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Short communication

Improved mass accuracy in PTR-TOF-MS: Another step towards better compound identification in PTR-MS

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ABSTRACT

Proton transfer reaction mass spectrometry (PTR-MS) provides on-line monitoring of volatile organic compounds (VOCs) with a low detection threshold and a fast response time. Commercially available set-ups are usually based on quadrupole analysers that, due to the unit mass resolution, do not provide useful analytical information besides the nominal mass of the ions detected. Recently new instruments based on time-of-flight (PTR-TOF-MS) analysers have been proposed and commercialized. They provide higher mass resolution and thus improve the analytical information contained in the spectra. Mass accuracy, however, is an issue that has not been considered in great detail in the published papers on PTR-TOF-MS so far. We show here that the mass accuracy obtained by a commercial apparatus can be improved by proper data analysis. In particular, internal calibration based on an improved algorithm allows for a mass accuracy that suffices for elemental determination in the most common situations. Achieving good mass accuracy is a fundamental step for further exploiting the analytical potential of PTR-MS.

1. Introduction

PTR-MS, in its quadrupole based version [1], is a useful technique for the on-line monitoring of most volatile organic compounds. To increase the analytical information contained in PTR-MS spectra the coupling with ion trap [2] or TOF analysers has been proposed [3,4] and recently PTR-TOF-MS instruments have become commercially available [5,6].

Up to now the published studies on PTR-TOF-MS concentrate on mass resolution [5], detection limit [5] and response time [7] but, to the best of our knowledge, no systematic evaluation of the mass accuracy achievable has been discussed.

This latter parameter, however, is of outmost importance in view of the possible identification of the elemental composition of observed spectrometric peaks with the help of isotope ratios and fragmentation patterns. For the small (up to 300 Da) volatile organic compounds commonly monitored by PTR-MS analysis, a mass accuracy of 5 ppm is usually sufficient for the exact determination of the elemental composition of molecules.

External calibration refers to fixing a set of calibration coefficient to be employed during the entire duration of mass spectral acquisition. A proper setting of calibration coefficients at the beginning of the experiment allows reaching good mass accuracy. However, our experience shows that, due to a lack of stability in instrumental parameters, external calibration in commercial PTR-TOF-MS instruments does not guarantee mass accuracy for a sufficiently long time.

A common solution to this problem is the use of an internal calibration based on the known exact mass of selected ions. In the case of PTR-MS useful choices are, for instance, NO^+, $O_2{}^+$ and protonated acetone at nominal masses 30, 32 and 59, which are always present at reasonable concentrations [8]. Other ions can be used if, for example, GC analysis can identify the nature of some of the most intense peaks.

A linear relation between the time-of-flight t and $\sqrt{m/z}$ has been used for the internal calibration of PTR-TOF-MS spectra [8]. This has the advantage that only two parameters are used but it does not consider corrections due to nonlinear effects.

Here we propose the use of a different calibration method that, by including a third parameter, allows for a better accuracy. Further, we evaluate the obtainable mass accuracy by using different sets of calibration peaks.

We compare our present results with results obtained with the commercial software supplied with the instruments and with the linear relation mentioned above. We further discuss the increased accuracy in mass determination achieved with the present method.

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Table 1
List of peaks considered in this paper. The last column indicates whether the peak has been used in the calibration or test procedure.

Nominal mass	Exact mass	Formula	Calibration/test
18	18.0338	NH_4^+	Test
21	21.0221	$H_3{}^{18}O^+$	Cal
30	29.9974	NO^+	Cal
59	59.0491	$H_7C_3O^+$	Cal
89	89.0597	$H_9C_4O_2^+$	Test
103	103.0754	$H_{11}C_5O_2^+$	Cal
117	117.0910	$H_{13}C_6O_2^+$	Test
131	131.1067	$H_{15}C_7O_2^+$	Cal
145	145.1223	$H_{17}C_8O_2^+$	Test
159	159.1380	$H_{19}C_9O_2^+$	Cal
173	173.1536	$H_{21}C_{10}O_2^+$	Test
187	187.1693	$H_{23}C_{11}O_2^+$	Cal
205	205.1951	$H_{25}C_{15}^+$	Test

2. Materials and methods

2.1. Samples

We measured volatile organic compounds in the head-space of apples of different cultivars enclosed for 30 min in glass jars (1000 ml) by both PTR-TOF-MS and SPME-GC/MS. GC data are not discussed here, but they have been used to confirm the identification of the observed PTR-MS peaks considered in the present study.

