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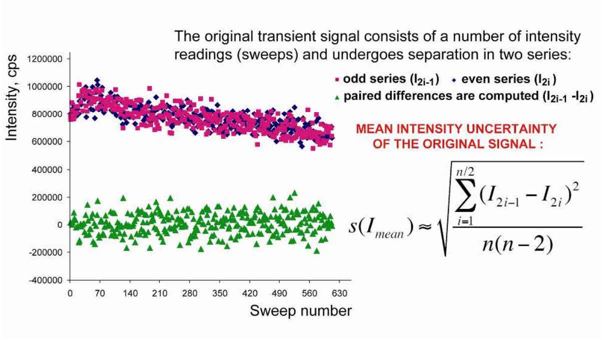

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A new method is proposed to calculate the mean intensity uncertainty of a transient LA-ICPMS signal. It is based on the statistical analysis of intensity differences for successive sweeps.

# Differencing as a method to estimate the uncertainty of a transient LA-ICPMS signal

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## Abstract

Laser ablation inductively coupled plasma mass spectrometry (LA-ICPMS) usually yields transient time resolved signals, of which the (floating mean) intensity changes with time. Estimating the mean intensity uncertainty of a transient signal is useful methodologically and also helps computing the concentration (concentration ratio) uncertainty, provided the intensity ratio is defined as a ratio of the mean intensities calculated over the sweeps constituting the signal. This mean intensity ratio definition is more accurate for strongly fluctuating signals compared to the alternative (mean of ratios, intercept) definitions. Here we present a new method to estimate the mean intensity uncertainty of transient LA-ICPMS data based on the ratio-of-means model. It invokes calculating the intensity differences of each two successive sweeps in the original signal and statistically treating a series of these differences instead of the original signal. The transient trend is usually eliminated from the differenced data, allowing to easily compute the uncertainty of the mean difference and to derive the mean intensity uncertainty for the original signal. By propagating the individual isotope mean intensity uncertainties, the isotope intensity ratio uncertainty can then be obtained.

## Introduction to the methodology of the LA-ICPMS signal treatment

Estimating the uncertainty is an integral part of an analytical result and is also important from a methodological point of view, since it allows evaluating and improving the performance of an analytical method. In the case of replicate measurements, the uncertainty can be calculated from the replicates. However, *in-situ* analytical methods such as laser ablation inductively coupled plasma mass spectrometry (LA-ICPMS) often do not allow acquiring replicates because of the small size of the sample or its inhomogeneity. In this case, the sample concentration [= mass content] or concentration ratio ($c^X/c^Y$) uncertainty has to be calculated from one single analysis according to the equation[1-3]:

$$\left(\frac{I^X}{I^Y}\right)_{mean} = \beta\frac{c^X}{c^Y} \qquad (1)$$

where $X$ and $Y$ are isotopes, of which the mean intensity ratio $(I^X/I^Y)_{mean}$ in the sample is estimated during the analysis. Coefficient $\beta$ can be called sensitivity ratio for isotopes $X$ and $Y$; it is closely related to parameters such as mass fractionation / bias[4]. It is estimated by analysing (an) external standard(s) with known isotope abundances (ratios). Propagating the uncertainties in squares yields:

$$Var\left(\frac{c^X}{c^Y}\right) = \beta^{-2}Var\left(\frac{I^X}{I^Y}\right)_{mean} + \beta^{-4}\left(\frac{I^X}{I^Y}\right)^2_{mean}Var(\beta) - 2\beta^{-3}\left(\frac{I^X}{I^Y}\right)Cov\left(\frac{I^X}{I^Y},\beta\right) \qquad (2)$$

Accordingly, the variance (square of standard deviation) of the concentration ratio depends on the variances and absolute values of the mean intensity ratio and mass bias and on their covariance, if there is any. The estimation of the mean intensity ratio variance using the differencing method is the topic of this work. The estimation of the variance of the sensitivity ratio is methodologically different and invokes approaches that are beyond the scope of this work; they include standard certification as well as the analysis of the intensity vs. concentration ratio statistics for the selected standard(s).

