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Evaluation of measurement uncertainty in analytical assays by means of Monte-Carlo simulation

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Abstract

The main limitations of the Guide to the expression of Uncertainty Measurement (GUM) approach for evaluating the measurement uncertainty of analytical assays are presented and explained. The advantages of using Monte-Carlo simulation against the GUM approach are outlined and discussed and the principle of propagation of distributions is explained. The procedure of Monte-Carlo analysis is illustrated by two case studies. A first simple example quoted from the EURACHEM Guide and dealing with the preparation of a calibration standard is used to present the technique with detail in a step-by-step way. In this case the results obtained by both approaches are very similar. A second example deals with the calibration of mass according to a strong non-linear model. In this case, the Monte-Carlo analysis leads to better results.

Keywords: Measurement uncertainty; Monte-Carlo simulation; ISO-GUM approach; Propagation of distributions

1. Introduction

The increasing implementation of accreditation and quality control procedures emphasizes the necessity of suitable methods for estimating the measurement uncertainty. It is well recognized the importance of measurement uncertainty and traceability to ensure the reliability of analytical assays. This is reflected in the accreditation standard EN-ISO/IEC 17025 that covers enhanced requirements concerning uncertainty and traceability [1].

A very well established approach for evaluating and reporting measurement uncertainty is set out in the 'Guide to the expression of Uncertainty Measurement (GUM)' published by ISO [2]. The GUM approach is recommended by the International Bureau of Weights and Measures (BIMP) [3] and is followed by the NIST guidelines [4] and the rules of the Laboratory of the Government Chemist [5]. EURACHEM/CITAC has also produced a guide that applies the GUM principles to analytical measurements [6].

The GUM approach estimates the overall uncertainty via the law of propagation of uncertainty, following identification and quantification of uncertainties in individual sources. This scheme is also referred as the uncertainty propagation or 'bottom-up' approach [3,7] and is summarized in four main steps: specification, identification, quantification, and combination. In the specification step, an algebraic relationship is established (whenever possible) between the analytical result Z, and the parameters or individual factors x_i that affect the analytical procedure:

$$Z = Z(x_1, x_2, \ldots, x_n) \quad (1)$$

In the identification step, all the sources of significant uncertainty in the analytical procedure are localized and then quantified in the quantification step. The uncertainties can be directly evaluated as a standard deviation from a series of repeated measurements (type A uncertainty) or by using previous information from manufacturer's certificates or analyst's experience leading to a confidence interval that must be converted to standard uncertainty depending on the probability density function of the parameter (type B uncertainty). In the combination step, the combined standard uncertainty $u(Z)$ is evaluated from the standard uncertainties of the individual parameters $u(x_i)$ and covariances $\mathrm{cov}(x_i, x_j)$

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between correlated parameters, according to the principles of error propagation:

$$u^2(Z) = \sum_{i=1}^{n} \left(\frac{\partial Z}{\partial x_i}\right)^2 u^2(x_i) + 2\sum_{i=1}^{n-1}\sum_{j=i+1}^{n} \left(\frac{\partial Z}{\partial x_i}\frac{\partial Z}{\partial x_j}\right) \mathrm{cov}(x_i, x_j) \quad (2)$$

If all parameters contributing to the measurement of Z are independent, $\mathrm{cov}(x_i, x_j) = 0$.

Once the combined standard uncertainty is evaluated, the expanded uncertainty $U(Z)$, is calculated by multiplying $u(Z)$ by a coverage factor k, assuming that the probability distribution function of Z is normal (when the conditions of the Central Limit Theorem are met). The value $k = 2$ has become the conventional coverage factor. Nevertheless, it is more advisable the use of the Student's t-tabulated value for the level of confidence chosen and the effective degrees of freedom calculated using the Welch–Satterthwaite approach [7,8], including correlation terms [9]:

$$\frac{u^4(Z)}{\nu_{\mathrm{eff}}} = \sum_{i=1}^{n} \frac{(\partial Z/\partial x_i)^4 u^4(x_i)}{\nu_i} + 2\sum_{i=1}^{n-1}\sum_{j=i+1}^{n} \times \frac{(\partial Z/\partial x_i)^2(\partial Z/\partial x_j)^2 \mathrm{cov}^2(x_i, x_j)}{\sqrt{\nu_i \nu_j}} \quad (3)$$