Our experimental dataset for analysis consists of 20 PTR-TOF-MS spectra of 5 different apple cultivars, resulting in a total set of 100 PTR-TOF-MS spectra. Taking into account the information deduced from the GC data, we identified 13 peaks present in all spectra. The ions corresponding to the known m/z values are listed in Table 1.

2.2. PTR-MS analysis

Measurements were performed as described in [9] but with a commercial PTR-TOF-MS 8000 apparatus supplied by Ionicon Analytik GmbH, Innsbruck (Austria) in its standard configuration [5]. The sampling time per channel in the TOF is 0.1 ns, amounting to about 350,000 channels for a mass spectrum up to 400 Th, and the ionisation conditions are controlled by drift voltage (600 V), drift temperature (110 °C) and drift pressure (2.25 mbar).

Fruits were taken from the storage room and placed in a glass jars (1000 ml, 30 °C) which were provided with two Teflon/silicone septa on opposite sides. After 30 min a Peek tube (110 °C, 0.055 in. diameter) was connected between the inlet of the PTR-MS and the headspace collecting jars and 100 standard cubic centimetres per minute were continuously extracted for 30 s, allowing to obtain 30 TOF spectra from virtually 0 up to 400 Th within this time. Every single spectrum is the sum of 28,600 acquisitions lasting for about 35 μs each.

2.3. Data analysis

Generally speaking, external calibration is sufficient to determine the nominal mass of all peaks in PTR-TOF-MS spectra. The further identification of specific ion peaks then relies on details of the PTR-MS technique or additional information. In the present case, we rely on the identification of a certain number of (calibration) peaks, including such typical ions as $H_3{}^{18}O^+$, NO^+ and acetone and, in addition, other intense peaks in ripened apple headspace such as the linear ester ion series at $m/z = 61 + n14$ and the sesquiterpene peak related in our samples mostly to farnesene (see Table 1). We choose 7 peaks at nominal masses 21, 30, 59, 103, 131, 159, 187 to be used as calibration peaks in the calibration of the dataset. The remaining known peaks in Table 1 are used as test peaks to check the performance of the calibration procedure. In the following, the former peaks will be denoted as “calibration peaks”, the latter peaks as “test peaks” (Table 1).

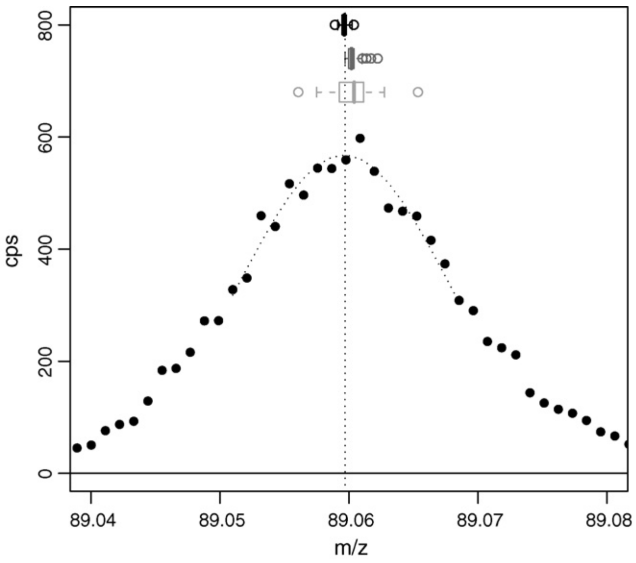

Fig. 1. Example of a test peak ($H_9C_4O_2^+$, nominal mass 89, exact mass 89.0597). The vertical dotted line represents the exact mass value of the ion. The boxplots summarise 100 mass values obtained after calibrating with 6 calibration peaks ($m/z = 59$, 159, 103, 30, 187 and 131.) using the commercial software (light grey), Eq. (1) (dark grey) and Eq. (2) (black). For details on boxplots see caption to Fig. 3.

