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Blank correction in IDMS: possible pitfalls

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The blank correction in isotope dilution mass spectrometry (IDMS) is investigated using the double IDMS exact matching technique. The effects of different amounts of blanks in the sample, reference and spike solutions are simulated for the determination of the mass fractions of Pb and Cu. The simulations are compared with and confirmed by the respective interlaboratory CCQM key comparisons. The most accurate results are obtained when the blend bx of the sample and spike and blend bz of the reference and spike are treated in the same way (digestion, matrix separation, choice of the same solvent, amounts of sample, reference and spike, *etc.*) starting from sample preparation. When applying this procedure, it is not necessary to subtract the blank subsequently. A similar "blank-matching" approach has previously been reported by Pagliano, Mester, and Meija (*Anal. Chem.*, 2015, **87**: 10724–10727). In the present study, it is shown that in the case where exact matching is applied, the subsequent blank subtraction is not only superfluous but also yields a systematically wrong result with a bias of up to ten times the uncertainty depending on the blank concentration. If the procedural blank is "small", a subsequent subtraction yields a result similar to that of the procedure presented in this work. This small effect has obviously hidden a systematic bias in the past. By varying the mass fraction of the blank w_{bl} in the range $0.0001\ \mu\text{g g}^{-1} < w_{\text{bl}} < 0.0025\ \mu\text{g g}^{-1}$ for Pb, a subsequent blank subtraction yields a significantly biased result of w_{x} from −0.57% to −14%, exceeding the associated standard uncertainty $u(w_{\text{x}})$ at $w_{\text{bl}} \approx 0.0004\ \mu\text{g g}^{-1}$.

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Introduction

Over the past decades, numerous measurement strategies have been established and further improved for the accurate determination of analyte amounts in more or less complex matrices using mass spectrometric techniques, like inductively coupled plasma mass spectrometry (ICP-MS).[1,2] In analytical chemistry as well as in related disciplines, like geochemistry, forensics, food chemistry, environmental analysis, and metrology in chemistry in general, a few measurement strategies have been crystallized, yielding the smallest uncertainties associated with the intended quantities.[1–4] The term "analyte amount" is just a generalized description; in terms of metrology, it usually refers to the "mass fraction" w_{x} of an analyte x (unit: g g^{-1}), directly pointing out the gravimetric treatment of the samples and procedures during analysis. If the analyte element consists of at least two stable isotopes, isotope dilution mass spectrometry (IDMS) yields the most accurate and precise (smallest associated measurement uncertainty) results of the targeted mass fraction w_{x} based on internal calibration.[5] The IDMS principle has been discussed in numerous textbooks and research papers over the past decades.[6–11] Briefly, in IDMS, the isotopic composition and thus molar mass of the analyte element are known. A blend bx is prepared from the sample x containing the analyte element, usually with a natural isotopic composition, and from the so-called spike material y. The latter contains the analyte element with one isotope enriched compared with the natural isotopic composition, preferably with an almost inverse isotopic composition. If the spike material is completely characterized and is a certified reference material (CRM) at its best, knowledge of the masses of the blend components and the isotope ratios in the parent materials and the blend is needed to yield w_{x} with the lowest associated uncertainty. This procedure is called single IDMS. In most cases, the spike is insufficiently characterized with respect to its isotopic composition and especially its chemical purity. To overcome this problem, a double IDMS must be applied. In double IDMS, a third material, the reference material z (sometimes called the primary standard or back-spike) with the same or similar isotopic composition as the analyte in the sample, is used to prepare a second blend bz consisting of spike y and reference material z. In double IDMS, the purity of the spike cancels out from the model equation, and the impact of the knowledge of the isotopic composition on the result and its uncertainty is drastically reduced. Double IDMS yields results with the lowest associated measurement uncertainties; it is completely understood, exhibits the highest metrological quality and serves as the primary method in metrology in chemistry with results traceable to the International System of Units (SI). Practical considerations of IDMS include that, due to the principle of measuring ratios of intensities, a loss of substances after blend preparation does not affect the result or its associated uncertainty. It is important that the sample, the

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spike, reference material and respective blends are treated in the same way during the entire preparation process (*e.g.* digestion and separation). This means that the respective blanks affect all materials in the same way ("blank-matching"). Several types of IDMS have been developed and applied: single IDMS, double IDMS, and triple and higher order IDMS.[12,13] With each additional blend, another quantity (like the usually difficult-to-determine ratios in the spike) can be eliminated from the model equation. However, the latter procedures require laborious preparation efforts but usually yield only a small improvement in slightly reduced measurement uncertainty. When using IDMS, in most cases, double IDMS is applied, yielding the smallest uncertainties. A special case that is the focus of this work is called exact-matching (double) IDMS.[14,15] In this method, the blends (bx) of the sample and spike, as well as the reference and spike (bz), are almost equal (with a ratio equal to unity). Moreover, the ratio of the amount of substances $n_{\mathrm{x}}/n_{\mathrm{z}}$ in sample x and reference z is equal to unity (exact-matching criterion). If the isotopic compositions of the sample and spike are equal, the molar masses in the final equation cancel out.

Before presenting the blank-matching procedure we applied, its implications and consequences, the disambiguation of the term blank used here and in the context of analytical chemistry should be briefly outlined. A guide for the term "blank" used in analytical chemistry was released by Eurachem in 2019, defining several types of blank.[16] In this guide, terms like calibration blank, procedural blank, reagent blank, solvent blank, and sample blank are outlined. In the isotope ratio IDMS literature, the term "procedural blank" is usually used. This is a combination of the first compound, procedural blank (according to ref. 16), which is generated from a sample without the respective matrix of the analyte, including the effects of sample tubes, bottles, vials, surfaces, and additional reagents.[17] The second compound of our investigated blank is the "solvent blank" according to ref. 16, which is self-explanatory. The third contribution is the sample blank emerging from the matrix and sample treatment (digestion and separation). The fourth contribution results from the very measurement: carry-over effects and contamination of machine surfaces (*e.g.* skimmer, sampler, and lenses). It is often very difficult to distinguish between these different blank contributions. Therefore, the term "procedural blank" used here is a composition of these four individual blanks and corresponds to what is usually determined in an ICP-MS lab by applying IDMS. Parallel to the development of IDMS methods, the handling and quantification of procedural blanks have evolved. Historically, the procedural blank must be determined quantitatively in a separate experiment and subtracted from the analyte results (within its matrix). Thus, the blank-corrected result is an indirect result of the blank and contaminated sample.[18] Moreover, the blank determination of analytes at an ultra-trace level is difficult and time-consuming.