Following the NIST guide [4], the degrees of freedom of a standard uncertainty $u(x_i)$ obtained from a type A evaluation is determined statistically from a series of N measurements x_{ik} ($k = 1$–N) as the standard deviation, $s(x_i)$, with $\nu_i = N - 1$ degrees of freedom. If m parameters are estimated by fitting a curve to N data points by the method of least squares, the degrees of freedom of the standard uncertainty of each parameter is $N - m$. The degrees of freedom associated with a standard uncertainty obtained from a type B evaluation are more problematic. However, it is a common practice to carry out such evaluations in a manner that ensures that an under-estimation is avoided. Under the assumption that this practice is followed, the degrees of freedom may be taken to be $\nu_i = \infty$. In some cases, for Gaussian distributions it is common to take $\nu_i = 50$ and this criterion has been implemented in some computer programs for evaluation of the measurement uncertainty [10,11].

GUM approach exhibit, however, some important limitations [12] which are considered in the following:

(1) Model linearization: the referred law of error propagation applied to obtain the combined uncertainty, comes from the truncation of a Taylor's series expansion until first order terms. This is a linear approximation that in some cases could need high order terms [1].
(2) Assumption of normality on Z: in the common practice of routine analysis, the distribution of the result is taken as normal and consequently, the expanded uncertainty $U(Z)$ is computed as the product of the coverage factor k and the combined uncertainty $u(Z)$, the coverage factor being assimilated to the normal variate (z-score). Thus, it is very common to find reported uncertainties obtained using a coverage factor $k = 2$, which gives a level of confidence of approximately 95% (95.45% actually).
(3) Computation of the effective degrees of freedom: if the distribution of Z is considered to be approximated by a Student's distribution, the coverage factor k is taken as the tabulated Student's t-value for a given significance level and the effective degrees of freedom (ν_{eff}) computed from the Welch–Satterthwaite equation. In the general case (including correlation terms), the analytical evaluation of the effective degrees of freedom is still an unsolved problem [9], type B uncertainties, generally contributing with infinite degrees of freedom.

In order to overcome these handicaps left by the GUM approach, the use of Monte-Carlo simulation can be considered for the evaluation of measurement uncertainty [9,12–14]. The Monte-Carlo method is a numerical procedure for solving mathematical problems by means of the simulation of random variables [15,16]. The values of any random variable can be 'simulated' by the suitable transformation of a rectangular random variable, uniformly distributed within the interval (0,1). Pseudo-random numbers, γ, distributed accordingly can be successfully generated by computational algorithms based on congruency methods. From these pseudo-random numbers, the values ξ of any other random variable X with a probability density function $p(x)$ within the interval (a,b) can be simulated by solving the integral equation:

$$\int_a^{\xi} p(x)\,\mathrm{d}x = \gamma \quad (4)$$

All these calculations are rapidly performed thanks to the high speed of modern computers by using the suitable software.

Thus, Monte-Carlo analysis is a tool for combining 'distributions' and thereby, propagating more than just statistical uncertainties. It uses random number generation for simulating the values of the random variables rather than analytic calculations and now it is increasingly popular due to high speed personal computers. The principle of propagation of distributions (Monte-Carlo simulation) against the propagation of uncertainty (GUM approach) is illustrated in Fig. 1. The model Z has three input quantities, namely X_1, X_2, and X_3 whose probability density functions are rectangular ($p(X_1)$), normal ($p(X_2)$), and triangular ($p(X_3)$), respectively. The propagation of these distributions by Monte-Carlo simulation according to the Z model leads to a resulting non-symmetric probability density function for Z, $p(Z)$. From $p(Z)$, the mean expected value of Z together with its uncertainty can be easily obtained as explained below.