## LA-ICPMS data treatment and EURACHEM/CITAC guidelines: beyond equations (1,2)

One can argue, perhaps appealing to the EURACHEM/CITAC guidelines on measurement uncertainties, that the individual concentrations constituting the concentration ratio in equations (1,2) are not only intensity dependent but are also functions of laser ablation and ICPMS parameters. Besides, it can be argued that the individual isotope intensities are also functions of some parameters. Questions could arise: (i) can and should we construct functions linking the individual isotope concentration to the instrumental parameters and propagate the uncertainties according to these functions? (ii) can we construct such functions for the individual isotope intensities? (iii) if we do not have such functions, are the sample intensity and intensity ratio uncertainties underestimated? These questions have partially been discussed in the EURACHEM/CITAC guided research on ICPMS uncertainties[5], where they receive negative answers (except question (ii) where arguments beyond the current ICPMS knowledge can be advanced using a mathematical apparatus developed for non-transient signals only, see Electronic Appendix 2). Early studies using an expression for the sensitivity based on instrumental parameters such as plasma temperature, ionisation and ion transmission efficiencies and applying this expression to uncertainty calculations[6] had no impact on the development of data quantification in LA-ICPMS, where the principle of internal standardisation, minimising the role of instrumental parameters, dominates. Thus, metrological LA-ICPMS studies do not make attempts to link instrumental parameters to concentrations and intensities and their uncertainties[3,5,7]. More detailed explanations regarding this question are given in Electronic Appendix 2.

**The different approaches to the definition of the mean intensity ratio**

A typical LA-ICPMS signal is time resolved, i.e. it contains a number of intensity readings (sweeps). Accordingly, it is possible to define the mean intensity ratio in equations (1-2) as[3,5,7,8]:

a) a ratio of the mean intensities calculated over all sweeps constituting the signal;
b) a mean of the intensity ratios calculated from each sweep individually;
c) an intercept value of a regression approximating a time series of the sweep intensity ratios.

Besides, a practice of averaging (‘integrating’) several, usually 3-5, sweep intensities before computing ratios exists[1,3,5,7], leading to the appearance of transitional forms between the definitions above.

The definitions above are usually understood in the ICPMS practice as equally unbiased. This is not true. It is possible to show that, for sufficiently large *n*,

$$\sum_{i=1}^{n} I_i^X \Big/ \sum_{i=1}^{n} I_i^Y \; (\mathit{ratio\ of\ means}) \le \sum_{i=1}^{n} \frac{I_i^X}{I_i^Y} \Big/ n \;\; (\mathit{mean\ of\ ratios}) \qquad (3)$$

The sign ‘less or equal’ in this expression is concerned with the extent of fluctuation of the studied signal. For ‘smooth’ distributions of the individual sweep intensities, the ratio of means is approximately equal to the mean of ratios. For strongly fluctuating sweep intensity distributions (more exactly, in case if the intensity of the isotope-denominator in expression (3) strongly fluctuates), the ratio of means is markedly less than the mean of ratios[3,8]. As the standard used for mass bias calibration rarely fluctuates the same way as the sample (with the latter often showing more fluctuation[3]), the concentration ratio in the sample becomes dependent on the extent of fluctuation of the standard and the sample signals. This dependence can be sufficiently strong, detrimental to the quality of analysis[3,8].

A positive bias in mean ratio estimates obtained using definition (b) has been known for ~ one century now; a historical introduction and a discussion relevant to mass spectrometry can be found in the literature of secondary ion mass spectrometry[8]. Definition (c) can be understood as a more general form of definition (b). For a non-transient distribution of the individual sweep intensity ratios, the mean is given by a trivial regression with a zero slope. For a transient distribution of such ratios often encountered, for example, in *U-Pb* LA-ICPMS dating applications, the mean is defined by the center of the linear ordinary least square regression [as the regression line passes through point (*mean time, mean ratio*)]. Unsurprisingly, definition (c) also yields biased ratio estimates; we showed in a recent work that the mean intensity ratio varies depending on the signal fluctuations and averaging, and the extent of this variation can be dramatic and not necessarily the same for the standard and the sample, leading to inaccuracies[3]. This deficiency of the mean of ratios and the regression based approach is attenuated[3] by averaging the individual sweep intensities before the intensity ratio vs. time data are regressed (and also by setting longer dwell times). For example, instead of applying a regression to the sequence

$$\left(\frac{I_1^X}{I_1^Y}, t_1\right), \left(\frac{I_2^X}{I_2^Y}, t_2\right), \left(\frac{I_2^X}{I_2^Y}, t_2\right) \qquad (4)$$

we could regress a sequence of the ratios of partial sums (the averaging factor, *k*, being set arbitrarily):

$$\left(\frac{I_1^X + \ldots + I_k^X}{I_1^Y + \ldots + I_k^Y}, \frac{t_1 + \ldots + t_k}{k}\right), \left(\frac{I_{k+1}^X + \ldots + I_{2k}^X}{I_{k+1}^Y + \ldots + I_{2k}^Y}, \frac{t_{k+1} + \ldots + t_{2k}}{k}\right), \ldots \qquad (5)$$

Still, for strongly fluctuating signals even averaging tens of sweeps before regression does not lead to accurate results (see Electronic Appendix 1, $I^{Pb207}/I^{U235}$ values). Thus, the regression-based definition of the mean intensity ratio should be used with caution, at least for strongly fluctuating signals.

