

Instrument response functions, mass bias and matrix effects in isotope ratio measurements and semi-quantitative analysis by single and multi-collector ICP-MS†

Christopher P. Ingle,^a Barry L. Sharp,^{*a} Matthew S. A. Horstwood,^b
Randall R. Parrish^b and D. John Lewis^c

www.rsc.org/jaas

^aDepartment of Chemistry, Loughborough University, Loughborough, Leicestershire, UK
LE11 3TU. E-mail: b.l.sharp@lboro.ac.uk

^bNERC Isotope Geosciences Laboratory, Keyworth, Nottingham, UK NG12 5CG

^cCentral Science Laboratory, Sand Hutton, York, UK YO41 1LZ

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This paper proposes a new approach to the estimation and correction of mass bias based on modelling the underlying instrument response function. Conventional definitions of mass bias are shown to be flawed and it is proposed that this quantity be recognised as merely the consequence of the instrument response function whose constants have a more fundamental importance. More accurate prediction of the bias in isotope ratio determinations is necessary and possible because of the improved precision afforded by multi-collector ICP-MS instrumentation. Isotope ratio measurements of Cd and Sn were used to study the variation of the mass bias with time, absolute mass and mass difference. No statistically significant variations were seen over a 20 min period, after which the data deviated significantly from the original measurement. After inclusion of the uncertainties in the natural abundances used to calculate the mass bias, no significant variation with increasing average isotope mass was observed. The reproducibility of the pattern of the points about the mean value suggested spectral interference and/or inaccurate values for the true isotope ratios. This was illustrative of the danger of using locally determined parameters to predict the mass bias. The variation of bias with mass difference showed a linear relationship, the implications of this for modelling are discussed. The common mass bias correction models are shown to be directly derivable from assumptions about the nature of the instrument response function. When the true instrument response function was investigated using a multi-element solution, a second order polynomial was found to provide the best fit to the data. The mass bias correction expression derived from such a model was used to calculate corrected Cd isotope ratios that were closer to the natural values than those obtained from the commonly used correction expressions. Increasing the concentration of a matrix element (bismuth or calcium) was found to significantly affect the value of Cd and Mg isotope ratios measured by multi-collector ICP-MS. The direction and magnitude of the effect was dependent on the position on the multi-collector array in which the isotopes were collected, with the heavier isotopes suffering higher levels of suppression. Measurements using an instrument with different multi-collector hardware did not show the same behaviour. A method of semi-quantitative analysis was developed that used the bias of 16 isotope ratios across the mass range to define the parameters in a quadratic instrument response function. This function was then applied to calculate the concentration of 24 analyte elements based on knowledge of ionisation efficiencies and the concentration of a single internal standard. This approach gave errors in the calculated concentrations that were comparable to the results obtained by using 6 internal standards, and did not require separate measurement of a standard solution to predetermine the instrument response.

Introduction

Mass bias occurs in analysis by inductively coupled plasma mass spectrometry (ICP-MS) when ions of different mass are transmitted through the spectrometer with different efficiencies, resulting in non-uniform sensitivity across the mass range and inaccurate isotope ratio measurements. Unfortunately the naming of the relative error in the measurement of an isotope ratio as the 'mass bias' appears to have endowed the quantity with the importance of a fundamental parameter rather than it being merely the consequence of instrument response. Note that here mass bias is considered to be entirely due to instrumental effects and that mass discrimination is a different phenomenon, arising only from chemical processes.

It was put forward some time ago that the majority of mass bias observed in a quadrupole ICP-MS system was due to processes occurring in the interface region, including the space charge effect.¹ Double focussing ICP-MS instruments typically utilise accelerating potentials of the order of 8 kV, much higher than those used in quadrupole systems,² and it was expected that the increased accelerating potentials would result in reduced space charge effects.^{3,4} Several groups have found, however, that the mass bias is similar for double focussing and quadrupole instrumentation,^{5,6} suggesting that the majority of the bias may originate in the field free regions between the sampler and the skimmer and/or immediately behind the skimmer. Maréchal *et al.*⁷ have also suggested that mass bias originates in the plasma itself.

The non-analyte species present in the ion beam are also said to contribute to the total mass bias.⁸ Among other effects, high

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concentrations of matrix elements result in an increased ion beam density, leading to greater space charge effects that exacerbate the loss of lighter ions from the ion beam, thereby enhancing the mass bias.

Commentary on current models

The mass bias, B , is corrected by one of two methods. External standardisation, wherein the isotope ratio of interest is measured in a standard solution, and the bias used to correct the same ratio in the sample, allows the mass bias to be measured at the same masses as the analyte, and at approximately the same abundances. The magnitude of the mass bias may change, however, in the presence of the sample matrix and/or in the time lapse between measurement of the standard and the sample. For internal standardisation, the mass bias is determined in the sample solution either using a known isotope ratio of an element added to the sample for that purpose, or using a pair of isotopes of the analyte element that are invariant in nature. The bias is then applied as part of a mathematical model to correct the analyte ratio. Internal standardisation provides near continuous monitoring of the mass bias and can be used to correct matrix effects, however inaccuracies may be introduced as the isotopes used to calculate the bias have masses, ionisation characteristics and isotopic abundances that are different to the analyte isotopes.

The mathematical models used are arbitrary and are based on linear, power or exponential functions.^{4,9} It is important to note that B is defined and determined locally for a specific isotope pair. Subsequent incorporation of B into one or other of the models requires two assumptions. The first is that B can be treated as a measure of the error per unit mass and is therefore constant over the range of interest. The second assumption sometimes made is that B has additive properties such that B measured from isotopes having two mass units separation is equal to twice that for unit mass separation over the same interval. Both these assumptions are incorrect. Defining B locally raises a further potential difficulty; it may incorporate a contribution from unsuspected spectral interferences which could vary from sample to sample, and thus make it unrepresentative of the bias at adjacent masses.

Previously, work in this laboratory showed¹⁰ that for the case where B_{xy} is locally defined for isotopes at masses x and y , the compound error is given by:

$$R^{\text{true}} = \frac{R^{\text{obs}}}{(1+B_{(i+1),i})(1+B_{(i+2),(i+1)}) \dots (1+B_{(j),(j-1)})} \quad (1)$$

where R^{true} and R^{obs} are the true and observed ratios of the isotopes i and j . Eqn. (1) is derived from the original equation¹⁰ simply by dividing both sides by the isotopic signal for isotope j .

