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# Application of non-traditional stable isotopes in analytical ecogeochemistry assessed by MC ICP-MS – A critical review

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## Abstract

*Analytical ecogeochemistry* is an evolving scientific field dedicated to the development of analytical methods and tools and their application to ecological questions. *Traditional* stable isotopic systems have been widely explored and have undergone continuous development during the last century. The variations of the isotopic composition of light elements (H, O, N, C and S) have provided the foundation of stable isotope analysis followed by the analysis of traditional geochemical isotope tracers (e.g. Pb, Sr, Nd, Hf). Questions in a considerable diversity of scientific fields have been addressed, many of which can be assigned to the field of ecogeochemistry. Over the past fifteen years, other stable isotopes (e.g. Li, Zn, Cu, Cl) have emerged gradually as novel tools for the investigation of scientific topics that arise in ecosystem research and have enabled novel discoveries and explorations. These systems are often referred to as *non-traditional isotopes*.

The small isotopic differences of interest that are increasingly being addressed for a growing number of isotopic systems represent a challenge to the analytical scientist and push the limits of today's instruments constantly. This underlines the importance of a metrologically sound concept of analytical protocols and procedures and a solid foundation of data processing strategies and uncertainty considerations before these small isotopic variations can be interpreted in the context of applied ecosystem research. This review focuses on the development of isotope research in ecogeochemistry, the requirements for successful detection of small isotopic shifts as well as highlights the most recent and innovative applications in the field.

## Keywords

analytical ecogeochemistry, non-traditional stable isotopes, isotope tracers, MC ICP-MS, chemical metrology

## **Introduction**

### ***The role of isotope ratios analysis in analytical ecogeochemistry***

*Analytical ecogeochemistry* deals with the development and application of tools of analytical chemistry to study dynamic biological and ecological processes within ecosystems and across ecosystem boundaries [1]. In this context, analytical ecogeochemistry may be conceptualized as a linkage between modern analytical chemistry and geochemical methods with ecology, within the frame of transdisciplinary research. Given the holistic concept of *The total human ecosystem* according to Naveh technical products of humans are considered as part of the ecosystem as well [2]. Isotope signatures have evolved as widely used tracers in many fields of related sciences because of their exceptional characteristics of naturally or anthropogenically induced abundance variation. In addition, the use of isotope enriched materials or spikes tracers introduced into ecological systems has experienced a tremendous boost during the last decade. The analysis of isotope amount ratios is *ergo* regarded as a key approach to investigate processes where isotope ratio fractionation carries information about whatever history behind. The emerging presence and the fast growth of this field of research are demonstrated by the continuously increasing number of Google Hits that - within the short period between September 2014 to April 2015 - has augmented by 15%.

### ***Mass spectrometry for isotope ratio determination in ecosystem research from then until today***

The field of conventional stable isotope studies has paved the way to the use of isotopes as environmental tracers [3]. The leading technique to measure the isotopic variability of light elements (H, C, O, N, S) has been gas source isotope ratio mass spectrometry (*aka* isotope ratio mass spectrometry - IRMS) since the early years of mass spectrometry [4]. The technique was developed based on Nier's initial mass spectrometer in the 1940s [5-7] and still forms the backbone of light stable isotopes until today. The number of applications of IRMS is tremendously manifold as the method offers versatile possibilities to explore diverse research problems [8]. The application of traditional stable isotopes has recently been extended to the use of so-called clumped isotopes making use of the effect that at lower temperatures heavy isotopes (e.g.  $^{13}\text{C}$ ,  $^{18}\text{O}$  and  $^{16}\text{O}$  to  $^{47}\text{CO}_2$ ) clump together as these molecules have higher thermodynamic stability [9].

With thermal ionisation mass spectrometry (TIMS), an additional technologically simple and, as a consequence, very reliable ion source has been used since the first half of the 20<sup>th</sup> century. Usually combined with a single-focusing magnetic sector mass analyser with subsequent ion detection by a multicollector array of Faraday cups and a few ion counters, these components are still the core of modern TIMS instruments. The first commercial instruments were launched as early as the 1960s. Traditionally, isotopic systems such as U-Th-Pb, Sm-Nd and Rb-Sr have been assessed by TIMS in the context of nuclear forensics, geochemistry, and industrial and material research. Until today, more

than 60 elements have been analysed by TIMS and the technique has found its way into many more fields of research covering a wide spectrum from the original areas of applications to fields related to life sciences and environmental sciences as well [10].

Looking back at history, since implemented in the early 1980s, multicollector-thermal ionisation mass spectrometry (MC-TIMS), had already developed to a well-established technique for isotope ratio measurements at the time the first multicollector detector array was coupled to an inductively coupled plasma (ICP) as ion source in 1992 and entered the market as multicollector ICP-MS (MC ICP-MS) [11]. Thereafter, geo- and cosmochemistry were the first research areas that were served by MC ICP-MS. They still represent the fields with the largest number of application publications even though many more fields and many more elements have been accessed over the years.

As a consequence, isotope ratio analysis via MC ICP-MS has developed as a promising additional technique, even though TIMS still holds its status as a reliable method for isotope ratio measurements – mainly because of the high precision capabilities and matrix-independence [12]. In contrast to TIMS, MC ICP-MS impresses because of the analytical ease of the method due to the reduced sample preparation required and high sample throughput as well as its capabilities to ionize a very broad set of elements [13]. Today, MC ICP-MS allows determining isotope ratios with measurement precisions comparable to those of TIMS (down to 0.001%) [10]. This might include preparatory work to fully separate the analyte isotopes from the matrix in order to overcome systematic errors derived from matrix-induced interferences as well as changes in instrumental isotopic fractionation (*aka* mass bias), which is significantly larger for MC ICP-MS [14-16] than for TIMS [12,17,18].

Today, these three mass spectrometric techniques (i.e. IRMS, MC ICP-MS and TIMS) can be regarded as key techniques being used in the field of stable isotope ratio analysis. Additionally, secondary ion mass spectrometry (SIMS) and glow discharge mass spectrometry (GDMS) are used for stable isotope ratio determination. However – up to the present day – the number of studies on non-traditional stable isotopes in the field of ecogeochemistry is by far lower than for IRMS, MC ICP-MS and TIMS. A comprehensive overview about SIMS and GDMS has been published recently in a book about sector field mass spectrometry and will thus not be discussed in detail in this review [19,20].

### ***What is a stable isotope?***

In contrast to radioactive isotopes, which disintegrate at predictable and measurable rates to form other isotopes by emitting a nuclear electron or a helium nucleus and radiation, *stable isotopes* do not decay into isotopes of other elements. This definition is based on pure logic. Other concepts have however been circulating over the years, that take into account half-lives above which an isotope is regarded as (quasi) stable. In this article, we focus on isotopes that are isotopes considered as stable

only if they do not have a reported half-life, which has not experimentally been determined by the time of publication [21,22]. Further explanations are given by Brand and Coplen [23].