Thus, the propagation of distributions provides a general probabilistic basis for uncertainty evaluation and is based on the direct use of the probability density functions assigned

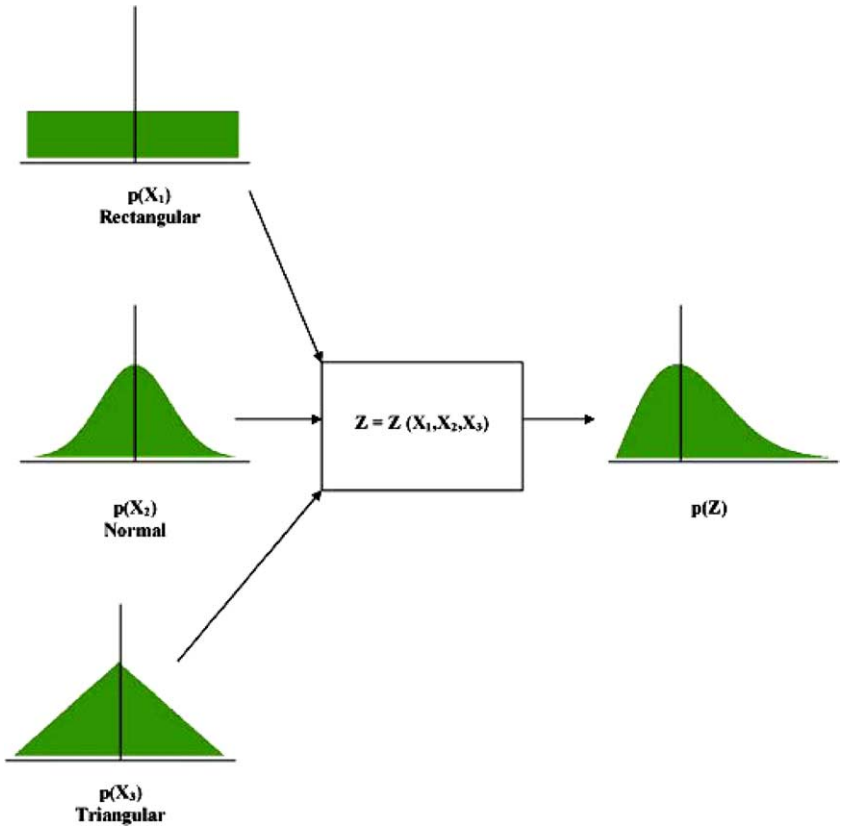

Fig. 1. Propagation of distributions. The model Z has three input parameters X_1, X_2, and X_3 with probability density functions of $p(X_1)$ (rectangular); $p(X_2)$ (normal); and $p(X_3)$ (triangular). The propagation of these distributions leads to a resulting non-symmetric probability density function for Z, $p(Z)$. From $p(Z)$, the mean expected value of Z together with its uncertainty.

to the values of the input quantities rather than just the use of their means and standard deviations (GUM approach). Now, a number of GUM supplementary guides are being prepared by a working group of the Joint Committee for Guides in Metrology (JCGM). The first supplemental guide, dealing with the numerical methods for the propagation of the distributions, is in an advanced stage and recognizes that Monte-Carlo simulations should be used instead of the typical uncertainty propagation for evaluating the uncertainty in the future [17].

The Monte-Carlo simulation is easy to apply and returns the information about the model distribution. However, it also has some limitations: model simulation runtime could be long in some complex cases. Also, the selection of the proper probability distribution functions for the model parameters may be difficult due to inaccurate data or to a lack of understanding of the underlying physical processes [18]. The accuracy of the numerical simulation depends on the quality of the random number generator, but the majority of commercial packages are suitable for this application [19].

In order to perform Monte-Carlo simulations, we need a computer program for generating the pseudo-random numbers and for solving the integral equation in order to simulate the values of the variables with a given probability distribution function. Those researchers with programming expertise may write the suitable routines and procedures or take the code available in FORTRAN and C language [20,21]. Final programming users may use commercial software.

There are several commercial software packages to carry out Monte-Carlo analysis. Among them Crystal Ball [22], LabView [23], @Risk [24], Analytica [25], Stella II [26], WINCERT [27], and Evaluator [28] are very suitable.

