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Title: Uncertainty evaluation for the quantification of low masses of benzo[a]pyrene: comparison between the Law of Propagation of Uncertainty and the Monte Carlo method.

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Abstract:

A proper evaluation of the uncertainty associated to the quantification of micropollutants in the environment, like Polycyclic Aromatic Hydrocarbons (PAHs), is crucial for the reliability of the measurement results. The present work describes a comparison between the uncertainty evaluation carried out according to the GUM uncertainty framework and the Monte Carlo (MC) method. This comparison was carried out starting from real data sets obtained from the quantification of benzo[a]pyrene (BaP), spiked on filters commonly used for airborne particulate matter sampling. BaP was chosen as target analyte as it is listed in the current European legislation as marker of the carcinogenic risk for the whole class of PAHs.

MC method, being useful for nonlinear models and when the resulting output distribution for the measurand is non-symmetric, can particularly fit the cases in which the results of intrinsically positive quantities are very small and the lower limit of a desired coverage interval, obtained

according to the GUM uncertainty framework, can be dramatically close to zero, if not even negative.

In the case under study, it was observed that the two approaches for the uncertainty evaluation provide different results for BaP masses in samples containing different masses of the analyte, MC method giving larger coverage intervals. In addition, in cases of analyte masses close to zero, the GUM uncertainty framework would give even negative lower limit of uncertainty coverage interval for the measurand, an unphysical result which is avoided when using MC method. MC simulations, indeed, can be configured in a way that only positive values are generated thus obtaining a coverage interval for the measurand that is always positive.

Keywords: Uncertainty evaluation, Monte Carlo method, GUM uncertainty framework, Benzo[a]pyrene, Polycyclic Aromatic Hydrocarbons.

1. Introduction

The quantification of low masses of Polycyclic Aromatic Hydrocarbons (PAHs) is an important issue as they are ubiquitous toxic contaminants which can be present in all the environmental compartments [1] even at trace levels. PAHs with five or more aromatic rings, among which the compounds having major toxicological relevance, are mainly absorbed onto fine and ultrafine particulate matter [2]. The most studied PAH is benzo[a]pyrene (BaP) which is classified as carcinogenic agent by the International Agency for Research on Cancer [3] and thus listed in the current European legislation as marker of the carcinogenic risk for the whole class of PAHs [4].

There are many difficulties in establishing a realistic uncertainty budget associated with measurement results for the quantification of chemical pollutants in environmental samples, among which the definition of the measurand and of a proper model equation, the small amount of different compounds to be determined and quantified, the effect of the matrix, the identification and quantification of the various uncertainty sources. In this framework, the evaluation of the uncertainty associated with the quantification of micropollutants like PAHs in the environment plays an important role to give reliability to the estimate obtained for the measurand. Examples of uncertainty evaluation for organic micropollutants can be found in literature [5-9] and the main approach adopted is the GUM uncertainty framework, as summarized in [10, G.6.6]. The approach proposed in the GUM relies on the Law of Propagation of Uncertainty (LPU), which requires the linearization of the measurement model. Monte Carlo (MC) method [11], instead, is based on the propagation of the whole probability distribution of the input quantities, thus providing a numerical approximation to the distribution to be associated to the measurand which is consistent with the measurement model and with the distributions assigned to the input quantities. In general, MC method fits better than the GUM approach to nonlinear models, it does not require any linear approximation of the model nor the determination of the effective degrees of freedom for calculating the expanded uncertainty to be associated to the measurand. In case of an asymmetric output density function, for example, MC method automatically provides a realistic coverage

interval, contrary to the approach prescribed within the GUM which resorts to the approximation of the output density function with a Student (symmetric) one. Therefore, MC method particularly fits the cases of results of chemical measurements dealing with intrinsically positive quantities having values close to zero. However, there are only few examples of its implementation in chemical measurements, mainly focused on case studies derived from literature [12-14]. The application of MC method to chemical measurements is also reported in [15], but the example given in the Guide does not concern models with correlated input quantities.

The present work aims at comparing the results obtained by application of the GUM uncertainty framework and the MC method to real data sets derived from the quantification of the mass of BaP spiked on filters commonly used for airborne particulate matter sampling. The development of a method to quantify BaP in ambient air is beyond the scope of the paper as it was addressed in [16]. The main outcome of the present work is that the application of the GUM uncertainty framework may lead to poorly reliable coverage intervals when the resulting output distribution for the measurand is non-symmetric. In the considered cases, the results of masses of BaP are very small and the lower limit of the uncertainty coverage interval can be dramatically close to zero, even negative for simulated results. This situation was faced by applying MC method.

2. Experimental

2.1 Materials and methods

A glass fiber filter (*Pall* & *Whatman*) having diameter of 47 mm, a type of filter commonly used for the sampling of airborne particulate matter, was spiked with the Certified Reference Material (CRM) NIST SRM 2260a, containing 36 Polycyclic Aromatic Hydrocarbons (PAHs). The spiked filter was extracted by Soxhlet, following the extraction procedure described in [16]. The same filter was subsequently extracted a second time thus obtaining a diluted sample. The mass of BaP

contained in a nominal volume of 1 µL of each extract was quantified by means of a gas chromatograph coupled with a mass spectrometer (GC-MS) Focus DSQ II (Thermofisher Scientific), equipped with a chromatographic column Agilent HP-5ms (film thickness 0.25 µm, internal diameter 0.25 mm, length 30 m).

