



# The next generation in high sensitivity and high resolution Proton-Transfer-Reaction Time-of-Flight Mass Spectrometry (PTR-TOFMS)

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## **Abstract**

Proton-Transfer-Reaction Time-of-Flight Mass Spectrometry (PTR-TOFMS) has revolutionized the PTR-MS community. First PTR-TOFMS prototypes published in the last decade performed rather low with 0.2 to 4 *cps/ppbv* sensitivity, detection limits in the ppbv range and a mass resolution of around 1000 *m/Δm*. IONICON's first commercial PTR-TOFMS was already a milestone compared to these prototypes with a sensitivity of up to 25 *cps/ppbv*, a single digit *pptv* level detection limit and a mass resolution of over 6000 *m/Δm*. Here we present another historical step in PTR-TOFMS technology, namely the overall improvement of every aspect of instrumental performance. We show that with these advancements we can now reach over 8000 *m/Δm* in mass resolution at a sensitivity of nearly 300 *cps/ppbv* and a detection limit below 1 *pptv*. This represents an improvement of over one order of magnitude in terms of sensitivity, which is a gigantic step in mass spectrometry. Furthermore we also improved the PTR-TOF 2000 model, which now measures up to high sensitivity PTR-QMS systems with a sensitivity of about 750 *cps/ppbv* and a detection limit of around 650 *ppqv* while still obtaining a maximum mass resolution of over 2400 *m/Δm*. All of these outstanding performance data are proven by measured results of certified gas standards and detailed information about the measurement process.

## **Introduction**

Since the first presentation of a high resolution and high sensitivity Proton-Transfer-Reaction Time-of-Flight Mass Spectrometry (PTR-TOFMS) instrument by us in 2009 (Jordan et al.<sup>i</sup>) this technology found growing importance in typical PTR-MS fields of application, such as environmental research<sup>ii</sup>, food and flavor science<sup>iii</sup>, biological research<sup>iv</sup> and medicine<sup>v</sup>. Moreover, PTR-TOFMS opened completely new application areas where not only high sensitivity but high selectivity is needed, e.g. explosives<sup>vi</sup>, chemical warfare<sup>vii</sup> and illicit and prescribed drug<sup>viii</sup> detection, as well as investigations of toxic industrial compounds<sup>ix</sup>. Although quadrupole mass filter based PTR-MS technology has its undisputed advantages, it becomes obvious that PTR-TOFMS will play a major part in the future and therefore every technical advance in this technology will have a great impact to the analytical community.

However, as in a TOF mass spectrometer the ions are pulsed, the instrument's sensitivity was so far somewhat lower compared to a mass filter working in continuous mode like e.g. quadrupoles. Blake<sup>x</sup> and Ennis et al.<sup>xi</sup> consequently reported in 2004 and 2005 on PTR-TOFMS prototype performance

data showing 0.17 *cps/ppbv* and 3.7 *cps/ppbv*, respectively. Blake added mass resolution data of around 1000  $m/\Delta m$  and Ennis presented a detection limit of 1 *ppbv*. Although the first coupling of a PTR ion source to a TOF mass spectrometer was a remarkable scientific achievement, the performance data were about two orders of magnitude below those from state-of-the-art PTR-QMS at that time. Therefore our publication<sup>i</sup> four years later, introducing a PTR-TOFMS with a mass resolution of over 6000  $m/\Delta m$ , a sensitivity of 15-25 *cps/ppbv* and a detection limit in the single digit *pptv* region can be considered as another milestone in PTR-TOFMS history.

In 2009 we published data from an improved version of a PTR-QMS (Jordan et al.<sup>xiii</sup>) demonstrating a sensitivity of nearly 1000 *cps/ppbv* and a detection limit in the *ppqv* region. As the response to this development from the scientific community was tremendously positive over the last few years, we started improvement and advancement work concerning sensitivity and detection limits also for our TOF based instruments. Here we present our latest performance data obtained with two "off-the-shelf" PTR-TOFMS models (PTR-TOF 8000 and PTR-TOF 2000).

