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Matrix separation of Sr and Pb for isotopic ratio analysis of Ca-rich samples via an automated simultaneous separation procedure

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Abstract

This paper presents a systematic investigation of the effects of Ca on the matrix separation of Sr and Pb and subsequent isotope-amount ratio measurements using a variety of synthetic solutions and reference materials with varying Ca content during the application of an automated analyte/matrix separation approach. The separation method based on the DGA resin was optimized by using increased column bed volumes, comparing two different column sizes (1-mL and 3-mL-bed volume). Certified reference materials (synthetic calcium carbonate – MACS-3, basalt – BCR-2, sagittal otolith – FEBS-1, bone meal – NIST SRM 1486, bone ash – NIST SRM 1400, and skim milk powder – BCR-063R) with varying Ca content, Ca/Sr and

Ca/Pb mass fraction ratios were separated using the optimized method and analyzed for the Sr and Pb isotopic composition by multi collector inductively coupled plasma mass spectrometry (MC ICP-MS). The developed separation method based on the 3-mL-bed volume column provides quantitative recoveries (84% to 105% for Sr, 77 % to 96% for Pb), while maintaining a quantitative separation of Sr and Pb. Procedural blank levels were $<0.04 \text{ ng g}^{-1}$ for Sr and $<0.05 \text{ ng g}^{-1}$ for Pb, respectively. The method allows for the automated extraction of Sr in Ca-rich matrices with Ca/Sr mass fraction ratios of up to 4051 corresponding to an absolute Ca load of $965 \mu\text{g} \pm 86 \mu\text{g}$ (BCR-063R, milk powder). Furthermore, the method allows for the simultaneous extraction of Pb from these matrices showing Ca/Pb mass fraction ratios of up to 42095 corresponding to an absolute Ca load of $761 \mu\text{g} \pm 122 \mu\text{g}$ on column (NIST SRM 1400, bone tissue), respectively. This results in at least 5-times higher tolerable Ca loads compared to previous methods. Measured $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values of FEBS-1 ($-1.58 \text{ ‰} \pm 0.23 \text{ ‰}$ ($U, k = 2$)), MACS-3 ($-4.11 \text{ ‰} \pm 0.29 \text{ ‰}$ ($U, k = 2$)) and NIST SRM 1400 ($3.87 \text{ ‰} \pm 0.23 \text{ ‰}$ ($U, k = 2$)) were in accordance with published results. Measured $\delta(^{208}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ ($-29.87 \text{ ‰} \pm 0.07 \text{ ‰}$ ($U, k = 2$)), $\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ ($-66.95 \text{ ‰} \pm 0.17 \text{ ‰}$ ($U, k = 2$)) and $\delta(^{208}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ ($51.55 \text{ ‰} \pm 0.26 \text{ ‰}$ ($U, k = 2$)) values of NIST SRM 1400 were also in accordance with published results. Furthermore, we propose a $n(^{87}\text{Sr})/n(^{86}\text{Sr})$ isotope-amount ratio of 0.70884 ± 0.00017 ($U, k = 2$) corresponding to a $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ value of $-2.11 \text{ ‰} \pm 0.24 \text{ ‰}$ ($U, k = 2$) for the BCR-063R reference material. Additionally, we propose a $n(^{208}\text{Pb})/n(^{206}\text{Pb})$ isotope-amount ratio of 2.0793 ± 0.0001 ($U, k = 2$) corresponding to a $\delta(^{208}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ of $-40.97 \text{ ‰} \pm 0.05 \text{ ‰}$ ($U, k = 2$), a $n(^{207}\text{Pb})/n(^{206}\text{Pb})$ isotope-amount ratio of 0.84995 ± 0.00008 ($U, k = 2$) corresponding to a $\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ of $-70.72 \text{ ‰} \pm 0.09 \text{ ‰}$ ($U, k = 2$) and a $n(^{208}\text{Pb})/n(^{204}\text{Pb})$ isotope-amount ratio of 38.221 ± 0.008 ($U, k = 2$) corresponding to a $\delta(^{208}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ of $40.82 \text{ ‰} \pm 0.23 \text{ ‰}$ ($U, k = 2$) for the reference material MACS-3.

Keywords

Analyte/matrix separation, MC ICP-MS, DGA Resin, Ca-rich samples, Extraction chromatography

1. Introduction

Sr and Pb isotope ratio analysis in Ca-rich matrices are highly relevant in a variety of fields such as archaeometry [1-3], food traceability and authentication [4] or geochemistry [5]. The accurate determination of Sr and Pb isotope ratios by multi collector inductively coupled plasma mass spectrometry (MC ICP-MS) requires the separation of the analytes from the sample matrix before their measurement, in order to avoid matrix-related effects [6], e.g. isobaric and polyatomic interferences, signal instability, varying instrumental isotopic fractionation effects and loss of sensitivity due to signal suppression and material deposition on the cones from aqueous solutions containing $>200 \mu\text{g g}^{-1}$ Ca [7] over time. Furthermore, quantitative extraction (i.e. full recovery) of the analytes is favorable in order to avoid effects caused by a possible isotope fractionation during sample preparation [8].

The presence of Ca poses problems in Sr isotope ratio analysis as Ca-based polyatomic interferences (Ca-argides and Ca-dimers) formed in the plasma potentially occur on all nominal Sr isotope masses resulting in biased isotope ratio measurements [6, 7, 9-12]. Beside numerous studies on the effects of Ca on Sr isotope ratios in laser ablation-based analysis of solid samples without the possibility of analyte/matrix separation prior to the measurement, solution-based analysis may also suffer from the presence of Ca, leading to biased Sr isotope ratios. Aqueous spiking experiments performed by Ehrlich *et al.* [7], Waight *et al.* [12] and Irrgeher *et al.* [13] demonstrated that for Ca/Sr mass fraction ratios of 10 or higher (with experiments being performed at Ca mass fractions $>2 \mu\text{g g}^{-1}$) pronounced matrix effects occur. In consequence, significant interferences on all Sr isotopes were observed, which resulted in overall lower $n(^{87}\text{Sr})/n(^{86}\text{Sr})$ isotope-amount ratios. Ehrlich *et al.* [7] noted that in case the $n(^{87}\text{Sr})/n(^{86}\text{Sr})$ isotope-amount ratio in carbonates is corrected for internal instrumental fractionation (IIF) via an accepted standard $n(^{86}\text{Sr})/n(^{88}\text{Sr})$ isotope-amount ratio, the impact of Ca-based polyatomic interferences is also corrected for. As a consequence, this indicates that unseparated samples can be processed. This concept is misleading since the correction for IIF is not an adequate approach for correction of other bias effects such as spectral interferences. Moreover, the ratio of Ca-bearing interferences between the masses 86, 87 and 88 do not correspond to the abundances of Sr. The concept holds therefore only true up to a $(^{88}\text{Sr})/(\text{Ca-Ca} + \text{Ca-Ar interferences})$ signal ratio of about 1/4000 taking an uncertainty of the final $n(^{86}\text{Sr})/n(^{88}\text{Sr})$ isotope-amount ratio of 100 ppm into account. Besides, measurements of $n(^i\text{Sr})/n(^i\text{Sr})$ isotope-amount ratios in unseparated samples containing phosphorous (e.g. hydroxyapatite samples such as teeth and bones) would suffer from additional polyatomic interferences ($(\text{Ar-P-O})^+$ and $(\text{Ca-P-O})^+$) on masses 85 (used for Rb correction), 87 and 88 respectively [10]. It has to be

noted, that today the approach of internal IIF correction needs to be considered with caution since recent studies proved significant mass-dependent fractionation of the stable isotopes of Sr [14, 15], negating the assumption of a constant $n(^{86}\text{Sr})/n(^{88}\text{Sr})$ isotope-amount ratio [10, 16]. As a consequence, an automatically linked correction for Ca-based polyatomic interferences with the IIF correction cannot be expected when applying state-of-the-art internal inter-elemental IIF correction following standard protocols [13, 16-20].

To distinguish Ca-argides from Sr, a resolving power of $(m/z)/(\Delta m/z)$ of ca. >9200 would be required [12], which cannot be achieved with today's commercially available sector field mass spectrometers [21, 22]. Besides, unwanted IIF effects due to the matrix should be avoided. Therefore, an effective Ca removal during sample preparation is crucial to obtain accurate Sr isotope ratios when analyzing Ca-rich sample matrices.