2.2 Calibration of the GC-MS

In order to calibrate the GC-MS, three reference solutions were prepared by gravimetric dilution of the NIST SRM 2260a. The concentration (ng μL^{-1}) of BaP in these solutions was calculated by converting the mass fractions using density values experimentally determined by a frequency densimeter (DMA 5000 Anton Paar) at 20 °C, which was also the operational temperature during the mass measurements. The uncertainty related to density, being in 10^{-7} g cm^{-3} was found to be negligible with respect to the uncertainty of the mass fraction of BaP in each solution. The values of BaP concentration (ng μL^{-1}) and associated uncertainties are reported in Table 1.

Aliquots of the NIST SRM 2270, containing perdeuterated benzo[a]pyrene (BaP-d_{12}), were added to the solutions in order to obtain standards with the same concentration of BaP-d_{12}, i.e. 0.2455 ng μL^{-1}, to be used as internal standard (IS), according to the prescription of [17]. An aliquot of 1 µL of each solution was then injected three times into the GC-MS for instrument calibration. The ratio of peak areas of the IS and of the analyte was used to determine the mass of BaP present in the injected volume. For each solution i (i =1, 2, 3), a calibration factor f_i is obtained by applying the following equation [17]:

$$f_i = (\overline{A_{\mathrm{IS}_i}} \cdot m_{\mathrm{R}i})/(\overline{A_{\mathrm{R}_i}} \cdot m_{\mathrm{IS}}) \quad (1)$$

where $\overline{A_{\mathrm{IS}_i}}$ and $\overline{A_{\mathrm{R}_i}}$ are the mean of the areas of the gas chromatographic peaks obtained in the three runs corresponding to BaP-d_{12} and BaP, respectively, whereas $m_{\mathrm{R}i}$ and m_{IS} are the masses (ng) of

BaP and BaP-d_{12} injected in each run. For each value, the LPU was applied for evaluating the associated uncertainty [10]. Table 2 shows, as an example, the uncertainty budget for f_1.

In the evaluation of the uncertainty associated to each f_i, the correlation between the chromatographic areas of the BaP and those of the IS in the same run was taken into account since, as expected, it was observed an evident linear relationship between the areas. The covariance term corresponding to the mean areas was calculated according to [10, Section 5.2.3].

In Table 3 the values obtained for the three calibration factors f_i and the corresponding uncertainties are reported.

The arithmetic mean of the f_i values, equal to 0.616, was taken as an estimate for the GC-MS calibration factor f, which was then used to quantify the unknown amount of BaP in the extracted samples. The standard uncertainty associated with f was calculated from the uncertainties associated with each f_i and the covariances between them, i.e. $u(f) = 1/3[u^2(f_1) + u^2(f_2) + u^2(f_3) + 2\mathrm{cov}(f_1, f_2) + 2\mathrm{cov}(f_1, f_3) + 2\mathrm{cov}(f_2, f_3)]^{1/2}$. The covariances are mainly due to the fact that the same IS mass was used for obtaining all the f_i and the calibration solutions were prepared by dilution of the same CRM. Considering, for example, f_1 and f_2, as defined by corresponding istances of eq. (1), their covariance is given by $\mathrm{cov}(f_1, f_2) = \frac{\partial f_1}{\partial m_{\mathrm{IS}}}\frac{\partial f_2}{\partial m_{\mathrm{IS}}}\mathrm{cov}(m_{\mathrm{IS}}, m_{\mathrm{IS}}) + \frac{\partial f_1}{\partial m_{\mathrm{R1}}}\frac{\partial f_2}{\partial m_{\mathrm{R2}}}\mathrm{cov}(m_{\mathrm{R1}}, m_{\mathrm{R2}})$, where $\mathrm{cov}(m_{\mathrm{IS}}, m_{\mathrm{IS}}) = u^2(m_{\mathrm{IS}})$ and $\mathrm{cov}(m_{\mathrm{R1}}, m_{\mathrm{R2}}) \cong \mathrm{cov}\left(m_{\mathrm{R1}}, \frac{1}{2}m_{\mathrm{R1}}\right) = \frac{1}{2}u^2(m_{\mathrm{R1}})$. The f value and its uncertainty are also reported in Table 3.

2.3 Quantification of BaP

After calibrating the GC-MS, the mass of BaP, contained in a nominal volume of 1 µL of each of two samples obtained by two consecutive Soxhlet extractions of a blank filter spiked with NIST SRM 2260a, was quantified according to [17], following the same approach of the calibration process. For each extract, three analytical runs were carried out. The following model equation was

used for calculating the measurand, i.e. the mass m_E of BaP contained in a nominal volume of 1 µl of the extracted samples:

$$m_E = (f\,\overline{A_E}\,m_{ISE})/\,\overline{A_{ISE}} \quad (2)$$

where m_{ISE} and $\overline{A_{ISE}}$ are the mass (ng) and the mean chromatographic area for the internal standard in the extract (ISE), f is the calibration factor (see Table 3) and $\overline{A_E}$ is the mean area of the chromatographic peak corresponding to BaP in the extract.

Two different methods were applied for the uncertainty evaluation of the quantities of interest: the GUM uncertainty framework [10] and the MC method for propagation of probability distributions [11].