### Experimental

The PTR technology is already well known (compare e.g. Blake et al.<sup>xiii</sup>) and therefore only a short description will be presented here. In Fig. 1 a schematic view of an IONICON PTR-TOFMS is presented. Assuming that the instrument is equipped with the switchable reagent ions (SRI) feature, either water vapor from a container holding distilled water (for  $H_3O^+$  mode), charcoal filtered air (for  $NO^+$  mode) or oxygen from an  $O_2$  cylinder (for  $O_2^+$  mode) is introduced into the ion source. Due to the sophisticated design of this source, the high purity level of the reagent ions makes an additional, signal diminishing mass filter, which is utilized e.g. in SIFT-MS instruments, between the ion source and the adjacent drift tube, obsolete. In the drift tube the chemical ionization via PTR ( $H_3O^+$ ) or for instance charge transfer ( $NO^+$ ,  $O_2^+$ ) takes place. Finally, a transfer lens system guides the ions into the TOF, where they are analyzed by their mass and detected on a microchannel plate (MCP) detector.

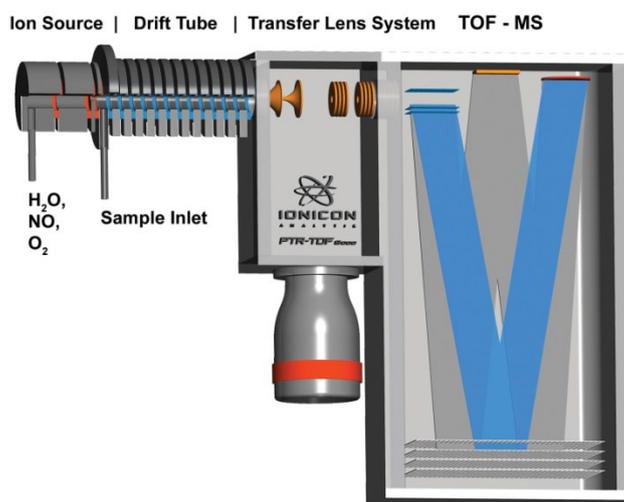


Fig. 1: Schematic view of an IONICON PTR-TOFMS with SRI

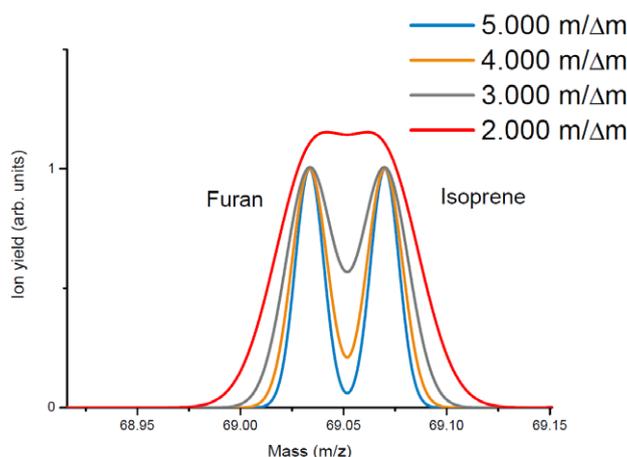
Although the PTR-TOF 8000 is capable of being operated in W-mode, in the present study we solely used the V-mode, as the achieved resolution in this mode is more than sufficient and the instrument's sensitivity is considerably higher. The PTR-TOF 2000 can only be used in V-mode and offers a shorter flight path, which leads on the one hand to a somewhat reduced mass resolution (see results section) but also to a higher sensitivity.

Both instrument types were adapted and improved by optimizing a variety of different experimental parameters, starting from the ion source all the way to the detector.

### ***PTR-TOF 8000 Results***

#### *Mass resolution*

In order to demonstrate the importance of high mass resolution and to determine reasonable resolution values for the simultaneous detection of isobaric substances, we calculated the resulting peak shapes at different mass resolutions (2000 to 5000  $m/\Delta m$ ) for the two isomers protonated furan ( $C_4H_4O.H^+$ ; 69.039  $m/z$ ) and isoprene ( $C_5H_8.H^+$ ; 69.070  $m/z$ ). Fig. 2 clearly demonstrates that with a resolution of 2000  $m/\Delta m$  the two peaks virtually "melt" together into one broad peak, thus making individual quantification difficult or even impossible, presuming that one of the two substances is present in much higher concentrations compared to the other. In contrast, at a resolution of 5000  $m/\Delta m$  the valley between the peaks is clearly below 10% and therefore the two compounds can be quantified independently.



