D4: Good Practice Guide on sample processing, treatment, uncertainty budgets, and the quantification of the so-called mass bias

21GRD09 MetroPOEM
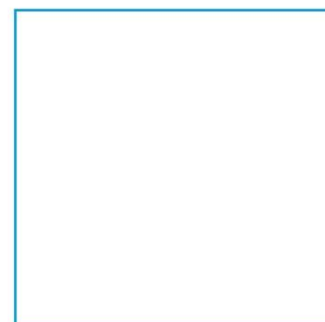
D4: Good Practice Guide on sample processing, treatment, uncertainty budgets, and the quantification of the so-called mass bias

Organisation name of the lead participant for the deliverable: LGC

Dmitriy Malinovskiy (LGC), Betül Engin (LGC), Philip Dunn (LGC), Tea Zuliani (JSI), Tjaša Žerdoner (JSI), Seena Prem Pranav (BAM), Marcus Oelze (BAM), Jochen Vogl (BAM), Oktay Cankur (TUBITAK), Lukas Flierl (PTB), Olaf Rienitz (PTB), Janine Eberhardt (PTB), Dirk Arnold (PTB), Ben Russell (NPL), Johanna Irrgeher (MUL), Shaun Lancaster (MUL), Stefan Wagner (MUL), Jixin Qiao (DTU), Daniel Pröfrock (Hereon), Dominik Wippermann (Hereon), Johanna Noireaux (LNE), Rasmus Andreasen (AU), Mihail-Razvan Ioan (IFIN-HH), Simon Jerome (NMBU)

Due date of the deliverable: September 2025 (M36)

Actual submission date of the deliverable: 30/09/2025

Glossary

CRC	Collision/Reaction Cell
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
ICP-MS/MS	Inductively Coupled Plasma Tandem Mass Spectrometry
ICP-TOF-MS	Inductively Coupled Plasma Time-of-Flight Mass Spectrometry
ICP-SFMS	Inductively Coupled Plasma Sector Field Mass Spectrometry
MC-ICP-MS	multicollector inductively coupled plasma mass spectrometer
TIMS	thermal ionisation mass spectrometer
IIF	instrumental isotopic fractionation
m/z	mass-to-charge ratio
SI	International System of Units

TABLE OF CONTENTS

1   Summary

This Good Practice Guide has been structured around the specific objectives and needs of the MetroPOEM project, namely to develop isotope ratio mass spectrometric methods for stable and long-lived radiogenic environmental pollutants, to produce recommendations for sample processing, treatment, uncertainty budgets, and quantification of instrumental mass bias, and the need for obtaining SI-traceable isotope amount ratios. The guide has reviewed and summarised the existing approaches to sample preparation and calibration of isotope ratio measurements. Continued progress made in evaluating and modelling instrumental isotope fractionation in ICP-based mass spectrometers, with recommendations for setting up high precision measurement protocols, are articulated in the section on correction for instrumental isotope fractionation. Separate sections on best practices for reporting results of isotope ratio measurements and constructing uncertainty budgets are also included.

The information presented should help an analyst to make an informed choice on suitable measurement strategy in the isotopic characterisation of materials. It is also anticipated that the present guide will help enhance awareness of the need for improving data comparability between different laboratories and support the community`s need for reliable isotope ratio data.

2   Introduction

2.1   Project background

Isotope ratio data hold immense significance in various fields of science and technology. They play a critical role in earth and environmental sciences, providing insight into a wide range of phenomena and giving rise to numerous applications. Both stable and long-lived radiogenic isotope ratios are useful markers of the origin of substances and geomaterials, in both small closed systems and on a global scale. Well-established applications of isotope ratios include absolute age determination, reconstruction of events and physico-chemical conditions that existed in the past, assessment of chemical transformation and migration pathways of pollutants in the environment, and quantification of weathering dynamics in climate research.

Advances in the technology made over the last 20 years have improved sensitivity of modern mass spectrometers and provided new means of resolving spectral interferences. As a result, precise and accurate isotope ratio measurements can now be performed at much lower concentrations of analyte and for difficult-to-analyse elements, which were previously inaccessible. The number of laboratories equipped with instrumentation capable of precise isotopic analysis have also increased worldwide. These changes bring about new possibilities for calibration of isotope ratio measurements and the need to produce reference standards with lower uncertainties.

2.2   Scope

As part of response to the aforementioned need, the project "Metrology for the harmonisation of measurements of environmental pollutants in Europe" (21GRD09, MetroPOEM) was initiated within the framework of the Metrology Partnership programme. An important objective of the project was to produce recommendations for sample processing, treatment, uncertainty budgets, and the quantification of instrumental mass bias in isotope ratio measurements. In implementing this objective, the present guide aims to advise on best practices for the determination of isotope ratios that can be traceable to the SI and on associated sample processing and data reduction.

Eight elements with stable and long-lived radiogenic isotopes were selected in MetroPOEM as models for the development and optimisation of measurement procedures, including Li, B, Cr, Ni, Cd, Sb, Pb, and U. These elements were considered in the section devoted to analyte separation prior to instrumental analysis and used as examples in other sections of the guide. Although main factors influencing isotope ratio measurement are common for all types of mass spectrometric instruments, the emphasis was given to ICP-MS based techniques, which are arguably the most widely used type of mass spectrometry for isotopic analysis of metals and metalloids in the last years.

3   Instrumentation for isotope ratio measurements

High precision isotopic analysis of most elements in the Periodic Table of the Elements that have two or more isotopes can be made by using either thermal ionization mass spectrometry (TIMS) or multi-collector inductively coupled plasma mass spectrometry (MC-ICP-MS). The notable exceptions are light elements (H, C, N, O, and S) and noble gases (He, Ne, Ar, Kr, Rn and Xe) which are measured by specialised gas source IRMS accurately and with higher precision. Both TIMS and MC-ICP-MS instruments are equipped with multiple detectors that detect ions with different mass-to-charge ratio (m/z) simultaneously. It is the capability of

simultaneous detection of ions with different m/z that allows these instruments to measure isotope ratios with highest precision.

It is worth noting that TIMS was one of the earliest types of mass spectrometry developed, with first measurements tracing back to the year of 1918 (Bürger et al., 2015). First commercial TIMS instruments were introduced on the market in the 1960s. The ICP-MS technology emerged later. MC-ICP-MS was presented to the isotope ratio community in the early 1990s (Walder, Freedman, 1992).

Isotopic analysis with precision inferior to that achieved by MC-ICP-MS and TIMS but still sufficient for resolving larger natural variations in the isotopic composition of selected elements (e.g., Li, B, Sr, and Pb) can be made by single collector ICP-MS instruments. There are a few types of single collector ICP-MS instruments which differ from each other by the principle of how ions produced in the plasma are separated in the mass analyser according to their mass-to-charge ratio. They can be broadly classified into quadrupole-based ICP-MS, sector-field ICP-MS, and time-of-flight ICP-MS.

Quadrupole ICP-MS makes use of a quadrupole for separating ions with different m/z. The principle of operation of the quadrupole was described extensively in textbooks and articles previously (e.g., Miller, Denton, 1986; Montaser, 1998; Thomas, 2004; Linge, Jarvis, 2009). Continuous progress in dealing with spectral interferences originating from the plasma led to the appearance of collision/reaction cell quadrupole ICP-MS (CRC-ICP-MS), and tandem mass spectrometry (ICP-MS/MS – also known as ICP-QQQ-MS). Details on these techniques can be found elsewhere (Tanner et al. 2002; Balcaen et al., 2015; Kroukamp, Abou-Shakra, 2020). Modern quadrupole-based ICP-MS instruments routinely achieve a resolution of one atomic mass unit (u) across the entire mass range.

The mass analyser in sector-field ICP-MS employs a magnetic field to separate ions by their mass-to-charge ratio (Rottmann et al., 2015). In addition to magnetic field, these instruments use an electrostatic analyser for focusing ions of different energies to provide more uniform kinetic energy spread of ions with the same mass-to-charge ratio. Due to the combination of the magnetic field analyser and electrostatic field analyser in their design, sector-field mass spectrometers are also called double-focusing mass spectrometers. These instruments can operate in different instrumental mass resolution modes and, when operating in high resolution mode, offer an order of the magnitude greater mass resolution over that achieved in quadrupole ICP-MS, however with compromising the overall sensitivity.

In time-of-flight ICP-MS, the mass analyser separates ions based on their differences in velocity as they travel through a field free flight region of the mass spectrometer. An important benefit associated with this way of ion separation is that the entire m/z range can be sampled in a very short period of time such that the contribution from ion source noise becomes vanishingly small in the measurement (Willie et al., 2005). Although sensitivity of time-of-flight ICP-MS is lower when compared to quadrupole-based ICP-MS, it has the advantages of faster measurement of multiple m/z at the same time and greater mass resolution.

All the above instrumental techniques were used in the MetroPOEM project to determine isotope ratios of selected elements as well as to evaluate the limits of the individual methods when it comes to high precision isotope ratio measurements.

4 Sample matrix separation

Isotopic analysis is susceptible to matrix effects. If the samples being analysed are not matched to the matrix of calibration standards, a measurement bias can occur. The use of an internal standard can reduce susceptibility to matrix effects. However, normalisation to an internal standard can only account for a small difference in matrices between samples and standards. The presence of heavy matrix in samples will render internal normalisation ineffective.

For techniques using solution sample introduction, a universal means of dealing with matrix effects is the separation of analyte from concomitant matrix elements. Such separation is a prerequisite for high precision isotopic analysis. It will not only allow for accurate correction for instrumental mass discrimination but also helps avoid potential spectral interferences originating from matrix elements.

There is a plethora of methods that have been used for chemical separation of an analyte from the sample matrix prior to isotopic analysis. These include ion-exchange chromatography, chelation ion chromatography, extraction chromatography, cold vapor generation, hydride generation, precipitation, co-precipitation, sublimation and distillation.

4.1 Chromatography-based methods

Chromatography refers to a group of methods that are used as a way of separating mixtures of compounds into their individual components (Modern chemical techniques, 2015). Ion-exchange chromatography, chelation ion chromatography, and extraction chromatography are the three variants that were used most widely as preparative techniques for sample matrix separation before isotope ratio measurement. The main reasons for a wide use of these methods are their applicability to nearly all elements

in the Periodic Table, ease of implementation when comparing to other methods, and efficiency of analyte purification.