3. Results and discussion

3.1 Uncertainty evaluation according to the GUM uncertainty framework

The uncertainty associated with the measurand defined by eq. (2) was evaluated by the LPU taking into account the uncertainty contributions coming from the input quantities in model (2) and the covariances present between them (again, the chromatographic areas were highly correlated). In Table 4 the mass of BaP in 1 µL of each extract is reported, together with its standard uncertainty and the expanded uncertainty at 95 % coverage probability. The expanded uncertainties were calculated choosing as coverage factor the 97.5^{th} percentile of a Student's *t*-distribution with effective degrees of freedom calculated according to the Welch-Satterthwaite equation [10], i.e. 4 and 3 degrees of freedom for the first and the second extraction, respectively. Note that the number of replicates for the two extracts was the same, but different values of the relative uncertainty associated with the mean areas were obtained in the two cases, hence, application of the Welch-

Satterthwaite formula for multiplicative models, as reported in the Example in [10, G.4.1], led to different values of the effective degrees of freedom.

Note also that the uncertainty associated to the mass of the internal standard, derived by its calibration certificate, was considered as having a very high number of degrees of freedom, so that it does not give contribution to the effective degrees of freedom for the measurand estimate. Moreover, when considering the correlation between m_{ISE} and f, which was found equal to -0.54, and using therefore the generalized expression of the Welch-Satterthwaite equation [18] for correlated input quantities, the corresponding contribution to the effective degrees of freedom for m_E resulted in being negligible.

Table 5 shows, as an example, the uncertainty budget for the sample containing the highest mass of BaP.

3.2 Uncertainty evaluation according to the propagation of distributions by MC

The same data sets were used for propagation of probability distributions by means of MC method in order to obtain an approximated distribution for the measurand, i.e. the mass of BaP in the extracts, and compare the resulting coverage intervals with those obtained according to the GUM uncertainty framework. At this purpose, suitable probability distributions were assigned to the input quantities of model (2), according to the criteria prescribed in [11, 19]. A bivariate Gaussian distribution was assigned to m_{ISE} and to f, since the available information on these quantities were their best estimates and their associated covariance matrix [11, Section 6.4.8]. Hence, the bivariate normal distribution had those best estimates as its (vector) expectation and matrix $\boldsymbol{\Sigma}$ as covariance matrix, with

$$\Sigma = \begin{bmatrix} u^2(f) & u(f, m_{ISE}) \\ u(f, m_{ISE}) & u^2(m_{ISE}) \end{bmatrix}$$

A scaled and shifted bivariate *t*-distribution with one degree of freedom was assigned to the chromatographic areas of the IS (A_{ISE}) and of the BaP (A_E) in the extract, since the two (N = 2) quantities were considered as having a bivariate normal distribution and, for each quantity, repeated (n = 3) measurements were available [19, Section 5.3.2]. Hence, the bivariate *t*-distribution resulted in having $[\overline{A_E}, \overline{A_{ISE}}]^T$ as the (vector) expectation and matrix $\boldsymbol{S}/n$ as the scale matrix, where $\boldsymbol{S}$ is defined by:

$$S = \frac{1}{\nu}\begin{bmatrix} \sum_{i=1}^{3}(A_{E_i} - \overline{A_E})^2 & \sum_{i=1}^{3}(A_{ISE\,i} - \overline{A_{ISE}})(A_{E_i} - \overline{A_E}) \\ \sum_{i=1}^{3}(A_{ISE\,i} - \overline{A_{ISE}})(A_{E_i} - \overline{A_E}) & \sum_{i=1}^{3}(A_{ISE\,i} - \overline{A_{ISE}})^2 \end{bmatrix}$$

Note that for $\nu = n - N = 1$, the mean value and the covariance matrix of the *t*-distribution are not defined, anyway a coverage (hyper) interval for that distribution can always be meaningfully determined [19, Section 5.5.1, Note 1]. Table 6 shows the values of the distributional parameters relevant to the above-mentioned bivariate normal and *t*-distributions, for the sample obtained with the first extraction.

The numerical simulation of the input probability distributions and their propagation through measurement model (2) were implemented in R environment [20] (in the Annex, the core of the code is reported). Random generation from multivariate normal and *t*-distributions was performed by applying R functions rmvnorm and rmvt available in the mvtnorm package [21]. For each input quantity, 10^6 values were drawn. Since only positive values of measurand m_E in model (2) are feasible, the joint input probability density functions were numerically truncated at zero by disregarding negative values drawn during the MC simulation [11, Section 9.4.2.1.1, Note], thus obtaining a number of corresponding simulated BaP mass values smaller than 10^6, but always higher than $7 \cdot 10^5$, which provided a good numerical distribution for the measurand. From such distribution, the shortest 95 % coverage interval was obtained, as shown in Section 3.3 (Table 7).

3.3 Comparison between the GUM uncertainty approach and propagation of distributions by MC

Figures 1 and 2 show the approximate numerical representation of the probability density function (pdf) for the BaP mass in the samples corresponding to the first and the second extraction, respectively, obtained by applying MC method. The figures show also the 95 % coverage intervals for the measurand m_E of model (2) obtained by applying the two different methods (symbols ● and ▲ indicate the limits of the coverage interval obtained according to the GUM uncertainty framework and by MC method, respectively). The relevant interval limits are reported in Table 7.