For three adjacent isotopes at masses N , $N+1$ and $N+2$, and making the assumption that B is in fact constant, the compound error in the ratio $(N+2)/N$ becomes:

$$\begin{aligned} R^{\text{true}} &= \frac{R^{\text{obs}}}{(1+B_{N+1,N})(1+B_{N+2,N+1})} = \frac{R^{\text{obs}}}{(1+B)(1+B)} \\ &= \frac{R^{\text{obs}}}{(1+B)^2} \end{aligned} \quad (2)$$

or in general terms,

$$R^{\text{true}} = \frac{R^{\text{obs}}}{(1+B)^{\Delta m}} \quad (3)$$

Where Δm is the mass difference between the isotopes that make up the ratio R . The above expression is identical to the power

law correction. Thus the power law is arrived at as a direct algebraic consequence of assuming the bias to be a constant. The series expansion of eqn. (3) is:

$$R^{\text{true}} = \frac{R^{\text{obs}}}{1 + \Delta m B + \frac{\Delta m(\Delta m - 1)B^2}{2!} + \dots} \quad (4)$$

The linear model is given by:

$$R^{\text{true}} = R^{\text{obs}} / (1 + B\Delta m) \quad (5)$$

The exponential model is expressed as:

$$R^{\text{true}} = R^{\text{obs}} / \exp(B\Delta m) \quad (6)$$

The series expansion of eqn. (6) is:

$$R^{\text{true}} = \frac{R^{\text{obs}}}{1 + \Delta m B + \frac{(\Delta m B)^2}{2!} + \dots} \quad (7)$$

Noting the series expansions, the linear and exponential models may be regarded as approximations to the power law model that may compensate for the error in the basic assumption that B is constant. For example if Δm is 2 and terms higher than second order in B are ignored, the linear correction factor is reduced by B^2 whereas the exponential correction factor is raised by B^2 , relative to that predicted by the power law.

That these models cannot be correct is evident since they predict that the bias is dependent on the mass difference between the isotopes, and not the absolute mass, thereby assuming the bias to be constant across the mass range. Thus the bias in ${}^6\text{Li}/{}^7\text{Li}$ is predicted to be the same as in ${}^{207}\text{Pb}/{}^{208}\text{Pb}$, which does not accord with common experience. Although the above equations are always written with B explicitly expressed as a constant, in practise the local determination of B enables the models to approximate data at any mass provided the mass increment is small.

These mass bias correction models have been shown to approximate data acquired by ICP-MS. Taylor *et al.*,⁴ using a multi-collector double focussing system, found the power and exponential laws to be most effective for the correction of mass bias in U measurements, as did Rehkämper and Mezger¹¹ for Pb. Park *et al.*¹² found the three correction equations to be almost equally effective when calculating a Sn isobaric interference for Cd ratios measured by single collector double focussing ICP-MS. Using quadrupole ICP-MS, Begley and Sharp⁹ found the linear and power law functions to be equivalent for Pb isotope measurements using Tl as an internal standard, and the linear model to be at least as valid as the two alternatives for the correction of Pt isotope ratios.

A different approach has been favoured for the correction of mass bias in thermal ionisation mass spectrometry (TIMS). The equation employed is:^{13,14}

$$R^{\text{true}} = R^{\text{obs}} / \left(\frac{m_2}{m_1} \right)^f \quad (8)$$

where m_1 and m_2 are the masses of the isotopes that make up the ratio R and f is the 'mass bias factor'. Note that f is still defined and measured locally, but this equation should be a much better approximation to the true picture as it indicates that the correction depends on the absolute masses of the isotopes that make up the ratio. This equation was first described by Russell *et al.*¹³ and is referred to as the Russell correction expression throughout this paper.

The mass bias factor, f can be determined using an internal standard isotope ratio, and applied to correct an analyte ratio in a single mathematical step. This is illustrated for the Tl

internal standardisation of Pb in eqn. (9), which is directly derivable from eqn. (8).

$$\left({}^{206}\text{Pb}/{}^{204}\text{Pb} \right)^{\text{corr}} = \frac{\left({}^{206}\text{Pb}/{}^{204}\text{Pb} \right)^{\text{obs}}}{\left(\frac{{}^{205}\text{Tl}/{}^{203}\text{Tl}}{{}^{205}\text{Tl}/{}^{203}\text{Tl}} \right)^{\text{obs}} \left(\frac{\ln(206/204)}{\ln(205/203)} \right)} \quad (9)$$

These correction expressions have been shown to be applicable to multi-collector ICP-MS for several isotope systems.^{7,15,16} In these cases it was found that the mass bias factors for the analyte and internal standard were not equal, but that the ratio of the two was constant during an analytical session, and could be used to successfully correct for the mass bias.

Maréchal *et al.*⁷ showed that the power model (eqn. (3)) and the Russell expression (eqn. (8)) can be regarded as particular cases of a 'generalised power law':

$$R^{\text{true}} = R^{\text{obs}}/g(m_2^n - m_1^n) \quad (10)$$

where g is a mass independent coefficient and n is an arbitrary number. It was shown that $n \sim 1$ for the power model and $n = 0$ for the Russell expression.⁷

This paper considers the instrumentally derived bias in isotope ratios from a different perspective, treating them as the direct consequence of the instrument response function, which logically must be continuous and smooth with mass. It is shown that the common mass bias correction expressions discussed above can be derived directly from functions of this type. To avoid confusion with the bias per mass unit, this paper uses the term E^{obs} to represent the fractional error in an isotope ratio measurement,

$$E^{\text{obs}} = (R^{\text{obs}} - R^{\text{true}})/R^{\text{true}} \quad (11)$$

where R^{obs} and R^{true} are the observed and true isotope ratios, the latter calculated using published natural abundance data.¹⁷

In the current study, the mass bias characteristics of a double focussing ICP-MS system operated in both single and multi-collector modes were investigated. Areas of particular interest included the variation of E^{obs} with mass, mass difference and time. Cd and Sn were measured for these investigations, giving coverage of the mass spectrum from m/z 108 to 124. The effect of increasing concentrations of matrix elements (bismuth and calcium) on the magnitude and variation of isotope ratio measurements was also examined.

A method of performing semi-quantitative analysis was developed, using E^{obs} for a series of measured isotope ratios to define the instrument response function. This approach allowed calculation of the concentration of more than 20 elements in a multi-element solution based on knowledge of the concentration of a single internal standard, without prior calibration.

Experimental

The experiments were performed on Thermo Elemental VG Axiom double focussing ICP-MS instruments at the NERC Isotope Geosciences Laboratory (NIGL), Keyworth, Nottingham and at the Central Science Laboratory (CSL), Sand Hutton, York. Both instruments were used in solution mode, without sample desolvation. All standard solutions were

Table 1 Instrument operating conditions and experimental acquisition parameters

Instrument parameters		
Forward power	1250 W	
Plasma gas	14 l min ⁻¹	
Auxiliary gas	0.85 l min ⁻¹	
Nebuliser	100 µl min ⁻¹ Meinhardt (pumped uptake) gas flow optimised for maximum signal at ¹¹⁵ In	
Resolution setting	400	
Lens settings	Optimised for maximum signal at ¹¹⁵ In	
Experimental parameters		
Detector	Single collector Electron multiplier	Multi-collector Nine Faraday collectors
Dwell time	10 ms	5 s
Data acquisition	3 peak widths 20 points per peak 10 sweeps	2 sets 25 points per set

prepared by dilution of 1000 µg ml⁻¹ single element stocks (Claritas PPT, Spex Certiprep Inc., Metuchen, NJ) using double Teflon distilled 2% nitric acid.

Data were acquired in both single and multi-collector modes; acquisition parameters for each mode and typical instrument operating conditions are given in Table 1. Measurements using the multi-collector were acquired statically; the collector positions and solution concentrations used are shown in Table 2. Prior to data acquisition, baselines 0.5 u either side of the axial mass were measured. These values are subtracted from the data by the instrument software prior to any calculations. For single collector determinations, electrostatic sector scanning was used with a secondary electron multiplier for ion detection. 2.5 ng ml⁻¹ Cd or Sn was used as the sample; the masses monitored corresponded to those available using the multi-collector array. The instrument was allowed to warm up for at least 1 h prior to recording any data. For a particular mode of data acquisition each set of analyses was performed on a single day and the order in which the solutions were analysed was randomised to minimise the effect of drift on the data.

