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HANDBOOK OF RARE EARTH ELEMENTS

ANALYTICS

Edited by Alfred Golloch

2ND EDITION



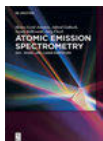
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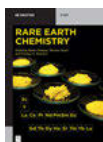
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Analytics

2nd revised and extended edition

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Alfred Golloch

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1 Introduction

Rare earth elements (REEs) are a group of chemical elements in the periodic table, including the 15 elements from lanthan (La,57) to lutetium (Lu, 71), scandium (Sc,21) and yttrium (Y,39). This grouping was agreed by IUPAC [1]. The elements scandium and yttrium differ in their atomic structure from the lanthanides but their chemical and physical properties are very similar.

	Main groups		Transition groups										Main groups					
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
	Ia s ¹	IIa s ²	IIIb d ¹	IVb d ²	Vb d ³	VIb d ⁴	VIIb d ⁵	VIIIb d ⁶ d ⁷ d ⁸			Ib d ⁹	II b d ¹⁰	IIIa p ¹	IVa p ²	Va p ³	VIa p ⁴	VIIa p ⁵	VIIIa p ⁶
1 1s	1 H																	2 He
2 2s 2p	3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
3 3s 3p	11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
4 4s 3d 4p	19 K	20 Ca	21 Sc	22 Ti	23 V	24 *Cr	25 Mn	26 Fe	27 Co	28 Ni	29 *Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
5 5s 4d 5p	37 Rb	38 Sr	39 Y	40 Zr	41 *Nb	42 *Mo	43 Tc	44 *Ru	45 *Rh	46 *Pd	47 *Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
6 6s 4f 5d 6p	55 Cs	56 Ba	57 *La	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 *Pt	79 *Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rr
7 7s 5f 6d	87 Fr	88 Ra	89 *Ac	104 Rf	105 Db	106 Sg	107 Bh	108 Hs	109 Mt	110 Ds	111 Rg	112 Cn	113 Nh	114 Fl	115 Mc	116 Lv	117 Ts	118 Og
Lanthanoids (4f-elements)			58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 *Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu		
Actinoids (5f-elements)			90 *Th	91 *Pa	92 *U	93 *Np	94 Pu	95 Am	96 *Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr		

Figure 1.1: Periodic table of elements [2].

The abundance of the REEs in the earth’s crust follows a pattern in the periodic table. Lanthanides with even atomic numbers are more common in nature than lanthanides with odd atomic numbers.

Figure 1.2 shows the pattern of the REEs abundance in the earth’s crust and it can also be noted that the abundance of the REEs with lower atomic numbers is higher than the abundance of the REEs with higher atomic numbers. Regarding this scope the first group is called “Light REEs, LREEs” and the second one “Heavy

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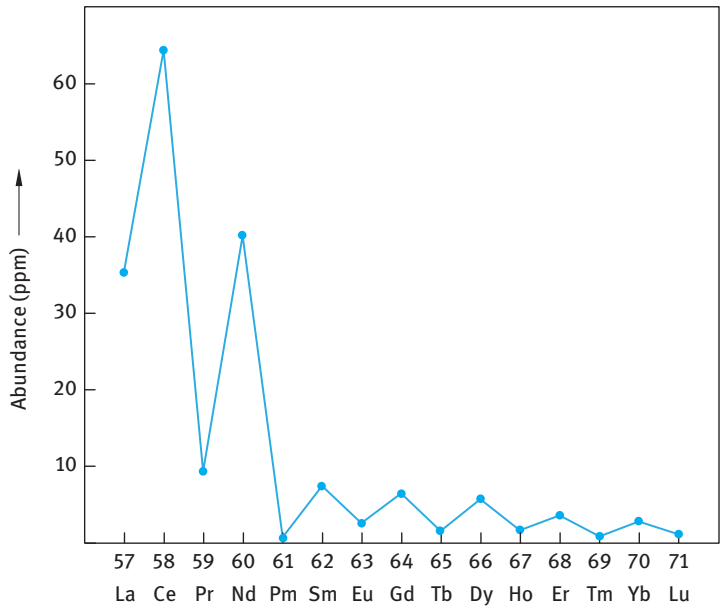


Figure 1.2: Abundance of the rare earth elements in the earth’s crust (Harkin rule) [2].

REEs, HREEs” (See Table 1.1). Other attempts have been made to subdivide the REEs into groups.

Table 1.1: Light and heavy REEs.

LREE	atomic number	HREE	atomic number
Sc	21	Y	30
La	57	Gd	64
Ce	58	Tb	65
Pr	59	Dy	66
Nd	60	Ho	67
Pm	61	Er	68
Sm	62	Tm	69
Eu	63	Yb	70
		Lu	71

In most deposits of REEs the share in LREEs is higher than 90% and the percentage of HREEs 2–3%. For “High-Tech” applications mainly HREEs are used and the demand for these elements is obvious.

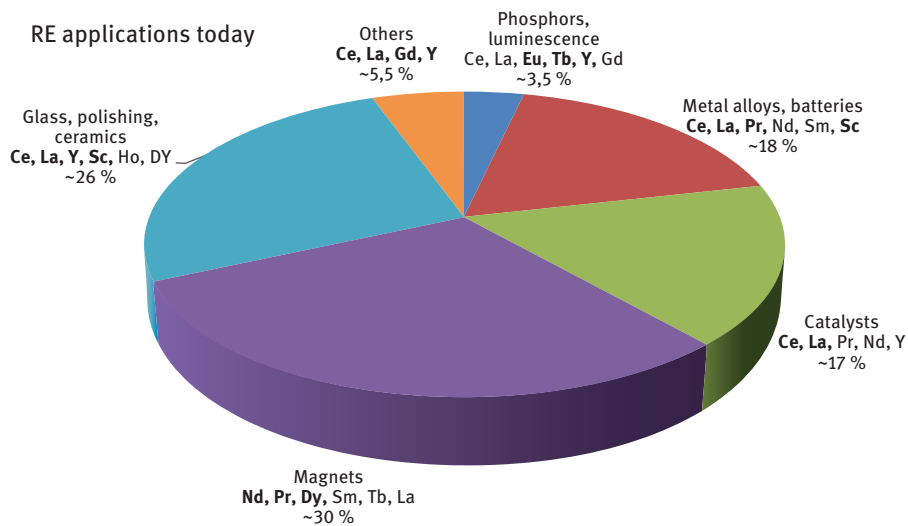


Figure 1.3: Main applications of rare earth elements [3].

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Alfred Golloch

2 Analytics of rare earth elements – basics and methods

2.1 Electronic configurations of RE elements and analytical properties

The electronic configuration of the rare earth elements (REEs) is the key for understanding the analytical properties of the elements. Table 2.1 shows the electronic configurations of the ground state of REEs atoms and of the ions.

Table 2.1: Electronic configuration of the rare earth elements [1].

Atomic number	Name	Symbol	Electronic configuration	
			Atom	Ion Ln ³⁺
57	Lanthanum	La	5d ¹ 6s ²	[Xe]
58	Cerium	Ce	4f ² 6s ²	4f ¹
59	Praseodymium	Pr	4f ³ 6s ²	4f ²
60	Neodymium	Nd	4f ⁴ 6s ²	4f ³
61	Promethium	Pm	4f ⁵ 6s ²	4f ⁴
62	Samarium	Sm	4f ⁶ 6s ²	4f ⁵
63	Europium	Eu	4f ⁷ 6s ²	4f ⁶
64	Gadolinium	Gd	4f ⁷ 5d ¹ 6s ²	4f ⁷
65	Terbium	Tb	4f ⁹ 6s ²	4f ⁸
66	Disprosium	Dy	4f ¹⁰ 6s ²	4f ⁹
67	Holmium	Ho	4f ¹¹ 6s ²	4f ¹⁰
68	Erbium	Er	4f ¹² 6s ²	4f ¹¹
69	Thulium	Tm	4f ¹³ 6s ²	4f ¹²
70	Ytterbium	Yb	4f ¹⁴ 6s ²	4f ¹³
71	Lutetium	Lu	4f ¹⁴ 5d ¹ 6s ²	4f ¹⁴
21	Scandium	Sc	3d ¹ 4s ²	[Ar]
39	Yttrium	Y	3d ¹ 5s ²	[Kr]

The ground state configurations for the majority of lanthanoides can be summarized as 4fⁿ 6s², except the following elements:

Lanthanum 5d¹ 6s²
Gadolinium 4f⁷ 5d¹ 6s²
Lutetium 4f¹⁴ 5d¹ 6s²
Scandium 3d¹ 4s²
Yttrium 4d¹ 5s²

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In general the f-levels of the lanthanoid atoms are filled with electrons and the N shell is filled up to the maximum of 32 electrons. The energy of 6 s, 5 d and 4 f levels are very similar and as the result there is an irregular fill of the energy levels. It can be noted that the half-full ($4 f^7$) and the completely filled 4f subshell are preferred. The fill of the inlying 4 f subshell with electrons slightly affects the chemical properties of the elements. The ground state configurations are not important for the analytical behaviour, but the trivalent ions configurations are more important. The trivalent ions are formally generated when the valence electrons are removed. The radii of the Ln^{3+} ions are very similar to the radii of Sc^{3+} and Y^{3+} ions. This electronic similarity causes the chemical similarity and that is the reason for including elements of group 3 of the periodic table in considerations of the chemistry of lanthanoides.

Chemistry of Ln^{3+} ions

The radii of the Ln^{3+} ions continuously decrease with the increasing atomic number of the elements (lanthanoid contraction). In general, the lowest detection limits are obtained for elements with a simple spectrum (Figure 2.1).

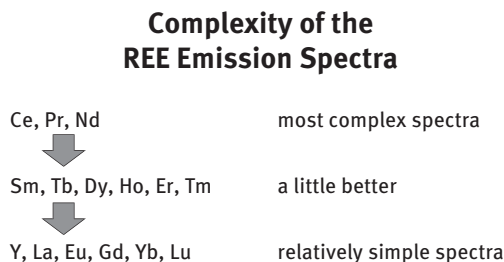


Figure 2.1: Structure of REE emission spectra.

The lanthanoid contraction is the reason for the resemblance of the 4 d and 5 d elements of the subgroups of the periodic table. The lanthanoid contraction is responsible for the regular amendment of some lanthanoides properties. The chemistry of the Ln^{3+} ions is similar to the chemistry of the Sc^{3+} and Y^{3+} ions. The solubility of the trifluorides LnF_3 is poor whereas the chlorides, bromides and iodides are slightly soluble. The oxalates can be used for precipitation of the Ln^{3+} ions. All the Ln^{3+} ions react with EDTA to form chelates in a ratio of (1:1).

Chemistry of Ln^{2+} and Ln^{4+} ions

Additional to the oxidation state (+3) the oxidation states (+2) and (+4) can be formed from the atoms of some lanthanoides. Table 2.2 presents the elements with “unusual” oxidation states.

Table 2.2: Some lanthanoides with “unusual” oxidation states.

Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
				+2	+2						+2	+2	
+3	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3	+3
+4	+4	+4					+4	+4					

The stability of compounds with the oxidation state (+2) decreases as following: $\text{Eu}^{2+} > \text{Yb}^{2+} > \text{Sm}^{2+} > \text{Tm}^{2+}$. In aqueous solution only Eu^{2+} ions are stable, the other Ln^{2+} ions decompose water. Compounds containing Ln^{2+} ions are similar to compounds of alkaline earth elements.

Examples of isotype compounds are:

SmF_2	CaF_2	YbI_2	CaI_2
TmF_2	CaF_2	EuSO_4	SrSO_4
EuF_2	SrF_2	YbO, EuO	BaO

Comparing the compounds with Ln^{4+} ions it can be noted that compounds with Ce^{4+} are the most stable ones. In aqueous solution only Ce^{4+} ions can exist but all other Ln^{4+} ions oxidize water. Only few solid compounds with Ln^{4+} ions exist, e.g. oxides like CeO_2 , PrO_2 , TbO_2 or fluorides like Cs_3NdF_7 and Cs_3DyF_7 .

2.2 The development of rare earth analytics from 1940 to present

Quotation [3]

“Before World War II, the rare earth were frequently determined as a group with a nonselective precipitant such as oxalic acid, hydrofluoric acid, or ammonium hydroxide. Indeed as recently as 1943, well-known textbooks on quantitative analysis contained such statements as “Beyond simply isolating the rare earth in this manner, there is little the analyst can do”. During and since World War II, however, knowledge of rare earths and the literature on their analytical chemistry have grown tremendously. [2]”

An approach to review the development of REEs analytics from 1940 to present results in the realisation of subdividing the time period. The study of corresponding publications showed that it would be useful to analyse and describe three time periods:

1940–1960

1960–1980

1980–present

2.2.1 Determination methods applied during the period from 1940–1960

Two publications appeared 1961 as chapter of a book [3] or in book form [4] dealing with the analytical chemistry of the rare earth elements. Both of the publications have been prepared in order to describe the development of the analytical chemistry during the 20 years from the beginning of the second world war II.

In addition to these two books a collection of papers was published presented at the conference on rare earth elements held in June 1956 at the Institute of Geochemistry and Analytical Chemistry im V.I. Vernadskii of the Academy of Sciences of USSR [5]. It was the aim of the conference to summarize the experience on rare earth elements gained in Russia during the past 20 years.

The publications stated above resumed for the first time the knowledge and experience on analytical chemistry of the rare earth elements after 20 years.

Only few methods for the determination of REEs were available such as:

- Gravimetric methods
- Titrimetric methods
- Spectrophotometry
- Spectrography
- X-ray absorption and emission spectrometry
- Radiochemical methods (NAA, tracer)

Gravimetric methods

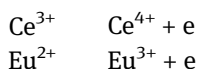
Various methods have been proposed

The precipitation of the rare earths as oxalates is the most frequently used method.

The oxalates are thermally decomposed

Titrimetric methods

Volumetric determination of individual rare earth in mixtures is restricted to cerium and possibly europium. Valence state variations are basis for the methods.



Spectrophotometry

The analytical methods of spectrophotometry are based upon:

Absorption spectra of the RE ions (350–750 nm region), Sc, Y, La have no absorption spectra in this region

Absorption spectra of coloured dye complexes

Instrumentation

Filter photometers (Standard)

Increasing application of monochromatic spectrophotometers

Spectrography (Emission spectrometry)

Instrumentation

Grating spectrograph

Excitation source dc-arc discharge

Graphite electrodes for nonconducting samples

Photoplate detection

Calibration

Techniques of internal standard

Observation of selected lines intensity ratio

Problems

Many spectra of REEs are very complex. Finding excitation conditions in order to produce spectra of sufficient precision

X-ray absorption and emission spectrometry**Radiochemical methods (NAA, tracer)**

These methods have been of no great importance for routine analysis of REEs

2.2.2 Separation methods applied during the period 1940–1960

The number of methods for separation of REEs was limited.

- Fractional precipitation
- Organic solvent extraction of complex compounds
- Ion exchange
- Paper or cellulose chromatography
- Electrolytic methods (reduction at a lithiums)

All these separation methods were not efficient and unsuitable for the separation of complex mixtures of REE, except ion exchange. This technique was continuously developed during this time period and the quality of separations was improved.

Conclusion: REE analysis 1940–1960

Spectrography was the only available method for trace analysis of REEs

2.2.3 Rare earths analysis during the period 1960–1980

A distinct progress in rare earth analysis made during the period from 1960–1972 was presented on a conference in Norway 1972 [6]. The results presented on the conference are substantially in accord with the progress reviewed in an additional publication [7]. New determination techniques were developed or implemented ones were significantly improved:

- Determination of rare earths by complexometry
- Emission spectrometry (arc/spark)
- Flame and plasma atomic absorption, emission, and fluorescence spectrometry
- X-ray excited optical fluorescence spectrometry
- X-ray fluorescence spectrometry
- Mass spectrometry and isotope dilution
- Neutron activation analysis

Determination of rare earths by complexometry [8]

The development of complexometric determination of the rare earths is a useful supplement of the gravimetric and titrimetric methods. The application of the method is limited on the determination of mixtures or pure REEs isolated from the others.

The volumetric determination of the rare earths was practically unknown before EDTA and related compounds (polyaminopolycarboxylic acids) were introduced in analytical chemistry.

Atomic emission spectrometry (arc/spark)

De Kalb EL in Ref. [6]

Atomic emission spectrometry is the most powerful tool for the analysis of RE materials. The efficiency of the method depends on the character of the spectrum. The spectra of many of the RE elements are very complex and the choice of a suitable spectrometer is restricted to those which can provide adequate resolution. A rough classification of spectra of the REEs is listed in Figure 2.2.

Atomic emission spectrometry can be used for the following applications:

- Determination of rare earths in a “pure” rare earth
- Determination of other impurities in a rare earth
- Determination of rare earths in a mixture of various rare earths
- Determination of rare earths impurities in other materials

The methods for the determination of RE impurities in an RE metal or oxide were developed by Fassel and co-workers [9–13]. Later the methods were modified by several analysts. The use of an ac-arc instead of a dc-arc improved the detection limits and the precision. Detection limits of 10–0,01 ppm RE impurity in RE matrix could be achieved.

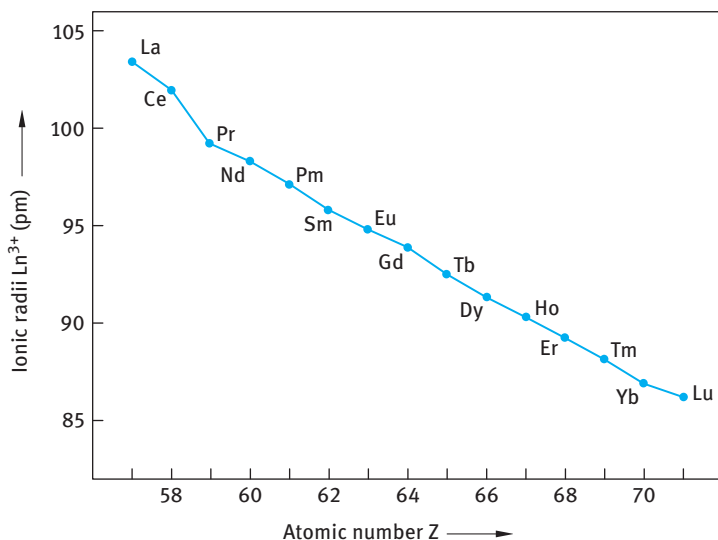


Figure 2.2: Lanthanoid contraction.

Flame and plasma atomic absorption, emission, and fluorescence spectrometry

Fassel VA, Kniseley RN, Butler CC in Ref. [6]

As mentioned above the atomic emission spectrometry (arc/spark) is available for the analysis of solid REE samples. A method for the determination of REEs in aqueous solutions is missing. During this time period several studies were prepared to ascertain if emission spectra of REEs can be generated using combustion flames. The result of the studies showed that with oxygen/hydrogen flames REE spectra could be generated. The character of the spectra did not correspond to atomic lines but to molecule emission bands. The analytical application was limited.

Flame emission spectrometry was improved by the studies of Fassel, Curry and Kniseley [14]. They detected that flame chemistry rather than flame temperature was an important consideration in the production of free atoms of the rare earths. Fuel-rich hydrocarbon flames significantly enhanced the emission intensities. The spectra are relatively simple.

Flame atomic absorption spectrometry (FAAS) and flame atomic fluorescence spectrometry (FAFS) have been also investigated for application of REEs analysis. A comparison of the results illustrated the much better detection limits of FES than those observed in FAAS:

Atomic flame emission spectrometry was successfully applied for mixtures of rare earth elements.

On the conference [6] the power and the potential of inductively coupled plasma-atomic emission spectrometry was presented. Some characteristics of ICP-AES were discussed and the arguments for use in analysis of REEs were convincing.

X-ray excited optical fluorescence spectroscopy (XEOF)

Cathode-ray excited emission spectroscopy (CREE)

These two special analytical methods have been developed and improved during the period 1960–1972. The application was focussed on special challenges e.g. trace analysis of REEs. The methods could not be established for routine analysis.

X-ray fluorescence analysis (XRF)

The first prototype of a x-ray fluorescence (secondary emission) spectrometer was launched 1948. Since then the technique was fast developed. Important contributions on x-ray fluorescence analysis were published 1955–61 Ref. [15–18]. The method is well established 1972 and all sample types can be analysed. Liquids, powders, metals or fused beads. XRF is applicable to the concentration range of REEs from 100 % down to absolute 0,01 %. These results were obtained with spectrometers equipped with wavelength dispersive optics. Spectrometers with energy dispersive detection technique were not available.

Mass spectrometry and isotope dilution

Mass spectrometry is a method which can be applied for trace REEs analysis and is preferred for analysis of small samples. Different instruments were applied. Here are some technical details:

Two types of ion sources were used: surface ionization filaments (Re wires) and high frequency spark. The sample preparation depends on the ion source, for Re filaments small amounts of the sample were dissolved. For spark source sample powder was mixed with high-purity graphite and tiny electrodes were pressed.

Mass spectrometers

Single or double focussing instruments

Registration of the spectra using electron multiplier or photoplate

Limits of determination: 0,1 ppm.

Neutron activation analysis

Eiliv Steinnes in [6]

The method is well established 1972 and preferred applications of REEs analysis are:

- Geological samples
- Reactor material
- High purity chemicals

- Metals
- Biological tissues
- Water

Advantages of the method

High sensitivity for a great number of elements

Good specificity

Freedom from reagent contamination

Relative freedom from matrix effects

Multi-element determination

Drawbacks

Nuclear reactors are not easily accessible

The equipment is relative expensive

In some cases considerable amounts of radioactivity

Sometimes it is time consuming to wait for the result.

2.2.4 Literature review 1978 [18]

This review compiled by Jones and Dixon confirmed the state of REE analytics presented on the conference in Norway 1972 [6].

- Spectroscopic methods were preferred for the determination of REEs
- NAA completed the tool box
- Increasing application of atomic absorption spectrometry
- Spark-source mass spectrometry was applied more often

Important separation methods with improved efficiency are:

- Liquid-liquid extraction
- Cation exchange
- Anion exchange

2.2.5 Situation of rare earth analytics 1980-present

Since about 1980 the very effective method of “Inductively coupled plasma- optical emission spectrometry ICP-OES” was available. This tool was a breakthrough for rare earths analytics. Both liquid samples and solid material could be analysed. Efficiency and precision of the method are excellent and the method was widely accepted.

About 1990 the superior technique of the “Inductively coupled plasma- mass spectrometry ICP-MS” was developed and available for rare earths analytics. This

method was an ideal supplement to ICP-OES and both of the methods are the workhorses in rare earths analytics.

A review summarizes the experience gained with the application of spectroscopic methods for REEs analytics.

Zawisza B, Pytlakowska K, Feist B, Polowniak M, Kita A, Sitko R. Determination of rare earth elements by spectroscopic techniques: a review.

J. Anal. At. Spectrometry 2011,26,2373–2390.

The determination methods and the separation techniques which were developed since 1980 have been discussed with some review articles. Recent modifications of the analytical methods are described and discussed in the chapter X-Y-Z of this handbook. The modern developments of separation techniques are also part of the chapter X of this book and provide the reader with important details of the application.

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Part I: **Sample preparation**

Beibei Chen, Man He, Huashan Zhang, Zucheng Jiang, Bin Hu

3 Chromatographic techniques for rare earth elements analysis

Abstract: The present capability of rare earth element (REE) analysis has been achieved by the development of two instrumental techniques. The efficiency of spectroscopic methods was extraordinarily improved for the detection and determination of REE traces in various materials. On the other hand, the determination of REEs very often depends on the preconcentration and separation of REEs, and chromatographic techniques are very powerful tools for the separation of REEs. By coupling with sensitive detectors, many ambitious analytical tasks can be fulfilled.

Liquid chromatography is the most widely used technique. Different combinations of stationary phases and mobile phases could be used in ion exchange chromatography, ion chromatography, ion pair reverse-phase chromatography and some other techniques. The application of gas chromatography is limited because only volatile compounds of REEs can be separated. Thin-layer and paper chromatography are techniques that cannot be directly coupled with suitable detectors, which limit their applications. For special demands, separations can be performed by capillary electrophoresis, which has very high separation efficiency.

3.1 Introduction

Separation of rare earth elements (REEs) is essential to promote the development of REEs industry. Due to the similar properties of REEs, conventional separation methods such as extraction and co-precipitation cannot achieve the separation of single REE. Chromatography (including liquid chromatography (LC) and gas chromatography (GC)) and capillary electrophoresis (CE) techniques are powerful separation techniques with high separation resolution, and have been successfully applied in separation of REEs. Among them, LC is the most widely used technique because it has the advantages of various separation modes, robustness, fast separation, and so on. Ion exchange chromatography (IEC) is the most suitable LC separation mode for REE ions. Besides IEC, ion chromatography (IC), ion pair reverse phase chromatography (RPC), extraction chromatography and centrifugal partition chromatography have also been used for separation of REEs. GC is only suitable for the separation of volatile or semi-volatile compounds. Therefore, it is not an optional separation technique for the separation of REE ions. CE is a good choice for the separation of charged REE ions. Compared with LC, CE presents better separation resolution, but it is less robust and the absolute limits of detection are relatively high. Therefore, the application of CE on separation of REEs is not as wide as that of LC. In this chapter, the state of art about the

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applications of chromatography and CE to the separation of REEs will be introduced, and the emphasis is laid on the applications of LC.

3.2 Liquid chromatography

LC method is the dominant method in the separation of REEs with high separation resolution. Modern LC methods can be classified into two types: column chromatography and planar chromatography. The representative for former one is high performance liquid chromatography (HPLC), which was the most important development in LC during 1960s and was firstly applied to the separation of REEs in 1972 utilizing an ion-exchange mode [1]. In addition to ion-exchange mode, other LC separation modes including IC, ion pair chromatography (IPC), normal and reverse phase (RP) LC, extraction chromatography and centrifugal partition chromatography have also been used for separation and determination of REEs, which greatly promoted the development of rare earth industry. Thin-layer chromatography (TLC) and paper chromatography (PC) are assigned to planar chromatography. These methods used to be important means for the separation of REEs before 1960s, while their application gradually decreased since the introduction of HPLC. When compared with planar chromatography methods, HPLC effectively shortens the analytical time. Moreover, HPLC can be easily combined with various detection techniques such as photometry, fluorescence spectrometry, inductively coupled plasma-optical emission spectrometry/ mass spectrometry (ICP-OES/MS) and electrochemical detection, and the detection sensitivity towards REEs can be greatly improved. Thus, HPLC is widely used in the separation and analysis of REEs. Among all the HPLC methods, IEC and RP ion pair chromatography (RPIPC) are the most widely used methods.

3.2.1 Ion exchange chromatography

With ion exchange resin as stationary phase, IEC is the main method for the analysis of REEs. It is mainly used for the separation of rare earth impurities from single rare earth matrix. Since Sisson et al. [1] successfully realized the HPLC separation of REEs with ion exchange resin as stationary phase in 1972, IEC is more and more widely used in the separation of REEs.

3.2.1.1 Ion exchanger

The stationary phase used in IEC is the ion exchanger, mainly strong acidic cation exchange resin (such as styrene-divinylbenzene copolymer) and strong basic anion exchange resin (organic resin). According to the physical structure of resin, the ion exchanger can be

divided into micro-reticular resin, macro-reticular resin, thin shell mold resin, porous covering resin, directly synthesized chelating resin and supported resin. Micro-reticular resin and macro-reticular resin are often used in classical IEC separation of REE, whereas the thin shell mold resin, macro-reticular resin and bonded phase porous ion exchanger are usually applied in high performance IEC separation of REE.

3.2.1.1.1 Organic resin

(1) Micro-reticular and macro-reticular ion exchange resin

Micro-reticular ion exchange resin, also known as gel resin, is a kind of traditional common resin. This resin is full of micropores with small porosity and pore size uniformity. The pore size is determined by the cross-linking degree. When the cross-linking degree is more than 8%, the pore size is less than 50 Å and a high exchange capacity is achieved (4.5–5.0 mmol/g for cation resin and 3.5–4.0 mmol/g for anion resin).

Macro-reticular ion exchange resin has large pore size and high surface area. Not only the gel pores but also the tunnel macropores (pore size larger than 200–1000 Å) exist in the skeleton structure of this kind of resin. The macroporous resin shows cavities under dry or swelling state, while the cavities of microporous resin only appear under the swelling state. Although the surface area of macroporous resin is large, the exchange capacity is low. With high permeability for large organic ions and stable swell-shrinking property in different eluents, the macroporous resin is quite suitable for ion exchange separation in organic solvent. Hoehlein et al. [2] employed macroporous resin AminexA-5 and common resin DowexAG-X8 for separation of La, Ce, Pr, Nd, Pm, Sm and Eu. The results showed that the theoretical plate number of macroporous resin is dozen times of common resin, and both the separation efficiency and the purity of obtained rare earths are relatively high. Dowex50W-X8 and AG50W-X were also successfully used for separation of REEs [3, 4].

(2) Exchange resin with thin shell

It is a type of ion exchange resin with core-shell structures. The core is a polystyrene rigid particle with low cross-linking degree (2%–5%) and a diameter of 10–30 µm, which is a hydrophobic inert nuclei without any exchange groups. The coating is a thin sulfonated or aminated resin film. Since the exchange groups are on the surface of resin, it has good permeability, high exchange speed, and high resolution. Besides, due to the rigidity of the inside core, swelling or shrinkage deformation of the resin is limited and the resin can be used in a wide pH range. Thus, the exchange resin with thin shell is an appropriate alternative for the carrier of high performance IEC stationary phase. The limitation of exchange resin with thin shell is that the exchange capacity is low. In order to avoid the ion diffusion towards resin center, the layer of ion exchange resin such as HC-Pellionex-SCX and AS-Pellionex-SAX [5] were coated on the surface of small glass beads or silicon dioxide particles.

3.2.1.1.2 Silica gel-based ion exchanger

Total porous silica gel and surface-covered silica gel are the two main kinds of silica gel used as carrier of ion exchanger. They belong to bonded phase porous ion exchanger. To form silica gel-based ion exchanger, the porous silica gel was covalently bound with alkyl or aryl and then grafted with quaternary amine or sulfonic acid group. With small particles (5–10 μm) of silica gel as carrier, the ion exchanger has a good chromatographic performance and high exchange capacity. This kind of ion exchanger could bear high column pressure and achieve rapid analysis; its physical and chemical parameters are easy to control, but it only can be used in acidic pH range. With α -hydroxyisobuturic acid (α -HIBA) as the eluent, a separation of REEs was realized on Nucleosil SA series of silica gel (10 μm particle size) based sulfonic acid cation exchanger [6].

The above-mentioned resins can be chosen according to different target analytes. Resin with thin shell is the primary choice for the separation of simple mixtures. For the samples that are difficult to separate or large sample injection dosage is required, bonded phase porous ion exchanger with particle size of 5–10 μm is a better choice. In some REEs separation, high stability of columns is required and the common ion exchange resin with diameter of 10 μm is generally used. Table 3.1 lists the characteristics of the above-mentioned ion exchange resins.

Table 3.1: The characteristics of several ion exchangers.

Characteristic	Thin shell mold resin	Bonded phase porous resin	Ploystyrene-divinylbenze resin
Diameter (μm)	30–40	5–10	7–10
Exchange capacity (mmol/g)	0.01–0.1	0.5–2	3–5
Anti-deformability and anti-pressure capability	Best	Good	Poor ^a
Shape	Spherical	Spherical or amorphous	Spherical
Pressure drop	Low	High	Highest
Separation efficiency	Moderate	High	Low
Packing way	Dry type filling	Homogenization	Homogenization
pH range	2–7.5	2–7.5	0–12 (anionic) 0–14 (cationic)
Regenerative speed	Fast	Moderate	Slow

^aDepends on the difference of cross-linking degree.

3.2.1.1.3 Chelating agent-loaded resin

Chelating agent-loaded resin, also known as chelate-forming resin or modified chelating resin, is a novel selective ion exchange resin. The selectivity of chelating agent-loaded resin is similar to that of the chelating agent when using for the enrichment of metal ions. Besides, it is easy to prepare. The reported chelating agent-loaded resins are divided into strong basic anion exchange resin and nonpolar adsorption resin

based on the resin matrix. And the chelating agents loaded on the two types of resins were water-soluble and hydrophobic agents, respectively.

There are mainly two kinds of mechanism for the adsorption of chelating agent on resin: anion exchange [7] and surface adsorption [8]. Besides anion exchange contributing to the adsorption of chelating agent on anion exchange resin, molecular adsorption between chelating agent and the resin is another important factor for the adsorption which is highly related to the molecular structure.

The stability of chelating agent-loaded resin is one of the most important factors to evaluate the performance of resin, and it directly affects the separation and detection of REEs and the regeneration of resin. The stability is dependent on the structure of chelating agents. To obtain a stable chelating agent-loaded resin, the chelating agent should have anionic groups and big conjugate system. In addition, different types of anion exchange resin as the carrier also have an influence on the stability. Generally, the stability of a strong base anion resin is better than a weak base anion resin. Moreover, the common anions such as NO_3^- , Cl^- , SO_4^{2-} , ClO_4^- and Ac^- and their concentration also affect the stability of loaded resin. The order of the effect of these anions correspond to their order in affinity to the resin [9]. Trichloroarsenazo and tribromoarsenazo-loaded resins have good stability, and have been used in the separation of REEs.

The mixture of di(2-ethylhexyl)phosphoric acid (P204) and 2-ethylhexyl hydrogen 2-ethylhexylphosphonate (P507) is a very strong complexing agent and can be used in acidic solution. After loading on C18 silica gel, the resin was packed in a column and applied for the preconcentration and separation of REEs from the seawater followed by the ICP-MS detection [10].

3.2.1.1.4 Chelating resin

Chelating resin is usually synthesized by chemical bonding of the chelating agent or the functional groups on the polymers, resulting in good selectivity. For example, polystyrene-divinylbenzene (PS-DVB) based Amberlite XAD-2 resin functionalized with ortho-vanillinthiosemicarbazone [11] exhibits good chemical stability, selectivity, reusability and fast equilibration rate for Th and U. Silica nano- and microparticles functionalized with a monolayer of diethylenetriaminepentaacetic acid (DTPA)-derived ligands [12] is chemically robust, and exhibits quick kinetics and good separation of the La(III), Ce(III), Pr(III), Nd(III), and Dy(III) ions. The novel supported ionic liquid phase (SILP) betainium sulfonyl(trifluoromethanesulfonylimide) poly(styrene-co-divinylbenzene) [Hbet-STFSI-PS-DVB] [13] was prepared for the separation of REEs (Sc, Y, Nd, Dy) from BR leachates, showing high reusability and stability.

3.2.1.2 Basic properties of ion exchange resins

2.1.2.1 Cross-linking degree

The cross-linking degree of PS-DVB based ion exchange resin was expressed by the percentage of divinylbenzene, which is the cross-linking agent of resin. A stereoscopic network structure could be formed in the long chain of polystyrene by adding the cross-linking agent. The cross-linking degree of polymeric ion exchange resin is usually ranging from 4% to 12%, while it is 8% for the commonly used ion exchanger in typical separation process. The property of resin is greatly affected by the cross-linking degree: the resin is tough and the mass transfer is slow for REE ions at high cross-linking degree (12–16%), while the opposite phenomenon is observed at low cross-linking degree (1–4%). In HPLC, ion exchange resin with small particle size (5–10 μm) and 8–12% of cross-linking degree have a relatively good separation result.

3.2.1.2.2 Swelling degree and thermal stability

When water is used as the mobile phase, the polymer-based ion exchange resin as stationary phase will absorb moisture and swell. The swelling degree of the ion exchanger is determined by the cross-linking degree. When the cross-linking degree is higher, the swelling degree is lower. In the solution with high ionic concentration, the swelling degree is low; on the contrary, the swelling degree is high and the maximum swelling would occur in pure water. A high swelling degree is along with a large exchange capacity for the same type resin. The swelling degree of strong acid cation exchange resin is in the order of $\text{H}^+ > \text{Na}^+ > \text{NH}_4^+ > \text{K}^+ > \text{Cs}^+$; and it is in the order of $\text{F}^- > \text{OH}^- > \text{HCO}_3^- > \text{SO}_4^{2-} > \text{Cl}^- > \text{NO}_3^- > \text{Br}^- > \text{I}^-$ for the swelling degree of strong basic anion exchange resin. Furthermore, the swelling is relevant to solvent polarity, and the resin swells slightly in nonpolar solvent.

The optimal performance of resin is also limited by the temperature. Sulfonic acid resin would react slowly with water and lose the sulfonic acid at 100 °C, while sulfonate resin would be stable at 200 °C. The hydroxyl type of anion exchange resin containing quaternary ammonium group begins to decompose at 50 °C, while the ammonium type of anion exchange resin is stable at 100 °C.

3.2.1.2.3 Exchange capacity

Ion exchange capacity reflects the exchange ability of resin, which is equal to the concentration of measured (titrated) exchangeable groups among the network structure inside the resin, and it would change along with pH value. The relative retention value and maximum sample volume of column is also increasing with the increase of the exchange capacity of anion exchange resin. In addition, capacity factor (k') of sample is directly proportional to the ion exchange capacity that usually depends on the employed type of resin.

3.2.1.3 Mobile phase

Generally, the mobile phase of IEC should meet the following requirements: (1) it is able to dissolve various kinds of salt and acid adequately and act as buffer solution for ion exchanging at the same time; (2) It merits good selectivity for interest analytes and good separation can be achieved with a proper solvent strength. Aqueous solutions with the addition of salt are usually used as the mobile phase in IEC, such as buffer solution and sometimes spiked with organic solvent (methanol, ethanol and acetonitrile)/water mixtures. The strength and selectivity of the mobile phase are often related to the buffer type, concentration and pH, as well as the type and quantity of organic solvent added.

3.2.1.3.1 Effect of ionic strength

The ionic strength of the mobile phase would be increased by changing the buffer concentration (under fixed pH value) or mixing with another acid, and the solvent strength is often increased with the increase of the ionic strength. With the increase of the ions concentration in the mobile phase, competitive exchanging between ionic exchange groups and mobile phase would be increased and the sample retention is decreased accordingly.

3.2.1.3.2 Effect of pH value

The retention of interest analytes in IEC could also be altered by varying the pH value of mobile phase or concentration of hydrogen ions. With the increase of pH value, the retention of target analyte would decrease in cation exchange chromatography, while the retention of target analyte would increase in anion exchange chromatography. Therefore, it is a very useful means to optimize the retention performance of analytes and separation selectivity in IEC by altering pH value and H^+ concentration of mobile phase.

3.2.1.3.3 Selection of complexing agent in mobile phase

In a simple ion exchange system for the separation of cation or anion, the separation of ions is dominated by the retention affinity difference between ions. For REEs with similar properties, the difference between their retention affinity is not enough for their separation on the resin. In order to improve the retention difference of adjacent REEs, complexing agent (H_nL) is added into mobile phase. It could broaden the retention value of target REEs and increase the separating factor (α) by utilizing the differences of stability constant (β) of rare earth complex anions (ML^{3-n}), resulting in the separation of adjacent REEs eventually. The formation of rare earth complex anions and stability constant (β) is expressed by the following formulas:

$$M^{3+} + mL^{n-} = ML_m^{(mn-3)-}$$

$$\beta = \frac{[ML_m^{(mn-3)-}]}{[M^{3+}][L^{n-}]^m}$$

Distribution coefficient (K_d') of rare earth ions in resin is as follows:

$$K_d' = \frac{[M']}{[M^{3+}] + [ML_m^{(mn-3)-}]}$$

$[M']$ is the concentration of rare earth ions in resin. It can be obtained by combining the above formulas:

$$K_d' = \frac{[M']}{[M^{3+}]} \bullet \frac{1}{(1 + \beta[L^{n-}]^m)}$$

There are no complex anion $ML_m^{(mn-3)-}$ if no complexing agent is added into mobile phase. In this case, distribution coefficient (K_d) shall be:

$$K_d = \frac{[M']}{[M^{3+}]}$$

So that K_d' can be expressed by the following formulas:

$$K_d' = K_d \bullet \frac{1}{1 + \beta[L^{n-}]^m}$$

From above we can see that distribution coefficient changes with formation of rare earth complex anions by adding complexing agent into mobile phase, and the separation factor (α) shall be measured by:

$$\alpha' = \frac{K'd_2}{K'd_1} = \frac{Kd_2}{Kd_1} \bullet \frac{1 + \beta_1[L^{n-}]^m}{1 + \beta_2[L^{n-}]^m}$$

$$\alpha' = \alpha \bullet \frac{1 + \beta_1[L^{n-}]^m}{1 + \beta_2[L^{n-}]^m}$$

Where α and α' refer the rare earth separation factor without and with the addition of complexing agent. As can be seen, the separation factor will change with the variation of complexing constant. Hence, adding appropriate complexing agent into mobile phase can increase the separation factor according to the following formula:

$$R_s = \frac{1}{4} \frac{\alpha - 1}{\alpha} \frac{k}{k - 1} \sqrt{N}$$

Where N refers column plate number, k refers capacity factor, R_s refers to resolution. As can be seen, R_s would vary significantly with a minor variation of the separation factor, thus affecting the retention properties of REEs remarkably. Therefore, it is important to select a proper complexing agent.

In the selection of complexing agent, big difference in stability constants between different REEs is needed. Besides, the complexing agent should be low cost and be featured with proper solubility in the mobile phase. For separating REEs in cation exchange chromatography, complexing agent in mobile phase can be carboxylic acid, hydroxy carboxylic acid, aminocarboxyl chelating agent and so on.

(1) Hydroxy carboxylic complexing agent

Hydroxy carboxylic acid includes α -HIBA, α -hydroxy- α -methylbutyric acid (α -H- α -MBA), lactic acid, malic acid and glycolic acid. The first three were the most frequently used complexing agents. The separation factors for adjacent REEs in cation exchange chromatography by using hydroxy carboxylic acid as eluent are shown in Table 3.2.

Table 3.2: The separation factors of cation exchange chromatography for the separation of adjacent REEs by using hydroxy carboxylic acid as eluent [26, 27].

Adjacent REEs	α -HIBA		α -H- α -MBA	Lactic acid	
	25 °C	87 °C	87 °C	25 °C	87 °C
La-Ce	2.1	2.1	3.0	2.10	1.83
Ce-Pr	1.7	1.7	1.6	2.04	1.73
Pr-Nd	1.4	1.5	1.4	1.38	1.36
Nd-Pm	1.6	1.5	1.4	1.38	1.36
Pm-Sm	1.7	1.7	1.8	1.32	1.32
Sm-Eu	1.9	1.7	2.0	1.20	1.28
Eu-Gd	1.5	1.4	1.4	1.04	1.22
Gd-Tb	1.9	1.9	1.9	1.50	1.73
Tb-Dy	1.8	1.8	1.8	1.65	1.56
Dy-Ho	2.0	1.6	1.8	1.45	1.38
Ho-Er	1.4	1.3	1.3	1.60	1.52
Er-Tm	1.6	1.4	1.7	1.55	1.47
Tm-Yb	1.5	1.4	1.4	1.54	1.43
Yb-Lu	1.4	1.3	2.4	1.40	1.31
Y-Ho	1.77	1.56	1.67		
Y-Dy	1.10	1.04	1.10		

α -HIBA is also named as α -hydroxy- α -methylpropionic acid. As early as 1956, Choppin et al. [14] used α -HIBA as eluent in cation exchange chromatography to separate actinide and lanthanide elements. It could be complexed with rare earth ions rapidly with many advantages such as small temperature coefficient, large separation factor and good separation uniformity. α -HIBA can separate adjacent REEs effectively at room temperature and it is the most effective and widely used

eluent [15, 16]. But it was difficult to separate Y and Dy because of their small separation factor. The slightly change of concentration and acidity of α -HIBA elution has a great influence on the separation effect of REEs; thus, these influencing factors should be controlled strictly.

The melting point of α -H- α -MBA is 67.5 °C, the dissociation constant is 1.87×10^{-4} (30 °C), the solubility is 1.679 g/L in water and the solubility of its sodium salt is 61.9 g/L (30 °C). As can be seen in Table 3.2, α -H- α -MBA has a better separation effect. It has been used as eluent for the separation of heavy REEs in cation exchange chromatography.

Lactic acid is also named as 2-hydroxy propionic acid. The melting point of lactic acid is 16.8 °C. With large temperature coefficient, lactic acid should be used at higher temperature (70–95 °C) and its separation factor is smaller than α -HIBA as shown in Table 3.2. Due to its self-polymerization, the separation repeatability of lactic acid is poor.

Complexing agents other than α -HIBA may be superior for certain separations (e.g., a particular detection system) or, indeed, for the separation of a particular combination of lanthanides. In the determination of individual lanthanides in rare earth ores and high-purity lanthanide reagents by HPLC-ICP-OES, using an IEX-210 SC cation exchanger, a concentration gradient of aqueous ammonium lactate was chosen [17] as the mobile phase. This eluent was preferred to be the common aqueous solutions of α -HIBA (or citrate, or EDTA) as the latter clogged the ICP torch. The ammonium lactate eluent produced efficient separations of the lanthanides. The mobile phase flow rate was adjusted to achieve a compromise between the requirements of HPLC for low flow rates for maximum column efficiency and that of ICP for high flow rates for strongest emission intensities. Comparative evaluation of three hydroxycarboxylic acids for the separation of lanthanides has been tested by Raut et al. [18]. α -HIBA was found to be the best for separation of heavier lanthanides (Tb to Lu), while α -H- α -MBA led to a better separation for lighter lanthanides (La to Eu). All the 14 lanthanides were separated by gradient HPLC employing both α -HIBA and α -H- α -MBA.

(2) Aminocarboxyl chelating agent

Aminocarboxyl chelating agent such as ethylenediaminetetraacetic acid (EDTA), hydroxyethyl ethylenediamine triacetic acid, diethylenetriaminepentaacetic acid (DTPA) and nitrilotriacetic acid (NTA) have been used as eluent in ion exchange separation of REEs. The complex of aminocarboxyl chelating agent with REEs is stable and the separation factor between adjacent REEs is relatively large, which is beneficial to the separation. Separation and analysis of the europium-gadolinium couple was achieved by adding EDTA into mobile phase of IEC [19]. However, both the formation speed and the dissociation speed of the complex are slow, which affect the speed of ion exchange and lead longer elution time, so the application of aminocarboxyl chelating agent on the separation of REEs is rare.

On the other hand, oxalic acid has been also used as chelating agent in the mobile phase with anion exchangers [20]. Oxalic acid forms negatively charged complexes with REEs that are separated by anion exchange chromatography. In this case, a reverse order of elution was produced, since La forms a weaker complex than Ce or Lu. The order of elution in this case is $\text{La} < \text{Ce} < \text{Lu}$.

3.2.1.4 Application of IEC in separation of REEs

In 1972, Sisson et al. [1] used AG 50W ion exchange resin as stationary phase and α -HIBA as mobile phase and realized the HPLC separation of REEs. From then on, IEC is widely used in separation of REEs.

IEC can be used to separate the rare earth samples in meso- to micro-analysis, and also the purification of single rare earth sample. It is a main method for the analysis of REEs and mainly used for the separation of rare earth impurities from single rare earth matrix. Table 3.3 lists the applications of IEC in separation of REEs.

In separation of REEs, cation exchange chromatography has been used more extensively. Anion exchange has not been as popular as cation exchange for REE separations because column performance is generally poorer than for separations based on cation exchange chromatography.

Rollin et al. [21] used IonPac CS10 column as stationary phase, 1 mol/L HCl and α -HIBA as mobile phase with gradient elution and post-column derivatization with Arsenazo III, and realized the separation of uranium, thorium and lanthanide elements by the detection of ultraviolet (UV) at 650 nm. This method could be used for the determination of lanthanide and actinide elements in nuclear materials. Recently, Borai et al. [22] developed a new method for group separation of some heavy metals from REEs followed by online sequential individual separation of REEs with a combination of chelation chromatography and ICP-OES. In this study, various chelating agents such as DTPA, PDCA (2,6-pyridinedicarboxylic acid), NTA, α -HIBA, and oxalic acid were used as mobile phases, and the elution capability and separation efficiency of the investigated eluents are mainly dependent on the number of carboxylic acid and geometrical structures. The results showed that heavy REEs and intermediate REEs could be efficiently separated by using 0.001 mol/L NTA at pH 3, while light REEs were separated by using 0.005 mol/L α -HIBA at pH 4 followed by 0.001 mol/L PDCA at pH 2.

The separation of the same type of metal chelates on dynamically coated cation or anion exchange columns introduces additional possibilities for improving the resolution. In the ion interaction technique, the exchange sites are dynamically coated on an RP C18 column using oxalate tetrabutylammonium [23] or tetra-n-butylammonium hydroxide (TBAOH) [24] as mobile phase and the separation is performed by an ion pair mechanism. The cation or anion exchange sites in the ion interaction method are similar to cation or anion exchange mode. However, the

sulphonic acid or ammonium exchange sites functionality is achieved by the octa-nesulphonate or tetrabutylammonium added together with the eluent.

On the other hand, a reversed chromatographic system where chelation takes place at the surface of the stationary phase or so-called high-performance chelation IC has attracted attention over the last decade, mainly due to the development of new efficient chelating exchange substrates. The chelating exchangers, as imminodiacetate functional groups [25], usually exhibit the opposite effect to cation exchange affinity for the REEs and give rise to the possibility of isocratic separation. Dybczynski et al. [26] developed a new RP-HPLC method for selective separation of yttrium from all REEs by employing NTA as a complexing agent in anion exchange mode. In the new RP-HPLC system with C18 column, TBAOH as an ion interaction reagent and NTA as a complexing agent enable baseline separation of yttrium from light and heavy REEs.

Traditionally, REEs are detected by post-column spectrophotometric reaction with strongly absorbing chromophores such as 4-(2-pyridylazo)resorcinol (PAR) or Arsenazo III, but the use of ICP-OES [17] and ICP-MS [27] detection has been increased in recent years.

Table 3.3: Application of IEC in separation of REEs.

Target analytes	Exchange materials or chromatographic column	Mobile phase	Comments	Ref.
REEs	Shimadzu Model LC-3A stainless steel column pack with strong cation exchange resin (IEX-21OSC)	0.4–1.0 mol/L ammonium lactate (pH 4.22)	HPLC coupled with ICP-OES detection	[17]
Lanthanide and actinide elements	IonPac CS10 cation exchange column	1 mol/L HCl and α -HIBA	Post-column derivatization with Arsenazo III and spectrophotometric detection at 650 nm	[21]
Neighboring lanthanide elements	CS-3 Dionex cation exchange column	α -HIBA with different concentration and pH	Dionex IC-2500 HPLC, post-column derivatization with 4-(2-pyridylazo)resorcinol (PAR)	[28]
REEs	Dowex 50W-X8 cation exchange	0.001 mol/L NTA at pH 3 (heavy REEs and intermediate REEs); 0.005 mol/L α -HIBA at pH 4.5 followed by 0.001 mol/L PDCA at pH 2 (light REEs)	Group separation of heavy metals from REEs followed by online individual separation of REEs	[22]

Table 3.3 (continued)

Target analytes	Exchange materials or chromatographic column	Mobile phase	Comments	Ref.
Separation of Y from REEs	Kromasil 100 C18 reversed-phase column	2 mmol/L NTA + 3 mmol/L TBAOH; $C_{Cl^-} < 10$ mmol/L, pH = 3.05.	Post-column derivatization with Arsenazo III and spectrophotometric detection at 658 nm	[24]
REEs	Hydrophilic polymer-based NTA gel	16–80 mmol/L HNO_3	Post-column derivatization with Arsenazo III and spectrophotometric detection at 658 nm; ICP-MS detection	[25]
Separation of Y from REEs	Kromasil 100 C18 reversed-phase column	0.5–4 mmol/L NTA + 0.8–16 mmol/L TBAOH + 2–130 mmol/L NaCl pH=2.3–6.0	Post-column derivatization with Arsenazo III and spectrophotometric detection at 658 nm	[26]
REEs	Conventional anion-exchange chromatographic column (IonPac AS9-HC)	5 mmol/L EDTA (pH 5.5–7.5)	ICP-MS detection	[27]
Lu, Tb, Tm, Er, Ho, Dy and Tb	Modified silica gel with chemically bound phosphonic acid	80 mmol/L α -HIBA, 5 mmol/L SDS (pH 3.5)	HPLC (flow rate, 0.75 mL/min); post-column derivatization with Arsenazo III and spectrophotometric detection at 660 nm	[29]
Th and Nd	AG* 1-X8 anion exchange resin for separation of Th, Eichrom LN spec resin for separation of Nd	11 mol/L HCl for elution of Th, 0.25 mol/L HCl for elution of Nd	SF-ICP-MS detection for Th, MC-ICP-MS detection for Nd	[30]
Separation of Sc from BR acid leachate	TiP material	pH 2.0	The selectivity toward Sc^{3+} is due to the matching between the lattice radius of Ti^{4+} and the ionic radius of Sc^{3+}	[31]

3.2.2 Ion chromatography

Since its commercial introduction in 1975 [32], IC has been recognized as a very useful tool for analyzing a broad range of cations and anions with excellent speed and sensitivity. The IC system usually consists of two ion exchange columns (separating column and suppressor column) and electric conductivity detector; the separation of the analytes is achieved in the separating column; and the suppressor column

absorbs counterions that interfere with the conductivity detection system. However, it was not particularly suitable for many metal ions including REEs because the hydroxide-type suppressor column precipitated the metal hydroxides. With the development of non-suppressed IC, the suppressor column is eliminated from the system by careful choosing the ion exchanger and eluent solution of low ionic strength as the mobile phase. This modification made the IC determination of REEs available. And then IC can be divided into two types: double column IC (suppressed IC) and single-column IC (non-suppressed IC) system.

3.2.2.1 Principle of the method

Taking the detection of the cation (such as monovalent cation) as an example, the eluent is diluted HCl or HNO₃, the separation column is packed with H⁺ type cationic exchange resin (R-SO₃⁻H⁺) with low exchange capacity and the suppression column is packed with strong basic anionic exchange resin (R-N⁺OH⁻) with high exchange capacity. The reaction on the separation column is $\text{RSO}_3^-\text{H}^+ + \text{Y}^+\text{Cl}^- \rightarrow \text{RSO}_3^- \text{Y}^+ + \text{H}^+ \text{Cl}^-$, then all kinds of cations are separated based on the different affinity with the resin; the reaction of elution on the suppression column is $\text{R}\cdot\text{N}^+\text{OH}^- + \text{H}^+\text{Cl}^- \rightarrow \text{R}\cdot\text{N}^+\text{Cl}^- + \text{H}_2\text{O}$, and water of low conductivity is eluted from the column; then the reaction of the determined cation (Y⁺) is $\text{R}\cdot\text{H}^+\text{OH}^- + \text{Y}^+\text{Cl}^- \rightarrow \text{R}\cdot\text{N}^+\text{Cl}^- + \text{Y}^+\text{OH}^-$. Therefore, the determined cation turns into hydroxide that dissolves in water and then was eluted from the column. Compared with water, the hydroxide has higher conductivity. The different hydroxide produce different response signals when they enter the electric conductivity detector and then a cationic chromatogram is obtained.

For anion (such as Cl⁻ and NO₃⁻) detection, the eluent is diluted sodium hydroxide, and the separation column is loaded with OH⁻ type cationic exchange resin with low exchange capacity. The reaction of the determined anion (X⁻) in the separation column is $\text{R}\cdot\text{N}^+\text{OH}^- + \text{Na}^+ \text{X}^- \rightarrow \text{R}\cdot\text{N}^+ \text{X}^- + \text{Na}^+ \text{OH}^-$. The suppression column is loaded with cationic resin (RSO₃⁻H⁺) with high exchange capacity, which reacts with the elution containing separated anions: $\text{RSO}_3^-\text{H}^+ + \text{Na}^+ \text{OH}^- \rightarrow \text{RSO}_3^-\text{Na}^+ + \text{H}_2\text{O}$; $\text{RSO}_3^-\text{H}^+ + \text{Y}^+ \text{Cl}^- \rightarrow \text{RSO}_3^-\text{Na}^+ + \text{H}^+ \text{X}^-$. In this case, the determined anions turn into acid and enter the electric conductivity detector together with water, then different response signal is produced and an anionic chromatogram is obtained.

In IC, both of the separation column and the suppressor column are packed with ion exchange resin. According to the features of this method such as narrow range of target concentration (10⁻⁹–10⁻⁶), small inject volume (<100 μL) and short analytical time, the ion exchange resin should meet these requirements: small-sized spherical particle, high stability under the high pressure, good mass transfer effect and fast equilibrium; sharp peak would be obtained after fast ion exchanging in the mobile phase; low degree of swelling and shrinkage, good chemical stability and thermostability;

properly lower exchange capacity that makes good resolution and short separating time. Table 3.4 is the comparison of the resin used in IC and IEC.

Table 3.4: The comparison of the resin used in IC and IEC.

The resin used in IEC	The resin used in IC
Capacity is 3–5 mmol/g	Capacity is 0.02 mmol/g
Large swelling	Small swelling
More diffusion paths	Less diffusion paths
High sample concentration	Low sample concentration
High elution concentration	Low elution concentration
Wide peak	Narrow peak

3.2.2.2 Double-column IC

Double-column IC is also named suppressed IC. It consists of the separation column, the suppression column and the electric conductivity detector. According to the interest analytes with different charge, it can be classified into anion chromatography and cation chromatography.

In double-column anion chromatography, the packing materials in the separation column are usually a covered type of aminated anion exchange resin, and the packing materials in the suppression column are strong acidic cation exchange resin with high capacity (hollow fiber membrane suppressor and tablet micro-membrane suppressor were employed later). The elution is a strong base-weak acid salt with low concentration, such as Na_2CO_3 , NaHCO_3 , NaB_4O_7 and sodium phenoxide.

As for double-column cation chromatography, the separation column is packed with sulfonated styrene-divinylbenzene copolymer coated thin-shell cation exchange resin with low exchange capacity, and the suppression column is packed with strong base anion exchange resin with high exchange capacity. The strong acid solution (such as HCl and HNO_3) at low concentration is often used as the eluent and assisted by low-concentration appropriate salt solution. However, this method is only applicable to alkali metal, ammonium, alkaline earth metal and organic amine. Cations that have precipitation reaction in the alkaline suppression column, for example, heavy metal, transition elements and REEs, are not suitable for this method.

3.2.2.3 Single-column IC

Single-column IC, also called non-suppressed IC, can be divided into single-column anion chromatography and single-column cation chromatography. In this method, there is no suppression column, but one separation column is used throughout the

process. Ion to be detected is introduced into the electric conductivity detector directly after separation. The instrument of single-column method is simple, and sharp peaks and excellent resolution can be obtained.

In single-column anion chromatography based on reducing the exchange capacity of the ion exchange resin and the eluent concentration and maintaining the retention value of the separated ion, the anion exchanger with low exchange capacity (0.007–0.04 mmol/g), small size (5–25 μm) and large aperture is employed. The eluent of this method is aromatic organic weak acid or its salt solution with low background conductance and low concentration, such as benzoic acid, citric acid, phthalate and so on. The type, concentration and pH value of the eluent will affect the separation of anion.

Single-column cation chromatography not only can separate and detect cations that can be detected by double-column method, but also can separate and detect the cations that cannot be detected by double-column method such as heavy metal, transition elements and REEs. The packing materials are mild sulfonated styrene-divinylbenzene copolymer with low exchange capacity or the silica gel bonded with sulfonated organic groups. The exchange capacity is not higher than 0.02 mmol/g and the particle size is less than 5 μm . Table 3.5 lists some commercial single-column cation chromatography column.

Table 3.5: Some commercial single-column cation chromatography column.

Type	Particle size (μm)	Exchange material	Exchange capacity (mmol/g)	Column dimension (mm)
TSKgelIC-Cation	10	PS/SVB, Thin shell mold resin -SO ₃ groups	0.012	50×4.6
TSKgelIC-CationSW	5	Silica particles, Surface- SO ₃ groups	0.45	50×4.6
Wescan-Cation	15	PS/SVB, Thin shell mold resin -SO ₃ groups	0.02	300×4.6
IC-PAK Cation (waters)	15	PS/SVB, Thin shell mold resin -SO ₃ groups	0.02	300×4.6
YSC-2	14	PS/SVB, Thin shell mold resin -SO ₃ groups	0.017	100×5

Note: PS/SVB is polystyrene-divinylbenzene copolymer.

3.2.2.4 Application of IC in separation of REEs

Single column method has been used for the separation of REEs and a low-capacity ion-exchange column is commonly used with an electrolyte solution of low ionic strength as the mobile phase. Sevenich et al. [33] developed a single-column method for lanthanide separation using a conductivity detector and ethylenediammonium/tartrate as eluent.

The substitution of tartrate with α -HIBA improved the separation slightly and elution times, predictably, decreased with increasing atomic number (Figure 3.1). The utilization of conductivity detection necessitated an isocratic elution system, which prevented efficient separation. Unfortunately, gradient elution in this system would dramatically alter the base line and complicate detection. Wang et al. [6] also employed non-suppressed IC for separation of the lanthanides. The system, consisting of a bonded-phase cation-exchange resin with 2-methylsuccinic acid as eluent, was distinguished from normal cation exchange by the low ionic strength (0.01–0.04 mol/L) of the eluent. The determination is completed after post-column derivatization and detection at 600 nm.

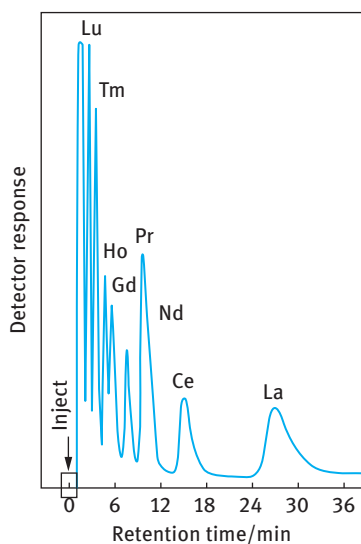


Figure 3.1: Separation of selected lanthanides (20 mg/L) on a sulphonated gel-type resin using 2 mmol/L ethylenediammonium and 2 mmol/L tartrate (pH 4.5) as eluent. Conductivity detection [33].

Nesterenko and Jones [34] achieved the isocratic separation of lanthanides and yttrium by using high performance chelation IC on iminodiacetic acid bonded silica. The obvious advantage of this approach is the possibility of prediction of elution order of lanthanides by utilizing a large amount of published values of stability constants of different complexes for selecting a proper chelating exchanger to achieve a reasonable separation. This work also shows that high performance chelation separations of complex metal mixtures such as the lanthanides and yttrium.

IC can be taken full advantage of in combination with element-selective detection techniques such as ICP-OES [35, 36] or ICP-MS [37–41]. In such applications, the eluent from the column is injected directly into the detection system. High sensitivity and anti-interference ability would be obtained. Neutron activation analysis (NAA) is also a reliable determination of individual REE at trace and ultra-trace levels. Dybczynski et al. [42] compared the performance of purely instrumental activation analysis (INAA) and radiochemical mode (RNAA) with pre- and post-irradiation

group separation for the determination of individual lanthanides with the special emphasis on Gd, Ho, Er, Tm, and Lu. The results showed that RNAA is able to determine all or nearly all lanthanides from one sample with reasonable accuracy in a variety of materials, while INAA is able to determine only certain members of the lanthanide series. The same separation scheme was also combined with IC yielding very good results [43, 44].

IC has wide applications in the analysis of REEs and the application of high-performance IC (HPIC) to the analysis of REEs has been reviewed [45]. Automation is also a trend for IC separation of REEs. Haley and Klinkhammer [46] realized the complete separation of REEs from small volume (5 mL) seawater samples by automated ion chromatography coupled with ICP-MS detection. Meynadier et al. [47] developed an automated separation of Sr prior to isotopic analysis from liquid samples (river water, seawater or solutions resulting from natural carbonate dissolution) by using HPIC technique. Table 3.6 is the application of IC in the separation and determination of REEs.

Table 3.6: Application of IC in the separation and determination of REEs.

Target analytes	Exchange materials or chromatographic column	Mobile phase	Comments	Ref.
Lanthanide elements	Bonded-phase cation-exchange resin NucleosilSA	0.01–0.04 mol/L 2-methylactic acid	Post-column derivatization with Arsenazo I and spectrophotometric detection at 600 nm	[6]
La, Nd, Gd, Ho, Tm, Yb, Lu REEs	Gel-type cation exchange resins Ion Pac CS5A column	4 mmol/L ethylenediamine and 3 mmol/L α -HIBA (pH 4.5) Gradient elution containing oxalic and α -HIBA	Use of a masking agent EDTA and a conductimetric detector Comparative evaluation of ICP-OES detection and UV-Vis spectrophotometric detection after post column derivatization with PAR	[33] [35]
REEs	Excelpak ICS-C15 column or Excelpak ICS-C35 column	α -HIBA or lactic acid	ICP-MS detection	[37]
lanthanides and Y	Dionex Ion Pac CS3 column	α -HIBA	ICP-MS detection compared with neutron activation analysis (NAA) as well as IC	[39]

Table 3.6 (continued)

Target analytes	Exchange materials or chromatographic column	Mobile phase	Comments	Ref.
REEs, Am, Cs, Ce	LUNA CSX	0.13 mol/L α -H- α -MBA (pH 3.6) during 20 min; then 0.22 mol/L α -H- α -MBA (pH 4.5)	Post-column derivatization with Arsenazo III and spectrophotometric detection at 654 nm (for REEs) ICP-MS detection (for Cs)	[41]
REEs	Ion Pac TMC-1 column	A gradient mixture of oxalic acid and diglycolic acid	Automated HPIC coupled with ICP-MS detection	[46]
Sr	Cation-exchange columns CS16 and GS16	40 mmol/L methanesulfonic acid	Automated HPIC coupled with thermal ionisation mass spectrometry (TIMS) detection	[47]
Lanthanide elements	IonPac CS5 column	8–25 mmol/L oxalic acid/ 0–23 mmol/L diglycolic acid (pH=3.0–5.5)	post-column spectrophotometric detection with PAR at 520 nm, separation of 13 REEs	[48]

3.2.3 Reversed phase ion pair chromatography (RPIPC)

Ion pair extraction has become a valuable liquid-liquid separation technique for isolating water-soluble ionic compounds by partitioning them between water and an immiscible liquid. The principle was extended to chromatography [49] during the 1970s and has been used in both the liquid-solid (adsorption) and liquid-liquid (partition) modes. Prior to 1980, normal-phase ion pair chromatography (NPIPC) was commonly used with silica or cellulose micro-particles coated with polar stationary phases and nonpolar mobile phases containing an ion pair reagent. However, the stability of NPIPC is poor and its application is limited. The current wide popularity of IPC stems from the use of bonded micro-particulate alkyl silica as nonpolar stationary phases associated with aqueous buffers containing low concentration of the ion-pairing reagent. The latter form of IPC has shown promise for lanthanide separations, which is named RPIPC. RPIPC is developed on the basis of RPC, by the addition of ion pair reagent in mobile phase, analyte ions form weak polar ion pair with ion pair reagent and the retention value would increase. Compared with general RPC, the retention of solute is increased and the separation selectivity and detection sensitivity are improved, which is greatly attributed to the addition of ion pair reagent.

3.2.3.1 Ion pair reagent

In RPIPC, the capacity factor of the sample is affected by the mobile phase composition, pH and the ion pair reagent. In other words, the species, concentration and property of the ion pair reagent in the mobile phase are the main factors for solute retention and isolation. The ion pair reagent includes cationic and anionic reagents. Some ion pair reagents that commonly used in rare earth separation are listed in Table 3.7.

Table 3.7: Some ion pair reagents that commonly used in rare earth separation.

	Name	Molecular formula	Number of carbon atoms
Anions	1-butyl sulfonate	$1\text{-CH}_3(\text{CH}_2)_4\text{SO}_3^-$	4
	1-hexyl sulfonate	$1\text{-CH}_3(\text{CH}_2)_5\text{SO}_3^-$	6
	1-octyl sulfonate	$1\text{-CH}_3(\text{CH}_2)_7\text{SO}_3^-$	8
	1-dodecyl sulfonate	$1\text{-CH}_3(\text{CH}_2)_{11}\text{SO}_3^-$	12
	1-eicosyl sulfonate	$1\text{-CH}_3(\text{CH}_2)_{19}\text{SO}_3^-$	20
Cations	Tetramethyl ammonium	$(\text{CH}_3)_4\text{N}^+$	4
	Tetraethyl ammonium	$(\text{CH}_3\text{CH}_2)_4\text{N}^+$	8
	Tetrabutyl ammonium	$(\text{CH}_3(\text{CH}_2)_3)_4\text{N}^+$	16
	Tetrahexyl ammonium	$(\text{CH}_3(\text{CH}_2)_5)_4\text{N}^+$	24
	Trioctyl methyl ammonium	$\text{CH}_3(\text{CH}_3(\text{CH}_2)_5)_3\text{N}^+$	25
	Tetraoctyl ammonium	$(\text{CH}_3(\text{CH}_2)_7)_4\text{N}^+$	32
	Tridecyl methyl ammonium	$\text{CH}_3(\text{CH}_3(\text{CH}_2)_9)_3\text{N}^+$	31

In the analysis of REEs by RPIPC, alkyl sodium sulfonate and alkyl sodium sulfate are widely used ion pair reagents. IPC of the 2- hydroxy-2-methylpropionic acid and ammonium 2-hydroxy-2-methylpropionate complexes with a C18 phase pre-treated with sodium eicosyl sulfate, ammonium dodecyl sulfate and ammonium octanesulfonate has been used for REE separation, respectively.

Knight et al. [50] used α -HIBA and octane sulfonic ion pair reagent as mobile phase in C18 RP column and achieved analysis of REEs in samples of hydrometallurgy uranium mine. Goetze et al. [51] used C18 RP column as stationary phase, tetrabutyl ammonium bromide and tetrahexyl ammonium bromide (water – methyl alcohol) as mobile phase, realizing the separation of heavy REEs. Saraswati et al. [52] used 4-(2-thiazolylazo)resorcinol as a chelating reagent in the reversed-phase HPLC separation of transition metals from REEs in low-alloy steels by increasing the concentration of the eluent (octane-1-sulphonate-tartaric acid). Zhang et al. [53] used C18 RP column as stationary phase, 100 mmol/L HAc and 200 mmol/L triethanolamine (methanol/water=85/15) as mobile phase, realizing the separation of REE-tetra-kis(4-methoxyphenyl)porphyrin (TMOPP)-Cl complex.

Tsakanika et al. [54] used α -HIBA and octane sulfonic ion pair reagent as mobile phase with gradient elution and derivatization with 4-(2-pyridylazo)resorcinol post-column, realizing the separation of scandium from other rare earth elements in laterite samples under the detection at 520 nm. Raut et al. [55] used α -HIBA and octane sulfonic sodium as mobile phase, and separated REEs from uranium and thorium in 11 min; this method was used in the analysis of REEs in rock samples. Santoyo et al. [56] used C18 RP column as stationary phase, α -HIBA and octane sulfonic sodium as mobile phase with gradient elution and derivatization with Arsenazo III post-column, realizing the separation of in 15 min under the detection at 658 nm. Jaison et al. [57] investigated the separation of REEs in different reverse-phase chromatographic column (C18, C8) and with different ion pair reagents (octane sulfonate, octane sulfate, nonane sulfonate, octadecylbenzene sulfonate, eicosyl sulfate), and then used C18 RP column as stationary phase, α -HIBA as mobile phase with gradient elution and derivatization with Arsenazo III post-column, realizing the separation and detection of 14 lanthanide elements and iron, thorium, uranium.

It should be mentioned that the concentration of ion pair agent in mobile phase should not be high, or the precipitation from ion pair agent might block up the column. So the concentration of ion pair agent should be as low as possible in an appropriate range.

3.2.3.2 Application of RPIPC in the separation of REEs

RPIPC always need a certain period of time to equilibrate the column because of the addition of ion pair reagent, and the column efficiency would decrease due to long-time service. However, the utilization of RPIPC has been gradually increased because it is easy to operate and the separation efficiency is excellent.

Figure 3.2 shows the anionic chromatogram of separating REE-oxalate complexes by RPIPC [23], which was successfully employed for the determination of trace rare earth impurity in HNO_3 solution or reference material. In Supelcosil LC-18 column, 1-octanesulfonate ion pair agent was used as mobile phase of α -HIBA, which exhibits good separation performance for all REE (Figure 3.3) [50]. This method was used for the analysis of REEs in samples of hydrometallurgy uranium mine.

By coupling RPHPLC with ICP-MS detection, Pedreira et al. [58–61] have completed a series of work on determination of trace REEs impurities in highly pure rare earth matrix. One of the major difficulties in the REEs separation is purification of yttrium from heavy REEs. With acetic acid as a novel eluent, Kifle and Wibetoe [62] realized selective separation of yttrium from the other REEs. The method is capable of base line separation of adjacent lighter and medium lanthanide as well as yttrium. However, the separation of heavier Lns remains unsatisfactory.

Santoyo and Verma [56] proposed an RPIPC method for determining lanthanides in synthetic standards by using a linear gradient program of α -HIBA eluent (0.05–0.5 mol/L, pH at 3.8) mixed with 0.01 mol/L sodium n-octanesulfonate. With the aid of a weighted

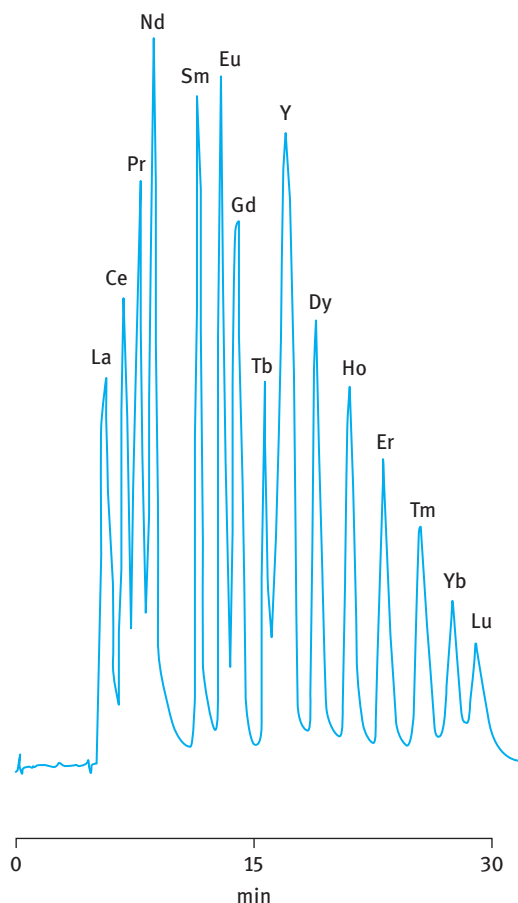


Figure 3.2: Chromatograms of separating REE-oxalate complexes by ion pair chromatography [23]. Column: Supelcosil LC-18 (5 μ m, 150 $\times$ 4.6mm); mobile phase: 0.5 mmol/L oxalic acid-2.5 mmol/L tetrabutylammonium hydroxide (pH4.6; detection at 658 nm following post-column derivation with Arsenazo III).

least-squares (WLS) regression model, the sensitivity and detection limits were estimated. It was found that the WLS method was able to compute the straight-line slopes and intercepts with considerably smaller errors than the conventional ordinary least-squares (OLS) regression method, and hence, to obtain a much better estimation of the limits of detection (LODs). They also achieved the determination of lanthanides in international geochemical reference materials by RPIPC using error propagation theory to estimate total analysis uncertainties [63].

Table 3.8 shows the application of RPIPC in REE separation. REE separation by RPIPC has attracted lots of attention due to its easy controlled separation condition, large theoretical plate number and high separation efficiency. Normally, REE complex

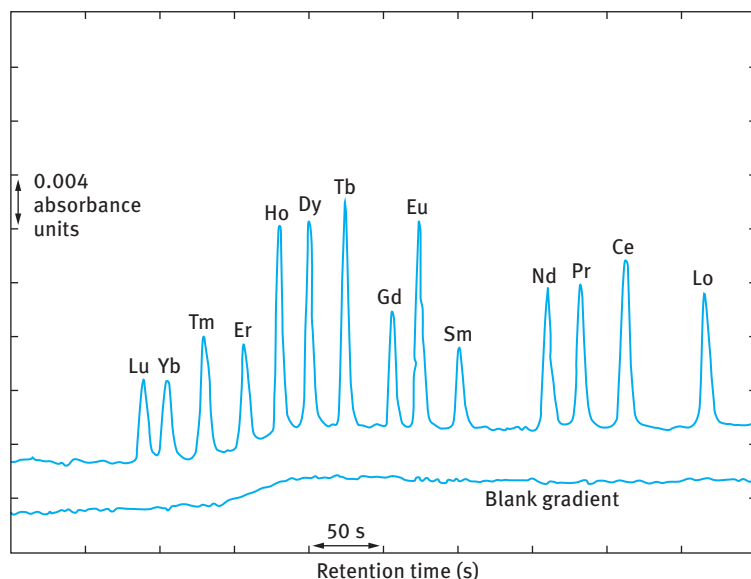


Figure 3.3: Gradient separation of the lanthanides: Supelcosil LC18 column; linear program at pH 4.6 from 0.05 mol/L HIBA to 0.40 mol/L HIBA over 10 min at 2.0 mL/min; modifier, l-octanesulfonate at 0.01 mol/L; detection at 653 nm after postcolumn reaction with Arsenazo 111; sample, 5 μ L of a solution containing 10 μ g/mL of each lanthanide [50].

can be hardly determined in the UV and visible region. Thus, derivatization by chromogenic agent was used in post-column derivation. Due to the uncertainty of the retention process, IPC was described by several different proliferations of names as the following: paired ion, soap, solvent-generated ion-exchange, ion-association and ion-interaction chromatography and dynamic ion exchange.

Table 3.8: Application of RPIPC in the separation of REEs.

Target analytes	Column	Mobile phase	Comments	Ref.
Selective separation of Y from all REEs	Kromasil 100 C18	0.5–4 mmol/L NTA+ 0.8–16 mmol/L TBAOH (tetra-n-butyl ammonium hydroxide)+2–130 mmol/L NaCl (pH=2.3–6.0)	Detection after post-column derivatization with Arsenazo III	[26]
Number of Fissions in Thorium-Uranium Dioxide Fuels	Supelcosil LC18 column	0.05–0.40 mol/L α -HIBA with 0.01 mol/L l-octanesulfonate (pH 4.6)	Detection at 653 nm after postcolumn reaction with Arsenazo (III)	[50]

Table 3.8 (continued)

Target analytes	Column	Mobile phase	Comments	Ref.
Er,Dy,Eu	Silcagel60 C8-RP	5 mmol/L phosphate buffer solution (pH6.5) and 7.5 mmol/L (C ₄ H ₉)NCl water and methanol (99+1)	RP-ion pair HPLC with EDTA complex	[51]
Transition and REEs	Spherisorb S-5 ODS-1 column	0.001 mol/L sodium octane-0.023 mol/L l-sulphonate-tartaric acid (pH 6.0),	Detection at 580 nm after postcolumn reaction with 4-(2-Thiazolylazo) resorcinol (TAR)	[52]
Y, Er, Tm, and Yb	YWG-C18 ODS	methanol/water (85/15,V/V) containing 100 mmol/L HAc and 200 mmol/L triethanolamine	SPD-10AV UV-Vis detector (428 nm)	[53]
Sc and REES	Vydac 201TP5415 RP C18	0.06–0.4 mol/L α -HIBA with 0.01 mol/L sodium 1-octane sulfonate (pH 3.7)	Detection at 520 nm after post-column derivatization with PAR	[54]
Th, U	C18-RP	Dual gradient elutions of α -HIBA and sodium 1-octane sulfonate	Detection at 650 nm after post-column derivatization using with Arsenazo III	[55]
Lanthanide elements in synthetic standards	C18 RP column	0.05–0.5 mol/L α -HIBA, with 0.01 mol/L sodium n-octanesulfonate (pH=3.8)	Detection at 658 nm after post-column reaction with Arsenazo III.	[56]
Lanthanide elements and iron, thorium, uranium.	C8, C18 RP column	7% (v/v) (0.007 mol/L) of different ion pair reagents with α -HIBA as gradient elution	Detection after post-column derivatization with Arsenazo III	[57]
Trace REEs in highly pure neodymium oxide	Shim-pack CLC-ODS column	0.7 mol/L lactic acid (pH 2.9) modified with 0.01 mol/L sodium laurylsulfonate	Detection at 655 nm after post-column reaction with Arsenazo III.	[60]
Separation of yttrium from the other REEs	0.3 mmol/L HDEHP coatedC-18 column	Isocratic elution with 0.3 mol/L CH ₃ COOH and 20 mmol/L n-octane sulphonate at pH 4.75	Detection at 658 nm after post-column reaction with Arsenazo III.	[62]

3.2.4 Extraction chromatography

Extraction chromatography (EXC) is a liquid-liquid partition chromatography that combining solvent extraction principles with chromatographic separation technology, which is known as reversed-phase partition chromatography. It is a novel technology for the separation of REEs with the merits of combining the advantages of solvent extraction (mainly selectivity) with the simplicity and ease of handling of

ion exchange materials. The separation mechanism involves ion pairing, ion exchange, coordination, simple partitioning or any combination of them [15].

3.2.4.1 Support material and stationary phase

In the extraction chromatography, a porous support implemented with a proper extractant were used as stationary phase. Normally, solid particles are used as the support material, which have many merits such as porous, uniform pore distribution, large specific surfaces, no expansion in mobile phase and no adsorption with ions in solution. Diatomite, silica gel, poly(tetrafluoroethylene) (PTFE), and polyethylene-vinyl acetate copolymer have been used as the stationary phase supports. For organic extractant, acidic organophosphorus extractant, such as P204, P507, P215 and so on. were commonly used. Selective separation of REEs can be attributed to studies of acidic phosphorus-based cation extractants and long-chain tertiary and quaternary amines as anion extractants. An acidic extractant is preferred to a neutral extractant [e.g., trioctyl-phosphine oxide (TOPO) and tributyl phosphate (TBP)] because of larger separation factors and the need for a lower acid concentration in the mobile phase. Recently, lipophilic diglycolamide (DGA) [64], N,N'-dimethyl-N,N'-dioctyl-3-oxa-DGA (DMDODGA) [65], di(2-ethylhexyl)-phosphoric acid (HDEHP) [66], 2-ethylhexyl, 2-ethylhexylphosphonic acid (H[(EH)EHP]) [67] and di(2,4,4-trimethylpentyl)-phosphinic acid (H[TMPeP]) [68] 2-ethylhexylphosphonic acid mono-2-ethylhexyl ester [69, 70], were also reported as extractant in EXC for separation of REEs. Compared to the extractant of N,N,N',N'-tetraoctyl-3-oxa-diglycolamide (TODGA), DMDODGA resin exhibits higher extraction strength for hydrometallurgical separation of REEs [65]. By comprehensively comparison of H[(EH)EHP], HDEHP and H[TMPeP] impregnated reversed phase column, best separation for the entire series of REEs was obtained with H[(EH)EHP], HDEHP was more appropriate for lighter REEs and H[TMPeP] was the best choice for separation of heavy REEs [68].

3.2.4.2 Application of extraction chromatography on the separation of REEs

The acidic organophosphorus extractant (such as P204, P507, P215, P229 and so on) as stationary phase of extraction chromatographic system is the most commonly used for separating REEs. Acidic organophosphorus extractants (P204 and P507) have been paid great attention for REEs separation. Tsuyoshi and Akiba [71] realized the separation and determination of Sm in the presence of a large amount of Nd by HPLC using reverse phase stationary phase dynamically modified with P204. Miranda et al. [72] studied the REEs fractionation by solvent extraction by use of HPLC as an analytical control technique with P204 as the extractant. Knutson et al. [73] accomplished an overloaded one-step separation of REEs through preparative

ion-exchange HPLC with a P204 impregnated column and nitric acid as eluent. An ICP-MS system was used for post column element detection.

The separation of rare earth impurities in high purity rare earth oxides and preparation of high purity rare earth elements were achieved with P507 levetrel resin as stationary phase and inorganic acid solution as mobile phase to separate matrix and other rare earth impurities. Qin et al. [74] proposed a new method to determine trace rare earth impurities in high-purity CeO_2 by using electrothermal vaporization (ETV) ICP-OES after HPLC separation with P507 resin as the stationary phase. They also developed a new method for the determination of trace rare earth impurities in high-purity La_2O_3 by HPLC combined with ICP-MS [75]. The chromatographic retention behavior of La and impurities in HPLC was studied with P507 resin as the stationary phase and HNO_3 as the mobile phase. Compared with the conventional open-column method, the proposed separation system shows a good performance with regard to short separation time, low reagent consumption, and simple operation. The method has been applied to the analysis of real samples of high-purity La_2O_3 with satisfactory results. Shuai et al. [76] proposed a rapid and effective method for separation and determination of trace rare earth impurities in high-purity La_2O_3 by combination of P507/HPLC separation with high sensitive ETV-ICP-OES determination. The results showed that a selective separation of La matrix can be obtained by using P507 resin as the stationary phase and the diluted HNO_3 as the mobile phase. This HPLC system possessed a series of outstanding characteristics in rapid speed, simple operation and low amounts of reagents consumed. Li et al. [77] adopted a single-step extraction chromatography separation method for Sm–Nd isotope analysis of micro-samples of silicate rocks by high-sensitivity thermal ionization mass spectrometry (TIMS) detection. The combination of single-stage separation with NdO^+ TIMS technique greatly improves sample throughput and reduces sample consumption. Thus, the method provides a straightforward, and time efficient way for the Nd isotope analysis in limited amount samples.

3.2.4.3 Centrifugal partition chromatography

Centrifugal partition chromatography is also called centrifugal countercurrent chromatography (CCC) or high-speed countercurrent chromatography (HSCCC), which is a kind of liquid-liquid extraction chromatography without the stationary phase support. On the basis of classic reflux chromatography, Murayama et al. [78] proposed a new method of centrifugal counter-current chromatography with a rotary seal joint. The key of the method is the rotating sealing device (Figure 3.4), which is simple and applicable to the preparative separation in a short time.

Centrifugal partition chromatography is used for the separation of the 2,4-dinitrobenzene derivatives of amino acids at first. Araki et al. [79] and Akiba et al. [80] separated REEs with suitable concentration of acid solution as mobile phase and P204 and P507 as stationary phase, respectively. The former separated Pr, Nd, and

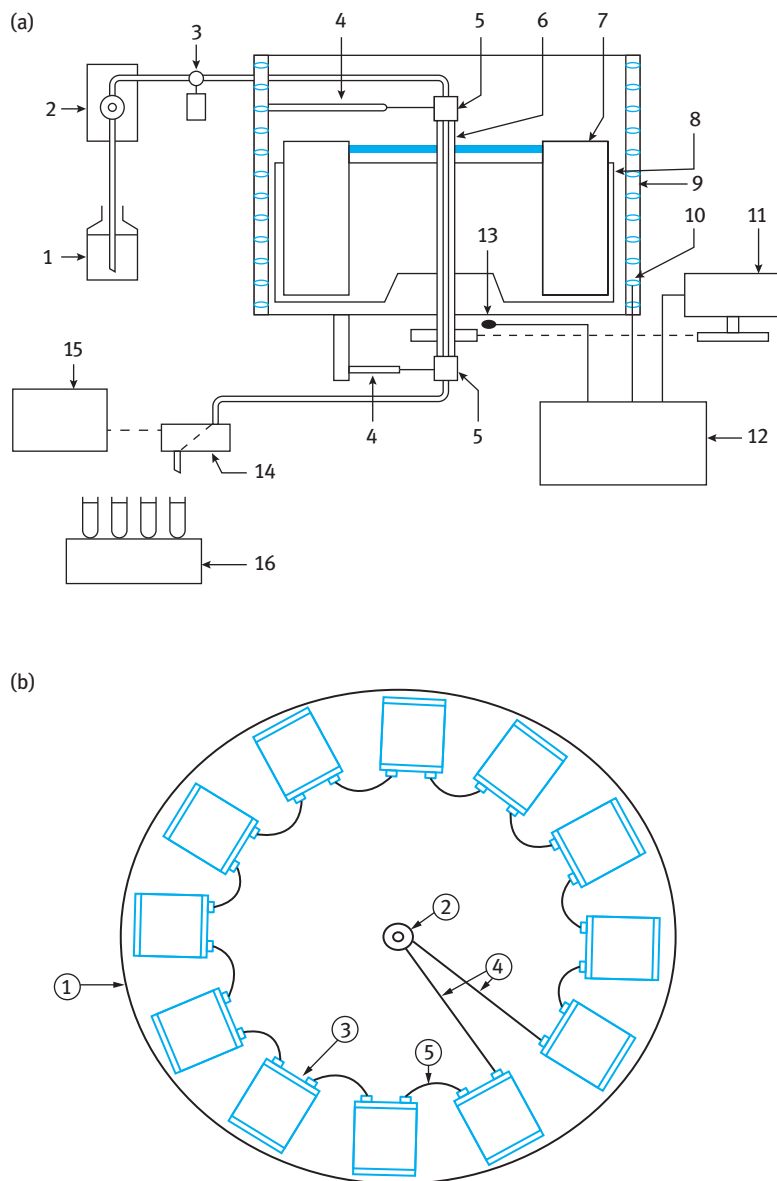


Figure 3.4: (a) The system of centrifugal partition chromatography. 1. The solvent reservoir; 2. High pressure constant flow pump; 3. Sample injector; 4. The joint of sealed rotating connection device; 5. The sealed rotating connection device; 6. Rotation axis; 7. Column storage chamber; 8. Rotator; 9. Heating and cooling device; 11. Motor; 12. Controller of temperature and speed; 13. Speed controlled sensor; 14. Monitor; 15. Recorder; 16. Collector. (b) The rotator of centrifugation distribution chromatography. 1. Centrifugal rotator; 2. The sealed rotating device; 3. Column storage chamber; 4. Connecting pipe; 5. Column storage chamber connecting pipe.

Er, Yb; the later realized the separation and detection of the adjacent REEs using post-column derivatization with Arsenazo III. Nakamura et al. [81] realized the mutual separation of heavy REEs by using HSCCC provided with a multilayer coiled column containing a toluene solution of 2-ethylhexylphosphonic acid (EHPA). The REEs were chromatographically eluted by a mobile phase with a stepwise pH gradient, as shown in Figure 3.5. By using CCC, they also realized the separation of yttrium from lanthanoid

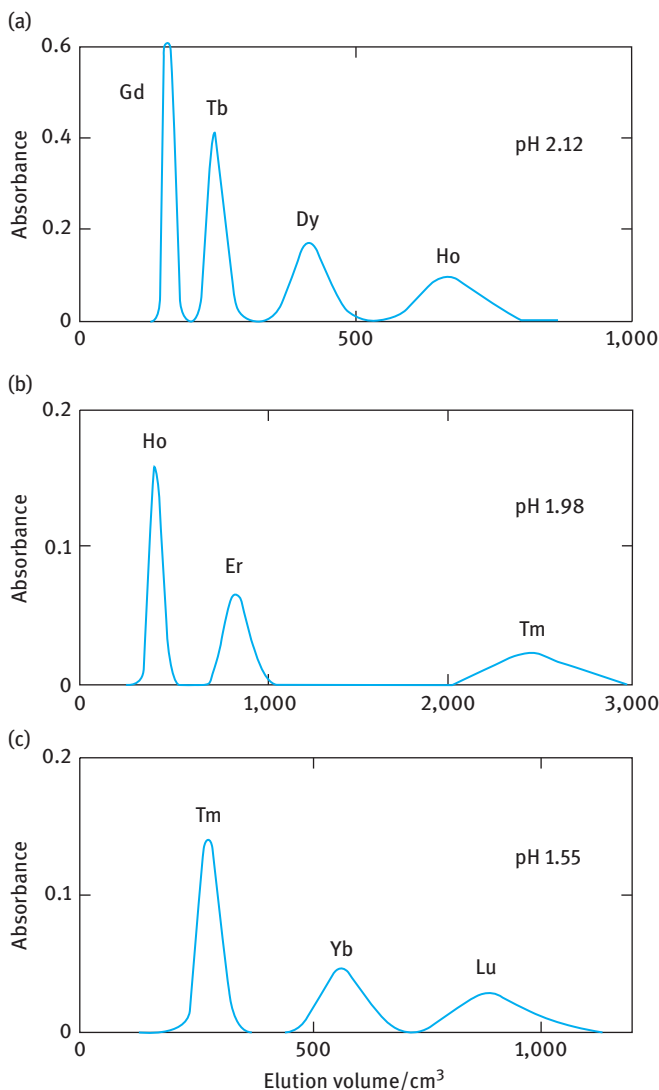


Figure 3.5: Chromatographic separation of heavy REEs. Stationary phase: 0.02 mol/L (EHPA)₂ in toluene, mobile phase: 0.1mol/L (H,Na)Cl₂CHCOO; sample: 5×10^{-4} mol/L lanthaooid in 10^{-3} mol/L HNO₃ [81].

elements [82] and purification of yttrium [83]. Tsuyoshi et al. achieved separation of praseodymium and neodymium [84] and purification of yttrium from xenotime [85] by using HSCCC with a toluene solution containing 2-ethylhexylphosphonic acid mono-2-ethylhexyl ester or di(2,4,4-trimethylpentyl) phosphinic acid as stationary phase.

Wu et al. [86] investigated the effects of concentration of extractant, pH and the flow rate of mobile phase on the separation efficiency of Am and Eu by HSCCC with dichlorophenyldithiophosphinic acid in xylene as the stationary phase and 0.1 mol/L NaClO_4 as mobile phase. The results show that the separation factor increases with the increasing of the concentration of extractant and the pH value of the mobile phase, furthermore, decreasing the flow rate of the mobile phase can also improve the separation efficiency between Am and Eu. Mutual separation between Am^{3+} and Eu^{3+} can be accomplished by optimizing the separation condition, the separation factor and separation efficiency between Am^{3+} and Eu^{3+} can reach 2.87 and 0.74, respectively. Hennebrüder et al. [87] developed an analytical scheme for the determination of REEs and Gd-DTPA in river water based on the preconcentration by means of CCC followed by ICP-MS detection. The analytical results obtained were compared with the preconcentration using SPE. It could be demonstrated that CCC results are comparable with those employing SPE. By employing the optimized conditions of CCC, the times for the enrichment of REEs (25 min) could be substantially shortened compared with the SPE procedure (120 min) for a single sample.

The literatures about centrifugal partition chromatography for the separation of REEs are listed in Table 3.9.

Table 3.9: Centrifugal partition chromatography for separation of REEs.

Target analytes	Stationary phase.	Mobile phase	Comments	Ref.
Rare earth	0.1 mol/L P204 in heptane; 0.1 mol/L P204 in dichloromethane	0.06 mol/L HCl (Ce, Pr); 0.07 mol/L HCl (Pr, Nd); 0.1 mol/L HCl (Er, Yb)	Detected after post-column reaction with Arsenazo III	[79]
Lanthanoid elements	0.02 mol/L P507 in kerosene	20% ethylene glycol chlorine acetate buffer solution (pH 1.27–2.94)	Detected after post-column reaction with Arsenazo III	[80]
Heavy REEs and Y	0.02 mol/L EHPPA in toluene	0.1 mol/L (H, Na) Cl_2CHCOOH	Detected after post-column reaction with Arsenazo III	[81]

Table 3.9 (continued)

Target analytes	Stationary phase.	Mobile phase	Comments	Ref.
Separation of Y from La	0.02 mol/L P204 in toluene (primary stationary phase), 0.25 mol/L Versatic 10 in toluene (secondary stationary phase)	0.1 mol/L chloroacetic acid; 0.01 mol/L CH ₃ COONa (in 0.1 mol/L NaNO ₃)	Detected after post-column reaction with Arsenazo III	[82]
REEs and Gd-DTPA	0.5 mol/L P204 in n-decane.	0.01 mol/L HNO ₃	ICP-MS detection	[87]
Rare earth	Three-tier connected spiral PTFE tube (300 m × 1.07 mm), 0.003 mol/L P204 in n-heptane	0–0.3 mol/L HCl gradient elution	Detected after post-column reaction with Arsenazo III	[88]
Lanthanide elements	P204: n-pentdecene: carbon tetrachloride (6:11:3)	0.5 mol/L HNO ₃	ICP-MS detection	[89]
Light REEs (Pr and Eu)	TBP: decane; carbon tetrachloride (6:7:7)	5 mol/L LiNO ₃ -1 mol/L HNO ₃	ICP-MS detection	[90]

3.2.5 Thin-layer chromatography (TLC) and paper chromatography (PC)

TLC and PC can be called as planar chromatography. These two methods used to be important means of REE separation, especially for the separation of adjacent REE. Since the introduction of HPLC in separation of REEs, application of planar chromatography especially paper chromatograph is decreasing.

In TLC and PC, the movement of target analytes (REEs) is usually expressed in rate of flow (R_f), which is defined as the ratio of the distance between the origin point of sample and the center point of target analytes and the distance between the origin point of sample and the front of mobile phase. The R_f value is always less than 1 and it is associated with the distribution coefficient of target analytes. When the distribution coefficient is larger, the distance of target analytes moved in the plane is smaller, so the R_f value is also smaller. R_f value is determined by the distribution coefficient. Besides, the property of the adsorbent, the thickness of the paper or thin layer, the composition and proportion of mobile phase, temperature, humidity and the degree of saturation vapor pressure also have effect on the R_f value. For example, temperature can affect the distribution coefficient and the composition of developing solvent. To ensure the stability of the R_f value, it is better to do the operation under the condition of constant temperature, humidity and vapor pressure of mobile phase. Generally, the separation is operated in a chromatographic cylinder or chromatographic box.

3.2.5.1 Paper chromatography

With paper as the carrier, the separation mechanism of PC is assigned to distribution behavior. PC is usually a normal-phase chromatography with less polar organic solvent as the mobile phase and the absorbed water on the supporting matrix (paper) as the stationary phase. The supporting matrix of PC for separation of REEs include cellulose, inorganic or organic ions infiltrated cellulose, ion exchanger (polymeric amine and acidic phosphate ester) infiltrated cellulose and chelating agent (such as 8-hydroxyquinoline) infiltrated cellulose. For the separation of REEs by using PC, inorganic acid aqueous solution or its mixture with organic solvent were used as mobile phase at times. And some complexing agents such as lactic acid [91] and EDTA [92] can be introduced into the mobile phase to improve the distribution property of REEs.

PC needs no expensive equipment and is suitable for the routine analysis of large numbers of samples. It was applied in REEs as early as 1955, Lederer et al. [93] employed ethanol-2 mol L⁻¹ HCl (9:1, V/V) as mobile phase for the separation of La, Ce, Pm, Eu, Dy and so on. Few years later, Dubuquoy et. al. [94] adopted a SA-2 ion-exchange paper with ammonium α -HIBA as developing solvent to separation La, Ce, Pr, Nd, Pm, and Sm from U fission. They also separated Lu, Yb, Tm, Y, Tb, and Eu by using SA-2 ion-exchange paper with different developing solvent [91] and a review about the separation of REEs by using SA-2 paper ion exchange chromatography was reported later [95]. In 1986, Chen and Yuan [92] used N₁₉₂₃ as stationary phase and 0.01 mol L⁻¹ EDTA (pH = 5) as developing solvent for the separation of light REEs and heavy REEs with their associated element Zr and U. Kostyuk [96] investigated the possibility of the separation of seven REEs (Pr, Nd, Sm, Eu, Gd, Er and Yb) by PC and optimized the separation conditions. The impregnation of PC by ammonium nitrate had given most successful results.

PC has been applied to the separation of lanthanides from other ions (such as main group, transition and actinide ions) and for group separation of the rare earths. Complete separation of all lanthanides by PC has apparently not yet been achieved although separation of the light rare earths (La, Ce, Pm, Nd, Sm and Eu) and other combinations has been successful [97]. Limitations imposed by the low intrinsic efficiency of PC may be overcome by utilizing a two-dimensional development although it is generally easier to use TLC or paper electrophoresis instead. PC can be combined usefully with coprecipitation, solvent extraction and IEC on columns for the selective determination of lanthanide mixtures. The detection of lanthanides separated by PC usually relies on spray reagents containing chromogenic complexing reagents such as Alizarin Red, 8-hydroxyquinoline, Arsenazo I, II or III and pyridylazoresorcinol.

A disadvantage of PC is the relatively long developing time required (2–20 h). Moreover, the separation effect among REEs by using PC is not satisfactory, so the application of paper chromatography on REEs is rare.

3.2.5.2 Thin-layer chromatography

TLC as an important branch of chromatographic analysis can get good separation effect without any sample pretreatment and its overall performance exceeded the PC and atmospheric column chromatography.

3.2.5.2.1 Stationary phase

According to the separation mechanism of TLC, the support material (sorbent) is divided into adsorptive carrier and distributive carrier. The main types of sorbent include silica gel, cellulose, alumina, organic Teflon40, Corvic and so on. Among them, silica gel is the most common used carrier, and cellulose is suitable for the light rare earth separation. The requirements for the sorbent are as follows: (1) it has huge surface area and sufficient adsorption capacity, different adsorption capacity for different components; (2) it is not dissolved in the solvent and developing agent and do not have chemical reaction with solvent or developing solvent or chemical composition in the sample; (3) the particles are uniform and wouldn't be broken during use.

3.2.5.2.2 Developing solvent

TLC for separation of REEs includes adsorption thin layer, distribution thin layer, ion exchange thin layer, gel thin layer and so on. Due to the different separation mechanism, the choice of developing solvent is a key factor for a successful TLC separation. The appropriate developing solvent was selected by considering the polarity of separated components, the type and activity of thin layer, and the polarity (elution force) of developing solvent. The first two factors determine the polarity of developing solvent and the elution capacity. Touchstone et al. [98] pointed out that the elution ability of the solvent is proportional to the dielectric constant, a large dielectric constant of the solvent would reduce the separation ability and increase the R_f value; on the contrary, the separation ability would be increasing and the R_f value would be decreasing. When the R_f value is too high, developing solvent with low dielectric constant should be chosen.

Generally, the developing solvent system for normal-phase thin-layer analysis of REEs is extractant-organic solvent-acid, for example, P204-ether- HNO_3 and TBP-hydrocarbon- HNO_3 which are preferable. As for RP thin layer, the layer is usually impregnated by extraction agent such as P204, TBP and TOPO; of which P204 is the best, TBP ranks second and TOPO is the worst. The commonly used developing solvent is inorganic acids, and nitric acid is the most widely used.

3.2.5.2.3 TLC separation of REEs

With high-performance TLC, it is possible to separate all the REE in a single step [99]. TLC has replaced PC as the preferred method for separating REEs. A wide

variety of stationary phases, mobile phase and detection methods have been investigated for TLC (as shown in Table 3.10).

TLC is divided into normal and RP TLC. The developing system in normal phase TLC is generally extractant-organic solvent-acid, for example P204-ether- HNO_3 . Specker et al. [99, 100] investigated different developing system for the separation of all REEs by TLC with employing silylanization silica as stationary phase; they finally chose P204-diethyl ether-tetrahydrofuran- HNO_3 as the developing system (as shown in Figure 3.6) [99]. Ishida et al. [101] used silica as stationary phase and NH_4NO_3 solution as mobile phase to separate REEs. They got a poor separation for the REEs. And then they used gradient elution with NH_4NO_3 and double phase TLC to realize the complete separation.

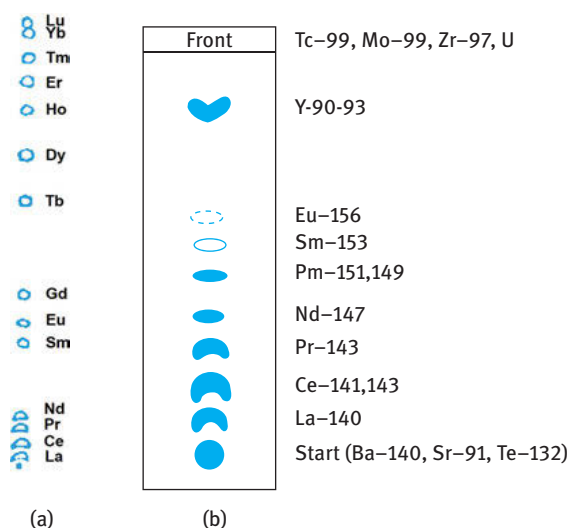


Figure 3.6: The thin layer chromatograms of REEs. (a) The mixture of REEs; (b) Uranium and nuclear fission products. Stationary phase: silanization diatomite; mobile phase: diethyl ether/tetrahydrofuran/P204/nitric acid [99].

The separation of single REE by normal phase TLC is not good, and the application area RP TLC is more widely. As early as 1964, Pierce and Flint [102] adopted RP TLC for the separation of REEs, and since then a lot of works on the separation of REEs by this method were reported. For example, Takeda and Ishida [103] used 0.1 mol/L trihydroxymethylamine and 0.1 mol/L HCl-impregnated silica (pH=7) as stationary phase, and different alkali metals nitrate solutions as mobile phase to separate all the REEs except Po. Later on, they used both carboxymethylcellulose-aqueous sodium nitrate systems [104] and carboxymethylcellulose-aqueous sodium chloride systems [105] for the separation of REEs, and Y has been separated from all of the REEs, except for La, which provides R_f values similar to those of Y.

Soran et al. [106] studied the separation of REEs by TLC with using silica H and ammonium nitrate impregnated saturated silica H as stationary phase, and di(2-ethylhexyl) dithiophosphoric acid as complexing agent in the mobile phase. They found that the best results were obtained by use of ethyl methyl ketone-tetrahydrofuran-di(2-ethylhexyl) dithiophosphoric acid (1 mol/L), 6.8 + 3.2 + 0.4 (v/v), as mobile phase. In another work, they also used mobile phase containing di(2-ethylhexyl) disulfophosphate and di(isobutyl) disulfophosphate to separate Ur, Th and REEs and demonstrated disulfophosphate played a great role in the separation of lanthanide and actinide [107].

Due to the limitation of the subsequent detection methods, TLC is difficult to be applied to the determination of REEs. However, it can be used in the initial separation analysis of REEs to provide reference information for further research. Table 3.10 shows the application of TLC in separation of REEs.

Table 3.10: Application of TLC in separation of REEs.

Elements	Stationary phase	Mobile phase/ developing solvent	Comments	Ref.
Adjacent lanthanides	silica gel (pH 7.0) pretreated with 0.1 mol/L tris(hydroxymethyl)-aminomethane and 0.1 mol/L HCl	Nitrate solution of alkaline earth metal	RF values of the lanthanides varied in a regular and characteristic way accompanied by the tetrad effect with increasing atomic number	[103]
REEs	Silica gel H and silica gel H impregnated with NH_4NO_3	Et Me ketone-THF-di(2-ethylhexyl) dithiophosphoric acid (1 mol/L), 6.8/3.2/0.4 (v/v/v)	—	[107]
REEs	Silica gel	Aqueous nitrate solutions of alkali metals	Spraying with aqueous 0.02% Arsenazo III and then 1 mol/L CH_3COOH	[108]
REEs	Whatman KC 18 reversed-phase thin-layer chromatography plates	1 mol/L lactate in 50% methanol	Reversed-phase TLC with spraying aqueous 0.1% Arsenazo III or 0.1% xylene orange	[109]
REEs	Silica gel without binder	0.1–2 mol/L ammonium sulfate solution (pH=5.4±0.1)	Spraying with aqueous 0.02% Arsenazo III and then an aqueous NH_3 , followed by gentle heating	[110]
REEs	DC-Trennung	Diethyl ether/HDEHP/ HNO_3 (100:1:3.5)	Increase the R_f differences between either the heavy or the light rare earths by variation of HDEHP and HNO_3 .	[111]

Table 3.10 (continued)

Elements	Stationary phase	Mobile phase/ developing solvent	Comments	Ref.
REEs and Y	Fixion 50-X8 sheet material with a layer of Dowex 50-X8 cation exchanger on the polymer base	0.1 mol/L oxalic acid- 2 mol/L NH ₄ Cl at pH(7.5–8.5)	Desorption of the REE group with 5 mol/L HCl followed by dilution and then determination by ICP-OES	[112]

3.3 Gas chromatography

GC is a simply operated and widely used separation and analysis method, which is highly selective, sensitive and effective. GC is suitable for the analysis of volatile and thermally stable analytes. This technique was firstly used in the separation of lanthanide elements-methylene pivalic acyl clathrates by Eisentrunk et al. in 1965 [113]. In the later study of GC separation for REEs, β -diketonates as ligand account for the largest proportion. The separation and determination of REEs by GC are summarized in Table 3.11.

Problems such as adsorption and low resolution of lanthanide β -diketonates has not been effectively solved through changing stationary phase, so the research works on GC separation of REEs decreased gradually, and there is almost no research on this aspect in recent years.

Table 3.11: The separation and determination of REEs by GC.

REEs	Chelates	Stationary phase	Column temperature	Ref.
Sc, Lu, Er	isobutyrylpivalylmethane	Silicone	210–280 °C	[114]
Nd, Gd, Er	isobutyrylpivalylmethane, trifluoroacetylacetone	Silicone E-30	160–280 °C	[115]
Y, La~Nd, Sm~Tb, Yb	hexafluoroacetylacetone + tributyl phosphate (TBP)	Dexsil 300GC	150–210 °C	[116]
Y, lanthanides	fluorinated β -diketonates + organic neutral donors	SE-3, QF-1	185–215 °C	[117]
yttrium group lanthanides	polyfluorinated β -diketonates +DBSO	Dexsil 300GC	140–215 °C	[118]
Y, lanthanides	hexafluoroacetylacetone + TBP	1.0% Silicone SE-30	250–275 °C	[119]
Sm, Eu, Gd, Tb, Dy, Ho, Er, Yb, Tm, Lu, Y	trifluoroacetyl-pivaloylmethane	SE-30	200 °C	[120]
Ho, Dy, Tb, Gd	trifluoroacetylacetone	PEG-20M, OV-17	240 °C	[121]

Table 3.11 (continued)

REEs	Chelates	Stationary phase	Column temperature	Ref.
Sc, Y, REEs	pivaloyltrifluoroacetone	Silicone	170–270 °C	[122, 123]
cerium group lanthanides	polyfluorinated β -diketone + DBSO	Dexsil 300GC	172–215 °C	[124]
lanthanides	β -diketone + DBSO	DB-5 HT capillary	50–300 °C	[125]

3.4 Capillary electrophoresis

CE is a kind of electrokinetic separation method performed in capillaries. In CE methods, analytes migrate through electrolyte solutions under the influence of an electric field. The separation is based on the ionic mobility. CE techniques include capillary zone electrophoresis (CZE), micellar electrokinetic chromatography (MEKC), capillary gel electrophoresis (CGE), capillary isoelectric focusing (CIEF) and capillary isotachopheresis (CITP). Among them, CZE and CITP are the most widely used CE modes in REEs separation and analysis.

3.4.1 Basic knowledge and principle

3.4.1.1 Zeta potential

The directional migration of the analytes in capillary is not only affected by the applied voltage, but also influenced by the charge on the inner surface of the capillary. When the electrolyte contacts with the inner surface of the capillary, a double electrode layer is formed. One layer next to the inner surface is the Stern layer, and the other one in a free state is the diffusion layer. The potential between the Stern layer and the starting edge of the diffusion layer is the Zeta potential (ζ_i) of the capillary wall. In fused silica capillary, when the pH of the solution is higher than 2.5, the Si-OH on the inner surface of the capillary is ionized as SiO⁻, making the inner surface of the capillary negative charged. Next to this negative charged surface, ions with opposite charges agglomerate forming the double electrode layer. The relationship between the Zeta potential and the thickness of the diffusion layer (δ) can be expressed as

$$\zeta_i = \frac{4\pi\delta e}{\varepsilon}$$

where ϵ is the dielectric constant and e is the total excess charge per unit area in the solution. The Zeta potential is proportional to the product of the charge numbers on the inner surface and the thickness of the diffusion layer, which is affected by the property of the ions with opposite charges, pH of the buffer solution, the equilibrium between the cations in the solution and the negative charged surface of the fused silica capillary and so on.

3.4.1.2 Electrophoresis

The electrophoresis is the directional migration of the charged analytes under the influence of an electric field. The migration velocity (U_{ep}) is expressed as

$$U_{ep} = \mu_{ep} \cdot E$$

where E is the electric field intensity and μ_{ep} is the mobility of the analytes. The ion mobility is the migration distance in a given buffer solution per unit time and per unit electric field intensity, which is

$$\mu_{ep} = \frac{\epsilon \zeta_i}{4\pi\eta}$$

where η is the viscosity of the medium, ζ_i is the Zeta potential of the target ion. ζ_i is related to the surface electric density of the target ion. If the charged number of the target ion is fixed, the larger the mass, the lower the Zeta potential. Different ions migrate in the electrolyte with the different mobility according to their specific mass and surface electric density, which is the separation base of the electrophoresis.

3.4.1.3 Electroosmotic flow

Electroosmotic flow (EOF) is an electrokinetic phenomenon generated along with the electrophoresis. Under the influence of an electric field, the electrolyte will directionally move relative to a stationary charged boundary. The mobility of EOF (μ_{eo}) is expressed as

$$\mu_{eo} = \frac{\epsilon \zeta_w}{4\pi\eta}$$

where ζ_w is the Zeta potential of the capillary wall. The formation of EOF is related to the double electric layer, which is mainly controlled by the SiO^- on the surface of fused silica capillary, or the adsorption on the surface of non-ionic capillary material (e.g., PTFE). EOF plays a great role in CE separation. The adjusting of the mobility and direction of EOF is important to improve the separation efficiency, selectivity and

resolution. Usually, the mobility of EOF is five- to sevenfold faster than the mobility of the charged ions, and the direction of EOF is from anode to cathode. Therefore, all the particles (cations, anions and neutral particles) will migrate from anode to cathode with the appeared mobility (μ_{ap}), which is the vector sum of μ_{eo} and μ_{ep} , and can be calculated as

$$\mu_{ap} = \mu_{eo} + \mu_{ep} = \frac{l}{t} \cdot \frac{L}{V}$$

where l is the distance between the injector and the detection window, t is the migration time, L is the length of the capillary, and V is the applied voltage.

3.4.1.4 Separation efficiency and resolution

In CE separation, the separation efficiency can be expressed as the theoretical plate numbers (N), which is calculated as

$$N = \frac{Vl}{2DL} \mu_{ap}$$

where D is the diffusion coefficient of the solute. The higher the electric field, the higher the separation efficiency; the higher the appeared mobility, the higher the separation efficiency; the lower the diffusion coefficient, the higher the separation efficiency.

The plate numbers can also be determined by experiments, which is calculated as

$$N = 5.54 \left(\frac{t}{W_{h_{1/2}}} \right)^2$$

where $W_{h_{1/2}}$ is the peak width at half peak height.

Resolution (R_s) is another factor to evaluate the separation degree in CE. For two analytes (1 and 2) next to each other, according to Giddings equation, R_s can be calculated as:

$$R_s = \frac{\sqrt{N}}{4} \left(\frac{\mu_{ap,2} - \mu_{ap,1}}{\mu_{ap,2} + \mu_{ap,1}} \right)$$

It can be seen that the difference in the appeared mobility of two analytes is the main factor that affects the resolution.

3.4.2 Influencing factors on CE separation

There are many factors that would affect CE separation, including voltage, buffer solution composition and pH, adducts and temperature and so on.

3.4.2.1 Voltage

Increasing voltage would result in improvement of separation efficiency and resolution; however, it would also cause the increase of Joule heat which is not beneficial for CE separation.

3.4.2.2 Buffer composition

Since CE is processed in buffer solution as background electrolyte, the selection of electrolyte has great influence on the migration and separation of analytes. There are some criteria for choosing the buffer solution: the buffer solution should have large buffering capacity in a certain pH range; the mobility of the electrolyte should be small, indicating large molecule and small charge to reduce the current; the influence of the electrolyte on the detection can be ignored.

3.4.2.3 Buffer pH

The buffer pH has great influence on EOF. At high pH, the Si-OH on the inner surface of capillary is ionized at a great degree, resulting in a high EOF; at low pH, the ionization of Si-OH was restricted, resulting in reduced EOF. The highly dependent of EOF on pH determined that the migration time of analytes is highly related to the buffer pH. Therefore, optimization of buffer pH is important to obtain an optimal CE separation of REEs.

3.4.2.4 Adducts

Adducts is another important factor to the separation of interest analytes in CE. The addition of an appropriate adduct can change the physical and chemical properties of capillary wall and the solutes via their interactions. The CE separation of metal cations is greatly dependent on the molar conductance of target cations. Since REEs cations have similar molar conductance, the CE separation of REEs cations usually involves the addition of complexes to improve the separation resolution. Commonly used complexes include oxalate, citrate, lactate, tartrate, nitrilotriacetic acid, EDTA,

α -HIBA, 8-hydroxyquinoline-5-sulphonic acid and so on. Among them, α -HIBA is the mostly frequently used adduct.

3.4.2.5 Temperature

The increase of temperature leads to the decrease of the solution viscosity and the increase of current, which cause the variation of EOF. Normally, increasing temperature would result in the reduction of the migration time.

3.4.3 Applications in REEs analysis

In CE separation of REEs, the migration direction of REEs is the same as the EOF. The tiny difference in charge and radius of REEs leads to a slight difference in mobility. For instance, the mobility of trivalent REE cations is varied from $72.3 \times 10^5 \text{ cm}^2/\text{V}$ (La) to $67.5 \times 10^5 \text{ cm}^2/\text{V}$ (Yb). Therefore, these REE cations cannot be well separated in conventional CE. The addition of complex in separation system would enlarge the difference in mobility of REEs, leading to an effective separation. Besides adducts, electrolyte composition, buffer pH and the property of capillary wall will also influence the separation of REEs. Janos [126] provided a review on separations of lanthanides by CE in 2003.

As early as 1970, the CE separation has shown its advantages of fast and high resolution in REEs separation. The applications of CE in separation of REEs are listed in Table 3.12. In 1970, Korchemmaya [127] achieved a CE separation of all the REEs in 15–20 min. Then, Foret et al. [128] separated 19 metal ions including 14 REEs in 5 min by using CZE. Later on, Jandick et al. [129] separated 24 elements including REEs in 5 min. Chen and Cassidy [130] compared the CE separation of REEs with different capillary coatings. With benzylamine aminotoluene and α -HIBA as complexes, 14 REEs could be separated in 6 min by using C1 coated capillary, while the separation time is 8 min when using C18 coated capillary. A comparison of CZE and ITP demonstrated that the selection of electrolyte and the optimization of CE conditions in ITP are much more complicated than that in CZE. In ITP, the leading catholyte should be acids with high mobility, and the trailing anodolyte should be weak acids [131]. The optimization of CZE conditions without such limitations is more convenient. Recently, Bottenus et al. designed and fabricated a fused-silica microfluidic device for ITP, and 14 REEs can be separated by ITP with 10 min in a serpentine fused-silica microchannel (70 μm wide $\times$ 70 μm tall $\times$ 33 cm long) [132].

UV (with indirect or direct UV mode) is the most widely used detector in CE analysis of REEs. To obtain higher sensitivity than UV detection, Saito et al. [133, 134] employed laser induced fluorescence (LIF) as CE detector for the detection of the complexes of lanthanides with fluorescein-thiocarbamyl-1-(4-aminobenzyl)

ethylenediamine-N,N,N',N'-tetraacetate (FTC-ABEDTA). The LODs were decreased to dozens pM level. With capacitively coupled contactless conductivity detection (C^4D) as subsequent detector, sensitive detection of REEs ions can be achieved without the need of visualization agent. Thi Anh Huong et al. constructed a portable in-house-made CE instrument with C^4D detector for determination of 14 REEs, and the best LOD was 0.24 mg/L [135]. Elemental-specific ICP-MS is one of the most sensitive methods for the determination of REEs. A combination of CE-ICP-MS is capable for the speciation of Ln and Ln-humic acids [136–138]. However, an interface with small dead volume and high transport efficiency between CE and ICP-MS is necessary. Recently, Lackey et al. developed a versatile and low cost interface to combine chip ITP with ICP-MS detection for the determination of REEs [139]. ESI-MS is a method of choice for elemental and molecular analysis of lanthanides, has also been employed as CE detector [140]. However, the LOD of Ln obtained by CE-ESI-MS is much higher than that by CE-ICP-MS. It is worth noting that with on line sample stacking technique, the sensitivity of CE based method for separation of REEs can be further enhanced.

The applications of CE in separation of REEs are listed in Table 3.12.

3.5 Supercritical fluid chromatography

Supercritical fluid chromatography (SFC) [169] was called high-pressure GC in the early time, which utilizes supercritical fluid as mobile phase. Lanthanide chelate is one of the first metal chelates that separated by SFC. In 1968, Karayanis et al. [170] separated lanthanide β -diketonates by utilizing supercritical CCl_2F_2 as mobile phase under the temperature lower than that used in GC. So SFC solves the problem of thermal instability of compounds exists in GC. A few years later, the separation of lanthanide chelates of acetylacetone (ACAC), trifluoroacetylacetone, thenoyltrifluoroacetone, dipivaloylmethane, and 6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedione with ethanol modified inert silylated column were investigated by Laintz et al. [171]. Mobile phases consisting of supercritical CO_2 were used and all of the compounds were shown to have good chromatographic performance. Furthermore, Wu et al. [172, 173] separated and analyzed lanthanide β -diketonates with good performance. However, due to the supercritical chromatography instruments are relatively complex, difficult to popularize, and show no obvious advantages when compared with HPLC, limiting the development of this technology in the separation and analysis of REEs. With the gradual improvement of HPLC technology, SFC has gradually been replaced by HPLC, actually it is rarely used now.

Table 3.12: The applications of CE in separation of REEs.