Theoretical methods

According to the basic version of the isotope dilution mass spectrometric approach, a single IDMS, briefly, the resulting double IDMS and its respective special variant (exact-matching double IDMS) should be described. Eqn (1) represents the basic single IDMS equation for determining the mass fraction w_{x} of an analyte (element) in a sample x of interest as follows:

$$w_{\mathrm{x}} = w_{\mathrm{y}} \times \frac{m_{\mathrm{yx}}}{m_{\mathrm{x}}} \times \frac{M_{\mathrm{x}}}{M_{\mathrm{y}}} \times \frac{\left(R_{\mathrm{bx}} - R_{\mathrm{y}}\right)}{\left(R_{\mathrm{x}} - R_{\mathrm{bx}}\right)} \times \frac{\sum\limits_{j} R_{\mathrm{x},j}}{\sum\limits_{j} R_{\mathrm{y},j}}. \tag{1}$$

The requirements are the known masses of (a) the sample solution m_{x} and (b) the spike solution m_{yx} (which is the same element as the analyte element with an artificially enriched isotope) in a blend bx consisting of the sample and spike material. Here, the spike material must be fully characterized (isotopic composition, molar mass M_{y}, and purity). In particular, the mass fraction w_{y} of the spike solution in blend bx must be known. R_{x}, R_{y}, and R_{bx} are the isotope ratios of the sample, spike and blend, respectively; $R_{\mathrm{x},i}$ and $R_{\mathrm{y},i}$ are the isotope ratios in x and y with respect to the reference isotope, respectively. One advantage is that once the spike is added to the sample and homogenization as well as isotopic equilibrium is achieved, a loss of the analyte does not change the result due to the measurement of ratios. In MC-ICP-MS, the relative standard uncertainties associated with R are in the range $\leq 1 \times 10^{-5}$. However, due to the limited number of available fully characterized spike materials y, a single IDMS is usually replaced by a double IDMS approach. In this case, the spike material y can be characterized using a second "reference" material z with a natural isotopic composition (similar to that of x). A second blend bz is prepared (containing spike y and reference material z). Another term for bz is "calibration blend". The analogue to eqn (1) is as follows:

$$w_{\mathrm{z}} = w_{\mathrm{y}} \times \frac{m_{\mathrm{yz}}}{m_{\mathrm{z}}} \times \frac{M_{\mathrm{z}}}{M_{\mathrm{y}}} \times \frac{\left(R_{\mathrm{bz}} - R_{\mathrm{y}}\right)}{\left(R_{\mathrm{z}} - R_{\mathrm{bz}}\right)} \times \frac{\sum\limits_{j} R_{\mathrm{z},j}}{\sum\limits_{j} R_{\mathrm{y},j}}, \tag{2}$$

yielding

$$w_{\mathrm{y}} = w_{\mathrm{z}} \times \frac{m_{\mathrm{z}}}{m_{\mathrm{yz}}} \times \frac{M_{\mathrm{y}}}{M_{\mathrm{z}}} \times \frac{\left(R_{\mathrm{z}} - R_{\mathrm{bz}}\right)}{\left(R_{\mathrm{bz}} - R_{\mathrm{y}}\right)} \times \frac{\sum\limits_{j} R_{\mathrm{y},j}}{\sum\limits_{j} R_{\mathrm{z},j}}. \tag{3}$$

Inserting eqn (3) into (1) provides the general double IDMS equation (also known as "reverse IDMS") as follows:

$$\begin{aligned} w_{\mathrm{x}} = w_{\mathrm{z}} \times \frac{m_{\mathrm{z}}}{m_{\mathrm{yz}}} \times \frac{M_{\mathrm{y}}}{M_{\mathrm{z}}} \times \frac{\left(R_{\mathrm{z}} - R_{\mathrm{bz}}\right)}{\left(R_{\mathrm{bz}} - R_{\mathrm{y}}\right)} \times \frac{\sum\limits_{j} R_{\mathrm{y},j}}{\sum\limits_{j} R_{\mathrm{z},j}} \times \frac{m_{\mathrm{yx}}}{m_{\mathrm{x}}} \times \frac{M_{\mathrm{x}}}{M_{\mathrm{y}}} \\ \times \frac{\left(R_{\mathrm{bx}} - R_{\mathrm{y}}\right)}{\left(R_{\mathrm{x}} - R_{\mathrm{bx}}\right)} \times \frac{\sum\limits_{j} R_{\mathrm{x},j}}{\sum\limits_{j} R_{\mathrm{y},j}}, \end{aligned} \tag{4}$$

$$w_{\mathrm{x}} = w_{\mathrm{z}} \times \frac{m_{\mathrm{yx}}}{m_{\mathrm{x}}} \times \frac{m_{\mathrm{z}}}{m_{\mathrm{yz}}} \times \frac{M_{\mathrm{x}}}{M_{\mathrm{z}}} \times \frac{\left(R_{\mathrm{bx}} - R_{\mathrm{y}}\right)}{\left(R_{\mathrm{x}} - R_{\mathrm{bx}}\right)} \times \frac{\left(R_{\mathrm{z}} - R_{\mathrm{bz}}\right)}{\left(R_{\mathrm{bz}} - R_{\mathrm{y}}\right)} \times \frac{\sum_{j} R_{\mathrm{x},j}}{\sum_{j} R_{\mathrm{z},j}}. \tag{5}$$

Eqn (5) no longer contains w_{y}; the masses in m_{z} and m_{yz} in the blend bz must be known as well as the molar masses M_{x} and M_{z}. The respective isotope ratios must be measured. If the isotopic composition of the sample x and the reference z are equal, it follows that $M_{\mathrm{x}} = M_{\mathrm{z}}$ and $\Sigma R_{\mathrm{x},j} = \Sigma R_{\mathrm{z},j}$, and eqn (5) reduces to the following equation:

$$w_{\mathrm{x}} = w_{\mathrm{z}} \times \frac{m_{\mathrm{yx}}}{m_{\mathrm{x}}} \times \frac{m_{\mathrm{z}}}{m_{\mathrm{yz}}} \times \frac{\left(R_{\mathrm{bx}} - R_{\mathrm{y}}\right)}{\left(R_{\mathrm{x}} - R_{\mathrm{bx}}\right)} \times \frac{\left(R_{\mathrm{z}} - R_{\mathrm{bz}}\right)}{\left(R_{\mathrm{bz}} - R_{\mathrm{y}}\right)}, \tag{6}$$

which is used in ref. 14 and 15.