The effect of high concentrations of (i) heavy and (ii) light, easily ionisable matrix elements was studied by separately spiking 200 ng ml⁻¹ Cd and Mg standard solutions with bismuth and calcium in concentrations of 1, 10, 50 and 100 µg ml⁻¹. Collector positions as in Table 2 were used for Cd acquisitions. Data for ²⁵Mg was collected in the axial position, ²⁴Mg and ²⁶Mg were detected by the L4 and H4 collectors respectively (note that the dispersion of the instrument is fixed, the mass range that can be covered by the multi-collector array is 10% of the mass of the axial isotope). The samples for each element were analysed in random order and a solution containing only Mg or Cd was measured before and after each spiked sample. 2% nitric acid was aspirated for at least 10 min between analysis of the doped and 'clean' solutions.

For investigations into the use of instrument response functions for semi-quantitative analysis, a multi-element standard solution containing 100 ng ml⁻¹ of Li, B, Mg, Sc, Ti, Co, Cu, Ge, Rb, Y, Mo, Rh, Sn, Ba, Nd, Gd, Er, Yb, W, Ir,

Table 2 Solutions measured for the multi-collector acquisitions and the masses monitored therein

	L4 ^a	L3 ^a	L2 ^a	L1 ^a	Ax ^b	H1 ^c	H2 ^c	H3 ^c	H4 ^c
200 ng ml ⁻¹ Cd	—	¹⁰⁸ Cd	—	¹¹⁰ Cd	¹¹¹ Cd	¹¹² Cd	¹¹³ Cd	¹¹⁴ Cd	¹¹⁶ Cd
200 ng ml ⁻¹ Sn	¹¹⁶ Sn	¹¹⁷ Sn	¹¹⁸ Sn	¹¹⁹ Sn	¹²⁰ Sn	—	¹²² Sn	—	¹²⁴ Sn

^aL1 to L4 refer to the low mass Faraday collectors. ^bAx = axial Faraday collector. ^cH1 to H4 refer to the high mass Faraday collectors.

Pt, Pb, Bi and U was prepared from single element stock solutions. Acquisitions were performed in single collector mode, using magnetic sector scanning (magnet settle time = 100 ms), a Faraday collector and a dwell time of 2 s. The scan parameters were 2 peak widths per isotope and 10 points per peak width. All non-overlapping isotopes were measured, giving a total of 79 isotopes in all.

Results and discussion

Variation of E^{obs} with time

Typical values for E^{obs} per unit mass for Cd and Sn isotope ratio measurements were 1.2–1.4% for the multi-collector and 1.0–2.4% for the single collector determinations. These values compare reasonably with literature values for elements of a similar mass, Heumann *et al.*⁶ found the mass bias to be 1.7% per mass unit on measurements of the $^{79}\text{Br}/^{81}\text{Br}$ ratio by single collector double focussing ICP-MS and Walder *et al.*¹⁸ found the bias using a multi-collector system to be approximately 1.2% per mass unit at m/z 144.

The variation of E^{obs} for multi-collector isotope ratio data over a 50 min period was examined. The changes in $^{114}\text{Cd}/^{112}\text{Cd}$ and $^{119}\text{Sn}/^{118}\text{Sn}$ were typical of the data recorded, E^{obs} for these ratios is plotted against time in Fig. 1. Note that because time was the independent variable, an arbitrary reference point has been chosen rather than the ensemble average. The instrument was stable to within two times the standard error of the population over a 20 to 30 min timescale, after which significant deviation from the original E^{obs} value was seen. Therefore in all acquisitions, only data acquired within a 20 min period was considered to be comparable.

Variation of E^{obs} with absolute mass

Isotope ratios with a mass difference between the isotopes (Δm) of one were used to investigate the change in E^{obs} with the average mass of the isotopes that make up a ratio; Cd and Sn have 8 such ratios between them. The time between starting the Cd and Sn measurements was kept to a minimum (approximately 10 min) to ensure that results for the two elements could be treated as a single data set. The data is presented in Fig. 2 for single and multi-collector modes of acquisition; each point is

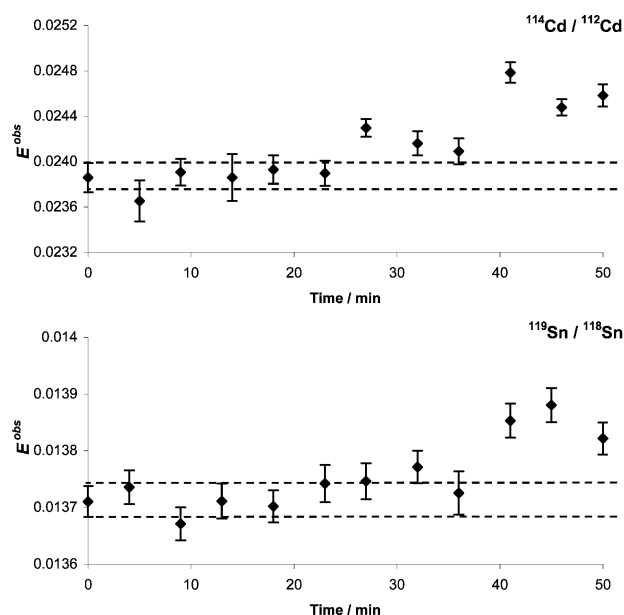


Fig. 1 Variation of E^{obs} for Cd and Sn in multi-collector mode, over a 50 min period. Error bars represent 2 times the standard error (SE) of the individual points, dotted lines mark $\pm 2 \times \sqrt{\sum (SE^2)/n}$ from the initial measurement.

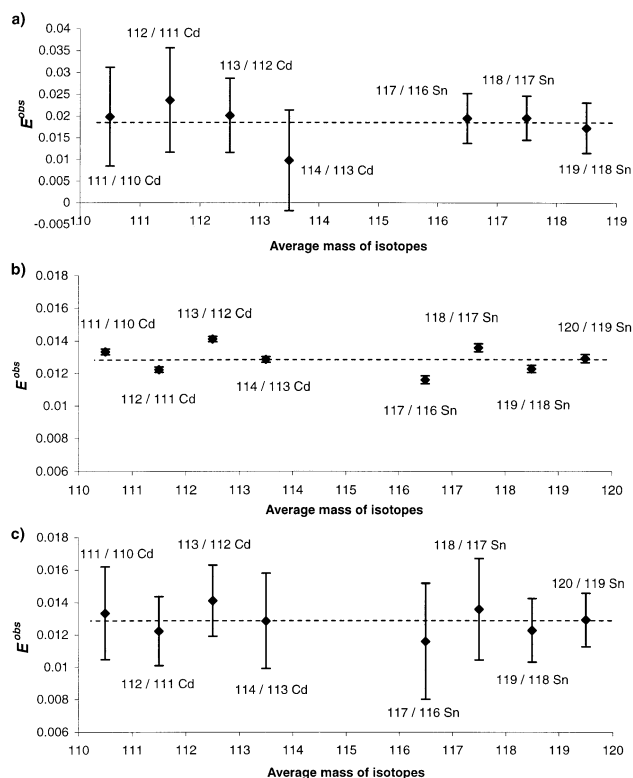


Fig. 2 E^{obs} vs. average mass of isotopes for ratios with a mass difference of 1 for (a) single collector, (b) and (c) multi-collector data. Dotted lines mark the mean E^{obs} value and error bars represent one standard deviation, in (a) and (b) for the measurement only, in (c) for the combined measurement and natural isotopic abundance uncertainty taken from ref. 17.

the mean of 50 integrations, error bars represent 1 standard deviation. The single collector data (Fig. 2a) showed no significant variation from the ensemble mean (dotted line) as the mean mass of the isotopes changed, owing to the magnitude of the error in the data.