Ion-exchange chromatography is based on a stoichiometric chemical reaction between ions in a solution and the oppositely charged functional groups on a stationary phase (Fritz, 2004). In essence, in the case of metal ions, it involves the use of eluents containing complexing acids and a column packed with an ion exchange resin.

Although related, chelation ion chromatography differs markedly from ion exchange chromatography in that it involves the formation of coordinate bonds between metal ions and complexing ligands immobilised on the surface of the ion-exchange resin (Nesterenko, Jones, 2019). Consequently, the retention of metals in chelation ion chromatography is largely controlled by stability constants of the metal complexes formed on the surface of the ion-exchanger.

Extraction chromatography is described as a technique that combines the selectivity of solvent extraction with the ease of operation of chromatographic methods (Siekierski, 1975; Horwitz et al., 2006; Pin, Rodruguez, 2014). To understand the basis of separation by this method it is worth noting that chemical and physical mechanisms used to separate the solutes include (1) ion-exchange, (2) adsorption, (3) partition, (4) affinity, and (5) size-exclusion mechanisms (Glen et al., 2012). Extraction chromatography refers to the separation where adsorption, partition or affinity driven mechanisms prevail. Well-known Sr-spec, Pb-spec, and TEVA resins, manufactured by Eichrom Technologies Inc, are the examples of element specific solid phase extraction resins based on extraction chromatography.

Guiding principles of chemical separation based on chromatography have been extensively reviewed in the literature (e.g., Harland, 1994; Fritz, 2004; Glen et al., 2012; Schönbächler, 2018; Nesterenko, Jones, 2019; Michalski, 2024). The performance of chromatographic separation of an analyte made for subsequent isotope ratio measurement can be assessed in terms of the following criteria:
- extent of reducing of total dissolved solids in sample solution after the separation,
- removal of known interfering elements,
- quantitative recovery of the analyte,
- absence of so-called "column matrix effect" caused by material stripped from the ion-exchange or solid phase extraction resin.

The importance of as efficient as possible purification of an analyte from matrix elements has been stressed by many studies (Albarede, Beard, 2004; Irrgeher, Prohaska, 2016). Although there is no commonly accepted criterion, it is recommended that concentrations of matrix elements in the purified sample solution to be at a concentration level lower than that of the analyte.

Reduction of total dissolved solids, removal of interfering elements, and recovery of analyte can be assessed by analysing aliquots of sample solutions taken before and after the separation.

To ensure that recovery of analyte is quantitative is essential. This is needed to avoid artificial isotopic fractionation on the column. On-column isotope fractionation with preferential elution of lighter or heavier isotopes is common in chromatography-based methods. In fact, this type of isotope fractionation was extensively studied and formed the basis for isotope enrichment of many elements (Kakihana, Oi, 1989; Malinovsky, Vanhaecke, 2014). Importantly, on-column isotope fractionation can only occur if recovery of analyte after the separation is not quantitative, implying that some fraction of analyte remained bound to the resin.

It should be noted that it is very difficult to quantify recovery with relative standard uncertainty at the level of 1% or better. In most cases, uncertainty of concentration measurements is higher due to the cumulative effect of many contributing factors in the measurement procedure. A question then remains whether "unaccounted" fraction of analyte can induce measurable isotope fractionation. An alternative way of checking for the absence of on-column isotope fractionation is to run standards with known isotopic composition through chromatographic columns and compare isotope ratios before and after the run. In this way, potential effect of organic material originated from the material of ion exchange resin can also be assessed (Pietruszka and Reznik, 2008).

4.2   Other methods for purification of analyte

Apart from chromatography-based methods, other methods can be used for purification of analyte in environmental samples. These include sublimation, distillation, cold vapor generation, hydride generation, precipitation/co-precipitation, and the method of diffusive gradients in thin films.

Sublimation, including its both macro- and micro-sublimation variants, was shown to be an effective method for separation of boron from sample matrix in a variety of sample types (Pi et al., 2014; Van Hoecke et al., 2014; Xiao et al., 2019; Wang et al., 2020). Micro-sublimation was employed for the separation of boron from seawater prior to isotopic analysis in MetroPOEM.

Several elements with specific combinations of physical and chemical properties, *e.g.*, Hg, Se, Sb and Te, can be separated from sample matrix by conversion of the analyte into cold vapor. Cold vapor generation is a widely used method for sample introduction in Hg isotopic analysis. It involves the conversion of soluble

Hg(II) in sample solutions into Hg(0) vapor by reduction with $SnCl_2$, followed by the introduction of gas phase containing Hg(0) into the plasma of MC-ICP-MS (Shi et al., 2023). Although selenium, antimony and tellurium do not have significant vapor pressure at room temperature, these elements can be converted into volatile hydrides, H_2Se, SbH_3, and H_2Te, respectively, by reduction using $NaBH_4$ or a similar compound. Due to high chemical selectivity of the process of reduction, cold vapor and hydride generation methods give very efficient separation of analyte from matrix elements. These methods also have an added benefit of improved sample transport efficiency.

The use of diffuse gradients in thin films is a novel method for *in-situ* purification and preconcentration of analytes from natural waters. This method has so far been demonstrated only for a few cases (Hanousek et al., 2016; Wagner et al., 2022). However, it shows good potential and offers many benefits for isotopic studies.

4.3   Automation in sample preparation

Automation has impacted most areas of sample preparation in analytical chemistry. The term analytical automation describes a process whereby an analytical instrument performs with only minimal involvement of an analyst. By definition, automated systems are designed to replace previously manual laboratory techniques and procedures with their mechanised versions.

Examples of automated systems designed for the needs of high precision isotopic analysis include the *prepFAST MC – High Precision Isotopic Analysis* and the *microFAST Isotope2 – Automated Precision Injection for Isotope Ratio Analysis*, both manufactured by Elemental Scientific. The *prepFAST MC* systems are fully automated, chromatography-based units that isolate elements of interest from the sample matrix and collect multiple discrete eluent fractions for precise isotopic analysis. They allow for sample loading, multiple acid washes, column conditioning and elution cycles. The interfacing and integration of computers into the system allow an analyst to control parameters of sampling time, volume and flow rate.

Importantly, the performance of an automated system for matrix removal needs to be verified using the same performance criteria as for a manual procedure. These criteria have been described above.

4.4   Separation procedures employed for the model elements of the project (Li, B, Cr, Ni, Cd, Sb, Pb, and U)

Lithium

Procedure at PTB.   This section describes the separation of lithium from seawater using DOWEX 50WX8-200 100-200 resin prepacked column. The procedure described can also be adapted to other sample matrices. In the present case – a seawater sample from the German North Sea coast - the lithium mass fraction (w(Li)) ranged from 140 ng/g to 170 ng/g. Therefore, the procedure described serves as an orientation.

A subsample of approximately 16 mL was transferred into a PFA-beaker. The aliquot was evaporated to dryness using a hot plate at 120 °C and stored in an oven at 80 °C overnight. After cooling to room temperature, the residuals were dissolved in roughly 16 mL deionized water. After the pretreatment, lithium was separated from the sample matrix using preconditioned DOWEX 50WX8-200 100-200 mesh resin, packed in a 30 cm-glass column (d_{in} = 0.9 cm) with $V_{resin} \approx$ 14.5 mL. The applied separation is summarized in Table 1 and is based on works by Velapoldi et al., 1978 and Rienitz, 2001. After the column separation the lithium fractions were evaporated to complete dryness (hot plate at 120 °C) and re-dissolved in 10 mL HNO_3 (w(HNO_3) = 0.01 g/g), leading to the final measurement solutions with w(Li) $\approx$ 120 ng/g. To assess a possible isotope fractionation during the column separation also three aliquots of an LSVEC solution were loaded onto the columns. In case of the three LSVEC subsamples, the same treatment was conducted, but due to the slightly higher lithium content 7.54 mL were loaded onto the column, all other volumes remained the same. These LSVEC aliquots were treated also as samples during the later measurements. The measurements against unprocessed LSVEC were repeated three times on different days, the resulting isotope ratios are shown in Figure 1. The plot shows that the developed separation procedure does not cause significant isotope fractionation.

Table 1: Elution scheme for lithium separation using DOWEX 50WX8-200 100-200 resin.

fraction	eluent	V/mL	
1	sample in H_2O	7.72	loading sample
2	H_2O	3×20	rinsing
3	0.4 mol/L HCl	70	waste
4	0.5 mol/L HCl	40	lithium fraction

5	5 mol/L HCl	100	Eluting and removing all other elements (reconditioning)
6	H$_2$O	100	adjusting pH ≈ 7
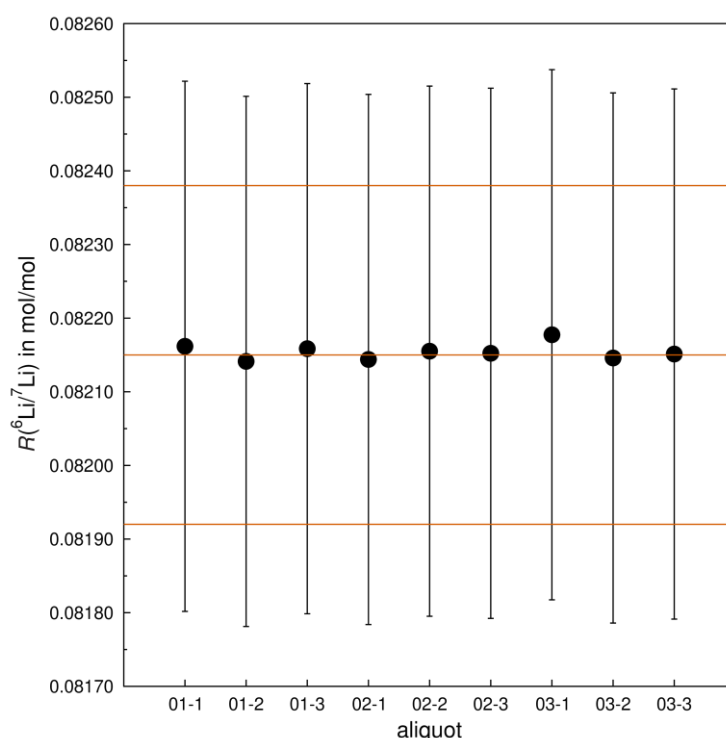
Figure 1: Absolute isotope ratio (R(^{6}Li/^{7}Li)) of the three LSVEC aliquots after being processed in the described way. Error bars indicate expanded uncertainties (k = 2). The light brown line represents the certified value with its uncertainty range.