2. The Monte-Carlo simulation approach for evaluating measurement uncertainty

The evaluation of the measurement uncertainty from Monte-Carlo simulation can be itemized in the following steps:

(1) Establishment of the model equation for the measurement process between the analytical result Z, and the parameters or individual factors x_i (equivalent to the specification step of GUM approach) as indicated in Eq. (1).
(2) Selection of the significant sources of uncertainty (analogous to the identification step of GUM approach).
(3) Identification of the probability density functions $p(x_i)$ corresponding to the uncertainty sources selected.
(4) Selection of the number M of Monte-Carlo trials.

(5) Extraction (simulation) of M samples $\{x_{i1}, x_{i2},\ldots, x_{iM}\}$ of each x_i significant uncertainty source, considered as a random variable with a probability density function $p(x_i)$.
(6) Computation of the M results $\{Z_1, Z_2,\ldots, Z_M\}$ by applying Eq. (1) to the M samples $\{x_{i1}, x_{i2},\ldots, x_{iM}\}$ for each variable x_i.

From the estimated set of results $\{Z_1, Z_2,\ldots, Z_M\}$, the 'combined uncertainty' $u(Z)$ can be calculated now easily as the standard deviation:

$$u(Z) = \sqrt{\frac{\sum_{i=1}^{M} Z_i^2 - \left(\sum_{i=1}^{M} Z_i\right)^2 / M}{M-1}} \quad (5)$$

Owing to high speed of modern computers, a large number of trials can be processed without time limitations. A value of $M = 100{,}000$ is typically enough, even with many input distributions. In case of correlated random variables, e.g. x_i and x_j, their values are suitably simulated from the joint probability density function $p(x_i,x_j)$.

Once the coverage probability, p, is selected, the confidence interval for the result is evaluated as $[Z_{(1+p)M/2} - Z_{(1-p)M/2}]$ whose extremes correspond to the 2.5 and 97.5% percentiles of the sorted Z values. When the skewness value of the Z forecast discrete distribution is near zero, the confidence interval becomes symmetric and the expanded uncertainty $U(Z)$ can be approximated to

$$U(Z) = \frac{Z_{(1+p)M/2} - Z_{(1-p)M/2}}{2} \quad (6)$$

and the corresponding coverage factor can be back-evaluated as $k = U(Z)/u(Z)$.

3. Comparison between GUM approach and Monte-Carlo analysis illustrated by two case studies

In order to compare the results obtained by using the two approaches, two worked examples have been selected. The first one quoted from the EURACHEM/CITAC Guide [6] deals with the uncertainty in the preparation of a calibration standard. This is a very simple case where non-linearity is weak and it is expected that both GUM approach and Monte-Carlo analysis yield the same results. In this example, the general way to perform Monte-Carlo analysis and the comparison with the GUM approach is shown step-by-step. The second case study concerns the calibration of a weight against a reference following a strong non-linear model. Here, high deviations between the both approaches are expected.

3.1. Uncertainty in the preparation of a calibration standard

This case study is quoted from the EURACHEM/CITAC Guide [6]: Example A1: preparation of a calibration standard (pp. 34–39). The goal is to prepare a calibration standard of high purity cadmium with a concentration of ca. $1000\,\mathrm{mg\,l^{-1}}$. The measurand is the concentration of standard solution, which depends upon the weighing of the high purity metal (Cd), its purity, and the volume of the liquid in which is dissolved.

3.1.1. GUM approach

(1) Specification step: the model equation is

$$C\_\mathrm{Cd} = \frac{1000mP}{V} \quad (7)$$

where C_Cd is the concentration of the standard ($\mathrm{mg\,l^{-1}}$), m is the mass of high purity cadmium dissolved (mg), P its purity, and V is the volume of the final solution (ml). The scale factor 1000 is to convert milliliter to liter.
(2) Identification step: the sources of significant uncertainty for each parameter affecting the measurand are:

Purity (P): the purity of the metal (Cd) is quoted in the supplier's certificate as $99.99 \pm 0.01\%$. P is therefore 0.9999 ± 0.0001. These values depend on the effectiveness of the surface cleaning of the high purity metal.