The greater precision achieved using the multi-collector array allowed significant changes in E^{obs} with average mass to be seen (Fig. 2b). The published natural isotopic abundances used to calculate E^{obs} have uncertainties associated with them;¹⁷ a plot of E^{obs} vs. average isotope mass for the multi-collector data including these uncertainties is given in Fig. 2c. The absolute uncertainties given in Rosman and Taylor¹⁷ were propagated into the standard deviation of the analysis using accepted error calculation expressions.¹⁹

As shown in Fig. 2c, the variation of E^{obs} including the natural isotopic abundance uncertainties was within one standard deviation of the mean value for both Cd and Sn isotope ratios. It was found, however, that the pattern of results around the mean value was reproduced in subsequent determinations. Fig. 3 shows E^{obs} relative to the mean value for the initial Cd measurements, and replicate data recorded 2 months later. The mean value of E^{obs} for the repeat measurements was 0.015, compared to 0.013 in the original determinations. Variation in the absolute value of E^{obs} was expected, however the reproducibility of the pattern of the individual E^{obs} values about the mean was not.

There are three possible explanations for deviation from the mean E^{obs} and the reproducibility of this. Firstly, imperfection in the gain calibration of the Faraday amplifiers could have led to uneven response across the multi-collector array. The reproduction of the same pattern of variation on different occasions and following recalibration of the amplifiers, along with the magnitude of the deviation, is strong evidence against this explanation. Secondly, there may have been spectral

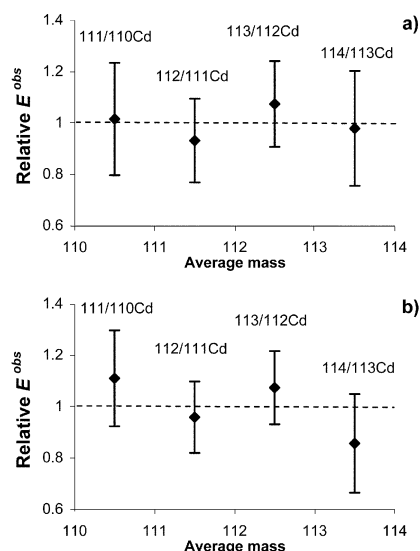


Fig. 3 E^{obs} relative to the mean E^{obs} value vs. average mass for Cd isotope ratios (a) original data, (b) + 2 months. Error bars represent the combined standard deviation, as in Fig 2c.

interferences affecting the analyses. The solution used in the measurements was investigated at resolution settings up to 10,000, but no resolvable spectral interferences were found. As the resolution of the system is increased, however, the sensitivity decreases meaning that even if they were present, low levels of resolvable spectral interferences such as Ar_2NO^+ , Ar_2O_2^+ , KrO_2^+ and KrNO^+ would not be seen. A number of oxide interferences fall in the mass range under investigation, and would not be separated using maximum resolution. None of the possible elements (Ru, Mo, Zr, Rb) were found at detectable levels in the analyte solutions, even at low resolution, therefore the oxides were almost certainly not present. Despite these observations, spectral interference, possibly in the form of a combination of species, may have been the cause of the observed pattern of deviation about the mean value of E^{obs} . As ICP-MS systems become more sensitive, and more precise measurements are performed using multi-collector detection techniques, it is inevitable that low level spectral interferences previously hidden by poor measurement precision will become problematic.

A third explanation for the observed patterns is that the natural isotope abundance values used to calculate E^{obs} did not match the true isotopic abundance in the analysed solutions. By decreasing the 'true' ^{112}Cd abundance value from 24.13 to 24.12%, and increasing ^{111}Cd and ^{113}Cd by 0.005% to maintain a total of 100%, all analyses in Fig 3a display the same E^{obs} . Similarly for Sn, small changes to the values used as the true isotopic abundance removed the variation completely. These changes are well within the uncertainty ranges of the natural isotopic abundances specified by Rosman and Taylor,¹⁷ suggesting a slight variation to the reference isotope ratios may be recommended. The reproducibility of the pattern of deviation indicates that this explanation is the most plausible.

Variation in E^{obs} with mass difference (Δm)

The change in E^{obs} with Δm was investigated by examining sets of ratios with a single isotope as denominator. Results for $^x\text{Sn}/^{117}\text{Sn}$ for single and multi-collector determinations are presented in Fig. 4 by way of example. The straight line trend was reproduced when other Sn isotopes were used as the reference point, and in similar examination of the Cd isotope ratios. When the $^x\text{Sn}/^{117}\text{Sn}$ multi-collector isotope ratio data was used to evaluate B for the power and exponential models using eqns. (3) and (6), and then multiplied by Δm to convert bias per mass unit into E^{obs} , the plots of E^{obs} vs. Δm were also

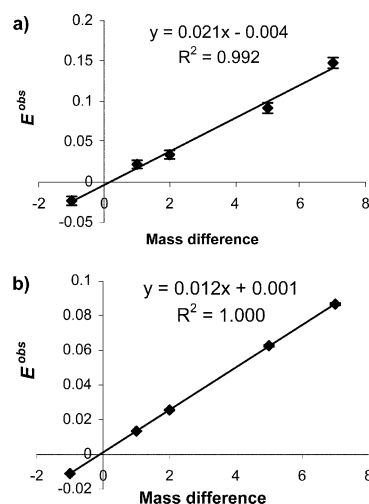


Fig. 4 E^{obs} vs. mass difference for $^x\text{Sn}/^{117}\text{Sn}$, where x = all other Sn isotopes, for (a) single collector (SC) and (b) multi-collector (MC) modes. Error bars represent the measurement standard deviation.

linear, with an R -squared value of 0.9995. This outcome is due to the relatively small mass range examined; over only eight mass units the power and exponential functions are approximately linear.

The multi-collector data always displayed a very strong linear relationship between E^{obs} and Δm . Upon further investigation, it was found that as the mass of the reference isotope decreased, the gradient of the regression line increased such that the gradient for $^x\text{Sn}/^{124}\text{Sn}$ was 0.0114 and that for $^x\text{Cd}/^{110}\text{Cd}$ was 0.0134, where x represents the other isotopes of Sn or Cd. The change in gradient across the mass range examined is illustrated in Fig. 5. The trend observed clearly demonstrated that E^{obs} did change with the mass analysed, and therefore that the power, linear and exponential mass bias correction expressions that are dependent solely on the mass difference between the isotopes are fundamentally incorrect.