For decades, separations of various isotopic systems (e.g. Sr, Pb, Nd) have been accomplished conventionally by mostly manual processing of samples using ion-exchange or ion-extraction resins. A comprehensive overview of applications of both manual and automated separation procedures and schemes including information on the used resin products and analyzed isotope systems was recently published by Retzmann *et al.* [23]. In 2012, a new, commercially available system (prepFAST-MCTM, Elemental Scientific, Omaha, USA) was introduced to the market, which allows for the fully automated separation of selected analyte elements from the matrix for subsequent isotope ratio analysis. Based on work conducted by Romaniello *et al.* [24] the manufacturer sells a commercially available method developed for Sr and Ca isotope ratio analysis using the DGA Resin (TrisKem International, Bruz, France) [25]. The method uses 5 mol L⁻¹ nitric acid for the final elution of the purified Sr fraction. Furthermore, Romaniello *et al.* [24] showed that the total amount of Ca, which can be loaded onto the DGA Resin in a 1-mL-bed volume column, is limited and the authors recommended to match a total Ca load of <100 µg Ca.

Recent studies by Retzmann *et al.* [23] present another separation protocol based on the DGA Resin. The new method allows to separate multiple analytes (Sr, Pb and Nd) from the same complex matrix solutions, even in the presence of large amounts of major component elements, such as Ca of up to 60 µg, on a 1-mL-bed volume column. Furthermore, the authors proved that 0.2 mol L⁻¹ nitric acid is applicable as alternative reagent for the elution of the Sr fraction from solutions of acid digested sediment samples. Nevertheless, a significant co-elution of Sr and Pb was described, which could not be overcome. As a consequence, the authors recommended to set a cut-off favoring a quantitative recovery of Sr, which resulted in a loss of around 10% of the total Pb amount.

One major limitation of both separation methods is the limited applicability to absolute Ca amounts <100 µg. This may result in insufficient Sr amounts present in the final elution solution for isotope ratio measurement, when separating Sr from Ca-rich samples such as bones, teeth or milk powder (as three commonly used matrices). This fact may become even more critical when analyzing Pb isotope ratios in the same samples, as the Pb content in Ca-rich matrices is often significantly lower than the Sr content. This results in rather large amounts of sample to be processed in analyte/matrix separation in order to achieve sufficient amounts of Sr and Pb (usually >10 ng) for accurate isotopic analysis. Consequently, substantial Ca loads have to be managed and a possible loss of Pb caused by an overlap of Sr and Pb could occur.

In this study, the effect of increasing Ca amounts on the separation efficiency of Sr, Pb and Ca using DGA Resin was systematically investigated with the aim to develop a robust automated sample preparation approach for the processing of samples with variable and substantially higher tolerable Ca contents (>100 µg). The optimized method was applied to various Ca-rich reference materials for subsequent Sr and Pb isotope ratio analysis as a proof of concept.

2. Experimental

Sample preparation and analyte/matrix separation were carried out at the University of Natural Resources and Life Sciences Tulln, Austria. Isotope ratio measurements were performed at the Helmholtz-Zentrum Geesthacht, Germany. All procedures were accomplished in cleanrooms (ISO class 8 according to ISO 14644-1) at both facilities.

2.1 Reagents, reference materials, resin and test solutions

Type I reagent-grade water (18 MΩ cm) (F+L GmbH, Vienna, Austria) was further purified by sub-boiling distillation (Milestone-MLS GmbH, Leutkirch, Germany). Analytical reagent-grade nitric acid (65% w/w, Merck-Millipore, Darmstadt, Germany) was purified by double sub-boiling using a Savillex DST-1000 sub-boiling distillation system (AHF Analysentechnik, Tübingen, Germany). Polyethylene (PE) flasks, tubes and pipette tips (VWR International, Radnor, USA), as well as perfluoroalkoxy (PFA) screw cap vials (Savillex, Eden Prairie, USA) were pre-cleaned in a two-stage washing procedure using nitric acid (10% w/w and 1% w/w respectively).

Dilutions of multielement stock solutions (Inorganic Ventures, Christiansburg, USA and ICP multielemental standard Merck VI, 10 mg L⁻¹; Merck-Millipore) were used to prepare calibration standards for quantification.

Certified reference materials MACS-3 (synthetic calcium carbonate, USGS, Reston, USA), BCR-2 (basalt, USGS), FEBS-1 (sagittal otolith, NRC, Ottawa, Canada), NIST SRM 1486 (bone meal, NIST, Gaithersburg, USA), NIST SRM 1400 (bone ash, NIST), and BCR-063R (milk powder, IRMM, Geel, Belgium) were analyzed throughout this study. More information related to the used reference materials can be found in Table 1 and in literature [26-28].

Details about preparation and handling of the DGA Resin (part. No. DN-B25-S, TrisKem International, mean particle size of 50 – 100 μm) can be found elsewhere [23].

Eight test solution containing 500 ng g^{-1} Sr (NIST SRM 987, highly purified SrCO_3 , NIST) and 50 ng g^{-1} Pb (NIST SRM 981, high purity lead metal, NIST), spiked with increasing Ca amounts (0, 1, 50, 100, 200, 300, 400, and 500 $\mu\text{g g}^{-1}$ – prepared from a 1 g L^{-1} single-element standard (Inorganic Ventures)) were prepared in 2 mol L^{-1} nitric acid to evaluate the retention behavior of Sr, Pb and Ca.

Table 1 Investigated reference materials and their Sr, Pb and Ca content as given in the original certificates.

Reference material	Material	Sr content [$\mu\text{g g}^{-1}$]	Pb content [$\mu\text{g g}^{-1}$]	Ca content [mg g^{-1}]	Ca/Sr mass fraction ratio	Ca/Pb mass fraction ratio
MACS-3	synthetic CaCO_3	6760 ± 350	56.5 ± 1.8	376.9 ± 5.2	55.8 ± 1.5	6671 ± 184
BCR-2	basalt	346 ± 14	11 ± 2	50.9 ± 0.8	147.1 ± 4.6	4627 ± 145
FEBS-1	otolith	2055 ± 79	0.40-0.77	383 ± 14	186.4 ± 1.4	957500-497403
NIST SRM 1486	bone meal	264 ± 7	1.335 ± 0.014	265.8 ± 2.4	1007 ± 18	199101 ± 3595
NIST SRM 1400	bone ash	249 ± 7	9.07 ± 0.12	381.8 ± 1.3	1533 ± 10	42095 ± 287
BCR-063R	milk powder	$3.33^* \pm 0.24^{**}$	0.0185 ± 0.0027	13.49 ± 0.10	4051 ± 56	729189 ± 10810

* no certified value, measured value ($n = 9$, replicate digest)

** 1 SD ($n = 9$)

2.2 Sample digestion

Between 3 mg and 140 mg of the reference materials MACS-3, FEBS-1, NIST SRM 1486, NIST SRM 1400 and BCR-063R were weighed into a 15 mL PFA screw cap beaker and submerged with 1.4 mL double sub-boiled nitric acid and 0.35 mL hydrogen peroxide (30%, w/w). The samples were digested for 2 hours at 120 °C on a hot plate. After digestion, the solution was transferred quantitatively to a test tube and diluted quantitatively to a final volume of 10 mL with sub-boiled water, leading to a final concentration of 2 mol L⁻¹ nitric acid.

BCR-2 reference material was leached according to Jweda *et al.* [27] in order to remove possible contamination of the reference material, which potentially originated from the grinding process of the reference material [29]. The leached powder was dried and 100 mg were digested according to Retzmann *et al.* [23]. 8 mL of the digested solution were evaporated on a hot plate and re-dissolved in 1 mL of 2 mol L⁻¹ nitric acid prior to separation.

Analyte recoveries in the digests were found to be quantitative throughout all the experiments. Therefore, a complete digestion can be assumed.

2.3 Multielemental analysis

Multielemental analyses of the samples were performed using a quadrupole inductively coupled plasma mass spectrometer, ICP-QMS (NexION 350D, PerkinElmer, Ontario, Canada) coupled to an ESI SC-2 DX FAST (Elemental Scientific) autosampler at the University of Natural Resources and Life Sciences Tulln. All samples were diluted by a factor of 10 prior to analysis using diluted nitric acid (2% w/w).

The multielemental screening to determine Sr, Pb and Ca concentrations in the collected fractions was accomplished by external calibration (9-point calibration ranging from 0.1 ng g⁻¹ to 150 ng g⁻¹) with standards prepared gravimetrically from a commercially available multielement stock solution (ICP multielement standard Merck VI, 30 Elements in nitric acid 10-1000 mg L⁻¹) including 10 ng g⁻¹ indium (In) (prepared from an In stock solution, Merck-Millipore) as internal normalization standard. General instrumental setting for the multielement measurements are cited in detail elsewhere [23]. The Limits of Quantification (*LOD*) were calculated according to DIN ISO 11843-2 [30]. Therefore, the *LOD* is defined as 3 x *SD* of the blank. Total combined uncertainties for multielement analysis were calculated using a simplified Kragten approach [31]. The significant number of digits of content and recoveries in section 3.1 and 3.2 (and corresponding tables) are given according to GUM and EURACHEM guidelines, whereby the uncertainty determines the significant number of digits to be presented with the value.