Mass (m): the second stage of the preparation involves weighing the high purity metal. A 100 ml quantity of a $1000\,\mathrm{mg\,l^{-1}}$ cadmium solution is to be prepared. The relevant mass of cadmium is determined by a tared weighing, giving $m = 0.10028\,\mathrm{g}$. The manufacturer's literature identifies three uncertainty sources for the tared weighing: the repeatability, the readability (digital resolution) of the balance scale, and the contribution due to the uncertainty in the calibration function of the scale. This calibration function has two potential uncertainty sources, identified as the sensitivity of the balance and its linearity. The sensitivity can be neglected because the mass by difference is done on the same balance over a very narrow range. Buoyancy correction is not considered.

Volume (V): the volume of the solution contained in the volumetric flask is subject to three major sources of uncertainty: the uncertainty in the certified internal volume of the flask, the variation in filling the flask to the mark, and the flask and solution temperatures differing from the temperature at which the volume of the flask was calibrated.
(3) Quantification step: the different uncertainties are calculated

Purity (P): the purity of cadmium is given on the certificate as 0.9999 ± 0.0001. Thus it is a type B uncertainty. Because there is no additional information about the uncertainty value, a rectangular distribution is assumed. To obtain the standard uncertainty $u(P)$ the value of 0.0001 has to be divided by $\sqrt{3}$:

$$u(P) = \frac{0.0001}{\sqrt{3}} = 0.0000577$$

Mass (m): the uncertainty associated with the mass of the cadmium is estimated, using the data from the calibration certificate and the manufacturer's recommendations on uncertainty estimation, is $u(m) = 0.05$ mg. This is a type B uncertainty and it is assumed a normal distribution.

Volume (V): the volume has three major influences; calibration, repeatability, and temperature effects that can be split into three contributions: V_c, V_r, and V_t.

(i) Calibration (V_c): the manufacturer quotes a volume for the flask of 100 ± 0.1 ml measured at a temperature of 20 °C. The value of the uncertainty is given without confidence level or distribution information, so an assumption is necessary. Here, the standard uncertainty is calculated as a type B one, assuming a triangular distribution, and $u(V\_c)$ is obtained by dividing 0.1 by $\sqrt{6}$:

$$u(V\_c) = \frac{0.1}{\sqrt{6}} = 0.0408$$

(ii) Repeatability (V_r): the uncertainty due to variations in filling can be estimated as a type A uncertainty from a repeatability experiment on a typical example of the flask used. A series of 10 fill and weigh experiments on a typical 100 ml flask gave a standard deviation of 0.02 ml. This can be used directly as a standard uncertainty. Thus $u(V\_r) = 0.02$.

(iii) Temperature: according to the manufacturer the flask has been calibrated at a temperature of 20 °C, whereas the laboratory temperature varies between the limits of ±4 °C. The type B uncertainty from this effect can be calculated from the estimate of the temperature range and the coefficient of the volume expansion. The volume expansion of the liquid is considerably larger than that of the flask, so only the former needs to be considered. The coefficient of volume expansion for water is $2.1 \times 10^{-4}\,°C^{-1}$, which leads to a volume variation of $\pm(100 \times 4 \times 2.1 \times 10^{-4}) = \pm 0.084$ ml. The standard uncertainty is calculated using the assumption of a rectangular distribution for the temperature variation:

$$u(V\_t) = \frac{0.084}{\sqrt{3}} = 0.0485$$

The volume V can be considered as a interim result with a interim model equation:

$$V = V\_c + V\_r + V\_t \quad (8)$$

However, for the sake of correctness, the expected value of V must be calculated also from Eq. (8), and therefore the value of 100 ml can be ascribed only to one of the three terms. It seems to be advisable to assign the value 100 ml to the expectation of V_r (because just this value was obtained by a series of 10 measurements with a standard deviation of 0.02) and to take zero for the expectations of both V_c and V_t. Accordingly, the expected value of V from Eq. (8) will be: $V = 100 + 0 + 0 = 100$ ml, and the interim combined standard uncertainty $u(V)$ of the volume V:

$$u(V) = \sqrt{u^2(V\_c) + u^2(V\_r) + u^2(V\_t)} = 0.0665$$

(4) Final step: calculation of the combined standard uncertainty of C_Cd.