As shown in Fig. 4a, the single collector data was not as closely linear as the multi-collector data, however a correlation coefficient of 0.99 is still suggestive of a strong linear relationship, and E^{obs} for all ratios considered was within one standard deviation of the line of best fit drawn through the data. The gradient of the plot for single collector data was significantly higher than that for the equivalent multi-collector data, a result that was repeated in subsequent acquisitions. The change in the gradient of the line of best fit with mass of the reference isotope was also generally greater for the single collector determinations. On changing the reference isotope from ^{116}Sn to ^{124}Sn , the gradient of the single collector plots decreased by approximately 20%, compared to a 10% decrease for multi-collector data. This discrepancy is most likely due to the difference in the modes of acquisition and the use of electrostatic sector scanning which introduces extra bias to the

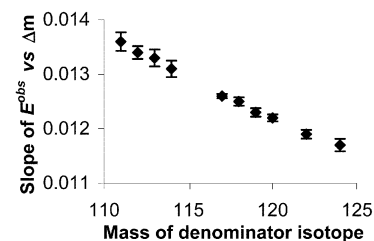


Fig. 5 Change in the gradient of the regression line of the plots of E^{obs} vs. mass difference with mass of the denominator isotope for multi-collector Cd and Sn data. Error bars are one standard deviation of the gradient of each regression line calculated using standard statistical techniques.¹⁹

system because the changes in the electrostatic sector voltage with mass, also affect the sensitivity.²

Effect of matrix elements on isotope ratio measurements in multi-collector mode

The use of Cd and Mg as analytes and calcium and bismuth as matrix elements enabled the influence of both analyte and matrix element mass to be investigated. The data were collected in static multi-collector mode.

It was found that in the presence of matrix, higher mass analyte isotopes were reduced in intensity relative to lower mass isotopes, and that the effect was enhanced as the concentration of matrix increased. The effect of these changes on isotope ratios is illustrated in Fig. 6 for the $^{108}\text{Cd}/^{111}\text{Cd}$ ratios with a bismuth matrix. ^{111}Cd was chosen as the reference isotope as it was collected on the axial channel of the multi-collector array. Fig. 6 clearly shows that the isotopes collected further away from the axial position were more strongly affected by the presence of the matrix. The response of $^{116}\text{Cd}/^{111}\text{Cd}$ did not fit the observed trend due to tin contamination in the bismuth solution added to the Cd standard.

The intensity changes observed led to a reduction in all values of E^{obs} . Although an important result, the underlying cause of the change in E^{obs} was the different responses of the ion signals to the high matrix concentrations, dependent on the position on the multi-collector array in which the isotopes were collected. This dependence on collector position was confirmed by examination of ratios with a constant mass difference of 2 between the isotopes. With $100\text{ }\mu\text{g ml}^{-1}$ calcium present, the ratios that displayed significant difference to those in the 'Cd only' solutions were $^{108}\text{Cd}/^{110}\text{Cd}$ (collector L3/collector L1), $^{112}\text{Cd}/^{114}\text{Cd}$ (H1/H3) and $^{114}\text{Cd}/^{116}\text{Cd}$ (H3/H4). The other ratios, involving only isotopes in the L1 to H2 range showed no significant difference from their values in the unspiked samples.

The observations were opposite to those expected, it was thought that the increased space charge due to the presence of the matrix would lead to increased losses of the lighter isotopes. Nonetheless, heavy-light element effects as previously reported^{1,8,20} were still seen. Mg was more seriously affected than Cd by the same concentration of matrix, and the changes

caused by the presence of bismuth were greater than those due to calcium.

One possible explanation for the collector dependent effects seen in this study is that non-analyte ions were detected by the Faraday collectors, possibly following collision with the walls of the flight tube, with the geometry of the double focussing system leading to maximum effect at the low mass end of the multi-collector array, and a gradual decline across to the higher collectors. A general increase in signal response across the array would not necessarily occur as the 'bouncing ion' effect would be small compared to the loss of analyte ions suggested by the data. Investigation of the baselines revealed that their magnitude was no different in the matrix doped and clean solutions, ruling out any non-analyte ion effect. Any 'bouncing' ions would result in an increased baseline level in the solutions doped with high levels of a matrix element.

Measurements using a second Axiom ICP-MS system showed a much lower degree of matrix effect. In the presence of $100\text{ }\mu\text{g ml}^{-1}$ of matrix element, Cd signal intensities were approximately 93% of the signal measured in bracketing Cd only solutions, compared to 65% in the original acquisitions. This was reflected in the isotope ratios, the maximum change in analyte ratio with the matrix was approximately half the magnitude of the changes observed in the original data. Additionally, the collector dependent matrix effects reported above were not apparent in the second set of acquisitions. The set-up of the two instruments was not identical, therefore it is unsurprising that different levels of matrix effects were observed. The nebulisers used were not the same and gas flows, torch position and ion lens tuning parameters were optimised for maximum signal on a daily basis. Therefore it was extremely unlikely that the secondary discharge in the two systems was equal. The instruments also differed in the hardware of their multi-collector array. At the time of the acquisitions, the Axiom at NIGL was fitted with multi-ion counters in addition to the nine Faraday collectors. It is possible that the presence of the extra detectors caused the collector dependent effects that were observed on this instrument, and not seen on the second system that was equipped with the standard single ion counter and multi-Faraday array. Alternatively, the dependence on collector

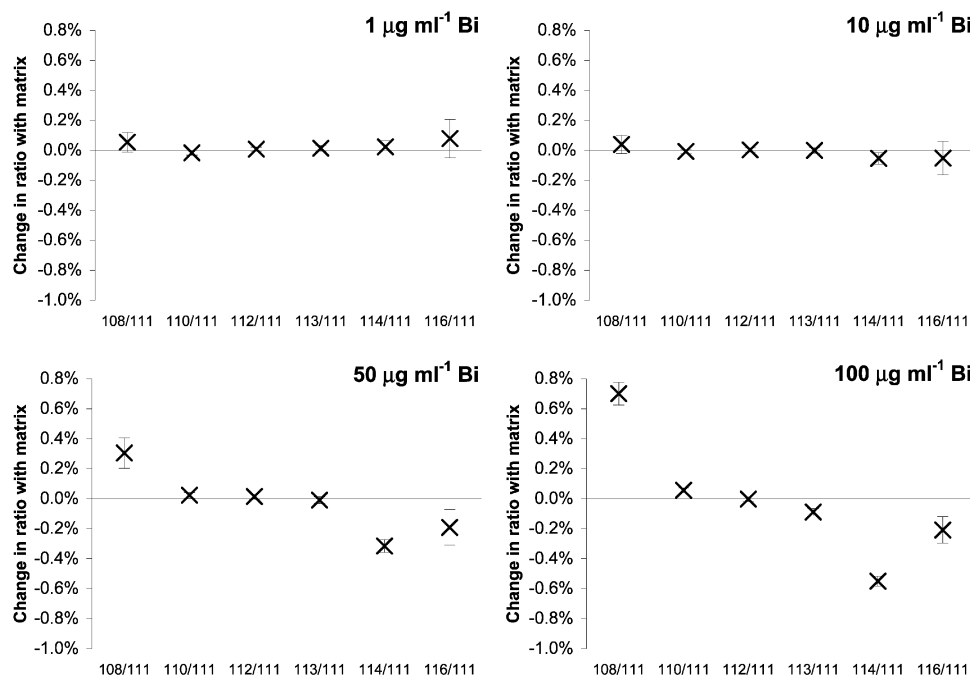


Fig. 6 Cd isotope ratios measured in the presence of increasing concentrations of bismuth matrix, relative to ratios measured in Cd only solutions. Error bars are one standard deviation.

position may only be apparent in systems where a significant matrix induced enhancement or reduction of the ion signal occurs.