Procedure at BAM. The chromatographic separation of lithium was performed using a two-step cation exchange column procedure (Rosner et al. 2007; Misra et al. 2009). Columns were packed with Bio-Rad AG50W-X12 (200-400mm mesh; 2.1meq/mL capacity). The initial separation step employs polypropylene columns (6.4mm internal diameter) packed with 3mL resin. The columns were pre-cleaned with 6M HCl and conditioned with 0.2M HCl prior to sample loading. Elution was carried out using 0.2M HCl, following the protocol outlined in Table 2, with the Li fraction collected in pre cleaned Teflon beakers. Fractions were evaporated to dryness at 100°C.

The dried residue was redissolved in 0.15M HCl and loaded onto a second, smaller Teflon column containing 0.5mL of the same resin. The protocol for the second column is outlined in Table 3. Separated Li were evaporated to dryness, followed by re-dissolution with a mixture of concentrated HNO$_3$ and hydrogen peroxide(H$_2$O$_2$) to remove trace amounts of organic residues, dried down again and redissolved in 2% HNO$_3$ to match the concentration of bracketing standards for MC-ICP-MS analysis.

Pre- and post-Li fractions from both column steps were screened by HR-ICP-MS (Element 2, Thermo Fischer Scientific) to verify quantitative recovery and the absence of Na.

Table 2. Elution protocol for the first lithium separation

Procedure	Eluent	Volume (mL)
Cleaning	6M HCl	18
Backwash	H$_2$O	
Cleaning	6M HCl	18
Conditioning	0.2M HCl	18
Sample loading	0.2M HCl	0.5

Fixing	0.2M HCl	1
Pre elution	0.2M HCl	21
Pre Li fraction	0.2M HCl	1
Li elution	0.2M HCl	26
Post Li fraction	0.2M HCl	1

Table 3. Elution protocol for lithium separation with second column

Procedure	Eluent	Volume (mL)
Cleaning	6N HCl	3
Conditioning	0.15M HCl	3
Sample loading	0.15M HCl	0.1
Fixing	0.15M HCl	0.3
Pre elution	0.15M HCl	3.3
Pre Li fraction	0.15M HCl	0.5
Li elution	0.15M HCl	7.5
Post Li fraction	0.15M HCl	0.5

Boron

Boron was separated from the seawater matrix using a micro-sublimation technique (Van Hoecke et al., 2014; Xiao et al., 2019). Aliquots of 30 µL sample solution were placed on the inner surface of the lid of a 5 mL Savillex® Teflon vial (conical interior, finned legs). The sample droplet was acidified with HNO_3 to pH ≤ 2. The vial is then tightly closed in an inverted position and wrapped with aluminium foil such that sides of the vial remained warm while the exposed base part acted as a condensation surface. Samples were heated at 95°C for 25h. During this procedure, boric acid volatilizes from the sample droplet and recondenses on the cooler upper surface of the vial. After cooling of the sample vial, the lid contains the residual matrix is replaced with a fresh, clean lid, thereby isolating the purified boric acid condensate. The condensate was diluted in 2% HNO_3 prior to boron isotope analysis by MC-ICP-MS.

Chromium

To separate Cr (total) from the seawater matrix, a coprecipitation procedure with $Mg(OH)_2$ and assisted by the addition of triethylamine adapted from Arslan et al. (2018) was tested. This procedure was then followed by a two-step Cr isolation method using AG1-X8 and AG50W-X8 (BioRad) resins as described in Yamakawa et al. (2009).

Nickel

To separate Ni from concomitant elements in seawater samples, a procedure modified from previous studies (Arı, Bakırdere, 2020; Beunon et al., 2020; Yang et al., 2024) was used. First stage of the procedure involved pre-concentration of the element by co-precipitation with $Mg(OH)_2$. The precipitate formed was then dissolved in 7 M HCl and run through strongly anion-exchange chromatographic column with AG®1-X8 BioRad resin, to separate chloro-anionic elements (Cu, Fe, Mn, Cd, Cr, Mo). Separation of Ni from Mg and other cationic elements in solution was achieved by chromatographic separation using Chelex-100 resin, following the guidelines described by Yang et al. (2024).

Cadmium

Most frequently, two different chemical purification protocols have been in use: (1) purification of Cd using the AG®1-X8 resin and (2) purification of Cd using AG®-MP-1M BioRad resin. In the present project, Cd was pre-concentrated from the seawater matrix by applying a procedure similar to that used for Ni. Namely, Cd was preconcentrated by triethylamine-assisted (TEA) $Mg(OH)_2$ coprecipitation by the procedure adopted from

Arslan et al. (2018). The precipitate was then dissolved in 2M HCl and Cd was isolated from the interfering elements on the AG®-MP-1M (BioRad) resin following the procedure described in Pallavicini et al. (2014).

Antimony

A combination of cation exchange chromatography and anion exchange chromatography can be used for chemical purification of Sb prior to isotope ratio measurements, following the procedure described by Lobo et al. (2012). The procedure involves two stages of separation. In the first stage, a sample solution in 0.14 M HF is loaded onto a chromatographic column filled with Dowex AG50-X8 cation-exchange resin to separate Sb from alkaline and alkaline earth elements, together with Mn, Fe, Cu and Pb. In the second stage, elements that tend to be in the anioinic form in aqueous solution, are separated from Sb by running the samples through Amberlite IRA 743 anion-exchange resin.

Lead

Procedure at MUL. The manual analyte/matrix separation protocol for extracting Pb from the sample solutions was adapted from a previously published method for the simultaneous separation of Sr and Pb (Reese et al., 2019). Columns were packed with 0.5 mL of the resin SR-B-100-A (mesh size: 100 μm – 150 μm) (Triskem International, Bruz, France). After a resin cleaning procedure, 4 mL of sample solution was loaded on the column, the matrix was eluted by 8 mol L^{-1} HNO_3 and finally Pb was eluted with 4 mL of MilliQ water and 4 mL of 8 mol L^{-1} HCl. The collected Pb eluates were evaporated to dryness at 85 °C and re-dissolved in 2 mL HNO_3 (w = 2 %).

The automated analyte/matrix separation protocol for extracting Pb form the sample solutions was performed using the seaFAST-Litre system available at ESI Omaha, USA. Aliquots of samples were sent to Omaha and followed a purification and preconcentration step by a factor of 10. Eluates were screened for recoveries and impurities at MUL and considered pure for further isotope ratio analysis by MC-ICP-MS.

Procedure at Hereon. Replicates of 20 mL each were dried on a heating block and subsequently dissolved in 8 M HNO_3. Matrix separation was done by manual column separation using Sr Resin (TrisKem International) in 2% HNO_3 and a separation protocol utilizing 6 M HNO_3, Type I reagent grade water and 8 M HCl as cleaning steps prior to sample loading. The column is conditioned in 8 M HNO3, before the sample is loaded. Matrix is removed by several rinsing steps using 8 M HNO_3 and Type I reagent grade water. Pb fractions are eluted using 8 M HCl. Pb fractions are dried on a heating Block and subsequently dissolved in 2% HNO_3 for measurement by MC-ICP-MS.

Uranium

This section describes the separation of uranium from seawater using Triskem UTEVA resin prepacked columns. The procedure described can be adapted to other types of samples. In the present case – a seawater sample from the German North Sea coast - the uranium mass fraction (w(U)) was approximately 3 ng/g.

Initially, a subsample of approximately 60 g was transferred into 300 mL PFA vessels. The subsample was evaporated to dryness at approximately 120 °C using a hot plate. The residues were re-dissolved in 35 mL HNO_3 (w(HNO_3) = 0.65 g/g) and 15 mL H_2O, evaporated to dryness again, and re-dissolved in 15 mL HNO_3 (c(HNO_3) = 3 mol/L). Afterwards the uranium was separated from the matrix using preconditioned Triskem UTEVA resin columns (UT-C50-A, Lot # FUTA240212, 2 mL pre-packed). The separation was carried out according to the modified Eichrom "Analytical Procedure Method No. ACS07" (Eichrom Technologies, 2015), with details shown in Table 4 below.

Table 4. Elution scheme used for uranium separation on Triskem UTEVA resin (2 mL pre-packed columns, Lot # FUTA240212).

Fraction	Eluent	V/mL	
1	0.05 mol/L HCl	15	removal of uranium impurities
2	3 mol/L HNO_3	5	preconditioning
3	sample in HNO_3	15	loading of sample
4	3 mol/L HNO_3	16	removal of matrix
5	7.5 mol/L HCl	3	conditioning
6	0.05 mol/L oxalic acid & 5 mol/L HCl	5	removal of Th
7	7.5 mol/L HCl	5	waste

| 8 | 0.05 mol/L HCl | 11 | uranium fraction |

The uranium fraction was collected in 15 mL PFA vessels, evaporated to dryness (hot plate at 120 °C) and the residue was re-dissolved in 1 mL HNO_3 (0.65 g/g) and 1 mL H_2O_2 (0.30 g/g).The sample was evaporated to dryness again on a hot plate at 80 °C (the temperature was increased from 50 °C to 80 °C in 10 °C steps over 3 h) . Finally, the residual was re-dissolved in 3.5 mL 0.025 g/g HNO_3 to prepare the measurement solutions with $w(U) \approx 50$ ng/g.