REEs	CE methods	Separation condition	Time (min)	LODs	Ref.
Ln, Y, Sc	CZE-UV (fused silica 50 cm × 75 µm)	borate buffer (20 mM, pH 11.0) + 1 mM CDTA	12	2–5 µM (Ln), 10 µM (Sc)	[141]
Ln	CZE-UV (fused silica 40 cm × 100 µm)	30 mM creatine + 7 mM α-HIBA + 30 mM acetate acid, pH 4.8	–	–	[142]
La, Ce, Tb, Gd	CZE-UV (fused silica 52 cm × 75 µm)	10 mM creatine + 2 mM α-HIBA + acetate buffer, pH 4.1	3.5	40 µg/L	[143]
La–Yb, alkalis, Ca, Mg	CZE-UV (fused silica 36.5 cm × 75 µm)	4 mM α-HIBA, pH 4.4	8	77–199 mg/mL	[144]
Ln	ITP (PTFE 20 cm × 0.05 mm)	0.027 M KOH + 0.015 M α-HIBA + acetate buffer + 0.0025% PVA, pH 4.92	20	5 nmol	[145]
La–Tm	CZE-UV (fused silica 50 cm × 50 µm)	30 mM creatine + 0.4 mM α-HIBA, acetate buffer, pH 4.0	11	–	[146]
Ln	CZE-UV (fused silica 57 cm × 75 µm)	4.25 mM α-HIBA, 8 mM acetate buffer, pH 4.4	10	0.03 nmol	[147]
Ln	CZE-UV (fused silica 35 cm × 50 µm)	0.02 M imidazole + 6 µM lactic acid, pH 3.4	6	5 µM	[148]
Ln	CZE-UV (fused silica 40 cm × 75 µm)	8 mM α-HIBA + 0.9 mM malonic acid + 30 mM creatine, ethylbutyric acid buffer, pH 4.8	5	–	[131]
Y, Ln except Pm	ITP (PTFE 25 cm × 0.32 mm)	Leadings: 20 mM ammonia; BGE: 7.5 mM α-HIBA + 2 mM malonic acid + 2-ethylbutyric acid, pH 4.8; Tailing: 20 mM carnitinehydrochloride; all with 0.1 % (w/w) HPC	–	–	[149]
La, Ce, Pr, Nd, Sm, Eu	ITP-UV (fused silica 50 cm × 50 µm)	Leading: 10 mM H ₂ SO ₄ ; BGE: 0.4 mM quinine sulfate + 8 mM α-HIBA; Tailing: 80 mM TRIS	3	6–11 nM	[150]
RE, Th, U (as DBCAs chelate)	CZE-Vis (fused silica 70 cm × 75 µm)	20 mM NaAc-HCl buffer + 0.2 mM DBCAs, pH 3.0,	10	48.1–72.3 nM	[151]
14 REEs	CZE-UV (fused silica 35 cm × 50 µm)	20 mM imidazole + 8 mM α-HIBA, pH 3.4 with HCl	10	5 nM	[152]
14 REEs	CZE-UV (fused silica 65 cm × 50 µm)	0.1 mM cupferron + 15 mM α-HIBA, pH 4.9	7	0.24–0.47 µg/mL	[153]
La–Lu	CZE-UV (fused silica 36.5 cm × 50 µm)	4 mM α-HIBA + 10 mM UVcat-1, pH 4.4 with HAC	<1	<0.1 ng	[154]

Ln	CZE-UV (fused silica 71 cm × 50 µm)	0.8 mM picolinic acid + 10 mM α-HIBA + 25 mM formic acid, pH 4.7	9	0.53–0.96 µg/mL	[155]
Ln (xenotime, monazite)	EKS-CZE-UV (fused silica 100 cm × 75 µm)	Leading: 100 mM ammonia + 7.5 mM α-HIBA + 2.0 mM malonic acid, 2 ethylbutyric acid, pH 4.8 Supporting: 10 mM 4-methylbenzylamine + 4 mM α-HIBA + 0.4 mM malonic acid, 2 ethylbutyric acid, pH 4.8 Tailing: 1M HCl	< 5 min	–	[156]
Ln (as ABEDTA chelate)	CZE-UV (fused silica 50 cm × 50 µm)	50 mM borate + 20 mM carbonate, pH 12.35 with NaOH	35	0.94 µM	[157]
16 REEs	CZE-UV (fused silica 50 cm × 75 µm)	17 mM creatinine + 7.8 mM α-HIBA + 175 mM HAC	12	–	[158]
Eu, Gd species	CZE-ICP-MS (fused silica 80 cm × 74 µm)	100 mM HAC + 10 mM NaAc, pH 3.7	< 8	125 (Eu), 250 (Gd) ng/L	[136]
Ln (as NBD-ABEDTA chelate)	CZE-UV (fused silica 60 cm × 50 µm)	9.5 mM borate + 33.5 mM IDA, pH 9.45	20	0.42 µM	[159]
REEs (geological samples)	CZE-UV (fused silica 60 cm × 75 µm)	17 mM creatinine + 7 mM α-HIBA + 140 mM HAC + 6.5 mM HCl	13	~10 (Y), ~20 (other REEs) µg/L	[160]
Ln-humic acid	CZE-ICP-MS (fused silica 80 cm × 74 µm)	100 mM HAC + 10 mM NaAc, pH 3.7		0.8–1.6 nM	[137]
Ln (as FTC-ABEDTA chelate)	CZE-LIF (fused silica 80 cm × 74 µm)	12 mM borate + 5.5 mM IDA + 9.0 mM citrate + 25 µM CyDTA, pH 9.60	23	91 pM	[133]
Ln	CZE-UV (fused silica 35.5 cm × 75 µm)	4 mM α-HIBA + 10 mM UVCat-1, pH 4.4	~3	0.67–16 ng (“odd–even” pattern)	[161]
Ln-humic acid	CZE-ICP-MS (fused silica 80 cm × 74 µm)	100 mM HAC + 10 mM NaAc, pH 3.7	–	–	[138]
Ln	CZE-ESI-MS (fused silica 120 cm × 50 µm)	0.8 mM picolinic acid + 10 mM α-HIBA + 25 mM formic acid, pH 4.7 with TRIS	< 30	Low mg/L	[140]

(continued)

Table 3.12 (continued)

REEs	CE methods	Separation condition	Time (min)	LODs	Ref.
Ln	LLLME + CZE-UV (fused silica 50 cm × 75 μm)	28 mM creatinine + 11.5 mM α-HIBA + 0.26 M HAC	20	0.19–0.70 μg/L	[162]
Nd (as FTC-ABEDTA chelate)	CZE-LIF (fused silica 80 cm × 74 μm)	12 mM borate + 25 μM CyDTA, pH 9.60	12	22 pM	[134]
Ln	ITP-CD / ICP-MS (fused silica or PVA coated 56 cm × 30 μm)	LE: 14 mM HMBA + 10 mM HAC, pH 4.5 with ammonia TE: 15 mM HAC	~30	–	[163]
Ln, Th, UO ₂ ²⁺	CZE-UV (fused silica 57 cm × 75 μm)	1 mM HTTA + 50 mM α-HIBA + 5 mM NaNO ₃ + 5% methanol, pH 5.2	12	–	[164]
Ln	Portable CZE-C ⁴ D (fused silica 53 cm × 50 μm)	20 mM arginine + 10 mM HIBA, pH 4.2	13.5	0.24 mg/L	[135]
Y, La, Ln without Pm	CZE-indirect UV (fused silica 60 cm × 75 μm)	12 mM benzimidazole, 8 mM dipropylglycolic acid, 10 mM glycolic acid, pH 3.0	12	0.2–1.2 μg/L	[165]
Ln	CZE-C ⁴ D (fused silica 61.5 cm × 50 μm)	4.5 mM 2-HIBA + 1 mM HAC, pH 4.5	6	2.77–8.26 nM	[166]
Th, U (as H ₂ SA ₂ en chelate)	MEKC-UV	60 mM HBO ₃ -Na ₂ B ₄ O ₇ + 13 mM SDS + 11.5% acetonitrile, pH 8	4	0.04–0.08 mg/L	[167]
Nd, Sm, Eu, Gd isotope	Stop-flow ITP-MC-ICP-MS (fused silica 120 cm × 50 μm)	LE: 14 mM HMBA, pH 4.5 with NH ₄ Ac TE: 15 mM HAC	< 25 min	20 ng	[168]
Ln	Chip ITP-C ⁴ D (a serpentine fused-silica microchannel (70 μm × 70 μm × 33 cm))	LE: 10 mM NH ₄ Ac, 7 mM HIBA, 1% PVP, pH 4.5 TE: 10 mM HAC, 7 mM HIBA, and 1% PVP, pH 3.0	< 10	~50 μM	[132]
Ln	Chip ITP-ICP-MS	LE: 10 mM NH ₄ Ac, 7 mM HIBA, 1% PVP, pH 4.5 TE: 10 mM HAC, 7 mM HIBA, and 1% PVP, pH 3.0	35	–	[139]

CDTA: cyclohexane-1,2-diaminetetraacetic acid; PVA: Polyvinyl alcohol; HPC: hydroxypropylcellulose; TRIS: tris(hydroxymethyl) aminomethane; DBC-As: 2-(2-arsenophenylazo)-1,8-dihydroxy-7-(4-chloro-2,6-dibromophenylazo)-naphthalene-3,6-disulfonic acid; EK5: electrokinetic supercharging; ABEDTA: 1-(4-aminobenzyl) ethylenediamine-N,N',N'-tetraacetate; NBD: nitrobenzofurazan; IDA: iminodiacetate; LIF: laser induced fluorescent; FTC: fluorescein-thiocarbamyl; CyDTA: trans-1,2-diaminocyclohexane-N,N',N'-tetraacetic acid, LLLME: liquid liquid liquid microextraction, HMBA: 2-hydroxy-2-methylbutyric acid; CD: conductivity detection; LE: leading electrolyte; TE: terminating electrolyte; H₂SA₂en: bis(salicylaldehyde) ethylenediamine; MC: multi collector; HTTA: 2-thenyltrifluoroacetone; PVP: polyvinylpyrrolidone

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4 Separation/Preconcentration techniques for rare earth elements analysis

Abstract: The main aim of this chapter exactly characterizes the contribution. The analytical chemistry of the rare earth elements (REEs) is highly complicated and the determination of a specific element is impossible without appropriate sample pretreatment. Sample pretreatment can be carried out either by separating REEs from the matrix or concentrating interest REEs. The separation of REEs from each other is mainly made by chromatography.

At the beginning of REE analysis, the method of precipitation/coprecipitation was applied for the treatment of REE mixtures. The method is inapplicable for the separation of trace REEs. The majority of the pretreatment methods used are based on the distribution of REEs in a two-phase system, a liquid-liquid or a liquid-solid system. Various techniques have been developed for liquid-liquid extraction (LLE), in particular liquid phase micro-extraction. The extraction is always combined with preconcentration of REEs in a single drop of extractant or in a hollow fiber filled with the extractant. Further modified techniques for special applications and for difficult REE separation have been developed. Compared to LLE, solid phase (micro-)extraction is preferred. The method is robust and easy to handle, and a variety of functionalized solid phase sorbents are available for the separation and preconcentration of REEs. At present, new solid materials (e.g. nanotubes, metal organic frameworks) and extraction modes (e.g., capillary microextraction) are developed and applied for the analysis of trace REEs.

4.1 Introduction

Rare earth elements (REEs) have been widely used in functional materials, catalysts, and other products in industry, diagnosis reagents of magnetic resonance imaging (MRI) in medicine and some fertilizers in agriculture (especially in China). As a result of their usage, more and more REEs are getting into the environment, food chain and organisms. The concentration of REEs in biological samples and environmental samples such as atmosphere, soil and natural water is around ppm-ppb level; the concentration of REEs in sea water is around ppt level; the requirements for ultra-high purity rare earth materials demand for a detection limit of ppb-ppt level for the ultra-trace REE impurities. Accordingly, much higher sensitivity is demanded for the quantification of trace/ultra-trace REEs in real-world samples. On the other hand, the separation among REEs has always been a challenging hot topic due to their similar chemical properties.

For the determination of trace REEs in biological and environmental samples, appropriate separation/preconcentration techniques are usually required to separate

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the complex matrix, preconcentrate interesting REEs and bring REEs in a suitable form for subsequent instrumental analysis. The most widely used techniques for the separation and/or preconcentration of trace REEs include precipitation/coprecipitation, liquid-liquid extraction (LLE), liquid phase microextraction (LPME), cloud point extraction (CPE), solid phase extraction (SPE) and solid phase microextraction.

4.2 Precipitation/coprecipitation

4.2.1 Oxalate precipitation

Precipitants for REEs include oxalic acid, diphenyl glycolic acid, cinnamic acid, mandelic acid (for the precipitation of Sc), methylene phosphoric acid (for the precipitation of La) and 8-hydroxy quinoline (for the precipitation of Eu, Gd and Sm). Among them, oxalic acid is the mostly employed precipitant for REEs. Oxalate gravimetric method based on the precipitation of RE oxalate had been used as a routine analytical method for the determination of total REEs and is suitable for the samples with content of REEs of above 5 %.

Oxalate gravimetric method is performed by weighing the burned precipitate obtained by oxalate precipitation and separation. Oxalic acid is spiked into the weak acidic solution containing REEs, resulting in colored RE oxalate precipitation as $\text{RE}_2(\text{C}_2\text{O}_4)_3 \cdot n\text{H}_2\text{O}$, $n = 5, 6, 9$ or 10 . Dimethyl oxalate or oxalic acid acetone is usually used as the precipitant in homogeneous precipitation; ammonium oxalate is preferred for a good separation when the content of iron is 40 times higher than that of REEs. Alkali metal oxalates are unsuitable as the precipitant for REEs for that alkali metal would form insoluble complex salt with REEs which would be introduced into the precipitate, or form soluble oxalic acid complexes with yttrium group REEs which lead to incomplete precipitation of REEs.

A series of factors influence the oxalate gravimetric method, including solubility of RE oxalate, oxalate activity, temperature, stirring and aging time, ammonium salt and other coexisting ions, and the medium. The details could be found in the book on REEs [1].

4.2.2 Co-precipitation

Coprecipitation is a conventional separation/preconcentration technique, which is suitable for the separation of trace REEs from the large number of common elements in complicated samples.

The carrier (also called trapping agent) is very important in coprecipitation. Generally, the carrier should meet the following requirements: (1) featuring with

similar chemical composition and structure to RE precipitate; (2) the usage should be as low as possible; (3) no interference for subsequent analysis and no need for secondary separation. The fluorides, hydroxides, oxalates or metal organic chelates of REEs are generally used as the carrier for their coprecipitation. It should be noted that if inductively coupled plasma-optical emission spectrometry/mass spectrometry (ICP-OES/MS) is employed for the subsequent detection, small amounts of interfering substances that remained in the precipitation will not interfere with the determination of REEs due to the good elemental selectivity of ICP-OES/MS. In other words, the requirement for separation efficiency in coprecipitation is not very stringent when ICP-OES/MS detection is used after coprecipitation.

Flotation technique for separation of REEs is another form of coprecipitation. Zhang et al. [2] employed $\text{Fe}(\text{OH})_3$ as the precipitant, oleic acid as the surfactant and processed the precipitation and flotation of trace REEs effectively under pH 8–9. Some representatives for trace REEs analysis by using coprecipitation and ICP-OES/MS determination are listed in Table 4.1.

Table 4.1: Application of co-precipitation-ICP-OES/MS for trace REEs analysis.

Sample	Analytes	Carrier	Operation process	Ref.
Soil, plant and environmental water	Ce, La, Y and Yb	Mixture of PAN and 5-Br-PADAP	Samples are adjusted to pH 8, spiked with co-precipitating agent (carrier), maintained at 60–80 °C for 30 min, filtered after 2 h settling; The precipitate is dissolved by HNO_3 and HClO_4 prior to ICP-OES detection.	[2]
silicate rocks	REEs and Y	Calcium oxalates	The rock sample was decomposed by HF and HClO_4 , followed by precipitation of REE and Y as oxalates, with calcium as carrier. The oxalate precipitate is ignited to the oxide, and then dissolved in diluted HNO_3 for ICP-OES detection.	[3]
Geological samples	REEs	Calcium oxalates	The sample was decomposed by HF, HNO_3 and HClO_4 , and the residue was dissolved in HCl. The solution was adjusted to pH 3.5–4, followed by precipitation of REE as oxalates and cation- exchange column separation in 6 mol/L HNO_3 .	[4]
Soils and sediments	REE. Cd. In. Tl. Th. Nb, Ta. Zr and Hf	$\text{Ti}(\text{OH})_4\text{-Fe}(\text{OH})_3$	The sample was alkaline fused by $\text{NaOH-Na}_2\text{O}_2$ and co-precipitated by $\text{Ti}(\text{OH})_4\text{-Fe}(\text{OH})_3$. The precipitate was dissolved with inverse aqua regia and determined by ICP-MS.	[5]

Table 4.1 (continued)

Sample	Analytes	Carrier	Operation process	Ref.
Sea water	REEs and Y, Mn, Co, Cr	Mg(OH) ₂	The sample was adjusted to pH 9.5 by aqueous NH ₃ , which led to precipitation of magnesium hydroxides. The Mg(OH) ₂ precipitate were dissolved in diluted HNO ₃ solution for subsequent ICP-MS detection.	[6]

4.3 Liquid liquid extraction (LLE)

LLE is generally a two-phase solvent extraction, aiming to separate interesting analyte based on its different distribution coefficients in two immiscible solvents. The greater the difference in the solubility of interesting analyte between the extraction solvent and original aqueous solution is, along with greater distribution coefficient, the better is the extraction performance for separation. The distribution coefficient depends on the extraction temperature, solvent and the characteristics of target analyte. The factors affecting the extraction performance mainly include the extraction solvent (extractant), the solubility difference between the extractant and original aqueous solution and the contacting of two phases during extraction. Under a certain condition for a specific analyte, the selection of extractant significantly determines the extraction performance.

Acetone, ether or alcohols were employed for the extraction of REEs in 1937, and new extractants and strategies for the extraction of REEs are emerging prominently. Tributyl phosphate was used to extract Ce⁴⁺ and RE³⁺ first in 1949 and then to separate RE³⁺ from each other successfully. Di(2-ethylhexyl)phosphate (P204), naphthenic acid and methyl trialkylammonium chloride were employed for the separation and purification of REEs in the production process from the 1970s.

LLE is commonly used for the separation of REEs from non-REEs, group separation of REEs and separation of single REE to improve the sensitivity and selectivity for REEs analysis. The affecting factors for LLE of REEs are mainly the selection of extractants, extractant concentration, medium pH and salting-out agents.

4.3.1 Extractants for REEs

In practical analysis, an appropriate extractant is required to feature with good selectivity, low water solubility, high extraction capacity, good stability and safety; in terms of chemical property, low density, high surface tension, low viscosity and high boiling point and flash point are required. According to the structure and

property, along with the extraction mechanism, the extractants for REEs can be divided into neutral phosphorus compounds, acidic phosphorus compounds, organic amines, neutral oxygen-containing compounds, chelates and others (including supramolecule, e.g., crown ethers and calixarene).

4.3.1.1 Neutral phosphorus

The basic structure is $(RO)_3PO$ or R_3PO , without dissociable H, alkyl or alkoxy connected with P. Their structure, property and other constants are listed in Table 4.2. These extractants have phosphoryl ($P=O$), and the high electron density on O atom favors the coordination with RE ions. The electronegativity of RO-group is higher than that of R-group (R is electron-donating group), and the electron density on O atom in $P=O$ is decreased, decreasing the complexation ability with REE ions (Table 4.3).

TBP and P350 are specific representatives of neutral phosphorus. REE ions could be well extracted by TBP in nitric acid above 10 mol/L and the partition coefficient

Table 4.2: Neutral phosphorus extractants for REEs extraction.

Name	Structural formula	Trade names and abbreviation	Solubility (H_2O , g/L)
Dibutyl Phosphate	$(nC_4H_9O)_3PO$	TBP	0.38
Diisoamyl methyl phosphonate	$CH_3P(O)(C_5H_{11}-i)$	P218, DAMP	3.39
Dimethyl methyl phosphate	CH_3PO	P350	0.14
heptyl ester	$(OCHCH_3(CH_2)_5CH_3)$		
Isopropyl bis-(2-ethylhexyl) phosphate	$i-C_3H_7(O)(OC_8H_{17}-i)_2$	P277	0.01
Dibutyl butanephosphonate	$C_4H_9P(O)(OC_4H_9)_2$	P205, DBBP	
Dibutyl butyl phosphate	$(C_4H_9)_2PO(OC_4H_9)$	P203, BDBP	
Trioctylphosphine oxide	$(nC_8H_{17})_3PO$	P201, TOPO	0.09
Dibutyltin oxide	$(nC_4H_9)_3PO$	TBPO	
Oxide di- (2-ethylhexyl) phosphine	$(CH_3(CH_2)_3)CH(C_2H_5)CH_2)_3PO$	TEHPO	

Table 4.3: The effect of substituent on REEs extraction by neutral phosphorus agent [7].

D_{RE}	Structure of extractants			
	$Bu_3PO(TBP)$	$Bu_2(BuO)PO$	$Bu(BuO)_2PO$	$(BuO)_3PO$
Ce	4.25	1.96	0.291	0.026
Pm	6.00	2.95	0.613	0.050
Y	12.3	3.61	0.419	0.044

Note: Extractant: 0.1mol/L (benzene as solvent); $[HNO_3]$ 3mol/L, Ce^{144} , Pm^{147} , Y^{90} .

is listed in Table 4.4. The extracted complex is $\text{RE}(\text{NO}_3)_3 \cdot 3\text{TBP}$. As can be seen from Table 4.4, the extraction ability of TBP for heavy RE ions is better than that for light RE ions, and the separation factor for neighboring RE ions is relative low, making it very difficult for the separation of neighboring single RE ions. P350 can extract RE ions well under low-acidity condition; compared with TBP, P350 presents higher extraction efficiency, higher separation factor and lower water solubility. The extracted complex is in the form of $\text{RE}(\text{NO}_3)_3 \cdot 3\text{P350}$, and the distribution ratio is increasing with the increase of the atomic number.

Table 4.4: Distribution coefficient for REEs extraction by TBP [8].

RE	La	Ce	Pr	Nd	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu	Y
HNO_3 (mol/L)	14	14	14	12.3	12.3	12.3	12.3	12.3	12.3	12.3	12.3	12.3	12.3	12.3	12.0
D	0.09	0.3	1.1					1.0	1.6	2.1	2.9	4.4	5.9	7.2	14

4.3.1.2 Acidic phosphorus

The basic structure is $(\text{RO})_2\text{PO}(\text{OH})$ or $(\text{RO})\text{PO}(\text{OH})_2$, and $\text{R}(\text{RO})\text{PO}(\text{OH})$ or $\text{R}_2\text{PO}(\text{OH})$. Neutral phosphorus is alkyl phosphates and acidic phosphorus is alkyl phosphoric acid, by substitution or esterification of one or two -OH in orthophosphate molecule. H^+ would easily dissociate from the left hydroxyl and make the molecule acidic. These compounds are called acidic phosphorus (Table 4.5).

Hydroxyl groups are involved in these extractants, and H is easily substituted by RE^{3+} ; $\text{P}=\text{O}$ would easily coordinate with RE^{3+} ; thus, these acidic phosphorus extractants exhibit good extraction ability for RE ions either under low-acidity or high-acidity condition. In $(\text{RO})_2\text{PO}(\text{OH})$, R-substitutes RO-group, increasing the electron density on O atom in -OH, making H difficult to dissociate and decreasing the replacement extent for RE^{3+} (Table 4.6).

Table 4.5: Acidic phosphorus extractants.

Name	Structural formula and pK_a	Trade names and abbreviation	Solubility (H_2O , g/L)
Di(isooctyl) phosphate	$(\text{C}_4\text{H}_9\text{CH}(\text{C}_2\text{H}_5)\text{CH}_2\text{O})_2\text{PO}(\text{OH})$ 3.32	P204, D2EHPA, HDEHP	0.02

Table 4.5 (continued)

Name	Structural formula and pK_a	Trade names and abbreviation	Solubility (H_2O , g/L)
Phosphoric acid ethylhexylester	$(C_4H_9CH(C_2H_5)CH_2O)PO(C_4H_9CH(C_2H_5)CH_2)(OH)$ 4.10	P507, HEHEHP, PC88A	0.08
Bis (1-methylheptyl) phosphate	$(C_6H_{13}CH(CH_3)O)_2PO(OH)$ 3.22	P215	0.02
Di-iso-octyl Phosphonate	$(C_4H_9CH(C_2H_5)CH_2)_2PO(OH)$ 4.98	P227	
Lauryl alcohol phosphate acid ester	$n - C_{12}H_{25}OPO(OH)_2$	P501, DDPA	0.20
Phosphoric acid diphenyl ethylhexyl ester	$(C_4H_9CH(C_2H_5)CH_2O)C_6H_5PO(OH)$ 3.12	P406, HEHPHP	
Dibutyl Phosphate	$(C_4H_9O)_2PO(OH)$	DBP	
Monoalkyl phosphate	$RCH_2CH_2OPO(OH)_2$	P538	0.05

4.3.1.3 Oxygen-containing organic extractants

Some alcohols, ketones and carboxylic acids can also be used as the extractants for REEs (Table 4.7). RE^{3+} is a hard acid; oxygen-containing organic extractants are hard bases, and they can form complexes according to HSAB theory, while the extraction mechanisms are different. For alcohols, ketones, ether and ester, RE ions are extracted by oxygen-based coordination or hydrogen bonding. For carboxylic acids, RE ions are extracted by ion exchanging between H^+ and RE ions; the acidity affects the extraction significantly; to decrease the water solubility of the carboxylic acids, carbochain of C_7 - C_9 are usually employed, and carbochain longer than C_{10} is unsuitable for the extraction due to the decreasing K_a . Fatty acid with branched-chain exhibits good extraction selectivity, along with steric effect.

4.3.1.4 Nitrogen-containing compounds

Amine-based extractants are one of the most useful nitrogen-containing extractants for RE ions, including primary amines, secondary amines, tertiary and quaternary ammonium salts. Organic amines with molecular weight of around 250–600 are suitable for the extraction of RE ions because they are insoluble in water; they can form stable salts in strong acid and the anion exchange ability in salts follow the order of $ClO_4^- > NO_3^-$

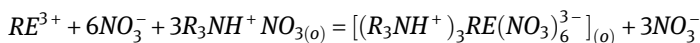
Table 4.6: The structure of acidic phosphate and their properties for REEs extraction [9].

Number	Structural formula	pK _a	Extraction equilibrium constants (K)				Separation factor (α)	
			Nd	Sm	Y	Yb	Sm/Nd	Yb/Y
1	(iso - C ₈ H ₁₇ O) ₂ P(O)OH	2.74	6.8×10 ⁻³	4.9×10 ⁻²	1.0×10 ⁻¹	3.7×10 ⁻¹	7.2	3.7
2	(sec - C ₈ H ₁₇ O) ₂ P(O)OH	3.19	5.6×10 ⁻⁴	6.4×10 ⁻³	4.1×10 ⁻¹	3.3	11.4	8.0
3	<i>i</i> - C ₈ H ₁₇ PO(OC ₈ H ₁₇ - <i>i</i>) ₂	4.09	8.4×10 ⁻⁵	8.8×10 ⁻⁴	1.4×10 ⁻¹	8.9×10 ⁻¹	10.5	6.4
4	C ₆ H ₅ PO(OC ₈ H ₁₇ - <i>i</i>)	2.99	2.2	4.2×10	1.7×10 ³	2.2×10 ⁻⁴	19.1	12.9
5	Cyc - C ₆ H ₁₁ PO(OC ₈ H ₁₇ - <i>i</i>)	3.87	1.6×10 ⁻³	2.8×10 ⁻²	3.4	3.5×10	17.5	10.3
6	(iso - C ₈ H ₁₇) ₂ PO(OH)	5.45	4.0×10 ⁻⁸	3.2×10 ⁻⁹	4.1×10 ⁻⁵	6.1×10 ⁻⁴	8.0	14.8
7	(<i>n</i> - C ₈ H ₁₇) ₂ PO(OH)	5.71	1.2×10 ⁻⁴	1.8×10 ⁻³	4.1×10	1.8	15	4.4
8	(iso - C ₈ H ₁₇ O)PO(OH) ₂	3.60	6.7×10 ⁻⁴	2.2×10 ⁵	6.4×10 ⁻⁴	2.0×10 ⁵	3.3	3.1
9	(iso - C ₁₈ H ₃₇ O)PO(OH) ₂	9.10	3.8×10 ⁵	4.1×10 ⁵	2.9×10 ⁵	9.8×10 ⁵	1.1	3.4
10	(iso - C ₁₈ H ₃₇ O)PO(OH) ₂	4.72	3.7×10 ⁻³	1.2×10 ⁻⁴	6.3×10 ³	8.1×10 ⁻³		
		10.40						
11	<i>iso</i> - C ₁₈ H ₃₇ PO(OH) ₂	3.88	7.6×10 ²	1.3×10 ³	9.4×10 ²	4.3×10 ³	1.6	4.6
		9.37						

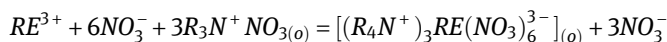
Table 4.7: Some oxygen containing extractants for REEs.

Name	Structural formula	Trade names and abbreviation	Solubility (H ₂ O, g/L)
Naphthenic Acid	<i>iso</i> – C ₁₈ H ₃₇ PO(OH) ₂ OH	Naphthenic Acid, Nphthanic	0.09
Versatic acid	R ₁ R ₂ C(CH ₃)COOH	C547, Versatic911	2.50
Methyl isobutyl ketone	R ₁ R ₂ C(CH ₃)COOH	4-Methyl-2-pentanone, MIBK, Hexone	19.1
sec-Caprylic alcohol	C ₆ H ₁₃ CH(CH ₃)OH	2-Octanol, Octanol 2	1.0
β-primary alcohol	RCHRCH ₂ OH	A1416	

>HSO₄[–]>F[–]; they form associated complex with RE anionic complex and extracted by organic solvents, thus amine-based extractants are also called as liquid ionic extractants.



Or



Quaternary ammonium salts can extract RE anionic complex in acidic or neutral solution. Table 4.8 lists some nitrogen-containing extractants for RE ions.

Table 4.8: Some nitrogen containing extractants for REEs.

Name	Structural formula	Trade names and abbreviation	solubility (H ₂ O, g/L)
Se-carbon primary amine	(C _n H _{2n+1}) ₂ CHNH ₂ (n = 9 – 11)	N1923, AH:9	0.04
Multi-branched hexadecyl tertiary carbon primary amine	CH ₃ C(CH ₃) ₂ [CH ₂ C(CH ₃) ₂] ₃ NH ₂	N116, Pirnene JM.T	0.05g (0.5 mol/L H ₂ SO ₄)
N-dodecyl (trialkyl methyl) amine	CH ₃ [C(CH ₂) ₂ CH ₂] ₂ C(CH ₃) ₂ NHCH ₂ CHCH(CH ₂ C(CH ₂) ₂)CH ₃	AmberliteL A-1	0.015–20g (0.5 mol/L H ₂ SO ₄)
N-lauryl (meth alkyl) amine	C(R ₁)(R ₂)R ₃ NHCH ₂ (CH ₂) ₁₀ CH ₃	AmberliteL A-2	
Dioctylamine	(CH ₃ (CH ₂) ₇) ₃ N	N204, TOA, TNOA	
Triisooctylamine	(CH ₃ C(CH ₃) ₂ CH ₂ CH(CH ₃)CH ₂) ₃ N	TIOA	
Triheptylamine	(C ₇ H ₁₅) ₃ N	N208	
Tribromoaniline	(C ₆ H ₅ CH ₂) ₃ N	TBA	
Trialkylamine	(C _n H _{2n+1}) ₃ N, n = 8 – 10	N235, Alamine336	0.01
Chloride methyl trialkyl amine	[(C _n H _{2n+1}) ₃ NCH ₃]Cl, n = 6 – 10	N263, Aliquat336	0.04

The separation performance of primary amine is unsatisfying to single RE, and the extraction of La to Sm by primary amine can be easily obtained while the extraction efficiency is decreased after Sm. Li et al. [10] used N1923 to extract REEs from sulfuric

acid matrix, and found that the extraction efficiency of REEs decreases as atomic number increases, exhibiting “tetrad effect”; while in perchloric acid medium, the extraction efficiency of REEs increases as atomic number increases, also exhibiting “tetrad effect” [11]. Secondary amine, e.g., N235, is mainly octyl, similar to trioctylamine, and can extract REEs in the presence of salting-out agents. Trioctylamine as a colorless viscous liquid is soluble in organic solvents, and its applications in metal ions extraction is reviewed [12].

N263, trialkyl methyl ammonium chloride, consisting of 8–10 carbon atoms in its alkyl carbon chain, is a quaternary ammonium salt that frequently used in REEs extraction. Its performance and composition are similar to Aliquat336. It is a viscous liquid, with high extraction capacity and excellent selectivity, and is suitable for a variety of inorganic acid system. The distribution ratio of REEs in the N263-LiNO₃ system is decreased with increasing the atomic number of REEs, showing an “inverted order” (Table 4.9); while a “positive sequence” is obtained in the N263-NH₄SCN system (Table 4.10). For amine extractants, the effect of their structure and spatial effects on the extraction efficiency is also very significant.

Table 4.9: Distribution ratio of REEs in N263- nitrate system.

RE ³⁺	La	Pr	Nd	Sm	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu	Y
Distribution ratio (D)	4.4	4.0	1.59	0.41	0.15	0.13	0.13	0.086	0.058	0.022	0.021	0.013	0.031
separation factor ($\alpha_{RE/Y}$)	140	128	50.7	13.2	4.8	4.3	4.2	2.7	1.86	0.70	0.67	0.43	

Note: HNO₃, 0.1mol/L; N263, 400g/L; V(o)/V(aq)=4:1.

Table 4.10: Distribution ratio of REEs in N263-thiocyanic acid system.

RE ³⁺	La	Pr	Nd	Sm	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu	Y
Distribution ratio (D)	0.52	1.09	1.29	2.06	7.19	3.05	3.30	4.76	7.26	17.87	30.94	59.30	2.14
separation factor ($\alpha_{RE/Y}$)	0.25	0.51	0.60	0.96	3.36	1.43	1.55	2.23	3.40	8.32	14.5	27.8	

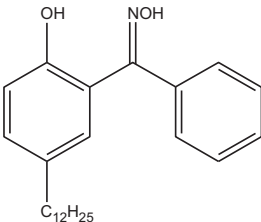
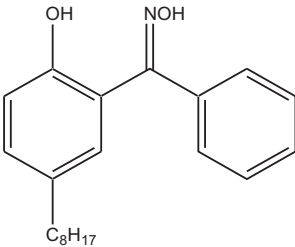
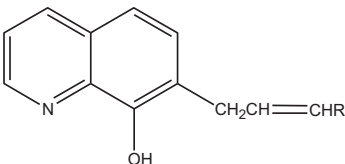
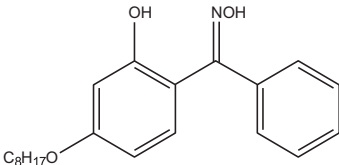
Note: NH₄NCS, pH=1; N263, 0.7mol/L; V(o)/V(aq)=4:1.

4.3.1.5 Chelate extractant for REEs

Chelate extractants can form stable electrically neutral complex with RE ions which can be extracted by organic solvents. Besides β -diketones (e.g., acetylacetone, thenoyl-trifluoroacetone [TTA], 1-phenyl-3-methyl-4-benzoyl-pyrazolone [PMBP]), homologs of

8-hydroxyquinoline and ketoxime derivatives (Table 4.11) are also commonly used chelating extractants for REEs.

Table 4.11: Some chelating agent for REEs extraction.

Name	Structural formula	Trade names and abbreviation	solubility (H ₂ O, g/L)
Lauryl hydroxamic acid	$i\text{-C}_{11}\text{H}_{23}\text{CONHOH}$	H106	0.02
5,8-Diethyl-7-hydroxy-6-dodecanone Oxime	$\text{CH}_3(\text{CH}_2)_3\text{CH}(\text{C}_2\text{H}_5)\text{CH}(\text{OH})\text{C}(\text{NOH})\text{CH}(\text{C}_2\text{H}_5)(\text{CH}_2)_3\text{CH}_3$	N509, LIX-63	
2-Hydroxy-5-dodecyl benzophenone oxime		3045, LIX64	
2-Hydroxy-5-octyl – benzophenone oxime		N510	0.005
2-Hydroxy-5-sec-octyl oxy benzophenone oxime		N530	0.001
7-Dodecenyl-8-hydroxyl-quinoline		N601, Kelex100	0.003

TTA, colorless acicular crystal, is soluble in benzene, methylbenzene and other organic solvents. RE^{3+} can be extracted by TTA at pH 3–4 (Table 4.12). TTA is usually employed to synergistically extract REEs with other solvents such as ethylenediamine, 2,2,2-terpyridine and neutral phosphorus reagents.

Table 4.12: Extraction constants for REEs extraction by PMBP and TTA [13].

RE ³⁺	La	Ce	Pr	Nd	Pm	Sm	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu	Y
pK _α (TTA)	10.51	9.45	8.85	8.58	8.06	7.68	7.57	7.51	7.03	7.25	7.2	6.96	6.72	6.77	
pK _α (PMBP)	7.19 4.40	6.56	5.81	5.67		5.00	4.77		4.42				3.89		

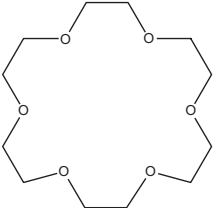
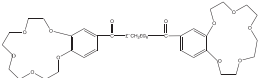
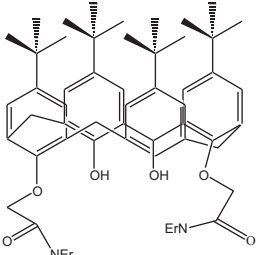
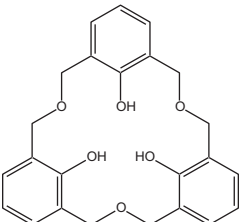
PMBP [5] is also a good β -diketone reagent for REEs extraction, with higher extraction capacity, acidity and faster reaction dynamic compared with TTA. It has become one of the main extraction agents for the separation and preconcentration of REEs. 1-pheny-3-methyl-4-acetyl-pyrazolone is a homolog of PMBP, and the extraction efficiency of heavy REEs could reach more than 90 % under pH3. Oxime and hydroxylamine compounds have been investigated for heavy REEs extraction. Haraguchi et al. [14] synthesized several N-phenyl hydroxamic acid. Among them, 2-hexyl-N-phenyl-decyl hydroxyl oxime acid is considered as the most suitable agent for the extraction of heavy REEs; the extraction capacity of N-*p*-methoxybenzoyl, -*p*(*n*, *iso*, *t*)-butylbenzoyl, -propoxybenzoyl, -*m*-nitrobenzoyl, -*m*-cyanobenzoyl-N-phenylhydroxylamine for REEs was discussed, along with the effects of substituent in extractant molecules and the acidity of the reagents on the separation factor between REEs. It was found that the smaller the K_a value of the extractant is, the greater the extraction constant is [15–18].

4.3.1.6 Supramolecular extractants and others

Crown ethers and calixarenes are supramolecular compounds which can be used for the complexing and extraction of REEs [19, 20]. In the presence of counter anions, 18-crown-6 and benzo15-crown-5 exhibit very high extraction efficiency for REEs. Inoue et al. [21] used dicrown ether to extract REEs-picric acid complexes, and the extraction efficiency was increased. Calixarene was also used for the extraction of REEs [22], and some supramolecular compounds as REEs extractants are listed in Table 4.13. 1,3-bis(diethylamide) calixarenes [4] exhibits a high extraction efficiency for REEs, which is 20–22 % higher than that obtained by crown ether and dicrown ether.

Sulfoxide with S-O bond is also a good extractant for REEs. Among them, dimethylsulfoxide was one of the most commonly used, which can form ion association complex soluble in benzene in the presence of anions, such as ClO_4^- or SCN^- . Besides, pentylsulfoxide, di-*n*-octylsulfoxide and tetramethylenesulfoxide are also effective for the extraction of REEs. Bis (2-ethylhexyl) sulfoxide can extract REE- SCN^- complex into benzene.

Table 4.13: Some supramolecular as REEs extractants.

Name	Structural formula	RE ³⁺	Conter anion	Solvent	References
18-Crown-6		La-Lu La-Ga	ClO ₄ ⁻ picricacid	CH ₂ Cl ₂ CH ₂ Cl ₂	[20, 23]
Octanedione 1,8-bis (4-benzo-15-crown-5)		La-Gd	picricacid	CH ₂ Cl ₂	[21]
1,3-bis (diethylamide) calixarenes [4]		La-Lu	picricacid	CH ₂ Cl ₂	[24]
hexahomotrioxacalix [3]arene		Sc, La, Y, Lu	DMSO		[25]

Light REEs can be extracted by employing crown ether 18-crown-6 [26] and benzo-15-crown-5 [27]; with the existence of pentadecafluorinecapilate, light REEs could be extracted by 18-crown-6 in ion association form [28].

4.3.2 Extractant concentration and extraction equilibrium constant

Distribution coefficient (D) is proportional to n th power of free extractant concentration; if free extractant concentration is increased by two times, D is increased by 2^n times. When P204 is used for the extraction of RE ions, D is proportional to 3 power

of the concentration of P204 dimer. The increase of the concentration of the extractant is beneficial to the extraction of interesting ions.

The higher the stability constant for the complex is formed by REE ions and the extractant, the complex is more stable and more easily to be extracted. Given a specific extractant for the extraction of RE ions, the stability of the complex is related to the charge and radius of RE ions. For RE ions with the same valence, the radius decreases with the increase of the atomic number, and the formed complex stability and extraction equilibrium constant increase with the increase of atomic number (Table 4.14), while the separation factors for the neighboring RE ions are not increasing with the increase of atomic number (Table 4.15). Thus, the extraction efficiency of REE ions and the separation factors for neighboring RE ions should be considered simultaneously, and the latter is sometimes more important.

Table 4.14: Extraction equilibrium constants (K) for REE extraction by P204.

RE ³⁺	Pm	Sm	Eu	Tb	Dy	Ho	Er	Yb	Lu	Y
log K	-1.73	-0.95	-0.83	0.4	0.88	1.25	1.75	2.27	2.94	1.63

Table 4.15: Separation factor for REE extraction by P204.

REE pair	Ce/La	Pr/Ce	Nd/Pr	Pm/Nd	Sm/Pm	Eu/Sm	Gd/Eu
Separation factor	2.8	1.5	1.3	2.7	3.2	2.2	1.5
REE pair	Tb/Gd	Dy/Tb	Ho/Dy	Er/Ho	Tm/Er	Yb/Tm	Lu/Yb
Separation factor	5.3	2.8	2.2	3.0	3.5	3.0	2.0

4.3.3 Medium pH

In acidic complex extraction system for REEs, the effect of pH on D of REE ions in two phases is very obvious. Within a specific acidic complex extraction system, D will increase by 10^n times (n is the valence of RE ions) when pH is increased by 1 unit. If the volume of two phases are the same, when $D = 1$, half of RE ions are extracted, and the pH is called half extraction pH value, denoted by $\text{pH}_{1/2}$.

$$\text{pH}_{1/2} = -1/n \log K - \log(\text{HL})_o$$

where K is the extraction equilibrium constant and $(\text{HL})_o$ is the concentration of extractant (HL) in organic phase. As can be seen, the higher K or $[\text{HL}]_o$ is, the lower the $\text{pH}_{1/2}$ is, indicating RE ions can be extracted more easily. So $\text{pH}_{1/2}$ is used to

show the extraction ability for metal ions with the same valence. The $\text{pH}_{1/2}$ for Y extraction by naphthenic acid is the highest among other ions (Table 4.16), indicating D of Y is the lowest.

P204 and P507 are specific representatives of acidic phosphorus extractants. The extraction ability of P204 is increasing with the increasing of the atomic number of REE (Table 4.17), and the difference between light and heavy REEs is obvious. P204 form dimeric polymer through hydrogen bonding in nonpolar solvents (e.g., benzene, CCl_4), REE ions coordinates with three dimers by replacing three H in it and form neutral six coordinate complex, which is easily dissolved in organic solvents, with the extraction mechanism of cation exchange. In the nitric acid or hydrochloric acid matrix, the extraction efficiency of P204 for REEs will decrease with the increase of the matrix acidity. The basic structure of P507 is similar to that of P204, the reaction for the extraction of REEs is similar along with the performance variation. Due to the C-P bond in P507, the extraction ability of P507 is lower than that of P204, while P507 is featured with easy back-extraction and uneasy emulsification.

Table 4.16: $\text{pH}_{1/2}$ for RE ions extraction by naphthenic acid.

RE ³⁺	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu	Y
$\text{pH}_{1/2}$	3.95	3.89	3.78	3.74	4.1	3.73	3.62	3.76	—	3.73	3.97	3.84	3.92	4.02	—	4.30

Table 4.17: Distribution ratio and separation factors (α) of REEs (III) by P204*.

RE ³⁺	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd
D	1.3×10^{-4}	3.6×10^{-4}	5.4×10^{-4}	7.0×10^{-4}	1.9×10^{-4}	5.9×10^{-4}	0.013	0.019
$\alpha_{Z_{n+1}/n}$	2.8	1.5	1.3	2.7	3.2	2.2	1.6	5.3
RE ³⁺	Tb	Dy	Ho	Er	Tm	Yb	Lu	Y
D	0.100	0.28	0.62	1.4	4.9	14.7	39.4	1.00
$\alpha_{Z_{n+1}/n}$	2.8	2.2	3.0	3.5	3.0	2.0		

*Extraction medium: HClO_4

4.3.4 Salting-out agent

In a neutral complex extraction system (e.g., REEs extraction by TBP), the extraction efficiency would be improved by adding salting-out agents (e.g., LiNO_3 , NH_4NO_3). The concentration of NO_3^- would be increased with the addition of salting-out agents, benefiting the increasing of D . Additionally, the hydration of salting-out agents would decrease the concentration of free water molecules in the extraction system, reducing

the concentration of hydrated RE ions and increasing the activity of RE ions. Dimethyl methyl phosphate heptyl ester (P350) presents much better performance for REEs extraction than TBP, the effect of concentration of salting-out agents LiNO_3 on D and separation factor (α) in the separation of La and Pr is very significant (Table 4.18).

In the ion association complex extraction system, the addition of salting-out agents would also help the extraction of REE ions (Table 4.19). In the extraction of REE ions by N263, salting-out agents can participate the ion association complex formation as reactants, and increase the average activity coefficient of $\text{RE}(\text{NO}_3)_n$. On the other hand, salting-out agents as complexing agents can improve the complexing of REE, and decrease the distribution ratio.

Table 4.18: Effect of LiNO_3 on the extraction of La^{3+} and Pr^{3+} by P350.

LiNO_3 (mol/L)	Distribution ratio		Separation factor (α) $\text{Pr}^{3+}/\text{La}^{3+}$
	$D(\text{Pr}^{3+})$	$D(\text{La}^{3+})$	
1	0.201	0.151	1.33
2	0.426	0.155	2.72
3	0.594	0.186	3.19
4	0.697	0.183	3.81
5	1.28	0.240	5.34
6	1.47	0.254	5.78

Table 4.19: Effect of salting-out agents on the extraction efficiency of Eu^{3+} .

$\text{Al}(\text{NO}_3)_3$		LiNO_3		NH_4NO_3	
C (mol/L)	EE (%)	C (mol/L)	EE (%)	C (mol/L)	EE (%)
0.2	2.2	0.6	3.6	2.0	16.6
0.4	12.2	1.2	18.9	4.1	51.1
0.8	62.1	2.4	74.5	5.1	67.1
1.2	92.7	3.7	95.9	7.1	88.8
1.6	98.8	4.9	99.5	8.2	94.0

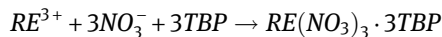
C: concentration; EE: Extraction efficiency

4.3.5 Extraction systems for REEs and their application

4.3.5.1 Neutral complex extraction system

In this extraction system, the extracted RE complexes are neutral salts such as $\text{RE}(\text{SCN})_3$ and $\text{RE}(\text{NO}_3)_3$, and the employed extractants are neutral organics such as TBP and trioctylphosphine oxide (TOPO). >P=O in neutral extratants would complex

with RE ions and form insoluble neutral complexes such as $\text{La}(\text{NO}_3)_3 \cdot 3\text{TBP}$ and $\text{Ce}(\text{SCN})_3 \cdot 4\text{TOPO}$ which can be extracted by organic solvents. The neutral extraction system for REEs is discussed as follows by using TBP as the representative.



The equilibrium constant (K)

$$K = \frac{[\text{RE}(\text{NO}_3)_3 \cdot 3\text{TBP}]}{[\text{RE}^{3+}][\text{NO}_3^-]^3[\text{TBP}]^3} \quad (1)$$

The distribution coefficient (D) of REE ions between two phases:

$$D = \frac{[\text{RE}(\text{NO}_3)_3 \cdot 3\text{TBP}]}{[\text{RE}^{3+}]} \quad (2)$$

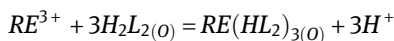
Combining eqs (1) and (2),

$$D = K[\text{NO}_3^-]^3[\text{TBP}]^3 \quad (3)$$

As can be seen, D of REE ions between two phases is proportional to the equilibrium constant, the concentration of NO_3^- in aqueous phase and concentration of TBP in organic phase under equilibrium condition. The size and charge of RE ions also affect the extraction process, and D for RE^{4+} is higher than the corresponding RE^{3+} ; for RE^{3+} , the smaller the radius, much more stable for the formed RE complexes. The order of the D for REEs extraction by TBP is as follows: $\text{Lu} > \text{Yb} > \text{Tm} > \text{Er} > \text{Ho} > \text{Dy} > \text{Y} > \text{Tb} > \text{Gd} > \text{Eu} > \text{Sm} > \text{Pm} > \text{Nd} > \text{Pr} > \text{Ce} > \text{La}$. In other words, D increases with the increase of atomic number, or with the decrease of atomic radius. The effect of NO_3^- concentration in aqueous phase on the extraction of light and heavy REEs is different [29].

4.3.5.2 Acidic complex extraction system

In acidic complex extraction system, organic weak acid (HL or H_2L) acts as the extractants, which can be chelate extractants (e.g. β -diketones), acidic phosphorus extraction agent (e.g., P204) or carboxylic acid (e.g. naphthenic acid). The extraction mechanism is based on the cation ions exchange between RE ions and H^+ in the employed extractants, and the hydrophobic complex formed by RE ions and the extractant is extracted into the organic solvents. P204 is a commonly used extractant for REEs extraction and separation, the reaction is as follows.



The extraction equilibrium constant (K):

$$K = \frac{[RE(HL_2)_3]_{(o)} \cdot [H^+]^3}{[RE^{3+}][H_2L_2]_{(o)}^3} \quad (4)$$

The distribution ratio (D) of REE ions between two phases:

$$D = \frac{[RE(HL_2)_3]_{(o)}}{[RE^{3+}]} \quad (5)$$

Substituting eq. (4) into eq. (5),

$$D = \frac{K[H_2L_2]_{(o)}^3}{[H^+]^3} \quad (6)$$

For REE ions with any valence, equation (6) is changed into

$$D = \frac{K[HL]_{(o)}^n}{[H^+]^n} \quad (7)$$

Taking the logarithm on both sides of the fomula,

$$\log D = \log K + n \log [HL]_{(o)} + npH \quad (8)$$

Equation (8) is the basic fomula for acidic extraction system for REEs.

Butyric acid, α -ethylbutyric acid, α -chloro fatty acid can be used to extract and separate REEs from non-REEs. The distribution ratio of REEs during the extraction by α -ethylbutyric acid shows “tetrad effect” with the increasing of their atomic numbers.

PMBP-benzene could extract REEs and Th into organic phase under pH 5.5, and the extracted REEs can be back-extracted by 2–3 mol/L formic acid, while Th left in the organic phase which can be back-extracted by 2.4–6 mol/L HCL. By using Arsenazo III, the determination of Th and REEs could be achieved simultaneously in one sample. In the solution of 15% ammonium thiocyanate and 60% sulfosalicylic acid, PMBP-benzene solution also can be used to separate REEs from a large amount of common elements under pH 5–5.7. After back-extracted by 0.01 mol/L HCL, the trace REEs in the steel and alloy could be determined by the arsenazoIII spectrophotometry [30].

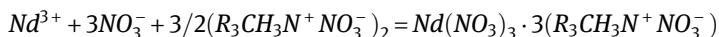
With P204 as the extractant, crude separation of yttrium and heavy REEs from light REEs groups in sulfuric acid system could be achieved by changing pH, extractant concentration and extraction series. Heavy REEs could be separated from light REEs in 0.7–0.9 mol/L HNO_3 by using P204-benzene extractant. In the extraction of REEs from 0.1 mol/L HCl into toluene by using 2-ethylhexyl-(3-pentadecylphenyl) phosphate acid, it could be found that the extraction of heavy REEs was better than

medium and light REEs and the obtained extraction efficiency was higher than that obtained by other organophosphorus extractants [31]. Bis(4-dicyclohexyl)phosphate acid (D4DCHPA) – xylene can also be used for REEs group separation [32].

4.3.5.3 Ion association complex extraction system

The extractants used in this system are organic amines and quaternary ammonium salt or oxygen-containing ketones, alcohols and ether, the extracted compounds are RE complex cations or anions. Organic amines associate with RE complex anions by ammonium, and oxygen-containing organic solvents associate with RE complex anions, forming associated complex which can be extracted into organic solvents. During the extraction process, the exchange between anions and anions occurs, and the extraction system and affecting factors are discussed as follows by using extraction of Nd^{3+} by N263 as the representative.

Before use, N263 is transformed into methyl trialkyl ammonium nitrate by nitric acid or nitrate, and the reaction is



The effect of acidity on the reaction is complicated because there are a variety of existing species of the complex anions and the extractant which affected by the acidity. Increasing the concentration of nitric acid help the formation of $\text{Nd}(\text{NO}_3^-)_{3-6}$ and the extraction; while $\text{R}_3\text{CH}_3\text{N}^+\cdot\text{NO}_3^-\cdot\text{H}_3\text{O}^+\cdot\text{NO}_3^-$ forms with the increase of nitric acid concentration, decreasing the concentration of $\text{R}_3\text{CH}_3\text{N}^+\cdot\text{NO}_3^-$ and deteriorating the extraction. Thus, the effect of acidity in a certain range on the extraction of RE ions is negligible. High concentration of the extractant is beneficial to REE extraction, while polymerization would occur among the extractants, worsening the separation factors between RE ions.

Above all, in the ion association complex extraction system, the extraction by using quaternary ammonium salts can be performed in diluted acidic matrix; the oxygen-containing organic extractants exhibit good extraction performance for REEs under high acidity and the extraction efficiency is affected by the acidity significantly.

N263-xylene was used to separate REEs in the steel from other coexisting elements, while the interference of Zr was masked by adding EDTA before extraction. Benzyl chloride dimethyl myristyl ammonium and 2,3-naphthalenediol-chloroform solution were used to extract REEs from sodium acetate buffer based on ion association reaction, followed by ICP-OES detection [33].

4.3.5.4 Synergistic extraction system

As early as in 1954, it was found that the distribution ratio for RE ions obtained by using TTA and TBP simultaneously is higher than the sum of the distribution obtained by either of them. With the development of extraction chemistry, the synergistic extraction of REEs has been getting more and more attention. The synergistic extraction system consisting of TTA and neutral phosphorus extractants is the most concerned one, three extraction systems as mentioned above can all be involved in the synergistic extraction system (Table 4.20). The system combining acidic chelating with neutral complexing also exhibits significant synergistic effect.

The mechanism for synergistic extraction is complicated. For the synergistic extraction system involving acidic and neutral extractants, it is based on adducting and substitution mechanism, also affected by the size, charge and coordination geometry of the ion (Table 4.21).

The system of TTA-TBP was applied for the separation of Eu^{3+} from Am [34]. PMBP-TOPO-benzene system can be effectively used to separate REEs, U and Th from niobite [35]. The extraction performance of the 5, 7-dichloro-8-hydroxyquinoline-chloroform solution for REEs (La, Eu and Lu) could be improved in the presence of tetrabutyl ammonium or TOPO [36].

Table 4.20: Classification of the synergistic extraction system.

Classification		Example
Dual heterogeneous synergistic extraction system	Chelating and neutral complexing	$\text{Eu}^{3+}/\text{H}_2\text{O}-\text{HNO}_3/\text{TTA}+\text{TBP}$ (Cyclohexane)
	Chelating and ion association	$\text{Th}^{4+}/\text{HCl}+\text{LiCl}/\text{TTA}+\text{TOA}(\text{Benzene})$
	Neutral complexing and ion association	$\text{PuO}_2^{2+}/\text{H}_2\text{O}-\text{HNO}_3/\text{TBP}+\text{TBAN}(\text{Kerosene})$
Dual homogeneous synergistic extraction system	Chelating synergistic extraction	$\text{RE}^{3+}/\text{H}_2\text{O}-\text{HNO}_3//$ $\text{HA}+\text{TTA}(\text{Benzene})$
	Neutral complexing synergistic extraction	$\text{RE}^{3+}/\text{H}_2\text{O}-\text{HNO}_3//$ $\text{TBPO}+\text{TOPO}(\text{Kerosene})$
	Ion association synergistic extraction	$\text{Pa}^{3+}/\text{H}_2\text{O}-\text{HCl}/\text{RCOR}+\text{ROH}$
Other synergistic extraction system	Ternary system involving chelating, neutral complexing and ion association	$\text{UO}_2^{2+}/\text{H}_2\text{O}-\text{H}_2\text{SO}_4/\text{D}_2$ $\text{EHPA}+\text{TBP}+\text{R}_3\text{A}(\text{Kerosene})$

4.4 Liquid phase microextraction

LPME is developed based on LLE [37, 38]. Compared with traditional LLE, LPME is environmentally friendly with the consumption of very small amount of organic solvent (only a few microliters or tens of microliters); the operation of LPME is much

Table 4.21: Synergistic extraction of REEs by β -diketones and TBP.

RE ³⁺	Extractants (cyclohexane as the solvent)					
	HFA-TBP		TAA-TBP		FHD-TBP	
	log β_1	log K	log β	log K	log β_2	log K
Eu	10.84	5.05	–	–2.22	10.00	10.06
Nd	10.50	4.35	–	–2.77	9.96	9.95
Tm	10.76	4.63	–	–2.62	10.20	10.47

HFA, hexafluoro acetylacetonate; FHD, decafluoro heptanedione

simpler, avoiding time-consuming step in LLE; and LPME can provide a comparable or even better enrichment factor (EF). LPME integrates the sampling, extraction and concentration in one step, and can be easily combined with various modern analytical instruments (e.g., HPLC, CE, GC, GFAAS). It has been employed in the fields of environmental monitoring, food safety and pharmaceutical analysis.

In 1996, Liu and Dasgupta [38] reported a drop-in-drop system (Figure 4.1) to extract sodium dodecyl sulfate, in which a 1.3- μ L microdrop of a water-immiscible organic solvent was immersed into a large flowing aqueous drop to accomplish the extraction process. At almost the same time, Jeannot and Cantwell [37] introduced a procedure that they termed solvent microextraction. In this configuration (Figure 4.2), a droplet of 1-octanol was held at the end of a Teflon rod and suspended in a stirred aqueous sample solution. After extraction, the Teflon rod was withdrawn from the aqueous solution; the organic phase was sampled with a microsyringe and injected into a GC system for analysis. One disadvantage of the aforementioned methods is that extraction and injection have to be performed separately with different apparatus. In order to overcome this shortcoming, Jeannot and Cantwell [39] developed a microextraction method in 1997, which was performed simply by suspending a 1- μ L drop directly from the tip of a microsyringe needle immersed in a stirred aqueous solution containing target analytes, the post-extraction microdrop was retracted back into the microsyringe and transferred into GC for further analysis. In this configuration, the microsyringe served as both the solvent holder and the GC sampling injector, which make the extraction and injection integrated in a single device (Figure 4.3). This represents a desirable convenience of the microextraction operation, and led to the appearance of some new LPME configurations, such as single-drop microextraction (SDME) and hollow fiber (HF)-LPME.

To extremely decrease the volume of the extractant phase and simplify the experimental apparatus and operation procedure, analysts have spent a lot of energy on the configuration of experimental apparatus and exploration of microextraction mechanisms. So far, the most representative techniques in LPME include SDME, HF-LPME, dispersive liquid-liquid microextraction (DLLME) and solidified floating organic drop microextraction (SFODME).

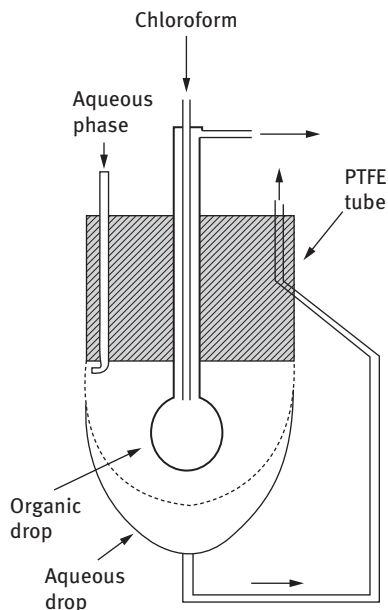


Figure 4.1: Schematic diagram of “drop in drop” system [38].

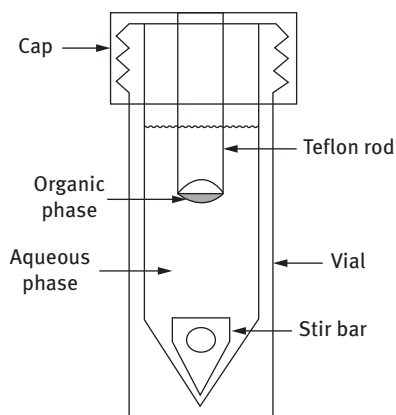


Figure 4.2: Schematic diagram of solvent microextraction based on Teflon rod [37].

4.4.1 Single drop microextraction

In this extraction mode (Figure 4.3), the extractant is suspended on the needle tip of the microsyringe, and immersed in the sample solution, contacting directly with target analytes and sample matrix. Since the extraction medium is in the form of a single drop, this type of microextraction is called SDME. Direct-SDME or direct immersion (DI)-SDME, in which the extraction medium without any special supporter, is simple and inexpensive.

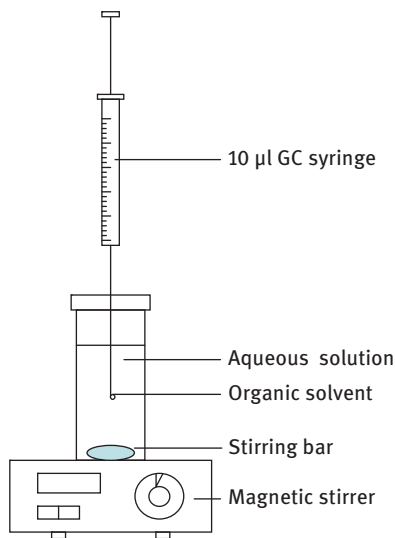


Figure 4.3: Schematic diagram of solvent microextraction based on microsyringe [39].

In direct-SDME, the analyte (A) is distributed between aqueous sample solution and organic solvent [40]:



The distribution coefficient of A between two phase ($K_{org/d}$) can be defined as

$$K_{org/d} = \frac{C_{eq,org}}{C_{eq,d}} \quad (10)$$

Where $C_{eq,org}$ and $C_{eq,d}$ are the concentration of A in organic phase (acceptor phase) and sample solution (donor phase), respectively, under equilibrium.

Then $C_{eq,org}$ can be calculated by eq. (11).

$$C_{eq,org} = \frac{K_{org/d} C_i V_d}{K_{org/d} V_{org} + V_d} \quad (11)$$

Where C_i is the initial concentration of A in sample solution, V_d and V_{org} are the volume of sample solution and organic solvent, respectively.

As can be seen from eq. (11), a high $K_{org/d}$ is beneficial to the extraction.

The two-phase micro-extraction mode is only applicable to a strong or moderate lipophilic analytes ($K_{org/d} > 500$) instead of strongly hydrophilic analytes [40]; for acidic or alkaline analyte, the analyte should be existing in deprotonated form for extraction by adjusting sample pH to increase the partition coefficient.

To achieve the LPME of REE ions, PMBP-benzene was used as the extraction solvent (10 µL), and a 500-fold EF for La was obtained [41]. In this microextraction procedure as shown in Figure 4.4, perfluoroalkoxy (PFA) tubing was used to connect the

extraction chamber, and a constant-flow pump and a 10- μ L microsyringe were employed to introduce the aqueous solution and extraction solvent, respectively. The sample solution was continuously pumped “around” the drop, allowing the analytes to be extracted efficiently. It is called continuous-flow microextraction. With some modification to the continuous-flow SDME setup that the waste outlet of tubing was placed into the sample reservoir, cycle-flow SDME was developed and successfully applied in the determination of trace metals in biological samples [42]. It allows further reduction in the sample size and non-attended operation since there is no danger of the sample vial running out.

Besides the two-phase microextraction mode mentioned above, Ma and Cantwell [43] combined solvent microextraction with simultaneous back extraction into a single microdrop, which was called three-phase (liquid-liquid-liquid) microextraction. As shown in Figure 4.5, *n*-octane was employed as an organic liquid membrane, confined inside a Teflon ring over a buffered aqueous sample solution. With the help of a microsyringe, a microdrop was left suspended inside the organic liquid membrane. The target analytes were initially extracted into the organic liquid membrane (neutral at high pH) and back extracted simultaneously into the acidic microdrop (protonated at low pH).

In three-phase SDME, the analytes are extracted from an aqueous donor phase to an aqueous acceptor drop covered with an organic layer. Due to the large volume ratio between the sample donor phase and the acceptor drop as well as the thin organic layer, high EFs can be obtained with three-phase SDME in a short time. The convenience and efficiency of in-line coupling with some analytical instrument, e.g., CE, are additional advantages of three-phase SDME. Most acidic or basic analytes can be enriched by adjusting the pH to promote neutral forms of the analytes in the donor phase and their charged forms in the acceptor phase in three-phase SDME.

Besides the acidic or basic analytes, three-phase microextraction coupled with CE-UV was employed for the analysis of trace REEs by using 40 mmol/L PMBP as the extractant and 4 % (v/v) formic acid as back-extraction solution [44]. Under the optimized conditions, the LODs of REEs were in the range of 0.19–0.70 ng/mL. The developed method was successfully applied to the determination of trace amounts of REEs in water samples.

4.4.2 Hollow fiber liquid phase microextraction

SDME is simple, inexpensive, rapid and available for headspace extraction, whereas requires careful and elaborate manual operations to overcome the problem of drop dislodgment, which would deteriorate the reproducibility. Prolonged extraction times and faster stirring rates are unfavorable in SDME, since they typically result in drop dissolution and/or dislodgment. In order to solve this problem, in 1999, Pedersen-Bjergaard and co-workers [45] introduced a method named HF-LPME, in

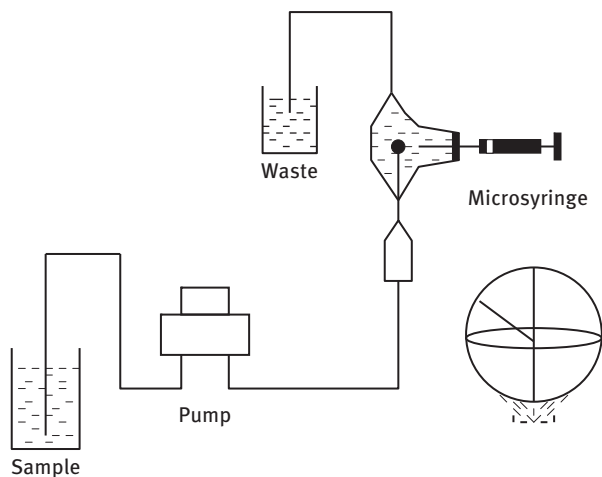


Figure 4.4: The experiment setup for continuous-flow SDME [41, 42].

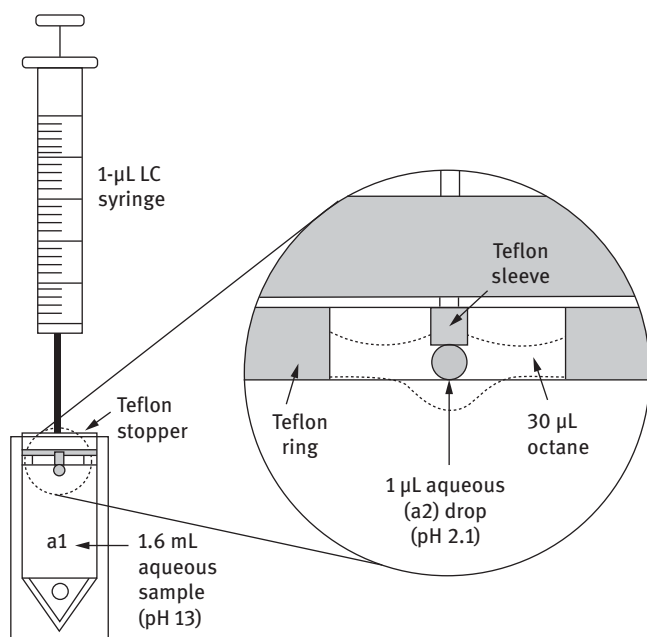


Figure 4.5: Schematic diagram of “Ma and Cantwell” type three phase-SDME [43].

which the micro-extract is contained within the lumen of a porous hollow fiber. With the hollow fiber supporting/protecting the micro-extract, HF-LPME is much more robust than SDME with extra sample clean-up ability. Similar to SDME, HF-LPME can also be performed in both two-phase and three-phase microextraction

modes. In the two-phase HF-LPME, the analyte is extracted from the aqueous sample into the organic phase immobilized in the pores and lumen of the hollow fiber. In the three-phase mode (hollow fiber liquid-liquid-liquid microextraction (HF-LLLME)), the analyte is extracted from the aqueous sample through the organic solvent immobilized in the pores of the hollow fiber into another aqueous phase (acceptor phase) presented inside the lumen of the hollow fiber.

4.4.2.1 Two phase HF-LPME

Figure 4.6 presents the schematic diagram of two-phase HF-LPME. In this operation mode, the extractants immobilized in the pores and the lumen of the hollow fiber are the same organic solvent, and the analytes are extracted from the aqueous sample (donor phase) directly into the organic acceptor solution. The extraction mechanism is similar to that specified in the section of Direct-SDME. HF-LPME is the most used LPME mode and it can be applied for the analytes with solubility in an organic solvent immiscible with water substantially higher than that in an aqueous medium.

Compared with direct-SDME, two-phase HF-LPME is much stable and simple in terms of operation due to the accommodation and protection of the organic solvents in the hollow fiber.

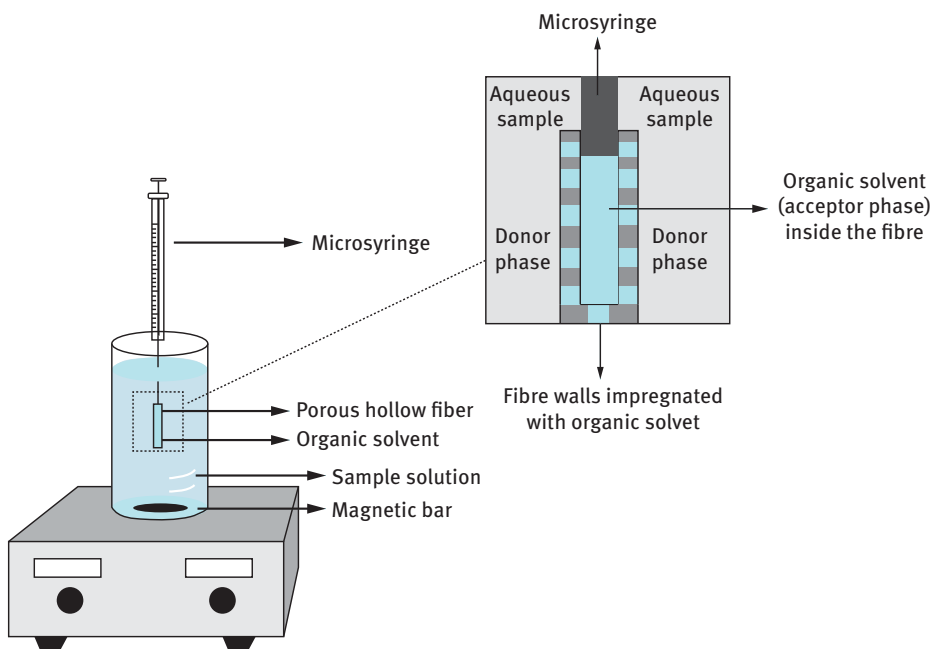


Figure 4.6: Schematic diagram of two phase HF-LPME.

4.4.2.2 Three phase HF-LPME

Figure 4.7 presents the schematic diagram of three-phase HF-LPME, also called HF-LLLME. The analyte is extracted from aqueous sample solution through a thin phase of organic solvent inside the lumen of the pores of a polypropylene hollow fiber and finally into an acidic/alkaline acceptor solution inside the hollow fiber. Up to now, this extraction mode is limited to basic or acidic analytes whose solubility can be adjusted in the donor and acceptor solution, without application on the analysis of REEs. For example, in order to extract basic compounds, pH of the sample has to be adjusted into the alkaline region to suppress the solubility of the analyte in aqueous sample solution (donor phase), whereas pH in the acceptor solution should be low to promote the solubility of analyte in the acceptor phase. In this manner, the basic compounds may easily be extracted into the organic phase and further into the acceptor phase. For acidic analytes, the pH adjustment is just reversed. Following extraction, the aqueous acceptor solution is directly injected into CE, HPLC/LC-MS or other detection techniques for subsequent analysis. In this three-phase system, the acceptor phase is aqueous, which is compatible with HPLC or CE analysis. The acceptor phase in three-phase HF-LPME can also be organic, involving two immiscible organic solvents immobilized in the pores of the HF and filled in its lumen, respectively.

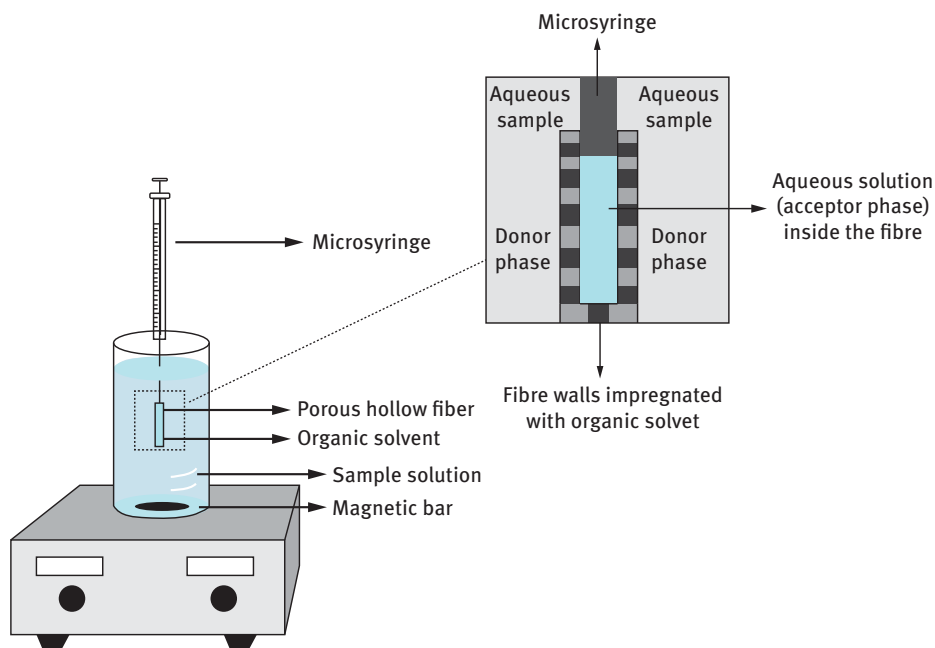
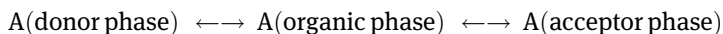


Figure 4.7: Schematic diagram of three phase HF-LPME.

In three-phase HF-LPME, the extraction process of analyte (A) can be specified as follows [40]:



The distribution coefficient of A between organic phase and donor phase ($K_{org/d}$) and that between acceptor phase and organic phase ($K_{a/org}$) can be expressed as:

$$K_{org/d} = \frac{C_{eq,org}}{C_{eq,d}} \quad (12)$$

$$K_{a/org} = \frac{C_{eq,a}}{C_{eq,org}} \quad (13)$$

Where $C_{eq,a}$ is the concentration of A in acceptor phase under equilibrium, and the total distribution coefficient of A between acceptor phase and donor phase ($K_{a/d}$) can be expressed as:

$$K_{a/d} = \frac{C_{eq,a}}{C_{eq,d}} = K_{org/d} K_{a/org} \quad (14)$$

In the three phase HF-LPME system, the extraction efficiency is not only affected by $K_{org/d}$, but also $K_{a/org}$, both of which determine the whole extraction process.

Under equilibrium, the concentration of A in acceptor phase ($C_{eq,a}$) can be calculated by

$$C_{eq,a} = \frac{K_{a/d} C_i V_d}{K_{a/d} V_a + K_{org/d} V_{org} + V_d} \quad (15)$$

Where C_i is the initial concentration of A in sample solution (donor phase), and V_d , V_a and V_{org} are the volume of sample solution, acceptor phase and organic solvent, respectively.

4.4.3 Dispersive liquid liquid microextraction

Based on ternary component solvent system, DLLME was introduced by Assadi and co-workers in 2006 [46]. The operation mode and required apparatus of DLLME are quite different from SDME and HF-LPME. Briefly, a mixture of a water-immiscible extraction solvent and a so-called dispersing solvent, miscible in both phases, is rapidly injected into the aqueous sample solution by a microsyringe, resulting in a cloudy solution which consists of fine particles of the extraction solvent dispersed in the aqueous phase. In this step, the disperser solvent could help the extraction solvent distributed homogeneously in the whole aqueous solution in a short time, resulting in a large contact area between extraction solvent and aqueous sample, and a consequent rapid attainment of extraction equilibrium. By centrifugation, a small volume of extraction

solvent (containing the extracted target analytes) sedimented in the bottom of the conical test tube was obtained and then transferred for subsequent analysis (Figure 4.8).

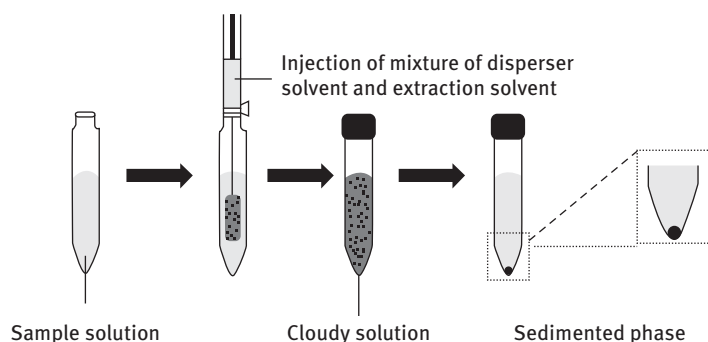


Figure 4.8: Schematic diagram of DLLME.

For DLLME, the extraction time is defined as the time from the injection of dispersant solution into the sample to centrifugation. Since the contact area between the extractants and the sample solution is quite large, the phase transition from water to the extraction phase is very fast. In DLLME, the EF is defined as the ratio of analyte concentration in the aqueous phase and extraction phase, and extraction recovery (R) (or extraction efficiency) is defined as the ratio of the total amount of analyte in the extraction phase and the aqueous solution. It can be expressed as

$$EF = \frac{C_{sed}}{C_o} \quad (16)$$

$$R = \frac{C_{sed} \times V_{sed}}{C_o \times V_{aq}} \quad (17)$$

$$R = \frac{V_{sed}}{V_{aq}} \times EF \quad (18)$$

Where C_{sed} is the concentration of analyte in the extraction phase, V_{sed} is the volume of extraction phase, C_o is the initial concentration of analyte in sample solution, V_{aq} is the volume of sample solution and R is extraction recovery (efficiency).

DLLME is a modified solvent extraction method, in which the extraction time is greatly reduced comparing with the other two methods mentioned above. The apparatus involved in the DLLME operation procedure just includes a microsyringe, a centrifuge and some conical test tubes. There is no need for magnetic stirrer, magneton for agitation, hollow fiber and no trouble in the possibility of extraction drop dislodgment. DLLME has some advantages such as simplicity of the operation, rapidity, low sample consumption, low cost, high recovery and high EF. Nevertheless, the reproducibility and anti-interference ability of DLLME are not very satisfactory.

The disperser solvent is required to be miscible with water and extractants, and acetone, methanol and acetonitrile are the mostly used disperser solvents. The extractants are usually required to be immiscible with water with higher density than water and good extraction capacity for target analytes.

Mallah et al. [47] used ionic liquids, 1-hydroxy-2,5-pyrrolidinedione (HYD), in a DLLME for determination of trace REEs in uranium dioxide powder. In this process, an appropriate mixture of extraction solvent and disperser solvent is rapidly injected into an aqueous sample containing Sm, Eu, Gd and Dy complexes with HYD, and consequently a cloudy solution is formed. After centrifugation of this solution, the whole enriched phase was determined by ICP-OES. The experimental results indicate that the hexafluorophosphate anions with a partial ion exchange mechanism in ionic liquid solvents play a key role in the electrical neutralization of the lanthanoid complex in DLLME.

Chandrasekaran [48] developed a method based on DLLME and ICP-QMS for the simultaneous extraction and preconcentration of 14 REEs in groundwater. In this method, the REEs are complexed with 2,6-pyridinedicarboxylic acid (2,6-PDCA) in the presence of Aliquat-336 (triprilylmethylammonium chloride), which enhanced the hydrophobicity of the ion association complex, benefiting the extraction into chloroform. The extraction was carried out after adjusting the pH of the water sample to 4. The REE ions were back extracted from the chloroform layer with nitric acid for determination by ICP-QMS. Under optimum conditions, an average EF of 97 was obtained for 50 mL of water sample for ICP-QMS determination.

DLLME would provide relatively high EFs (e.g., 100-fold), while is generally suitable for water sample analysis due to limited anti-interference capability. Since SPE has excellent sample cleanup ability, DLLME has high EFs, and the desorption solvent of SPE matches the DLLME well, the coupling of SPE and DLLME will endow the dual extraction technique both excellent anti-interference ability and high EFs. Guo et al. [49] proposed a simple and efficient two-step method based on dispersive (D)-SPE and DLLME for the separation and preconcentration of 15 REEs from environmental water and sediment samples, followed by electrothermal vaporization (ETV)-ICP-MS detection. With Chelex 100 as the adsorbent of D-SPE, target REEs were first extracted and the retained REEs were then desorbed by 0.1 mol/L HNO_3 . After 125 mmol/L Tris and 40 mmol/L PMBP were added into the above elution solution, target REEs were further preconcentrated into CCl_4 by DLLME. The developed dual extraction technique exhibited high EFs (234–566-fold) and good anti-interference ability.

4.4.4 Solidified floating organic drop microextraction

Solidified floating organic drop microextraction (SFODME) is another new LPME technique introduced by Khalili Zanjani et al. [50], in which small volume of an organic solvent with a melting point near the room temperature (in the range of 10–30°C) is

floated on the surface of aqueous solution. The aqueous phase is then stirred for a prescribed period of time, and the sample is transferred into an ice bath. When the organic solvent is solidified, it is transferred into a small conical vial and the melted organic solvent is used for subsequent determination (Figure 4.9). Compared with conventional solvent extraction, it also has the advantage of great reduction in the amount of organic solvent and thus great enhancement of the EF. It is featured with simple operation, easy batch operation and high stirring rate sustainable, and easy separation of organic phase from aqueous phase after solidification.

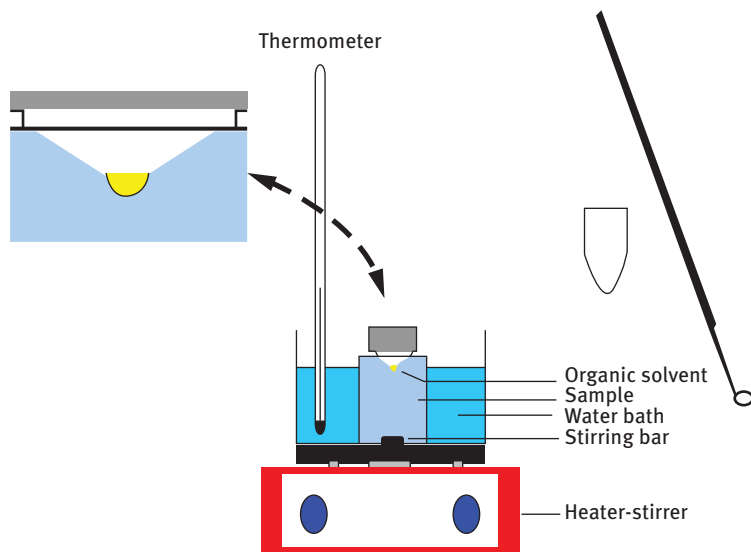


Figure 4.9: Schematic diagram of SFODME apparatus [50].

SFODME is based on equilibrium extraction. The affecting factors can be found in eq. (1-11) and (1-12), and eq. (1-13) presents the calculation of EF [51].

$$C_{o,f} = KC_{aq,f} = \frac{KC_{aq,i}}{1 + K(V_o/V_{aq})} \quad (19)$$

$$\frac{dC_o}{dt} = \frac{A_i \beta \times (KC_{aq} - C_o)}{V_o} \quad (20)$$

$$EF = \frac{C_{o,f}}{C_{aq,i}} \quad (21)$$

Where $C_{o,f}$ is the final concentration of analyte in organic phase, $C_{aq,f}$ and $C_{aq,i}$ are the final and initial concentration of analyte in sample solution (water phase), V_o and V_{aq} are the volume of organic phase and sample solution (water phase) at a certain time (t), A_i is the contact area between organic phase and water phase, β is

the mass transfer coefficient, C_{of} is the final concentration of analyte in organic phase obtained by the calibration.

In SFODME, the main affecting factor is the selection of organic extraction solvent. It should meet the following requirements: (1) immiscible with water; (2) melting point is around room temperature (10–30 °C); (3) good extraction ability for target analytes; (4) the density is less than water; (5) compatible to the employed instruments (e.g. GC, HPLC, AAS, ICP-OES). The suitable organic solvents include *n*-undecyl alcohol, *n*-dodecanol, 2-dodecanol, 1-bromo-hexadecane, 1, 10-dichlorodecane and 1-chloro-octadecyl, and *n*-undecyl and *n*-dodecanol are the most commonly used organic solvents in SFODME.

Chen et al. [52] employed a SFODME-based method for the determination of trace Dy and Y in biological and environmental water samples followed by ETV-ICP-MS detection. 1-(2-pyridylazo)-2-naphthol (PAN) was used as both chelating reagent in SFODME and chemical modifier in ETV for separation, preconcentration and volatilization of the REEs prior to their determination.

4.4.5 Affecting factors

The affecting factors are different in different LPME extraction modes. The main affecting factors include extraction solvent, sample pH, stirring rate, extraction time, extraction temperature and ionic strength. For the extraction of REEs, the selection of chelating agent is very important, which refers to the section of “LLE of REEs”.

In general, the selection of extractants is mainly based on “like dissolves like” principle. The following properties are preferred practically: (1) insoluble in water or very low solubility in water; (2) high boiling point and low saturated vapor pressure, to reduce the evaporation loss during extraction; (3) the distribution coefficient of analytes between the organic and aqueous phases is high. Table 4.22 lists the common organic solvents with corresponding properties.

Sample pH is usually adjusted to make target analytes existing in non-ionic form reducing their solubility in water and promoting the extraction. For the REEs extraction system which is mainly based on chelation or complexation reactions, pH mainly affects the stability of chelates or complexes, thus affecting the extraction.

Stirring rate is a dynamic factor affecting the extraction. In LPME process, the mass transfer of analytes is determined by the diffusion rate and the thickness of diffusion layer between sample solution and the organic solvent. Based on the theory of convection-diffusion, efficient stirring can accelerate the diffusion rate of the analyte and reduces the thickness of the diffusion layer. Thus, increasing the stirring rate would generally accelerate the extraction, and reduce the extraction time. While, when the stirring rate is too high, some negative impact would occur, e.g., single drops in SDME is unstable, bubbles adhered on the surface of the hollow

Table 4.22: Physical properties of the extractants used in LPME.

Extractant	Boiling point (°C)	Vapor pressure (Torr)	Water solubility (mg/L)	Density (g/cm ³)	Viscosity (cP)	Surface tension (dyn /cm)	Dipole moment (D)	Dielectric constant
Cyclohexane	80.7	97.8	55	0.78	0.9	24.65	0.00	2.02(20°C)
n-Hexane	68.7	151.3	12	0.65	0.29	17.94	0.08	1.88
Octane	125.7	14.0	6.6x10 ⁻³	0.70	0.51	21.18	0.00	1.95(20°C)
Iso-octane	99.2	49	2.4	0.69	0.50(20°C)	18.8	0.00	1.94(20°C)
Decane	174.2	1.3	0.05	0.73	0.86	23.37	0.00	1.99(20°C)
Benzene	80.1	95.2	1791	0.87	0.60	28.2	0.00	2.27
Toluene	110.6	28.5	515	0.86	0.55	27.92	0.31	2.38
o-Xylene	144.4	6.6	175	0.88	0.76	29.49	0.45	2.57(20°C)
m-Xylene	139.1	8.3	146	0.86	0.58	28.10	0.30	2.37(20°C)
p-Xylene	138.4	8.7	156	0.86	0.60	27.76	0.02	2.27(20°C)
Ethylbenzen	136.2	9.6	152	0.86	0.64	28.48	0.37	2.40(20°C)
1-Octanol	195.2	0.08	5.38	0.82	7.36	26.92	1.76	10.34(20°C)
Benzyl alcohol	205.4	0.11	800	1.04	4.65(30°C)	39.44	1.66	13.1(20°C)
MIBK	117.4	18.8	1700.0	0.80	0.55	23.64(20°C)	—	13.11(20°C)
Chlorobenzene	131.7	11.7	327	1.10(20°C)	0.72(20°C)	31.98(30°C)	1.62	5.62
Phenetole	172	1.28	—	0.97(20°C)	1.16(25°C)	32.85(22°C)	3.33	4.22
Dichlorometane	39.6	435.8	1990	1.32	0.39(30°C)	26.54(30°C)	1.14	8.93
Chloroform	61.2	194.8	8500	1.48	0.54	26.53	1.15	4.81(20°C)
Tetrachloroethene	76.6	115.2	770	1.58	0.90	26.13	0.00	2.23
1,2-Dichloro-ethane	83.5	83.3(20°C)	8100(20°C)	1.25	0.73(30°C)	30.84(30°C)	1.83	10.37
1,2-Dichloro-benzene	180.5	1.3	156	1.30	1.32	26.48(20°C)	2.14	9.93
Tetrachloroethylene	121.1	18.5	150	1.61	0.80(30°C)	31.30	0.00	2.28
Bromobenzene	155.9	4.2	424	1.48	1.01(30°C)	35.09(30°C)	1.55	5.40
Nitrobenzene	210.8	0.28	1900(20°C)	1.20	1.62(30°C)	42.17(30°C)	4.00	34.78

(continued)

Table 4.22 (continued)

Extractant	Boiling point (°C)	Vapor pressure (Torr)	Water solubility (mg/L)	Density (g/cm ³)	Viscosity (cP)	Surface tension (dyn /cm)	Dipole moment (D)	Dielectric constant
Carbon disulfide	46.2	361.6	2100(20°C)	1.29	0.36(20°C)	32.25(20°C)	0.06	2.64
[C ₄ MIM][PF ₆]	—	—	18800	1.36–1.37	148–450	48.8,49.8	—	—
[C ₆ MIM][PF ₆]	—	—	7500	1.29–1.31	560–586	—	—	—
[C ₈ MIM][PF ₆]	—	—	2000	1.20–1.23	682–710	34.2–36.5	—	—
[C ₆ MIM][Tf ₂ N]	—	—	3400	1.33	—	—	—	—
Water	100.0	23.8	∞	1.00	0.89	71.81	1.82	78.36

MIBK: 4-Methyl-2-pentanone; [C₄MIM][PF₆]: 1-butyl-3-methylimidazolium hexafluorophosphate; [C₆MIM][PF₆]: 1-hexyl-3-methylimidazolium hexafluorophosphate; [C₈MIM][PF₆]: 1-octyl-3-methylimidazolium hexafluorophosphate; [C₆MIM][Tf₂N]: 1-hexyl-3-methylimidazolium bis (trifluoromethylsulfonyl) imide.

fiber membrane appear (HF-LPME) and impede extraction, or the dissolving loss of the organic extraction solvent is accelerated.

LPME of target analytes is a process based on their distribution between the sample solution and the extraction phase, and the maximum extraction efficiency would be obtained when the extraction equilibrium is reached. For the analytes with high distribution coefficient and fast mass transfer speed, the extraction equilibrium can be achieved in a short time, which is an incomplete extraction under equilibrium. However, for analytes with relatively low distribution coefficient or low mass transfer rate, long time are needed to reach the extraction equilibrium. In this case, the extraction is usually processed under non-equilibrium state, during which the extraction time is strictly controlled to ensure the reproducibility.

Extraction temperature has a double impact on the extraction process in terms of thermodynamics and kinetics. In general, increasing the sample temperature would increase molecular motion, the diffusion coefficient of the analyte, and the mass transfer rate of the analyte, thus speeding up the extraction. However, increasing the extraction temperature would reduce the partition coefficient of the analyte, increase the water solubility of the organic solvent, lowering the extraction efficiency. Moreover, when the temperature is too high, small bubbles would occur in the aqueous phase, which is attached to the surface of the extraction solvent, hindering the extraction.

The addition of some inorganic salt, e.g., NaCl, Na₂SO₄, would increase the ionic strength of the sample solution, decrease the solubility of analytes in sample solution due to salt-out effect, increasing the distribution of analytes in the extraction phase and thus the extraction efficiency. While sometimes the salt addition would inhibit the extraction which is explained by that the salt would change the physical property of the extraction film and thus the diffusion rate of target analyte in the extraction phase.

4.5 Cloud point extraction (CPE)

Cloud point extraction (CPE) is based on the fact that most nonionic surfactants can form micelles in aqueous solutions and become turbid when they are heated beyond a temperature called the cloud point temperature (CPT). Above the CPT the micellar solution separates into a small volume of surfactant-rich phase and a diluted aqueous phase, in which the surfactant concentration is close to the critical micellar concentration (CMC). Any analyte solubilized in the hydrophobic core of the micelles, will be separated and concentrated in the small volume (usually in the range of 50–250 μ L) of the surfactant-rich phase. This process is reversible, and two phases would combine into one phase when the temperature is lower than CMC.

4.5.1 Application of CPE for trace REEs analysis

REEs react with complexants and produce hydrophobic complexes that are entrapped into the micelles and then into the surfactant-rich phase. Due to the viscosity and organic content of the surfactant-rich phase, appropriate sample introduction systems or nebulizers are required, such as employment of a free-clogging nebulizer, chemical vapor generation and micronebulization/aerosol desolvation. Table 4.23 lists the REEs extraction systems by CPE, along with subsequent detection technique.

4.5.2 Affecting factors

4.5.2.1 Surfactants

Surfactants generally consist of a hydrophobic and a hydrophilic moiety, and the CPT is related to the chain length of hydrophilic and hydrophobic moiety in the surfactants. With the same hydrophobic moiety, CPT would increase with the increase of hydrophilic chain length; on the contrary, CPT declines with the increase of the hydrophobic chain length. Besides nonionic surfactants, amphoteric ionic surfactant exhibits cloud point phenomenon. Some anionic surfactants (e.g., sodium dodecyl sulfate [SDS], sodium dodecyl benzene sulfonate [SDBS] and sodium dodecyl sulfonate [SDSA]) in aqueous high concentration HCl medium would also appear phase separation. Table 4.24 lists the frequently used surfactants in CPE, along with the structure, CMC and CPT.

Increasing the surfactant concentration would improve the extraction efficiency, increase the ratio of two-phase volume, and simultaneously reduce the EF and distribution coefficient. In order to increase EF, a low surfactant concentration is preferred, while too low surfactant concentration would lead to difficult separation of the sedimented phase from sample solution, deteriorating the accuracy and reproducibility.

4.5.2.2 Sample pH and chelating agent

For the extraction of REE ions, a chelating agent is necessary to transform REEs into a hydrophobic form, which is then extracted into the surfactants. pH should be appropriate for the formation of REEs complex. However, most of the complexation system for REEs occurs in slightly acidic pH (Figure 4.10), which is incompatible with digested solid samples which is generally strong acidic. Ohashi et al. [58] show good extraction in a more acidic media (pH = 3) for La^{3+} , Eu^{3+} and Lu^{3+} , while higher concentrations of surfactant were needed to counter the effect of the acidic media on the extraction. The EF would be reduced and LOD would be deteriorated due to the low extraction efficiency.

Table 4.23: Applications of CPE for trace REEs analysis.

Analytes	Surfactant	Complexant	Enrichment factor	Detection	LOD	Sample	Ref.
REEs	Triton X-114	8-HQ	7.9–9.2	ICP-OES	41.4 (Yb) –448 ng/L (Gd)	Tea leaves and mushroom	[53]
REEs	Triton X-114	No complexant	5.4–8.1		69.0 (Sc)-509.5 ng/L (Sm)		
Dy, Er, Eu,	PONPE-7.5	TTA	9–14	ICP-OES	2 (Pr)- 103 (Lu) ng/L	River water	[54]
Gd, Ho, La, Lu, Pr,		PAN	70	NAA	0.27 (Yb)-3.07 (Eu) ng/g		[55]
Sm, Tb, Tm and Yb							
Eu	Triton X-114	Alizarin red S	22	FAAS	6 ng/mL	Water	[56]
REEs	Triton X-114	(i-pr)DGA	140	ICP-MS	0.2 to 30 ng/L	Soil	[57]

8-HQ: 8-hydroquinoline; TTA: 1-(2-thenoyl)-3,3,3-trifluoroacetone; (i-pr)DGA: N,N,N',N'-tetraisopropyl diglycolamide.

Table 4.24: Surfactants commonly used in CPE.

Surfactants		CMC (mmol/L)	CPT (°C)
Chemical name	Commercial name in series		
Polyoxyethylene fatty alcohol	Brij 30	0.02–0.06	2–7
	Brij 35	0.06	>100
	Brij 56	0.0006	64–69
P-tert-octyl phenyl polyethylene glycol ether	Triton X-100	0.17–0.30	64–65
	Triton X-114	0.20–0.35	22–5
N-alkyl phenyl polyethylene glycol ether	PONPE-7.5	0.085	5–20
	PONPE-10	0.07–0.085	62–65
Amphoteric ionic surfactants	C ₉ APSO ₄	4.5	65
	C ₈ -lecithin		45

The behaviors of La^{3+} , Eu^{3+} and Lu^{3+} in CPE with and without di(2-ethylhexyl) phosphoric acid (HDEHP) as the complexant, Triton X-100 as the surfactant, were investigated [58]. It was suggested that the extraction of Ln^{3+} into the surfactant-rich phase without chelating agent was caused by the impurities contained in Triton X-100. The extraction efficiency of above 91 % for tested REEs was obtained using 3.0×10^{-5} mol/L HDEHP and 2.0 % (v/v) Triton X-100. From the equilibrium analysis, it was clarified that Ln^{3+} was extracted as $\text{Ln}(\text{DEHP})_3$ into the surfactant-rich phase. Besides, Li et al. [53] proposed an on-line CPE system with ICP-OES detection with/without 8-HQ as complexant for trace analysis of REEs in biological samples. The experimental results indicated that: (1) the use of on-line CPE greatly simplifies the extraction procedure; (2) LODs for REEs obtained by on-line CPE-ICP-OES with 8-HQ as chelating agent were slightly better than that obtained by on-line CPE-ICP-OES without a chelating agent, and the RSDs of the two methods were comparable; (3) both on-line CPE-ICP-OES systems had good selectivity and could be used for the biological sample analysis.

4.5.2.3 Extraction temperature and time & centrifugation time

The extraction temperature and time are determined by the properties of surfactants and the extracted compounds. Generally, the extraction temperature is 15–20°C higher than the CPT of the employed surfactant. Increasing extraction time would increase the extraction efficiency, while too long extraction time hardly affect the extraction efficiency, and 30 min extraction is commonly used for a good extraction efficiency.

Increasing the centrifugation time would initially increase the extraction efficiency and distribution coefficient, which will be constant after a long extraction time. For a CPE system with relative high CPT, too long centrifugation would lead to the reversion of phase separation, decreasing the extraction efficiency.

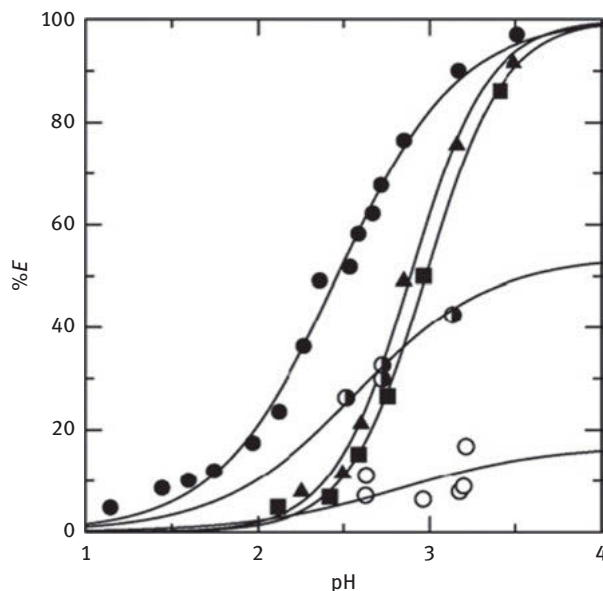


Figure 4.10: Extraction percentage of La(III), Eu(III) and Lu(III) vs. pH without chelating agents. Circle, La(III); triangle, Eu(III); square, Lu(III); closed, Aldrich (lot no. 13112LB); half closed, Aldrich (lot no. 03615HC); open, Nacalai Tesque; Ln(III), 3.6×10^{-5} mol/L; Triton X-100, 2.0% (v/v); $I = 0.01$ mol/L (pH > 2.0) and 0.1 mol/L (pH < 2.0) with (H, Na)ClO₄ [58].

4.5.2.4 Ionic strength

The ionic strength hardly affects the extraction efficiency and distribution coefficient. The addition of some inert salt would change the cloud point of the surfactant, favoring the separation of two phases.

4.6 Solid phase extraction and solid phase microextraction

Solid phase extraction (SPE) is currently the most frequently used sample pretreatment technique in real sample analysis [59], featuring with high EFs, rapid phase separation, low organic solvent consumption, simple operation, as well as easy-to-automate. The principal goals of SPE are trace enrichment (concentration), matrix simplification (sample clean-up) and medium exchange (transfer from the sample matrix to a different solvent or to the gas phase) [60]. Usually, the analytes are transferred from a mobile phase (gas, fluid or liquid) [61] to the solid phase where they

are retained for the duration of the sampling process. The solid phase is then isolated from the sample and the analytes are recovered by elution using a liquid or fluid, or by thermal desorption into the gas phase. The adsorption process of target analytes on the adsorbents depends on the physical/chemical form of analytes, specific surface properties of the adsorbent and the experimental conditions, such as pH, temperature and analytes concentration. The adsorption involves interactions between the analytes and sorbents with various functional groups and ion exchange processes.

The adsorbent plays a key role in SPE-based methodology because it determines the selectivity, affinity and capacity. The ideal SPE adsorbents are expected to feature with the following characteristics: (1) porosity, having a large specific surface area; (2) low blank; (3) high chemical and mechanical stability; (4) fast kinetics of adsorption and desorption; (5) reversible adsorption; (6) high selectivity; (7) high recovery rate. Besides the conventional materials such as organic chelate resin [62], activated carbon [63], activated alumina [64] and microcrystalline material [65], a variety of novel materials including carbonaceous materials [66–68], molecular/ion imprinted polymers [69, 70], nanostructured materials [71–74], mesoporous materials [75–77], restricted access materials (RAM) [78, 79], monolithic materials [80, 81], magnetic materials and metal-organic frameworks (MOFs) [82–84], have been employed in SPE. The application of various SPE adsorbents in trace REEs analysis is listed in Table 4.25.

4.6.1 Carbon nanotubes and graphene oxide

Carbon nanotubes (CNTs), which were first discovered by Iijima [123], have led research to new area in many interdisciplinary investigations as the advantages of CNTs are unique structural, electronic, optoelectronic, semiconductor, mechanical, chemical and physical properties. CNTs can be described as a graphite sheet rolled up into a nanoscale-tube (which are single-wall carbon nanotubes [SWCNTs]), or with additional graphene tubes around the core of an SWCNT (which are multi-wall CNTs (MWCNTs)). These CNTs have diameters in the range between fractions of nanometers and tens of nanometers and lengths up to several centimeters with both their ends normally capped by fullerene-like structures.

Although raw CNTs walls are not reactive, oxidation of CNTs (by using such as HNO_3 , NaOCl and KMnO_4 solutions) can lead to surface functionalization with oxygen-containing groups (e.g., carboxylic, carbonyl and hydroxyl group), allowing retention of cations [124]. These functional groups cause a rise in negative charge on carbon surface and the oxygen atoms in functional groups donate single pair of electrons to metal ions, consequently increasing their cation exchange capacity [125]. It is commonly believed that the chemical interaction between the metal ions and the surface functional groups of CNTs is the major sorption mechanism.

Table 4.25: Application of various SPE adsorbents in trace REEs analysis.

Materials	Elements	Detection	LOD (ng L ⁻¹)	Adsorption capacity (mg g ⁻¹)	Samples	References
C ₁₈ silica cartridge modified with PAN	Ce, Dy, La, Sm and Y,	ICP-OES	11–37		Spring, well, tap water and seawater	[85]
Silica gel column	La, Eu and Yb (PMBP complex)	ICP-OES	34–82		GBW07603, Lake water and synthetic seawater	[86]
Microcolumn packed with MWNTs	La, Sm, Eu, Gd, Tb, Ho	ICP-OES	3–57	7.23–9.93	GBW07605, Lake water and synthetic seawater	[87]
Ion-Imprinted Polystyrene Resins	Yb and Yb	FAAS, ICP- OES		8.9±0.2 (Y)		[88]
Maleic acid grafted PTFE fibers	Y, La, Nd, Eu, Gd, Tb and Yb All lanthanides except Pm	ICP-MS	0.001–0.02	0.31 mmol g ⁻¹ (La)	GBW07312, GBW07313, GBW07405, seawater, river water	[89]
Fullerene derivatives poly(b- styryl)-(12-methanofullerene- C60)-61- formo hydroxamic acid Carbon Nanofibers	Ce, La, Pr, Nd, Sm and Gd.	ICP-MS	0.9–3.5	1.25–2.15 mmol g ⁻¹	Standard reference material (BCR-1, SO-Z, NBS 163), seawater	[66]
	La, Eu, Gd, and Yb	ICP-MS	0.36–0.6	14.2–19.1	Tea leaves GBW07605	[90]
Mesoporous TiO ₂	V, Ce, Dy, Eu, La and Yb	ICP-OES	30–350	13.1–26.5	GBW08571 coal fly ash, water samples (river, pond, well and lake)	[91]
					GBW07401	

(continued)

Table 4.25 (continued)

Materials	Elements	Detection	LOD (ng L ⁻¹)	Adsorption capacity (mg g ⁻¹)	Samples	References
Tulsion CH-90 resin	^{152,154} Eu	Nal (TI) gamma scintillation detector		0.31 mmol g ⁻¹		[92]
Chitosan-based chelating resin functionalized with EDTA	All REEs except Pm	ICP-MS	0.12–5.6		seawater	[93]
Nano-pore samarium (II)- imprinted polymer	Sm	ICP-OES				[94]
silica gel modified with MTPB	Sc	ICP-OES	85 ng g ⁻¹	0.6 mmol g ⁻¹	shrubby leaves, Tibet soil, balsam pear leaves and lotus leaves	[95]
Octadecyl silica minicolumn.	Ce, Dy, La, Sm, Y, Yb,	ICP-OES	90–400		Seawater, tap water and well	[96]
Microcartridge containing C18- derivatized silica particles	La, Gd	CZE with diode array detector	0.02 (La) 0.08 (Gd)		Tap water	[97]
Syringe-driven chelating columns	All lanthanides except Pm	ICP-MS	0.005–0.09		Seawater	[98]
Amberlite XAD-4 resin with monoaza	La, Nd and Sm	ICP-OES	3900–7400	0.055–0.066 mmol g ⁻¹		[99]
dibenzo 18-crown-6						
Bis-(2-ethylhexyl)-phosphate (HDEHP) coated reverse phase C18	Gd and Gd based MRI contrast agents	ICP-MS	22–38		surface water, waste water	[100]
Bentonite modified with N-(2- hydroxyethyl) ethylenediamine	Sm	ICP-OES	600	17.7	GBW07602, waste water	[101]

MWNTs with tannic acid	La, Tb and Lu	MPT-AES	3.97–8.55	[102]
Activated carbon modified with benzoyl hydrazine	Eu	ICP-OES	73 ng g ⁻¹ 59.8	[103]
TiO ₂ –graphene composite	La, Tb, and Ho	MPT-AES	1600–2800	[104]
Nanoporous silica functionalized with N'-[(2-hydroxy phenyl) methyl] benzohydrazide	Dy	ICP-OES	50	[105]
High-dispersion-type MW-CNTs attached to polymerbeads (TSK TM)	All REEs except Sc and Pm	ICP-MS	0.016–0.159	[106]
Walnut shell packed microcolumn	All REEs except Sc and Pm	ICP-MS	0.01–0.17	[107]
Eu-imprinted polymer nanoparticles	Eu	Electro-chemistry	23000	[108]
TiO ₂ nanotube packed microcolumn	La, Ce, Eu, Gd, Lu and Yb	ICP-MS	10.1–14.7	[109]
Carbon-ferrite magnetic nanocomposite	La, Sm, Nd and Pr	ICP-OES	500–10000	[110]
4-(2-thiazolylazo) resorcinol immobilized Chromosorb 106	All lanthanides except La and Pm	ICP-MS	0.06–0.31	[111]
Pr ³⁺ ion surface-imprinted HQ-PHEMA/SiO ₂	Pr ³⁺	UV-Vis (with EDTA titration)	0.013 mmol g ⁻¹	[112]
Oxidized multiwalled carbon nanotubes packed minicolumn	Sc	ICP-OES	4	[113]

(continued)

Table 4.25 (continued)

Materials	Elements	Detection	LOD (ng L ⁻¹)	Adsorption capacity (mg g ⁻¹)	Samples	References
2,6-pyridinedicarboxaldehyde-functionalized Amberlite XAD-4 resin	Nd, Sm, Eu, Gd, Tb, Dy, Ho, Yb, Lu, and Ce	ICP-OES	7–150	0.0490–0.0667 mmol g ⁻¹	SPS-SW2 Batch 127 seawater, tap water	[114]
8-hydroxy-2-quinolinecarboxaldehyde functionalized Amberlite XAD-4 resin packed minicolumn	Pr, Sm, Eu, Gd, Tb, Dy, Ho, Tm, Yb, and Lu	ICP-OES	10–420	0.0496–0.112	SPS-SW2 Batch 127 seawater, tap water	[115]
Coriolus versicolor immobilised Amberlite XAD-4	La	ICP-OES	270	16.6 mg for 0.25 g C. versicolor immobilised on 1.0 g of Amberlite XAD-4	Tap water, river water	[116]
Y(III) imprinted polymer	Y	ICP-OES	900	18.5	standard rock reference material, radioyttrium	[117]
Fe ₃ O ₄ @SiO ₂ @polyaniline-graphene oxide composite	All REEs except Sc and Pm	ICP-MS	0.04–1.49	7.7–16.3	GBW07605, tea leaves, lake water, river water	[118]
Fe ₃ O ₄ @SiO ₂ -(CH ₂) ₃ -S-cinchonidine	Eu	ICP-OES	40	26.5	Mineral water, agricultural water, tap water, spring water	[119]
Double-ion imprinted polymer @magnetic nanoparticles	Ce and Gd	Electro-chemistry	70 (Ce) 190 (Gd)			[120]
Transcarpathian clinoptilolite (thermally activated at 350 °C)	Tb	UV-Vis	750	≈6.0	Synthetic water	[121]
Graphene oxide-TiO ₂ composite	La, Ce, Eu, Dy and Yb	ICP-OES	130–410	16.6–28.7	River water, lake water, seawater, sediment	[122]

The oxidation of MWCNTs with concentrated nitric acid lead to the surface functionalization with oxygen-containing groups, and the isoelectric point (IEP) of MWCNTs shifts to the lower pH values. When the pH of the solution is higher than the IEP of the oxidized MWCNTs, the negative charge on the surface provides electrostatic attractions that are favorable for adsorbing cations. The decrease of pH leads to the neutralization of surface charge, so the adsorption of cations onto MWCNTs decreases quickly. Liang et al. [126] investigated the adsorption behavior of REEs on MWCNTs and quantitative adsorption (>95 %) for target REEs ions was obtained when the pH exceeded 3.0; pH 4.0 was selected as the optimum condition for the SPE of REE ions, followed by elution with 1.0 mol/L HNO_3 and ICP-OES detection. The detection limits of this method for REEs was between 3 and 57 ng/L.

Su et al. [118] prepared a $\text{Fe}_3\text{O}_4@\text{SiO}_2$ @polyaniline-graphene oxide composite (MPANI-GO) through a simple non-covalent method and applied it to magnetic solid phase extraction (MSPE) of trace REEs in tea leaves and environmental water samples followed by ICP-MS detection. The GO plays a key role in the adsorption of REEs on MPANI-GO and the function of MPANI was mainly to anchor and magnetically functionalize GO. The adsorption mechanism of the REEs on the MPANI-GO could be attributed to the chelation of the functional groups of GO containing hydroxyl, epoxide, carboxyl and carbonyl groups with REEs. When 0.5 mol/L HNO_3 was used as the eluting agent, the MPANI-GO can be reused for more than 30 times without obvious decrease of the recoveries of REEs. It should be also noted that the prepared magnetic nanoparticles are superparamagnetic, which could be attracted to a magnetic field but retain no residual magnetism after the field is removed. During the extraction, the suspended superparamagnetic nanoparticles adhered to the target REEs can be removed very fast from a matrix using a magnetic field, and they do not agglomerate after removal of the field.

4.6.2 Silica-based materials

Modified silica gel merits good selectivity, high mass-exchange characteristics and good mechanical stability. Immobilization of organic functional groups on a siliceous surface has been successfully employed to produce varieties of modified silica gel. In this process, an organic reagent or a synthesized organic molecule containing desired functional group is directly attached to the support, or to the original chain bonded to the support via a sequence of reactions to increase the main chain, where other basic centers can be added to ensure the enhancement of a specific adsorption. Based on the hard-soft acid-base theory, chemically stable metal chelates can be formed between REEs and β -diketone reagents (e.g., acetylacetone, trifluoroacetylacetone and hexafluoroacetylacetone) under suitable experimental conditions. These reagents, as derivatization reagents, have been successfully applied in GC analytical systems. Zhang et al. [127] prepared an acetylacetone-modified silica gel (ACACSG)

for the preconcentration of trace REEs in environmental and biological samples. The maximum adsorption percentages for target REEs were obtained at pH 6.0–8.0. Two possible mechanisms could be used for the explanation of the adsorption of the REEs on ACACSG. First, REEs were adsorbed through the affinity of =O of acetylacetone. Second, the REEs were adsorbed on ACACSG by electrostatic action between REEs and the charge on silica gel surface. In the acidic medium, the first mechanism plays a dominating role. When the pH increases, the -OH on the surface of silica gel provides the ability of binding cation. The adsorption percentage of REEs onto ACACSG increases quickly when both mechanisms work.

4.6.3 Chelating resin and ionic-exchange resin

Various chelating agents have been immobilized on polymeric supports to produce chelating sorbents for determination of REEs by SPE in natural water samples. These functional groups include 8-HQ [128], iminodiacetate (IDA) [129, 130], hydroxamic acid [131], 2-amino-5-hydroxy benzoic acid [132], 2,6-diacetylpyridine [133] and fluorinated β -diketone [134]. Chemical immobilization offers the ability to customize the sorption medium with different functional groups to improve selectivity, sorption capacity and reusability.

Fu et al. [135] synthesized alkyl phosphinic acid resin (APAR) for on-line preconcentration of trace REEs, followed by ICP-MS determination. REEs in seawater could be on-line concentrated on the APAR packed column, and eluted from the column with 0.5 mL 0.1 mol/L HNO_3 within 30 s. An EF of nearly 400 was achieved for all REEs when the seawater sample volume was 200 mL, while the matrix and coexisting spectrally interfering ions such as Ba, Sn and Sb could be simultaneously separated. Zeereen et al. [111] prepared a new chelating resin by immobilizing 4-(2-thiazolylazo) resorcinol (TAR) on Chromosorb 106 and investigated the adsorption behavior of REEs on it. It was found that the REEs were quantitatively retained from saline solutions on the Chromosorb 106-TAR resin at pH 5.0 and can be eluted with 1 % (v/v) HNO_3 . The resin possesses large sorption capacity for REEs ranging from 81.1 (Lu) to 108 (Nd) $\mu\text{mol/g}$. Gupte et al. [136] employed resorcin [4] calixpyrrole and its azo derivative impregnated Amberlite XAD-2 resin for the preconcentration of La^{3+} and Ce^{3+} . The resin was found to be highly selective for these two REE ions in the presence of various electrolytes at a particular pH. Table 4.26 presents some adsorption capacity for La^{3+} and Ce^{3+} .

Separation of REEs by ion chromatography on a Dionex Ion Pac CS3 column (sulfonic acid type) has been achieved by both isocratic and gradient elution with HIBA as the mobile phase [137]. It was shown that the plate height for Y was distinctly smaller than those for REEs with similar ionic radii. An improved combined isocratic-gradient elution procedure was devised for separation of Sc, Y, La and the lanthanides in one run. By using strongly basic anion-exchanger (QAE-SephadexA-25), Gd complexed with negatively charged humic substances (humic and fulvic acids) was

Table 4.26: Adsorption capacity (mg/g) of La^{3+} and Ce^{3+} on some chelating resin [136].

Adsorbents	La^{3+}	Ce^{3+}
Aliquat-336–Amberlite XAD-4	4.73	
Amberlite XAD-4 resin–bicine ligands	48.6	
Calix[4]arene-o-vanillinsemicarbazone–merrifield resin	25.2	28.1
Amberlite XAD-16 (AXAD-16)-N,N-dihexylcarbamoymethyl	188	–
Phosphonic acid, Amberlite XAD-4-(o-vanillinsemicarbazone)	2.30	2.48
Calix[4]arene-semicarbazone–merrifield's peptide resin	1.88	1.44
Merrifield chloromethylated resin–(dimethyl amino-phosphonomethyl)-phosphonic acid (MCM-DAPPA)	169	
azocalix[4]pyrrole Amberlite XAD-2 polymeric chelating resin	107, 111	88.2, 89.9

collected from sample solution [138]. A Gd-based MRI contrast agent (diethylene-triamine-N,N,N',N'',N'''-pentaacetato aquo gadolinium(III), Gd-DTPA²⁻) was simultaneously collected on the same column. The Gd-DTPA complex was desorbed by anion-exchange with 50-mmol/L tetramethyl ammonium sulfate, leaving Gd-humic complexes on the column. The Gd-humic complexes were subsequently dissociated with 1 mol/L nitric acid to desorb the humic fraction of Gd. The 2-step desorption with small volumes of the eluting agents allowed 100-fold preconcentration for the fractionation analysis of Gd at low ng/L levels by ICP-MS. On the other hand, Gd(III) neither complexed with humic substances nor DTPA, i.e., free species, was not adsorbed on the column.

The details on relevant chromatographic separation of REEs can be referred from the section of “Liquid chromatographic separations of REEs”.

4.6.4 Metal oxide nanostructured materials

Nanoparticles are often defined as particles of less than 100 nm in diameter. The nanoparticles exhibit new or enhanced size-dependent properties compared with larger particles of the same material. Depending on the chemistry of the constituent atoms, nanoparticles are known to exhibit remarkable adsorption properties due to their enhanced surface area and large interface volume. Nano-sized inorganic oxides are widely used in SPE for the preconcentration/separation of metal ions because it can adsorb metal ions with high adsorption capacity. Different types of nanoparticles, such as nanometer-sized powder materials, mesoporous nanoparticles and magnetic nanoparticles, have been applied in SPE of REE ions.

The effect of pH on the adsorption characteristics of La^{3+} and La complexes of citric acid, 2-hydroxyisobutyric acid (HIBA), and humic acid on nanometer-sized TiO_2 was investigated [139]. An obvious difference was found between the adsorption of free La^{3+} and La complexes on nanometer-sized TiO_2 with pH changing from 4.0 to 6.5. Quantitative adsorption of lanthanum citrate, lanthanum HIBA and lanthanum humic complexes were achieved with pH ranging from 4.0 to 8.0, whereas free La^{3+} cannot be quantitatively adsorbed until the pH value is up to 6.5. However, if the pH value was lower than 4.0 (pH 3.5 for lanthanum citrate), the adsorption of lanthanum citrate and lanthanum humate complexes declined remarkably due to incomplete complexing between La^{3+} and the organic ligands (the first acid dissociation constants [pK_a] of the citric acid and the 2-hydroxyisobutyric acid are 3.13 and 3.72, respectively).

These nanometer-sized metal oxides are not selective and unsuitable for samples with complicated matrices. In order to improve selectivity of the nanoparticles, the modification of the adsorption material is usually required. The most often used method is to load specific chelate reagent physically or chemically on the surface of this material. The former method is simple but the loaded reagent is prone to leakage. PAN, PMBP, 8-HQ and dithizone were commonly used as modifiers on metal oxides nanoparticles. Due to the chelating ability of the loaded reagent with the target analytes, selectivity of the nanoparticles could be improved.

Jon et al. [140] employed PMBP physically immobilized nanometer Al_2O_3 as the adsorbents for the extraction of REE ions Sc^{3+} , Y^{3+} and La^{3+} . The interesting ions can be adsorbed quantitatively on the above material at pH = 4.5 and the analytes adsorbed on the column can be eluted with 0.5 mol/L HCl. The dynamic adsorption capacity of target REEs on the modified nanometer Al_2O_3 are 5.7 (Sc), 13.1 (Y) and 15.5 (La) mg/g, respectively. Comparatively, the chemically bonded materials are more stable than that obtained by physical method, and could be used repeatedly. Yan et al. [141] prepared magnetic $\text{Fe}_3\text{O}_4@\text{TiO}_2@\text{P204}$ NPs by fabricating P204 onto $\text{Fe}_3\text{O}_4@\text{TiO}_2$ NPs on Lewis acid-base interaction between Ti and phosphate group. The prepared $\text{Fe}_3\text{O}_4@\text{TiO}_2@\text{P204}$ NPs possess good selectivity, high adsorption capacity and quick adsorption/desorption kinetics toward REEs.

Mesoporous nanoparticles are special kind of mesoporous materials. The particle size of the material was less than 100 nm, while it has mesoporous on the particles. The application of the material as adsorbent has been viewed in three perspectives: (1) As a new nanometer material with unsaturated surface atoms that can bind with other atoms, it possess highly chemical activity, very high adsorption capacity and selective adsorption of metal ions. (2) Due to its large surface area, mesoporous material provides more active sites, this results in achieving equilibrium adsorption in short time. (3) By virtue of mesoporous structure, fast adsorption and desorption can be obtained. Huang et al. [77] employed mesoporous TiO_2 nanoparticles as column packing sorbent for flow injection micro-column preconcentration on-line coupled with ICP-OES determination of trace metals (including REEs) in environmental samples. The results showed mesoporous TiO_2 possesses a high adsorption capacity toward the metal ions

and the adsorbent was suitable for the preconcentration of trace metal ions in samples with complicated matrix, and is highly stable with long column life time, enabling more than one hundred of load and elution cycles to be performed without loss of analytical performance.

4.6.5 Ion-imprinted materials

Ion-imprinted polymers (IIPs) are similar to molecular-imprinted polymers (MIPs); they can recognize metal ions after imprinting and retain all the virtues of MIPs. IIPs have outstanding advantages such as predetermined selectivity in addition to being simple and convenient to prepare. Traditional IIP exhibits poor site accessibility to target ions because the functionality is totally embedded by high cross-linking density in the polymer matrices. In order to obtain IIP with high selectivity and easy site accessibility for target ions, efforts have been made to deal with the issue of accessibility by imprinting on the matrix surfaces.

Recently, surface imprinting technique attracted extensive research interest due to good accessibility to the target species, low mass-transfer resistance, and completed removal of templates, fast adsorption kinetics and ease of preparation. Meng et al. [142] prepared a novel Ce^{3+} ion imprinted silica based on the supported material of ordered mesoporous silica SBA-15 by surface imprinting technique via reversible addition-fragmentation chain transfer polymerization. The results showed that the synthesized material possessed high-ordered mesoporous structure and showed high selectivity and satisfied adsorption capacity for adsorption of Ce^{3+} . Zhang et al. [143] synthesized Dy^{3+} -imprinted TTA modified silica gel sorbent by surface imprinting technique and employed it as a selective SPE sorbent for on-line extraction and subsequent ICP-OES determination of Dy^{3+} . The selectivity coefficient for Dy^{3+} in the presence of competitive ions, e.g., La^{3+} , Nd^{3+} and Gd^{3+} , was above 350. The static adsorption capacity and selectivity coefficient of the imprinted sorbent are higher than those of the non-imprinted sorbent, and the imprinted TTA modified silica gel sorbent offered a fast kinetics for the adsorption and desorption of Dy^{3+} . With a sample loading flow rate of 2.5 mL/min for 48 s preconcentration and elution flow rate of 1.5 mL/min for 8 s elution, an EF of 10 and the sample frequency of 40 samples/h were obtained.

4.6.6 Metal-organic frameworks

MOFs are a new class of hybrid inorganic-organic microporous crystalline materials self-assembled straightforwardly from metal ions with organic linkers via coordination bonds. Due to their unique physical and chemical properties, (e.g., permanent nanoscale pore structure, uniform pore size, large specific surface area and good thermal stability), MOFs exhibited great application prospect in hydrogen storage,

gas separation, catalyst, sensors and biological imaging. The inherent high-specific surface area (appr. 5,000 m²/g) indicates a large adsorption capacity; the uniform pore structure with certain pore size allows a selective adsorption of molecular with less pore size; the functionalization in their pores or outer surface can be achieved easily. While the application of MOFs-based sorbents is mainly limited in simple water samples or simulated samples (in organic solvents) presently.

Ln³⁺@bio-MOF-1 were synthesized via postsynthetic cation exchange of bio-MOF-1 with Tb³⁺, Sm³⁺, Eu³⁺ or Yb³⁺, and their photophysical properties were studied [144]. It is demonstrated that bio-MOF-1 encapsulates and sensitizes visible and near-infrared emitting lanthanide cations in aqueous solution. The development and application of MOFs in trace REEs is greatly expected although it is relatively scarce presently.

4.6.7 Restricted access materials

RAMs are a class of biocompatible adsorbent particles enabling the direct extraction of analytes from biological fluid (e.g., plasma and urine). The separation mechanism is based on the hydrophilic effect and size exclusion. To be brief, a hydrophilic barrier enables the small molecules to permeate through the inner part of the material; meanwhile, it excludes the macromolecules by physical or chemical means on the surface of the material. They have been successfully used as separation media for the analysis of environmental and biological samples in recent years. In LC pre-column, the commercialized alkyl-diol silica (ADS) was frequently applied as RAM for the clean-up of complex biological samples, such as blood, serum, urine and milk. The mechanism was explained by that the outer surface (hydrophilic diol group) repelled macromolecules (such as proteins, nucleic acids), while the internal surface, comprising hydrophobic reversed-phase (C₄, C₈ or C₁₈), retained analytes that penetrate through the porous layer.

Yan et al. [145] prepared restricted accessed magnetic nanoparticles by self-assembly of a nonionic surfactant (Tween-20) onto the PAR functionalized magnetic nanoparticles (MNPs). It was found that the as-prepared restricted accessed Fe₃O₄@SiO₂@PAR nanoparticles have a porous structure with BET surface area of around 99.4 m²/g, average pore size of about 6.14 nm and pore volume of 0.47 cm³/g, respectively. Besides, the prepared restricted accessed Fe₃O₄@SiO₂@PAR showed a good size exclusion property toward protein, providing an application potential for the direct analysis of biological samples. Based on it, a novel method of restricted accessed MSPE combined with ICP-MS was developed for the direct determination of trace metal ions in human fluids. Under the optimum conditions, the adsorption capacity of La³⁺ and Nd³⁺ on restricted accessed Fe₃O₄@SiO₂@PAR were 33.7 and 36.9 mg/g, respectively.

4.6.8 Capillary microextraction

In 1990, Pawliszyn et al. proposed solid phase microextraction (SPME) [146] as a new pretreatment technique. It integrates extraction, preconcentration and sampling into one step, featuring with simple operation, low consumption of solvents/sample, good reproducibility, high efficiency and can be hyphenated with various detection techniques. It was commercialized by Supelco Corporation in 1993 and has been applied extensively in a variety of fields [147–149]. While the application of SPME in the analysis of trace elements and their species is relatively scarce [150].

Eisert and Pawliszyn [151] proposed another operation mode for fiber-SPME in 1997 – capillary microextraction (CME) – also called in-tube SPME. Figure 4.11 presents a schematic diagram of in-tube SPME combined with LC-MS system [152].

The main difference between fiber-SPME and CME is the coating which is coated on the surface of the fiber for the former one while on the inside surface in the capillary for the latter. Compared with fiber-SPME, CME can be easily online combined with HPLC or CE, improving the producibility; the problem of coating easily swelling or falling off in some organic solvents is overcome, lowering the analytical cost; it can be used for strong polar analytes analysis, widening the application field. The thickness of the extraction coating in CME (0.1–1.5 μm) is far less than that in fiber-SPME (10–100 μm), and the contacting surface between the coating and analytes is larger than that in fiber-SPME, shortening the required time to attain the equilibrium. In CME analysis, sample solution should be clean, otherwise the particles would block the capillary column or the flow channel.

CME can be divided into three operation modes [153], which include open-tubular CME, packed CME and monolithic CME. The application of CME in trace REEs analysis is scarce presently.