The relationship between the instrument response function and E^{obs}

The instrument response is defined in terms of the sensitivity, S , and is dependent on the mass examined, m , such that

$$S = f(m) \quad (12)$$

Where f is a continuous function with no singularities.

The intensity observed at $m = m_1$ is given by

$$I_{m_1}^{\text{obs}} = S_{m_1} \times A_{m_1} \times C \times \eta \quad (13)$$

Where A_{m_1} is the abundance of the isotope at $m = m_1$, C is the elemental concentration, and η the fractional ionisation of the element. $I_{m_2}^{\text{obs}}$ is similarly defined, and if the two isotopes at $m = m_1$ and $m = m_2$ are of the same element, the observed isotope ratio can be calculated:

$$R^{\text{obs}} = \frac{I_{m_2}^{\text{obs}}}{I_{m_1}^{\text{obs}}} = \frac{S_{m_2} \times A_{m_2} \times C \times \eta}{S_{m_1} \times A_{m_1} \times C \times \eta} \quad (14)$$

$$R^{\text{obs}} = \frac{S_{m_2}}{S_{m_1}} \times R^{\text{true}}$$

The fractional error in the measured ratio, E^{obs} , is given by:

$$E^{\text{obs}} = \frac{R^{\text{obs}} - R^{\text{true}}}{R^{\text{true}}} \quad (15)$$

Note that E^{obs} is not the mass bias per mass unit, but is the deviation of a particular isotope ratio from the expected value (see earlier discussion).

Substituting eqn. (14):

$$E^{\text{obs}} = \frac{S_{m_2}}{S_{m_1}} - 1 \quad (16)$$

The function S could take any form, however there are certain conditions that should be fulfilled. At $m = 0$, the instrument response should be equal to a constant, ϕ , that is non-zero but arbitrary, and that cancels when isotope ratios are calculated. It is not logical that an isotope ratio could be dependent on the instrument response at zero mass. The function should also include one or more other constants which help to define the change in response with mass. If all these constants are set to zero, S should equal ϕ for all values of m .

It is possible to define plausible instrument response functions that can be shown to lead to the common mass bias correction expressions.

(i) Instrument response: $S = \phi(1 + k)^m$, a power law model where k is an arbitrary constant. Substituting into the above equations for the ratio of two isotopes at masses m_1 and m_2 ,

$$R^{\text{obs}} = (1 + k)^{m_2 - m_1} \times R^{\text{true}} \quad (17)$$

$$E^{\text{obs}} = (1 + k)^{m_2 - m_1} - 1 \quad (18)$$

If k is defined as the bias per unit mass, eqn. (17) is equivalent to the standard power law mass bias correction model given in eqn. (3), with k being numerically equal to B .

(ii) Instrument response: $S = \phi e^{km}$ Then,

$$R^{\text{obs}} = e^{k(m_2 - m_1)} \times R^{\text{true}} \quad (19)$$

$$E^{\text{obs}} = e^{k(m_2 - m_1)} - 1 \quad (20)$$

As before, if k is defined as the bias per unit mass, eqn. (19) is

equivalent to the standard exponential correction model given in eqn. (6).

Expanding either of the expressions for R^{obs} given above, and assuming k to be small (terms in k^n with $n > 1$ are ignored) yields

$$R^{\text{obs}} = (1 + k(m_2 - m_1)) \times R^{\text{true}} \quad (21)$$

and therefore,

$$E^{\text{obs}} = k(m_2 - m_1) \quad (22)$$

Defining k as the bias per unit mass, eqn. (21) is the same as the linear correction model (eqn. (5)). This again shows that the linear model is an approximation of the other models.

As mentioned above, these expressions for E^{obs} are all dependent on the mass difference between the isotopes and not the absolute masses, and as such are completely detached from the real situation.

(iii) Instrument response: $S = \phi(m)^k$ (Note this function does not equal ϕ when $m = 0$)

Then,

$$R^{\text{obs}} = \left(\frac{m_2}{m_1}\right)^k \times R^{\text{true}} \quad (23)$$

$$E^{\text{obs}} = \left(\frac{m_2}{m_1}\right)^k - 1 \quad (24)$$

Eqn. (23) is equivalent to the correction expression given by Russell *et al.*¹³ (eqn. (8)). The expression for E^{obs} does depend on the absolute masses of the isotopes involved in the ratio, and as such this instrument response function is more likely to be representative of the true instrument behaviour than the other models considered thus far.

The constant k can be determined using optimisation software such as the Solver function in Microsoft Excel[®] to find the value of k that minimises the sum of the squared differences between E^{obs} calculated from instrumental data and that predicted by the response model. Using E^{obs} rather than S for the optimisation eliminates the requirement to evaluate ϕ as well as k .

Internal standardisation can also be used to determine constants in the instrument response function. The equations given above for R^{obs} can be rearranged to allow determination of k from measurement of a known isotope ratio. As with the above method, this approach requires that the true form of the instrument response function is known.

A multi-element standard solution was measured in order to determine the response function of the instrument used in this study. The solution contained 19 elements ranging in mass from m/z 6 (Li) to 193 (Ir). Molar concentration, isotopic abundance and fractional ionisation (calculated using the Saha equation and assuming $T = 7500$ K and $n_e = 10^{21} \text{ m}^{-3}$) were taken into account, and the instrument response was plotted against mass. Masses affected by spectral interference or contamination could easily be eliminated as they were not part of the smooth trend defined by the remaining isotopes.

The theoretical instrument response function for each of the models was calculated across the same mass range, Solver optimisation was used to determine the values of the constants in the response functions, as described above. The value of ϕ was ascertained using Solver to minimise the sum of the square differences between the experimental instrument response, and that predicted by the models at each mass. The optimised forms of the power and exponential models are compared to the true instrument response in Fig. 7a and b respectively. As illustrated, both models provided poor fit to the experimental data, the functions are simply the wrong shape. Regression analysis was performed using the experimental response as the