TOF spectra are characterized by proportionality between the square root of the m/z value and the ion time-of-flight, at least on an idealized basis, and thus, as discussed in [8], the following fitting formula for the internal calibration procedure should hold:

$$t - t_0 = A\sqrt{\frac{m}{z}}, \tag{1}$$

where t_0 and A are constants to be determined. However, our comprehensive data analysis, in accordance with theoretical rea-

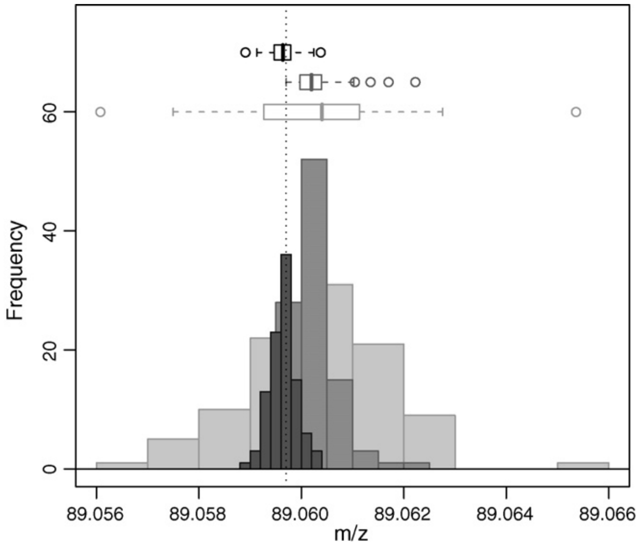

Fig. 2. Histograms of estimated values for a test peak ($H_9C_4O_2^+$, nominal mass 89, exact mass 89.0597) following calibration of the 100 measured spectra using the commercial software (light grey histogram), Eq. (1) (dark grey histogram) or Eq. (2) (black histogram), with 6 calibration peaks at $m/z = 59$, 159, 103, 30, 187 and 131. For the sake of clarity, different bin sizes have been used in the two cases. The vertical dotted line represents the exact mass value of the ion. Boxplots as in Fig. 1.

sons [10], suggests that non-negligible deviations from Eq. (1) are present in our data.

We therefore propose to account for the deviations by replacing Eq. (1) with a relation

$$Bt^2 + Ct + D = \frac{m}{z}, \tag{2}$$

where B, C and D are suitable fitting constants. We assume that Eq. (2) is a good trade-off between computational/experimental effort (only 3 parameters) and proper accurate modelling of TOF optics which would require more parameters.

Internal calibration of our data begins with the determination of the calibration peak centroids: a time-of-flight value is estimated as the mean parameter of the Gaussian which best fits the peak after calibration. In order to limit errors due to asymmetry in the peak shape, only intensities above 50% of the maximum are considered for the Gaussian fit, as proposed in [11]. Alternatively, one could fit modified Gaussian functions to match the asymmetries, for example the one proposed in [12]. Calibration peak centroids give the (uncalibrated) time-of-flight values to be used together with exact m/z values, to fit the parameters B, C and D of Eq. (2).

Internal calibration is performed with an increasing number of calibration peaks by using, besides $m/z = 59$ and 89, the following additional calibration peaks $m/z = 103$, 30, 187, 131, 21.

Test peak centroids are also determined and their m/z values are estimated via Eq. (2). Estimated values can then be compared with the *a priori* known m/z value of the corresponding ion. Here, we will use two different definitions for the mass accuracy: (i) MMD (maximum mass deviation) defined as the 95th percentile of mass deviation observed and corresponding to the case in which we determine the mass of a peak from a single spectrum and (ii) ME, the median error, corresponding to the more favourable case in which we can measure several spectra, as in the presented apple data.

All calculations have been carried out in Matlab (Eigenvectors Inc., Seattle, WA, USA), implementing routines for automatic determination of calibration coefficients.