2.4 Sr and Pb isotope ratio analysis

Sr and Pb isotopic ratio measurements were performed at the Helmholtz-Zentrum Geesthacht (Department of Marine Bioanalytical Chemistry) using a multi collector ICP-MS (MC ICP-MS) instrument (Nu Plasma II, Nu Instruments Ltd, Wrexham, UK). The instrument was equipped with a desolvation nebulization membrane unit (APEX Ω , Elemental Scientific, Omaha, USA) as sample introduction system. Separated Sr fractions were directly diluted with nitric acid (2% w/w) to achieve a Sr concentration in the measurement solution of 65 ng g⁻¹. A solution of NIST SRM 987 (NIST) with a concentration of 65 ng g⁻¹ was used as isotopic reference for standard-sample bracketing (SSB) in Sr isotopic analysis. The separated Pb fractions were evaporated to dryness on a hot plate at 85°C and re-dissolved in nitric acid (2 % w/w) prior to isotopic analysis to achieve a Pb concentration in the measurement solution of 10 ng g⁻¹. A solution of NIST SRM 981 (NIST) with a concentration of 10 ng g⁻¹ was used as isotopic reference for SSB in Pb isotopic analysis.

Concentrations of samples and SSB-standards were matched within $\pm 10\%$. Separated Sr fractions and NIST SRM 987 solutions were spiked with a Zr solution (Merck-Millipore) to allow for internal inter-elemental IIF correction as described in detail elsewhere [13, 16-19, 23]. Data collection for both isotopic systems was accomplished by recording a total of 60 measurements per sample over a period of 300 s with an integration time of 10 s. The ‘measure zero’ method implemented in the Nu Plasma instrument software was used for blank correction by aspirating solutions of ultra-pure nitric acid (2% w/w) prior to every set of 5 samples. The obtained instrumental precision for $n(^{87}\text{Sr})/n(^{86}\text{Sr})$ was typically 6 ppm, for $n(^{208}\text{Pb})/n(^{206}\text{Pb})$ 20 ppm, respectively. A detailed description of the instrument configuration can be found in Retzmann *et al.* [23].

The $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ and $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values (in ‰) and absolute $n(^{87}\text{Sr})/n(^{86}\text{Sr})$ isotope-amount ratios were calculated after correction of residual Rb interferences of $^{87}\text{Rb}^+$ on $^{87}\text{Sr}^+$ as described in Retzmann *et al.* [23]. Isotope ratios $\delta(^{208}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$, $\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$, $\delta(^{208}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ and absolute Pb isotope-amount ratios were calculated after correction of residual Hg interferences of $^{204}\text{Hg}^+$ on $^{204}\text{Pb}^+$ as described in Retzmann *et al.* [23]. All values provided for Sr and Pb isotopic composition in certified reference materials were corrected for IIF using standard SSB according to [13, 16-19, 23]. Since Ca showed significant signal suppression effects on the Zr intensity, additional IIF correction using Zr as internal standard was not applicable for the unseparated samples (see section 3.3.3). As a consequence, all data were corrected for IIF by SSB. The long-term stability

of the mass fractionation was monitored over time using the reference values. No significant change could be observed within a measurement sequence. As the natural fractionation of $n(^{88}\text{Sr})/n(^{86}\text{Sr})$ is significant with respect to the uncertainties obtained for $n(^{87}\text{Sr})/n(^{86}\text{Sr})$ after internal IIF correction, this approach was considered inappropriate and not applied in this study. A comprehensive investigation on the different calibration approaches is provided elsewhere [16, 20].

Total combined uncertainties for Sr and Pb isotope ratio analysis were calculated using a simplified Kragten approach according to the protocol of Horsky *et al.* [16] who presented a detailed instructive procedure for the calculation of combined uncertainties for Sr isotope-amount ratios using three strategies of correction for IIF including traditional internal correction, standard-sample bracketing, and a combination of both, using Zr as internal standard. Note, in Fig. 1, 2, 3, 4 and Table 3, 4 the significant number of digits of all isotope ratios are given according to GUM and EURACHEM guidelines, whereby the uncertainty determines the significant number of digits to be presented with the value.

2.5 Matrix separation

All matrix separations were performed using the fully automated, low pressure chromatographic sample handling system (prepFAST-MCTM Elemental Scientific) [25]. Self-packed columns with either 1-mL or 3-mL-bed volume (ESI part. No. CF-1000 or CF-3000) of DGA Resin were used in this study. A detailed description of the packing procedure and the function of the prepFAST-MCTM system in general can be found elsewhere [23].

The ‘calibration mode’ of the prepFAST-MCTM was utilized for method optimization and the creation of elution profiles of the individual targeted analytes. The stepwise elution of the separated elements from the column was achieved in this operating mode by pumping small, defined volumes of reagent (e.g. 1 or 2 mL) through the column. Every fraction was eluted into a separate vessel to allow for multielement analysis of individual fractions. The elution steps of Sr (Sr $V = 3$ mL and 8 mL) and Pb ($V = 4$ mL and 10 mL) were collected as two pooled single fractions to determine blank concentrations, as well as to analyze Sr and Pb isotope ratios.

2.6 Optimization of the separation method

Separations of eight synthetic test solutions containing 500 ng g⁻¹ Sr, 50 ng g⁻¹ Pb beside varying amounts of Ca (0, 1, 50, 100, 200, 300, 400, and 500 µg g⁻¹) have been carried out to evaluate the effect of Ca as well as the retention behavior of Sr and Pb on the column. A total amount of 500 ng Sr was chosen to ensure that no additional sampled treatment such as evaporation after the separation was necessary for isotope ratio measurements. Since Pb usually occurs at lower

levels than Sr, a total amount of 50 ng Pb was chosen suitable for subsequent Pb isotope ratio measurements. Therefore, an evaporation step prior to isotope ratio analysis of Pb was necessary.

The effect of Ca on the separation efficiency was systematically investigated following two different approaches:

Approach 1 – separation with a 1-mL-bed volume column

In recent publications [23, 24], 1-mL-bed volume columns have been used for the separation of Sr and Pb using the prepFAST-MCTM system. Based on the results of the previous work [23], an elution scheme for the simultaneous separation of Sr and Pb using 0.2 mol L⁻¹ and 5 mol L⁻¹ nitric acid, respectively was applied (see Table 2 a).

Table 2 a) Elution parameters of the separation procedure for Sr and Pb using a 1-mL-bed volume column; b) elution parameters of the optimized separation procedure of Sr and Pb using a 3-mL-bed volume column

Purpose/ Analyte	<u>a) Sr/Pb method 1-mL-bed volume</u>		<u>b) Sr/Pb method 3-mL-bed volume</u>	
	Volume/flow rate	c (acid)	Volume/flow rate	c (acid)
Condition column	6 mL / 2 mL min ⁻¹	2 mol L ⁻¹ HNO ₃	8 mL / 2 mL min ⁻¹	2 mol L ⁻¹ HNO ₃
Load sample	1 mL* / 1 mL min ⁻¹	2 mol L ⁻¹ HNO ₃	1 mL* / 1 mL min ⁻¹	2 mol L ⁻¹ HNO ₃
Elute matrix	6 mL / 2 mL min ⁻¹	2 mol L ⁻¹ HNO ₃	8 mL / 2 mL min ⁻¹	2 mol L ⁻¹ HNO ₃
Elute Sr	3 mL / 1 mL min ⁻¹	0.2 mol L ⁻¹ HNO ₃	8 mL / 1 mL min ⁻¹	0.2 mol L ⁻¹ HNO ₃
Elute Pb	4 mL / 1 mL min ⁻¹	5 mol L ⁻¹ HNO ₃	10 mL / 1 mL min ⁻¹	5 mol L ⁻¹ HNO ₃
Elute Ca/wash column	10 mL / 1 mL min ⁻¹	0.1 mol L ⁻¹ HCl	15 mL / 1 mL min ⁻¹	0.1 mol L ⁻¹ HCl

* except for MACS-3 (0.5 mL) and BCR-063R (5 mL)

Approach 2 – separation with 3-mL-bed volume column

Additional experiments were carried out with the largest column (3-mL-bed volume) available from ESI. The elution volumes were adjusted according to Table 2 b to test the applicability of the larger column bed volume.