In this case, the molar masses need not be known, and mass bias correction is no longer necessary (because the calibration factors cancel out). The exact-matching conditions are as follows:

$$R_{\mathrm{bx}}/R_{\mathrm{bz}} \approx 1 \tag{7}$$

and

$$n_{\mathrm{bx}} \approx n_{\mathrm{bz}}. \tag{8}$$

The isotope ratios of the blends can be expressed as follows:

$$R_{\mathrm{bx}} = \frac{n_{\mathrm{bx},2}}{n_{\mathrm{bx},1}} = \frac{n_{\mathrm{x},2} + n_{\mathrm{y},2}}{n_{\mathrm{x},1} + n_{\mathrm{y},1}} = \frac{\dfrac{m_{\mathrm{x}} \times w_{\mathrm{x}}}{M_{\mathrm{x}}} \times x_{\mathrm{x},2} + \dfrac{m_{\mathrm{yx}} \times w_{\mathrm{y}}}{M_{\mathrm{y}}} \times x_{\mathrm{y},2}}{\dfrac{m_{\mathrm{x}} \times w_{\mathrm{x}}}{M_{\mathrm{x}}} \times x_{\mathrm{x},1} + \dfrac{m_{\mathrm{yx}} \times w_{\mathrm{y}}}{M_{\mathrm{y}}} \times x_{\mathrm{y},1}}, \tag{9}$$

$$R_{\mathrm{bz}} = \frac{n_{\mathrm{bz},2}}{n_{\mathrm{bz},1}} = \frac{n_{\mathrm{z},2} + n_{\mathrm{y},2}}{n_{\mathrm{z},1} + n_{\mathrm{y},1}} = \frac{\dfrac{m_{\mathrm{z}} \times w_{\mathrm{z}}}{M_{\mathrm{z}}} \times x_{\mathrm{z},2} + \dfrac{m_{\mathrm{yz}} \times w_{\mathrm{y}}}{M_{\mathrm{y}}} \times x_{\mathrm{y},2}}{\dfrac{m_{\mathrm{z}} \times w_{\mathrm{z}}}{M_{\mathrm{z}}} \times x_{\mathrm{z},1} + \dfrac{m_{\mathrm{yz}} \times w_{\mathrm{y}}}{M_{\mathrm{y}}} \times x_{\mathrm{y},1}}. \tag{10}$$

Eqn (9) and (10) denote the compositions of the respective isotope ratios of blends bx and bz according to the initial preparation of masses m_{x}, m_{yx}, m_{z}, and m_{yz} using sample x and spike and reference solutions y and z. In this established procedure used to determine w_{x}, no indication of an additional blank contribution is included *a priori*. Since every analytical procedure is accompanied by blank contamination (of the analyte element), the application of eqn (5) and (6) already include a procedural blank induced when the sample, spike and blends were prepared (*e.g.* digested) consecutively under slightly different conditions. Thus, it seems reasonable to subtract the amount of procedural blank after the application of eqn (5) or (6). However, this requires the additional determination of the mass fraction of the procedural blank $w_{\mathrm{x,bl}}$ in a separate measurement. There are at least three main challenges to this. First, the content of the procedural blank is usually very small and therefore difficult to measure; second, an additional blank determination is time-consuming; and third, the uncertainty associated with the blank mass fraction $w_{\mathrm{x,bl}}$ adds to the uncertainty of the final result $u(w_{\mathrm{x}})$. Nevertheless, this approach has been applied in numerous studies in the past decades, emphasizing a subsequent blank subtraction.[18–20] In 2015, Pagliano, Mester, and Meija published a sophisticated method called "blank-matching isotope dilution", showing that the efforts of a separated determination of the procedural blank and its subsequent subtraction from the initial result can be shortened and improved.[21] In their approach, a separate blank determination and elimination is not necessary if the sample, spike and blend solutions are treated from the beginning of the preparation in the same way. This means that in the case of digestion steps, all components are treated equally at the same time under the same conditions using the same amounts. Since the procedural blank is apparent in the same amount in all these solutions, it virtually cancels out when applying eqn (5) and (6). Moreover, laborious separate blank measurements are no longer required. This technique has been applied in our laboratory for more than two decades. However, an additional subtraction of a procedural blank leads to an overestimation of the blank, thus yielding a systematically biased w_{x}. In this study, we show the effect and amount of the respective bias by simulations if a subsequent (and overestimated) blank subtraction is performed. This, in turn, proves that only the blank-matching procedure is similar to that described in ref. 21 yields the correct value, and a subsequent subtraction induces a (usually slightly but sometimes completely) incorrect result. Thus, we demonstrate that blank-matching and subsequent subtraction yield different results.

Simulation of procedural blank impact

Although eqn (5) as the "full" double IDMS expression does not include any blank contributions of natural isotopic composition, its application should theoretically yield exactly the same result w_{x} as can be calculated from the gravimetric preparation.

In practice, however, the blend bx can be prepared with an excess of acids used, *e.g.*, for digestion and other preparation steps. These additional solutions contain a blank (bl) with a natural isotopic composition.

Assuming that this additional blank contribution (bl) is included in $R^{*}_{\mathrm{bx}}(R^{*}_{\mathrm{bz}},\ R^{*}_{\mathrm{x}},\ \text{and}\ R^{*}_{\mathrm{z}})$, eqn (9) and (10) are compared as follows:

$$R^{*}_{\mathrm{bx}} = \frac{n^{*}_{\mathrm{bx},2}}{n^{*}_{\mathrm{bx},1}} = \frac{\dfrac{m_{\mathrm{x}} \times w_{\mathrm{x}}}{M_{\mathrm{x}}} \times x_{\mathrm{x},2} + \dfrac{m_{\mathrm{yx}} \times w_{\mathrm{y}}}{M_{\mathrm{y}}} \times x_{\mathrm{y},2} + \dfrac{m_{\mathrm{bl}} \times w_{\mathrm{bl}}}{M_{\mathrm{x,IUPAC}}} \times x_{\mathrm{x,2,IUPAC}}}{\dfrac{m_{\mathrm{x}} \times w_{\mathrm{x}}}{M_{\mathrm{x}}} \times x_{\mathrm{x},1} + \dfrac{m_{\mathrm{yx}} \times w_{\mathrm{y}}}{M_{\mathrm{y}}} \times x_{\mathrm{y},1} + \dfrac{m_{\mathrm{bl}} \times w_{\mathrm{bl}}}{M_{\mathrm{x,IUPAC}}} \times x_{\mathrm{x,1,IUPAC}}}, \tag{11}$$

$$R^*_{\mathrm{bz}} = \frac{n^*_{\mathrm{bz},2}}{n^*_{\mathrm{bz},1}} = \frac{\dfrac{m_{\mathrm{z}} \times w_{\mathrm{z}}}{M_{\mathrm{z}}} \times x_{\mathrm{z},2} + \dfrac{m_{\mathrm{yz}} \times w_y}{M_{\mathrm{y}}} \times x_{\mathrm{y},2} + \dfrac{m_{\mathrm{bl}} \times w_{\mathrm{bl}}}{M_{\mathrm{x,IUPAC}}} \times x_{\mathrm{x,2,IUPAC}}}{\dfrac{m_{\mathrm{z}} \times w_{\mathrm{z}}}{M_{\mathrm{z}}} \times x_{\mathrm{z},1} + \dfrac{m_{\mathrm{yx}} \times w_y}{M_{\mathrm{y}}} \times x_{\mathrm{y},1} + \dfrac{m_{\mathrm{bl}} \times w_{\mathrm{bl}}}{M_{\mathrm{x,IUPAC}}} \times x_{\mathrm{x,1,IUPAC}}}, \tag{12}$$

$$R^*_{\mathrm{x},2} = \frac{\dfrac{m_{\mathrm{x}} \times w_{\mathrm{x}}}{M_{\mathrm{x,sample}}} \times x_{\mathrm{x},2} + \dfrac{m_{\mathrm{bl}} \times w_{\mathrm{bl}}}{M_{\mathrm{x,IUPAC}}} \times x_{\mathrm{x,2,IUPAC}}}{\dfrac{m_{\mathrm{x}} \times w_{\mathrm{x}}}{M_{\mathrm{x,sample}}} \times x_{\mathrm{x},1} + \dfrac{m_{\mathrm{bl}} \times w_{\mathrm{bl}}}{M_{\mathrm{x,IUPAC}}} \times x_{\mathrm{x,1,IUPAC}}}. \tag{13}$$