For comparison, we further determine mass accuracy by using Eq. (1) and by employing the commercial software which is provided with the PTR-TOF-MS (TofViewer 1.4, Ionicon Analytik).

3. Results and discussion

As an example, we discuss the (test) peak at $m/z = 89$ depicted in Fig. 1. The mass spectrometric peak has an approximate Gaus-

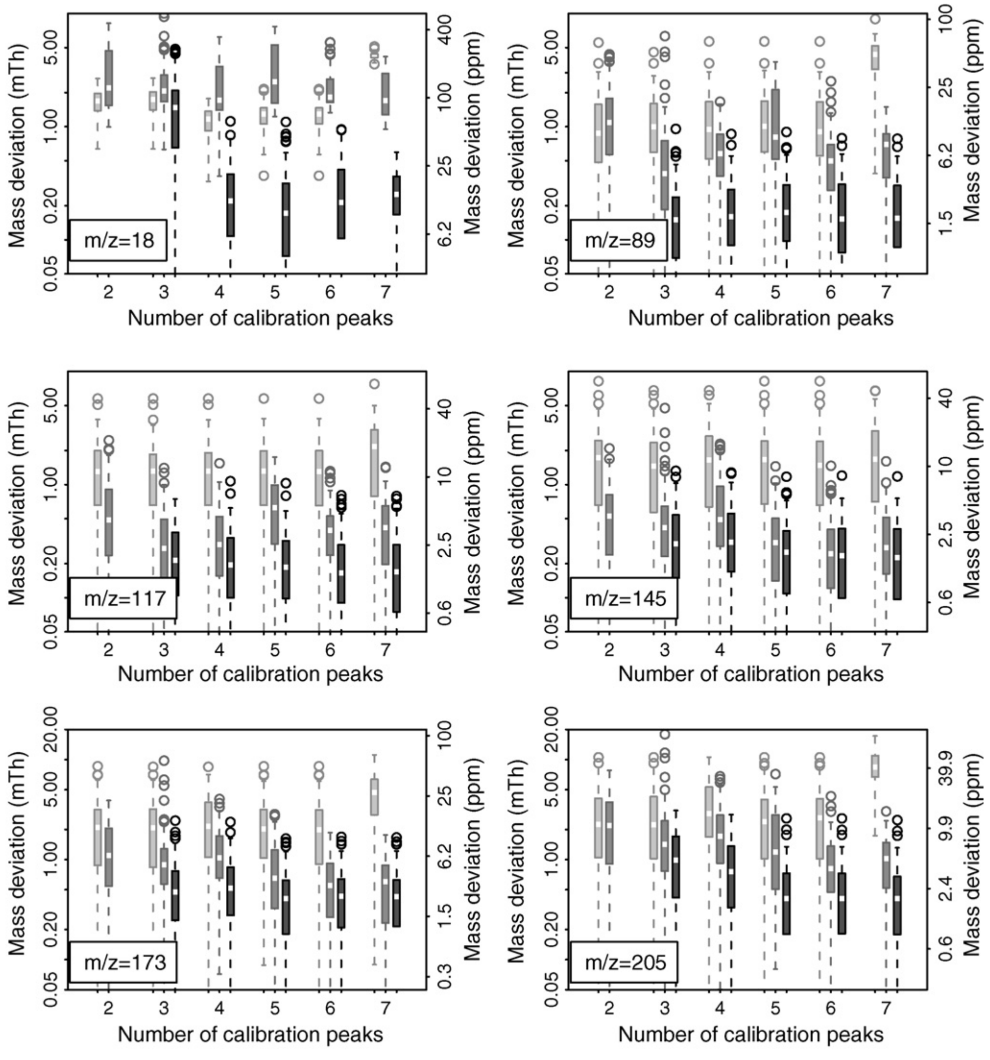

Fig. 3. Calibration errors for the test peaks (difference between measured and calculated mass value) as a function of the number of calibration peaks. Results obtained using our calibration method (black), that is Eq. (2), are compared with those obtained using Eq. (1) (dark grey) and using the commercial software (light grey). Each "box" represents the interquartile range of the 100 spectra and the line inside each box is the sample median. Data that are more than 1.5 times the interquartile range away from the edges of the box are marked as outliers (circles). All other values fall within the plotted whisker.