2.7 Application to matrix reference materials and blanks

Both approaches were applied in ‘calibration mode’ of the prepFAST-MCTM system for the separation of various digests of Ca-rich certified reference materials: MACS-3, BCR-2, FEBS-1, NIST SRM 1486, NIST SRM 1400, and BCR-063R. The selected reference materials covered a variety of different matrices as well as varying Ca, Sr and Pb concentrations. A detailed description of the used reference materials can be found in Table 1. The Ca/Sr mass fraction ratios ranged from 55.8 ± 1.5 to 4051 ± 56 , whereas the Pb concentration ranged from

18.5 ng g⁻¹ ± 2.7 ng g⁻¹ to 56.5 µg g⁻¹ ± 1.8 µg g⁻¹, respectively. The amount of sample was adjusted to a Sr amount of at least 270 ng (BCR-063R) and a maximum of 890 ng (MACS-3) for each separation (see Table 3). The amount of Sr was adjusted to ensure that no evaporation after the separation was necessary to allow for direct isotope ratio measurement of the obtained sample solution.

A sample load of 1 mL 2 mol L⁻¹ nitric acid was treated as blank. Blank values were determined by collecting Sr ($V = 3$ mL and 8 mL) and Pb ($V = 4$ mL and 10 mL) fractions.

2.8 Sr and Pb isotope ratio analysis of reference materials

In order to demonstrate the capability of the developed separation method, Sr isotope ratio analysis were performed on the Sr fractions of FEBS-1, MACS-3, NIST SRM 1400 and BCR-063R separated with either 1-mL- and 3-mL-bed volume columns in ‘calibration mode’ of the prepFAST-MCTM system generating pooled single fractions for Sr (see Table 2). The amount of sample was adjusted to a Sr amount of at least 270 ng (BCR-063R) (see EMS Table 1). Pb isotope ratio analysis were performed on the Pb fractions of MACS-3, NIST SRM 1400 and NIST SRM 981 (without Ca spiking) separated with 3-mL-bed volume columns in ‘calibration mode’ of the prepFAST-MCTM system generating pooled single fractions for Pb (see Table 2). The amount of sample was adjusted to Pb amounts between 14 and 18 ng (MACS-3 and NIST SRM 1400) (see EMS Table 1), to ensure appropriate amounts for MC ICP-MS measurements applying 10¹¹ Ω amplifiers. In order to demonstrate the need for separation, the unprocessed digest of the reference materials FEBS-1, NIST SRM 1400 and BCR-063R were analyzed for Sr and Pb amount-of-substance ratios analyzed as well.

The separated Sr fractions were diluted with 2% w/w nitric acid and directly measured via MC ICP-MS, while the unprocessed digests were evaporated to dryness and re-dissolved in 2% w/w nitric acid. The corresponding Pb fractions of the reference materials NIST SRM 981, MACS-3 and NIST SRM 1400 were evaporated to dryness and re-dissolved in 2% w/w nitric acid. All samples were separated in duplicates.

3. Results and Discussion

3.1 Elution behavior of Ca, Sr and Pb

Approach 1 – 1-mL-bed volume column

Fig. 1 a and b display column calibration profiles for the separation of test solutions containing 500 ng g⁻¹ Sr and 50 ng g⁻¹ Pb doped with 100 µg g⁻¹ Ca (Fig. 1 a) and 500 µg g⁻¹ Ca (Fig. 1 b)

respectively using a 1-mL-bed volume column. The increasing Ca amount leads to a shift of the elution window of the Pb peak towards the Sr peak, leading to an increased proportion of Pb in the Sr fraction and an increase of retained Ca within the final Sr fraction (see Fig. 1 a and b, and Fig. 2). Ca/Sr mass fraction ratios ≤ 2 in the eluted Sr fraction ($V = 3$ mL) are found for Ca loads ≤ 200 μg when a 1-mL-bed volume column is applied (see Fig. 2).

The elution of Ca in the final Sr fraction substantially increases (corresponding to Ca/Sr mass fraction ratio of 39 and higher in the eluted Sr fraction) for Ca loads of >300 μg (see Fig. 2). Based on these results, the maximum Ca load should be <200 μg for the 1-mL-bed volume column. This is in accordance with results presented by Romaniello *et al.* [24] who suggested a maximum total amount of <100 μg Ca to be loaded onto the DGA Resin with a bed volume of 1-mL.

Even for low Ca loads, the separation of Pb and Sr cannot be entirely achieved when a 1-mL-bed volume column is used. In Ca-free solutions approximately 7% of Pb co-elutes in the Sr fraction, which is in agreement with previous results as well [23]. Retzmann *et al.* [23] demonstrated, that elution with nitric acid concentrations ranging from 0.1 mol L⁻¹ to 0.5 mol L⁻¹ did not result in a decrease of this co-elution effect.

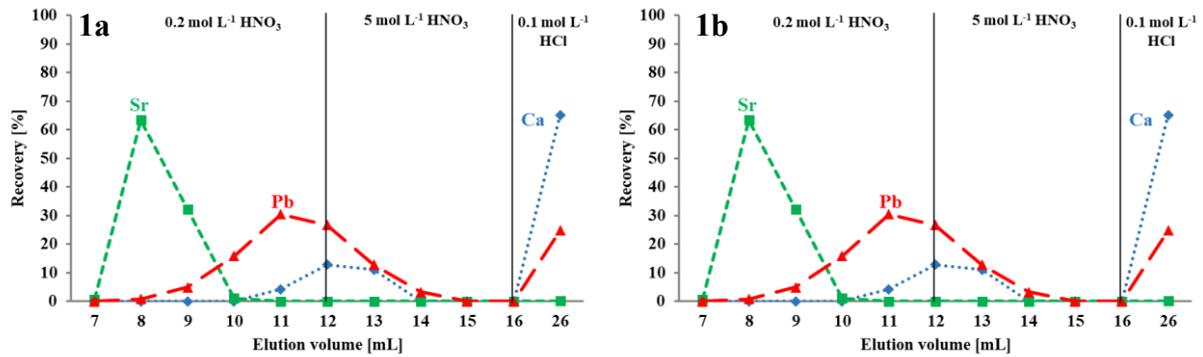
Based on these experiments, the elution volumes to collect pooled single fractions for Sr and Pb of the separation utilizing the 1-mL-bed volume column were chosen accordingly, as given in Table 2 a.

Approach 2 – 3-mL-bed volume column

Fig. 1 c and d show selected column calibration profiles for the separation of Sr, Pb and Ca in test solutions containing 500 ng g⁻¹ Sr, 50 ng g⁻¹ Pb doped with 100 $\mu\text{g g}^{-1}$ Ca (Fig. 1 c) and 500 $\mu\text{g g}^{-1}$ Ca respectively (Fig. 1 d) using a 3-mL-bed volume DGA column. The 3-mL-bed volume column offers superior efficiency for the separation of Sr from Ca and Pb based on the significantly larger amount of the DGA Resin, which can handle higher matrix loads. No significant increase in the Ca/Sr mass fraction ratio ($\text{Ca/Sr} < 1$) in the eluted Sr fraction ($V = 8$ mL) are observed for Ca loads of up to 500 μg (see Fig. 2). This allows for Sr isotope analysis without significant bias caused by the presence of Ca in the measurement solution. Furthermore, Sr and Pb are now separated without any overlap during elution, even in the presence of Ca amounts of up to 500 μg . This is a significant improvement in comparison to the separations realized when applying a 1-mL-bed volume column, where a Pb proportion of around 10% in the Sr fraction needs to be accounted for.

Based on the results of these experiments, the elution volumes to collect pooled single fractions for Sr and Pb of the separation utilizing the 3-mL-bed volume column were chosen accordingly, as given in Table 2 b.