### ***What is a non-traditional stable isotope?***

The line between *traditional* and *non-traditional* stable isotopes was never drawn with intention or even defined. Instead it has rather developed over the time with the history of the mass spectrometric techniques used for stable isotope analysis. The so-called light elements (H, C, O, N and S) have been analysed since the 1940s using IRMS and are conventionally referred to as the *traditional* stable isotopes. As there is no definition or alliance about these terms, one is generally free to assign isotopes or isotopic systems to either group. This assignment will continue as a dynamic process with time as elements will exceed the border from *non-traditional* to *traditional* isotopes. This becomes increasingly clear today, as the group of traditional stable isotopes may absorb also *heavy* stable isotopes such as those of Sr, Hf or Pb. Further, stable isotopes of these elements may somehow fall into both groups: traditional as well as non-traditional stable isotopes, depending on the isotopes of interest and the ratios being calculated. The natural variation of the  $^{87}\text{Sr}/^{86}\text{Sr}$  isotope ratio, as a result of the radioactive decay of  $^{87}\text{Rb}$ , has been used for decades in geochronology and can – in good conscience – be considered as a traditional isotope ratio. In contrast to that the other three naturally occurring isotopes  $^{84}\text{Sr}$ ,  $^{86}\text{Sr}$  and  $^{88}\text{Sr}$  have been taken as invariant in nature until the early 2000s when first papers about an observed variation were published. This was mainly as a reward for recent advances in mass spectrometry, which made it possible to measure small isotopic variations with the needed accuracy [24,31]. Isotope ratios of  $^{88}\text{Sr}/^{86}\text{Sr}$  and  $^{88}\text{Sr}/^{84}\text{Sr}$  would thus rather fall into the group of non-traditional stable isotope ratios. Often, metal stable isotopes are considered as non-traditional, as they have not been subject to isotopic analysis until the turn of the last millennium, when a first review chapter on the topic was published [12]. At that time, instrumental developments allowed for the first measurable isotopic variations of these elements with significance and thus opened a completely new field of isotopic research.

### ***The balance between analytical method development and the applications***

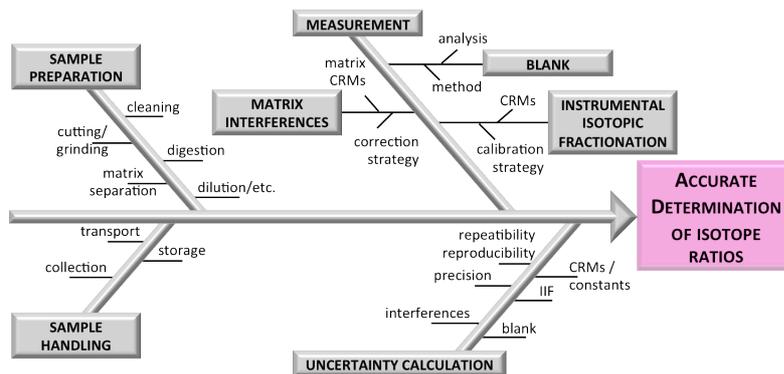
As analytical ecogeochemistry is dedicated to both the development as well as the application of analytical methods and tools to ecological questions, a major core issue of today's research in the field of non-traditional stable isotopes to be faced with is assigned to an existing and possible increasing imbalance between analytical method development and applications. As we are dealing with very small isotopic variations that call for isotope ratio data with the highest accuracy and

lowest uncertainties possible – in other words with the best analytical quality achievable - analytical method developments to implement routines for the analysis and application of, for instance, metal isotope ratios of Cu, Zn, Sn or Cd to a specific environmental research question will not be a task to be completed within a week or two. Still, only well-established and validated methods can guarantee that small isotopic variations are certain and not a result of analytical sloppiness. Interpretation of analytically sound data is a challenge *per se* anyway and as analytical chemists we know that the consequences of providing data of lacking of quality can cause tremendous impact and has to be regarded as irresponsible. Conversely, there is no use of brilliant isotopic data if no or wrong interpretation is undertaken. As a consequence, a combination of sound analytical science and the profound knowledge in the applied disciplines is an essential basis: *Transdisciplinarity* is highly required, joining methodological knowledge about chemical analysis and the quality of data including uncertainties with the research question itself in the corresponding field of application [25].

#### ***Factors influencing the metrological quality of isotope ratios***

The key issue in the accurate analysis of non-traditional stable isotopes or - put another way - isotope ratios underlying rather small isotopic fractionation effects (with terrestrial ranges of a few per mille only) is to deconvolve isotopic fractionation related to processes before the analysis from those fractionation effects attributed to the analytical procedure, either during sample preparation or measurement. Thus, profound analytical work and careful method development are of utmost importance in order to guarantee a validated measurement method.

To design metrologically sound measurement protocols for assessing isotope amount ratios a number of key issues have to be respected during sampling, sample preparation, the measurement (correction for blank, spectral and non-spectral interferences, calibration and correction for instrumental isotopic fractionation) and data processing including the calculation of combined uncertainties (**Fig. 1**). Some of these aspects will be discussed in further detail in the following sections focused on MC ICP-MS but are applicable to other mass spectrometric techniques in many aspects.



**Fig. 1** Factors that affect the metrological quality of isotope ratio determination

### *Collection, transportation and storage of samples*

Sound analytical procedures start with the sampling design, including the preparation of items and consumables needed for the collection of the sample. Certainly, the effort that has to be put into the preparation of e.g. contamination-free sampling containers depends strongly on the sample matrix and the analyte of interest as specific problems and techniques are associated with each type of sample. In case of elemental and isotopic analysis at low levels (ng/g levels and below) this implies validated procedures for decontamination of sample containers and lab ware. The correct choice of suitable materials for the containers, consumables and lab clothing used [26-29]. Issues related to the sampling procedure, transportation and storage for different types of samples are comprehensively given in [30].

### *Sample preparation*

Isotopic analysis involves - if needed - the transformation of the sample, which can be either sampled as a liquid, solid or gaseous matrix, into a measurable (physical) status. In many cases, especially for MC ICP-MS analysis, this involves matrix digestion or extraction (and pre-concentration) in order to finally end up with the sample in a liquid form and the analyte dissolved in a solution that can be directly introduced into the mass spectrometer. In case a laser ablation system is coupled to MC ICP-MS for solid sample analysis, the sample may require cleaning, grinding, and cutting or similar preparation steps prior to analysis. As many isotopes suffer from severe interferences, either originating from components of the sample itself or the analytical setup (e.g. Ar, Kr from the plasma gas or O and N from ambient air or nitric acid in the sample solution), the analytical setup has to be designed accordingly. This would for example apply to the purity of plasma gas (e.g. to account for Kr traces in the Ar gas during Sr isotope amount ratio measurements) or the use of desolvation membranes (e.g. to reduce the formation of hydrides).

In many cases samples need to be processed through an analytical matrix separation procedure (following either single stage or multiple stage protocols) in order to provide interference-free measurements and best-as-possible matrix matching between the sample and the standards used for calibration. Matrix separation eliminates major isobaric and polyatomic interferences (e.g.  $\text{Rb}^+$  and  $(\text{CaCa})^+$  on  $\text{Sr}^+$  or  $(\text{ZnAr})^+$  on  $\text{Cd}^+$ ). In addition, matrix dependent instrumental isotopic fractionation is minimized if a near-perfect matrix matching is achieved. Today, both off-line and on-line separation procedures coexist. Specific cation-exchange resin products are available from different suppliers for the separation of the elements of interest. These are based on the different retention behaviors of the analyte ion and the interfering components. Some elements require more complex purification protocols than others. The complexity spans from a single pass procedure through one column (e.g. Sr [31]) to multiple-step procedures (e.g. Cd [32]). Some protocols even combine the separation of different elements, e.g. for Nd, Sr and Pb [33]. Recently an automated separation system, the prepFAST-MC™ (Elemental Scientific, Mainz, Germany), was launched on the market and allows for automated sample purification [34]. The system even makes sample preparation directly at the sampling site possible without the need to store the sample and transport it to the laboratory for further processing. This allows for sample preparation of a fresh sample on site [35]. Ion separation of samples require strict control of method blanks and good recoveries, preferably  $R = 100\%$ . This precludes possible effects of on-column isotope fractionation, which have been observed [36-38]. Alternatively, matrix-matched isotope certified reference materials (iCRM) should be processed but the possibilities are limited here due to the scarcity of appropriate iCRM (see below).