By applying the law of error propagation to Eq. (7) after evaluating partial derivatives we get:

$$u(C\_Cd) = \sqrt{\left(\frac{1000P}{V}\right)^2 u^2(m) + \left(\frac{1000m}{V}\right)^2 u^2(P) + \left(-\frac{1000mP}{V^2}\right)^2 u^2(V)}$$

The sensitivity coefficients are:

$$\frac{\partial C\_Cd}{\partial m} = \frac{1000P}{V} = 9.999$$

$$\frac{\partial C\_Cd}{\partial P} = \frac{1000m}{V} = 1002.8$$

$$\frac{\partial C\_Cd}{\partial V} = -\frac{1000mP}{V^2} = -10.027$$

that lead to the value of the combined uncertainty $u(C\_Cd) = 0.8354$

The final uncertainty budget can be summarized in Table 1.

The computation of the expanded standard uncertainty can be obtained upon normality assumption for about the 95% confidence level using a coverage factor $k = 2$: $U(C\_Cd) = 1.6708$. This is a coarse evaluation. The use of the Student tabulated value as coverage factor is more advisable. Thus, the effective degrees of freedom must be computed from Eq. (3) disregarding the correlation terms. First, we evaluate the effective degrees of freedom of the interim result V defined in Eq. (8) by taking the degrees of freedom for V_c, V_r, and V_r as depicted in Table 1:

$$\nu_{\text{eff}}(V) = \frac{(0.0665)^4}{(0.02)^4/9} = 1100$$

Then, the effective degrees of freedom for C_Cd are computed:

$$\nu_{\text{eff}}(C\_Cd) = \frac{(0.8354)^4}{[(9.999 \times 0.05)^4/50] + [(10.027 \times 0.0665)^4/1100]} = 340$$

Student's t-distribution typical tables cover until 100–120 degrees of freedom, thus, for evaluating the t-value for

Table 1
Uncertainty budget for the studied example

Quantity	Features	Degrees of freedom	Expectation	Uncertainty (type)
C_Cd	Result	Calculated	1002.6997	0.8354 (Calculated)
m	Normal distribution	50[a]	100.28	0.05 (Type B)
P	Uniform distribution	∞	0.9999	0.0000577 (Type B)
V	Interim result	Calculated	100	0.0665 (Calculated)
V_c	Triangular distribution	∞	0	0.0408 (Type B)
V_r	Observations, Student's distribution	9	100	0.02 (Type A)
V_t	Uniform distribution	∞	0	0.0485 (Type B)

[a] The degrees of freedom for a variable normally distributed with type A uncertainty are taken as 50 according to [10,11].

95% confidence level and 340 degrees of freedom a numerical computation was necessary, leading to $t = 1.9669$, very close to the limiting normal value 1.96. Accordingly, $U(C\_\mathrm{Cd}) = 1.6432$.

3.1.2. Monte-Carlo analysis

Authors use the package Crystal Ball 2002. This program is a user-friendly and customizable Excel add-in that easily enables Monte-Carlo simulations. Thus, using Crystal Ball the value contained in an Excel cell can represent a random variable featured by its expected value (the value of the cell) and its assumed probability density function (Normal, Uniform, Triangular, Lognormal, Weibull, Binomial, Poisson...) together with a given dispersion measurement (standard deviation, interval). For each parameter affecting to the measurand, an Excel cell is built. The measurand value is computed in another Excel cell by applying the corresponding mathematical operations with the parameters cells. Then the measurand cell than contains the computed value is chosen as forecast cell and the simulation is started once the number of trials M (and other features) is selected.