The index "IUPAC" indicates a natural blank composition. In the case of an analyte element with 4 stable isotopes (Pb), the molar mass in the sample, including the natural blank, consists of the following:

$$M^*_{\mathrm{x}} = \frac{R^*_{\mathrm{x},1}}{\sum R^*_{\mathrm{x},i}} M_{1,\mathrm{IUPAC}} + \frac{R^*_{x,2}}{\sum R^*_{\mathrm{x},i}} \times M_{2,\mathrm{IUPAC}} + \frac{R^*_{x,3}}{\sum R^*_{\mathrm{x},i}} \times M_{3,\mathrm{IUPAC}} + \frac{R^*_{\mathrm{x},4}}{\sum R^*_{\mathrm{x},i}} \times M_{4,\mathrm{IUPAC}}, \tag{14}$$

$$R^*_{\mathrm{z},2} = \frac{\dfrac{m_{\mathrm{z}} \times w_{\mathrm{z}}}{M_{\mathrm{z}}} \times x_{z,2} + \dfrac{m_{\mathrm{bl}} \times w_{\mathrm{bl}}}{M_{\mathrm{x,IUPAC}}} \times x_{\mathrm{x,2,IUPAC}}}{\dfrac{m_{\mathrm{z}} \times w_{\mathrm{z}}}{M_{\mathrm{z}}} \times x_{\mathrm{z},1} + \dfrac{m_{\mathrm{bl}} \times w_{\mathrm{bl}}}{M_{x,\mathrm{IUPAC}}} \times x_{\mathrm{x,1,IUPAC}}}. \tag{15}$$

In the case of 4 isotopes, the molar mass in the reference, including the natural blank, is as follows:

$$M^*_{\mathrm{z}} = \frac{R^*_{\mathrm{z},1}}{\sum R^*_{\mathrm{z},i}} \times M_{1,\mathrm{IUPAC}} + \frac{R^*_{\mathrm{z},2}}{\sum R^*_{\mathrm{z},i}} \times M_{2,\mathrm{IUPAC}} + \frac{R^*_{\mathrm{z},3}}{\sum R^*_{\mathrm{z},i}} \times M_{3,\mathrm{IUPAC}} + \frac{R^*_{\mathrm{z},4}}{\sum R^*_{\mathrm{z},i}} \times M_{4,\mathrm{IUPAC}}. \tag{16}$$

Experimental

Materials and sample preparation

The chemicals used, sample preparation procedures, and measurement techniques have been described in detail elsewhere.[22,23] Here, a brief description is provided to understand the potential influences of the experimental blank sources. High purity reagents and materials were used to reduce additional contamination (blank) sources. All sample solutions were based on aqueous HNO_3 (0.15 mol kg^{-1} → $w(HNO_3) = 0.0094$ g g^{-1} ≈ 1%). The purification of HNO_3 for the Pb measurements ($w(HNO_3) = 0.65$ g g^{-1}, EMSURE™ for analysis, Supelco) was performed in a perfluoroalkoxy alkane (PFA) sub boiling distillation system (OmniPure™, Teledyne CETAC Technologies, USA). Aqueous HNO_3 (0.15 mol kg^{-1}) solutions were used as blank solutions and for rinsing during mass spectrometric determinations. The purified water was generated using a water purification system (Merck KGaA), yielding a final resistivity of ≥18 MΩ cm. The purified labware (vials and bottles) used was mainly made of PFA. The masses used during gravimetric

Table 1 Instrumental parameters[a]

	Neptune XT™ MC-ICP-MS (Pb)	Element 2 HR-ICP-MS (Cu)
General parameters		
Radio frequency power/W	1200	1200
Cool gas (Ar)/L min^{-1}	16.0	16.0
Auxiliary gas (Ar)/L min^{-1}	0.8	0.8
Nebulizer gas (Ar)/L min^{-1}	1.0–1.2	1.1
Nebulizer (sample flow rate/μL min^{-1})	PFA, self-aspirating (50)	PTFE, Meinhard (200)
Sampler, orifice/mm	Nickel, 1.1	Nickel, 1.1
Skimmer, orifice/mm	Nickel ("H-type"), 0.8	Nickel ("H-type"), 0.8
Mass resolution $M/\Delta M$	400 (LR, pseudo low res. mode)	300 (LR), 10000 (HR)
Sample introduction system	ASX110FR autosampler (CETAC™)	—
	In a class-100 laminar flow hood	—
Spray chamber	Double pass cyclonic/Scott (quartz)	Cyclonic (PEEK)
Torch, injector tube, and bonnet	Quartz	Quartz
Data acquisition		
Operation mode	Static	Scanning (counting mode HR, and analogue mode LR)
Rotating amplifiers	Applied	—
Baseline measurement	Defocusing at the start (30 s)	—
Integration time/s	2.1	—
Number of integrations/cycle	1	—
Number of cycles/block	1	—
Number of blocks	20	—
Detectors	Faraday cups: L3 (^{202}Hg), L1(^{204}Pb), C (^{206}Pb), H1(^{207}Pb), H2 (^{208}Pb) with $R = 10^{11}$ Ω	Single collector (SEM)

[a] PTFE: polytetrafluoroethylene; PEEK: polyether ether ketone; and SEM: secondary electron multiplier.

Table 2 Results (PTB) of the double IDMS determinations used as reference values[22,23]

Element	Unit	Mass fraction w_x	Expanded uncertainty U	k
Pb	mg kg^{-1}	0.2189	0.0046	2.11
Cu	mg kg^{-1}	0.3589	0.0049	2.13

preparation were corrected for air buoyancy. The argon gas used for mass spectrometric measurements had purities of 5.0 (Pb) and 4.6 (Cu).