**Uncertainty of the ratio of mean intensities and of the mean intensities constituting this ratio**

Definition (a), based on the ratio of two mean intensities, is (almost) unbiased regarding the signal fluctuations and their averaging[3,8]. This work focuses on the estimation of the intensity and intensity ratio uncertainty in the framework of definition (a) using the differencing method. The mean intensity ratio is defined as follows:

$$\left(\frac{I^X}{I^Y}\right)_{mean} = \frac{I^X_{mean}}{I^Y_{mean}} = \left(\sum_{i=1}^{n} I_i^X / n\right) \Big/ \left(\sum_{i=1}^{n} I_i^Y / n\right) = \sum_{i=1}^{n} I_i^X \Big/ \sum_{i=1}^{n} I_i^Y \qquad (6)$$

where $n$ is the number of sweeps constituting the analysis. Propagating the related uncertainties in squares gives the following equation for the variance of the mean intensity ratio[3,5,9]:

$$Var\left(\frac{I^X}{I^Y}\right)_{mean} = \left(\frac{1}{I^Y_{mean}}\right)^2 Var(I^X_{mean}) + \frac{(I^X_{mean})^2}{(I^Y_{mean})^4} Var(I^Y_{mean}) - 2\left(\frac{1}{I^Y_{mean}}\right)\left(\frac{I^X_{mean}}{(I^Y_{mean})^2}\right) Cov(I^X_{mean}, I^Y_{mean}) \qquad (7)$$

In the presence of a non-negligible background, the mean background intensity is subtracted from the mean signal intensity for each of the isotopes; in the equations above, the corresponding net intensities and their uncertainties [$Var(I_{net})=Var(I_{gross})+Var(I_{bkgr})$] are then used. We will not detail this merely technical aspect; henceforth, background corrections are omitted to improve formulae readability.

Estimating the uncertainties of mean intensities for the individual isotopes and of their covariance (if there is any) are pre-requisites for using equation (7). The mean intensity uncertainty obtained by ICPMS from an individual analysis can be calculated using two basic approaches, the Poisson and the intensity-of-the-mean-of-the-individual sweeps approach. Currently, the Poisson approach to ICPMS signals is restricted by low intensities, where the familiar formula is valid (provided time is known precisely and omitting the dead time correction to the uncertainty)[5,10,11]:

$$s(I_{mean}) = s\left(\frac{N}{t}\right) = \frac{s(N)}{t} = \frac{\sqrt{N}}{t} = \sqrt{\frac{I_{mean}}{t}} \qquad (8)$$

A more detailed discussion on the Poisson distribution in ICPMS is given in Electronic Appendix 2.

A more universal approach valid also for high-intensity signals is to use the time resolved structure of ICPMS signals and estimate the mean intensity uncertainty as the uncertainty of the mean of the individual sweep intensities:

$$s(I_{mean}) = \frac{s(I_{individual\ sweep})}{\sqrt{n}} = \sqrt{\frac{\sum_{i=1}^{n}(I_i - I_{mean})^2}{n(n-1)}} \qquad (9)$$

where $I_i$ is an individual sweep intensity and $n$ is the total number of sweeps.

This approach is widely used to treat non-transient ICPMS data (e.g. the background noise and raster ablation signals). However, it fails on transient signals, where the mean intensity is different for the different parts of the signal. In an extreme case of an idealised, precise transient signal, of which the sweep intensities rapidly decrease with time in a strictly linear way, formula (9) still yields a high uncertainty value. How to obtain the mean intensity uncertainty for a transient signal, as well as the covariance of two mean intensities, to enable the uncertainty calculation according to equation (7)?

**Differencing as a method to eliminate the transient trend and to estimate the mean intensities uncertainties and covariance**

ICPMS signals belong to a large group of statistical processes that are called *time series*. A time series represents a series of values registered with some periodicity during a time interval. Time series are common in econometrics and technical sciences; thus, a mathematical apparatus exists to handle them[12,13]. One frequently used approach to handle a transient time series is to eliminate the trend and transform the series to a non-transient form. Eliminating the trend can be done by differencing, i.e. by creating a new – non-transient - series of values, each of which representing a difference of the neighbouring values from the original series. Selecting the neighbouring values from the original time series can be done in many ways, with or without a logarithmic or other transformation of the original values[10]. In the following, we will consider a differencing model that fits for our purpose to estimate the uncertainty of the mean intensity of a transient LA-ICPMS signal.