To validate that the separation procedure does not induce uranium isotope fractionation, it was applied to four aliquots (each ~1.5 g) of a stock solution of IRMM-184 (Rienitz, 2001). This solution had a uranium mass fraction of roughly 50 ng/g. After separation, the isotope ratios ($R(^{234}U/^{238}U)$ and $R(^{235}U/^{238}U)$) of the four aliquots were determined using MC-ICP-MS and IRMM-184 as certified reference material in a sample-reference bracketing scheme. Please note that reference IRMM-184 was an unprocessed aliquot of the before mentioned stock solution. Details of the MC-ICP-MS measurements are given in the next section. **Fehler! Verweisquelle konnte nicht gefunden werden.**2 and **Fehler! Verweisquelle konnte nicht gefunden werden.** show the determined isotope ratios $R(^{234}U/^{238}U)$ and $R(^{235}U/^{238}U)$, respectively. In addition to the single results for each aliquot, the certified value for IRMM-184 is shown as horizontal red dashed line together with its error range of plus/minus the expanded uncertainty ($k = 2$). Since in all cases the isotope ratios of the four aliquots agree with each other and the certified value, it can be concluded that the presented procedure does not cause measurable isotope fractionation.
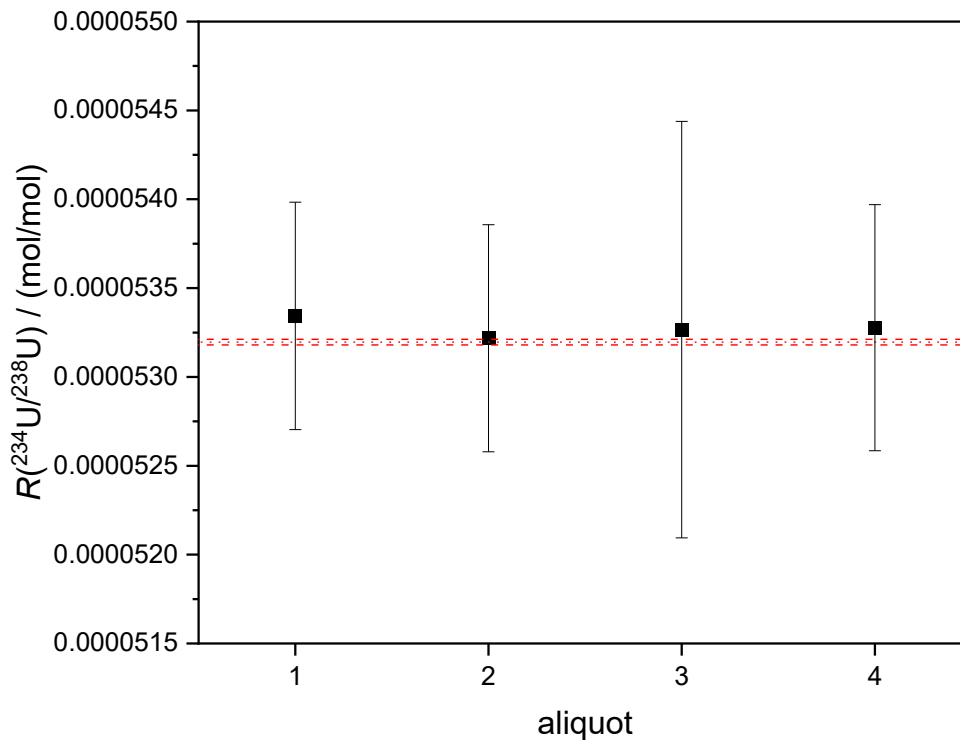
Figure 2 Absolute isotope ratio $R(^{234}U/^{238}U)$ of the four aliquots of IRMM-184 after being processed in the described way. Error bars indicate expanded uncertainties ($k = 2$). The red dashed line represents the certified value with its uncertainty range.
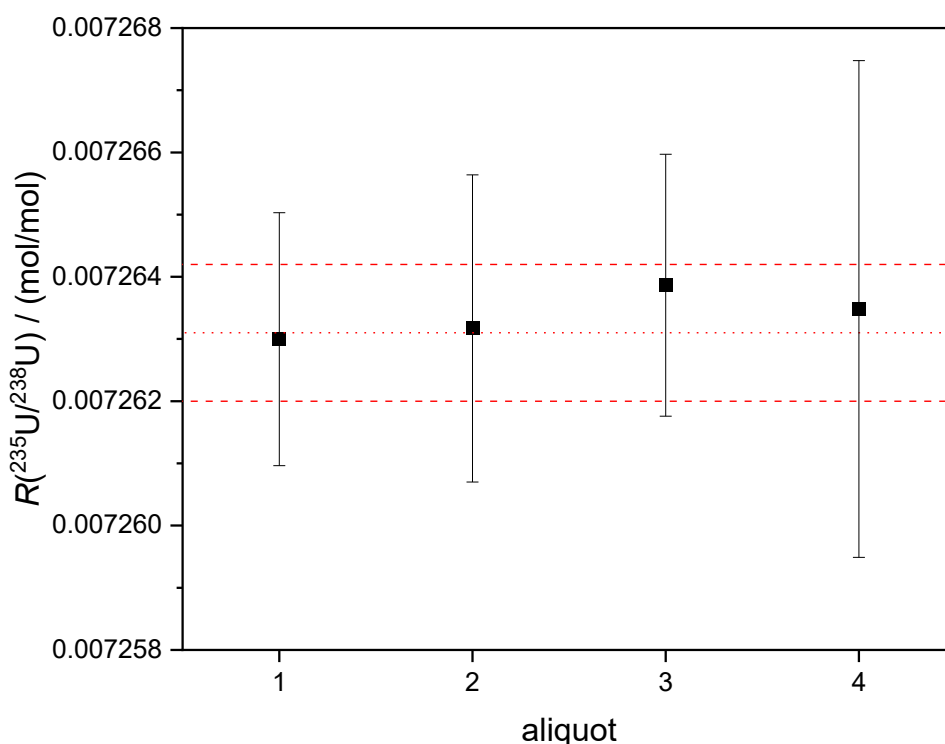
Figure 3: Absolute isotope ratio R(^{235}U/^{238}U) of the four aliquots of IRMM-184 after being processed in the described way. Error bars indicate expanded uncertainties (k = 2). The red dashed line represents the certified value with its uncertainty range

5   Correction for instrumental isotope fractionation

Isotope ratios as measured by mass spectrometry are biased from their true values. In the literature, this bias is termed interchangeably as instrumental mass bias, instrumental mass discrimination, and instrumental isotope fractionation. The phenomenon was investigated by many research groups over decades (e.g., Nier, 1950; McKinney et al., 1950; Russell et al., 1978; Hart, Zindler, 1989; Albarède, Beard, 2004; Baxter et al., 2012; Meija et al., 2012; Yang et al., 2018). The following methods can be used to correct for it.

5.1   Calibration by using synthetic isotope mixtures

Originally proposed by Alfred O. Nier in 1950, this method has become the gold standard for performing the higher order isotopic characterisation of materials. At the core of this method are synthetic mixtures of highly enriched isotopes, prepared under full gravimetric control and used for calibration of measured isotope ratios. Detailed description of the measurement principle and selected applications can be found elsewhere (Qi et al, 1998; Ponzevera et al., 2006; De Bievre et al., 2012; Meija, 2012; Yang et al., 2018, Stoll-Werian et al., 2019; Dunn et al, 2024). Although being laborious and with costly materials involved, the method offers two important advantages. First, it does not need to rely on any previously characterised isotope standard. Second, the method produces results that are directly traceable to the SI units.

Measurement by this method involves weighing operations to prepare calibration mixtures from isotopically enriched parent materials, isotope ratio measurements of samples, calibration mixtures and parent materials, and chemical characterisation of impurities in parent isotopically enriched materials. Provided that up-to-date instrumentation is used, the calibration by using synthetic isotope mixtures has the potential to determine isotope amount ratios in samples with lowest uncertainties.

Accounting for chemical impurities in parent isotopically enriched materials is essential. Mass fraction of chemical impurities is subtracted from masses of parent materials, taken to prepare isotope mixtures, to know accurate masses of enriched isotopes used in mixing. A challenge here arises from the need to quantify non-metals, including oxygen, nitrogen, and hydrogen. A recent development in the field is the development of the variant of the method that determines mixing proportions of enriched isotopes with the aid of ion chromatography, rendering the determination of impurities in the parent materials superfluous (Flierl et al., 2024).

5.2 Double and triple spike methods

Double and triple spike methods are also based on the use of enriched isotopes. What makes them different to the method of synthetic isotope mixtures is that enriched isotopes are added directly to the samples to be measured. Conventionally, the methods are applicable to elements having at least four stable or long-lived radiogenic isotopes (Rudge et al., 2009). However, a modification of the approach applicable to elements with three isotopes was reported (Chew, Walczyk, 2013; Coath et al., 2017). The double spike technique involves measuring isotope ratios of four isotopes, the abundances of two of which have been altered by the addition of enriched isotopic spikes. The triple spike technique involves measuring isotope ratios of four isotopes, the abundances of three of which have been altered by the addition of enriched isotopic spikes (Galer, 1999).

Measurements by these methods include weighing operations to add appropriate amounts of enriched spikes, isotope ratio measurements of unspiked sample, spiked sample, enriched isotopic materials, and an isotope standard with known isotopic composition. The latter is needed to calibrate isotope ratios of enriched isotopic materials. An estimate of the chemical purity of the spike materials is also required.

Data reduction algorithm allows to invert measured data to obtain isotope ratios of the sample corrected for instrumental isotope fractionation. The double spike inversion formulas were derived in early works and revised later (Compston, Oversby, 1969; Dobson, 1970; Rudge et al., 2009). It is noteworthy that the conventional double spike inversion assumes mass-dependent isotope fractionation. As a consequence, this approach is not a suitable analytical method for isotopic analysis of samples in which mass-independent isotope fractionation can occur (Bigeleisen, 1996; Malinovsky, Vanhaecke, 2011; Buchachenko, 2013). To address the issue, an analytical equation to calculate a correction that needs to be applied in the presence of isotopic anomalies in samples was suggested (Hu, Dauphas, 2017).

A known advantage of the double spike method is that the requirement to quantitative recovery of an analyte can be relaxed. Once the isotopically enriched spike equilibrates with the sample prior to chemical separation, quantitative yield after the procedure is not necessary. Selected applications of the method are described elsewhere (Johnson, Beard, 1999; Siebert et al., 2001; Mead, Johnson, 2010; Gall et al., 2012; Creech et al., 2013; Liu et al., 2020).