#### *Measurement related factors*

Blank: In every analytical procedure it is essential to monitor the background levels of the analyte of interest. Significant amounts of analyte may be present in the system (in absence of the sample), thus potentially biasing the analytical result. Usually, so-called *method blanks* are processed following the entire method in the same manner as the sample itself but in absence of the analyte. As such, background levels of the analyte e.g. present at trace amounts in the used chemicals, consumables and instrument parts such as tubings, cones and connectors can be accounted for. Isotope amount ratio determination can be biased if the method blank either originating from, for instance sampling, digestions and extractions, ion exchange chromatography but also the measurement itself contributes significantly to the total amount of analyte. Therefore, it is recommended to monitor each preparatory step separately in order to identify sources of contamination as well as to critically monitor the limits of detection for the single steps in the sample preparation procedure and during the measurement itself. During the measurement, different strategies of recording instrumental background are possible depending on the isotopic system of

interest as well as the instrumentation used. In MC ICP-MS *on-peak* zeros are often applied, where a blank is recorded prior to the measurement of the sample. Alternatively, zero by electrostatic analyser deflection or measurements at half-masses can be applied.

Matrix and Interferences: In spectroscopy interferences alter, modify, or disrupt a measured signal. Different types of interferences are usually distinguished, conventionally grouped into spectral (or spectroscopic) interferences, non-spectral interferences and interferences that originate from the system (mostly from the electronics and the detection unit). Non-spectral interferences are in most cases referred to matrix effects or matrix interferences [39]. Matrix-matching between the calibration standard and the samples is of utmost importance as a variable remaining matrix can induce a systematic bias [40]. More details on spectral interferences and possible corrections in MC ICP-MS are given elsewhere [41].

Instrumental isotopic fractionation: In mass spectrometry, the term *instrumental isotopic fractionation* (IIF) (also *instrumental mass bias*, *instrumental mass discrimination* or *instrumental mass fractionation*) describes an observed bias of the true isotope ratio to the one measured in a given sample. It is essential to differentiate between isotopic fractionation coming from instrumental phenomena and isotopic fractionation caused by e.g. natural effects. The concept of terminology related to *fractionation* in this context is described in Coplen [42] Basically, *fractionation* is a commonly used term, which is used to describe different phenomena of natural as well as instrumental processes in mass spectrometry. [43] The general term *fractionation* comprises processes that lead to the separation between two different entities (e.g. chemical compounds, elements or isotopes). *Isotopic fractionation* is the recommended term to be used for the effects leading to differences in isotope ratios of one element (e.g. between two substances). *Instrumental isotopic fractionation* can both arise from mass dependent and mass independent effects. The understanding of the factors that cause instrumental isotopic fractionation is still limited. The detected, erroneous values of isotope ratios can derive from many different effects in a mass spectrometer from sample introduction, ion formation, ion extraction, ion separation to ion detection. A preferential transmission of heavier isotopes can be considered as major cause of instrumental isotopic fractionation between nuclides [44]. In ICP-MS, the ionization source and the interface are believed to play a major role in IIF, mainly due to the large pressure drop between the ion source and the expansion region. These phenomena have recently been described in more detail for ICP-MS, GDMS, TIMS, SIMS and IRMS [17].

In order to cope with the systematic error introduced into the isotope ratio data assessed, different calibration strategies can be applied, also strongly dependent on the underlying mass spectrometric technique. Calibration for IIF requires the choice of an appropriate mathematical model to describe

the phenomena in the mass spectrometer that lead to the isotope ratio bias, best by method validation using matrix-matched, certified if possible, standard reference materials.

IIF correction is of particular importance when absolute isotope ratios are assessed. In case of the use of  $\delta$ -values (generally used e.g. in IRMS, but also in MC ICP-MS) all factors contributing to a bias of the measured ratio to the true ratio are accounted for irrespective of their origin (e.g. instrumental mass fractionation, dead time and detector cross calibration for different detector yields of multiple detectors). In case  $\delta$ -values are assessed, the standard and the sample should behave as identically as possible. Matrix-matched isotope reference materials would be preferable. However, if no iCRM is available in-house preparation of matrix-matched iCRMs (e.g. an isotope reference material doped with matrix elements at levels that are to be expected in the measured sample) would, for instance, be an option. In isotope amount ratio analyses, calibration of the mass spectrometer is achieved by establishing a relationship between the 'true' isotope amount ratio of a certified standard or a stable isotope amount ratio in the sample and the value obtained from the measurement of the same isotope amount ratio. This is necessary since all mass spectrometric techniques are subject to the effect of mass discrimination resulting in a systematic shift from the 'true' isotope amount ratio in a sample/or standard to the measured isotope amount ratio in the same. With the objective to calibrate a mass spectrometer for the effect of mass discrimination, a number of different strategies have been proposed over the years, of which a few have developed as frequently applied approaches for isotope amount ratio analysis. Details can be retrieved from [16,44,45].

Many of the effects at the origin of IIF are mass dependent and follow distinct mathematical models, which can e.g. be linear or exponential functions and this can be corrected for accordingly (see below). Moreover, mass independent isotopic fractionation has been observed [46-49]. In literature, possible causes of mass independent isotopic fractionation in MC ICP-MS were attributed to the nuclear field shift, the magnetic isotope effect, the oxide formation rate or high first ionization potentials [50].

Metrological traceability and the use of certified reference materials: Metrological traceability requires the establishment of a calibration hierarchy, providing that all input parameters into a model equation are traceable to a common reference through a documented unbroken chain of calibrations - if possible, the SI-unit [51]. In ecosystem research, this guarantees comparability between laboratories and published isotope ratio data, independent on the method of isotope ratio analysis or measuring institution. This is of crucial importance since ecological questions often demand for a large dataset provided by different laboratories at different times. Above all, the processing of (international) certified reference materials (CRMs) (either provided with a certificate

or calibrated against a certified standard) meets the requirements to establish traceability. This is often the limiting factor in the process chain as the availability of CRMs, especially those certified for isotope ratios and representing matrix-matched materials, is very limited. Metrological authorities that provide certified reference materials (e.g. the National Institute of Standards and Technology (NIST), the Federal Institute for Materials Research and Testing (BAM), the National Research Council Canada (NRC), the International Atomic Energy Agency (IAEA) or the Institute for Reference Materials and Measurements (IRMM) in Belgium) are continuously increasing the supply even though the demand can certainly not be met. Matrix matching of reference materials used for data reduction is preferable to the use of non-matrix-matched CRMs since near-perfect similarity in behavior of the analyte in the sample and in the standard is favored. As a consequence, a trend towards the preparation of in-house standards for the analysis of samples to cope with the non-availability of commercially available reference materials can be observed. A summary paper of existing isotope reference materials and their correct use can be found in the respective documents [52-54]. The role of reference materials for the analysis of non-traditional isotope research has also been discussed in [55,56].

#### *Relative notation vs. absolute notation of isotope amount ratios*

Isotope ratio notations in both absolute as well as relative values coexist. As different laboratories perform different data correction strategies (for e.g. for blank and instrumental isotopic fractionation) international comparability is generally difficult to establish when using absolute isotope ratios even if certified reference materials are being used. In addition to that, many existing isotope certified reference materials are provided with high uncertainties assigned to the certified values. The delta notation provides a means to circumvent the use of the stated uncertainties of CRMs (except for heterogeneities). Additionally, it allows small differences in number ratios to be expressed without precisely knowing the absolute isotopic abundances of an element. However, the use of delta values makes measurement results easily comparable on an international level if analysts use CRMs as anchor to a common reference.

Relative isotope ratios are expressed in delta ( $\delta$ ) values as the isotope ratio between two nuclides of an element of an unknown sample to a preferably internationally accepted standard and are expressed in parts per thousand (or per mille, ‰) [42].

Alternatively, a notation in epsilon ( $\epsilon$ ) values as the ratio of an unknown sample to a preferably internationally reference material in parts per ten thousand has arisen during the last years to express very small variations in the isotopic composition. This notation however is recommended to be omitted [42].