From Figure 1 it can be seen that the two approaches give quite different results in terms of coverage intervals. Although the assumed output distribution in the GUM uncertainty framework is a Student *t*-distribution with quite few (4) degrees of freedom, hence leading to a large coverage factor for the calculation of the corresponding expanded uncertainty, the MC coverage interval is two and a half times larger than that obtained in the GUM uncertainty framework, and it is also asymmetric with respect to the measurand estimate. Due to the very few degrees of freedom of the input bivariate Student *t*-distribution of the mean areas (therefore, very different from a Gaussian distribution) and due to the fact that both the bivariate Student *t* and Gaussian input distributions were feasibly truncated in zero, the MC output distribution has in fact a very long right tail (not well visible in Figure 1 whose plot is graphically truncated) and is also asymmetric. This is an example of those situations in which "the conditions required by the Central Limit Theorem may not be well met and the approach of G.6.4[1] may lead to an unacceptable result" [10, Section G.6.5]: "the PDF for the output quantity is not a Gaussian distribution or a scaled and shifted *t*-distribution" [11].

At the lower mass (Fig. 2), again the MC coverage interval is two and a half times larger than the one obtained in the GUM uncertainty framework. The probability distribution provided by MC

[1] Such approach assigns to the measurand estimate a scaled and shifted *t*-distribution with degrees of freedom given by the Welch-Satterthwaite formula.

method is now clearly truncated at zero, the smallest possible feasible value for the measurand, hence sharpening the asymmetry in its shape and, consequently, in the MC coverage interval.

Eventually, a numerical simulation was carried out in order to study the situation at very low mass values of BaP. In order to simulate a small m_E, the experimental results obtained for the sample of the second extraction were used as they were, but the areas corresponding to the BaP were all decreased by a common constant term. This led to a (simulated) mass value of $3 \cdot 10^{-3}$ ng, which is close to the minimum mass of BaP, i.e. $2.5 \cdot 10^{-3}$ ng, detectable with the method described in [16]. Incidentally, all the distributional parameters of the input probability distributions remained the same as those used for the second extraction, with the exception of the $\overline{A_E}$ value, which changed from 85114 a.u. to 18114 a.u.. The comparison of the results obtained by applying the two methods to this data set is presented in Figure 3. It can be seen that the GUM uncertainty framework would lead to a coverage interval streching into a region of negative unfeasible values. MC simulation, instead, would provide only positive numbers, thus producing a realistic coverage interval.

Table 7 compares the 95 % coverage intervals as obtained by resorting to the GUM uncertainty framework and the MC method.

4. Conclusions

In the present work two approaches for the measurement uncertainty evaluation were compared. The GUM uncertainty framework and the Monte Carlo method were applied to the analysis of BaP, chosen as a marker of a class of organic micropollutants, the PAHs.

In the determination of different values of BaP masses, it was noticed that the two methods gave different results, MC method leading to larger coverage intervals. For decreasing mass values, the approximate numerical representation of the probability density function provided by MC method becomes more asymmetric and more clearly truncated at zero.

For the simulated mass value close to zero ($3 \cdot 10^{-3}$ ng) it comes out that the GUM uncertainty framework leads to a coverage interval streching into a region of negative unfeasible values for the measurand. This is the consequence of blindly assigning a shifted and rescaled *t*-distribution to the measurand when this is not an acceptable approximation for the output pdf. MC simulation, instead, can be configured in a way that only positive values are generated (discarding negative values), thus obtaining a coverage interval for the measurand that is always feasible.

6. Annex

Core of the MC simulation code

```
# Uncertainty evaluation for BaP quantification
library(mvtnorm)
set.seed(234)                                                    # Fixed for validation purposes
M = 1000000                                                      # Number of MC trials

# INPUT - Experimental values, uncertainties and covariances
fm = 0.6164727577
ufm = 0.016602461
Aemean = 7619522
uAemean = 1039644.199
mISEm = 0.245544554
umISEm = 0.003613861
Aisemean = 2808070
uAisemean = 417849.1067
cov_fm_mISEm = -3.27889E-05
corr_fm_mISEm = -3.27889E-05/(ufm*umISEm)

# Assignment of the pdf to the input variables
# Bivariate normal distribution
MATCOV_fm_mISEm = matrix(c(ufm^2, cov_fm_mISEm, cov_fm_mISEm, umISEm^2), ncol=2)
A = rmvnorm(M, mean = c(fm, mISEm), sigma = MATCOV_fm_mISEm , method="chol")
fold = A[,1]
mISEold = A[,2]
# Bivariate Student distribution
S = matrix(c(6.48516E+12, 2.58914E+12, 2.58914E+12, 1.04759E+12), ncol=2)      # See Suppl. 2, Sec 5.3.2.1
B = rmvt(M, delta = c(Aemean, Aisemean), sigma = S/3, df = 1, type = "shifted")
Aeold = B[,1]
Aiseold = B[,2]

# Propagation of the input pdfs through the model
f = fold[fold >= 0 & Aeold >= 0 & mISEold >= 0 & Aiseold >= 0]                 # Only positive values retained
Ae = Aeold[fold >= 0 & Aeold >= 0 & mISEold >= 0 & Aiseold >= 0]               # Only positive values retained
mISE = mISEold[fold >= 0 & Aeold >= 0 & mISEold >= 0 & Aiseold >= 0]           # Only positive values retained
Aise = Aiseold[fold >= 0 & Aeold >= 0 & mISEold >= 0 & Aiseold >= 0]           # Only positive values retained
meS = (f*Ae*mISE)/Aise                                                         # Measurement model
meS = sort(meS)
MS = length(meS)
summary(meS)

# Measurand estimate and standard deviation
meSmean = mean(meS)
meSsd = sd(meS)

# Shortest coverage interval with coverage probability p = 1-alpha
alpha = 0.05
a = 0
i = 1
step = 0.00001
s = seq(1/MS, alpha/2, step)
dataInt = matrix(rep(0, 3*length(seq(1/MS, alpha/2, step))),  ncol = 3, byrow=TRUE)

for(a in s)
        {dataInt[i,] = c(meS[ceiling(MS*a)], meS[ceiling(MS*a+MS*(1-alpha))], meS[ceiling(MS*a+MS*(1-alpha))]
        - meS[ceiling(MS*a)])
         i = i + 1}
extremes = dataInt[dataInt[,3]==min(dataInt[,3]),][1:2]
```