5.3 Sample-standard bracketing (external standardisation)

The sample-standard bracketing method assumes that variations in instrumental isotope fractionation between an unknown sample and two isotope standards, one preceding and one following the sample, are small relative to the standard deviation of the measurement. This assumption is valid in the techniques operating at steady state, such as ICP-MS. Data reduction after measurement involves interpolating the magnitude of instrumental isotope fractionation of an unknown sample from the observed instrumental fractionation of bracketing standards. With the above assumption, the relationships between them can be described as follows:

$$K \approx \frac{R_{std}}{r_{std,1}} \approx \frac{R_{smp}}{r_{smp}} \approx \frac{R_{std}}{r_{std,2}} \qquad (1)$$

where K is the calibration factor, relating true and measured values of an isotope ratio, R_{smp} and R_{std} are true isotope ratios of sample and isotope standard, respectively; $r_{std,1}$ and $r_{std,2}$ are measured isotope ratios of the preceding standard and the following standard. Re-arranging Eq (1) gives

$$R_{smp} = r_{smp} \times \frac{R_{std}}{2} \times \left(\frac{1}{r_{std,1}} + \frac{1}{r_{std,2}} \right) \qquad (2)$$

Sample-standard bracketing also forms the basis for the determination of relative isotope ratios. In a situation when samples and isotope standards are matrix-matched, delta value of an unknown sample relative to a chosen isotope standard can be calculated using measured isotope ratios:

$$\delta_{std}{}^{i/j}E = \frac{r_{smp}}{r_{std}} - 1 \qquad (3)$$

where delta value δ expresses the abundance of isotope i of element E in a sample relative to the abundance of the same isotope in isotope standard; $r_{sample} = I_{smp}(^iE)/I_{smp}(^jE)$ and $r_{std} = I_{std}(^iE)/I_{std}(^jE)$ are measured ratios of the isotopes in sample and isotope standard.

The use of an internal standard can facilitate correction for small differences in matrix composition between samples and standards. This is achieved by normalisation of measured isotope ratios of an analyte to those of an internal standard. Another element from the same or adjacent mass region with interference-free isotopes can act as an internal standard. In this approach, measured isotope ratios of samples and standards are first corrected for instrumental isotope fractionation by using one of the empirical approaches, described in the section 5.4, and then used for the calculation of delta values:

$$\delta_{std}{}^{i/j}E = \frac{R'_{smp}}{R'_{std}} - 1 \qquad (4)$$

where $R'_{smp} = \left(I_{smp}(^{i}E)/I_{smp}(^{j}E)\right)_{corr}$ and $R'_{std} = \left(I_{std}(^{i}E)/I_{std}(^{j}E)\right)_{corr}$ are isotope ratios of sample and isotope standard corrected for instrumental isotope fractionation by using one of the empirical approaches detailed below.

5.4 Internal standardisation

In analytical chemistry, an internal standard is a known amount of a substance, different from the analyte of interest, that is added to all samples, blanks and calibration standards to correct for fluctuations in instrument response during analysis and as an aid for calibration (Skoog et al., 2018; Burns, Walker, 2019). In isotope ratio measurements, the purpose of using an internal standard is twofold. First, it helps correcting for drift and signal instability due to noise from the ion source and electronic lenses, and due to matrix effects. Second, the internal standard can be used as a calibrant of the measurement.

A number of models for the relationship between measured isotope ratios of two different elements were developed. The genesis and performance characteristics of these models are described in detail elsewhere (Longerich et al., 1987; Maréchal, et al., 1999; Ingle et al., 2003; Young et al., 2010; Baxter et al., 2012; Meija et al., 2012; Malinovsky et al., 2016; Tong et al., 2019).

When high precision isotopic analysis is concerned, the most used are the models based on exponential and power laws. Although it was noted that these models can be viewed as two variants of the generalised power law (Maréchal et al., 1999), practical calculations using them yield slightly different results. The calculations involved in these models are summarised in Table 5 on the example of Ni and Cu isotopes.

Table 5. Models commonly used to correct for instrumental isotope fractionation.

Name	Functional form	Parameters of the models explained
Exponential model	$R_{^{62}Ni/^{60}Ni} = \left(\dfrac{A_r(^{62}Ni)}{A_r(^{60}Ni)}\right)^{f} \cdot r_{^{62}Ni/^{60}Ni}$	Ni is the analyte. Cu is the admixed internal standard. $R_{^{62}Ni/^{60}Ni}$ is the true Ni isotope ratio. $r_{^{62}Ni/^{60}Ni}$ is the measured Ni isotope ratio. $R_{^{65}Cu/^{63}Cu}$ is the certified Cu isotope ratio. $r_{^{65}Cu/^{63}Cu}$ is the measured Cu isotope ratio. $A_r(^{62}Ni)$ and $A_r(^{60}Ni)$ are the relative atomic masses of Ni isotopes; $A_r(^{65}Cu)$ and $A_r(^{63}Cu)$ are the relative atomic masses of Cu isotopes. f is the exponential model mass fractionation coefficient calculated as
Power model	$R_{^{62}Ni/^{60}Ni} = r_{^{62}Ni/^{60}Ni} \cdot g^{\left(A_r(^{62}Ni) - A_r(^{60}Ni)\right)}$	$f = \dfrac{\ln\left(\dfrac{R_{^{65}Cu/^{63}Cu}}{r_{^{65}Cu/^{63}Cu}}\right)}{\ln\left(A_r(^{65}Cu)/A_r(^{63}Cu)\right)};$ g is the power model mass fractionation coefficient calculated as $g = \left(\dfrac{R_{^{65}Cu/^{63}Cu}}{r_{^{65}Cu/^{63}Cu}}\right)^{\left(\frac{1}{A_r(^{65}Cu) - A_r(^{63}Cu)}\right)}$

The exponential and power models can be effective in correcting for signal instability and temporal drift in instrumental mass bias over a measurement session. Normalisation procedures based on these models are also valuable for minimising matrix effects between samples and standards in the determination of delta values. However, in absolute isotope ratio measurements, the assumptions on the functional form of the relationship between measured isotope ratios do not guarantee accuracy of results.

A model that is free from any assumptions, and thus offering significant benefit in higher order measurements, is the so-called regression model. It is based on correlated temporal drift between simultaneously measured isotope ratios of an analyte and an internal standard. Isotope amount ratios of an

analyte, corrected for instrumental isotope fractionation, can be calculated by the following formula, written with isotopes of Ni and Cu as examples.

$$R_{62_{Ni}/60_{Ni}} = e^a \cdot R_{65_{Cu}/63_{Cu}}^b \qquad (5)$$

where $R_{62_{Ni}/60_{Ni}}$ is $n(^{62}Ni)/n(^{60}Ni)$, the mass bias corrected isotope ratio of the analyte; $R_{65_{Cu}/63_{Cu}}$ is the known $n(^{65}Cu)/n(^{63}Cu)$ isotope ratio of the internal standard; b and a are the slope and intercept of a linear regression through data points of measured $I(^{62}Ni)/I(^{60}Ni)$ isotope ratios and measured $I(^{65}Cu)/I(^{63}Cu)$ isotope ratios in ln-ln space, $\ln(I(^{62}Ni)/I(^{60}Ni))$ versus $\ln(I(^{65}Cu)/I(^{63}Cu))$.

To obtain accurate and precise results by the regression model, it is necessary to find measurement conditions that will allow establishing a high level of correlation between variations in measured isotope ratios of the analyte and internal standard. This can be achieved either through running measurement over long time or in a series of short-term measurements with incremental changes of one of major instrumental parameters, such as RF power in ICP-MS (Malinovsky et al., 2016).

It should also be noted that an interesting calibration approach was reported recently by Vogl (2021). This approach does not fit into any of the above four categories of calibration methods. However, it is based on the theory of mass-dependent isotope fractionation, commonly employed in the internal standardisation. This approach makes use of the difference in the instrumental isotope fractionation of two different types of mass spectrometers during measurement of the same sample. Using the measurement data, two different fractionation lines can be constructed in a three-isotope diagram. The point of interception of these lines should correspond to true isotope ratio of the sample.

6   Reporting isotope ratio data

Results of isotope ratio measurements can be reported in two ways: as relative isotope ratios or as absolute isotope ratios, also known as isotope amount ratios, isotope abundance ratios, and isotope number ratios. General guidelines for reporting isotope ratio data were published and help clarify relevant terminology and recommended requirements for publishing isotope delta results (De Laeter et al., 2003; Coplen, 2011; Brand et al., 2014; Prohaska et al., 2022; Skrzypek et al., 2022). Useful guiding documents are also listed on the website of the IUPAC Commission on Isotopic Abundances and Atomic Weights (CIAAW, 2025).

Relative isotope ratios are expressed as isotope delta values. The isotope delta (symbol δ), of an element E in a material P is defined by the isotope number ratios of an element E in substance P and in an international standard (Std) (Brand et al. 2014; Skrzypek et al. 2022):

$$\delta_{Std}\left(^{i/j}E, P\right) = \frac{R\left(^{i/j}E,P\right)}{R\left(^{i/j}E,Std\right)} - 1 \qquad (6)$$

Isotope delta values are small numbers and therefore are commonly expressed in the per mil notation (‰), by multiplying by 1000.

The isotope number ratio in a substance P is defined as (Prohaska et al., 2022):

$$R\left(^{i/j}E, P\right) = N\left(^{i}E,P\right)/N\left(^{j}E,P\right) \qquad (7)$$

where $N(^iE,P)$ and $N(^jE,P)$ are the numbers of atoms of each isotope making the isotope ratio of the chemical element E in substance P. It is recommended that ^iE denotes the higher and ^jE the lower atomic mass number of the isotopes involved.

Reporting isotope ratios as isotope amount ratios is needed to ensure traceability of measurement results to the SI units. The knowledge of absolute isotope ratios is also essential in the determination of atomic weights of elements, accurate mass balance calculations and in many other applications.

7   Measurement uncertainty budgets

The uncertainty budget is a statement of a measurement uncertainty, of the components of that measurement uncertainty, and of their calculation and combination (JCGM 200:2012). It comprises all known sources of uncertainty in the analysis. It is recommended that uncertainties be estimated according to the ISO *Guide to the Expression of Uncertainty in Measurement*, commonly known as the GUM (JCGM 100:2008).