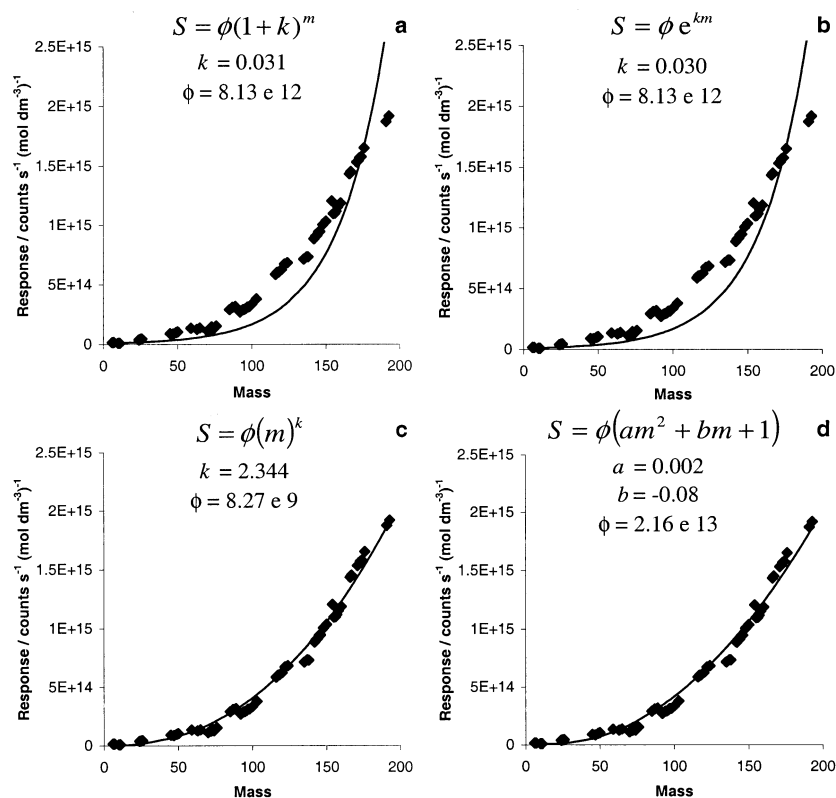


Fig. 7 Comparison of experimental (◆) and theoretical (—) instrument response functions.

y -variable and the response predicted by the models as the x -variable, and the standard deviation of the y residuals, $s_{y/x}$ was calculated using eqn. (25).

$$s_{y/x} = \sqrt{\frac{\sum_i (y_i - \hat{y}_i)^2}{(n-2)}} \quad (25)$$

The \hat{y}_i values are the points on the calculated regression line corresponding to the individual x -values (masses), n is the number of points (61). Clearly smaller values of $s_{y/x}$ demonstrate better fit to the data. For both the power and exponential models, $s_{y/x}$ was 2×10^{14} . The magnitude of this value was due to the fact that the elemental concentrations were converted into molar form before calculation of the instrument response at the individual masses (the units for the response were $\text{counts s}^{-1} (\text{mol dm}^{-3})^{-1}$). For the Russell *et al.* response function, the fit to the experimental data after optimisation of the constants was very good, as shown in Fig. 7c. The standard deviation of the y residuals, $s_{y/x}$ was 6×10^{13} , showing significantly better fit than the power and exponential models.

The shape of the experimental response function in Fig. 7 clearly approximates a polynomial model. Thus the theoretical response function $S = \phi(am^2 + bm + 1)$ was considered. After optimisation, good fit to the experimental data was observed for this model (Fig. 7d), $s_{y/x}$ was 6×10^{13} . The polynomial response function was as good a match to the data as $S = \phi(m)^k$ (Russell law).

For the polynomial instrument response function,

$$R^{\text{obs}} = \frac{am_2^2 + bm_2 + 1}{am_1^2 + bm_1 + 1} \times R^{\text{true}} \quad (26)$$

$$E^{\text{obs}} = \frac{a(m_2^2 - m_1^2) + b(m_2 - m_1)}{am_1^2 + bm_1 + 1} \quad (27)$$

Note that E^{obs} is dependent on the absolute masses of the isotopes. When the optimisation method was used to determine the constants, it was found that Solver could not find optima

for a and b from certain starting values. Initial values of -1 for both parameters generally provided successful optimisation. Internal standardisation can also be applied to find the values a and b , although measurement of two known isotope ratios is required.

The different instrument response models were applied to the correction of multi-collector Cd isotope ratio data; Fig. 8 summarises the results. Initial measurement of a Cd standard solution was used to find the optimum parameters for each instrument response function, using Solver in Microsoft Excel[®] as described above. The parameters were then used to correct isotope ratios measured in a separate 200 ng ml^{-1} standard solution. The ratios that were corrected were not the same as those used in the optimisation. As shown in Fig. 8, ratios with low mass difference and centred close to the axial collector were corrected to within one standard deviation of the natural ratios by all models. The power and exponential instrument response functions however gave poor correction when the mass difference between the isotopes increased and as collectors further from the axis were employed. The polynomial and 'Russell' response functions consistently provided better correction of isotope ratio data; ratios corrected using the polynomial model were closest to the published natural values. The conclusion of this study is that for all ICP-MS systems, the true instrument response function should be investigated by measurement of a multi-element standard solution, and the function that provides best fit to the data should be used to derive the isotope ratio correction model.

The effect of the presence of a matrix element on the isotope ratio correction provided by the models was also investigated. Parameters in the instrument response functions were optimised separately for each sample as above, and used to correct other Cd ratios measured in the same solution. The 'residual bias' of Cd isotope ratios corrected using each model was calculated for clean standards and solutions spiked with increasing levels of matrix elements. The results for a Cd + $100 \text{ } \mu\text{g ml}^{-1}$ calcium solution, relative to those for a clean Cd standard are presented in Fig. 9 by way of example. The

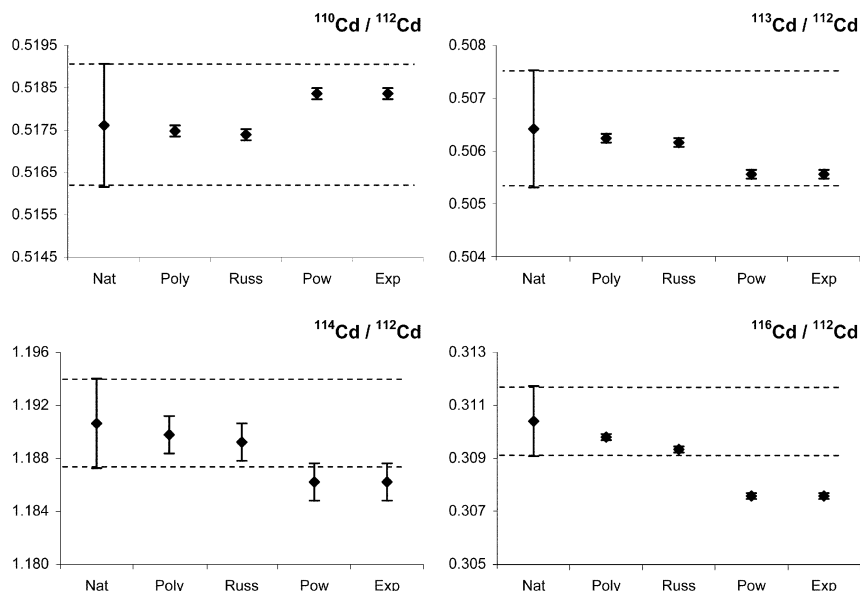


Fig. 8 Corrected Cd isotope ratio data from a 200 ng ml^{-1} standard solution. Nat = natural ratio, Poly = polynomial correction model, Russ = Russell, Pow = power, Exp = exponential correction models. Dotted lines = ± 1 sd of the natural ratio. Error bars are one standard deviation, natural isotope ratios and errors calculated from ref. 17.

Russell, power and exponential models resulted in a higher residual bias when the matrix was present, compared to the clean standard solutions, for all isotope ratios investigated. After correction using the polynomial model, most, but not all, of the ratios had a residual bias that was lower in the matrix doped samples than in the 'Cd only' solutions. This slightly unexpected result derives from the fact that the matrix induced changes in the absolute intensities occurred in a manner that reduced the magnitude of E^{obs} , as described above. Although not universal, this result suggests that the two parameter polynomial model is more adaptive to matrix induced changes in E^{obs} than the other functions investigated.

