Simultaneous on-line vacuum single- and multi-photon ionization on an orthogonal acceleration time-of-flight mass spectrometer platform†

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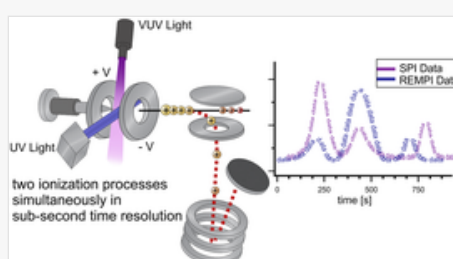
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Abstract

The development of orthogonal acceleration time-of-flight (oa-tof) technology is driven forward due to higher mass accuracy and resolving power than conventional linear/reflectron tof instruments. This is achieved with a more accurate definition of starting energies and coordinates of ions by spatial separation of ion generation and orthogonal ion extraction. Consequently, the ability to cover the whole mass spectral range without scanning is not given anymore. Therefore, continuous ion sources are favored for ensuring high duty cycles and thus high temporal resolution. For pulsed ion sources, high repetition rates are mandatory for covering large m/z ranges without losing their high temporal resolution. We have combined an oa-tof with deuterium lamp single-photon ionization (SPI) as a continuous ion source together with a pulsed 2000 Hz excimer (KrF) laser for resonance enhanced multi-photon ionization (REMPI). These two ionization techniques can be used simultaneously. To the best of our knowledge, this system is the first of its kind in combining a vacuum pulsed ionization source with an oa-tof instrument without any other ion storage hardware. The combination of a soft broadband ionization for organics (SPI) in combination with a very sensitive and selective soft ionization (REMPI) can be used for covering the whole mass range or in targeted on-line monitoring cases one or several smaller mass ranges. To demonstrate the simultaneous SPI/REMPI-oa-tof technique, two applicative areas are explored: on-line monitoring of coffee roast gas emissions and e-cigarette vapor. The complementary information from SPI and REMPI signals are combined in a way to exploit the advantages of both ionization types. In a further development step, a second data acquisition card is built into the system. This modification allows the independent storage of data from both ionization methods without mixing. For demonstration, a third example with a GC measurement is provided. The last example shows the possibility of modified sensitivities for different mass regions in REMPI data acquisition without affecting the SPI channel. The newly developed system shows high robustness in terms of measurements in real industrial environments. The simultaneous measurement technique provides a higher density of information in a single measurement, saving time and resources.

Introduction

The idea of spatially separating the ion generation and ion extraction in a time-of-flight mass spectrometer (tofMS) was introduced by Benson *et al.* in 1956.[1] Nevertheless, he was unable to construct such an instrument due to the lack of suitable electronic devices at that time. The groups of Chernushevich/Dodonov *et al.* and Guilhaus *et al.* developed such an instrument independently in 1987 and 1989, respectively.[2,3] Basically, ions are generated and transferred with a relatively low potential into an extraction zone and from thereon extracted perpendicular to the first axis with a high potential pulse into the mass separator. Nowadays, such a geometry introduced by Benson *et al.* is called orthogonal acceleration tofMS (oa-tofMS). This special geometry can narrow the initial energy and velocity spread of produced ions, so that a higher mass resolution can be achieved than in conventional tofMS.[4] Usually, continuous ion-producing sources are favored, like single photon ionization (SPI) lamps or electrospray ionization.[4–6] The oa-tofMS geometry requires this circumstance. By guiding the ions from the transfer region into the mass separator, an essential benefit of conventional tofMS is lost. By one extraction, only a part of the produced ions is guided to the detector and consequently, a part, instead of a whole spectrum, is covered. However, this disadvantage, especially for continuous ion sources, does not have to impact the on-line monitoring feasibility of oa-tofMS. Depending on the flight time of the highest supposed mass, the mass separator can be operated at several dozen kHz. Single extraction are "stitched" together for covering the whole spectral range. Therefore, whole spectra can be covered even at several 10 Hz, when needed. Only the duty cycle (produced ions *vs.* detected ions) is lower in an oa-tofMS compared to a conventional tofMS and can be in the range of up to 30%.[7] In a wide series of commercial products, oa-tof based mass separators play a vital role. The latter drawback of the reduced duty cycle due to the oa-tof geometry can be compensated with ion traps before the mass separator.[8] By combining other hardware components as quadrupoles and ion traps with oa-tof mass analyzers, modern instruments are capable of a wide series of experiments with high mass accuracy and mass resolution. MS/MS experiments, MALDI- or ion mobility coupling enable impressive insights into a wide variety of matrices.[9–11] Despite, oa-tof multi-reflectron instruments reach remarkable mass resolutions for tof-instruments up to more than 50 000 ($m/\Delta m$).[12,13] Nevertheless, using these instruments for process monitoring is not always possible.