Pb samples. The initial Pb sample material/matrix was rice flour distributed for the CCQM-K158 interlaboratory comparison.[23] 0.8 g of rice sample material was weighed into quartz vials. Then, 2 g of Pb spike (y) solution ($w_{\mathrm{Pb}} \approx 22$ ng g^{-1}) and 2.5 g of 0.15 mol per kg HNO_3 (sub-boiled) were added to the sample. Prior to microwave-assisted acid digestion, 5 mL HNO_3 (65%, sub-boiled) and 3 mL H_2O_2 (30%, Suprapur) were added. The latter is the amount of material that mainly contributes to the procedural blank. The following certified reference materials (CRMs) were used: NIST SRM 981 (for mass bias correction and molar mass determination), BAM-Y004 (BAM-A-primary-Pb-1 for element content), and NIST SRM 991 (spike), highly enriched in ^{206}Pb ($x(^{206}\mathrm{Pb}) = 0.999\ 79$ mol mol^{-1}). In the same way, the reference/spike-blends were prepared by adding 2.5 g Pb reference (z) solution ($w_{\mathrm{Pb}} \approx 65$ ng g^{-1}) instead of the rice flour sample. During one digestion run, four sample/spike-blends were digested together with four reference/spike blends in an MLS ultraCLAVE III™ microwave oven ($p(\mathrm{Ar}) = 50$ bar, $\vartheta = 250$ °C, $t = 2$ hours). After digestion, the samples were evaporated on a heating block at $\vartheta = 140$ °C to dryness. The residues were redissolved in 8 mL HNO_3 (1 mol L^{-1}) and subsequently transferred to Triskem™ Pb resin columns. These are used to separate the Pb fraction (in 6 mol per L HCl) completely from the matrix. HCl was removed by evaporation to dryness on a hot plate at 140 °C. Then, the residues were redissolved in 2.5 mL HNO_3 (65%, sub-boiled) to get rid of potentially abraded column material. The dried residues were redissolved in 8 mL HNO_3 (0.15 mol kg^{-1}) to obtain measurement solutions with $w_{\mathrm{Pb}} \approx 26$ ng g^{-1}.

Cu samples. The Cu samples were taken from ampoules distributed within the CCQM-K100 interlaboratory comparison.[22] 2.6 g Cu sample material (Cu in fuel ethanol) was blended with 3.7 g Cu spike solution (Chemotrade # 52-5 Cu-65) enriched in ^{65}Cu ($x(^{65}\mathrm{Cu}) = 0.9970$ mol mol^{-1}) with $w_{\mathrm{Cu}} = 0.1$ µg g^{-1} in a quartz vessel. After homogenization, the solutions were evaporated to dryness on a hotplate at $\vartheta = 100$ °C. After the addition of 5 mL HNO_3 (65%, sub-boiled), the solutions were evaporated to dryness ($\vartheta = 150$ °C). The measurement solutions were prepared by adding 10 mL HNO_3 (0.15 mol kg^{-1}) to the residues.

BAM-A-primary-Cu-1 (BAM) as the calibration standard (z) was used as a reference material; as the spike material (y), Cu (#52-5 Cu-65, Chemotrade™ Germany) was applied. The respective reference–spike blends consisted of 4.6 g reference Cu solution ($w_{\mathrm{Cu}} = 0.2$ µg g^{-1}) and 3.7 g Cu spike solution ($w_{\mathrm{Cu}} = 0.1$ µg g^{-1}).

Mass spectrometry

Pb content was determined using a multicollector-inductively coupled plasma mass spectrometer (MC-ICP-MS) Neptune XT™ (Thermo Fisher Scientific GmbH, Bremen, Germany). The Ar gas load was removed using a high-throughput jet-interface OnTool Booster™ pump (Pfeiffer, Germany). To avoid any oil diffusion or contamination, the turbomolecular pumps are backed by a dry scroll pump (nXDS6i™, Edwards). The correction of Hg interference with Pb was performed during the molar

Table 3 Uncertainty budget of $w_{\mathrm{Pb}} = w_x$. Molar masses M were taken from ref. 26 and 27

Quantity	Value	Unit	Standard uncertainty	Sensitivity coefficient	Index
w_{dry}	0.98435	g g^{-1}	3.35×10^{-3}	−0.22	12.1%
f_{smp}	1.00000	1	6.50×10^{-3}	0.22	44.2%
f_{exp}	1.00000	1	3.80×10^{-3}	0.22	15.1%
w_z	0.0650504	µg g^{-1}	97.6×10^{-6}	3.4	2.4%
m_{yx}	2.066418	g	800×10^{-6}	0.11	0.2%
m_x	0.80619	g	4.00×10^{-3}	−0.27	25.7%
m_z	2.45942	g	800×10^{-6}	0.089	0.1%
m_{yz}	2.052304	g	800×10^{-6}	−0.11	0.2%
r_{bx} (^{206}Pb/^{208}Pb)	0.9840883	V/V	52.2×10^{-6}	−0.45	0.0%
r_{bz} (^{206}Pb/^{208}Pb)	0.9814721	V/V	59.9×10^{-6}	0.42	0.0%
x_y (^{206}Pb)	0.9997900	mol mol^{-1}	10.0×10^{-6}	75×10^{-9}	0.0%
x_y (^{208}Pb)	130.0×10^{-6}	mol mol^{-1}	10.0×10^{-6}	-580×10^{-6}	0.0%
M (^{204}Pb)	203.97302800	g mol^{-1}	1.50×10^{-6}	-940×10^{-9}	0.0%
M (^{206}Pb)	205.97444900	g mol^{-1}	1.50×10^{-6}	18×10^{-6}	0.0%
M (^{207}Pb)	206.97588000	g mol^{-1}	1.50×10^{-6}	-12×10^{-6}	0.0%
M (^{208}Pb)	207.97663600	g mol^{-1}	1.50×10^{-6}	-4.8×10^{-6}	0.0%
r_x (^{204}Pb/^{208}Pb)	0.02530368	V/V	4.81×10^{-6}	0.11	0.0%
r_x (^{206}Pb/^{208}Pb)	0.493402	V/V	113×10^{-6}	0.56	0.0%
r_x (^{207}Pb/^{208}Pb)	0.4024912	V/V	52.3×10^{-6}	0.11	0.0%
$r_{z,\mathrm{IDMS}}$ (^{206}Pb/^{208}Pb)	0.4572387	V/V	43.0×10^{-6}	0.063	0.0%
w_x	**0.21865**	**µg g^{-1}**	**2.14×10^{-3}**		

Table 4 Uncertainty budget of $w_{Cu} = w_x$

Quantity	Value	Unit	Standard uncertainty	Sensitivity coefficient	Index
f_{exp}	1.00000	1	2.60×10^{-3}	0.36	16.8%
w_z	0.199845	$\mu g\ g^{-1}$	300×10^{-6}	1.8	5.6%
m_{yx}	2.930800	g	800×10^{-6}	0.12	0.2%
m_x	2.559000	g	800×10^{-6}	−0.14	0.2%
m_z	4.216500	g	800×10^{-6}	0.085	0.0%
m_{yz}	2.939300	g	800×10^{-6}	−0.12	0.2%
r_{bx} (^{65}Cu/^{63}Cu)	0.91357	mol mol^{-1}	1.92×10^{-3}	−0.77	42.0%
r_{bz} (^{65}Cu/^{63}Cu)	0.95703	mol mol^{-1}	1.91×10^{-3}	0.70	35.0%
x_y (^{65}Cu)	0.994400	mol mol^{-1}	500×10^{-6}	-89×10^{-6}	0.0%
x_y (^{63}Cu)	5.600×10^{-3}	mol mol^{-1}	500×10^{-6}	0.016	0.0%
x (^{65}Cu)	0.308300	mol mol^{-1}	150×10^{-6}	0.094	0.0%
x (^{63}Cu)	0.691700	mol mol^{-1}	150×10^{-6}	−0.042	0.0%
$\boldsymbol{w_x}$	**0.35892**	**$\mu g\ g^{-1}$**	**2.28×10^{-3}**		