In case isotope ratios are expressed in delta ( $\delta$ ) values [42] no further model for mass discrimination correction has to be applied. In this case all sources of mass discrimination are expected to be similar for the used reference material and the sample under investigation and without exactly knowing the absolute isotopic abundances of an element. This facilitates comparability of internationally published data. In contrast, comparability between isotope ratios given as absolute values is far more complex due to the need of taking e.g. correction approaches, calibration processes or used reference values into account. Thus, several sources of uncertainty entailed with absolute isotope ratio measurements will be eliminated when  $\delta$ -values will finally replace absolute values, as the impact of using different strategies for mass bias correction as well as the impact of uncertainties on reference materials will be significantly reduced or excluded. An example is given for Sr in this topical issue by Horsky *et al.* [40].

In order to establish international transparency of used CRMs, recently, W.A. Brand *et al.* [57] have reported a comprehensive list of reference materials, which should be used as primary reference ( $\delta = 0$ ) along with delta values of other reference materials, which are commonly used as delta reference. The primary reference has per definition a  $\delta$  of 0 as well as an uncertainty of 0 (even though the uncertainty as a result of the homogeneity of the CRM has to be taken into account for the calculation of combined standard measurement uncertainties).

#### *Uncertainty*

It is important to avoid isotope ratio data being reported with only the standard deviation or standard error of the measurement, even though also studies without even reporting measurement errors exist [58]. As many other factors contribute to the uncertainty of isotope ratios, this is not acceptable, since significant differences in the isotopic composition between samples can only be assured, if all possible sources of uncertainty are considered. Instead, combined uncertainties should be calculated and assigned to isotope data. This is especially important when small isotopic effects are being looked at as in the case of non-traditional isotopes. Else, interpretations of natural effects are based on non-significant differences. The major sources of uncertainty of the measurement itself definitely include blank correction, IIF correction, potential interference corrections, uncertainties of standard reference materials used, used constants (i.e. atomic weights and isotope abundances from tables). Repeatability and reproducibility are considered as within-run-precision or between-run-precision and often presented as the only value of uncertainty in isotopic studies [59]. The calculation of combined (measurement) uncertainties represents an integral part during method development or latest in method validation. Amongst others the *Joint Committee for Guides in Metrology (JCGM)* publishes regularly guidelines for the calculation of uncertainty in measurements in order to provide users with standard procedures for uncertainty assessment and to counteract the lack of international consensus on the expression of uncertainty in measurement. In this topical issue,

Horsky *et al.* give a tutorial review on how to calculate combined uncertainties for isotope ratio analysis on the example of strontium isotope ratios for an ecogeochemical research question [40].

#### *International comparability of isotope ratio data and the movement towards isotope databases*

Given the above mentioned issues, transparency of the establishment of isotope ratio data finally being published in a scientific paper is of paramount and essential significance for the establishment of international comparability, even though not trivial. Users need to make sure to provide information on the applied data reduction, calibration system and reference constants in detail. In order to provide international consent on reported values for isotopic determinations, the Commission on Isotopic Abundance and Atomic Weights (CIAAW) associated to the IUPAC (International Union of Pure and Applied Chemistry) meets biennially to revise isotope abundances and thus the of Atomic Weight values. These values are published in the Table of Isotopic Composition of the Elements (*aka* TICE) [60] and the Table of Standard Atomic Weights (*aka* TSAW) [61]. As a consequence, it is highly recommended to customarily update constant values that are used in laboratories on a regular basis for data processing. Secondly, transparent report of which constants are being used together with the pertinent references is crucial in order to allow for comparability and conformability. This becomes especially important today as isotope databases are being created, which logically demand comparability of the input data.

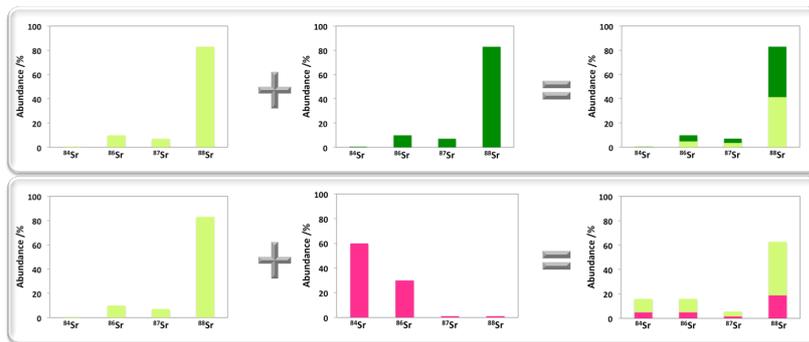
#### *The isotope line-up under investigation*

Both the natural variation of the isotopic composition as well as the application of isotope enriched spikes provide unique tools and have been widely applied to study ecogeochemical processes. Almost 50 different isotope systems have been investigated by ICP-MS so far, with - besides Sr, Pb, Nd and U - Ca, S, Cu, Hf, and Zn being the most prominent and considerably pushing the limits of plasma based mass spectrometry.

Within a short literature wrap-up that is given below, an overview about the fields of application as well as selected examples on novel isotopic signatures based on natural variation, case studies exploiting the potential of isotope enriched tracers and the combination of isotopic systems for the study of ecosystem processes on different spatial scales will be presented to underpin the opportunities substantiated by the field of analytical ecogeochemistry.

Basically, two general scenarios are possible when isotope signatures are being used in ecogeochemistry: (1) One can either analyse the natural isotopic composition of a sample as intrinsic mark or (2) an artificially introduced isotope enriched tracer - an extrinsic mark - that alter the isotopic composition of an element to an extent that the measured isotope signatures deviate with significance from what can be found in a natural environment (**Fig. 2**). Below, examples for both

scenarios will be described.



**Fig. 2** Principle of isotopic mixing on the example of Sr isotopes – 1 mixture of natural sources, 2 mixture of natural source and enriched stable isotope tracer

### *NATURAL ISOTOPIC FRACTIONATION (intrinsic marking)*

In order to successfully use the natural isotopic composition of an element as a tag for tracing or to describe natural processes, a significant variation of the isotopic composition of the element chosen as tracer has to exist between the entities to be differentiated. The isotopic mark can only be assessed if the element is available at concentrations detectable considering the methodological sensitivity of the analytical protocol and instruments available. Finally, the isotopic variation used as indicator for movement, transport, mixture, impact should be significant with respect to the performance characteristics of the method. These preconditions often imply also a minimum residence, exposure or take-up time of a characteristic tracer signature into a sample (e.g. at a specific site), so that the tracer can finally be successfully linked to e.g. either locally specific geochemical data or an identifiable dietary source. From these aspects, it is also clear that extracting information from elements and their isotope ratios for tracing will not work for every research question [62].

### *Isotope fractionation*

Natural isotopic variation is caused by very diverse reasons, most of which are supposedly based on mass-dependent phenomena: This includes metabolic processes, natural physical processes (e.g. based on temperature effects, sea level effects) or equilibrium fractionation [63] and biological and biochemical (e.g. photosynthesis, microbiological activity, trophic level, metabolism, physiology), climatic (e.g. precipitation, temperature, diffusion) processes. The isotopic composition can also be altered by anthropogenic input factors such as the use of fertilizers in agriculture or industrial emission. Especially those elements, whose isotopic fractionation or variation in nature is caused by geological processes, represent (in most cases) chemical labels of long-term integrated information that – within the period of record – can be considered as stable. In addition to natural processes that

cause variations in the isotopic composition of elements, a number of technological effects can cause changes in the isotopic composition of elements. This includes fractionation during technological processing by e.g. electrolysis, distillation, and nuclear applications. As the induced isotopic shifts may be specific for e.g. a certain production process or plant, these isotopes are increasingly being used as environmental tracers (e.g. U, Pb, Cu, Zn, Sn).