High variances in concentration, particle rich sampling streams, highly polar matrices with high loads of water and oils can be very challenging. Simple systems with a minimum set of robust hardware parts are therefore better suited for this niche application. The combination of an oa-tofMS with a pulsed ionization source and no other ion storage hardware parts is uncommon. Only the implementation of matrix-assisted laser ionization was tested intensively.[2,14] Due to the dependence on the rate of the pulsed ion source and the fact that only a part of the produced ions are guided into the mass separator, spectra accumulation can be very time-intensive.[15] Therefore, this direct combination has not established itself in the MALDI community yet.

Besides of the mass analyzer, process monitoring can be additionally simplified with a soft ionization method, especially when complex matrices are analyzed.

For a soft, continuous vacuum ionization, deuterium SPI lamps can be used, which have an upper energy limit of 10.78 eV (115 nm, MgF_2 window).[16] Due to the Lyman-alpha emission line at 10.2 eV (121.5 nm), this energy should considerably contribute to the ionization.[17] SPI serves as a soft broadband ionization method. Most organic compounds below an ionization energy of 10.78 eV may be ionized with different ion yields. Thus, background gases such as, $e.g.$, N_2, O_2, H_2O, CO_2, or Ar are not ionized due to their higher ionization energies.[18] Photoionization additionally can be achieved by resonance enhanced multiphoton ionization (REMPI). For REMPI, usually, short UV wavelengths are used. Krypton-fluoride excimer laser serve a wavelength of 248 nm. The main point in this aspect is that REMPI uses at least two photons (excitation and ionization) for ionization. Only little excess energy is transferred into the molecule, but only molecules with relatively long-lasting excited states can be ionized efficiently. Thus, REMPI is a very soft, selective, and sensitive ionization method typically for compounds with aromatic moieties. Nevertheless, the efficiency of ionization with REMPI depends further on the structure of the investigated analyte.[19,20] In an alkylated row, ionization efficiency ranges usually within an order of magnitude, whereas among different substance classes much greater differences of several orders of magnitude exist. Further theory and applications of photoionization techniques are described elsewhere.[18,21–23]

Typical tof-instruments allow considerable higher operating frequencies as most UV laser systems are able to serve. Thus, there is therefore free (temporal) space between the laser pulses, which could be utilized for another ionization approach. This idea is not new. Combing different ionization principles leads to benefits according to a higher load of information over a given sample or process and, therefore, shorter analysis times. This can be achieved by either using different MS with different ionization methods on the same sample inlet[24,25] or multiple ionization sources, mass separators, and detectors in the same instrument,[26] or by using the same ionization chamber, mass separator, and detector on different time scales.[27,28] Despite the benefits, these concepts are rarely applied and not broadly used. Drawbacks are given if the time scale of switching between ionization principles is too large for fast processes. In the approach of Mühlberger $et~al.$[28] even three ionization principles are used: SPI, REMPI, and electron ionization (EI), but REMPI and SPI where switched once a second, which makes it less suitable to gas chromatography (GC). In addition, instrumental parameters need to be carefully set as different ionization concepts might generate drastically different numbers of ions, which could cause space charge, ion transmission issues, as well as, problems with the linear range of the detector.[27,28]

In this work, we show the simultaneous combination of soft broadband SPI and soft selective REMPI on an oa-tof platform. The combination is used for enhancing the information density the system delivers in a single run. This work will show how this implementation is performed and gives application examples for monitoring of e-cigarette (e-cig) vapor and coffee roast gas as industry relevant applications. Furthermore, the development for separating data recording for SPI and REMPI is shown and presented with a further application example on GC-measurements of coffee extracts.

Materials and methods

Mass analyzer, light sources, data acquisition & timing

The mass spectrometer was assembled and bought (without Laser) by Photonion (Photonion GmbH, Germany). The system can be operated with three ionization apertures: a deuterium lamp type L7293 (Hamamatsu Photonics K.K., Japan), a krypton-fluoride excimer laser 0–12 mJ, 3 × 6 mm spot size (MLase AG, Germany) with a freely triggerable

repetition rate of up to 2000 Hz and with electron ionization. The mass spectrometer is a Kaesdorf type OFT10 (Stefan Kaesdorf, Germany) with a first drift length of 129 mm (center of ion generation to center of ion extraction) and a second drift length of 1032 mm. The flight time of an imagery ion of the mass 500 m/z is 37 µs in the mass separator with the voltage set used in this work. The signals are enhanced by a factor of ten and recorded with a 1-channel, 14-bit, 2 gigasamples Acqiris ADQ14 acquisition card (Acqiris SA, Switzerland). For timing, a 6-channel, 25 ps resolution Bergmann BME_SG08p (Bergmann Messgeräte Entwicklung KG, Germany) delay generator card is used. In a further development step of the measurement system, a second identical data acquisition card is set in the instrument. The data acquisition and timing software is self-written and based on Labview 2018 (National Instruments Corp., USA).