Semi-quantitative analysis using E^{obs}

ICP-MS is an ideal technique for semi-quantitative analysis, allowing rapid determination of the concentration of a large number of elements in a wide range of sample types, with a reasonable degree of accuracy (30 to 50%).²¹ In general, prior measurement of a standard or reference material is performed to determine relative sensitivity factors for the analyte elements, which are then used to calculate sample concentrations. This procedure is equivalent to a one point calibration for each element; any elements that are to be quantified in the sample must also be present in the reference solution. Spectral

overlaps and matrix effects may be problematic if the standard and sample are not well matched in terms of matrix components.

Alternatively the instrument response function can be determined by using the intensities of selected isotopes across the mass range. Unknowns are determined by interpolation from this function. This is the most commonly used method of semi-quantitative analysis, and has the advantage of requiring only a few standard isotopes to model the entire mass range, however extrapolation of the function may lead to inaccurate determinations.

Another method of determining the response function suggests itself from the above discussion of the relationship between E^{obs} and the instrument response. Firstly, a number of isotope ratios that are free from spectral interference were measured across the mass range. This was performed as part of the semi-quantitative analysis; the elements involved could be analytes as long as their natural isotopic ratio was known and constant. The values of E^{obs} were then calculated using eqn. (15), and the sum of the squared differences between these measured values of E^{obs} , and those calculated from eqn. (16), was minimised by altering the value of the constant(s) in the instrument response function, using optimisation software as described.

These parameters were then used to calculate the concentration of the analyte elements, *via* the following procedure. The numerical value of the instrument response for the internal standard was calculated from the data, using rearrangement of eqn. (13), including the calculated value for its fractional ionisation. The concentration of all other elements was then evaluated using the instrument response function to calculate the relative response at each analyte mass, and factors for the degree of ionisation and isotopic abundance.

The principal advantages of this method are that any matrix induced variations are taken into account as the samples themselves are used to determine the instrument response, and that quantification requires knowledge of only one elemental concentration, that of the internal standard. The instrument response function is determined using only a series of isotope ratios. Spectral interference remains a potential problem, as for any other method of quantitation.

To test this method of semi-quantitative analysis, a multi-element standard solution containing 24 elements was analysed. A total of 14 isotope ratios were used for optimisation of

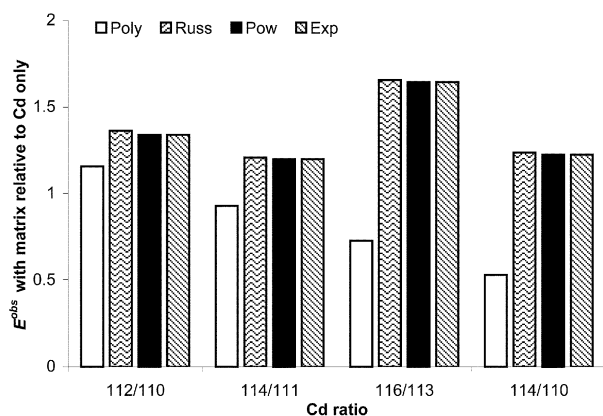


Fig. 9 Residual E^{obs} for a series of Cd isotope ratios, calculated after correction using the different models for a 200 ng ml^{-1} Cd + 100 µg ml^{-1} Ca solution, relative to that in a clean 200 ng ml^{-1} Cd standard.

Table 3 Percentage difference between calculated and true concentrations for semi-quantitative analysis using isotope ratios and internal standards to define the instrument response function

Isotope ratios method		Internal standards method
Li	16%	Std ^a
B	4%	−285%
Mg	350%	666%
Sc	101%	78%
Ti	72%	54%
Co	43%	Std ^a
Cu	13%	3%
Ge	−11%	−15%
Rb	22%	20%
Y	19%	16%
Mo	−5%	−5%
Rh	Std ^a	Std ^a
Sn	15%	−1%
Ba	1%	Std ^a
Nd	11%	12%
Gd	11%	22%
Er	26%	47%
Yb	25%	51%
W	−23%	−4%
Ir	21%	57%
Pt	−16%	10%
Pb	1%	35%
Bi	−15%	Std ^a
U	−7%	Std ^a

^aStd = element used as an internal standard.

the constants in the instrument response function. These were ^{26/24}Mg, ^{49/47}Ti, ^{65/63}Cu, ^{72/70}Ge, ^{87/85}Rb, ^{94/92}Mo, ^{100/98}Mo, ^{122/120}Sn, ^{137/135}Ba, ^{148/146}Nd, ^{160/158}Gd, ^{176/174}Yb, ^{186/184}W and ^{193/191}Ir. The concentration of 23 analyte elements was calculated using the optimised response function and Rh as an internal standard, and the percentage error in the calculated concentration of each element was evaluated. Table 3 gives the results of this calculation and the percentage errors obtained when 6 internal standards were used to determine the instrument response function. For both approaches, a polynomial instrument response of the form $S = \phi(am^2 + bm + 1)$ was assumed. Using isotope ratios to define the instrument response function, 17 of the 23 calculated element concentrations were within 25% of their true value, including Li, B, Pb and U. By the internal standards method, the calculated concentrations of 11 out of the remaining 18 analyte elements were within 25% of the true values. The majority of the elements in this range were the same for the internal standards method as for the E^{obs} approach, suggesting that contamination (Mg) and/or spectral interferences (argon or nitric acid based for Sc and Ti; oxide interferences for Er and Yb) may have been responsible. A greater number of elements could be quantified using the isotope ratio approach, as this method required only one internal standard, compared to six for the alternative procedure.

Conclusion

This paper proposes a new approach to the modelling and correction of instrumentally derived bias in isotope ratio measurements. The first step is to characterise the instrument response function over as wide a range of masses as possible. A smooth continuous function is used (in contrast to the locally defined mass bias) because no other choice is logical, and it follows that data points that fall off this curve must be due to spectral interference, poor calibration of individual detectors, erroneous prediction of the degree of ionisation, or that the true isotopic abundances in the sample are not equal to the published values. The instrument response function is then used to define the expression that should be used to correct isotope ratio data, from eqn. (14). The constants in the

response function are determined at the time of analysis using rearrangement of this equation, and measurement of an internal or external standard. The corrected analyte isotope ratio can then be evaluated by substitution of the constants and the masses of the isotopes into the correction expression. The use of internal standardisation to determine the constants is preferred as the presence of the sample matrix is expected to influence the values.

Ultimately the response function applied will depend on the individual instrument used to perform the analysis, and may even vary between different systems that are of the same make and model, particularly if different operating conditions are employed. Continuing improvements in performance and increasing numbers of collectors will allow (and indeed require) more refined functions to accurately model the data. The use of this approach for quadrupole ICP-MS systems may be hindered by the achievable isotope ratio precision that will prevent discrimination between similar correction models. More success may be anticipated at low masses where the mass-to-mass variation in error is much larger, although this has not been tested here. The approach outlined in this paper should be applicable to other kinds of mass spectrometer. For example, time of flight instruments can acquire data for a large mass range simultaneously (from the plasma's point of view) and therefore it should be possible to define the instrument response function of these systems with great precision, allowing a detailed mass bias model to be constructed. Additionally, the increasing use of isotope ratio data from organic mass spectrometry will require accurate corrections for the instrumentally derived error.

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