Wu et al. [154] prepared a Congo red (CR) modified SWCNTs coated fused-silica capillary for CME of trace La, Eu, Dy and Y in human hair followed by fluorinating assisted (F)ETV-ICP-OES determination. The maximum adsorption capacities of the CR-SWCNTs coated capillary evaluated from the breakthrough curve were 0.8, 0.7, 0.7 and 0.7 $\mu\text{g}/\text{m}$ for La, Eu, Dy and Y, respectively. The proposed method was applied to the analysis of real-world human hair sample, featuring with simplicity, high sensitivity and less sample/reagents consumption. Zhang et al. [155] synthesized an IDA modified poly(glycidyl methacrylate-trimethylolpropane trimethacrylate) [poly(IDAGMA-TRIM)] monolithic capillary and used it for the selective extraction and preconcentration of REEs. Based on it, a novel method of poly(IDA-GMA-TRIM)-based CME on-line coupled to ICP-MS was developed for the determination of ultra-trace REEs in biological samples (urine and serum). Under the optimal conditions, the LODs for REEs were in the range of 0.08 (Er)-0.97 ng/L (Nd) with a sampling frequency of 8.5/h. Cai et al. [156] prepared poly(glycidyl methacrylate-ethylene dimethacrylate) (GMA-EDMA)-Au NPs monolithic capillary, and further modified with mercaptosuccinic acid (MSA). The grafted massive carboxyl groups with good affinity to REEs helped to improve

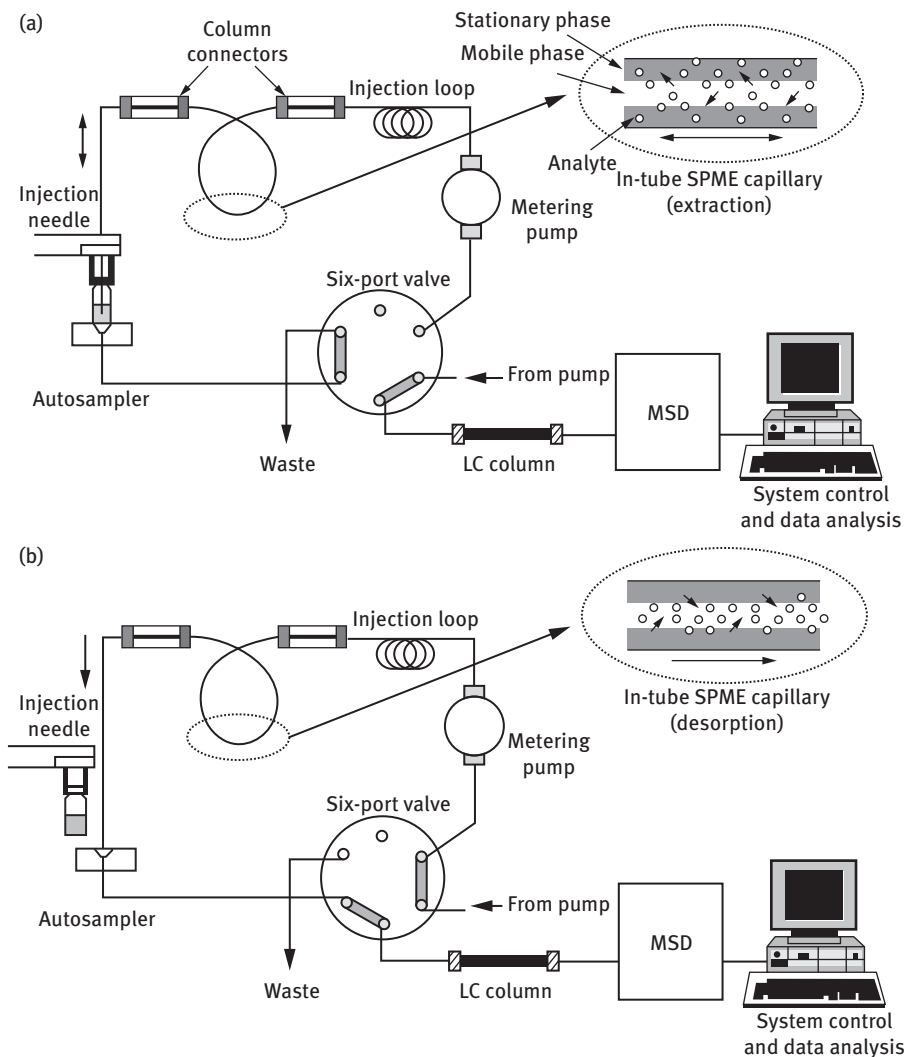


Figure 4.11: Schematic diagram of the in-tube SPME/LC/MS system [152]. (a) load position (extraction phase); (b) injection position (desorption phase).

the adsorption capacity by 3–6.5 times after Au NPs introduction. The monolith is featured with good anti-interference ability and long lifespan with attractive potential for the analysis of REEs in environmental waters (including seawater) and human blood samples with complex matrix.

A novel method of TiO₂ nanoparticles (NPs) functionalized monolithic CME on-line coupling with ICP-MS was developed for the sequential determination of Gd³⁺ and Gd-based contrast agents in human urine samples [157]. The monolithic capillary was

prepared by embedding anatase TiO_2 NPs in the poly(methacrylic acid-ethylene glycol dimethacrylate) (MAA-EDMA) framework. Gd-based contrast agents (e.g., gadolinium-diethylene triamine pentaacetic acid (Gd-DTPA) and Gd-DTPA-bismethylamide (Gd-DTPA-BMA)) and Gd^{3+} display different adsorption behaviors on the monolithic capillary. As shown in Figure 4.12, in the presence of PBS, Gd^{3+} was adsorbed completely

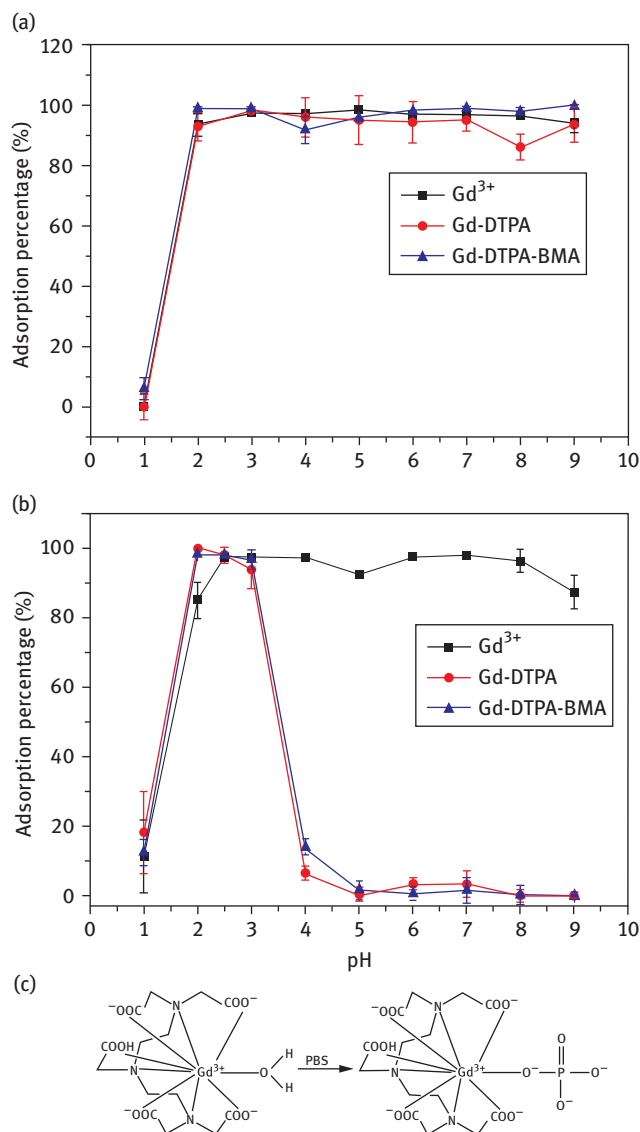


Figure 4.12: Effect of pH on the adsorption behavior of Gd^{3+} , Gd-DTPA and Gd-DTPA-BMA in the absence (a) or presence (b) of PBS, and the formation of the deduced ternary complex (c) [157].

on the poly(MAA-EDMA-TiO₂ NPs) monolithic capillary in a relatively wide pH range (2–9), whereas Gd-DTPA could be retained quantitatively on the monolith under pH of 2–3 and a sharp decrease of adsorption percentage of Gd-DTPA was observed when pH was higher than 4. It was speculated that in the presence of PBS, Gd-DTPA first reacted with PO₄³⁻ to form a ternary complex (structure shown in Figure 4.12) because the interaction between Gd-DTPA and phosphate is stronger than that between Gd-DTPA and TiO₂ NPs. This ternary complex could be easily adsorbed by the prepared poly(MAA-EDMA TiO₂ NPs) monolithic capillary due to the good affinity of TiO₂ NPs to phosphate group at pH 2–3.

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Part II: **Methods for the elemental analysis of rare earths and for the analysis of rare earth containing molecular compounds**

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5 Analysis and speciation of lanthanoids by ICP-MS

Abstract: Inductively coupled plasma mass spectrometry (ICP-MS) is based on the formation of positively charged atomic ions in a high-frequency inductively coupled argon plasma at atmospheric pressure. The ions are extracted and transferred from the plasma source into a mass analyzer operated at a high vacuum via an interface equipped with sampling and skimmer cones. The ions are separated in the mass analyzer according to their mass to charge ratio. The ions are converted at a conversion dynode and are detected by use of a secondary electron multiplier or a Faraday cup.

From an analytical point of view, ICP-MS is a well-established technique for multi-elemental analysis in particular for elements at trace- and ultra-trace levels. Furthermore, methods based on ICP-MS offer simple quantification concepts, for which usually (liquid) standards are applied, low matrix effects compared to other conventional analytical techniques, and relative limits of detection (LODs) in the low pg g^{-1} (part per trillion, ppt) range and absolute LODs down to the attomolar range. For these applications, ICP-MS excels by a high sensitivity which is independent of the molecular structure and a wide linear dynamic range. It has found acceptance in various application areas and during the last decade, ICP-MS is being more and more applied for the detection of rare earth elements particularly in the life sciences.

Due to the fact that all molecules introduced into the high temperature of the plasma in the ion source were completely dissociated and broken down into atoms, which are subsequently ionized, all elemental species information is completely lost. However, if the different species are separated before they enter the plasma by using adequate fractionation or separation techniques, then ICP-MS can be used as a very sensitive element-specific detector. In this chapter, a more detailed discussion of this feature of ICP-MS will be presented with emphasis on the speciation of gadolinium-containing contrast agents.

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5.1 Introduction

Inductively coupled plasma mass spectrometry (ICP-MS) is one of the most successful analytical methods in atomic spectroscopy. It has found widespread acceptance in various application areas including environmental (e.g., drinking, river, sea, and waste water) [1, 2], geological (e.g., trace element patterning), clinical (e.g., determination of trace metals in blood, serum, and urine) [3] and industrial [4] analysis. ICP-MS is a multi-element detection method that offers simple calibration and quantification most often by liquid standards and excels by limits of detection (LODs) in the sub pg mL^{-1} range.

5.2 Fundamentals of ICP-MS

In MS, the fundamental properties of electric, magnetic, and radio frequency (RF) fields are used to separate ions with different mass to charge ratios. The ions to be separated are generated in an ion source which is the inductively coupled high-frequency plasma in the case of ICP-MS. Therefore, most ICP-MS instruments consist of the following components which are schematically shown in Figure 5.1.

- A sample introduction system where the sample is converted to a physical state which is optimized for the function of the ion source. In the case of ICP-MS, sample introduction is most often realized by pneumatic nebulization of a liquid sample.
- A plasma ion source, where ions are generated from atoms by use of external energies from an inductively coupled high-frequency electromagnetic field. In the plasma source, the aerosol is dried, decomposed, dissociated and atomized, excited, and finally positively ionized.
- An interface system, which consists of sampling and skimmer cones and a vacuum fore-pump, by which the ions are extracted from the plasma. This device is also needed to reduce the pressure from the ion source to the vacuum needed in the mass analyzer region.
- A lens system to focus the ions into the mass analyzer.
- The mass analyzer (quadrupole [ICP-QMS], magnetic sector field [ICP-SFMS], time-of-flight analyzer [ICP-TOFMS]) where the ions are separated based on their mass to charge ratio.
- A unit by which the ions are detected (secondary electron multiplier [SEM] or Faraday cup).
- A computer that controls all functions of the mass spectrometer, acquires data and delivers the mass spectrum, where the mass to charge ratios of the ions are represented with their measured intensities.

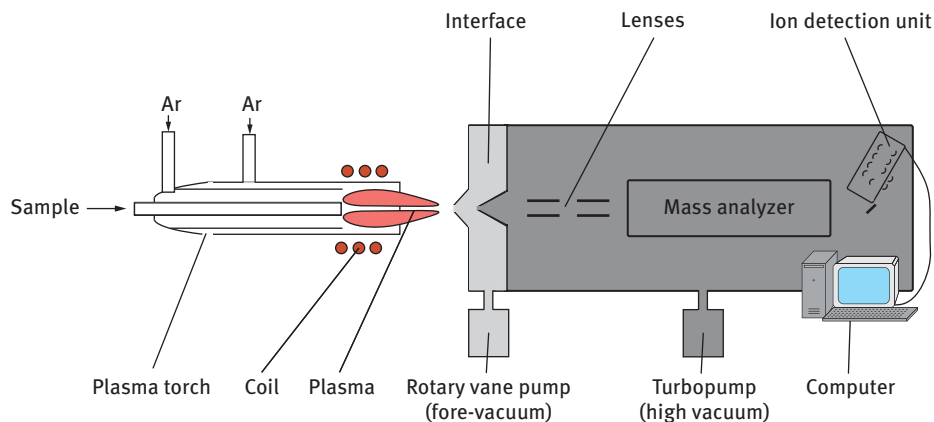


Figure 5.1: Schematic view of an ICP-MS instrument (with courtesy of Frank Bierkandt).

5.2.1 Sample preparation

ICP-MS is a method that is conventionally used for liquid analysis. For this purpose, the sample, in particular solid or particulate materials, has to be converted into a solution from which an aerosol is generated by a pneumatic nebulizer (see Section 2.2). The aerosol is transported continuously by a transport gas (most often argon (Ar)) and a tubing to the plasma ion source, which is operated at atmospheric pressure.

Most often, digestion by use of mineral acids (e.g., HNO_3) at high temperatures and high pressures is required to get solids and medical samples such as body fluids, tissues, and bones into solutions. These mineral acids are often combined with oxidizing reagents (e.g., H_2O_2) in particular if carbon-rich materials have to be digested. Microwave-assisted digestions are generally sufficient to get many environmental and medical relevant materials into clear solutions, which are compatible with the needs of ICP-MS (for more details, see Ref. [5]).

Analyte quantification is commonly carried out by calibration with external single or multi-element standards and sample handling is usually assisted by an auto-sampler to measure up to hundred samples a day and in some routine analytical labs, the ICP-MS instruments are even working overnight. When instrumental drift or matrix effects are expected, an internal standard can be added in liquid form to compensate for intensity drift, as well as transport and ionization effects. The matrix load of an ICP-MS is usually limited to less than $1,000 \mu\text{g mL}^{-1}$ and even at low $\mu\text{g mL}^{-1}$ levels matrix effects have to be compensated. An alternative to internal standards, matrix addition is a laborious but sensible approach if accurate data are needed and higher salt loads can be tolerated, which is the case for rare earth elements (REE). They have to be analyzed in geological or environmental samples at

ultra-trace levels due to the very low natural abundances of all these elements and thus dilution most often should be avoided.

Special care is needed in the case of speciation analysis of gadolinium (Gd)-based contrast agents (GBCAs). To preserve the original species (cholate form) during all sample preparation steps, the common addition of nitric or hydrochloric acids to the samples has to be avoided to prevent the degradation of the chelates.

5.2.2 Sample introduction

The robustness of the ion source and the fact that the ion source is operated at atmospheric pressure enables a large variety of sample introduction systems to be used. The most common samples are in a liquid form and have to be converted into an aerosol. The aerosol is tolerated by the plasma if the droplets are small enough to be vaporized and the water load is not getting too high to affect the plasma properties. Commonly, pneumatic and, in particular, concentric nebulizers are used for aerosol generation (for a more detailed description and additional references, see Refs. [6, 7]).

The most common pneumatic nebulizer consists of a nozzle in front of a concentrically centered capillary containing the analyte solution in which the liquid is accelerated by the Venturi effect using a pressurized nebulizer gas (argon). By the turbulences generated in front of the nozzle, the liquid surface is disrupted and the liquid is dispersed into small droplets which are transported by the nebulizer gas via tubing to the plasma ion source.

Pneumatic nebulizers are typically combined with a spray chamber for the removal of the larger droplets [6–8]. Additionally, cooling of the spray chamber significantly reduces the solvent load of the plasma and as a result, water- and acid-based interferences. An alternative way to reduce the solvent load, which is particularly important if organic solvents are nebulized, is the use of a desolvation system. The desolvation system in most cases consists of a heated selective membrane, through which the gaseous solvent molecules are transported, whereas the dried aerosol is retained in the gas stream and transported to the plasma.

The main drawback of conventional nebulizers is their low efficiency (most often less than 5 %), which means that only a few percent of the sample liquid is injected into the plasma. This limitation can be overcome by the application of high-efficiency nebulizers among which the ultrasonic nebulizer is one of the most successful ones. Micro-concentric pneumatic nebulizers working at extremely low sample introduction rates also achieve higher efficiency (Figure 5.2). They are most often combined with separation systems requiring low mobile phase flow rates (capillary electrophoresis [CE], nano-high-performance liquid chromatography [HPLC]).

Nebulizers and spray chambers manufactured from inert polymers (such as Teflon or PFA) have to be used when aggressive chemicals, such as HF are applied. In

this context, these nebulizers are most often combined with a torch injector tube manufactured from sapphire and cones made from Pt.

Many alternative sample introduction systems have been investigated with the aim of improving the sensitivity, reducing spectral interferences, or handling small volumes of sample. Other sample introduction systems are used in the context of speciation (e.g., chromatographic systems) or for direct analysis of solids (e.g., laser ablation, electro-thermal vaporization).

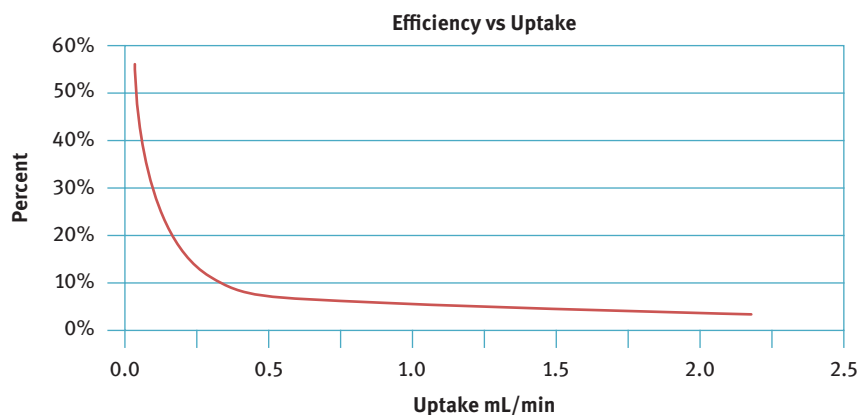


Figure 5.2: The relationship between uptake rate and nebulizer efficiency (the percentage of the sample that reaches the plasma as opposed to going down the drain) (reproduced with permission from Glass Expansion GmbH, Germany).

5.2.3 The ion source

The ICP is one of the most successful analytical ion sources in atomic MS. This plasma is generated electrodeless in an atmospheric pressure discharge gas (argon) by application of high-frequency voltages to an induction coil located at the top of a torch consisting of three concentric quartz tubes. Usually, three different argon flows are used. A relatively low gas flow rate (called inner gas, nebulizer gas, sample gas, transport, or carrier gas) of about 1 L min^{-1} is used for aerosol production of the liquid sample and to transport and inject the aerosol into the hot core of the plasma plume. A much higher flow rate ($10\text{--}15 \text{ L min}^{-1}$) (called outer gas, plasma gas, or coolant gas) is introduced tangentially. This flow of argon thermally isolates the plasma from the outer quartz tube and thus prevents melting. The third flow (argon support gas, intermediate gas, auxiliary gas) is optionally used for the alignment of the plasma in the torch. The outer quartz tube is surrounded by a water-cooled induction coil connected to an RF generator power supply with a frequency of 27 MHz. An oscillating magnetic field induces high-frequency oscillating electrons

and an ion current in a closed circular path, by which the plasma gas is heated to high temperatures (gas-kinetic temperature of 6,000–8,000 K, ionization temperature ca. 7,500 K, excitation temperature of 6,500–7,000 K, electron temperature ca. 10,000 K). The plasma is ignited by a high-voltage spark.

The ICP is thus maintained by inductive heating in the high-frequency electromagnetic field, but an electrical power of up to 1,500 W is required for continuous operation. The injected aerosol travels through a narrow axial channel, surrounded by the high-temperature plasma core forming a donut-shaped structure, where volatilization, atomization, excitation, and ionization of the sample components take place. Predominantly positively singly charged ions are generated from most elements of the periodic table. The fraction of ionization of a given element is usually calculated by use of the so-called Saha–Eggert equation if the electron densities and electron temperatures are known. From this formula, it can be estimated that most elements with first ionization potentials below 8 eV (e.g., lanthanoids) are completely ionized and elements with potentials in a range between 8 and 12 eV (e.g., S, Se, Br, I) are partly ionized. Thus, the mass spectrum acquired during a mass scan consists mainly of isotopes of singly charged elemental ions.

Due to the high temperatures and the high electron densities, the ICP is a very robust electrical flame, which shows only little matrix effects. The fundamental plasma properties and analytical figures of merit are not significantly affected when the sample composition is altered. This is a tremendous advantage over many other analytical methods. Therefore, these plasmas are operated in ICP-optical emission spectrometry (ICP-OES) with quite high concentrations in the percent range; however, due to space charge effects in ICP-MS the maximum concentration tolerated is limited (see Section 2.1).

5.2.4 Interface

As mentioned before, the plasma of the ion source is operated at atmospheric pressure, whereas the mass spectrometer has to be operated under high vacuum conditions. Thus, an interface is required to extract the ions from the plasma and to stepwise reduce the pressure on the way to the mass analyzer. Due to the fact that the interface is in direct contact with the hot plasma, it is usually water-cooled and made of materials with high thermal conductivity and sufficient chemical resistance. It generally consists of two cones, both often made of nickel (Ni): the sampler, which is in direct contact with the plasma and the skimmer cone, which separates the first pumping stage from the second one. In the center of the metallic cone, an orifice (0.8–1.2 mm) is used for the extraction of the ions from the plasma. The second cone (skimmer) is typically pointed and has a smaller orifice. The cones are placed coaxially at a distance of a few millimeters allowing a sequential pressure decrease. When analyzing corrosive solutions or measuring low Ni concentrations, platinum cones are preferred to avoid abrasion of the cone metal and Ni

background, respectively. In order to reduce the effects of electrostatic coupling between the load coil and the plasma discharge – resulting in an electrical discharge between plasma and sampler cone – the load coil is usually grounded at the side facing the sampler cone.

The ions generated in the plasma are sucked into the sampler orifice by the pressure drop between the atmospheric plasma and the low pressure of a few mbar in the first vacuum stage. The ions are accelerated in this first pumping stage to ultrasonic velocities and are picked up by the skimmer by the flow dynamics of the hot expanding argon gas. Behind the skimmer cone, a lens system is arranged for ion focusing.

5.2.5 Lens system

Behind the skimmer, an additional pressure drop is generated by turbo-molecular pumps. Electrostatic fields can then be applied to an electrostatic lens system to accelerate the ions and focus them into the mass analyzer region. For reduction of the noise coming from neutrals and photons, different technical means (ion mirrors, photon stops, Omega-lenses, bent geometries in case of sector field and time-of-flight instruments) are applied to hinder them from reaching the detector.

5.2.6 Mass analyzers

Ions are separated in the mass analyzer based on their mass to charge ratio by using the fundamental properties of electric, magnetic, or RF fields. The most commonly used mass analyzer in ICP-MS is the ICP-QMS. Historically, it was first coupled to an ICP by Robert Samuel Houk in 1980 (for more details, see the famous publication [5]) and was already commercially available a few years later in 1983. Since then, it had become one of the most successful multi-element techniques in atomic spectrometry.

5.2.6.1 Quadrupole analyzer

The quadrupole analyzer usually consists of four cylindrical metallic rods arranged symmetrically around a central axis. The pair of facing rods is supplied by positive RF and direct current (DC) voltages, whereas the second pair is supplied by negative RF and DC voltages. For a given combination of these voltages, only ions of a given single mass to charge value have a stable trajectory and are transmitted through the rod system whereas all others hit the wall or the rods and thus are removed from the ion beam. Ramping the ratio between the RF and the DC voltage

offset allows fast scanning across the whole analytical mass range sequentially. ICP-QMS provides a unit mass resolution all over the mass range, which means that one peak (isotope) is separated from the neighboring peak (isotope) only. They do not reach high-resolution mode, and thus spectral interferences can limit applications of ICP-QMS.

Among spectral interferences, polyatomic species are most problematic, because they are less predictable and depend on the sample composition and the operational parameters of the ICP-MS system. The formation of cluster ions from the most dominant species in the plasma (Ar, H, O, C, N) and the matrix solution (water, mineral acids, salts, etc.) is a major source of polyatomic interferences in ICP-MS.

Other technical means are therefore required to overcome these limitations by spectral interferences. Collision and reaction cell as well as double focusing sector field devices are used to overcome this limitation.

5.2.6.2 ICP-QMS combined with collision and reaction cells

Collision and reaction cells (CRCs) can be used exclusively in quadrupole instruments. In this approach, a pressurized cell usually is located behind the skimmer cone. Two types of gases are used in the cell: inert buffer gases (collision cell) and chemically reactive (reaction cell) gases. In the first case, the buffer gas collides with the ions from the plasma. Big molecular ions, in particular polyatomic molecular species, collide more often with the buffer gas than atomic ions due to the higher impact cross-section. This results in a higher energy loss. At the exit of the collision cell, a retarding field is applied where only the atomic ions have sufficient kinetic energy to overcome the barrier (a process called kinetic energy discrimination (KED)). In the second approach, a reaction gas is applied that either reacts with the analyte element to shift it to an un-interfered mass range or with the polyatomic species to produce molecular ions with a significant shift of the mass. Also, charge transfer reactions are often applied to neutralize the interfering species directly. In modern instrumentation both approaches are accessible. Recently, a new technology was launched to the market, where a quadrupole mass filter is arranged in front of the reaction cell so that only preselected ions can enter the cell for reactions. This approach significantly reduces the number of unwanted reactions in the cell. Due to its similarity to organic mass spectrometers, this new approach is also known as MS/MS approach, because two quadrupoles are used synchronized to each other.

Although very powerful and quite often used, collision and reaction cell devices have a significant disadvantage; the loss of multi-element capability.

5.2.6.3 ICP-sector field mass analyzer

Most of the hardware items of a sector field device are identical to quadrupole devices. This holds true for the sample introduction, the ICP, the interface, as well as the detector and computer system. However, they contain a more complex lens system, an entrance and an exit slit and a magnetic and an electric sector field. The lens system is needed for acceleration of all ions to high energies >8,000 electron volts (eV) and for beam shaping to adopt the circular geometry of the ion beam behind the skimmer to a more linear geometry which fits the shape of the entrance and exit slit (for more details, see Ref. [9]). The high energies are required for optimal function of the magnetic sector, which is used to separate the ions due to their mass to charge ratio. The electric sector is needed to compensate for differences in ion energy, which otherwise can compromise the resolving power of the magnetic field.

In general, sector field instruments (for more details see Ref. [9]) are equipped with up to two single detectors (Faraday cup, secondary electron multiplier, or channeltron detectors) and are usually operated in scanning mode for multi-element analysis. In contrast to this type of sector field instruments, a multi-collector (MC)-ICP-MS is operated in static mode and is equipped with multiple detectors (Faraday cups, multiple ion counting systems, or channel plates). The MC-ICP-MS has the advantage that all isotopes of an element are measured at the same time, which improves the precision of signal intensity measurements by orders of magnitude in comparison to all scanning devices. Due to the fact that MC-ICP-SFMS instruments are mainly applied for isotope ratio measurements, they are not yet applied for REE analysis and thus will be discussed elsewhere in more detail [9–11].

Compared to quadrupole devices, sector field instruments show a higher sensitivity (slope of the calibration graph) at a low resolving power and significantly reduced background due to their bent geometry (less than 1 count per second (cps) in the mass range above 100 Da) and thus lower detection limits are achieved. The main advantage of sector field instruments is the capability to apply a high mass resolving power that separates the spectroscopic interferences from the signal of the isotope of interest by variation of the slit width of the entrance and exit slit.

The resolution of the ICP-SFMS instrument is defined by

$$R = (m/z) / \Delta(m/z)$$

R: mass resolution [without units].

m: nominal mass of measured signal (peak) [should be given as a reference, because the mass resolution of a sector field instrument is constant over the mass range, and thus the peak width (Δm) of a signal increases proportional to mass. This is quite opposite to a quadrupole machine, where the peak width is constant over the whole mass range and thus the resolution increases with increasing mass].

Δm : mass difference between a peak at the nominal mass m and a peak at $m + \Delta m$.

z : absolute charge number of the isotope of interest.

Commercial instruments provide a resolution R of up to 10,000 by which most of the common spectral interferences originating from polyatomic species can be resolved from the isotope of interest. However, it should be mentioned that the sensitivity is indirectly proportional to the resolution; higher resolutions are paid for by a loss in sensitivity. In Table 5.1, typical spectral interferences and the respective theoretical resolution for separation from the analyte isotopes are compiled.

Table 5.1: Mass resolution (R) necessary to separate typical interferences.

Nominal mass (m/z)	Polyatomic species	Analyte isotope	Resolution R
Solvent H_2O and HNO_3			
31	$^{14}\text{N}^{16}\text{O}^1\text{H}^+$	$^{31}\text{P}^+$	968
	$^{15}\text{N}^{16}\text{O}^+$	$^{31}\text{P}^+$	1,458
54	$^{40}\text{Ar}^{14}\text{N}^+$	$^{54}\text{Cr}^+$	2,031
	$^{40}\text{Ar}^{14}\text{N}^+$	$^{54}\text{Fe}^+$	2,088
Solvent HCl			
51	$^{35}\text{Cl}^{16}\text{O}^+$	$^{51}\text{V}^+$	2,572
52	$^{35}\text{Cl}^{16}\text{O}^1\text{H}^+$	$^{52}\text{Cr}^+$	1,671
75	$^{40}\text{Ar}^{35}\text{Cl}^+$	$^{75}\text{As}^+$	7,775
Solvent H_2SO_4			
48	$^{32}\text{S}^{16}\text{O}^+$	$^{48}\text{Tl}^+$	2,519
64	$^{32}\text{S}_2^+$	$^{64}\text{Zn}^+$	4,261
64	$^{32}\text{S}^{16}\text{O}_2^+$	$^{64}\text{Zn}^+$	1,952
65	$^{32}\text{S}^{33}\text{S}^+$	$^{65}\text{Cu}^+$	1,939

From Table 5.1, it can be seen that a resolution of about 4,000 (referred to as medium resolution, MR) is already sufficient to separate most isotopes from polyatomic species. However, the resolution of commercial instruments is often not sufficient to overcome isobaric interferences from isotopes of different elements located at the same nominal mass (e.g., ^{54}Cr and ^{54}Fe) for which a resolution of more than 100,000 (73,900 to separate ^{54}Cr from ^{54}Fe) is required.

5.2.6.4 Time-of-flight mass analyzer

In a “time-of-flight” mass analyzer (ICP-TOFMS), the ions are accelerated in an electric field by a voltage applied to a grounded plate and an ion transparent grid. All ions in the electric field receive the same energy. They are separated according to the difference in time that they need to reach the detector in a fixed distance. After

passing the grid the ions travel in a field-free region with velocities dependent on their mass. Low-mass ions hit the detector first, followed by heavier ions. Thus, the detector registers ion signals with μs time resolution. Depending on manufacturer up to 30,000 full mass spectra can be recorded per second. These instruments are therefore very useful for measurement of very short transient signals.

A specialized ICP-TOFMS – well known under the name “mass cytometer” – is schematically shown in Figure 5.3. This instrument [12] was introduced to the market as a trademark “CyTOF™” by the company DVS Sciences Inc. (now Fluidigm, CA, USA). The instrument addresses the challenges of a special detector for biological and medical cell flow cytometry.

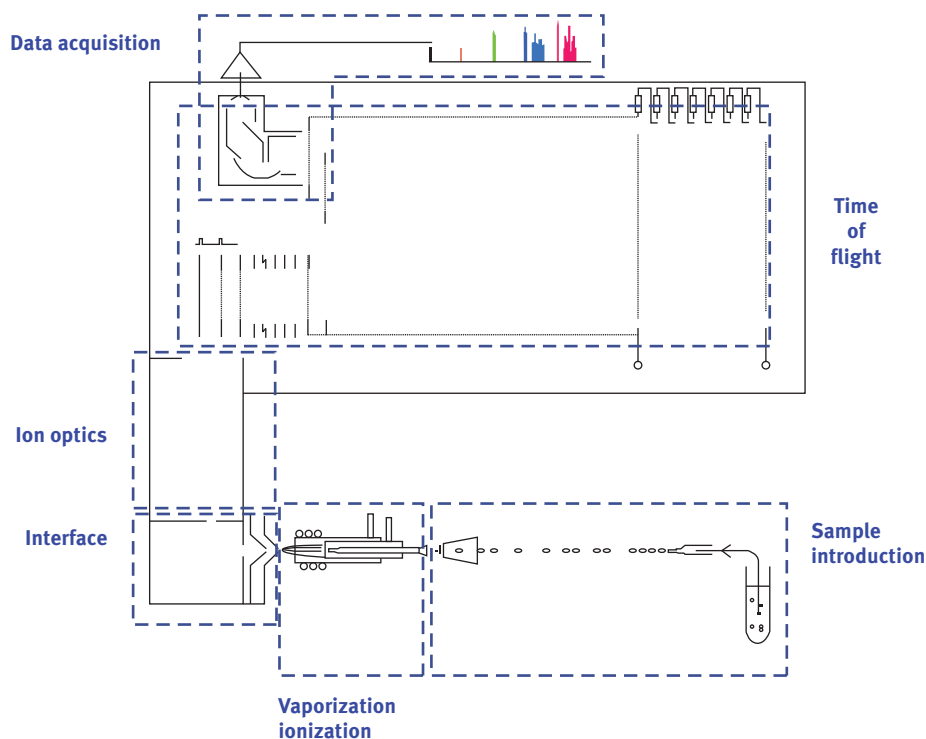


Figure 5.3: Schematic set-up of a mass cytometer (see Ref. [12]).

It employs a fast ICP-TOFMS with an integral electrostatic quadrupole deflector minimizing the exposure of ion optics and detector to unionized particles and an RF- quadrupole ion guide is used as a low-mass cut-off filter ($m/z < \text{approx. } 82$) rejecting abundant interfering plasma species (for instance Ar^+ , ArO^+ , Ar_2^+). But this mass cut-off also limits the range of detectable masses to >82 Da with a mass resolution $R = 600$. The sample introduction of the CyTOF™ is based on a concentric

nebulizer designed and used to nebulize a cell suspension with a sample uptake rate of $<60 \mu\text{L min}^{-1}$. The nebulizer is connected to a heated spray chamber, to which a make-up argon gas flow (typically at 0.7 L min^{-1}) is supplied via a mass flow controller. In the spray chamber, the droplets with embedded cells are dried (all water and droplets without cells are vaporized) and transported to the ICP in a laminar flow. The instrument allows multi-element analysis of a few thousand single cells just in the time frame of a second.

This instrument opens a new door for the application of lanthanoid elements. A whole article (see: Novel Applications of Lanthanoids as Analytical or Diagnostic Tools in the Life Sciences by ICP-MS-based Techniques) is dedicated to this new technology, because lanthanoids are applied in this application for tagging of antibodies to detect biomarkers in highly multiplexed immune-assays, and is therefore of high interest in clinical diagnosis and cell biology.

5.2.7 Detector and computer

Most ICP-MS instruments are equipped with an ion-to-electron conversion dynode and an electron multiplier (discrete dynode detector or channeltron), which can be operated in analogue or counting mode. That allows coping with a large variation in the number of ions that reach the detector per unit of time (count per second, cps) so that a linear dynamic range of up to 9 orders of magnitude can be achieved. For sector field instruments, an additional detector, a Faraday cup, is optional which allows extending the linear dynamic range even to 12 orders of magnitude.

Finally, a computer, which controls all functions of the mass spectrometer, the generator, and the vacuum system, acquires data and delivers the mass spectrum, where the mass to charge ratios of all measured isotopes are represented by their intensities. Most instruments provide all software needed for the calculation of mean and integrated intensity values and standard deviations of the measured intensities. From these values, calibration, drift correction, and quantification of specific elements can be performed. The operator selects all isotopes needed for analysis and arranges the samples in a given sequence defined in the software and finally evaluates the results of the whole sequence with the software.

Specialized software for peripherals, in particular special sample introduction systems, as well as for performing time-resolved measurements, for instance in hyphenated techniques, is also usually provided by the instrument manufacturers.

5.3 Analytical figures of merit

All multi-element methods in atomic spectrometry are in principle suited for the analysis of lanthanoids. However, analysis by ICP-OES of lanthanoids, in particular REE, can be problematic due to very line-rich emission spectra causing significant spectral interferences. In comparison, the mass spectrum in ICP-MS is quite simple and consists only of peaks of all isotopes of the element of interest. In the mass range of the REE, polyatomic molecules are not observed and thus ICP-MS is often applied in industry, geology, and life sciences. Concerning spectral interferences, the main limitation of REE analysis is oxide formation which is rather a big problem compared to other elements. Careful tuning allows reducing this value below 1 %, but if all REE are present at similar concentrations, as is the case for many geological applications, then this problem can become an important issue.

For most of the applications, in particular for industrial quality and purity control of starting products, the oxide problem can be neglected. The LODs are quite low for lanthanoids because their natural background is rather low. However, the LODs strongly depend on the application and thus will be discussed in more detail in the application section of this book.

The analysis of lanthanoids, and in particular of REE, is a general topic of this book, thus different applications will be presented where different analytical methods are applied for multi-element analysis in different matrices (environment, geological samples, new materials) and of course, ICP-MS can be applied for all these applications – a critical review is presented elsewhere [13].

In the next sections, we want to focus on a quite new application of ICP-MS where this method is used for a speciation analysis mainly of Gd-based contrast agents in environmental waters [14].

5.4 Speciation of Gd-based contrast agents

Speciation has been defined by the International Union for Pure and Applied Chemistry (IUPAC) as “the analytical activity of identifying and/or measuring the quantities of one or more individual chemical species in a sample; the chemical species are specific forms of an element defined as to isotopic composition, electronic or oxidation state, and/or complex or molecular structure; the speciation of an element is the distribution of an element amongst defined chemical species in a system.” [15].

The most important tool for speciation studies of metals is the combination of a separation and/or a fractionation technique with ICP-MS, and most often the ICP-MS instrument is only used as a metal-specific detector, which provides a time-resolved intensity measurement for the isotope of interest. The compound of interest then is identified by standards having the same retention time and if standards are available, they also can be used for calibration, just to get quantitative results.

Different separation and fractionation techniques are described in the literature, and their selection depends strongly on the compounds of interest. So far, the most common separation techniques applied in ICP-MS couplings are HPLC, GC, and CE. They allow speciation analysis aiming to solve analytical problems in the life sciences and environmental research.

ICP-MS, by itself or hyphenated to separation techniques, is a powerful tool for the analysis of contrast agents for magnetic resonance imaging (MRI).

MRI has become the most powerful imaging technique for the non-invasive examination of human anatomy, physiology, and pathophysiology. It allows high spatial resolution and the ability to distinguish soft tissues and with the use of contrast agents, the contrast of images is improved that led to the development of new imaging protocols. The first contrast agent approved by the Food and Drug Administration (FDA) had the trade name Magnevist[®] (Schering AG, Germany) and comprised paramagnetic gadolinium (Gd) in a chelate form. In subsequent years, various paramagnetic contrast agents based on metal ions such as gadolinium, manganese, and superparamagnetic iron oxide nanoparticles have been developed with Gd-based contrast agents (GBCA) being the most frequently used. Since the Gd ion is highly toxic for humans, accumulates in bone, liver, and spleen and forms insoluble hydroxides and phosphates at physiological pH, it cannot be administered in its ionic form. Therefore, it is complexed with polyaminocarboxylates to produce the water-soluble, thermodynamically-stable, and kinetically-inert chelates that offer safe application and fast excretion. The strategies of designing stable GBCA ligands are discussed in detail in Ref. [16].

Nine different GBCAs are clinically approved and are applied in about 30% of all clinical MRI studies. These GBCAs are quite similar in terms of safety, efficacy, biodistribution, mechanism of action, and pharmacokinetic behavior. Based on chemical structure, GBCAs can be classified into open-chain (linear) and macrocyclic chelates as shown in Figure 5.4. According to the number of carboxylic groups, ionic or non-ionic complexes are formed. These metal complexes are characterized by their exceptionally high thermodynamic stability constants [17]. Generally, macrocyclic chelates have more desirable kinetics of decomplexation compared to their linear counterparts. The dissociation half-lives ($t_{1/2}$) of the three macrocyclic GBCA (Gadovist[®], Dotarem[®], ProHance[®]) were estimated under test conditions to be 1000 years at pH 7.4 [17, 18] but might be substantially shorter under physiological conditions e.g., with competing salts [19]. Because of their similar extracellular distribution, administration of any of the contrast agents results in the same diagnostic information. The only exception is cartilage where the distribution of anionic agents is lower than neutral agents because of repulsion from the negatively charged glycosaminoglycans [20].

GBCAs are administered intravenously, eliminated rapidly by the kidneys, and excreted unchanged in the urine. Due to the concentration level in which the contrast agents are administered (about 1 g kg⁻¹ body weight) and the demand for detailed information even in low concentrations, an analytical method with low

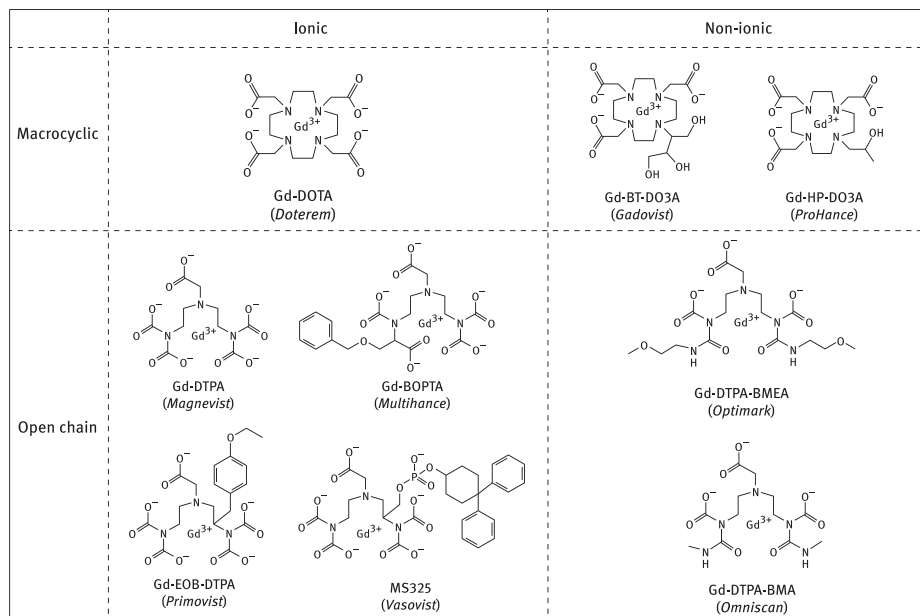


Figure 5.4: Structures of the Gd complexes employed as MRI contrast agents. The chelates can be classified into ionic and nonionic complexes and into complexes with linear (open chain) and macrocyclic ligands.

detection limits is required for the analysis of Gd in the human body fluids. ICP-MS is often used for this kind of studies.

As described in Section 2.1 sample preparation is necessary for most ICP-MS applications, especially for samples with a high matrix content such as human body fluids. Many studies in the past included an acid-based digestion step in their procedure to free samples from unwanted organic compounds. Although Gd is not normally considered as a contaminant easily picked up from the environment, sample preparation has to be carried out with care. Analysis of blood and urine samples for Gd with ICP-MS has been shown to be reproducible with high precision. ICP-MS has been successfully employed in several studies investigating the excretion and pharmacokinetics of contrast agents [21].

The clinical studies have demonstrated that Gd chelates are excreted unchanged. However, the discovery of nephrogenic systemic fibrosis (NSF), a rare but fatal cutaneous disease that has been linked to these compounds [22, 23], demonstrated the need for further investigations concerning the total concentration of Gd (using ICP-MS) as well as its spatial distribution within tissues using imaging techniques such as laser ablation coupled to ICP-MS (LA-ICP-MS). In this respect, potential species transformations within the patient's body came especially into focus. Because analytes are completely ionized in the plasma, ICP-MS only detects Gd signals without molecular information. The analysis strategy needed to be extended for the characterization of the respective Gd species.

Hyphenation to a separation system is the method of choice. The coupling of HPLC to mass spectrometers has in particular been the focus of researchers for speciation analysis. The strategy and methods employed for speciation are summarised in Figure 5.5.

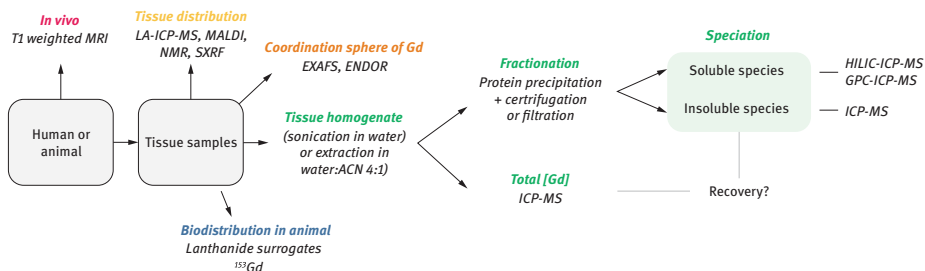


Figure 5.5: The strategy and methods used in the speciation of GBCAs. Abbreviations: ACN: acetonitrile; ENDOR: Electron Nuclear Double Resonance; EXAFS: Extended X-ray Absorption Fine Structure; GPC: Gel Permeation Chromatography; NMR: Nuclear Magnetic Resonance; SXRF: Synchrotron X-ray Fluorescence. (reproduced with permission from Ref. [24]).

All Gd chelates that are being used as the active ingredient in contrast agent formulations can be separated on a range of HPLC columns. As the complexes are highly polar or even ionic, finding a suitable column is crucial. The type of stationary phase determines its ability to separate analytes of different nature. Hydrophilic interaction chromatographic (HILIC) stationary phases have been applied for the separation of the complexes with great success.

HILIC columns can consist of any polar material and several surfaces, including for example amide- or silanol-bonded phases. The Gd chelates have been separated on zwitterionic bonded phases with great efficiency. The separation mechanism is described as hydrophilic partitioning combined with ionic interactions. Eluents are similar to reversed-phase chromatography, often based on acetonitrile or methanol.

Other stationary phases that have been used for contrast agent separation are porous graphitic carbon, C₁₈, as well as silica-based gel-filtration columns and size-exclusion columns. Many of these columns, however, were generally not suitable for the simultaneous separation of all available Gd complexes, but only for two or three of the complexes.

Hyphenation of HPLC systems to an ICP-MS requires an interface. In the simplest case, fitting tubing for the transfer of the HPLC outflow directly into the nebulizer of the ICP-MS is sufficient. When the flow is very high, a splitting might be necessary. Often, the addition of oxygen is necessary after nebulization. Common ICP-MS instruments tolerate about 2 % organic solvent. Higher percentages overburden the plasma and the plasma extinguishes or carbon depositions on skimmer and sampler cones can cause signal drift effects. The addition of oxygen results in the reaction of the organic content to carbon dioxide. Alternatively, desolvation system could be used to reduce the solvent load. The use of common organic solvents like acetonitrile or methanol in HPLC characteristic percentages is therefore possible.

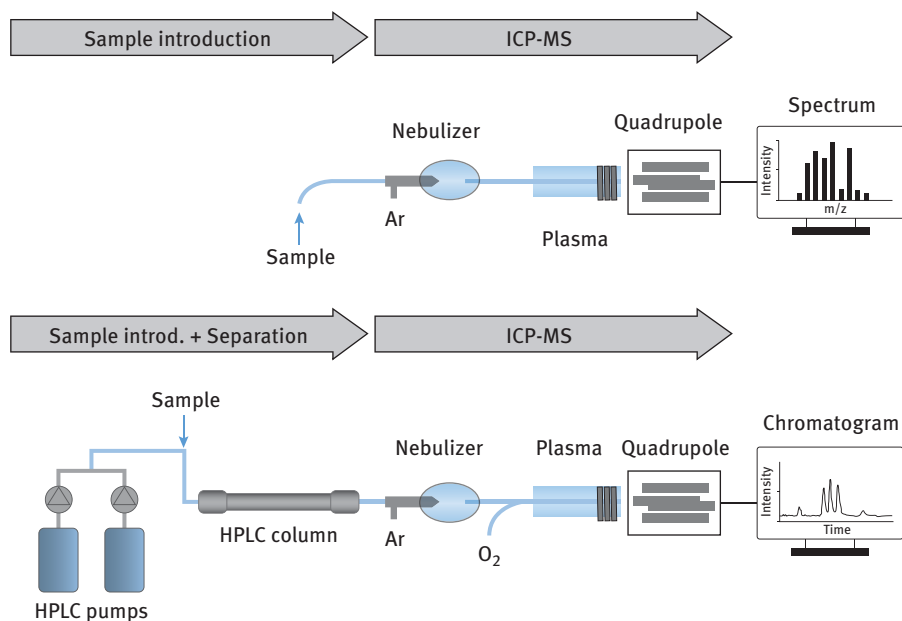


Figure 5.6: Schematic of direct sample introduction into an ICP-QMS (top) and hyphenation of an HPLC system to an ICP-QMS (bottom).

Figure 5.6 shows the difference between a common ICP-QMS set-up for the analysis of Gd concentrations in directly introduced samples as described in Section 2.2 and an HPLC system hyphenated to an ICP-QMS. When the sample is introduced directly into the plasma, a spectrum is recorded and the intensity documented. The concentration of the analyte can be determined with the intensity of the selected isotope and respective calibration measurements as described in Section 3.

In the HPLC system, two pumps provide a mixture of two solvents for chromatographic separation. The sample is introduced into the flow which then enters the column. On the column, the analytes are separated. At their respective retention time, the analytes exit the column and are being transferred with the HPLC flow into the nebulizer and subsequently into the plasma. The plasma ionizes all analytes, but due to the distinct retention time and transient signal recording, the chromatographic peaks can be assigned to the respective substance. This is done by comparing the chromatogram of the sample with chromatograms of standard solutions with known analyte composition and concentration that were run under the same conditions. Analytes in the samples can then be identified by comparing retention times which are specific for individual molecules.

Figure 5.7 gives an overview of different analytical methods for Gd quantification and speciation, respectively.

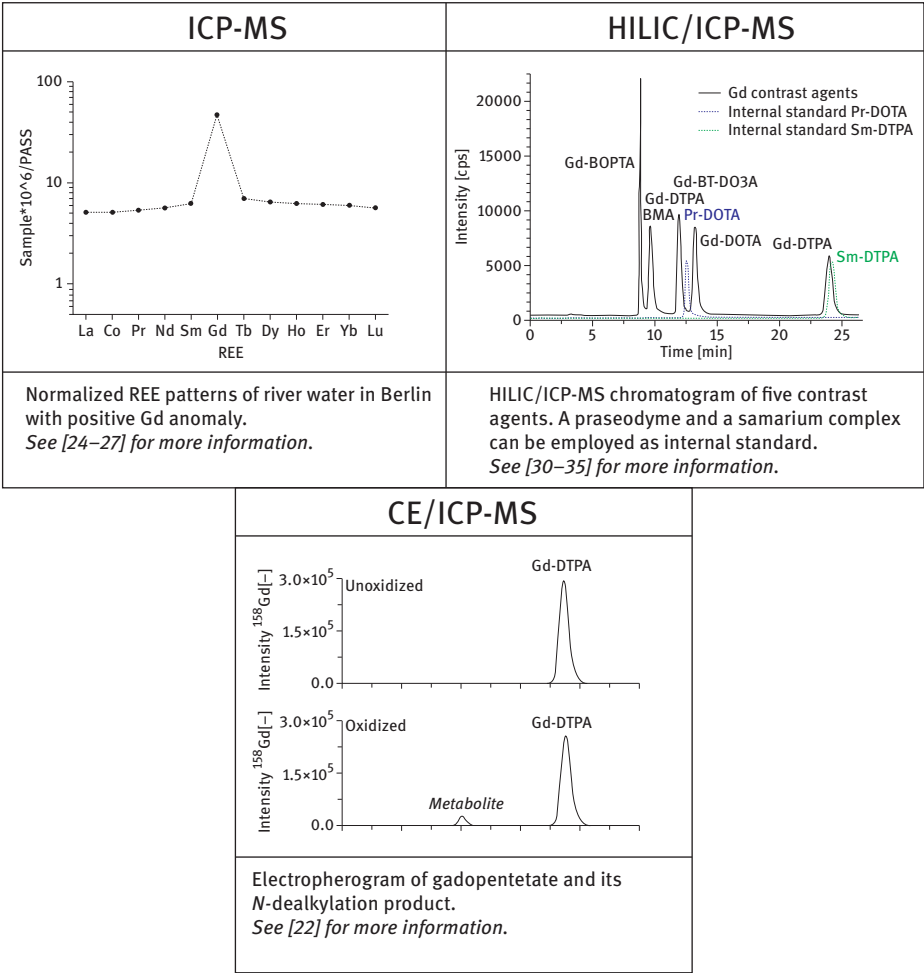


Figure 5.7: ICP-MS was employed for the determination of rare earth element concentration in river water. A chromatogram and an electropherogram show the power of separation techniques hyphenated to ICP-MS for Gd species analysis. For more information, see references ¹ [25–28], ² [29–34] and ³ [35].

5.5 Analysis of Gd-based contrast agents in medical samples

The contrast agents are excreted rapidly and especially fast in the first few hours after administration. Excretion monitoring and the assessment of pharmacokinetics were the first studies carried out with ICP-MS. The excretion can be monitored well with the procedure mentioned above. Elimination rates can be determined and total

excretion from the patient's body could be confirmed. In comparison to other analytical methods such as ICP-OES or total reflection X-ray spectroscopy, ICP-MS exhibits the necessary low detection limits for full monitoring of Gd concentrations.

ICP-QMS has also been applied for the analysis of Gd in tissues, bone, fingernails, and hair. The high sensitivity of the method showed great potential for accurate pharmacokinetic studies down to very low concentration levels in a wide range of sample matrices [36–38].

With the ability for speciation analysis and therefore the distinction between different Gd species, several studies concerning the potential of contrast agent transformation were carried out. The first analysis of urine samples of an MRI patient using HPLC/ICP-QMS showed that the injected Gd-based contrast agent, gadopentate, was excreted fast, undissociated, and almost quantitatively (>99 %). The separation of free Gd ions and gadopentetate was carried out with a size-exclusion chromatographic column [39]. The assessment of complex stability identified a difference between linear and macrocyclic ligands. HPLC/ICP-QMS analysis detected Gd ions in human serum samples of chelates with linear ligands, indicating their release from the complex [40]. Similar results were found in a study concerning the potential transmetalation of the complexes with iron and zinc ions. Transmetalation and the associated release of toxic Gd ions were shown to take place in samples with Gd complexes with the less kinetically stable linear ligands but not in samples with macrocyclic ligands which remain intact (Figure 5.8). These results were shown by the complementary employment of HILIC/ICP-QMS and HILIC hyphenated to electrospray ionization (ESI)-MS [41]. The combination of the two analytical methods was also successfully employed for the investigation of metabolic reactions of the contrast agents. Electrochemical simulation of the oxidative metabolism and subsequent analysis of the respective samples utilizing HILIC/ICP-MS and HILIC/ESI-MS indicated a ligand dealkylation and therefore destabilization of the complex. The same study employed another separation technique hyphenated to ICP-QMS to achieve more information; ionic reaction products, especially Gd ions, were investigated using CE/ICP-QMS [35].

ICP-MS has been used to evaluate the total amount of Gd in human bone and brain samples from patients with normal renal functions. The study revealed that Gd deposition in bone is much higher than in the brain and is more pronounced for linear GBCA in comparison to macrocyclic GBCA [43, 44].

The analysis of a skin biopsy sample from a suspected nephrogenic systemic fibrosis patient was carried out by LA-ICP-QMS and HILIC/ICP-QMS. The complementary results revealed the presence of the intact Gd complex that had been administered 8 years before the analysis [45].

Due to the cumulative evidence of deposition of Gd in tissue, the recent recommendations by the FDA [46] and the European Medicines Agency (EMA) [47] are to limit the clinical use, even market withdrawal, of linear GBCAs.

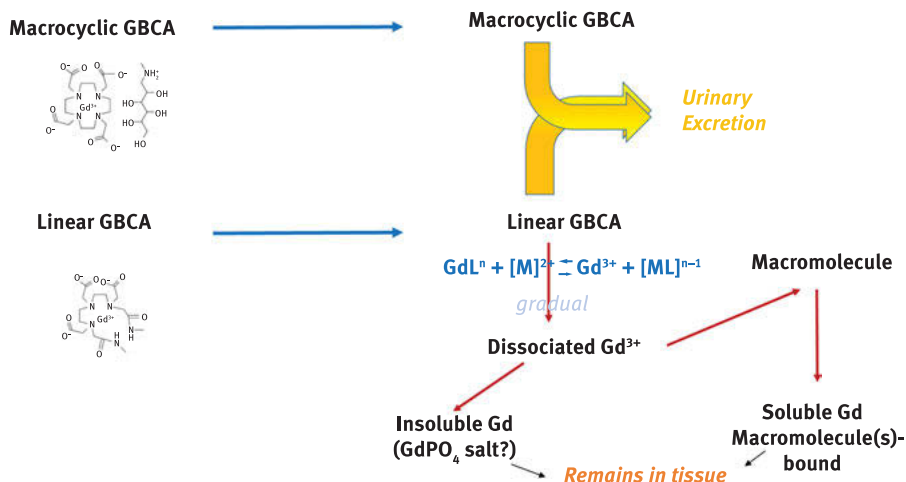


Figure 5.8: The probable in vivo behavior of linear and macrocyclic GBCAs. Abbreviations: GdL: chelated Gd; M: endogenous metal; ML: chelated metal. (reproduced with permission from Ref. [42]).

As can be seen from the presented studies, ICP-MS is a powerful tool for the investigation of contrast agents and their behavior in the human body. It is very important, however, to choose the appropriate analytical strategy corresponding to the objective of the study. The hyphenation of separation techniques to ICP-MS is most often necessary for species identification.

HPLC/ICP-MS will undoubtedly continue to be one of the most important analytical techniques for the detailed investigation of contrast agents as well as a whole range of other (metallo-)drugs. The constant development of new stationary phases as well as the constant improvement of ICP-MS detection limits will encourage speciation analysis of pharmaceuticals in the future.

5.6 Imaging of Gd-based contrast agents in tissues

The spatial distribution of GBCAs within tissues is of primary safety concern. Besides, it can reveal the potential correlation between Gd deposition and histopathological tissue changes as well the potential co-localization of Gd with other elements. Laser ablation – inductively coupled plasma – mass spectrometric imaging (LA-ICP-MS) is an important imaging tool for the investigation of GBCA distribution in tissues and to overcome the relative insensitivity of MRI. Owing to its high sensitivity, accuracy, multi-elemental analytical capabilities, and large linear dynamic range, LA-ICP-MS is the method of choice for the precise investigation of the distribution of GBCAs in various tissue samples.

5.6.1 Brain

GBCAs are considered safe, effective, and classically believed not to cross intact blood-brain barrier (BBB). Nevertheless, inspired by the recently discovered link between nephrogenic systemic fibrosis and GBCA, the long-term safety of GBCA, especially when administered repeatedly, has become a hot topic in radiology. Gadolinium depositions have been found in several organs, especially bone and brain, not only for patients with impaired kidney function but also for healthy people. Since the clinical impact is not clear yet, there is a strong need for further research to identify localization and mechanisms of gadolinium depositions in the brain (chelated or unchelated) as well as to gather knowledge about long-term consequences as repetitive MRI is performed for clinical decisions and trials. The proposed mechanisms for gadolinium or GBCA uptake into the brain are shown in Figure 5.9.

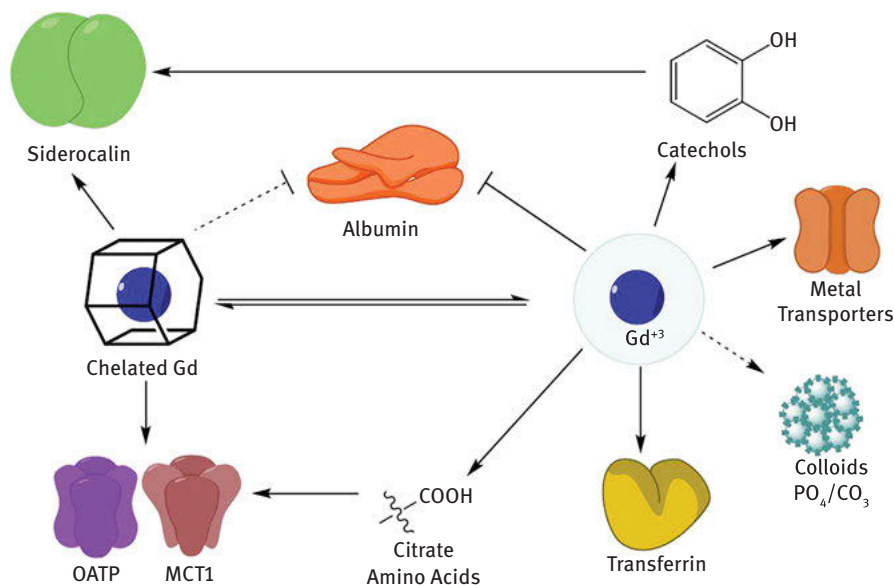


Figure 5.9: Proposed mechanisms for Gd or GBCA uptake into the brain. Binding targets of Gd or chelated Gd associated with uptake are indicated by an arrow, and processes that limit uptake (i.e., binding to albumin) are denoted by a bar. Abbreviations: MCT1: Monocarboxylate Transporter 1; OATP: Organic Anion-Transporting Polypeptide. (reproduced with permission from Ref. [48]).

LA-ICP-MS has been used to investigate the distribution of linear and macrocyclic GBCAs in rat brains. The results showed local accumulation of Gd only after the administration of linear GBCAs although no histological changes in the brain have been detected [49]. However, human post-mortem case studies have revealed the local deposition and concentration of Gd originating from macrocyclic GBCAs in the cerebellum that had seemingly

intact BBB and no evident signal changes by MRI and the potential time-dependent wash-out of macrocyclic GBCAs from the brain. The data also demonstrated the co-localization of Gd with elements such as phosphorus, copper, iron, and zinc (Figure 5.10) which corroborates the hypothetical transmetallation reactions [50, 51] (for more details, see the critical review Ref. [42]).

It has to be emphasized that neither signs of adverse health effects nor morphological changes have been linked to Gd deposition in the brain. Nevertheless, further research needs to be conducted to study the potential mechanisms underlying Gd deposition and the long-term adverse health effects especially in patients with neurological diseases with an impaired BBB e.g., multiple sclerosis.

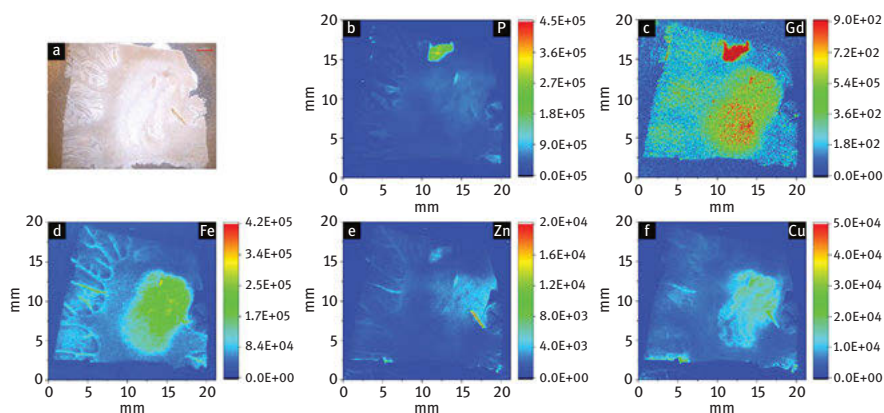


Figure 5.10: Images of cerebellum of a patient who received the macrocyclic GBCA, Gadovist®, 2 weeks before death. a) Light image of an autopsy section through the cerebellum. b-f) LA-ICP-MS element distribution maps of P, Gd, Fe, Zn, and Cu. (modified with permission from Ref. [51]).

5.6.2 Other tissues

The spatial distribution of GBCAs in histological sections of human skin and rodent skin and kidneys has been demonstrated using LA-ICP-MS and was correlated with *in vivo* MRI [49, 52, 53]. However, LA-ICP-MS doesn't provide any structural information about the analytes. Therefore, matrix-assisted laser desorption/ionization – mass spectrometry (MALDI-MS) has been used for the analysis of the spatial distribution of different chemical forms of the Gd-based analytes. In contrast to LA-ICP-MS, MALDI-MS allows repetitive measurements of the samples as the sample is not consumed. At the same time, the sample preparation for MALDI-MS doesn't usually interfere with LA-ICP-MS which allows the same sample to be analyzed by both techniques with MALDI-MS analysis performed always first. MALDI-MS has shown the distribution of GBCA in mice liver tissues after the administration of linear GBCA and employed fragmentation

experiments to confirm the identity of the analyte [54]. Another study demonstrated in situ quantification of the GBCAs with high spatial resolution using MALDI-MS after in vivo MRI. The results of the MRI and MALDI-MS were in agreement [55].

The complementarity of LA-ICP-MS and MALDI-MS imaging has been demonstrated by the successful detection and localization of the macrocyclic GBCA, Gadovist™, in mice organs such as heart, kidney, and liver. The MALDI-MS data revealed the co-localization of the Gadovist™ $[\text{Gd}(\text{BT-DO3A})+\text{H}]^+$ and free chelate $[(\text{BT-DO3A})+\text{H}]^+$ and the LA-ICP-MS images have confirmed that Gd distribution [56]. The complementary MALDI-MS and LA-ICP-MS images of Gadovist™ distribution in the heart, kidneys, and liver are shown in Figure 5.11. In addition, MALDI-MS measurements didn't detect any

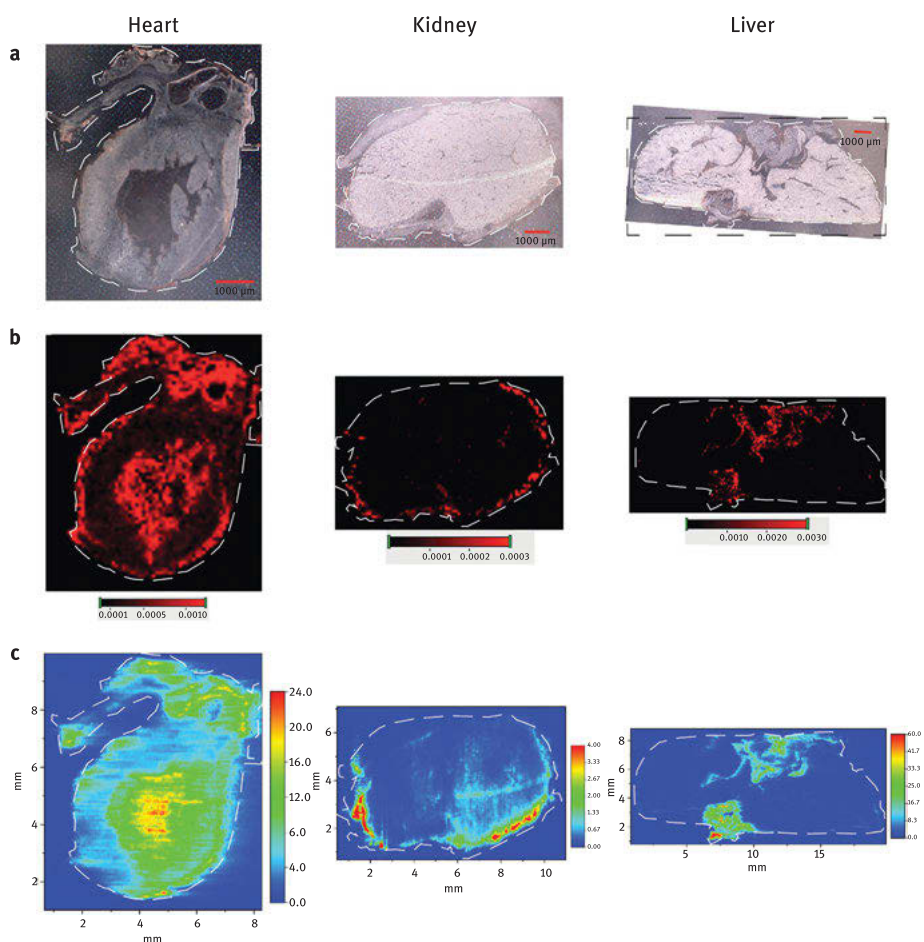


Figure 5.11: Distribution of Gadovist™ in mouse heart, kidney, and liver tissues. a) Optical images. b) MALDI-MS images of the chelated form $[\text{Gd}(\text{BT-DO3A})+\text{H}]^+$. c) Corresponding LA-ICP-MS images showing the distribution of Gd. (reproduced with permission from Ref. [56]).

degradation or transmetalation products of Gadovist™ which supports the hypothesis that the macrocyclic GBCAs remain intact. The high sensitivity of LA-ICP-MS allowed the detection of Gd deposition in mice brain which was not detected by MALDI-MS.

5.7 Analysis of Gd-based contrast agents in environmental samples

A second challenge concerning Gd-based MRI contrast agents was the discovery of high Gd concentrations in surface waters. In an extensive study, rivers, tap water, seawater as well as the effluent of a wastewater-treatment plant and a hospital were sampled. The concentrations of REEs, determined by ICP-QMS, were normalized to post-Archaeon Australian Shale and showed a distinct Gd anomaly that indicated its anthropogenic nature [25]. Many studies were carried out since, all with ICP-QMS, all showing a similar pattern. Positive Gd anomalies ranging between 1.5 and 240 pmol L⁻¹ were exposed in many rivers that run through populated areas [26–28]. In sharp contrast, rivers in thinly populated areas did not show Gd anomalies [25]. The Gd source was soon to be traced back to the employment of MRI contrast agents [25]. Effluents of wastewater treatment plants were analyzed with ICP-SFMS and significant output of Gd by the plants was proven. A balancing of Gd input and output with ICP-SFMS, employing isotope dilution analysis to avoid matrix effects, showed that only about 10 % Gd is removed during treatment [57, 58].

In most studies, sample preparation consisted of filtration and acidification before ICP-QMS analysis. For an even more efficient determination of trace levels of Gd in natural water samples, a pre-concentration method based on solid-phase extraction was developed by Raju et al. A C₁₈ phase coated with bis-(2-ethylhexyl)-phosphate yielded in hundredfold-Gd enrichment. Recovery for several Gd complexes was >95 % [29].

Due to the toxicity of the un-complexed Gd ion, studies soon focused on the investigation of the present Gd species. Wastewater treatment plant effluent was analyzed complementary with ICP-QMS and HILIC/ICP-QMS. The results showed that the complexes are mostly intact. However, total concentrations determined by ICP-QMS were higher than the concentration of complexed Gd determined with HILIC/ICP-QMS, indicating species transformation [30].

The dilution of Gd discharged by a wastewater treatment plant into the adjacent channel was monitored utilizing ICP-QMS. The highest concentration was found close to the plant outlet as expected. Already after 2 km, the Gd concentration was constant [31]. Samples from a nature reserve into which the effluent from a wastewater-treatment plant enters the environment were examined by HILIC/ICP-SFMS. Samples were introduced as dry aerosol generated by desolvation, a process that improved detection limits for all major Gd complexes to well below 0.1 nmol L⁻¹.

Several contrast agents were determined and the mass balancing showed that the contrast agent concentration accounts for about 80 % of the total Gd concentration [32]. The analyte enrichment through surface evaporation enhanced the ability to analyze samples with very low Gd concentrations. Lake water samples were gently heated by infrared light by Raju et al. HILIC/ICP-QMS analysis of the samples detected Gd complex concentrations in the ng L^{-1} range [33].

Gd complexes are not only found in surface waters; the analysis of tap water samples with HILIC/ICP-QMS proved the presence of several of the chelates in river-bank filtration water. The application of a praseodymium complex as an internal standard successfully corrected intensity drifts as well as changes in sample volume and matrix effects [34].

HILIC/ICP-QMS was also an appropriate analytical technique for the investigation of the uptake of GBCAs by plants. The complexes could be extracted from cress plants that were exposed to the contrast agents. The highest Gd concentration relative to the concentration in the growing solution was observed in the leaves. Lower concentrations were determined in stem and roots, indicating a concentration gradient. Speciation analysis was important for these experiments to demonstrate that Gd is transported from the roots to the leaves in the complex form [31]. An overview of studies employing different HPLC columns for the separation of Gd complexes is presented in Table 5.2.

Table 5.2: Overview of different studies employing different HPLC columns for the separation of Gd complexes as well as different ICP-MS systems. The detection limit (LOD) is presented for five of the most used and most investigated Gd contrast agents [34].

Method		LOD in pmol L^{-1} (absolute mass in fmol)				
		Gd-BOPTA	Gd-DTPA	Gd-DOTA	Gd-DTPA-BMA	Gd-BT-DO3A
Lindner et al. [34]	ZIC-cHILIC-ICP-QMS	14 (0.14)	13 (0.13)	14 (0.14)	22 (0.22)	19 (0.19)
Lindner et al. [31]	ZIC-HILIC-ICP-QMS	400 (2.00)	250 (1.25)	310 (1.55)	260 (1.30)	390 (1.95)
Birka et al. [45]	HILIC-ICP-SFMS (desolvation nebulizer)		90 (0.18)	100 (0.20)		80 (0.16)
Telgmann et al. [41]	HILIC-ICP-SFMS	830 (1.66)	830 (1.66)	830 (1.66)	830 (1.66)	830 (1.66)
Raju et al. [33]	ZIC-HILIC-ICP-QMS	130 (0.65)	170 (0.85)	110 (0.55)	120 (0.60)	150 (0.75)
Künnemeyer et al. [30]	ZIC-HILIC-ICP-QMS	1,000 (4.00)	1,000 (4.00)	1,000 (4.00)	1,000 (4.00)	1,000 (4.00)

5.8 Summary and outlook

ICP-MS is a powerful tool for the analysis of lanthanoids in various matrices. This method will always be applied if multi-element analysis of as many as possible lanthanoids is required with the lowest limit of detection.

Concerning speciation, the determination of Gd concentrations in environmental samples will remain a focus for future research in analytical chemistry. In particular, the question of how far a bio-enrichment can occur in the biosphere of aquatic compartments has to be answered. The application of MRI GBCAs will continue and no sewage treatment stage is in sight to prevent Gd from reaching surface waters. The improvement of ICP-MS detection limits through instrument upgrades, advanced pre-concentration methods, or enhanced sample introduction systems, will be of major interest for environmental studies because of the low Gd concentration in many samples. This will be especially important for speciation analysis to give a detailed overview of the contrast agent behavior during and after wastewater treatment.

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6 Inductively coupled plasma optical emission spectrometry for rare earth elements analysis

Abstract: Inductively coupled plasma optical emission spectrometry (ICP-OES) merits multielements capability, high sensitivity, good reproducibility, low matrix effect and wide dynamic linear range for rare earth elements (REEs) analysis. But the spectral interference in trace REEs analysis by ICP-OES is a serious problem due to the complicated emission spectra of REEs, which demands some correction technology including interference factor method, derivative spectrum, Kalman filtering algorithm and partial least-squares (PLS) method. Matrix-matching calibration, internal standard, correction factor and sample dilution are usually employed to overcome or decrease the matrix effect. Coupled with various sample introduction techniques, the analytical performance of ICP-OES for REEs analysis would be improved. Compared with conventional pneumatic nebulization (PN), acid effect and matrix effect are decreased to some extent in flow injection ICP-OES, with higher tolerable matrix concentration and better reproducibility. By using electrothermal vaporization as sample introduction system, direct analysis of solid samples by ICP-OES is achieved and the vaporization behavior of refractory REEs with high boiling point, which can easily form involatile carbides in the graphite tube, could be improved by using chemical modifier, such as polytetrafluoroethylene and 1-phenyl-3-methyl-4-benzoyl- 5-pyrazone. Laser ablation-ICP-OES is suitable for the analysis of both conductive and nonconductive solid samples, with the absolute detection limit of ng-pg level and extremely low sample consumption (0.2% of that in conventional PN introduction). ICP-OES has been extensively employed for trace REEs analysis in high-purity materials, and environmental and biological samples.

6.1 Introduction

Atomic emission spectrometry is a methodology for elemental qualitative, semi- quantitative and quantitative analysis, which is based on the characteristic electro- magnetic radiation emitted from atoms/ions under heat/electrical excitation. Atomic emission spectrometry involves three steps: (i) The sample is vaporized, atom generation in the gas phase occurs, the atoms are excited and optical radiation under the action of the energy source is emitted. (ii) The compound radiation emitted by the optical source is dispersed according to the wavelength order by the monochromator, forming a spectrum. (iii) The wavelength and the intensity of the spectral lines are detected by the detector. The qualification depends on the wavelength of characteristic resonance

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emission line and quantification depends on the proportional relation between the signal intensity and analytes concentration.

Inductively coupled plasma (ICP) is a partially ionized gas, which is formed by the working gas in a high-frequency electromagnetic field when high-frequency current flows through the induction coil. The generated flame-shaped discharge (plasma torch) presents high temperature of around 10,000 K, which is an excellent radiation source/energy source with good performance in terms of vaporization, atomization, excitation and ionization in atomic emission spectrometry.

The plasma torch is in a cyclic structure, favoring the sample introduction from the center channel of plasma and maintaining a stable flame; carrier gas with low flow rate (less than 1 L/min) can easily penetrate the ICP, making the residence time for sample at the center channel of around 2–3 ms, complete evaporation and atomization of the sample; the high temperature provided by ICP is higher than that provided by any flame favoring the excitation of atoms and ions; samples are heated indirectly in the center channel, causing little influence on the properties of ICP discharge; ICP is a thin light source with low self-absorption phenomena, and it's an electrodeless discharge without electrode contamination.

By using ICP as the light/energy source for atomic emission spectrometry, inductively coupled plasma atomic emission spectrometry (ICP-AES), also termed inductively coupled plasma optical emission spectrometry (ICP-OES), was proposed in 1960s and developed rapidly since 1970s. ICP-OES has been demonstrated to feature multielemental analysis ability, wide dynamic linear range, low chemical interference/matrix effect, good stability and reproducibility, low detection limit, and various sample introduction techniques available for different demands in real sample analysis.

As the light source of atomic emission spectrometry, ICP can provide high temperature for the sufficient dissociation, atomization, excitation and ionization of target analytes, low background and relatively high signal-to-background ratio due to the long residence time of analytes in it. The detection limit is mainly determined by standard deviation of background signal and background equivalent concentration (BEC), and Table 6.1 lists BEC and detection limits of REEs in ICP-OES.

The merits of ICP-OES in trace REEs analysis can be specified as follows:

(1) Low detection limits

In general, ICP-OES provides excellent detection capability for REEs with the detection limit of ng/mL level. For the elements with single oxide dissociation energy of above 7 eV (e.g., REEs, Nb, Zr), the detection limit obtained by ICP-OES is 1–2 magnitudes lower than that obtained by flame atomic absorption spectrometry (FAAS) and atomic fluorescence spectrometry (AFS). Table 6.2 lists the detection limits of REEs obtained by ICP-OES for their sensitive lines.

(2) Good reproducibility

Without internal standard, the relative standard deviation (RSD) can be maintained at around 1–2 %.

(3) Low matrix effect

Compared with FAAS and AFS, ICP-OES exhibits low matrix effect.

(4) Wide linear range

The linear range for REEs analysis by ICP-OES can achieve 5 magnitudes. For example, a good linear relationship can be obtained in the concentration range of 0.01–100 mg/L for the calibration standard of Yb and Tm.

Table 6.1: The analytic lines, background equivalent concentration (BEC) and detection limits (C_L) of REEs [1].

Analytic lines (nm)	BEC ($\mu\text{g/mL}$)	C_L (ng/mL)
Sc II 361.384	0.035	1.0
Sc II 357.253	0.16	4.5
Sc II 337.215	0.22	6.2
Y II 371.030	0.042	1.2
Y II 324.228	0.084	2.4
Y II 377.433	0.14	4.0
Y II 437.494	0.15	4.2
Y II 224.306	0.25	7.0
La II 333.749	0.27	7.6
La II 412.323	0.27	7.6
La II 398.852	0.30	8.5
Ce II 413.765	0.60	17.0
Ce II 413.380	0.60	17.0
Ce II 395.254	0.60	17.0
Ce II 418.660	0.60	17.0
Ce II 399.924	0.71	20.0
Ce II 446.021	0.81	23.0
Ce II 429.667	0.81	23.0
Pr II 390.844	0.53	15.0
Pr II 414.311	0.53	15.0
Pr II 417.939	0.53	15.0
Pr II 422.535	0.71	20.0
Pr II 411.846	1.41	40.0
Nd II 401.225	1.41	40.0
Nd II 430.358	1.77	50.0
Nd II 406.109	1.77	50.0
Nd II 386.340	3.54	100.0
Sm II 359.260	0.32	9.0
Sm II 442.435	0.64	18.0
Sm II 360.949	0.64	18.0
Sm II 363.429	0.71	20.0
Sm II 428.079	0.78	22.0
Sm II 446.734	0.78	22.0
Sm II 356.827	0.78	22.0
Eu II 381.967	0.025	0.7
Eu II 420.505	0.071	2.0

Table 6.1 (continued)

Analytic lines (nm)	BEC (μg/mL)	C _L (ng/mL)
Eu II 272.778	0.46	13.0
Eu II 443.556	0.54	15.0
Eu II 281.294	0.71	20.0
Gd II 342.247	0.24	6.7
Gd II 336.223	0.35	10.0
Gd II 335.047	0.35	10.0
Gd II 310.050	0.53	15.0
Gd II 354.936	0.53	15.0
Tb II 350.917	0.46	13.0
Tb II 367.653	0.78	22.0
Tb II 387.417	0.78	22.0
Tb II 332.440	2.12	60.0
Tb II 374.725	2.12	60.0
Dy II 353.170	0.23	6.5
Dy II 340.780	0.96	27.0
Dy II 338.502	1.27	36.0
Ho II 345.600	0.25	7.0
Ho II 339.898	0.35	10.0
Er II 337.271	0.11	3.0
Er II 349.910	0.13	3.7
Er II 326.478	0.14	4.0
Tm II 313.126	0.14	4.0
Tm II 346.220	0.25	7.0
Tm II 376.133	0.35	10.0
Tm II 336.261	0.35	10.0
Tm II 376.192	0.42	12.0
Tm II 250.908	0.71	20.0
Yb II 328.937	0.071	2.0
Yb II 369.119	0.11	3.0
Yb II 289.138	0.22	6.0
Lu II 261.542	0.026	0.74
Lu II 291.139	0.21	6.0

II is the primary ionization ion line.

Table 6.2: Sensitive lines and detection limits of REEs in ICP-OES.

Serial number	Element	Wavelength (nm)	Detection limits (ng/mL)	Serial number	Element	Wavelength (nm)	Detection limits (ng/mL)
1	Ce II	413.77	32	1	Eu II	381.97	1.8
2		413.38	33	2		412.97	2.9
3		395.25	35	3		420.51	2.9
4		418.66	35	4		393.04	3.8
5		399.92	39	5		390.71	5.1

Table 6.2 (continued)

Serial number	Element	Wavelength (nm)	Detection limits (ng/mL)	Serial number	Element	Wavelength (nm)	Detection limits (ng/mL)
6		393.11	40	6		272.78	5.4
7		446.02	41	7		372.49	5.9
8		394.28	45	8		397.20	6.3
9		429.67	46	9		443.56	8.0
10		407.58	47	10		281.39	8.7
1	Dy II	353.17	6.7	1	Gd II	342.25	9.3
2		364.54	15	2		336.22	13
3		340.28	18	3		335.05	14
4		353.60	20	4		335.86	14
5		394.47	21	5		310.05	15
6		396.84	21	6		376.84	17
7		338.50	22	7		303.28	18
8		400.05	23	8		344.00	20
9		387.21	24	9		358.50	20
10		407.80	27	10		364.62	20
1	Er II	337.27	6.7	1	Ho II	345.60	3.3
2		349.91	11	2		339.90	8.7
3		323.06	12	3		389.10	11
4		326.48	12	4		347.43	12
5		369.27	12	5		341.65	12
6		390.63	14	6		381.07	13
7		291.04	18	7		348.48	13
8		296.45	18	8		379.68	17
9		331.24	20	9		351.56	18
10		339.20	21	10		345.31	20
1	La II	333.75	6.7	1	Pr II	390.84	25
2		379.48	6.7	2		414.31	25
3		408.67	6.7	3		417.94	27
4		412.32	6.7	4		422.54	28
5		398.85	7.3	5		422.29	31
6		379.08	7.3	6		406.28	31
7		399.58	8.7	7		411.85	33
8		407.74	9.3	8		418.95	40
9		387.16	10	9		440.88	41
10		375.91	10	10		400.86	43
1	Lu II	261.54	0.67	1	Sc II	361.38	1.0
2		291.14	4.1	2		357.25	1.3
3		219.55	5.5	3		363.08	1.4
4		307.76	5.9	4		364.28	1.8
5		289.48	6.7	5		424.68	1.8
6		339.71	6.7	6		357.64	2.5
7		350.74	7.3	7		335.37	2.5
8		270.17	8.0	8		337.22	2.9
9		290.03	8.0	9		358.09	3.0
10		275.47	8.0	10		255.24	3.1

Table 6.2 (continued)

Serial number	Element	Wavelength (nm)	Detection limits (ng/mL)	Serial number	Element	Wavelength (nm)	Detection limits (ng/mL)
1	Nd II	401.23	33	1	Sm II	359.26	29
2		430.36	50	2		442.43	36
3		406.11	64	3		360.95	38
4		415.61	71	4		363.43	44
5		410.95	77	5		428.08	46
6		386.34	87	6		446.73	49
7		404.08	87	7		367.08	50
8		417.73	91	8		356.83	51
9		385.37	100	9		373.13	52
10		394.15	100	10		443.43	55
1	Tb II	350.92	15	1	Y II	371.03	2.3
2		384.87	37	2		324.23	3.0
3		367.64	40	3		360.07	3.2
4		387.42	41	4		371.43	3.5
5		356.17	42	5		437.49	4.3
6		356.85	43	6		378.87	5.0
7		370.29	43	7		361.11	5.0
8		332.44	57	8		321.67	5.3
9		389.92	64	9		363.31	5.5
10		374.73	67	10		224.31	6.1
1	Tm II	313.13	3.5	1	Yb II	328.94	1.2
2		346.22	5.4	2		369.42	2.0
3		386.80	6.5	3		289.14	5.7
4		342.51	6.7	4		222.45	5.9
5		376.13	7.3	5		211.67	6.3
6		379.58	7.3	6		212.67	6.3
7		336.26	7.3	7		218.57	8.7
8		317.28	8.7	8		275.05	11
9		376.19	8.7	9		297.06	11
10		313.39	8.7	10		365.38	14

6.1.1 Spectral interference

The ICP-OES spectra of REEs are complex in ICP-OES detection, and Table 6.3 lists the commonly used spectral lines for REEs analysis. As can be seen, the spectral interferences among REEs are obvious, and the spectral interferences in the determination of trace REEs, especially REEs impurities in rare earth matrix, have become a prominent and challenging issue. Taking the analysis of other 14 REEs (except Sc) impurities in Eu or Gd matrix as an example, 113 emission spectral interference lines in MIT Table [2] can be found for Eu in the range of analytical line ± 0.1 nm, and 57 emission spectral interference lines can be found for Gd.

Table 6.3: Commonly used spectral lines (nm) for REEs analysis.

Sc	Y	La	Ce	Pr	Nd	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
335.37	319.56	324.51	306.30	390.84	383.65	356.83	281.39	310.05	329.31	330.89	339.90	323.26	313.13	289.14	261.54
361.38	324.23	333.75	380.15	400.87	392.10	360.95	381.97	335.05	332.44	340.78	345.31	326.48	313.39	297.06	291.14
390.75	332.79	338.09	394.21	405.65	394.15	363.43	390.71	335.86	350.92	353.17	345.60	331.24	325.80	303.11	307.76
391.18	344.88	392.76	401.24	410.07	401.22	366.14	393.05	336.22	356.17	353.60	347.43	337.27	329.10	328.94	327.90
402.04	360.07	392.92	413.76	417.94	406.11	367.08	397.20	342.25	367.63	364.54	389.10	349.91	336.26	346.44	329.17
424.68	361.10	394.91	418.66	420.67	424.74	373.91	412.97	344.00	370.39	389.85	405.39	369.26	342.51	347.88	331.21
	362.09	398.85	422.26	422.30	430.36	388.53	459.40	365.46	384.87	400.05	410.38	390.63	344.15	369.42	347.25
	363.32	399.57	446.02	422.53	445.16	425.64	462.72	367.12	431.88	404.60	416.30	400.80	346.22	398.80	451.86
	321.03	403.17	456.24	430.58	463.42	427.97	466.19	368.41	432.64	410.39			371.79		513.51
	328.26	408.67	569.92	440.88	489.69	428.08		371.27	433.84	418.68			379.57		
	407.74	433.37		446.87	492.45	429.67		376.84		421.17			388.31		
	410.24	452.61		449.65	495.48	442.05		396.63					409.42		
	437.49	550.13		493.97		442.43		422.58							
				495.14		443.39		440.19							
						443.43									
						446.73									
						476.03									
						478.31									
						488.40									

The spectral interferences observed in ICP-OES are induced by overlapping of spectral lines, partial overlapping, molecular spectra and continuous background. There are three cases for the spectral interferences of REEs: (1) the analytical line is completely overlapped by the matrix line; (2) a strong matrix line appears on one side of the analytical line, causing partial overlapping; (3) the analytical line locates between two weak matrix lines or a weak matrix line appears on one side of the analytical line. The analytical line of the first two cases should not be chosen and it's better to select another analytical line. For the third case, the spectral interference depends on the matrix concentration to a great extent. If the concentration of matrix is high, the effect of spectral interference is very serious; while if the concentration of matrix is low, the spectral interference is not distinct and can be ignored when the content of target REEs is high, and the interference effect is serious and it is difficult to distinguish and recognize the analytical line accurately when the signal of target REEs is very weak.

Even if a spectrometer with high resolution is adopted, it is still difficult to completely overcome the spectral interferences for the analysis of a complex RE system. The severity of the spectral interferences is determined by not only the complex spectrum of REE matrix, but also the concentration of REE matrix. The higher the matrix concentration is, the spectral interference is more serious. Based on it, high dilution is expected to be a simple and feasible approach to reduce the spectral interferences with a premise that the analytical sensitivity is enough.

Although commercial spectrometry instrument can easily process the correction of background interference, it cannot automatically deduct the spectral interference caused by spectral overlap or partial overlap. How to judge the existence of the spectral interference and how to effectively correct the interference have become a challenge in REEs analysis. Fortunately, the prediction and correction of spectral interference between REEs spectral lines can be achieved based on the established database of REEs spectral lines. Some spectral correction technologies have been employed in trace REEs analysis by ICP-OES, including interference coefficient method, derivative spectrometry, Kalman filtering method, self-modeling curve resolution method (SMCRM) and partial least-squares method (PLS).

Interference coefficient method (or interference factor method) is the simplest method which has been widely used in spectral correction, possessing the ability of simultaneous correction of spectral interference and background interference. The Interference coefficient is obtained by the ratio of interference equivalent concentration (IEC) and the concentration of interference compounds. The limitation of the method is that it's unsuitable for the analysis of samples with changing matrix composition.

Derivative spectrometry was widely used in molecular absorption spectrometry and then introduced for spectral interference correction in ICP-OES analysis. Compared with interference factor method, derivative spectrometry exhibits more adaptability, which not only can correct the spectral interference but also can reduce IEC

and improve the resolution. Kalman filtering is a more effective way to resolve serious spectral interference than derivative spectrophotometry. It can be used to correct the spectral interference of almost completely overlapping lines of Er 324.750/Cu324.754 (nm) and Nd 359.259/Sm359.260 (nm) in synthetic samples [3].

SMCRM is a mathematical method based on the resolution factor. By using SMCRM, the overlapping peaks can be decomposed into the original real shape without the need of firstly assuming the parameter and distribution function of the peaks. PLS is a stoichiometry method and is especially effective for the complex multicomponent system that can interact with each other.

It should be pointed out that these spectral interference correction technologies mentioned above are based on mathematical model and can only be used to correct spectral interference in simple matrix sample, with not enough application potential in real complex sample analysis.

To effectively resolve the spectral interference problem in trace REE analysis, some appropriate and effective measures are considered: (1) selecting another analytical line when the detection sensitivity is enough is an ideal choice, reflecting the high selectivity of atomic emission spectrometry; (2) adoption of spectrometer with high resolution and dispersive power, which is essential for analysis REEs in complex matrix; (3) using properly diluted sample solution for detection under the premise that the detection sensitivity can meet the analytical requirements; (4) using a chemical separation technology to remove REE matrix; (5) resolving the spectral interference by correction techniques.

The existence of REEs matrix has obvious effects on the spectral background. As can be seen from Figure 6.1, the intensity of the background is increased with the increase of matrix concentration. But the impact is not the same for different spectrum regions. The emission intensity of background is affected by many factors including operating parameters of ICP, apparatus properties such as dispersive power and stray light, and the spectral complexity and concentration of sample matrix. Under a certain operation condition of the instrument, the emission intensity of background mainly depends on the spectral complexity and concentration of the matrix. The emission intensity of background caused by REEs matrix (e.g., Ce, Nd, Tb) with abundant spectral lines is much stronger than that caused by REEs matrix (e.g., La, Eu) with simple spectral lines. In addition, the intensity of the background also depends on the concentration of the matrix. Taking high-purity terbium oxide as an example, when the concentration of Tb₄O₇ is 10 mg/mL, the spectrum of the matrix is very complex. Even a spectrometer with high dispersion rate (36,000/mm optical grating, 0.26 nm/mm reciprocal linear dispersion power) is unable to overcome such serious spectral interference and strong background interference, which makes quantitative determination impossible. However, the detection limit of 0.31–30 µg/g for REEs impurity by ICP-OES detection is still achieved when the concentration of Tb matrix is reduced to 1 mg/mL [4]. When the trace REEs impurities in 99 % purity

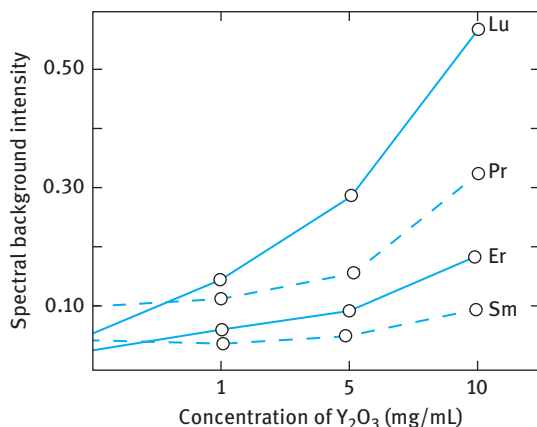


Figure 6.1: The effect of matrix concentration on the spectral background intensity [5].

Tb_4O_7 is analyzed by a spectrometer with a moderate dispersion rate, the adopted matrix concentration was only 0.2 mg/mL.

The background interference caused by continuous spectrum or stray light can be easily deducted by the off-peak method. Presently, most of the instruments have been allocated with the function of automatic background correction. Sometimes the on-peak method is also employed for correction, during which matrix blank is detected immediately after each sample analysis to ensure the consistency of matrix interference value.

To understand the impact of the existence of matrix on the increase of background, background factor is proposed, which refers to the background intensity ratio between the mixed solution of 1 mg/mL matrix and corresponding analyte and the solution containing only the analytes with same concentration. Table 6.4 lists the background factors and corresponding detection limits obtained from the analysis of high-purity Tb_4O_7 samples. As can be seen from Table 6.4, the existence of matrix increases the detection limit, and the increase of background clearly makes a contribution to the increase of detection limit.

6.1.2 Matrix effect

In general, matrix effects include spectral interferences and non-spectral interferences. Non-spectral interferences are mainly caused by sample atomization, transmission, desolvation and the variation of the spectral excitation parameters. The combined influences lead to the variation of analytes' spectral intensity.

In the ICP-OES analysis of high-purity REEs, matrix effect generally exhibits an inhibition effect on the analytical signal (Figure 6.2). In other words, when RE

Table 6.4: Background factors and corresponding detection limits (Tb matrix concentration: 1 mg/mL) [6].

Element	Line (nm)	Background factors	detection limits (ng/mL)	
			In water solution	In matrix solution
Y	371.030	3.62	0.4	1.2
Sm	466.734	1.80	4.0	3.0
Eu	393.048	5.85	0.7	6.0
Gd	310.050	3.67	3.0	12.0
Dy	387.211	2.53	3.0	7.0
Er	390.631	1.83	6.0	8.0

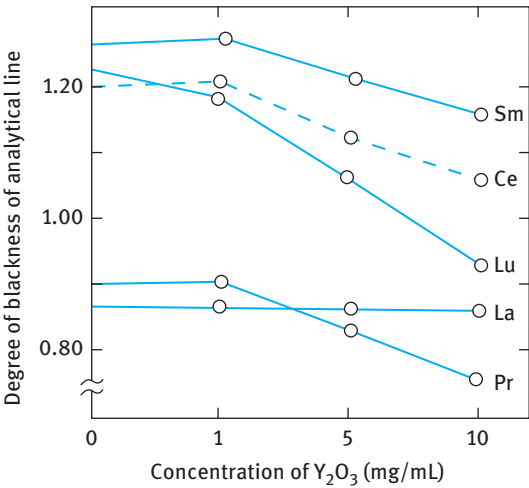


Figure 6.2: The effect of Y₂O₃ matrix concentration on target REE signals.

matrix concentration exceeds a certain value in the solution, the normalized intensity of the analytes ($I_{\text{matrix}}/I_{\text{no matrix}}$) values should be less than 1. However, due to the excellent properties of ICP light source, when RE matrix concentration is less than 1.0 mg/mL, the existence of the matrix has no significant impact on the signal intensity of target analytes [7]. Besides, the severity of the REEs matrix effects is related to the medium and sample injection mode. It is reported that in contrast with the sample injection mode of water/non-desolvation, the matrix effect is more serious when the sample solution containing ethanol was introduced into the ICP with desolvation. Moreover, as the desolvation temperature increases, matrix effect is further increased [8].

Table 6.5 lists the detection limit of REEs with and without the existence of RE matrix. It shows that the existence of the matrix deteriorates the detection limit.

Table 6.5: The influence of REE matrix on the detection limit of trace REEs.

Elements	Detection limit (µg/mL)		Elements	Detection limit (µg/mL)	
	without matrix	with matrix*		without matrix	with matrix*
La	0.025	0.04	Tb	0.20	0.40
Ce	2.5	1.0	Dy	0.10	0.80
Pr	0.25	0.80	Ho	0.10	0.40
Nd	0.05	0.06	Er	0.05	0.20
Sm	0.10	0.60	Yb	0.50	1.2
Eu	0.005	0.01	Lu	0.05	0.06
Gd	0.025	0.10	Y	0.02	0.02

*matrix (Tm₂O₃) concentration: 10 mg/mL.

The mechanism for signal inhibition caused by matrix effect is still unclear, while there are some tendentious opinions.

The influence on sampling efficiency: The existence of a large number of REE matrix results in a decrease of sampling efficiency of target REEs, which is considered as an important factor.

The influence on excitation temperature of ICP: The existence of matrix leads to the decrease of the excitation temperature of ICP, because the evaporation and dissociation process consume a portion of energy of the ICP excitation source when the matrix is introduced into ICP.

The influence on ionization process of analytes: Based on the investigation of intensity ratio of spectral line in different types for target elements, it is found that the introduction of the matrix decreases the ionization degree of analytes in ICP.

Elastic collisions happen between analytes particles in the excited states and matrix particles in the ground state, which leads to the transfer of excitation energy.

To overcome matrix effects in REEs analysis, we can take the following measures:

(1) Matrix matching

This is the most commonly used method, processing matrix matching between the tested sample solution and standard series to eliminate the matrix effect. The main problem is that higher-purity matrix is very expensive and sometimes unavailable. In general, in the analysis of high-purity rare earth with purity of 99.99 %, we should use high-purity rare earth with purity of 99.999–99.9999 % as the matrix for matching at least. Otherwise, the blank value generated by the matching matrix cannot be ignored.

(2) Internal standard compensation

To overcome the problem of the matrix-matching method, internal standard is another effective way to eliminate the matrix effect. In high-purity REEs analysis, internal standard is the spiked elements, which has similar physical and chemical properties with target elements. Internal standard method is based on the similarity

of the matrix effects on internal standard lines and analytical lines, the spectral line intensity ratio of which is irrelevant or insensitive to the existence/concentration of the matrix. Therefore, internal standard can be used to compensate for the influences of matrix. Table 6.6 lists the application of the internal standard method in high-purity REEs analysis. As can be seen, when Sc is used as the internal standard for the determination of trace REEs impurities in high-purity yttrium oxide, the analysis results obtained by internal standard method are generally consistent to that obtained by matrix-matching method.

Table 6.6: The results of trace REEs impurities in high purity yttrium oxide using internal standard method and matrix matching method.

Method	measured value (μg/g)						
	La	Ce	Pr	Nd	Sm	Gd	Dy
internal standard method	16.0	160	<8	160	4.9	9.0	7.4
matrix matching method	17.0	180	<8	150	6.0	8.0	7.0

Internal standard lines (nm): Sc 432.501 or Sc 337.215.

(3) Correction factor

Based on the single matrix and controllable concentration of high-purity REEs analysis, the correction factor method provides an alternative way for the compensation of matrix effect. The correction factor method is based on the fact that under a certain working conditions of ICP, the intensity of the analytical lines is mainly dominated by the properties and concentrations of REE matrix; in other words, the matrix effect is constant or nearly constant. Therefore, we can use a correction factor to compensate the matrix effect. Table 6.7 lists the analytical results obtained by

Table 6.7: The application of the correction factor method in high purity yttrium oxide analysis.

Elements	Spiked amount (μg/mL)	measured value (μg/mL)		
		non-correction	correction factor method	matrix matching method
La	0.05	0.038	0.046	0.051
Ce	0.05	0.036	0.047	0.049
Pr	0.10	0.085	0.120	0.097
Nd	0.10	0.062	0.080	0.095
Eu	0.05	0.036	0.049	0.043
Gd	0.05	0.038	0.042	0.038
Tb	0.05	0.034	0.043	0.065
Dy	0.10	0.062	0.080	0.095
Er	0.10	0.065	0.091	0.10
Lu	0.10	0.082	0.10	0.11

correction factor and matrix-matching method. As can be seen, although the matrix effect can be corrected with the correction factor method to a certain extent, the real application of this method still requires further investigation. The limitation of the correction factor method is that it is unsuitable to the situation in which matrix composition is varied.

(4) Dilution method

When the matrix spectrum is very complex, highly diluted samples can be adopted for instrumental analysis. For instance, when the matrix is diluted to 1 mg/mL in the determination of REEs impurities in Dy_2O_3 , the sample solution can be directly analyzed, and the non-spectral interference effect has been reduced to a negligible degree. Thus, the quantification can be performed without matrix matching. There are other similar reports, such as Ref. [4]. When the matrix (Tb) is diluted to 0.2 mg/mL, spectral interferences and non-spectral interferences are reduced greatly and can be ignored, and the sensitivity of the method can still meet the analysis requirements of Tb_4O_7 with purity of 99%. Therefore, the dilution method is a simple way to reduce the matrix effects. The shortcoming of this method is that the sensitivity will be reduced.

6.1.3 Acid effect

Acid effect in ICP-OES is a kind of non-spectral interference. The presence of HNO_3 , HCl , HClO_4 , H_2SO_4 or H_3PO_4 would reduce the uptake amount of the solution and decrease the signal intensity of interest analytes. The effect is increasing with the order of $\text{HNO}_3 < \text{HCl} < \text{HClO}_4 < \text{H}_2\text{SO}_4 < \text{H}_3\text{PO}_4$, and no difference to atomic lines and ionic lines. This interference can be greatly reduced by employing peristaltic pump for sample introduction, indicating that the uptake rate variation caused by nebulization interference is the main reason.

To overcome the acid effect, some strategies can be taken:

- (1) Improvement of the working conditions of sample introduction system. Inorganic acid would lead to variation of the aerosol transportation, resulting in matrix interference. Therefore, improved nebulizer has become one of the effective ways to overcome the acid effects, such as micro-concentric nebulizer, high-efficient nebulizer, and the desolvation system has been demonstrated to be effective.
- (2) Use of high RF power and low carrier gas flow rate. Acid effect would decrease the energy transfer in the plasma, especially those acids featuring with low viscosity and low density (hydrochloric acid, nitric acid, perchloric acid) which would affect the excitation temperature and electron density of the plasma, and this influencing is much more serious than that caused by sample introduction system. Thereby increasing the RF power of the plasma (>1.2 kW) and prolonging the retention time of the analyte in the central channel of the plasma would

strengthen the plasma state, and the signal intensity variation would be maintained constant as possible with the introduction of different amount of matrix.

- (3) Commonly used methods to overcome matrix interference. Matrix-matching, standard addition and internal standard methods could be used to decrease the acid effect.

6.1.4 Sensitivity-enhancing effect of organic solvent

Since Fassel et al. directly introduced organic solvent to ICP for the first time in 1976, the reports on organic solvent have been increasing, and the investigation of organic solvent in ICP has become a hot topic in this field. The research on the application of organic solvent in ICP is mainly concentrated on three points: (1) the effects of enhanced sensitivity caused by organic solvent on spectral lines and its mechanism; (2) the hyphenation of solvent extraction with it; (3) the direct analysis of metal or metalloid elements in organic samples.

6.1.4.1 Affecting factors

The main factors that can influence the analytical functions of organic ICP are summarized as follows:

(1) Forward power

A high forward power must be provided to keep a steady discharge of organic ICP. When the solutions containing inorganic matter, organic matter, or both inorganic matter and organic matter are separately introduced to ICP, it is found that the incident power of organic ICP is about 0.5 kW higher than that of aqueous ICP on the same conditions. The possible reason is that the particles formed during organic molecular decomposition process give rise to the conductance and thermal conduction of aerosol tunnel.

Additionally, the analytical intensity of spectral line is increasing with an increase of the power, while the increasing rate of background intensity is lower, resulting in an improvement of the signal/noise ratio of spectral line. Besides, increasing the incident power would allow more uptake amount of samples with no quenching of the plasma.

(2) Gas flow rate and observation height

The increasing of cooling gas flow rate could weaken the emittance of cyanogen molecular band and has no obvious influence on the intensity of spectral line. When organic solvents are introduced into the plasma, auxiliary gas would not be shut down in order to prevent the deposition of carbon particles on the wall of middle and inside tube of torch. Carrier gas flow rate affects the intensity of spectral line seriously, which varies with the properties of spectral line, namely hard line or

soft line. Generally, the best observation height for the analysis of organic solutions is lower than that for the analysis of aqueous solutions.

(3) Uptake rate of solutions and ICP tolerance

It is found that the solvent with higher vapor pressure, such as methanol, acetone, benzene and cyclohexane, is difficult to be introduced, but for the solvent with lower vapor pressure the situation is contrary. One of the reasons for ICP quenching is the unstability of the plasma and impedance unmatching which is caused by the sudden entering of too much organic solvent with higher vapor pressure.

There are two ways to improve the tolerance capacity of ICP for organic solvents. One is to increase the incident power, and the other is to control the uptake rate of the solvent. Generally speaking, the higher the evaporation factor of solvent is, the slower the ultimate uptake rate is.

6.1.4.2 Enhanced sensitivity caused by organic solvents in REEs analysis

It has been long observed that the introduction of organic solvent could enhance the spectral line intensity of REEs and improve the detection sensitivity of ICP-OES for REEs.

6.1.4.2.1 Enhanced sensitivity by ethanol

By using the conventional pneumatic nebulization (PN) sample introduction system, 15–30 % (v/v) ethanol solution are found to effectively improve the spectral line detection for most elements in ICP-OES. Based on the investigation of the effects of ethanol on the spectral line intensity of REEs, it is found that the spectral line intensity of REEs is increased, and the background intensity decreases with the increase of ethanol concentration. What's more, the sensitivity-enhancing effect on the ionic spectral line is higher than that on the atomic spectral line. Thus, the introduction of ethanol is beneficial to improve the detection limit of REEs (Table 6.8).

The introduction of ethanol also affects the stability of ICP discharge, especially when the working power of ICP is relatively low. The lower the working power is, the less the amount of ethanol the plasma can tolerate. So a higher working power should be employed when ethanol is introduced to ICP compared with aqueous solution.

Introducing ethanol to ICP would cause some negative effects, such as the instability of ICP discharging, the deposition of carbon particles formed during the decomposition of organic matter at high temperature and the resulting molecular spectrum of cyano group, which would cover the corresponding band of light spectrum.

Table 6.8: The effect of ethanol on the detection limit of REEs.

Element	Wavelength	Detection limit (ng/mL)		Element	Wavelength	Detection limit (ng/mL)	
	(nm)	Ethanol	Water		(nm)	Ethanol	Water
La	333.749	14	29	Dy	364.540	25	33
Ce	418.963	71	90	Ho	339.898	14	19
Pr	422.293	95	120	Er	337.271	2.3	3.0
Nd	401.225	52	146	Tm	313.126	4.7	8.7
Sm	442.434	99	190	Yb	328.937	0.78	0.87
Eu	381.967	8	12	Lu	261.542	1.7	3.0
Gd	303.285	56	71	Y	324.228	3.0	5.4
Tb	387.417	230	570				

6.1.4.2.2 Mechanism for sensitivity enhancing effect of ethanol

Some research showed that the enhanced sensitivity caused by ethanol on the spectral line of REEs can be attributed to the improved nebulization efficiency and atomization efficiency based on the introduction of ethanol.

In order to investigate the influence of ethanol on nebulization efficiency, Chen et al. [9] compared two mixing situations, mixing ethanol with water in solutions and mixing two aerosols of ethanol with water. The results show that the sensitivity-enhancing effect caused by mixing ethanol with water in solutions is obviously higher than that by mixing aerosols, indicating that the sensitivity-enhancing effect of ethanol depends on the improvement of sample nebulization and mass transfer process. Because the surface tension of ethanol is lower than that of water, ethanol is easier to form tiny droplet. Similar conclusion was obtained in some Refs [10, 11], and it is specified that the sensitivity enhancing of the REEs spectral line is caused by the decreasing of the droplet diameter and the increasing of the transition rate of target elements.

To investigate the effect of ethanol on the nebulization efficiency, the mixed aerosol of ethanol and water in different ratios are introduced into the plasma, and the results are shown in Figure 6.3. As can be seen, with the increase of ethanol concentration, the intensity of REE spectral line is increased obviously; when the concentration of ethanol is higher than 60 % (v/v), the increasing of the spectral line intensity is sharper. The results show that REE compounds may experience a process of first dissociating and then recombining, forming monoxide of REEs finally which is difficult to dissociate. While when the existence amount of ethanol is enough, the possibility of forming REEs monoxide is reduced because of the strong reducing property of carbon particles or carbon-containing free radicals which occur in high temperature, thus improving the atomization efficiency.

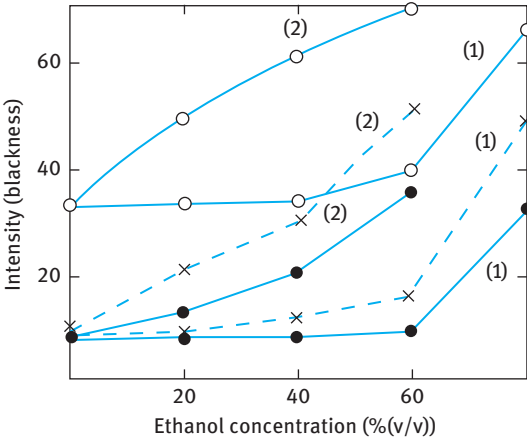


Figure 6.3: The effect of ethanol on nebulization and atomization efficiency [9] ×-Ho, •-Tm, o-Y; (1) introduction after aerosol mixing, (2) introduction after solution mixing.

6.1.4.2.3 Organic solvent and pre-desolvation

Yang et al. [12] proposed that the combination of the sensitivity-enhancing effects of organic solvent (ethanol) and desolvation would improve the detection sensitivity of REEs.

(1) Effect of desolvation temperature

As can be seen from Figure 6.4, the signal-to-noise ratio of REEs is gradually increased with the increasing of the desolvation temperature from 150 to 300 °C. And the detection limits of interest REEs are obviously improved when the desolvation temperature is 300 °C and the concentration of ethanol is 95 % (v/v). Compared with non-desolvation aqueous solution, the detection limits of REEs are decreased about one order of magnitude (Table 6.9).

Table 6.9: The detection limit of REEs with/without desolvation [12].

Elements	Line (nm)	Detection limit (ng/mL)		
		Non-desolvation (Water)	Desolvation (Water)	Desolvation (95% Ethanol)
La	399.575	49	28	5.0
Eu	281.395	41	22	3.7
Gd	342.247	23	13	2.5
Yb	289.139	21	14	3.0
Lu	347.148	53	21	4.9

It should be pointed out that (i) desolvation also depends on the concentration of matrix concentration. The improvement of the detection limits is obvious without the

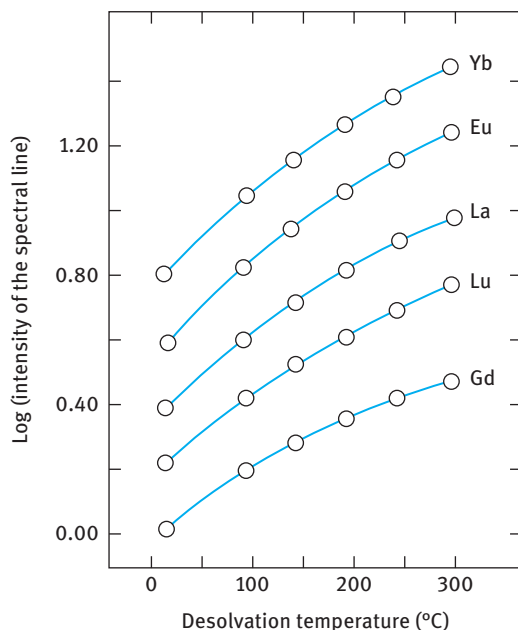


Figure 6.4: The effect of desolvation temperature on the spectral line intensity of REEs [12].

matrix existing, and the improvement is more and weaker when the concentration of matrix is increasing. Thus, there is a strict limit on the total salinity of the sample solution for desolvation sampling, generally less than 5 mg/mL. Otherwise, the high salinity not only affects the improvement of the detection limits but also causes torch blockage; (ii) compared with non-desolvation, the matrix effect is obviously enhanced (Figure 6.5) when the sample is introduced into the plasma under desolvation. As can be seen, the spectral line intensity of the elements is decreased clearly when the concentration of Y matrix is up to 1 mg/mL. Moreover, the analytical signal is decreased by nearly 50 % when the concentration of Y matrix is up to 5 mg/mL; the matrix effect increases with the increasing of the desolvation temperature.

(2) The effect of ethanol concentration

Figure 6.6 shows the effect of the ethanol concentration on the spectral line intensity of REEs with the desolvation temperature of 300 °C. As can be seen, the signal of analyte is gradually raising with the increasing of ethanol concentration up to 95% (v/v).

Based on the investigation of the effect of ethanol concentration and desolvation temperature on the sampling rate of the analytes into the plasma (the quantity of the analytes entering the plasma excitation area in unit time), it can be concluded that (i) the loss rate of analytes in transportation would drop to 50% with the increase of ethanol concentration, specifically, 95% loss of the analyte in aqueous solution to 50% loss in 95% ethanol. (ii) The desolvation efficiency is increased

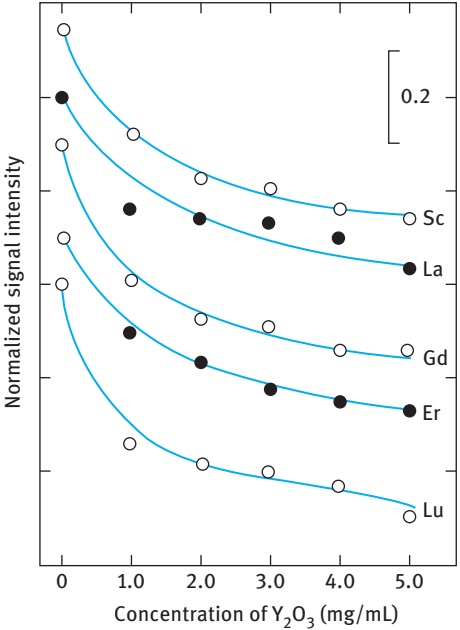


Figure 6.5: The effect of Y matrix on spectral line intensity of REEs under pre-desolvation [12].

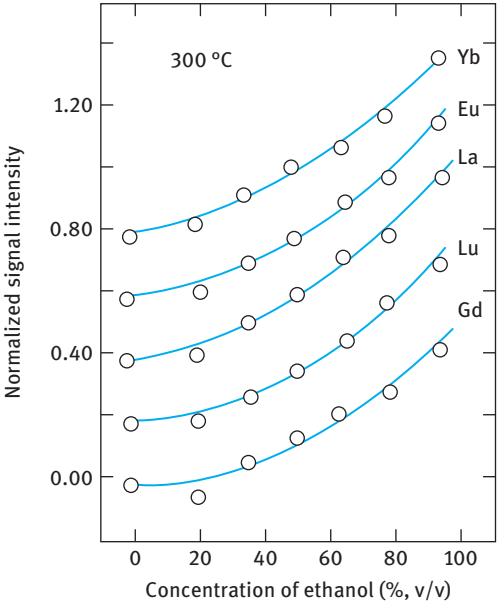


Figure 6.6: Effect of ethanol concentration on the signal intensity of REEs in ICP-OES.

from 32 to 73% with the increase of the desolvation temperature, and the loss of analytes is further decreased. Above all, it can be assumed that the reason why it can improve the detection sensitivity of REEs through the combination of ethanol with desolvation is that the uptaking rate of analytes into the torch is enhanced and the effect of the solvent on the plasma is excluded or decreased during the process.

(3) Matrix effect in ethanol/desolvation system

Yang et al. [7, 12] systematically investigated the matrix effects in ethanol/desolvation system and compared it with normal non-desolvation system. It was found that the existence of 1 mg/mL Y matrix has no obvious effect on the normalization intensity of target analyte, while the spectral line intensity is obviously decreased with desolvation sampling under the same condition.

The performance of matrix effect observed under the condition of ethanol/desolvation can be described as follows: (i) The effect on the sampling efficiency: it showed that when the concentration of matrix is in the range of 1–5 mg/mL, the sampling efficiency of analytes is decreased nearly 40% compared with that obtained under no matrix existence. (ii) The effect on the excitation conditions of ICP: it was found that the ionizability of target element (Yb) is decreased when the matrix was introduced into ICP based on the investigation of the intensity ratio of the spectral line in different types (atomic line and ionic line). Moreover, the ICP temperature was measured and it was found that the excitation temperature of the plasma is decreased with the introduction of matrix to the plasma, probably due to that the process of matrix evaporation and dissociation consumes a part of energy of ICP.

(4) Sensitivity-enhancing effects by other solvents for REEs analysis

Chen et al. [13] investigated the sensitivity-enhancing effects of five organic solvents, including butyl acetate, methylisobutylketone, chloroform xylene and phenoxin, and on target REEs, and combine it with liquid extraction technique. In this process, target REE ions formed organometallic chelates firstly with the organic agent PMBP, and the compound was extracted from aqueous solution to organic phase using appropriate organic solvents and then directly introduced into ICP. The sensitivity-enhancing factor obtained by five organic solvents for La and Y is listed in Table 6.10. It can be found that the introduction of all tested organic solvents exhibited sensitivity-enhancing effects in different degree, and the order is butyl acetate > MIBK > $\text{HCCl}_3 \approx \text{phenoxin} \approx \text{CCl}_4$. A comparison of the detection limit and RSD for La and Y obtained in different solvents is listed in Table 6.11.

Based on the distribution ratio difference of La in TBP- HNO_3 system with other REEs, the selective extraction and separation of REEs impurities (Eu-Lu and Y) from La matrix were processed by using TBP as the extractant [14]. The organic phase was directly introduced into ICP for detection and the detection limit of the method is ranging from 0.34 to 9.3 ng/mL.

Table 6.10: Sensitivity Enhancing factor of organic solvent on La and Y.

Solvent	Enhance Factor ($I_{\text{organic solution}}/I_{\text{aqueous solution}}$)			
	La 333.7nm	La 338.0	Y 324.2nm	Y 371.0nm
Methylisobutylketone	2.7	2.7	6.8	7.8
Butyl acetate	6.3	4.9	14.2	16.4
Xylene	2.2	3.3	3.6	13.6
Chloroform	3.1	3.6	6.3	11.4
Phenoxin	2.0	2.4	3.0	4.7

Table 6.11: Detection limit and precision for La and Y in different solvents.

Solvent	La		Y	
	DL (ng/mL)	RSD (%)	DL (ng/mL)	RSD (%)
Water	26	1.2	2.6	3.6
Butyl acetate	2.9	2.4	0.18	1.0
Methylisobutylketone	6.3	3.5	0.31	2.1
Xylene	10.3	4.2	0.86	6.4
Chloroform	15.8	6.1	0.70	4.7
Phenoxin	19.4	2.9	2.6	3.1

6.2 Sample introduction for ICP

The analytical performance of plasma source spectrometry is highly dependent on the employed sample introduction techniques. Therefore, the research on new sample introduction techniques has always received the greatest attention. An “ideal” sample introduction technique should meet these requirements: (i) high sample introduction efficiency; (ii) low sample mass requirement and (iii) powerful ability to analyze a wide variety of samples with complex matrix. However, it is difficult to realize the above-mentioned criteria even with a PN, which is the most popular sample introduction technique in ICP-OES.

6.2.1 Pneumatic nebulization and ultrasonic nebulization

Conventional PN sample introduction is characterized with several shortcomings including low transport efficiency (ca. 10%), large sample mass requirement and possible risk of blockage in the nebulizer during the analysis of samples containing high concentration of dissolved salts or slurries. Although Babington nebulizer can

be applied to the direct analysis of these samples, it was particle diameter dependent and severely suffered from the matrix effect.

By using an ultrasonic nebulizer coupled to a desolvation system the amount of solvent entering the plasma can be drastically reduced and sensitivity improved. Bentlin et al. [15] compared pneumatic and ultrasonic nebulization in terms of the detection limits for both radially and axially viewed plasma, by monitoring the most sensitive spectral lines when possible. It was found that the lowest detection limits were obtained by using ultrasonic nebulization and axially viewed plasma (Table 6.12). The best detection limits obtained with ultrasonic nebulization are mainly due to the greater aerosol output of the ultrasonic nebulizer (the sample uptake rate and aerosol transportation to the plasma are higher than those of the MicroMist nebulizer). The detection limits found using ultrasonic nebulization and axially viewed plasma are lower than those reported for La, Ce, Nd, Sm, Eu, Er and Yb, measured using ultrasonic nebulization ICP-OES and matrix removal [16]. For comparison purposes, the detection limits obtained by PN-ICP-MS [17] are also shown in Table 6.12. It can be seen that detection limits found using ultrasonic nebulization and axially viewed plasma are in general only one order of magnitude higher, or less, than those found by ICP-MS.

Table 6.12: Selected spectral lines of the lanthanides and respective detection limits (mg/L) by ICP-OES as a function of the nebulizer and plasma view [15].

Analyte	Pneumatic		Ultrasonic		ICP-OES [16]	ICP-MS[17]
	Axial	Radial	Axial	Radial		
La (II) 398.852	0.164	0.818	0.010	0.073	0.30	0.004
Ce (II) 413.380	1.436	4.799	0.069	0.272	0.93b	0.004
Pr (II) 414.311	1.114	2.767	0.036	0.237	—	0.003
Pr (II) 390.844a	0.834	3.401	0.041	0.205	—	—
Nd (II) 406.109	1.252	2.696	0.060	0.194	0.51c	0.018
Sm (II) 360.949	0.804	2.023	0.062	0.417	—	0.016
Sm (II) 359.260a	2.077	3.398	0.039	0.221	0.25	—
Eu (II) 381.967	0.034	0.140	0.003	0.019	0.045	0.011
Gd (II) 335.047	0.504	2.684	0.036	0.309	—	0.013
Gd (II) 342.247a	0.196	0.659	0.012	0.106	0.72	—
Tb (II) 350.917	0.349	1.942	0.023	0.211	—	0.004
Tb (II) 367.635a	1.354	4.610	0.039	0.239	—	—
Dy (II) 353.170	0.165	0.579	0.007	0.045	—	0.011
Ho (II) 345.600	0.167	0.512	0.008	0.065	—	0.004
Er (II) 349.910	0.160	0.922	0.013	0.137	0.12d	0.012
Tm (II) 384.802	0.433	1.050	0.009	0.080	—	0.003
Yb (II) 328.937	0.018	0.061	0.003	0.090	0.01	0.010
Lu (II) 261.542	0.017	0.124	0.003	0.014	0.006	0.003

6.2.2 Flow injection

In 1975, Ruzicka and Hansen [18] published their research works, which marked the establishment of a new analytical technique—flow injection analysis (FIA). In 1981, Fang [19] introduced the instrument, principle and application of FIA in China for the first time. The application of FIA in atomic spectrometry is originated in atomic absorption analysis (AAS), and it was until 1980 when Ito et al. [20] introduced FIA into ICP-OES. From then on, FIA was applied widely in ICP-OES as an on-line/pretreatment technology for trace analysis. Fu et al. [21] reviewed the application of FIA in REEs analysis in China, which was mainly concentrated on the hyphenation of FIA with spectrophotometry, and electroanalysis and ICP-OES analysis were discussed as well. The hyphenation of FIA with ICP-OES merits low sample consumption, simple operation, rapidity, good reproducibility, low pollution and easy automation, demonstrating that it is a kind of promising sampling technique. The characteristics of FIA coupled with atomic spectroscopy can be summarized as follows:

- (1) Sample volume is usually 10–300 μL .
- (2) Sample throughput can be as high as 500 h^{-1} .
- (3) The absolute detection limit can be improved.
- (4) The clogging of nebulizer can be prevented effectively.
- (5) The impact caused by matrix or acidity variation can be reduced.
- (6) An improved reproducibility can be obtained over common continuous sampling.
- (7) Online dilution is available for the determination of target elements with different concentration.
- (8) The sensitivity-enhancing effect of organic solvent can be fully utilized, and the resistance for organic solvent in FIA-ICP-OES system is apparently higher than that in common ICP-OES system.