Standard gas mixture

As standard gas, a mixture of benzene, toluene, p-xylene, and mesitylen, each with the concentration of 1 ppmv is used (supplier: air liquid).

Coffee

The coffee was kindly supplied by Probat (Probat-Werke von Gimborn Maschinenfabrik GmbH, Germany) and is of the type Arabica Columbia Excelsior. The roasting on the industrial site was done in a tangential coffee roaster (Jupiter 500 Hybrid, Probat GmbH).

For the lab experiments, the coffee (Arabica Columbia) was roasted using an IKAWA roster (IKAWA Ltd, London) to a dark roast with 70 points on the colorette scale (Colorette 3a, Probat GmbH), which corresponds roughly to 17.1 points for the $L*$ value in the CIElab $L*a*b*$ notation (own reference data). The coffee was allowed to degas overnight and was milled using a cone grinder (Baratza Sette 270, coffee circle; Berlin) at the fineness of 7H. Afterward, the coffee was processed in a French press using 24 g of coffee and 200 ml (±5 ml) of hot water (93 °C, ±1 °C). After 2 min the plunger was pressed down and the coffee extract was transferred in a flask. Once the extract has cooled to 60 °C, 6 ml of hexane (purity >97%, (Merck KGaA, Darmstadt, Germany) has been added. The flask has been closed and allowed to stand for 12 h under gentle stirring. On the following day, 3 ml of the hexane extract could be recovered, of which an aliquot of 1 ml was used for the GC analysis.

e-Cigarette

The e-cig is a Vype e-Pen 2 (British American Tobacco plc. England) with a liquid called "dark cherry" and was vaped by coupling the system to a Borgwaldt LM1 (Borgwaldt KC GmbH, Germany).
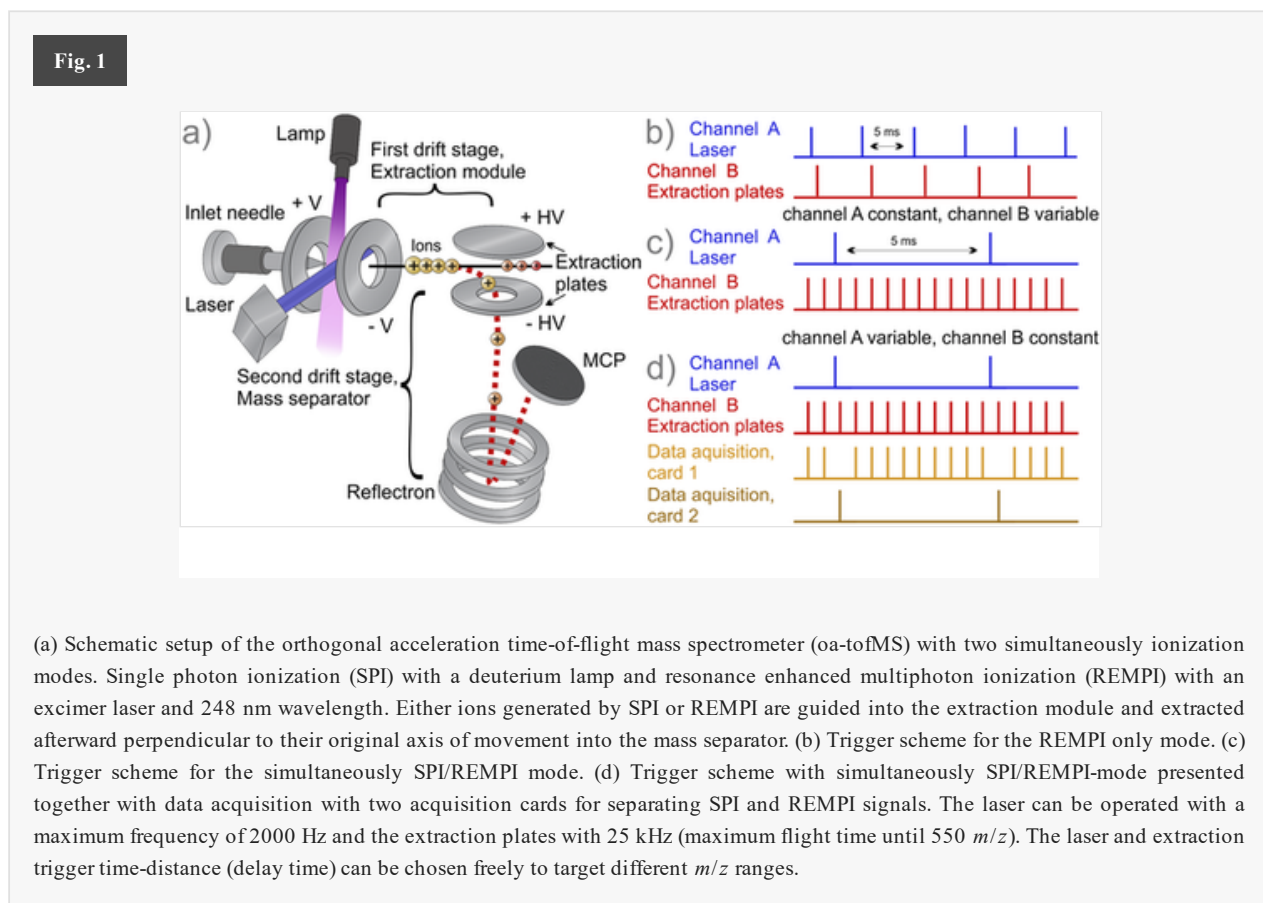
Gas chromatography