In our example, the model equation (and the interim one) has been set already, and the sources of uncertainty, identified. The selection of the probability density functions for the different parameters can be done from the information gathered in Table 1. Thus P is a random variable uniformly distributed with expectation 0.9999 and range 0.9998–1.0000 (cell B1), m is normally distributed with mean 100.28 and standard deviation 0.05 (cell B2), V_c follows a triangular distribution with zero mean and interval ±0.1 (cell B3), V_r can be assumed to follow a normal distribution with expectation 100 and standard deviation 0.02 (cell B4), and finally, V_t is uniformly distributed with zero mean and interval ±0.084 (cell B5). The value of the result cell is then computed as $f_x = (1000 \times \mathrm{B1} \times \mathrm{B2})/(\mathrm{B3} + \mathrm{B4} + \mathrm{B5})$ and then is selected as the forecast cell. A value of $M = 100{,}000$ trials was selected. From the report, the following data were quoted:

Mean value: 1002.6985
Median: 1002.6968
Standard deviation: 0.8348
Skewness: −0.0030
Confidence interval for 95%: [1001.0760, 1004.3245]

According to the skewness value for the forecast distribution, the confidence interval can be considered symmetric and hence, the expanded uncertainty may be computed as $U(C\_\mathrm{Cd}) = (1004.3245 - 1001.0760)/2 = 1.6240$ that corresponds to a coverage factor $k = 1.945$.

The comparison of the results obtained by using both approaches (rounded to two decimal places) is shown in Table 2. In this case, there are no significant differences in the uncertainties computed from both approaches. However, Monte-Carlo analysis is more straightforward to carry out (assuming that the computer program performing Monte-Carlo simulation is available) and it is immune to the drawbacks of the GUM approach. This can be concluded in the next example.

3.2. Uncertainty in mass calibration

This case study was adapted from [29] and deals with the calibration of a weight against a reference. In this example the model is intrinsically non-linear in nature and the Monte-Carlo simulation will give better and different results compared with GUM. Here both approaches will be applied in a rather summarized presentation because in the precedent example they were fully step-by-step explained.

A weighing balance operating in air of density 'a' is used to compare the mass m_W of W with the mass m_R of R. As their densities ρ_W and ρ_R are different in general, it is necessary consider the buoyancy effect. By applying the Archimedes' principle we obtain:

$$m_\mathrm{W}\left(1 - \frac{a}{\rho_\mathrm{W}}\right) = (m_\mathrm{R} + \delta m_\mathrm{R})\left(1 - \frac{a}{\rho_\mathrm{R}}\right) \quad (9)$$

where δm_R is the mass of a small weight of density ρ_R that is added to R so as to balance it with W. Because weights are generally used in air (density close to 1.2 kg m^{-3}), it is usual

Table 2
Comparison of the results obtained using the GUM approach and Monte-Carlo simulation (MCS) to the preparation of a calibration standard

	GUM	MCS
Mean value	1002.70	1002.70
Standard uncertainty	0.84	0.83
Coverage factor	1.97	1.94
Expanded uncertainty	1.64	1.62

Table 3
Input parameters and their assigned probability density functions for the mass calibration model

X_i	$p(X_i)$	Features
$m_{R,c}$	Normal	100 g, 0.050 mg
$\delta m_{R,c}$	Normal	1.234 mg, 0.020 mg
a	Rectangular	1.2 kg m^{-3}, 0.1 kg m^{-3}
ρ_W	Rectangular	8000 kg m^{-3}, 1000 kg m^{-3}
ρ_R	Rectangular	8000 kg m^{-3}, 50 kg m^{-3}

The normal distribution is featured by its mean and standard deviation, and the uniform distribution by its mean and a semi-width.

to work in terms of 'conventional' values. The conventional mass $m_{W,c}$ of W is defined to be the mass of a hypothetical weight of density $\rho_0 = 8000\,\mathrm{kg\,m^{-3}}$ that balances W in air at density $a_0 = 1.2\,\mathrm{kg\,m^{-3}}$. Accordingly:

$$m_W\left(1 - \frac{a_0}{\rho_W}\right) = m_{W,c}\left(1 - \frac{a_0}{\rho_0}\right)$$

In terms of conventional values, the measurement model (9) becomes in good approximation [30]

$$m_{W,c} = (m_{R,c} + \delta m_{R,c})\left(1 + (a - a_0)\left(\frac{1}{\rho_W} - \frac{1}{\rho_R}\right)\right) \quad (10)$$

with $a_0 = 1.2\,\mathrm{kg\,m^{-3}}$.