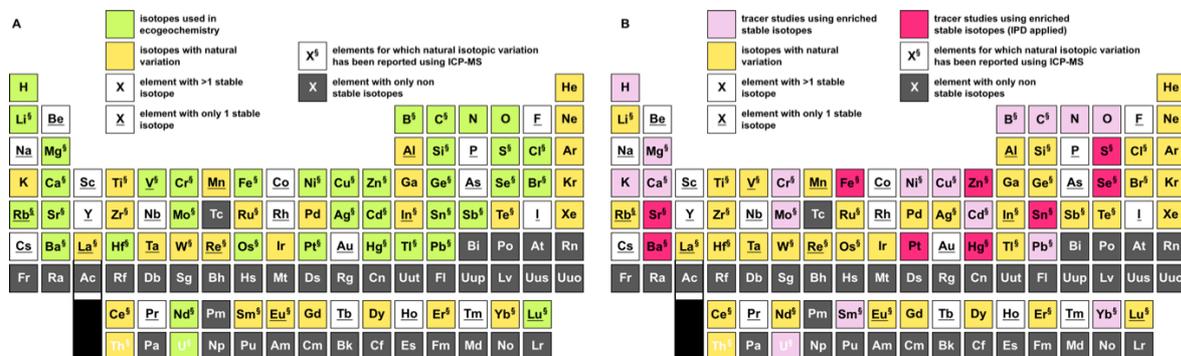
Details about the theoretical principles of isotope effects and isotope fractionation can be found in Hoefs [64,65] and Faure [66]. Furthermore, only recently, J. G. Wiedehold gave a comprehensive review about the origin of metal and metalloid isotope variation providing a detailed discussion about the basic concepts of known fractionation processes of metals [67].

Isotopic systems have been of interest in ecosystem research ever since and have proven to be very powerful tools in both paleoecological as well as modern timescales and across a wide range of spatial dimensions [68-70]. The effective and successful use of the variation of the natural isotopic composition of an element as tag for tracing requires some preconditions to be met: A significant variation of the isotopic composition (i.e. to be measurable by existing analytical tools) of the element chosen as tracer is necessary besides the take-up, integration and record of the isotope tracer (preferably in a time resolved manner) in a sufficient amount and without (or with determinable) fractionation.

From the early years of ecosystem research, a clear focus has been laid on applying light stable isotopes (H, C, N, S and O). The variation of the isotopic composition of the light stable isotopes is mainly induced by natural biological and biochemical activities (e.g. photosynthesis, microbiological activity, trophic level, metabolism, physiology) and climatic processes (e.g. precipitation, temperature, diffusion) [64,71]. Isotope systematics of e.g. N and C have been applied frequently to assess estuarine food-web eutrophication in the coastal zone caused by anthropogenic activity and thus contribute to the development of management strategies to cope with these additional input sources [72-74]. Besides, noble gases (He, Ne, Ar, Kr and Xe) have been assessed for the investigation of aquatic ecosystems, for e.g. tracing climatic variations [75].

More and more, new isotopic systems have been recognized for their potential to interpret ecosystem processes [76,77]. The isotopic variation of these elements is dominated by chemical and physical reactions (such as e.g. radioactive decay or redox reactions) or diffusion (in natural or industrial (and thus anthropogenically induced) processes). In many cases, natural processes depend on the environmental conditions (e.g. temperature or pH) like (bio)mineralization or weathering. Therefore, the isotopic composition of these elements can be used as a fingerprint with the relation to the source of the element but also to decipher processes behind fractionation.

Browsing through literature certainly gives an impression of which isotopic systems have already been exhaustively or at least comparably well studied. **Fig. 3A** highlights the isotopic systems that have already been used in the field of analytical ecogeochemistry.



**Fig. 3 (A)** Periodic table of the elements: elements for which isotope ratio data acquired in the field of analytical ecogeochemistry have been published (highlighted in green). **(B)** Periodic table of the elements: elements for which provenance studies or other using isotopically enriched tracers have been published (highlighted in shiny pink). Tracer studies where isotope pattern deconvolution (IPD) has been applied for data evaluation are highlighted in pink)

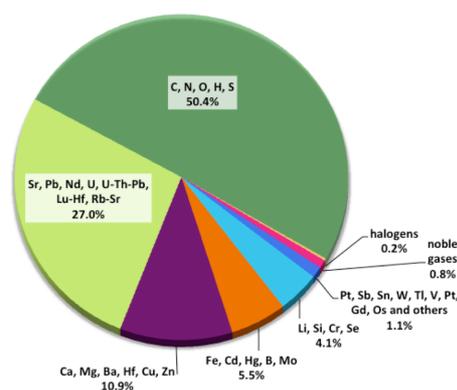
In literature, the isotopic systems are frequently grouped and discussed in the context of their fields of application and can be roughly classified into the following subcategories, with the one or other category crossing the boundaries:

- Geochronological, cosmochemical and radionuclide applications
- Forensic and archaeometric applications
- Industrial applications and material science
- Environmental and (paleo)climatic applications
- Biological and medical applications
- Applications in life-science research

Only recently, the applications of long-established as well as novel isotopic systems have been summarized in a number of comprehensive book chapters and reviews, e.g. geochronological dating [66,78,79] describing U-Th-Pb, Lu-Hf, Pt-Re-Os; forensic applications with a focus on Pb (e.g. crime scene investigation) [80], U and Pu (nuclear forensics) [80], food forensics (Sr, S, Pb, B) [79,80] and environmental applications (Pb, Ag, Cd, Cu, Hg, Sb, Zn) [79,80]; archaeometric applications (Pb, Sr, Nd, Os, Cu, Sn, Sb, B) [79,81]; applications at the geosphere-biosphere interface [82] (Cu, Zn, Fe, Mo, Sr, Ca, Mg, Nd); paleoredox proxy stable metal isotope ratios of U, Mo and Cr [83]; state-of-the-art on the use of stable isotope techniques for studying mineral and trace element metabolism in

humans with special emphasis on the elements Ca, Fe, Zn, Mg, Se, Cu and Mo [84]; other applications in life sciences [79] using Cu, Fe, Zn, Ca, Hg, Sr; and speciation analysis with a focus on the isotopes of Hg, S, Pb, Sb, Cl, Br [85]. In 2015, Wiederhold did another approach to differentiate among applications and distinguished between source- and process-tracing, exemplifying the different types of fractionation processes (e.g. biological cycling, sorption, precipitation) along with published case studies on the different isotopic systems [67].

The isotope ratio charts are headed by the set of the most popular isotopic systems H, N, O, C and S, followed by well-established traditional geochemical isotope tracers such as U-Th-Pb, Lu-Hf, Rb-Sr, Pb, U, Nd and Sr. The ranking list is continued by elements such as Ca, Mg, Hf, Cu and Zn followed by the group of Fe, Cd, Hg, B and Mo as well as Li, Si, Cr, Se. Halogens and noble gases represent a small but considerable group. Finally, there is a list of very novel systems, where for some of them only a handful of papers exist, as they represent challenging and complex systems to analyse. These include e.g. Sb, Pt, Gd, Sn, V and Os. (**Fig. 4**)



**Fig. 4** Distribution of publications between 2010 and 2015 for selected groups of elements

In the group of non-traditional isotopes that has been studied increasingly during the last couple of years, cadmium has drawn much interest. Cd has seven stable isotopes and is considered as one of the ‘newcomers’ in the field of isotope tracers as it can be used to differentiate between natural and anthropogenic sources. Natural isotopic variation of cadmium is mainly caused by mass-dependent processes (with mass-independent fractionation also been reported [86]) and believed to happen e.g. during biological uptake. Industrial Cd emissions are prone to processes that involve evaporation and condensation, which induce significant fractionation effects ( $< 1 \text{ ‰}$  for  $^{114}\text{Cd}/^{110}\text{Cd}$ ), thus providing potential signatures to trace human sources of Cd in the environment [32]. The extent of isotopic fractionation of Cd is rather low compared to the traditional systems, not significantly exceeding the range from  $-3.6 \text{ ‰}$  to  $+3.4 \text{ ‰}$  in terrestrial materials [87]. So far, the largest Cd isotope fractionations were determined in oceanic environments (up to  $4 \text{ ‰}$  for  $^{114}\text{Cd}/^{110}\text{Cd}$ ) and attributed to biological uptake and utilization of dissolved seawater Cd [88]. In the context of aquatic

ecosystems, until today, Cd isotope ratios were used e.g. to trace Cd cycling in riverine and shelf environments in the water mixing zone of Siberian rivers with the Arctic Sea [89] or to trace anthropogenic sources in riverine sediments of a river catchment in North China [90]. Moreover, a correlation of Cd and P and its connection in nutrient utilization is speculated even though still rather unknown [91]. Furthermore, cadmium isotope ratios were found to be a useful tracer for the assignment of soil Cd to industrial sources rather than to its origin from fertilizers [92]. Further details on Cd isotopes can be retrieved e.g. from [79,93].