1-mL-bed volume column



3-mL-bed volume column

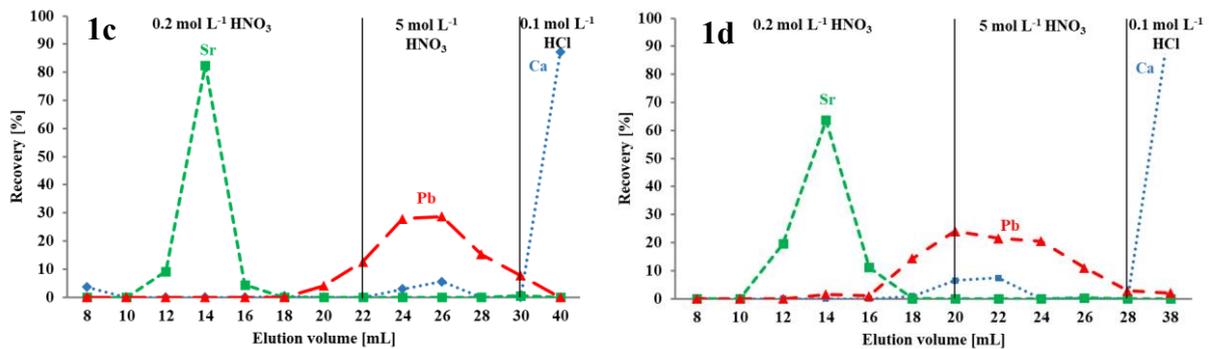


Fig. 1 a) and b) 1-mL-bed volume column: elution profiles of Sr, Pb and Ca for the separation of a test solution containing 500 ng g^{-1} Sr, 50 ng g^{-1} Pb and 100 µg g^{-1} Ca (1a, left) or 500 µg g^{-1} Ca (1b, right). c) and d) 3-mL-bed volume column: elution profiles of Sr, Pb and Ca for the separation of a test solution containing 500 ng g^{-1} Sr, 50 ng g^{-1} Pb and 100 µg g^{-1} Ca (1c, left) or 500 µg g^{-1} Ca (1d, right).

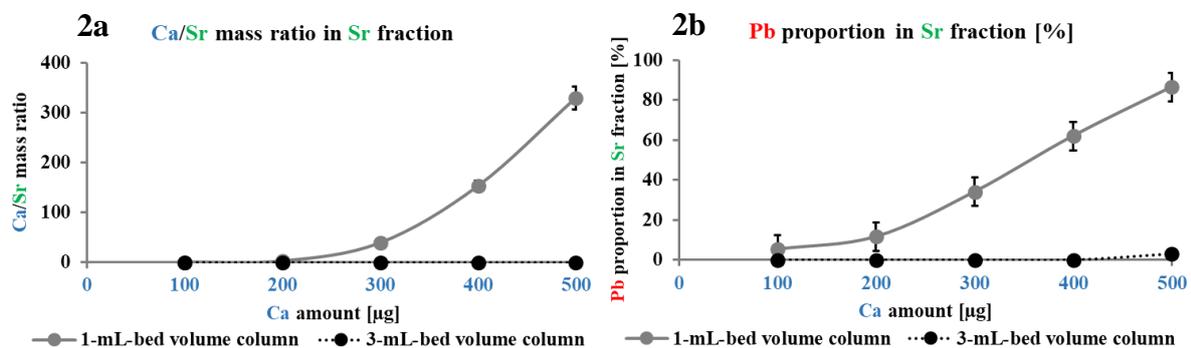


Fig. 2 a) Ca/Sr mass fraction ratios retrieved in the Sr fraction (3 mL for 1-mL-bed volume column, 8 mL for 3-mL-bed volume column) calculated for the separation of different test solutions containing 500 ng g^{-1} Sr, 50 ng g^{-1} Pb spiked with 100 to 500 µg g^{-1} Ca. b) The proportion of Pb co-eluted in the Sr fraction (3 mL for 1-mL-bed volume column, 8 mL for 3-mL-bed volume column) calculated for the separation of different test solutions containing 500 ng g^{-1} Sr, 50 ng g^{-1} Pb spiked with 100 to 500 µg g^{-1} Ca. Errors correspond to *expanded uncertainties* U ($k = 2$), if not visible uncertainties are smaller than spot size.

3.2 Elution behavior of Ca, Sr and Pb separated from different reference materials and blanks for 1-mL and 3-mL-bed volume columns

3.2.1 Approach 1 – 1-mL-bed volume column

The 1-mL-bed volume column achieves Sr recoveries $\geq 85.6\%$ for all investigated reference materials (see Table 3). Despite these recoveries, only for the reference materials FEBS-1, MACS-3 and BCR-2 a satisfying separation of Sr (570 ng - 890 ng on column) from Ca (50 μg - 130 μg on column) is achieved, due to the lower Ca/Sr mass fraction ratios ($\text{Ca/Sr} \leq 186$) in these materials compared to the other reference materials (NIST SRM 1400, NIST SRM 1486, BCR-063R) (see Table 1). Overall Pb (2.6 ng – 14.8 ng on column) recoveries ranging from 3.87% to 87.2% are achieved for the reference materials MACS-3, BCR-2, NIST SRM 1400 and NIST SRM 1486 along with up to 95% of Pb eluting in the Sr fractions (see Table 3). Only in case of MACS-3 and BCR-2, the co-elution of Pb in the Sr fraction is $<10\%$, which is in good agreement with previous results [23]. It should be noted that low Pb concentrations are challenging in MC ICP-MS analysis, unless detectors other than Faraday cups with generally applied $10^{11} \Omega$ amplifiers are used (e.g. secondary electron multiplier detectors or Faraday cups with 10^{12} or $10^{13} \Omega$ amplifiers). Therefore, Pb amounts in the range of 10 ng are favorable in setups such as the one used in the previous study [23]. Separations of NIST SRM 1400, NIST SRM 1486 and BCR-063R with absolute Ca loads $\geq 500 \mu\text{g}$ (Ca/Sr mass fraction ratios ≥ 1000) lead to significant amounts of Ca co-eluting during Sr elution (see Table 3).

Procedural blanks of 0.13 ng g^{-1} Sr and 0.03 ng g^{-1} Pb respectively were obtained, when using the 1-mL-bed volume columns.

3.2.2 Approach 2 – 3-mL-bed volume column

The 3-mL-bed volume column achieves similar Sr recoveries for all investigated reference materials when compared to the 1-mL-bed volume column. Recoveries of Sr for the different reference materials range from $84\% \pm 16\%$ (FEBS-1) to $104.8\% \pm 7.3\%$ (NIST SRM 1486) (see Table 3). Though, the observed Ca/Sr mass fraction ratios in the separated Sr fractions are significantly lower with values of <1 , indicating a complete separation of both analytes even in the presence of Ca loads up to $761 \mu\text{g} \pm 122 \mu\text{g}$ (NIST SRM 1400) (see Table 3). In case of Ca loads of $952 \mu\text{g} \pm 66 \mu\text{g}$ (BCR-063R), minor residual Ca is present in the Sr fraction leading to low Ca/Sr mass fraction ratios with values of <10 (see Table 3). Furthermore, the greater column size enables the complete separation of Pb from Sr. The increased separation efficiency without any overlap of the Sr and Pb peaks has already been shown for test-solutions in section 3.1 and could herewith be confirmed for real samples showing $<10\%$ of Pb in Sr fraction with

maximum Ca loads of $761 \mu\text{g} \pm 122 \mu\text{g}$ (NIST SRM 1400) (see Table 3). This is advantageous as possible isotope fractionation due to incomplete recovery for one of the analytes is avoided and sufficient amounts of Pb for isotope ratio measurements can be collected. Pb recoveries for the reference materials MACS-3, BCR-2 and NIST SRM 1400 with a Pb load on-column between $7.6 \text{ ng} \pm 1.6 \text{ ng}$ and $14.8 \text{ ng} \pm 1.0 \text{ ng}$ range from $76.7\% \pm 5.4\%$ and $96\% \pm 13\%$, while Pb recovery for the reference material NIST SRM 1486 with a Pb load on-column of $2.62 \text{ ng} \pm 0.25 \text{ ng}$ is only $59.6\% \pm 4.2\%$ (see Table 3). Our data indicates a complete separation of Sr from Pb for Ca loads up to $500 \mu\text{g}$. Higher Ca loads would lead to the co-elution of Pb in the Sr fraction (see Table 3). Pb separation for the materials FEBS-1 and BCR-063R are not considered, due to the overall low concentration of Pb in these materials.

In case of the reference materials MACS-3 and BCR-2, sample loads could be increased by a factor of 5 to collect enough Pb for isotope ratio measurements without overloading the 3-mL-bed volume column with Ca originating from the specific matrix.

Procedural blanks of $<0.04 \text{ ng g}^{-1}$ Sr and $<0.05 \text{ ng g}^{-1}$ Pb respectively have been realized, when using the 3-mL-bed volume column. Overall, the determined blank levels are comparable to those measured in a previous study [23].

Table 3 Recoveries for different Ca-rich certified reference materials when applying the developed separation procedure to 1-mL- and 3-mL-bed volume columns. Errors correspond to *expanded uncertainties* U ($k = 2$).