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TABLES

Solution	**BaP concentration ng µL^{-1}**	**Expanded uncertainty $U(x)$ (k = 2) ng µL^{-1}**
1	1.032	0.019
2	0.5166	0.0093
3	0.2574	0.0046

Table 1. BaP concentration (ng µL^{-1}) in calibration solutions for GC-MS and associated expanded uncertainties (k = 2). The choice of k = 2 is justified by considering that the solutions were obtained by gravimetrically diluting a CRM, where both the mass standards and the CRM are characterised by sufficiently high degrees of freedom.

Uncertainty component $u(x_i)$	**Uncertainty source**	**Standard uncertainty value** $u(x_i)$	**Sensitivity coefficient** $\partial f_1 / \partial x_i$	**Contribution to** $u(f_1)$ $\lvert\partial f_1 / \partial x_i\rvert \cdot u(x_i)$
$u(\overline{A_{IS}})$	Area of the gas chromatographic peak of the IS	$2.7 \cdot 10^5$ a.u.	$5.0 \cdot 10^{-7}$ (a.u.)$^{-1}$	0.13
$u(m_R)$	Mass of BaP	$1.9 \cdot 10^{-2}$ ng	$5.9 \cdot 10^{-1}$ ng^{-1}	0.011
$u(\overline{A_R})$	Area of the gas chromatographic peak of BaP	$1.9 \cdot 10^6$ a.u.	$-7.4 \cdot 10^{-8}$ (a.u.)$^{-1}$	0.14
$u(m_{IS})$	Mass of the IS	$3.6 \cdot 10^{-3}$ ng	-2.5 ng^{-1}	0.0090
		$cov(x_i, x_j)$	$(\partial f_1 / \partial x_i) \cdot (\partial f_1 / \partial x_j)$	**Contribution to** $u^2(f_1)$ $2(\partial f_1 / \partial x_i) \cdot (\partial f_1 / \partial x_j) \cdot cov(x_i, x_j)$
$cov(\overline{A_{IS}}, \overline{A_R})$	Covariance between $\overline{A_{IS}}$ and $\overline{A_R}$	$5.1 \cdot 10^{11}$(a.u.)^2	$-3.7 \cdot 10^{-14}$ (a.u.)$^{-2}$	$-3.8 \cdot 10^{-2}$
$u_c(f_1) = 0.017$				

Table 2. Uncertainty budget for calibration factor f_1.

Solution	f_i	$u(f_i)$
1	0.614	0.017
2	0.631	0.019
3	0.604	0.024
	f	$u(f)$
	0.616	**0.017**

Table 3 Values of calibration factors f_i, calculated for each calibration solution, and value of the calibration factor f, with associated standard uncertainties.

Sample	**Mass of BaP, m_E ng**	**$u(m_E)$ ng**	**$U(m_E)$ ng**
First extraction	0.411	0.013	0.035
Second extraction	0.014	0.002	0.006

Table 4. Mass of BaP in the samples with the associated standard and expanded uncertainties for a 95 % coverage probability obtained by multiplying the standard uncertainty by the corresponding Student-*t* quantile, i.e., according to R language, t(0.975,4) = 2.78 and t(0.975,3) = 3.18, respectively.