**Fig. 2: Calculated peak-shapes for two isobaric compounds at different mass resolutions**

In such a complex instrumentation like a PTR-TOFMS even the smallest variations in orifice diameters, vacuum conditions, electric fields, etc. have enormous effects on the resulting performance. Therefore, in order to present typical, meaningful and valid data from our currently manufactured instrument series, we measured the resolution on two independent off-the-shelf PTR-TOF 8000 systems.

The mass resolution determination was performed utilizing a standard gas mixture (Restek; USA) containing the compounds listed in Tab. 1 at concentration levels of about 100 *ppbv* each (in nitrogen). The gas cylinder was connected to the respective PTR-TOF 8000 inlet via a T-piece with

one end open for the overflow. Additionally, in order to get more data points in the low mass region, some high intensity lab air compounds (e.g. acetone, isoprene, etc.) were analyzed. In Fig. 3 the results for the two instruments are presented. It can be seen that for both instruments the resolution is increasing with increasing mass-to-charge ratio. Therefore the maximum achievable resolution can be calculated using an appropriate fitting function. The instrument used in Fig. 3 a) reaches a maximum resolution of about 7000  $m/\Delta m$ , whereas in b) the resolution goes up to nearly 8300  $m/\Delta m$ . According to the calculations in Fig. 2 these resolutions are more than sufficient for separating isomeric compounds, even when their exact masses are closer to each other than for furan and isoprene.

Compound	Molecular composition	Protonated mass ( $m/z$ )
Benzene	C <sub>6</sub> H <sub>6</sub>	79.054
Toluene	C <sub>7</sub> H <sub>8</sub>	93.070
Styrene	C <sub>8</sub> H <sub>8</sub>	105.070
Ethylbenzene	C <sub>8</sub> H <sub>10</sub>	107.086
Xylene	C <sub>8</sub> H <sub>10</sub>	107.086
Chlorobenzene	C <sub>6</sub> H <sub>5</sub> Cl	113.015
Trimethylbenzene	C <sub>9</sub> H <sub>12</sub>	121.101
Dichlorobenzene	C <sub>6</sub> H <sub>4</sub> Cl <sub>2</sub>	146.976
Trichlorobenzene	C <sub>6</sub> H <sub>3</sub> Cl <sub>3</sub>	180.937

Tab. 1: Standard gas components used for the present study

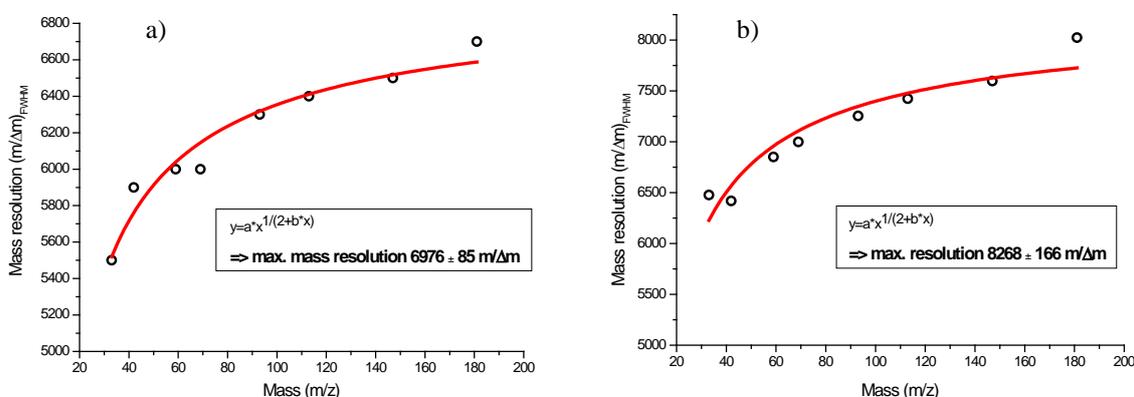


Fig. 3: Measured resolutions for different mass compounds, recorded with two different PTR-TOF 8000 instruments