6.2.2.1 FIA coupled with ICP-OES for direct determination of trace REEs

Chen et al. [22] applied FIA-ICP-OES for the determination of 14 trace REEs in the high-purity Y_2O_3 directly. When the employed sample volume was 1 mL in which the matrix concentration was 40 mg/mL, detection limit for target REEs was in the range of 0.25–12.5 g/g, with RSD of 1.0–2.9%. This method can be used for the rapid and accurate determination of trace REEs in Y_2O_3 with 99.99 % purity.

Compared with conventional PN, FIA-ICP-OES has the following obvious advantages:

- (1) Both of acid and matrix effects can be reduced to a certain extent, and these two interferences can be further reduced with the decrease of sample injection volume (Figure 6.7), which is probably due to the dilution effect of carrying flow on the sample and the sampling mode of peristaltic pump. Luo et al. [23] investigated the chemical/physical interference by using three injection modes,

PN, peristaltic pump uptake and flow injection, and it was found that the acid effect was effectively eliminated or reduced in FIA system.

- (2) High concentration of matrix in sample solution is allowable. It was found in the experiment that no clogging happened in nebulizer or ICP center tube when 50 mg/mL Y_2O_3 matrix was introduced into the plasma by FIA system continuously for a long time. Apparently, it is closely related to the dilution effect of carrying flow and the rapid contact of sample solution with the nebulizer or central tube.
- (3) Reproducibility of the method can be further improved. Table 6.13 lists a comparison of analytical performance obtained by PN and FIA-ICP-OES for REEs.

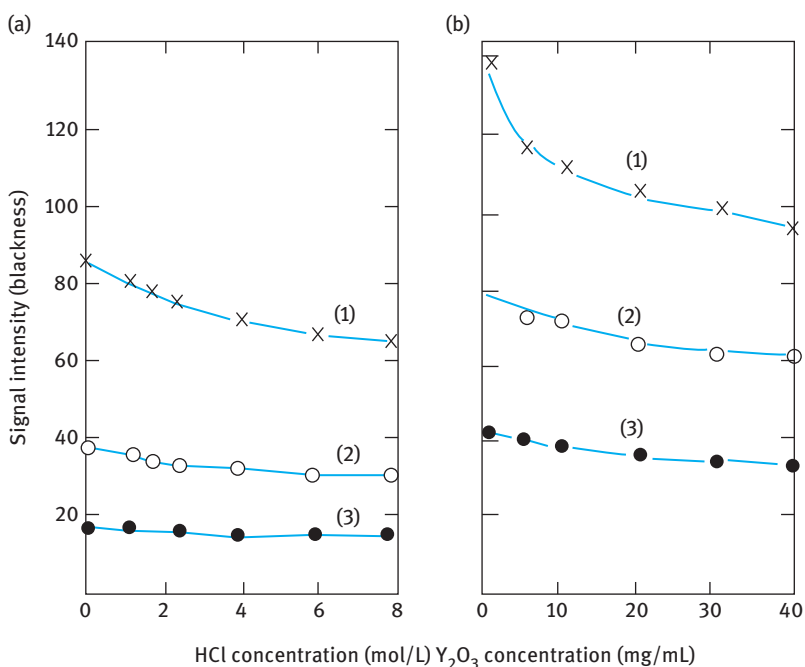


Figure 6.7: The effect of HCl and matrix concentration on the signal intensity of REEs. (a) HCl, Gd 335.1 nm, (b) Y_2O_3 , Er 337.2 nm; (1) continuous pneumatic nebulization, (2) FIA, 1 mL, (3) FIA, 0.36 mL.

6.2.2.2 Standard addition method in FIA

In this method, sample solution is used as the carrying flow, the standard solutions with different concentrations are successively injected into the carrying flow by the sampling valve, and they flow through a coil of a certain length to mix sufficiently, followed by introducing directly into the nebulization system and subsequent ICP-

Table 6.13: A comparison of analytical performance of REEs in Y₂O₃ matrix [22].

Analytes	LOD (μg/g)			RSD (%)	
	C(10mg/mL)	F(20mg/mL)	F(40mg/mL)	FIA	PN
La	5	10	2.5	1.0	2.1
Ce	10	50	12.5	2.5	4.1
Pr	10	50	12.5	2.4	3.0
Nd	10	10	12.5	2.5	4.4
Sm	10	50	12.5	2.2	3.4
Eu	1	1	0.25	1.3	1.0
Gd	1	5	2.5	2.6	5.5
Tb	5	5	1.25	2.9	6.5
Dy	1	1	0.25	1.2	3.5
Ho	1	1	0.25	2.8	5.5
Er	1	1	0.25	1.8	3.3
Tm	5	5	1.25	2.2	5.5
Yb	1	1	0.25	1.0	1.6
Lu	10	10	2.5	2.2	6.5

C, continuous nebulization; F, flow injection; (), matrix concentration.

OES detection. The obtained curve is shown in Figure 6.8, and the cross point which is made by the working curve and the concentration axis is the determined concentration of target analyte in the sample solution. This standard addition method is called flow injection reverse standard addition method, also called interpolating standard addition method.

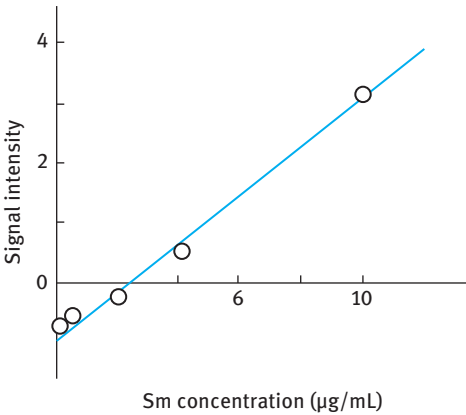


Figure 6.8: The curve of Sm concentration vs signal intensity in flow injection reverse standard addition method (Sm 359.2 nm) [24].

The reverse standard addition method was applied to the determination of single REE in the mixed REEs sample [24], featuring with simple operation, rapid analysis, good accuracy, and it is insusceptible to the variation of sample composition. Yet a large volume of sample solution is consumed in this method. The main influencing factors in this method include the length of mixing tube, injection volume, flow rate and signal integration interval. In order to obtain accurate results, the spiked amount of the standard series solutions should be closed to the concentration of target analytes in the real sample.

Three standard addition methods in FIA-ICP-OES analysis are compared in terms of the analytical performance, including (i) interpolating standard addition method (sample solution is the carrying flow), spiking standard series with fixed volume into the carrying flow; (ii) gradient correction technology, spiking standard series with different concentration into sample solution; (iii) the method in which water carrying flow is in front of the sample solution, which is followed by the standard series. The order of the precision is (i) > (iii) > (ii), (ii) > (i) > (iii) for the simplicity, and (ii) > (i) > (iii) in sample consumption.

6.2.2.3 On-line separation/preconcentration-ICP-OES for trace REEs analysis

Online flow injection (FI) combined with ICP-OES detection is widely used for the analysis of metals and metalloids. The advantages are summarized as follows:

(i) high enrichment efficiency; (ii) low sample/reagent consumption; (iii) simple operation and high analytical efficiency. Yet the injection volume and sample throughput restrain mutually; the improvement of detection limit is limited; the separation device/operation is relatively complex. The commonly used online separation/preconcentration system is shown in Figure 6.9. Table 6.14 lists the representative application of online FI separation/preconcentration ICP-OES for trace REEs analysis.

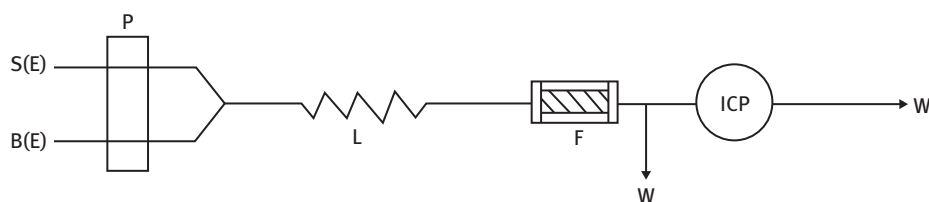


Figure 6.9: On-line separation/preconcentration system combined with ICP [26] (P, pump; E, elution solution; R, reagent; S, sample; L, reaction/mixing coil; F, microcolumn; W, waste).

Table 6.14: On-line FI separation/preconcentration-ICP-OES for trace REEs analysis.

Sample	Analytes	Stationary phase	Elution	Enrichment factors	Sample throughput(h ⁻¹)	LOD	Ref.
Mineral	REEs	chelate resin	1 mol/L HCl	99	–	sub-ng/mL	[25]
High purity zinc	La, Nd, Eu, Gd, Tb, Dy, Ho, Lu	DSC-arsenazo loaded activated carbon	4 mol/L HCl	12	–	ng/mL	[26]
Water samples	La	P507 chelating resin	1 mol/L HCl	30	60	0.7 ng/mL	[27]
Mineral	14 REEs	P507 extraction-eluting resin	3.5 mol/L HNO ₃	8–15	14	0.05–	[28]
Natural water and coal fly ash	Co, Cd, Cr, Cu, Mn, Ni, V, Ce, Dy, Eu, La and Yb	Mesoporous TiO ₂	2 mol/L HCl	10	20	0.5 µg/g	[29]
Acid drainage	Sc	oxidized multiwalled carbon nanotubes	30% (v/v) HNO ₃	225	10	0.36 µg/L	[30]
Environmental water	REEs	CCTS-AHBA resin	2 mol/L HNO ₃	21.1–30.8	–	1–18 ng/L	[31]
Urine samples	La	Amberlite XAD-7 resin	2 mol/L HNO ₃	100	–	90 ng/L	[31]

CCTS-AHBA, Functional moiety of 2-amino-5-hydroxy benzoic acid (AHBA) chemically bonded to amino group of cross-linked chitosan (CCTS)

6.2.3 Laser ablation

As an inefficient solid sampling technique, laser ablation (LA) has been successfully employed in ICP-OES. Arrowsmith et al. [32] reported the strategy by using LA as the sampling system and ICP as the excitation unit. The schematic diagram of the apparatus is presented in Figure 6.10.

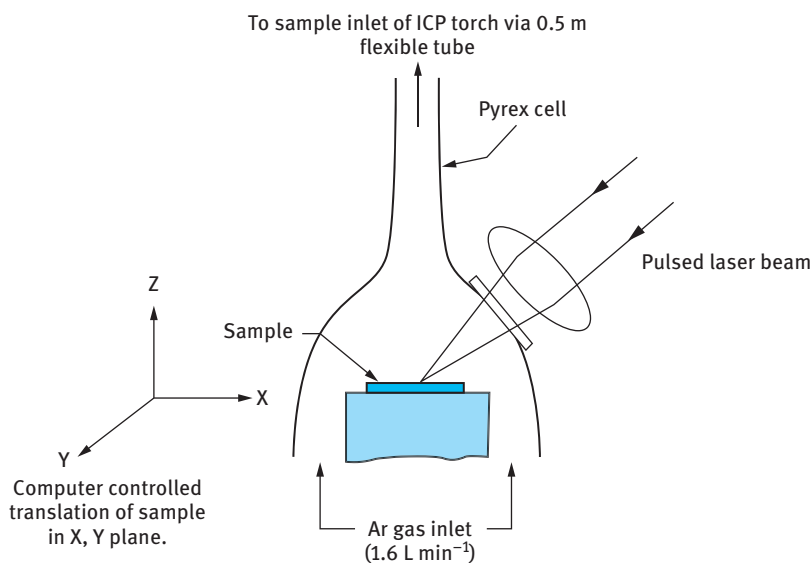


Figure 6.10: Schematic diagram of the laser ablation housing for 45° laser beam angle of incidence [32].

LA-ICP-OES is featured with low absolute detection limit (ng to pg level); the ability for conductor and nonconductor analysis, especially those solid samples difficult to decompose (e.g., complicated minerals, ceramics); supplementary means of micro-analysis; non-destructive analytical techniques; and low sample consumption, just 0.2% of that needed in conventional PN sampling.

Lin et al. [33] employed LA-ICP-OES for the direct determination of refractory elements (including REEs) in minerals without chemical separation, and relative detection limits of $\mu\text{g/g}$ or much lower were achieved. In the sample preparation, graphite, caprolactam and polychlorotrifluoroethylene (2:2:4) were used as the diluent, and the sample was mixed with the diluent with the ratio of 1:4. The mixed sample (6 mg) was pressed into discs ($\text{Ø}25 \text{ mm} \times 1.5 \text{ mm}$) and used for direct detection. The obtained detection limit for the refractory elements is listed in Table 6.15.

The addition of a certain amount of organic fluorinating reagent benefits the improvement of the vaporization behavior of target analytes, decreasing the effect of existing form of matrix and target analytes on the vaporization process. If the

Table 6.15: The detection limits for refractory elements by LA-ICP-OES.

Element	Relative detection limit (μg/g)	Absolute detection limit (ng)	Element	Relative detection limit (μg/g)	Absolute detection limit (ng)
Ba	2.6	3.1	Ce	11	13
Cu	0.1	0.12	Cr	9.7	1.2
La	6.1	7.3	Mn	10	12
Nb	8.0	9.6	Sc	17	20
Sr	3.0	3.6	Ti	—	—
V	11	13	Y	4.5	5.4
Yb	0.62	0.74	Zr	4.5	5.4

concentrated analytes can be introduced into plasma completely, the detection limit will be decreased efficiently. Under a certain condition, trace REEs were selectively adsorbed on an ionic-exchange paper, which was then vaporized by continuous laser and introduced into ICP for detection. The detection limit of ng/g can be obtained (Table 6.16).

Table 6.16: Trace REEs analysis by LA-ICP-OES combined with chemical separation/preconcentration technique.

Element	Wavelength (nm)	Detection limit (ng/g)	Element	Wavelength (nm)	Detection limit (ng/g)
La	379.1	1	Dy	353.1	0.1
Ce	371.1	30	Ho	345.6	0.6
Pr	390.8	10	Er	369.3	1
Nd	406.1	10	Tm	346.2	0.1
Sm	359.2	1	Yb	328.9	0.1
Eu	381.9	0.1	Lu	350.7	1
Gd	342.2	1	Y	371.0	0.1
Tb	350.9	1			

6.2.4 Electrothermal vaporization

This technique was developed from the atomizer source in graphite furnace atomic absorption spectrometry (GFAAS) and has gained renewed interest by the atomic spectroscopy community due to its outstanding characteristics compared with conventional PN. Firstly, ETV has high transport efficiency (approximately 80%), which is useful to promote the detection limits for the analysis of real samples. Secondly, the ETV steps of sample vaporization and its excitation/ionization are separated spatiotemporally, which is helpful in removing the matrix and reducing non-spectroscopic or spectroscopic interferences from the matrix. Thirdly, the low sample mass requirement of ETV

is favorable to some situations in which only a small amount of sample is available. Finally, ETV is quite suitable for direct analysis of solid samples, which leads to increasing applications in trace analysis.

Since the precursory reports of using a tantalum filament device as a vaporizer for ICP in 1974 [34] and employing a graphite furnace for sample introduction for ICP in 1978 [35], ETV-ICP-OES has been developed as an important tool for the determination of trace elements. When ETV sample introduction devices were hyphenated to ICP-MS [36], the performance of high sensitivity and solid sample analysis potential of ETV-ICP-MS attracted great attention for the determination of elements at trace and ultra-trace levels. Nowadays, ETV-ICP-OES/MS has been considered as one of the most versatile methods with respect to its accommodation of different types of samples with complex matrices (non-aqueous solutions, high dissolved salt or acid concentrations, slurries, and solid samples), especially solid samples.

6.2.4.1 Analytical performance

ETV-ICP-OES merits wide linear range, simultaneous multielement detection ability and good anti-interference capability in comparison with GFAAS. ICP-OES equipped with an ETV device offers 1–2 orders of magnitude improvements in detection limits, compared with conventional pneumatic nebulizer as sample introduction for the determination of many elements. The absolute detection limits generally range from sub-nanogram to picogram level for ETV-ICP-OES and from picogram to femtogram level for ETV-ICP-MS. Table 6.17 compares the analytical performance of ETV/PN-ICP-OES with GFAAS.

Table 6.17: Analytical performance of ETV-ICP-OES, PN-ICP-OES and GFAAS.

Analytical performance	ETV-ICP-OES	GFAAS	PN-ICP-OES
Detection limit	+	+	–
Anti-interference	+	–	++
Multielement simultaneous determination	–	–	+
Linear range	–	–	+
Micro sample introduction	+	+	–
Analytical rate	+	+	+
Analytical cost	–	+	–

Note: + represents good performance; – represents bad or average performance.

6.2.4.2 ETV devices and operation parameters

The vaporizers used in ETV are usually modified from a metal coil atomizer (tungsten, platinum, tantalum, etc.) or a graphite furnace. The metal coil device has smaller size than the latter, which facilitates its use in some miniaturized analysis

instruments. However, its inherent potential to interact with oxygen and evaporate at high temperature prevents its application as an atomizer. Consequently, the graphite furnace is employed most often, even though it suffers from “memory” effect at high temperature due to analyte transferring into the inner surface of graphite tube and formation of refractory carbides. The use of pyrolytic graphite-coated tube or metallic carbide-coated tube could improve the performance of graphite furnace ETV.

Many designs have been studied in order to obtain a high transport efficiency of analyte from ETV to ICP. One of the most used designs is the horizontal flow-through type. The carrier gas flows through the longitudinally heated graphite tube from one end to the other toward the plasma. In order to form a stable aerosol, a finely designed cold gas flow was usually incorporated at the outlet of the graphite furnace. The by-pass cold gas is favorable for minimizing aerosol condensation and deposition in the transferring tubing.

Some factors are usually considered in the design of the electrothermal vaporization (ETV) device: (i) avoiding the condensation and deposition of sample aerosol in the internal surface of evaporation chamber; (ii) providing maximum vapor density for transmission; (iii) reducing the pulse effect (piston effect) in the ICP to keep the stability; (iv) achieving long retention time of analytes in the plasma and maximizing the atomization/excitation efficiency. A schematic diagram of ETV-ICP system by using a graphite furnace as the vaporizer is presented in Figure 6.11.

It should be noted that the role played by graphite furnace in GFAAS and in ETV-ICP-OES/MS is different. For GFAAS, the graphite furnace is used not only as a vaporizer but also as an atomizer, in which the sample drying, ashing and atomization take place. Sometimes, it is difficult to achieve a complete atomization for refractory elements and carbide-forming elements, due to restricted maximum available temperature (2,800–3,000 °C) and the small size of space in the graphite furnace. However, for ETV-ICP-OES/MS, the graphite furnace is only used as a vaporizer, in which the sample undergoes drying, ashing and evaporation. In this case, a complete vaporization of the analyte and its efficient transportation into ICP, in which excitation/ionization of the analyte occurs, are only necessary for adjusting the graphite furnace as sample introduction device.

Good performance of ETV-ICP-OES/MS depends on its operation conditions. A higher flow rate of carrier gas would decrease the dilution effect on aerosol, whereas a lower gas flow rate would lead to a longer retention time of analyte in the plasma, which is favorable for multielement detection. Optimization of ICP-OES/MS should also be carried out usually with a conventional PN method, before its connection with ETV. Similar to GFAAS, the temperature programs for ETV-ICP-OES/MS also consist of drying, ashing and vaporization steps. During the drying step, the sample overheating and plasma overloading should be prevented. Successful removal of matrix may be realized by proper usage of drying and ashing steps. The optimized vaporization

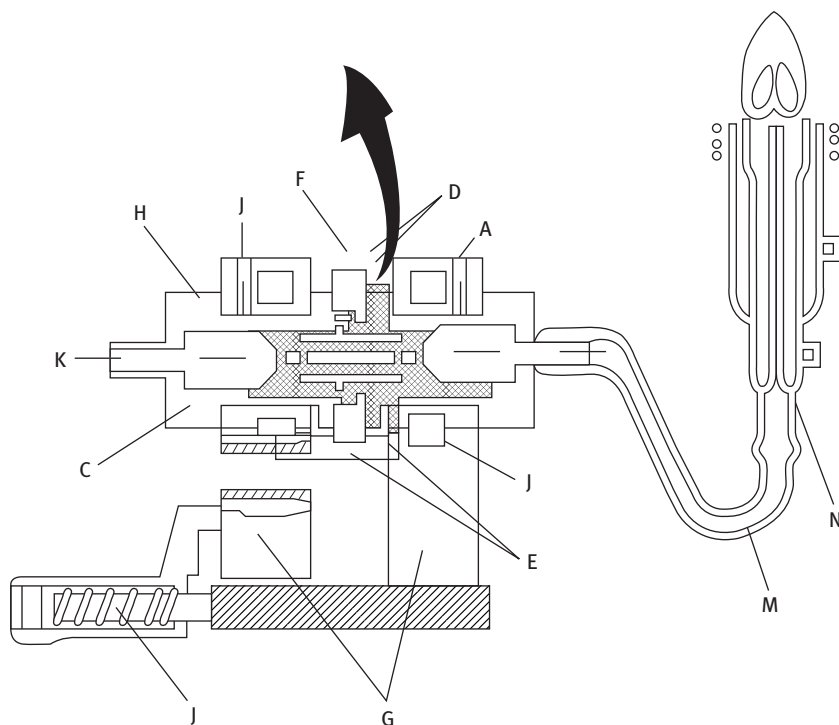


Figure 6.11: Schematic diagram of ETV-ICP system by using a graphite furnace as the vaporizer (A, graphite tube; B, sampling hole; C, graphite seat; D, seat cover; E, packing ring; F, filling plug; G, electrothermal unit; H, pipe connector; I, cooling water pipe; J, compression spring; K, carrier gas; L, outside flow air; M, PTFE tube; N, ICP torch) [37].

temperature should be chosen for good signal profiles and the highest intensities of analytes of interest.

6.2.4.3 Limit of conventional ETV system

Low vaporization and transportation efficiency of interesting analytes sometimes occurred in conventional ETV-ICP-OES, which is mainly caused by the following situations: (i) the analytes vaporized out before vaporization step in the temperature programs, which is called ashing loss; (ii) incomplete vaporization of interest analytes leads to a decrease in the transportation efficiency; (iii) the deposition of analytes in the internal surface of ETV device and the transportation tubing result in a decreased transportation efficiency.

To achieve complete vaporization of refractory elements and those that can easily form nonvolatile carbides with graphite at high temperature, the following strategies can be adopted:

- (1) Employing refractory metal (e.g., Ta) as the vaporizer. The disadvantage of this vaporizer is that these metals can easily react with active substances in air and sample to become brittle at high temperature. Moreover, the vaporization of these metals at high temperature may cause spectral interferences.
- (2) Coating the graphite tube with metallic carbides. While it could improve the detection limits of several elements it led to worse detection limits of some others.
- (3) Use of chemical modifiers. Chemical modifiers could be spiked to react with interest analytes (or matrix), forming volatile compounds which can be vaporized out. It is proved to be efficient and effective to resolve this problem.

The most widespread and efficient type of chemical reaction is halogenating reaction, especially fluorination and chlorination reaction. The halogenating reaction can easily happen at high temperature to a great number of elements and the formed halide is more volatile than their oxide substances. Besides, metal chelating and alkylating reactions can also be employed.

The chemical modifiers can be divided into inorganic and organic chemical modifiers. Comparatively, organic chemical modifiers are more commonly used in ETV-ICP-OES system, probably due to the more degradability of organic reagents, which can easily release active substances.

The chemical modifiers can be spiked into ETV system in gaseous or solid form. Gaseous chemical modifier (e.g., Freon) is mixed into the carrier gas (Ar), and the reaction process is happening between gaseous chemical modifiers and solid samples; solid modifiers are mixed with the sample evenly or prepared into slurry solution, followed by introducing into the vaporizer. Slurry sample introduction inherits the advantages of direct solid sample introduction and liquid sample introduction.

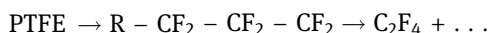
6.3 ETV-ICP-OES for REE analysis

When ETV-ICP-OES is used for the determination of refractory elements and easily forming carbides elements (e.g., REEs), incomplete vaporization of the analytes and memory effects are the major difficulties. The application of a suitable chemical modifier has been proved to be one of the most efficient methods.

6.3.1 Fluorination-assisted ETV-ICP-OES for REEs analysis

Halogenation with halocarbon vapors (CCl_4 , CF_2Cl_2 , CHF_3 , etc.) has been successfully introduced into GFAAS and ETV-ICP-OES/MS for volatilization of refractory elements or for in situ removal of matrix. When polytetrafluoroethylene (PTFE) emulsion was used as a halogenating reagent in ETV, the vaporization of refractory elements and carbide-forming elements from the graphite tube and their transport into the plasma could be dramatically improved.

PTFE is high molecular polymer with a decomposition temperature of 415 °C and would decompose into a series of monomers of tetrafluoroethylene at temperature higher than its decomposition temperature.



At high temperature, the decomposition products of PTFE and C_2F_4 would react with the oxides of many elements, forming corresponding fluoride. Compared with other halogenating reagents, PTFE presents several advantages: (i) high fluorine content; (ii) sufficient chemical activity of F; (iii) suitable decomposition temperature (about 415 °C), favoring the elimination of organic matrix; (iv) low amount of inorganic impurities; and (v) easy to use, and can be easily mixed with sample in any ratio.

FETV technique for sample introduction, using PTFE slurry as fluorinating reagent to promote the volatility of REEs, has been proved to be effective and efficient. By the use of PTFE as a fluorinating reagent, the vaporization and transport efficiency of trace REEs in ETV-ICP-OES are dramatically improved, which leads to the promotion of detection limits by one or two orders of magnitude in comparison with that obtained with an ETV technique without the use of PTFE.

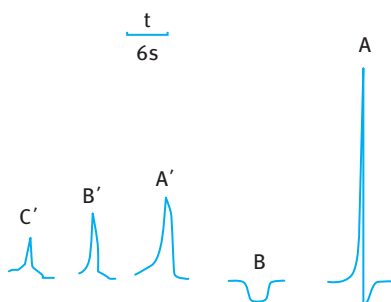
6.3.1.1 Vaporization mechanism of REEs fluorination

REEs are refractory metals with high boiling points for the elements or their oxides. Besides, REEs would easily form very stable involatile carbide on the surface of graphite tube. Table 6.18 lists some physicochemical characteristics of REEs and related compounds.

Figure 6.12 presents the typical signal profiles of Yb in the absence and presence of PTFE. As can be seen, the signal of Yb obtained in the absence of PTFE is very weak, the peak is broad, and asymmetry with tailing and the memory signal is obvious. In the presence of PTFE, the signal peak of Yb is strong, sharp and symmetrical, and the memory signal is negligible. The results indicate that refractory RE oxides reacted with fluorinating reagent in the presence of PTFE and form fluorides with low boiling point which is vaporized and transported into ICP.

Table 618: Melting and boiling points (°C) for REEs and corresponding compounds.

Element	Metal		Oxide		Carbide		Fluoride	
	Melting point	Boiling points	Melting point	Boiling points	Melting point	Boiling points	Melting point	Boiling points
Sc	1538	2730	–	4450	1797	–	1515	1527
Y	1530	3304	–	4300	1950	–	1152	2230
La	920	3470	2217	4200	2360	–	1493	2327
Ce	795	3475	2397	3300	2290	–	1430	2327
Pr	919	3130	2042	–	2160	–	1395	2327
Nd	1019	3127	2211	–	–	–	1374	2327
Sm	1072	1803	2262	–	–	–	1306	2327
Eu	826	1440	2002	–	2265	–	1276	2327
Gd	1306	3000	2322	–	2097	–	1231	2277
Tb	1360	2800	2337	–	2245	–	1172	2280
Dy	1500	2600	2352	–	–	–	1154	2230
Ho	1461	2600	2367	–	2280	–	1143	2230
Er	1497	2900	2387	–	2180	–	1140	2230
Tm	1545	1730	2392	–	2180	–	1158	2230
Yb	824	1430	2372	3227	–	–	1157	2230
Lu	1652	3300	2467	–	–	–	1182	2230

**Figure 6.12:** Signal profiles of Yb in the absence and presence of PTFE [38] A, 0.5 mg/L Yb, 6% PTFE; B, 10 mg/L Yb, 6% PTFE cleaning signal; A', 2mg/L Yb, without PTFE; B' and C' are the 1st and 2nd cleaning signal, respectively.

6.3.1.1.1 Transportation process

Deposition loss is usually employed for the evaluation of the transportation efficiency of analytes in the transportation process. Table 6.19 lists the deposition loss of analytes with and without the presence of PTFE. As can be seen, although the deposition loss is reduced under the presence of PTFE, it's not very much. And the deposition loss is mainly caused by rapid temperature decreasing.

While the premise for evaluating the transportation efficiency with deposition loss is the complete vaporization of target analytes, this is not true in practical process. Thus, the relative deposition loss is proposed for a better understanding of the transportation efficiency, which is defined as the ratio of the deposition loss amount of target analytes to the vaporized amount of corresponding elements. Table 6.20 presents

Table 6.19: The deposition loss of analytes with and without the presence of PTFE.

Element	Deposition loss (%)	
	Without PTFE	With PTFE
La	19.2	15.7
Yb	24.6	14.9
Y	25.8	13.5

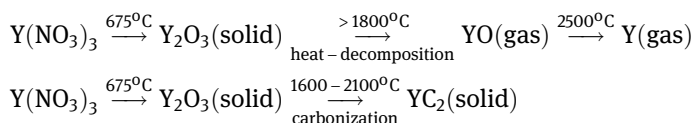
Table 6.20: The relative deposition loss of target analytes with and without the presence of PTFE.

Element	Relative deposition loss (%)	
	Without PTFE	With PTFE
La	63.0	16.0
Yb	32.5	15.6
Y	67.6	13.5

the relative deposition loss of target analytes with and without the presence of PTFE. It shows that the relative deposition loss with the presence of PTFE is reduced by two times (Yb) to five times (La) over that without the presence of PTFE, indicating that the introduction greatly improves the transportation of REEs in ETV system. The reason may be specified by two factors. (i) The formed fluoride is transported in the form of a molecule, whose transportation rate is higher than that of the conventional atom transportation form. (ii) Besides the reactive small molecular decomposed from the PTFE under high temperature, other nonreactive small molecular and tiny particles are formed by the gas flow, and it can act as a “condensation nuclei” of gaseous fluorides in the condition of rapid ETV heating, improving the transportation efficiency of target analytes [39].

6.3.1.1.2 Vaporization process of REEs and the mechanisms

Without the presence of PTFE, REEs is vaporized in atomic vapor form in ETV-ICP-OES; the vaporization process can be described as follows by taking Y as the representative.



The formed YC_2 is very stable and cannot decompose during the ETV heating program. Yet $\text{Y}_2\text{O}_3(\text{solid}) \rightarrow 2\text{YO}(\text{gas}) + \text{O}(\text{gas})$ would happen from the thermodynamics'

point of view. Thus, Y is vaporized in the form of gaseous atom and the vaporization is incomplete.

With the presence of PTFE, the situation is contrary. The target REEs are vaporized out under a relatively low temperature and the vaporization efficiency of above 98% can be achieved. RE oxides react with PTFE as in the following process. The thermodynamics data listed in Table 6.21 can also prove the feasibility.

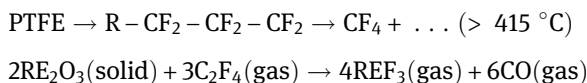


Table 6.21: ΔG (kJ) for the fluorinating reaction of La, Y and Yb with the presence of PTFE.

Reaction	1000 K	1500 K	2000 K
$2\text{La}_2\text{O}_3(\text{s}) + \text{C}_2\text{F}_4(\text{g}) \rightarrow 4\text{LaF}_3(\text{g}) + 6\text{CO}(\text{g})$	–	–2202	–
$2\text{Y}_2\text{O}_3(\text{s}) + \text{C}_2\text{F}_4(\text{g}) \rightarrow 4\text{YF}_3(\text{g}) + 6\text{CO}(\text{g})$	–1172	–1725	–2203
$2\text{Yb}_2\text{O}_3(\text{s}) + \text{C}_2\text{F}_4(\text{g}) \rightarrow 4\text{YbF}_3(\text{g}) + 6\text{CO}(\text{g})$	–524	–983	–

6.3.1.2 Affecting factors for fluorination vaporization

The main factors influencing the formation and vaporization of fluorides include the amount of fluorinating reagents, ashing temperature, vaporization temperature and matrix concentration.

(1) Amount of fluorinating reagents (PTFE slurry)

The concentration of fluorinating reagents is one of the main impactors which influence the completion of fluorination reaction. Figure 6.13 represents the effect of PTFE concentration on the vaporization signal intensity of La. It indicates that the signal intensity is increased with the increase of the concentration of PTFE and maintains constant when the concentration of PTFE is above 4% (m/V). Yet when the concentration of PTFE is increased further, the plasma is unstable and quenched sometimes, probably due to the rapid decomposition of PTFE in the plasma and the resulting un-matching impedance. Generally, 6% PTFE is employed in the experiment.

(2) Ashing temperature

The selection of ashing temperature should consider the following factors. (i) It is beneficial to the removal of the matrix, especially organic matrix; (ii) It helps the rapid formation of RE fluorides; (iii) No loss of analytical signal. Figure 6.14 represents the effect of ashing temperature on the vaporization signal of La. An obvious ashing loss is observed when the temperature is higher than 1,800 °C. In other words, an ashing temperature up to 1,500 °C can be employed, and a lot of interference components (organic compounds and part of inorganic matrix) can be completely removed under this temperature. This temperature is much higher than the decomposition

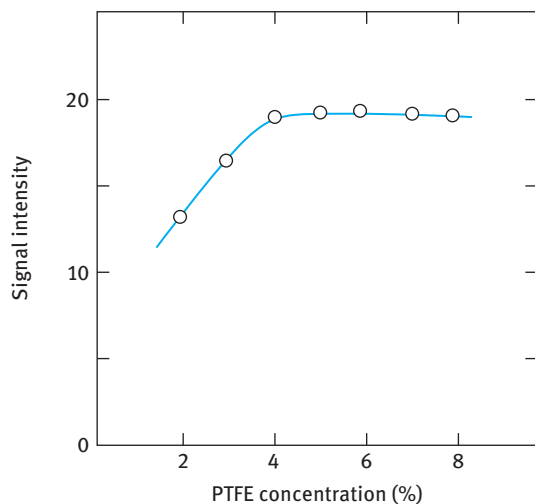


Figure 6.13: Effect of PTFE slurry concentration on the signal intensity of La [40].

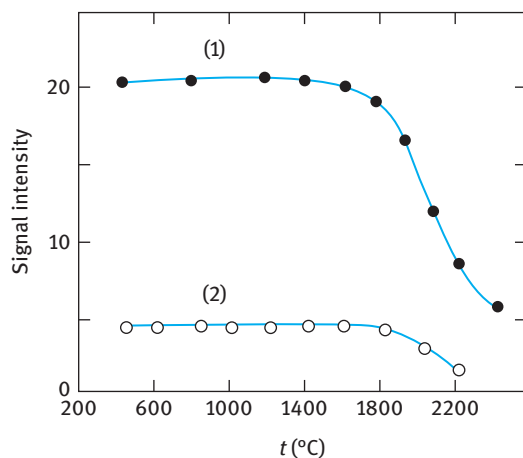


Figure 6.14: Ashing curve of La [40] (1) 0.2 mg/L La, 6% PTFE; (2) biological sample, 6% PTFE.

temperature of PTFE (415 °C), indicating that there is no obvious loss of the formed fluorides at such a high temperature. Thus, for the elements with boiling points higher than 415 °C for their fluorides (e.g., REEs), the selection of ashing temperature should refer to the boiling point of corresponding fluorides; for the elements with boiling points lower than 415 °C for their fluorides (e.g., Si), the selection of ashing temperature should refer to the decomposition temperature of PTFE, $T_{\text{ashing}} < 415$ °C. In general, the ashing time affects the extent of fluorination reaction to some extent.

(3) Vaporization temperature

Figure 6.15 provides the effect of vaporization temperature on the signal intensity of La. It shows that the vaporization efficiency is increased with the increase of the vaporization temperature, along with the increasing of the signal intensity. And the signal intensity maintains constant when the temperature is above a certain level (e.g., 2,400 °C). Compared with conventional ETV, the optimal vaporization temperature in fluorination-assisted ETV is lower.

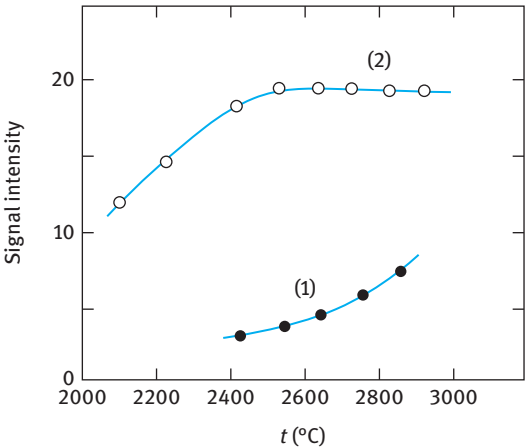


Figure 6.15: The effect of vaporization temperature on the signal intensity of La [40] (1) 2 mg/L La; (2) 0.2 mg/L La, 6% PTFE.

(4) Matrix concentration

Matrix effect is one of the main factors evaluating the analytical performance of the method.

Alkali and alkaline earth metals are common matrix elements in many real-world samples. Table 6.22 lists the tolerance limit of alkali and alkaline earth metals in the determination of La and other refractory metals by FETV-ICP-OES. As can be

Table 6.22: Matrix effect of alkali and alkaline earth metals.

Element and wavelength (nm)	Concentration of target element (mg/L)	Tolerance limit (mg/mL)			
		K	Na	Ca	Mg
La 333.749	0.5	5.0	5.0	5.0	5.0
Mo 202.030	0.1	5.0	5.0	5.0	5.0
Cr 267.716	0.4	5.0	5.0	5.0	5.0
B 249.678	0.3	5.0	5.0	5.0	5.0

seen, the highest tolerance limit of alkali and alkaline earth metals exceeds 5 mg/mL, which is approximately 10^4 – 10^5 times of the concentration of target element.

Table 6.23 lists the tolerance limit of transitional metals in the determination of La and other refractory metals by FETV-ICP-OES. As can be seen, the effect of transitional metals on the fluorination-assisted vaporization of interest elements is not very obvious.

Table 6.23: Matrix effect of transitional metals.

Element and wavelength (nm)	Concentration of target element (mg/L)	Tolerance limit (mg/mL)				
		Cu	Mn	Pb	Zn	Fe*
La 333.749	0.5	5.0	5.0	5.0	5.0	5.0
Mo 202.030	0.1	5.0	—	—	4.0	2.0
Cr 267.716	0.4	5.0	—	—	5.0	5.0
B 249.678	0.3	5.0	—	5.0	5.0	—

*when the concentration of Fe is above 2 mg/mL, Fe 202.050 nm interfere Mo 202.030 nm.

Figure 6.16 presents the effect of RE matrix (Y, Yb) on the signal intensity of La. No obvious variation of the signal intensity is observed when the concentration of matrix (Y, Yb) is below 2 mg/mL. When the concentration of matrix is above 2 mg/mL, the signal intensity of La is decreased sharply, probably due to the two competition reactions. One happens between target analytes and fluorinating reagents, the other

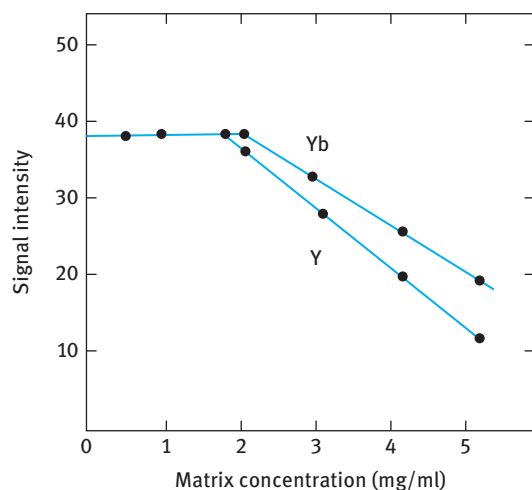


Figure 6.16: The effect of RE matrix (Y, Yb) on the signal intensity of La [38].

happens between the RE matrix and fluorinating reagents, and they may cause the incomplete vaporization of La or variation of the vaporization rate.

6.3.1.3 Analytical performance

Table 6.24 presents the detection limits of REEs obtained by FETV-ICP-OES. As can be seen, the absolute detection limit of sub ng/pg is obtained for REEs by FETV-ICP-OES. Compared with conventional ETV-ICP-OES detection system, the detection is improved by about 2 orders of magnitude; the relative detection limit is comparable or superior to that obtained by PN-ICP-OES. RSD of less than 5% can be achieved in FETV-ICP-OES, and the dynamic linear range covers 3–4 orders of magnitude. As mentioned above, the tolerance limit of coexisting ions is about 10^4 – 10^5 times of target REEs in FETV-ICP-OES measurement, which is one order of magnitude higher than that obtained in conventional ETV-ICP-OES.

Table 6.24: Detection limits of REEs [41].

Element	Wavelength (nm)	PN-ICP-OES	Conventional ETV-ICP-OES		FETV-ICP-OES		
		ng/mL	ng/mL	ng	ng/mL	ng	ng [42]
La	333.7	263	500	5.0	4.0	0.08	
Ce	413.7	86			14	0.28	
Pr	401.2	83			17	0.34	
Nd	390.8	290			10	0.20	
Sm	359.3	52			9.6	0.19	
Eu	381.9	18			1.8	0.036	0.012
Gd	342.2	29			8.2	0.16	
Tb	350.9	30			8.7	0.17	
Dy	353.1	22			3.7	0.07	
Ho	345.6	15			2.5	0.05	
Er	337.2	21			3.0	0.06	0.034
Tm	313.3	46			1.6	0.03	
Yb	328.9	7			1.2	0.02	0.018
Lu	261.5	1.1			0.2	0.004	0.054
Y	371.0	23	621	12	0.6	0.012	0.025
Sc	361.3	7			0.2	0.004	0.017

6.3.2 Low temperature ETV-ICP-OES for REEs analysis

The use of organic chelating reagents as chemical modifiers in the ETV-ICP-OES has some characteristics including the following: (i) refractory elements can be vaporized at lower temperatures, which is beneficial to prolong the lifetime of evaporator;

and (ii) organic chelating reagents can be used both as chemical modifiers and as extracting reagents; thus, the application potential and the determination sensitivity of the method can be further improved.

A series of chelating reagents including EDTA, polyhydroxy compounds, 8-hydroxyquinoline, 1-phenyl-3-methyl-4-benzoyl-5-pyrazone (PMBP), acetylacetone, thenoyltrifluoroacetone (TTA), diethyldithiocarbamate and ammonium pyrrolidinecarbodithioate have been tested as chemical modifiers for ETV-ICP-OES/MS determination of trace elements. Peng and Jiang [44] firstly attempted to use the reaction of PMBP and REEs in ETV, which form volatile and chemically stable REEs chelates for the subsequent vaporization. It was found that PMBP chelates of La, Y, Eu and Sc could be vaporized from graphite tube at 1,000, 1,200, 1,200, and 900 °C, respectively. The proposed method was successfully employed for trace REEs (La, Eu, Y and Sc) analysis in environmental samples. By using PMBP as the chemical modifier in ETV-ICP-OES analysis of refractory REEs, the vaporization temperature (900–1,200 °C) of interest REEs is significantly decreased compared to that in conventional ETV system, the formation of RE carbides is effectively avoided, and the detection limit of REEs (ng/mL level) is comparable to that in FETV-ICP-OES. Fan et al. [43] developed a method of ETV-ICP-OES for the determination of trace Sc and Y, based on gaseous compound introduction into the plasma as their TTA complexes. As can be seen from Figure 6.17, a weaker signal intensity could be detected for Sc and Y at the temperature of 300 and 500 °C, respectively, indicating that the TTA complexes of Sc(III) and Y(III) formed and started to vaporize into ICP [43]. With the elevation of vaporization temperature, the signal intensity for both Sc and Y increased notably, and the maximum emission signal was obtained at 800 °C for Sc and 900 °C for Y. These maximum signals remained constant with further increases of vaporization temperature up to 1,500 °C.

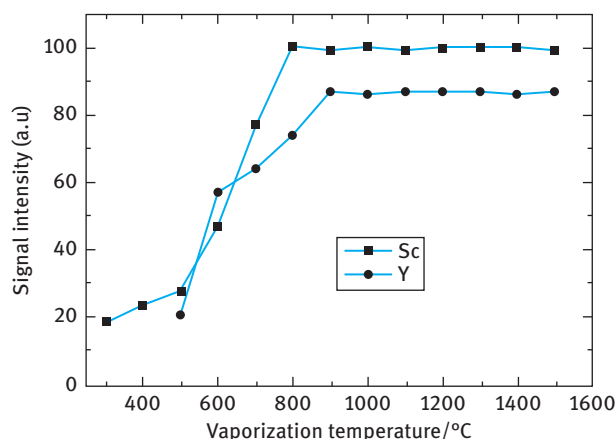


Figure 6.17: Effect of vaporization temperature on the signal intensity of Sc and Y (Sc and Y, 2 ng; TTA, 0.8 mmol/L) [43].

Besides, low-temperature ETV-ICP-OES can be easily combined with sample pretreatment techniques for further improvement in the detection limit of target REEs. Chen et al. [45] employed PBMP as both the extractant and chemical modifier and realized the quantification of trace Eu in high-purity ZrO_2 by ETV-ICP-OES.

Above all, compared with conventional ETV system, low-temperature (LT)ETV merits the following: (i) the vaporization of REEs can be performed at fairly low temperature in LT-ETV; (ii) the lifetime of graphite tube can be prolonged; (iii) the formation of refractory carbides is effectively prevented; (iv) the sensitivity is improved significantly; (v) it's easy to combine with chemical separation/preconcentration technique.

6.4 Application of ICP-OES in the quantification of REEs in real samples

6.4.1 High purity REE analysis by ICP-OES

High-purity REE refers to RE metals or oxides with the purity higher than 99.9%, which are mainly used in optical, electric, magnetic and other functional materials. The metal impurities in these high-purity REE materials are in $\mu\text{g/g}$ level or much lower. ICP-OES can be employed for the analysis of high-purity REE (99.9–99.99%) with good reproducibility, no need for complicated sample pretreatment process and multielement analysis ability. The application of ICP-OES for the analysis of high-purity REE is presented in Table 6.25.

Yet the sensitivity of ICP-OES is not high enough for the analysis of REE with purity higher than 99.99%; the spectral interference is serious, especially for those REE matrix with complex spectral background; matrix matching is often needed due to the matrix effect; and direct solid sample analysis is expected. It should be pointed out that the ability of analyzing high-purity REE by ICP-OES is affected by the complex spectral background of REE matrix, and the high dilution of the sample along with the low nebulization efficiency limits the determination performance of ICP-OES to a great extent.

6.4.1.1 Detection limit of REEs in REE matrix

The conventional detection limit (C_L) is obtained with the absence of other coexisting elements, no consideration of matrix effect in real-world sample. Boumans proposed real detection limit ($C_{L,i}$) which can be expressed as

Table 6.25: Application of ICP-OES in the determination of REEs impurities in high purity REE.

Matrix	Determined elements	Instrument types	Reciprocal linear dispersion (nm/mm)	Limit of determination or purity	Ref.
Ce	La,Pr,Nd,Sm,Y	PGS-2/ Spectrographic	0.37	99.99%	[47]
La	Part of the REEs	7502B/ Multichannel	0.55	99%-99.9%	[6]
Tb	Y,Sm,Eu,Gd,Dy, Ho,Er	JY38/Scanning	0.26	10%-100 µg/g	[5]
La	Ce,Pr,Nd,Sm	JY38/Scanning	0.26	ng/mL grade	[48]
Pr	La,Ce,Nd,Sm,Y	JY38/Scanning	0.26	99.95%	[49]
Sm	14 REEs	ICPS-1000/ Scanning	–	99.95%	[50]
Nd	14 REEs	WSP-1/ Spectrographic	0.46	high purity	[51]
Eu	14 REEs	PGS-2/ Spectrographic	0.37	0.5–30 µg/g	[46]
Eu	14 REEs	ICPS-1000/ Scanning	–	1–10 µg/g	[52]
Gd	14 REEs	WPG-100/ Spectrographic	0.8	1.3–36 µg/g	[53]
Tb	Ce,Pr,Nd,Sm,Eu, Gd,Dy,Ho,Er,Y	WSP-1/ Spectrographic	0.46	99.8%	[54]
Tm	14 REEs	PGS-2/ Spectrographic	0.74	99.95%	[55]
Sc	14 REEs	PGS-2/ Spectrographic	0.37	99.99%	[47]
Tm	14 REEs	PGS-2/ Spectrographic	0.74	99.99%	[56]
Lu	14 REEs	PGS-2/ Spectrographic	0.74	99.99%	[57]
Y	14 REEs	PGS-2/ Spectrographic	0.74	99.99%	[58]
La	14 REEs	PGS-2/ Spectrographic	0.74	99.99%	[59]
Ce	14 REEs	PGS-2/ Spectrographic	0.36	99.95%	[60]

$$C_{L,t} = \frac{2}{5} \times \frac{X_i(\lambda_a)}{S_a} + C_L$$

where k is the sensitivity of the analytical line, and $X_i(\lambda_a)$ is the net signal of interference obtained at the analytical line. Thus, $C_{L,t}$ is often higher than C_L .

Velichkov employed $C_{L,t}$ for the selection of analytical line in the determination of single RE in high-purity RE materials [61]. Table 6.26 lists a comparison of detection limits for REEs obtained under different circumstances, where A represents the detection limit with the presence of matrix ($C_{L,t}$), B represents the detection limit without the presence of matrix (C_L) and C is the detection limit obtained after the removal of matrix. As can be seen, in the presence of RE matrix, the obtained real detection limit is higher than the obtained conventional detection limit; the increase of the detection limit depends on the spectrum complexity of the RE matrix, and the detection limit is much higher when the spectrum of RE matrix is more complicated;

Table 6.26: The detection limits of REEs under different conditions [61].

Element	Analytical lines (nm)	Detection limits corresponding to dissolved solids (matrix is Pr or Sm)(%)		
		A	B	C
Sc II	424.683	4.6×10^{-4}	1.5×10^{-4}	1.8×10^{-5}
Y II	324.228	1.0×10^{-3}	—	2.4×10^{-5}
La II	333.749	4.1×10^{-3}	—	7.6×10^{-5}
Ce II	446.021	1.7×10^{-2}	2.1×10^{-3}	2.3×10^{-4}
Pr II	418.948	—	1.6×10^{-2}	4.1×10^{-4}
Nd II	430.358	—	1.3×10^{-3}	5.0×10^{-4}
Sm II	360.949	4.4×10^{-3}	—	1.8×10^{-4}
Eu II	412.970	—	1.3×10^{-3}	1.4×10^{-4}
Gd II	272.778	1.5×10^{-3}	—	1.3×10^{-4}
	301.013	3.1×10^{-3}	—	1.8×10^{-4}
	310.050	—	6.9×10^{-3}	1.8×10^{-4}
Tb II	370.286	—	1.0×10^{-2}	2.7×10^{-4}
Dy II	353.170	5.9×10^{-3}	6.5×10^{-4}	—
Ho II	339.898	—	4.0×10^{-4}	6.5×10^{-5}
Er II	337.271	—	2.6×10^{-4}	3.0×10^{-5}
Tm II	346.220	—	3.3×10^{-4}	7.0×10^{-5}
Yb II	289.138	9.5×10^{-4}	—	6.0×10^{-5}
Lu II	328.937	—	4.2×10^{-4}	2.0×10^{-5}
	261.542	1.0×10^{-4}	1.6×10^{-4}	7.4×10^{-6}

$C_{L,t}$ is increasing with the increase of the matrix concentration; the detection limit could be improved by removing the matrix and enriching target analytes.

6.4.1.2 Analytical line and internal line

For the direct determination of trace REEs impurities in high-purity RE, the selection of analytical lines should consider the following factors: (i) sensitive analytical lines are commonly considered; (ii) when the most sensitive line is interfered, other sensitive lines should be selected instead; (iii) the interference type (partly or complete overlapping) and extent should be investigated by wavelength scanning; (iv) instrument with high dispersive power can be used to avoid or reduce the spectral interference; (v) appropriate dilution of the sample can reduce the spectral interference caused by the matrix to some extent.

Application of a certain internal standard would avoid the problems caused by variation of ICP discharging parameters and nebulization condition, ensuring the reproducibility and accuracy of the method. Table 6.27 lists the analytical lines of REEs in high-purity RE matrix.

Table 6.27: Reference analytical lines for ICP-OES detection of REE impurities in high purity RE matrix.

Matrix	Analytical lines of RE impurities (nm)							
	Ce	La	Pr	Nd	Sm	Eu	Gd	Tb
La	338.10	—	474.02	384.90	408.67	480.67	333.75	—
Ce	—	418.66	456.05	415.47	413.38	446.02	418.66	413.38
Pr	422.54	417.94	—	410.07	440.88	422.29	414.31	422.52
Nd	406.11	406.11	—	—	430.35	406.11	415.61	399.46
Sm	359.26	373.91	446.73	336.59	—	442.43	388.5	359.26
Eu	388.97	397.19	—	309.71	272.77	—	372.49	412.97
Gd	364.62	354.93	—	376.84	376.84	335.05	—	385.24
Tb	332.44	350.91	—	350.92	332.44	387.42	367.64	—
Dy	340.78	353.17	—	—	394.46	338.50	394.46	400.04
Ho	345.60	345.60	—	450.39	381.07	345.60	—	381.07
Er	337.27	337.27	—	390.63	337.27	349.91	369.27	349.91
Tm	336.26	342.51	—	336.29	384.80	329.1	313.13	—
Yb	369.42	328.93	—	398.80	328.93	328.93	297.06	—
Ln	347.20	307.76	—	350.74	261.54	291.14	307.76	—
Y	324.22	371.02	332.78	354.90	371.02	324.22	371.02	377.43

Matrix	Analytical lines of rare earth impurities (nm)						
	Dy	Tm	Yb	Lu	Y	Y	Sc
La	379.48	423.83	423.83	423.83	408.67	408.67	333.74
Ce	404.08	424.86	429.66	418.66	413.76	413.38	422.57
Pr	390.84	440.88	418.95	417.94	417.94	422.53	422.39
Nd	401.25	438.56	415.60	406.10	401.22	396.31	410.34
Sm	359.26	428.08	446.73	425.64	356.82	428.08	403.43
Eu	381.97	420.50	393.05	397.19	443.55	390.71	393.05
Gd	342.25	335.08	354.93	354.93	335.04	342.24	342.24
Tb	350.92	400.55	400.55	356.17	387.41	350.91	350.91
Dy	—	444.97	397.85	353.17	400.04	353.17	400.04
Ho	345.60	442.05	348.48	345.60	347.42	339.89	345.60
Er	369.26	390.63	390.63	369.26	337.27	337.27	323.05
Tm	346.22	—	367.13	346.22	342.51	342.51	342.51
Yb	328.94	328.93	—	328.93	369.42	328.93	328.93
Ln	350.74	350.74	350.74	—	261.54	291.13	347.24
Y	377.43	371.02	437.49	324.22	—	—	324.22

6.4.1.3 Matrix concentration and solid detection limit

The relative solid detection limit of the method could be improved by increasing the concentration of the sample (matrix concentration), while matrix effect would deteriorate the detection limit. Thus, it is necessary to select an appropriate

concentration of the sample matrix. The aqueous detection limit of target analyte can be expressed as:

$$C_L = \frac{k \cdot (RSD)_B \cdot C_o}{I_L/I_B}$$

where k is an integer determined by confidence, generally $k = 3$, $(RSD)_B$ is the RSD of background signal, I_L/I_B is the signal-to-background ratio, and C_o is the concentration of target analyte.

Actually, the solid detection limit in the original sample is more interested in high-purity RE analysis. Dividing both sides of the formula by the matrix concentration (C_{matrix}) simultaneously, the solid detection limit can be obtained:

$$C'_L = \frac{k \cdot (RSD)_B \cdot C'_o}{I_L/I_B}$$

where C'_o is the content of target analyte in solid sample. For a specific sample, C'_o , k and $(RSD)_B$ are constants; thus, C'_L is proportional to reciprocal of I_L/I_B .

To find the appropriate matrix concentration, the following procedure can be processed.

The sample solution is diluted stepwise and a series of sample solutions with different matrix concentration are obtained. The corresponding I_L/I_B is determined and plotted to matrix concentration (C_{matrix}), resulting to a curve of relationship between the solid detection limit and matrix concentration (Figure 6.18). As can be seen, with the increasing of the matrix concentration, the solid detection limit of target analyte is decreased; with further increasing of the matrix concentration, the solid detection limit decreases slowly and becomes constant. Based on it, an appropriate matrix concentration can be selected.

Besides, when the matrix concentration is too high, nebulizer clogging or analytes deposition on ICP torch would occur. Consequently, matrix concentration of less than 10 mg/mL is usually employed.

6.4.2 REE ores analysis by ICP-OES

Acid or alkaline digestion is usually employed to transform the ores into aqueous solution prior to ICP-OES detection. Table 6.28 lists the application of ICP-OES for the direct determination of REEs in ores. It should be pointed out that the sensitivity of ICP-OES is limited and the possible spectral interference caused by coexisting ions should be corrected.

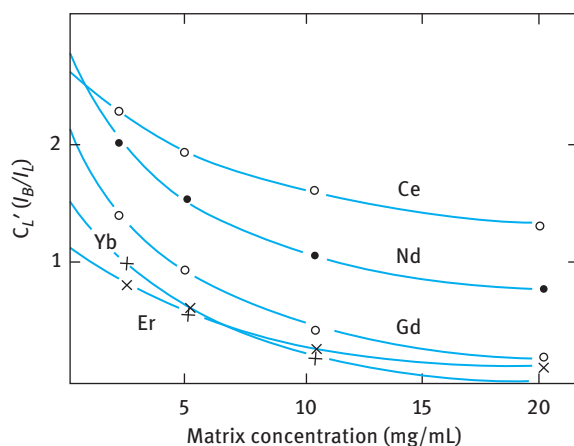


Figure 6.18: Relationship between the solid detection limit and matrix concentration [46].

Table 6.28: Application of ICP-OES for the direct determination of REEs in ores.

Sample	Target analyte	Sample preparation	Detection limit	Reference
Phosphate Mine	REEs	Sample is digested by $\text{HNO}_3 + \text{HF} + \text{HCl}$, vaporized, and diluted by diluted HNO_3 for ICP-OES detection	40–300 $\mu\text{g/g}$	[62]
Geological samples	13 REEs	Sample is microwave-digested by $\text{HNO}_3 + \text{HF}$ at 14 atm, vaporized, and diluted by 2 mol/L HNO_3 for ICP-OES detection	0.01–1 $\mu\text{g/g}$	[63]
Sediments	La, Sc, Y, etc.	Sample is digested by $\text{HNO}_3 + \text{HF} + \text{HClO}_4$, vaporized, and diluted by diluted HCl for ICP-OES detection	$\mu\text{g/g}$ level	[64]
Phosphate Mine	REEs	Sample is digested by hot H_2SO_4 , filtered, and the filtrate is diluted to the REEs concentration range of 10–500 $\mu\text{g/mL}$ for subsequent ICP-OES detection	1–40 ng/mL	[65]
Monazite	REEs	Sample is digested by H_2SO_4 and vaporized, the residue is decomposed by HCl , and diluted with water, spiked with Cd as internal standard	ng/mL level	[66]

6.4.3 Trace REE analysis by ICP-OES in alloys and other samples

ICP-OES has been widely employed in the determination of REEs and non-REEs in various types of RE alloys (e.g., aluminum alloys, copper alloys, magnetic and superconducting materials). The operation is very simple, and the sample is often decomposed by using some inorganic acids, diluted properly, and can be directly introduced into ICP for subsequent detection, no need for any chemical separation pretreatment. Main components and trace components can be determined simultaneously; for example,

the content of Pr and Sm in Pr-Sm-Co alloy is determined by ICP-OES to be 12–20%. Besides, the reproducibility of ICP-OES detection can be maintained at around 1 %. Table 6.29 lists the application of ICP-OES in the analysis of REEs in metal and alloy samples.

Table 6.29: Application of ICP-OES in the analysis of REEs in metal and alloy samples.

Sample	analyte	Sample preparation	Detection limit	Reference
Magnetic materials	REEs	Sample is digested by $\text{HNO}_3 + \text{HF} + \text{HClO}_4$, vaporized, and diluted by diluted HCl for ICP-OES detection	1–40 $\mu\text{g/g}$	[67]
RE-Co magnetic materials	Sm, Ce, Y, Mn, Hf, Co, Fe, Cu, Zr	Sample is digested by aqua regia and prepared into sample solution with matrix concentration of 5 mg/mL. 4 mL of the sample solution is diluted to 1 L with 1.2 mol/L HCl for ICP-OES detection, with Be as the internal standard.	–	[68]
Rare Earth Steel	La, Ce, Pr, Nd	Sample is digested by $\text{HNO}_3 + \text{HCl} + \text{HClO}_4$, vaporized, and diluted by 0.1 mol/L HClO_4 for ICP-OES detection	0.1–1 $\mu\text{g/g}$	[69]

Certain REEs, e.g., Dy, Er, Eu, Gd, Sm and Tm, are known as high neutron absorbers and act as neutron poisons in nuclear fuel, even at trace levels. For ICP-OES determination of trace REEs in uranium dioxide (UO_2) samples and nuclear grade uranium compounds, such as uranyl nitrate hexahydrate [$\text{UO}_2(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$], uranium hexafluoride (UF_6), triuranium octoxide (U_3O_8) and uranium trioxide (UO_3), the matrix effect and spectral interference should be considered. As a standard test method, ASTM C1287-8 involves a matrix-matching for the calibration construction with a need for highly pure uranium [70]. It would suffer from the radioactive contamination due to the use of high concentration of uranium, especially those containing enriched uranium-235. The other strategy is separating REEs from uranium matrix before ICP-OES detection. Durani et al. [71] separated REEs in fluoride form from uranium matrix with activated charcoal prior to ICP-OES analysis. Besides, separation of uranium matrix can be achieved by using CyDTA/ammonium hydroxide in presence of 1,10-phenanthroline [72] or precipitation by a mixture of hydroxide-peroxide [73], followed by estimation of impurities in the filtrate; solvent extraction is another alternative, such as separation of uranium from 6 M HNO_3 using di(2-ethylhexyl) phosphoric acid/toluene [74]. Recently, Baghaliannejad et al. [75] used tri(2-ethylhexyl)phosphate for the removal of uranium matrix. After the solvent extraction, uranium concentration in the raffinate was reduced to less than 10 mg/L (initial value of ~40,000 mg/L). The matrix interference and spectral interferences in ICP-OES were significantly alleviated.

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7 Application of spark atomic emission spectrometry for the determination of rare earth elements in metals and alloys

Abstract: Within the framework of determining the chemical composition of solids using rapid analysis methods, spark atomic emission spectrometry numbers among the standard procedures of most laboratories found within the metal-producing and -processing industries as well as many other companies and institutes nowadays. For analysis purposes, samples must be both electrically conductive and sufficiently homogeneous. Prior to routine use, a spark spectrometer must first be calibrated using certified standard samples. Subsequently, only about 20 to 30 seconds are needed to perform a complete quantitative analysis, during which around 70 chemical elements can be determined across all materials. These requirements mean that of all rare earth applications only those in which they are found as alloying or trace elements within the field of metallurgy are of importance for spark emission spectrometry. In this context, the most common rare earths are lanthanum (La) and cerium (Ce), followed by praseodymium (Pr), neodymium (Nd), scandium (Sc), yttrium (Y) and samarium (Sm), while the materials are mainly aluminium, magnesium, cast iron, steel and zinc alloys. The calibration functions of several examples will be shown, discussed and validated. The detection limits lie in the µg/g region regardless of the given matrix and are thus sufficient for most applications. Repeatability for concentrations larger than 0.1 % is less than 1 % relative, and is in the percentage range for low concentrations.

7.1 Introduction

In the past few decades, spark emission spectrometry has become a standard procedure for quickly determining the composition of metals and metal alloys and now forms an integral part of almost every laboratory within the metal-producing industry, but also increasingly the metal-processing sector. While the focus was on determining only main elements during the early years, up to thirty or more elements can now be analysed simultaneously.

The use of rare earths in many different applications has increased at an extremely brisk rate. But for which of these applications can spark emission spectrometry serve as an analysis method? After an introduction to the method, the following will shed light on this question and present a selection of analytical performance data.

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7.2 Spark emission spectrometry basics

Spark emission spectrometry belongs to the group of optical atomic emission spectrometric analysis methods [1]. All of these methods have in common that free atoms or ions must initially be excited from a base energy state (E_0) to a higher energy state (E_1) by the application of energy and the associated change of state of the outer electron shells. During a spontaneous emission of radiation these free atoms or ions then fall back into their base state, either directly or via the detour of an excitation state, a sort of “halfway house” in energy terms. The attribute “optical” here points to the fact that the emitted radiation is ultraviolet, visible or infrared light.

Planck’s Law describes the link between energy and the spectral wavelength of the emitted radiation:

$$\Delta E_{10} = E_1 - E_0 = h \cdot \nu_{10} = \frac{h \cdot c}{\lambda_{10}}$$

ΔE_{10} : Energy difference between the excited state 1 and the base state 0; E_1 : Energy of the excited state 1; E_0 : Energy of the base state 0; h : Planck constant; ν_{10} : Frequency of the emitted radiation; c : speed of light; λ_{10} : Wavelength of the emitted radiation

Every chemical element displays a collective of individual energy transitions, its line spectrum. An example of such a spectrum can be found in Figure 7.1, which presents several iron lines ranging between 270 and 273 nm.

As a result, proving the existence of one or more such lines enables qualitative analysis. But the fact that the intensity of the radiation is proportionate to the number of atoms or ions present makes it possible to perform both qualitative and quantitative analyses.

Solid samples must first be transitioned into a gaseous state and dissociated to guarantee excitation is free from interferences from any neighbouring atoms or ions. In the case of spark emission spectrometry, this energy is supplied by an electric spark, i.e. a brief electrical discharge between (at least) two electrodes. The sample itself actually constitutes one of these electrodes, namely the cathode. It therefore follows that, as a fundamental prerequisite of the method, the sample must be electrically conductive or at least powdered and mixed with an electrically conductive material such as graphite. However, generally self-conductive compact samples such as metals or metal alloys are analysed. Tungsten has established itself as a material for the so-called counter electrode, a metal that is characterised by both a high melting point and by extreme hardness, both of which are essential if the counter electrode is to remain easy to clean using mechanical means.

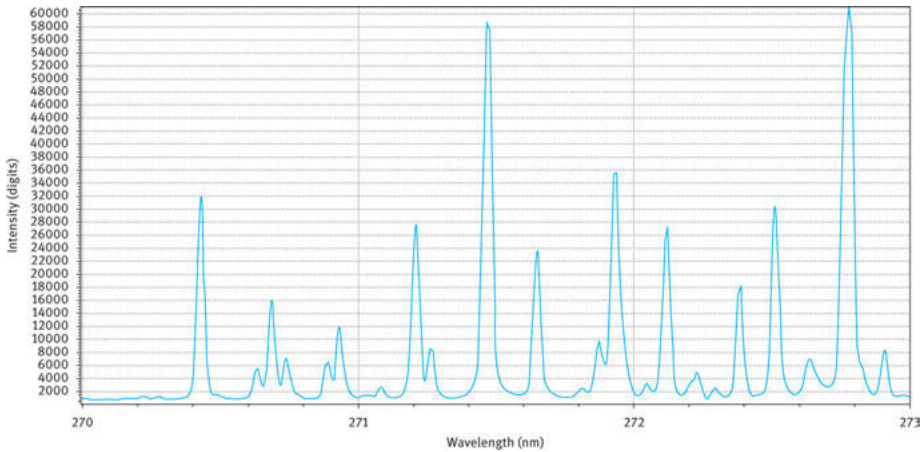


Figure 7.1: Line spectrum of iron in a pure iron sample between 270 and 273 nm.

The spark discharge usually occurs in an argon atmosphere and not in air, for which there are diverse reasons:

- argon comes with the advantage of delivering good transparency of element lines below 190 nm,
- no oxidation processes occur and
- the heavy Ar ions cause an extreme cathode fall region, meaning the majority of the energy is transferred to the surface of the sample, which acts as the cathode, and not to the counter electrode. The temperature at the sample is consequently high, while the temperature at the counter electrode remains low.

A high-voltage ignition pulse initially causes an electrical spark to be discharged from the counter electrode to the sample, during which sample material (approx. 30 ng per spark discharge) is removed and transported into the plasma, which consists of Ar atoms, Ar ions and electrons. At temperatures $>10,000\text{ }^{\circ}\text{C}$, a part of the sample material is vaporised, dissociated into atoms or ions and thermally excited to emit light (see above). The sample retains a so-called spark spot, which is characterised by a very fine metal distribution owing to fused micro-regions. Figure 7.2 shows a schematic of such a system.

However, not just the element lines of the vaporised elements are emitted within this Ar plasma, but equally a spectral background. This is mainly made up of the line spectrum of the plasma gas and continuum radiation, which results from the recombination processes between positive ions and electrons as well as electron *bremsstrahlung* (braking radiation). This, in turn, results from the change in kinetic energy that occurs given collisions between free-moving electrons and heavy plasma portions such as ions and atoms [2]. However, as the described processes are not only dependent on the electron and ion density, but also on the gas composition and

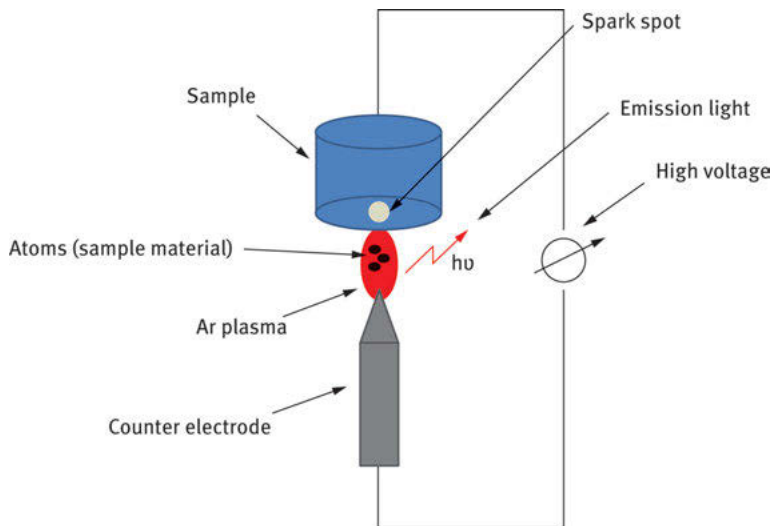


Figure 7.2: Spark emission between the sample and the counter electrode.

temperature, the intensity of the background radiation is sample- and wavelength-specific.

Yet the analytical method used with spark emission spectrometry does not rely on observing a single spark discharge, but is actually based on a longer sparking process that is made up of several steps. To begin with, the area between the sample and the counter electrode is purged with argon to displace any excess air. What follows is the so-called pre-sparking period, in which several thousand spark discharges with a frequency of up to 1,000 Hz serve to remelt and thus to homogenise a portion of the sample surface. Structural influences such as inclusions can thus be eliminated or reduced. In the best possible case, this pre-sparking period ends in a so-called stationary sparking state, which is to say a point in time at which the magnitude of the emitted radiation no longer changes. This pre-sparking period is followed by the actual analysis process, during which the emitted radiation is measured and integrated over several thousand individual spark discharges, and finally converted into percentages by weight with the help of calibration functions.

7.3 Setup of a spark emission spectrometer

Modern spark emission spectrometers can generally be divided into mobile units for positive material identification purposes and stationary laboratory devices. But since mobile spectrometers have to be small, easy to handle and simple to transport, they also come with compromises in terms of spectral resolution, stability and, ultimately,

their analytical capabilities. Among other things, the larger and better stabilised optical system that characterises laboratory spectrometers results in improved analysis capabilities; these devices range from small table-top units right up to automated high-end analysers.

Since they are based on the same physical principle, almost all spark spectrometers are similar in design. As an example, the following will discuss the QSG 750-II laboratory spectrometer made by the company OBLF GmbH, shown in Figure 7.3. The dimensions of the device are 100 cm (width), 90 cm (depth) and 130 cm (height).

The general design of a spark emission spectrometer is shown in Figure 7.4. The following then briefly describes the individual components.



Figure 7.3: OBLF QSG 750-II spark emission spectrometer. Source: OBLF GmbH.

Argon supply

The spark spectrometer is usually supplied with argon (1) of quality 4.8 (purity of 99.998 %). Should elements such as nitrogen or oxygen need to be analysed, argon supply using quality 5.0 or 6.0 is recommended, or the use of a gas purifier (3) for cleaning the argon. In this case, argon flows with a primary pressure of approx. 10 bar (2) through small pipes that are filled with various chemicals. While titanium causes chemical bonding of nitrogen and oxygen, copper oxide makes carbon monoxide and

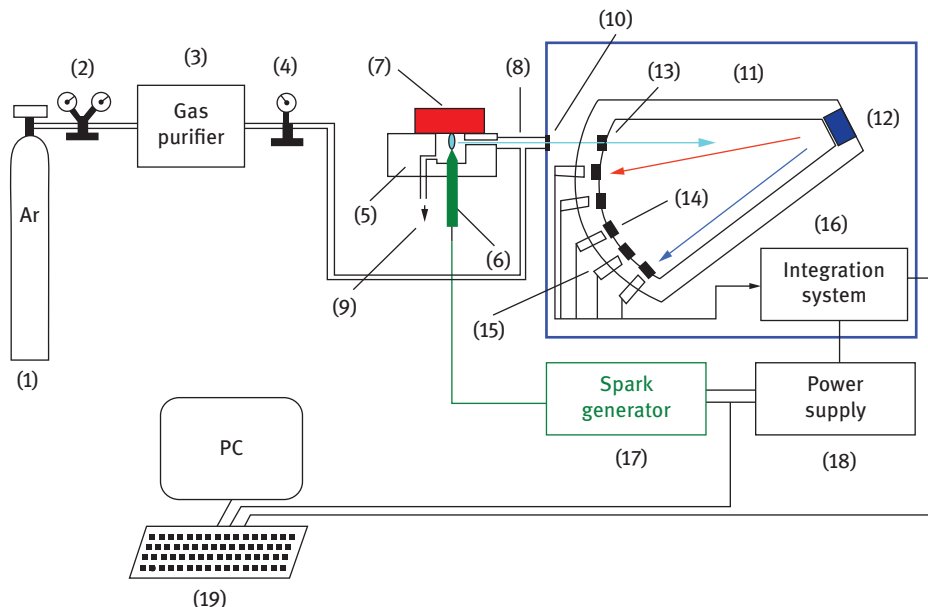


Figure 7.4: Schematic of a spark emission spectrometer [1]: 1: Ar cylinder, 2: Reducing valve (output 10 bar), 3: Gas purifier, 4: Reducing valve (3 bar), 5: Spark stand, 6: Counter electrode, 7: Sample, 8: Light tube, 9: Gas outlet, 10: Entrance window and vacuum lock, 11: Optical frame, 12: Optical grating, 13: Entrance slit, 14: Exit slit, 15: Photomultiplier, 16: Integration system, 17: Spark generator, 18: Power supply, 19: Control and evaluation PC.

hydrocarbons oxidise into carbon dioxide and water, which are then physically bonded to a molecular sieve. Downstream of the gas purifier argon pressure is reduced to 3 bar (4).

Spark stand

The spark stand (5) consists of a top plate and a chamber with the counter electrode (6). The top plate is a hardened stainless steel plate with a circular opening (diameter: 12 mm), onto which the sample (7) is positioned in such a way that the opening is completely blocked off to prevent any ingress of air. The spark stand chamber is constructed in such a way as to ensure it is well purged by the argon flow. The argon that is contaminated with burn-off (9) lands in a filter or is directly discharged into the open air.

Spectrometer optical system

The emission light generated in the spark stand reaches the evacuated optical system via a light pipe (8) and an entrance window (10), which is made of quartz or magnesium fluoride. The vacuumised optical system is under 0.005 mbar of pressure and contains a polychromator array with a Paschen-Runge mount assembly (11). In this regard, the concave reflection grating (12), the entrance slit (13) and the exit slits (14) are arranged in a Rowland circle. In this case, the grating and exit slits are rigid, the entrance slit can be moved in order to vary the target area of the light on the grating. Depending on the respective analytical task, the number of lines on the reflection grating can differ. The default number is at 2,400 lines per millimetre, which results in a reciprocal linear dispersion of 0.56 nm / mm. The width of the entrance slit is less than 20 µm, while the width of the exit slits varies between 25 and 50 µm. The light that escapes through the exit slits is then detected with the help of photomultiplier tubes (15) and integrated into the data acquisition system (16). Following an analogue-to-digital conversion, these measured values are transferred to the spectrometer's PC where the measured intensities are then converted into percentages by weight. As an alternative to photomultiplier tubes other spark spectrometers use semiconductor sensors (CCD or CMOS) for light detection purposes.

Spark generator

As one of the core elements of any spark emission spectrometer, the spark generator (17) is responsible for generating the spark discharge. Classic discharge circuits contain a power supply, a reservoir capacitor, a coil, a resistor and the analysis spark gap. So-called medium-voltage discharges, in which the applied voltage lies within a range from 400 to 1,500 V, have established themselves for practical use. But as such a voltage is insufficient to ignite the analysis spark gap, ignition is effected externally either with the help of a so-called auxiliary spark gap or by using a high-voltage pulse. Subsequently the reservoir capacitor can discharge via the now electrically conductive spark gap, with the discharge characteristics being dictated by the capacity of the capacitor, the inductivity of the coil and the size of the discharge resistor. The resulting supercritical attenuation ensures a unipolar discharge.

Modern spark generators, however, increasingly use transistor switches. In contrast to the classic spark generation method, these transistor switches are characterised by a current cut-out function. As long as the switch is closed, energy flows into the spark gap. Apart from the specific inductivity used, the maximum current is only dependent on the length of time the transistor switch is activated. The type of spark generation employed in this case is called a gated discharge source (GDS) and is also the type used in the QSG 750-II. Should the switch be activated again during the current decay time, energy will continue to flow into the spark gap and

the discharge period as well as the light emission period will be prolonged. This makes it possible to generate both short, spark-like as well as longer, arc-like discharges. The graph at Figure 7.5 shows the respective emitted light intensity curves as a function of time for various discharge types:

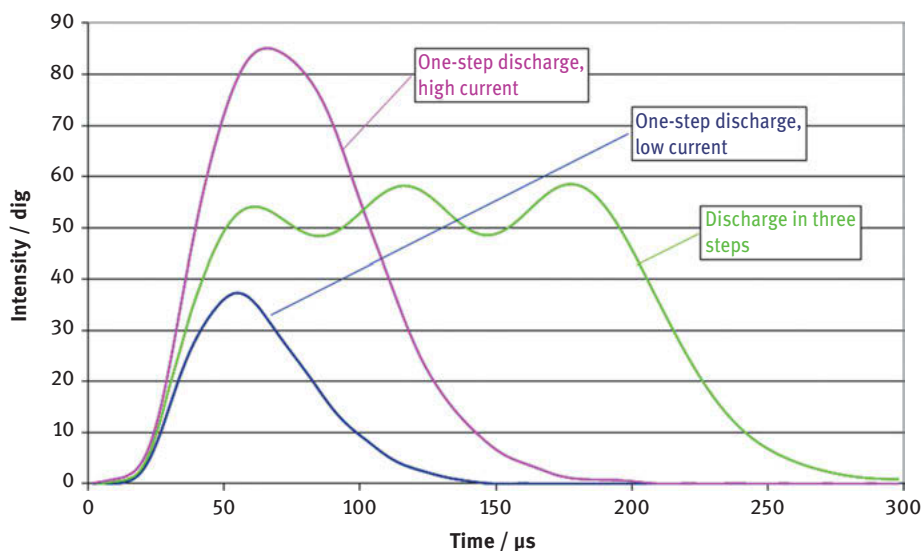


Figure 7.5: Emission curve with various discharge types.

Given a shorter discharge time (blue function), the maximum light emission is also lower and is reached earlier than with a longer discharge time (pink function). The green function finally shows the curve produced upon the transistor switch being reactivated twice.

Power supply

A central power supply (18) supplies all voltages needed for the spark generator, data acquisition and all other systems.

Operation and evaluation PC

A conventional PC (19) serves to operate the spectrometer and to evaluate measured data.

7.4 The analysis process

A spectrometer-compliant sample must be provided prior to any actual analysis. This must be a homogeneous, electrically conductive solid sample that can be well positioned on the spark stand. One side of the sample must display a surface with a diameter of >12 mm. Samples of smaller diameters (between 7 and 12 mm) can be analysed using a special overlay mask. Wires with diameters of <7 mm can fundamentally also be sparked using a special wire sample holder, but in this case analytical adjustments need to be made to guarantee correct analysis. The sample thickness should be between 0.2 and approx. 60 mm. Thinner metal sheets are difficult to analyse due to the applied heat and the danger of burning through. Higher samples can be fixed on the spark stand using extra-long retainers.

The sample surface to be used for analysis purposes must first be prepared prior to the process. This sample preparation serves to remove scale and any surface contamination. Various methods have established themselves for different metals. While turning or milling are standard methods for soft metals such as aluminium, magnesium, copper, lead or zinc, grinding with a grain size of 60 or 80 is preferred for iron, nickel or cobalt alloys. In contrast to image analysers for which a polished and “perfect” sample surface is preferred, electrical sparks like points of attack on the sample such as the striations left by grinding or milling. This guarantees that the sparks spread out evenly over the sample surface.

Once the prepared sample is at hand, it is placed on the spark stand and the analysis can begin. The time taken for an individual measurement varies according to the type of sample between 15 and 50 seconds. On the one hand, this is dictated by the sample-specific pre-sparking period. While, for instance, standard steels already display a homogenised structure after a pre-sparking time of nine seconds, it can take around 40 seconds to homogenise the many and dominant manganese sulphide precipitations found in semi-finished free-cutting steels. On the other hand, the integration process can consist of one or several cycles with various excitation energies. In contrast to the standard steel elements, exciting nitrogen atoms requires much more powerful spark discharges. However, as a result of the elevated spectral background these are counterproductive with regard to standard steel elements. Consequently, the only option for the spectrometer is to analyse the elements over various integration cycles. Finally, the measuring frequency also plays a central role. To ensure adequate statistical certainty, approx. 1,000–3,000 individual spark events are averaged or integrated. As matrices such as zinc degrade considerably more strongly than, for instance, iron, the pause between two individual spark discharges must be substantially longer. This leads to a spark succession frequency of 100–200 Hz in contrast to 800 Hz with iron.

In practice, though, an analysis never consists of taking a measurement at only one spot on the sample. As samples can display segregations or blowholes, a complete analysis is always made up of at least two so-called sparkings at different places

on the sample. Using the statistical software function, the comparability of both individual results is then verified. Should a sufficient degree of certainty be given, both individual results are automatically averaged and the analysis is completed.

One of the latest developments in the field of spark emission spectrometry was introduced at the CETAS conference in Luxembourg (city) in the year 2011 and constituted the launch of a so-called double electrode spark stand, which features two electrodes instead of only one [3]. These two electrodes permit two spark processes to be conducted on the sample surface without having to reposition the sample in between sparkings. The purging process at the beginning of the analysis naturally needs to be completed only once. The pre-sparking process is conducted at double the frequency in an alternate manner. Depending on the analysis system, the actual measuring process can also be performed alternately. This makes it possible to carry out two spark processes in about the same space of time it would take to complete one using a standard system. If both spark processes are comparable, the analysis is completed. The advantage of the system is of particular benefit to users who are called upon to carry out numerous analyses per day.

7.5 Quantitative analysis

Simply proving the existence of an element within a sample, which is to say performing a qualitative analysis, is generally not sufficient for users of spark emission spectrometry. Instead, the aim is to deliver as precise a determination of the composition of a sample as possible, which requires a quantitative analysis.

7.5.1 Calibration and recalibration

Although a theoretical connection exists between the measured intensity of an element line and the concentration of the element within the plasma and the sample, respectively, a direct determination is made impossible due to a surfeit of underlying parameters. For this reason a spark emission spectrometer must be calibrated using certified samples. In contrast to other analysis methods, the evaluation function is not the calibration function $I = f(c)$, but rather the analysis function $c = f(I)$ (I = intensity, c = percentage by weight). As the amount and composition of the sample material that enters the plasma from the sample are dependent on numerous parameters such as viscosity, vaporisation enthalpy and thermal conductivity, and as the composition of the vaporised material can in turn influence the plasma temperature and the associated excitation processes, the measured intensity must be standardised. The intensity of a reference line, usually the line of the matrix element such as iron in a steel sample, is used as a standardisation factor. When

multiplied by the so-called scaling factor S_{kt} , a typical intensity of the reference line, an absolute intensity $I_{abs,El}$ delivers the relative intensity $I_{rel,El}$:

$$I_{rel, El} = \frac{I_{abs, El}}{I_{abs, Ref}} * S_{kt}$$

$I_{rel,El}$ = Relative element intensity, $I_{abs,El}$ = Absolute element intensity, $I_{abs,Ref}$ = Absolute reference intensity, S_{kt} = scaling factor

Owing to the resolution of the spectral unit and the line broadening within the plasma, spectral interferences can occur due to the overlapping of element lines, but also due to band coincidences of any non-dissociated molecules. The analysis function takes these “additive interference signals” into account by means of a linear correction.

Apart from these spectral interferences, the sample’s physical and chemical properties and the resulting vaporisation and excitation characteristics within the plasma also affect any analytes, an effect that is not fully compensated by the signal’s reference to the matrix intensity. The severity of this “matrix effect” is dependent on the concentration of the interfering element as well as of the analyte itself and is also taken into account in the analysis function.

Theoretically there is a linear correlation between the concentration of the analytes within the sample and the measured intensity, but this is usually only given if the concentration is low. Owing to the optically dense spark plasma, higher concentrations give rise to a self-absorption effect, i.e. non-excited atoms or ions in their base state absorb light emitted by their own kind, which in turn leads to their excitation.

The emission lines to be used in the respective application are mostly specified by the spectrometer manufacturer. The selection is based on information provided by the customer in the form of matrices, elements and concentration ranges or materials that need to be analysed. Material databases or reference literature such as the Key to Steel [4] enable spectrometer manufacturers to collate the first-named information themselves.

Unfortunately, not all elements can be measured with only one emission line each, for which the reasons are as follows:

- The self-absorption effect causes the curve of an analysis line to rise too steeply upwards of a certain concentration → the line cannot be used for high element concentrations.
- The spectral background is too large to achieve a good signal-to-background ratio → the line cannot be used for low element concentrations.
- The slope of the analysis function is too high → the line is not sensitive enough and cannot be used for low element concentrations.
- The spectral interferences are extremely high, e.g. due to matrix lines or due to main alloy components → if available, a different line should be used.

Calibrating a spark emission spectrometer involves a lot of effort since a sufficient number of certified samples is required for each analyte; this is necessary not only to describe a basic function, but also to calculate all requisite additive and matrix corrections. As a result, it is not uncommon for the calibration of a complex steel matrix to require around 300 to 400 samples – for which reason this “basic calibration” is performed only once in the course of a spectrometer’s lifecycle. However, as changes in the analysis sensitivity, e.g. due to soiling of the spark stand and the entrance window or fluctuations in argon quality, can lead to variations in measured intensities, it must be mathematically possible to return the system to its calibrated state with the help of recalibration samples. In the event of a commonly performed two-point recalibration, two recalibration samples are supplied for each analysis channel: a “low sample” and a “high sample”, each of which contains a low or high concentration, respectively, of the analyte. The “target intensities” of these samples are initially recorded prior to the start of the actual calibration. The recalibration samples then form part of the scope of delivery and remain with the customer. After renewed analysis at a later point in time (to ascertain “actual intensities”), target and actual intensities are used to generate correction factors with whose help every intensity of a production sample can be corrected to reflect the state of the original calibration. Depending on the number of samples, some users perform such a recalibration on a daily or a monthly basis.

7.5.2 Evaluation of calibration and analysis results

Once calibrated, the spectrometer program displays graphs of the analysis functions. An example is shown in Figure 7.6, which details a calibration of chromium in low-alloy steel.

Relative intensity is plotted on the x axis and relative concentration on the y axis. Relative concentration is defined by the absolute concentration of the element, divided by the matrix concentration (in this case the iron concentration), multiplied by 100 %. Each measuring point represents a certified standard sample.

The quality of the smoothing function is given by the correlation coefficient R and residual scatter SR . A_0 to A_3 represent the coefficients of the function, which in this case is of the third degree.

In accordance with DIN 32 645 [5] the detection limit of an analysis process is calculated using the following formula:

$$\chi_{DL} = \Phi_{n;\alpha} * s_L / b$$

χ_{DL} : Detection limit; $\Phi_{n;\alpha}$: Factor to quickly estimate the detection limit; n : number of measurements to ascertain s_L ; α : Significance level; s_L : Standard deviation of the intensity of a pure metal sample; b : slope of the calibration line (sensitivity)

The quick estimation factor $\Phi_{n;\alpha}$ is dependent on the number of measurements n that are taken and the significance level α . As a result, the detection limit must

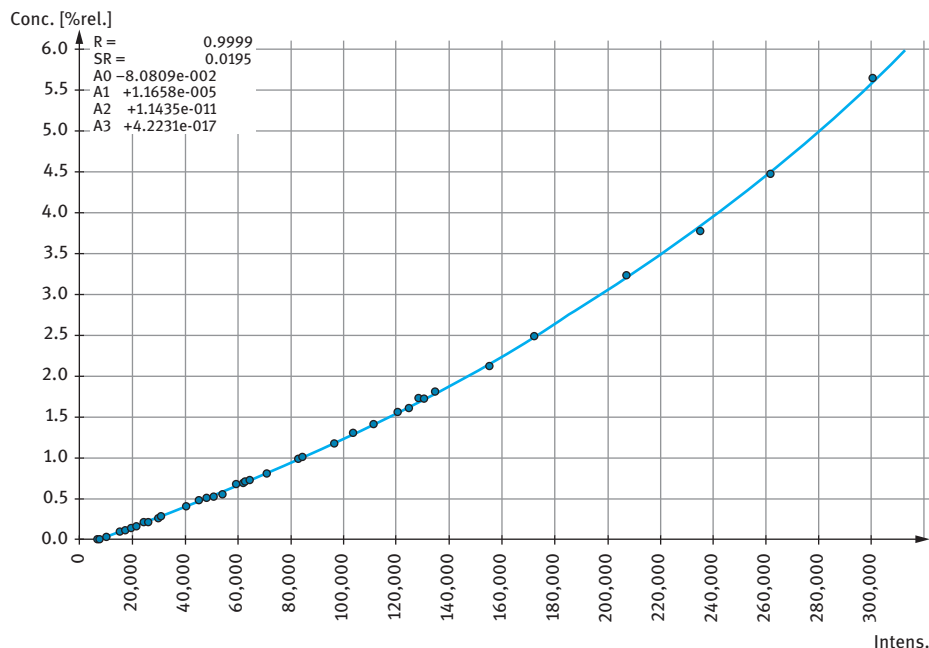


Figure 7.6: Analysis function of chromium in low-alloy steel.

always be specified along with the data for n and α . For reasons of uniformity, a factor of three, which corresponds to 10 measurements and a significance level of 0.01, is mostly used for spectrometry purposes.

Further factors used to assess the analysis process are accuracy, repeatability and reproducibility. Calibration quality is decisive for the accuracy of the analysis data. Validation measurements taken after calibration provide a good impression of the analysis results. Repeatability generally refers to the standard deviation of a multiple analysis that has been completed in a short time. Reproducibility, on the other hand, refers to long-term stability over a period of several hours, days, weeks or months. This is dependent on not just the spectrometer's stability itself, but also on parameters such as the recalibration and sample preparation.

7.6 Using spark emission spectrometry

Spark emission spectrometry provides many advantages in comparison to other analysis methods:

- short analysis times,
- numerous elements that can be analysed,

- direct analysis using a solid sample,
- relatively few requirements regarding the sample,
- fully functional in rough environments,
- simple operation, even by staff with little experience and
- the option of automation.

As a result of all these benefits, spark emission spectrometry has established itself as a standard procedure in almost all enterprises within the metal-producing industry during the last 40 years. Nowadays, no steel plant is in a position to manufacture its products without having tracked the production process with the help of spark discharges. In the same vein, almost all foundries as well as manufacturers of aluminium, copper, magnesium, nickel, cobalt, titanium, tin, lead and zinc alloys as well as, in part, precious metals are equipped with spark emission spectrometers nowadays. However, quality assurance requirements mean metal-processing companies are also often called upon to not simply put their trust in the supplied works certificates of the primary producer, but to carry out incoming quality control measures themselves. Thanks to the flexibility of the technology, further areas of application can be found among materials testers and other establishments such as universities and institutes where there such testing is carried out. In such cases, the equipment not only serves the provision of external services such as contract laboratories, but is also used for research and teaching purposes.

Many application areas of spark emission spectrometry, even though not all, are covered by operation procedures and standards, e.g. for the analysis of carbon and low-alloy steels [6, 7], austenitic steels [8], manganese steels [9], cast iron [10], aluminium and aluminium alloys [11], magnesium and magnesium alloys [12], as well as zinc and zinc alloys [13]. In many industrial sectors, inter-laboratory comparability is established with the help of round-robin tests, which are often carried out by sector institutes within, e.g., the steel or foundry industries.

The number of elements requiring analysis has risen dramatically, especially in the last few years. While the focus was only on standard steel elements like carbon, silicon, manganese, phosphorous and sulphur as well as chromium, nickel or molybdenum alloys 40 years ago, the number of elements requiring analysis can amount to 30 or more in a modern steel plant.

The following Figure 7.7 shows elements within the periodic table that are analysable in the various matrices and/or that are routinely analysed more or less often.

General and advanced literature on the topic of spark emission spectrometry can be found, among others, in the works by Slickers [14], Thomsen [15] and Joosten [16].

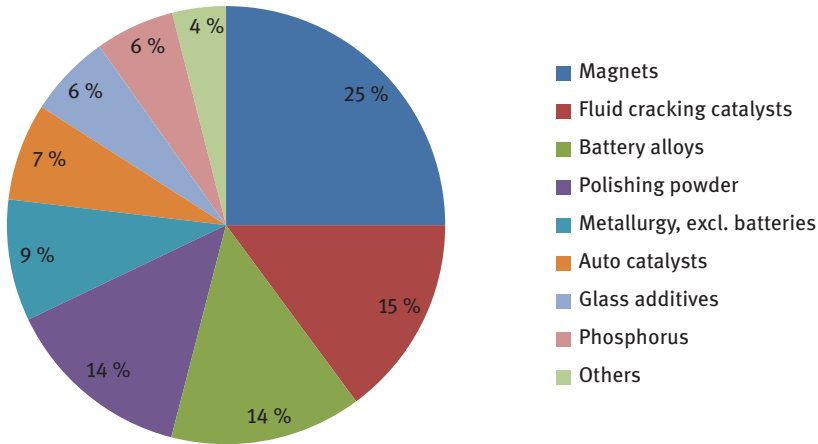


Figure 7.8: Industrial use of rare earths in 2010. Source: CIBC [17].

with the aim of producing materials with specific mechanical properties. Several applications will be briefly presented in the following.

Magnesium alloys

Mainly Ce, La, Nd and Pr, but increasingly also other rare earths, are used in the production of high-tensile materials that are required in the aviation or automotive industries [18, 19]; concentration range of up to 5 %.

Aluminium alloys

In this case, Sc increases strength and comes with structure-stabilising as well as grain-size-refining effects, especially in AlLi alloys [20], Ce and La also improve material properties, e.g. ductility [21]; concentration range <1 %.

Cast iron and steel

Ce and La increase the number of and optimise the size distribution of graphite spheres in spheroidal graphite [22], while various other rare earths improve the material properties of steel [23]; concentration range <0.1 %.

Zinc alloys

Ce and La reduce grain boundary effects in ZnAl alloys, above all in GalfanTM, which are used as coating materials for sheet and/or plate steel. These rare earths result in improved corrosion resistance, a more homogeneous grain distribution and ultimately make the material more weldable, paintable and ductile; concentration range <0.1 % [24].

Performing general analyses of the named alloys and materials has long belonged to the main tasks to which spark emission spectrometry is put, but the inclusion of rare earths is a more recent development.

7.7.2 Spectrometric prerequisites

Once the prerequisites for an analysable sample have been met, suitable wavelengths must first be found for the respective elements. Wavelength tables such as those published by Saidel, Prokofjew and Raiski [25] and the Massachusetts Institute of Technology [26] can serve as a basis, or online databanks such as the one hosted by the American NIST Institute [27]. Table 7.1 provides an overview of the most commonly used wavelengths or wavelengths that research has shown to be the most promising, all of which fall within a range from 290 to 460 nm.

In each case, Table 7.1 also details several neighbouring wavelengths of other rare earths that constitute potential spectral interferences and should or must be taken into consideration during calibration. The severity of these spectral interferences is dependent on the analysis and interference lines, the distance between both of these, the resolution of the optical system and the width of the exit slits. It must be stated, though, that due to the fact that rare earth elements all share a certain similarity at atomic level, it is not possible to analyse any of the rare earths without there also being interferences from others. How severe these interferences are and whether they are of real-life importance can only be determined with regard to each respective application.

However, since calibration depends on more than samples containing the respective rare earth element, but must also include samples with differing concentrations of potential interference elements, the question initially poses itself as to whether there are enough commercially available reference samples that satisfy the requirements.

7.7.3 Calibration samples

In general, in-house or certified reference samples can be used for calibration purposes. In-house samples come with the advantage of being as close to the company's own production output in terms of composition. However, prior to being used as a calibration sample, such in-house samples need to be analysed to determine "target concentrations", a process that is usually completed with the help of a wet-chemical

Table 7.1: Potential analysis and interference lines of rare earths.

Element	Most used or possible wavelength / nm	Interference wavelength / nm
Sc	402.04	Sm 402.00, Nd 402.09, Dy 402.09
Y	467.48	Nd 467.46, Er 467.48
La	433.37	Pr 433.31, Pr 433.39, Sm 433.41
Ce	399.92	Nd 399.87, Pr 399.92
	413.76	Gd 413.71, Nd 413.80, Pr 413.82
Pr	422.53	Gd 422.51, Dy 422.52, Sm 422.53, Gd 422.59
Nd	406.11	Gd 406.13
	410.95	Sm 410.94, Pr 410.94, La 410.95
Sm	356.83	Lu 356.78, Nd 356.89
	443.43	Ce 443.37, Pr 443.49
Eu	459.40	Ce 459.96, Sm 495.53
Gd	364.62	Pr 364.47, Dy 364.59, Pr 364.63
	379.64	Tm 379.59
Tb	387.42	Ho 387.41, Pr 387.45
Dy	353.17	Tb 353.17
	421.17	Nd 421.13, Pr 421.19, Gd 421.20
Ho	293.68	Yb 293.72
Er	369.27	Sm 369.28, 369.28
	400.80	Sm 400.81
Tm	376.13	Gd 376.09, Nd 376.16
Yb	398.80	Gd 398.78, La 398.85
Lu	451.86	Dy 451.85

or spectrometric reference procedure. Often, though, suitable sample material is not yet available prior to equipment calibration. Not just for this reason, but mainly due to quality assurance requirements (laboratory certification or accreditation), calibration must include nationally and/or internationally certified reference samples.

As an example, the following table (Table 7.2) lists the number of samples by matrix along with the highest concentration that can be made available by one of the largest and best known manufacturers and distributors of such samples.

In contrast to samples with standard elements for steel and aluminium, which are available in their hundreds and that even permit individual calibrations for special alloys, the sample range for rare earths is rather sparse. While elements with the highest industrial application density, which is to say Sc, La and Ce in aluminium, La, Ce and Nd in magnesium as well as Ce and La in cast iron, steel and zinc, are naturally the most commonly available, the variety of samples is only just sufficient to complete a basic calibration for some of these elements.

Especially in recent times, though, requests are repeatedly reaching spectrometer manufacturers for the analysis of additional rare earths, e.g. Sm and Er in aluminium, or Sm, Y, Er and Gd in magnesium. With the help of a few still existing, but unfortunately no longer commercially available, samples and a few that are only available on

Table 7.2: Certified reference samples for rare earths, available for purchase. Source: Brammer Standard Company, Inc. [28].

Elem.	Al		Mg		Cast iron		Steel		Zn		Ni		Co		Ti	
	No.	Max/ %	No.	Max/ %	No.	Max/ %	No.	Max/ %	No.	Max/ %	No.	Max/ %	No.	Max/ %	No.	Max/ %
Sc	20	0.54														
Y			4	4.3											1	0.005
La	6	0.03	15	0.37	6	0.02	2	0.02	16	0.08			2	0.06		
Ce	10	0.05	28	4.16	49	0.11	7	0.06	18	0.09						
Pr			2	0.07												
Nd	2	0.002	6	0.18												
Sm																
Eu																
Gd			2	0.05												
Tb																
Dy																
Ho																
Er																
Tm																
Yb																
Lu																

the Chinese market, OBLF can at present perform calibrations up to higher concentrations and/or for further elements. Table 7.3 details the maximum concentrations available at present.

Table 7.3: Maximum concentrations of calibration samples held by OBLF.

Element	Al	Mg	Cast iron	Steel	Zn	Ni	Co	Ti
	Max / %	Max / %	Max / %	Max / %	Max / %	Max / %	Max / %	Max / %
Sc	0.3							
Y	0.01	4.8				0.8		0.008
La	0.3	1.2	0.03	0.02	0.06	0.5	0.05	
Ce	0.6	3	0.1	0.05	0.07	1.5		
Pr	0.08	0.5						
Nd	0.25	3.2						
Sm	0.02	0.1						
Eu		0.01						
Gd		0.3						
Tb		0.05						
Dy		0.35						
Ho		0.07						
Er		0.15						
Tm		0.015						
Yb		0.1						
Lu		0.01						

However, overall it can be said that there is a great need for certified reference samples, a situation that no doubt not only results from the fact that samples are difficult as well as work-intensive to produce and certify, but also due to the demand for them.

Using existing and/or reference samples provided by the customer, it is possible to carry out calibrations. In the following, several examples from the aluminium, magnesium, iron and zinc matrices will be presented and analytical performance data discussed.

7.8 Analysis of aluminium alloys

7.8.1 Calibration (analysis function) and accuracy

Of the rare earth elements, Sc, Y, La, Ce, Pr, Nd and Sm can in general be calibrated in aluminium at present. As the most often analysed elements, Ce and La (Figures 7.9 and 7.10) serve as examples for analysis functions. Wavelength 413.76 nm was used for Ce and 433.37 for La. Both functions display a linear curve within the concentration range of up to 0.6 % (Ce) and 0.24 % (La). For Ce, an additive Ti correction (413.73 nm) of 21 µg/g / % Ce is necessary. The lowest concentration range requires an additive Mg correction, which is not based on a line overlapping, but rather on a shift of the background signal, and thus constitutes a matrix correction.

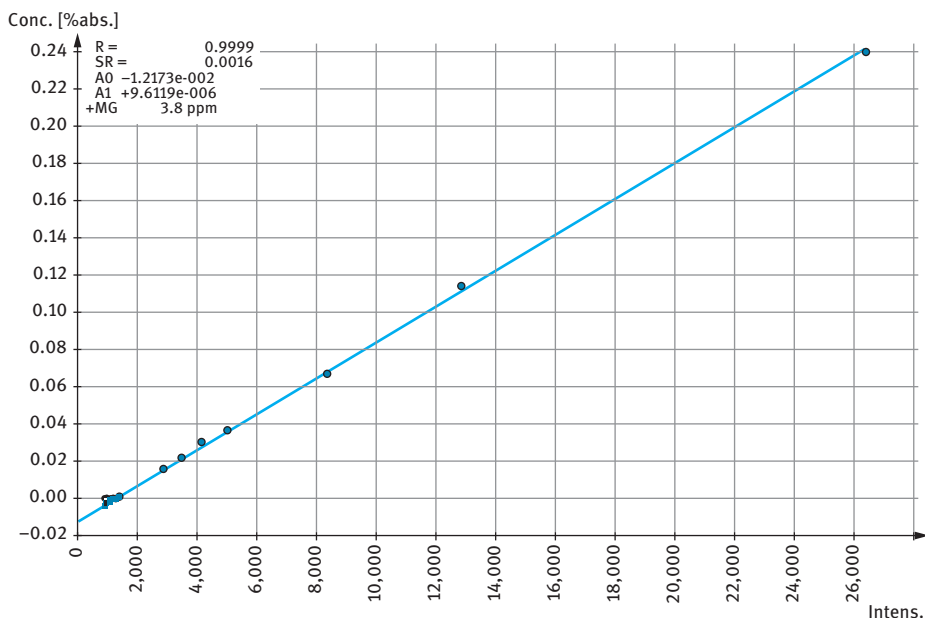


Figure 7.9: Analysis function of La in aluminium.

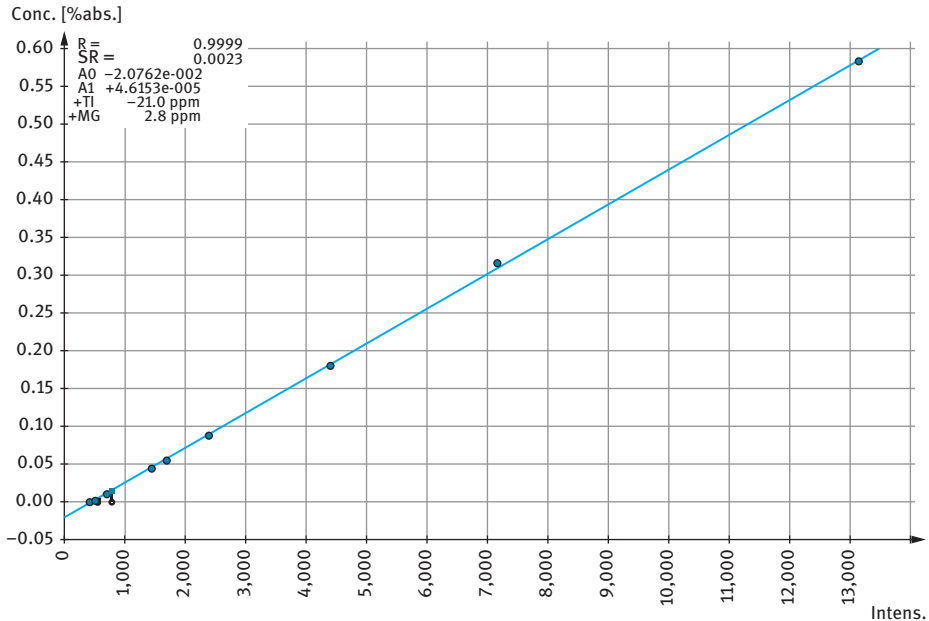


Figure 7.10: Analysis function of Ce in aluminium.

Table 7.4 details the validation as a test of the accuracy of the calibration. The sample set was a Chinese series that already served as a basic calibration framework. As a result, the requirement of an independent validation using independent samples could not be met due to a lack of suitable samples, as was also the case for the other matrices.

The degree of correspondence with the certified values is very good. However, if rare earth samples with a higher number and variety of concentrations were to be routinely analysed, more samples would have to be included in the calibration due to the interference situation.

Table 7.4: Validation of La and Ce in aluminium (Meas. val. = Measured value).

Sample	La in aluminium		Ce in aluminium	
	Setpoint / %	Meas. val. / %	Setpoint / %	Meas. val. / %
SE1	0.022	0.021	0.054	0.056
SE2	0.037	0.036	0.087	0.089
SE3	0.067	0.067	0.180	0.181
SE4	0.114	0.112	0.316	0.309
SE5	0.239	0.237	0.584	0.579

7.8.2 Detection limits

A 10-fold analysis of a pure aluminium sample delivered the detection limits of the individual elements. These are detailed in Table 7.5 for all elements determined in aluminium.

Table 7.5: Detection limits in aluminium (* = calibration is possible, but has yet to be carried out).

Element	Sc	Y	La	Ce	Pr	Nd	Sm
Detection limit/ $\mu\text{g/g}$	0.1	*	3	3	3	3	2

7.8.3 Repeatability

To determine repeatability, several samples were sparked 10 times in quick succession, followed by a calculation of the mean values and standard deviations. A comparison of the values for Ce and La is shown in the following tables (Figures 7.11 and 7.12).

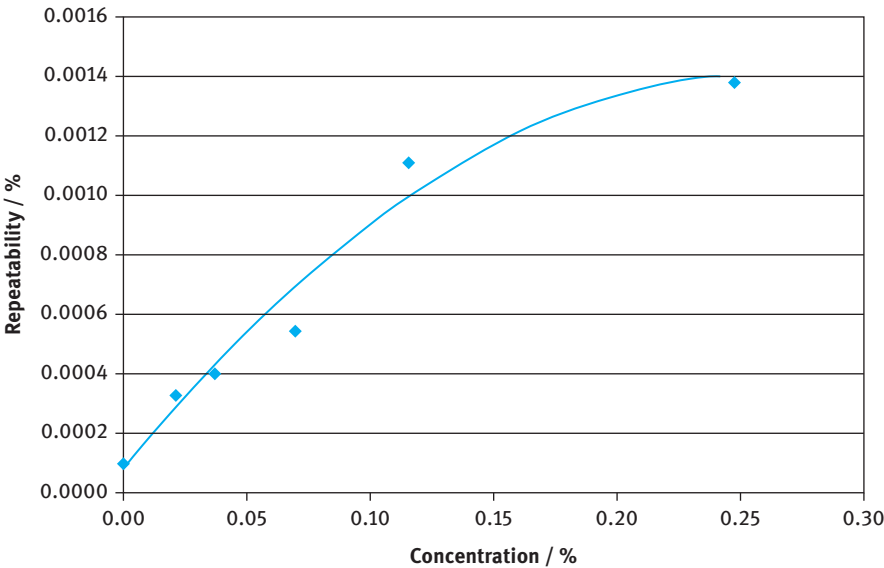


Figure 7.11: Representation of repeatability of La in aluminium.

Given an example concentration of 0.2 %, repeatability for La corresponds to a relative standard deviation of 0.6 %, and for Ce with a concentration of 0.5 % to a relative standard deviation of 0.7 %.

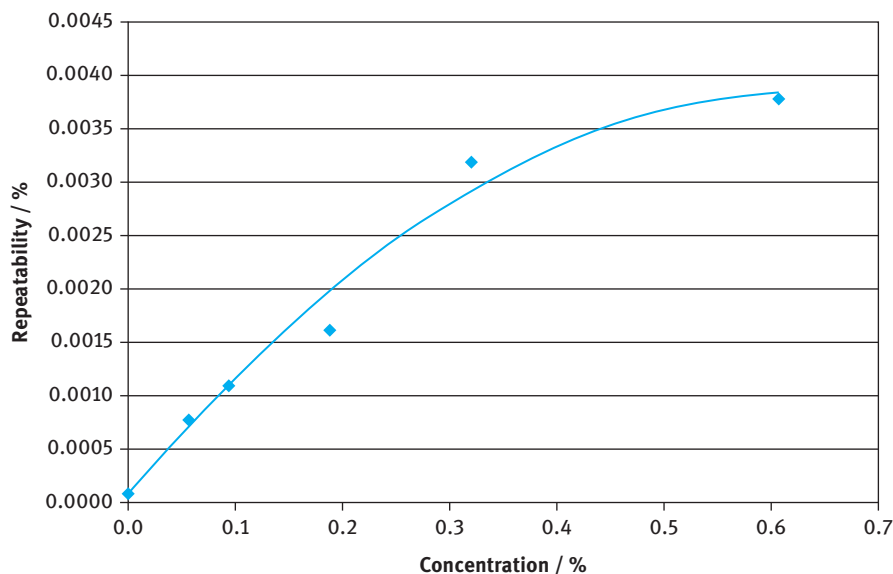


Figure 7.12: Representation of repeatability of Ce in aluminium.

7.9 Analysis of magnesium alloys

7.9.1 Calibration (analysis function) and accuracy

The calibration samples provided by the Norwegian company Norsk Hydro were still available for purchase up until a few years ago, but unfortunately are now no longer commercially available. A few of these samples are still held by OBLF and can be used for calibration purposes. In comparison to the values cited at Brammer Standard (see Table 7.2), the OBLF calibration limits are considerably higher and permit – at least as a basic function – the calibration of almost all rare earths. As a rule, the elements ordered by customers are mainly La, Ce, Nd, Pr and less often Y and Sm. As La and Ce were discussed for aluminium, the focus will now be on the elements Nd and Pr, as examples, for magnesium. The analysis functions of up to 3 % in the case of Nd and up to 0.5 % in the case of Pr are shown in Figures 7.13 and 7.14.

In contrast to Pr, the Nd samples do not display a linear function, which can be explained by the self-absorption effect. In this case, a second-degree polynomial serves to describe the function. As the concentrations of rare earths are generally higher in comparison to aluminium, some of the spectral interferences described in Table 1 are easily visible. The interference of Y on Pr is particularly noticeable, but not mentioned in the table. Going by the measured calibration samples, the interference is, however, clear to see.

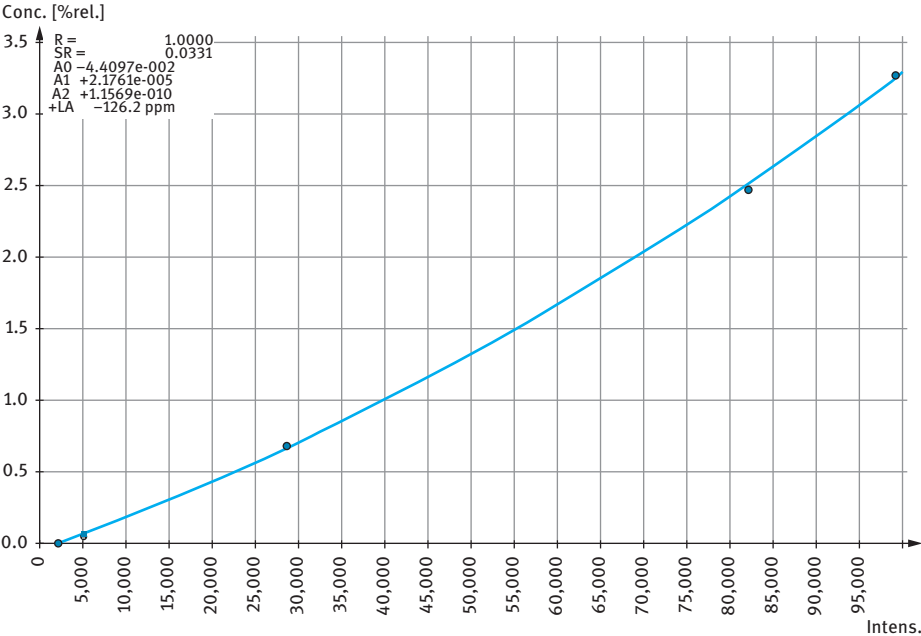


Figure 7.13: Analysis function of Nd in magnesium.

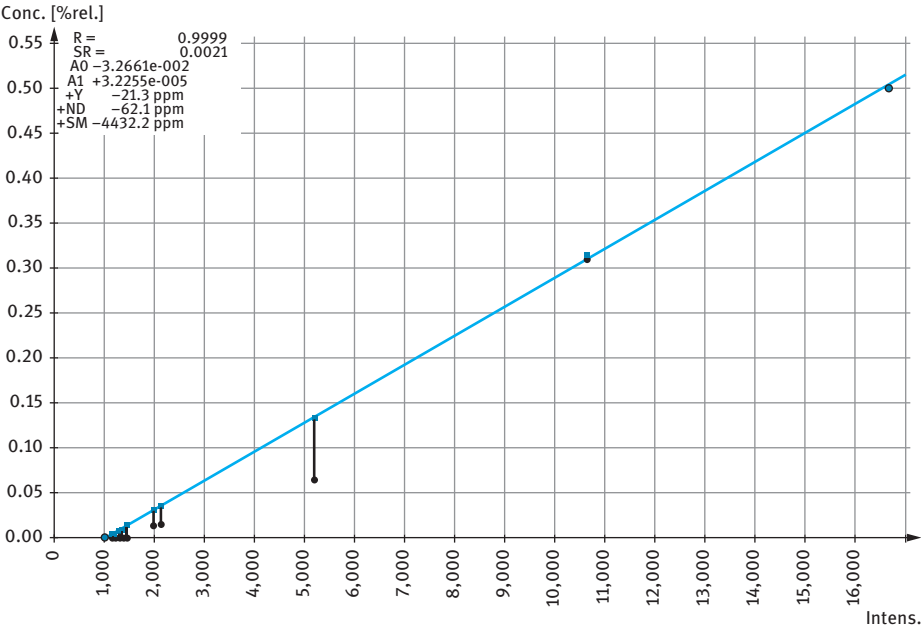


Figure 7.14: Analysis function of Pr in magnesium.

Some of these samples were subsequently sparked in concentration mode. The results are shown in Table 7.6.

Table 7.6: Validation of Nd and Pr in magnesium (Meas. val. = Measured value).

Sample	Nd in magnesium		Pr in magnesium	
	Setpoint / %	Meas. val. / %	Setpoint / %	Meas. val. / %
MGH2B	0.044	0.041	0.013	0.013
MGF1B	0.050	0.050	0.48	0.48
AEH93	0.61	0.59	0.28	0.27
MGY1A	2.26	2.30	0.059	0.059
MGH1B	3.05	3.02	0.014	0.015

The degree of correspondence is again very good in this case. However, in practice care must be exercised when dealing with materials that are alloyed with a large variety of rare earths. This would most definitely require a more extensive calibration, ideally using the precise materials required in each case.

7.9.2 Detection limits

Table 7.7: Detection limits in magnesium (* = calibration possible, but has yet to be carried out).

Element	Y	La	Ce	Pr	Nd	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
Detection limit/ $\mu\text{g/g}$	12	5	10	8	9	27	*	*	*	*	*	5	*	*	*

The detection limits in Table 7.7 show that spark emission spectrometry is not a suitable method for analysing rare earths in the lowest $\mu\text{g/g}$ or even sub- $\mu\text{g/g}$ ranges. In such cases, a wet-chemical method would no doubt deliver more reliable data. The advantages of spark analysis can, by contrast, be seen in the possibility of analysing higher concentrations, coupled with the high speed of the method.

7.9.3 Repeatability

Figures 7.15 and 7.16 again show the repeatability of Nd and Pr as examples. In the case of Nd, the relative standard deviations lie within the 2 % region at 0.6 % and for Pr with a concentration of 0.5 % also at 0.6 %, and are thus within the normal spark spectrometry range.

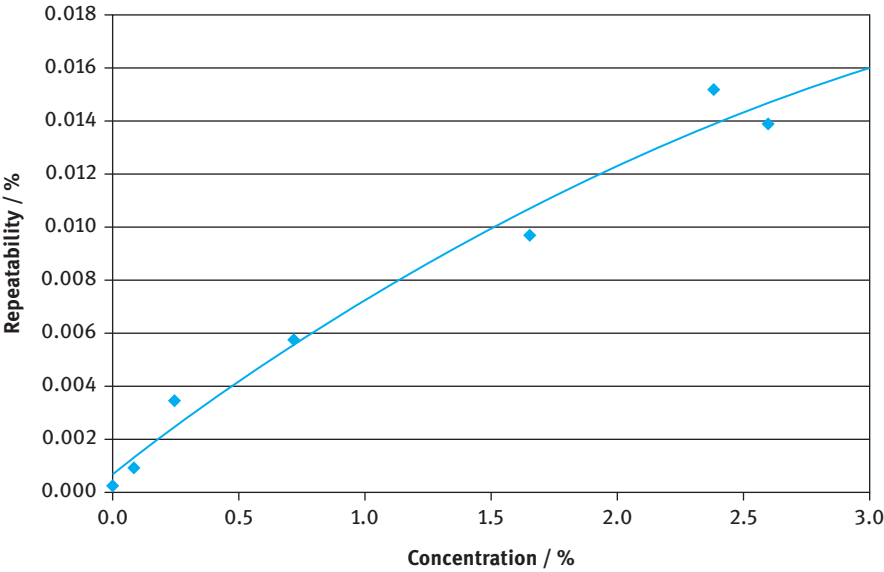


Figure 7.15: Representation of repeatability of Nd in magnesium.

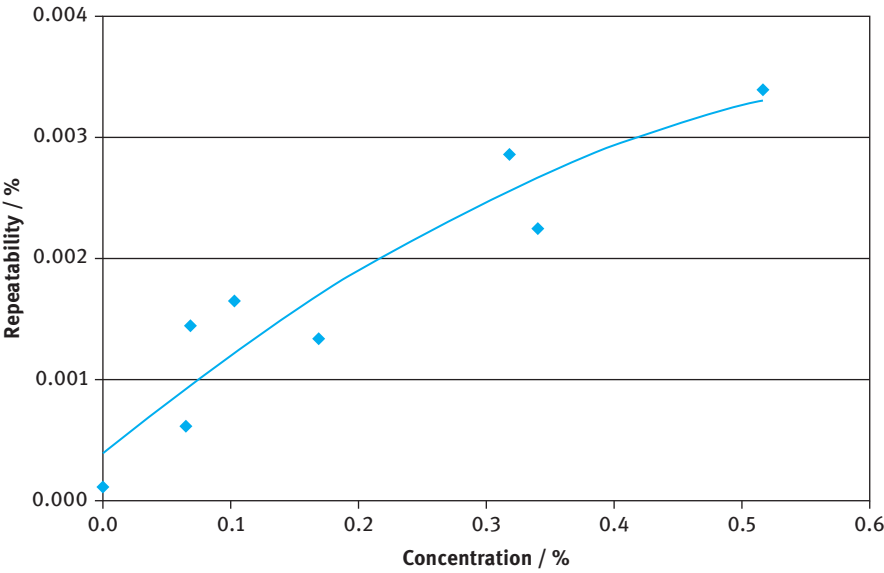


Figure 7.16: Representation of repeatability of Pr in magnesium.

7.10 Analysis of iron alloys

7.10.1 Calibration (analysis function) and accuracy

Although the use of rare earths in the area of steel production has yet to make great strides, the use of La and Ce in cast iron has almost become a standard application nowadays. For that reason, the focus will be on cast iron in the following. Figures 7.17 and 7.18 detail the analysis functions.

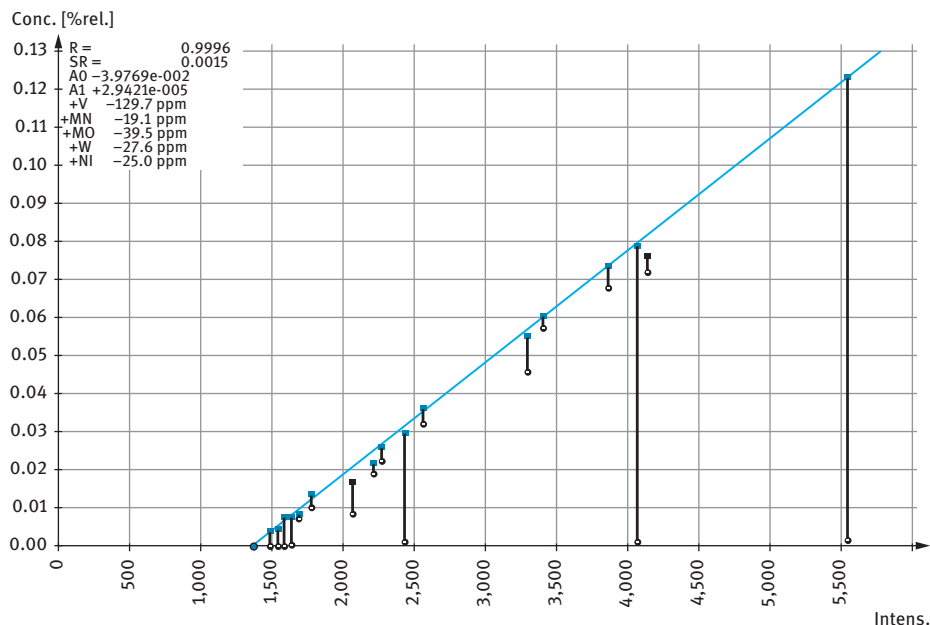


Figure 7.17: Analysis function of Ce in cast iron.

In comparison to the aluminium and magnesium matrices, the spectral interferences affecting the analysis functions are substantially more severe with a height of many $\mu\text{g/g}\%$, especially of elements that are characteristic of cast iron, e.g. C, Mn, Cr and Ni. While these interferences can be corrected with relative ease, they also make routine analysis anything but simple. As shown in Table 7.8, the validation looks good for both elements, but when analysing unknown samples of differing composition, deviations of $\pm 0.001\text{--}0.002\%$ may well arise, even down to the lowest concentrations. In such a case a selective calibration would again be helpful.

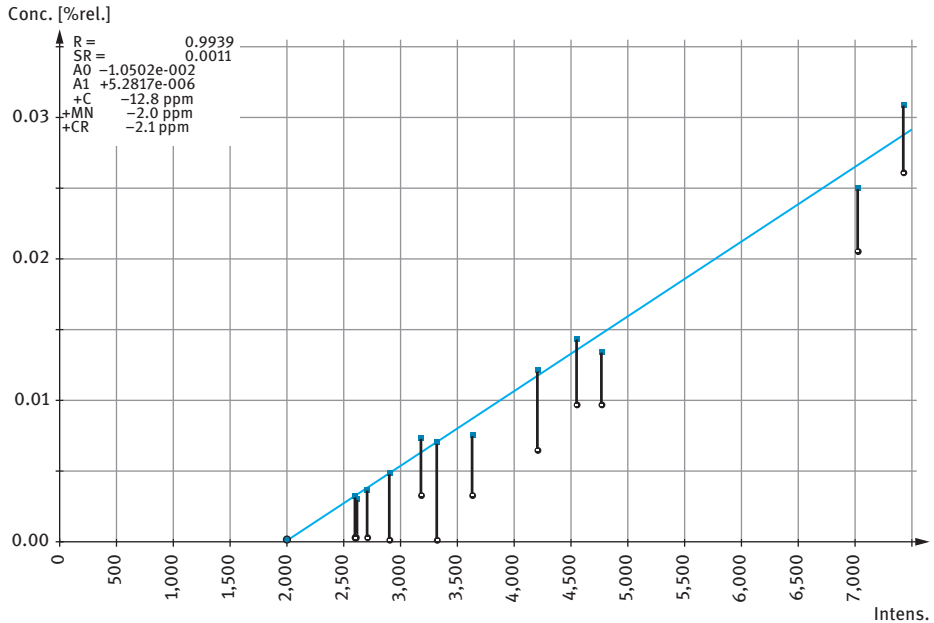


Figure 7.18: Analysis function of La in cast iron.