Reference material	On column load			n	1-mL-bed volume				n	3-mL-bed volume			
	Ca [μg]	Sr [ng]	Pb [ng]		Sr recovery [%]	Pb recovery [%]	Ca/Sr mass fraction ratio*	Pb proportion in [%] in Sr fraction*		Sr recovery [%]	Pb recovery [%]	Ca/Sr mass fraction ratio**	Pb proportion in [%] in Sr fraction**
MACS-3	53 ± 12	891 ± 135	7.6 ± 1.7	1	124.2 ± 8.7	87.2 ± 6.1	<1	9.24 ± 0.65	3	100 ± 13	83 ± 14	<1	$<LOD$
BCR-2	91 ± 6	567 ± 40	14.8 ± 1.0	1	102.9 ± 7.2	77.4 ± 5.42	<1	6.02 ± 0.42	1	103.2 ± 7.2	76.7 ± 5.4	<1	$<LOD$
FEBS-1	132 ± 10	650 ± 46	$<LOD$	3	87 ± 21	$<LOD$	<1	$<LOD$	3	84 ± 16	$<LOD$	<1	$<LOD$
NIST SRM 1486	504 ± 68	484 ± 86	2.62 ± 0.25	1	94.8 ± 6.6	15.4 ± 1.1	200 ± 28	53.18 ± 3.7	1	104.8 ± 7.3	59.6 ± 4.2	<1	$<LOD$
NIST SRM 1400	761 ± 122	411 ± 81	14.1 ± 2.4	3	88.8 ± 8.2	3.87 ± 0.27	874 ± 249	95.2 ± 15	5	96.1 ± 8.7	96 ± 13	<1	7.54 ± 0.53
BCR-063R	965 ± 86	271 ± 55	$<LOD$	3	85.6 ± 8.8	$<LOD$	2686 ± 682	$<LOD$	3	97.0 ± 8.1	$<LOD$	7.3 ± 5.7	

* 3-mL-Sr fraction.

** 8-mL-Sr fraction.

3.3 Sr and Pb isotope ratio analysis of reference materials

$\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ and $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values for four different reference materials (MACS-3, FEBS-1, NIST SRM 1400 and BCR-063R) were assessed in unseparated samples as well after their separation, applying 1-mL- or 3-mL-bed volume columns (see Fig. 3). These four reference materials were chosen based on the availability of published isotope ratio data

and the brought range of varying Ca/Sr mass fraction ratios (MACS-3: 55.8, FEBS-1: 186.4, NIST SRM 1400: 1007 and BCR-063R: 4051), that they represent. Complete isotopic data is given in the electronic supplementary (see Table S1, Appendix A). In the following, all results of Sr and Pb delta values and isotope-amount ratios are given with errors corresponding to total combined uncertainties calculated as described in 2.4 with a coverage factor of $k = 2$. Note that combined uncertainties include not only internal instrumental precision, but also the contribution of the blank, the correction for interferences and the repeatability of bracketing standards.

3.3.1 Sr isotope ratio analysis of unseparated samples

While the unseparated FEBS-1 sample shows a $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ value of $-1.92\text{‰} \pm 0.26\text{‰}$, which is lower than the published results by Yang *et al.* [32], the unseparated NIST SRM 1400 sample gives a significantly higher $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ value (with $6.65\text{‰} \pm 0.26\text{‰}$) than the published results by Romaniello *et al.* [24] (see Fig. 3 and Table S1, Appendix A). The unseparated reference material BCR-063R shows extreme shifts in $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ value ($12.85\text{‰} \pm 0.26\text{‰}$) and $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ value ($-16.57\text{‰} \pm 0.60\text{‰}$) compared to the separated samples. These shifts can be explained by a combination of matrix-based interferences caused by Rb, Ca and P present in the samples.

The high signal of the isobaric interference caused by ^{87}Rb cannot be corrected by simple mathematical correction during Sr isotope ratio measurements also taking into account different mass fractionation between Sr and Rb isotopes [13]. Residual uncorrected Rb will lead to higher $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values [13]. With a Rb/Sr mass fraction ratio of 4.93 ± 0.06 ($SD, n = 6$) in the unseparated sample of BCR-063R, Rb represents the main contributor of the observed bias, leading to a shift towards a higher $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ value ($12.85\text{‰} \pm 0.26\text{‰}$) as compared to the separated sample, since all given $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values are mathematical corrected for ^{87}Rb (as described in section 2.4) (see Fig. 3 and Table S1, Appendix A). Previous studies, e.g. by Irrgeher *et al.* [13], already demonstrated the limitation of mathematical correction for residual ^{87}Rb on $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values for samples with Rb/Sr mass fractions $\geq 0.001\%$.

Since the Rb/Sr mass fraction ratio and thus total Rb mass fraction in carbonates and hydroxyapatites are significantly lower (Rb/Sr < 0.01), the effect of Rb can be corrected for by mathematical correction. Therefore, the effect can be considered negligible for these unseparated samples [9]. On the other hand, significant interferences on all Sr isotopes by Ca-argides and Ca-dimers are known, reporting lower $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ (main interference:

($^{42}\text{Ca}^{44}\text{Ca}$)⁺ if no phosphorus is present in the measurement solution) and higher $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values (main interferences: ($^{48}\text{Ca}^{40}\text{Ca}$)⁺ and ($^{48}\text{Ca}^{40}\text{Ar}$)⁺) [9, 10, 13]. Hence, the observation of a lower $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ value of (-1.92 ‰ ± 0.26 ‰) of the unseparated FEBS-1 samples compared to the separated samples is in accordance with bias caused by the presence of Ca-argides and Ca-dimers from Ca in the matrix as reported in literature (see Fig. 3 and Table S1, Appendix A). If P is present in the matrix (as for reference material NIST SRM 1400; P content of 17.91% ± 0.19%), the additional interferences ($^{40}\text{Ar}^{31}\text{P}^{16}\text{O}$)⁺ and ($^{40}\text{Ca}^{31}\text{P}^{16}\text{O}$)⁺ might occur [10, 11], leading to increased $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values. When analyzing inorganic and biogenic apatite matrices ($w(\text{Ca}) = 0.4$, $w(\text{P}) = 0.18$, $w(\text{Sr}) \geq 0.0003$) using LA MC ICP-MS, Horstwood *et al.* [11] observed shifts between 0.3 ‰ and 4.0 ‰ caused by P-based interferences. The shifts in the $n(^{87}\text{Sr})/n(^{86}\text{Sr})$ isotope-amount ratios were mathematically corrected with uncertainties of ca. 0.05% for calcium phosphate samples with Ca/Sr mass fraction ratios up-to 1333 using a set of reference materials with characterized $n(^{87}\text{Sr})/n(^{86}\text{Sr})$ isotope-amount ratios. Limiting uncertainties of 0.1-0.2% had been seen for calcium phosphate samples with Ca/Sr mass fraction ratios >1333 ($w(\text{Ca}) = 0.4$, $w(\text{P}) = 0.18$, $w(\text{Sr}) < 0.0003$) [11]. The observed higher $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ value of 6.65 ‰ ± 0.26 ‰ of the unseparated NIST SRM 1400 sample is in accordance with the bias caused by the presence of the molecular interferences generated from Ar, Ca and P as reported in literature [10, 11] (see Fig. 3 and Table S1, Appendix A).

3.3.2 Sr isotope ratio analysis of samples separated by using 1-mL- and 3-mL-bed volume columns

$\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values of MACS-3 separated using 1-mL- (-4.16 ‰ ± 0.29 ‰) and 3-mL-bed volume (-4.11 ‰ ± 0.26 ‰) overlap within uncertainties with the published results by Jochum *et al.* [33] (see Fig. 3, Table 4 and Table S1, Appendix A). $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ of MACS-3 separated using 1-mL-bed volume (-0.53 ‰ ± 0.37 ‰) overlap within uncertainties with those of the samples separated using 3-mL-bed volume (-0.40 ‰ ± 0.53 ‰) (see Fig. 3 and Table S1, Appendix A). Hence, the separation of MACS-3 by applying the 1-mL-bed volume column can be considered as successful as by using the 3-mL-bed volume column. Same is true for $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values of FEBS-1 separated using 1-mL- (-1.59 ‰ ± 0.23 ‰) and 3-mL-bed volume (-1.58 ‰ ± 0.23 ‰), as well as $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values of -0.16 ‰ ± 0.46 ‰ using 1-mL- and -0.07 ‰ ± 0.46 ‰ using 3-mL-bed volume, which all overlap within uncertainties with the published results by Yang *et al.* [32] (see Fig. 3, Table 4 and Table S1, Appendix A).