Individual components of uncertainty and their contributions to total uncertainties will be different for different measurement methods and calibration approaches described above. In identifying individual uncertainty components, it is advisable to follow the practice when all uncertainty terms are associated with a physical cause (Saunders et al., 2008). This ensures that each of the identified sources of uncertainty can have a mathematical model allowing quantitative estimation and propagation of uncertainty.

Uncertainty budgets and uncertainty propagation for measurements with the calibration approach based on synthetic isotope mixtures were described in detail in works by Qi et al. (1998); Wolff-Briche et al. (2000), Mana et al., 2010; Vogl et al. (2016), Dunn et al. (2024), and Flierl et al. (2024). Uncertainty propagation in the

double spike method was discussed in works by Powell et al. (1998) and Rudge et al. (2009). Discussion on uncertainty budgets and uncertainty propagation for measurements using the internal standardisation was given by Meija et al. (2010), Malinovskiy et al. (2016), and Tong et al. (2019).

8 References

Albarède, F., Beard, B.L. (2004). Analytical methods for non-traditional isotopes. In: Johnson, C.M., Beard, B.L., Albarede, F. (Eds.) *Reviews in Mineralogy and Geochemistry: Geochemistry of Non-Traditional Stable Isotopes*, 55, 113-152. https://doi.org/10.2138/gsrmg.55.1.113.

Arı, B., Bakırdere. S. (2020). A primary reference method for the characterization of Cd, Cr, Cu, Ni, Pb and Zn in a candidate certified reference seawater material: TEA/Mg(OH)$_2$ assisted IDMS by triple quadrupole ICP-MS/MS. *Anal. Chim. Acta* 1140, 178-189. https://doi.org/10.1016/j.aca.2020.10.004.

Arslan, Z., Oymak, T., White, J. (2018). Triethylamine-assisted Mg(OH)$_2$ coprecipitation/preconcentration for determination of trace metals and rare earth elements in seawater by inductively coupled plasma mass spectrometry (ICP-MS). *Anal. Chim. Acta*, 1008, 18–28. https://doi.org/10.1016/j.aca.2018.01.017

Balcaen, L., Bolea-Fernandez, E., Resano, M., Vanhaecke, F. (2015). Inductively coupled plasma – Tandem mass spectrometry (ICP-MS/MS): A powerful and universal tool for the interference-free determination of (ultra)trace elements – A tutorial review. *Anal. Chim. Acta*, 894, 7-19. https://doi.org/10.1016/j.aca.2015.08.053.

Baxter, D. C., Rodushkin, I., Engström, E. (2012). Isotope abundance ratio measurements by inductively coupled plasma-sector field mass spectrometry. *J. Anal. At. Spectrom*. 27, 1355-1381. https://doi.org/10.1039/C2JA30153A.

Beunon, H., Chernonozhkin, S.M., Mattielli, N., Goderis, S., Doucet, L.S., Vinciane Debaille, V., Vanhaecke, F. (2020). Innovative two-step isolation of Ni prior to stable isotope ratio measurements by MC-ICP-MS: application to igneous geological reference materials. *J. Anal. At. Spectrom*. 35, 2213-2223. https://doi.org/10.1039/D0JA00163E.

Bigeleisen, J. (1996). Nuclear size and shape effects in chemical reactions. Isotope chemistry of the heavy elements. *J. Am. Chem. Soc*. 118, 3676-3680. https://doi.org/10.1021/ja954076k

Brand, W.A., Coplen, T.B., Vogl, J., Rosner, M., Prohaska T. (2014). Assessment of international reference materials for isotope-ratio analysis (IUPAC Technical Report). *Pure Appl. Chem*. 86, 425-467; https://doi.org/10.1515/pac-2013-1023

Buchachenko, A.L. (2013). Mass-Independent Isotope Effects. *J. Phys. Chem*. B 117, 2231−2238. https://doi.org/10.1021/jp308727w.

Bürger, S., Vogl, J., Kloetzli,U., Nunes, L., and Lavelle, M. (2015). Thermal Ionisation Mass Spectrometry. In T. Prohaska, J. Irrgeher, A. Zitek, N. Jakubowski (Eds.), *Sector Field Mass Spectrometry for Elemental and Isotopic Analysis* (pp. 381-428), The Royal Society of Chemistry.

Burns, D.T., Walker, M.J. (2019). Origins of the method of standard additions and of the use of an internal standard in quantitative instrumental chemical analyses. *Anal. Bioanal. Chem*. 411, 2749–2753. https://doi.org/10.1007/s00216-019-01754-w.

Chew, G., Walczyk, T. (2013). Measurement of Isotope Abundance Variations in Nature by Gravimetric Spiking Isotope Dilution Analysis (GS-IDA). *Anal. Chem*. 85, 3667-3673. https://doi.org/10.1021/ac3034807

CIAAW. (2025). Retrieved from https://www.ciaaw.org/publications.htm#P5

Coath, C.D., Elliott, T., Hin, R.C. (2017). Double-spike inversion for three-isotope systems. *Chem. Geol*. 451, 78-89. http://dx.doi.org/10.1016/j.chemgeo.2016.12.025

Compston,W., Oversby, V.M. (1969). Lead isotopic analysis using a double spike. *J. Geophys. Res*. 74, 4338–4348. https://doi.org/10.1029/JB074i017p04338.

Coplen, T. (2011). Guidelines and recommended terms for expression of stable isotope-ratio and gas-ratio measurement results. *Rapid Commun. Mass Spectrom*. 25, 2538–2560. https://doi.org/10.1002/rcm.5129.

Cosmochim. Acta 34, 1241–1244. https://doi.org/10.1016/0016-7037(70)90060-8.

Creech, J., Baker, J., Handler, M., Schiller, M., and Bizzarro, M. (2013). Platinum stable isotope ratio measurements by double-spike multiple collector ICPMS. *J. Anal. At. Spectrom*. 28, 853-865. https://doi.org/10.1039/C3JA50022E

De Laeter, J.R., John Karl Böhlke, J.K., P. De Bièvre, P., Hidaka, H., Peiser, H.S., Rosman, K. J. R., Taylor, P. D. P. (2003). Atomic weights of the elements. Review 2000 (IUPAC Technical Report). *Pure Appl. Chem*. 75, 683-800. https://doi.org/10.1351/pac200375060683.

Dodson, M.H. (1970). Simplified equations for double-spiked isotopic analyses. *Geochim. Cosmochim. Acta* 34, 1241-1244. https://doi.org/10.1016/0016-7037(70)90060-8

Dunn, P.J.H., Malinovsky, D., Ogrinc, N., Potočnik, D., Flierl, L., Rienitz, O., Paul, D., Meijer, H.A.J. (2024). Re-determination of R(13C/12C) for Vienna Peedee belemnite (VPDB). Rapid Commun. Mass Spectrom. 38, e9773. https://doi.org/10.1002/rcm.9773.

Eichrom Technologies, LLC 2014. Analytical Procedure "Uranium in Soil", Method No. ACS07. https://www.eichrom.com/wp-content/uploads/2018/02/acs07-16_uranium-in-soil.pdf

Flierl, L., Rienitz, O., Vogl, J., Pramann, A. (2024). An advancement of the gravimetric isotope mixture method rendering the knowledge of the spike purity superfluous *Anal. Bioanal. Chem.* 416, 5325–5333. https://doi.org/10.1007/s00216-024-05465-9.

Fritz, J.S. (2004). Early milestones in the development of ion-exchange chromatography: a personal account. *J. Chromatogr. A* 1039, 3-12. https://doi.org/10.1016/j.chroma.2003.12.068

Galer, S.J.G. (1999). Optimal double and triple spiking for high precision lead isotopic measurement. *Chem. Geol.* 157, 255-274. https://doi.org/10.1016/S0009-2541(98)00203-4

Gall, L., Williams, H., Siebert, C., and Alex Halliday, A. (2012). Determination of mass-dependent variations in nickel isotope compositions using double spiking and MC-ICPMS. *J. Anal. At. Spectrom.* 27, 137-145. https://doi.org/10.1039/C1JA10209E

Glen, L., Hortin, M.D., Goldberger, B.A. (2012). Chromatography and extraction. In: Burtis, C.A., Ashwood, E.R., Bruns, D.E. (Eds.) *Tietz textbook of clinical chemistry and molecular diagnostics, 5th edition. Geochemistry* (pp. 307-328), Elsevier Saunders.

Hanousek, O., Santner, J., Mason, S., Berger, T. W., Wenzel, W. W., Prohaska, T. (2016). Diffusive gradients in thin films measurement of sulfur stable isotope variations in labile soil sulfate. *Anal. Bioanal. Chem.* 408, 8333-8341. https://doi.org/10.1007/s00216-016-9801-8

Harland, C.E. (1994). *Ion Exchange: Theory and Practice*. The Royal Society of Chemistry. London

Hart, S.R., Zindler, A. (1989). Isotope fractionation laws: a test using calcium. Int. J. Mass Spectrom. Ion Processes. 89 (2-3), 287-301. https://doi.org/10.1016/0168-1176(89)83065-4.

Horwitz, E. P.; McAlister, D. R.; Dietz, M. L. (2006). Extraction chromatography versus solvent extraction: How similar are they? *Separ. Sci Technol*. 41 (10), 2163-2182. https://doi.org/10.1080/01496390600742849

Hu, J.Y., Dauphas, N. (2017). Double-spike data reduction in the presence of isotopic anomalies. *J. Anal. At. Spectrom.* 32, 2024-2033. https://doi.org/10.1039/C7JA00187H.

Introduction to Ion Exchange Chromatography. (2025). Retrieved from https://www.bio-rad.com/en-uk/applications-technologies/introduction-ion-exchange-chromatography?ID=LUSN6ZE8Z#:~:text=Ion%20exchange%20chromatography%20is%20a,Bio%2DRad%20for%20these%20techniques.

Irrgeher, J., Prohaska, T. (2016). Application of non-traditional stable isotopes in analytical ecogeochemistry assessed by MC ICP-MS - A critical review. *Anal. Bioanal. Chem.* 408, 369–385. https://doi.org/10.1007/s00216-015-9025-3.