Table 5 Assignment of the individual results (mass fractions) in different ways to account for blank contributions

Result	Derivation	Blank	Blank subtraction
w_x	Eqn (5), reference value	Exact-matching measurement	—
$w_{x,c}$	Eqn (5) using R^*_{bx}, R^*_{bz} (eqn. (11) and (12)), R^*_x (eqn (13)) and R^*_z (eqn (15))	Simulation with blank impact on R^*_{bx}, R^*_{bz}, R^*_x, and R^*_z taken into account	No
$w_{x,c,cl}$	See $w_{x,c}$ and "classical" (cl) subsequent blank subtraction	See above plus blank subtraction	Yes

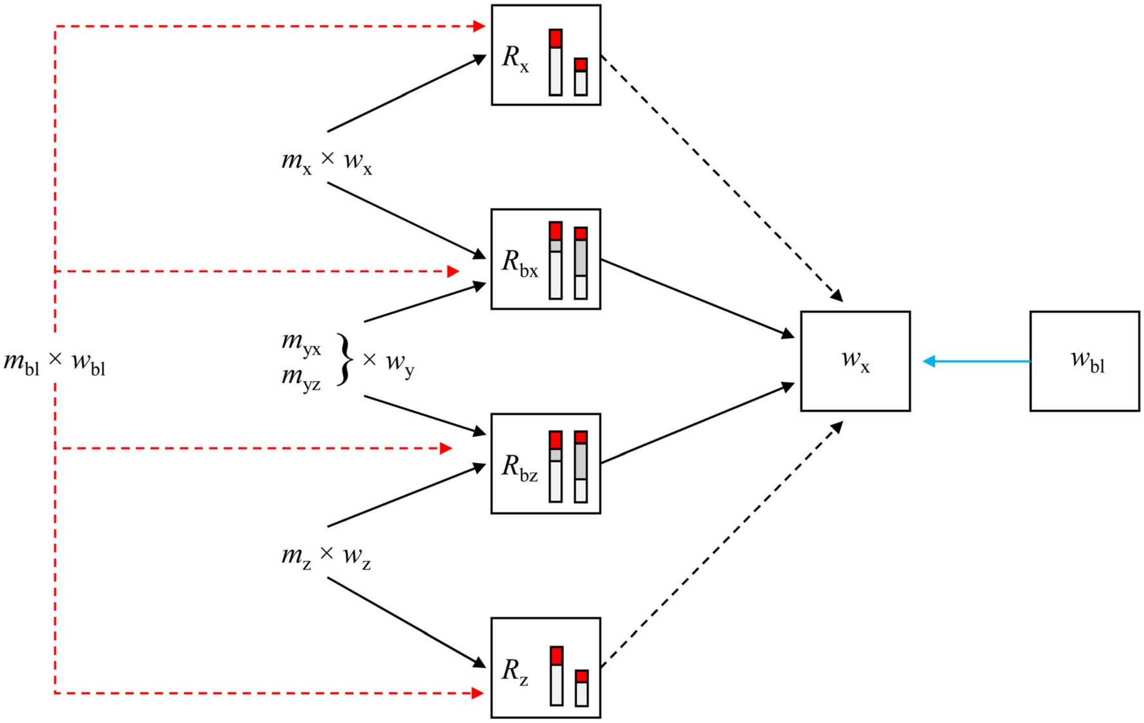

Fig. 1 Impact of the blank on the isotope ratios and final result w_x. The blank impacts both blend ratios R_{bx} and R_{bz}. In the case of a different isotopic pattern in the sample x, reference z and blank bl, *e.g.* Pb, the blend also impacts the ratios R_x and R_z. w_x depends on the altered isotope ratios in a complex way (see text for details), while the direct subtraction of the blend impacts w_x straightforwardly.

mass determination. The mass bias of $^{206}Pb/^{208}Pb$ was used to calculate the $^{202}Hg/^{204}Hg$ mass bias *via* exponential law, and the mass bias-corrected ^{204}Hg signal was then subtracted from the $m/z = 204$ signal to calculate the ^{204}Pb signal.[24]

Cu was analyzed using a high-resolution inductively coupled plasma mass spectrometer (HR-ICP-MS) Element 2™ (Thermo Fisher Scientific GmbH, Bremen, Germany).

The instrumental parameters of the mass spectrometers are listed in Table 1.

Results and discussion

Pb and Cu measurements

As a basis for the discussion of the blank effects according to the simulations, the results of the underlying measurements are summarized in Table 2. Detailed reports are given elsewhere.[22,23] Both Pb and Cu measurements and evaluations were carried out using the exact-matching double IDMS approach. Samples and blends (bx, bz) were treated in the same way during the entire preparation steps (*e.g.* same digestion procedures). Due to this blank matching, it was not necessary to determine a potential blank in a separate experiment, which would systematically bias the results, as shown hereinafter.

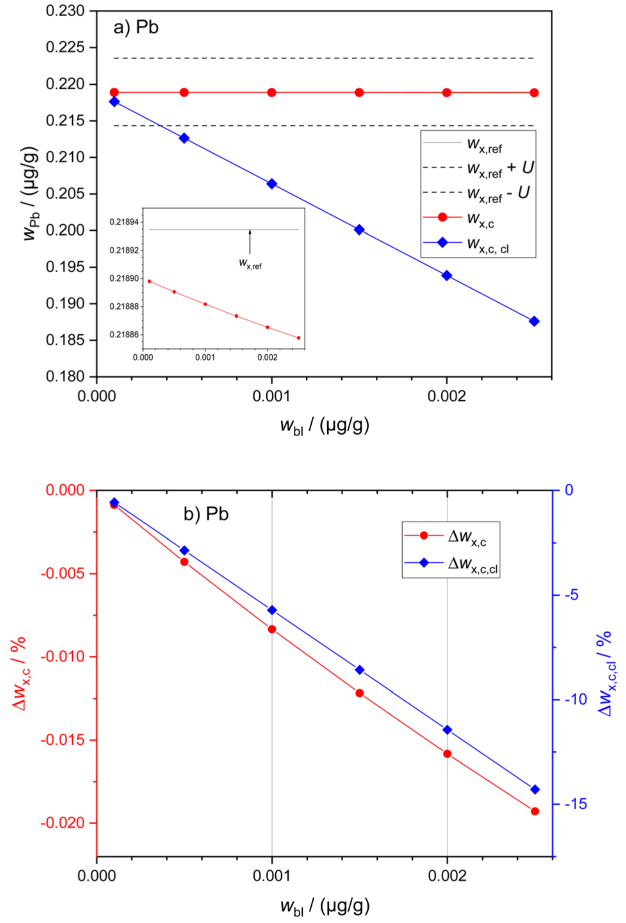

Fig. 2 Simulation of the mass fractions $w_{x,c}$ (red) and $w_{x,c,cl}$ (blue) of Pb after consideration of the blank contributions. The black solid line (a) refers to the reference value w_x (Table 2). The dashed lines indicate the expanded uncertainty range associated with w_x (experimentally determined). In (a), the absolute variation of w_{Pb} is shown. With its 500 times enlargement of the y-axis the inset reveals the most subtle variations. In (b), the relative changes in w_{Pb} are displayed.