Antimony (Sb) is one of the isotopic systems that has been investigated scarcely. The natural isotopic variation is rather small, with only about 0.05% reported among industrially important Sb materials [94]. Larger fractionation (up to 1.8 ‰) has been e.g. observed in natural environments between Sb(III) and Sb(V) in aqueous solutions (hydrothermal deposits and seawater reservoirs) [95]. Only two isotopes exist, thus calibration is usually performed using secondary calibration methods, e.g. using external intra-elemental calibration, usually performed using Sn. The mass fractions found in natural samples are often low and sample preparation is tedious in order to separate Sb from the matrix. Sb isotope ratios have served authenticity studies or archaeometric investigations in order to determine the origin of artifacts, e.g. glasses, as well [96,97]. Sb was shown to also reflect seawater redox conditions in its fractionation behavior. Further, Sb isotope ratios were determined in different geological samples and significant, even though smaller variation was observed. Thus, Sb may be used as a paleoredox tracer in oceanic systems or geochemical tracer [95]. Sb is considered an emerging contaminant, present in unpolluted systems at levels  $< 1 \mu\text{g L}^{-1}$  [98]. However, the low levels represent a challenge, especially when it comes to isotope ratios measurements. Further, contamination-free laboratory handling is required as Sb is used as softening agent in the production of plastic material, especially bottles [99,100]. Besides, soil contamination by Sb is constantly increasing mainly due to mining, shooting activities and industrial use [101].

Vanadium represents another system marginally studied and rather challenging, as only two isotopes are present that depict only small isotopic variation in nature. In 2011, Nielsen *et al.* [102] and Prytulak *et al.* [103] published two landmark papers on the analytical method development as well as the use of V isotope ratios. The articles contain both details on chemical separation and mass spectrometric protocols as well as data on V isotope signatures in six widely available reference materials. In 2013, the same authors report  $\delta^{51}\text{V}$  values ranging from 0.27 ‰ to 1.29 ‰ (relative to Alfa Aesar V standard solution) for 64 mantle-derived mafic and ultramafic rocks from diverse localities [104]. Isotopic effects of oxidation state, partial melting, and mineral fractionation factors are discussed in the context of V isotope signatures. V isotope ratios were later combined with Ni and Mo isotope ratios determined in a set of globally distributed crude oils, to investigate potential

stable isotope fractionation. In their study, Ventura *et al.* succeeded to measure the small isotopic variation of V in a complex matrix [105]. The data were combined with Ni and Mo isotope ratios.

Whilst Mo has been discussed in various book chapters recently (see above), Ni isotope ratios, which show a very narrow range of natural variation, have only recently enjoyed more popularity, particularly in geological science. In 2012, Gall *et al.* presented a 3-step purification procedure combining different ion exchange resins. The separation is based on the ability of Ni to form strong complexes with ammonia and dimethylglyoxime for accurately determine Ni isotope ratios using MC ICP-MS [106]. The authors present a natural isotopic variation of Ni in geological material, mainly USGS reference materials, in the range of 0 to +0.2 ‰. In 2013, Gueguen *et al.* published a range for  $\delta^{60/58}\text{Ni}_{\text{NIST SRM 986}}$  between -0.13 and +0.16 ‰ for igneous- and mantle derived rocks. Manganese nodules (Nod A1; P1), shale (SDO-1), coal (CLB-1) and a metal-contaminated soil (NIST SRM 2711) showed values ranging between +0.14 and +1.06 ‰, whereas komatiite-hosted Ni-rich sulfides varied from -0.10 to -1.03 ‰ [107]. Another application focused on the determination of Ni isotope signatures in the soluble phase of rivers, published by Cameron and Vance in 2014, showed that that  $\delta^{60/58}\text{Ni}_{\text{NIST SRM 986}}$  varies between +0.29 to +1.34 ‰. Interestingly, the nickel isotope ratios of rivers are significantly heavier (by up to 1 ‰) than the range for silicate rocks on the continents [108]. In a recent study on biogeochemical Ni cycling, Ratié *et al.* observed an overall trend of heavier isotope depletion between different phases during weathering ( $\Delta^{60}\text{Ni}_{\text{Soil-Bedrock}} = -0.47$  ‰) when studying bedrock, ore and soil samples for tropical weathering effects [109].

Another newcomer in the field of isotope ratio analysis in analytical ecogeochemistry is platinum. In 2002, the IRMM-010 as isotope reference material based on metallic Pt was only recently launched on the market of CRMs [110]. Creech *et al.* presented a method based on double spike MC ICP-MS for the analysis of geological standard reference materials with values of  $\delta^{198/194}\text{Pt}_{\text{IRMM-010}}$  up to 0.4 ‰ [111]. This shows the potential of Pt to be used as geochemical tracer. The system however requires matrix separation [112], especially considering the complex matrices in which Pt (and Pd) are usually of interest (e.g. road dust, geological materials).

Even though ytterbium has not yet found its way to the use of isotopic signatures in environmental samples, first methods to accurately determine Yb isotope ratios in standards have been developed [113,114]. Only recently, Wang *et al.* published comprehensive approach for the measurement of Yb including the suggestion of new Atomic Weight values [115].

Only very few studies have been dedicated to method development for Sn isotope ratio analysis by MC ICP-MS, which may stem from the complexity of the system with 10 stable isotopes, the one with the highest number of naturally occurring stable isotopes. Consequently, also a fair set of isobaric interferences, mainly from Cd, In, Te, Xe have to be handled [116]. Applications direct to the use of

Sn isotopic signatures to determine the origin of Sn in e.g. geological samples or processed Sn in e.g. Bronze products. In 2010 Hausteine *et al.* [117] showed that Sn isotope ratios vary significantly between tin ores originating from the German Erzgebirge and Cornwall, based on a large dataset. This opened doors to use Sn isotope ratio data for provenancing of historic Bronze remnants and thus elucidate possible trading history. Studies were also successfully conducted on corroded Bronze artefacts by the same group [118]. Yamazaki *et al.* investigated bronze artefacts for tin isotope ratio and the assessment of the possible use of Sn isotope signatures for provenancing [119]. The variation of  $\delta^{124/120}\text{Sn}_{\text{NIST SRM 3161a}}$  in six samples taken from excavations spread over China was about 0.4 ‰. The analytical method includes ion/matrix separation and MC ICP-MS analysis including calibration of the mass spectrometer by means of Sb isotopes. Mass-dependent isotope fractionation was shown for cassiterite samples from Japan and China (revealing fractionation of 0.77 ‰ in  $^{124}\text{Sn}/^{120}\text{Sn}$ ) as well by Yamazaki *et al.* [120].

Environmental studies on silver are very rare. One promising paper about Ag isotopes was published by Luo *et al.* in 2010 who presented a sound analytical method coping with the challenge of matrix separation and stabilization of Ag in solution (for the prevention of solution ageing and loss of Ag within short times) as well as accurate measurement using MC ICP-MS (by applying Pd for calibration).  $\delta^{109/107}\text{Ag}_{\text{SRM978a}}$  values for different natural materials are reported, including sediment CRM PACS-2, domestic sludge SRM 2781, industrial sludge 2782, and the fish liver CRM DOLT-4. The isotopic values ranged from  $-0.284 \pm 0.014$  ‰ for CRM DOLT-4 as biological material to  $+0.044 \pm 0.014$  ‰ for industrial sludge SRM 2782. Considering the high precision achieved, the authors showed that Ag has a notable potential for monitoring small natural isotopic fractionations in nature [121].