Let us consider a transient LA-ICPMS signal made of a series of sweep intensities $I_1, I_2, I_3, I_4, \ldots, I_n$, where $n$ is an even integer value representing the total number of sweeps. This series can be split in two new series, of which the first (odd) contains values $I_1, I_3, \ldots, I_{n-1}$, and the second (even) – values $I_2, I_4, \ldots, I_n$. Let us designate the mean intensity for the odd series as $a$:

$$a = \frac{I_1 + I_3 + \ldots + I_{n-1}}{n/2}$$

and the mean intensity for the even series as $b$:

$$b = \frac{I_2 + I_4 + \ldots + I_n}{n/2}$$

The mean intensity of the original series is easily derivable: $I_{mean}=(a+b)/2$.

Its variance is given as follows: $Var(I_{mean}) = Var\left(\frac{a+b}{2}\right) = \frac{1}{4}(Var(a) + Var(b) + 2Cov(a,b))$ (10)

Let us create a series of differences $I_1$-$I_2$, $I_3$-$I_4$, …, $I_{n-1}$-$I_n$. This series is usually not transient, even if the original series is transient (Fig. 1a and b; section 'Limitations related to the presence of a trend…'). The mean value for this series is $a$-$b$. Its variance is as follows:

$$Var(I_{2i-1} - I_{2i})_{mean} = Var\left(a-b\right) = Var(a) + Var(b) - 2Cov(a,b) \quad (11)$$

The covariance term in equations (10) and (11) needs to be discussed. Do the odd and the even series represent two independent samples of the same stochastic process, meaning a zero covariance? One widely known example where it holds true is the calculation of the critical intensity value ($L_c$) for detection decision by differencing two sequential background estimates[1,10,14-17]:

$$L_c = ks(I_{mean\ bkgr\ 1} - I_{mean\ bkgr\ 2}) = k\sqrt{(Var(I_{mean\ bkgr\ 1}) + Var(I_{mean\ bkgr\ 2}) - 2Cov(I_{mean\ bkgr\ 1}, I_{mean\ bkgr\ 2})} =$$
$$= k\sqrt{(Var(I_{mean\ bkgr\ 1}) + Var(I_{mean\ bkgr\ 2})} = k\sqrt{2}s(I_{mean\ bkgr})$$

(12)

where coefficient $k$ describes a desired confidence level.

However, mean intensity estimates $a$ and $b$ are not exactly sequential compared to the background estimates above, and their difference depends on the fine structure of the LA-ICPMS signal, which is poorly studied at present. Specifically, it depends on the presence of short-term trends in the sweep intensity vs. time distribution: intensities belonging to two neighbour sweeps follow a short-term trend and do not differ much, even if the intensity variance over all sweeps is significant. In the extreme case, the even intensity series can be approximately represented as a time shifted copy of the odd series; then, $Cov(a,b) \approx Var(a)$. To ensure that the odd and the even series are indeed independent, either one or both of the following requirements must be met: 1) the intensity collection time (dwell time) per sweep and per isotope is sufficiently long (several ms at least); 2) the analytical protocol includes a number of isotopes collected sequentially. These requirements serve to eliminate short-term trends from the ICPMS data (and, generally, from any time series). In the following, we will assume that the data meet these requirements, resulting in a zero covariance between the odd and the even series. Tests presented in section 'Discussion of examples' support this assumption.

The uncertainty of the mean difference can be easily calculated:

$$Var(I_{2i-1} - I_{2i})_{mean} = \frac{Var(I_{2i-1} - I_{2i})_{individual}}{n/2} = \frac{\sum_{i=1}^{n/2}\left[(I_{2i-1} - I_{2i}) - (I_{2i-1} - I_{2i})_{mean}\right]^2}{n/2(n/2-1)} \quad (13)$$

Gaussian confidence limits can be assigned to this uncertainty, provided the even and the odd sweep intensities are Gauss distributed; a goodness of fit test (e.g. a $\chi^2$ test) can also be made for the differences if the latter statement is questioned.