JCGM 100:2008(E). (2008). Evaluation of measurement data - Guide to the expression of uncertainty in measurements (GUM:1995). International Organisation for Standardization, Geneva. https://doi.org/10.59161/JCGM100-2008E

JCGM 200:2012. (2012). International vocabulary of metrology, 3rd edition. https://doi.org/10.59161/JCGM200-2012.

Johnson, C.M., Beard, B.L. (1999). Correction of instrumentally produced mass fractionation during isotopic analysis of Fe by thermal ionization mass spectrometry. *Int. J. Mass Spectrom.* 193, 87–99. https://doi.org/10.1016/S1387-3806(99)00158-X.

Kakihana, K., Oi, T. (1989). Theory of isotope separation by displacement chromatography. J*. Chromatogr. A* 483, 179-188. https://doi.org/10.1016/S0021-9673(01)93120-6.

Karasiński, J., Tupys, A., Yang, L., Mester, Z., Halicz, L., Bulska, E. (2020). Novel Approach for the Accurate Determination of Se Isotope Ratio by Multicollector ICP-MS. *Anal. Chem.* 92, 16097–16104. https://doi.org/10.1021/acs.analchem.0c03768.

Kroukamp, E., Abou-Shakra, F. (2020). Multi-Quadrupole ICP-MS: Pushing Limits of Detection to the Next Decimal. *Spectroscopy*, 35, 16-22. https://www.spectroscopyonline.com/view/multi-quadrupole-icp-ms-pushing-limits-of-detection-to-the-next-decimal.

Linge, K.L., Jarvis, K.E. (2009). Quadrupole ICP-MS: Introduction to Instrumentation, Measurement Techniques and Analytical Capabilities. *Geostand. Geoanal. Res.* 33, 445-467. https://doi.org/10.1111/j.1751-908X.2009.00039.x

Liu, F., Zhaofeng Zhang, Z., Xin Li, X., An, Y. (2020). A practical guide to the double-spike technique for calcium isotope measurements by thermal ionization mass spectrometry (TIMS). Int. J. Mass Spectrom. 450, 116307. https://doi.org/10.1016/j.ijms.2020.116307.

Lobo, L., Devulder, V., Degryse, P., Vanhaecke, F. (2012). Investigation of natural isotopic variation of Sb in stibnite ores via multi-collector ICP-mass spectrometry – perspectives for Sb isotopic analysis of Roman glass. *J. Anal. At. Spectrom.* 27, 1304-1310. https://doi.org/10.1039/C2JA30062A

Longerich, H.P., Fryer, B.J., Strong, D.F. (1987). Determination of lead isotope ratios by inductively coupled plasma-mass spectrometry (ICP-MS). *Spectrochim. Acta Part B*, 42, 39–48. https://doi.org/10.1016/0584-8547(87)80048-4.

Malinovsky, D., Dunn, P.J.H., Goenaga-Infante, H. (2016). Calibration of Mo isotope amount ratio measurements by MC-ICPMS using normalisation to an internal standard and improved experimental design. *J. Anal. At. Spectrom*., 31, 1978-1988. https://doi.org/10.1039/C6JA00184J

Malinovsky, D., Vanhaecke, F. (2011). Mass-independent isotope fractionation of heavy elements measured by MC-ICPMS: a unique probe in environmental sciences. Anal. Bioanal. Chem. 400, 1619–1624. https://doi.org/10.1007/s00216-011-4856-z.

Malinovsky, D., Vanhaecke, F. (2014). Molybdenum isotope enrichment by anion-exchange chromatography. *J. Anal. At. Spectrom*. 29, 1090-1097. https://doi.org/10.1039/c4ja00013g.

Mana, G., Massa, E., Valkiers, S., Willenberg, G.D. (2010). Uncertainty assessment of Si molar mass measurements. *Int. J. Mass Spectrom*. 289, 6–10. https://doi.org/10.1016/j.ijms.2009.09.005.

Maréchal, C.N., Télouk, P., Albarède, F. (1999). Precise analysis of copper and zinc isotopic compositions by plasma-source mass spectrometry. *Chem. Geol.* 156, 251-273. https://doi.org/10.1016/S0009-2541(98)00191-0.

McKinney, C.R., McCrea, J.M., Epstein, S., H. A. Allen, H.A., Urey H.C. (1950). Improvements in Mass Spectrometers for the Measurement of Small Differences in Isotope Abundance Ratios. *Rev. Sci. Instrum*. 21, 724–730. https://doi.org/10.1063/1.1745698.

Mead, C., Johnson, T.M. (2010). Hg stable isotope analysis by the double-spike method. *Anal. Bioanal. Chem.* 397(4), 1529-38. https://doi.org/10.1007/s00216-010-3701-0.

Meija, J. (2012). Calibration of isotope amount ratios by analysis of isotope mixtures. *Anal. Bioanal. Chem*. 403, 2071–2076. https://doi.org/10.1007/s00216-012-5785-1.

Meija, J. (2025). Elusive isotope ratios. *Nat. Phys.* 21, 1170. https://doi.org/10.1038/s41567-025-02955-0.

Meija, J., Yang, L., Mester, Z., Sturgeon, R. (2012). Correction of instrumental mass discrimination for isotope ratio determination with Multi-Collector Inductively Coupled Plasma Mass Spectrometry. In F.Vanhaecke, P. Degryse (Eds.), *Isotopic Analysis* (pp. 107-129). Wiley-VCH Verlag.

Michalski, R. (2024). Applications of ion chromatography in environmental analysis. In: Nesterenko, P.N., Poole, C.F., Sun, Y. (Eds.) *Ion-Exchange Chromatography and Related Techniques* (pp. 333-349). Elsevier.

Miller, P.E., Denton, M.B. (1986) The quadrupole mass filter: Basic operating concepts. *J Chem Educ.* 63, 617-622. https://doi.org/10.1021/ed063p617

Misra, Sambuddha and Froelich, Philip N (2009). Measurement of lithium isotope ratios by quadrupole-ICP-MS: application to seawater and natural carbonates. *J. Anal. At. Spectrom*., 24, 1524-1533. https://doi.org/10.1039/B907122A

Modern chemical techniques (2015). *Royal Society of Chemistry*. Retrieved from https://edu.rsc.org/resources/chromatography/1301.article.

Montaser, A. (1998). *Inductively Coupled Plasma Mass Spectrometry*. Wiley & Sons.

Nesterenko, P.N., Jones, P. (2019). Ion Exchange|Chelation Ion Chromatography. In: Worsfold, P., Townshend, A., Poole, C., Miró, M. (Eds.) *Encyclopedia of Analytical Science*, 3rd Edition (pp. 155-169).

Ngere, J.B., Ebrahimi, K.H., Williams, R., Pires, E., Walsby-Tickle, J., McCullagh, J.S.O. (2023). Ion-Exchange Chromatography Coupled to Mass Spectrometry in Life Science, Environmental, and Medical Research. *Anal. Chem*. 95, 152−166. https://doi.org/10.1021/acs.analchem.2c04298

Nier, A.O. (1950). A Redetermination of the Relative Abundances of the Isotopes of Carbon, Nitrogen, Oxygen, Argon, and Potassium. *Phys. Rev.* 77, 789–793. https://doi.org/10.1103/PhysRev.77.789

Pallavicini, N., Engström, E., Baxter, D.C., Öhlander, B., Ingri, J., Rodushkin, I. (2014). Cadmium isotope ratio measurements in environmental matrices by MC-ICP-MS. *J. Anal. At. Spectrom*. 29, 1570–1584, https://doi.org/10.1039/c4ja00125g

Pi, J-l., You, C.-F., Chung, C-H. (2014). "Micro-sublimation separation of boron in rock samples for isotopic measurement by MC-ICPMS." *J. Anal. At. Spectrom. 29*, 861-867. https://doi.org/10.1039/C3JA50344E

Pietruszka, A.J., Reznik, A.D. (2008). Identification of a matrix effect in the MC-ICP-MS due to sample purification using ion exchange resin: An isotopic case study of molybdenum. *Int. J. Mass Spectrom.* 270, 23-30. https://doi.org/10.1016/j.ijms.2007.11.001

Pin, C., Rodriguez, L. (2014). Separation Methods Based on Liquid–Liquid Extraction, Extraction Chromatography, and Other Miscellaneous Solid Phase Extraction Processes. In: Turekian, K.K., Holland, H.D. (Eds.) *Treatise on Geochemistry, 2nd edition. Volume 15: Analytical Geochemistry* (pp. 147-170), Elsevier.

Ponzevera, E., Quétel, C. R., Berglund, M., Taylor, P.D.P. (2006). Mass Discrimination During MC-ICPMS Isotopic Ratio Measurements: Investigation by Means of Synthetic Isotopic Mixtures (IRMM-007 Series) and Application to the Calibration of Natural-Like Zinc Materials (Including IRMM-3702 and IRMM-651). *J. Am. Soc. Mass Spectrom.* 17; 1412-1427. https://doi.org/10.1016/j.jasms.2006.06.001

Powell, R., Woodhead, J., Hergt, J. (1998). Uncertainties on lead isotope analyses: deconvolution in the double-spike method. *Chem. Geol*. 148, 95–104. https://doi.org/10.1016/S0009-2541(98)00023-0.

Prohaska, T., Irrgeher, J., Benefield, J., Böhlke, J.K., Chesson, L., Coplen, T.B., Ding, T., Dunn, P.J.H., Gröning, M., Holden, N.E., Meijer, H.A.J., Moossen, H., Possolo, A. Takahashi, Y., Vogl, J., Walczyk,

T., Wang, J., Wieser, M.E., Yoneda, S., Zhu, X.K., Meija, J. (2022). Standard atomic weights of the elements 2021 (IUPAC Technical Report). *Pure Appl. Chem*. 94, 573-600. https://doi.org/10.1515/pac-2019-0603.

Qi, H.P., M. Berglund, M., P. D. P. Taylor, P.D.P., Hendrickx, F., A. Verbruggen, A., De Bièvre, P. (1998). Preparation and characterisation of synthetic mixtures of lithium isotopes. *Fresenius J. Anal. Chem*. 361, 767–773. https://doi.org/10.1007/s002160051013.