Uncertainty component $u(x_i)$	**Uncertainty source**	**Standard uncertainty value, $u(x_i)$**	$\partial m_E/\partial x_i$	**Contribution to $u(m_E)$ $\lvert\partial m_E/\partial x_i\rvert \cdot u(x_i)$**
$u(\overline{A_{ISE}})$	Area of the gas chromatographic peak of the IS	$4.2 \cdot 10^5$ a.u.	$-1.5 \cdot 10^{-7}$ ng (a.u.)$^{-1}$	$6.1 \cdot 10^{-2}$ ng
$u(f)$	Calibration factor for BaP	$1.7 \cdot 10^{-2}$	$6.7 \cdot 10^{-1}$ ng	$1.1 \cdot 10^{-2}$ ng
$u(\overline{A_E})$	Area of the gas chromatographic peak of the BaP	$1.0 \cdot 10^6$ a.u.	$5.4 \cdot 10^{-8}$ ng (a.u.)$^{-1}$	$5.6 \cdot 10^{-2}$ ng
$u(m_{ISE})$	Mass of the IS	$3.6 \cdot 10^{-3}$ ng	1.7	$6.0 \cdot 10^{-3}$ ng
		$\mathrm{cov}(x_i, x_j)$	**$\partial m_E/\partial x_i \cdot \partial m_E/\partial x_j$**	**Contribution to $u^2(m_E)$ $2(\partial f_1/\partial x_i) \cdot (\partial f_1/\partial x_j) \cdot \mathrm{cov}(x_i, x_j)$**
$\mathrm{cov}(\overline{A_{ISE}}, \overline{A_E})$	Covariance between $\overline{A_{ISE}}$ e $\overline{A_E}$	$4.3 \cdot 10^{11}$ (a.u.)^2	$-7.9 \cdot 10^{-15}$ ng^2 (a.u.)$^{-2}$	$-6.8 \cdot 10^{-3}$ ng^2
$\mathrm{cov}(m_{ISE}, f)$	Covariance between m_{ISE} e f	$-3.3 \cdot 10^{-5}$ ng	1.1 ng	$-7.3 \cdot 10^{-5}$ ng^2
$u_c(m_E) = 0.013$ ng				

Table 5. Uncertainty budget for the mass of BaP (in 1 µL) of the sample obtained with the first extraction.

Distributional parameter	Value
f	0.616
m_{ISE}	0.2455 ng
$u(f)$	0.017
$u(m_{\mathrm{ISE}})$	0.0036 ng
$u(f, m_{\mathrm{ISE}})$	-3.3E-05 ng
$\overline{A_{\mathrm{E}}}$	7619522 a.u.
$\overline{A_{\mathrm{ISE}}}$	2808070 a.u.
S_{11}	$6.48516 \cdot 10^{12}$ (a.u.)^2
S_{22}	$1.04759 \cdot 10^{12}$ (a.u.)^2
$S_{12} = S_{21}$	$2.58914 \cdot 10^{12}$ (a.u.)^2

Table 6. Distributional parameters of the input probability distributions for model (2), for the sample obtained with the first extraction.

	Estimate of BaP mass **ng**	**95 % Coverage Intervals (GUM uncertainty framework)** **ng**	**95 % Coverage Intervals (MC method)** **ng**
First extraction	0.411	[0.376, 0.446]	[0.331, 0.511]
Second extraction	0.014	[0.008, 0.020]	$[7 \cdot 10^{-9}, 0.032]$
Simulated very low extraction	0.003	[-0.004, 0.010]	$[8 \cdot 10^{-9}, 0.020]$

Table 7. BaP mass estimates and 95 % coverage intervals for the three considered samples.