Combining equations (10), (11) and (13) then gives, for the mean intensity $I_{mean}$ of the original signal:

$$Var(I_{mean}) = Var\left(\frac{a+b}{2}\right) = \frac{1}{4}(Var(a)+Var(b)) = \frac{Var(a-b)}{4} = \frac{Var(I_{2i-1}-I_{2i})_{mean}}{4} =$$

$$= \frac{Var(I_{2i-1}-I_{2i})_{individual}}{2n} = \frac{\sum_{i=1}^{n/2}\left[(I_{2i-1}-I_{2i})-(I_{2i-1}-I_{2i})_{mean}\right]^2}{n(n-2)}$$

$$s(I_{mean}) = \frac{s(I_{2i-1}-I_{2i})_{individual}}{\sqrt{2n}} = \sqrt{\frac{\sum_{i=1}^{n/2}\left[(I_{2i-1}-I_{2i})-(I_{2i-1}-I_{2i})_{mean}\right]^2}{n(n-2)}}\left[\approx\sqrt{\frac{\sum_{i=1}^{n/2}(I_{2i-1}-I_{2i})^2}{n(n-2)}}\right] \quad (14)$$

In this stage, both mean intensities and their variances are known and formula (7) can be applied to compute the intensity ratio uncertainty, provided the mean intensities for two isotopes involved in the ratio calculation show a zero covariance. The latter is not given *a priori*: an appreciable mean intensities covariance exists in multi-collector ICPMS measurements, where the individual sweep intensities for different isotopes are acquired simultaneously and increase or decrease simultaneously, reflecting the pattern of plasma and sampling system fluctuations; some covariance can also be present in mono-collector ICPMS measurements. Generally, it needs to be estimated[3,7,9].

To estimate the covariance, the differencing method needs to be generalised. If *a* and *b* are the mean intensities for the odd and the even series for isotope *X*, respectively, and *c* and *d* – those for isotope *Y*, then we obtain:

$$\begin{aligned} Cov(I^X_{mean}, I^Y_{mean}) &= Cov\left(\frac{a+b}{2},\frac{c+d}{2}\right) = \frac{1}{4}Cov(a+b,c+d) = \\ &= \frac{1}{4}\big(Cov(a,c)+Cov(b,d)+Cov(a,d)+Cov(b,c)\big) \end{aligned} \quad (15)$$

On the other hand, $Cov(a-b,c-d) = Cov(a,c)+Cov(b,d)-Cov(a,d)-Cov(b,c)$.

Series *a* and *c*, *b* and *d* are complementary, i.e. they contain sweep intensities belonging to the same sweep, where a covariance is likely to appear. Series *a* and *d*, *b* and *c* are not complementary, since they contain individual sweep intensities from the different (odd vs. even) sweeps. Following the state-of-the-art approach[3,7,9] to the covariance calculation in LA-ICPMS and thus omitting the covariance between sweep intensities from the different sweeps, we neglect *Cov (a,d)* and *Cov (b,c)* terms in the equation above and arrive to the following formula:

$$Cov(I^X_{mean}, I^Y_{mean}) = \frac{1}{4}\big(Cov(a,c)+Cov(b,d)\big) = \frac{1}{4}Cov(a-b,c-d) =$$

$$= \frac{\sum_{i=1}^{n/2}\left[(I^X_{2i-1}-I^X_{2i})-(I^X_{2i-1}-I^X_{2i})_{mean}\right]\left[(I^Y_{2i-1}-I^Y_{2i})-(I^Y_{2i-1}-I^Y_{2i})_{mean}\right]}{n(n-2)}\left[\approx\frac{\sum_{i=1}^{n/2}(I^X_{2i-1}-I^X_{2i})(I^Y_{2i-1}-I^Y_{2i})}{n(n-2)}\right] \quad (16)$$

Since variance is a special case of covariance [*Cov(x,x)=Var(x)*], formula (14) can be considered as a special case of formula (16).

## Discussion of examples

The performance of the differencing method can be shown with the following examples: (i) an idealised, precise linear signal; (ii) a real non-transient signal as a special case of a transient signal; (iii) a real transient signal; (iv) a replicate series of transient signals. Tables containing generalised intensity data and the resulting uncertainties for examples (ii-iv) are available as Electronic Appendix 3, all original data and calculations are provided in Electronic Appendix 4.

(i) For the first case, we consider a trivial 'signal', of which the intensity decreases with time (sweep number $i$) following a strictly linear pattern: $I_i=ai+b$, where $a$ is the slope of the line and $b$ is the intercept. In this case, $I_i-I_{i+1}=-a$ for any pair of sequentially acquired sweeps. The uncertainty of a constant value is zero, which is also easy to obtain using formulae (13,14) (although not the approximate variant of formula (14) given in brackets: it yields an uncertainty close to zero only asymptotically, at large $n$). In contrast, applying formula (9) to this example yields a positive uncertainty depending on $a$.