For gas chromatography (GC), a gas chromatograph HP 6890 series is used with a 30 m HP-5 column. For a depiction of the linear range of the system in Fig. 3, an isothermal program with 110 °C oven temperature and injector temperature of 230 °C at a split of 1 : 5 is used. For the GC analysis of coffee extracts, the following temperature program is applied: 60 °C (1 min) to 220 °C with 20 K min^{-1}, from 220 to 270 °C with 10 K min^{-1} hold for 6 min. The split/splitless injector is operated at 270 °C with 1.6 ml flow of Helium with on-column injection (1 min). Data recording is started at 1 min after injection (due to manual data acquisition start).

Two versions of data acquisition have been used. In the first setup, all data has been stored together with both ionization techniques on the 14-bit acquisition card. The second setup consists of two acquisition cards. The SPI and REMPI spectra are accordingly stored separately.

Instrument development

For the first experiments, a simpler setup using a single data acquisition card is used. The measurement with continuous lamp ionization is an established analytical procedure,[27,29,30] but by intending to have a second simultaneous non-continuous ionization proceeding at the same timescale, there is the need to set a synchronized timing. The standard mode of an oa-tof (without any additional hardware parts) is continuous ion generation and, related to the ionization, unsynchronized ion extraction. Accordingly, the ions extracted into the mass separator are randomly distributed as they are continuously produced with no defined starting time point for ion generation. By installing a pulsed ion source in

the system, ions are no longer continuously generated. In consequence, ion extraction has to be synchronized as well. By knowing the fill-up time of the extraction module for a given m/z value, it is possible to set the trigger delays for ionization and extraction in order to scan the entire m/z range of interest, monitoring a single m/z range or monitoring multiple m/z ranges. As usual for oa-tofMS, several single extractions (also called waveforms) are merged for a full spectrum. Fig. 1 shows the basic schematic setup of the system together with trigger schemes for different measurement modes. The system can be operated in SPI, REMPI, or simultaneously SPI/REMPI mode.

Fig. 1

(a) Schematic setup of the orthogonal acceleration time-of-flight mass spectrometer (oa-tofMS) with two simultaneously ionization modes. Single photon ionization (SPI) with a deuterium lamp and resonance enhanced multiphoton ionization (REMPI) with an excimer laser and 248 nm wavelength. Either ions generated by SPI or REMPI are guided into the extraction module and extracted afterward perpendicular to their original axis of movement into the mass separator. (b) Trigger scheme for the REMPI only mode. (c) Trigger scheme for the simultaneously SPI/REMPI mode. (d) Trigger scheme with simultaneously SPI/REMPI-mode presented together with data acquisition with two acquisition cards for separating SPI and REMPI signals. The laser can be operated with a maximum frequency of 2000 Hz and the extraction plates with 25 kHz (maximum flight time until 550 m/z). The laser and extraction trigger time-distance (delay time) can be chosen freely to target different m/z ranges.