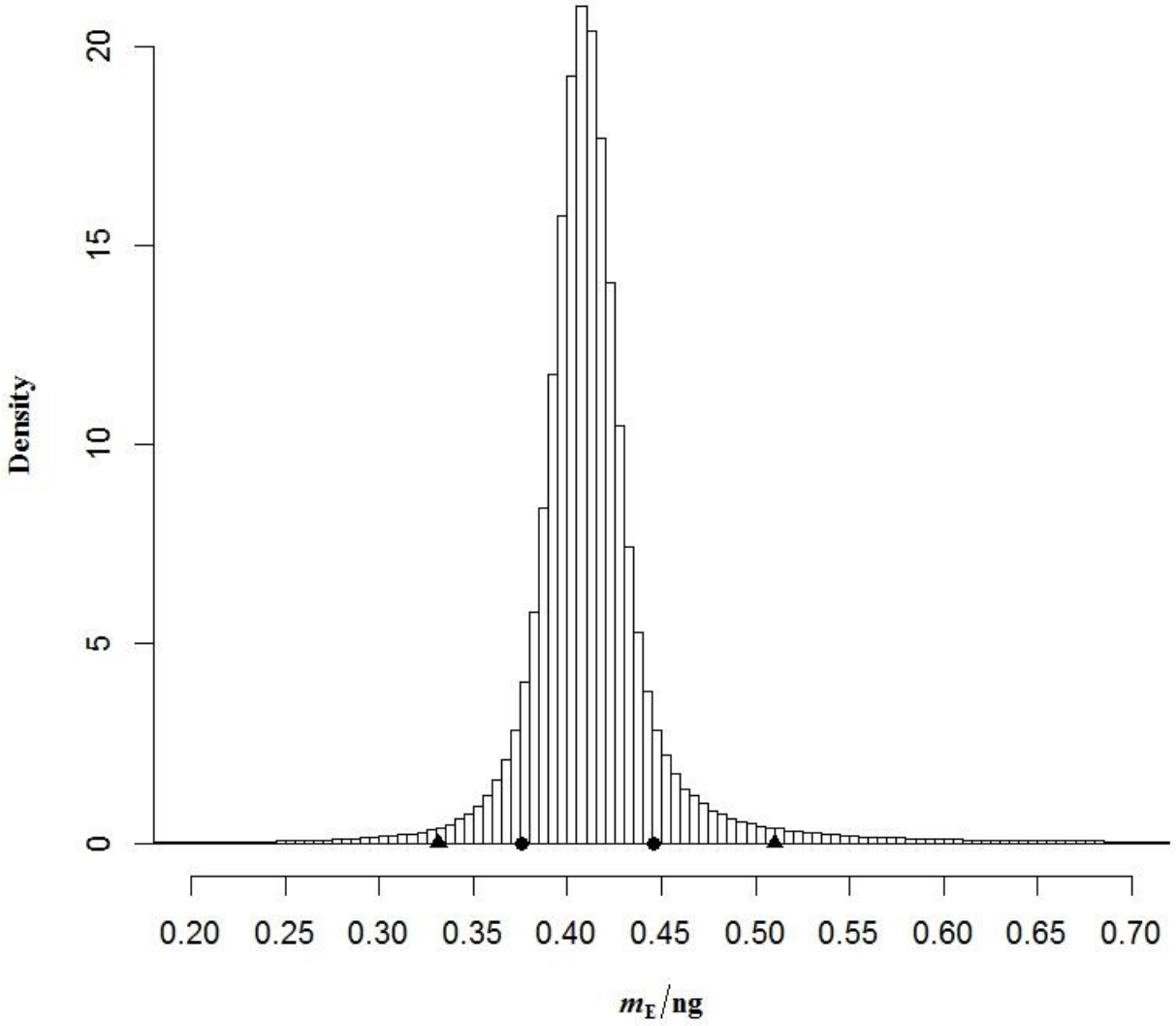
FIGURE CAPTIONS

Figure 1. Approximate numerical representation of the probability density function (pdf) for the mass m_E of BaP in the nominal volume of 1 µL of the sample obtained with the first extraction. Symbols ● and ▲ indicate the limits of the coverage interval obtained according to the GUM uncertainty framework and by MC simulation, respectively, as reported in Table 7.

Figure 2. Approximate numerical representation of the probability density function (pdf) for the mass m_E of BaP for the nominal volume of 1 µL of the sample obtained with the second extraction. Symbols ● and ▲ indicate the limits of the coverage interval obtained according to the GUM uncertainty framework and by MC simulation, respectively, as reported in Table 7. Symbol **x** indicates the minimum detectable mass of the analytical method.

Figure 3. Approximate numerical representation of the probability density function (pdf) for the mass m_E of BaP for the nominal volume of 1 µL of the sample simulated at very low level. Symbols ● and ▲ indicate the limits of the coverage interval obtained according to the GUM uncertainty framework and by MC simulation, respectively, as reported in Table 7. Symbol **x** indicates the minimum detectable mass of the analytical method.

FIGURE 1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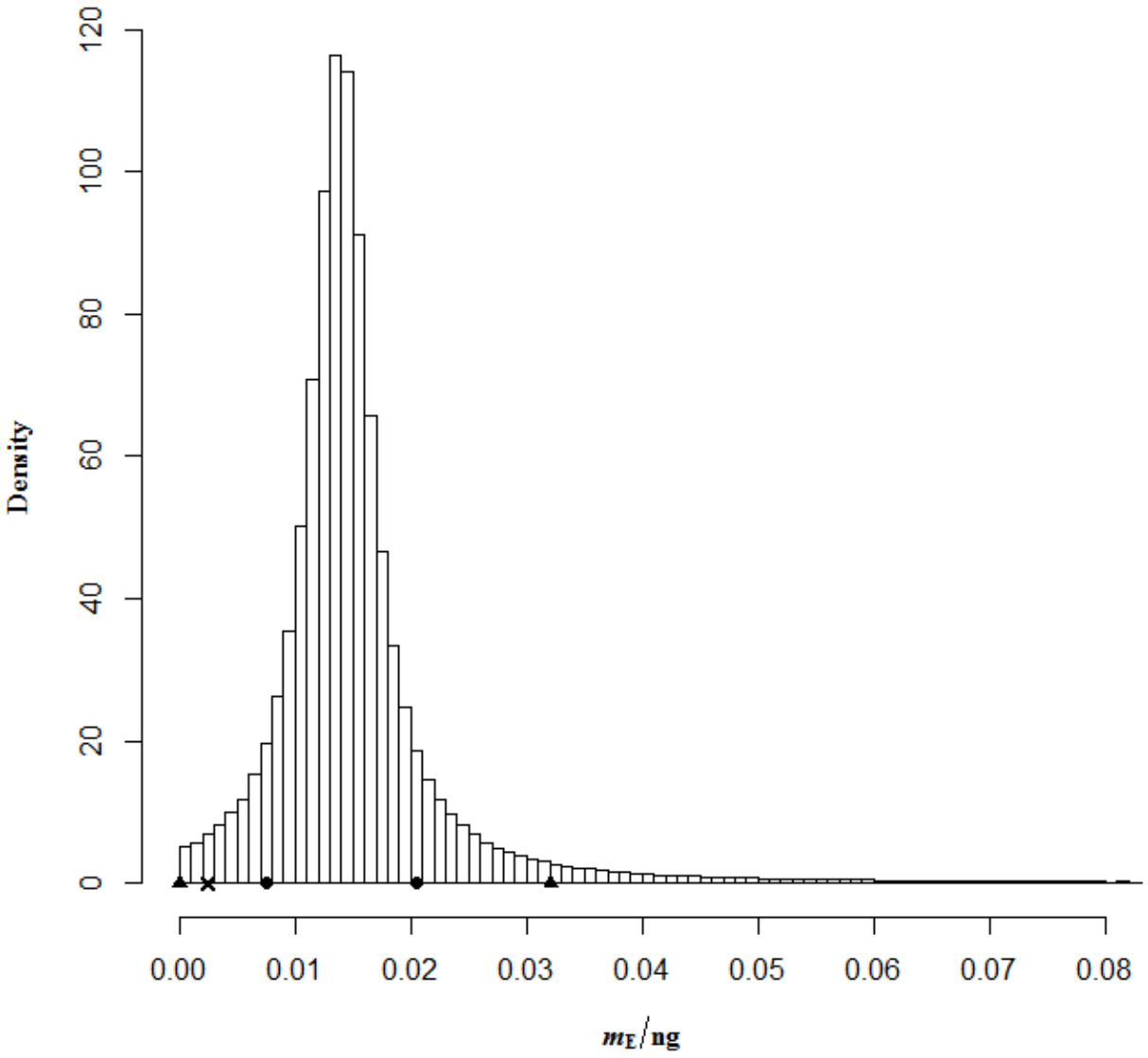
10
15
20
0.20
0.25
0.30
0.35
0.40
0.45
0.50
0.55
0.60
0.65
0.70
m_E/ng