(ii) The second case treats a real non-transient signal as a special case of transient signal (Fig. 1a, Table 1 in Electronic Appendix 3). The mean intensity of $U^{238}$ computed over 232 sweeps is 2592175 cps, the standard deviation of the mean obtained using formula (9) is 6334 cps, the same uncertainty obtained using formula (14) is 6806 cps, and using formula (14), approximate variant, - 6807 cps. The difference in the uncertainties obtained from formulae (9) and (14) is 7.4 %. This is acceptable, as the values compared are single measurement based estimates and have, therefore, their own uncertainties: a new measurement yields a new uncertainty estimate generally different from the previous one. The extent of such differences can amount to 5-10% for values obtained by the differencing method. No appreciable covariance between the neighbour sweeps is observed (see Electronic Appendix 4).

(iii) We continue with transient signals (Fig. 1b, Table 2 in Electronic Appendix 3). The mean intensity of $U^{238}$ computed over 612 sweeps is 772893 cps, the standard deviation of the mean obtained using formula (9) is 3720 cps, the same uncertainty obtained from formula (14) is 2185 cps, and from its approximate variant of it – 2191 cps. The difference in the uncertainties obtained from formulae (9) and (14) is 70.3 % (!), with formula (9) overestimating the uncertainty. We repeat the calculations using the intensity of $Pb^{207}$. The mean intensity of $Pb^{207}$ computed over 612 sweeps is only 4424 cps, reflecting the low sample abundance of this isotope. The standard deviation of the mean obtained using formula (9) is 38.4 cps, the same uncertainty obtained from formula (14) is 36.4 cps, and from the approximate variant of this formula – 36.5 cps. The difference in the uncertainties obtained from formulae (9) and (14) becomes small. This example shows the relative roles of the signal transience and signal scatter. At high intensities, the signal transience is well recognisable relative to the scatter, while at low intensities the transient nature of the signal vanishes in its fluctuations (leaving aside the U-Pb ablation related fractionation, which also contributes to a less transient behaviour of $Pb^{207}$ intensity[18]). Let us cut off a substantial part of the signal and leave only the last segment of it showing little transience. Formulae (9) and (14) yield consistent results for both $Pb^{207}$ and $U^{238}$ in this case, reflecting the approximate identity of these formulae for non-transient signals (see Electronic Appendix 4).

Recently, a method has been proposed that relies on formula (9) applied to short segments of a transient signal and not to the signal as a whole[3]. The signal transience within each of the segments is neglected. Each segment yields an uncertainty corresponding to its own mean intensity. The uncertainty of the mean intensity over all segments is derived by propagating the individual segment uncertainties. This very straightforward method can be practically implemented, especially if the signal transience is weak, much less significant than the between-sweeps intensity scatter. In the example of a transient $U^{238}$ signal above (Fig. 1b) this method yields a standard deviation of the mean of 2351 cps, which is comparable to 2185 cps obtained by the differencing method, additionally confirming the validity of the latter (see Electronic Appendix 4).

(iv) Finally, we consider a replicate series of transient signals (Table 3 in Electronic Appendix 3). We will compare uncertainty estimates obtained using the differencing method with those calculated based on the replicate series of intensity (intensity ratio) values, each of which being outcome of an individual analysis. This approach is conditional, since the (short-term) signal stability observed during one measurement is compared to that obtained during the acquisition of many measurements, which takes longer and which can introduce either an additional fluctuation or trend (drift) in the distribution of values obtained from the individual measurements. The doubly stochastic Poisson distribution with a mean randomly varying from analysis to analysis is a good example to illustrate this[19-21]; another example related to the non-stationary background behaviour can be found in our recent work[17]. Thus, an uncertainty estimate obtained from a single analysis is, in the most general case, a minimum estimate compared to the uncertainty obtained from replicate measurements; the both approximately coincide, if a good instrument stability could be achieved. Table 3 presents mean intensities, their uncertainties, as well as the $I^{Pb206}/I^{U238}$ and $I^{Pb207}/I^{U235}$ ratios with the corresponding uncertainties for a series of 18 single collector LA-ICPMS analyses of the SRM 610 doped glass standard from NIST. The core part of the standard glass disc, considered to be homogeneous in Th and U[22-24] and probably homogeneous[24,25] in Pb, was analysed using a spot size of 35 µm and an on-sample energy density of 5 J/cm$^2$; the analytical list was similar to that typically used for U/Pb dating of zircon. Mean intensity uncertainties for Hg$^{201}$, Pb$^{204}$, U$^{235}$ and U$^{238}$ isotopes obtained by the differencing method coincide with those calculated from the eighteen replicates at a level of 5% or better. Pb$^{206}$, Pb$^{207}$, Pb$^{208}$ and Th$^{232}$ show less match: the uncertainty values computed from the replicates are up to 24% higher than those obtained from the individual analyses using the differencing method. In the case of Pb$^{208}$ and Th$^{232}$, this mismatch is (at least partly) concerned with a transient trend, or drift, observed in the replicate values: the intensities systematically change during the acquisition of replicates (Electronic Appendix 4). The $I^{Pb206}/I^{U238}$ ratio uncertainty calculated from the replicates is 0.0025. The corresponding uncertainty obtained from the individual analyses by the differencing method amounts, on average, to 0.0024 (computed using formula (7), omitting the covariance term) and to 0.0026 (including the covariance term in this formula), which is a surprisingly good match. Similarly matched values are obtained for the $I^{Pb207}/I^{U235}$ ratio (Table 3 in Electronic Appendix 3). These particular examples also demonstrate a subordinate role of covariance corrections for results obtained using a single collector ICPMS.