In Fig. 1(a), the operation with SPI and REMPI is schematically shown. The system is compromised of the basic components for general functionality without any special electronics and hardware enhancements like quadrupoles or ion traps. This setup ensures the robustness and repeatability, which is highly mandatory for process monitoring of complex matrices with very variable concentrations. Consequently, the setup consist of as few parts as possible In Fig. 1(b), the trigger scheme is depicted for the REMPI mode only, the laser is set on a continuous sequence and the triggering for the extraction plates is done afterward in a variable distance. The delay of laser and extraction trigger defines which m/z values are guided into the mass separator. The laser frequency can be adjusted up to 2000 Hz. The data acquisition is synchronized with the trigger for the extraction plates. This scheme was the first operation mode of the system and was used as a proof-of-concept. In order to be able to work with the high extraction rates for SPI, the REMPI laser trigger has to be variable and the extraction plate trigger is fixed. This ensures appropriate programming of the timing card for every use case.
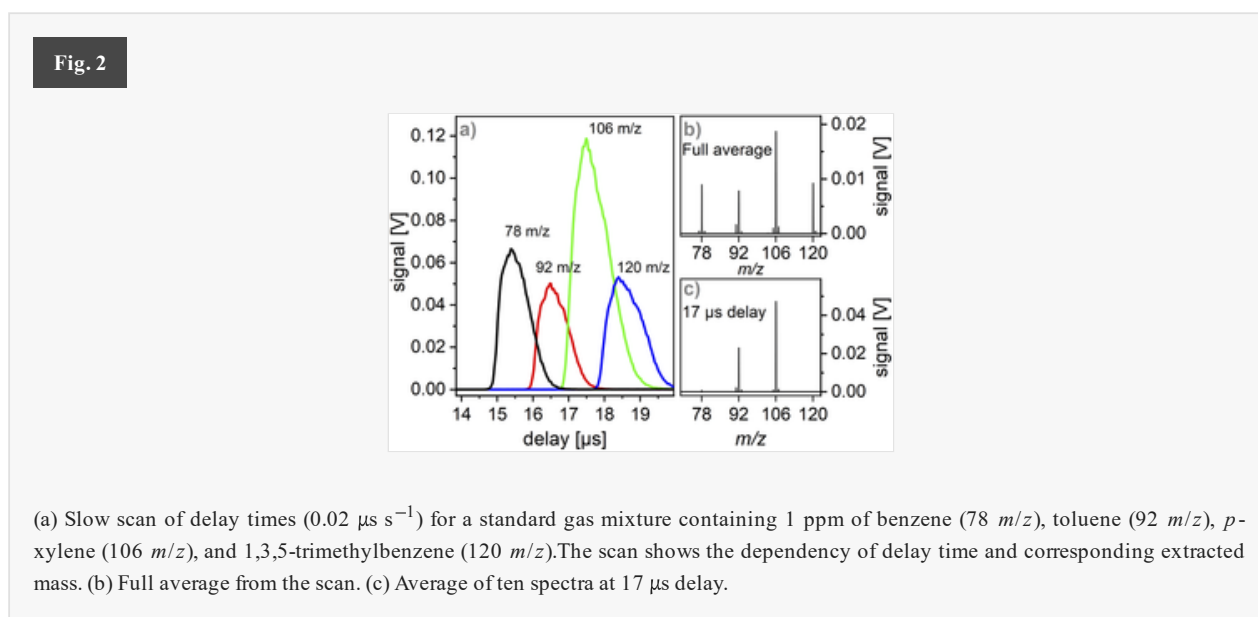
In Fig. 1(c), the trigger scheme for the SPI/REMPI-mode is presented. For SPI, more extractions have to be averaged. It is improbable having several ions guided into the mass separator in one single extraction. Consequently, for a sufficient time resolution and signal-to-noise ratio, a high repetition rate and averaging of several hundred extractions is needed. The upper limit of extractions depends on the tof-geometry. The fill-up time of the extraction module and maximum expected m/z value defines the upper boundary. For practical reasons, it has turned out to be useful working with 20 000 Hz (several common divisors with the 2000 Hz laser, what eases programming). Higher extraction rates up to 25 000 Hz are also possible in the here presented instrument. For the operation with REMPI, the photon density and ion yield are considerably higher. Therefore, in a single extraction just after a laser pulse, the resulting spectrum is nearly exclusively filled with ions resulting from the REMPI ionization. With a base frequency rate of 20 000 Hz, the time between two extractions is 50 μs. A part of the created ions is guided into the mass separator by triggering the laser just before an extraction in a particular delay time (*e.g.*, 22 μs before). The data acquisition is again synchronized with the trigger for the extraction plates. A full spectrum can be "stitched" together by scanning through different defined delay times.

In a further measurement system development, a second data acquisition card is installed. This modification allows the recording of SPI and REMPI signals separated from each other. The trigger scheme for the data acquisition is depicted in Fig. 1(d). The channels for data acquisition are triggered in dependence on the laser trigger. If the laser is not triggered, all data is collected by card one. If a laser trigger is present, card two will be triggered in order to record the signals from the following extraction. As mentioned before, the deuterium lamp produces ions continuously but at a low efficiency compared to the laser ionization. At low laser repetition rates (*e.g.*, 50 or 100 Hz), the signals in channel two can be regarded as nearly only produced by REMPI. Nonetheless, at higher laser repetition rates, the contribution of SPI ions in channel two can no longer be neglected in many cases. In post-processing, the data of card two can be subtracted by the signals of card one.