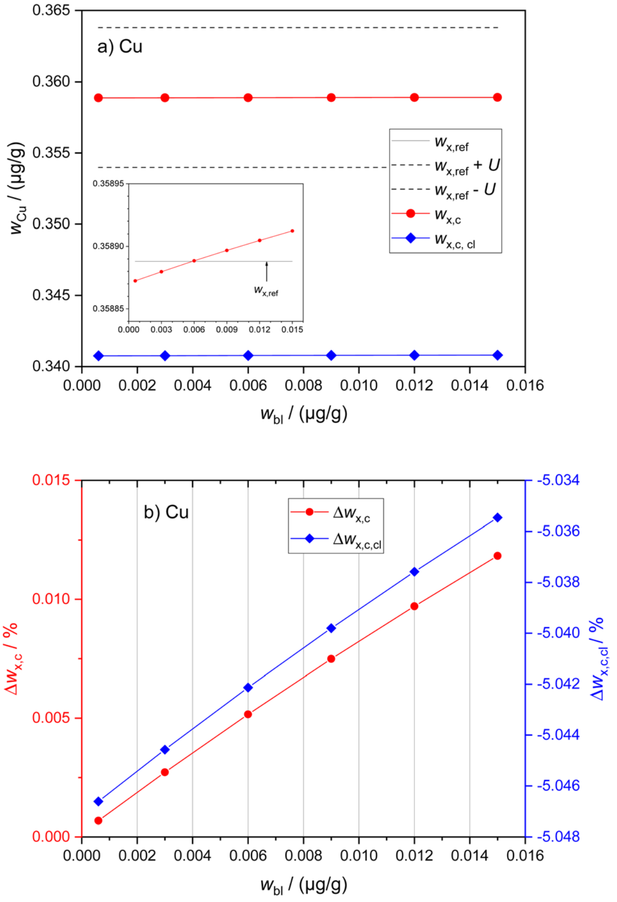

Fig. 3 Simulation of the mass fractions $w_{x,c}$ (red) and $w_{x,c,cl}$ (blue) of Cu after consideration of the blank contributions. The black solid line (a) refers to the reference value w_x (Table 2). The dashed lines indicate the expanded uncertainty range associated with w_x (experimentally determined). In (a), the absolute variation of w_{Cu} is shown. With its 230 times enlargement of the y-axis the inset reveals the most subtle variations. In (b), the relative changes in w_{Cu} are displayed.

The determination of the contents of Pb and Cu yielded relatively expanded uncertainties of 2.1% and 1.4%, respectively. These results have been confirmed in the context of interlaboratory comparisons and can be used as validated anchor points in our study.

A representative uncertainty budget for w_{Pb} according to the "Guide to the Expression of Uncertainty in Measurement" (GUM) is shown in Table 3.[25] The budget was calculated using the GUM Workbench Pro™ software (version 2.4.1. 392; Metrodata GmbH, Germany).

Main uncertainty contributions stem from the handling and treatment of liquids and samples during digestion and column separation by 44%, which is summarized by a factor f_{smp} (according to a type A contribution). A similar contribution is estimated by a factor f_{exp} by 15%, which indicates uncertainty contributions due to sampling and homogeneity issues. The

Table 6 Some examples of Pb mass fractions and their deviation from the correct result ($w_x = 0.2189$ µg g^{-1}) under different conditions (scenario A: exact matching, B: more blend bz, and C: more blend bx) calculated ignoring the blank completely (option 1) and subtracting it (option 2). For more details on the blends, see the SI

Scenario		A	B	C
n_{bl}/n_x/%		5.7	5.7	5.7
Option 1	n_{bl}/n_z/%	5.7	11	3.1
Option 2	n_{bl}/n_z/%	0.57	1.1	0.31
n_x/n_z/(mol mol^{-1})		1.002	1.996	0.539
R_{bx}/R_{bz}/(mol mol^{-1}) (mol mol^{-1})$^{-1}$		1.001	0.994	1.002
Option 1	Δw_x/%	−0.0083	−5.1	2.6
Option 2	Δw_x/%	−0.60	−1.2	−0.32

only quantity entering the original double IDMS eqn (5) is m_x with a contribution of 26%. The measurements of the intensity ratios (which will be transferred into isotope ratios) do not contribute a significant amount.

For Cu, a representative uncertainty budget according to the GUM is illustrated in Table 4, which is calculated using the GUM Workbench Pro™ software.[25]

In the case of the Cu exact-matching double IDMS, the main uncertainty contributions result from the intensity ratios $r_{bx}(^{65}\mathrm{Cu}/^{63}\mathrm{Cu})$ (42%) and $r_{bz}(^{65}\mathrm{Cu}/^{63}\mathrm{Cu})$ (35%) which is a direct consequence of the less precise single collector measurements. The factor f_{exp} denotes the contributions due to liquid handling and sample preparation (17%, type A).

Pb and Cu blank simulations

In order to assess the origin and impact of the blank, we used the experimentally determined mass fractions w_x presented in Table 2 as reference values, validated during interlaboratory comparisons. These w_x values were evaluated using the double IDMS eqn (5) in the case of Pb and eqn (6) in the case of Cu ($M_x = M_z$ and $\Sigma R_{x,j} = \Sigma R_{z,j}$), applying an exact-matching preparation; all samples and blends were equally treated throughout the whole preparation process. To get an idea about the blank impact, a stepwise consideration of the blank was simulated. In total, two additional (biased) results for w_x are finally simulated: $w_{x,c}$ and $w_{x,c,cl}$. Table 5 summarizes the individual properties and meanings of the symbols used. The blank contribution was considered in a respective quantity marked with an * (*e.g.* R_x^*). Fig. 1 schematically describes the different simulated (and biased) results. Detailed calculations using Pb and Cu as representative analytes are given in the SI (with a stepwise contribution of quantities, including the blank).