## Limitations related to the presence of a trend in the series of differenced intensities

U/Pb signals in examples (ii-iv) are characterised by a strong scattering of the individual sweep intensities. This reflects the specifics of U/Pb data acquisition protocols that imply a fast intensity acquisition and include a large number of sweeps. Such conditions are not always met in LA-ICPMS: for example, trace element data obtained by sector field LA-ICPMS are usually collected with longer time intervals between the successive sweep intensity acquisitions because of the increased total number of isotopes analysed and of magnet hysteresis. Besides, high ablation rates (high repetition rate and fluence) are often employed to improve the detection limit. The resulting signals show a non-linear, exponential intensity decay with time; the difference between two successive sweep intensities is essentially defined by the exponential dependence above, and not only by the intensity fluctuations between the sweeps. As a result, differencing the sweep intensity data does not always help to remove the trend completely (see Electronic Appendix 6 for an example). As a pre-requisite for using the differencing method, a need to test the differenced data for the presence of a trend arises. Detecting a trend in a time series is an elaborated statistical problem. Some well-known approaches are based on the Abbe[27], Foster-Stuart[28] and Cox-Stuart[29] tests. Here, we consider only the Abbe test, as it is suitable for detecting non-monotonous trends[27], it has a comparatively high power[30], and is intrinsically linked to the differencing method itself[27]. The idea of this test is to compare the uncertainty of the mean obtained by the differencing method (similar to formula 14) to that obtained using formula (9) that does not account for a trend. If the ratio of these uncertainty estimates is low, a trend is present. In Electronic Appendix 6, we show how to apply this test to differenced intensities from an LA-ICPMS signal and provide a formal description of the test. We recommend the Abbe test (possibly in combination with other tests) to be applied to the differenced series before the differencing method is employed, especially if the data acquisition protocol is prone to a trend in the differenced data.

## Concluding remarks

The differencing can be considered as a simple and elegant method to estimate the uncertainty of transient LA-ICPMS signals. Alternatives are few. The mean-of-ratios and the related intercept approaches were mentioned in the *Introduction*; their inaccuracy for strongly fluctuating signals was a stimulus to create the differencing method. The Poisson representation of ICPMS signals, in the general case, requires estimating the total uncertainty via the autocovariance function of a doubly stochastic Poisson process, which is difficult in the case of a transient signal and is beyond the current ICPMS knowledge (see Electronic Appendix 2). We will give a more detailed analysis of questions related to the 'poissonicity' of ICPMS signals in a forthcoming work.

The current status of uncertainty quantification in LA-ICPMS is such that only for high precision isotope ratio work uncertainty values are required by the ICPMS user. For example, such values are usually requested for reporting U/Pb ages based on the $Pb^{206}/U^{238}$ and $Pb^{207}/U^{235}$ concentration ratios in minerals with elevated abundances of uranium (e.g., the mineral zircon, tetr. $ZrSiO_4$). The uncertainty estimation for each U/Pb age is a complex error propagation process[3,7,26]. One of the key entry parameters for this process is the uncertainty of the mean intensity ratio, and the differencing method helps to obtain it. The differencing method extends the existing metrological tools to treat the ICPMS signal, especially for strongly fluctuating signals and at high signal intensities, where the ordinary Poisson approach [$s(N)=\sqrt{N}$] is not applicable.