Results and discussion

Analytical figure of merit

REMPI as a pulsed source cannot rely on the unsynchronized averaging which is possible with continuous SPI. Therefore, the dependence of delay time and mass range is to be determined as a first analytical step. By changing the delay times, certain mass regions can be targeted. In Fig. 2, a scan of delay times is shown in steps of 0.02 μs s^{-1} resolution for a standard gas mixture covering 78–120 m/z. Fig. 2(b) shows the average mass spectrum over the entire scan. The usual fast scanning of delay times is done at a slow rate in order to visualize ion distribution in the extraction zone. The length of the transfer module and the applied voltages determine this dependency of extracted mass to delay time. As it can be seen, a single mass can be extracted at multiple delay times with varying efficiency. This behavior is exemplarily indicated by the spectrum in Fig. 2(c) for a delay time of 17 μs.

(a) Slow scan of delay times (0.02 μs s^{-1}) for a standard gas mixture containing 1 ppm of benzene (78 m/z), toluene (92 m/z), p-xylene (106 m/z), and 1,3,5-trimethylbenzene (120 m/z).The scan shows the dependency of delay time and corresponding extracted mass. (b) Full average from the scan. (c) Average of ten spectra at 17 μs delay.
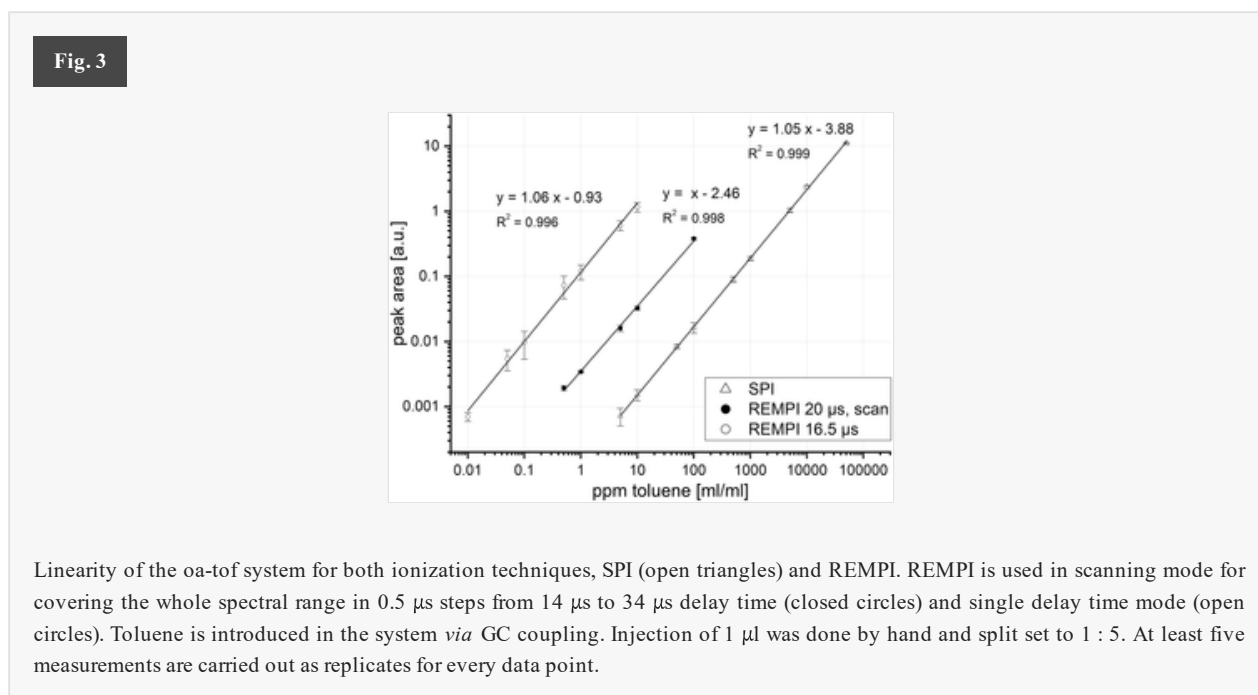
The spatial distance, respectively time-difference between adjacent masses decreases at higher masses. In a field-free drift tube, the reduction in time difference is proportional to the square root of the mass-to-charge ratio.[4] Consequently, the duty cycle of the system is enhanced at higher masses as more adjacent mass-to-charge ratios are able to enter the mass separator simultaneously and the instrument becomes more sensitive. The dependency of delay time and extracted mass is depicted in Fig. S1 in the ESI[†] for a broader mass range. The delay times can be set for every laser shot independently. The ability of a sub-second time resolution of the instrument is maintained in scanning mode for the usage of several 100 up to 2000 Hz (laser) and averaging of the entire scans at every sub-second. The exact laser and trigger parameter settings depend on the individual experimental setup, but a 10 Hz data recording by covering a spectral distance of 0–500 m/z is feasible. Therefore, the suitability of the system for gas-phase online monitoring and gas chromatography hyphenation is given. If the signal response for a particular component is reaching the upper linear range of the detector, it is also possible to skip the corresponding mass region or only extract a part of the generated ion packet. For example, in Fig. 2, the extraction for 106 m/z could be skipped from 16.5 μs to 17.5 μs for lowering the signal response. However, the signal intensity of neighboring masses is likewise affected. Thus, single masses cannot be addressed, only mass ranges. Additionally, by changing the potentials of the first drift stage, the curves in Fig. 2 can be narrowed or widened, revealing the spatial distribution of the corresponding ions in the extraction zone. This