In case of the separation of NIST SRM 1400 using the 1-mL-bed volume column, the co-eluted Ca (Ca/Sr mass fraction ratio of 874 ± 249 , resulting in a mass fraction of Ca $>40 \mu\text{g g}^{-1}$ in the measurement solution for MC ICP-MS (see Table 3)), caused significant shifts in the isotopic composition resulting in a $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ of $2.18 \text{‰} \pm 0.23 \text{‰}$ and in a $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ value of $-3.69 \text{‰} \pm 0.46 \text{‰}$ compared to the published results by Romaniello *et al.* [24] (see Fig. 3, Table 4 and Table S1, Appendix A). The shifts towards lower $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ and $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values can be explained as a result from interferences caused by residual Ca, as described for carbonates in section 3.3.1. Even though mathematical correction for Ca-argide and Ca-dimer interferences were successfully performed in LA-MC ICP-MS measurements of carbonates ($w(\text{Ca}) = 0.4$, $w(\text{Sr}) \geq 0.0003$) with Ca/Sr mass fraction ratios up to 1333 [9, 11, 32, 34], several considerations negate the application of such a correction approach to solution-based Sr isotope ratio measurements: 1) The internal inter-elemental IIF correction requires a close matching of sample and the standard solutions, as matrix-induced IIF, e.g. resulting from residual Ca, cannot be fully compensated for [13, 17]. Therefore, complete separation of the matrix elements is still the method of choice; 2) Pronounced matrix effects occur due to e.g. instability and loss of sensitivity originating from material deposition on the cones from aqueous solutions containing $>2 \mu\text{g g}^{-1}$ Ca [7, 12, 13] leading to suppression of Sr and Zr signals over time (further discussed in section 3.3.3); 3) As known from literature, mathematical corrections of interferences negatively impact the uncertainty of isotope ratio measurements by an increase of up to 40% (comparison of solution-based MC ICP-MS to LA MC ICP-MS measurements [10]). Further, the instrumental measurement setup would require measurements in dynamic mode to monitor Ca at the Ca-masses as sensitivity for detecting the low signals of Ca-dimers and Ca-argides using Faraday cups will not be sufficient. Therefore, matrix separation is indispensable for precise isotope-amount ratio analysis as mathematical corrections for interferences solely cannot provide comparable combined uncertainties.

$\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ ($3.87 \text{‰} \pm 0.23 \text{‰}$) and $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ values ($-0.32 \text{‰} \pm 0.46 \text{‰}$) of the NIST SRM 1400 samples separated using the 3-mL-bed volume overlap within uncertainties with the published results by Romaniello *et al.* [24] (see Fig. 3, Table 4 and Table S1, Appendix A). Hence, a successful separation of NIST SRM 1400 was only achieved when using the 3-mL-bed volume column, proving the suitability of larger resin volumes for handling substantial higher Ca loads.

Observations similar to those of NIST SRM 1400 were made for the reference material BCR-063R separated with the 1-mL-bed volume column. Ca co-eluted in the Sr fraction leading to, shifts towards lower $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ ($-4.30 \text{‰} \pm 0.23 \text{‰}$) and $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$

values ($-4.95 \text{ ‰} \pm 0.46 \text{ ‰}$) (see Fig. 3 and Table S1, Appendix A). Proving the suitability of the developed method for high Ca loads via analysis of NIST SRM 1400 with similar Ca loads as for BCR-063R, we suggest a $n(^{87}\text{Sr})/n(^{86}\text{Sr})$ isotope-amount ratio of 0.70884 ± 0.00017 (U , $k = 2$) corresponding to a $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ value of $-2.11 \text{ ‰} \pm 0.24 \text{ ‰}$ (U , $k = 2$) for the BCR-063R reference material (see Table 4 and Table S1, Appendix A).

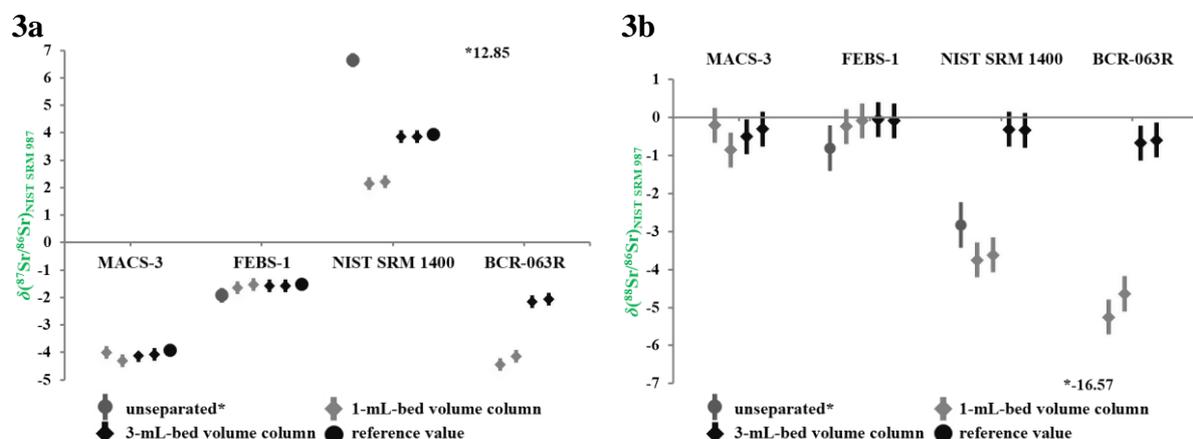


Fig. 3 a) $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ and b) $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ for different Ca-rich reference materials when applying the developed separation procedure using 1-mL and 3-mL-bed volume columns including published values reported for FEBS-1 [32], MACS-3 [33] and NIST SRM 1400 [24]. All samples except unseparated samples were ion exchanged and measured in duplicates. Errors correspond to *expanded uncertainties* U ($k = 2$). Values exceeding the y-scale are indicated with *.

Table 4 Published values for $\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$, $\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$, $\delta(^{208}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$, $\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$, $\delta(^{208}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ and $\delta(^{207}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ of the used Ca-rich reference materials including values provided in this study.

CRM	Reference	Method	$\delta(^{87}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$ $n(^{87}\text{Sr})/n(^{86}\text{Sr})$	$\delta(^{88}\text{Sr}/^{86}\text{Sr})_{\text{NIST SRM 987}}$	$\delta(^{208}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ $n(^{208}\text{Pb})/n(^{206}\text{Pb})$	$\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ $n(^{207}\text{Pb})/n(^{206}\text{Pb})$	$\delta(^{208}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ $n(^{208}\text{Pb})/n(^{204}\text{Pb})$
NIST SRM 981	certificate	-			0 ± 0.37 2.1681 ± 0.0008	0 ± 0.36 0.91464 ± 0.00033	0 ± 0.87 36.722 ± 0.031
FEBS-1	[32]	MC ICP-MS	-1.64 ± 0.02 * 0.709172 ± 0.000006	-	-	-	-
MACS-3	[33]	TIMS	-3.92 ± 0.01 * 0.7075532 ± 0.000037	-	-	-	-
	this study	MC ICP-MS		-	-40.97 ± 0.05 2.07928 ± 0.00007	-70.72 ± 0.09 0.84995 ± 0.00008	40.82 ± 0.23 38.221 ± 0.008
NIST SRM 1400	[24]	MC ICP-MS	3.93 ± 0.03 * 0.713129 ± 0.000019	-0.32 ± 0.03	-	-	-
	[35]	TIMS	-	-	-30.49 ± 1.38 * 2.102 ± 0.003 **	-68.49 ± 1.09 * 0.852 ± 0.001 **	-
	provided by NIST ([36] and [37])	TIMS	-	-	-30.12 ± 0.37 *** 2.1028 ± 0.0008 ***	-67.83 ± 0.36 *** 0.8526 ± 0.0003 ***	51.09 ± 0.86 *** 38.598 ± 0.031 ***
BCR-63R	this study	MC ICP-MS	-2.11 ± 0.24 0.70884 ± 0.00017				

* calculated δ -value using certified value of NIST SRM 981 and NIST SRM 987.