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**Supporting information**
A collection of signals used in this article and additional discussions on the quantification of ICPMS data are provided in Electronic Appendices 1-6.

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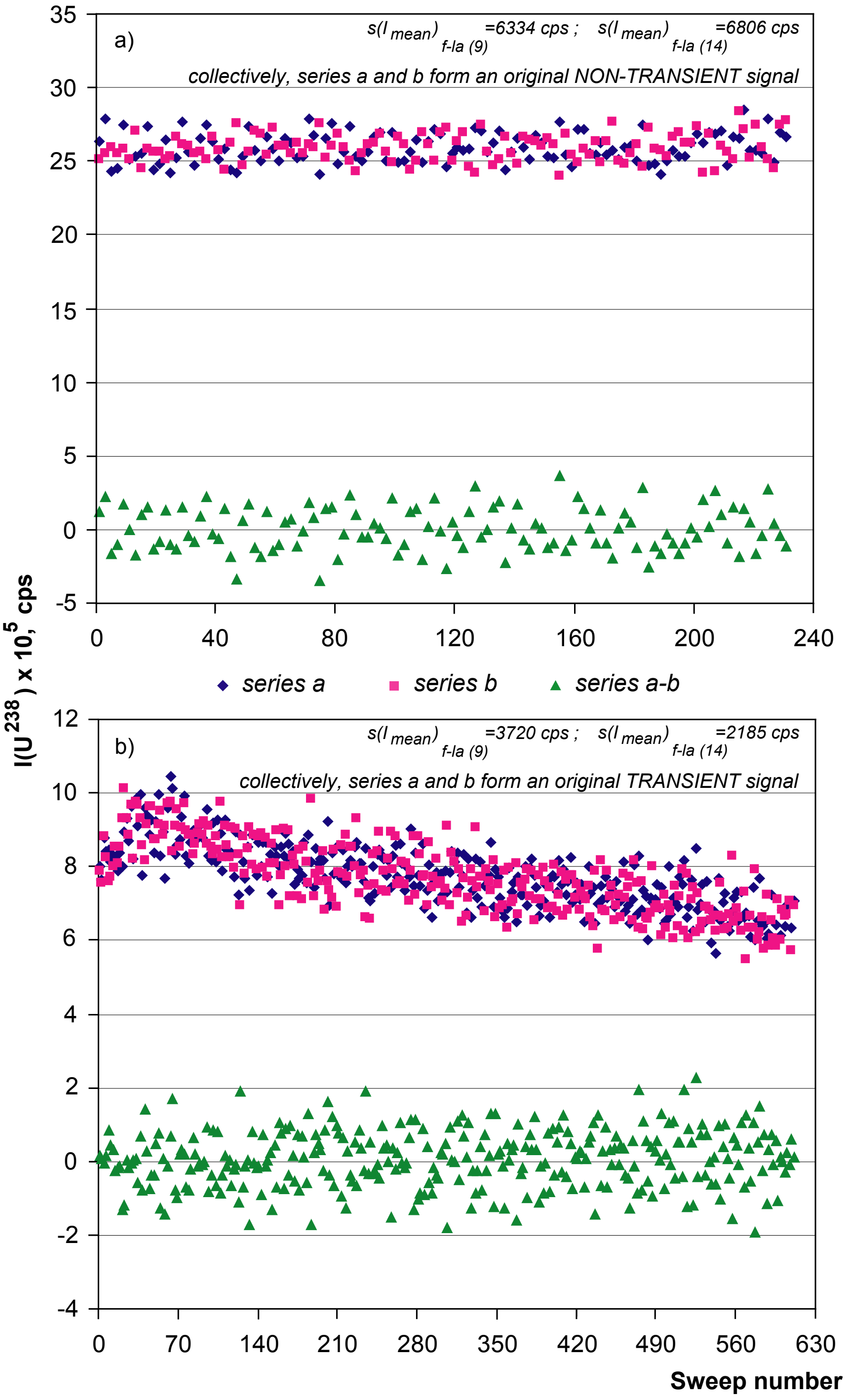

Fig. 1. LA-ICPMS signals separated in series *a* and *b* corresponding to the odd and the even sweeps, respectively, and a signal transform obtained by differencing these series. The differencing eliminates the trend and allows estimating the uncertainty of the transformed data irrespective of the absence or presence of transience in the original signal (Fig. 1a and b, respectively). See Tables 1,2 in Electronic Appendix 3 and Electronic Appendix 4 for the data and Electronic Appendix 5 for a discussion on their graphical comparison.