approach of skipping signals might help simplify sample extraction protocols, as single high concentrated analytes no longer influence the measurement negatively.

The delay time *vs.* signal curves in Fig. 2 represents the presence of ion packages in the extraction zone. At the maximum peak height of the curves, the ion packages seem to have the perfect angle for being guided into the mass separator. However, all curves reveal a tailing. The corresponding ions travel longer through the extraction zone and are extracted in even steeper angles relative to their initial trajectory of movement. Additionally, it is observed that the mass resolution changes along the delay curve. For toluene, the highest mass resolution (very low transmission efficiency) of nearly 5000 ($m/\Delta m \; fwhm$) is given at 16 μs delay. At 16.5 μs, the highest signal for toluene, a mass resolution of 4600 is achieved. At *ca.* 17.5 μs, a resolution of 2600 is gained. At the last point, ions might also be affected by a turn-around effect. The averaged mass resolution (over the whole curve) for toluene in Fig. 2 is approximately 4100. In addition, a slight shift in peak position can be observed for ions extracted with higher delay times. This circumstance also effects the mass accuracy to a small extent.

In order to demonstrate the response linearity and limit of detection of the system in usage of the available ionization techniques, Fig. 3 is provided. The linearity of photoionization MS over several orders of magnitude has been proven by various authors.[30–32] The measurements were performed using liquid injections of different concentrations of toluene in ethanol introduced *via* a GC coupling. As it can be seen, the highest linear range of five orders of magnitude can be reached with the SPI mode (marked with open triangles). In this mode, the lowest measured concentration is 0.005 μl ml^{-1} toluene (4 ng μl^{-1} on column; signal-to-noise, S/N = 3), whereas the highest is 50 μl ml^{-1}. The extraction rate was set to 20 000 Hz and the data storage after averaging to 4 Hz. The rate of ion generation *via* this ionization mode is low enough, allowing only a few or no ions to reach the detector in a single extraction. In order of extremely high concentrations of a given compound, a saturation of the detector can thus be avoided. For the REMPI mode, two techniques are applied. The scan (closed circles), which covers a wide mass range, and the single delay time extraction (open circles).

Fig. 3

Linearity of the oa-tof system for both ionization techniques, SPI (open triangles) and REMPI. REMPI is used in scanning mode for covering the whole spectral range in 0.5 μs steps from 14 μs to 34 μs delay time (closed circles) and single delay time mode (open circles). Toluene is introduced in the system *via* GC coupling. Injection of 1 μl was done by hand and split set to 1 : 5. At least five measurements are carried out as replicates for every data point.

Since both, photon density and ionization efficiency, are enhanced using the KrF laser, the lower detection limits become reasonable in Fig. 3. In the REMPI scanning mode, compared to SPI, one additional order of magnitude can be achieved for toluene as a detection limit. In the most sensitive mode, the single delay time mode, the duty cycle for toluene is highest. After every laser shot, toluene is extracted into the mass separator. The minimum concentrated sample is detectable at 0.00001 μl ml^{-1}. The split for GC injection was set to 1 : 5 and no purge-and-trap or other techniques were applied, which would further lower the detection limit.

By combining the two ionization techniques, their advantages can be used effectively. On-line instruments, such as the one presented in this manuscript, are ideal for process monitoring. Furthermore, vacuum ionization techniques such as SPI and REMPI offer high robustness in terms of being largely insensitive to matrix effects. This aspect is very beneficial in case of fast-changing concentration ratios and, therefore, highly dynamic changes in the ion populations in

the ion chamber. In the following, two distinct examples for process monitoring exploiting the mentioned aspect for the developed SPI/REMPI tof-MS in terms of using REMPI in the mass regions of interest.