Table 2
Statistical mass accuracy (median error) and maximum mass deviation (MMD) of test peaks in the case of calibration based on the 6 peaks at $m/z = 59$, 159, 103, 30, 187 and 131.

Nominal mass	Median error		MMD	
	mTh	ppm	mTh	ppm
18	0.21	11.7	0.77	42.8
89	0.15	1.7	0.55	6.1
117	0.17	1.4	0.64	5.5
145	0.24	1.6	0.65	4.5
173	0.43	2.5	1.2	6.7
205	0.40	2.0	1.2	5.7

sian shape corresponding in this case to a resolution of about 4000 ($m/\Delta m_{50\%}$). Calibrating with 6 peaks (at nominal masses: 30, 59, 103, 131, 159, 187) it is possible to determine the exact mass with good approximation. Fig. 2 shows the distribution of the mass determinations for this peak obtained for the 100 measured spectra.

Our calibration procedure provides a rather narrow histogram with a MMD accuracy of 6.1 ppm and a ME of 1.7 ppm. In contrast, the commercial software gives estimated masses distributed over a much broader range, MMD and ME being 30 ppm and 10 ppm respectively.

Fig. 3 displays the absolute differences between the estimated and the exact m/z values for the present selected test peaks. A box plot is constructed for each number of calibration peaks considered. Table 2 summarises as an example present values for the mass accuracy when using 6 calibration peaks. Note that in general the mass accuracy increases with an increasing number of calibration peaks. This finding is in accordance with the fact that calibration parameters are better estimated by using more calibration peaks. Interestingly, this is not the case of the commercial software. It leads to substantially lower mass accuracies and shows no improvements when calibrating with more ions. Moreover, systematic discrepancies between estimated and known ion m/z value often appear, e.g., as it is evident from Fig. 1 ($m/z = 18$).

A calibration using Eq. (1) provides a mass accuracy that lies between our method and the commercial software. For example, with Eq. (1) we obtain 7.8 ppm and 13 ppm for MMD and ME, respectively, for the test peak at $m/z = 89$, when calibrating with 6 calibration peaks.

Our present results, i.e., the improved mass accuracy, can be better appreciated in terms of “acceptable uncertainty” [13] of mass determination. For instance, suppose we measure $m/z = 205.1951$ for the mass of an ion whose structure is to be determined. Considering ions encompassing C_{0-100}, H_{0-100}, N_{0-20}, O_{0-20} and S_{0-20}, as it is plausible when dealing with VOCs emitted by food samples, there exists just one possible structural sum formula within an uncertainty of 19 ppm. Increasing the uncertainty to 33 ppm leads however to 5 possible sum formulas. Therefore, it is clear that reaching an acceptable uncertainty is a fundamental step for further exploiting the analytical potential of PTR-MS. For instance, we reach a MMD of 5.7 ppm for the test peak $m/z = 205$ when using 6 calibration peaks, while calibration with the commercial software results in a MMD of more than 33 ppm (see Fig. 3).

Finally, despite its simplicity, Eq. (2) proves to quite successfully increase mass accuracies to useful values. The accuracy is lower for mass peaks with low nominal masses, for example the test peak at $m/z = 18$. However, the increased uncertainty is balanced by a drop in the acceptable mass accuracy needed to support elemental determination in the sum formula in this case.

4. Conclusions

We present a method to provide an accurate determination of peak positions in TOF mass spectra highlighting the accuracy to which a peak position can be measured in PTR-TOF-MS apparatuses. The relatively good accuracy achieved here for the commercial TOF analyser coupled with proton transfer ionisation provides a method that combines the sensitivity and speed of PTR-MS with analytical features that helps the determination of the exact elemental composition of the measured peaks. Moreover an accurate calibration permits to enhance signal to noise ratio by the averaging of several spectra referring, for instance, to the same sample.

We are evaluating whether improvement of mass spectral analysis (baseline correction, noise reduction) can further improve the analytical properties of this interesting technology and how this is related to instrumental resolution.

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