Table 7.8: Validation of Ce and La in cast iron (Meas. val. = Measured value).

Sample	La in cast iron		Ce in cast iron	
	Setpoint / %	Meas. val. / %	Setpoint / %	Meas. val. / %
246B	0.003	0.002	0.007	0.008
244B	0.009	0.010	0.018	0.020
249B	0.006	0.006	0.021	0.022
669/11	—	—	0.042	0.044
247B	0.019	0.020	0.053	0.053
667/11	—	—	0.062	0.062

7.10.2 Detection limits

The detection limits detailed in Table 7.9 show that analysis is possible within the µg/g range. However, calibration should be carried out using samples that are as close to the material as possible in order to minimise the above-mentioned inter-elemental influences.

Table 7.9: Detection limits in cast iron and steel.

Element	La	Ce
Detection limit/ $\mu\text{g/g}$	2	5

7.10.3 Repeatability

The degrees of repeatability of La and Ce are shown for a series of samples in Figures 7.19 and 7.20. With the exception of the highest La samples, the values correlate to the concentration in a linear fashion. At 0.05 % the relative standard deviation is at approx. 1.8–2 %.

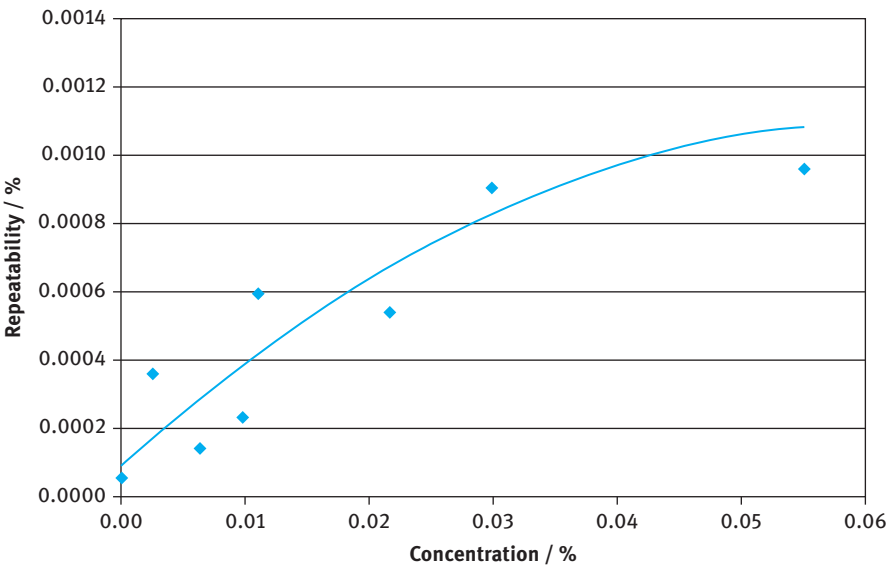


Figure 7.19: Representation of repeatability of La in cast iron.

7.10.4 Long-term stability

Long-term stability is a key criterion for assessing analytical performance. Routine use and evaluation of control samples are good options for ascertaining this long-term stability. As an example, Figure 7.21 shows the La concentration curve of a control sample analysed at a foundry over a period of approx. four weeks. In each case the mean value is shown, calculated on the basis of two spark events. Several hundred production samples were also analysed in between the control sample measurements on each day. Recalibration was carried out on a weekly basis.

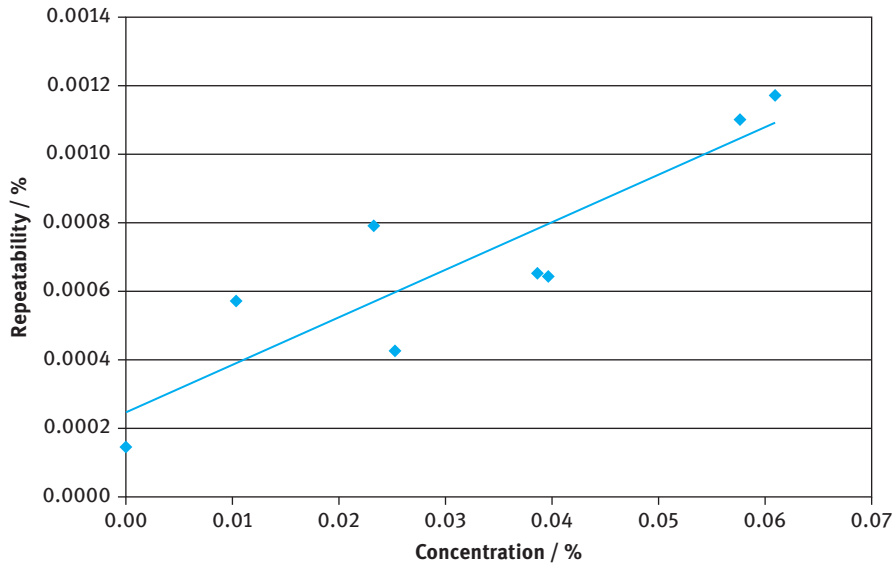


Figure 7.20: Representation of repeatability of Ce in cast iron.

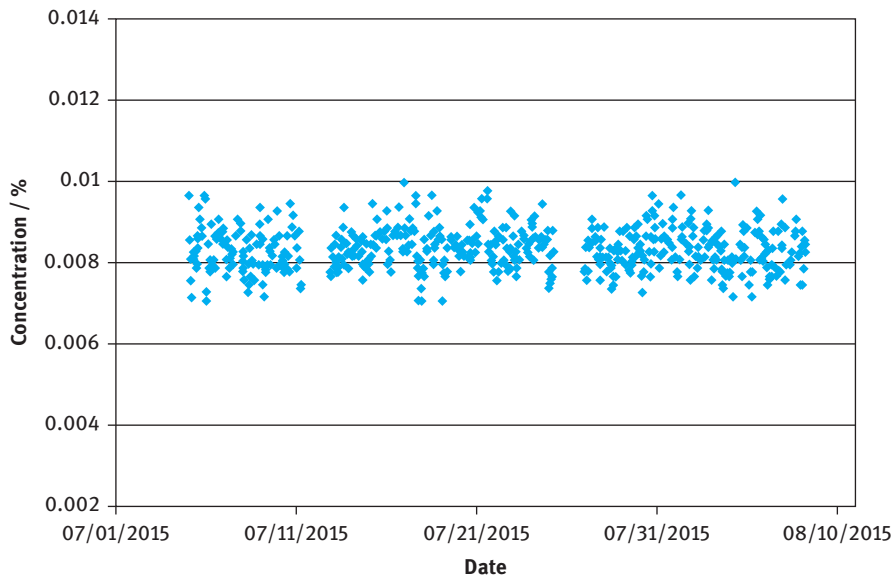


Figure 7.21: Signal record regarding the long-term stability of La in cast iron.

Over the entire period, the standard deviation remained at 0.0005 %, which makes it only approx. 0.0001 % higher than the standard deviation for repeatability.

7.11 Analysis of zinc alloys

7.11.1 Calibration (analysis function) and accuracy

The only two rare earths that are used in zinc alloys are La and Ce, and predominantly in an alloy called Galfan™, which is used as a coating for sheet steel [28]. It therefore comes as little surprise that only these elements are available as certified samples and can be calibrated. At present customer requests for analysis of these two elements are still relatively few so that only few reference samples are available at OBLF. The following calibrations (Figures 7.22 and 7.23) were therefore carried out with three (for La) and four (for Ce) reference samples.

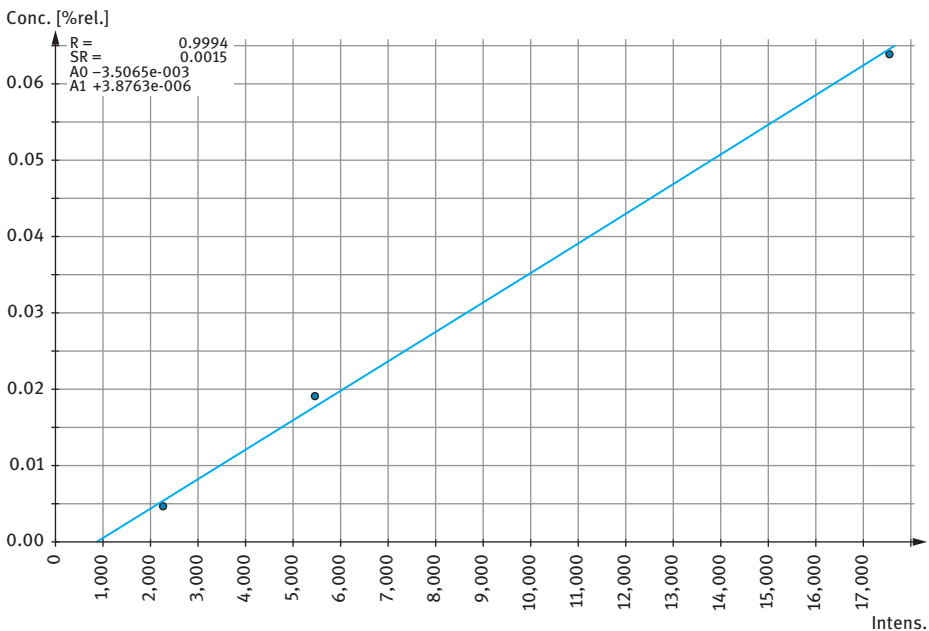


Figure 7.22: Analysis function of La in zinc.

Since no further rare earths are present, but also – with the exception of aluminium and copper – as a result of further material elements only being present in low concentrations, the functions are not affected by other elements.

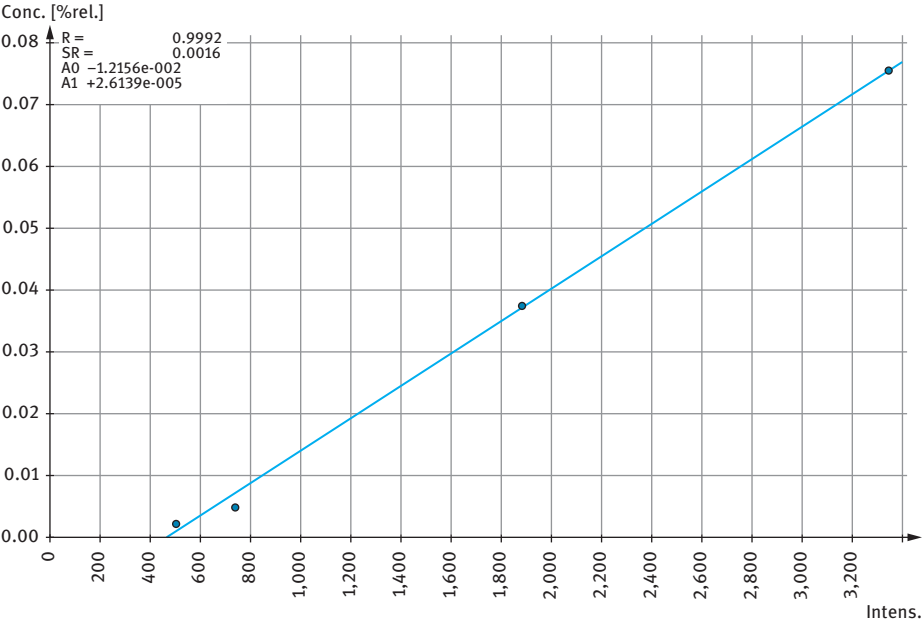


Figure 7.23: Analysis function of Ce in zinc.

7.11.2 Detection limits

The detection limits ascertained via the generated calibration function are shown in Table 7.10 and were at 1 µg/g for La and 4 µg/g for Ce. According to the ASTM standard, the sum of La and Ce must range between 0.03 and 0.10 %, which are nowhere near the ascertained detection limits [29].

Table 7.10: Detection limits in zinc.

Element	La	Ce
Detection limit/µg/g	1	4

7.11.3 Repeatability

A 10-fold analysis of two samples resulted in the repeatability values shown in Figures 7.24 and 7.25. In the upper region at 0.01 % for La and at 0.025 % for Ce they are at 3 % relative. Based on the detection limits and repeatability the analytical

prerequisites are given for routinely determining La and Ce in zinc alloys. Calibration should, however, be extended and validated with further standard samples.

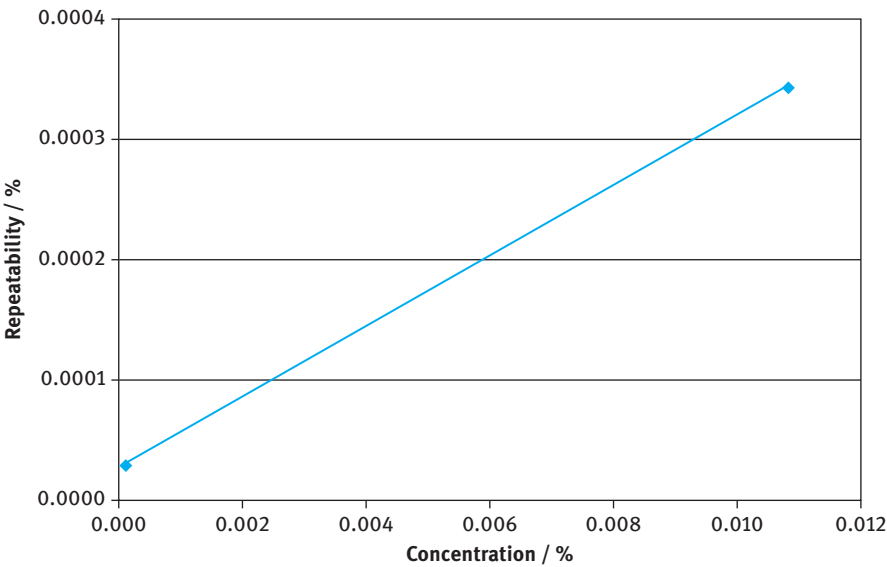


Figure 7.24: Representation of repeatability of La in zinc.

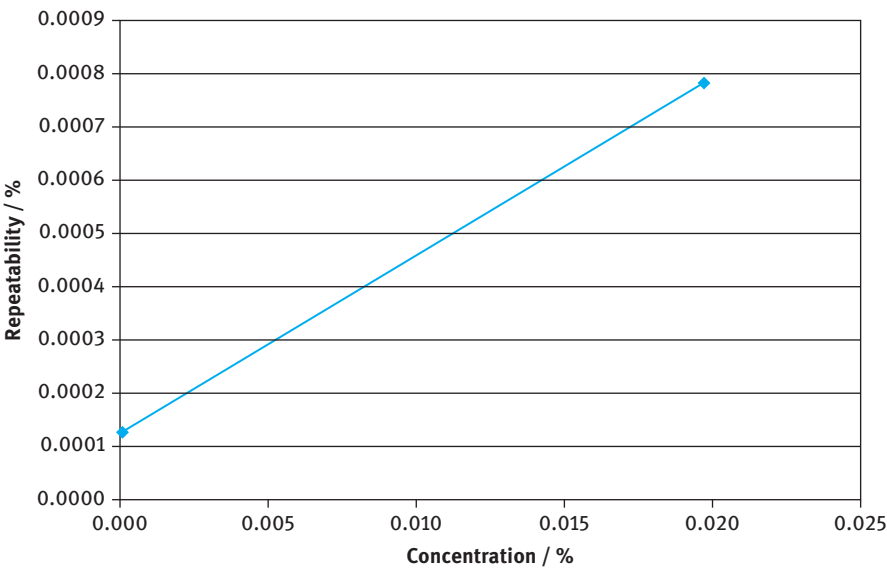


Figure 7.25: Representation of repeatability of Ce in zinc.

7.12 Conclusion

Spark emission spectrometry is a means of analysing and determining the chemical composition of metallic (conductive) solid samples both quickly and without involving lengthy sample preparation. Applications involving rare earths need to be metals or metal alloys if they are to satisfy the requirement of metallic conductivity and homogeneous element distribution. In this context, iron (cast iron and steel), aluminium, magnesium and zinc alloys are additionally alloyed with rare earths in a range from a few tens of $\mu\text{g/g}$ to several percent. At present, calibration samples are mainly available for the most common alloys and the most commonly used rare earths. As this spectrum is constantly growing, there is a backlog demand for calibration standards that contain more than certified concentrations of Ce and La.

Analytical performance data show that detection limits are in the $\mu\text{g/g}$ region regardless of the specific matrix. Repeatability values for concentrations larger than 0.1 % are, in part, considerably lower than 1 % relative; for concentrations less than 0.1 % these values range between one and three percent relative. Using the reproducibility of cast iron as an example shows that processability is given.

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8 Photophysical properties and characterisation of lanthanoids

Abstract: The special photophysical properties of the lanthanoids are among the most fascinating characteristics of these elements and are the basis of many technological applications. The fundamental understanding of these properties is crucial for a further improvement of lanthanoid luminophores. At the same time, the photophysical characterisation of lanthanoid coordination compounds can help to understand their overall properties, such as their composition in solution.

This chapter starts with a short introduction to the basic photophysical properties of trivalent lanthanoids and the most important implications for the design of luminescent lanthanoid coordination compounds. Afterwards, the established standard techniques for the characterisation of lanthanoid luminophores are introduced with concrete advice for the successful performance of the experiments. In the last section of the chapter short introductions to two emergent fields of study are given: The circularly polarised luminescence (CPL) of lanthanoids and energy transfer processes between lanthanoids.

8.1 Introduction

A broad variety of applications in technology and research rely on the unique photophysical properties of the lanthanoids [1]. For example, europium is widely used in fluorescence lamps, in displays and for anti-counterfeiting labeling in euro notes, and lanthanoids such as neodymium, ytterbium or erbium are often the key component of laser media. The emission spectra of trivalent lanthanoid luminophores consist of very narrow bands whose positions and shape are almost independent of the coordination sphere around the lanthanoid. This allows for unambiguous identification of individual lanthanoids and makes them the perfect luminophores for multiplexing applications. Typically, lanthanoid luminophores are significantly more resistant to photobleaching than organic luminophores. Long luminescence lifetimes up to the millisecond range allow for timegated imaging applications and the near-infrared emission of some of the lanthanoids allows for the utilization of the biological window for tissue. These properties lead to the successful utilisation of lanthanoid luminescence for biomedical applications. More recently also less commonly described phenomena such as energy transfer processes between lanthanoids and circularly polarised luminescence of lanthanoid luminophores started to become a focus of research. Key to the next innovations based on lanthanoid luminescence are the careful design and characterisation of novel lanthanoid luminophores with improved properties.

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The aim of this chapter is to give a general introduction to the principles of the photophysics of trivalent lanthanoids in molecular species and to explain the most important experiments pertinent to the photophysical characterisation of these luminophores.

8.2 Photophysical properties of lanthanoids

8.2.1 Electronic structure, energy levels and transitions

The unique photophysical properties of the trivalent lanthanoids are a consequence of their special electronic structure. For all Ln^{3+} (which is the most commonly observed oxidation state of all lanthanoids) the valence electrons are located in the 4f-orbitals. These orbitals happen to be spatially closer to the atomic nucleus than the energetically lower and therefore completely filled 5s- and 5p-Orbitals. This unusual circumstance leads to shielding of the f-electrons from the surroundings of the Ln^{3+} , which hinders electronic interactions such as covalent bonding and ligand field effects operative in d-transition metal complexes. This makes the energies of electronic f-f-transitions largely independent of the environment of the metal ion and consequently allows for a simple and unambiguous identification of a particular lanthanoid and the assignment of its characteristic transitions. In this situation also the vibronic coupling of electronic states with vibrations, which usually leads to considerable broadening, does not have a significant influence, which explains the observed very narrow linewidths.

The electronic states of the trivalent lanthanoid ions are typically described within the Russel-Saunders coupling scheme using term symbols $^{2S+1}L_J$, with $2S+1$ being the spin multiplicity, S being the total spin quantum number, L being the total angular momentum quantum number (given by the letters $S, P, D, F, G, H \dots$ for $L = 0, 1, 2, 3, 4, 5, \dots$) and J being the total spin-orbit coupling quantum number ($J = L + S, \dots, |L - S|$). Every term $^{2S+1}L_J$ consists of $2J+1$ individual Stark levels, which can become distinguishable in the presence of a ligand field [2–4].

With the aid of Hund's rules, the term symbols $^{2S+1}L_J$ describing the electronic ground states of the individual lanthanoids can easily be identified. The determination of the energetic order and position of the excited states is less straightforward but they have been calculated for lanthanoids in different media (Figure 8.1) [6–10]. Importantly, in the case of Ln^{3+} the ligand field effects are much smaller than in the case of transition metals. They are usually on the order of a few hundred wave-numbers at most and therefore constitute only the fine structure of the individual bands, not the overall shape of the spectrum. Consequently, for the interpretation of emission spectra of lanthanoids the energies of the different $^{2S+1}L_J$ can be assumed to be independent of the coordination environment. In most cases, ligand

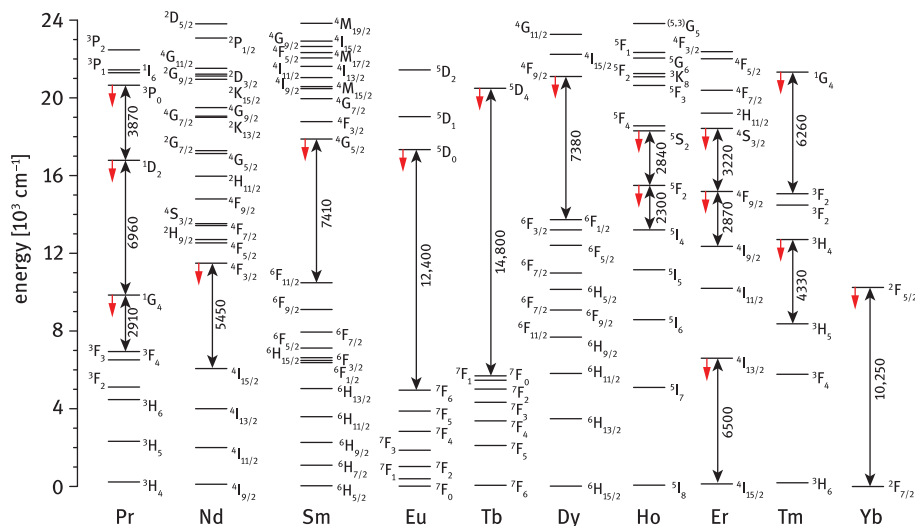


Figure 8.1: Partial energy-level diagram for selected trivalent lanthanoid ions (calculated energies for Ln^{3+} (aq) [6–9]; exception: Yb^{3+} in LaF_3 [10]). Downward arrows: prominent emitting levels; double-headed arrows: energy gap ΔE between emitting level and next lower level (in cm^{-1}). Term symbols $^{2S+1}L_J$ on the left of the lanthanoid manifolds are aligned in height with the quantum number J , the ones on the right with their multiplicities $2S + 1$. Figure originally published in reference [5], *Handbook on the Physics and Chemistry of Rare Earths* (Eds.: J.-C. G Bünzli, V. K. Pecchasky) 53, E. Kreidt, C. Kruck, M. Seitz, *Nonradiative Deactivation of Lanthanoid Luminescence by Multiphonon Relaxation in Molecular Complexes*, 35–79, Copyright Elsevier 2018.

field effects are in fact not discussed in the analysis of the photophysical properties of lanthanoids, though it is indeed possible to extract valuable information from the observable fine structure of the transitions.

The intensities of transitions between different electronic states of Ln^{3+} can be analysed with the Judd-Ofelt theory [11]. All transitions are f-f-transitions and hence are in principle Laporte(parity)-forbidden, some are also spin-forbidden [4]. Fortunately, there are some mechanisms such as J -mixing and orbital mixing which ease the applicability of these rules and make the transitions observable [12, 13]. The forbidden or “weakly allowed” nature of the transitions accounts for the very long luminescence lifetimes being observable for some of the lanthanoids and can hence be considered to be beneficial for the emissive properties of lanthanoid lumino-phores. But at the same time it is a major problem for their excitation. With extinction coefficients typically below $10 \text{ M}^{-1} \text{ cm}^{-1}$, direct f-f excitation with conventional light sources is usually not feasible and is only practical with strong lasers. This problem can be circumvented with the aid of the so called “antenna effect”.

8.2.2 Antenna effect

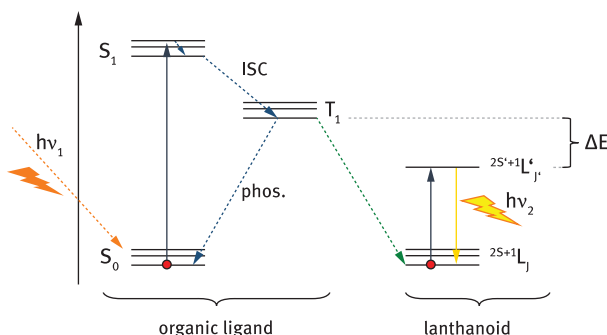


Figure 8.2: Indirect excitation of a lanthanoid via the antenna effect. By absorption of light the organic ligand is brought to an excited singlet state S_1 , from which an intersystem crossing (ISC) to the excited triplet state T_1 occurs. The direct relaxation of the system which leads to ligand-centered phosphorescence (phos) is forbidden and hence the T_1 state is long-lived enough to transfer energy to the coordinated lanthanoid, which consequently reaches an excited state $^{2S'+1}L'_J$.

In contrast to the direct excitation of lanthanoid luminophores, an indirect excitation with the aid of the antenna effect (Figure 8.2) can be very efficient and is the commonly used strategy for the preparation of luminescent lanthanoid coordination compounds [13, 14]. To make use of it, a ligand containing chromophoric groups with high extinction coefficients, for example an aromatic ligand, is brought in close proximity to the lanthanoid. The S_1 state of such a ligand can easily be populated with a conventional light source and moderate light intensities. From the S_1 state an energetically lower T_1 state can be populated via intersystem crossing (ISC). From this long-lived triplet state the energy can be transferred to the lanthanoid, populating one of its excited states [15]. An important design criterium for the preparation of highly luminescent lanthanoid luminophors is to make this process as efficient as possible. To avoid thermally induced backtransfer of energy from the lanthanoid to the ligand, the energetic difference ΔE (see Figure 8.2) between the triplet state of the ligand and the emissive state of the lanthanoid should roughly be greater than 2000 cm^{-1} [16]. Usually one antenna chromophore can be used for the excitation of several different lanthanoids, which allows for the preparation of isostructural complexes of different lanthanoids with identical chemical properties and excitation wavelengths, but different emission spectra. Together with the very small linewidths of the transitions of the lanthanoids, this makes them optimal luminophores for multiplexing applications [17, 18].

8.2.3 Quenching and strategies for the improvement of lanthanoid luminophores

After the lanthanoid has reached an excited state, the emission of a photon is not the only pathway which allows the system to relax to the ground state. Excited states of lanthanoids are very susceptible to multiphonon quenching via high-energy oscillators such as C-H, N-H or O-H bonds. During these processes, energy is transferred from the excited lanthanoid to a resonant overtone of a vibrational mode of the bond, leading to a loss of energy for the desired luminescence process [5].

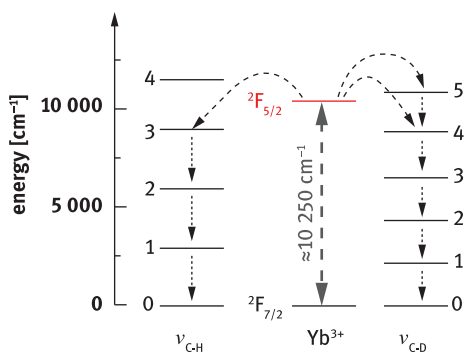


Figure 8.3: Energy transfer from the $^2F_{5/2}$ state of Yb^{3+} to overtones of C-H or C-D oscillators. Since the fundamental vibration of the C-D oscillator is lower in energy compared to the C-H oscillator, a higher overtone is necessary for C-D which is more difficult to populate. The energy transfer to the C-D oscillator is hence less likely to occur and the non-radiative quenching of the Yb^{3+} is reduced.

The most efficient approach to suppress these processes and to realise highly luminescent lanthanoid luminophors is to avoid such oscillators in the close proximity to the lanthanoid. The simplest strategy for that is the use of deuterated solvents. Another important strategy is a ligand design which allows to exclude solvent molecules from the first coordination sphere around the lanthanoid. But especially in the case of the C-H bonds of the ligand such a rigorous treatment is usually not possible. Instead, a commonly applied strategy is the deuteration (sometimes also fluorination) of the corresponding bonds [19–21]. The fundamental vibrations of the resulting oscillators are lower in energy ($\nu_{C-D} < \nu_{C-H}$, see Figure 8.3) and hence a higher overtone is needed to be in resonance with the excited state. Since such a higher overtone is less likely to be populated, the quenching becomes less likely and the luminescence properties of the luminophore are improved [5]. Especially in the case of lanthanoids emitting in the NIR impressive improvements of the luminescence lifetimes and quantum yields could be realised by deuteration of the ligand scaffold [21–23].

8.2.4 Definition of parameters

The processes outlined above can be quantified and related with a number of parameters such as luminescence lifetimes and quantum yields. Definitions of the most commonly used parameters are given in this section, the techniques applied for their measurement are the topic of section 8.3.

Observable luminescence lifetime τ_{obs}

The observable luminescence lifetime, which can also be given as the observable deactivation rate $k_{obs} = 1/\tau_{obs}$, is often experimentally well accessible [24]. For a sample consisting of i luminescent species the luminescence intensity I after excitation will decrease exponentially as

$$I(t) = \sum_i I_{0,i} \cdot e^{\frac{-t}{\tau_{obs,i}}} + B \quad (8.1)$$

With $I_{0,i}$ being the initial intensity after excitation, $\tau_{obs,i}$ being the observable luminescence lifetime and B being the background emission. In the case of a sample consisting of only one luminescent species ($i = 1$), after subtraction of B , τ_{obs} simply relates to the time at which the luminescence intensity has decreased to $1/e$ or 36.8% of the initial intensity I_0 .

Radiative luminescence lifetime τ_{rad}

The radiative lifetime refers to the luminescence lifetime in the theoretical case of the absence of any nonradiative deactivation processes and hence reflects the intrinsic properties of the emissive f-f transition [25]. Unfortunately, the direct experimental determination of τ_{rad} is not straightforward for most lanthanoids, with Eu^{3+} being an exception, and only few values for τ_{rad} are reported in literature (see section 8.2.5 and 8.3.5.2) [26, 27].

Absolute quantum yield ϕ_{Ln}^L

The absolute quantum yield is the experimentally directly accessible measure for the ratio of photons emitted by the sample (N_{em}) and the photons previously absorbed by the sample (N_{abs}) [24, 28]:

$$\phi_{Ln}^L = \frac{N_{em}}{N_{abs}} \quad (8.2)$$

For imaging applications this can be considered among the most relevant parameters and a lot of research on lanthanoid luminophores focusses on the optimisation of ϕ_{Ln}^L .

Intrinsic quantum yield ϕ_{Ln}^{Ln}

Somewhat analogously to the radiative luminescence lifetime τ_{rad} , the intrinsic quantum yield ϕ_{Ln}^{Ln} focusses on the lanthanoid after reaching the excited state [27]. It describes the fraction of energy which is successfully transformed into emitted photons from the excited state of the lanthanoid. Differently to τ_{rad} , quenching processes and for example the backtransfer of energy upon the ligand have an impact upon ϕ_{Ln}^{Ln} . The intrinsic quantum yield is calculated from the luminescence lifetimes τ_{rad} and τ_{obs} :

$$\phi_{Ln}^{Ln} = \frac{\tau_{obs}}{\tau_{rad}} \quad (8.3)$$

Sensitisation efficiency η_{sens}

The sensitisation efficiency describes the overall efficiency of the indirect sensitisation of the lanthanoid via the antenna effect. This is for example dependent on the efficiency of the intersystem crossing by which the triplet state of the antenna is populated, and the efficiency of the subsequent energy transfer process to the lanthanoid [27, 29, 30].

$$\eta_{sens} = \frac{\phi_{Ln}^L}{\phi_{Ln}^{Ln}} \quad (8.4)$$

8.2.5 Information available from luminescence data and the special case Eu^{3+}

Since ligand field effects are typically considered to be negligible for lanthanoid luminophores, usually the luminescence properties of these compounds are not assumed to provide substantial insights into their structure or composition. An exception to that is Eu^{3+} , where a substantial amount of information can be obtained about the local environment around the lanthanoid ion from simple emission spectra [31].

The transitions commonly observed in Eu^{3+} emission spectra start from the non-degenerate $^5\text{D}_0$ level and end in the $^7\text{F}_j$ manifold (see Figure 8.4). Of the seven terms ($j = 0-6$) of the $^7\text{F}_j$ manifold, usually the transitions to the five lowest in energy can

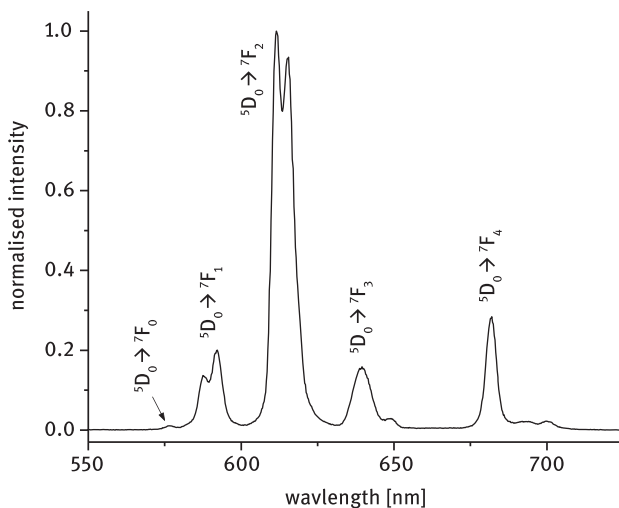


Figure 8.4: Steady state emission spectrum of a Eu^{3+} complex.

be detected ($J = 0, 1, 2, 3, 4$). In the case of the $^5\text{D}_0 \rightarrow ^7\text{F}_0$ transition, both, the start and the final level are non-degenerate, so that only a single line can be observed for this transition. If this transition appears to consist of several lines, or if the peak exhibits a deformation or shoulder, this is a strong indication for the presence of several emissive species in the sample. This doesn't have to be caused by impurities of the sample. The differences between the species can for example relate to different solvent molecules or anions being present in the first coordination sphere around the lanthanoid, or might point towards rearrangement processes of the organic ligands. According to the Laporte rule the $^5\text{D}_0 \rightarrow ^7\text{F}_0$ transition is strictly forbidden, and even in coordination polyhedra of low symmetry it is usually very weak and sometimes cannot be observed at all. In these cases alternatively the $^5\text{D}_0 \rightarrow ^7\text{F}_1$ transition can be used to extract information about the number of emissive Eu^{3+} centres. With $J = 1$, the $^7\text{F}_1$ level has three Stark levels, so depending on the symmetry a total of up to three lines can be expected for this transition, and the presence of additional lines or shoulders again points towards the presence of several emissive species. From the splitting of the individual components of the $^5\text{D}_0 \rightarrow ^7\text{F}_1$ transition the second-order crystal-field parameter $^2\text{B}_0$ can be extracted, providing useful insights for the analysis of the magnetic properties of the studied complex [32, 33]. As it is a magnetic dipole transition, the overall intensity of the $^5\text{D}_0 \rightarrow ^7\text{F}_1$ transition can be expected to be largely independent of the coordinative environment around the lanthanoid. With the aid of this transition, the radiative lifetime τ_{rad} of a Eu^{3+} complex can be determined from a simple corrected emission spectrum of the compound. It is calculated from the ratio of the integrated total emission intensity I_{tot} and the intensity of the magnetic dipole $^5\text{D}_0 \rightarrow ^7\text{F}_1$ transition I_{MD} :

$$\frac{1}{\tau_{rad}} = A_{MD,0} \cdot n^3 \left(\frac{I_{tot}}{I_{MD}} \right) \quad (8.5)$$

with $A_{MD,0}$ being the constant probability of the spontaneous emission in vacuo (14.65 s^{-1}) and n being the refractive index of the surrounding medium [26, 27]. For other lanthanoids τ_{rad} can be determined from absorption spectra (see section 8.3.5.2). In contrast to the $^5D_0 \rightarrow ^7F_1$ transition of Eu^{3+} , its $^5D_0 \rightarrow ^7F_2$ transition is a so-called hypersensitive transition, and the intensity of this transition can be considered to be a measure for the asymmetry in the coordination polyhedron and the polarisability of the donor atoms. A high intensity of this transition correlates to a low symmetry around the Eu^{3+} ion. The intensity of the $^5D_0 \rightarrow ^7F_2$ transition is directly proportional to the Judd-Ofelt intensity parameter Ω_2 .

In the last few years the general perspective on the amount of information that can be obtained from emission spectra of lanthanoid luminophores has started to change. With more elaborate spectrometers, allowing for high-resolution measurements at very low temperatures, the subtle ligand field effects in lanthanoid coordination compounds can in fact be monitored and analysed. This does for example allow for the study of the influence of individual ligands on the electronic structure of the coordinated lanthanoid [34]. In this context the value of luminescence experiments for the characterisation and development of lanthanoid single molecule magnet is currently also getting more attention.

8.3 Photophysical characterisation

8.3.1 Set up of a spectrometer

In Figure 8.5 the very general setup of a luminescence spectrometer is shown schematically. For most applications, the most practical choice for the light source are xenon lamps which are combined with one or several monochromators and one or several excitation slits for spectral selection. Alternatively, LEDs can be used if no variation of the excitation wavelength is necessary, and lasers are typically used for the direct excitation of the f-f-transitions. For steady state emission spectra continuous light sources are used, for the recording of time-resolved luminescence decay profiles pulsed light sources are necessary. As last element in the excitation light path a filter can be installed, which is typically done to remove second order excitation signals.

To minimize the fraction of the excitation light which reaches the detector, the emission light path is orientated rectangular to the excitation light path. After an optional filter, the emitted light is passed through one or several monochromators and one or several emission slits for spectral selection before it reaches the detector. Most

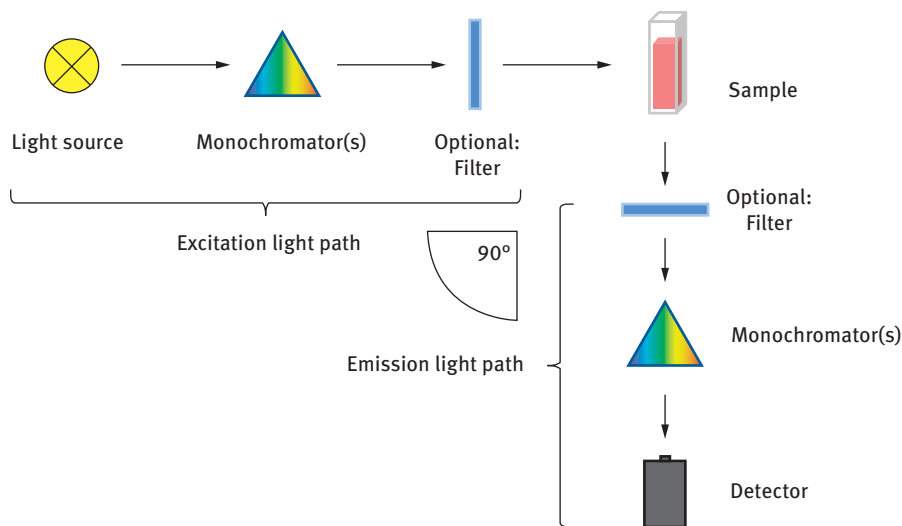


Figure 8.5: Schematic representation of the general setup of a luminescence spectrometer.

detectors are photomultipliers and are optimised for wavelengths below 1000 nm. Detectors optimised for the near-infrared are available, but usually less sensitive and more expensive.

In the following sections general strategies for the photophysical characterisation of lanthanoid luminophores in the solution state are described.

8.3.2 Cuvettes and sample preparation

Most commonly experiments for the solution state characterisation of the photophysical properties of lanthanoid coordination compounds are performed in rectangular glass fluorescence cuvettes with 10 mm path lengths. Standard cuvettes made from a wide variety of glasses and with different closures such as stoppers or lids are available, and also a variety of more specialised cuvettes can be purchased from different suppliers. Most important for the choice of glass is of course the range of wavelengths which is to be studied. Cuvettes with PTFE stoppers are the most practical for many applications. New cuvettes should be checked for luminescent impurities in the glass prior to use, and when results from several experiments are to be compared directly (for example during the measurement of quantum yields with the optically dilute method) it is beneficial to use cuvettes from the same lot.

To avoid cross contamination a careful cleaning of the cuvettes is key. The simplest way to ensure a complete removal of traces of previous samples makes use of the high solubility of lanthanoid nitrates in water by storing the precleaned cuvettes (and stoppers/lids, if the material is sufficiently stable) in half concentrated

nitric acid, which can be removed prior to use by washing the cuvettes several times with water and acetone. If spectroscopic grade solvents aren't available, HPLC grade solvents or NMR solvents can be a good alternative to ensure a sufficient purity of the sample. Solvents from new sources or new batches should be checked for purity prior to use. For samples containing air stable lanthanoid luminophores degassing of the solvents is usually not necessary. Whenever a biological application of the studied compound is targeted, a study of the photophysical properties in water is of course desirable. Hence the use of organic or deuterated solvents can help to enhance the luminescence and facilitate analysis. Generally, samples should be filtered, for which for example a bit of cotton wool stuffed into a single use pasteur pipette can be used.

In most cases it is easiest to adjust the concentration of the sample via UV/Vis. To avoid concentration effects samples should be relatively dilute, often maximum absorptions between 0.1 and 0.2 are a good choice. A rigorous control of absorption usually is only necessary when spectra are going to be interpreted quantitatively, for example for the determination of quantum yields. When the absorptions measured for a series of experiments are similar enough the spectra obtained can usually be normalised for the absorption to allow for a direct comparison, albeit this can only give a rather rough intensity ratio.

8.3.3 Characterisation of the antenna

As outlined in section 8.2.2, in most cases lanthanoid luminophores make use of the so-called antenna effect, which allows for an indirect sensitisation of the lanthanoid. To allow for a most efficient indirect sensitisation during the photophysical characterisation of a lanthanoid luminophore it is important to understand the photophysical properties of the antenna ligand, i.e. to know its absorption maximum. This can be determined with the aid of a simple UV/Vis scan experiment. Due to the low extinction coefficient of the f-f-transitions of Ln^{3+} , they cannot be excited in such an experiment and hence for a series of complexes of one ligand and several lanthanoids more or less identical UV/Vis spectra can be expected. Small deviations can occur when different ionic sizes of the lanthanoids lead to a slightly different arrangement of the ligand around the lanthanoid.

To avoid energy backtransfer processes from the lanthanoid to the ligand, the energetic difference between the triplet state of the ligand and the excited state of the lanthanoid should be at least 2000 cm^{-1} . Accordingly, from the energy of this triplet state it can be concluded for which lanthanoids the ligand could be a suitable antenna. For the determination of the energy of the triplet state complexes of non-emissive lanthanoids such as La^{3+} , Lu^{3+} , Gd^{3+} or Y^{3+} are prepared and their emission spectra at low temperature (77 K) are recorded. In these systems the energy cannot be transferred from the ligand to the lanthanoid and so the triplet state

of the ligand will often be depopulated via phosphorescence. The energy of the triplet state can be estimated from the observed phosphorescence maximum if the band is featureless or from a high-energy shoulder of the band if vibrational progressions are visible. Usually these experiments are performed with the aid of liquid N₂ dewar cuvettes which can be fitted into the sample holder of the spectrometer. The sample, prepared in a solvent or solvent mixture suitable to give a frozen glass matrix at 77K (for example mixtures of methanol and ethanol (1:1, v/v) or water and glycerol (1:1, v/v)), can then be filled in a simple NMR tube which is carefully placed in liquid N₂ to freeze the sample.

8.3.4 Steady state emission spectra

Though the emission spectra of lanthanoid coordination compounds are often considered to be largely independent of the individual structure of the complex they can provide valuable insights and are an important basis for the subsequent more detailed analysis of lanthanoid luminophores.

Usually the absorption maximum determined via UV/Vis spectroscopy is the excitation wavelength λ_{exc} of choice for any subsequent characterisation of a lanthanoid luminophore, such as the acquisition of steady state emission spectra. Apart from λ_{exc} , typically the most important parameter to be optimised during the acquisition of steady state emission spectra are the slit widths in the excitation and emission pathway of the spectrometer. Especially the emission slit width should be chosen as narrow as possible to allow for a good resolution of the individual features of the emission spectrum. Often it is unproblematic to increase the slit width in the excitation pathway a bit more to increase the overall intensity of the detected luminescence, but depending on the overall configuration of the spectrometer this can sometimes lead to different unfavourable phenomena related to stray light. Most importantly the width of potential second order emission peaks is related to the slit width in the emission pathway. The simplest way to check if a feature of a spectrum is a second order emission peak is to shift the excitation wavelengths a few nanometres and to check if the questionable peak shifts the twofold number of nanometres. Alternatively, and to check for any type of artifact caused by the set-up of the spectrometer, the sample cuvette can be replaced with a blank cuvette with pure solvent. Second order emission peaks can usually be removed by the installation of a low-pass filter before the sample, optimally also a high-pass filter is installed in the emission pathway (see Figure 8.5).

Another feature of steady state emission spectra which can sometimes be observed unexpectedly are transitions from higher excited states such as the $^5\text{D}_1$, $^5\text{D}_2$ or $^5\text{D}_3$ states of Eu^{3+} . This phenomenon is more common in the emission spectra of solid samples but can sometimes also be observed for molecular samples in solution.

Most commonly, steady state emission spectra are recorded at room temperature. At lower temperature the fine-structures of transitions are usually better resolved so that individual Stark levels can be measured more reliably. Such spectra can for example be recorded with the aid of the relatively affordable N₂ dewars which can be mounted in the sample holder, as described for the determination of the triplet level of the ligand in section 8.3.3.

8.3.5 Determination of luminescence lifetimes

8.3.5.1 Observable luminescence lifetime τ_{obs}

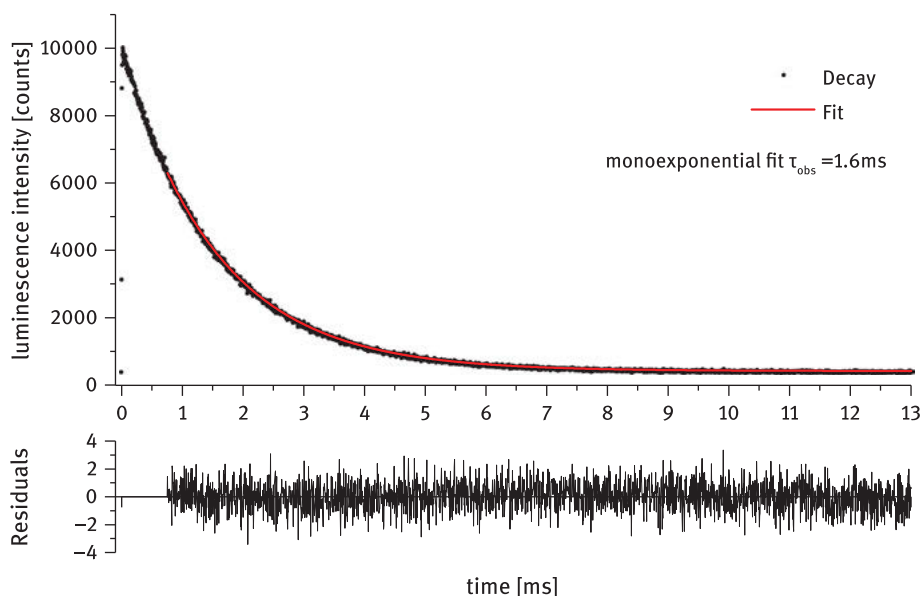


Figure 8.6: Prototypical luminescence decay of a europium complex. Modified from Reference [35].

For the determination of the observable luminescence lifetime the decay of luminescence intensity at a given wavelength is recorded (see Figure 8.6). Since in many cases (e.g. for Eu³⁺ and Tb³⁺) all transitions of a lanthanoid luminophore start from only one excited state, the observable luminescence lifetimes τ_{obs} for all transitions should be identical. Typically, from an optimised steady state emission spectrum recorded at a given excitation wavelength λ_{exc} the emission maximum is picked as wavelength which is detected during the luminescence decay experiment. To allow for maximum intensity to be detected during the experiment, the slit widths in the emission and excitation pathways are set to a high value. Care has to be given that an eventual second order emission peak does not overlap with the recorded wavelength.

After the luminescence decay has been recorded the data is fitted according to equation 8.1 to give the luminescence lifetime. Whenever a mono-exponential fit according to $I(t) = e^{-\frac{t}{\tau_{obs}}}$ does not provide a sufficiently good agreeance with the decay data, it should be checked if multi-exponential fittings can provide a better description of the experimental data. If the decay is best described by a multi-exponential fit this points towards the presence of several different emissive species in the sample, for example with different solvent molecules or ions being bound to the lanthanoid. The pre-exponential factors then relate to the relative occurrence of the different species in the sample. These species can be interconverting, and the equilibrium can be dependent on several parameters such as the concentration of the sample, the water content or the purification of the complex under study. Whenever Eu^{3+} complexes are studied and a multiexponential luminescence decay was determined, the steady state emission spectrum should be checked for any feature giving evidence of the presence of several species (see section 8.2.5).

Typical observable luminescence lifetimes τ_{obs} of the different lanthanoids vary over a broad range. For strongly luminescent lanthanoids such as Eu^{3+} or Tb^{3+} often values in the millisecond range can be reported, for most other lanthanoids τ_{obs} is usually significantly shorter and in the range of micro- or even nanoseconds. In line with the energy gap law and as a rule of thumb, shorter luminescence lifetimes can be expected for lanthanoids with smaller energy gaps between the emissive and the next lower state [36, 37]. These lanthanoids are more susceptible to non-radiative deactivation via multiphonon quenching (see section 8.2.3) and often it can be a challenge to determine their luminescence lifetimes. To control multiphonon quenching and to enhance the luminescence of such samples the use of deuterated solvents is inevitable in many cases. The effect of the deuteration of the solvent will be more pronounced for lanthanoid complexes in which the ligand does not completely saturate the coordination sphere of the metal ion and solvent can bind directly to the lanthanoid. This can be used to determine the number of directly bound solvent molecules q with the aid of luminescence lifetimes determined in pairs of protonated and deuterated solvents. For several lanthanoids empirical equations have been developed for that purpose (see Table 8.1 for some of the most common examples). Especially the equations for Eu^{3+} and Tb^{3+} often provide valuable insights, but more care has to be given when the respective equations for the less commonly studied lanthanoids such as neodymium [38–40], samarium [41] or dysprosium [41] are used.

Generally, for values of τ_{obs} uncertainties should be expected to be in the range of $\pm 10\%$.

Table 8.1: Empirical equations for the determination of the number of bound solvent molecules q . Solvent molecules in the second coordination sphere and beyond can be considered by subtraction of α from the difference of lifetimes.

Ln^{3+}	solvent	q [solvent molecules]	reference
Eu^{3+}	$\text{H}_2\text{O}/\text{D}_2\text{O}$	$q = A \left[\tau_{\text{H}_2\text{O}}^{-1} - \tau_{\text{D}_2\text{O}}^{-1} - \alpha \right]$ With: $A = 1.11 \text{ ms}$ and $\alpha = 0.30 \text{ ms}^{-1}$ Hydroxy, amine, and amide oscillators can be treated explicitly	[42]
Eu^{3+}	$\text{H}_2\text{O}/\text{D}_2\text{O}$	$q = A \left[\tau_{\text{H}_2\text{O}}^{-1} - \tau_{\text{D}_2\text{O}}^{-1} - \alpha \right]$ With: $A = 1.2 \text{ ms}$ $\alpha = 0.25 \text{ ms}^{-1}$ Carbonyl-bound amide NH oscillators can be treated explicitly	[43]
Tb^{3+}	$\text{H}_2\text{O}/\text{D}_2\text{O}$	$q = A \left[\tau_{\text{H}_2\text{O}}^{-1} - \tau_{\text{D}_2\text{O}}^{-1} - \alpha \right]$ With: $A = 5 \text{ ms}$ $\alpha = 0.06 \text{ ms}^{-1}$	[43]
Yb^{3+}	$\text{H}_2\text{O}/\text{D}_2\text{O}$	$q = A \left[\tau_{\text{H}_2\text{O}}^{-1} - \tau_{\text{D}_2\text{O}}^{-1} - \alpha \right]$ With: $A = 1.0 \text{ } \mu\text{s}$ $\alpha = 0.20 \text{ } \mu\text{s}^{-1}$	[43]
Yb^{3+}	$\text{CH}_3\text{OH}/\text{CD}_3\text{OD}$	$q = A \left[\tau_{\text{CH}_3\text{OH}}^{-1} - \tau_{\text{CD}_3\text{OD}}^{-1} - \alpha \right]$ With: $A = 2.0 \text{ } \mu\text{s}$ $\alpha = 0.1 \text{ } \mu\text{s}^{-1}$	[38]

8.3.5.2 Radiative lifetime τ_{rad}

As described in section 8.2.5, in the case of Eu^{3+} the radiative lifetime τ_{rad} can be determined from steady state emission spectra. For this purpose, the spectra have to be corrected for grating and detector efficiencies. The overall intensity and the intensity of the magnetic dipole $^5\text{D}_0 \rightarrow ^7\text{F}_1$ transition are then integrated and with the aid of equation 8.5 the radiative lifetime τ_{rad} can be calculated.

The determination of τ_{rad} for other lanthanoids is more complicated and significantly fewer values have been reported in literature. In some cases, for a transition to the electronic ground state of a lanthanoid luminophore, τ_{rad} could be calculated from the corresponding absorption spectrum with the modified Einstein relation given in equation 8.6:

$$\frac{1}{\tau_{\text{rad}}} = 2303 \cdot \frac{8\pi c n^2 \tilde{\nu}_{ul}^2}{N_A} \frac{g_l}{g_u} \int \epsilon(\tilde{\nu}) d\tilde{\nu} \quad (8.6)$$

$$\text{With } \tilde{\nu}_{ul}^2 = \frac{\int \tilde{\nu} \cdot \varepsilon(\tilde{\nu}) d\tilde{\nu}}{\int \varepsilon(\tilde{\nu}) d\tilde{\nu}}$$

With c being the speed of light (in cm s^{-1}), n being the refractive index of the medium, $\tilde{\nu}$ being the frequency of the transition in cm^{-1} , N_A being Avogadro's constant, g_l and g_u being the degeneracies of the ground and excited states ($2J+1$ for trivalent lanthanoids), respectively and $\varepsilon(\tilde{\nu})$ being the absorption spectrum of the transition (in $\text{M}^{-1} \text{cm}^{-1}$ vs. wavenumbers). This strategy has for example been used to calculate the radiative lifetimes τ_{rad} of Er^{3+} , Nd^{3+} or Yb^{3+} complexes [26, 30, 44]. However, due to the very low extinction coefficients of lanthanoids it is typically a challenge to record the absorption spectra necessary for this method, with large amounts of the sample material and special cuvettes with a long light path being necessary. As a consequence, the calculation of τ_{rad} for lanthanoids other than Eu^{3+} is rather exotic.

8.3.6 Absolute quantum yields ϕ_{Ln}^L

8.3.6.1 Relative methods

Since they do not require specialised equipment, the most commonly used methods for the determination of absolute quantum yields ϕ_{Ln}^L are relative methods, in which the compound under study is compared to a reference compound with a known quantum yield [24, 28]:

$$\phi_x = \phi_{Ln}^L = \phi_s \cdot \left(\frac{I_{em,x}}{I_{em,s}} \right) \cdot \left(\frac{A_{ex,s}}{A_{ex,x}} \right) \cdot \left(\frac{I_{ex,s}}{I_{ex,x}} \right) \cdot \left(\frac{n_x}{n_s} \right)^2 \quad (8.7)$$

with ϕ_x being the quantum yield of the compound under study, ϕ_s being the quantum yield of the standard compound. $I_{em,x}$ and $I_{em,s}$ are the integrated intensities of emission of both compounds from corrected spectra, $A_{ex,x}$ and $A_{ex,s}$ are the absorbance of the samples at the excitation wavelength, $I_{ex,x}$ and $I_{ex,s}$ are the intensities of the light source at the excitation wavelength, and n_x and n_s are the refractive indices of the sample solutions. At sufficient dilutions these can be approximated to be equivalent to the refractive indices of the solvents.

Equation 8.7 already gives some important indications for the planning and execution of such experiments for the determination of ϕ_{Ln}^L . If possible, the samples of both, standard compound and compound under study should be prepared in the same solvent and should be excited at the same wavelength. All parameters of the spectrometer such as slit widths should be kept constant for all measurements. Generally, the reference compound should be as similar to the compound under study as possible, i.e. the emission range and intensity of both should be comparable, but

at the same time the standard compound has to be available with reliably high purity. Most of the established standard compounds [45, 46] described in literature are based on organic chromophores such as quinine sulfate in sulfuric acid, which of course limits the comparability to lanthanoid luminophores and reduces the reliability of the obtained values. By now also some lanthanoid based standard compounds have been described, and though they might be considered less established they can be a very valuable alternative [47–49]. If possible two different standards should be used and referenced against each other.

The determination of the absolute quantum yield via equation 8.7 relies on various different values which all have to be expected to have a non-neglectable uncertainty. Hence the absolute error of the determined absolute quantum yield can be expected to be rather big. More reliable values can be expected when the optically dilute method is used, where a series of samples with different concentrations of both, the standard compound and the new compound, are studied in parallel and analysed with a linear regression.

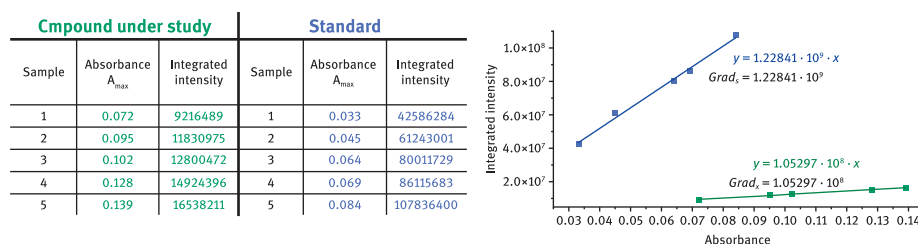


Figure 8.7: Obtaining $Grad_s$ and $Grad_x$ from experimental data for the determination of a quantum yield with the optically dilute method. For five samples of the compound under study and the standard, the maximum absorbance was determined from corrected UV/Vis spectra and the integrated intensity was derived from corrected steady state emission spectra.

For both compounds, the integrated intensities from corrected spectra are plotted against the maximum absorbance (see Figure 8.7), so that the linearly fitted slopes $Grad_x$ and $Grad_s$ can be extracted. Together with refractive indices of the samples the quantum yield can be calculated as:

$$\phi_x = \phi_{Ln}^L = \phi_s \cdot \left(\frac{Grad_x}{Grad_s} \right) \cdot \left(\frac{n_x}{n_s} \right)^2 \quad (8.8)$$

To obtain reliable values for $Grad_x$ and $Grad_s$, at least four samples of both compounds should be studied, with concentrations optimally spanning over about one order of magnitude. Often it is beneficial to prepare the samples with the highest and lowest concentration first to make sure that with a given set of parameters of the spectrometer all samples can be studied, i.e. the intensity detected for the samples with the lowest concentrations has to be sufficient to allow for a reliable

integration, and the intensity of the samples with the highest concentration must still be significantly below the detector limit.

Even with this more reliable method, uncertainties for the determined absolute quantum yields ϕ_{Ln}^L should be estimated to be at least in the range of $\pm 15\%$.

8.3.6.2 Absolute method

According to equation 8.2 it would obviously be most straightforward to determine the quantum yield by quantification of the number of photons absorbed by the sample (N_{abs}) and the number of photons emitted by the sample (N_{em}). But with standard setups it is typically not possible to determine which fraction of the light emitted by the luminophore actually reaches the detector, so that N_{em} cannot be determined. In the case of the relative methods for the determination of quantum yields the use of standard compounds compensates for that. Alternatively, quantum yields can be determined with the aid of integration spheres [50]. These extensions, which are available for many spectrometers, are in principle spherical detectors in which the sample can be placed. This allows to quantify the emitted light independently from scattering, and hence to relate the number of emitted photons to the number of photons used for excitation of the sample. With the aid of integration spheres it is possible to determine quantum yields from just the measurement of a blank and the sample, without the use of standard compounds. Nevertheless, a careful calibration of the setup is necessary, and it is favourable to test its reliability by the parallel measurement of a compound with a known quantum yield.

8.4 Less commonly studied phenomena

8.4.1 Circularly polarised luminescence (CPL)

Circularly polarised luminescence (CPL) generally describes the phenomenon observed when a chiral luminophore after excitation with unpolarised light emits different intensities of left and right handed polarised light at a specific wavelength [51–56]. This property of a luminophore can be quantified with the dissymmetry factor g_{lum} , which is calculated as the quotient of the difference of the intensities of left (I_L) and right (I_R) handed polarised light and the half of the total luminescence ($I_L + I_R$):

$$g_{lum} = \frac{I_L - I_R}{1/2 (I_L + I_R)} = \frac{\Delta I}{I} \quad (8.9)$$

This chiroptical property can in principle be found in any class of luminophores, but while for most organic luminophores or luminescent transition metal complexes typically g_{lum} values in the range of 10^{-4} to 10^{-2} are reported, for lanthanoid luminophores very commonly g_{lum} values between 0.1 and 1.0 are determined. This is another consequence of the special electronic structure of the lanthanoids [57, 58]. The highest dissymmetry factor in solution reported until now ($g_{\text{lum}} = 1.38$) was found for the $^5D_0 \rightarrow ^7F_1$ transition of $\text{Cs}[\text{Eu}(+)\text{-hfbc}]_4$ ((+)-hfbc = 3-heptafluoro-butylryl-(+)-campherato) [59]. Generally the highest dissymmetry factors can be expected for transitions which are magnetic dipole allowed and electric dipole forbidden, and the $^5D_0 \rightarrow ^7F_1$ transition of Eu^{3+} fulfils this selection rule optimally. A detailed theoretical analysis of the suitability of the transitions of many lanthanoids for the observance of strong CPL had already been performed in 1980 by Frederick S. Richardson, and has since then been validated by experimental findings [60]. Often the strongly luminescent Tb^{3+} is considered to be the second best lanthanoid for the preparation of strong CPL emitters, but more recently there is also a growing number of remarkably strong CPL emitters based on further lanthanoids such as Sm^{3+} or Dy^{3+} [61–64]. This is again in line with Richardson's prediction. Typically, these lanthanoids have a rather high susceptibility to multiphonon quenching and hence their complexes tend to be only weakly luminescent, which hinders the detection of CPL. After some early reports around 1999 [65–67], more recently also new examples of near-infrared CPL of lanthanoid complexes have been reported [68].

Importantly and in sharp contrast to the unpolarised total luminescence of the lanthanoids, their CPL is very dependent on the specific arrangement of the ligands around the lanthanoid. Subtle changes in the ligand field can have a significant influence upon the CPL properties of a compound. Though there have been efforts [53, 58, 64, 69, 70], it is not yet possible to do a detailed correlation of the structure of a lanthanoid luminophore and its CPL properties, which obviously hinders the targeted design of strong CPL emitters.

Currently CPL is gaining more and more attention and is turning into a focus point of the interest in lanthanoid luminophores. By now for example applications in the construction of novel OLED materials [71] or for the realisation of innovative approaches for bioimaging [72] are coming into reach. In this context the study of CPL in the near-infrared is especially interesting.

8.4.2 Energy transfer processes between lanthanoids and upconversion

After a lanthanoid ion has reached an excited state, apart from the emission of light also several alternative processes can occur, for example the transfer of energy to another lanthanoid ion. Depending on the different electronic states of the involved

lanthanoids this can result in a downshifting process, a quantum cutting process or an upconversion process (see Figure 8.8).

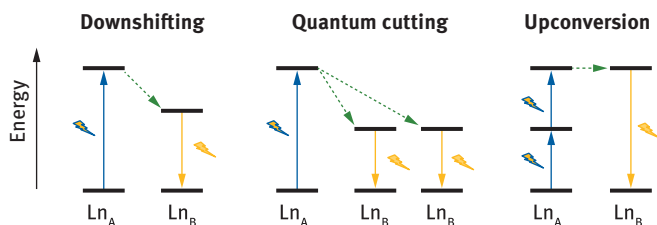


Figure 8.8: Examples for energy transfer processes between lanthanoids Ln_A and Ln_B . Blue arrows refer to excitation processes, green dotted arrows refer to the actual transfer of energy and yellow arrows indicate emissive processes.

After a downshifting process a photon of a lower energy can be emitted, a quantum cutting process conceptually allows to transform one photon of a high energy into two photons of a lower energy and during an upconversion process the energy of two photons of low energy is fused to give one photon of a higher energy. In principle such processes can be observed in various systems based on all kinds of luminophores, in the case of the lanthanoids they are facilitated by the long lifetimes of the excited states and the ladder-like arrangement of the energy levels which is found for many lanthanoids.

Especially upconversion processes have an enormous potential for various applications, for example for the construction of more efficient solar energy conversion devices or for the development of novel luminophores for bioimaging [73]. These could for example be excited with low energetic near-infrared light, for which biological tissue is transparent and which is less phototoxic. Several different upconversion mechanisms have been described, some of them are visualised in Figure 8.9 [74, 75].

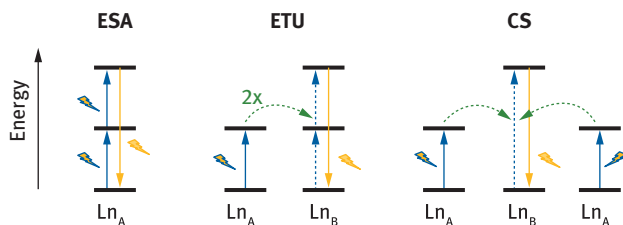


Figure 8.9: Examples for lanthanoid centered upconversion processes: ESA (excited state absorption), ETU (energy transfer upconversion) and CS (cooperative sensitisation). Blue arrows refer to excitation processes, green dotted arrows refer to the transfer of energy and blue dotted arrows refer to the coupled excitation processes. Yellow arrows indicate emissive processes.

An excited state absorption (ESA) process does not require an energy transfer process between several lanthanoids. Initially, the lanthanoid absorbs a photon to reach an intermediate energy level. While this state is populated, the lanthanoid absorbs another photon with an energy matching the energetic difference to a higher excited state. From this state a photon with an energy equal to the sum of energies of the absorbed photons can be emitted. Importantly, with this mechanism the three states do not have to be equidistant. When light of several wavelengths is used, ESA processes are in principle possible for a wide variety of lanthanoids. But of practical importance for ESA-up-conversion are especially lanthanoids with a ladder-like arrangement of energy levels such as Er^{3+} , Ho^{3+} , Tm^{3+} and Nd^{3+} . During an energy transfer upconversion (ETU) one lanthanoid (Ln_A , often referred to as the sensitiser) absorbs the photons and then transfers the energy to a second lanthanoid (Ln_B , often referred to as the activator). This stays at an intermediate energy level until Ln_A has absorbed a second photon and transferred it onto Ln_B , which then reaches the higher excited state from which an upconverted photon is emitted. The by far most common sensitiser is Yb^{3+} , which is due to the presence of only one excited state and the relatively large absorption cross section of the corresponding transition [74]. Suitable activators to which the energy can be transferred to are for example Er^{3+} , Tm^{3+} and Ho^{3+} , from which Er^{3+} is typically regarded as the activator which allows for the best ETU-efficiencies. The cooperative sensitisation (CS) is highly related to the ETU process. In this case Ln_B lacks the intermediate energy level, so instead of a stepwise sensitisation a simultaneous sensitisation from two lanthanoids Ln_A has to take place. An example for such a process is the cooperative energy transfer from two Yb^{3+} -ion to one Tb^{3+} - or Eu^{3+} -ion [76].

A plethora of examples for lanthanoid-centered upconversion has been reported for nanoparticles (upconverting nanoparticles, UCNPs) [77–79]. They consist of an optically inactive host material which is doped with photophysically active guest-ions. UCNPs are quite accessible, they can be prepared for example via coprecipitation, thermal decomposition or solvothermal synthesis. Unfortunately, these processes do not allow for a targeted design of the photophysical properties of such nanoparticles. By variation of the dopants the properties can be modified, but typically the optimisation of UCNPs is some kind of a trial and error process. The preparation of nanoparticles generally is a statistical process and hence an exact reproducibility is usually not given. Apart from that, the exact distribution of the lanthanoids in the host material cannot be determined, and in every single nanoparticle different relative arrangements of lanthanoids will occur. This drastically hinders the potential of UCNPs for an improvement of the fundamental understanding of lanthanoid-centered upconversion. Molecular systems in which lanthanoids are combined in a well-defined way would provide far better opportunities for such studies, but unfortunately there is only a very limited number of examples for such compounds [80].

One important problem for the realisation of these systems results from the high chemical similarity of the different lanthanoids, which makes it very difficult to prepare heteropolymetallic lanthanoid coordination compounds in a non-statistical

fashion. In principle it is also possible to observe upconversion after twofold excitation of a single lanthanoid ion (ESA upconversion) or after energy transfer between two ions of the same lanthanoid. While such processes are commonly reported for solid state materials, molecular examples are sparse, and generally it is indeed significantly more difficult to realise lanthanoid centered upconversion in the molecular state. One main reason for that is that the low energy excited states which are intermediately populated during the upconversion process are especially susceptible to nonradiative deactivation, which is far more likely to occur in the molecular state and in solution than it is in nanoparticles.

8.5 Summary and outlook

The outstanding photophysical properties of the lanthanoids such as their fingerprint-like emission spectra and their long luminescence lifetimes are among the most fascinating features of these special elements. These properties are indispensable for diverse fields of technology such as bioimaging, display development or for laser media. All these fields could already benefit from the improved understanding of the fundamental principles of lanthanoid photophysics and the resulting improvement of lanthanoid luminophores of the last decades, and further developments can be anticipated for the future. Apart from that, lanthanoid luminescence is getting more and more attention in emerging fields such as circularly polarised luminescence (CPL) or in new contexts such as the magnetic properties of the lanthanoids. Apart from the development of new strategies for the design of lanthanoid luminophores and their incorporation into materials and devices, the characterisation of these luminophores in terms of their fundamental photophysical properties will be key.

Though ligand field effects are small for lanthanoid complexes and the overall shape of their emission spectra is largely independent from the nature of the coordinating ligands, the careful characterisation of their photophysical properties can provide valuable insights. More elaborate spectrometers even allow to study the fine structure of the observed transitions and help to understand the electronic fine structure of individual complexes. Such techniques and studies will further increase the analytical potential of lanthanoid photophysics.

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9 Use of X-ray fluorescence analysis for the determination of rare earth elements

Abstract: X-ray fluorescence spectrometry is a powerful tool for the analysis of solid material. That is the reason why the technique was applied for the determination of rare earth elements since about 1970. At present energy dispersive XRF (EDXRF) and wavelength dispersive XRF (WDXRF) are used for the analysis of pressed powder pellets or fused Li-borate beads containing rare earth elements. The production of reliable results can only be achieved by careful optimization of the parameter in particular the selection of spectral lines. The quantification is based on a calibration realized by using reference samples.

9.1 Introduction

The use of X-ray fluorescence spectroscopy (XRF) for the analysis of rare earth elements (REE) is divided into the analysis of minors and traces in materials with natural origin and the analysis of industrial products containing REEs as main, minor or trace components.

The advantage of XRF is the direct analysis of solid material which could be presented directly as powder or pressed pellet. The disadvantage could be a high error and a high average lower limit of detection (LLD) of about 1 to 10 µg/g.

Nevertheless XRF is very often used as a rapid method with high throughput. For some applications the measurement error could be reduced by using fusion technology as sample preparation method. The LLD could be further reduced by using preconcentration methods.

One typical application is the analysis of REE in geological materials as overview or screening in addition to other techniques like ICP-OES or ICP-MS.

Other typical applications are the analysis of REE as tracer in polymers [1], as impurity in pure chemicals, as component in glass for e.g. light-emitting diodes (LED), as component in polishing powders, as component in magnets and generally as component in recycling processes.

For all these applications the sample preparation procedure as well as the measurement conditions have to be adapted to the REE present in the samples.

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9.2 Principle of X-ray fluorescence analysis

X-ray fluorescence radiation is an electromagnetic radiation with high energy. Energetically it lies between γ radiation and UV radiation.

X-ray fluorescence is generated by, among other processes, the ionization of the inner shell of an atom if radiation with high energy (0.1–100 keV) interacts with an atom. However, the probability that it will occur is small and is also dependent on the atomic number of the atom. Most of the excitation energy is translated into heat, which is the reason that XRF instruments always need to be more or less cooled.

If ionization of an inner shell does occur, i.e., an electron is removed, then the hole is filled by an electron from a higher energy shell. The energy difference is released as X-ray fluorescence radiation and is characteristic for the element. Depending on which transition takes place, it is called K, L or M radiation.

Figure 9.1 shows the typical electron transitions for the different shells. The lower line represents the innermost shell of an atom. The arrows symbolize an electron transition that is accompanied by the formation of an X-ray fluorescence line, such as, e.g., $K\alpha_1$. The intensity of the lines decreases in the order $K\alpha$, $K\beta$, $L\alpha$, $L\beta$.

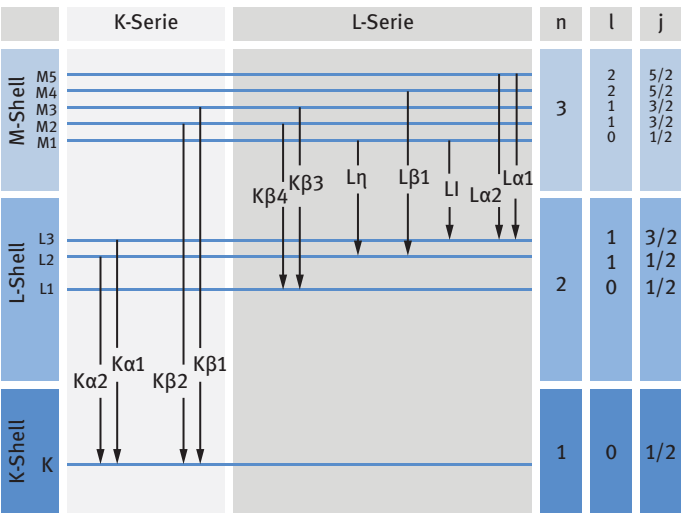


Figure 9.1: Transition of electrons in inner shells (a schematic setup of the energy levels for the single X-ray emission lines of the K- and L-series).

E.g. an electron e_K is leaving the K-shell if the energy $h \cdot \nu$ of the exciting radiation is higher than the binding energy $h \cdot \nu_K$ of the electron e_K (Figure 9.2). The characteristic X-ray fluorescence radiation is created. However if this fluorescence radiation leads to an ionization of the M-shell an electron e_M will leave the atom. This effect is called Auger effect and is in competition to the fluorescence effect. The fluorescence yield

9.3 XRF methods

Depending on the method of detection, instrument technology is divided into energy dispersive (EDXRF) and wavelength dispersive (WDXRF) X-ray fluorescence analysis [2–9].

9.3.1 Energy dispersive X-ray fluorescence analysis (EDXRF)

With EDXRF, the sample is excited by the X-ray tube directly or through a filter (Figure 9.3). A semiconductor detector (e.g., silicon-lithium semiconductor, pin diode or silicon drift chamber) analyzes the X-ray fluorescence radiation that comes directly from the sample.

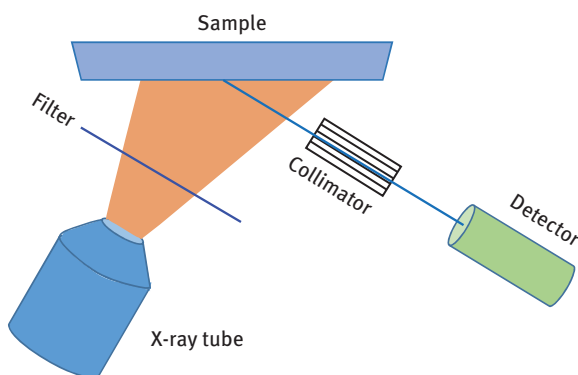


Figure 9.3: A schematic setup of an energy dispersive X-ray fluorescence spectrometer (EDXRF) with direct excitation.

Here, the detector together with the associated electronics counts and sorts, according to energy, all of the photons that reach it. A pulse height spectrum that indicates the number of photons or impulses for a given energy is established. The detector typically has only a few μs for processing, so that in case of a modern silicon drift detector (SDD) processing is accordingly limited to approximately 1,000,000 pulses per second. Using a filter, a portion of the exciting radiation can be screened out to avoid overloading the detector.

XRF with polarizing excitation represents an alternative design for EDXRF (Figure 9.4). Here, the radiation coming from the tube is deflected by 90° and is then used to irradiate the sample. The detector must be perpendicular to the plane determined by the tube, target and sample. The most important effect is that by deflecting the X-ray radiation by 90° , the radiation is polarized and the spectral background in

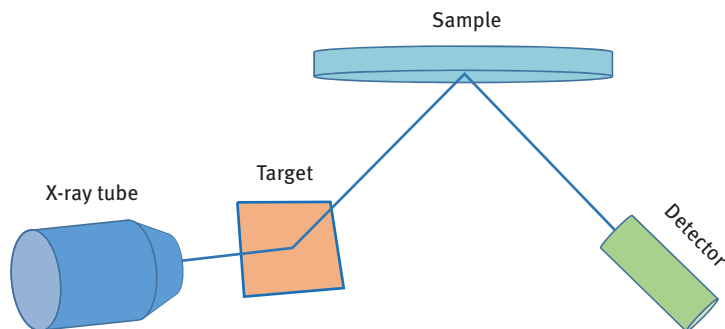


Figure 9.4: Configuration of an energy dispersive X-ray fluorescence spectrometer (EDXRF) with polarized excitation.

the spectrum is reduced. The analysis of REE by EDXRF suffers from big overlaps between the spectroscopic lines so that detector resolution becomes the limiting factor.

9.3.2 Wavelength dispersive X-ray analysis (WDXRF)

WDXRF uses, like some EDXRF, direct excitation (Figure 9.5). Here it is also possible to work with filters to block or weaken components of the excitation radiation. The major difference is the method of detection of the X-ray fluorescence radiation for WDXRF. Using a goniometer, only one wavelength from the spectrum is fed to the detector, i.e., it measures only one line from one element. In order to conduct multiple element analyses, it is necessary to create a serial measuring program that drives to and analyzes all of the lines of interest; one after another. There are, however so-called simultaneous spectrometers: In this case, there is a set channel for each element consisting of a fixed crystal with corresponding detector arranged around the sample. When combined with a goniometer this forms a very fast, high performance XRF instrument that is especially useful for process control.

Most of the XRF spectrometer nowadays are equipped with an X-ray tube with a Rh target. Nevertheless for the analysis of REE an X-ray tube with Au or W target would be a better choice than Rh to excite the K and L-lines of the REE [10].

The analysis of REE by WDXRF remains still a challenge even if the resolution of the goniometer is much better than for EDXRF. There are still a lot of line overlaps which cannot be totally resolved. The final performance of the XRF analysis of REE is therefore strongly depending on the availability of overlap free analyte lines which could be used for the determination.

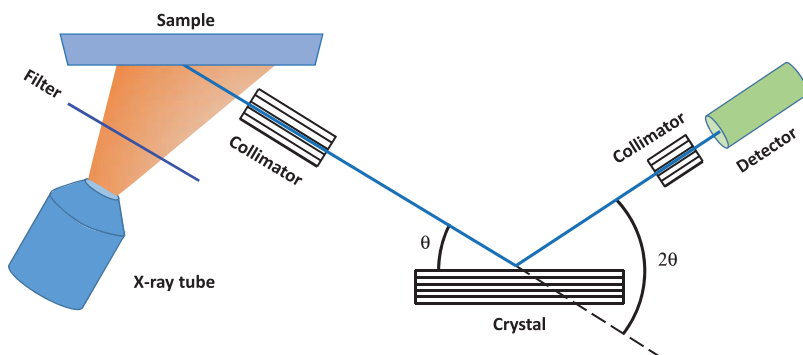


Figure 9.5: Schematic setup of a wavelength dispersive X-ray fluorescence spectrometer (WDXRF).

9.3.3 Comparison of EDXRF – WDXRF

In general, it is possible to say that the two techniques are complimentary; one supplements the other. EDXRF has a time advantage, as all elements are measured simultaneously, whereas the (serial) WDXRF measures the elements one after another.

WDXRF has a resolution and sensitivity advantage which is especially useful in the range of atomic numbers up to 30 and 55 to 80 which also includes most of REEs.

9.3.4 Other XRF techniques

9.3.4.1 Handheld XRF instruments

As the X-ray tubes became smaller, it became possible to construct very small portable X-ray fluorescence instruments (Figure 9.6). These usually have the form of a pistol, with which a given material can be directly analyzed onsite. These handheld XRF instruments are based on EDXRF with direct excitation. Combined with a low power X-ray tube they suffer from low resolution and low sensitivity for REE analysis.

Nevertheless these portable XRFs are used successfully in on-site field studies for geochemical exploration. Although the measurement has become very simple in this way, it is important not to neglect the aspects of sample preparation [24, 25].

9.3.4.2 Total reflection XRF

Total reflection is a special version of XRF which works only with liquid samples. Therefore the sample needs to be digested first and then a small amount is dried on a

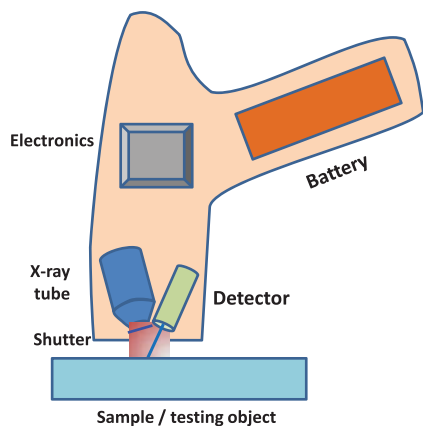


Figure 9.6: Handheld XRF instrument based on EDXRF.

quartz disk which then is irradiated by X-rays under total reflection conditions [11]. An example for the determination of REE in geological materials is described in [12].

9.4 Sample preparation

The performance of XRF for REE analysis is strongly depending on sample preparation. However the sample preparation strategy must be in agreement with the chosen measurement conditions especially the analyte lines, K- or L-series .

9.4.1 Pressed pellets techniques

Pressing a sample leads to a defined density in the pellet. This guarantees reproducible sample preparation.

The Following Procedures are Used to Press Samples:

- Direct pressing
- Pressing in aluminium trays
- Pressing in rings
- Pressing with binders
- Pressing onto a backing material

It is important for XRF that the pressed sample is mechanically stable. The sample is subject to a vacuum when placed into the analytical instrument and returned to an air environment after the measurement. High stability is required to be sure that the sample does not break during these procedures. Only a few materials display this type of stability, which can be increased by pressing into aluminum trays. Mixing with a binder is obligatory for most materials.

Manually mixing with mortar and pestle is arduous and not very effective. This is why I recommend using a simple mixer, whereby the high reproducibility is also ensured.

In practice: Making a pellet

The complete procedure for making a pellet, from preparation of the sample to pressing, is shown in Figure 9.7 [2].



Figure 9.7: Illustration of all steps to produce a pressed pellet with binder.

After grinding the sample, 4 g of the sample are mixed with 1 g binder (e.g., wax [2]). Before pressing, the pressing tool can be covered with a pellet film, which prevents subsequent sticking, simplifies cleaning and prevents contamination of the pellet from the hardened steel (Cr, Fe). Aluminum cups help stabilize the pellet and enable easy labeling, but have no additional usefulness. Table 9.2 presents figures based on experience for the pressure required depending on the diameter of the pressed pellet.

Here it is important to remember that the pressing procedure must be reproducible, i.e., the same density must be obtained in each pressed pellet. Direct pressing from 0 to, e.g., 30 tons can prevent the air contained in the sample from completely escaping. This leads to cracks in the pressed pellet. Use of a lower pressure or a pressing procedure in several steps is recommended.

Table 9.2: Recommended pressure depending on the diameter of the pressed pellet.

Diameter	Pressure
32 mm	15–20 t
40 mm	20–30 t
35 mm ring inside	max. 30 t

When there is not enough sample material, but a stable pressed pellet is still required, then the sample can be pressed onto a backing. In literature [13] this is presented for yttriumoxide: 400 mg of sample (dissolved in acid and precipitated as oxalate) are mixed with an equal amount of boric acid and then pressed on a boric acid layer as backing. However since 01 December 2010 boric acid is classified as GHS08 health hazard which means that it should be replaced by a non hazardous material. In [2] a cellulose type material called BOREOX is presented as a good non hazardous replacement.

It has to be mentioned that sample thickness should always be higher than the penetration depth of the XRF line used for calibration. Table 9.3 lists recommended minimum sample thicknesses or masses depending on K- or L-lines for REE analysis.

Table 9.3: Minimum required sample thickness [2] or mass [10] of a pressed pellet for REE analysis depending on the analyte line and pellet diameter.

REE XRF lines	Minimum Sample Thickness	Minimum Mass / Diameter
L-lines	0.5 mm	2 g / D30 mm
K-lines	8 mm	20 g / D30 mm
		40 g / D40 mm

In [23] the preparation of coal ashes as pressed pellets is described. 3.0000g at 105°C dried ash is well mixed with 1.5000g cellulose and 0,4500g graphite, then grinded in a disc mill and then pressed with 20kN.

9.4.2 Fusion technology

In XRF, most solid samples are prepared as pressed pellets, whereby the achievable precision suffers from so called particle size effects. They describe the phenomenon that the intensity of X-ray fluorescence is depending on particle size and shape. If the achieved precision with pressed pellets is not sufficient, the sample must be prepared using a fusion process.

The fusion provides an ideally homogeneous sample with a defined density and without particle size effects. In addition, homogeneity and a perfect surface lead to a much smaller calibration error.

Figure 9.8 shows the fundamentals of the fusion process.

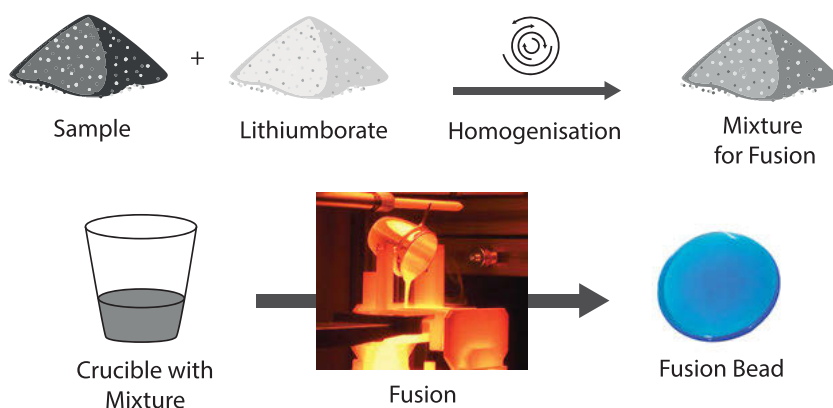


Figure 9.8: Principle of the fusion process.

The following conditions must be fulfilled for fusion of a sample:

- Finely ground oxidic sample material
- Borate as the fusion material and glass forming agent
- Platinum-gold crucible
- Platinum-gold casting dishes
- Temperatures higher than the Borate melting point

Modern automatic fusion systems are used to obtain reproducible fusions. As base for the technique either a muffle furnace, a gas burner or an induction furnace is used. In most of the systems the sample is mixed with the flux then placed into a platinum crucible. The crucible is set onto the melting position and then the sample is fully automatically oxidized, melted, stirred and cast. After approximately 10–15 minutes, the cold fusion bead can be placed into the XRF for measurement.

For ICP-OES or ICP-MS measurements the melted sample could be cast directly into the acid instead of casting a bead.

Further sample preparations methods using fusion known from literature

Rock samples are mixed 1:5 with lithiumtetraborate and fused at 1000°C in a muffle furnace. Then dissolved in HF and HNO₃ followed by a separation of REE from the matrix by anion exchange and subsequent preconcentration. Finally the REE are coprecipitated with rhodizonate and tannin. The precipitate is collected on membrane filter which is measured with XRF [14].

To fuse REE rock samples 3 different dilutions between sample and flux are suggested by [15]: 1:1 for REE, 1:2 for Th and U and 1:10 for major and minor elements. It is a challenge to perform a low dilution fusion with a ratio 1:1 to avoid inclusions and bubbles. Therefore the fusion had to be repeated a second time and LiCl was added to avoid devitrification. The LLDs achieved with this method are in the range of 0.6 µg/g (Th, U) and 0.7–6.5 µg/g for REE.

The authors of reference [16] describe a method for raw materials with major and minor concentrations of REE: the REEs are separated from the main matrix by dissolving them with HF/HNO₃ and Na₂CO₃/Na₂O₂ and final precipitation as oxalate. Then a fusion of the residue with Lithiumtetraborate was done. Cr and Mo were used as internal standard. Results are presented for light rare earth elements, Y and Th over a wide concentration range (La, Ce, Nd, Pr 0.02–25%; Sm, Gd, Eu, Y and Th 0.005–1%).

In [10] Monazite samples were fused with pure lithiumtetraborate or a mixture of lithiumtetraborate and lithiummetaborate (90:10) in a ratio of 0.5 g sample and 9.5 g flux and a few drops of LiBr (25%) as releasing agent.

9.4.3 Additional sample preparation techniques

[17] describes the analysis of REEs in Apatit. The sample is dissolved in HNO₃, then the REEs are separated by a mixed solvent anion exchange and kept by the resin which is then analysed by XRF on top of a disc.

Another preconcentration method in combination with a thin film measurement is presented in [18]: 1 g sample was fused with 4 g Na₂O₂ and finally dissolved in acid. The REEs were separated from the main components by ion exchange. The XRF measurement was done at an ion-exchange paper.

Also in [19] the XRF measurements were performed directly on a filter. After digestion of the sample with acid the REEs are preconcentrated by using an Arsenazo III complex which was collected on a filter by chemofiltration.

9.5 Practical application of REEs determination

Reference materials

To perform and to verify an XRF calibration reference materials are required. Table 9.4 lists the reference materials mentioned in the literature cited in this article. Most of them are already sold out. However there are replacements and many other reference materials which could easily be explored by free accessible databases in the internet. Table 9.5 gives an overview.

Table 9.4: Reference materials cited in REE literature.

Reference material	Producer
SRM 613	NIST, National Institute of Standards and Technology, USA
JG-1a, JR-2, JR-3, JG-1, JB-1	GSJ, Geological Survey of Japan
SARM 1 (NIM-G)	SARM, Mintek South Africa
IGS-36	BGS, British Geological Survey
BCR-1, G-2, GSP-1, BHVO-1	USGS, U.S. Geological Survey

Table 9.5: Free accessible databases for the search of reference materials containing REEs.

Database	Reference
FLUXearch	www.fluxearch.com
COMAR	www.comar.bam.de
GeoReM	georem.mpch-mainz.gwdg.de

Measuring parameters

Starting the configuration of an XRF spectrometer for the determination of REE first the spectral line for calibration must be selected. REEs have 3 K-lines and about 7 L-lines which could be used. However the sensitivity of the analyte lines differ a lot. From the K-line series the $K\alpha_1$ line and for the L-lines the $L\alpha_1$ and $L\beta_1$ show the highest sensitivity.

K series lines could be used for La, Ce, Pr, Nd, Sm if pressed pellets are used as sample preparation. Based on the large penetration depth particle size effects will be reduced.

Figure 9.9 shows the K series lines for La to Sm measured with WDXRF equipped with a Rh target X-ray tube, 60 kV excitation, LIF 220 crystal, 0.15° fine collimator and SC as detector. The graph demonstrates how the sensitivity decreases from La to Sm.

For comparison Figure 9.10 shows the K series lines of the elements La to Sm measured with an EDXRF equipped with a W target X-ray tube, 60 kV excitation combined with a Al_2O_3 polarizer target and a Silicon drift detector (SDD). The resolution

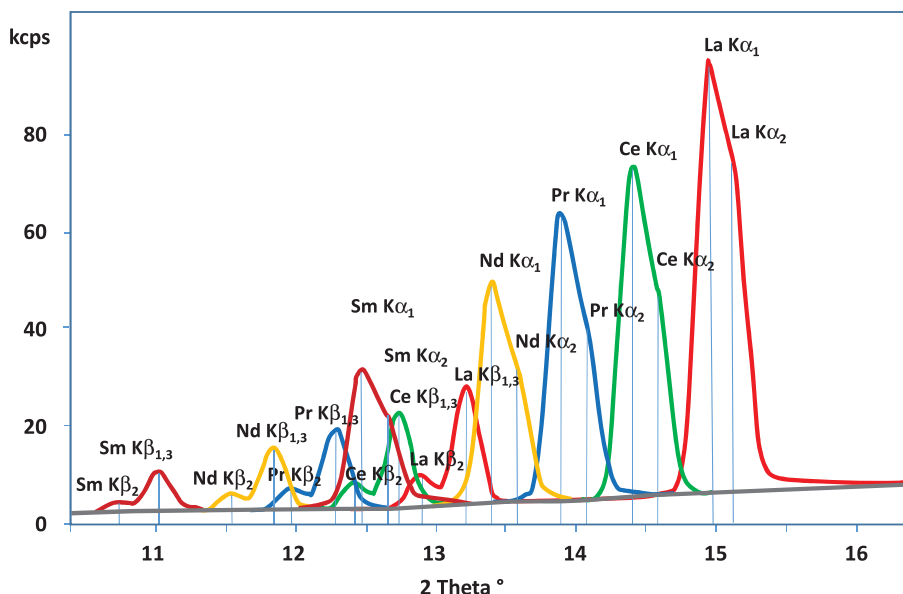


Figure 9.9: Overlapped K-line spectra of REE measured at 40000 µg/g single element samples from FLUXANA, WDXRF, Rh tube 60kV, LIF 220, 0.15°, SC.

is better than in WDXRF and there are less line overlaps in the spectrum. Based on the fact that the concentrations for the REE shown in Figure 9.9 are 40000 µg/g each and the concentrations for the REE shown in Figure 9.10 are only 100 µg/g each it can be seen that also the sensitivity is much higher.

L series lines must be used with fusion disks because of infinite thickness limitations. Figures 9.11–13 show the complete L-line spectra of La, Gd and Lu as an example measured with WDXRF, Rh target X-ray tube, 40 kV excitation, LIF 220 crystal, 0.15° fine collimator and flow counter detector (FPC). The L-lines show always the same line pattern (out of the $L\beta_4$ line).

For comparison Figure 9.14 shows the overlap of single element L-line spectra of the REE measured with an EDXRF with W target X-ray tube, 40 kV excitation with a Mo secondary target and a SDD. However the resolution of the detector is not sufficient to resolve the different lines.

The most difficult work in creating a measurement programme for REEs is the selection of the analyte lines and the corresponding background positions. Because of the high numbers of line overlaps a general recommendation is very difficult. Figures 9.15–9.18 show a full scan of all analyte lines in the region of the REE lines. This measurement was performed on the glass drift monitor sample FLX-S13 from FLUXANA which contains most of the elements which show lines in this spectrum. The detailed study of all line marks gives a good impression of where to select the analyte lines and the corresponding background positions for the required application.

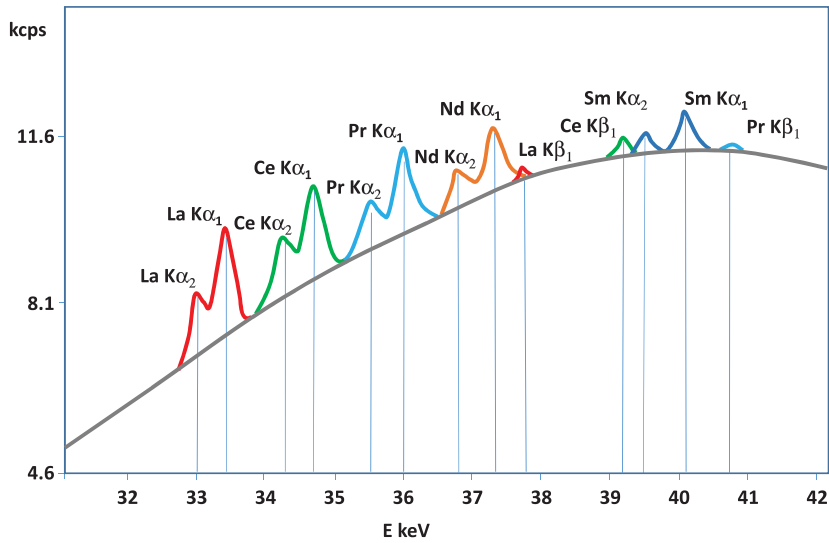


Figure 9.10: Overlapped K-line spectra of REE measured at 100 µg/g single element samples from FLUXANA, EDXRF, W tube, 60 kV, Al_2O_3 polarizer, SDD.

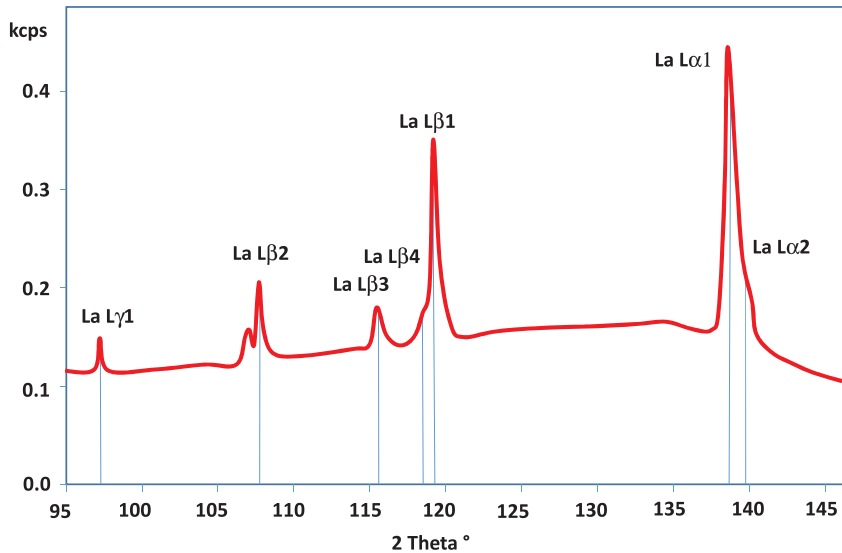


Figure 9.11: L series lines of 100 µg/g La in cellulose measured with WDXRF, Rh-tube, 40 kV, LIF 220, 0.15°, FPC.

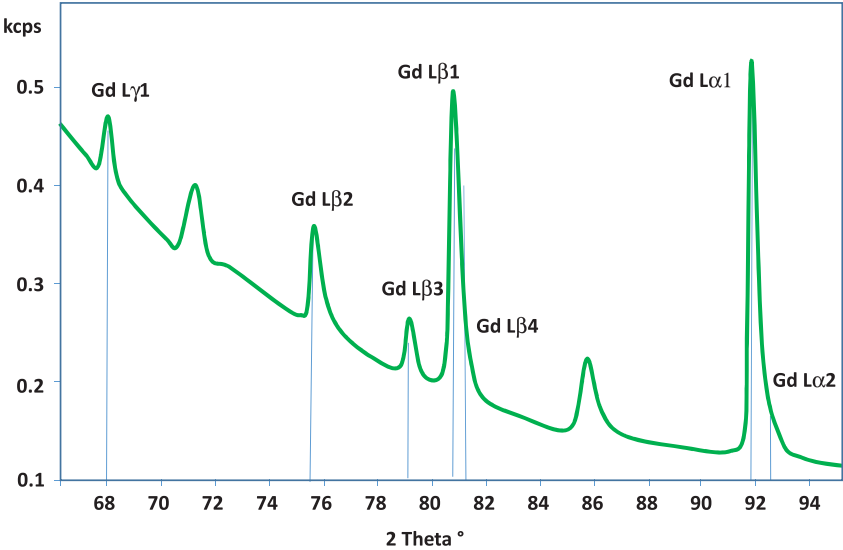


Figure 9.12: L series lines of 100 $\mu\text{g/g}$ Gd in cellulose measured with WDXRF, Rh-tube, 40 kV, LIF 220, 0.15°, FPC.

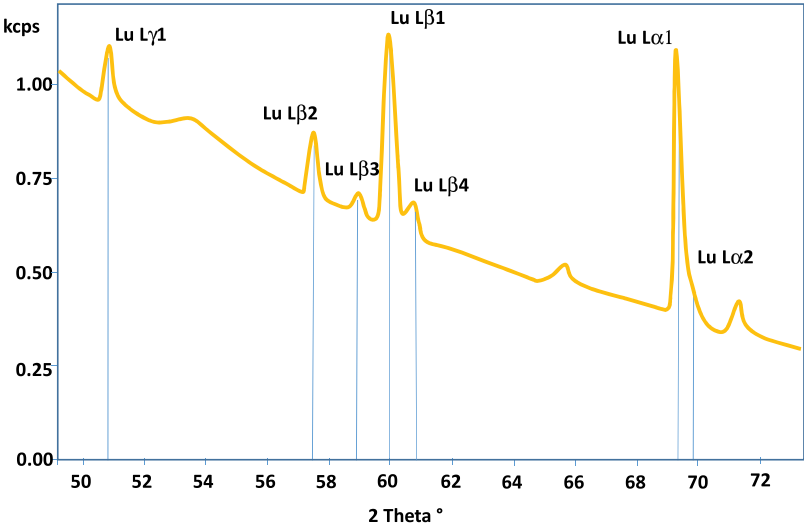


Figure 9.13: L series lines of 100 $\mu\text{g/g}$ Lu in cellulose measured with WDXRF, Rh-tube, 40 kV, LIF 220, 0.15°, FPC.

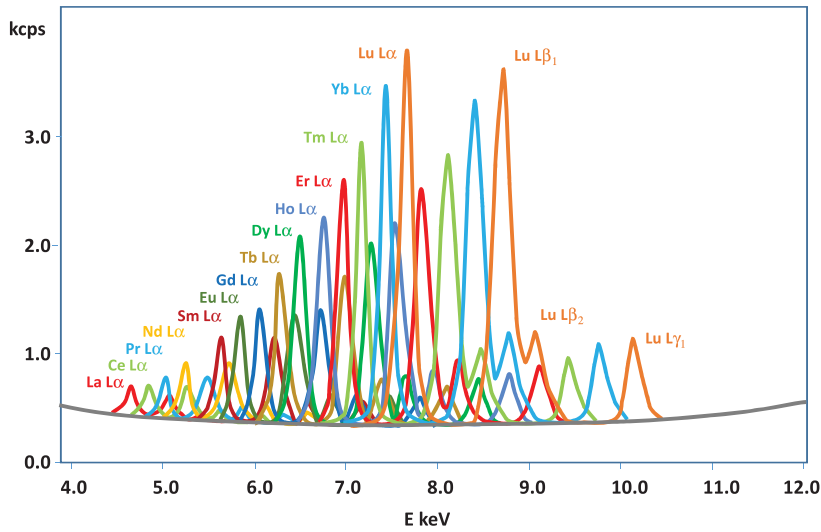


Figure 9.14: Overlapped L-line spectra of REE measured at 100 µg/g single element samples from FLUXANA, EDXRF, W tube, 40 kV, Mo secondary target, SDD.

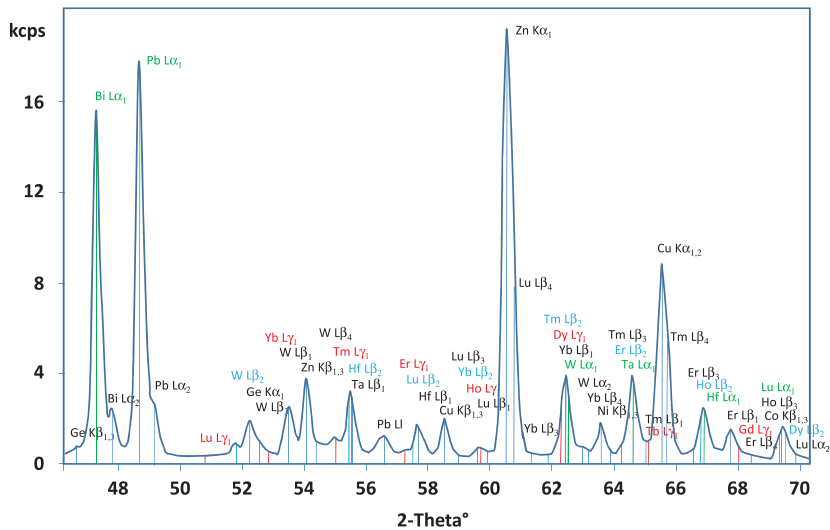


Figure 9.15: Scan 1/4 of FLUXANA drift monitor sample FLX-S13 with WDXRF, Rh tube 40 kV, LIF 220, 0.15°, FPC.

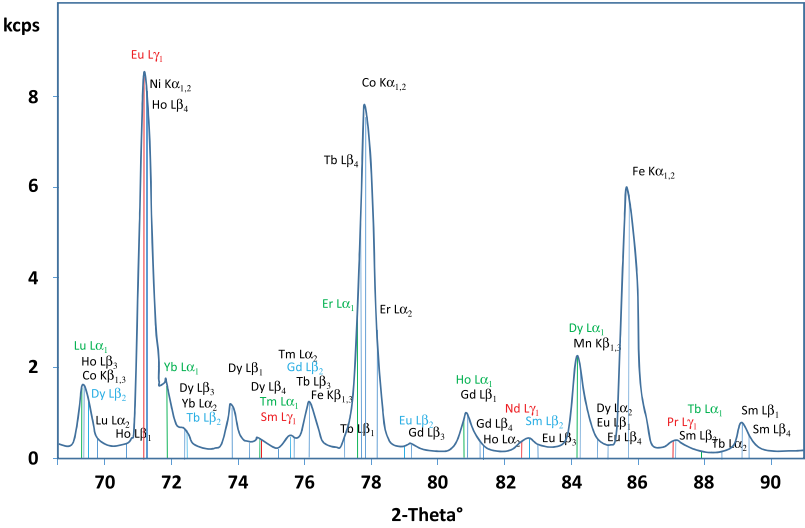


Figure 9.16: Scan 2/4 of FLUXANA drift monitor sample FLX-S13 with WDXRF, Rh tube 40 kV, LIF 220, 0.15°, FPC.

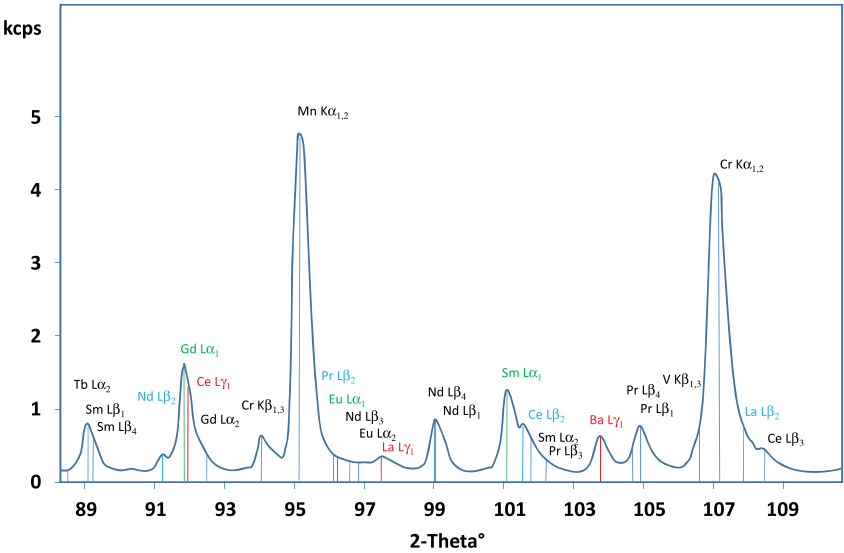


Figure 9.17: Scan 3/4 of FLUXANA drift monitor sample FLX-S13 with WDXRF, Rh tube 40 kV, LIF 220, 0.15°, FPC.

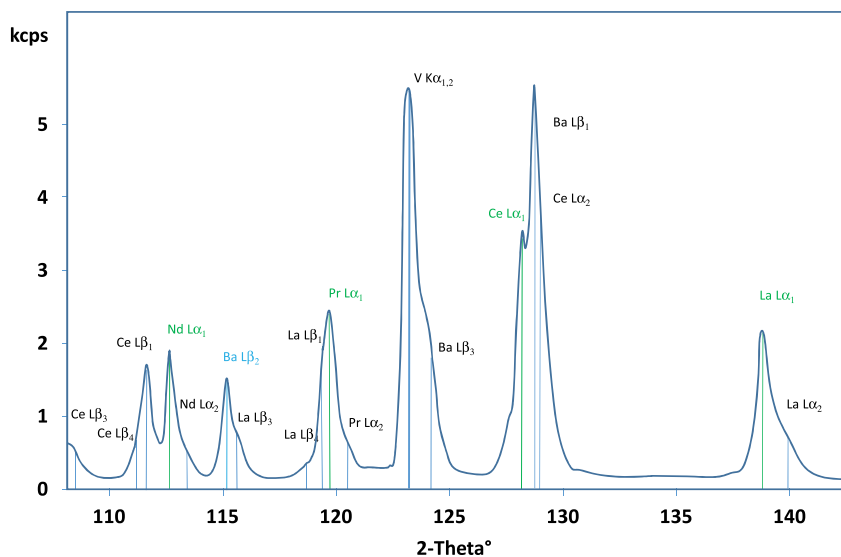


Figure 9.18: Scan 4/4 of FLUXANA drift monitor sample FLX-S13 with WDXRF, Rh tube 40 kV, LIF 220, 0.15°, FPC.

Table 9.6 lists all X-ray fluorescence lines of REE which show relevant intensities and Figure 9.19 lists all line overlaps which have to be taken into account for REE.

Analyte lines

Table 9.7 gives an indication which analyte lines should be selected for the analysis of REE. The selection considers a minimum of line overlaps which have to be taken into account by spectrum scans or the measurement of single element standards. Also background positions have to be chosen based on individual measurements on the samples which have to be investigated.

A complete measurement program for WDXRF equipped with Rh target tube to measure rock samples is presented in [15].

Lower limit of detection (LLD)

Figures 9.20 and 9.21 show LLDs of REE in different matrices and measured with WDXRF equipped with a Rh target tube and EDXRF equipped with a W target tube, both working with 60 kV. While EDXRF shows here a higher sensitivity for the K lines, WDXRF shows a higher sensitivity for most of the L lines.

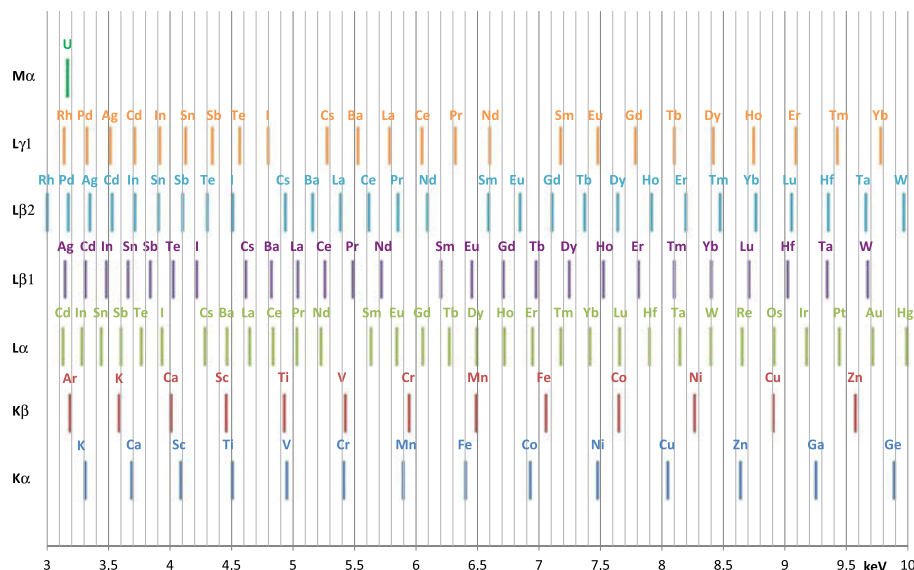


Figure 9.19: X-ray fluorescence line overlaps relevant for REE in the range of 3 to 10 keV [2].

9.6 Calibration

The calibration strategy is depending on the sample preparation. For pressed pellets particle size effects and matrix effects dominate the interelement corrections. To build up a calibration many standard materials analysed by other analytical methods are required. Most of the instrument manufacturers offer such calibration packages already. In fused bead sample preparation the sample is totally dissolved and doesn't show any particle size effects. Additionally matrix effects could be reduced because of the dilution or the presence of a strong absorber element. Fusion shows the advantage of building an independent calibration traceable to the weights of pure chemicals. An example of building such a calibration is given in [15]. For such a calibration less calibration samples are required and the need of external standard materials is small. Also FLUXANA offers calibration sets for REE applications as fused beads.

Attention has to be paid to sample thickness if K lines are used for analysis. There is a possible risk that the samples are not infinitely thick for the high energies of K lines. If a Rh target tube is used a possible correction for the imperfect thickness and additionally for any kind of matrix effects could be the normalization to the Rh Kα Compton Peak because no absorption edges are found in between.

Table 9.6: Fluorescence lines from REE in keV [20, 21].

Z	Element	K α_1	K α_2	K β_1	L α_1	L α_2	L β_1	L β_2	L β_3	L β_4	L γ_1	M α_1
57	La	33.4418	33.0341	37.801	4.65097	4.63423	5.0421	5.3835	5.1434	5.0618	5.7885	0.833
58	Ce	34.7197	34.2789	39.2573	4.8402	4.823	5.2622	5.6134	5.3653	5.2774	6.052	0.883
59	Pr	36.0263	35.5502	40.7482	5.0337	5.0135	5.4889	5.85	5.5918	5.4981	6.3221	0.929
60	Nd	37.361	36.8474	42.2713	5.2304	5.2077	5.7216	6.0894	5.8294	5.7216	6.6021	0.978
62	Sm	40.1181	39.5224	45.413	5.6361	5.609	6.2051	6.586	6.3180	6.1962	7.178	1.081
63	Eu	41.5422	40.9019	47.0379	5.8457	5.8166	6.4564	6.8432	6.3716	6.4378	7.4803	1.131
64	Gd	42.9962	42.3089	48.697	6.0572	6.025	6.7132	7.1028	6.8310	6.6873	7.7858	1.185
65	Tb	44.4816	43.7441	50.382	6.2728	6.238	6.978	7.3667	7.0961	6.9403	8.102	1.24
66	Dy	45.9984	45.2078	52.119	6.4952	6.4577	7.2477	7.6357	7.3702	7.2039	8.4188	1.293
67	Ho	47.5467	46.6997	53.877	6.7198	6.6795	7.5253	7.911	7.6518	7.4711	8.747	1.348
68	Er	49.1277	48.2211	55.681	6.9487	6.905	7.8109	8.189	7.9392	7.7453	9.089	1.406
69	Tm	50.7416	49.7726	57.517	7.1799	7.1331	8.101	8.468	8.2309	8.0258	9.426	1.462
70	Yb	52.3889	51.354	59.37	7.4156	7.3673	8.4018	8.7588	8.5368	8.3132	9.7801	1.521
71	Lu	54.0698	52.965	61.283	7.6555	7.6049	8.709	9.0489	8.8470	8.6065	10.1434	1.581

Table 9.7: Recommended analyte lines of REE from the author with alternatives in brackets. For comparison also the recommendations from literature are given.

Z	Element	Author	[10]	[22]	[3]	[16]
57	La	$L\alpha_1$	$L\alpha_1$	$L\alpha_1$	$L\alpha_1, L\beta_1$	$L\alpha_1$
58	Ce	$L\beta_1 (L\alpha_1)$	$L\beta_1$	$L\alpha_1$	$L\beta_1$	$L\beta_1$
59	Pr	$L\beta_1 (L\alpha_1)$	$L\beta_1$	$L\beta_1$	$L\beta_1$	$L\beta_1$
60	Nd	$L\alpha_1$	$L\beta_1$	$L\alpha_1$	$L\alpha_1$	$L\beta_1$
62	Sm	$L\beta_1 (L\alpha_1)$	$L\beta_1$	$L\beta_1$	$L\alpha_1, L\beta_1$	$L\beta_1$
63	Eu	$L\alpha_1 (L\beta_1)$	$L\alpha_1$		$L\alpha_1$	$L\beta_1$
64	Gd	$L\alpha_1$	$L\alpha_1$	$L\alpha_1$	$L\alpha_1$	$L\beta_1$
65	Tb	$L\alpha_1$	$L\alpha_1$	$L\alpha_1$	$L\alpha_1$	
66	Dy	$L\beta_1$	$L\alpha_1$	$L\beta_1$	$L\beta_1$	
67	Ho	$L\beta_1$	$L\alpha_1$	$L\beta_1$	$L\alpha_1$	
68	Er	$L\alpha_1$	$L\alpha_1$	$L\beta_1$	$L\alpha_1$	
69	Tm	$L\alpha_1$	$L\alpha_1$		$L\alpha_1$	
70	Yb	$L\alpha_1$	$L\alpha_1$	$L\alpha_1$	$L\alpha_1$	
71	Lu	$L\alpha_1 (L\beta_1)$	$L\alpha_1$		$L\alpha_1$	

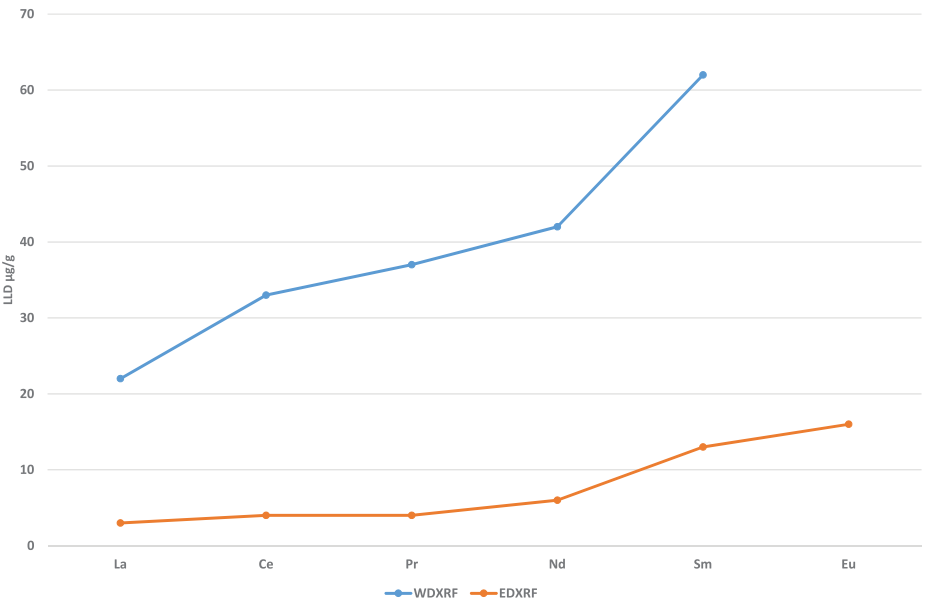


Figure 9.20: LLD of REE measured with $K\alpha_1$ -line (WDXRF: 20s per line in lithiumtetraborate matrix, EDXRF: 600s in cellulose matrix).

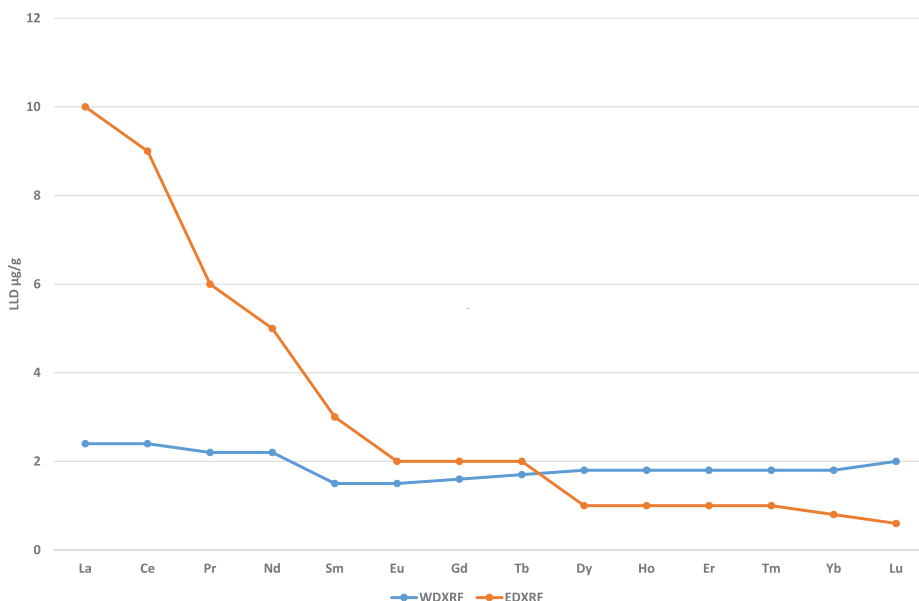


Figure 9.21: LLD of REE measured with La_{α_1} -line (WDXRF: 20s per line, EDXRF: 600s, both in cellulose matrix).

Other calibration strategies mentioned in literature

[16] for the calibration of REE an empirical correction in combination with internal standard elements Cr and Mo.

[22] an overview about the use of an internal standard like Sr for Y, the use of standard addition for REE in rock samples and dried solutions on filters.

[23] for the calibration of REE in coal ash using pressed pellets, an empirical matrix correction using background positions as internal standard.

9.7 Summary

The analysis of REE with X-ray fluorescence analysis remains a challenge. An XRF application of REE requires an extensive and careful development by the analyst. The significance of the final result depends on the choice of the sample preparation method, the measurement conditions, the calibration strategy and the selection of standard materials.

The choice of fusion or pressed pellets will influence the sensitivity. Sample thickness must be in agreement with line selection. The choice of the analyte line

and the corresponding background has to take into account possible line overlaps. Calibration must consider matrix effects and interelement effects.

In literature several examples are given how to use XRF successfully for REE analysis. However there could be always limitations based on particle size effects, line overlaps or poor sensitivity, so that other techniques like for example ICP-MS have to be used instead.

Finally an intense study of the application problem has to prove that XRF could be used successfully to analyse REE in a certain sample type.

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10 Neutron activation analysis of the rare earth elements

Abstract: Neutron activation analysis has been the analytical method of choice for REE analysis at the trace element level from the early 1960ies through the 1980ies. At that time, irradiation facilities were widely available and fairly easily accessible. The development of high-resolution gamma-ray detectors in the mid-1960ies eliminated, for many applications, the need for chemical separation of the REE from the matrix material, making neutron activation analysis a reliable and effective analytical tool. While not as precise as isotope-dilution mass spectrometry, neutron activation analysis was competitive by allowing the analysis of about half of the rare earths (La, Ce, Nd, Sm, Eu, Tb, Yb, Lu). The development of ICP mass spectrometry since the 1980ies, together with decommissioning of research reactors and the lack of installation of new ones in Europe and North America has led to the rapid decline of neutron activation analysis.

10.1 Introduction

The principle of neutron activation analysis (NAA) was proposed by von Hevesy and Levi in 1936 [1, 2], following the detection of the neutron by Chadwick in 1932 [3]. The practical application of NAA had to await the development of neutron-generating devices, in particular the nuclear reactor, after World War II, which made high neutron fluxes ($10^{12} \text{ cm}^{-2} \text{ s}^{-1}$ and above) available for analytical purposes. For more than 20 years, from the mid-1960ies to the late 1980ies, NAA remained the most widely employed method for the analysis of the rare earth elements as well as a number of other elements, present at the trace element level in geological and other materials. Scholarly accounts of the state of NAA towards the end of this period are provided by Potts [4] and, with particular regard to the REE, by Henderson and Pankhurst [5].

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From the early days of NAA, REE studies have focused on geological materials (meteorites, magmatic, metamorphic and sedimentary rocks). Soils, and environmental samples, including water and atmospheric dust, are more recent additions. Archaeological samples, in particular pottery, have also generated some interest. Applications in forensics have followed. Many biological, including medical, studies have employed NAA as an analytical tool but in this field the REE are of little – if any – interest. For a recent literature compilation see Munita et al. [6].

10.2 Principles of neutron activation: Activation equation, cross sections

An atomic nucleus that is hit by a neutron (n) may undergo a variety of nuclear reactions, depending upon the energy of the neutron. At low to intermediate kinetic energies, below about one million electron Volts (MeV), (n,γ) reactions prevail, meaning that the neutron is captured by the nucleus which then emits a γ -ray. Higher kinetic energies of the neutron cause reactions such as (n,p), by which the neutron is captured and a proton p is emitted, or (n,α), which indicates that an α -particle (a helium nucleus) is emitted. As neutrons do not carry an electric charge, they experience no repulsion by an atomic nucleus. For this reason, neutrons with very small kinetic energies can be captured by a nucleus. In fact, “thermal” neutrons are most commonly utilized in NAA. Thermal neutrons carry kinetic energies less than about 0.1 electron volts (eV, $1 \text{ eV} = 1.602 \times 10^{-19} \text{ J}$). Using the relation $E = k_B \times T$, where k_B is Boltzmann’s constant ($8.617 \times 10^{-5} \text{ eV/K}$), we calculate that a temperature of 300 K corresponds to an energy of just 0.026 eV.

If a target, which contains atomic nuclei of kind X , is exposed to a beam of neutrons (or other particles), the number N of nuclei Y , formed by a reaction, can be calculated:

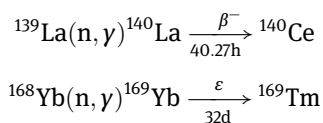
$$\frac{dN_Y}{dt} = \sigma \times \Phi \times N_X \quad (10.1)$$

where dN_Y/dt is the production rate of Y , σ is the cross section (cm^2), Φ is the flux of neutrons ($\text{cm}^{-2}\text{s}^{-1}$), assumed to remain constant across the target, and N_X the number of nuclei X , also assumed to remain essentially constant. The cross section σ indicates the probability of the reaction to occur. It is commonly associated with the apparent cross section of nucleus A for a neutron that approaches the nucleus. The word “barn” has been coined as the unit for the cross section where $1 \text{ barn (b)} = 10^{-24} \text{ cm}^2$; 1 b corresponds approximately to the cross section of the uranium nucleus. For thermal neutrons, σ decreases approximately as a function of $1/v$, where v is the speed of the neutron. The slower the neutron is, the larger is the probability that it is captured by a nucleus. Above the thermal energy range there is the range of epithermal

energies up to about 100 eV. This range is characterized by sharp peaks at well-defined energies that correspond to resonances, the formation of a compound nucleus in discrete excited states. Activation with epithermal neutrons is of advantage for the analysis of elements such as U and Th in biological and geological samples, but not the REE [e.g. [7]].