This model is used to evaluate the uncertainty for the calibration of a weight of nominal mass 100 g. The GUM approach and Monte-Carlo simulation are used to estimate the measurand $m_{W,c}$, its uncertainty $u(m_{W,c})$ and a 95% coverage interval.

In Table 3 are shown the input parameters (X_i) for this model as well as the assigned probability distribution functions $p(X_i)$.

3.2.1. GUM approach

Table 4 lists the partial derivatives and sensitivity coefficients for the measurement model (10) with respect to the input parameters. As can be seen by the fact of evaluating partial derivatives at the mean expected values of each input parameter, the sensitivity coefficients indicate that for the purposes of GUM the measurement model (10) could be replaced by the simple additive model

$$m_{W,c} = m_{R,c} + \delta m_{R,c}$$

The cause of this paradox lays in the first order Taylor's expansion which deviates from intrinsic non-linear models, like this. The result obtained is $m_{W,c} = 101.234$, with a combined uncertainty of $u(m_{W,c}) = 0.0539$ and an expanded uncertainty obtained upon normality assumption for about the 95% confidence level using a coverage factor $k = 2$: $U(m_{W,c}) = 0.1078$.

Table 4
Partial derivatives and model sensitivities for the mass calibration

X_i	Partial derivative	Sensitivity coefficient
$m_{R,c}$	$1 + (a - a_0)\left(\frac{1}{\rho_W} - \frac{1}{\rho_R}\right)$	1
$\delta m_{R,c}$	$1 + (a - a_0)\left(\frac{1}{\rho_W} - \frac{1}{\rho_R}\right)$	1
a	$(m_{R,c} + \delta m_{R,c})\left(\frac{1}{\rho_W} - \frac{1}{\rho_R}\right)$	0
ρ_W	$-(m_{R,c} + \delta m_{R,c})(a - a_0)\left(\frac{1}{\rho_W^2}\right)$	0
ρ_R	$-(m_{R,c} + \delta m_{R,c})(a - a_0)\left(\frac{1}{\rho_R^2}\right)$	0

Table 5
Comparison of the results obtained using the GUM approach and Monte-Carlo simulation (MCS) to the calibration of mass

	GUM	MCS
Mean value	101.2340	101.2338
Standard uncertainty	0.0539	0.0755
Coverage factor	2.0	1.95
Expanded uncertainty	0.1078	0.1472

3.2.2. Monte-Carlo analysis

The selection of the probability density functions for the different parameters can be done from the information gathered in Table 3. Thus $m_{R,c}$ is a random variable normally distributed with expectation 100 and standard deviation 0.050 (cell B1), $\delta m_{R,c}$ is normally distributed with mean 1.234 and standard deviation 0.020 (cell B2), a follows a rectangular distribution with mean 1.2 and interval ±0.1 (cell B3), ρ_W can be assumed to follow a rectangular distribution with mean 8000 and interval ±1000 (cell B4), and finally, ρ_R is also rectangular distributed with 8000 mean and interval ±0.050 (cell B5). The value of the measurand $m_{W,c}$ result cell is then computed as $f_x = (B1 + B2) \times (B3 - 1.2) \times ((1/B4) - (1/B5))$ and then is selected as the forecast cell. A value of $M = 100{,}000$ trials was selected. The results were:

Mean value: 101.2338
Median: 101.2340
Standard deviation: 0.0755
Skewness: 0.0010
Confidence interval for 95%: [101.0845, 101.3842]

The comparison of the results obtained by using both approaches (rounded to two decimal places) is shown in Table 5.

As can be seen, Monte-Carlo analysis provides results more reliable that the produced by the GUM approach, because in this case, the model equation has strong non-linear nature.

4. Conclusion

Monte-Carlo analysis is a method of choice for evaluating the measurement uncertainty of analytical assays because it

is not prone to the main handicaps of the GUM approach. The only weakness of the method is the need of a suitable computer program and a high speed personal computer.

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