FIGURE 2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40
60
80
100
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0.01
0.02
0.03
0.04
0.05
0.06
0.07
0.08
m_E/ng
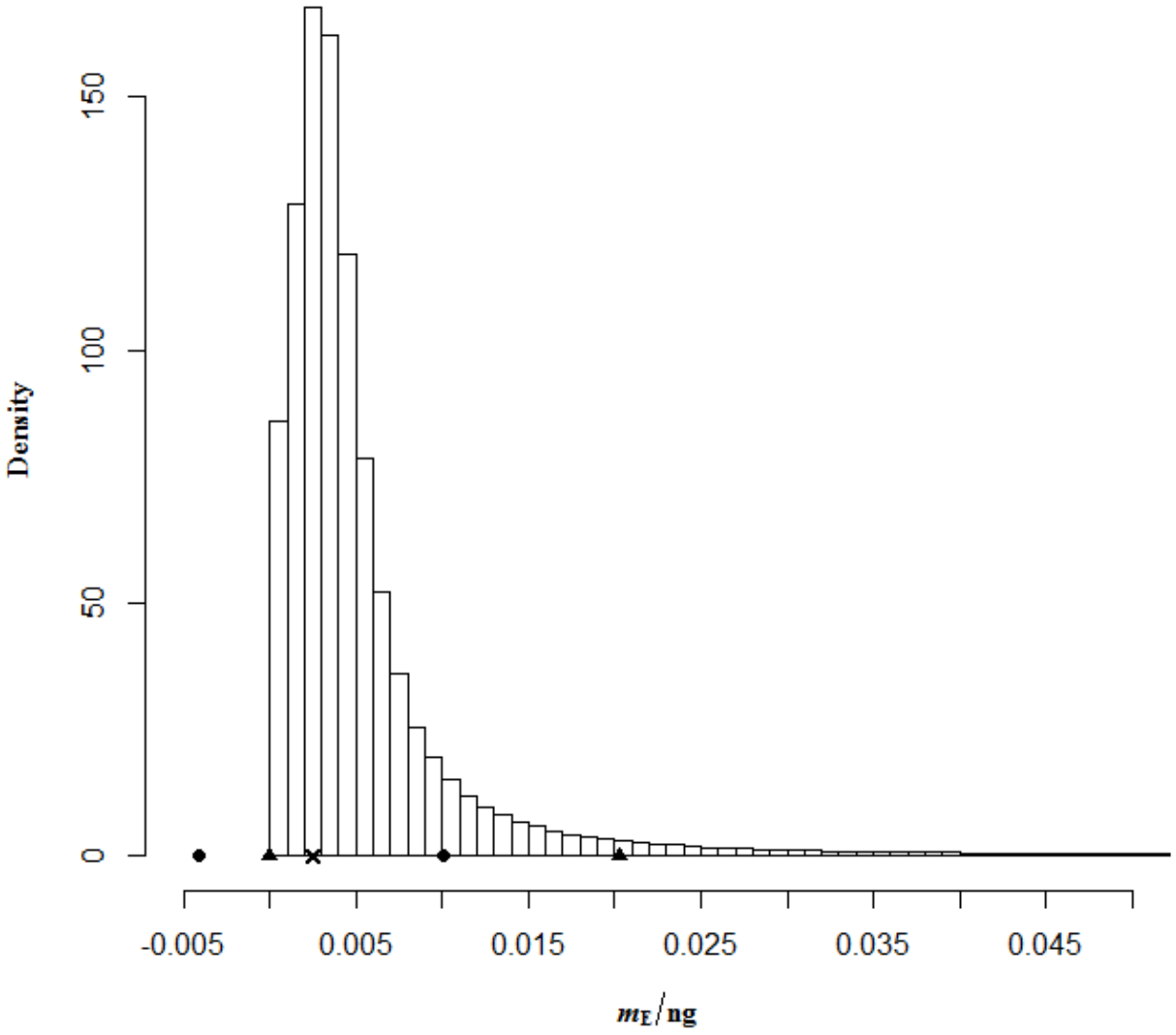
FIGURE 3