Moreover, the isotopic systems of the halogens chlorine and bromine should be highlighted. The isotopic variation of chlorine isotopes is fairly large in industrially produced organic chlorine compounds (i.e.  $\delta^{37}\text{Cl}_{\text{SMOC}}$  values (-7 to +6 ‰)) compared to the variation in natural samples (i.e. <1 ‰) [57]. In 2004, Stewart *et al.* published a comprehensive review on the variation of stable chlorine in natural and anthropogenic materials [122]. Traditionally, Cl isotope ratios have been analysed using IRMS, but more and more MC ICP-MS conquers to successfully measure Cl isotope ratios, as well [123]. One major issue is related to continuous environmental pollution by chlorinated aliphatic hydrocarbons, which have been widely used in industries and found their way into the environment. Natural pathways and attenuation can be monitored using Cl isotope ratios (often in combination with C isotopes). Wiegert *et al.* showed the potential of a remediation strategy of chlorinated ethenes through the use of microbacteria based on C and Cl isotope ratios measurements, as dechlorination was indicated by Cl isotope ratios [124]. In 2012 Elsner *et al.* presented a review on compound-specific stable isotope analysis of environmental organic

contaminants, also elucidating the use of Cl isotope ratios to trace chlorine-containing organic compounds [125]. Cl isotope ratios have also been used to trace water sources. For example, Eggenkamp *et al.* investigated the origin of the ground water circulating near the "salinas" (very unique terrestrial inland salt exploitation still in operation) at Rio Maior in Portugal and got insight about groundwater streams and mixing of different water sources [126].

Terrestrial  $\delta^{81}\text{Br}_{\text{SMOB}}$  values range between  $-0.8$  to  $+3.3$  ‰ [57]. In 2010, Gelman and Halicz presented the coupling of gas chromatography to MC ICP-MS for the determination of Br isotopes in organobromine compounds, which represent contaminants to the environment. A difference in the isotopic composition of approximately 2 ‰ between dibromoethane and the brominated aromatic compounds was observed, which is expected to derive from the different production synthesis approaches [127]. The same authors developed a method using on-line oxidation of bromide into bromine and its subsequent introduction into MC ICP-MS by a continuous He flow and analysed different seawater samples for  $\delta^{81}\text{Br}_{\text{SMOB}}$ , showing  $\delta^{81}\text{Br}_{\text{SMOB}}$  values that overlapped within uncertainties [128]. In another study, Du *et al.* [129] presented data on Br isotope ratios in natural waters collected in China. Geothermal groundwater, oilfield water, saline groundwater and salt lake water were analysed and different fractionation effects between bromine and chlorine were shown. The authors hypothesize on different sources and evolutionary processes behind the fractionation. Wei *et al.* presented recently an improved analytical method for the determination of Br isotope ratios for the application to trace Br in its geochemical cycle, pointing to a future project dedicated to study the processes of ore genesis of rare and dispersed mineral deposits in western China [130]. Another method, however using conventional sample introduction for Br isotope ratios analysis by MC ICP-MS was presented in this topical issue by de Gois *et al.* for the analysis of seawater samples [131]. Zakon *et al.* coupled gas chromatography to MC ICP-MS for simultaneous measurement of S, Cl and Br isotope ratios in different (reference) materials [132]. Further details about Cl and Br isotope fractionation can be found in [133,134].

In nature, selenium occurs in four different oxidation states (Se(VI), Se(IV), Se(0), and Se(-II)). The chemical behavior, mobility and bioavailability are strongly dependent on the prevalent redox conditions. A link between Se isotopic fractionation and oxidation processes was for example shown by Schilling *et al.* [135]. The authors showed that Se isotopic fractionation may be induced by microbial or abiotic reduction of Se(VI) and/or Se(IV) to less oxidized Se soil pools. Se isotope ratios bear the potential to show historic redox changes in the ancient oceans through assessment of the Se isotopic signatures recorded in ancient sedimentary rocks [136]. Further, studies on mass independent fractionation of Se in accordance with mass independent fractionation of S isotopes has gained interest during the last years [137]. Se isotopes and Se isotopic fractionation in the context of the study of the mineral and trace element metabolism in humans was comprehensively discussed

recently by Walczyk [84].

Chromium represents another element that occurs in different oxidation states in the natural environment (Cr(+III) and Cr(+VI)); being toxic in the oxidation state +VI. A connection between redox reactions and isotopic fractionation has been shown by e.g. Ellis *et al.* in 2002 [138]. Isotopic fractionation of chromium during reduction processes of hexavalent Cr in laboratory experiments as well as natural waters (from contaminated study sites) revealed  $^{53}\text{Cr}/^{52}\text{Cr}$  shifts of  $3.4 \pm 0.1 \text{ ‰}$  towards lighter ratios from the reactant to the product. The isotopic shifts seem to indicate the extent of reduction, which renders toxic Cr(VI) in the environment immobile and less toxic. Both Cr and Se isotope fractionation were also investigated in another context by Johnson and Bullen, who studied the mass-dependent fractionation of the two elements in low-temperature environments [139]. They showed that based on the redox properties of Se and Cr in the context of isotope fractionation, these elements are potential candidates as recorders of marine chemistry and paleoredox conditions.

In several studies on silicon as well as on lithium isotope ratio fractionation promising characteristics of these elements as indicators of environmental processes were shown. The combination of Si and O isotope ratios to study present and past climate and environmental processes has gained much interest during the last years [140,141]. One big field of research is that dedicated to the study of isotopic fractionation during Si consumption of diatoms from water, which was studied e.g. by Cardinal *et al.* [142]. In their study in the Australian Sector of the Southern Ocean, the authors gained insight about processes that led to significant isotopic variation of Si, showing also significant dependence of fractionation on the latitudinal position.

Another paleoclimate tracer was found in lithium isotope ratios. In a landmark paper by Misra and Froelich [143] a 68-million-year record of lithium isotopes in seawater ( $\delta^7\text{Li}$ ) was reconstructed from planktonic foraminifera. The authors showed that with increased mountain building and changes in continental silicate chemical weathering regimes through the Cenozoic, the isotopic signature of riverine dissolved  $\delta^7\text{Li}$  (measured relative to NIST SRM 8545) increased from about 3 ‰ to 23 ‰. Further applications of Li isotope as tracers in marine and terrestrial environments are given in a handbook by Burton and Vigier [144].

#### *Isoscapes and their analytical application to ecogeochemical questions*

*Isoscapes* are defined as spatially distributed isotope patterns across landscapes and represent a fundamental tool to track any natural sample to its source, in case natural isotope ratios are used as intrinsic labels [145]. Such isotope landscapes have already been established for both terrestrial and aquatic ecosystems with a focus on light stable isotopes. Isoscapes are generated by combining a hypothesis with geospatial data available, predictions, interpolation based on geological data for