Neutron capture of an atomic nucleus results in the formation of an isotope of the same element in an excited state. A prompt γ -ray is released immediately and carries away part or all of the excitation energy, depending upon the existence and stability of excitation levels. Prompt γ -ray NAA is one of the methods of neutron activation. It requires the detector to be set up close to the neutron source, e.g. a reactor. It may be the method of choice if only stable isotopes of an element are produced during neutron irradiation or if only radioactive isotopes with very short half-lives are generated. Among the REE, only Sm and Gd can be reasonably well analysed at normal concentrations in rock samples [8]; prompt γ -ray NAA will not further be considered here.

In many cases, Y is a radioactive isotope that decays with its characteristic half-life $t_{1/2}$ into a stable isotope or into another radioactive isotope of a different element. The decay results in the formation of an element with a higher atomic number $Z+1$ by emission of an electron (β^- -decay) or of an element with a lower atomic number $Z-1$, either by the nucleus capturing an orbiting electron or, more rarely, by emission of a positron from the nucleus (β^+ -decay), for example:



where ϵ denotes electron capture, h and d are time in hours, respectively days. Half-life and decay constant λ are related by

$$t_{1/2} = \ln(2)/\lambda \quad (10.2)$$

At least a fraction of the decays by β^- , β^+ or ϵ results in the formation of a nucleus in an excited state. The excitation energy is immediately released by emission of one or more γ -rays with characteristic energies. These γ -rays are registered and evaluated in NAA.

A decay scheme is used to illustrate the decay of a radioactive isotope. This is shown in a simplified form in Figure 10.1 for the decay of ${}^{140}\text{La}$ into stable ${}^{140}\text{Ce}$. Almost all β^- -decays go into excited levels of ${}^{140}\text{Ce}$ which decay through γ -ray emission. The four strongest decays at 328.8 keV (kilo electron Volts), 487.0 keV, 815.8 keV and 1596.6 keV are most suitable for γ -ray counting.

If nuclide Y , produced according to equation (10.1), is radioactive it will start to decay during neutron irradiation and we must subtract its rate of decay

$$-\frac{dN_Y}{dt} = \lambda \times N_Y$$

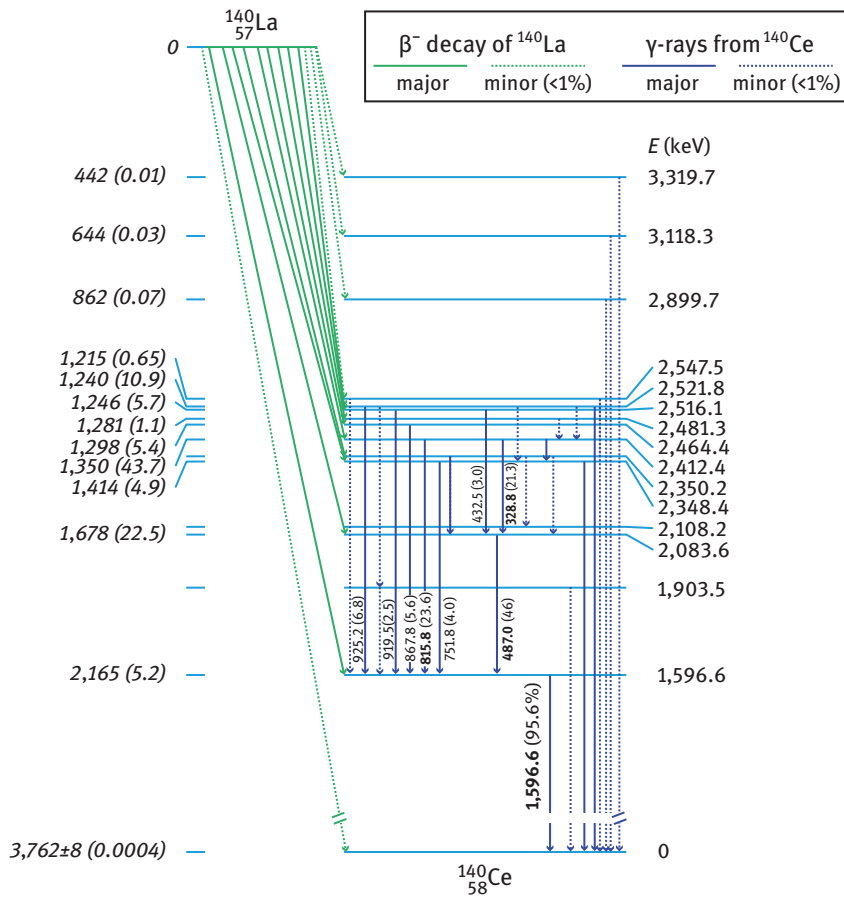


Figure 10.1: Decay of radioactive ^{140}La into stable ^{140}Ce . β^- -decays into various excited states and into the ground state of ^{140}Ce are displayed by green arrows; decay of the various excited states by γ -emission is shown by dark blue arrows. Levels of excited states of ^{140}Ce are shown in light blue. The total decay energy between the ground state of ^{140}La and the ground state of ^{140}Ce amounts to 3762 keV. More than 99% of all β^- -decays end up at excited levels of ^{140}Ce which release their excitation energies through γ -emission. Values in parentheses are γ -ray abundances per 100 β^- -decays. Modified after [49].

from equation (10.1) which gives:

$$\frac{dN_Y}{dt} = \sigma \times \Phi \times N_X - \lambda \times N_Y \quad (10.3)$$

Assuming that N_X remains essentially constant during irradiation and that $N_Y = 0$ at the beginning of irradiation, the integration of this equation provides:

$$N_Y = \frac{\sigma \times \Phi \times N_X}{\lambda} \times (1 - e^{-\lambda \times t}) \quad (10.4)$$

with t being the duration of irradiation and N_Y being the number of radioactive nuclei at the end of irradiation. As NAA counts the number of decays within a defined period of time, it is convenient to replace N_Y by the activity A_Y , where $A = \lambda \times N$. We then obtain

$$A_Y = \sigma \times \Phi \times N_X \times (1 - e^{-\lambda \times t}) \quad (10.5)$$

Typical irradiation times range from seconds to days. For a given nuclide 50 % of the maximum activity is generated after irradiating the sample for one half-life ($t = t_{1/2} = \ln(2)/\lambda$), 90 % are produced after 3.3 half-lives. After the end of irradiation the induced activity decays away as a function of decay time t_d :

$$A_Y = \sigma \times \Phi \times N_X \times (1 - e^{-\lambda \times t}) \times e^{-\lambda \times t_d} \quad (10.6)$$

After a decay time of 7 half-lives less than 1 % of the activity at the end of irradiation is still present; this is an approximate limit where a nuclide can be quantitatively measured with an acceptable precision. In a natural sample such as a piece of rock or pottery, many radioactive nuclides with different half-lives will be produced during irradiation. A nuclide with a short half-life, such as ^{165}Dy (2.35 h) has well reached its saturation activity after an irradiation time of one day whereas a nuclide with a long half-life, such as ^{160}Tb (72.3 d) has achieved only about 1 % at that time. Whereas the activity of ^{165}Dy must be counted within about 12 hours after the end of irradiation, the activity of nuclides with long half-lives is counted much later when all short-lived activities have decayed.

Normally NAA is used as a relative method; this eliminates the need to precisely know the value of the neutron flux Φ (and flux variations) as well as the cross section σ . Instead, single- or multi-element standards are irradiated together with the samples of interest (see section 10.4.2). However, considerable efforts have also been undertaken to develop the single-comparator method where only one element or isotope, in particular ^{197}Au , is required for standardization ([9–11]). Greenberg et al. [12] even argue that NAA, based on the comparator method, fulfils the requirements of being a primary ratio method of measurement as defined by the *Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM)* of the Bureau International des Poids et Mesures, meaning “a primary method of measurement that measures the value of a ratio of an unknown to a standard of the same quantity; its operation must be completely described by a measurement equation”.

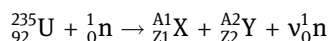
10.3 Equipment

10.3.1 Neutron sources

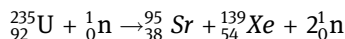
Obviously, NAA depends upon the availability of powerful neutron sources. By far the most important source is the fission reactor. Other sources are accelerators and the bombardment of light nuclei by α - or γ -rays.

10.3.1.1 The fission reactor

Research fission reactors produce neutrons through fission of ^{235}U by using uranium fuel enriched in this isotope. ^{235}U is fissionable by thermal neutrons with a high (n,f) cross section of 586 b (f = fission). Fission of ^{235}U produces two large fragments plus, on average, 2.5 neutrons that are required to entertain a chain reaction. Schematically, the fission reaction can be written as



with X and Y denoting the two fragments with mass A and atomic number Z and ν being the number of neutrons generated per reaction. The two large fragments centre around masses 90 to 100 and 133 to 143, respectively, for example



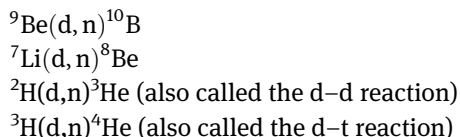
^{95}Sr and ^{139}Xe are both radioactive and undergo several β^- -decays into stable ^{95}Mo and ^{139}La , respectively. In a sample to be analysed, ^{235}U , of course, undergoes the same fission by thermal neutrons. This will lead to the production of light REE and may constitute a major source of error in NAA in particular of Ce and Nd if abundances of uranium exceed those of the light REE ([13] and section 10.4.5).

The neutrons released during fission of ^{235}U are fast neutrons that, on average, carry away a total energy of about 5 MeV. Before they can be absorbed by another ^{235}U nucleus or be utilized for standard NAA, they must be thermalized through elastic collisions with a moderator, i.e. with nuclei of light elements, in particular hydrogen, carbon and oxygen until equilibrium is achieved with the thermal motion of the moderator. Current research reactors reach thermal neutron flux densities between about 10^{12} and $10^{15} \text{ n}\cdot\text{cm}^{-2}\cdot\text{s}^{-1}$.

In 2012 there were about 382 research reactors in operation worldwide [14] with many facing decommissioning within a few years. In Germany, for example, only the research in Mainz is currently (as of mid 2020) in operation whereas some 40 years ago there were about a dozen. It is evident, therefore, that today NAA is of little importance in this country and in many others, as small new neutron generating facilities, in particular neutron generators, are still in the state of development.

10.3.1.2 Accelerators, neutron generators, isotopic neutron sources

Accelerator-generated neutrons have been employed in NAA since the 1970ies. Charged particle accelerators (cyclotron, linear accelerator, Van der Graaf accelerator) can be used to bombard isotopes of light elements with deuterium, causing reactions such as [15]:



(d,n) denotes that the target (isotopes of Be, Li, H) is bombarded with deuterons leading to the formation of a compound nucleus which emits a neutron and decays into isotopes of B, Be and He, respectively.

The last three reactions provide monoenergetic neutrons or nearly so. The d-d and the d-t reactions generate high neutron yields already at low bombarding energies and therefore are particularly useful to manufacture neutron generators with small footprints (in principle, tabletop machines) and thus have been in the focus of research in recent years [14, 16–18]. The d-d fusion reaction currently is capable of producing 10^{10} n/s, using a neutron generator in which a deuterium beam, produced with a radio-frequency generated plasma and 100 to 140 kV of acceleration voltage, is focused on a target, commonly metal hydride [17, 19]. However, the maximum thermal neutron flux at sample position was only $2 \times 10^7 \text{ n} \times \text{cm}^{-2} \times \text{s}^{-1}$, insufficient for trace element analysis. The d-d reaction is being explored for prompt γ -ray NAA as well as for standard NAA. Deuterium (${}^2\text{H}$) has the advantage over tritium (${}^3\text{H}$) to be easily available and stable whereas the latter is radioactive (half-life 12.3 years [a]) and must be manufactured through nuclear reactions. Neutron generators employing the d-d reaction contain no radioactivity and thus are safe when switched off. The d-t reaction produces high-energy neutrons (14.7 MeV). Such fast neutrons may be employed in the determination of light elements like carbon, nitrogen and oxygen through (n,p), (n, α) and (n,2n) reactions; these elements are not well activated by (n, γ) reactions [20].

Isotopic neutron sources have been (and are) of little importance in NAA due to rather low neutron intensities of less than 10^7 n/s [14]. They require an α -emitting radioactive source such as ${}^{241}\text{Am}$ (half-life 432.2 a) or ${}^{226}\text{Ra}$ (1600 y) and a target, in particular Be, to induce (α ,n) reactions, e.g. ${}^9\text{Be}(\alpha, \text{n}){}^{12}\text{C}$. Photon activation using a radioactive source of high-energy γ -rays, in particular ${}^{124}\text{Sb}$ (half-life 60.3 d) is essentially limited to the analysis of Be through the reaction ${}^9\text{Be}(\gamma, \text{n}){}^8\text{Be}$ where the latter instantaneously disintegrates into two ${}^4\text{He}$ atoms. Upon decaying into ${}^{124}\text{Te}$, ${}^{124}\text{Sb}$ emits a γ -ray of energy 1.69 MeV which is just barely energetic enough to induce the (γ ,n) reaction on ${}^9\text{Be}$ which requires a threshold energy of 1.67 MeV. Almost all other (γ ,n) reactions have threshold energies in excess of 8 MeV [15]. Photons exceeding this energy are produced as bremsstrahlung by firing a high-energy electron beam from an accelerator on a target metal. In this way, some REE

can be analysed by photon activation in geological and biological materials if present at concentration levels of tens of ppm [21, 21].

10.3.2 The counting system

A NAA counting system consists of a detector and the pulse-processing electronics. The latter comprises preamplifier, main amplifier, a multichannel analyser that includes an analogue-to-digital converter and an output device (computer) (Figure 10.2) [4]. The amplifiers are required to amplify the small signal registered in the detector and to achieve a high signal-to-noise ratio. The multichannel analyser sorts and stores the incoming signals as a function of γ -ray energy. Evaluation of the spectra (calculation of photopeak areas) is carried out by dedicated software on a computer.

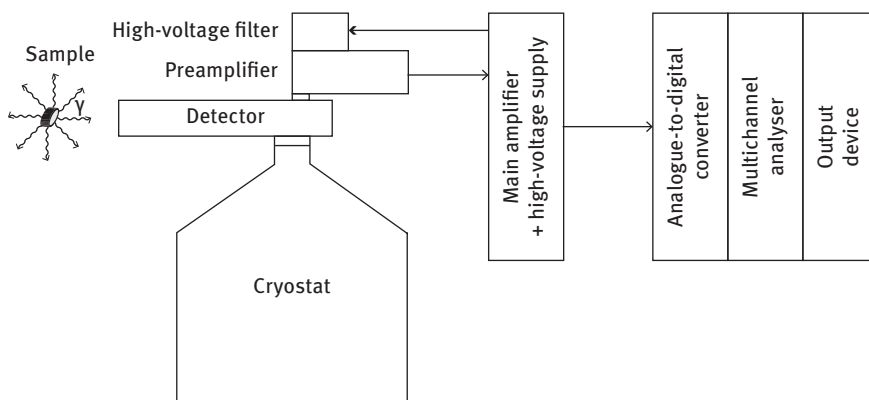


Figure 10.2: Schematic sketch of an NAA counting system (modified after [4]).

10.3.2.1 Detectors

During the early years of NAA the most suitable detector was a scintillation detector, commonly a big transparent single crystal (or polycrystalline material) of NaI doped with Tl as an activator (order of 0.1 mole-%), connected to a photocathode and a photomultiplier. The energy of γ -rays entering such a crystal is absorbed and transferred to electrons which are caught by the activator. A tiny flash of light is then emitted during transition from the excited to the ground state. The light is converted to an electric signal by the photocathode and the signal is amplified by a photomultiplier. The advantage of the Tl-doped NaI detector is that the crystals are fairly easy to grow from the melt to large sizes [22]. Sizes of 3 inch (diameter) by 3 inch (height) were the standard in the 1960ies. They were able to register a large fraction of the incoming γ -rays. In contrast to semiconducting diodes they also can be operated at ambient temperatures.

The main disadvantage of the Tl-doped NaI detector is its poor energy resolution. NAA of the REE in geological materials at that time required the chemical separation of each rare earth element using time-consuming ion-exchange techniques [23]. NaI scintillation detectors are still used when it is important to detect as large a fraction of the incoming γ -rays as possible, for example in nuclear medicine or environmental sciences.

The high-resolution Ge semiconductors that are used today were developed in the early 1960ies [24, 25]. Ge has a higher atomic number than Si that is used as detector material in X-ray fluorescence and therefore Ge is much better suited to stop the high-energy γ -rays. Moreover, to create an electron–hole pair requires only an energy of 2.95 eV at the operating temperature of about 80 K (3.72 eV in Si at the same temperature). Absorption of a 1 MeV γ -ray will then create about 3.4×10^5 electrons equivalent to a charge of 5.7×10^{-14} coulombs [4]. Until the 1980ies the process of growing germanium left unacceptably high levels of impurity inside the crystal which acted as p-type (“positive holes” in the valence band, due, for example to atoms with three valence electrons instead of the four in germanium, causing the formation of acceptor levels in the forbidden energy region between valence band and conduction band) or n-type semiconductors (negative charges, for example by atoms with five valence atoms, forming donor levels). Such impurities cause conduction of the germanium under an electrostatic field even in the absence of ionizing radiation. In order to compensate for this effect, Li which enters interstitial sites in the Ge, was diffused into a cylinder of p-type Ge, leaving only the central part of the cylinder as a p-type semiconductor [4]. These crystals were thus called coaxial Ge(Li) detectors. As lithium diffuses fairly rapidly through germanium at room temperature, these crystals had always to be cooled to the temperature of liquid nitrogen, even if not in use. High-purity Ge became gradually available during the 1970ies, initially as small crystals only, eliminating the need of Li drifting. These crystals were first used to manufacture “planar” (disk-shaped) Ge detectors with a volume typically less than 10^0 cm^3 and an active area of 0.1 mm^2 that were employed in the detection of low-energy γ -rays ($\approx 60\text{--}250 \text{ keV}$). The maximum volume of high-purity Ge detectors has increased about linearly from the mid-1970ies (less than 100 cm^3) to about 800 cm^3 in 2003 [26], thus permitting the fabrication of detectors for any need.

The quality of a detector is judged by its efficiency to detect a signal as well as its resolution. The absolute efficiency is the fraction of γ -rays emitted from a sample that cause an event in the detector. This parameter is strongly dependent upon the geometry, in particular the distance between sample and detector, as the sample will emit photons isotropically in all directions (Figure 10.2). More important is the relative efficiency which permits a comparison to be made between different detectors. Relative efficiency is the relative photopeak efficiency (total absorption of a γ -ray in the crystal by the photoelectric effect, see below) of a detector compared to that of a 3 inch $\times$ 3 inch NaI(Tl) detector at an energy of 1333 keV (^{60}Co) and a distance of 25 cm between source and detector [27]. Obviously relative efficiency

increases with the volume of the detector and values of more than 100 % are nowadays reached for high-purity Ge detectors. The efficiency decreases with γ -energy, above about 300 keV approximately proportional to $E^{-0.5}$. A large Ge(Li) or Ge detector possesses a maximum efficiency at about 100 keV and it decreases by about one order of magnitude at 1333 keV. A planar Ge detector has a maximum efficiency below about 50 keV and it is lower by about one order of magnitude at 200 keV.

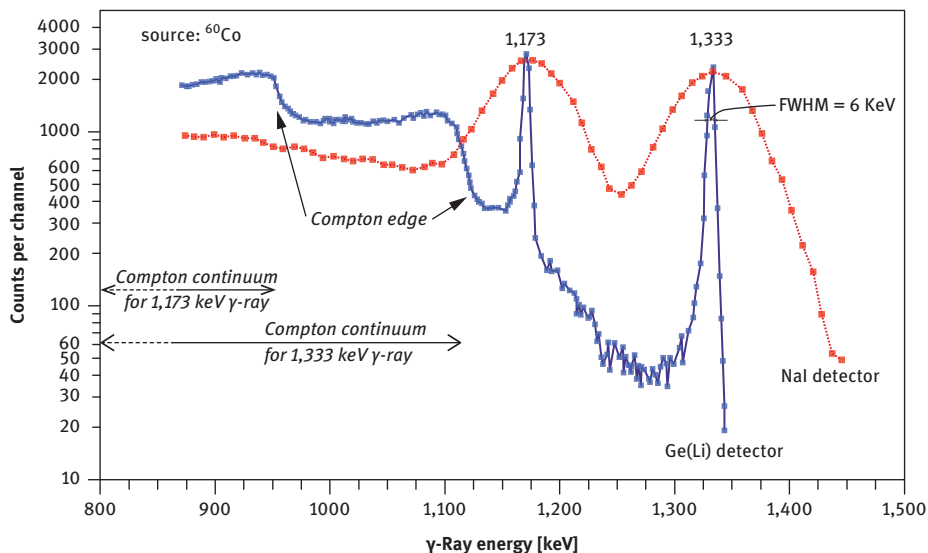


Figure 10.3: The high-energy part of a γ -ray spectrum of ^{60}Co showing the superior energy resolution of a Li-drift Ge detector over a Tl-doped NaI scintillation detector [24]; $\text{keV} = 1000 \text{ eV}$. The resolution of the Ge(Li) detector is shown for the 1333 keV γ -ray (FWHM = full width at half maximum).

The resolution of a detector is reported as full width at half maximum (FWHM), that is the width of a peak at half its maximum intensity. For coaxial Ge(Li) and big high-purity Ge detectors resolution is usually specified for the 1333 keV line of ^{60}Co (see Figure 10.3), either as an absolute value in keV or as a relative one ($100 \times \text{FWHM}$ divided by the energy of the γ -peak). For planar Ge detectors resolution is reported for the 122.1 keV γ -peak of ^{57}Co or the 121.8 keV peak of ^{152}Eu . In the former case, resolution is about 2 keV absolute or 0.15 % relative, 20 to 30 times better than the resolution of a NaI(Tl) detector, in the latter case it may be about 0.55 keV absolute or 0.45 % relative. As high-energy γ -rays are much less likely to be absorbed in a planar Ge detector than in a high-volume Ge detector, the Compton background (see next section) is much diminished which makes the planar detector the detector of choice for registering γ -rays with energies below $\approx 150 \text{ keV}$.

10.3.2.2 Interaction of electromagnetic radiation with matter

The absorption of X-rays or γ -rays by matter follows an exponential relation

$$I = I_0 \times \exp(-\mu \times d) \quad (10.7)$$

where I_0 is the initial intensity of the photon beam, I is the remaining intensity after having travelled distance d (cm) through matter and μ (cm^{-1}) is the absorption coefficient. The latter is the sum of three terms, the photoelectric effect, the Compton effect and the pair-production effect.

In the *photoelectric effect* the entire energy of the photon is transferred to an orbital electron, in about 80 % of cases to a K electron and in 20 % to an L electron [15]. The energy of the electron corresponds to the energy of the photon minus the binding energy of the electron. Instantaneously an electron from the next higher shell fills the gap, thus emitting a characteristic X-ray. The energies of the photoelectron and the X-ray are absorbed by ionization of detector atoms. The photoelectric effect is most important for atoms with high atomic number (approximately proportional to Z^4) and low photon energies (roughly proportional to E^{-3}). It is essentially these photons that are of interest in NAA as this effect produces the sharp photopeaks.

The *Compton effect* is the result of elastic scattering between a photon and an electron, most likely an outer orbital one, of the interacting atom. Only part of the energy of the photon is transferred to the electron, thereby reducing the energy of the photon that is deflected at an angle θ relative to its incident direction. The energy of the scattered photon is dependent upon θ [15]:

$$E_\gamma = \frac{E_0}{1 + \frac{E_0}{m_0 \times c^2} \times (1 - \cos \theta)} \quad (10.8)$$

where E_γ is the energy of the photon after collision, E_0 is the energy of the photon prior to collision and $m_0 \times c^2$ is the rest mass of the electron ($9.109 \times 10^{-31} \text{ kg} \times 299792458^2 \text{ m}^2/\text{s}^2 = 8.187 \times 10^{-14} \text{ J}$ or 511 keV as $1 \text{ eV} = 1.602 \times 10^{-19} \text{ J}$). E_γ attains its maximum for $\theta = 0^\circ$ ($E_\gamma = E_0$) and its minimum value for $\theta = 180^\circ$ ($E_0/[1 + 2E_0/(m_0 \times c^2)]$). For $\theta = 180^\circ$ the maximum energy of the Compton electron

$$E_{e-\max} = E_0 - E_{\gamma-\min}$$

will then be:

$$E_{e-\max} = \frac{E_0}{1 + \frac{m_0 \times c^2}{2E_0}} \quad (10.9)$$

As E_γ may vary continuously between its minimum and maximum values, so may the energy of the Compton electron E_e between the value calculated from eq. 9) and zero. The scattered photon can undergo further Compton interactions, be totally absorbed by the photoelectric effect or escape from the detector. If only the energy of the scattered electron is absorbed in the detector whereas the scattered photon escapes, it contributes to the Compton continuum, a region with an undesired high background in a γ -spectrum. For the 1333 keV γ -ray of ^{60}Co , eq. 9 provides a value of 1119 keV; this is called the Compton edge (see Figure 10.3). Similarly, the 1173 keV line of ^{60}Co produces a Compton edge at 949 keV and a Compton continuum below that value. γ -ray absorption due to the Compton effect dominates μ at intermediate energies and also decreases with energy, but less steeply so than the photoelectric effect.

At very high energies of the γ -rays the *pair production effect* begins to dominate μ , for Ge in excess of about 10 MeV. Such a photon can interact with the strong electromagnetic field of an absorber nucleus to produce an electron–positron pair. The minimum energy of the photon that can give rise to pair production equals the rest masses of electron plus positron (511 keV each = 1022 keV). Excess energies of the incident photon will be shared as kinetic energy by electron and positron. After the positron has lost its kinetic energy, it annihilates by reaction with another electron, generating two 511 keV γ -rays that may subsequently be absorbed through the photoelectric effect or the Compton effect.

10.4 Practical considerations

10.4.1 Instrumental versus radiochemical NAA

Two types of NAA are commonly distinguished, instrumental NAA (INAA) and radiochemical NAA (RNAA). In INAA γ -ray counting is carried out after neutron irradiation without further manipulation of the sample, except, maybe, of re-packaging. As NAA is a true multi-element method, for a rock like basalt INAA typically permits the analysis of about 15 to 20 elements (Na, Sc, Cr, Mn, Fe, Co, Sb, Cs, La, Ce, Nd, Sm, Eu, Tb, Yb, Lu, Hf, Ta, Th, U), depending upon their concentration. Even up to 30 elements may be analysed by using a low-background technique [28].

In RNAA the sample is chemically treated after irradiation in order to separate the element(s) of interest from the matrix prior to counting of the photopeaks. This, of course, requires access to a laboratory where radiochemistry can be carried out. Apart from taking time, this generates additional radioactive waste, in particular in liquid form. All naturally occurring REE from La to Lu are, in principle, accessible to RNAA.

In geochemistry Sc and Y are not normally considered when plotting REE abundances. Y is not accessible to NAA as ^{90}Y , produced from the only stable isotope ^{89}Y with a high cross-section of 100 b, does not emit γ -rays of significant abundance. In most cases, the abundance of Y can well be inferred from Ho (average Y/Ho in rocks is 29). Exceptions are highly evolved magmatic systems rich in H_2O and halogens and aqueous solutions [29]. In contrast, Sc differs significantly from the lanthanides in its geochemical behaviour.

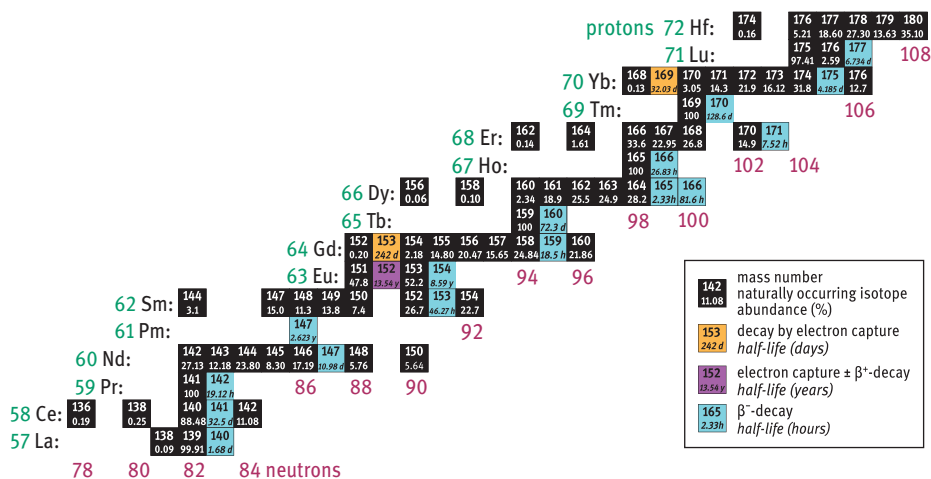


Figure 10.4: Excerpt from the chart of the nuclides [32] showing naturally occurring isotopes of the REE and Hf in black and radioactive ones employed in NAA in various colours. Small fractions (<5 %) of ^{142}Pr , ^{154}Eu and ^{170}Tm also decay by electron capture to ^{142}Ce , ^{154}Sm and ^{170}Er , respectively. Whereas La, Ce, Nd, Sm, Eu, Tb, Yb and Lu can commonly be analysed by INAA in geological samples, the analysis of Pr and Er always requires RNAA. (see also Table 10.1). Numbers attached to arrows (both in grey) at masses 140, 141, 142, and 147 are yields (in %) for the fission of ^{235}U with thermal neutrons (see section 10.4.5). Among the naturally occurring REE nuclides, some are very weakly radioactive and form the basis of decay systems that are used in geochronology and isotope geochemistry: ^{147}Sm decays, with a half-life of 106×10^9 years, by α -emission into ^{143}Nd [50]. ^{176}Lu decays by β^- -emission into ^{176}Hf (half-life 37.2×10^9 years [51]). ^{138}La undergoes a branched decay, by electron capture into ^{138}Ba and by β^- -emission into ^{138}Ce ; only the latter is of some importance (partial decay constant $\lambda_{\beta} \approx 2.37 \times 10^{-12} \text{ a}^{-1}$, [52]).

Figure 10.4 shows the naturally occurring nuclides from La to Lu (+ Hf) together with those employed in NAA. Table 10.1 provides additional information on cross sections for neutron absorption and γ -lines that can be evaluated for analysis (analytical photopeak data from [30, 31]; other data from [32] and from [33]). In natural rocks where the light REE (La – Nd) are present at the 10^0 to 10^1 ppm level and the heavy REE (Ho – Lu) at the 10^0 ppm level, the elements La, Ce, Nd, Sm, Eu, Tb, Yb and Lu can normally be analysed by INAA whereas Pr and Er can only be measured after REE separation from the matrix activity. Due to the short half-life of ^{165}Dy (2.35 h),

Table 10.1: Information on isotopes, reaction cross-sections and analytical photopeaks for the REE, Y, and some elements that are commonly analysed by INAA.

Isotope mass number	nat. abundance (atom-%)	activation cross section [b]	product isotope	half-life [#]	analytical photopeaks [keV]*	decay product (s)	method	irradiation time [#]	comment
La 139	99.91	9	¹⁴⁰ La	40.2724 h	328.75 (21.3), 487.03 (45.7), 815.8 (23.6), 1596.2 (96.0)	¹⁴⁰ Ce	INAA, RNAA	short, long	
Ce 140	88.48	0.58	¹⁴¹ Ce	32.5 d	145.45 (49.3)	¹⁴¹ Pr	INAA, RNAA	long	
Pr 141	100	11.5	¹⁴² Pr	19.12 h	1575.9 (3.7)	¹⁴² Nd	RNAA	long	4 b for formation of metastable ¹⁴² Pr which decays into ground state with half-life of 14.6 minutes; 7.5 b for formation of ¹⁴² Pr in ground state
Nd 146	17.19	1.4	¹⁴⁷ Nd	10.98 d	91.10 (28.3), 531.0 (13.5)	¹⁴⁷ Pm → ¹⁴⁷ Sm	INAA, RNAA	long	
Sm 152	26.7	206	¹⁵³ Sm	46.284 h	103.18 (28.2)	¹⁵³ Eu	INAA, RNAA	short, long	
Eu 151	47.8	3150	^{152m} Eu	9.31 h	121.78 (9.0), 841.6 (13.0), 963.5 (12.0)	¹⁵² Gd (72 %), ¹⁵² Sm (28 %)	INAA, RNAA	short	^{152m} Eu is a metastable state of ¹⁵² Eu
151	47.8	6000	¹⁵² Eu	13.537 a	121.78 (33.2), 344.27 (31.4), 778.85 (15.2), 964.0 (17.3), 1407.92 (24.3)	¹⁵² Gd (27.9 %), ¹⁵² Sm (72.1 %)	INAA, RNAA	long	

Gd	152	0.20	900	¹⁵³ Gd	240.4 d	97.50 (30.0), 103.20 (22.5)	¹⁵³ Eu	RNAA, rarely INAA	long	1700 b for formation of metastable ^{165m} Dy which decays into the ground state with a half-life of 1.3 minutes; 1000 b for formation of ¹⁶⁵ Dy 2000 b for neutron capture of ^{165m} Dy, 3500 b for neutron capture of ¹⁶⁵ Dy in the ground state
Tb	159	100	23.1	¹⁶⁰ Tb	72.3 d	86.79 (20.9), 298.54 (35.0)	¹⁶⁰ Dy	INAA, RNAA	long	
Dy	164	28.2	2700	¹⁶⁵ Dy	2.334 h	94.60 (4.0)	¹⁶⁵ Ho	RNAA, rarely INAA	short	
	165	0	5500	¹⁶⁶ Dy	81.6 h	82.45 (12.0)	¹⁶⁶ Ho	RNAA	long	
Ho	165	100	61	¹⁶⁶ Ho	26.83 h	80.60 (5.4)	¹⁶⁶ Er	RNAA, rarely INAA	short, long	
Er	170	14.9	6	¹⁷¹ Er	7.516 h	111.60 (25.0), 124.03 (11.0), 295.90 (28.0), 308.30 (63.0)	¹⁷¹ Tm → ¹⁷¹ Yb	RNAA	long, short	
Tm	169	100	105	¹⁷⁰ Tm	128.6 d	84.26 (10.0)	¹⁷⁰ Yb	RNAA, rarely INAA	long	

(continued)

Table 10.1 (continued)

Isotope mass number	nat. abundance (atom-%)	activation cross section [b]	product isotope	half-life [#]	analytical photopeaks [keV]*	decay product (s)	method	irradiation time [#]	comment
Yb 168	0.13	2400	¹⁶⁹ Yb	32.026 d	63.50 (45.0), 110.00 (18.0), 130.70 (11.0), 177.00 (22.0), 197.80 (40.0), 307.50 (10.0)	¹⁶⁹ Tm	INAA, RNAA	long	
174	31.8	100	¹⁷⁵ Yb	4.185 d	113.50 (1.9), 282.60 (3.7), 396.10 (6.0)	¹⁷⁵ Lu	INAA, RNAA	long, short	
Lu 176	2.59	1780	¹⁷⁷ Lu	6.734 d	112.96 (6.5), 208.34 (11.0)	¹⁷⁷ Hf	INAA, RNAA	long, short	
Y 89	100	1.25	⁹⁰ Y	64 h	1760.7 (0.02)	⁹⁰ Zr	(RNAA)		no useful γ-rays; requires β ⁻ counting
Na 23	100	0.53	²⁴ Na	14.959 h	1368.6 (100), 2754.1 (98.85)	²⁴ Mg	INAA	short, long	
Sc 45	100	27	⁴⁶ Sc	83.79 d	889.3 (100), 1120.5 (100)	⁴⁶ Ti	INAA	long	
Cr 50	4.345	16	⁵¹ Cr	27.7 d	320.1 (9.8)	⁵¹ V	INAA	long	
Mn 55	100	13.3	⁵⁶ Mn	2.5785 h	846.6 (99.0), 1811.2 (30.0), 2112.6 (15.5)	⁵⁶ Fe	INAA	short	
Fe 58	0.28	1.3	⁵⁹ Fe	44.503 d	142.54 (0.81), 192.23 (2.80), 1099.27 (56.0), 1291.58 (44.0)	⁵⁹ Co	INAA	long	
Co 59	100	37.2	⁶⁰ Co	5.2714 a	1173.23 (99.88), 1332.52 (100)	⁶⁰ Ni	INAA	long	

Sb	123	42.64	4.06	^{124}Sb	60.2 d	602.71 (98.1), 722.78 (10.8), 1691.04 (50.0)	^{124}Te	INAA	long	
Cs	133	100	29	^{134}Cs	2.0648 a	569.33 (15.8), 604.7 (98.0), 795.79 (89.0)	^{134}Ba	INAA	long	
Hf	180	35.1	13	^{181}Hf	42.39 d	133.05 (41.0), 136.25 (6.9), 345.95 (12.0), 482.16 (83.0)	^{181}Ta	INAA	long	
Ta	181	99.988	20	^{182}Ta	114.43 5	100.10 (11.9), 152.44 (7.1), 222.11 (7.98), 1121.19 (37.0), 1188.95 (17.1), 1221.31 (28.9), 1230.93 (12.1)	^{182}W	INAA	long	
Th	232	100	7.37	^{233}Pa	26.967 d	98.44 (13.5), 111.0 (4.85), 300.11 (6.6), 311.9 (38.0), 340.47 (4.43)	^{233}U	INAA	long	^{233}Th decays with a half-life of 22.3 m to ^{233}Pa which has a half-life of 27.0 d
U	238	99.2745	2.7	^{239}Np	2.3565 d	99.5 (11.0), 103.7 (18.0), 106.13 (21.06), 117.7 (6.3), 228.19 (9.5), 277.6 (12.1)	^{239}Pu	INAA	long, short	^{239}U decays with a half-life of 23.5 m to ^{239}Np which has a half-life of 2.356 d
										# short: minutes, long: hours to days
										#h hours, d days, a years
										*bold face: preferred γ -line for analysis if two or more lines can be used; values in parentheses: relative intensities (in %)

Dy can only be measured after a separate short (few minutes) irradiation and immediate transfer of the activated samples from the reactor to the laboratory for γ -ray counting which must be finished within about five half-lives when the induced activity has decayed to about 3 % of the value at the end of irradiation. This short irradiation is also beneficial for the determination of ^{166}Ho the signal of which is severely enhanced by second-order activation of ^{164}Dy in irradiations of long duration (section 10.4.5).

10.4.2 Samples and standards

Samples and standards are commonly irradiated as solids but liquids and even gases can also be used if care is taken to avoid leakage during and after neutron irradiation. Sealed SiO_2 glass tubes or ampoules are particularly suited as containers for liquids and gases. Biological samples may be freeze-dried prior to irradiation. Geological samples, if necessary, can simply be dried in an oven to remove moisture. During neutron irradiation prompt γ -rays are emitted by the sample due to neutron absorption and scattering; in addition, decay of the formed radioactive isotopes releases radiation. Partial absorption of this radiation by the sample produces heat. This causes radiolytic decomposition of H_2O and biological materials during long irradiations (hours and more, depending upon the neutron flux) and a build-up of pressure in the sample containers; organic material may even carbonize [15].

Geological samples will normally be present as finely ground powders but irradiation of rock chips or single mineral grains is also acceptable, provided that they are representative of the bulk samples. It is useful to have a broad idea on the range of REE concentrations to be expected in order to adjust the quantity of sample for irradiation. Quantities between less than 1 milligram and a few grams are used with the most typical quantities being on the order of 100 mg. Pulverized samples can be put into aluminium or SiO_2 glass containers and sealed; coarse grains or chips can be simply wrapped in Al foil. For short irradiations or irradiation in reactors with low neutron fluxes polyethylene foil or vials may also be used. In high-flux reactors polyethylene foil becomes brittle within minutes. In addition, in the manufacturing process compounds of antimony are employed as catalysers (for example, [34]) that are a source of high-energy γ -rays from the decay of ^{124}Sb and, consequently, cause an appreciable Compton background during counting. SiO_2 tubes and Al foil are available at very high purity, eliminating the need to transfer the irradiated samples to inactive containers before γ -ray counting. Safely encapsulating powder in Al foil, however, is difficult and thus not advisable. If low-purity Al containers are used, the samples must be transferred to inactive containers prior to γ -ray counting.

Although equation (10.6) can be solved for N_x , the number of atomic nuclei of interest, thus making NAA an absolute analytical method, this equation is not practical

to employ. Firstly, the absolute value of the activity A_Y cannot be easily derived and depends upon the counting geometry (mainly the distance between sample and detector) and the efficiency of the detector. Secondly and more importantly, the neutron flux Φ is not precisely known and may fluctuate. Major- and minor-element isotopes of geological and biological samples (H, C, N, O, Na, Mg, Al, Si, P, S, Ca, Ti, Fe) have small cross sections for neutron absorption (less than a few barns). Therefore, it can be safely assumed that the neutron flux remains constant across a set of samples during irradiation. The neutron flux, however, varies as a function of distance in the core region of a reactor. Whereas flux variations across samples are small in the core of a large graphite-moderated reactor ($\leq 0.5\%$ /cm), they may reach 10% /cm in the core of a small water-moderated reactor [15]. These uncertainties are eliminated by the irradiation of two or more sets of standards and, sometimes, flux monitors together with the samples. The single-comparator method, not further considered here, requires precise knowledge of γ -ray intensities, isotopic abundances and thermal neutron cross sections from which a “ k_0 -factor” can be calculated [35, 36, 12].

The flux monitor may be a thin rod or wire of a metal such as Fe, Co or Au. Short wires (few centimetres) may be wrapped around each sample in order to precisely record the neutron dose (flux $\times$ time) at the position of the sample. Thin metal sheets may be placed inside aluminium cans, large containers used for irradiation, in between individual samples or layers of samples [4]. Flux monitors are recommended if samples are to be irradiated in small research reactors and accelerators and/or if the highest possible analytical precision is to be achieved.

Standards can be prepared from commercially available multi-element or single element standard solutions for ICP-MS analysis. They may, of course, also be prepared by dissolving metals or compounds. If oxides are used, care has to be employed with regard to their exact stoichiometry. Terbium, for example, forms a stable oxide Tb_4O_7 instead of the normal REE_2O_3 composition. If stock solutions must be diluted, this should be done shortly before use in order to minimize loss of elements by adsorption to the walls of polyethylene or PTFE containers. Appropriate quantities of the solutions may be pipetted on small sheets of high-purity Al foil or into SiO_2 glass containers and dried. Quantities varying between a few micrograms (Sm, Eu, Lu) and about 100 micrograms (Gd) are considered reasonable. This is at least one order of magnitude more than present in most geological samples. When combining several elements in preparing standards, interferences of γ -lines must be avoided. For example, uranium concentrations in geological samples can often be obtained through the decay of ^{239}Np ($^{238}U(n, \gamma)^{239}U \xrightarrow{23.5\text{ m}} ^{239}Np \xrightarrow{2.35\text{ d}} ^{239}Pu$), which has a half-life only slightly larger than ^{153}Sm and has a fairly intense photopeak at 103.70 keV that cannot be resolved from the 103.18 keV photopeak of ^{153}Sm . Moreover, neutron absorption by ^{235}U causes fission, producing nuclides in the mass range of the light REE with high yields. Gd and Ho are subject to interference by second-order reactions of Eu and Dy; pure standards of Eu and Dy are required to correct for these interferences (section 10.4.5).

International reference standards should also be included in a set of samples in order to estimate the accuracy of the concentration data. As REE (and other trace element concentrations) are vastly different in different types of geological materials, it is advisable to select a standard similar in composition to the samples, for example a standard granite for the analysis of granites or a standard ultramafic rock for the analysis of peridotites. These rocks will have REE concentrations that typically differ by more than two orders of magnitude.

For the purpose of neutron irradiation in a reactor, the samples are packed into an aluminium can which may have a diameter of 1.5 to 3 cm and a length of ≈ 10 cm. 10–40 samples fit into such a can, each ≈ 100 mg sample sealed in SiO_2 glass or an aluminium container. In order to correct for neutron flux gradients, the position of each sample and standard inside the can must be known. As the induced activity A_γ is a linear function of the neutron flux (equation (10.6)) and as the irradiation time is the same for all samples and all standards, two sets of element standards, one set placed at the bottom and the other at the top of the irradiation can, are sufficient to correct for neutron flux variations by linear interpolation. More sets of standards or flux monitors, of course, will improve the flux correction at the cost of additional time for γ -ray counting. In large research reactors the variation in neutron flux between top and bottom of an aluminium can with a length of 10 cm will typically be on the order of 10 % only.

10.4.3 Counting strategies

Before irradiating the samples, the subsequent counting strategies should be considered and irradiation parameters adjusted:

If concentrations for all REE are desired, radiochemical separation is indispensable. In this case, each sample is split in two portions. One split should be irradiated for a short time (on the order of ten minutes) and immediately (after a delay of no more than one hour) be transferred to the radiochemistry laboratory. This split serves for γ -ray counting of ^{165}Dy and ^{166}Ho , and possibly ^{171}Er , $^{152\text{m}}\text{Eu}$, ^{140}La and ^{153}Sm . The second split should be irradiated for at least several hours up to about one week, depending upon the expected REE concentrations. After a delay of one to two days (“cooling time”) these samples are transferred to the laboratory for performing radiochemical separation of the REE and subsequent counting. The most critical isotope to be measured is ^{171}Er ($t_{1/2} = 7.52$ h); for its detection, not much more than one day ($\approx$ three half-lives) should be allowed to pass between the end of irradiation and γ -ray counting, together with isotopes having half-lives less than about one week (^{142}Pr , ^{166}Ho , ^{140}La , ^{153}Sm , ^{175}Yb , ^{177}Lu). Two to four weeks later, after the short-lived activities have decayed, the longer-lived nuclides can be measured, i.e. ^{147}Nd , ^{141}Ce , (^{177}Lu), ^{169}Yb , ^{160}Tb , ^{170}Tm , ^{153}Gd , and ^{152}Eu . ^{142}Pr and ^{140}La have no low-energy γ -lines; for their detection, a large-volume $\text{Ge}(\text{Li})$ or Ge detector

must be used. All other REE nuclides listed in Table 10.1 can, in principle, be analysed using a planar Ge detector. In the energy range below ≈ 150 keV the planar detector is the preferred one due to its lower Compton background and better resolution.

If no radiochemistry laboratory is accessible or if other elements, in addition to the REE are to be measured, then INAA is the method of choice. In this case the short irradiation is of little benefit as ^{56}Mn and, in favourable cases ^{165}Dy , are the only nuclides that cannot be detected in geological samples after the long irradiation.

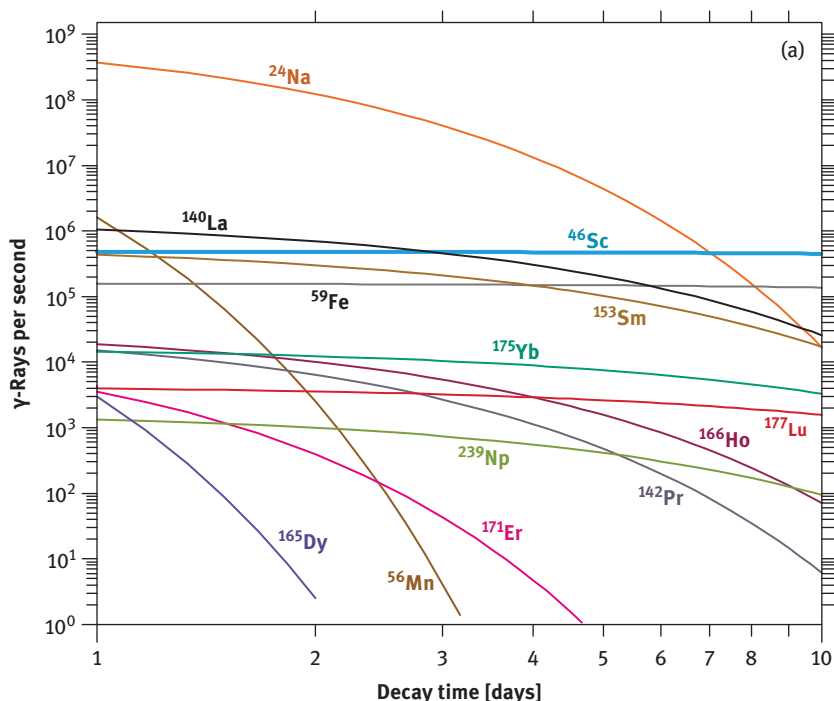


Figure 10.5: γ -activities of a number of nuclides as a function of cooling time for the international standard rock basalt BCR-1 released by the US Geological Survey. For each nuclide only the activity of the main γ -ray, displayed in boldface in Table 10.1, has been calculated as $A = \lambda \times N \times \text{relative intensity}$ (where more than one γ -line is highlighted, the one with the higher intensity was used, except for ^{239}Np (277.6 keV)). The energy-dependent efficiency of the detectors has not been considered. Calculations were performed for a thermal neutron flux of $5 \times 10^{13} \text{ cm}^{-2} \text{ s}^{-1}$ and an irradiation time of 24 h. Recommended concentrations in BCR-1 are: Na 2.43, Sc 32.8, Mn 1410, Fe 9.41, Co 36.3, La 25.0, Ce 53.7, Pr 6.9, Nd 28.7, Sm 6.58, Eu 1.96, Gd 6.68, Tb 1.05, Dy 6.35, Ho 1.11, Er 3.61, Tm 0.59, Yb 3.39, Lu 0.512, Hf 4.90, Ta 0.79, Th 6.04, U 1.71 (all values in ppm, except Na and Fe in %) [48]. Although many of these activities are high, be aware that only a small fraction of the γ -rays are registered by the detector. In INAA the activity is dominated by ^{24}Na during the first week after irradiation. Afterwards, ^{46}Sc , ^{59}Fe and ^{60}Co are the main contributors. All these nuclides release high-energy γ -rays during decay, thus causing a high Compton background, in particular in the large-volume Ge detector.

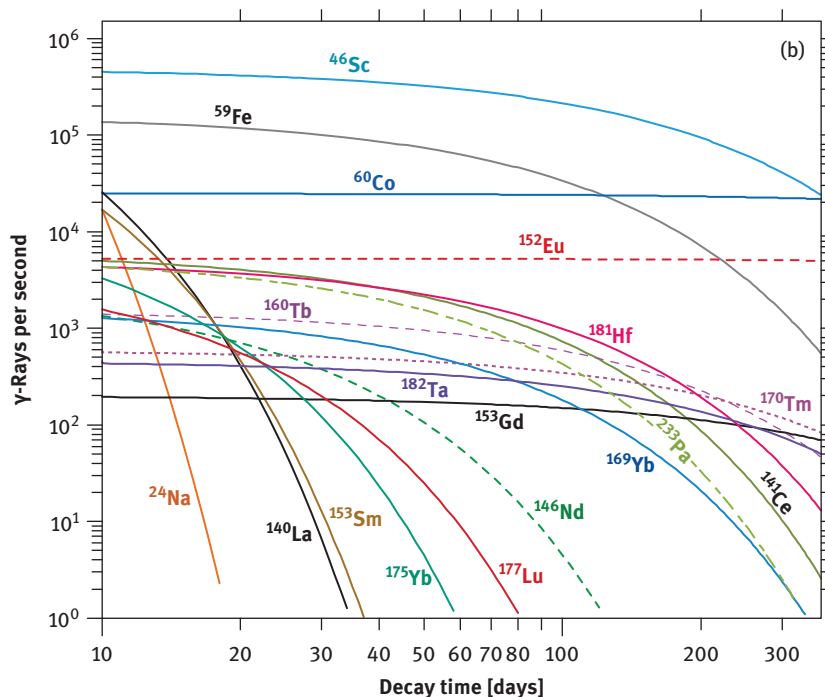


Figure 10.5 (continued)

tion. The long (hours to days) irradiation requires a cooling time of about two days or more before the first series of γ -ray counting can be started, targeting at ^{140}La , ^{153}Sm , ^{175}Yb , ^{177}Lu , ^{24}Na , and ^{239}Np . At that time ^{24}Na may still constitute the main activity in many geological and biological samples (Figure 10.5a); its high-energy γ -rays contribute highly to the Compton background. The second γ -ray counting may take place about three to five weeks after the end of irradiation. At this time, the short-lived nuclides have decayed to negligible values and the Compton background of geological samples is now determined by ^{59}Fe and ^{46}Sc and, maybe, ^{60}Co (Figure 10.6b). Among the REE, ^{141}Ce , ^{147}Nd , ^{152}Eu , ^{160}Tb and ^{169}Yb can now be expected to be detectable as shown in Figure 10.6b–c for the case of a volcanic rock.

As the behaviour of the REE in nature is predictable and mainly a function of the differences in ionic radii and, in the case of Ce and Eu, of oxygen fugacity, the REE patterns of rocks and minerals can commonly be constructed from the elements accessible by INAA. Under reducing conditions a portion of the Eu will be divalent, giving rise to Eu behaving differently from Sm or Gd, visible as a Eu anomaly in many rocks. The magnitude of this anomaly can only be interpolated between Sm and Tb as Gd cannot be measured precisely by INAA. Moreover, the ^{153}Gd photopeak at 97.5 keV is interfered by the 98.44 keV photopeak of ^{233}Pa (from the decay

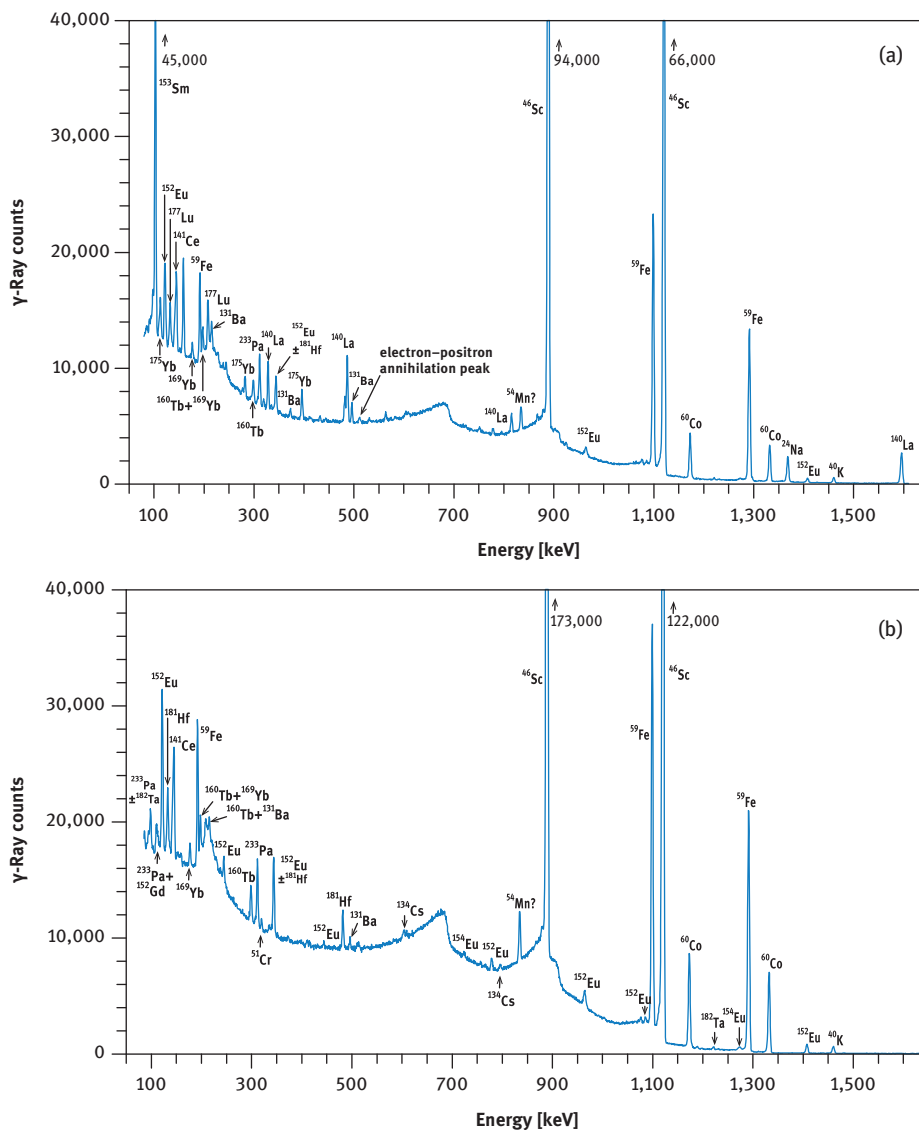


Figure 10.6: γ -ray spectra of international reference rock basalt BCR-1. (a) Spectrum taken with a coaxial Ge(Li) detector about 8 days after end of irradiation, (b) spectrum taken with a coaxial Ge(Li) detector about 30 days after end of irradiation, (c) part of spectrum taken with a planar Ge detector about 28 days after end of irradiation. Irradiation conditions: neutron flux $5 \times 10^{13} \text{ cm}^{-2} \times \text{s}^{-1}$ for 12 hours at the research reactor “DIDO” of the former “Kernforschungsanlage Jülich” (now “Forschungszentrum Jülich”) in September 1993. γ -ray counting was performed at the former “Institut für Kernchemie”, University of Cologne. The dead-time of the counting system was kept below 3 % by adjusting the distance between sample and detector. Counting times were 3 hours (a), 4 hours (b) and 10 hours (c).

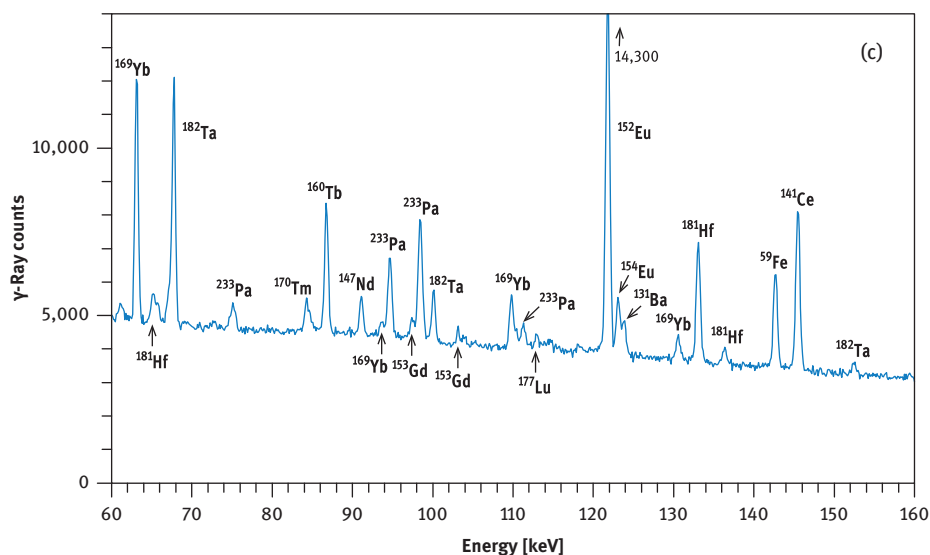


Figure 10.6 (continued)

of ^{233}Th , Figure 10.6c). For measuring Gd by INAA, it therefore is useful to let ^{233}Pa decay for about half a year (7 half-lives of this isotope) – if time is not essential.

10.4.4 RNAA – a fast separation scheme

Radiochemical neutron activation involves the separation of the elements of interest from the matrix activity. At the time when the samples arrive at the laboratory, one or two days after the end of irradiation, geological and biological materials are highly radioactive. All chemical work, therefore, must be carried out minimizing the exposure of the operator to the radiation. This includes manipulating the samples behind protective shielding (usually made by bricks of lead, about 5 cm thick) and following a quick-and-dirty chemical procedure. As all chemicals that are used during digestion of the samples and separating the REE are inactive, there is little danger of introducing contamination, except through cross-contamination between samples. Prior to the development of the high-resolution Ge detectors all REE had to be separated from one another which involved time- and labour-consuming extraction or ion-exchange techniques [37, 38].

With the advent of the coaxial Ge(Li) and planar Ge detectors, the chemical work was reduced to separating the REE as a group from the matrix. At the University of Cologne we have applied the separation technique outlined in Figure 10.7 and described in more detail by Carl [39]. In many geological samples ^{46}Sc accounts for the main activity between about one week and one year after the end of irradiation.

It is, therefore, indispensable to remove at least the major portion of ^{46}Sc from the REE. We achieved this by precipitating Sc using phytic acid [40]. Chemical yields of the REE were typically between about 90 % and 95 % as determined from the analysis of international reference materials or by re-irradiation and γ -ray counting of samples. To our experience, two people working together can process about 20 samples in 10 hours.

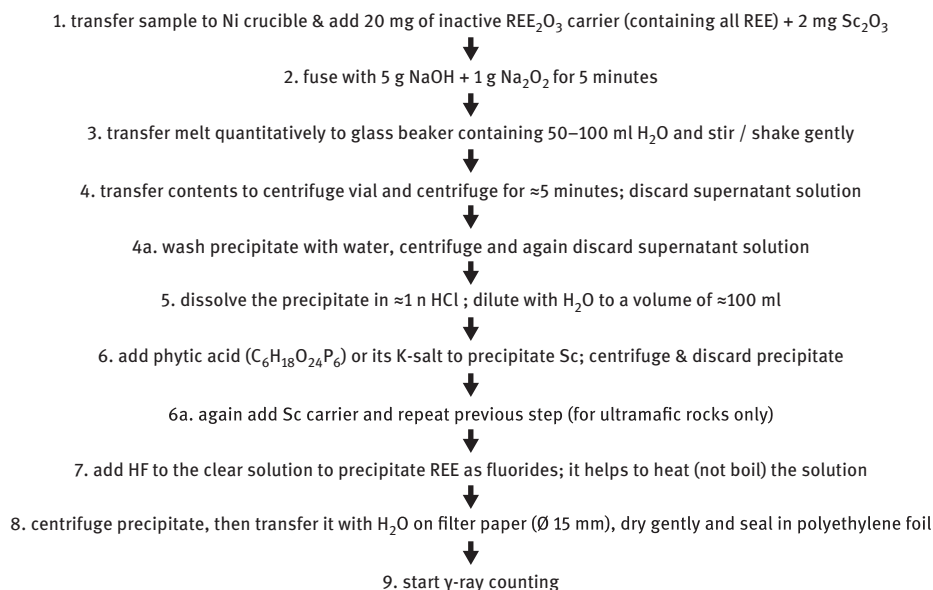


Figure 10.7: Separation scheme for REE from silicate minerals and rocks (modified after [39]). Steps 4a and 6a should be included if samples with very low REE concentrations are processed.

By employing this separation scheme and irradiating $\approx 10^{-1}$ g of sample at a flux of $8 \times 10^{13} \text{ n} \times \text{cm}^{-2} \times \text{s}^{-1}$ we were able to analyse the REE in minerals from peridotites containing ppb levels of the REE only (Figure 10.8). Even sub-ppb levels are accessible for the most sensitive elements La, Sm, Eu, Yb, and Lu. In contrast, by INAA we would have detected only Eu, Yb and Lu in orthopyroxene and none of the REE in olivine.

Biological samples may benefit from post-irradiation separation of the REE by ion-exchange techniques [41]. When high-purity chemicals are used, the REE may, of course, be separated from the matrix prior to irradiation. For recent separation schemes employing a variety of ion-exchange resins see for example [42]. Preconcentration techniques are also required for the analysis of materials with very low REE abundances like natural waters [43].

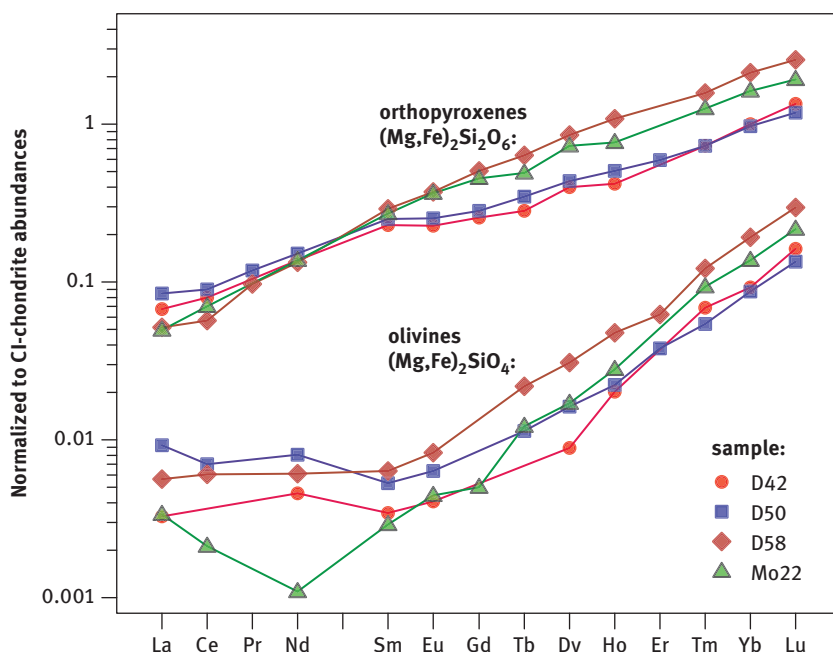


Figure 10.8: REE in olivines $(\text{Mg,Fe})_2\text{SiO}_4$ and orthopyroxenes $(\text{Mg,Fe})_2\text{Si}_2\text{O}_6$ from peridotites (redrawn from data published in [53]). Peridotites are rocks from the Earth's upper mantle brought to the surface as inclusions in basaltic volcanic rocks. REE were separated from the matrix (sample weights between 100 and 300 mg) according to the procedure outlined in Figure 10.7. CI-chondrite normalization values from [54]. The sample with the lowest REE concentration has REE abundances corresponding to detected quantities of approximately 1 ng for La, 1.5 ng for Ce, 0.7 ng for Nd and 0.5 ng for Sm. Even lower concentrations were observed in spinel $(\text{Mg,Fe})(\text{Al,Cr})_2\text{O}_4$, corresponding to detected quantities of ≈ 0.06 ng for La, 0.03 ng for Sm and 0.06 ng for Lu [53]. The patterns indicate crystal-chemical control of REE^{3+} incorporation into the lattice of olivine and orthopyroxene with the largest of the REE being most strongly excluded from incorporation. Higher than expected concentrations of the light REE in olivine are likely to be due to physical contamination, in particular fluid inclusions.

10.4.5 Data reduction and sources of error

Data reduction following γ -ray spectroscopy comprises calculation of the peak area and standard error. This procedure is comparable to the task encountered in energy-dispersive X-ray spectroscopy and is discussed in detail by Potts [4]. In most cases (La, Ce, Nd, Sm, Eu, Tb, Yb and Lu in INAA and all REE in RNAA), well-resolved γ -ray lines can be chosen to evaluate the net peak area by subtracting the interpolated background from the total peak area. Deconvolution of photopeaks is rarely required. As the 1σ -error is estimated from the square root of γ -ray counts of total peak as well as background, 1σ of the net peak area N_{Peak} is calculated as $\sqrt{N_{\text{Peak}} + 2N_{\text{Background}}}$. As the

background is particularly high at low energies (Figure 10.6a–c), its value may contribute more to the total error in this region than the photopeak, at least in INAA. If the counts at the background are of the same magnitude as the net peak area, a couple of thousand counts must be accumulated for the net peak area in order to keep the standard error below about 3 %. At high energies the background is low and the error of a photopeak is determined by the number of counts in the peak, but due to the much lower efficiency of the detector at high energies, the number of counts is much smaller, again leading to higher 1σ -errors. The energy dependence of the efficiency is seen in Figure 10.6a by comparing the γ -lines of ^{140}La at 487 keV and 1596 keV. According to Table 10.1 the 1596 keV-line should be more intense by about a factor of two compared to the 487 keV-line whereas in Figure 10.6a the latter line is the stronger one by a factor of almost two.

Although NAA is poor in interferences from competing reactions, leading to the formation of the same nuclide, caution must be exercised when analysing Gd and Ho. “Second-order reactions” may severely enhance the signals of ^{153}Gd and ^{166}Ho ([44, 45]). Such interferences arise during long irradiations and/or high neutron fluxes, when a radioactive nuclide $^{A+1}_{Z}X$, formed during irradiation from a stable isotope ^A_ZX of element X , decays into a stable isotope $^{A+1}_{Z+1}Y$, the (n,γ) -reaction of which – producing $^{A+2}_{Z+1}Y$ – is used to determine the concentration of element Y . Alternatively, $^{A+1}_{Z}X$ may capture another neutron to form $^{A+2}_{Z}X$ which decays into $^{A+2}_{Z+1}Y$.

Second-order activation can be calculated from the Bateman–Rubinson equation [46, 15]:

$$N_n(t) = \Lambda_1^* \times \Lambda_2^* \dots \Lambda_{n-1}^* \times N_1^0 \times \sum_{i=1}^n C_i \times e^{(-\Lambda_i \times t)} \quad (10.10)$$

where $N_n(t)$ is the number of nuclides $^{A+2}_{Z+1}Y$ produced after irradiation time t in a reactor from the interfering reaction, N_1^0 is the initial number of (inactive) nuclides ^A_ZX . $\Lambda_i = \lambda_i + \sigma_i \times \Phi$ and $\Lambda_i^* = \lambda_i^* + \sigma_i^* \times \Phi$ where λ_i is the decay constant of nuclide i , λ_i^* is the partial decay constant (producing, for example, ^{152}Gd from $^{152\text{m}}\text{Eu}$ whereas λ_i is the total decay constant, generating $^{152}\text{Gd} + ^{152}\text{Sm}$ from $^{152\text{m}}\text{Eu}$), σ_i is the total reaction cross section and σ_i^* the partial cross section (leading, for example, from ^{151}Eu to $^{152\text{m}}\text{Eu}$, whereas σ_i is the value leading from ^{151}Eu to $^{152\text{m}}\text{Eu} + ^{152}\text{Eu}$); Φ is the neutron flux.

The factors C_i are defined as

$$C_i = \prod_{j=1}^i \frac{1}{\Lambda_j - \Lambda_i} \quad (j \neq i)$$

In the above example, $n = 4$ (^A_ZX , $^{A+1}_{Z}X$, $^{A+1}_{Z+1}Y$, $^{A+2}_{Z+1}Y$), C_1 is then calculated as

$$C_1 = \frac{1}{\Lambda_2 - \Lambda_1} \times \frac{1}{\Lambda_3 - \Lambda_1} \times \frac{1}{\Lambda_4 - \Lambda_1}.$$

^{151}Eu possesses a cross section of 3150 b to form $^{152\text{m}}\text{Eu}$. 72 % of this nuclide decay into stable ^{152}Gd (Table 10.1). Thus, for this branching decay $\lambda^* = \ln(2)/(9.31 \times 3600) \times 0.72 = 1.489 \times 10^{-5} \text{ [s}^{-1}\text{]}$. Whereas ^{151}Eu has a natural abundance of almost 50 %, the

abundance of ^{152}Gd is only 0.20 %. For a sample with a chondritic meteorite Gd/Eu abundance ratio (≈ 3.5), irradiating a sample at a flux of $5 \times 10^{13} \text{ n} \times \text{cm}^{-2} \times \text{s}^{-1}$ for just one day enhances the total amount of ^{153}Gd by more than 10 %. For an elemental Eu/Gd ratio of 1:1 the increase is about 50 % and a neutron flux of $1 \times 10^{14} \text{ n} \times \text{cm}^{-2} \times \text{s}^{-1}$ will almost double the ^{153}Gd signal (Figure 10.9). 5 days of irradiation at $5 \times 10^{13} \text{ n} \times \text{cm}^{-2} \times \text{s}^{-1}$ will more than double the ^{153}Gd signal for a chondritic Eu/Gd ratio and increase it by a factor of 4 for a 1:1 ratio. A standard of pure Eu must be used to correct for this interference by counting ^{152}Eu and ^{153}Gd in standard and unknowns. Reducing the irradiation time to much less than one day or the neutron flux is not a good option in this case in view of the long half-life of ^{153}Gd and, hence, its low activity (compare Figure 10.5b).

^{164}Dy forms ^{165}Dy by neutron capture with a cross section of 2700 b which decays into stable ^{165}Ho with a half-life of 2.35 h, thus increasing the concentration of Ho as a function of irradiation time and neutron flux in the reactor. ^{165}Dy may also

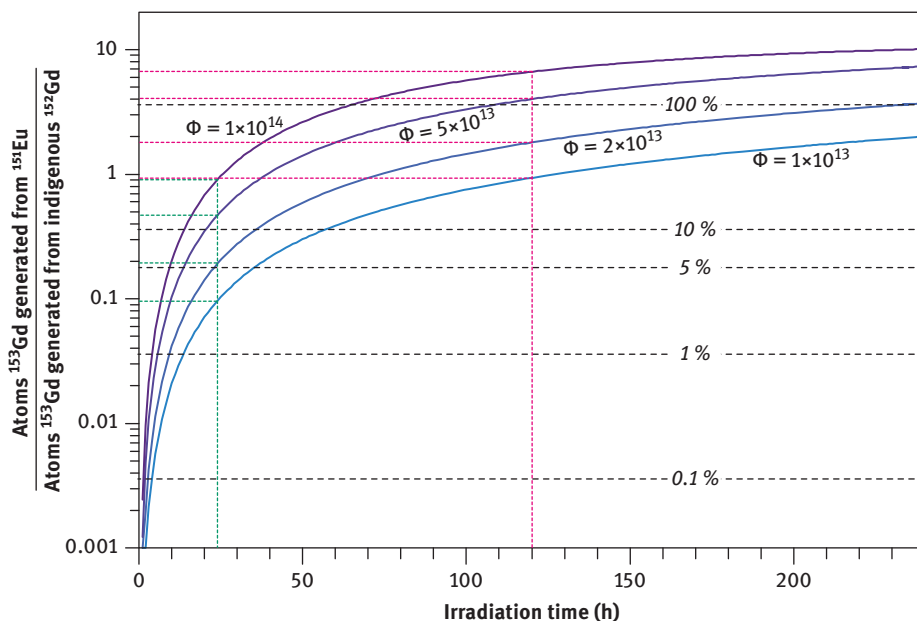


Figure 10.9: Interference from ^{151}Eu on the ^{153}Gd signal as a function of irradiation time and neutron flux as computed from equation (10.10). ^{153}Gd , activated from ^{152}Gd indigenous to the sample, was calculated from equation (10.4). The y-axis has been scaled to a 1:1 elemental Eu/Gd ratio. Most geological samples will have lower ratios, closer to the chondritic one ($\approx 1/3.5$, chondritic ratios are indicated by black broken lines). Green and red broken lines serve to illustrate the interference for irradiation times of 1 and 5 days, respectively. Calculations have been carried out employing the Bateman–Robinson equation [46, 15], using isotopic abundances, activation cross sections and half-lives as given in Table 10.1. For equal concentrations of Eu and Gd in a sample, for example 1 ppm, irradiating the sample for one day at a neutron flux of $1 \times 10^{13} \text{ n} \times \text{cm}^{-2} \times \text{s}^{-1}$ will increase the ^{153}Gd signal by about 10 % whereas irradiation at a flux of $1 \times 10^{14} \text{ n} \times \text{cm}^{-2} \times \text{s}^{-1}$ will almost double the signal.

capture another neutron ($\sigma = 3500$) to form ^{166}Dy , which decays into ^{166}Ho with a half-life of 81.5 h, about three times longer than the half-life of ^{166}Ho . This has the consequence that the interference of Dy on the determination of the Ho content is not only dependent upon the neutron flux and duration of irradiation but also on the time when the decay of ^{166}Ho is counted. The interference can only be kept small (<3 %) if the sample is irradiated for no longer than about one hour and γ -ray counting is carried out within about three half-lives of ^{166}Ho [45].

A second source of error arises from the presence of uranium in a sample if its concentration matches, or is even higher than, those of Ce and Nd (see also section 10.3.1.1). In these cases fission of ^{235}U by thermal neutrons produces fragments with masses within the range of the light REE. Particularly high, for our concern, are the fission yields Y_i for masses 140 (6.268 %), 141 (5.837 %), 142 (5.796 %) and 147 (2.265 %) (data taken from [32]). Initially, these nuclides have an excess number of neutrons, leading them to decay by β^- -emission into stable nuclides. The decay of nuclide 142 ends at stable ^{142}Ce , thus shielding ^{142}Pr from being affected by U fission. The decay of nuclide 140 is somewhat modulated by ^{140}Ba due to its half-life of 12.75 d. As ^{140}La is analysed within a few days after the end of irradiation and $\sigma_{(n,\gamma)}$ is much higher for ^{139}La than for ^{140}Ce and ^{147}Nd , contribution from fission of ^{235}U is expected to remain small. No long-lived nuclides, however, are encountered during decay of nuclides 141 and 147 until they reach ^{141}Ce and ^{147}Nd .

The activity ratio of ^{141}Ce produced by fission of ^{235}U relative to ^{141}Ce produced by the (n, γ) reaction from ^{140}Ce can be estimated from Equation 10.5:

$$\frac{A_{235\text{U}}(n, f)}{A_{141\text{Ce}}(n, \gamma)} = \frac{\sigma_{(n, f)} \times \Phi \times N_{235\text{U}} \times Y_{i141} (1 - e^{-\lambda_{141} \times t})}{\sigma_{(n, \gamma)} \times \Phi \times N_{140\text{Ce}} \times (1 - e^{-\lambda_{141} \times t})}$$

The neutron flux Φ and the irradiation time, of course, are identical for uranium and cerium in the sample. The equation thus simplifies to

$$\frac{A_{235\text{U}}(n, f)}{A_{141\text{Ce}}(n, \gamma)} = \frac{\sigma_{(n, f)} \times N_{235\text{U}} \times Y_{i141}}{\sigma_{(n, \gamma)} \times N_{140\text{Ce}}} = \frac{\sigma_{(n, f)} \times \frac{c_{235\text{U}}}{U_{\text{at. weight}}} \times Ab_{235\text{U}} \times N_{\text{Av}} \times Y_{i141}}{\sigma_{(n, \gamma)} \times \frac{c_{140\text{Ce}}}{\text{Ce}_{\text{at. weight}}} \times Ab_{140\text{Ce}} \times N_{\text{Av}}}$$

where c stands for concentrations, Ab for isotope abundances and N_{Av} for Avogadro's number. If concentrations of U and Ce are equal, this results in:

$$\frac{A_{235\text{U}}(n, f)}{A_{141\text{Ce}}(n, \gamma)} = \frac{586 \times \frac{1}{238.03} \times 0.0072 \times 0.06268}{0.58 \times \frac{1}{140.115} \times 0.8848} = 0.30$$

For the contribution to ^{147}Nd from fission of ^{235}U in the case of equal concentrations the result is:

$$\frac{A_{235\text{U}}(n, f)}{A_{147\text{Nd}}(n, \gamma)} = \frac{586 \times \frac{1}{238.03} \times 0.0072 \times 0.02265}{1.4 \times \frac{1}{144.24} \times 0.1719} = 0.24$$

Interferences of this magnitude can be corrected reasonably well by γ -counting of ^{239}Np , ^{141}Ce and ^{147}Nd in pure uranium standards and in samples, provided that concentrations of Ce, Nd and U are at least on the order of 10^1 ppm to allow γ -ray counting by INAA with small statistical errors. For most geological materials fission interference is much smaller. The average concentrations in the continental crust are estimated at 1.3 ppm U, 43 ppm Ce and 20 ppm Nd [47]. The basalt standard BCR-1 contains only 1.7 ppm U compared to 53.7 ppm Ce and 28.7 ppm Nd [48]. In alkaline rocks such as syenites, however, uranium may become strongly enriched. For example, for the international standard syenite SY-2 a U concentration of 284 ppm is reported, compared to 73 ppm Nd [48]. In NAA of this rock, the contribution from ^{235}U fission to the ^{147}Nd photopeak would match the contribution from ^{146}Nd . – Analysing the light REE in uranium ores, Gd in compounds of Eu, and Ho in compounds of Dy by NAA without pre-irradiation chemical separation would surely be a challenge.

10.5 Conclusion

NAA is an effective and sensitive tool for REE analysis of geological and environmental materials. Its role is nowadays greatly diminished by the decommissioning of nuclear research reactors in parts of the world as well as by the development of competitive techniques, namely ICP-MS. INAA is a true multi-element and non-destructive technique capable of routinely determining the concentrations of some 15 to 20 elements in geological samples. Both, INAA and RNAA are little susceptible to contamination because no pre-irradiation treatment of samples is necessary. On the other hand, NAA takes a long time to complete (one month or more) due to the necessity of letting short-lived activities decay in order to decrease the background during γ -ray counting. Potential health risks of the analyst through exposure to γ - and β^- -radiation must also be considered as well as the requirements for disposing nuclear waste when selecting NAA as the analytical method for REE analysis.

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11 Automated quantitative rare earth elements mineralogy by scanning electron microscopy

Abstract: Increasing industrial demand of Rare Earth Elements (REE) stems from the central role they play for advanced technologies and the accelerating move away from carbon-based fuels. However, REE production is often hampered by the chemical, mineralogical as well as textural complexity of the ores with a need for better understanding of their salient properties. This is not only essential for in-depth genetic interpretations but also for a robust assessment of ore quality and economic viability. The design of energy and cost-efficient processing of REE ores depends heavily on information on REE deportment. Detailed knowledge about the mineralogical siting of REEs can be gained from the application of automated quantitative process mineralogy. This technique assigns numeric values to compositional and textural properties of mineral matter. Scanning electron microscopy (SEM) combined with a suitable software package for acquisition of backscatter electron and X-ray signals, phase assignment and image analysis is one of the most efficient tools for quantitative mineralogy. Different SEM-based automated quantitative mineralogy systems, which are commercially available, are briefly characterized.

Using examples of quantitative REE mineralogy this chapter illustrates capabilities and limitations of automated SEM-based systems. Chemical variability of REE minerals and analytical uncertainty can reduce performance of phase assignment. This is shown for the REE phases parisite and synchysite. In another example from a monazite REE deposit the quantitative mineralogical parameters surface roughness and mineral association derived from image analysis are applied for automated discrimination of apatite formed in a breakdown reaction of monazite and apatite formed by metamorphism prior to monazite breakdown.

SEM-based automated mineralogy fulfills all requirements for characterization of complex unconventional REE ores that will become increasingly important for supply of REEs in the future.

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11.1 Introduction

The Rare Earth Elements (REE) comprise the lanthanides, a group of 15 metals, as well as scandium and yttrium because they tend to occur in the same mineral assemblage as the lanthanides and exhibit similar chemical properties. All the rare earths except promethium (Pm) are available in the geological environment. Following a common pattern within the periodic table, the lanthanides with even atomic numbers are more common in nature, and in general, REE with lower atomic numbers are more common ionic constituents in most REE minerals and occur in greater abundance than the REE with higher atomic numbers. The trends in the Earth's crustal abundance suggest a division between light and heavy REEs [1, 2]. Although variation exists, commonly the lanthanides are subdivided according to their atomic weight into light rare earths (LREE) comprising lanthanum (La) through gadolinium (Gd), and heavy rare earths (HREE) including terbium (Tb) through lutetium (Lu), and yttrium (Y).

Industrial consumption of REE indicates that demand is driven by the rapid development of emerging industries. These include hybrid electric vehicles and wind power generators, which rely on the use of rare earths such as neodymium for permanent magnets. Other consumer sectors include FCC catalysts, battery alloys, metallurgical products, phosphors, ceramics, catalytic converters, as well as chemical, military and satellite industries [3–7].

Given this global demand for green and sustainable products in energy, military, and manufacturing industries, REE demand throughout the world is projected to increase [8]. Consequently, the REEs are still increasingly becoming more attractive commodity targets for the mineral industry. Almost all current mine production of REEs is derived from less than ten minerals. The most extensively mined ore minerals by far are bastnaesite and monazite, and with lesser importance loparite and xenotime [9]. There is, however, a problem especially with monazite as it may contain deleterious impurities like thorium (Th), which imparts an unwanted radioactivity to the ores. The cost of handling and disposing of radioactive material is a serious impediment to the economic extraction of the more radioactive REE-rich minerals [10].

Another problem arises from the fact that the REE portfolio produced by current mining is dominated by Ce and La since LREE-bearing minerals like bastnaesite, monazite and loparite are the principal economic sources of REE. On the demand side, high-performance permanent magnets are among the largest REE demand drivers, but their manufacturing requires HREEs like Pr, Nd, Tb and Dy, which are of low natural abundance. As these magnet elements are coproduced with all other REEs, an increase in the demand for Pr, Nd, Tb or Dy in their key applications leads to an increase in the production of the other companion REEs with potential implications on their supply and demand. For example, an increase in the demand for Dy and other heavy REEs leads to an oversupply of the coproduced LREEs La and Ce which are geologically more abundant and, thus, generally cheaper than the HREEs. Cerium and La make up about 70 to 80 %

of the REE in bastnaesite and monazite dominated deposits, but their worth is two orders of magnitude less than that of Dy and Tb, per kilogram on the RE oxide market [11].

The imbalance between the market demand and the abundance of naturally occurring REEs in ore deposits can be assessed by the critical REE ratio $(Nd + Eu + Tb + Dy + Eu)/(La + Ce) \times 100$ [12]. For bastnaesite and/or monazite ores critical ratios range from about 15 to 27. Higher ratios, more in favor of the expensive REEs of up to 175 are recorded from ion adsorption deposits mined in Southern China. But these deposits are generally of low grade between 300 and 3500 ppm total REE oxides and are small compared to other REE deposits with tonnages ranging from 0.5–0.01 Mt [13].

This unfavorable ratio of LREE over HREE can be tackled by finding more technical applications of LREE and increase their demand by developing process technologies to leave unwanted elements on the mine site [14] or by shifting the focus from conventional high-LREE ores to unconventional REE ores with HREE enrichments. The distribution of individual REEs in minerals is not even and certain minerals will hold enrichments or depletions of light or heavy REEs, respectively. This renders most REE ores mineralogically and chemically complex. Together with a wide textural variability this demands sufficient understanding of the salient characteristics of REE ores, essential for a robust assessment of the quality and economic viability of a potential REE deposit. In that sense, it is important to identify and quantify all the REE-phases present in the ore and to evaluate the elemental deportment of the different REEs into the different REE-bearing phases.

Following the production chain, mineral processing requires additional information on mineral associations, grain size distributions as well as liberation characteristics of the valuable mineral phases. Nowadays mineral processing is generally capable of sequential separation of multiple mineral phases, but when the REEs are found in two or more mineral hosts, with each behaving differently during extraction, beneficiation can become relatively inefficient and costly [15, 16]. From that it would appear that deposits in which the REEs are preferentially concentrated in a single mineral phase have a competitive advantage. On the other hand, mining of REEs as by-product of additional or major commodities has a significant price advantage since extraction costs are shared by the bundle of metals mined. However, poly-metallic ores, by nature, contain a complex and diverse mineral assemblage, which may require special beneficiation strategies to become technically and economically viable. The design of cost efficient processing for such ores as well as the reliability of geometallurgical programs heavily depend on information that can be made available employing quantitative process mineralogy [14, 17–19].

11.2 Quantitative and automated mineralogy

Quantitative mineralogy assigns numeric values to compositional and textural properties of mineral matter (e.g. rocks, ores, processing products). Compositional properties

are related to the kind and quantity of mineral phases in a sample. This is known as the modal composition, which specifies the relative proportions in volume- or mass-% from highly abundant rock forming minerals to less abundant accessory phases.

Textural properties comprise a multitude of information on the grains forming the sample as well as on their spatial arrangement. Grains are characterized by their size and shape. Further quantitative mineralogical parameters related to size are grain size distributions, either of the total sample or a specific mineral fraction. The spatial distribution of grains can be described by properties such as alignment, orientation or spacing [20]. Quantitative mineralogy thus attempts to convert rock properties to numerical parameters, which often are only described in a qualitative way by geoscientists. As numeric procedures can only handle quantitative data this represents an important contribution to the development of computer models for beneficiation processes or geometallurgical optimization [18, 21].

A variety of methods including polarization microscopy, multispectral imaging in optical microscopy, electron microscopy, X-ray diffraction, differential thermal analysis, infrared and optical emission spectrometry has been applied in the last decades for quantitative mineralogical studies, e.g. [22–26].

To enhance the speed and efficiency of sample throughput and to increase the information on spatially or mineralogically heterogeneous ore bodies, which can only be characterized by large sample sets, and in order to circumvent the investigator-specific individual component inherent in petrographic studies, there have been numerous technical attempts to generate quantitative mineralogical information in an unattended way. These analytical procedures, which are mainly based on X-ray diffraction, as well as on optical and electron microscopy, are described by the term “automated mineralogy” [27, and references therein]. As shown above to be relevant for process mineralogy, particularly for the beneficiation of mineralogically and texturally complex REE ores, automated mineralogy systems must be capable to provide mineral identification and quantification. Furthermore, to account for target elements of mining but also in order to identify deleterious elements (e.g. U, Th) such systems should allow element detection. Any of the previously mentioned textural properties can only be quantified if information on phases and chemistry are related to images. Imaging must be performed with high spatial resolution to be suitable for fine-grained rocks. Thus, also accessory phases or complex intergrowth of minerals can reliably be quantified. Finally, all datasets must be available in digital form for image analysis. Scanning electron microscopy meets most of these requirements and is one of the most efficient tools for automated quantitative mineralogy. Today, scanning electron microscope (SEM) based automated mineralogy is an established technology and commercially available systems are applied by mining companies all over the world [18, 27, 28].

11.3 Scanning electron microscopy

In an SEM an electron beam is generated from a tungsten filament or a field emission gun. The electron beam is focussed and can be directed on a single spot or it can be scanned over a specimen. Among the interactions between the electrons penetrating the specimen and the sample elements the electrons scattered back from the incident beam (backscatter electrons, BSE) and fluorescence X-ray photons generated by excitation of atoms in the specimen are most important for quantitative mineralogy. Both yield information on sample composition (Figure 11.1).

The intensity of the BSE signal is primarily correlated to the mean atomic number of the sample [29]. This allows differentiation of minerals, in particular minerals containing elements with higher atomic number, such as the REE, are characterized by high BSE-intensity and can be distinguished from silicates or carbonates composed of lighter elements. The energy of fluorescence photons is characteristic of the excited elements while their intensity is proportional to the concentration of these elements. Modern SEMs are equipped with one or more fast energy dispersive detectors (EDS) that acquire spectra built by approximately 1000 to 5000 fluorescence photons detected within 2–5 milliseconds. As both, BSE and fluorescence photons, are generated by an interaction of sample atoms and electrons they represent a larger volume of the specimen than only the area of the incident electron beam ([30], Figure 11.1). In an untilted sample the volume of interaction depends on mean atomic number, density and beam energy [31, 32]. The latter is a function of the potential applied for acceleration of

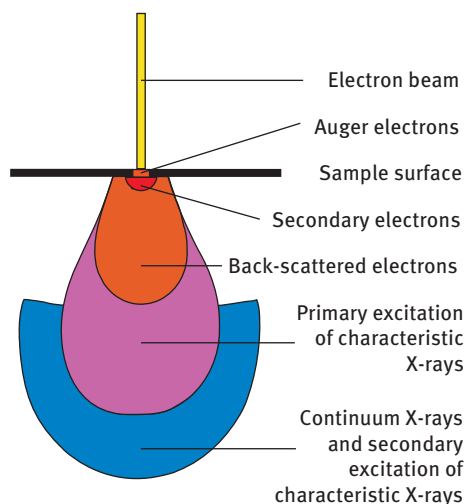


Figure 11.1: Schematic sketch showing interaction volume of electrons in sample, not to scale, according to [29, 31, 32]. Pear shape is typical of materials with low mean atomic numbers such as silicate or carbonate minerals.

electrons emitted from the electron gun. At usual analytical conditions, i.e. acceleration voltages between 15 and 25 kV, the width of the interaction volume limits the spatial resolution of the technique in most mineral matrices to values between 2 and 5 μm .

Polished samples – either as a thin section on glass or a polished epoxy resin mount – are preferred to avoid surface effects having negative influence on BSE and X-ray intensities by absorption and secondary excitation. As most mineral samples are not conductive, the samples are coated with carbon prior to analysis.

11.4 SEM-based automated quantitative mineralogy

11.4.1 General characteristics, functions

In addition to fast EDS and BSE detectors, basic instrument components of an SEM, which is suitable for automated mineralogy, are a large specimen stage performing precise automated stepwise movements and an electron source providing a stable and strong beam that generates a constant and high rate of fluorescence X-rays in the sample. These components permit to handle a series of samples in unattended operation in one vacuum chamber cycle [18, 27].

Finally, specific software packages are the key components that make such SEM applicable for automated quantitative mineralogy. They control the entire analytical procedure of one or more samples in an unattended way. This comprises control and optimisation of instrumental parameters as well as acquisition and storage of spatially resolved BSE and X-ray signals. Furthermore, software packages must offer a diversity of image analysis functions.

Grains with coherent properties and their boundaries must be identified in an image built up by the signals according to the scanning pattern (segmentation, e.g. [33, 34]). Signal acquisition can be optimized with respect to speed of analysis or spatial resolution of spectral information. These two alternatives are reflected by different analytical modes (Figure 11.2). In the fastest mode, grains can in a first step be discriminated on the basis of their BSE intensity, which is calibrated to a range of atomic numbers. In a second step, a single X-ray analysis is performed on each grain for phase assignment in combination with the BSE values. The alternative mode employs acquisition of BSE intensity and X-ray fluorescence spectra while the specimen is scanned step-by-step in a grid pattern. Phase assignment is then performed for each step, which is represented by an image pixel in the resulting data set. Depending on the step size of the grid pattern this mode yields highest spatial resolution of spectral information. However, due to time needed by the EDS detectors for acquisition of X-ray spectra, this analytical mode is more time consuming.

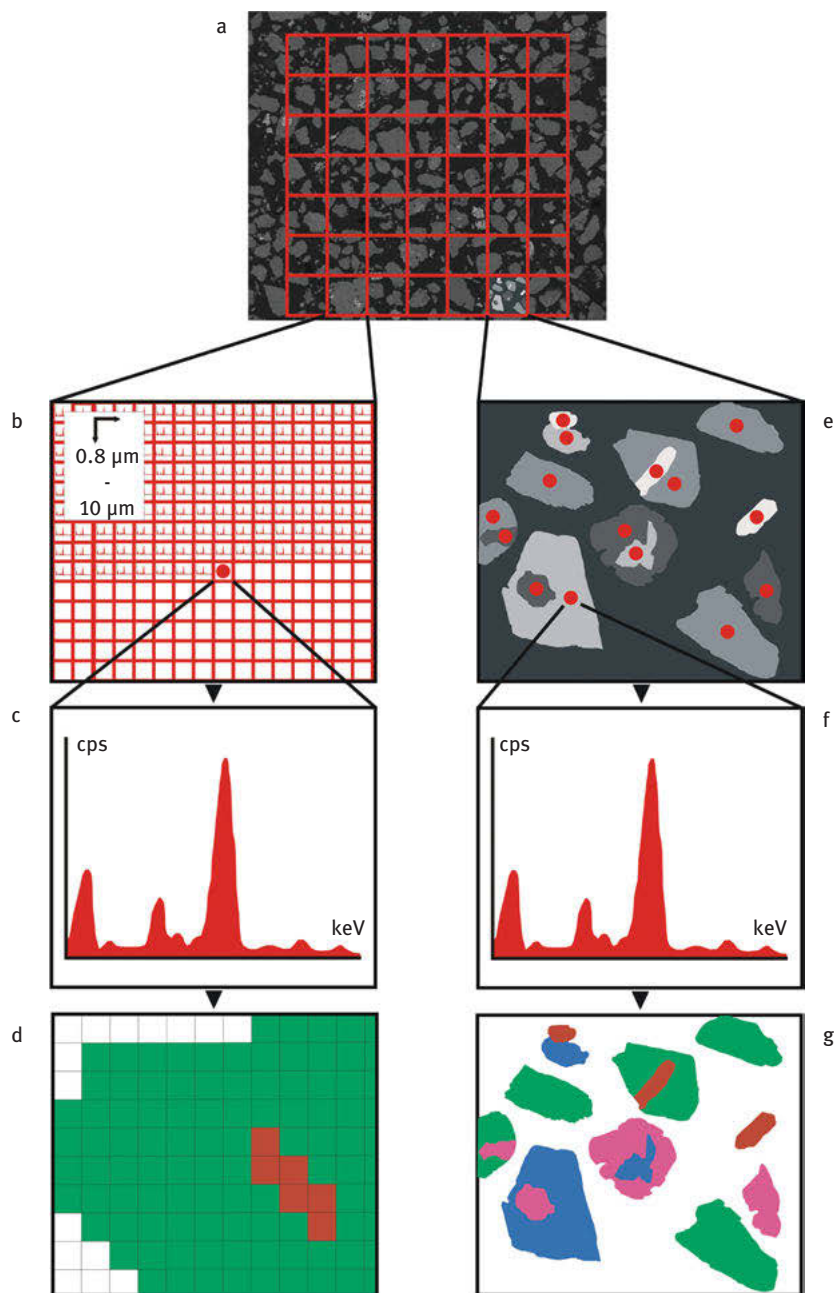


Figure 11.2: Acquisition modes of SEM based automated mineralogy systems, optimized with respect to spatial resolution of spectral information (a, b, c, d) or with respect to speed of analysis (a, e, f, g). a) Pattern of frames on a carbon-coated polished grain mount. Frames are sequentially scanned, acquisition of BSE image, segmentation of grains and discrimination of sample areas formed by resin

Various combinations of the two analytical modes, e.g. spectral analyses of points along lines or less dense grids in combination with BSE mapping, may be applied in accordance with the capabilities of the automated mineralogy system and the analytical task [18, 28].

Independent of the mode of data acquisition BSE threshold values lower than generated in any sample mineral can be set in order to stop analysis outside of a thin section area or a particle. This saves time and reduces hardware contamination avoiding evaporation of epoxy resin used in sample mounts.

In a further step the segmented grains are mineralogically identified by comparing their BSE and spectral characteristics with a library of standard mineral data. Algorithms performing data comparison can either quantify match of the full spectrum or they quantify a match of relative element proportion values derived from relative peak intensities detected in selected intervals of the spectrum. An alternative way of mineral assignment is to transfer spectral data to element concentrations and to compare analytical results with a standard mineral composition library with respect to chemical match. Final mineral assignment can either be carried out looking for the best match with one phase of the mineral library or for the first match in a predefined list of standard mineral data generated from the library.

Despite of large libraries implemented in all available automated mineralogy systems standard mineral datasets usually have to be reworked and adapted in a case specific way to cover the chemical complexity of all target minerals in a given sample set.

The way of mineral identification outlined here shows that phases, which have similar or identical BSE and spectral properties, can hardly be distinguished. This limitation is most obvious for polymorphs, which are mineralogically distinct due to different structures, but have identical chemical composition, e.g. calcite/aragonite, rutile/anatase, kaolinite/dickite, lepidocrocite/goethite, diaspor/boehmite [27, 35]. But also minerals, which mainly differ with respect to OH-groups in their structure or light elements (e.g. H, C) that are not detected by EDS or used for coating, can hardly be

Figure 11.2 (continued)

(black in BSE intensity image) that will not be scanned in further steps. b) Each frame is scanned with an electron beam step width varying between 0.8 μm (minimum value) and usually 10 μm .

c) Acquisition of BSE intensity and fluorescence spectrum with EDS X-ray detectors usually on the basis of 1000 to 5000 counts, d) Phase assignment to each pixel by correlation of X-ray and BSE data using a mineral library implemented in the software. Plot of mineral image after selection of different colours for various mineral phases, e) Discrimination of grains defined by areas of homogeneous BSE intensity, f) Performance of a single X-ray analysis in the centre of each grain (see 2c), g) Phase assignment for each grain based on X-ray data and BSE intensity calibrated to a range of atomic numbers using mineral library data of the software. Data provided by both acquisition modes (see 2d, f) are the basis for further automated image analysis and generation of quantitative mineralogical data (e.g. modal composition, particle size and size distribution, mineral association, particle shape, textural parameters).

distinguished (e.g. gibbsite, $\text{Al}(\text{OH})_3$ and diaspore/boehmite, AlOOH , [36]). Examples of REE-minerals are discussed below.

Distinction of individual mineral grains may also be limited in aggregates or rock domains formed by the same and chemically homogeneous mineral. In such cases, input options of additional image data obtained by detection of electron backscatter diffraction (EBSD) or polarization microscopy indicative of individual crystallographic grain orientation represent an important progress.

The generation of fluorescence radiation in a volume of interaction leads to mixed signals, if it extends over two or more different minerals. Such signals do not match with any of the standard data contained in a mineral library and consequently do not permit phase assignment. This effect is inevitable at grain-boundaries (edge-effect) and becomes increasingly pronounced with decreasing grains size [37]. Boni et al. [36] evaluate the consequences for mineral assignment to Al-hydroxide and clay phases in a study on bauxites.

Data automatically obtained in the SEM are transformed to digital images displaying mineral species with user-defined colours. An example of a polished rock sample (fieldscan) is given in Figure 11.3, which shows a rock formed by a groundmass of plagioclase and muscovite as well as by larger irregularly shaped quartz grains indicated by different colours. Less abundant mineral phases, such as the REE-mineral monazite (REEPO_4) as well as apatite or clinozoisite-epidote are detected by QEMSCAN and can easily be recognized due to dark blue, dusky pink and lavender colour coding, respectively.

The time consuming effort of high-resolution pixel-by-pixel X-ray mapping is highly appropriate for the study of materials composed of fine-grained minerals with similar BSE properties. This is illustrated in Figure 11.3. While phase assignment for muscovite, plagioclase and quartz is clear using X-ray data, these minerals, which are characterised by similar and relatively low densities, can hardly be distinguished in BSE images at a BSE scale suitable for distinction of heavier phases.

Proportions of different minerals (i.e. modal abundance) can be calculated simply by counting pixels quantifying the area assigned to each mineral (Figure 11.4). According to the Delesse principle this is equivalent to volume proportions [38, 39]. Using density information that is included in the database implemented in the software package modal abundance in volume-% can be transferred to mass-%.

These basic digital image data allow computation of quantitative textural parameters. Grains, either imaged in a mount of separate grains or numerically de-agglomerated from an image of a rock sample, can further be characterized in terms of size parameters (area, perimeter, diameter). Many software packages derive these values after calculation of equal area circles or ellipses for each grain. Furthermore, grains can be characterized with respect to their shape applying mathematical shape parameters. Numerous parameters converting quantitative geometrical values of grain-radius, -diameter, -area or -perimeter to grain shape are described in the literature (i.e. aspect ratio [40], circularity [41], convexity [42], eccentricity [43], projection shape factor [44], projection sphericity [45], radial shape factor, roughness factor [44], solidity [42], surface roughness [43]).

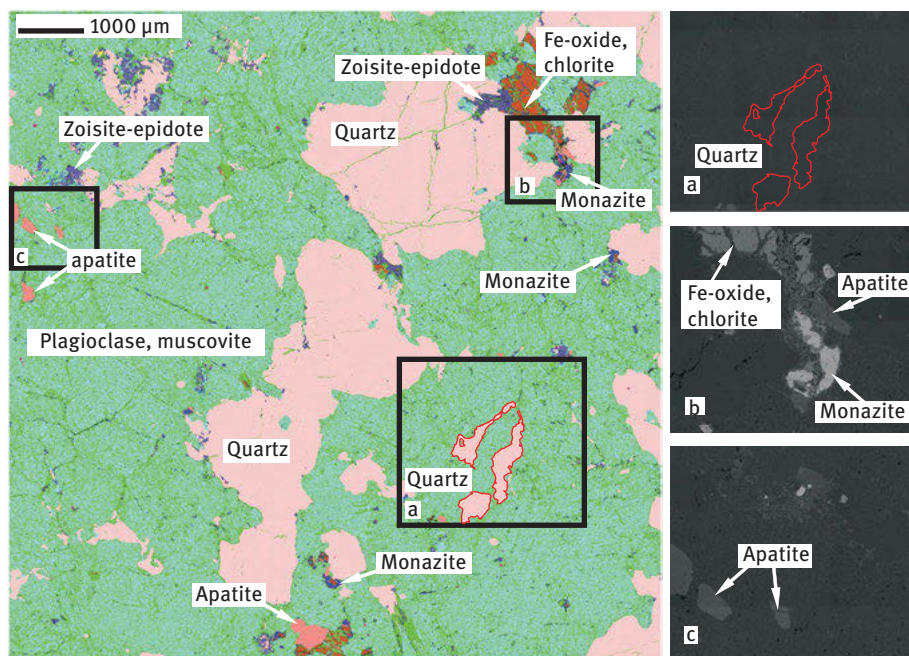


Figure 11.3: Mineral map (QEMSCAN fieldscan image) of a monazite (REEPO_4) bearing rock. Minerals are indicated by colour coding as shown in the image (apatite = dusky pink, chlorite = dark green, Fe-oxide = brown, monazite = dark blue, muscovite = light green, plagioclase = cyan, quartz = pink, zoisite-epidote = lavender). The sample areas of insets a, b and c are alternatively displayed as BSE image on the right side. The REE-mineral monazite is characterized by a high density compared to other phases and thus shows highest BSE intensity. Contours of three quartz grains are highlighted by red lines in inset a. BSE scaling appropriate for distinction of minerals with elevated density (e.g. apatite, Fe-oxide and monazite) in insets b and c is not suitable for distinction of lighter phases like muscovite, plagioclase and quartz, which dominate in inset a.

Image data can also be used for the quantification of textural parameters that describe orientation as well as contact relationships or mineral associations. Orientation can be expressed as a statistics on the angles of long axes of elongated particles. Pixels along shared boundaries of two phases can be counted yielding a statistics of mineral associations if applied to all mineral grains forming contacts in a rock sample (Figure 11.4).

Finally, quantitative image analysis data can be combined to derive parameters that are directly applicable to processing of ores and to the evaluation of beneficiation processes. Mineral liberation serves as a good example. It may be either defined as the modal proportion of an ore mineral in a particle or as the proportion of an ore mineral boundary, which is associated with the mounting resin to the total boundary of a particle. The latter indicates the free surface of an ore mineral amenable to processing operations (e.g. flotation, hydrometallurgy).

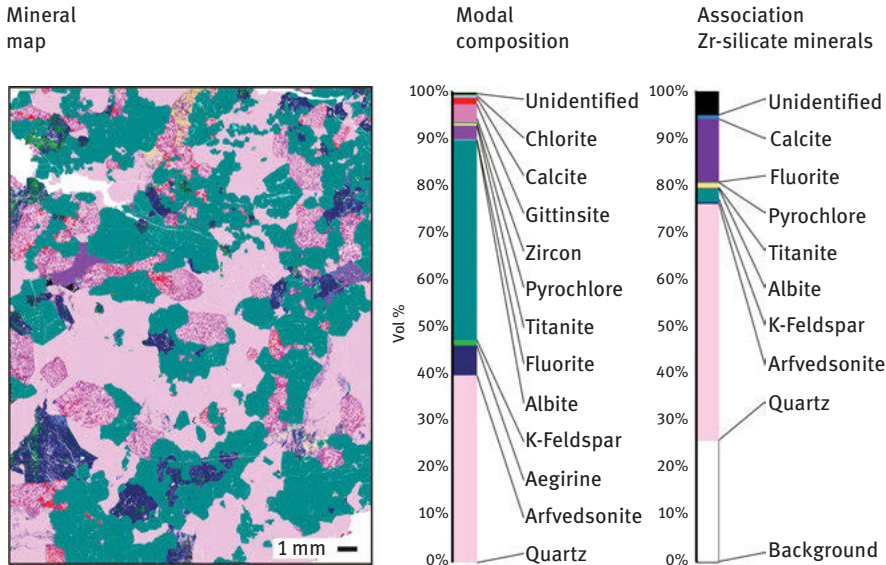


Figure 11.4: Example of a mineral map and first steps of image analysis leading to quantification of modal composition and mineral association obtained by automated analysis (QEMSCAN fieldscan image) of an alkaline granite, which is mainly composed of the minerals K-feldspar (dark cyan), quartz (pink) and arfvedsonite (navy blue). Postmagmatic alteration caused abundant formation of the silicates gittinsite ($\text{CaZrSi}_2\text{O}_7$, red) and zircon (ZrSiO_4 , magenta) as well as pyrochlore ($\text{Ca}_2\text{Nb}_2\text{O}_7$, dark green), which are major ore minerals for the rare metals Zr and Nb. Observation indicates that Zr-silicates occur in clusters of fine grains that are mainly hosted by quartz.

Quantification of pixels assigned to different minerals allow to calculate the modal composition in vol.-%. The association of the Zr-silicate minerals gittinsite and zircon with other phases is quantified by the number of pixels sharing boundaries with image pixels representing Zr-silicate phases. This yields quantitative confirmation of the observation showing quartz as major host of Zr-silicate aggregates. Furthermore, fluorite is also indicated as important phase associated with Zr-silicates. This is valuable information not only for an investigation of ore forming processes but also for studies to improve beneficiation, which make mineral processing more efficient and environmental friendly [16, 19, 46].

11.4.2 Analytical systems

11.4.2.1 Semi automated image analysis of SEM data

Numerous concepts exist to apply image analysis of BSE intensity and element distribution maps for mineral determination, petrography or ore characterization. While

some are specifically designed to handle data obtained from SEM or EMP, e.g. XRMapAnal [47], others are based on algorithms for general image analysis, e.g. ImageJ [48], or otherwise applied for multispectral remote sensing data, e.g. ArcGIS ESRI, Erdas Imagine, Multispec [48, 49]. Many of these approaches do not allow control of SEM stage or data acquisition. They require a user controlled transfer of element map data from SEM to image analysis software and are based on case specific adjustments for segmentation and phase assignment. Hence, such concepts can better be characterized as semi-automated [47] and will not be considered here in more detail.

11.4.2.2 First generations of automated mineralogy systems

As outlined by Sandmann [50] early generations of SEM based automated analytical systems were developed starting in the late 1960's by the Royal School of Mines London, UK (Geoscan-Minic), the Pennsylvania State University, USA (CESEMI) and by the Commonwealth Scientific and Industrial Research Organisation (CSIRO) in Australia in the middle of the 1970's as QEM*SEM automated mineragraphy [30, 35, 51]. A later version was commercialized as QEMSCAN (Quantitative Evaluation of Minerals by Scanning Electron Microscopy) by Intellection Pty Ltd. and FEI Company until 2015 when further development stopped. The MLA (Mineral Liberation Analyzer) was developed by the JKMRC (Julius Kruttschnitt Mineral Research Centre, University of Queensland) in the 1990's and later also provided by the FEI Company. In contrast to QEMSCAN, which performs phase assignment on the basis of BSE and spectral data obtained pixel-by-pixel (see Figure 11.2a – d), MLA achieves segmentation mainly using BSE imaging and final phase assignment on a limited number of spectral analyses on spots indicated in the segmented image (see Figure 11.2a, e, f, g) [34, 52, 53]. Both systems, which originally were developed to support Australia's growing mining industry have for long time been dominating the international automated mineralogy technology market [35, 50]. Hence, a large number of publications demonstrates the applicability of both, MLA and QEMSCAN, for many different geoscientific and mining related fields, e.g. exploration and process mineralogy [53–62], sediment and coal petrography [63–66], metamorphic petrology [67], environmental mineralogy [68].

A comprehensive literature overview and more details on the history of automated SEMs as well as a detailed overview of additional and mainly non-commercial systems developed in industry and academic institutions in the last 50 years is given by [50].

11.4.2.3 Current automated mineralogy systems

The Advanced Mineral Identification and Characterization System (AMICS) was originally developed by Yingsheng Technology (Darra, Australia) and is now distributed by **Bruker Nano GmbH** (Berlin, Germany). It consists of the QUANTAX EDS system as

well as of the AMICS software and can be linked to various scanning electron microscope platforms. Details of sample preparation, analytical modes and application to gold ore characterization are described by [18]. Zhang et al. [69] use the system in a process mineralogy study to optimize the extraction of rare alkaline elements from a lepidolite ore mineral concentrate.

Oxford Instruments (Abingdon, UK) offers a combination of automated mineralogy software and energy dispersive silicon drift detectors (X-Max^N) that can be operated on SEMs of different manufacturers. The Aztec feature SEM software platform for particle analysis completed by the AZTec Mineral or the earlier version INCA Mineral performs automated acquisition of BSE data for segmentation and separation of grains as well as of spectral EDS data from individual grains for phase assignment. The system can be extended with an electron backscatter diffraction (EBSD) detector for simultaneous generation of microstructural information, which can be used to support grain boundary identification. Applicability to process-mineralogy and geometallurgy was shown in recent studies [70, 71].

Tescan (Tescan Orsay Holding a.s., Brno-Kohoutovice, Czech Republik) produces the automated mineralogy system TIMA-X (Tescan Integrated Mineral Analyzer). The hardware basis is either formed by a MIRA field emission or a VEGA thermal emission SEM equipped with SE, BSE and up to four EDS detectors. In addition a detector for simultaneous recording of cathodoluminescence (CL) data or a Raman spectroscopy system can be added. Sample exchange can be carried out in an unattended way by the Automated Loading System. The software offers various modes of data acquisition combining BSE mapping and spectral analysis at different spatial resolution using various point patterns [28]. The TIMA-X software has pre-defined reporting tools supporting petrographic and textural studies as well as ore characterization or process mineralogy. It is in detail described by [28]. In the last years, the TIMA system has been applied to various geoscientific fields, such as ore geology, sedimentary and igneous petrology, palaeontology, environmental as well as process mineralogy [28, 72–74].

The Maps Mineralogy Software by **Thermo Fisher Scientific Inc.** (Waltham, Massachusetts, USA) is one of the latest developments in the field of commercial automated mineralogy systems. In combination with a Thermo ScientificTM Apreo or other SEMs of this company it allows simultaneous detection of BSE, EDS and CL data. The system offers various signal acquisition modes but mainly performs phase assignment on the basis of spectral information. In order to make use of the higher resolution that can be obtained in BSE images the spatial resolution of chemical information, which is physically limited by the interaction volume of the electron beam, is also enhanced. This approach is based on the deconvolution of mixed EDS signals and identification of mineral phases and their relative proportions in the interaction volume.

The Mineralogic Mining System was released by **Zeiss** (Carl Zeiss Microscopy GmbH, Jena, Germany) in 2014. It can be run on different SEM platforms offered by the company (e.g. Zeiss EVO, Zeiss SIGMA HD). The software allows various modes of data acquisition [75]. Mineral classification can be performed using BSE greyscale values as

well as in combination with X-ray spectra that are acquired by one or more EDS detectors for all image pixels. Prior to phase assignment X-ray data are transferred to quantitative element concentrations [75, 76]. Element wt.-% values are then compared to minimum and maximum ranges indicative of phases of interest listed in a database. The use of quantitative values (i.e. data directly related to mineral stoichiometry) makes phase assignment independent of instrumental parameters affecting the EDS spectrum (e.g. acceleration voltage, [75]). To enhance the volume of information and to support phase identification the system allows the correlation of SEM data with images obtained from external sources (e.g. polarization light and cathodoluminescence microscopy, 2D virtual slices through 3D X-ray tomographic datasets, [76]).

Some manufacturers or consultancy companies offer SEM based automated mineralogy systems, which are portable and adapted to oil and gas well-site or mineral processing plant conditions, addressing the needs of the industry.

11.5 Quantitative REE mineralogy

REE-minerals, i.e. phases in which REE + Y are the dominant atoms within a single set of crystal-structural sites [77], and other REE-rich minerals show a large range of compositions. This can be observed for the elements of the lanthanide group, but also for other high-field-strength-elements (e.g. Ti, Y, Zr, Nb, Th, U) and for other metals and metalloids with lower charge (e.g. Na, Ca, Sr, Ba, Al, Fe, Si). Many elements have an ionic character or form anionic groups in crystal structures of REE-minerals (e.g. O, OH, F, Cl, CO₃, PO₄, SiO₄, SO₄, VO₄, AsO₄). Accordingly, REE-minerals or REE-rich minerals occur in many mineral classes, such as the silicates, oxides, carbonates, phosphates, halogenides, arsenates, vanadates or sulphates [78]. REE-minerals are thus chemically highly variable and show complex formulae.

Owing to mainly identical charges (3⁺) and/or minor variations in ionic radii, various REE isostructurally substitute each other or other elements (Na, Ca, Th) in mineral phases [77]. Most REE minerals are thus characterized by a range of chemical compositions rather than by one specific stoichiometry.

Enhanced growth of such minerals and formation of REE ores often takes place in poly-stage magmatic to hydrothermal or supergene processes leading to polymineralic associations of fine grained and intricately intergrown mineral phases [19, 79]. Figure 11.5 displays examples of different REE-ore minerals and their complex textures.

These material characteristics represent a major obstacle to efficient processing of such ores. Quantitative data reflecting the mineralogical, chemical and textural diversity and heterogeneity of REE-ores is thus not only desirable for the study of ore formation, it is indispensable for the success of beneficiation processes and later metallurgical extraction of REE [14]. Therefore, quantitative mineralogical data also represents a key to environmental friendly and responsible sourcing of the REE [80].

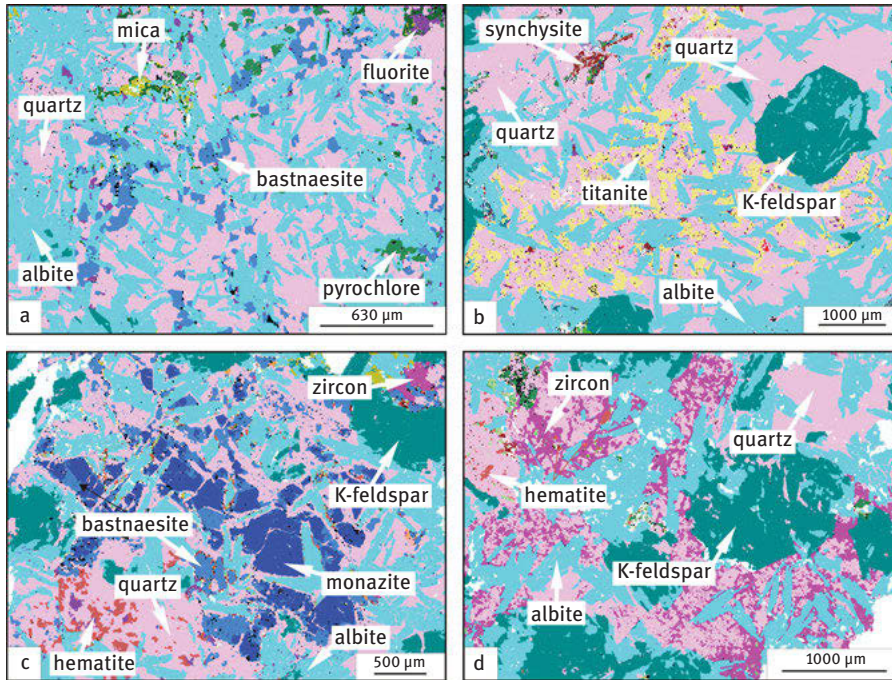


Figure 11.5: Examples of different REE-ore minerals from the alkaline granite hosted Zr-REE-Nb deposit of Khalzan Buregtei (Mongolia). All images were obtained with a QEMSCAN system. a) Bastnaesite, a LREE-fluoro-carbonate mineral intergrown with lath shaped albite and quartz. b) Y-rich REE-fluoro-carbonate synchysite-(Y) associated with Na- and K-rich feldspars, albite and K-feldspar, respectively, Ca-Ti-Nb-silicate titanite and quartz. c) LREE-phosphate monazite in part replaced by LREE-fluoro-carbonate bastnaesite. d) fine grained intergrowth of quartz and zircon. The latter is one of the important carriers of HREE in the deposit [19].

Automated mineralogy systems are highly appropriate to generate such data and hence have increasingly been applied in the last years in REE deportment and process mineralogical studies of REE ores from various deposit types, e.g. peralkaline intrusive rocks, carbonatites and their weathering products or placers [2, 19, 37, 81–84].

Identification and separation of different minerals on the basis of BSE and spectral signals excited by an electron beam are a prerequisite for successful application of an automated mineralogy system. Owing to the presence of REE and eventually other HFSE the REE-minerals are characterized by relatively high BSE intensities, which can easily be filtered by setting an appropriate BSE threshold (e.g. bright phase search, [28]). Acceleration voltages of 15 to 25 kV applied in SEMs allow excitation of characteristic L- and M-radiation of the REE. Despite of potential overlap with K-lines of elements ranging between V to Ni the REE L-lines can in many REE minerals be detected. However, characteristic L-lines of the REE are confined to a short interval, e.g. energies of La L α and Lu L α vary only between 4.651 and 7.654 keV. This leads to substantial interference among

the REEs. It precludes the determination of REE patterns which could be applied for differentiation of REE minerals. Rather, either single and very prominent REE signals (e.g. Ce K α) or the entire group of REE signals are recorded for the purpose of automated mineralogy. Next to the detection of the bulk REE, identification of REE minerals is mainly based on the additional detection of other elements, or combinations of elements, that are major constituents of these phases (e.g. Ca, Si, F, P, [37, 85]).

However, due to compositional variabilities of REE minerals, the capabilities of REE mineral identification in automated mineralogy can be limited. This is illustrated using the common fluoro-carbonate REE-ore minerals parisite and synchysite, which can in a simplified way be expressed as $\text{CaREE}_2(\text{CO}_3)_3(\text{F}, \text{OH})_2$ and $\text{CaREE}(\text{CO}_3)_2(\text{F}, \text{OH})$, respectively. They do not only show incorporation of the different lanthanoids La, Ce, Pr, Nd or Sm but also replacement of these elements by Y and Th as well as of Ca by other elements such as Sr, Ba or Fe. A review of published data [86–89] on these minerals reveals the following compositional ranges for both minerals (in part recalculated for $\text{Ca} + \text{Sr} + \text{Ba} + \text{Fe} = 1$ per 3 CO_3):

Parisite: $\text{Ca}_{0.89-1.00}\text{Sr}_{0.00-0.04}\text{Ba}_{0.00-0.09}\text{Fe}_{0.00-0.03}\text{La}_{0.29-0.67}\text{Ce}_{0.77-1.16}\text{Pr}_{0.08-0.11}\text{Nd}_{0.18-0.37}\text{Sm}_{0.01-0.05}\text{Eu}_{0.00-0.01}\text{Gd}_{0.00-0.02}\text{Y}_{0.00-0.04}\text{Th}_{0.00-0.01}(\text{CO}_3)_3(\text{F}, \text{OH})_2$

Synchysite: $\text{Ca}_{0.89-1.00}\text{Sr}_{0.00-0.03}\text{Fe}_{0.00-0.03}\text{La}_{0.24-0.39}\text{Ce}_{0.47-0.53}\text{Pr}_{0.03-0.06}\text{Nd}_{0.08-0.19}\text{Sm}_{0.01-0.02}(\text{CO}_3)_2(\text{F}, \text{OH})$

Calculated fluorescence spectra representative of these variable compositions obtained in an SEM analysis are displayed in Figure 11.6. In accordance with the mineral stoichiometry parisite is characterised by higher signals of REE as well as F and lower signals of Ca compared to synchysite. However, the signal ranges of La, Ce, Pr and Nd for both minerals show an overlap. Furthermore, automated quantitative mineralogical systems dominantly use spectral information from limited photon counts (e.g. 1000–10000) for phase assignment – independent of the software solutions offered by different companies. Thus, counting statistics, detector noise as well as surface effects lead to uncertainty of signal intensity. In consequence, chemical variability of REE minerals as illustrated by the example in Figure 11.6 and analytical uncertainty can reduce the performance of mineral distinction and phase assignment. In such cases, minerals that cannot be distinguished have to be combined in a group or groups of phases [37, 85].

Monazite (REEPO_4) is one of the most important ore minerals for light REE (Figure 11.5abcd). It is an important constituent of magmatic as well as of placer deposits and belongs to the first mineral phases used for extraction of REE [1].

In addition to a quantitative evaluation of a REE ore, which implies the determination of the modal abundance of monazite or other REE minerals, it is important to understand ore-forming processes. The definition of parameters controlling monazite stability that are indicated by monazite-forming as well as by monazite-consuming mineral reactions is a valuable basis for such study. This is illustrated in Figure 11.7, which displays details of the QEMSCAN image in Figure 11.3 showing a monazite bearing metamorphic rock.

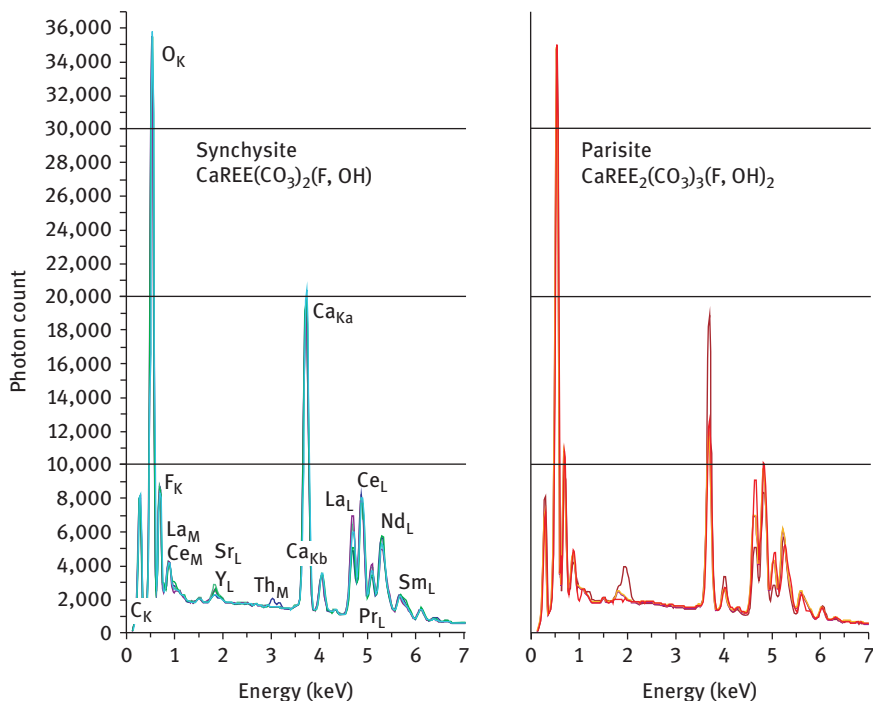
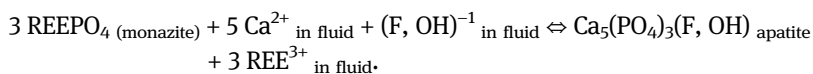


Figure 11.6: Fluorescence spectra of synchysite and parisite, calculated for mineral compositions published by [86–89], calculation performed with the iDiscover® software by Thermo Fisher Scientific Inc. (formerly distributed by FEI-company) assuming an acceleration voltage of 15 kV. The indices K and L denote spectral information belonging to the K- and L-series, respectively. Only in the case of Ca K_α (K_α) and K_β (K_β) radiation is indicated.