In PTR-MS analysis usually low mass compounds, i.e. below 100  $m/z$ , play an important role. Therefore we additionally investigated a sample containing "typical" VOCs (volatile organic compounds) like methylketene, butene and benzene, all having a molecular mass well below 100  $amu$ . In Fig. 4 close-ups of the corresponding mass spectrum areas are presented. Even though the compounds possess (low) masses between 50 and 80  $m/z$ , for all three a resolution of about 7000  $m/\Delta m$  can be reached. Moreover, although the ion yield of methylketene in Fig. 4 a) is over one

order of magnitude higher than that for butene, the two mass peaks show no overlap and can therefore be quantified individually without any crosstalk.

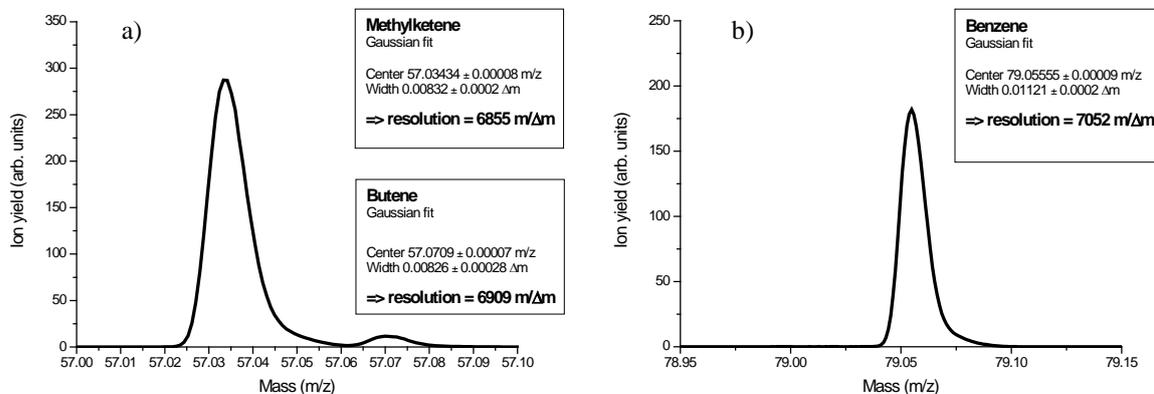


Fig. 4: Resolution determination for three low mass compounds utilizing a PTR-TOF 8000

#### Sensitivity and detection limit

High mass resolution is definitely one of the biggest advantages of a TOF based PTR-MS instrument. However, the benefit of a high resolution PTR-TOFMS is considerably reduced in case the instrument's sensitivity is insufficient for the analysis of low-concentration VOCs. In environmental research for example, compounds like sesquiterpene are usually present in concentrations in the single digit *pptv* region<sup>i</sup>, therefore a detection limit around 1 *pptv* is needed in order to perform a useful analysis.

For determining the sensitivities and the detection limits of the improved PTR-TOF 8000 we utilized the same standard gas mixture and experimental setup as described in the previous section (see Tab. 1). The pulse frequency, i.e. the number of "ion packages" that are injected into the TOF flight path per second, is not only controlling the accessible mass range but is also affecting the sensitivity. If the pulse frequency is doubled, twice the amount of ions will be detected per second on one *m/z* measuring point, i.e. the relationship between the pulse frequency and the sensitivity is linear. Thus, stating a PTR-TOFMS' sensitivity without stating the pulse frequency is of very limited significance. For the measurements presented in Fig. 5 we chose a frequency of 40 *kHz* which covers quite well the mass range expected from the gas standard used. Only for mass 79 *m/z* (protonated benzene) we used a frequency of 60 *kHz*, which reflects real-life conditions, where only such a mass range would be selected which covers the expected compounds while not "wasting" sensitivity.