calibrating the isoscape followed by sampling and data acquisition, which finally form the starting point for modeling. West *et al.* published a book [146] and comprehensive compendium [147] about the topic including a summary on data collection and processing, recommendations for appropriate model development and an overview of existing applications. The sampling strategy for generating an isoscape is crucial and strongly depends on the relative geographic distances where significant differences in the isotopic landscape are expected due to e.g. variations in the underlying geology. These factors are to be combined with the research question. Depending on the possible track of sample under investigation, both large-scale and small-scale scenarios are possible. It is obvious that more effort has to be put into isotopic mapping of a large area of interest at the same spatial resolution compared to a small territory. Nonetheless, the moving or transport distance of a sample under investigation as well as the expected degree of isotopic variation in the area vigorously trigger these decisions. Additionally, all relevant input sources and fluxes (e.g. heterogeneity of the geological underground, hydrological mixing, mixing of groundwater sources, mixing of air sources or anthropogenic input sources) within the observed zone need to be determined as they account for the complexity of establishing an isoscape. Isoscapes have been established for light stable isotopes, e.g. O and H, have been assessed and are widely used e.g. for climatic models [148]. These isoscapes include the temporal variation, as well. In case of heavy or so-called non-traditional isotopes, the application and establishment of isoscapes can be considered as something new and truly challenging. In case of e.g. the Sr isotopic system, the establishment of a suitable isoscape is not exclusively based on geospatial data and isotopic analysis of the underlying bedrock. The major interest lies very often in the Sr fraction, which is bioavailable to a plant or animal or human organism: Sr entering the food web is made up of a mixture of different input sources (e.g. Sr from weathered rocks, hydrological fluxes, precipitation, etc.) that account for the Sr fraction, which is taken up by plants and animals. Thus, an isotope map suitable to support e.g. migration research or authenticity studies has to take several input sources that are considered to be significant into account. Isoscapes for the bioavailable Sr isotope patterns have been established in areas of the United Kingdom [149,150] and North America [151], representing the first isotope maps of their kind. Apart from Sr, there have only been a few attempts to establish isoscapes so far. One example on the use of Nd isotopes was published by Brems *et al.*, where the Mediterranean coast beach sand was characterized and mapped for Nd in order to provenance Roman ancient glass to the possible origin of the raw material [152]. The major challenge when establishing isoscapes seems to lie in the assignment of the determining input factors and the establishment of a suitable and thus correct model to define an algorithm for interpolation between analysed samples (i.e. geospatial data points).

### ISOTOPIC LABELING USING ENRICHED STABLE ISOTOPES (*extrinsic marking*)

Enriched stable isotopes can be introduced as *extrinsic* tracers into a system and a notable number of elements have been applied to study biological and ecological processes (**Fig. 3B**). The intentional transfer of enriched stable isotope tracers into biological systems hereby aims at artificially inducing a significant change in the natural isotopic composition of an element: This allows for e.g. studying the fate and fluxes of metals, trace elements and elemental species in an ecosystem or organism or provides an intrinsic marker of particular compartments (such as of chemicals, individual plants or groups of animals - just to name a few examples). The use of enriched stable isotopes as tracers for various applications has been summarized and discussed comprehensively by Stürup *et al.* [153]. The authors picture in detail the advantages of using enriched stable isotope tracers over radioisotopes, as well.

The method as such can be considered as outstanding tool for tracer studies in environmental systems. Nonetheless, the introduction of an isotopically enriched tracer makes human interference into the natural system under investigation unpreventable. Therefore, the least impact on the natural conditions by the administration of an isotope tracer is of priority and may require elaborated preparatory measures to envelop or incorporate the tracer isotope material into a suitable vector for e.g. oral or intravenous admission. Furthermore, possible negative impacts (e.g. toxicity, medical intolerance) of tracers on the system (e.g. an organism, the environment under investigation) have to be taken into account as well as the selected tracer dose has to be set to acceptable levels still given that the tracer levels introduce a significant mark in the sample over the observation period. This will finally leave the analytical chemist with the challenge of deducing very low molar amounts of tracer material in the biological sample. In case of systems with more than two stable isotopes, multiple isotopic spikes enhance the discrimination power significantly [154].

Due to the shoreless potential of the methodology, the number of publications dealing with applications of isotope spikes as tracers to address research questions in *real world systems* is constantly increasing. A number of examples proved the applicability in human studies, as well (e.g. Ni in humans [155], Zn in feces [156], Cu in blood of patients with Parkinson's disease in comparison to healthy patients [157].) Only recently, Urgast and Feldmann [158] gave a general perspective on the capabilities of using also laser ablation-(multiple collector)-inductively coupled plasma mass spectrometry (LA-(MC) ICP-MS) for imaging of biological samples carrying an introduced stable isotope tracer, including a short discussion on the beneficial characteristics as well as the limitations of the method. Besides the simple detection of the enriched stable isotope tracer, alternative data processing strategies are required, which enable the gain of significantly more information about tracer pathways. Regression-based isotope pattern deconvolution (IPD) analyses as simplified alternative evaluation strategy to double spike isotope dilution calculations has first been suggested

by Meija *et al.* [159] in 2006. Details about the basic mathematical considerations behind multiple linear regression models being used for the evaluation of isotope data can be found elsewhere [159-161]. The outstanding advantage of this mathematical tool lies in the possibility of deducing the individual contribution of each input source (referred to as molar fraction) to a blend of the natural isotope source and the introduced isotopically enriched tracer, thus allowing for the deconvolution of interconverting analytes [162]. Based on IPD, even molar spike fractions of < 0.1% can be determined accurately, which was shown on the example of Sr isotope ratio analysis using LA-MC ICP-MS on fish otoliths containing a Sr double spike for transgenerational marking of fish [154,163]. Since 2007, isotope pattern deconvolution involving enriched isotopes in biological entities has been successfully applied for e.g.,  $^{57}\text{Fe}$  in cucumber plants [164];  $^{74}\text{Se}$  and  $^{77}\text{Se}$  in lactating rats [165] and  $^{77}\text{Se}$  in human serum [166];  $^{135}\text{Ba}$  and  $^{137}\text{Ba}$  in fish tissues [167,168];  $^{67}\text{Zn}$  and  $^{70}\text{Zn}$  in rat brain thin sections [169,170]. The methodology has also been picked up for forensic and environmental applications such as the authentication of explosives tagged with a dual isotope spike of tin ( $^{117}\text{Sn}$  and  $^{119}\text{Sn}$ ) [171] or the analyses of platinum ( $^{194}\text{Pt}$ ) in environmental samples [172]. One big field of application lies in transgenerational marking of fish as example of applying an extrinsic isotope tag, a concept developed by Schroder [173] and Buckley [174] based on the findings by Volk [175] and Kalish [176] who showed that the chemical composition of the maternal habitat is transferred to the eggs and consequently to the otolith region of the offspring fish. Since then, the method has been applied successfully and accepted as highly potential labeling tool for tracking of fish. Important ecological questions like larval dispersal, homing of fish and the success of restoration measures by directly marking fish that migrate into those sections for spawning could be tackled [168,177]. Until today, above all, stable Sr spikes [154,178] and Ba isotopes [168] have been successfully used in this context.

## Conclusions

Undisputedly, isotope ratio analysis has achieved impressive results in analytical ecogeochemistry over the last decades. Currently, trends go towards the exploitation of more and more isotopic systems for diverse questions, since the small isotopic shifts are believed to elucidate natural processes, which could not be tackled using other indicators so far. However, pioneering work is still required to explore the small isotopic variations in these systems with the required accuracy and uncertainty in order to avoid that scientific conclusions are drawn from analytical artifacts. Assuming that sample preparation and matrix separation are not sources for erroneous results, measurements need to be undertaken with appropriate data reduction including enhanced calibration strategies and uncertainty propagation. The latter is often neglected and analytical errors published in a number of studies are still limited to measurement precisions. This is often not sufficient on a long-

term perspective, especially when it comes to fundamental interpretation phantasies to draw conclusions from (metrologically) non-significantly different data points. A sound metrological basis is therefore the ultimate requirement: Method validation including the consideration of possible input factors to the final uncertainty on the isotope values must always be verified and fulfilled in order to obtain accurate measurement results. Needless to say that there is a tremendous and increasing demand for reliable matrix reference materials as we face an uncountable range of matrices in analytical ecogeochemistry. All these considerations put the analytical chemist in an extremely responsible position even though a specific application may be the major trigger for the measurement.

The isotopic forecast in analytical ecogeochemistry is very promising and certainly there is still much more to discover. Isotopic systems will continue to be auspicious tools to tell the one or other new story in the future.

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### **Conflict of Interest**

The authors declare no conflict of interest.

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