Monazite (REEPO₄) shown by dark blue colour coding is surrounded by a corona of apatite (Ca₅(PO₄)₃(OH, F) (dusky pink), which formed by a breakdown reaction indicating the limit of monazite stability. The reaction can be formulated in a simplified way as:



The abundance of apatite thus could be considered as an indicator for this breakdown reaction, which was probably triggered by a retrograde albitization of plagioclase releasing Ca²⁺ to the fluid. However, the image shows that next to fine grained and irregularly shaped apatite from the coronas a second type can be observed. Apatite of this type, which is texturally not associated to monazite and which forms larger rounded grains with smooth boundaries is genetically not related to monazite. Rather, it belongs to the original metamorphic assemblage.

Both types of apatite must be distinguished in order to indicate apatite as monazite breakdown product, which has the potential to inherit REE of the monazite. Shape parameters allow transferring the descriptive characterization of both types to measurable numeric data in an automated quantitative mineralogical approach that is independent of the experience or optical impression of a mineralogist performing individual microscopic grains inspection.

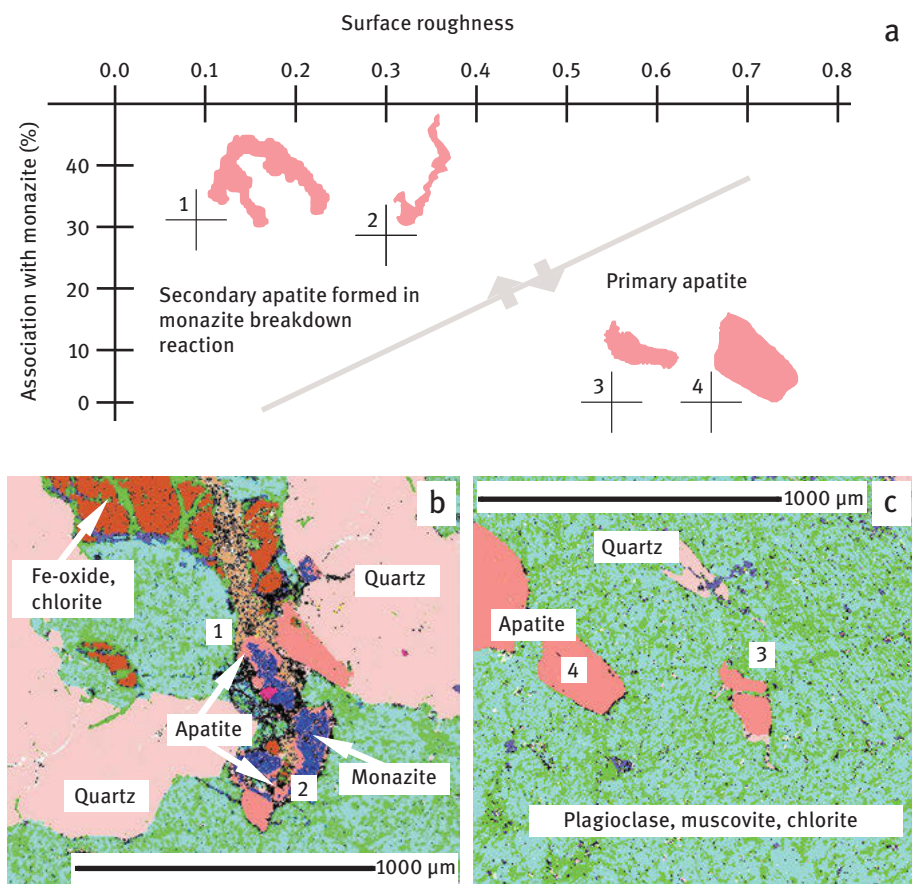


Figure 11.7: Example of image analysis applied to the distinction and quantification of primary apatite and apatite formed by breakdown of monazite. a) grains 1–4 are characterized by the parameters association and surface roughness. Association indicates the proportion of monazite pixels in contact with an apatite grain in % of the total amount of pixels defining the perimeter of the apatite grain. The surface roughness is defined as $(2 \times \pi \times (\text{area pixels} / \pi)^{1/2} / \text{perimeter pixels})$. Apatite formed by reaction of monazite (grains 1 and 2) is characterized by high association and low surface roughness values. b) Position of apatite grains 1 and 2 in a reaction rim around monazite, sample area is identical to inset b in Figure 11.3. c) Examples of primary metamorphic apatite grains (3 and 4) in a matrix composed of plagioclase and muscovite with minor chlorite, sample area identical to inset c in Figure 11.3.

The surface roughness parameter compares the actual perimeter of a grain (formed by neighbouring pixels of the same kind) with the perimeter of a circle with equivalent area quantified by the amount of pixels representing the grain. Thus the regularly shaped apatite grains with smooth boundaries, which belong to the metamorphic assemblage are characterised by high roughness parameters close to 1, whereas the irregularly shaped apatite grains forming the coronas around unstable monazite yield low roughness parameters < 0.4 .

Grain association is another parameter of image analysis that can be applied for discrimination of both types, because apatite formed by monazite breakdown generally is in contact with monazite. In contrast, metamorphic apatite is almost exclusively associated to other minerals than monazite.

A combination of both parameters, roughness and association, thus provides a criterion for visualization of textural complexity and automated discrimination of both types of apatite, which is illustrated in Figure 11.7. In a series of samples image analysis could be applied to quantify volumes of both reaction partners and consequently to show progress of monazite breakdown.

11.6 Concluding remarks

Starting with concepts from the 1960's SEM based automated quantitative mineralogy is a field that has shown significant progress in the last years due to an increasing number of new hard- and software developments of SEM and detector manufacturers. It is a valuable tool to quantify mineralogical and textural rock properties and therefore broadly applied in petrographic studies, ore evaluation or process mineralogy.

Enhanced crystallization of REE minerals during ore formation is mainly linked to a polystage succession of magmatic, post-magmatic or even weathering processes, which makes REE ores mineralogically and texturally exceptionally complex. The examples shown in this chapter underline the capabilities of SEM based automated systems for quantitative mineralogical characterization in particular for complex polymineralic REE mineral assemblages. As REE ore processing strongly depends on such data automated mineralogy is indispensable for efficient and environmental friendly ore beneficiation and extraction of the REE, which still show increasing demand in the world.

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Part III: **Application of rare earth elements analysis**

Sven Sindern, Tobias Fusswinkel

12 Analysis of rare earth elements in rock and mineral samples by ICP-MS and LA-ICP-MS

Abstract: The group of the REE serves as valuable indicator of numerous geological processes such as magma formation or fluid-rock interaction. The decay systems of the radioactive REE isotopes ^{138}La , ^{147}Sm and ^{176}Lu are used for geochronometric dating of a range of events, starting from first steps of planetary formation to younger stages of geodynamic development. Thus, the abundance of all REE occurring in a large range of concentrations as well as precise isotope ratios must be analysed in different geomaterials.

The inductively coupled plasma (ICP) ion source and various types of mass spectrometers (MS) represent the basis to fulfil the analytical requirements of geoscientific studies. Today, ICP-quadrupole MS (QMS), ICP-sector field MS (SF-MS) with a single detector or multiple ion collection (MC-ICP-MS) are standard instruments for REE analyses in the geosciences. Due to a need for in situ analysis, laser ablation (LA) –ICP-MS has become an important trace element microprobe technique, which is widely applied for determination of REE concentrations and isotope compositions in geoscientific laboratories.

The quality of concentration analysis or isotope ratio determination of the REE by ICP-MS and LA-ICP-MS is affected by many parameters. Most significant are interferences caused by polyatomic oxide and hydroxide ion species formed in the plasma as well as fractionation effects leading to non-stoichiometric behaviour during element determination or to biased isotope ratio measurements. Laser induced fractionation and isobaric interferences have to be considered as additional effects for LA-ICP-MS. As analyte elements and matrix are unseparated mineral standards matching the matrix of samples are a prerequisite for accurate and precise REE concentration and isotope ratio determination. Application of fs-lasers instead of the more common ns-lasers in LA-ICP-MS systems turns out to be a significant step to reduce laser induced fractionation and to overcome effects of sample matrices.

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12.1 Introduction

In nature, the rare earth elements (REE, i.e. lanthanides) are an ubiquitously distributed group of elements and present in many earth materials, although at low concentration. Ranked by abundance in the earth's crust ([1], noble gases not considered) they rank between position 24 (Ce, 60 µg/g) and 61 (Tm, 0.3 µg/g). Their concentrations are similar to those of common metals such as Zn (65 µg/g), Ni (56 µg/g), Cu (25 µg/g) and Pb (14,8 µg/g) but significantly higher than the concentrations of precious metals like Ag (0.07 µg/g), Au (0.0025 µg/g) or Pt (0.0004 µg/g), [1]. Only within a rare but complex group of minerals, the REE reach major element levels.

The geochemical behaviour of the REE is controlled by their ionic radii, charge and complexation behaviour [2]. Owing to their electron structure and progressive filling of the 4f orbitals the REE are characterized by the principal oxidation number of +3 and a steadily decreasing ionic radius with increasing atomic number (lanthanide contraction). Accordingly, within the group of the REE slightly different geochemical properties can be observed leading to gradually varying smooth distribution patterns (e.g. [3, 4]) that are characteristic of different rock types (Figure 12.1). Exceptions to this behaviour can be observed for Ce and Eu, which may adopt the oxidation numbers +4 and +2, respectively, depending on the geochemical system. Furthermore, smoothly varying REE patterns can show significant perturbations as a consequence of fractionation caused by contrasting complexation behaviour of different REE. This is a function of the electron configuration of different REE as well as of the type of the complexing ligand and thus of the geochemical environment in which a mineral or rock was formed [2].

The group of the REE thus serves as highly valuable indicator of numerous geological processes like magma formation and differentiation [9], as well as interaction of hydrothermal fluids and rocks including the formation of ore deposits, e.g [2, 10]. The REE can also reflect redox conditions in magmatic, hydrothermal or sedimentary systems (e.g. [11, 12]), and more and more they show the anthropogenic emission of REE used in medical or technical applications to natural environments [13–15], Figure 12.1.

Three of the REE (i.e. La, Sm and Lu) have natural radioactive isotopes with half-lives in the order of magnitude of the earth's age. Thus, considerable decay of the radioactive parent isotopes (^{138}La , ^{147}Sm and ^{176}Lu) and increase of the radiogenic daughter isotopes (^{138}Ce , ^{138}Ba , ^{143}Nd and ^{176}Hf) occur within the timescale of the earth's history and can be used for geochronometric dating, starting from first steps of planetary formation taking place after onset of solar system condensation, to crust formation and younger geodynamic or ore forming events [16–27]. Figure 12.2 illustrates the concept of the Sm-Nd isochron dating of a metamorphic rock. Application of the ^{138}La - ^{138}Ce / ^{138}Ba -, ^{147}Sm - ^{143}Nd - and ^{176}Lu - ^{176}Hf -decay systems requires determination of isotope ratios, particularly in minerals that strongly fractionate the parent over the daughter isotope [28, 29]. To use the latter decay system, Hf isotopes must be analysed, which is addressed in this chapter, too, although this element does not belong to the REE.

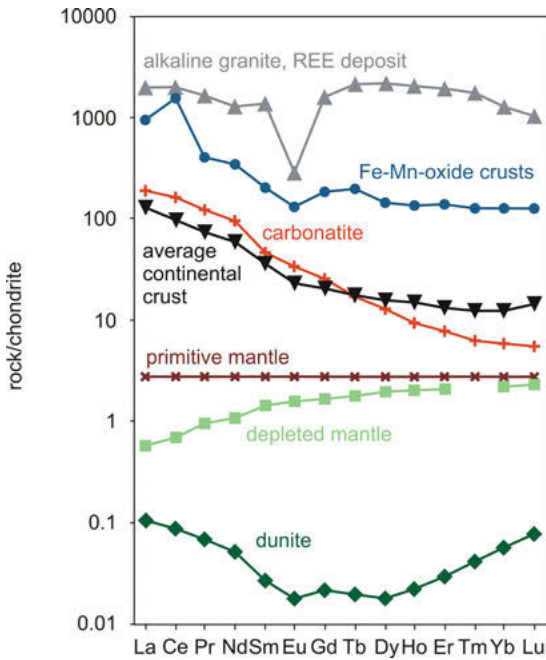


Figure 12.1: Chondrite-normalized REE patterns for major domains of the silicate earth and different rock types indicative of geological formation processes, chondrite values of [5]. Diverging patterns of the average continental crust [1] and depleted mantle [6] relative to primitive mantle [5] reflect REE fractionation during formation of magmatic melts. Dunites (values of DTS-1 by [7]) are residual rocks of the earth's mantle formed after extraction of melts. Carbonatites [2] and alkaline granites [8] represent melts ascending in the crust. They can enrich REE and form deposits of these elements. Fe-Mn-oxide crusts are precipitates of seawater [2] and reveal REE fractionation due to differences in marine particle reactivity. In particular, they show fractionation of Ce due to precipitation of CeO_2 .

For the application of the short-lived ^{146}Sm - ^{142}Nd decay system for the study of early differentiation of the earth, see [30, 31].

Furthermore, stable isotopes may also show isotopic fractionation serving as indicator of a natural process. Slight anomalies of the $^{153}\text{Eu}/^{151}\text{Eu}$ ratio in meteorite samples are interpreted to reflect early stages of planetary history, such as magnetic separation processes in the early ionized fraction of the solar nebula [32].

In nature, REE concentration patterns as well as isotope compositions can vary on a mineral grain scale. Complexly zoned REE-rich minerals, such as zircon, monazite or garnet, can therefore serve as monitor for major geodynamic processes, e.g. crust formation or growth and collapse of mountain chains [34, 35], if they are studied in detail.

These brief explanations show that a large range of analytical capabilities is required for the study of the REE in geosciences. Usually all members of the group of REE must be addressed in determination of element concentrations in order to

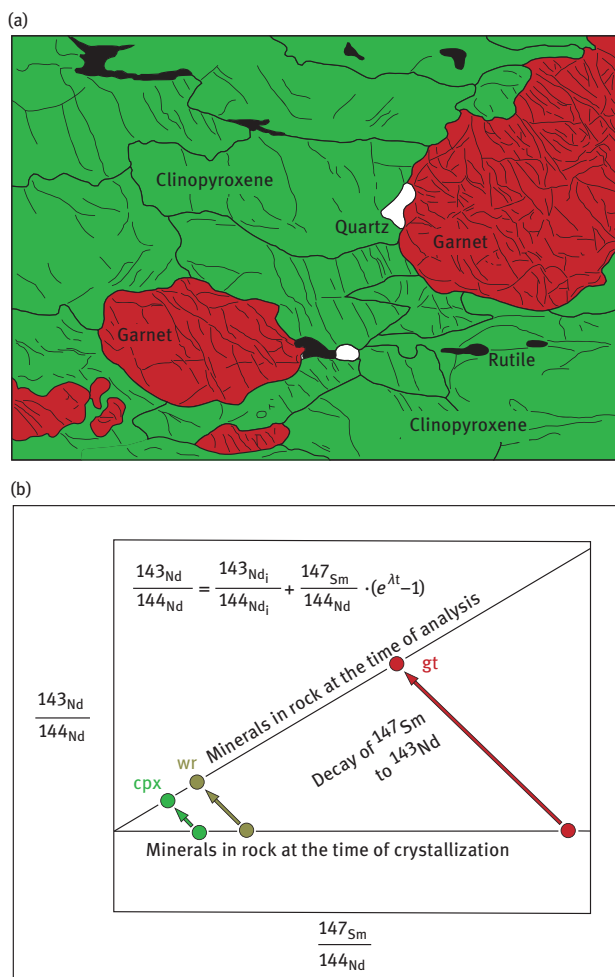


Figure 12.2: Samarium-neodymium isochron dating of rock formation. (a) eclogite – a metamorphic rock formed during subduction of oceanic crust – composed of the minerals clinopyroxene (green), garnet (red) with minor amounts of quartz (white) and rutile (black), sketch drawing according [33]. (b) isochron diagram showing the principles of dating using the ^{147}Sm - ^{143}Nd system according to the decay equation displayed in the upper part of the diagram. The index “i” indicates the initial ratio of $^{143}\text{Nd}/^{144}\text{Nd}$ present at the time of crystallization of the rock, and λ denotes the decay constant of ^{147}Sm ($\lambda = 6.54 \times 10^{-12} \text{ y}^{-1}$, e.g. [20]). Rock-forming minerals, garnet (gt) and clinopyroxene (cpx), accessories (not considered) and accordingly also a whole rock sample (wr) initially are at isotopic equilibrium during formation of the eclogite (i.e. at metamorphic crystallization) and plot on a horizontal line. Due to radioactive decay of ^{147}Sm to ^{143}Nd the isotopic signatures of mineral fractions and whole rock shift in an undisturbed system to a position on a line with positive slope – the isochron. Its slope ($e^{\lambda t} - 1$) indicates the time elapsed since rock formation and can be calculated after determination of $^{147}\text{Sm}/^{144}\text{Nd}$ and $^{143}\text{Nd}/^{144}\text{Nd}$ ratios [20, 28].

reveal the characteristic distribution patterns. Thus, the concentration range between several wt.-% down to the sub- $\mu\text{g/g}$ or ng/l level has to be covered in different earth materials like minerals, bulk rock or soil samples as well as natural water. Furthermore, precise determination of isotope ratios is a prerequisite for application of the ^{138}La - $^{138}\text{Ce}/^{138}\text{Ba}$ -, the ^{147}Sm - ^{143}Nd - and ^{176}Lu - ^{176}Hf -decay systems or for the investigation of fractionation of heavy stable isotopes (e.g. $^{153}\text{Eu}/^{151}\text{Eu}$). Both, element as well as isotope analyses, are performed on bulk samples after chemical processing but also in-situ using probe techniques, which allow analytical work with high spatial resolution. The inductively coupled plasma (ICP) ion source and various types of mass spectrometers (MS) represent the basis to fulfil the analytical requirements in the geosciences. This will be addressed in the following sections of this chapter. The important role of ICP-MS and laser ablation (LA) as efficient technique for sample introduction and in situ analysis of solid matter to fulfil the analytical requirements in the geosciences are highlighted.

12.2 Technical development

Starting in the 1980's ICP-Quadrupole MS (ICP-QMS) has become the standard instrument for REE analyses in the geosciences. Within a few years ICP-QMS based analytical procedures replaced instrumental neutron activation analysis or procedures applying isotope dilution thermal ionization mass spectrometry (TIMS), which represented the standard methods since the 1960's. The most important advantages of ICP-QMS were lower acquisition and operating cost, relatively low duration of analysis and large sample throughput as well as the option to cover all REE in one step [36–41].

The combination of the ICP ion source with magnetic sector field (SF) mass filters represented a major step in the field of isotope geochemistry and cosmochemistry [42, 43]. Owing to the flat top peak signals and the ability of the plasma source to ionize most elements, ICP-SFMS systems allow precise isotope ratio measurements also for poorly ionizing elements, such as Zr, Hf or W. In particular, geochronometry applying the Lu-Hf system was limited due to insufficient sensitivity of conventionally used thermal ionization mass spectrometry for Hf [16]. The application of multiple ion collection (MC) in MC-ICP-SFMS instruments and simultaneous mass detection was a further step to enhance the precision of isotope ratio measurements [44, 45].

In contrast to quadrupole mass spectrometers, double-focussing ICP-SFMS systems, either with multiple or single ion collection, can be operated with significantly higher resolution at still reasonable sensitivity [46, 47]. Despite of prices approximately more than 5 times higher than those of quadrupole instruments, (MC)-ICP-SFMS have become common equipment in most isotope geochemistry laboratories worldwide. In the last years instruments with tandem configuration have become technically more evolved and commercially available. In such mass spectrometers, a

further quadrupole mass filter is placed between the interface and that quadrupole or octopole, which serves as reaction or collision cell. This allows a control of ionic species that enter the cell, which enhances the efficiency of the reaction or collision process and improves the performance of the main quadrupole [48].

Due to particular need for in situ trace element and isotope ratio determination with high spatial resolution, laser ablation (LA)-ICP-MS has become an important technique in geosciences. After first steps in the late 1980's [39, 49–51], the potential of a technique for REE analysis avoiding the step of sample dissolution was intensively explored [52–54]. Time-of-flight mass spectrometers (ICP-TOFMS), which almost simultaneously acquire complete mass spectra [55], represent an alternative to ICP-QMS and ICP-SFMS in LA-ICP-MS instrument set ups. Due to limited ion counting rate and low sensitivity of such mass spectrometers LA-ICP-TOFMS systems have not been as effective as those applying QMS or SFMS analyzers [56]. Owing to technical developments of the last years, however, LA-ICP-TOFMS shows capabilities to determine concentrations of trace elements (including the REE) that are comparable to other LA-ICP-MS instruments or even superior if only small sample volumes are available [55] and references therein [57]. Simultaneous and fast detection of mass spectra can also be performed by array detector Mattauch-Herzog (MH-MS) and distance-of-flight mass spectrometers (DOF-MS), which thus have been considered as promising instruments for LA systems [58–60]. However, geoscientific applications so far are rare [61].

In comparison to secondary ionization mass spectrometry (SIMS), which has comparable analytical capabilities and which can also be considered an alternative method, LA-ICP-MS requires larger spot sizes but is significantly cheaper, faster and does not require vacuum [62]. LA-ICP-MS thus turned out to be one of the “most affordable and most widely applicable trace element micro probe” techniques in geoscientific laboratories [60, 63, 64].

For LA-ICP-MS analysis a pulsed high-energy laser beam is focused on the surface of a solid sample, which is placed in an air-tight sample chamber flushed with a carrier gas (Figure 12.3). Irradiation causes release of aerosol particles from the sample surface, which are transported to the ICP ion source in which they are vaporized and finally ionized (e.g. [63, 65] and references therein). Helium allows better uptake of aerosol particles than Ar and supports more complete vaporization of the aerosol in the plasma [66]. It therefore usually serves as carrier gas [67, 68]. Admixture of water to the sample aerosol enhances vaporization and thus increases sensitivity [66]. Small flows of other gases (e.g. N₂, H₂) may be added to the carrier gas to suppress oxide formation and to enhance sensitivity [69, 70].

Improvements of instrument sensitivity and stability as well as of sample chamber design in the last years allow to split the carrier gas flow and to transport the laser aerosol to two different instruments. Using such laser-ablation split-stream (LASS) setup different analytical tasks (e.g. determination of isotope ratios, trace element composition) can be performed simultaneously [71, 72].

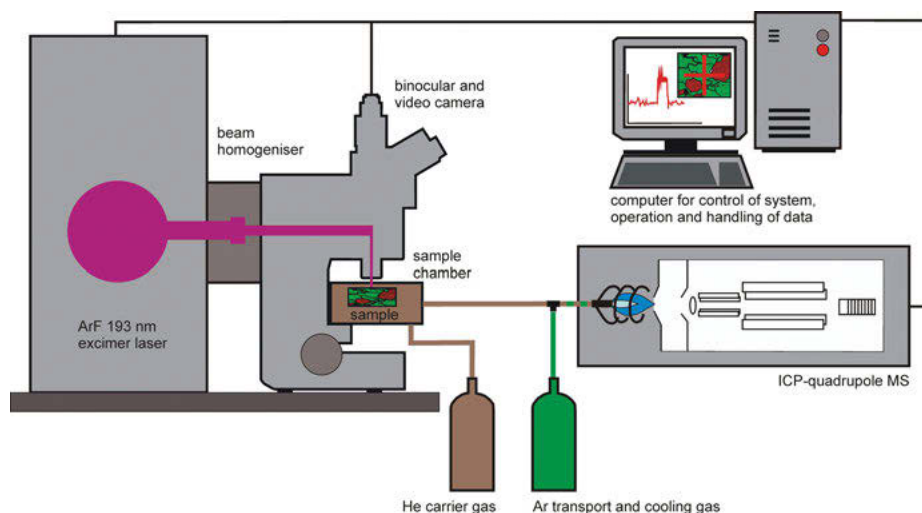


Figure 12.3: Schematic diagram of a common LA-ICP-MS system based on a ns-ArF excimer laser and an ICP-QMS, not to scale.

After intensive technical development in the last 25 years different lasers providing pulsed laser light are used in LA-ICP-MS systems. Lasers differ with respect to the pulse length, which can be in the range of 3–20 ns (ns-lasers) or in the sub-picosecond range (often 60 fs to 150 fs, generalized as fs-lasers, [70, 73–75]). Furthermore, lasers differ with respect to the type. In commercial instruments ns laserlight is either produced in solid state Nd:YAG or ArF excimer lasers. The latter laser type, which is more expensive but delivers higher photon energy, has a fundamental wavelength of 193 nm, whereas in a Nd:YAG laser such light is produced from the fundamental wavelength of 1064 nm using an Optical Parameter Oscillator ([56] and references therein). Solid state Nd:YAG ns lasers emitting light with 266 or 213 nm, which have been most common in earlier commercial systems, become less attractive for application in geoscientific laboratories.

Femtosecond lasers, which are based on solid state lasers (Ti:sapphire), use light ranging in energy between UV and IR. In contrast to ns lasers they have larger optical parts and more complex beam paths requiring finer tuning and more effort to maintain stability throughout analytical sessions [76]. Despite technical improvements in the last years and superior analytical properties (see below) worldwide application of fs lasers in LA systems is still rare compared to use of ns lasers. In addition to technical reasons, this may be due to the high price of fs LA systems [76].

12.3 Physical and chemical effects on concentration and isotope ratio determination

The quality of concentration- or isotope ratio determination by ICP-MS and LA-ICP-MS is affected by many factors. In addition to general aspects related to previous analytical activity (e.g. memory effects, contamination) or general technical conditions (e.g. signal drift, dead time of ion detector, plasma stability) there are further factors, which are specifically associated with physical and chemical processes in the ICP-source leading to interference and fractionation (e.g. [77]).

The occurrence of polyatomic ion species due to oxide and hydroxide formation of the REE and Ba as well as of BaCl in the plasma is a well-known phenomenon causing serious interference mainly on Eu, Gd, Tb, Yb and Lu [37, 38]. Oxide production is influenced by the availability of oxygen, which is significantly higher in solution –ICP-MS than at “dry plasma” conditions in LA-ICP-MS [39, 78]. In contrast to sample introduction by solution, LA-ICP-MS allows routine analytical procedures during which oxide contributions to most REE isotopes chosen for analysis can be neglected [79].

In addition to interferences, fractionating effects have to be considered. Plasma temperature is important for the degree of ionization and ion energies, which have an effect on mass dependent vaporization, diffusion or ion trajectories in the plasma ([80] and references therein). In addition, space charge effects causing mutual repulsion of positively charged ions lead to enhanced deflection of the lighter masses in the ion beam [81, 82]. In combination, these physical processes, which occur in the plasma, between sampler and skimmer cones as well as immediately behind the skimmer cone, are the reason for mass dependent fractionation [80, 83]. Any instrumental parameter affecting these physical processes in plasma and interface region, in turn, has an influence on fractionation that is reflected by non-stoichiometric behavior during element determination or by biased isotope ratio measurement. Such instrumental parameters are: Nebulizer gas flow, extraction lens voltage, torch position, RF power or cone design [80, 82]. Furthermore, as the total ion current also affects physical conditions in the plasma sample, related parameters like concentration or sample matrix influence mass dependent fractionation, too.

Other instrumental factors, such as focusing and shape of the ion beam, collision or scatter of ions in the flight tube or in the ion collection system, inefficient suppression of secondary electrons or nonlinear response of resistors lead to mass-independent fractionation effects [44]. These are most obvious if the beam is split into various parts in MC-ICP-MS.

All of these factors leading to elemental and isotopic fractionation are independent of the method of sample introduction (solution or laser ablation). Such instrumental mass bias must be distinguished from laser induced fractionation processes, which are specifically associated with sample uptake by laser ablation (Figure 12.4). The physical processes of aerosol formation and interaction occurring during ablation are controlled

by absorption of the laser energy by the solid sample. Thus, in addition to the sample matrix, instrumental parameters that influence absorption also have an effect on laser induced fractionation. Numerous studies conducted in this field have shown that laser wavelength, power density, carrier gas composition, laser spot size as well as laser pulse duration are most important [78, 84]. Fundamental differences of ablation mechanisms can be observed below and above a pulse duration frontier of a few picoseconds [76]. At shorter pulses, i.e. fs pulses, the interaction between laser light and solid matter is ultra-fast and the photonic energy is almost entirely absorbed at the spot of the laser beam. Sample heating is laterally and in depth confined to a zone $< 1 \mu\text{m}$ to this spot, which significantly reduces the formation of melts [70, 76] and references therein, [78]. At longer laser pulses, i.e. ns pulses, heat diffusion is a dominant process of energy transfer and consumption in the sample leading to extensive melting of the sample matter below and around the laser spot. Different element volatilities between subsolidus phases (vapor and melt) forming in the ablation pit or condensing around it cause non-congruent evaporation and redistribution of elements, which effects non-stoichiometry of the ablated matter [73, 76, 78 references therein, 85, 86].

Differential transport properties of ablation products (i.e. melt droplets, vapor phase condensates, solid fragments and agglomerates) were invoked to cause fractionation during passage through the transfer tubing [78, 87]. Most studies on laser induced fractionation point to the crucial role of melt formation at the ablation site (Figure 12.4). Thus, fs-LA-ICP-MS can be regarded as major step to reduce laser induced fractionation and to overcome effects of sample matrices on fractionation [70, 76, 88, 89].

While incomplete vaporization and ionization of larger particles in the plasma are shown to lead to preferential transmission of more volatile elements and lighter isotopes, enhanced loading of the plasma with aerosol particles causes element dependent suppression of signal intensity [78, 80, 90, 91]. Poitrasson and d'Abzac [76] point out that aerosol particle size related effects are significantly reduced in fs laser systems, because they produce aerosol particles with confined modal distribution and diameters smaller than $0.2 \mu\text{m}$ that are easily decomposed in ICP-MS torches. In contrast, ablation derived aerosols produced in ns lasers can show sizes $> 1 \mu\text{m}$ and thus have a more pronounced impact on fractionation [76, 90]. Although the latter effects occur in the plasma they are controlled by the properties of ablation derived aerosols and thus belong to laser induced fractionation.

While in fs laser systems ablation yield and laser induced fractionation appear not to be significantly affected by the wavelength, this is an important parameter for ns lasers [76]. For ns-LA-ICP-MS the application of deep UV wavelengths (in particular 193 nm) turned out to be best with respect to absorption, ablation yield and aerosol particle size distribution in transparent matrices [63, 90, 92]. This allows efficient ablation of silicates (e.g. zircon, feldspar) or oxides (e.g. quartz) that constitute a dominant part among mineral and rock samples.

Other studies explore the role of the position of a sample in a large-volume open design ablation cell on variation of Sm-Nd inter-element and Nd isotope fractionation [93]. Two-volume ablation cells help to establish constant conditions of fractionation [73, 76] and references therein.

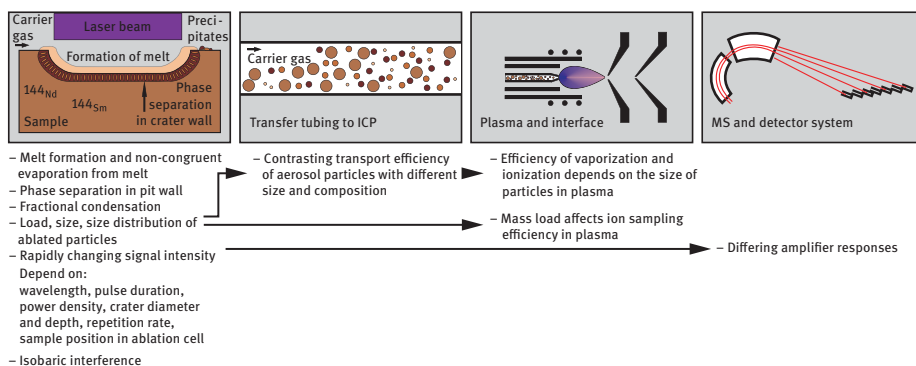


Figure 12.4: Schematic overview of processes causing laser-induced fractionation and interference in (ns-)LA-ICP-MS system on the way of an analyte element from the ablation pit in a solid sample with unseparated matrix via transfer tubing and ICP interface to the detector system, according to [73, 78, 85, 86, 90, 93].

For ns-LA-ICP-MS the application of deep UV wavelengths (in particular 193 nm) turned out to be absorbed best by transparent matrices [63, 90, 92]. This allows efficient ablation of silicates (e.g. zircon, feldspar) or oxides (e.g. quartz) that constitute a dominant part among mineral and rock samples.

12.4 Determination of REE concentrations

12.4.1 Sample preparation

The standard procedure of operation requires sample supply to the ICP ion source as liquid aerosol droplets via a nebulizer and a spray chamber. Therefore, dissolution is the first sample preparation step of earth materials after homogenization and separation of a representative aliquot.

As a characteristic feature of the REE deportment in earth materials their abundance is often controlled by accessory minerals such as allanite, apatite, monazite, xenotime or zircon, e.g. [94]. Some of these accessories are of low solubility, which has to be considered for the choice of dissolution procedures. Acid dissolution is usually performed with mixtures of either HNO_3 or HClO_4 and HF necessary to attack silicates and quartz that are dominant in many rocks. Evaporation to dryness

leads to disappearance of Si. Residues are taken up with either HCl or HNO₃. Pressure containers are preferred because they allow digestion of accessory minerals of low solubility.

Procedures employing microwave digestion systems are also successfully applied for analysis of REE in silicate rocks [95]. Furthermore, effective digestion of solid earth materials can be achieved by fusion dissolution with lithium borate. Glasses formed in this step can further easily be digested in HCl or HNO₃, e.g. [46].

Bulk rock REE analyses are also performed on homogenized solid samples applying LA as sampling tool. For this purpose pressed powder pellets have been applied [52, 96]. Limited precision due to heterogeneity on the scale of a single laser spot is compensated by averaging results from a raster of laser spots [39]. Better homogenization of rock samples is achieved in samples, which are fused – either directly or using a flux. Application of the relatively expensive method of direct fusion for REE analysis in rock samples is less common [97, 98] but sometimes rock glasses suitable for LA-ICP-MS are provided by natural volcanic processes [99]. Flux-based methods, using mixtures of Li-borates added to the sample at ratios ranging between 7:1 and 5:1 are applied most often [39, 46, 53, 100, 101].

12.4.2 Quantification

Quantification of REE concentrations by solution-ICP-MS is mainly based on external calibration using dilutions of stock solutions, e.g. [36, 37]. The methods of standard additions and isotope dilution are alternative ways of calibration, which are less vulnerable to complex matrices in earth materials and thus offer better accuracy and precision of REE analysis [102]. However, both methods require labour intensive and time consuming steps of sample handling, which also leads to higher costs of analyses. Therefore, they are usually not applied as routine methods in geoscientific laboratories.

Drift of signal intensity is corrected by internal standards for which elements that are naturally not contained in the sample are added at defined concentrations. For analysis of REE in earth materials Ru or Rh and Re are appropriate as their masses bracket the range of masses of the REE [103].

While one or more isotopes free of isobaric interferences exist for each REE, the interferences caused by polyatomic oxide and hydroxide species can be significant for the group of the REE and require correction applying experimentally derived factors accounting for yields of formation of interfering ions in the plasma [37, 45] unless high mass resolution is available using double focussing ICP-SFMS. Increasing the resolution ($m/\Delta m$) to values in the range of 8000–10000 REE-oxide ions can be separated from REE-atom ions, which, however, leads to a significant decrease in sensitivity [46, 104]. Several authors explore the effects of high resolution, collision cell technology and doubly charged ions to minimize interferences [40, 105, 106].

Detection limits and precision are not entirely dependent on instrumental parameters as they are also affected by factors such as laboratory blank and numerous processes during the entire analytical procedure starting from the sample preparation and ending with data reduction and concentration calculation. Using solution ICP-MS for determination of REE concentrations, even with quadrupole mass filters, detection limits ranging around 1 ng/g (in solid samples) and run-to-run (external) precision < 5 % for REE concentrations $\geq 0.1 \mu\text{g/g}$ can be reached. Accuracy of REE determinations based on repeated dissolution and analysis of certified rock standards varies between 5 and 10 % [37, 103].

Quantification of REE concentration in homogenized rock or mineral samples by LA-ICP-MS is mainly performed after external calibration using solid reference materials. As reference materials either synthetic glasses or rock glasses produced by melting of natural rocks or minerals as well as synthetic crystalline material or natural minerals are applied for REE analysis [107, 108]. Synthetic polyethylene based REE standards have been tested but are not common today [109]. The glasses 610 and 612 synthesized by the National Institute of Standards and Technology (NIST) are certainly most widely applied for LA-ICP-MS mineral and rock analysis, see GeoReM database by [110, 111]. Mineral standards, for which REE concentrations are known, are e.g. zircon 91500 [112], zircon Plesovice [113] or titanite TIT-200 [114]. An alternative technique based on simultaneous ablation of a Li-borate blank disc and nebulization of a standard solution was tested by [115].

It has to be considered for external LA-ICP-MS calibration that the absolute mass of material ablated per time unit (ablation yield) varies between different materials [63, 78, 86], which leads to systematic errors if standard materials are different to samples. Therefore at least one element with independently determined concentrations in standard and sample serving as internal reference standard is required for quantification of concentrations using the equation:

$$\frac{C_a^u}{C_r^u} = \frac{C_a^{st}}{C_r^{st}} \cdot \frac{I_a^u \cdot I_r^{st}}{I_r^u \cdot I_a^{st}} \cdot \frac{S_a^u \cdot S_r^{st}}{S_r^u \cdot S_a^{st}}$$

[63, 116]. Here, C and I denote concentrations and signal intensities, respectively, in an unknown sample (upper index u) and a standard (upper index st). The lower index a indicates the analyte element, whereas r marks the internal reference element. Usually external calibration standards and samples are analyzed in a bracketing sequence, which also helps to correct for drift effects.

As physical processes responsible for laser induced fractionation are controlled by material dependent absorption of laser energy in the solid (see above), signal intensities obtained in a standard are not representative for an individual sample unless both matrices are identical. Such differences in sensitivity can be corrected with element specific factors (S) accounting for contrast of sensitivity between internal reference element and the analyte element [78]. Owing to their overall similarity sensitivities within the group of the REE as well as those of Y and Sc are almost

identical. Furthermore, sensitivities of the REE are not significantly different from those of the alkaline earth elements Mg, Ca, Sr and Ba [86]. Therefore Ca, which is abundant in many rock types and minerals as well as in the NIST 600 series standards, can be recommended as suitable internal standard element for REE analysis. In such case, errors due to insufficiently constrained sensitivity correction factors are minimized. Whenever using a LA-ICP-MS system affected by mass- and element-dependent fractionation (particularly for ns-LA-ICP-MS) these errors can only be neglected if matrix-matched standards are applied.

This has an effect on accuracy of LA-ICP-MS, which is known to be < 10 % when analyzing silicate minerals without matrix matching but may be reduced to < 5 % if matrix matched standards are used [36, 78]. External precision has improved since the early days of REE analysis by LA-ICP-MS (e.g. [109]) and now is similar to precision of solution ICP-MS. Jochum et al. report precision of 0.8–3.5 % (RSD) for REE analysis by 193 nm ns-LA-ICP-SFMS in the concentration range of 38 and 51 µg/g in natural glass standards after repeated analysis [117]. The potential to improve precision as well as to overcome matrix dependency using fs-LA-ICP-MS is shown by [118, 119]. Detection limits for LA-ICP-MS significantly depend on the size of the laser pit and on the isotope used for detection next to the sensitivity of the instrument. For a beam diameter of 100 µm sensitive LA-ICP-SFMS systems can reach detection limits for REE as low as 0.001 µg/g [101, 117].

In addition to concentration analysis laser ablation operated in a raster mode is increasingly used as a tool for chemical imaging in the last years [64]. REE element distribution maps, which can hardly be obtained by electron microprobe due to limited detection capabilities and which require time-consuming and relatively expensive analytical sessions by secondary ion mass spectrometry can alternatively be generated by LA-ICP-MS. Acquisition of mass spectra by LA-ICP-QMS is a key property allowing to scan samples at enhanced speed and laser repetition rates, which in turn helps to generate multi trace element maps of mineral grains, including the REE, with high spatial resolution [55] and references therein, [120, 121]. Recently [55] performed LA-ICP-TOFMS mapping of Y and HREE distribution in garnet at a lateral resolution of only 5 µm, which is superior to spatial resolution achieved by LA-ICP-QMS instruments. Sample ablation cells used for mapping must be optimized to have fast washout of aerosols because this results in reduced laser pulse response duration. Fast response, in turn, enhances the temporal resolution of the signal obtained during laser scans, which is equivalent to enhanced spatial resolution of the element map (64, 121). The fastest ablation cells currently applied for trace element mapping in geo- as well as in biosciences reach washout times < 10 ms [122, 123].

12.5 Determination of isotope ratios by multi collector (MC) -ICP-MS

The application of the ^{138}La -, ^{147}Sm -, ^{146}Sm - or ^{176}Lu -decay for geo- or cosmo-chronological studies or the use of isotope ratios as geochemical tracers requires the precise determination of isotope ratios (Figure 12.2). These include ratios of the radiogenic daughter isotopes and a non-radiogenic stable reference isotope of the same element in the denominator (i.e. $^{138}\text{Ce}/^{142}\text{Ce}$, $^{143}\text{Nd}/^{144}\text{Nd}$, $^{142}\text{Nd}/^{144}\text{Nd}$, $^{176}\text{Hf}/^{177}\text{Hf}$) as well as ratios of the radiogenic parent isotope and the reference (i.e. $^{138}\text{La}/^{142}\text{Ce}$, $^{147}\text{Sm}/^{144}\text{Nd}$, $^{146}\text{Sm}/^{144}\text{Nd}$, $^{176}\text{Lu}/^{177}\text{Hf}$).

For this analytical task MC-ICP-MS offers best ionization of REE and Hf in the ICP source as well as most precise isotope ratio determination due to multiple ion collection, which allows simultaneous mass detection. This enhances precision because effects due to fluctuations in signal intensity cancel out [44, 45]. Isotope ratio determination is either performed in static mode with stable magnetic field or in dynamic mode, in which the field is changed to detect individual masses in different collectors. While the static mode allows faster analysis, the latter helps to circumvent errors caused by different efficiencies within the array of ion-collectors [44].

The following parts, therefore, focus on MC-ICP-MS. For isotope ratio determination by MC-ICP-MS sample uptake is done by solution as well as by laser ablation.

12.5.1 Solution MC-ICP-MS

For solution MC-ICP-MS powdered bulk rock samples or mineral grains must be dissolved. Due to blank restrictions and in order to keep the sample matrix simple, only acid dissolution, mainly with mixtures of HF and HClO_4 or HNO_3 , is performed using Teflon® vessels (with steel-jacket if necessary) in clean-air laboratory environment.

While ratios of two isotopes of the same element can be determined in one step, isotope ratios involving two elements (e.g. $^{147}\text{Sm}/^{144}\text{Nd}$, $^{176}\text{Lu}/^{177}\text{Hf}$) are determined in two separate steps of concentration analysis using isotope dilution, e.g. [28]. Therefore, mixed spike solutions, usually enriched in the isotopes ^{149}Sm - ^{150}Nd , ^{176}Lu - ^{178}Hf or ^{176}Lu - ^{180}Hf are added to the sample solution.

To keep the matrix of the elements as simple as possible, which helps to optimize signal stability and to minimize mass discriminating effects (see above) and in order to avoid isobaric interferences of atomic ions (e.g. ^{144}Sm , ^{144}Nd) as well as of molecular species forming with elements of lower masses and Ar, O, N or C, element fractions are isolated from the spiked sample solutions, e.g. [44]. Several methods of extracting the REE and Hf from the bulk rock or mineral matrix and subsequent purification of Nd, Sm and Lu employing different chromatographic materials (e.g. Biorad® AG50WX8 cationic resin, Eichrom® TRU resin, resins conditioned

with α -hydroxyiso-butyric acid/ α HIBA, Teflon[®] based resins conditioned with di(2-ethylhexyl)orthophosphoric acid/HDEHP) but also liquid-liquid extraction have been developed [124–136].

Despite chemical isolation trace impurities can occur in the fractions of analyte elements, which imposes the problem of isobaric interferences (e.g. ^{176}Yb - ^{176}Lu , ^{144}Sm - ^{144}Nd). Correction of interference related signal intensities can be performed using interference-free masses, such as ^{173}Yb , ^{175}Lu , ^{146}Nd or ^{145}Nd or ^{149}Sm as monitors for the presence of the interfering masses, e.g. [131].

Correction of mass bias due to fractionation effects in the ICP ion source or detection system can be performed by bracketing of the sample analysis with two standard analyses. This requires identical fractionation properties of sample and standard solutions [44]. For independent calculation of bias caused by mass dependent factors, different mathematical approaches are known among which an exponential law is applied most [44, 45]. For the latter, a stable reference isotope ratio unaffected by interferences is required for normalization. While the $^{146}\text{Nd}/^{144}\text{Nd}$ -, $^{147}\text{Sm}/^{153}\text{Sm}$ - and $^{179}\text{Hf}/^{177}\text{Hf}$ -ratios can be used for correction of unknown isotope ratios of Nd, Sm and Hf, respectively, Lu only has the two isotopes ^{176}Lu and ^{175}Lu . Mass bias of the $^{176}\text{Lu}/^{175}\text{Lu}$ ratio can be evaluated using an interference-free isotope ratio of another REE after doping of the solution (e.g. $^{167}\text{Er}/^{166}\text{Er}$, [137]) or using Yb occurring in the Lu fraction due to incomplete chromatographic separation. To avoid the incorrect assumption of identical fractionation properties of Lu and Yb, the difference in mass discrimination is externally evaluated by repeated systematic analysis of mixed Yb and Lu standard solutions – a method also allowing assessment of isobaric interference by ^{176}Yb on ^{176}Lu [15, 41]. Alternatively, normalization to the $^{187}\text{Re}/^{185}\text{Re}$ -ratio of an admixed standard solution is used for correction [138].

Any mass independent fractionation must be corrected using factors derived from analysis of standard solutions with known isotopic composition. Thus, often a final normalization to a standard solution run during analytical sessions is applied to yield accurate and reproducible isotope ratio measurements [44, 137]. For normalization or general evaluation of accuracy and correction procedures for determination of the radiogenic isotope ratios standard solutions prepared with pure metals or oxides such as La Jolla, Ames-Nd or JNdi-1 for Nd, JMC 475 for Hf or JMC 304, Ames-Ce for Ce are common [110, 139–141].

Precision of isotope ratio determination by MC-ICP-MS depends on instrumental properties and correction procedures as well as on concentration of the analyte element or analysis time. For common analytical conditions applied for rock and mineral analysis external precision (2σ) obtained from repeated analysis of standard solutions is often reported to be ≤ 20 ppm for $^{176}\text{Hf}/^{177}\text{Hf}$ or $^{143}\text{Nd}/^{144}\text{Nd}$, e.g. [83, 137, 142]. For the latter element precision of MC-ICP-MS is comparable to values determined by TIMS, e.g. [143].

12.5.2 LA-MC-ICP-MS

Determination of Sm-Nd isotopes with LA-MC-ICP-MS has in the last years increasingly been applied to minerals that enrich the light REE. Minerals, such as monazite, apatite, titanite or allanite, in which Nd can reach concentrations of several wt.-%, are highly suitable for this technique because precise isotope ratio analysis can be performed also in small laser spots [144]. Isotopes of the Lu-Hf system are mainly analysed in zircon. Such measurements in combination with other in situ trace element and isotope (U-Pb, O) data obtained from the same single crystal make zircon next to monazite or titanite one of the most important tracers of the earth's crustal evolution [69, 72, 145]. Modern LASS technology leads to optimum results for this task because age information, isotope or trace element signatures (including REE patterns) are obtained simultaneously from the same spot. This petrochronological approach links growth history of a single crystal to the magmatic and metamorphic evolution of an entire crustal segment and thus represents an important tool to unravel continental geodynamics [71, 72]. REE-minerals are important phases for petrochronological studies [72, 146].

LA-MC-ICP-MS thus combines the advantage of in situ analysis at high spatial resolution with the convenience of a method that does not require time-consuming dissolution and chromatographic sample preparation. However, leaving analyte elements and matrix unseparated leads to analytical tasks that require further consideration.

Isobaric interferences are more crucial for in situ analysis than for solution-ICP-MS. The signal of ^{144}Nd can be affected by a contribution of ^{144}Sm as high as 4 % in monazite because this mineral, like other light REE-rich minerals, contains significant amounts of Sm in addition to Nd [147]. Likewise, the REE isotopes ^{176}Lu and ^{176}Yb interfere to higher degrees with ^{176}Hf in in situ mineral analyses than in elemental fractions after chemical separation. Correction of an interfering isotope (e.g. ^{144}Sm) can be performed using its ratio with an interference-free isotope (e.g. ^{149}Sm) and additional correction of mass-bias on the ratio. However, stable non-radiogenic ratios used for normalization in mass bias correction procedures may also be affected by interfering matrix elements (e.g. ^{142}Ce on ^{142}Nd) that can have high concentrations in unseparated solid mineral matter. Different procedures for such correction are given in [93, 144, 147].

In general, due to laser-induced fractionation (see above), which occurs in addition to fractionation caused in plasma and interface, mass bias is a more pronounced effect of in-situ LA-MC-ICP-MS isotope ratio determination – particularly if ns-lasers are applied. Furthermore, inter-element fractionation affecting analyses of parent-reference ratios (e.g. $^{147}\text{Sm}/^{144}\text{Nd}$, $^{176}\text{Lu}/^{177}\text{Hf}$) cannot always adequately be corrected using stable isotope ratios of only one element.

In many laboratories both, insufficiently corrected mass bias of daughter-reference ratios as well as fractionation of parent-reference ratios, are corrected using mineral standards often analysed in a standard-sample bracketing mode [93]. Thus, well

characterized and homogeneous mineral standards matching the matrix of REE-enriched minerals including zircon or titanite are a prerequisite for accurate and precise isotope ratio measurement, in particular for ns-LA-MS-ICP-MS, which is still more often applied than fs-LA-MS-ICP-MS. Instead of mineral standards of zircon or titanite [112, 148–150], synthetic glass standards have also successfully been applied [93, 147]. The application of fs-lasers significantly limits fractionation effects and thus matrix matching is considered to be less crucial for fs-LA-ICP-MS [64, 76].

Precision of LA-MC-ICP-MS isotope ratio determination depends on signal intensity, and thus on the concentration of the analyte element as well as on the pit diameter. Furthermore, integration time and correction procedures also control precision [80, 149]. McFarlane and McCulloch report internal precision of the $^{143}\text{Nd}/^{144}\text{Nd}$ ratio as good as in TIMS instruments (< 10 ppm, 2σ) for monazite with Nd at 9 wt.-% and a crater diameter of 50 μm [144]. External precision reaches best values between 60–95 ppm (2σ) for analytical conditions applicable to natural minerals (e.g. zircon, $^{176}\text{Hf}/^{177}\text{Hf}$, [69, 149]).

12.6 Concluding remarks

In the last 35 years ICP-MS has been a rapidly developing technique. The robust and versatile ICP-source allows efficient ionization and can be combined with different systems of sample input as well as with different mass-spectrometers (quadrupole, magnetic sector field, time-of-flight) at various detector configurations (single-, multi-collector). Recent advances, e.g. in the field of fs-LA-ICP-MS and MC-ICP-MS, show that the technical and methodological evolution is still ongoing – certainly also driven by the analytical needs of the geosciences.

The introduction of ICP-MS as a standard instrument in geochemical laboratories significantly enhanced the availability of REE analyses of rocks and minerals and due to the excellent ionization capability of the source ICP-MS also marked a major step in isotope geochemistry and cosmochemistry. Taking the role of the REE as indicator elements for geological processes and as geochronometers based on the decay of La-, Sm- and Lu-isotopes into consideration, the advent of ICP-MS can be considered an important step in the geosciences.

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13 Novel applications of lanthanoids as analytical or diagnostic tools in the life sciences by ICP-MS based techniques

Abstract: Inductively coupled plasma-mass spectrometry (ICP-MS) is a well-established analytical method offering high sensitivity and multi-element analysis. ICP-MS has found acceptance in various application areas ranging from material analysis to applications in the life sciences. Within the last 15 years new strategies for the sensitive detection and accurate quantification of biomolecules in complex biomedical samples have been developed. Recent instrumental improvements have contributed to this progress.

As most of the biomolecules do not contain endogenous metals detectable with ICP-MS, bioconjugation with artificial metal-containing tags based on metal-loaded chelate complexes or nanoparticles is increasingly applied to determine biomolecules indirectly. Especially, the combination of immunohistochemical workflows using lanthanoid-tagged antibodies and ICP-MS detection provides new insights in the complexity and interdependency of cellular processes. Single-cell ICP-MS, also termed as mass cytometry, allows high-dimensional analysis of biomarkers in cell populations at single-cell resolution. For that purpose, lanthanoid isotope labelled antibodies are used to detect their corresponding target molecules. The visualisation of the elemental distribution is possible with laser ablation ICP-MS (LA-ICPMS) at high spatial resolution. Especially, the combination of LA with ICP time-of-flight mass spectrometry, also referred to as imaging mass cytometry (IMC), opens new possibilities for multiparametric tissue imaging at the single-cell level and even below. The lanthanoid localisation and concentration can be linked to their conjugated antibody target providing valuable information about surface markers, intracellular signalling molecules to measure biological function, and the network state of an individual cell in a tissue.

This book chapter focuses on new applications, where the multi-element capabilities of ICP-MS are used for the detection of lanthanoids applied as artificial elemental stains or tags for biomolecules and in particular antibodies.

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13.1 Introduction

Inductively coupled plasma-mass spectrometry (ICP-MS) is a well-established analytical technique for multi-element analysis. All metals and some non-metals like phosphorous and sulphur can be determined at low concentration levels. Furthermore, isotope analysis and isotope ratio measurements are possible. An ICP-MS set-up consists of a sample introduction system, typically for liquid samples, the inductively coupled argon plasma with a temperature of about 8000 Kelvin as an ion source, and a mass spectrometer. The sample introduction system is used to generate a fine aerosol, which is then introduced into the argon plasma where vaporization, atomization and finally ionization takes place. Afterwards the ions are separated in the mass spectrometer according to their mass-to-charge ratio and detected. Different types of mass analysers are in use, quadrupole mass filters, magnetic sector-field systems, and time-of-flight analysers, using different physical principles for mass separation. Further details about ICP-MS can be found in chapter 5 or in the literature [1]. ICP-MS excels by a high sensitivity, which is independent of the molecular structure of the analyte, a wide linear dynamic range and excellent multi-element capabilities. An ICP-MS instrument can be combined with either chromatographic separation systems or special sample introduction systems for solid samples, like electrothermal vaporization or laser ablation (LA) systems [2]. LA-ICPMS is widely spread in geology and for the analysis of different conducting and non-conducting materials (e.g. metals, ceramics, polymers) [3, 4]. In the last few years, the analysis of cells and tissue samples is gaining importance providing new insights into biochemical processes in healthy or diseased stages. In this context, the conjugation of metal-containing tags to biomolecules, that do not contain an endogenous metal, typically peptides, proteins, DNA, RNA and antibodies, is a rapidly growing field of research. These tags, particularly chelate complexes loaded with lanthanoids (Ln), are covalently bound to the molecule of interest using suitable reactive groups as part of a metal-loaded chelate complex or a nanoparticle. In this book chapter we focus on ICP-MS based approaches to detect and quantify biomolecules by using lanthanoids.

The determination of proteins, peptides and nucleic acids is an important topic in life sciences. In this context, lanthanoid elements can be used for the targeted analysis and quantification of proteins and nucleic acids by ICP-MS after previous chromatographic separation. Another emerging field of activity is the analysis of individual cells as the heterogeneity of cell populations has been widely recognized [5]. Single-cell (SC) analysis using a combination of high-throughput and multiparameter approaches is capable of reflecting cell-to-cell variability and thereby unraveling the complexity and interdependency of cellular processes in individual cells of a heterogeneous population. Nowadays, flow cytometry is the gold standard to detect protein

expression levels by using fluorescent probes [6–8]. Within the last few years, single-cell analysis by ICP-MS, also termed as mass cytometry when metal-conjugated antibodies are used, is becoming more and more popular [9–11]. This technique enables multiparametric analysis by detecting up to 100 biomarkers simultaneously at the single-cell level.

In recent years, significant progress has been made in the development and application of imaging techniques [12] such as matrix-assisted laser desorption/ionization MS (MALDI-MS) and secondary ion mass spectrometry (SIMS) for the determination of the distribution of organic compounds and elements in biological tissue samples. Laser ablation in combination with ICP-MS is increasingly used to map the distribution of contrast agents or other metal-containing drugs in connection with disease related changes and therapy progress. Recent instrumental improvements concerning sample chamber design and thereby aerosol wash-out time have contributed to better sensitivity and spatial resolution opening the way for sub-cellular mapping [13, 14]. The combination of immunohistochemistry and LA-ICP time-of-flight mass spectrometry (LA-ICP-TOFMS), also referred to as imaging mass cytometry (IMC), opens new possibilities for multiparametric tissue imaging at the single-cell level and possibly with sub-cellular resolution [15, 16]. Here, elemental tags containing lanthanoid isotopes play a crucial role. Furthermore, 3-dimensional elemental imaging provides information on tissue architecture, microenvironment, and cell-to-cell interactions.

This book chapter is not meant to cover all the work that has been done and published in recent years using lanthanoids as analytical or diagnostic tools in combination with ICP-MS based detection. Here, only the main aspects and some typical applications can be discussed to show the fascinating possibilities of the techniques in the biomedical context.

13.2 Bio-conjugation of biomolecules

The examination of tissue or cell samples on a molecular level is crucial to understand health and disease. Modern biomedical research requires highly sensitive and multiplexed detection of biomarkers to understand the complex processes in conjunction with diagnosis, progression and treatment of various diseases. Analytical approaches using elemental labelling of biomolecules are gaining in importance [17, 18].

Fluorescently or metal-labelled antibodies have become an integral part of basic science and clinical research. Based on the specific binding between antibodies and their corresponding antigens, proteins and peptides can be detected. In this context, ICP-MS based detection methods are increasingly becoming an important complement in bioanalysis due to the high sensitivity and selectivity provided by ICP-MS. Thus, highly multiparametric analysis is possible, which is not feasible

with fluorescence microscopy due to the limited number of spectrally resolvable fluorochromes and the difficulty in measuring simultaneously targets that differ in abundance by an order of magnitude or more. However, sometimes it is very helpful, e.g. for method validation, to use tags which are detectable with two or more independent analytical techniques. Such multifunctional tags like lanthanide-containing nanoparticles allow both fluorescence analysis and ICP-MS detection providing a more comprehensive information about the sample. Besides, special designed molecular tags composed of a lanthanide loaded chelate complex and a fluorescent moiety were successfully applied for biomolecule analysis. With the detection of different tags in the same probe, a so-called seeing and counting approach became possible by using fluorescence imaging for visualisation and ICP-MS for quantification of biomolecules in cell samples [19, 20]. It should be taken into account that the different parts of the tag do not have a negative effect on each other, e.g. a possible quenching of the fluorescent tag caused by the metal tag. Furthermore, steric hinderance due to the large size of the tag should be considered and the ratio of diverse functional parts should allow a similar dosage when using different detection methods.

An overview about modification and cross linking of various biomolecule classes by using different reagents is given by Hermanson [21]. Besides, several review articles provide an overview about different types of exogenous mass-tags and ICP-MS based quantitative analysis of biomolecules [17, 18, 22, 23]. For the determination of low biomolecule concentrations, the development of tags containing several metal ions is important. Furthermore, it is essential to optimize labelling strategies in terms of specificity and efficiency.

13.2.1 Bioconjugation by lanthanoid-containing tags

Exogenous metal-containing tags used for ICP-MS detection can be classified as several types:

1. Metal chelates based on macrocyclic chelating agents loaded with a metal, typically a lanthanoid ion.
2. Metal-chelating polymer-based tags loaded with a heavy metal, typically a lanthanoid ion.
3. Metal-containing nanoparticles (NPs), e.g. noble metal NPs, quantum dots or upconversion NPs.

For ICP-MS based application, typically bifunctional ligands are applied as tagging reagents. They consist of two parts, a metal chelating compound and a reactive groups, which connects the chelate complex – if possible covalently – to the biomolecule of interest and in particular to an antibody via functional groups like sulfhydryl groups of cysteine residues or the amino group at the N-terminal. Macrocyclic compounds based on 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) or

linear chelates such as diethylene-triamine-tetraacetic acid (DTTA) or diethylene-triamine-pentaacetic acid (DTPA) are promising chelates and can be loaded with different metals, preferentially lanthanoids or their isotopes [24–26]. Lanthanoids form stable complexes, thus avoiding toxic reactions in cells and tissue. The chelating compounds applied offer improved water solubility and have a high-stability constant in order to be resistant against metal exchange, which otherwise could compromise their application. Besides that, complex chemistry is well-established for medical applications, e.g. Gd-based contrast agents for magnetic resonance imaging. A short summary about the labelling chemistry is given by Linscheid [27].

Metal-coding for the determination of proteins and peptides was first discussed by Whetstone et al. [28]. Shortly afterwards Krause et al. [29] applied for a patent for a DOTA-based reagent named metal-coded affinity tag (MeCAT) with a cysteine reactive maleimide group and a biotin modification for purification and enrichment of tagged peptides via biotin-avidin affinity chromatography. As reactive group, terminal maleimidoethylacetamide residues are used for conjugation to sulfhydryl (SH) groups after selective reduction of the proteins or antibody's cysteine-based disulfide bridges. Alternatively, isothiocyanatobenzyl residues (SCN) and N-hydroxysuccinimid ester (NHS) are often applied, because they bind preferentially to amino-groups of amino acids. In both cases, the conjugation with the biomolecule is critical, because it significantly changes the physical and chemical properties of the antibody and it might also affect the antibody's binding efficiency and specificity in an immunoassay. However, the same type of chelate-containing tag can be loaded with different lanthanoid ions. Thereby, each type of antibody can easily be conjugated with a different element and, finally, the ensemble of tagged antibodies can be applied simultaneously in a single immunoassay. The detection capabilities can be improved by using a dual labelling strategy, i.e. different metal-containing tags bound to the same molecule [30, 31]. Amino groups were labelled with NHS-DOTA and thiol groups with iodoacetamide DOTA. The use of the same metal improves the detection limit, two different metals enable the differentiation by ICP-MS based detection.

To get a deeper insight into the antibody structure after reduction with tris(2-carboxyethyl)phosphine (TCEP) and tagging with bifunctional ligands containing maleimide residues as a reactive group (here MeCAT) Mueller et al. [32] used size exclusion chromatography (SEC)-ICP-MS and liquid chromatography–time-of-flight (LC-TOF)-MS. The results indicated that not only the hinge region of the antibody is reduced, but many smaller antibody fragments are generated, too. Several fragments could be identified carrying different numbers of lanthanoid-containing tags. However, a dot blot immunoassay revealed the functionality and the antigen specificity of isolated antibody fragments. The findings demonstrated that it is difficult to calculate the exact tagging degree. Furthermore, as all free and available amino or cysteine groups can potentially react with the tagging reagent, the number of metals per antibody and the locations of the labels cannot be controlled. This non-controllable antibody labelling chemistry limits the quantification. To overcome this, Kanje et al. [33]

developed a strategy resulting in a controlled labelling degree of one. Small antibody binding domains of protein G, C2_{FC} and C2_{Fab}, were conjugated with MeCAT after introducing a cysteine into the C-terminus of the protein. Afterwards, antibodies were labelled with these modified C2 domains by mixing and subjecting them to far-UV light (365 nm). This methodology allows a specific antibody labelling regardless of stabilizers in its buffer and without any further pre-treatment. In a proof-of-principle experiment, the amount of different labelled antibody–antigen complexes in a multiplex Western blot immunoassay was quantitatively determined by LA-ICPMS by using a spiked membrane as calibration sample.

Besides, glycoproteins and in particular antibodies, which are always glycosylated in nature, can be derivatized at their sugar residues after oxidation to aldehydes, which then can react with lanthanoid-containing chelating tags carrying a hydrazide or primary amine as reactive group [21]. In a similar way, the 5′- and 3′-end ribose sugars of RNA can be oxidized to aldehydes, using the reactive groups mentioned before [34]. A different way for DNA detection is based on the application of base-complementary oligonucleotide groups synthesized with reactive amino or SH groups and afterwards using the same conjugation chemistry as for antibodies.

Historically, chelating compounds were first employed in combination with radioactive tracers. Lewis et al. [35] conducted a bio-conjugation with the radioactive isotopes ¹¹¹In and ⁹⁰Y by using an NHS linker attached to DOTA. McDevitt et al. presented a method for binding ²²⁵Ac to SCN-DOTA and attaching of the complex to an immunoglobulin G (IgG) antibody [36]. To overcome health hazards caused by radioactive materials and by limiting the handling of such assays to laboratories specialized in radiochemistry, fluorescent lanthanoids (Eu, Sm, Tb, Dy) replaced the radioactive central ions shortly afterwards. The first example of an immunoreaction in combination with ICP-MS detection was introduced by Zhang et al. [37]. The authors used an Eu-tagged antibody for the detection of the thyroid-stimulating hormone (TSH) in human serum. The Eu signal measured after acid digestion was directly proportional to the serum TSH concentration. The precision was better than 10 % and the ICP-MS based assay covered the whole diagnostic relevant range. The TSH results obtained by ICP-MS were in good agreement with the result from a radioimmunoassay, which was used for validation. Shortly afterwards, the first ICP-MS based immunoassays for the simultaneous determination of several proteins in biological samples were published. Both nano-gold and lanthanide-labelled antibodies were used in these multiparametric assays [38, 39]. The development has since continued and currently heavy metal isotope tags (mass tags) are composed of metal-chelating polymers (MCPs) that carry 20 to 50 lanthanide atoms per tag, corresponding to 50 to 250 metal atoms per antibody-MCP conjugate [40–42]. The use of MCPs leads to a sensitivity increase, since the ICP-MS signal increases linearly with the number of atoms of a given element enabling profound profiling of functional molecular networks at single cell resolution and below [43–47]. 50 to 250 metal atoms per conjugate are enough to detect highly abundant biomarkers (10⁴–10⁷ per cell) [42].

DNA-based elemental tags are an attractive alternative to metal chelating polymers. As the water solubility of polymer tags decreases with increasing chain length, the number of metals which can be attached is limited. To overcome this limitation Hu et al. [48] synthesized an elemental tag loaded with hundreds of metal ions by coupling alkyne-DNA chains with Ln-DOTA complexes. Polymerase chain reaction (PCR) was used to create DNA chains with multiple alkynyl groups. Afterwards, the metal loaded azido-monoamide-DOTA (metal-DOTA-N₃) complex was conjugated to the DNA strands via the alkynyl groups by a Cu(I)-catalysed Huisgen cycloaddition reaction (click chemistry reaction). The resulting DNA-based elemental tags showed excellent water-solubility and biocompatibility. The sensitivity of the ICP-MS detection can be improved by increasing the length of DNA chains as the number of metal complexes increases with available alkyne groups.

To detect also low abundant biomarkers, nanoparticles containing hundreds, or thousands of atoms can be applied as tags to generate the required signal amplification. In the last few years, the bioanalytical use of nanoparticles has increased enormously [49]. Usually, fluorescent nanomaterials are applied instead of molecular fluorescent dyes [50]. Especially lanthanide-doped micro- and nanoparticles and lanthanide-containing inorganic nanoparticles are promising tags [22, 51, 52]. One advantage is, that they can be used for flow and mass cytometry, respectively.

Rare-earth doped inorganic nanoparticles, termed upconversion NPs (UCNPs), consist of a host matrix (e.g. NaYF₄, NaGdF₄, Y₂O₃ or Gd₂O₃) and dopant lanthanoid ions as sensitizer and activator. They are used in different fields of application due to their unique optical, electronic and magnetic properties [53, 54]. The properties of UCNPs are variable adjustable and depend on the selection, combination, and amount of lanthanoids as well as the host matrix, stoichiometry and particle size. Particularly, surface modifications and functionalisation of UCNPs expands the range of biomedical applications [55]. For biolabeling experiments, the surfaces must be modified to produce hydrophilic particles while maintaining their physicochemical properties and their colloidal stability in aqueous, buffer-containing media. Furthermore, additional functional groups for the attachment of bioaffinity agents are required. The review article from Heuer-Jungemann et al. [56] provides a comprehensive overview about NP coatings and surface ligands. Special functionalised UCNPs are of particular importance for the bioconjugation with antibodies. UCNPs offer an enhanced sensitivity in cell assays. In a proof-of-principle experiment with microgels (diameter 700 nm) as artificial cells, Lin et al. [57] determined a mass cytometry signal, which was about 2 orders of magnitude higher for streptavidin as model biomarker when using biotinylated NaHoF₄ NPs (with 15 000 Ho atoms per NP) compared to a biotinylated MCP with about 50 Tb³⁺ ions per probe. The sensitivity was only limited by the level of nonspecific adsorption of the NPs. Pichaandi et al. [58] determined a 30- or 450-fold signal enhancement for direct CD14 detection on cells using NaHoF₄ NPs (diameter about 12 nm) instead of metal chelating polymers conjugated to primary antibodies. Lanthanide nanoparticles can be functionalized with different coatings like PEGylated ligands or PAMAM dendrimers to improve NP stability

and biocompatibility, to allow antibody conjugation and to decrease nonspecific cellular binding. Thereby, lanthanide nanoparticles bioconjugated to antibodies are promising reagents for multiparametric, high-sensitivity analysis at sub-cellular resolution.

Alternatively, polymer particles, e.g. polystyrene (PS) NPs, can be loaded with lanthanoids [59]. Majonis et al. reported the first dual-purpose probe with fluorescent and mass tags contained in a single poly(N-alkylacrylamide) polymer [60]. Antibody-polymer conjugates were prepared and used in a multiplexed immunoassay based on both mass and flow cytometry to detect specific cell biomarkers.

Wu et al. [61] showed that the small size of semiconducting polymer dots (Pdots, diameter typically 10–30 nm) in combination with a high loading density of lanthanides (1000–2000 lanthanoid ions per tag) enables efficient and specific cell labeling with low nonspecific binding. Compared to conventional MCPs, a sensitivity increase by a factor of 4 to 6 could be determined. Pdots consist of polystyrene-grafted ethylene oxide functionalized with carboxyl groups (PS-PEG-COOH) and a lanthanoid chelated polymer. Antibodies can easily be conjugated via 1-ethyl-3-(3-(dimethylamino) propyl)-carbodiimide (EDC) chemistry. However, the relatively broad size distribution of Pdots limits currently their application. PS particles with a size of 1–5 μm can contain between 10^4 to 10^8 metal ions per particle and are mainly used as internal standards for cell studies. They show a small bead-to-bead variation of the metal content and are completely atomized and ionized in the ICP.

The 15 lanthanoid elements provide at least 37 isotopes that are non-redundantly unique masses allowing the design of highly multiplexed/multiparametric assays. Some of the isotopes are affected by isobaric interferences due to elements with multiple naturally occurring isotopes or, to a certain extent, by interferences based on oxide formation. However, this limitation has been solved by using highly enriched and stable isotopes. Lanthanoid-based tags enable also isotope dilution analysis as quantification method due to the possibility to use isotopically enriched metals.

In summary, lanthanoid-based elemental tags are in widespread use due to the following advantages:

1. All lanthanoids show a similar chemistry, thus a method once elaborated for one element can easily be transferred to other elements of this group.
2. The background values of lanthanoid elements in biological or medical samples are quite low enabling very sensitive analysis due to high signal-to-background ratios.
3. All lanthanoids can easily be ionized in the ICP with an efficiency near 100 % due to a low first ionization potential. Thus, the sensitivity in ICP-MS is high and the limits of detection (LODs) are quite low.
4. Lanthanoids are nearly not hampered by spectral interferences. Besides, many isotopes can be obtained in an enriched form with purities better than 95 %.

Additionally, lanthanoid-containing tags can be used for both ICP-MS and fluorescence detection due to their dual-functionality. This is also important for method validation purposes.

13.3 Principles of mass cytometry and imaging mass cytometry

13.3.1 Single-cell ICP-MS/mass cytometry

Differences between cells occur at many levels, even when two cells are considered identical, for example because they come from the division of the same mother cell. These cell-to-cell variations can be more pronounced, the more different origins the cells have or the more differentiated they are. In any case, the study of cells at the single-cell level includes analyzing the differences in their genomes, transcriptomes, proteomes, metabolomes, metallomes and even in cell-to-cell interactions. Single-cell analysis permits to discover small cell populations, or even individuals, that would be hidden within the average in bulk studies. These cell-to-cell variations have important implications in many biological *in vitro* and *in vivo* studies and, especially, with regard to understanding pathological processes, such as cancer.

The gold standard for single-cell analysis is flow cytometry. This technique allows the detection of protein expression in a cell-to-cell basis by the use of fluorescent probes. Most commonly, cell samples are treated with antibodies, tagged with fluorescent molecules. The cell suspension is then introduced into a liquid stream that aligns the cells in the center of a capillary, making the cells to pass, one by one, through a light beam that excites the fluorescent tags. The fluorescent, dispersed and transmitted light is then registered in detectors at specific wavelengths and angles. After relatively simple data processing, each cell can be characterized in terms of their fluorescence at different wavelengths, together with their transmission and dispersion of the light, which are related with the cell size and shape, respectively.

Despite the clear utility of flow cytometry, it is not free of disadvantages, being optical limitations the most important ones. In this regard, flow cytometry is limited by fluorescence quenching and autofluorescence of the samples. Regarding the number of proteins to be simultaneously analyzed, the limitation comes from the broad emission and absorption spectra of the fluorescent tags, which can lead to spectral overlaps that complicate and limit the strategies to perform highly multiparametric experiments.

Trying to overcome the limitations of flow cytometry, Scott Tanner and colleagues developed mass cytometry [62], a technique for multiparametric analysis of single cells

based on ICP-MS detection. The basic idea of this new workflow was the use of metal (lanthanoid) tags to modify the antibodies, as opposed to the traditional fluorescent tags in flow cytometry. Figure 13.1 shows the schematic workflow for single-cell mass cytometry analysis.

The mass cytometer was introduced to the market in 2009 as CyTOF™ by DVS Sciences Inc. (now Fluidigm) and is an adaptation of an ICP-MS with a time-of-flight (TOF) mass analyzer, therefore an ICP-TOF-MS [63]. TOF mass analyzers can perform very fast scans in a broad mass range, allowing to measure very short transient signals with μs time resolution. The sample introduction system is a critical part in single-cell analysis by ICP-MS and it is based, in the CyTOF, on a micro-concentric pneumatic nebulizer. The nebulizer is connected to a spray chamber that uses a make-up argon gas flow. A heating system helps dry the droplets in which the cells are embedded while they are transported into the plasma. This sample introduction system allows to use a sample flow rate of $45 \mu\text{L min}^{-1}$. After passing through the heated spray chamber, the dried cells enter the plasma, where they are atomized and ionized, creating an ion cloud that enters the high vacuum in the instrument and travels through the ion optics and filters, the time-of-flight mass analyzer and finally they are registered by the detector and the data acquisition system.

In a mass cytometer, every cell produces an ion cloud that generates a Gaussian transient signal when it arrives at the detector, lasting up to $400 \mu\text{s}$, and generates a series of spectra with the information of all the metals associated to the cells, including those isotopes used as tags or stains. After data processing, mass cytometry data can be visualized in a similar manner to traditional flow cytometry. However, due to the high number of parameters that mass cytometry can obtain data interpretation in two-dimensional plots becomes very difficult. Thus, sophisticated data postprocessing and statistical methods usually need to be applied for the interpretation of mass cytometry data [64].

Due to the risk of signal overlaps coming from two or more cells, the maximum cell introduction rate of the mass cytometer is limited to around $1000 \text{ cells s}^{-1}$. This is a low frequency for the analysis in comparison to fluorescent flow cytometry, which can achieve around $10000 \text{ cells s}^{-1}$, but the capability of CyTOF to analyze up to 100 biomarkers simultaneously in a single cell greatly improves the up to 15 different tags that the most advanced flow cytometry instruments and methods can achieve after tough optimization procedures.

Single-cell analysis by ICP-MS (SC-ICP-MS) is not exclusive of CyTOF. Many groups are currently performing single-cell analysis using quadrupole-, sector field- and other TOF-based instruments. Due to the sequential nature of the measurements in quadrupole and sector field ICP-MS instruments, single-cell analysis at low integration times is only possible in a mono-isotopic manner. Nonetheless, non-CyTOF TOF instruments are also capable of performing multiparametric single-cell analysis (mass cytometry by definition), since they are based on the same principles. The advantages of using these technologies are the higher availability of these instruments, which are not specifically

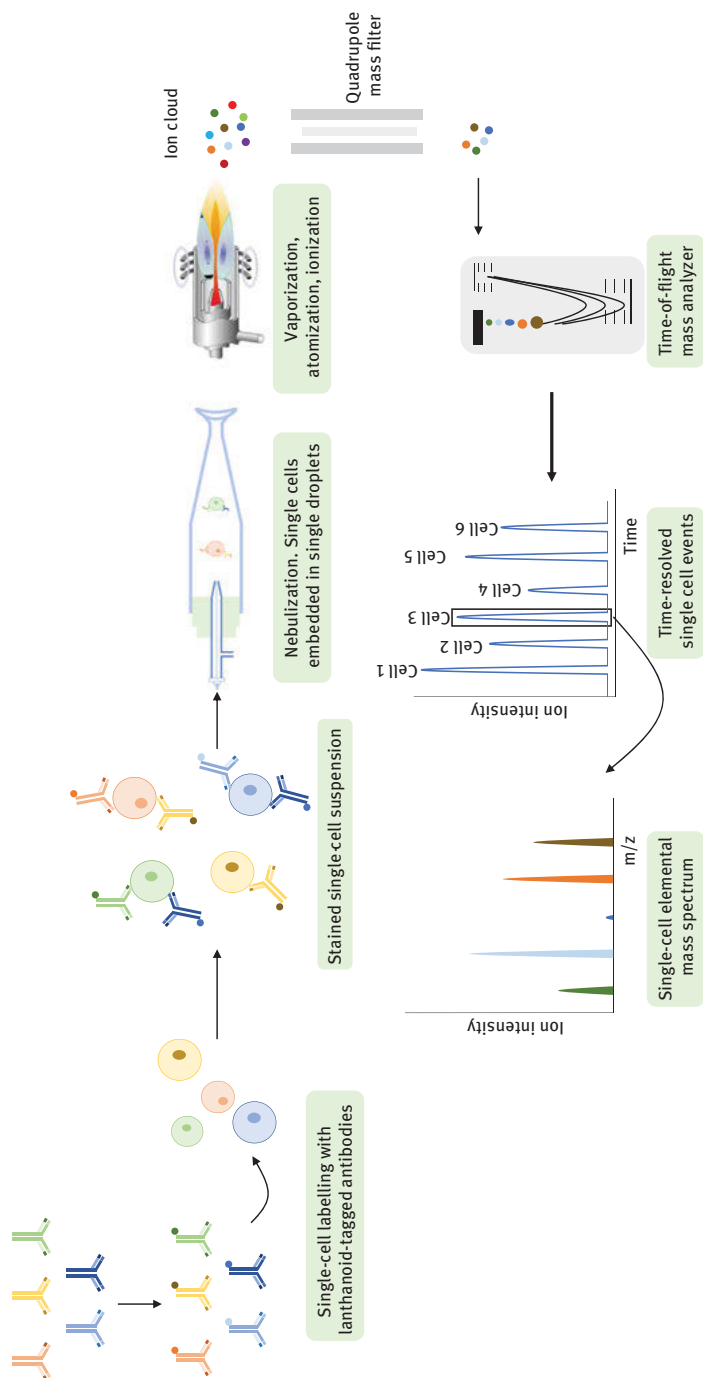


Figure 13.1: General workflow for single-cell mass cytometric analysis. A panel of selected antibodies is labelled with different metal atoms (lanthanoids), which are used for staining a single cell suspension. Once the antibodies have recognized their epitopes in the cells, the stained cell suspension is washed several times and sprayed in the ICP-MS sample introduction system, where, ideally, each cell is embedded in a solvent droplet. Once each droplet reaches the plasma, the solvent is vaporized and the different molecules are atomized and ionized, including the metal atoms used for labelling. The produced ion cloud is then filtered through a quadrupole that filters out the low-mass ions, reducing some interferences, and the remaining ions are separated in the TOF mass analyzer according to their m/z . Each cell is then detected as a short transient signal. The spectrum for each cell contains information about the amounts of bound antibodies and, therefore, the expression of the markers of interest can be deduced after adequate data analysis.

intended for single-cell analysis, and the accessibility to the whole mass range, which is limited in the CyTOF to elements with atomic mass above 75 Da in the newest systems. This opens the door to the detection and quantification of biologically interesting light elements, such as sulphur or phosphorus, and light metals, such as copper, zinc, iron, calcium, etc., which are naturally present in the cells and their up- or down-regulation can be related to relevant changes at the sub-cellular level.

Quantification in single-cell analysis

Element quantification in single cells follows the same principles as in single particle analysis. This means comparing the intensity of the single cell events with the slope of an external standard calibration curve, which is constructed by means of ionic standard solutions. A critical step in this strategy is the determination of the transport efficiency of the ionic standards, since it is different to this of the single cells and needs to be corrected. Transport efficiency can be calculated by different methods: (i) by measuring the amount of sample over time that is introduced into the instrument and comparing it with the amount of sample that is discarded through the waste outlet of the sample introduction system, which is not possible in total consumption systems; (ii) by measuring a particle suspension with a known concentration of particles and comparing the particles that can be detected with the actual number concentration; and (iii) by comparing the actual mass of an element in a particle suspension of a known size with the mass obtained if transport efficiency was 100%. All these strategies need to make some assumptions and have, therefore, some limitations, but they are mostly used in SC-ICP-MS works.

In most mass cytometry applications, accurate determination of the concentration of any species is not a central issue. In fact, mass cytometry usually relies on comparing the expression levels of the biomarkers of interest with control molecules or between different samples. However, absolute quantification of elements in single cells is interesting, for example, when calculating nanoparticle [65–67] or metallodrug uptake [68].

Regarding quantification of lanthanoids as antibody labels, not many researchers have addressed this challenge, although this would mean to directly quantify the number of proteins expressed by a single cell. Recently, absolute quantification of lanthanoid-labelled antibodies by SC-ICP-MS has been realized as a strategy to quantify the expression of transferrin receptor 1 (TfR1) in breast cancer single cells using a triple-quadrupole ICP-MS system [69].

Knowing the different sensitivity for the different lanthanoids also in CyTOF, Tricot et al. compared the effect of the sensitivity differences on the intensity of lanthanoid-tagged antibody probes, showing the importance of signal calibration or standardization when comparing the expression of different biomarkers labelled

with different lanthanoids [70]. In this case, they calculate the transport efficiency by comparing the signal intensity when either ionic solutions or nanoparticles suspensions are introduced in the continuous measurement mode in the CyTOF.

13.3.2 Imaging mass cytometry (LA-ICPMS)

Laser ablation in combination with inductively coupled plasma mass spectrometry (LA-ICPMS) is an element specific technique providing spatially resolved information on the low μm scale with limits of detection in the sub $\mu\text{g g}^{-1}$ range. Recent technological advancements in the field of low dispersion laser ablation setups have significantly improved the speed of analysis, sensitivity and sample throughput of LA-ICPMS measurements [13, 14]. With current LA setups, spot sizes down to 1 μm are available and high-throughput imaging at pixel acquisition rates of >200 Hz has become feasible [71]. Depending on the specific analytical problem, different instrumental setups are possible. On the ICP-MS side, low limits of detection can be reached using quadrupole-based instruments, while multi-element detection of short transient signals delivered by low dispersion LA setups is only enabled by TOF-based instruments [14].

Imaging mass cytometry (IMC) combines the concept of mass cytometry and high-resolution LA-ICP-TOFMS imaging. In this case, CyTOF instruments by Fluidigm are used for multiplexed single-cell analysis. Tissue sections or cells immobilized on slides are stained with panels of antibodies, which are conjugated to metal-chelating polymers carrying stable isotopes from the lanthanoid series [15, 72]. Samples are routinely scanned with a 1 μm spot size and pixel acquisition rates of 200 Hz. IMC allows the simultaneous detection of around 35 antigens and nucleic acid sequences in formalin-fixed paraffin-embedded (FFPE) tissue section and cultured cells with (sub-)cellular resolution. In contrast to mass cytometry, cells often overlap and are packed together in tissue sections, which results in less well-defined clusters in scatter plots and cell classifications for IMC. This problem can be addressed by analyzing multiple markers against the cell population of interest. To visualize the tissue, structure navigational aids and counterstaining procedures are required in IMC. For this purpose, the total ion current is used or iridium- and rhodium-containing DNA intercalators are employed, which provide information about nuclear size, shape and texture that can be used for measuring nuclear cytoplasmic distribution of intracellular proteins [15]. For counterstaining procedures, OsO_4 or RuO_4 is used in IMC studies [73, 74]. Imaging mass cytometry produces large amounts of spatially-resolved high-dimensional data, which constitutes a challenge for data analysis. Therefore, different software toolboxes have been developed for IMC enabling the analysis of cell phenotypes and their interactions in tissues [75, 76].

Calibration concepts and internal standardization for bioimaging by LA-ICPMS

Information about the localization of a metal, a metal species or biomolecule in biological samples is not always sufficient as biological responses are triggered by their concentration. Accurate quantification for biological samples by LA-ICPMS is challenging as it is limited by the availability of suitable and, in the ideal case, certified reference materials. Therefore, different calibration concepts have been exploited for bioimaging studies by LA-ICPMS, which are summarized in several reviews [77–79]. The most common calibration approach is based on matrix-matched standards, which are in-house prepared and characterized. Different materials have been suggested for the fabrication of matrix-matched standards to guarantee physical and chemical behaviors in terms of ablation and ionization characteristics, which are comparable to the biological sample material. This includes homogenates of a target organ such as liver [80], kidney [81], brain tissue [82] or whole blood [83], which are spiked with elemental standard solutions and sectioned to the same thickness as the sample. As drawbacks, these procedures can be laborious and involve the handling of biological material. Alternatively, polymer-based calibration standards [84] and printed standards [85, 86] using commercially available ink printers have been proposed. With the aim to mimic biological material, more universal matrix mimics such as gelatin have been used either as gelatin sections or as gelatin droplets spiked with elemental standard solutions. In order to ensure homogeneous distribution of analytes within gelatin droplets, it was found that the correct drying/setting conditions are essential parameters [87]. One study reported on the miniaturization of a droplet-based approach, which was accomplished by the generation of a microarray of gelatin standards using machining by the LA system itself. Using this approach, the quantitative distribution of Cu was studied in a model algae organism [88]. External calibration based on gelatin was employed to determine the expression levels of membrane receptors in two breast cancer cell lines by LA-ICPMS [89]. Automation of droplet deposition was accomplished by use of a MicroFab Jetlab micro-dispensing unit to create a rectangular grid of gold standard solutions. The calibration method was applied to quantify the number of Au nanoparticles in human erythroleukemia cells [90] and of a peptide-Au cluster in single cells [91]. Alternatively, micro-array spotters have been proposed to generate calibration standards in an automated and reproducible way. ICP-MS standard solutions were printed on nitrocellulose membrane [92] and on target glass slides [93] with volumes in the pL range [92, 94]. In this regard, single-cell analysis by LA-ICPMS was performed to quantify an Ir-DNA intercalator and an mDOTA-Ho dye in adherent 3T3 fibroblast cells [92]. Calibration standards using Ag NP suspensions were prepared in similar manner to investigate the quantitative distribution of Ag NPs in a multicellular tumor spheroid model [94].

Alternatively, (online) isotope dilution strategies have been proposed, which offer higher accuracy and precision as compared to external calibration as the isotope ratio remains constant even when instrumental drift or plasma fluctuations occur. The isotopically enriched spike can either be coated/blended on the sample or it can be added after the laser system as aerosol. Online isotope dilution analysis (IDA) was performed with LA-ICP-TOFMS using Pt spiked gelatin as matrix-matched standard to study the quantitative Pt distribution in kidney after cisplatin treatment [95]. In another study, the measurement uncertainty was determined by online IDA and it was found that it was reduced by up to two times compared to external calibration [96]. One study applied an online IDA approach to IHC-assisted LA-ICPMS for the quantification of metal labels. Anti-tyrosine hydroxylase was labelled with Yb isotopes, incubated on mouse brain sections and results were compared to external calibration [97].

Internal standardization is required to overcome effects related to instrumental drift where a high number of samples is ablated over a longer time period and to provide day-to-day reproducibility and interlaboratory comparability. For internal standardization by LA-ICPMS, different strategies are employed for quantitative elemental bioimaging including the use of an element naturally occurring in the sample and the addition of an internal standard layer between the sample and support or on top of the sample [79, 98]. In several studies, inks from a commercial inkjet printer were spiked with different elements used as internal standard and printed on top of electroblot membranes [99] or tissue sections [86, 100]. In addition, internal standard-spiked gelatin was proposed to correct for instrumental drift [81].

13.4 Applications

The different applications, where bio-conjugation (tagging) of biomolecules is used in combination with ICP-MS analysis can be divided into two main categories: (i) Identification and quantification strategies for proteins, peptides, RNA and DNA and (ii) Immunoassays and metallo-stains. They all have in common that lanthanoids are used to enable ICP-MS detection.

13.4.1 Identification and quantification strategies for proteins, peptides, RNA and DNA using ICP-MS based detection

Quantitative protein and peptide analysis are important topics in the life sciences. For this purpose, sensitive analytical methods are required to quantify such molecules at very low concentration levels in biological and biomedical samples. Several review

articles provide a general and comprehensive overview about lanthanoid elements as labels for ICP-MS based analysis of proteins and nucleic acids [22, 26, 27, 101, 102]. In combination with separation techniques such as capillary electrophoresis (CE) and high-performance liquid chromatography (HPLC) very sensitive relative and absolute quantification can be carried out in multiplexed experiments using the multielement capability of ICP-MS instruments. Since ICP-MS is not capable of differentiating between different proteins, their identification has to be conducted via electrospray ionization (ESI) and/or MALDI-MS and MS/MS. Figure 13.2 shows the general analytical strategy for protein determination by using lanthanoid-based probes.

A comprehensive summary of various applications for the quantification of proteins and nucleic acids using artificial tags in combination with ICP-MS detection is given by Liu et al. [22]. Furthermore, numerous applications of ICP-MS based immunoassays are discussed in the article. Here, only a few examples are presented.

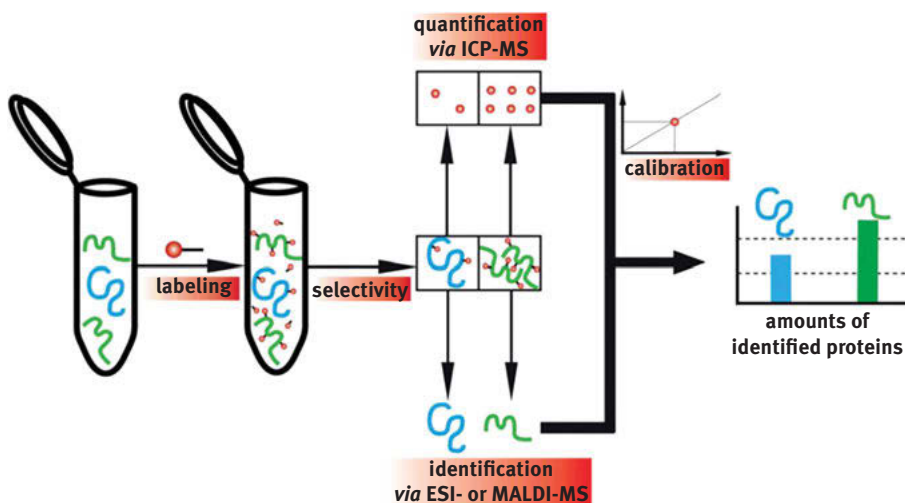


Figure 13.2: General idea and strategy of determining protein amounts by labelling with DOTA–lanthanoid complexes and quantification by ICP-MS. DOTA-lanthanoid complexes are covalently bound to proteins. Identification is carried out via ESI- and/or MALDI-MS and MS/MS and quantification by ICP-MS. The combination of both, identification and quantity, yield a useful quantification. Since ICP-MS is not capable of differentiating between different proteins, methods have to be employed for ensuring selectivity for different proteins prior to ICP-MS analysis and calibration. Reproduced from Ref. [26] with permission from The Royal Society of Chemistry.

The first MS-based application using a ligand based on DOTA loaded with lanthanoid ions was presented by Whetstone et al. [28] already in 2004. The authors showed that this approach is applicable in combination with reversed phase chromatographic separation of peptides and subsequent MS/MS experiments. Liu et al. [103] demonstrated the labelling of peptides using DTPA complexes loaded with

yttrium and terbium followed by the identification of differently tagged peptides using tandem MS.

The interplay between molecular and elemental mass spectrometry opens new opportunities. The labelled peptides or proteins can be identified accurately after chromatographic separation using the molecular mass spectrum. An absolute quantification is possible with ICP-MS using inorganic calibration standard solutions if the stoichiometry of the elemental tag and the labelling efficiency of the biomolecule are known. In a study conducted by Ahrends et al. [104], reaction parameters for the tagging of peptides and proteins with MeCAT were optimized. Afterwards, the workflow was successfully applied for the analysis of proteins from an eye lens of a wild boar (*Sus scrofa*) as a model system to demonstrate the applicability for complex biological samples. The developed method was also used to investigate changes in an *Escherichia coli* proteome [105]. Liquid chromatography (LC) ICP-MS was used for the separation and quantification of metal-tagged polypeptides from a lysate. The quantitative information from ICP-MS was then used for calibrating the organic mass spectrometer ESI-MS. The low matrix effects caused by biological samples in ICP-MS and the use of simple, non-species-specific metal-containing element standards opened a new possibility for the absolute quantification of cysteine-containing proteins and peptides. These can afterwards be used as home-made calibration samples in organic MS. Furthermore, the stability of MeCAT complexes under harsh analytical conditions including high salt content, low pH and increased temperature was demonstrated. It was shown that the developed technique is suitable to common proteomic workflows. The Linscheid group compared the relative quantification of peptides from α -lactalbumin using a gel-based workflow in combination with both organic and inorganic mass spectrometric methods [106]. The analysis of MeCAT labelled peptides using LC/ESI-MS and LC/ESI-MS/MS with infrared multiphoton dissociation (IRMPD) revealed that both the molecular masses and the specific fragments resulting from the MS/MS experiments can be used for relative quantification as different lanthanoids lead to different molecular masses for the same labelled peptides which can be distinguished easily. In summary, no significant differences between the methods were detected indicating that ICP-MS is the gold standard, but organic MS can be adequate in many cases. This finding is also important for method validation.

The combination of isotope dilution analysis with ICP-MS improves the quantification of biomolecules as matrix effects and signal drifts of the MS instrument can be eliminated efficiently. Chemical and physical analyte losses during the analytical workflow are compensated when applying species-specific isotope dilution. Esteban-Fernandez et al. [107] used MeCAT-Ln reagents for absolute peptide and standard protein quantification by LC-ICP-MS. Either external calibration with elemental standards or, for precise analyses, label-specific isotope dilution analysis using poly-isotopic elements were employed for absolute quantification. For external calibration any Ln-containing molecule or salt can be used as long as the ICP-MS sensitivity is kept at the same level (e.g. when using LC-ICP-MS). In one experiment, selected peptides were tagged with MeCAT-Eu and quantified by isotope dilution ICP-MS. A peptide mix at different concentrations was separated by

reversed-phase (RP) chromatography before ICP-MS detection and thus, calibration and quantification were performed in one run. For quantitative protein identification, a lysozyme and a bovine serum albumin tryptic digest were tagged with MeCAT-Eu. Afterwards the resulting peptides were analysed by LC-ICP-MS and LC-(RP)-ESI-ion trap Fourier transform ion cyclotron resonance MS.

Zhang et al. [108] developed a dual-labelling strategy for conjugating -SH and -NH₂ groups of a peptide using an element tag (maleimide-DOTA loaded with Eu) and a common fluorescent tag (fluorescein isothiocyanate). HPLC-ICP-MS in combination with isotope dilution analysis as well as capillary electrophoresis with laser-induced fluorescence detection (CE-LIF) were applied for the peptide determination.

Oxidative transformation of cysteine thiol groups into other functional groups is a significant post-translational modification in pathological and physiological processes. Since the formation of sulfenic acid (SA) displays a transient state of thiol oxidation, its formation can be considered a redox-sensitive sensor for the presence of reactive oxygen/reactive nitrogen species (ROS/RNS). Thereby, SA is an important biomarker in connection with age-related diseases like cancer and Alzheimer's disease. For the relative and absolute quantification of SA in peptides and proteins, an ICP-MS-based method was published by El-Khatib et al. [109]. For this purpose, a new metal-containing reagent (Ln-DOTA-Dimedone) was synthesized, which reacts specifically with SA. Species-independent signal intensities, high sensitivity and multiplexing capability of ICP-MS together with the labelling specificity of Ln-DOTA-Dimedone and Ln-MeCAT enabled the determination of SA and thiol residues in a simultaneous detection approach. Later, the SA detection was further improved by Sharar et al. [110] using a synthesised reagent, which reacts specifically with SA. In a proof-of-concept experiment, SA was generated in model peptides by oxidation with hydrogen peroxide. The short-lived SA was then captured by the linear alkyne β -ketoester (KE) previously linked to a Ln-DOTA complex by click chemistry. Finally, the resulting lanthanoid containing reagent (Ln-DOTA-KE) allowed highly sensitive elemental (ICP) and molecular (ESI) mass spectrometric SA detection and quantification in peptides.

Nucleic acids (deoxyribonucleic acid (DNA) and ribonucleic acid (RNA)) carry the genetic information and are therefore very important analytes in genomic research. Nucleic acids can be determined with ICP-MS via phosphorous. However, low sensitivity and mass interferences on ³¹P hinder the analysis, especially in real samples with low concentrations. Exogenous mass tags can overcome this limitation. First Merkoçi et al. [111] developed a DNA assay using gold nanoparticles immune-connected through peptide sequences followed by ICP-MS detection after dissolving. Later, lanthanoids were also used as artificial tags for DNA and RNA analysis. For example, Ornatsky et al. [112] simultaneously detected specific messenger RNA (mRNA) and proteins in leukaemia cell lines using different metal-containing tags. Another example is the analysis of micro-RNAs (miRNAs) which is of great significance for clinical diagnosis. The combination of an amplification strategy

using multicomponent nucleic acid enzymes, lanthanoid labelling and ICP-MS detection allowed the simultaneous detection of three miRNAs (miRNA-21, miRNA-155, and miRNA-10b) [113]. The specificity and cross-reactivity of the developed method was confirmed with solutions containing one, two, or three miRNAs.

In a proof-of-concept experiment, three thiolated complementary DNA probes (derivatized with Eu, Tb and Ho, respectively) were applied by López-Fernández et al. [114] for the detection of three oligonucleotides by ICP-MS using size exclusion chromatography for separation. The LODs achieved range between 5 and 11 fmol absolute. Han et al. [115] reported a multiplexing assay to determine 15 DNA targets each with 25–30 bases related to different diseases (cancer, hereditary pathia and virus) after labelling with different rare earth elements. Thiol-functionalized DNA was covalently conjugated with maleimide-DOTA, and then lanthanide ions were chelated in the macrocycle DOTA. The identification of each DNA target was performed by the recognition of mass spectrum of its own labelled lanthanide. Absolute DNA quantification was achieved with isotope dilution analysis using solution nebulization ICP-MS after hybridization of DNA targets. Two targets were simultaneously analysed using a specially designed two-strand system labelled with both natural isotopes (Dy or Er) and isotopically enriched isotopes (^{161}Dy or ^{168}Er).

For the ultrasensitive determination of nucleic acids classic amplification techniques can be applied to generate a signal enhancement. Brückner et al. [31] described a hybridization assay based on biotin–streptavidin affinity in combination with lanthanoid-tagged reporter oligonucleotide probes and biotinylated capture oligonucleotide probes. For the improvement of the sensitivity and sequence specificity of the assays, a target amplification using the ligase chain reaction (LCR) was applied. This amplification step resulted in a 6,000-fold sensitivity increase. Finally, an LOD of only 2.6 amol was achieved with a double-stranded DNA target. However, until now most of the developed methods for the analysis of nucleic acids by using metal-containing tags are proof-of-concept studies.

Classical immunoassays can also be combined with ICP-MS detection. In this case, antibodies bio-conjugated with metal-based tags are used. Two different detection methods can be applied including solution nebulization ICP-MS and LA-ICPMS. The latter is explained in subchapter 13.3.2. Immunoassays are based on the specific binding of antibodies with their corresponding antigens and thus can be used for identification of proteins (antigens) and/or their quantification. For this purpose, it is common to tag the antibody by a compound which can be easily detected by photometry, fluorescence, or spectrometric detection, in particular, ICP-MS. Usually, antibodies of the IgG-type are employed for this purpose. The first description of an antibody carrying a tag for subsequent detection was published by Coons et al. in 1941 [116], who introduced the coupling with fluorescein by an isothiocyanate derivate. The first clinical immunoassay was developed for the determination of insulin in human blood by Yalow and Berson in 1960 [117].

When using conventional pneumatic nebulization ICP-MS for detection, the antibody tag linked to the desired analyte is typically dissolved by acids after the immune reaction and the resulting solution is subsequently analysed. An advantage is that this type of assay is relatively simple and fast and can easily be quantified by liquid standard solutions. Both, one-parameter assays and multi-parameter assays are possible. The analytical figures of merits of such an immunoassay are directly related to the antibody affinity, the number of tags per antibody, the element background in the sample and the number of antigens. As the sample is always diluted due to the dissolution process, the limit of detection of this type of assay is typically degraded compared to a direct analysis using e.g. LA-ICPMS. However, it is advantageous that this type of assay can easily be quantified by liquid standard solutions. The review article from Giesen et al. [118] provides a detailed overview about ICP-MS-based immunoassays. An example for a recently published immunoassay using solution nebulization ICP-MS is the determination of carcinoembryonic antigens (CEA), which are widely applied in cancer diagnosis [48]. The immunoassay procedure used was similar to a conventional sandwich-capture format enzyme-linked immunosorbent assay (ELISA). Here, a novel DNA-based elemental tag, modified with a biotin group and streptavidin as a cross-linker, was attached to the antibody. After the immune reaction, the lanthanoid ions were dissociated from the complex and detected by ICP-MS. Furthermore, a multiplex detection of alpha-fetoprotein (AFP) and ferritin (FER) has been demonstrated using the corresponding antibodies tagged with Pr and Ho, respectively. To increase the sensitivity, Liu et al. [119] used UCNPs ($\text{NaYF}_4\text{:Yb,Er@NaYF}_4$ NPs) as artificial tags to determine AFP in blood serum, an important biomarker of liver cancer. The NPs were bio-conjugated to the mouse anti-human AFP antibody and afterwards used in a sandwich immunoassay with ICP-MS detection. The received limits of detections (3σ) of 0.31 ng mL^{-1} based on ^{89}Y signal and 0.22 ng mL^{-1} based on ^{174}Yb signal are comparable with other approaches. Besides, UCNPs as tags allow both ICP-MS analysis and fluorescence detection.

The multi-element capability of ICP-MS was utilised by Sun et al. [120]. The authors developed a combinatorial immunoassay for the simultaneous detection of 12 different clinically relevant biomarkers by using magnetic microparticles (MMPs) as a platform. First, capture antibodies were immobilized on the MMPs. Afterwards, protein targets were added and mixed with the detection antibodies labelled with different Ln-DTPA chelate complexes. Via the antigen-antibody reaction sandwich conjugates of MMP-protein-lanthanide complexes were synthesized. Magnetic separation was used to remove excess Ln-labelled antibodies, followed by digestion with nitric acid and ICP-MS quantification.

Shuck et al. [121] developed sensitive and rapid methods of protein quantification based on an antibody-based multiplex assay using solution nebulisation ICP-MS. The practical applicability of the method, termed metal-assisted protein quantitation (MAPq), was successfully demonstrated for the quantitative analysis of low-abundance nuclear and cytoplasmic proteins that do not require cell sorting, i.e. single-cell analysis by mass

cytometry. By using primary antibodies conjugated with lanthanoid-chelating polymers, up to 35 proteins could be analysed simultaneously in cultured cells and mouse tissue with a limit of quantification (LOQ) of 5 pg mL^{-1} . MAPq was found to be at least 10 times more sensitive than Western blots and could therefore detect changes in protein expression not accessible with conventional approaches.

Immunoassays can also be combined with size-exclusion chromatography (SEC) and ICP-MS detection. In this case, antibodies were labelled with lanthanoid-containing tags. After the immunoreaction, the antibody-antigen complexes were separated and detected by SEC-ICP-MS. Perez et al. [122] applied this strategy to determine four cancer biomarkers (CEA, sErbB2, CA 15.3 and CA 125) in human serum using the corresponding antibodies labelled with MCPs. The results were validated using sandwich-type immunoassays with electrochemiluminescence detection. With the Ln-polymer tags both sensitivity and LOQs could be improved up to a factor of 10 compared to Ln-DOTA complexes. For example, an LOQ of 0.18 ng mL^{-1} was calculated for CEA. Thereby, even biomarkers below the threshold reference values used in clinical analysis could be detected. In combination with post-column isotope dilution analysis, the precise absolute quantification of proteins is possible [123]. The SEC separation of the labelled antibody, added in excess to the protein sample, and the immunocomplexes enabled the determination of the Ln:sulphur stoichiometry of the labelled antibody. The differences in Ln:sulphur ratios between the labelled antibody and the immunocomplex peak were accounted for and used to calculate the concentration of the immunoglobulin protein. The procedure was validated by direct labelling of the target protein with another lanthanoid for parallel, simultaneous quantification. A very good agreement of the results was found.

13.4.2 Application of lanthanoids in single-cell ICP-MS / mass cytometry

As explained in section 13.3.1, mass cytometry uses mainly lanthanoid-labelled antibodies that allow a sensitive detection of the biomarker expression at the single-cell level. Mass-tag reagents include lanthanoid-chelating polymers and other nonpolymer-based reagents that include DNA intercalators, cell cycle tags and metal-chelated ligands, such as lanthanoid-loaded maleimide-DOTA. However, DNA intercalators and cell cycle tags are based on non-lanthanoid metals (mainly platinum and iridium) or non-metals (iodine), respectively, and therefore, only applications using polymeric mass-tag reagents and maleimide-DOTA complexes will be reviewed.

The number of single-cell applications using maleimide-DOTA reagents is rather limited because this molecule can only chelate one lanthanoid atom per DOTA group, therefore limiting the sensitivity to detect cellular biomarkers in comparison to polymeric tags. The use of lanthanoid-loaded DOTA has been reported in a single-cell study of apoptosis and cell differentiation caused by As_2O_3 by the conjugation of DOTA-Nd to

Annexin-V and DOTA-Dy to an anti-CD11b antibody, being Annexin-V an apoptosis-related protein and CD11b related to cell differentiation [124].

In comparison to maleimide-DOTA mass tags, polymer tags can host several tens of lanthanoid atoms per polymer molecule. Specifically, Maxpar® polymers (Fluidigm), which are mainly used as mass-tags in mass cytometry, host 20–50 atoms of lanthanoid per molecule [125] and the final lanthanoid:antibody stoichiometry is usually sufficient to detect relatively abundant biomarkers (10^4 – 10^7 molecules per cell). There is still, however, room for improvements in sensitivity by increasing the number of lanthanoid atoms, for example, by the development of branched polymers that contain a higher number of chelating groups.

The use of lanthanoid-loaded Maxpar polymers has been reported for single-cell biomarker analysis in a high number of publications, especially in mass cytometry studies using CyTOF. The field of immunology is a clear and active application field for mass cytometry that is especially benefitted by the high multiplexity of this technique, given the high complexity of the immune system. Some examples of applications of lanthanoid detection by mass cytometry in this field include the quantification of multiple transcription factors to understand and model the immune organization in mice [126]. Cytokine expression patterns, together with immune populations in peripheral blood mononuclear cells and their activation status were analyzed by mass cytometry using a panel of 45 lanthanoid-labelled antibodies to study the implications of immunity in narcolepsy [127]. Cytokine staining was also used in combination with other cell markers to identify cell signatures in human patients with multiple sclerosis [128].

Lanthanoid-labelled antibodies have been used for cell cycle determination. This is possible by the use of lanthanoid-labelled antibodies against specific cell cycle-related proteins (phosphorylated retinoblastoma protein (pRb), cyclin B1, Ki-67 and the phosphorylated histone H3 (p-HH3)), together with the analysis of the incorporation of the modified nucleotide 5-iodo-2'-deoxyuridine (IdU) [129]. This combination allows for the determination of all five cycle phases, but additional markers can be used to provide additional information on subset cell cycle states or checkpoints activation.

In an attempt to increase the throughput of mass cytometry and, at the same time, decrease staining irreproducibility between different batches of cells, the concept of barcoding has been introduced. Cellular barcoding consists of the codification of different types of samples using a combination of isotopically pure metals. Once each different cell sample is codified, all samples are pooled together, stained with an antibody panel and run in the mass cytometer. After the measurement, the barcoding is decoded and each cell can be assigned to its initial sample. Initially, barcoding was achieved using DOTA-chelated lanthanoids. By the combination of only seven lanthanoids, up to 128 different combinations for barcoding could be achieved [130]. This barcoding strategy, however, used most lanthanoid channels in the mass cytometer, and has been now replaced by palladium-based barcoding, by combination of the six stable isotopes of this metal [131].

Some simplified mass cytometry experiments with only one analyte marker have been proposed because they can be applied to quadrupole-based ICP-MS instruments, which are limited to monitoring only one isotope per run in SC-ICP-MS. For example, an experiment proposed using ^{142}Nd -loaded MaxPar polymer to tag an anti-transferrin receptor 1 (anti-TfR1) antibody. By means of external calibration and characterization of the labelled antibody, quantification of the TfR1 expression was accomplished at the single-cell level [69]. Another interesting mono-isotopic approach was published by Liang et al. [132]. They used clickable labeling with the azide-DOTA-europium tag and the metabolic assembly of alkyne-D-alanine (aDA) for signal amplification and applied this approach to bacterial counting by SC-ICP-MS.

Lanthanoid-loaded polystyrene beads are used for the standard instrument tuning procedure and signal normalization in CyTOF instruments. The first attempts were made with in-house loaded polystyrene microspheres further conjugated to diethylene triamine pentaacetic acid (DTPA), which was then loaded with Tb, Ho and Tm ions [133]. But another version was later made commercial as CyTOF calibration standard beads. These beads are about 3 μm in diameter and are doped with cerium, europium, holmium and lutetium in their natural isotope ratios, therefore containing isotopes 140, 142, 151, 153, 165, 175 and 176. The lanthanoid-loaded beads are used for daily tune of the instrument, as a quality control in terms of transport efficiency and sensitivity, but they can also be mixed with the samples for real-time normalization of the results. Therefore, the detection of the beads in the same run as the cell sample allows to monitor and correct for short-term fluctuations and changes during data acquisition by means of a normalization algorithm. This strategy also ensures comparability of mass cytometry data over days and weeks by normalizing the intensities to the intensity of the beads [134]. Besides being a standard tuning and normalization procedure with CyTOF, other authors also used lanthanoid-loaded polystyrene beads as a standard for quality control and tuning using quadrupole-based and other TOF-based ICP-MS systems, especially for transport efficiency calculation [69, 135].

13.4.3 Protein determination after separation by gel electrophoresis and by immuno-microarrays

Most ICP-MS based applications use a conventional sample introduction system based on the nebulisation of solutions. For the separation of biomolecules, separation systems like HPLC or CE can be coupled to an ICP-MS instrument. For the direct analysis of solid materials, the combination with a laser ablation system is possible. Thus, various kinds of solid samples like metals and geological samples, but also gels, membranes and tissues can be examined. The potential of LA-ICPMS to map and detect biomolecules was first described by Neilsen et al. [136] The authors used gel electrophoresis (GE) for separation followed by LA imaging to identify and quantify Co binding proteins in blood serum. Over the following years this combination

was increasingly used for the separation of metalloproteins containing e.g. Cu, Se or Zn using isoelectric focusing electrophoresis (IEF) as well as one- or two-dimensional polyacrylamide gel electrophoresis (PAGE) under both native and denaturing conditions [137]. With the development of exogenous metal-containing tags the application area expanded [22]. Besides, LA-ICPMS can be used for the readout of microarray using an immune reaction for (multiplexed) biomarker detection. The following paragraph provides an overview about the current analytical possibilities by means of a few selected examples.

There are two possibilities to analyse the metal content of proteins in gels by ICP-MS. One way is to cut out spots or parts of spots and remove or solubilize the gel matrix e.g. by using soluble gels or digestion with nitric acid and hydrogen peroxide. Spot mineralization showed an LOQ near 50 pg of protein (about 750 amol) although the detection of lower amounts of protein is possible [138]. The other way is to use LA-ICPMS directly or after electroblotting to transfer the proteins onto a thin membrane. Quantitative LA-ICPMS is still a challenge due to the lack of suitable calibration samples, fractionation effects and the heterogeneity of biological samples. However, a sensitive and accurate absolute quantification of proteins is possible with label-specific isotope dilution analysis. This was shown for Yb-DOTA-labelled proteins mixed with known amounts of protein standards labelled with isotopically enriched ^{171}Yb [138]. The proteins were separated by sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE) and analysed via LA-ICPMS directly in the gel. Using direct laser ablation of the gel, an LOQ of about 1 ng for human serum albumin (ca. 15 fmol) was successfully detected. The described approach works well for the absolute quantification of abundant proteins in biological samples, e.g. lysozyme as model sample or human serum albumin and transferrin in blood serum. A disadvantage of this procedure is that the protein must be available for labelling with the isotopically enriched tag.

He et al. [139] applied metal-coded affinity tags based on click chemistry to analyze the proteome of *Escherichia coli* (*E. coli*) in response to heat stress. For this purpose, differentially labelled samples were separated by two dimensional GE and afterwards scanned by LA-ICPMS to detect the differential expression of proteins in the spots. ESI-MS was applied to identify the proteins that showed the differential expression. Due to the excellent sensitivity of LA-ICPMS, an upregulated protein with very low abundance was found that was nearly invisible by conventional silver staining.

Western blot assays (also known as immuno-blot assays) are a common method for antibody-based protein detection. Proteins are first separated by GE, transferred onto a thin membrane using electro-blotting, and, subsequently, immuno-reacted with antibodies which bind specifically to the target proteins. LA-ICPMS can be used for detection and quantification when using metal-tagged antibodies. Waentig et al. [140] labelled different antibodies (chicken anti-bovine serum albumin, rabbit anti-chicken lysozyme and rabbit anti-bovine casein) with chelate complexes based on DOTA containing different lanthanoid ions and used them afterwards in a Western blot assay in

combination with LA-ICPMS detection. For validation, chemiluminescence detection as conventional method was applied, which gives a similar sensitivity but was more time consuming. These results demonstrate the potential of the developed methodology for the simultaneous identification and quantification of proteins after separation by GE. A Western blot assay was also used by de Bang et al. [141] for the multiplexed quantification of five thylakoid proteins extracted from chloroplasts of the plant species *Arabidopsis thaliana*. To correct for bias origination from the blotting procedure a cerium-labelled lysozyme was introduced as an internal reference protein. This allowed correction for up to 50 % difference in protein transfer efficiency during membrane blotting. For comparison between different membranes and protein quantification, matrix-matched calibration samples based on a nitrocellulose membrane spiked with multi-element solutions with different lanthanoid concentrations were used. Thus, a quantitative measure of the relative abundances of different proteins in the plant extract was achieved. The method was capable of measuring the L subunit in a photosystem I protein of an *Arabidopsis* mutant containing only less than 5 % of this particular protein, relative to the wild-type.

Jakubowski and co-workers elaborated methods for the quantification of cytochromes P450 (CYP) in liver microsomes using lanthanoid-labelling. CYPs are a family of iron containing enzymes. The analysis of CYPs patterns is important for toxicological and pharmacological studies as these enzymes are strongly involved in the metabolism of xenobiotics (e.g. toxicants, drugs). For these studies, rats were treated with several known inducers (xenobiotic or cancerogenic compounds), which are specific for different types or subsets of CYPs. Starting with an immunoassay for two CYPs, CYP1A1 and CYP2E1 [142], the number of targets was increased in the following years [143, 144]. Protein samples from liver microsomes were electrophoretically separated and subsequently transferred to a nitrocellulose membrane by electroblotting. For the multiplexed analysis of chemically induced alterations of cytochrome P450 protein expressions, different lanthanoid-tagged antibodies were used [143]. Competition of antibody binding was neglectable as the quantitative data obtained with single immunoassays were comparable to the multiplex assay. After optimisation of the labelling strategies for antibodies using different commercially available lanthanoid-containing tags, LODs in the lower fmol range were reached in a Western blot immunoassay. In dot-blot experiments for pure antibodies even sub-fmol LODs can be achieved [145]. This enables the use of a high-throughput microarray. Instead of sample separation by GE and blotting procedures, which are time consuming and vulnerable to sample losses, microarrays allow the high-throughput analysis of e.g. expression profiles. On a microarray, hundreds of protein spots are arranged on a single microscopic slide by use of a spotter. After spotting, the array is incubated with metal-tagged antibodies directed against biomarkers indicative for a specific disease or for an expression of relevant proteins. First, such microarray platforms were applied with fluorescently labelled antibodies. In this case LA-ICPMS can provide valuable service, too. Waentig et al. [144] successfully applied a multi-parametric microarray for the simultaneous analysis of 8 different cytochromes

using differentially lanthanoid tagged antibodies. The methodology presented shows excellent detection limits in the lower attomol range and a very good linearity which is a prerequisite for the development of further quantification strategies. Such an assay looks promising for a personalized diagnosis because hundreds of patient samples can be tested for various biomarkers in one run. Another example for the detection of multiple proteins in spots on an immuno-microarray using LA-ICPMS for the readout was published by Hu et al. [146]. Carcinoembryonic antigen (CEA), r-fetoprotein IgG (AFP) and human IgG have been detected simultaneously on the basis of sandwich-type immunoreactions with the corresponding antibodies tagged with lanthanoids (Eu, Sm) and colloidal gold, respectively. Because several analytes can be detected from one spot in a single measurement, LA-ICPMS as readout method for microarrays might be used more widely in the future.

13.4.4 Application of lanthanoids in LA-ICPMS/imaging mass cytometry

In the following subchapter selected applications will be presented, where antibodies conjugated with metals/metal nanoclusters/lanthanoids in combination with conventional LA-ICPMS setups were used. This approach is sometimes called ‘immuno-mass spectrometry imaging’ [147, 148], in contrast to ‘imaging mass cytometry’ (chapter 13.3.2), where dedicated CyTOF instruments by Fluidigm are employed for analysis [15].

LA-ICPMS applications

One recent study showed the potential of a low dispersion LA setup in combination with ICP-MS to study the localization and quantification of membranous receptors in two breast cancer cell lines [89]. Multimodal imaging of membranous receptors was performed based on fluorescence confocal microscopy (FCM) and LA-ICPMS by employing receptor-specific hybrid tracers, containing both a fluorophore and a DTPA single-lanthanoid chelate based on Ho (Figure 13.3) [89]. Sub-cellular imaging by LA-ICPMS demonstrated the specific binding of the hybrid tracer to the cell membrane. External calibration based on gelatin standards was used to determine the expression levels of the membrane receptors by LA-ICPMS. Quantitative results were in accordance with the expression levels determined by flow cytometry and mass cytometry. The study also demonstrated complementary characteristics for both imaging modalities, allowing a more distinct discrimination between both cell lines [89].

For imaging of proteins in biological tissues by LA-ICPMS, small metal nanoclusters (NCs) with fluorescent properties were proposed as elemental labels [149]. The

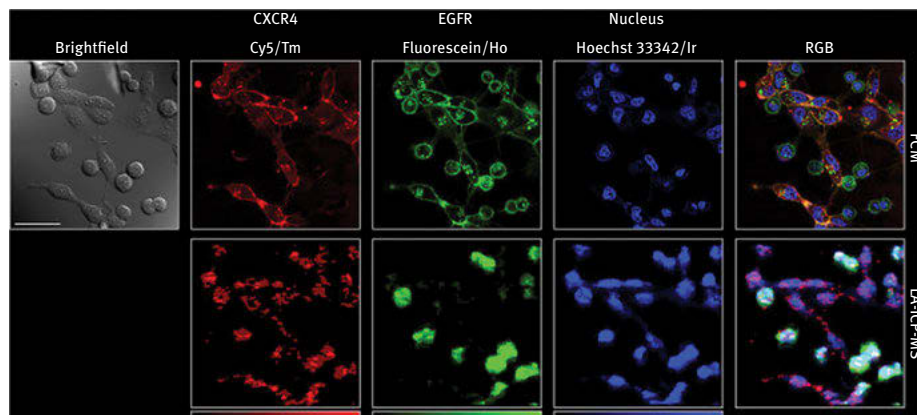


Figure 13.3: Composite of fluorescence and elemental images of breast cancer cells stained with hybrid tracers, obtained by fluorescence confocal microscopy and LA-ICPMS imaging with the corresponding brightfield microscopic image. Images are reprinted with the permission of Ref. [89], copyright by Elsevier.

main advantage of this method is the signal amplification that can be achieved by labelling of antibodies with metal nanoclusters, as each NC has several hundreds of metal atoms. In addition, metal NCs provide multimodal imaging capabilities through fluorescence and MS analysis in the same tissue section. Using this strategy, LA-ICPMS was used to localize specific proteins in human ocular tissue sections [150] and to visualize proteins of interest in neurodegenerative diseases in an eye tissue section [151]. In another study, simultaneous quantification of iron and ferroportin was carried out in tissue sections of the hippocampus region from Alzheimer disease (AD) patients and healthy controls (HC). For imaging of ferroportin, gold nanoclusters were used and for quantification of iron, laboratory-made gelatin standards were employed. Increased concentrations of iron were found in AD patients compared to HC donors, whereas similar concentrations of ferroportin were observed in AD donors with respect to HC donors [152]. Antibody-conjugated AuNPs in combination with LA-ICPMS detection were used for quantitative imaging of amyloid beta ($A\beta$) peptide in the brain of an Alzheimer's disease mouse model. Quantitative imaging of Au was performed with homogenized brain sections as external calibrants, which were made by immersing in gold standard solution with different concentrations [153]. One study investigated the distribution of the protein MMP-11 of the matrix metalloproteinase family, which is overexpressed in cancer cells, in human breast cancer tissue by LA-ICPMS. Visualization was accomplished by an Au-NP-based immunohistochemical assay. It was shown that the expression of MMP-11 was increased and more heterogeneous in metastatic specimens compared to non-metastatic tumor samples [154]. A recent study reported on an immuno-mass spectrometry imaging method to quantify dystrophin for Duchenne muscular dystrophy (DMD). For this purpose, gadolinium (Gd)-labeled anti-dystrophin

antibodies and LA-ICPMS were used to simultaneously quantify and localize dystrophin in muscle sections. The relative expression of dystrophin was quantified in murine and human skeletal muscle sections following k-means clustering segmentation, before application to DMD patients with different gene mutations [148]. In one work for immune-mass spectrometry imaging using quadrupole-based LA-ICPMS, significantly improved signal-to-noise ratios for lanthanoids were achieved by specific tuning of ion-optics and quadrupole parameters [147]. This provided increased transmission of low-level high-mass elements, which are typically used as labels for antibodies, at the expense of highly abundant endogenous low-mass elements. The lower limits of detection enabled to map at higher spatial resolution and to visualize important microstructures in brain tissue. This method improved the analysis of endogenous elements and tyrosine hydroxylase as a proxy for the concentration of dopamine in murine brains in the region of the hippocampus and the substantia nigra [147].

Imaging mass cytometry applications

Imaging mass cytometry (IMC) has become an emerging technique in recent years in the field of medical research, cancer research, immunoprofiling, etc. Numerous studies using IMC have been published and a comprehensive overview can be found in dedicated review articles [15, 72], while only selected applications will be presented here.

In a pioneering study by Giesen et al. (2014) [44], imaging mass cytometry was applied to human breast cancer samples using a spot size of 1 μm and allowing the multiplexed analysis to highlight tumor heterogeneity and identify cell subpopulations. In a recent study, the cellular architecture of breast cancer tissue was characterized based on cellular composition and tissue organization by imaging mass cytometry [47]. Topological single-cell network analysis of high-dimensional mass cytometry images was performed for 35 biomarkers in breast cancer tissue from 350 patients. Analysis revealed multicellular structures of the tumor microenvironment and novel subgroups of breast cancer that are associated with distinct clinical outcomes. In relation to patient outcome, the information yielded by the multicellular structures was superior to that yielded by single-cell data alone [47]. To define the phenogenomic landscape of breast cancer, IMC and multiplatform genomics were employed. Single-cell analysis revealed cell phenotypes spanning epithelial, stromal and immune types in 480 tumors using the quantification of the expression of 37 proteins by IMC. Distinct combinations of cell phenotypes and cell–cell interactions were associated with genomic subtypes of breast cancer, which can reveal a better understanding of the phenotypic impact of genomic alterations [155]. The assessment of HER2 ICD/ECD, cytotoxic T-cell infiltration and other structural and signaling proteins was performed by IMC in a cohort of patients treated with trastuzumab to discover associations with trastuzumab benefit. The proximity of

CD8 cells as a function of the expression of the ECD of HER2 provides evidence for the role of the immune system in the mechanism of action of trastuzumab [156].