Similar to the resolution, also the sensitivity increases with increasing *m/z* ratio. It has to be noted, that this is in contrast to quadrupole based PTR-MS instruments, where the sensitivity is seriously decreasing for high *m/z* ratios. This fact is of special importance for fields of application that are dealing with high mass compounds (above 200 *m/z*), like e.g. drug or explosives detection<sup>(viii, xiv)</sup>. In Fig. 5 a) the resulting sensitivities are shown. Compared to our original publication on the first PTR-TOFMS in 2009<sup>i</sup>, the instrumental improvements lead to an increase in sensitivity of more than

one order of magnitude, now reaching nearly 300 cps/ppbv for 147 m/z at 40 kHz and even higher for heavier compounds. The fact, that in Fig. 5 a) the sensitivity of 181 m/z is slightly suppressed can be explained by the fact that we set the operating voltage of the MCP to a slightly lower value than what would be the optimum for the detection of a compound on 181 m/z in order to prolong its lifetime. In general it can be said that increasing the MCP voltage increases the detection sensitivity for high mass compounds. However, increasing the MCP voltage also shortens the overall lifetime of the detector and therefore it is always a trade-off between these two factors which voltage should be chosen.

The limits of detection (LODs) were calculated using the 3 $\sigma$  method (with  $\sigma$  being the standard deviation of the background signal) for 1 s and for 1 min integration time. The results are shown in Fig. 5 b). For 1 s the LODs are between 35 and 10 pptv, for 1 min integration time between 3 and 0.8 pptv. One outlier is mass 93 m/z, which can be explained by the rather high background we experience on this m/z ratio due to some contamination inside the instrument.

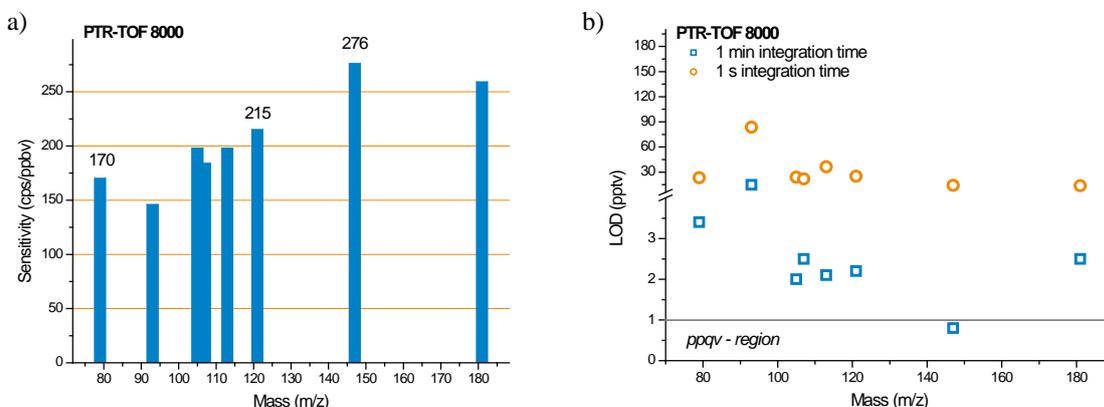


Fig. 5: Measured sensitivities and limits of detection for a PTR-TOF 8000

These data now prove that for the first time we reach the detection limit of a PTR-QMS (sub pptv region) with a PTR-TOF 8000, with the advantage of high mass resolution (up to 8000  $m/\Delta m$ ) and increasing sensitivity for high mass compounds.

### **PTR-TOF 2000 Results**

#### *Mass resolution*

The determination of the PTR-TOF 2000 mass resolution was performed the same way as described for the PTR-TOF 8000, i.e. utilizing the gas standard stated in Tab. 1 and several lab air compounds. Fig. 6 shows the obtained results. As expected from this compact TOF mass spectrometer the resolution is somewhat lower than for the PTR-TOF 8000, however for masses above about 80 m/z the resolution already exceeds 2000  $m/\Delta m$  and can therefore still be considered as very high, i.e. many isobaric substances can already be separated and individually quantified. The maximum achievable resolution for this instrument is 2440  $m/\Delta m$ .