** (SD , $n = 5$).

*** *Expanded uncertainty* U ($k = 2$) is estimated from NIST SRM 981.

3.3.3 Effects of residual Ca on IIF correction of Sr isotope ratios using Zr as internal standard

As described in e.g. Yang *et al.* [17] close matching of Sr/Zr signal intensities between standard and sample (max. $\pm 10\%$ offset) are required to improve accuracy of IIF correction. During the measurements performed in this study, a significant suppression of the Zr and partly Sr intensities for specific samples were observed when following the established approach for calibration using internal inter-elemental IIF correction [13, 16-20, 23]. The observed decrease of the Zr and partly Sr signal originated most likely from residual matrix components, mainly Ca, leading to a decreased ionization efficiency. When setting the Zr and Sr signals from BCR-63R solutions separated with a 3-mL-bed volume column with an ^{88}Sr signal of 11.5V as 100%-anchor, a signal suppression by 60% for ^{90}Zr (4.4 V) and 25% for ^{88}Sr (8.7 V) was observed, when analyzing BCR-063R sample solutions separated with a 1-mL-bed volume column. This results in a $^{90}\text{Zr}/^{88}\text{Sr}$ intensity ratio of 0.4. Since the required matching of the Sr and Zr signal intensities when using Zr as internal dopant for correction of instrumental isotopic fractionation was not given for all samples, conventional IIF correction via standard sample bracketing without internal correction via Zr was applied. In addition, Ca based interferences are also present on Zr isotopes. Moreover, little is known whether the effect of the matrix on the IIF of Zr is the same as on the IIF of Sr. Therefore, the concept of using Zr to correct for variations in the IIF remains questionable in case of substantial matrix differences between standard and sample.

3.3.4 Pb isotope ratio analysis of samples separated by using 3-mL-bed volume columns

The reference materials MACS-3 and NIST SRM 1400 were analyzed for their isotopic composition of Pb (see Table 1). Only in case of NIST SRM 1400, Pb isotope-amount ratios have been published before [35-37]. In addition, a separated NIST SRM 981 solution (without Ca spiking) was used as a third reference standard. Since separations applying the 1-mL-bed volume column lack in quantitative Pb recovery due to overlaps of Sr and Pb elution as described in section 3.1, all reference materials were separated using a 3-mL-bed volume column. Results for the Pb isotope ratio analysis are shown in Fig. 4.

Separated NIST SRM 981 displayed a $\delta(^{208}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ value of $0.17\text{‰} \pm 0.10\text{‰}$, a $\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ value of $-0.20\text{‰} \pm 0.04\text{‰}$ and a $\delta(^{208}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ value of $0.58\text{‰} \pm 0.51\text{‰}$, which overlapped within uncertainty with the anchor values from the certificate (Table 4 and Table S1, Appendix A, note: *Expanded uncertainties* $U(k=2)$ of NIST SRM 981 were calculated according to the certificate).

The reference material NIST SRM 1400 showed a $\delta(^{208}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ value of $-29.87 \text{ ‰} \pm 0.07 \text{ ‰}$, a $\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ value of $-66.95 \text{ ‰} \pm 0.17 \text{ ‰}$ and a $\delta(^{208}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ values of $51.55 \text{ ‰} \pm 0.26 \text{ ‰}$. The measured isotope ratio of $\delta(^{208}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ and $\delta(^{208}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ in this study overlapped within uncertainty with the values published by Aung *et al.* [35] and reported by NIST [36, 37] (see Fig. 4 a and c, Table 4 and Table S1, Appendix A). (Note: Pb isotope-amount ratios from NIST were reported in the literature [36, 37] without an uncertainty. Hence, *expanded uncertainty* U ($k = 2$) for these values were estimated in accordance to uncertainties of NIST SRM 981, see Table 4). In case of $\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$, the measured isotope ratios were slightly higher than the values published by Aung *et al.* [35] and reported by NIST [36, 37] (see Fig. 4 b, Table 4 and Table S1, Appendix A). Nevertheless, the uncertainty of $\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ had to be estimated, since the Pb isotope-amount ratios provided by NIST [36, 37] were reported without an uncertainty. Combining the measured isotope ratios of both NIST SRM reference materials, a successful separation when using the 3-mL-bed volume column led to accurate Pb isotope-amount ratios.

To the best of the author's knowledge there are no published results for Pb delta values or isotope-amount ratios for the reference material MACS-3 available. Proving the suitability of the developed method for high Ca loads via analysis of NIST SRM 1400 with higher Ca loads as MACS-3 (see Table S1, Appendix A), we suggest a $n(^{208}\text{Pb})/n(^{206}\text{Pb})$ isotope-amount ratio of 2.0793 ± 0.0001 ($U, k = 2$) corresponding to a $\delta(^{208}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ of $-40.97 \text{ ‰} \pm 0.05 \text{ ‰}$ ($U, k = 2$), a $n(^{207}\text{Pb})/n(^{206}\text{Pb})$ isotope-amount ratio of 0.84995 ± 0.00008 ($U, k = 2$) corresponding to a $\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ of $-70.72 \text{ ‰} \pm 0.09 \text{ ‰}$ ($U, k = 2$) and a $n(^{208}\text{Pb})/n(^{204}\text{Pb})$ isotope-amount ratio of 38.221 ± 0.008 ($U, k = 2$) corresponding to a $\delta(^{208}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ of $40.82 \text{ ‰} \pm 0.23 \text{ ‰}$ ($U, k = 2$) for the reference material MACS-3 (see Table 4 and Table S1, Appendix A).

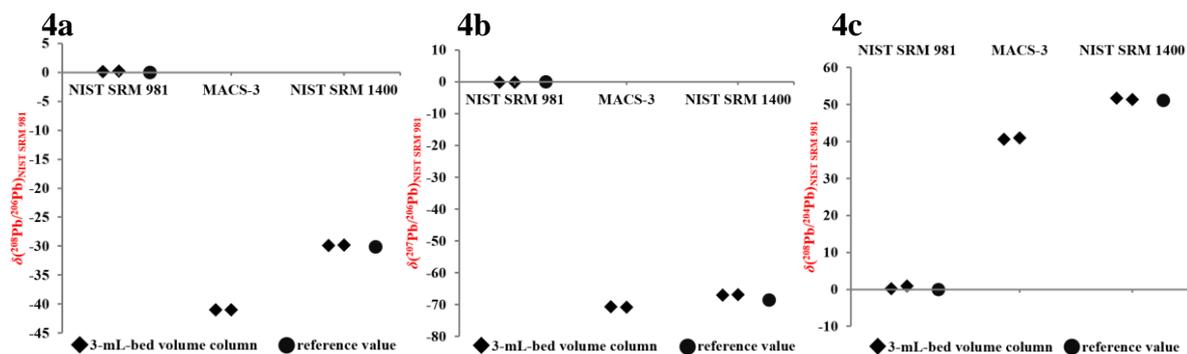


Fig. 4 a) $\delta(^{208}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$, b) $\delta(^{207}\text{Pb}/^{206}\text{Pb})_{\text{NIST SRM 981}}$ and c) $\delta(^{208}\text{Pb}/^{204}\text{Pb})_{\text{NIST SRM 981}}$ for different reference materials when applying the developed separation procedure using 3-mL-bed volume columns including published values reported by NIST (for NIST SRM 1400 cited in [36, 37]). All samples were ion exchanged and measured in duplicates. Errors correspond to *expanded uncertainties* U ($k = 2$), if not visible uncertainties are smaller than spot size.

4. Conclusion

The separation efficiency of Sr from Ca and Sr from Pb when using DGA Resin highly depends on the Ca amount loaded onto the column. In this paper, the behavior of the resin during its application for the simultaneous separation of Ca, Sr and Pb has been characterized in detail for the first time. Recent separation approaches using the DGA Resin were limited to Ca loads $<100 \mu\text{g}$ and a non-quantitative recovery of Pb in case of its utilization for a simultaneous separation of Sr and Pb. Our experiments confirmed significantly biased results of Sr isotope ratio analysis for samples with insufficient Ca separation, which were mainly caused by Ca-based polyatomic interferences. Furthermore, signal suppression by residual Ca effects the IIF corrections for Sr isotope ratio analysis, which underlines the necessity of an efficient analyte/matrix separation (especially Ca), when aiming at accurate isotope ratio analysis of variable, complex sample matrices.

In case of challenging separations and high matrix loads, a larger column bed volume of 3 mL resulted in a significantly increased matrix tolerance and separation efficiency. As a consequence, Sr and Ca separation could be accomplished along with the separation of Sr from Pb without any overlap for Ca loads of up to $500 \mu\text{g}$. Sr and Pb isotope ratio analysis proved that the increase of the column bed volume to 3 mL allows for the accurate analysis of isotope ratios in Ca-rich matrices with Ca/Sr mass fraction ratios up to ≤ 4051 and Ca/Pb mass fraction ratios up to 42095 (such as present in NIST SRM 1400). Overall, the increased Ca tolerance significantly improves the robustness and applicability of the described automated analyte/matrix separation approach, which is in particular advantageous when dealing with large sample sets of different matrices and varying concentration ranges as typical for large scale environmental studies.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at [doi](#).

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