The three-dimensional (3D) multicellular tumor spheroid model reflects the tumor microenvironment in terms of pathophysiologic gradients and cell types and has become an advanced *in vitro* model and research tool. Recently, the first use of IMC for single-cell phenotyping in a 3D tumor spheroid model was presented using a pixel size of 1 μm [157]. Multimodal mass spectrometry imaging techniques based on desorption electrospray ionization (DESI), IMC and LA-ICPMS imaging were employed to characterize an *in vitro* 3D lung adenocarcinoma model. Protein markers of proliferation (K_i -67) and hypoxia (glucose transporter 1) as determined by IMC defined metabolic signaling in the tumor spheroid model, which complemented the metabolite data obtained by DESI. The endogenous elemental compositions of Mg, Zn, and Cu as determined by LA-ICPMS corresponded to the protein information and further validated the presence of a hypoxic gradient [157].

Regarding metal-based anticancer drug research, cisplatin is routinely used as reagent for cell viability for single cell mass cytometry [158]; however up to date, only few imaging mass cytometry studies addressed metal-based anticancer drug research. One pioneering study by Chang et al. (2016) investigated cisplatin localization in pancreas tumor sections of mice together with markers for cell lineage definition, DNA damage response, cell proliferation and functional state [159]. It was shown that cisplatin was binding to collagen fibers (Figure 13.4) and that stroma-bound cisplatin was slowly released. Preferential binding of cisplatin to collagen-rich structures was also shown by IMC in gastric cancer, where higher tumor Pt concentration correlated with improved pathological response [160].

One IMC study addressed peripheral sensory neuropathy, one of the most common and dose-limiting side effects of oxaliplatin. While Pt was not detectable in plasma samples of the patients, it was readily detectable in skin biopsies even up to 66 months post application, which can provide a possible mechanism for oxaliplatin-induced peripheral sensory neuropathy [161].

Imaging mass cytometry was also used to study the immune cell and cytokine alterations in postmortem tissues of COVID-19 patients [162]. IMC revealed monocyte, macrophage, and dendritic cell infiltration in the lung, intestine, kidney, and liver tissues. In lungs and intestine, an overproduction of the immunosuppressive cytokine interleukin (IL)-10 and a higher expression of the tumor necrosis factor (TNF)- α expression was observed. The results suggested that IL-10 and TNF- α as immunosuppressive and pro-inflammatory agents, might be prognostic and could serve as therapeutic targets for COVID-19 [162].

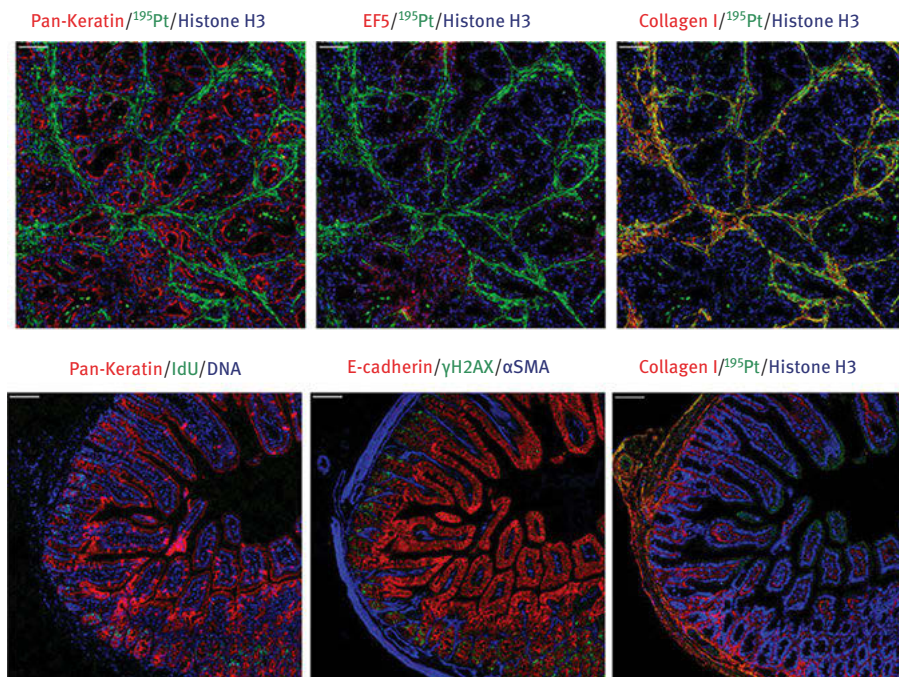


Figure 13.4: Imaging mass cytometry shows the preferential binding of cisplatin to collagen-rich structures in tumor tissue and small intestine. Top: Images of Pan-Keratin, EF5, collagen, ^{195}Pt , and Histone H3 in tumor tissue of mice after treatment with cisplatin. Bottom: Images of Pan-Keratin, IdU, DNA, E-cadherin, γH2AX , αSMA , Collagen I, ^{195}Pt , and Histone H3 of small intestine from cisplatin-treated mice. Images are reprinted with the permission of Ref. [159], copyright by Springer Nature.

Future perspectives: Three-dimensional LA-ICPMS imaging

Three-dimensional LA-ICPMS imaging provides invaluable information on the tissue architecture, cell-to-cell interactions and the tissue microenvironment. In LA-ICPMS, three-dimensional volumes can only be constructed from a series of 2D images of sequential sections of the sample due to matrix-dependent ablation rates. For reconstruction, elemental images of adjacent sections are stacked and aligned through registration approaches to reflect the true 3D morphology of the sample. In pioneering studies by Hare et al. (2012) [163] and Paul et al. (2015) [164], C57BL/6 mouse brains were mapped in 3D by LA-ICPMS by serial sectioning and subsequent volume reconstruction based on image registration. Metal distributions within the complete mouse brain were reconstructed and it was shown that discrete regions of metal distribution corresponded to specific areas of neurological functionality. In addition, gold nanoparticles and ytterbium-tagged tyrosine hydroxylase antibodies were used to assess the co-localization of Fe and dopamine throughout the entire mouse brain.

[164]. Super-resolution reconstruction was applied for 3D LA-ICPMS imaging of dystrophin (using Gd-labeled antibodies) in murine muscle fibers to improve spatial resolution and provide superior image clarity [165]. A 3D correlative map of metal distribution and skeletal growth was constructed in a mouse embryo at developmental stage E14. This was achieved by registering LA-ICPMS data to micro-computed tomography (μ -CT) using endogenous fiducial markers [166].

Van Malderen et al. (2017) used 3D LA-ICPMS imaging to visualize and quantify the toxic trace metal distribution pattern in structural compartments of wheat and rye grains exposed to natural background concentrations [167]. LA-ICP-TOFMS in combination with laboratory-based absorption μ -CT was used to study the 3D multi-elemental distribution profile within a freshwater microorganism *Ceriodaphnia dubia* [168]. In another study, a workflow based on a low dispersion LA-ICPMS setup was developed to reconstruct the 3D elemental distribution in single HeLa cells with a spatial resolution of 1 μ m. Cells were stained with uranyl acetate and an Ir-based DNA intercalator. As complementary method, micro-computer tomography was employed to acquire a reference frame of the morphology of the cells. A sequential series of 132 sections was prepared and the scanning speed was significantly increased by a bidirectional scanning strategy using a pixel acquisition rate of 250 pixels sec^{-1} [169]. Recently, a proof-of-principle study of 3D imaging was performed in imaging mass cytometry on a breast tumor tissue sample. Compared to 2D imaging, this approach allowed distinguishing invasive tumor cells from surrounding glandular tissue. The identified regions of micrometastasis correlated with areas of stroma strongly expressing phosphorylated ribosomal protein S6. Machine-learning methods enabled classification of cell types and interactions in 3D providing the identification of clusters of epithelial basal cells, T cells and phenotypes displaying distinct molecular profiles [170]. Table 13.1 provides a comprehensive overview about both LA-ICPMS and IMC applications mentioned in the text.

Table 13.1: Comprehensive overview about recent LA-ICPMS bioimaging and IMC applications mentioned in subchapter 13.4.4.

Sample	Analytes	Label	Spatial resolution	Reference	Comment
LA-ICPMS imaging					
HeLa cells	Nucleus	Ir intercalator	1 μ m	2019, Ref. [169]	3D reconstruction of elemental tags in single HeLa cells.
Breast cancer cells	Membranous receptors	Lanthanoid label	2 μ m	2019, Ref. [89]	Quantification of membranous receptor levels on subcellular level.
Fibroblast cells	Fibroblast cells	m-DOTA-Ho	30 μ m	2018, Ref. [92]	Quantification of Ho and Ir in single fibroblast cells.

Table 13.1 (continued)

Sample	Analytes	Label	Spatial resolution	Reference	Comment
Brain tissue	Fe, ferroportin	Au-nanocluster	10 μm	2019, Ref. [152]	Quantification of Fe and ferroportin in brain tissue from Alzheimer's disease.
Ocular tissue sections	Metallothioneins	Au-nanocluster	4 μm	2018, 2020, Ref. [150, 151]	Localisation of metallothioneins in eye tissue by use of metal-nanoclusters for signal amplification.
Brain tissue	Amyloid beta peptide	Au-NPs	100 μm	2021, Ref. [153]	Quantitative imaging of amyloid beta peptide in brain.
Breast cancer	MMP-11 protein	Au-NPs	30 μm	2019, Ref. [154]	Imaging of MMP-11 protein in human breast cancer tissue of patients with and without metastases.
Muscle tissue	Dystrophin	Gd-ABs	15 μm , 7.5 μm	2021, Ref. [148]	Imaging of dystrophin in skeletal muscle tissue of patients.
Imaging mass cytometry					
Breast cancer	35 biomarkers	Lanthanoide-antibodies	1 μm	2020, Ref. [47]	Single-cell pathology landscape of breast cancer revealed by IMC.
Breast cancer	37 proteins	Lanthanoide-antibodies	1 μm	2020, Ref. [155]	Characterisation of the phenogenomic landscape of breast cancer.
Breast cancer	18 proteins related to HER2	Lanthanoide-antibodies	1 μm	2019, Ref. [156]	Relationship between trastuzumab treatment nad HER2 related proteins in breast cancer tissue of patients.
Tumor spheroid	Hypoxia, proliferation	Lanthanoide-antibodies	1 μm	2020, Ref. [157]	First IMC study in a 3D multicellular tumor model.
Pancreas cancer	Collagen, histidin, Pt	Lanthanoide-antibodies	1 μm	2016, Ref. [159]	IMC revealed extensive binding of cisplatin to collagen in pancreas cancer.
Gastric cancer	Collagen, Pt	Lanthanoide-antibodies	1 μm	2019, Ref. [160]	Preferential binding of cisplatin to collagen-rich structures was demonstrated in gastric cancer.
Skin biopsies	Nerve fiber, Pt	Lanthanoide-antibodies	1 μm	2018, Ref. [161]	Platinum deposition in skin biopsies of patients treated with oxaliplatin.
Tissue of COVID-19 patients	Immune cells	Lanthanoide-antibodies	1 μm	2020, Ref. [162]	IMC revealed the immune cell composition and cytokine alterations in postmortem tissues of COVID-19 patients.

13.5 Lanthanoid-containing nanoparticles for medical applications

Metal-containing nanoparticles (NPs) are nowadays used in numerous fields ranging from industrial to medical applications. They are made of various substances resulting in different physicochemical properties and functionalities. There is a growing list of specially designed nanoparticles for biomedical applications like diagnosis, imaging or theranostics [171]. Presently, many of them are in an early stage, while others are translated into clinical use. Nanoparticles doped with REE are interesting for clinical diagnosis and toxicological studies. Besides, NPs can be used as artificial tags for the indirect determination of biomarkers using mass cytometry or IMC (see subchapters 13.4.2 and 13.4.4). Due to their low background levels in biological samples, lanthanoid-containing NPs can be easily detected with ICP-MS. Therefore, LA-ICPMS is meanwhile a powerful complement to other imaging techniques.

For magnetic resonance imaging (MRI), contrast agents are used to enhance the visualisation of tissue morphology and pathology [172]. Most of the contrast agents are Gd-containing substances, but also superparamagnetic iron oxide nanoparticles (e.g. magnetite or maghemite) coated with different organic modifiers are investigated [173]. These iron oxide NPs combine magnetic properties with biodegradability and low toxicity. For their development, Prussian blue iron staining of tissue or cell samples is often applied for histological iron detection. However, this staining approach is unspecific as such samples contain substantial endogenous iron. Hence, Scharlach et al. [174] used specially synthesised very small iron oxide particles doped with europium (5 wt% Eu^{3+} instead of Fe^{3+}) to distinguish between administered iron oxide NPs and endogenous iron. LA-ICPMS imaging revealed high Eu signals in liver tissue and aortic root sections from ApoE^{-/-} mice suggesting an NP accumulation.

Magnetic NPs can also be used as drugs for improved cancer treatment using magnetic fluid hyperthermia (MFH). The spatial distribution of the NPs is directly related to the effective area of tumor cell damage. Therefore, Hsieh et al. [175] studied the local accumulation of Gd-doped iron oxide nanoparticles in tumor tissue after MFH by LA-ICPMS.

Promising carbon-based nanomaterials, e.g. liposomes for imaging or therapy [176], cannot directly be detected in biological samples with ICP-MS, as no species-specific information is accessible. However, the embedding or encapsulating with lanthanoids enables their localisation and quantification. Organic nanocarriers containing gadolinium are for example used as MRI contrast agent for tumor imaging [177] or as potential drug for real-time gene therapy monitoring in the brain [178]. Pugh et al. [179] imaged rat brain sections after administration of Gd-tagged liposome NPs, a drug under development for treatment of dementia. In this context, LA-ICPMS and MRI images provide complementary spatially resolved information and allow cross-

validation. Liang et al. [180] applied dual labelling of polyvinylpyrrolidone (PVP) modified graphene oxide with lanthanum and cerium to analyse the biodistribution of graphene oxide nanosheets in different rat organs after intravenous injection.

Upconversion NPs (UCNPs) are very promising tags for multiparametric, high-sensitivity analysis at sub-cellular resolution, and are also attractive probes for multimodal imaging approaches. But until now the knowledge about their pharmacokinetics and toxicity is limited. Li et al. [181] studied the distribution of polyethylene glycol (PEG) coated $\text{NaYF}_4:\text{Yb}/\text{Tm}/\text{Gd}$ nanoparticles (PEG-UCNPs) in different mice organs. The metallic NP components Y, Yb, Tm and Gd exhibited similar distribution patterns in the LA-ICPMS maps. The NPs are mainly accumulated in the spleen and, to lower extent, in liver and kidney. Fe, Cu and Zn showed a rather homogeneous distribution in the kidney, indicating that PEG-UCNPs are not nephrotoxic. Tailor-made nanomaterials consisting of different elements enable multimodal imaging *in vivo* and *ex vivo*. Europium-doped gadolinium orthovanadate nanocrystals functionalized with poly(acrylic acid) are such a promising multifunctional material for cellular imaging using MRI (via Gd^{3+}), confocal laser scanning microscopy (via Eu^{3+}) and LA-ICPMS (all metals) [182]. Cell labelling is of special interest for cell tracking experiments, e.g. of stem cells, which are auspicious candidates for the treatment of various diseases and disorders. The elemental distribution maps of two different cell types (human lung epithelial cells, A549 and human adipose-derived stem cells, MSCs) incubated with the nanocrystals showed spatial similarities between the different elements confirming both the cellular uptake of the nanocrystals and their stability during the labelling process.

Imaging by LA-ICPMS is increasingly used for toxicological studies. NPs can interact with the body in manifold ways depending on the uptake route (e.g. ingestion, inhalation, skin exposure or injection). They can even enter deep sub-organs via the blood stream. The knowledge about factors influencing NP uptake and behaviour inside cells is important because their beneficial or detrimental effects arise from interaction at (sub-)cellular level. Dressler et al. [183] studied potential harmful effects of lanthanum oxide nanoparticles in Wistar rats after repeated oral administration. LA-ICPMS images of femur bones revealed a La accumulation on the surface of the bone up to a depth of about 5 μm . One of the main elements in bone, Ca^{2+} , and La^{3+} have similar chemical properties (e.g. ionic radius, donor atom preference and coordination chemistry), so that La^{3+} can possibly occupy calcium binding sites in bones. This toxicological study proved that at least parts of the La_2O_3 NPs are remaining in the body after 1 month, probably transported as NPs by the blood stream.

The multi-element capability of LA-ICPMS enables the elucidation of interactions between the NPs and tissue alterations by means of endogenous elements. This can lead to a better understanding of the biodistribution, toxicity, and pharmacokinetics of both widely used and special designed NPs.

13.6 Summary and outlook

In the last decade, different ICP-MS-based methods for the detection and quantification of various kinds of biomolecules (peptides, proteins, DNA, RNA, and antibodies) using lanthanoids as metal-containing tags have successfully been developed and applied for the analysis of complex real biological and biomedical samples. Especially, analytical approaches using metal tagged antibodies have become an integral part of current biomedical research. Recent improvements concerning both the instrumental part and software solutions for data evaluation and visualisation have made a significant contribution to this. The immunoassays and metal-staining techniques in combination with ICP-MS detection presented in this chapter are up to now mainly used for basic research. However, they have the potential to be applied in personalized diagnosis medicine in the near future. Imaging of regulatory networks within individual cells and interrogating interactions among cells in tissue samples contributes to a deeper understanding of the molecular mechanisms of diseases and supports drug development and targeted therapy. Recent proof-of-principle experiments using LA-ICPMS for 3D imaging provide valuable information on tissue architecture, microenvironment, and cell-to-cell interactions, e.g. by distinguishing invasive tumor cells from the surrounding tissue. In combination with other molecular imaging techniques like MALDI-MS new insights into the complex biomolecular pathways involved on human diseases and metabolic disorders are expected. Furthermore, together with MRI an important step towards bridging the gap between the *ex vivo* and *in vivo* imaging is possible.

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14 Lanthanoides in glass and glass ceramics

Abstract: Many types of glass contain lanthanoides, among them special glass for optical applications is the one with the highest content of lanthanoides. The precise determination of the lanthanoides' concentration is performed by ICP-OES. However, up to now there are no established standard processes, guaranteeing a uniform approach to the lanthanoid analysis. The knowledge of the lanthanoides' concentrations is necessary on the microscale in some cases, especially if a suitable separation and recycling procedure is to be applied. Here, the analysis is performed by EDX or WDX in the scanning electron microscope. The new quantitative methodology of 3D multi-energy X-ray imaging enables both effective sorting as a pre-step to recycling and a quantitative 3D representation of the distribution of lanthanoides in components.

14.1 Introduction

Glass is one of the oldest materials used by mankind: The first glass was produced in ancient Egypt about 4,000 years B.C. Nowadays, it exists in plenty of types and it can be either a mass product with millions of tons of annual production, but also a specialty product with only a few kg of annual production. Currently, about 100 million tons of glass is produced worldwide. There are different types of glass [1]:

1. Container glass (44% total market amount by weight)
2. Flat glass (29% total market amount by weight)
3. Glass fibers (12% total market amount by weight)
4. Specialty and technical glass and glass ceramics (15% total market amount by weight).

The first two glass types, covering almost seventy five percent of the global market volume (in tons, not in money!) are only covered by soda-lime glass, and besides of coloring elements, the main components of such glass are Na_2O , K_2O , CaO , MgO , Al_2O_3 , and SiO_2 , leading to silicate glass. Glass fibers also usually consist of silicate glass, with the main component SiO_2 . For specialty glass, other elements, like boron oxide, lead oxide, germanium oxide, phosphorous oxide, and others can be the network-forming main component. Regarding special applications, even non-oxidic glass like fluoride glass (for specific optical glass fibers) or chalcogenide glass (for infrared optics) is needed and can be doped with lanthanoides for these applications.

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Glass fibers and in particular specialty and technical glass can contain a much larger number of elements than container glass and flat glass. When the composition of the glass is developed, one of the unique material properties of glass is used: Glass as an amorphous component can dissolve almost all elements in considerable amounts. Therefore, glass chemists have developed glass compositions, containing almost all elements of the periodic system of elements: Modern glass compositions can consist of more than 15 intentionally added cations, each playing a unique role in the final glass or glass ceramics.

Nevertheless, being in a metastable state, glass has always a tendency to crystallize. While this is an unwanted effect for typical container and flat glass or glass fibers, the crystallization of glass is willingly triggered in the case of glass ceramics in order to get new materials with new and specific properties.

Due to the very broad and large application of specialty glass, lanthanoides can be added to the glass for many different reasons, the most relevant being:

1. Coloring agents, amounts < 2–3 wt% [2]
2. Mechanical properties, amount < 10–15 wt% [3]
3. Tuning optical properties, amount < 60 wt% [4]
4. Crystallization agent, amount < 3 wt% [5]
5. High Abbe number glass, amount < 50 wt%
6. Laser glass, amount < 5 wt%

For the production of specialty glass chemicals of high purity are needed. In contrast to container glass and flat glass. Therefore, a good recycling strategy of lanthanoides from specialty glass would be very helpful. At present, a successful recycling is hindered by many different glass systems, corroborated with the fact that almost all lanthanoides containing specialty glass is not a component of glass ware but in a system where it has to be extracted. One example for this might be the current cell phone camera: The optical system consists of lenses or prisms made by special glass, containing a large amount of pure lanthanoides like lanthanum oxide or neodymium oxide (up to 20%). However, the amount of the glass per cell phone is very small, and, depending on the manufacturer, different glass types are used. Another example might be dental glass ceramics. Here, various lanthanoides like samarium, ytterbium, or terbium are added in order to get a natural fluorescence. These lanthanoides are very rare and expensive, but a recycling even of production waste is currently not possible, since the different materials contain different types and amounts of lanthanoides.

Regarding all aspects, a precise knowledge of the chemical composition is mandatory in order to establish lanthanoid recycling strategies.

14.2 Literature survey of rare earth chemical analysis in glass

LA-ICP-MS (Laser-Ablation Inductively Coupled Plasma Mass Spectrometry) Glass samples containing rare earth oxides, especially trace concentrations, mostly were analyzed using LA-ICP-MS. Historical samples [6–14] and historical silicate ceramics [15] were analyzed also applying this method.

LA-ICP-AES (Laser-Ablation Inductively Coupled Plasma Atomic Emission Spectrometry) [8].

This method was applied for the analysis of:

- nuclear waste glass ceramics [16, 17]
- reference glass [18–24]
- various glass materials [25, 26]

ICP-MS analysis of solutions

The analysis of solutions containing rare earth elements by ICP-MS was published in several papers [17, 20, 21, 27–29].

The dissolution of the sample was performed by hydrofluoric acid digestion, microwave digestion or melting with lithium metaborate and subsequent dissolution of the melt.

14.3 Analytical methods for the determination of main components of glass (except lanthanoides)

Details of XRF and ICP are presented in chapter X and Y of this book. Comparing methods it is to be mentioned: it is easier to prepare a multi element standard solution for ICP than to produce or acquire a solid standard for XRF or ICP analysis. On the other hand, direct measurements of solids needs less time that a procedure with decomposition of the solid. The reproducibility of XRF is better than of ICP. The detection limits are lower for ICP, especially ICP-MS.

There are some specific features of glass analysis:

In the case of XRF, glass can either be measured directly or, because of its relative low melting point, converted to a fused bead by remelting without fluxing agent. The benefit is a higher sensitivity that means lower detection limits compared to sample preparation by diluting with a fluxing agent.

Some glass contains B_2O_3 or Li_2O or both of them. If a complete analysis of the glass sample (a sum of 100%) is required, these components have to be determined. For physical reasons it is impossible to measure Li_2O by XRF. B_2O_3 can be determined in glass samples prepared without fluxing agent. Because of an information

depth of the boron radiation below 1 μm , it is necessary to have planar polished surfaces [39]. Otherwise the B_2O_3 determination is performed as the Li_2O determination e.g. by ICP-OES in solution after decomposition (see next chapter).

For the analysis with ICP, glass can be decomposed by hydrofluoric acid digestion which leads to an acid solution free of Si (in most cases the main component of the glass) and B. Therefore a higher sample weight can be used which lowers the detection limits.

SiO_2 is determined gravimetrically after melting the sample with sodium carbonate, dissolving the melt in HCl and precipitation of the SiO_2 . The precipitated SiO_2 is filtered, ignited and then weighed [40, 42].

B_2O_3 is determined by ICP-OES after melting the sample with sodium carbonate, dissolving the melt in HCl and filtering from precipitated material [41, 42].

Fluorine in glass can be determined by XRF or by wet chemistry [42, 43]. One digestion method is the pyrohydrolysis in a tube furnace at 1050 $^{\circ}\text{C}$ with superheated water vapor in presence of a catalyst. The fugitive fluorine components are distilled into water. The second method is sintering the glass powder with a mixture of sodium carbonate and zinc oxide at 1000 $^{\circ}\text{C}$. After cooling the melt is extracted. In both cases the fluoride ion can be measured electrometrically (fluoride sensitive electrode), by ion chromatography or photometrically (alizarin-EDTA-complex).

14.4 Preparation of sample solutions for glass analysis by ICP-OES

14.4.1 Hydrofluoric acid digestion

The most common procedure for dissolution of glass samples in order to analyze the components except SiO_2 and B_2O_3 is the hydrofluoric acid digestion. The advantage of this method is the removal of the matrix components SiO_2 (and B_2O_3 if present) and of the harmful hydrofluoric acid by evaporation. Several variations exist:

14.4.1.1 Hydrofluoric acid – sulfuric acid digestion (procedure B) [44]

The powdered glass sample is weighed into a platinum dish and soaked with deionized water. Then hydrofluoric acid and sulfuric acid are added carefully. The mixture is heated slowly on a heating plate until the sulfuric acid begins to fume. After cooling the mixture is heated with additional hydrofluoric acid until all liquid is evaporated. After heating in a muffle furnace and cooling the dry residue is dissolved in hydrochloric acid.

14.4.1.2 Hydrofluoric acid – perchloric acid digestion (procedure C) [44]

The powdered glass sample is weighed into a platinum dish and soaked with deionized water. Then hydrofluoric acid and perchloric acid are added. After stirring and waiting for 30 to 60 minutes the mixture is heated on a heating plate until all liquid is evaporated. After cooling the evaporation is repeated with hydrofluoric acid and perchloric acid. After cooling again the dry residue is dissolved in hydrochloric acid.

14.4.1.3 Modified hydrofluoric acid – perchloric acid digestion

In several laboratories a modified procedure is used: The powdered glass sample is weighed into a graphite crucible. Then a mixture of HNO_3 , HF and HClO_4 is added. By heating it to 110 °C and then to 140 °C all acids are evaporated. After cooling the dry residue is dissolved in hydrochloric acid.

This procedure can be performed in a closed system where the harmful hydrofluoric acid is neutralized after evaporation by a sodium hydroxide solution.

14.4.2 Melt digestion

Some components which resist the hydrofluoric acid digestion can be dissolved by melt digestion. The disadvantage of the method is a high concentration of matrix elements (e.g. Na, Si) in the measuring solution which limits the range for the application in an ICP-OES spectrometer. The solution has to be diluted, and the use of an ultrasonic nebulizer is rather impossible. Several variations exist:

14.4.2.1 Sodium carbonate melt digestion (procedure A) [44]

The powdered glass sample is weighed into a platinum dish, mixed with sodium carbonate and then heated to 1000 °C. After cooling the melt is dissolved with water and nitric acid.

14.4.2.2 Sodium carbonate / potassium carbonate melt digestion (procedure 10.4) [45]

The powdered glass sample is weighed into a platinum crucible, mixed with sodium carbonate, potassium carbonate and sodium peroxide and then heated to 1000 °C. After cooling the melt is dissolved with water and nitric acid.

14.5 ICP-OES analysis of rare earth elements

ICP-OES measurements can be performed according to DIN 51086–2 [45]. Specific wavelengths for some rare earth elements are given (Table 14.1). DIN 51086–2 is being extended for the missing rare earth elements (Table 14.2).

Table 14.1: Frequently used emission lines for the analysis of rare earth elements in glass by ICP-OES, lower limits of the range of application for 1 g sample weight in 100 ml solution and important disturbing elements according to DIN 51086–2 [45].

Element	Emission line [nm]	Lower limit of the range of application [mg/kg]	Important disturbing elements
Ce	413.380	30	Fe, V
	418.660	30	
Er	337.271	5	V
	349.910	10	
Eu	381.967	1	Fe
	412.970	2	
La	333.749	5	Fe, Ti
	408.672	5	
Nd	401.225	30	Cr, Ti
	430.358	40	
Pr	390.844	20	Fe, U, Ni
	414.311		
Yb	328.937	1	Y
	369.419		

14.6 Analysis of special optical glass

Two samples of optical glass were analyzed in ISC by hydrofluoric acid – perchloric acid digestion described in chapter 4.1.3. SiO_2 and B_2O_3 were determined according to DIN [40, 41]. The results are given in Table 14.3.

It can be seen that the sum of determined components for both samples is near to 100%. Due to the fact that the measurement precision for ICP-OES is higher compared to ICP-MS definitely no important component was overlooked.

Li_2O cannot be determined by XRF. The measurement of B_2O_3 is difficult or impossible in case of borate fused beads. The XRF quantification to 100% can hardly be performed without information from other methods, e.g. ICP-OES.

Table 14.2: Frequently used emission lines for the analysis of rare earth elements in glass by ICP-OES, lower limits of the range of application for 1 g sample weight in 100 ml solution and important disturbing elements according to extension of DIN 51086–2 (in processing).

Element	Emission line [nm]	Lower limit of the range of application [mg/kg]	Important disturbing elements
Dy	353.171	0.5	Ce, Mn, Th
	387.211	1	Ho, Sm
	394.468	0.5	Ce, Eu, Er
Gd	342.246	0.5	Ce
	376.840	1	Th, W, Eu
Ho	345.600	2	Ce, Dy, Nd
	348.484	3	Tm, Hf
	381.074	2	
Lu	219.556	0.5	W, Ta
	261.541	0.5	Ni
	547.668	1	
Sm	359.259	3	Nd, Gd, Th, W
	388.528	3	Pr, Cr, Zr, Nb, Ta, Ce, Co
	446.734	5	Ce, Gd
Tb	332.440	5	Cr, Nb, Th
	350.914	3	Ho
	367.636	2	Nb, Cr, Fe, Er, Dy
Tm	313.125	0.5	Tb
	336.261	5	Zr, Th, Ti
	384.802	1	Ce, Y, U, Er

No spectral interferences emerge from the main components of glass (Si, Na, K, Mg, Ca, Al, B). The spectra of minor elements as Fe, Ti, Cr show interferences with some rare earth lines, however, many interference emerge between the rare earth and many other elements.

14.7 Analysis of glass by topochemical analysis

A precise analysis of element contents in glass and glass ceramics is obtained by methods described above. Sometimes, it might be useful to determine the element contents locally too, i.e. on a scale of micrometers or nanometers. This is not necessary for glass of a high-grade purity and homogeneity, but e.g. for glass ceramics. Glass ceramics are formed by tempering glass that contains nucleating agents, such

Table 14.3: Analytical results for two optical glass samples, concentrations are given in mass%.

Element oxide	Sample 1 %	Sample 2 %
SiO ₂	4.98	10.21
B ₂ O ₃	30.3	12.9
BaO	0.49	0.48
CaO	–	15.2
ZnO	2.94	–
ZrO ₂	7.85	7.44
La₂O₃	44.9	24.8
Y ₂ O ₃	7.94	–
TiO ₂	–	8.93
Nb ₂ O ₅	0.48	19.8
Sum	99.9	99.8

as titanium or zirconium oxide. Crystals are formed during a defined heat treatment because of these nucleating agents. At the end of the production process a microstructure, consisting of crystals and glass is formed (Figure 14.1). During development of glass ceramics local analyses of the elemental concentrations are mandatory to understand what happens during heat treatment. In case of recycling of glass ceramics, the total concentration of the single elements rather plays the predominant role. To measure them exactly, it is necessary to chemically dissolve first the glassy as well as the crystalline phases and then analyse them by ICP. The knowledge of the chemical composition of the various glassy and especially crystalline phases may be useful here to develop appropriate chemical dissolution and precipitation routines. For these two reasons, i.e. for the development of glass ceramics on one hand and for the development of chemical dissolution and separation processes on the other, a closer look at a sample is needed by using the so-called topochemical analysis EDX. Topochemical analysis EDX is usually performed in two ways: First, an EDX device (Energy Dispersive X-ray Analytics) is mounted on a SEM (Scanning Electron Microscope) or a TEM (Transmission Electron Microscope). Second, it can be combined with a WDX (Wave Length Dispersive X-ray Analytics) device, which is either a stand-alone device or it is mounted on a SEM. The functionality of these two methods is described in other chapters of this book. This chapter describes the procedure of the analysis and should be considered in more detail.

In both methods, a focused electron beam impinges on the sample surface and penetrates into the sample. By inelastic interaction processes between the primary

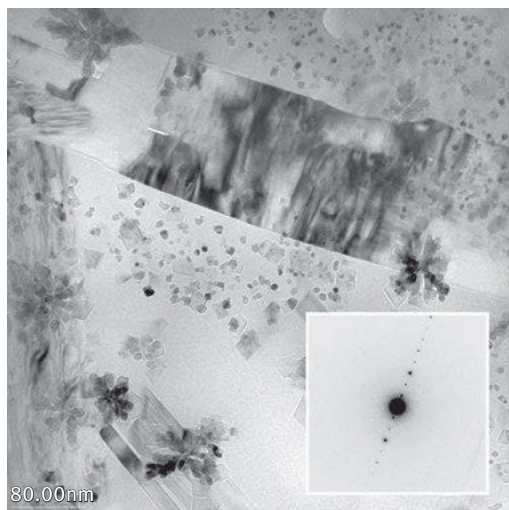


Figure 14.1: Transmission electron micrograph of a glass ceramic. Image Fraunhofer ISC.

electrons (the electrons of the electron beam) and the electrons of the atoms of the sample, heat energy arises (amongst others) that leads to a local heating of the sample. The degree of heating depends on the kinetic energy of the primary electrons, the current intensity (beam current), i.e. how many primary electrons per unit time are incident on the sample surface, as well as the cross section of the electron beam, i.e. the size of the incident on the sample. In extreme cases, temperatures of 1000 °C may arise during the analysis by EDS in transmission electron microscopy. (Figure 14.2) shows the resulting temperature during the analysis by EDS in TEM, depending on the current strength and thermal conductivity. It may happen that samples melt or vaporize locally when no appropriate care in the analysis is taken.

During analyses in a scanning electron microscope by EDS or WDS, the resulting temperatures are lower, but can still be significant (Figure 14.3).

The local stoichiometry changes by melting or even vaporizing, but this is trivial. It is also soon obvious that increased atomic mobility – that means increased diffusivity – arises due to the increased temperature. But another effect happens, namely the formation of a space charge inside the sample. It arises because here a part of the primary electrons is quasi landfilled. Spray and Rae described this effect in 1995 [47]. The following (Figure 14.4) is obtained from this article.

Due to the increased diffusivity by temperature rise and the driving force created by the space charge region, the very mobile ions such as Na^+ , but also Li^+ diffuse deeper into the sample and the stoichiometry in the analysis area changes.

Lanthanoides are not directly affected by this effect due to their usually relatively low diffusion rate. But as the concentration of other elements changes in the

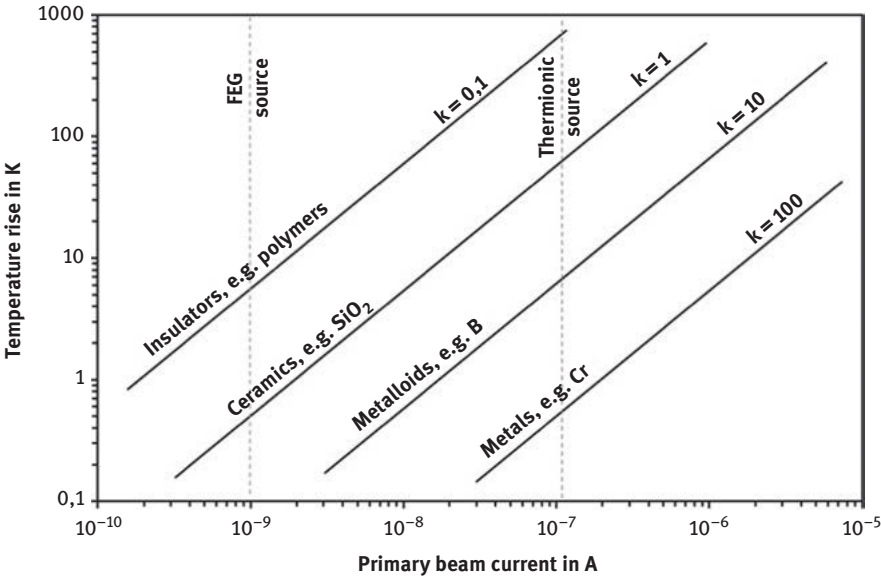


Figure 14.2: Possible local sample temperatures during the analysis in TEM by EDS, depending on the beam current and the thermal conductivity k [51].

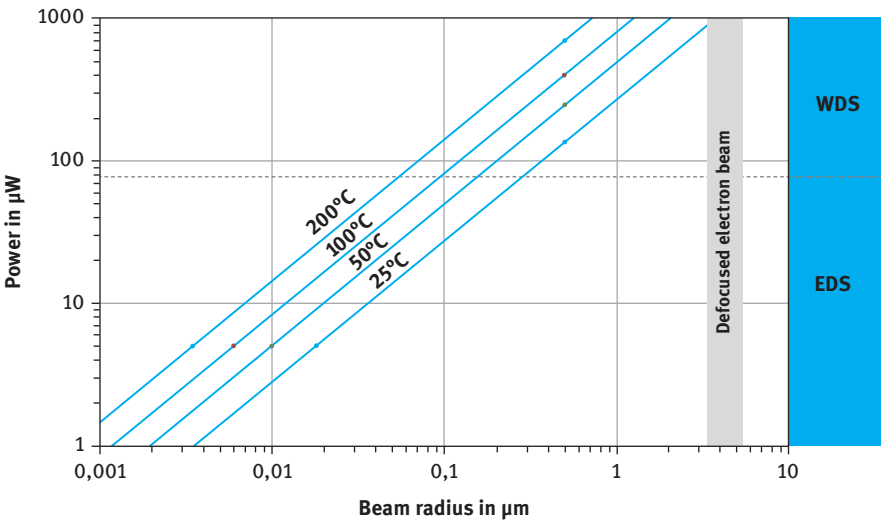


Figure 14.3: Local sample temperature depending on the diameter of the electron beam and the electron beam power [47].

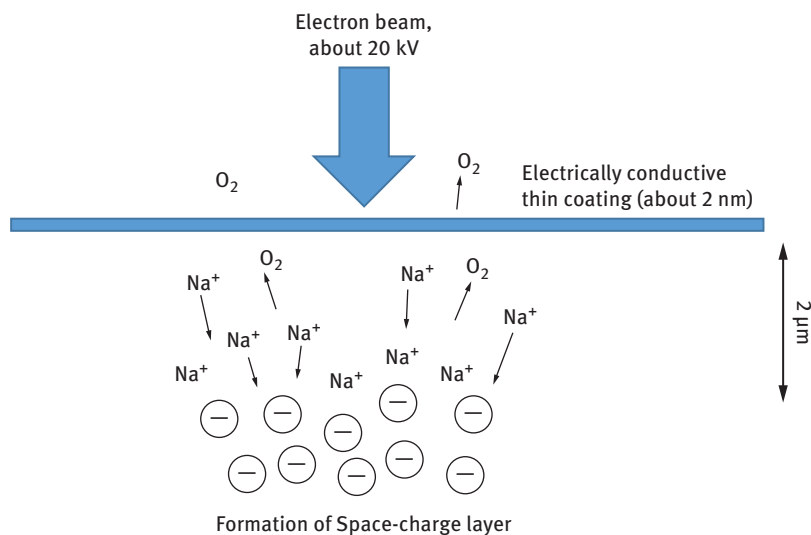


Figure 14.4: Formation of a space charge zone during the EDS or WDS analysis [47].

environment of lanthanoides, a false concentration of lanthanoides is measured! This effect should be also taken into consideration.

There is another important parameter to be considered during local analysis: the pressure. In the electron microscope is a very low pressure of about 10–5 mbar.

If the vapor pressure of some elements is very high, then a change in the stoichiometry is carried out by evaporation also.

To prevent these two effects, a consistent cooling of the samples is recommended during the analysis in order to avoid an increase in temperature and therefore an increased diffusivity.

A final aspect concerns the different hydrolytic resistance of glass. This has to be considered in the preparation that should be water-free, it should be carried out with petroleum for example. If water is used and the glass is very sensitive to an aqueous attack, then the alkali and alkaline earth metal ions are especially leached. With the standard soda-lime glass for windows changes of 10% in the sodium concentration may arise.

In summary, the following recommendations for a good local chemical analysis with EDS and WDS can be made:

- Use cooling stages (liquid nitrogen) to avoid high sample temperature
- Avoid water during grinding & polishing
- If possible: Avoid high beam current and focussing of the beam
- Observe the time dependent peak development during the measurement
- Don't forget that the surface of glass can be strongly different from the bulk

In the articles [46–51,] the thermal effects are described based on studies.

14.8 Analysis of glass by multi-energy x-ray imaging as a quantitative method for materials characterization

X-ray imaging is an established method for the characterization of material samples. Two-dimensional, radiographic methods as well as three-dimensional computed tomography are used very successfully in many fields. However both usually have a drawback: They provide only qualitative information rather than quantitatively exact physical properties. Multi-energy X-ray imaging as a quantitative method for material characterization solve this drawback and is applicable for two- and three-dimensional analysis. There are multiple methods which benefit from usage of that energy information, classical “dual energy” approach [52a] as well as with newest generation “spectral”, i.e. energy resolving, X-ray detectors [52b, 52c]. Multi-energy x-ray imaging opens up novel opportunities in the sorting and recycling sector, including for the recovery of rare earths from waste glass. For example, it is possible to classify raw material based on ingredients or material-dependent inclusions with industry-typical throughput.

In X-ray imaging, three quantities of the object define the attenuation of X-rays and thereby image contrast: the atomic number, the integral over the density along the x-ray path through the object and the x-ray energy. For homogeneous material the integral along the x-ray path is just the product of density and thickness and is called areal density. Computed tomography directly provides the attenuation coefficient depending on the atomic number, the density and energy only. In reality usually more than one element is present, but the attenuation coefficient of a compound object is simply the linear combination of its constituents. Generally, the attenuation coefficients depend on both the energy of the X-ray photons and the type of material. If an object is imaged using different X-ray spectra or using an energy resolving detector, information on the type of material becomes available. Those so called “dual energy” techniques have been known since the mid-70s [52] and are established in medical imaging. One technique and its application using gamma emission lines (mono-energetic) can be found in [53]. However, that method is limited to the availability of radioactive sources. The Fraunhofer IIS employ a basis material decomposition (BMD) technique that allows obtaining the areal density of a given set of chosen basis materials in a radiographic image. Multiple images from different angles can then be used for a computed tomography reconstruction resulting in the partial density of the respective basis material [54, 55].

Furthermore, multi-energy K-edge imaging allows to quantitatively determine the areal density of elements with a K absorption edge in the relevant part of the x-ray spectrum. In the macroscopic scale (millimeters to centimeters), that applies to elements with an atomic number $Z > \sim 55$, allowing the application to lanthanides ($Z=57 \dots 71$).

Figure 14.5 shows an example with solder and tantalum materials, applying a spectral (multi energy) method for basis material decomposition [56]. In conventional x-ray imaging all these material specific structures overlap in one single image. Multi energy X-ray material decomposition can not only separate solder from copper, but – by using the K-edge – also tantalum ($Z=73$). In these images, the brightness correlates with the areal density in the respective material channel.

As lanthanides have an atomic number close to tantalum, the K-edges are also in the same energy range, allowing the method to be applied to these elements as well.

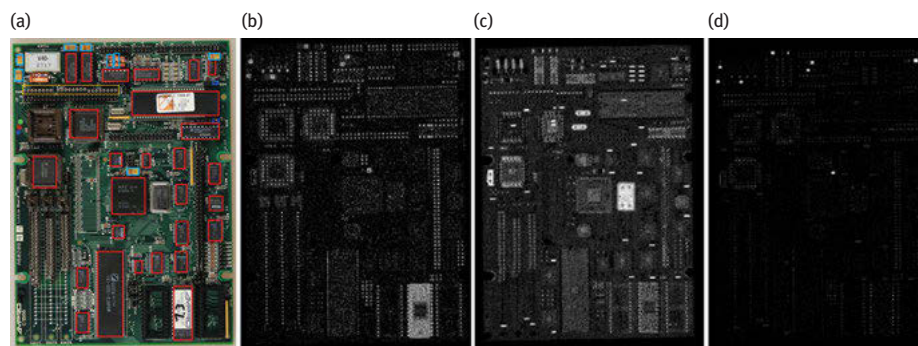


Figure 14.5: (a) visual image of a printed circuit board with multiple components labeled, IC in red and tantalum capacitors in blue. (b) multi energy BMD: solder channel. (c) multi energy BMD: copper channel. (d) multi energy BMD: tantalum channel.

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15 Recycling of rare earth elements

Abstract: Any development of an effective process for rare earth (RE) recycling has become more and more challenging, especially in recent years. Since 2011, when commodity prices of REs had met their all-time maximum, prices have dropped rapidly by more than 90%. An economic process able to offset these fluctuations has to take unconventional methods into account beside well-known strategies like acid/basic leaching. The solid-state chlorination provides such an alternative for mobilizing RE elements from waste streams. Instead of hydrochloric acid this kind of chlorination decomposes NH_4Cl thermally to release up to 400 °C hot $\text{HCl}_{(\text{g})}$. After cooling the resulting solid metal chlorides may be easily dissolved in pH-adjusted water. Without producing strongly acidic wastes and with NH_4Cl as cheap source for hydrogen chloride, solid-state chlorination provides various advantages in terms of costs and disposal. This method was examined, adjusted and optimized for RE recycling from fluorescent lamp scraps as well as magnets. Thereby many surprising influences and trends required various analytic methods to examine the reasons and special mechanisms behind them.

15.1 Recycling of rare earth elements

The development of efficient and economic strategies for RE recycling depends on different factors, for instance, commodity prices, location and size of deposits, costs for disposal as well as hazard potential. Due to great worldwide deposits of RE containing ores and low commodity prices, only a few recycling processes are currently able to work on an industrial scale. However, the majority focuses only on production wastes or end-of-life (EoL) products with especially high RE content [1–4]. Recycling of $\text{Fe}_{14}\text{Nd}_2\text{B}$ and SmCo magnets from production waste has been state of the art for a couple of decades. Currently 10–30% of the starting alloys still accumulate as different wastes during manufacturing, such as slurry, powder or chips [4]. Most of these chiefly pyrometallurgical processes remove the plastic sockets, then grind the waste and blend the resulting powder with new

Note: In 2014 the Institute of Chemical Technology at Freiberg University of Mining and Technology and FNE Entsorgungsdienste Freiberg GmbH were awarded the Technology Transfer Prize by the Saxon Ministry of Science and the Arts for the development and application of the SepSELSA process for RE recycling.

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starting alloys [2, 5, 6]. This strategy avoids an expensive and costly reduction of RE elements.

Regarding EoL products fluorescent lamp scraps and NiMH batteries currently serve as sources for efficient RE recycling. Although spent magnets often contain more than 30 wt.% of REM as well as there are many scientific articles dealing with this topic, yet none of the proposed strategies or processes has met the requirements for an upscale to industrial production [3, 4, 7–10]. The reasons are versatile: (i) Removing the small magnets from their sockets and housings in, for example, hard drives or electric motors often proves to be very complicated [7, 8, 11]; (ii) Besides prices for RE oxides decreased in part by more than 98% since 2011. (iii) Since EoL products contain REs mostly in oxidized state, either because of their application (fluorescent powders, polishing agents, ceramics, glass) or due to corrosion (magnets, alloys, batteries), pyrometallurgical treatment must not be used for recycling. The same applies for impurities, accompanying elements (e.g. Ni, Co, Zn) and housings coming along with EoL waste. Disadvantageously, the expensive RE reduction using fused salt electrolysis cannot be avoided in a hydrometallurgical process.

Nevertheless, Umicore and Solvay Rare Earths have already developed a wet chemical EoL recycling for fluorescent lamps (2008) and NiMH batteries (2011) on an industrial scale [7, 12]. By now Osram has patented a process for RE recovery from fluorescent lamp scraps, too [13]. In case of permanent magnets, the MORE project (2011–14), a joint project of Siemens, Mercedes, Umicore and several German scientific institutes and universities, examined three different strategies to recycle magnets from spent electric motors. Whereas both mechanical strategies, namely the reuse of undamaged magnets as well as blending the grinded magnets with starting alloys, missed the requirements for new permanent magnets, the third hydrometallurgical route yielded the REs as sellable oxides [7, 8]. But neither the MORE project nor one of the wet chemical processes developed in scientific literature has succeeded in reducing the gap between laboratory bench and industrial process so far [3, 4, 7–10]. Against this background, unconventional recycling processes get more and more attractive. One approach, the so-called solid-state chlorination, shows numerous amazing effects for RE recycling and combines high yields with an extremely low demand for chemicals with minor costs for disposal. Within the SepSELSA project this method was adjusted and optimized for RE recovery from fluorescent lamp scraps [14–16]. Unexpected trends and side reactions required many different methods of analysis. In this context the optimization based on statistical designs, as they are used for development of analytic techniques, proved most helpful.

15.2 Recycling from fluorescent lamp scraps

Approximately 250–300 t of Hg-contaminated fluorescent lamp scraps with average RE contents of about 10 wt.% are deposited downhole in Germany every year [13]. Additionally, the RE content in lamp phosphors can reach up to 27.9 wt.%, with only 10% being recovered, though [17]. In 2009, when the regulation EG 245 came into force, higher standards for light quality were applied so that the older and RE-free halophosphate fluorescent materials could not achieve anymore [18]. Furthermore, the eradication of the traditional incandescent bulbs, thus, the amount of three-band fluorescent materials and the RE content are going to rise prospectively. In this regard, EoL fluorescent lamps were examined to develop a RE recycling process.

15.2.1 Starting material

EoL scraps always contain a mixture of different fluorescent materials whose composition varies in a wide range due to joint repository and disposal. Alongside three-band materials and the older halophosphate these wastes embody residues of glass and metallic sockets, too. In general, the particular fluorescent materials are composed of a host lattice and one or more doped activator elements. RE elements serve mainly as activators, except for yttrium which forms a host lattice, too (Y_2O_3 : Eu^{3+}). Overall fluorescent lamp scraps may consist of up to 19 different elements. Table 15.1 summarizes the most common components of EoL wastes.

Table 15.1: Components of EoL fluorescent lamp scraps [16, 19].

Component	Emission colour	RE content
$\text{Y}_2\text{O}_3:\text{Eu}^{3+}$	Red	55% (mainly Y, 4–10% Eu)
$\text{BaMgAl}_{10}\text{O}_{17}:\text{Eu}^{2+}$	Blue	10% (<5% Eu)
$(\text{Ca}, \text{Sr}, \text{Ba})_5(\text{PO}_4)_3\text{Cl}:\text{Eu}^{2+}$	Blue	
$\text{La}(\text{PO}_4):\text{Ce}^{3+}, \text{Tb}^{3+}$	Green	35% (~10% Tb)
$(\text{Ce}^{3+}, \text{Tb}^{3+})\text{MgAl}_{11}\text{O}_{19}$	Green	
$(\text{Gd}^{3+}, \text{Ce}^{3+}, \text{Tb}^{3+})\text{MgB}_5\text{O}_{10}$	Green	

The EoL fluorescent lamp waste was supplied as a fine, Hg-free powder and characterized by X-ray diffraction (XRD) after removing most of the glass and plastic. The morphology and elemental composition (Table 15.2) were obtained by atomic emission spectrometry with inductively coupled plasma (ICP-OES) after an acid treatment using aqua regia at 90°C for 2h. Therefore, SEM-EDX spectroscopy was used to correlate each particle by its composition with the respective fluorescent material.

By developing an efficient recycling process all efforts were concentrated on yttrium and europium representing the main part of the six RE elements with a share of

Table 15.2: Elemental composition of lamp powder waste.

Element	Concentration (wt.%)
Ca	41.35 ± 0.47
P	13.28 ± 0.21
Al	3.11 ± 0.01
Fe	1.60 ± 0.03
Ba	1.17 ± 0.01
Na	1.08 ± 0.01
Sr	1.06 ± 0.01
Mn	0.44 ± 0.01
Mg	0.35 ± 0.01
K	0.22 ± 0.01
Si	0.11 ± 0.01
Ni	0.03 ± 0.01
Y	33.13 ± 0.21
Eu	2.04 ± 0.01
Gd	0.33 ± 0.01
Ce	0.30 ± 0.01
La	0.26 ± 0.01
Tb	0.14 ± 0.01

97%. Yttrium solely occurs in the red-light-emitting fluorescent material together with Eu^{3+} as activator. Regarding all elements, Y and Eu concentrations amounted to 33.13 and 2.04 wt.%, respectively.

In contrast, Eu^{2+} serves also as activator in blue fluorescent materials such as $\text{BaMgAl}_{10}\text{O}_{17}:\text{Eu}^{2+}$ and $(\text{Ca}, \text{Sr}, \text{Ba})_5(\text{PO}_4)_3\text{Cl}:\text{Eu}^{2+}$. The remaining REs (lanthanum, cerium, gadolinium and terbium) are components of blue and green emitting materials, but with quite low concentrations (<0.33 wt.%).

Furthermore, Ca (41.35 wt.%) and P (13.28 wt.%) were quantified as the main components in accordance with the lighting devices composition which corroborate the major presence of red phosphors, few existences of green phosphors, and traces of SiO_2 , Na_2O and K_2O [19, 20].

The analysis of all water-based samples was conducted via atomic emission spectroscopy using an inductive coupled plasma (iCAP 6500 duo von Thermo Scientific, USA). The samples were diluted to element concentrations between 1 and 25 mg/L. For fluorescent lamp wastes three dilutions (1:10, 1:100 and 1:1000) were applied, due to very different concentrations of yttrium and the other elements. Although all samples were analysed in a low dilution of 1:10, the concentration of lanthanum, cerium, gadolinium and terbium hardly exceeded the detection limit (~ 0.1 mg/L) proving a high selectivity for yttrium and europium.

For magnet analyses, a dilution of 1:500 was sufficient. Further pre-treatment of the samples was not required. Before transferring each sample to the plasma torch, a Mira Mist nebulizer connected to a cyclone spray chamber was used to produce an aerosol from the sample. For quantification, an average was calculated from intensities of three consecutive measurements (Table 15.3).

Table 15.3: Measured wavelengths λ for particular RE elements.

Fluorescent lamp wastes SmCo magnets	λ (nm)
Y	371.029
Co	228.616
Eu	381.967
Nd	401.225
	406.109
Gd	342.247
Dy	394.468
Tb	350.917
La	379.478
Sm	359.260
Ce	456.236

Contrary to natural RE ores wastes only contain a reduced number of RE elements. Thus, there are only few relevant disturbances that have to be considered, like for terbium and dysprosium at $\lambda = 353.170$ nm [21].

SEM-EDX analysis (Figure 15.1) show the morphology as well as the composition and distribution of the elements on the particles surface. The sample is very heterogeneous and the size of the particles is quite different. Considering the possible differences between the small and large particles, two different spectra were done. It mainly represents presents particles of around 1–5 μm , and to a lesser extent particle of ~20–50 μm . A contrast was applied to the same region depicted in Figure 15.1a and the results confirm that the smaller particles correspond to RE (Figure 15.1b–1d). The elemental surface analysis using the EDX probe identified Y and Eu as the main RE and a weak signal of Ce, and Si, Ca, Br, Na, P and Fe as non-RE. It is notorious the localization of Si in the bigger particles (Figure 15.1a–1b), which could be associated to the glass big particles remaining in the powder. Additionally, in Figure 15.1d is observed the homogeneous distribution of Y, Eu, Ca and P on the lamp powder waste surface.

Each analysis via X-ray diffraction was conducted with a Bruker D2 Phaser with a Lynxeye® detector using a Cu K α radiation; $\lambda = 1.541$ Å, 40 kV, 30 mA with an opening angle of 5° 2 θ . The X-ray tube was operated at 30 kV and 10 mA. The XRD patterns were collected with a step of 0.02° and 1s dwell time.

The crystalline phases detected in XRD (Figure 15.2) are related with red phosphors ($\text{Y}_{0.95}\text{Eu}_{0.04}\text{O}_3$ (JCPDS 25-1011), green phosphors $\text{LaPO}_4\text{:Ce}^{3+}$, Tb^{3+} $\text{CeMgAl}_{11}\text{O}_{19}\text{:Ce}^{3+}$, Tb^{3+} (JCPDS 36-0073), $(\text{Gd}, \text{Mg})\text{B}_5\text{O}_{12}\text{:Ce}^{3+}$, Tb^{3+} and $\text{Ca}_5(\text{PO}_4)_3\text{F}$ (fluorapatite), blue phosphor ($\text{Ba}_{0.9}\text{Eu}_{0.1}\text{MgAl}_{10}\text{O}_{17}$) and the presence of SiO_2 , Na_2O and K_2O .

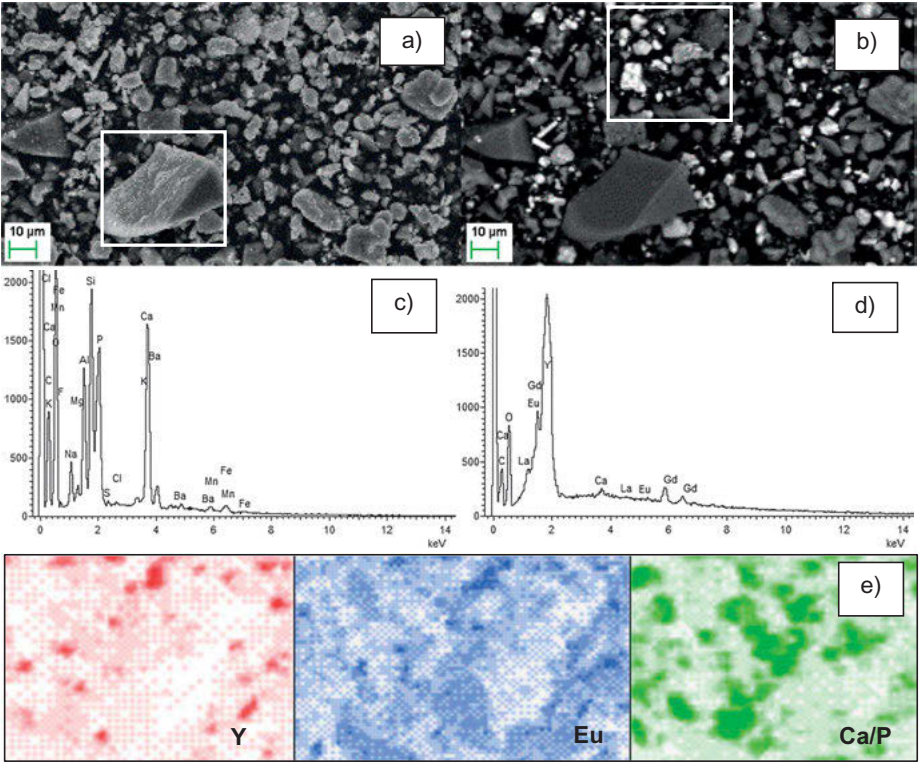


Figure 15.1: SEM-EDX characterization of fluorescent lamp scrap. (a) Particles view (Si/Al), (b) Particles view (RE) using light contrast applied (Signal QBSD), (c) Elemental composition of large particles, (d) Elemental composition of smaller particles [22], (e) Elemental distribution of Y, Eu, Ca and P.

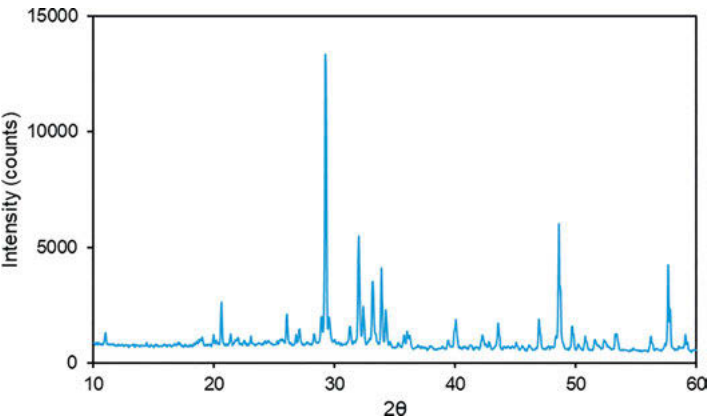


Figure 15.2: XRD pattern of the starting fluorescent lamp scrap.

15.2.2 Acid treatment

As is well known, leaching is usually done in hydrometallurgical processes as the first step prior to the extraction of metals, including RE, from secondary resources. In the proposed RE recovery process, a first leaching (L1) was carried out considering the purpose of maximizing the calcium elimination to prevent co-precipitation or co-extraction in further stages of the process, as well as reducing the RE losses. Pure water, acetic acid 1 M, gluconic acid 1 M and nitric acid 1 M were the leaching agents investigated using a contact time of 10 min, solid:liquid (S:L) ratio of 10% w/v and magnetic stirring of 200 rpm. The efficacy in removing Ca was: pure water < acetic acid (pKa 4.76) < gluconic acid (pKa 3.60) < nitric acid [22] following the increased acidic character (Figure 15.3a).

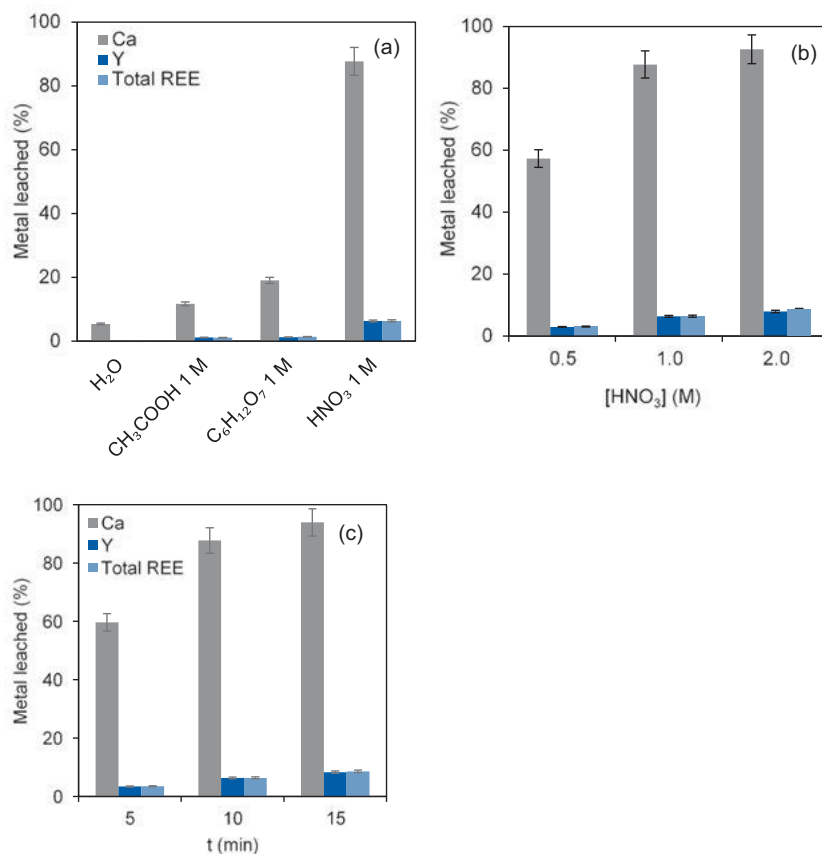


Figure 15.3: Ca, Y and total RE leached (%). S:L ratio of 10% w/v, magnetic stirring – 200 rpm. a) Effect of different leaching agents for 10 min. b) Effect of nitric acid concentration for 10 min. c) Effect of contact time using nitric acid 1 M [22].

Both the concentration of HNO_3 and the contact time using this leaching agent were investigated (Figure 15.3b-15.3c). The higher the HNO_3 concentration, the more metal is leached, reaching the maximum at 92.6 and 7.9 wt.% for Ca and Y, respectively. However, the metal recovery difference between 1 M HNO_3 and 2 M HNO_3 is less significant compared to 0.5 M HNO_3 . The same trend was observed in the contact time study, where the RE losses were minimized by reducing contact time. The optimal leaching conditions to minimise RE losses and maximise Ca elimination from fluorescent lamp wastes is 1 M HNO_3 for 10 min.

15.2.3 Liquid membranes

Despite the Ca elimination by the first acid treatment minimising the RE losses, 4–7% of these metals were lost in the leachate too. Considering the development of an efficient RE recovery process from fluorescent lamp wastes, these losses have been recovered by liquid membranes. Although solvent extraction is the most common technique to recover and separate RE, consumption of organic solvents as diluents in large amounts is problematic [23]. Furthermore, extraction is less efficient for the separation of metal ions and their pre-concentration compared to membrane separation processes. Membranes have the benefit of selective and fast ion transport because of their large mass transfer interfacial areas [24]. Considering the RE losses, for RE recovery from leachate L1, polymer inclusion membranes (PIMs) or supported liquid membranes (SLMs) get on the shortlist. Even though the PIMs are considered to be more stable than the SLMs, almost none of the hydrometallurgical processes in industrial scale have so far been using PIMs. This fact is mainly due to the limited performance, what is owed to their flat configuration as well as their high costs. Hence, SLM is the most appropriate technique, giving way to process intensification and industrial implementation [25]. Despite that there are a lot of liquid membrane types, supported or unsupported liquid phase serving as a membrane barrier between two phases of aqueous solutions, the supported ones reduce the membrane stability problems [26]. Hollow fibre renewal liquid membranes offer several potential advantages like high mass transfer rate, long-time stability of the liquid membrane, no leakage between the phases, low extractant consumption, wide range of operating parameters and easy scale-up [27,28]. Thus, it was chosen for carrying out the transport investigation experiments using a Liqui-CelTM (G-502) as a module.

The lab-scale plant worked with 4 L of the feed leachate L1 solution. 400 mL of Na_2EDTA 0.05 M and 50 mL of organic phase (Cyanex 923 diluted in kerosene) were used as the pseudo-emulsion containing stripping/organic in accordance with the low O:A ratios reported by Zahakifar et al. [29]. The streams of the feed and stripping/organic flowed at 50 L/h and a low transmembrane pressure ($P_f - P_s = 0.2$ bar) between shell and lumen side were applied.

A series of four experiments were carried out using a Cyanex 923 concentration range from 0 up to 0.3 M (Figure 15.4a). Considering the power viscosity of $(-2/3)$ [25], and the concentration range considered, the dependence on the permeability of this carrier concentration is linear (Figure 15.4b). Hence, viscosity of the organic phase is not the parameter that restricts RE transport, but the diffusion. However, metal transport is not controlled by the diffusion at higher carrier concentrations and the equation relating both parameters is not linear. Pavón et al., reported a permeability mathematical model which predict the RE transport for any Cyanex 923 concentration considering the viscosity of the organic phase and the diffusion process [25].

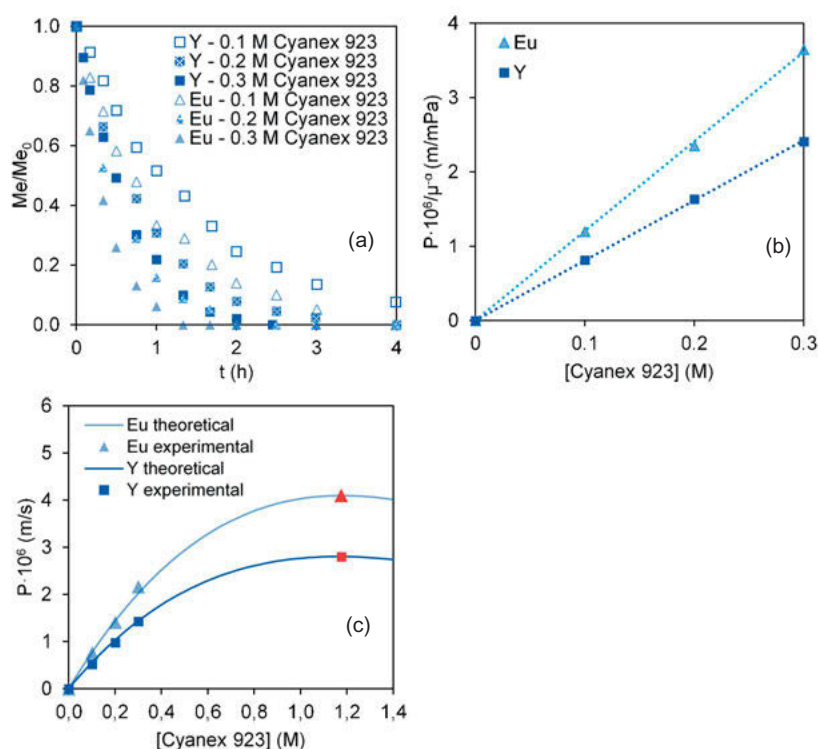


Figure 15.4: a) Effect of Cyanex 923 concentration on the RE transport. b) Effect of the concentration of Cyanex 923 from 0 up to 0.3 M on the permeability of the RE. c) Permeability of RE dependences on the Cyanex 923 using the mathematical model reported by Pavón et al. [25].

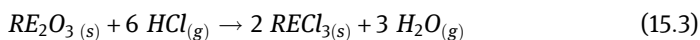
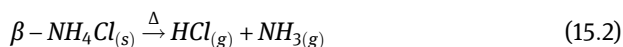
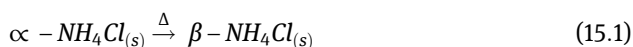
Considering the purpose of maximising RE permeabilities in order to optimise the transport process, 51 min are required using 1.18 M of Cyanex 923. Under these conditions, the maximum RE permeabilities are $2.80 \cdot 10^6$ and $4.10 \cdot 10^6$ m/s for yttrium and europium, respectively.

15.2.4 Solid state chlorination

Hydrometallurgical routes frequently encompass various acid treatments, which are cost-intensive and harmful if released into the environment. To avoid these problems, an unconventional method called solid-state chlorination (SSC) has emerged as a powerful alternative for RE recovery, which profits from higher efficiency and reduced costs. SSC is based on the conversion of the metal content of the raw material into water-soluble metal chlorides by converting them with dry HCl gas. The recovery and separation of the metal is considerably facilitated, since is sufficient to dissolve the formed metal chlorides in water.

The solid obtained after filtration in the L1 stage (solid_{L1}), reacts with gaseous $\text{HCl}_{(g)}$ which is produced by the $\text{NH}_4\text{Cl}_{(s)}$ decomposition. At 184 °C $\text{NH}_4\text{Cl}_{(s)}$ changes phase and thermal decomposition occurs at $T \geq 220^\circ\text{C}$ (Eqs. (15.1)-(15.2)) releasing gaseous $\text{NH}_{3(g)}$ and $\text{HCl}_{(g)}$. Although the maximal thermal decomposition is at $\sim 320^\circ\text{C}$, the decomposition already starts occurring at temperature far below its maximum since the partial pressures of $\text{NH}_{3(g)}$ and $\text{HCl}_{(g)}$ are never exactly zero.

RE yield is enhanced at lower temperatures compared to experiments conducted above 338 °C [15] because two different main reactions are involved in the process: (i) $\text{NH}_4\text{Cl}_{(s)}$ decomposition and (ii) RE chlorination (Eq. (15.3)).



In addition, the thermal decomposition is reversible, which allows recovering unreacted NH_4Cl in a subsequent step by allowing the gaseous phase to cool down. Whereas $\text{Y}_2\text{O}_3:\text{Eu}^{3+}$ reacts very fast to YCl_3 and EuCl_3 , all of the phosphate, aluminate and borate fluorescent materials remain almost unaltered. However, by leaching the chlorinated solid with 100 g of distilled water all formed metal chlorides dissolve.

Although several reactor types are at hand for conducting this SSC, only a few ones are suited for industrial production due to the requirement of continuously operating reactors. The SSC was conducted in an inert-gas flushed rotary kiln (Figure 15.5) which can be operated batch-wise or continuously to enable industrial implementation. In fact, this SSC process is presently operated on a technical scale by FNE Entsorgungsdienste Freiberg GmbH.

The mixture of NH_4Cl and solid_{L1} was placed between two tapers in the horizontal quartz tube. The $\text{NH}_{3(g)}$ excess produced during the NH_4Cl decomposition was firstly introduced to a scrubbing bottle with glass wool to remove solid particles and then, absorbed in a second scrubbing bottle containing deionised water.

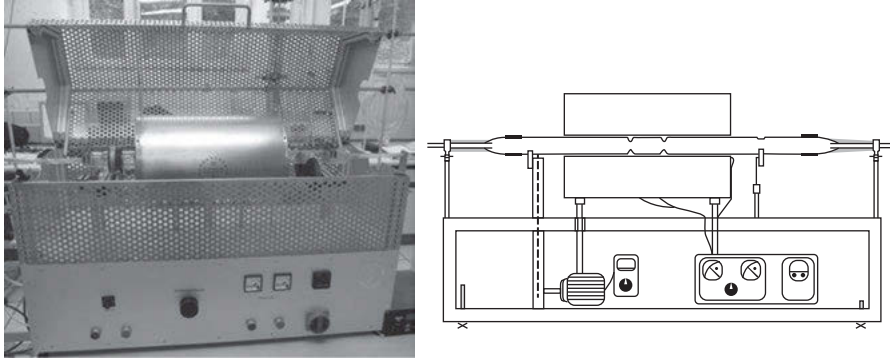


Figure 15.5: Rotary kiln used for simultaneous optimization.

15.2.4.1 Starting material

The solid_{L1} is mainly composed by calcium, phosphor, yttrium and europium (Table 15.4). These two RE represent ~97 wt.% of the RE content (~12 wt.%). The recovery of cerium, gadolinium and lanthanum would not be cost-effective due to their low concentrations. These three RE are contained in the blue and green phosphors, which however are considerably acid-resistant. Acidic digestion therefore requires efforts, which quickly render recycling of La, Ce and Gd less profitable.

Table 15.4: Elemental composition of the solid_{L1} obtained after L1 stage (REF).

Element	Concentration (wt.%)
Ca	6.94 ± 0.42
Al	3.54 ± 0.31
P	3.51 ± 0.23
Na	1.04 ± 0.15
Sr	0.96 ± 0.05
Ba	0.70 ± 0.03
Mg	0.29 ± 0.03
K	0.22 ± 0.02
Mn	0.16 ± 0.01
Fe	0.13 ± 0.02
Si	0.08 ± 0.01
Ni	0.03 ± 0.01
Y	73.70 ± 1.61
Eu	5.30 ± 0.08
Ce	1.02 ± 0.10

Table 15.4 (continued)

Element	Concentration (wt.%)
Gd	1.01 ± 0.06
La	0.92 ± 0.10
Tb	0.47 ± 0.04

The particle size distribution of the starting material is important, as the available area of the gas-solid reaction interface greatly affects the chlorination process. In this sense, the solid_{L1} was examined by laser diffraction analysis (MasterSize 3000, Malvern Panalytical). The results showed that 5.92 μm is the particle size with a highest volume fraction of 4.54% (Figure 15.6). Most particles are in the range of 2.75–8.70 μm (~60.76%). The d_{10} -, d_{50} - and d_{90} - values are 2.42, 8.68 and 58.90 μm , respectively. The volume fraction with a maximum of 0.2% in the range of 750–3,500 μm correspond to elements which originated from glasses in the original fluorescent lamp waste, such as Al-Si [22], which were not leached in the L1 stage.

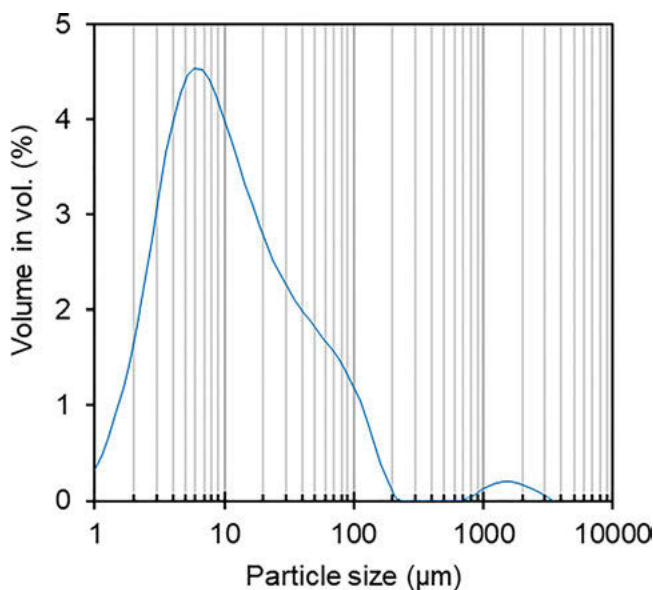


Figure 15.6: Particle-size distribution of the starting material [34].

The particle size distribution is smaller than in other literature studies [30, 31], being beneficial for the reaction rate because the area of the gas-solid phase reaction interface can increase in the chlorination process.

15.2.4.2 Optimization

15.2.4.2.1 Choice of optimization method

There are two fundamental approaches for optimization: (a) sequential and (b) simultaneous. Most commonly the optimum is determined by varying one influence factor after another while keeping all remaining reaction conditions constant. This one-factor-at-the-time strategy requires less experiments to obtain an optimum, but massive problems occur, when two or more factors correlate with each other (Figure 15.7). Moreover, this error may go unnoticed.

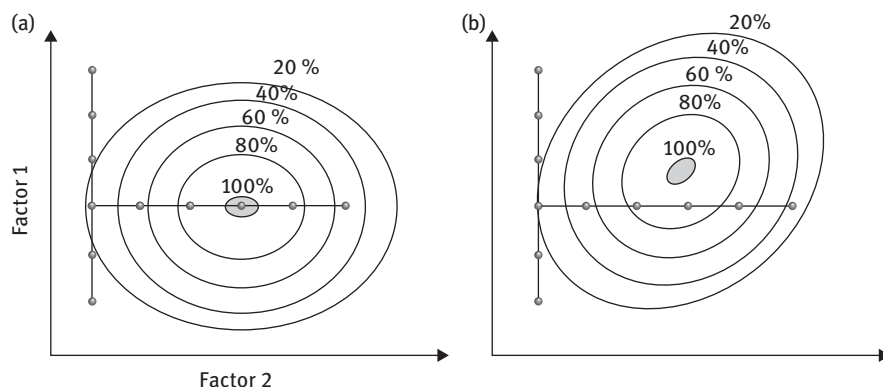


Figure 15.7: Response surfaces for sequential optimization without (a) and with correlation (b) between both factors (modified according to Ref. [32]).

Without any correlation the optimum at 100 % is achieved accurately (Figure 15.7a). But if one factor cannot be varied independently without changing the second factor as well, the depicted one-factor-at-the-time strategy yields only an ostensible optimum instead (Figure 15.7b) [32]. Especially in complex reaction systems avoiding all correlations is often impossible. So a change of optimization methods is absolutely necessary. In this regard, the sequential simplex method using a geometric algorithm suits to determine the global optimum, but with a previously unknown count of experiments. However, the simplex method relies on prompt analyses, because every next experiment within this algorithm requires an evaluation of the previous one. If there is no prompt analysis at hand, statistical designs provide an alternative. These designs alter all factors at the same time on the basis of a symmetric plan. The evaluation takes place after conducting all experiments [32, 33]. By generating a model equation from the results covering all influences, it becomes possible to estimate the target value (e.g. the yield) at every point of the examined area. For solid-state chlorination a three-stage Box Behnken plan was applied for optimization involving a polynomial of the second degree as model equation:

$$y = b_0 + \sum_{i=1}^N b_i x_i + \sum_{1 \leq i \leq j}^N b_{ij} x_i x_j + \sum_{i=1}^N b_{ii} x_i^2 \quad (15.4)$$

where y is the target value (RE yield in the permeate); x_i is the factor (temperature, residence time or $\text{NH}_4\text{Cl}:\text{solid}_{\text{L1}}$ ratio (AFR)); N is the number of factors (3); b_0 is the ordinate section (0); and b_i , b_{ij} , b_{ii} are the regression parameters of linear, squared and cross effects.

Determining all regression parameters is a mathematical problem of multiple linear regressions. Already the number of three factors renders the required calculations rather laborious. They are therefore commonly conducted by evaluation software such as Statgraphics (Statpoint Technologies, Inc.). By knowing the model equation, the optimum can be calculated within the examined area. Despite the chosen optimization method three preconditions must be fulfilled: (i) the experiments have to be repeatable with a preferably low distribution of measurement values, (ii) all factors must have an influence on the target value and (iii) have to be varied in an appropriate range, where the influence exceeds the experimental error. Therefore, attempts of orientation are necessarily conducted during a sequential pre-optimization of the solid-state chlorination.

15.2.4.2.2 Attempts of orientation

The yields of yttrium and europium calculated from their concentrations in the permeate were chosen as target values (simplified: Y_{yield} and Eu_{yield}) in the optimisation. The percentages of each element dissolved in the permeate and analysed by ICP-OES refers directly to the metal chlorides produced by solid-state chlorination, because all original components of the fluorescent lamp wastes are insoluble in the 2,4 pentanedione/ethanol mixture.

Considering the decomposition temperature of $\text{NH}_4\text{Cl}_{(\text{s})}$, as well as the RE chlorination temperature range, seven experiments were carried out as orientation to determine the factor levels in the Box-Behnken design.

The experiments with altered temperatures were conducted at an AFR of 1 g/g and with a constant residence time of 60 min. Starting at 250 °C, the RE yields increase reaching their respective maximum at 300 °C. However, the RE yields drops at higher temperatures (Figure 15.8a).

Why this RE yield decreased unexpectedly can be explained by the two consecutive reactions depicted in Eq. (15.5). RE are chlorinated ($\text{RECl}_{3(\text{s})}$) once the $\text{REO}_{(\text{s})}$ species are in contact with $\text{HCl}_{(\text{g})}$, after the $\text{NH}_4\text{Cl}_{(\text{s})}$ decomposition. Subsequently, $\text{RECl}_{3(\text{s})}$ species can be extracted by the leaching organic solution. However, when the temperature increases, the second reaction could be more favored, thus, producing the anionic species ($\text{RECl}_4^-_{(\text{aq})}$) which are not extractable by the 2,4 pentanedione/ethanol mixture.

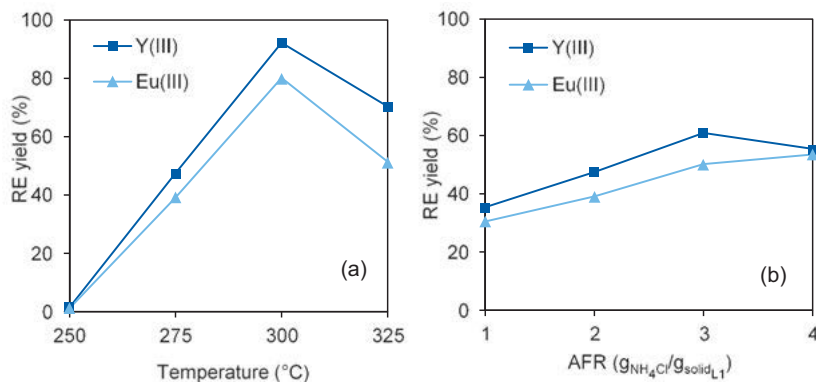


Figure 15.8: Effect of chlorination temperature (a) and AFR ratio (b) on the RE yield [34].



The $RECl_4^-$ anionic species is not extractable with the 2,4 pentanedione/ethanol mixture, reducing the RE yields [34]. Hence, the highest level of the temperature ≤ 300 °C to avoid the second reaction depicted in Eq. 15.5.

As second influence on solid-state chlorination the AFR was examined at 275 °C by varying the ratio between 1 and 4 g/g. Initially, Y yield increase until reach their maximum at 3 g/g, but afterwards decreased (Figure 15.8b). This trend turns against all expectations whereby Y yield should rise while more $HCl_{(g)}$ is available for chlorination.

In order to understand this fact, other elements should be examined. However, the leaching solution has to be change because the organic mixture used only dissolves these critical metals. The experiments were repeated but using distilled water in the leaching stage (Figure 15.9).

Other examined element follows a distinct trend contrary to yttrium: calcium. Although the calcium content in the solid treated in the solid-state chlorination is low compared to yttrium, it has a negative influence on Y yield (Figure 15.9). Ca yield increases constantly till 31.7% for all the AFR studied range, while Y drops after reach the optimum of 54.3% at 2 g/g. Actually Ca^{2+} does not drop Y yields by itself, but along with Ca^{2+} mobilized phosphate ions precipitate dissolved Y^{3+} as YPO_4 . Since solubility of precipitation of YPO_4 is much lower than for $Ca_3(PO_4)_2$ precipitation of Y^{3+} increases with rising amounts of calcium entering the solution [35, 36].

15.2.4.2.3 Simultaneous optimization

Suitable statistical designs for three factors (Temperature, residence time and AFR) are central composite design, complete factorial design or the Box-Behnken plan. 3^3

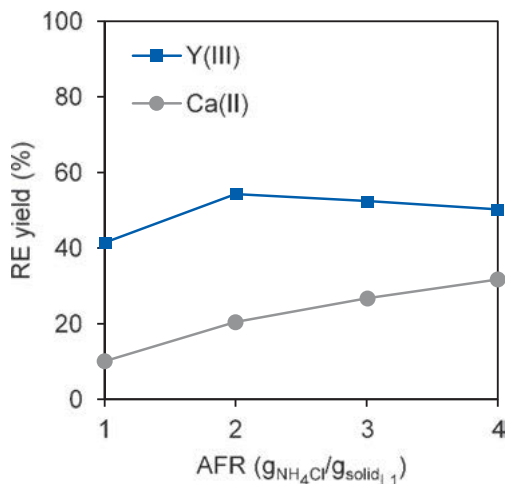


Figure 15.9: Effect of the AFR ratio on RE yield using distilled water in the leaching stage [34].

Box-Behnken design (Figure 15.10) was chosen since it allows for modelling linear as well as non-linear dependences with comparatively low experimental effort.

3³-Box-Behnken design

Target value:

RE yield in the permeate

Factors:

Temperature

Residence time

NH₄Cl/solid_{L1} ratio (AFR)

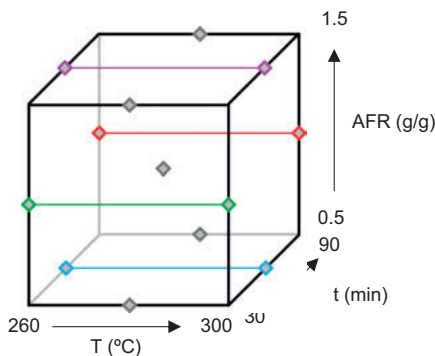


Figure 15.10: Statistical design used for the optimization of the solid-state chlorination of fluorescent lamp wastes.

Such a plan of three factors and three levels to even examine non-linear dependencies needs 15 experiments with a three-fold determination of the centre. Residence time, as second factor, was altered from 30 to 90 min, taking into account that the rotary kiln heats up with ~10 K/min. Lower times for chlorination would distort the results, since chlorination already starts during heating phase as soon as temperature rises above 220 °C.

Finishing all experiments, evaluation commences by looking at the resulting Pareto diagram (Figure 15.11). The diagram depicts all sized influences of the nine effects which can influence the yield: three linear (A, B, C), three squared effects (AA, BB, CC) and three binary correlations (AB, BC, AC) and compares them with the experimental error (blue line). Where the bars cross the blue line, there is a significant influence on RE yield.

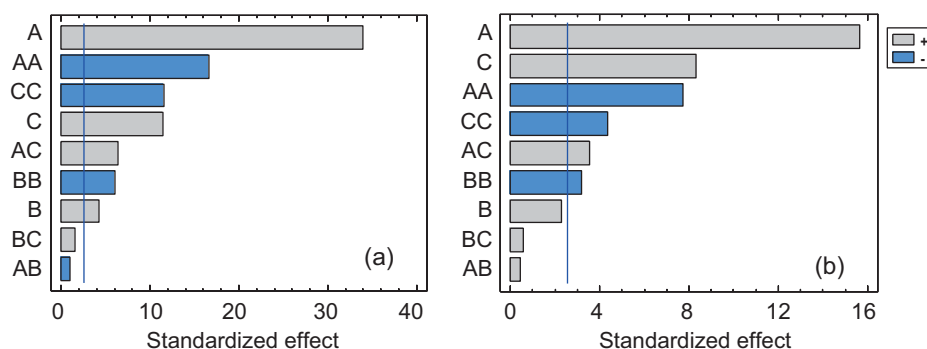


Figure 15.11: Pareto diagram with all linear (A, B, C), square (AA, BB, CC) and cross (AB, AC, BC) effects. a) Y, b) Eu [34].

The Pareto diagram shows that seven of nine effects are significant for Y_{yield} (Figure 15.11a). Only the AB and BC binary correlations are insignificant to both yield optimisation and, therefore both correlations were removed from Eq. (15.4).

Although the concentrations of both RE in the fluorescent lamp waste are different (Table 15.4), both optimisations are similar. It can be explained by the similarities of the chemical properties of these metals [37] and the difficulty of their selective separation [38]. As expected, temperature is the main effect influencing RE yield. While AFR provides the second highest linear factor and the residence time is significant, its influence remains on low level. This indicates a very fast chlorination being almost finished at 30 min.

Finally, the model equations (Eqs. (15.6)-(15.7)) for both RE are formed by removing non-significant effects and calculating the regression parameters:

$$Y_{\text{yield}}(\%) = -5076.04 + 35.0526 \cdot A + 1.33439 \cdot B - 92.9237 \cdot C - 0.0612 \cdot A^2 + 0.9156 \cdot A \cdot C - 0.0099 \cdot B^2 - 70.1363 \cdot C^2 \quad (15.6)$$

$$Eu_{\text{yield}}(\%) = -4661.69 + 32.3075 \cdot A + 1.41159 \cdot B - 140.722 \cdot C - 0.0567 \cdot A^2 + 0.9984 \cdot A \cdot C - 0.0105 \cdot B^2 - 52.6316 \cdot C^2 \quad (15.7)$$

where A is the temperature in $^{\circ}\text{C}$; B is the residence time in min; and C is the ratio of $\text{NH}_4\text{Cl}:\text{solid}_{\text{L1}}$ in g/g.

For Y the estimated optimum of 95.7% was predicted using the following reaction conditions: 295.9 °C, 67 min and AFR of 1.27 g/g. For Eu the optimum of 96.6% can be reached at 298.1 °C, 67 min and AFR of 1.49 g/g. Considering the different concentrations in fluorescent lamp waste, validation of the mathematical model was carried out by a twofold experiment using the optimized parameters for Y. Figure 15.12 shows how the RE yields depend on temperature and residence time with an AFR constant of 1.27 g/g. Both response surfaces are almost identical, what is a clear advantage considering the goal of recovering all RE by one single process.

Even the proven global optimum at 295.9 °C reveals a difference of 42.1 °C compared to the actual decomposition temperature of NH_4Cl (338 °C). Under this reaction condition NH_4Cl only decomposes partially and forms a dynamic equilibrium between gaseous phase and solid NH_4Cl . At least two contrary effects must influence RE yields to describe this trend.

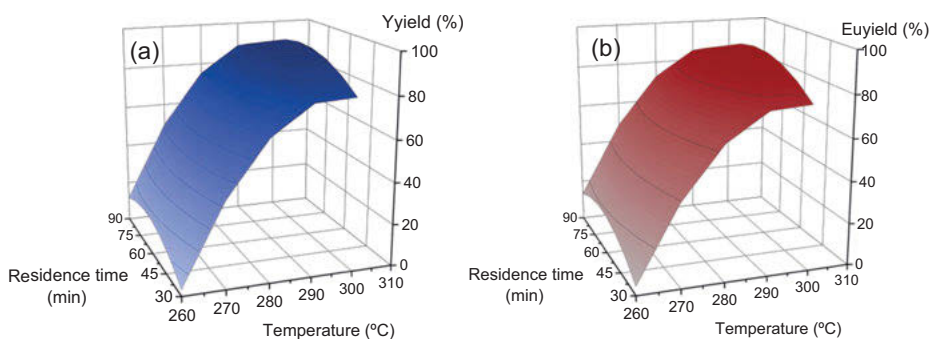


Figure 15.12: RE yield depending on temperature and residence time keeping constant AFR at 1.27 g/g. (a) Y, (b) Eu [34].

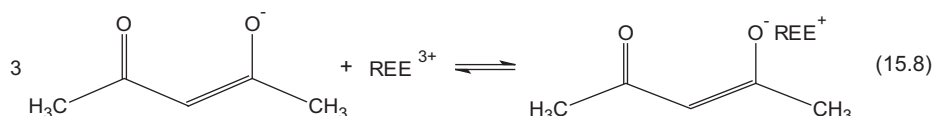
The reason for this trend must be related to the thermodynamics of decomposition. According to Eq. (15.2), every mole of NH_4Cl produces 2 moles of gas. So, 54 g of NH_4Cl decompose to 102 L of gaseous products at 350 °C. The faster the gaseous phase expands, the more unreacted $\text{HCl}_{(\text{g})}$ is driven out of the reaction zone.

On the contrary, improving RE yields requires a reduction of the gas phase volume. However, reducing temperature only poorly serves to decrease the molar volume. Truly, cooling from 350 °C to 25 °C halves the molar volume from 51 L/mol to 24.4 L/mol. For NH_4Cl this trend overlaps with the decomposition equilibrium, reducing the gas volume massively, when temperature drops below 338 °C. This way it becomes feasible to almost halve the gas volume by simply reducing temperature from 350 °C to 295.9 °C (optimum) instead. Endothermic decomposition on the one hand and expansion of gas volume on the other are the two contrary trends greatly affecting temperature dependence, which shift the optimum to quite low temperatures.

Although lower temperatures generally demand an extended reaction time (cross effect BC), RE yields only showed a slight time dependence between 30 and 90 min. Due to the batch operation shorter reaction times < 30 min cannot be examined with this rotary kiln. Therefore, continuous operation is required to reduce influences on RE yields by preheating.

15.2.5 Leaching optimisation

After the solid-state chlorination under optimal reaction conditions and leaching with 2,4 pentanedione/ethanol mixture the leachate is mainly composed of REs (~99.9%, [34]). The volume used of the leaching solution was utilized in excess (50 mL) to ensure the RE complete complexation (Eq. (15.8)).



Different experiments were carried out keeping the optimized parameters for the solid-state chlorination unchanged, but varying different L:S ratios to optimize the leaching solution volume. The solid consisted of 1 g of solid_{L1} and 1.27 g of NH₄Cl_(s). The excess of the leaching solution can be significantly reduced to almost its half (30 mL of the 2,4 pentanedione/ethanol, [34]), while obtaining the same RE yields and minimizing operational costs. Thus, the process obeys the rules of sustainability.

15.2.6 Recycling process

The organic leaching mixture was re-used after the RE had been removed by precipitation with NaOH. Both RE were re-dissolved in chloridic medium (pH ~ 1.5) to separate yttrium from the mixture using Cyanex 572 dissolved in kerosene as extractant via solvent extraction.

A cross-flow solvent extraction process with two stages was required for separating the RE yielding 99.4% Y in the organic phase with 0.15 mol/L of Cyanex 572 after two solvent extraction stages. Yttrium was fully recovered from the organic phase after re-extraction with 3 mol/L HCl in 99.9% purity. Europium was obtained in the raffinate flow with 97.4% purity. This SX process was followed by precipitation of yttrium and europium oxalate by addition of 0.8 mol/L oxalic acid [39] after pH conditioning by NaOH. Subsequently, this oxalate residue was filtered, dried and calcined at 800 °C for 2 h [40, 41]. Y₂O_{3(s)} and Eu₂O_{3(s)} were identified by XRD (Figure 15.13).

Figure 15.14 depicts how yttrium and europium may be recovered by combining solid-state chlorination with solvent extraction process.

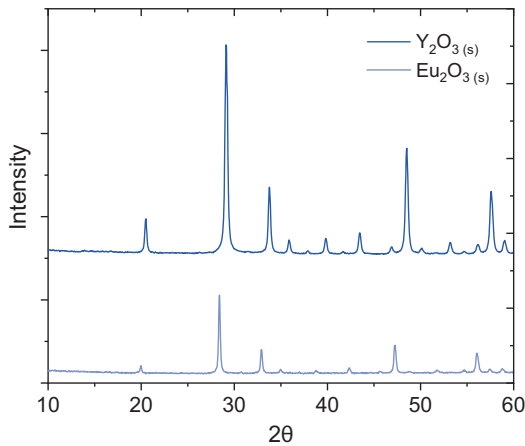


Figure 15.13: XRD pattern of the REO obtained after calcination at 800 °C for 2h.

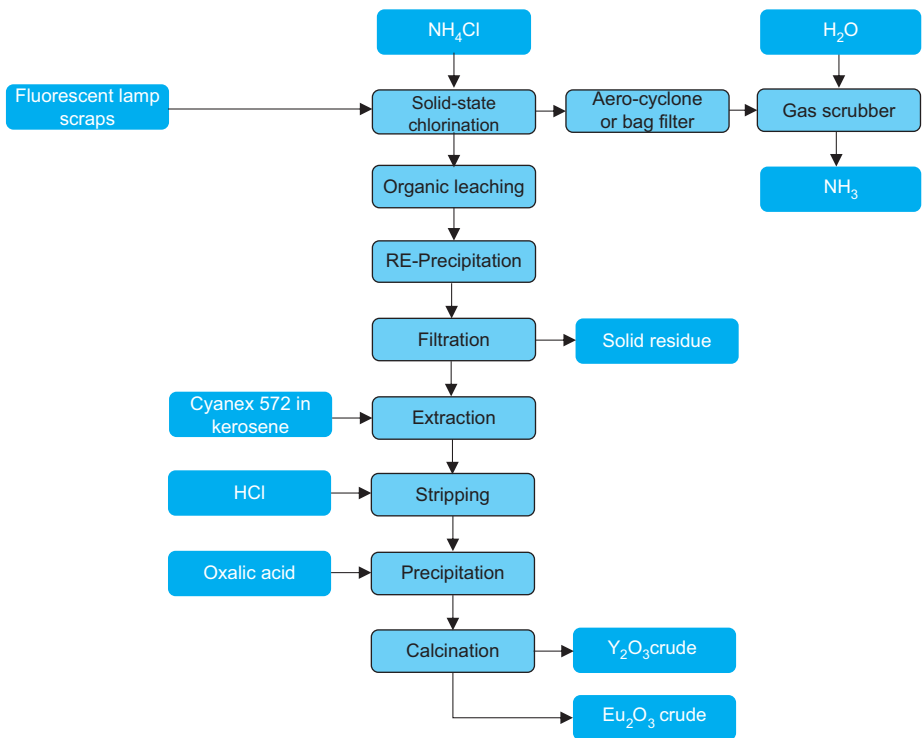


Figure 15.14: Scheme of the recycling process for fluorescent lamp scraps.

thus reduced by at least 50%. Furthermore, the organic mixture uses in the leaching stage provides a RE separation in one only step (without conditioning).

Yet a general statement on process economy cannot be made without taking into account the commodity prices, location, desired production output, personnel requirement, etc. Whereas wet chemical treatment of fluorescent lamp scraps went uneconomic between 2014 and 2016 solid-state chlorination remained at least economic for higher concentrated production wastes, although commodity prices have dropped by another 80%. At present, the main obstacles for scaling up the entire process are the rotary kiln design, which implies with several different heating zones and the implementation of membrane processes.

15.3 RE metal recycling from SmCo magnets

Permanent magnets containing RE metals belong to the strongest magnetic alloys currently available with magnetic energy densities up to 450 kJ/m [31, 32]. Because of versatile applications in, for example, hard drives, electric motors, wind power stations or MRI scanners the demand for neodymium, dysprosium, praseodymium, samarium and terbium substantially increased within last years.

Among RE alloys, SmCo magnets are the second most important group. Nevertheless, they are not collected separately, and recycling processes have to focus on recovering NdFeB magnets as well as SmCo ones within one process. Global demand for SmCo magnets is projected to expand at 6.3% annual pace to 388 € million in 2023 due to the increase electronic production and the rise need for magnets with resistance to high temperatures and corrosive environments in industrial applications. Although the recycling of rare earths from EoL permanent magnets is a widely studied field of research, with rare earth prices falling, they have become increasingly uneconomical. In this context, solid-state chlorination has been intensively investigated as a powerful alternative strategy for magnets recycling, too.

15.3.1 Starting material

Prior to chemical or mechanical treatment magnet recycling starts with the systematic collection of EoL magnets and their separation from electronic scrap. Particularly the latter still represents a major challenge. Because of sintering the starting materials during production, the SmCo₅ magnets alloys are not completely homogeneous. Consequently, from grinding no distinct particles with homogeneous composition are obtained.

The EoL magnets examined by solid-state chlorination were SmCo alloys, which were demagnetized before they were ground to particle size $\leq 100 \mu\text{m}$. Because of the

ignoble character of SmCo alloys they may easily be dissolved in 37% hydrochloric acid and analysed via ICP-OES afterwards. The results (Table 15.5) suggests that the starting material consists of rather SmCo₅ than Sm₂Co₁₇ with impurities of NdFeB magnets due to the traces amounts of terbium and neodymium.

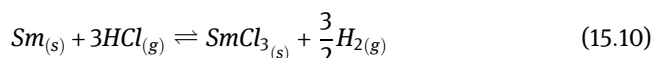
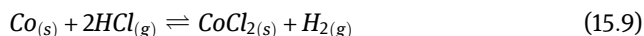
Table 15.5: Elemental composition of SmCo₅ magnet scrap.

Element	Concentration (wt.%)
Co	66.7
Sm	32.3
Tb	0.6
Nd	0.4

15.3.2 Solid-state chlorination optimization

15.3.2.1 Attempts of orientation

Applying solid-state chlorination for magnet recycling also has to meet requirements first, namely the forming of water soluble as well as nonvolatile metal chlorides. There are mainly two reactions taking place during chlorination process (Eqs. (15.9)-(15.10)), beside NH₄Cl decomposition.



CoCl_{2(s)} is obtained as by-product, whereas SmCl_{3(s)} contributes to Sm yield and it easily transferred into aqueous solution during subsequent leaching.

The conditions examined in the solid-state chlorination were the same as in NdFeB magnet recycling [30], because both magnets share some few similarities in their composition (¹/₃ RE metal, ²/₃ transition metal). Hence, SmCo₅ was expected to show a comparable reaction behavior in the process optimization.

15.3.2.2 Simultaneous optimization

The optimization of the solid-state chlorination was conducted by using a 3⁴ Box-Behnken design (Figure 15.16) and using a buffer solution, instead of an organic mixture, during the leaching step. The target value was represented by the yield of

all REs in the pregnant solution. Temperature, residence time, NH_4Cl mass and buffer mass were the four factors examined by this design of experiment (DOE).

3⁴-Box-Behnken design

Target value:

Sm yield in the permeate

Factors:

A: Temperature

B: Residence time

C: NH_4Cl mass

D: Buffer mass

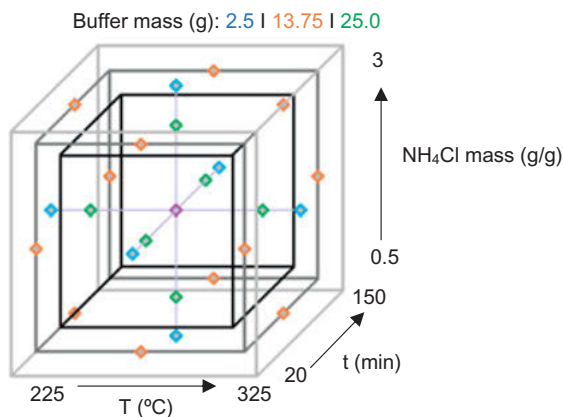
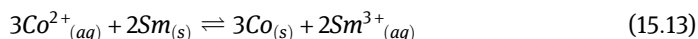
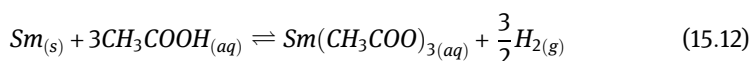
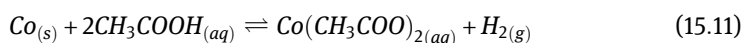


Figure 15.16: Statistical design used for the SmCo_5 solid-state chlorination optimization.

An acetic acid buffer system was used for dissolving the chloride metals since SmCo alloys are most likely to be recycled along with NdFeB magnets. This is owed to the fact that waste collecting systems do not differentiate between both types of magnet, for which reason both types appear as a non-separable waste-stream. There are two reactions taking place during the buffer leaching, i) acid-mediated metal dissolution (Eqs. (15.11)-(15.12)) and ii) cementation (Eq. (15.13)):



In this case, the use of this buffer solution in the leaching step contributes to Sm yield [43], thus, the optimization has to consider influences originating from both steps (leaching and chlorination). For this reason, the DOE examined for SmCo_5 contains four factors, instead of three (used in the solid-state chlorination optimization for fluorescent lamp scraps).

After conduction all 27 experiments, Sm and Co yields were evaluated by using the Statgraphics as statistical program. All the linear (A, B, C, D), squared (AA, BB, CC, DD), and cross effects (AB, AC, AD, BC, BD, CD), which could influence element yields significantly were examined. Only six of them (AA, DD, AB, AD, BD and CD) are insignificant for Sm yield and removed by the stepwise method (Figure 15.17).

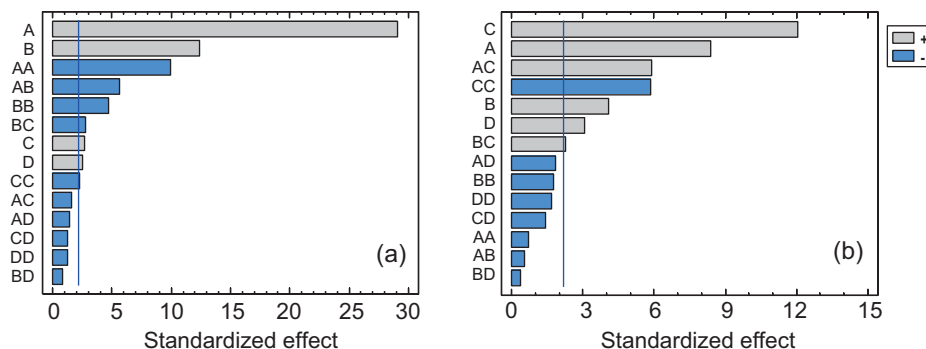


Figure 15.17: Pareto diagram with all linear, square and cross effects influencing (a) Sm yield, (b) Co yield.

Temperature, in linear and squared terms, affects Sm yield appearing among the top three influences. Residence time provides the second highest effect whereas NH_4Cl mass as well as buffer mass are only significant to a modest degree. As expected, AB correlation also influences on the RE yield due to the van't Hoff's rule for all chemical reactions.

Seven effects were determined to have significant influence on Co yield (Figure 15.17b). Comparing the significant effects for both metals, it can be noticed that, the most obvious difference is the strong influence of the NH_4Cl mass occurring as linear (C), squared (CC) and two cross effects (AC, BC). The reason lies in the selectivity for the more ignoble REs over nobler metals such as Co during chlorination.

All regression parameters have been calculated by multi-linear regression to achieve the model equation (Eqs. (15.14)-(15.15)).

$$\begin{aligned} \text{Sm}_{\text{yield}}(\%) = & -254.637 + 1.94905 \cdot A + 0.683843 \cdot B + 3.62502 \cdot C + 0.113218 \cdot D \\ & - 1.5140710 \cdot 10^{-3} \cdot AB - 3.00915 \cdot 10^{-2} \cdot BC + 2.77388 \end{aligned} \quad (15.14)$$

$$\begin{aligned} \text{Co}_{\text{yield}}(\%) = & 41.79 - 0.151528 \cdot A - 0.0271909 \cdot B - 29.1162 \cdot C + 0.352821 \cdot D \\ & + 0.211928 \cdot AC + 0.0625849 \cdot BC - 6.26815 \cdot C^2 \end{aligned} \quad (15.15)$$

where A is the temperature in $^{\circ}\text{C}$; B is the residence time in min; C is the NH_4Cl mass in g/g; and D is the buffer mass in g.

Eq. (15.15) predicts the complete Sm recovery (100%) using the following reaction conditions: 325°C , 70 min, 3 g/g NH_4Cl and 25 g buffer. The validation of the mathematical model was carried out by a double fold experiment using these Sm-optimized parameters, obtaining $99.7 \pm 0.1\%$ of Sm yields. Regarding model equation which estimates Co yield, it describes less accurately than Eq. (15.16) does for Sm yields due to the average difference between model and measured Co yield (3.3%).

Using the optimized reaction conditions for the Sm-optimum yield, $75.5 \pm 3.3\%$ of Co were predicted by Eq. (15.15). For preventing Co from being chlorinated and

dissolved, high temperatures and low NH_4Cl masses seem favourable. According to the results obtained, the two-step digestion can make use of a selectivity for Sm.

The selectivity for Sm was determined as a function of chlorination temperature and NH_4Cl mass keeping constant the residence time (70 min), buffer mass (25 g) and SmCo_5 mass (1 g). It was calculated with aid of both model equations (Eqs. (15.14)-(15.15)) as well as Eq. (15.16). The amount of digestion media utilized to dissolve Sm and Co in the permeate as Sm^{3+} and Co^{2+} ions (n_{EQ} in mol) was determined by Eqs. (15.17)-(15.18).

$$\text{Sm}_{\text{selectivity}}(\%) = \frac{n_{EQ\text{Sm}}}{n_{EQ\text{Sm}} + n_{EQ\text{Co}}} \quad (15.16)$$

$$n_{EQ\text{Sm}} = \frac{\text{Sm}_{\text{yield}} \cdot C_{\text{Sm}} \cdot m_{\text{SmCo}_5} \cdot z_{\text{oxSm}}}{M_{\text{Sm}}} \quad (15.17)$$

$$n_{EQ\text{Co}} = \frac{\text{Co}_{\text{yield}} \cdot C_{\text{Co}} \cdot m_{\text{SmCo}_5} \cdot z_{\text{oxCo}}}{M_{\text{Co}}} \quad (15.18)$$

where Sm_{yield} and Co_{yield} are the calculated yields by using model equations in %, $C_{\text{Sm/Co}}$ are the element concentration in the SmCo_5 magnets in wt.-%, z_{ox} is the oxidation state of the particular element, m_{SmCo_5} is the mass of the digested SmCo_5 magnet powder (1 g) and $M_{\text{Sm/Co}}$ is the molar mass in g/mol. Figure 15.18 shows the maximum $\text{Sm}_{\text{selectivity}}$ (58.6%) at the lowest NH_4Cl mass (0.5 g/g $_{\text{SmCo}_5}$) and at the highest temperature (325 °C). With these reaction parameters, 99.4% of Sm can be recovered, remaining the 80% of Co unchlorinated and undissolved.

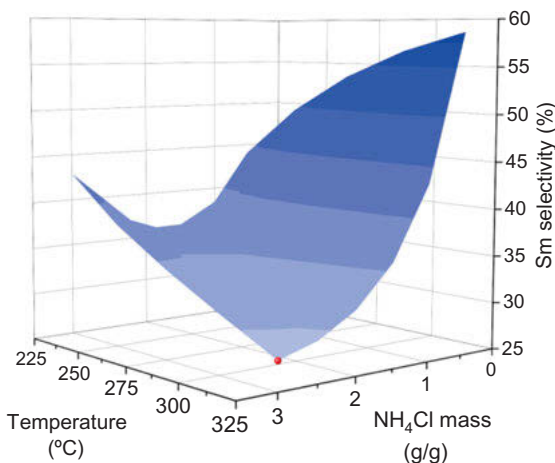


Figure 15.18: $\text{Sm}_{\text{selectivity}}$ as a function of chlorination temperature and NH_4Cl mass (magnet mass, residence time and buffer mass are kept constant at 1 g, 70 min and 25 g, respectively). Sm maximum is represented by bold point.

An automated mineralogy system (mineral liberation analyser, MLA) was used to examine the possible selectivity of Sm and Co. This system combines SEM-EDX measurements with a software that allows for, among other modes, automated measurement of particles. To demonstrate selectivity, sample preparation is most essential. 1 g of all solid powders were mixed with the same volume of graphite to separate agglomerated particles from each other.

The resulting graphite/sample mixture was casted with epoxy resin to a cylinder of 25–30 mm in diameter and hardened for 12 h. Subsequent grinding with SiC and polishing with a diamond suspension uncovered a smooth surface showing different cross sections of the particles.

The SmCo_5 material was chlorinated at more gentle conditions (Table 15.6) to avoid the easy mechanical unstable behaviour due to the formed chlorides, thus, becoming unmeasurable because the disintegration during polishing. Coating the surface with carbon to conduct electrons represents the last step of preparation.

Table 15.6: Solid-state chlorination and sample preparation for MLA to investigate partial selectivity.

No	$m_{\text{NH}_4\text{Cl}}$ [g]	Δ [g]	Temperature [°C]	Δ [°C]	Sample preparation for MLA
Optimum	3.0		325		Not measurable
1	3.0		275	–50	Not measurable
2	1.75	–1.25	275	–50	Not measurable
3	0.5	–2.50	275	–50	Not measurable
4	1.75	–1.25	225	–100	Measurable
5	0.5	–2.50	225	–100	Measurable
6	0.25	–2.75	225	–100	Measurable

*All experiments were conducted with 1 g SmCo_5 powder, residence time was set to 85 min.

By electrons backscattered on a gold standard the SEM was calibrated on greyscale to enable the distinction between particles and background (e.g. epoxy resins, cracks). On this basis the measuring range of EDX is determined as well. Typical are the measurements of tens to hundreds of thousands of particles leading to millions of spectra per sample. All these spectra are compared with a reference list (Table 15.7), formerly created for the material. This list also contains the element concentrations calculated from the spectra. Since magnets do not consist of classical minerals, no pre-recorded spectra were available and comparative spectra were collected at different locations of the sample and added to the reference list instead. However, a pinpoint measurement is limited to an accuracy of 0.1–2 μm , due to the pear-shaped excitation. Therefore, mainly mixed spectra are obtained during measurement of small sized particles or locations where compositions change strongly. Thus, assigning each measuring point to one of the references from the list is not conducted strictly, but with a previously defined tolerance, which was set to 80%. Every element concentration of the reference list is coloured differently, becoming possible to assign

Table 15.7: Grouping of reference spectra for MLA of SmCo_5 magnets.

Colour	[Co] (wt.-%)	[Sm] (wt.-%)	[Cl] (wt.-%)	[O] (wt.-%)	Comments
	61.0	39.0	0.0	0.0	Starting-material
	67.0	33.0	0.0	0.0	
	10.2	77.8	0.4	11.6	
	59.7	25.3	4.0	11.1	Chlorinated layer

the respective colour to each measuring point for graphic illustration of the entire examined surface (Figure 15.19).

The chlorinated powder was examined with an MLA and compared with the starting material. Since particles were cut and polished during sample preparation, it became possible to analyse the cross section to determine the composition depending on particle radius. Spectra of similar composition were combined to coloured material phases, representing the heterogeneity of particles as well as the collection of mixed spectra on spots with changing composition. The reaction mechanism is different from the one observed during the chlorination of NdFeB magnets due to the high selectivity in SmCo_5 magnets.

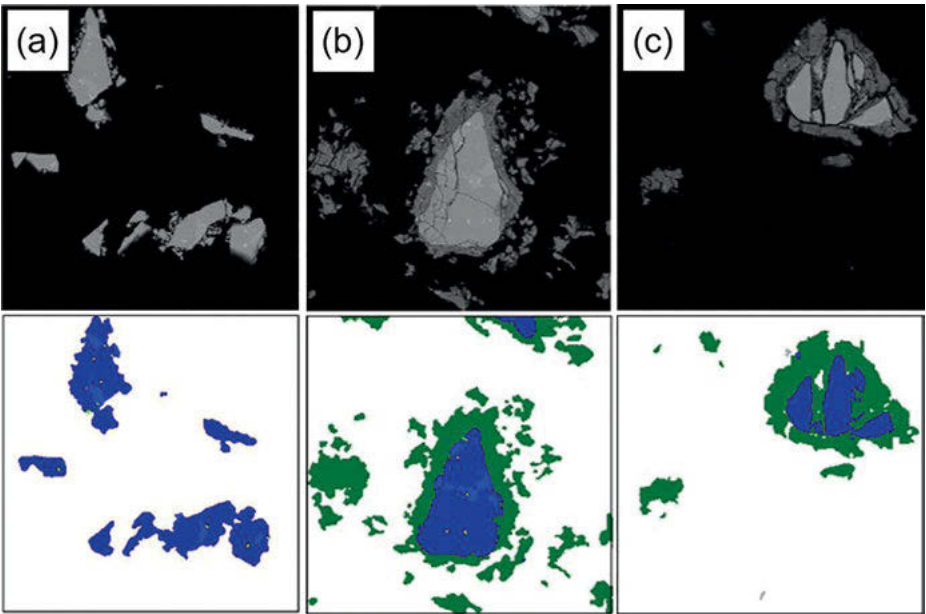


Figure 15.19: MLA examined samples of (a) untreated as well as (b) under- and (c) over-stoichiometric chlorinated magnet powders [49].

Three different phases can be seen in Figure 15.19a, which corresponds to the unchlorinated SmCo_5 powder. Besides two main phases where Co is the main component, the third one is especially rich in Sm (green areas on the right image). A thick chlorinated layer has formed covering the particles (Figure 15.19b) when the chlorination was conducted with 0.25 g/g NH_4Cl at 225 °C.

In this regard, chlorinated layer refers to a layer containing only 4 wt.% chloride, whereas fully chlorinated SmCo_5 magnets would consist of 51 wt.% chloride. In contrast to NdFeB magnets, SmCo_5 reacts differently, since the transition metal (Co) is incapable of shielding the more ignoble Sm from reacting with $\text{HCl}_{(\text{g})}$. Therefore, Co and Sm are almost chlorinated separately enabling the observed selective reaction. Overstoichiometric amounts of NH_4Cl during solid-state chlorination, cause a fast disintegration of particles. The chlorinated layer appears also within the particle core (Figure 15.19c), when the NH_4Cl excess was 12.5% (No. 4 in Table 15.6). This indicates that particles easily break apart in addition to losing their outer layer.

SEI were recorded by a scanning electron microscopy (SEM) from JEOL (model JSM 7001 F) coupled with an energy-dispersive X-ray spectroscopy (EDX) from Bruker (Quantax Esprit 1.9.3). The powder samples were applied directly to a messing tab of 10 mm in diameter. A small adhesive coal bed fixed the powder on the surface. Afterwards all samples were vaporized with carbon to conduct the electrons. For taking pictures in high resolution and to avoid overexposure, the voltage was kept at 3.0 kV at a short working distance of 7.1 mm. Thus, all SEI at magnifications of 400–500 were sufficient to provide a decent overview of surface and particle structure. In contrast, EDX analysis was conducted at 15.0 kV at 13 mm (distance to the detector). The magnification of the images was 10 times higher (3,500–5,500) to show particles in more detail.

In order to have a direct proof how particle disintegration leads to the selectivity for Sm, solid-state chlorination was conducted under optimum conditions to produce Sm-enriched layers. The resulting particles, especially their unpolished surface, were afterwards examined with SEM-EDX. Starting from unchlorinated SmCo_5 magnets, selectivity should lead to a distinct separation of SmCl_3 and CoCl_2 on the particle surface during chlorination.

Assignment is possible by back-scattered electron analysis (BSE), as elements with high atomic numbers ($_{62}\text{Sm}$) reach higher intensities and appear white or light grey, while elements with lower atomic numbers can be seen in dark grey ($_{27}\text{Co}$). Two domains are observed on the surface of the particles (Figure 15.20). The EDX analysis disclosed that the white domains consist almost exclusively of SmCl_3 (Table 15.8).

While in the white domains the concentration of Co amounts to only 2 wt.%, the situation in the grey domains is opposite. They contain 51.8 wt.% Co on average and are almost free of Sm.

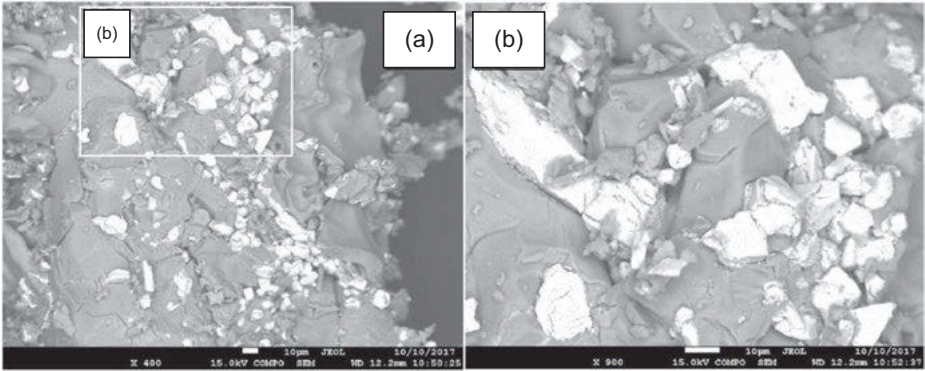


Figure 15.20: BSE images of SmCo_5 powder chlorinated under optimum conditions [49].

Table 15.8: Composition of both domains from Figure 15.20.

Colour	[Co] (wt.-%)	[Sm] (wt.-%)	[Cl] (wt.-%)	[O] (wt.-%)
Grey	51.8	0.5	45.2	2.5
White	2.0	60.6	32.4	5.0

15.3.3 Recycling process

Except for some few differences the desired process resembles the one developed for fluorescent lamp scraps (Figure 15.21). At first EoL magnets need to be demagnetized and ground to particle sizes $<100\ \mu\text{m}$ prior to chlorination to their metal chlorides. In the course of aqueous work-up, acetate buffer prevents hydroxides from precipitating and enhances RE yields by additionally leaching the magnets through cementation. Due to comparatively high pH values (~ 3), any further adjustment of pH values is redundant [44–46]. For precipitation purposes oxalic acid can be added to the permeate after filtration with the aim of retrieving RE oxalates. Calcining the latter leads to marketable RE oxides, achieving quantitative yields at $\text{pH} \geq 1$.

In general, designing an entire process is not necessarily the aim of developing recycling strategies. Instead extending an industrial process by one or at most a few steps facilitates upscaling. Since at present there is no industrial recycling technology available, EoL recycling has to be implemented in primary RE production from their minerals and ores (Figure 15.22). This situation may be changed by transferring the solid-state chlorination on an industrial scale.

Hitherto, all processes finally furnish a mostly acidic RE concentrate, which is used for further purification and RE separation. At this point permeates coming

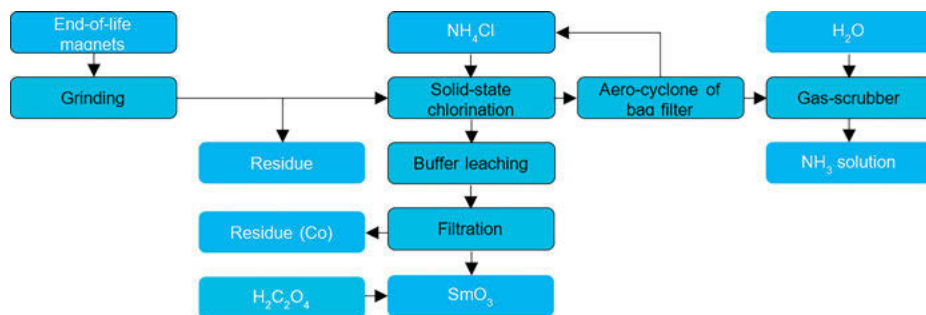


Figure 15.21: Scheme of the process developed for recycling SmCo₅ magnets.

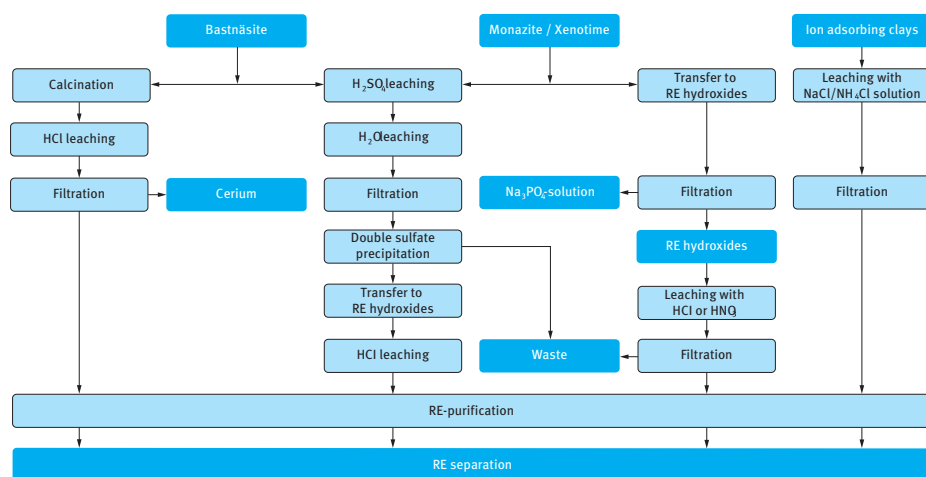


Figure 15.22: Applied industrial processes for primary RE production from different minerals [44–46, 50].

from solid-state chlorination could be fed into primary production. Applying solid-state chlorination for primary production is conceivable, but only for carbonatic bastnäsite (Ce,La,Nd,Y)[(F,OH)CO₃]. Chlorinating monazite (La,Ce,Nd)[PO₄], xenotime (Y,Yb)[PO₄] or clays leads nowhere, since solid-state chlorination is not suited to mobilize REs from phosphates, borates or aluminates. Even industrial processes need two steps to dissolve RE elements from both phosphatic minerals. Initially either concentrated H₂SO₄ or NaOH_(aq) transfers all RE phosphates to sulphates and hydroxides, respectively. After phosphate ions were removed all RE salts are dissolved by adding acids or simply by diluting with water. For ion adsorbing clays treatment with a solution of NaCl and NH₄Cl already suffices to desorb RE ions.

15.3.4 Summary

As was shown, the solid-state chlorination of EoL magnets is saving costs for both chemicals and disposal. The chlorination protocol using NH_4Cl provides all the benefits already discussed for fluorescent lamp scraps. The selectivity of the chlorination step allows for designing processes very flexibly. In case of low commodity prices for rare earth metals, NH_4Cl demand can be reduced by 38–78%, compared to acid leaching with mineral acids. Revenues from selling the pure by-product (NH_3 solution) can contribute additionally to process economics. By using an acetate buffer which partially leaches the magnet powder and additionally enhances RE yields by a supporting cementation reaction. In this regard, a first continuously operated reactor with a performance of 3 kg/h is built in Freiberg (Germany). This first demonstration plant capable of recycling REs from NdFeB as well as SmCo₅ magnets is in operation since July 2020.

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