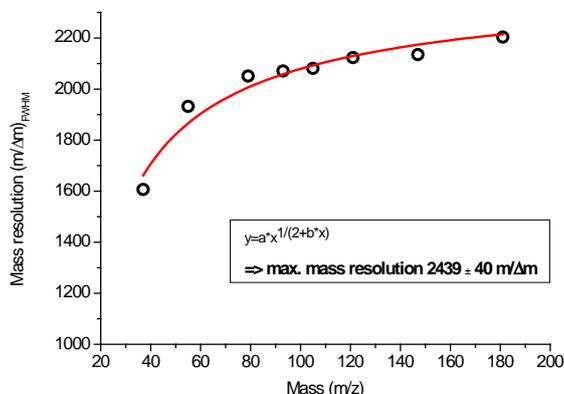


Fig. 6: Measured resolutions for different mass compounds, recorded with a PTR-TOF 2000 instrument

*Sensitivity and detection limit*

Also the sensitivity and the detection limit of the PTR-TOF 2000 were determined in a similar way as for the PTR-TOF 8000. It has to be noted that the pulse frequency for this instrument is generally higher because of the shorter flight path. The frequencies used for the three exemplary compounds are stated directly in Fig. 7 a). In this figure it can be seen that the highest sensitivity of about 740 cps/ppbv is reached at 121 m/z. Although the instrument is more sensitive for high mass compounds, the sensitivity for 181 m/z is with 580 cps/ppbv lower than for 121 m/z, which is because of the lower pulse frequency used for this compound (130 kHz and 100 kHz, respectively). In summary it can be said that the overall sensitivity of the PTR-TOF 2000 is about 2 to 3.5 times higher than that of the PTR-TOF 8000 and therefore now in the same region as a high sensitivity quadrupole based PTR-MS instrument<sup>xii</sup>.

The 3σ limits of detection are displayed in Fig. 7 b). Here especially the LODs for 1 s integration time are tremendously improved, i.e. they are between 7 and 12 pptv for the PTR-TOF 2000. The best detection limit is obtained at 121 m/z with 640 ppqv for 1 min integration time. Again, this is comparable to the best performances achieved so far only by PTR-QMS instruments<sup>xii</sup>.

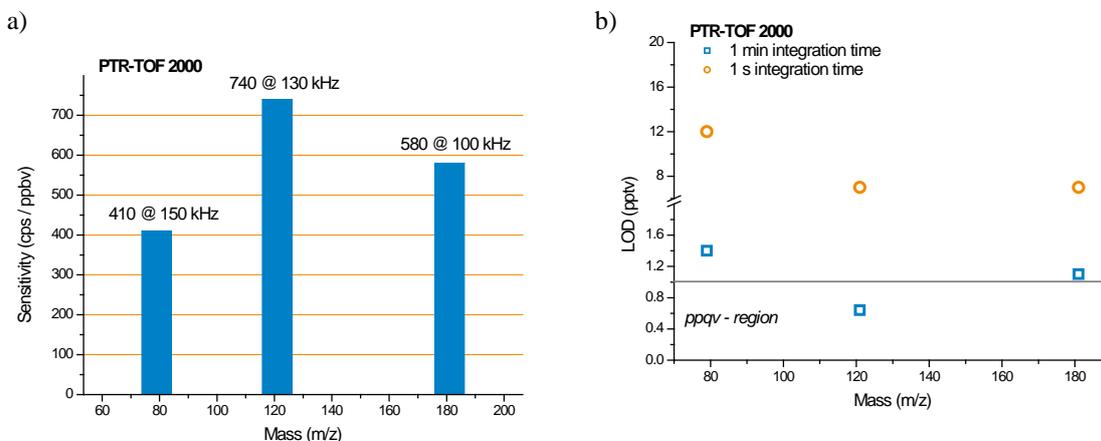


Fig. 7: Measured sensitivities and limits of detection for a PTR-TOF 2000

### Conclusion

We conclude that the sum of the sophisticated advances and improvements on our two PTR-TOFMS systems, namely the PTR-TOF 8000 and the PTR-TOF 2000 lead to an increase in instrumental performance of over one order of magnitude. For both instrument types we reach LODs in the *ppqv* region and for the PTR-TOF 2000 a maximum sensitivity of about 750 *cps/ppbv*. These outstanding instrumental performances in combination with the well-known advantages of a TOF mass spectrometer (virtually unlimited mass range, obtaining whole mass spectra in split seconds, increasing sensitivity with increasing *m/z* values, etc.) consolidate IONICON's PTR-MS systems as the gold standard in real-time, high sensitivity, high selectivity trace gas analysis.

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