Reese, A., Zimmermann, T., Pröfrock, D., Irrgeher, J. (2019). Extreme spatial variation of Sr, Nd and Pb isotopic signatures and 48 element mass fractions in surface sediment of the Elbe River Estuary - Suitable tracers for processes in dynamic environments? *Sci. Tot. Environ*. 668, 512-523. https://doi.org/10.1016/j.scitotenv.2019.02.401

Rienitz, O. 2001. Entwicklung chemisch-analytischer Primärmethoden zur Bestimmung physiologisch relevanter anorganischer Bestandteile in Humanserum. Wirtschaftsverl. NW, Verlag für neue Wissenschaft.

Rosner, M., Ball, L., Peucker-Ehrenbrink, B., Blusztajn, J., Bach, W. and Erzinger, J. (2007), A Simplified, Accurate and Fast Method for Lithium Isotope Analysis of Rocks and Fluids, and δ^7Li Values of Seawater and Rock Reference Materials. *Geostand. Geoanal. Res*. 31: 77-88. https://doi.org/10.1111/j.1751-908X.2007.00843.x

Rottmann, L., Jakubowski, N., Konegger-Kappel, S., Hanousek, O., Prohaska, T. (2015). Technical background. In T. Prohaska, J. Irrgeher, A. Zitek, N. Jakubowski (Eds.), *Sector Field Mass Spectrometry for Elemental and Isotopic Analysis* (pp. 44-96), The Royal Society of Chemistry.

Rudge, J.F., Reynolds, B.C., Bourdon, B. (2009). The double spike toolbox. *Chem. Geol*. 265, 420–431. https://doi.org/10.1016/j.chemgeo.2009.05.010.

Saunders, P., Fischer, J., Sadli, M. et al. (2008). Uncertainty Budgets for Calibration of Radiation Thermometers below the Silver Point. *Int. J. Thermophys*. 29, 1066–1083. https://doi.org/10.1007/s10765-008-0385-1.

Schönbächler, M. (2018). Ion Exchange Chromatography. In: White, W.M. (eds) *Encyclopedia of Geochemistry. Encyclopedia of Earth Sciences Series*. Springer, Cham. https://doi.org/10.1007/978-3-319-39312-4_113

Shi, M., Bergquist, B., Zhou, A., Zhao, Y., Sun, R., Chen, J., Zheng, W. (2023). The efficiency of Hg cold vapor generation and its influence on Hg isotope analysis by MC-ICP-MS. *J. Anal. At. Spectrom*. 38, 1076-1087. https://doi.org/10.1039/D3JA00056G.

Siebert, C., Nägler, T.F., Kramers, J.D. (2001). Determination of molybdenum isotope fractionation by double-spike multicollector inductively coupled plasma mass spectrometry. *Geochem. Geophys. Geosys*. 2, 1032. https://doi.org/10.1029/2000GC000124

Siekierski, S., (1975). Chapter 1. Theoretical Aspects of Extraction Chromatography. *J. Chromatogr. Library* 2, 1-16. https://doi.org/10.1016/S0301-4770(08)60967-7.

Skoog, D.A., Holler, F.J., Crouch, S.R. (2018). *Principles of instrumental analysis* (7th ed.). Cengage Learning.

Skrzypek, G., Allison, C.E., Böhlke, J.K., Bontempo, Luana, Brewer, Paul, Camin, Federica, Carter, James F., Chartrand, Michelle M. G., Coplen, Tyler B., Gröning, Manfred, Hélie, Jean-François, Esquivel-Hernández, Germain, Kraft, Rebecca A., Magdas, Dana A., Mann, Jacqueline L., Meija, Juris, Meijer, Harro A. J., Moossen, Heiko, Ogrinc, Nives, Perini, Matteo, Possolo, Antonio, Rogers, Karyne M., Schimmelmann, Arndt, Shemesh, Aldo, Soto, David X., Thomas, Freddy, Wielgosz, Robert, Winchester, Michael R., Yan, Zhao and Dunn, P.J. H. (2022). Minimum requirements for publishing hydrogen, carbon, nitrogen, oxygen and sulfur stable-isotope delta results (IUPAC Technical Report). *Pure Appl. Chem*. 94(11–12), 1249–1255. https://doi.org/10.1515/pac-2021-1108.

Stoll-Werian, A., Flierl, L., Rienitz, O., Noordmann, J., Kessel, R., Pramann, A. (2019). Absolute isotope ratios – Analytical solution for the determination of calibration factors for any number of isotopes and isotopologues. *Spectrochim. Acta Part B*, 157, 76-83. https://doi.org/10.1016/j.sab.2019.04.008.

Tanner, S.D., Baranov, V.I., Bandura, D.R. (2002). Reaction cells and collision cells for ICP-MS: a tutorial review. *Spectrochim. Acta Part B: Atom. Spectroscopy*, 57(9), 1361-1452. https://doi.org/10.1016/S0584-8547(02)00069-1

Thomas, R. (2004). *Practical Guide to ICP-MS*. Marcel Dekker Inc., New York.

Tong, S., Meija, J., Zhou, L., Methven, B., Mester, Z., Yang, L. (2019). High-Precision Measurements of the Isotopic Composition of Common Lead Using MC-ICPMS: Comparison of Calibration Strategies Based on Full Gravimetric Isotope Mixture and Regression Models. *Anal. Chem*. 91(6), 4164–4171. https://doi.org/10.1021/acs.analchem.9b00020.

Van Hoecke, K., Devulder, V., Claeys, P., Degryse, P., Vanhaecke, F. (2014). Comparison of microsublimation and ion exchange chromatography for boron isolation preceding its isotopic analysis via multi-collector ICP-MS. *J. Anal. At. Spectrom*. 29, 1819-1826. https://doi.org/10.1039/C4JA00111G

Vance, D., Thirlwall, M. (2002). An assessment of mass discrimination in MC-ICPMS using Nd isotopes. *Chem. Geol*. 185, 227-240. https://doi.org/10.1016/S0009-2541(01)00402-8.

Velapoldi, R.A., Paule, R.C., Schaffer, R., Mandel, J. and Moody, J.R. 1978. Standard Reference Materials: A Reference Method for the Determination of Sodium in Serum. National Bureau of Standards.

Vogl, J. (2021). The triple-isotope calibration approach: a universal and standard-free calibration approach for obtaining absolute isotope ratios of multi-isotopic elements. *Anal. Bioanal. Chem.* 413(3), 821–826. https://doi.org/10.1007/s00216-020-03050-4.

Wagner, S., Santner, J., Irrgeher, J., Puschenreiter, M., Happel, S., Prohaska, T. (2022). Selective diffusive gradients in thin films (DGT) for the simultaneous assessment of labile Sr and Pb concentrations and isotope ratios in soils. *Anal. Chem.* 94, 6338-6346. https://doi.org/10.1021/acs.analchem.2c00546

Walder, A.J., and Freedman, P.A. (1992). Isotopic Ratio Measurement Using a Double Focusing Magnetic Sector Mass Analyser with an Inductively Coupled Plasma as an Ion Source. *J. Anal. At. Spectrom.*, 7, 571-575. https://doi.org/10.1039/JA9920700571

Wang, T-H., You, C-F, Chung, C-H., Liu, H-C., Lin, Y-P. (2020). Macro-sublimation: Purification of boron in low-concentration geological samples for isotopic determination by MC-ICPMS. *Microchem. J.* 152, 104424. https://doi.org/10.1016/j.microc.2019.104424

Willie, S., Mester, Z., Sturgeon, R. (2005). Isotope ratio precision with transient sample introduction using ICP orthogonal acceleration time-of-flight mass spectrometry. *J. Anal. At. Spectrom.* 20, 1358-1364. https://doi.org/10.1039/B505309A

Wilschefski, S.C., and Baxter, M.R. (2019). Inductively Coupled Plasma Mass Spectrometry: Introduction to Analytical Aspects. *Clin. Biochem. Rev.,* 40(3), 115–133. https://doi.org/10.33176/AACB-19-00024.

Wolff Briche, C.S.J., Held, A., Dyckmans, B., Berglund, M., De Bièvre. P., Taylor, P.D.P. (2000). Gravimetric preparation of synthetic mixtures of platinum isotopes. *Int. J. Mass Spectrom.* 202, 9–18. https://doi.org/10.1016/S1387-3806(00)00185-8.

Xiao, J., Vogl, J., Rosner, M., Deng, L., Jin, Z. (2019). A validated analytical procedure for boron isotope analysis in plants by MC-ICP-MS, *Talanta* 96, 389-394. https://doi.org/10.1016/j.talanta.2018.12.087

Yamakawa et al. (2009). Chemical separation and mass spectrometry of Cr, Fe, Ni, Zn, and Cu in terrestrial and extraterrestrial materials using thermal ionization mass spectrometry. *Anal Chem.* 81(23), 9787-94. https://doi.org/10.1021/ac901762a.

Yang, L. Accurate and precise determination of isotopic ratios by MC-ICP-MS: a review. *Mass Spectrom. Rev.* 2009, 28, 990– 1011. https://doi.org/10.1002/mas.20251

Yang, L., Methven, B., Mester, Z., Meija, J. (2023). Determination of the isotopic composition of copper in a certified reference material HICU-1 by MC-ICP-MS using gravimetric isotope mixture calibration. *J. Anal. At. Spectrom.* 38, 2080-2086. https://doi.org/10.1039/d3ja00212h.

Yang, L., Sturgeon, R.E., Mester, Z., Meija, J. (2010). Metrological Triangle for Measurements of Isotope Amount Ratios of Silver, Indium, and Antimony Using Multicollector-Inductively Coupled Plasma Mass Spectrometry: The 21st Century Harvard Method. *Anal. Chem.* 82, 8978–8982. https://doi.org/10.1021/ac1019396.

Yang, L., Tong, S., Lian Zhou, L., Hu, Z., Mester, Z., Meija, J. (2018). A critical review on isotopic fractionation correction methods for accurate isotope amount ratio measurements by MC-ICP-MS. *J. Anal. At. Spectrom.* 33, 1849-1861. https://doi.org/10.1039/C8JA00210J

Yang, T., Huiyang Yu, H., Zhu, Z., Ding, R., Wang, J., Zhu, B. (2024). Development of a Chelex-100 based three-step chromatographic procedure for nickel isotope analysis in geological samples. J*. Anal. At. Spectrom.* 39, 1270-127. https://doi.org/10.1039/D4JA00007B.