Table 7 Some examples of Cu mass fractions and their deviation from the correct result ($w_x = 0.3589$ µg g^{-1}) under different conditions (scenario A: exact matching, B: more blend bz, and C: more blend bx) calculated ignoring the blank completely (option 1) and subtracting it (option 2). For more details on the blends, see the SI

Scenario		A	B	C
n_{bl}/n_x/%		5.0	5.0	5.0
Option 1	n_{bl}/n_z/%	5.0	10	2.5
Option 2	n_{bl}/n_z/%	0.50	1.0	0.25
n_x/n_z/(mol mol^{-1})		0.999	2.024	0.501
R_{bx}/R_{bz}/(mol mol^{-1}) (mol mol^{-1})$^{-1}$		1.001	1.001	0.999
Option 1	Δw_x/%	0.0052	−4.7	2.5
Option 2	Δw_x/%	−0.53	−1.1	−0.27

In the case of Pb, in the simulations, an additional solvent contributing mainly to the blank bl with $m_{sln} = 10$ g (*e.g.* mass of added acids during digestion) was used as a constant value. If the respective mass fraction w_{Pb} of this blank is varied within 0.0001 µg g^{-1} $\leq w_{bl} \leq$ 0.0025 µg g^{-1}, the deviation of $w_{x,c}$ (including all quantities influenced by a procedural blank) from the reference value w_x varies then from −0.00088% to −0.019% (compare SI). This deviation is very small and can be neglected in practice since $U_{rel}(w_x) = 2.1\%$. Instead, if a subsequent classical (index cl) blank subtraction is performed, $w_{x,c,cl}$ deviates from −0.57% to −14.30%. Assuming a potential (realistic) procedural blank w_{bl} (Pb) in the range of 1–10%, this corresponds to $w_{bl}(\mathrm{Pb}) = 2$ ng g^{-1} up to 20 ng g^{-1} (similar to Cu).

Fig. 2a shows the absolute variation of $w_{x,c}(\mathrm{Pb})$ and $w_{x,c,cl}(\mathrm{Pb})$ *vs.* w_{bl} in detail.

The inclusion of the relevant blank contributions is shown with the values $w_{x,c}$ (red lines). In the displayed range of w_{bl}, the impact of the blank on w_{Pb} is still covered by the expanded uncertainty $U_{rel}(w_{Pb}) = 2.1\%$.

A subsequent subtraction of the procedural blank after the consideration of all input quantities (blue lines (values $w_{x,c,cl}$) in Fig. 2a and b) induces already at $w_{bl} > 0.0005$ µg g^{-1} a deviation of $w_{x,c,cl}$ from w_x of −2.9%, which is larger than the expanded uncertainty associated with w_x, indicating a systematically biased result due to the subsequent (additional) blank subtraction. When increasing the mass fraction of the blank from $w_{bl} = 0.0005$ µg g^{-1} to $w_{bl} = 0.001$ µg g^{-1}, the result of w_{Pb} is even more strongly biased. This is clear proof that a subsequent blank subtraction yields a (strong) blank overcorrection and thus a systematically wrong result.

The simulations for the second example, Cu, are shown in Fig. 3a and b. For the Cu simulations, a blank bl with $m_{bl} = 8$ g (*e.g.* mass of added acids during digestion) was used as an estimation (constant value).

In the case of Cu, the calculation of w_x was performed and simplified using eqn (6) (thus, $M_x = M_z$ and $\Sigma R_{x,j} = \Sigma R_{z,j}$; and only R_{bx}^* and R_{bz}^* enter as blank contributors). This procedure was used in the experiment. Therefore, the respective calculation scheme of w_{Cu} yields $w_{x,a}$ and $w_{x,a,cl}$ (compare the SI). For comparison with Pb, $w_{x,c}$ and $w_{x,c,cl}$ were calculated, which almost agree with the results of $w_{x,a}$ and $w_{x,a,cl}$.

By varying the respective mass fraction w_{Cu} in the blank within 0.0006 µg g^{-1} $\leq w_{bl} \leq$ 0.015 µg g^{-1}, the deviation of $w_{x,a}$ from the reference value w_x varies from 0.00052% to 0.012% which is so small that it can also be neglected compared to the expanded uncertainty $U_{rel}(w_x) = 1.4\%$ associated with w_x. If, however, a subsequent classical blank subtraction is done, $w_{x,a,cl}$ deviates from −5.056% to −5.046%. This means that a subsequent subtraction of the blank always induces a clearly biased value (compare Fig. 3a and b for $w_{x,c}$ and $w_{x,c,cl}$).

In Tables 6 (for Pb) and 7 (for Cu), some examples of different simulated scenarios of a perfect (A) and slightly deviating (B and C) exact-matching IDMS protocol are listed. For two options ((1) all solutions were treated in the same way from the beginning; (2) bz was not digested and/or separated using, *e.g.*, a column), the relative deviations from the reference values of some selected results are shown (for details, see the tables). The calculations and assumptions can be found in the SI.

Conclusions

In the context of the metrological analysis of contents (*e.g.* mass fractions) of analytes (*e.g.* elements) in complex matrices, the discussion on how to consider the influence of the procedural blank remains important. This study quantitatively investigated blank correction effects in a wider range. Two representative analytes (Pb and Cu) were chosen, which were experimentally analyzed during interlaboratory comparisons using the exact-matching double IDMS method. The results were used as a kind of (validated) reference in this study. In the simulations, blank contributions with varying mass fractions of the respective blanks were considered. In the case of Pb (see Table 6), when the blank in the calculation is completely ignored, the mass fraction is biased by a negligible value of <0.05% assuming exact matching (and blank matching) of the blends bx and bz ($0.99 \leq n_x/n_z \leq 1.01$ and $0.99 \leq R_{bx}/R_{bz} \leq 1.01$) is achieved, and a blank of 5.7% of the analyte amount is considered in both bx and bz. The bias due to the blank is therefore well within the limits of the uncertainty associated with the mass fraction. However, the result is biased under the same conditions by nearly 6% when the blank is subtracted. When preparing the blend bz differently in a way that it does not undergo the sample preparation steps (like digestion and separation) so that the blank in blend bz is much lower than the blank in blend bx, the results are completely different. In the case that the blank in blend bz is only 10% of the blank in bx with all other parameters unchanged, ignoring the blank in the calculation yields a mass fraction that is about 5.1% too large, while the subtraction yields a mass fraction that is approximately 0.5% too low. In the case that the exact matching condition $n_x \approx n_z$ is especially ignored, the subtraction yields a result 1.2% too small, a deviation already in the same order of magnitude as the uncertainty. In the case of Cu, it is no surprise that nearly the same behaviour of the deviation Δw_x of the calculated result from the correct one is observed (see Table 7). Conditions can be assumed (and experimentally adjusted) where the subtraction leads to results that are much closer to the correct mass fraction, but in practice, it is hardly predictable if and when these conditions are achieved, while exact matching always yields results with deviations from the correct result well within the limits of the uncertainty, remaining virtually independent of the amount of blank. Therefore, the exact matching, as described by Pagliano, Mester, and Meija[21] and Henrion,[14] is a much safer bet because the classical blank subtraction might yield the correct result (under the best of conditions and sometimes purely by coincidence), but it does not have to, and it is virtually impossible to know when it does.

Conflicts of interest

The authors declare no competing interests.

Data availability

The data supporting this article are in the supplementary information (SI). Supplementary information: all calculations leading to the results and conclusions shown above are demonstrated in detail. See DOI: https://doi.org/10.1039/d6ja00070c.

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