Example I: Coffee roast gas monitoring

The suitability of the presented platform for process monitoring is evaluated in the following. As an industrial-relevant example, its use in the gas phase monitoring of coffee roasting is demonstrated. Monitoring this process is challenging as extremely high concentration differences are given from the beginning to the end of the roasting. Furthermore, especially in the industrial sector, the roster is refilled as fast as possible after a roast and roasts are typically quenched with water. The amount is app. 5 to 20% of the batch weight (depending on the roasting recipe and roaster type). Monitoring these rapid changes in humidity and concentrations, as well as high throughput, requires a robust and reliable device. Rapid humidity and concentration changes are not problematic. Space-charge-related problems are negligible in a wide range and water is not ionized directly by photoionization. The high throughput and associated contamination of the measurement system can be compensated with a thoroughly heated sampling system. At least 250 °C are needed. Further details for the basic suitability of tofMS and photoionization for monitoring coffee roast gas can be found in the manuscripts by Heide et al.[33] and Czech et al.[34]

In this work, the basic application of oa-tofMS with simultaneous SPI/REMPI-mode and storage in one data acquisition card shall be shown on the example of coffee roasting. Fig. 4 presents three independent roasts of the same coffee (Columbia Excelsior) roasted in an industrial type *Jupiter 500* tangential roaster. Each spectrum is averaged over a whole roast. In Fig. 4(a) results of the SPI-mode are shown. SPI is very suitable for the high-concentrated "bulk" components in the coffee roast gas phase. Due to the ionization with a deuterium lamp, the sensitivity of the instrument is moderate (0.5 ppm toluene in gas phase in one second were observed), which is, in this case, not a disadvantage. Pyrolysis products out of the biomass of the raw beans and Maillard reaction products like acetone (58 *m/z*), furan (68 *m/z*), pyridine (79 *m/z*), furfuryl alcohol (98 *m/z*), hydroxymethylfurfural (126 *m/z*), and of course caffeine (194 *m/z*) occur in very high concentrations in the gas phase. A very efficient continuous ionization method would lead to a more complex setup, as a dilution of the roast gas would be necessary for staying in the linear range of the system.

Fig. 4
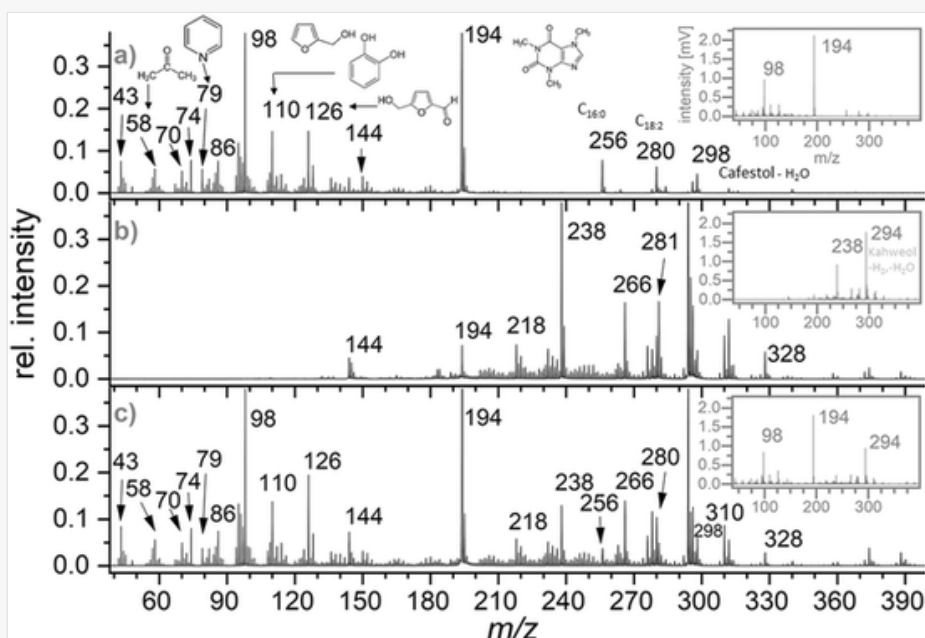
Spectra of three independent normalized spectra over a whole coffee roast with three different ionization modes. (a) SPI-mode spectrum, (b) REMPI-mode spectrum with extraction of masses above *ca.* 200 *m/z* and (c) simultaneous SPI/REMPI mode. Both ionization methods are applied and REMPI is set to the higher spectral range in order to not interfere with spectral information from SPI. Data storage is done on the same acquisition card. In grey: corresponding full-scale spectra without normalization. Structures are assigned tentatively according to previous work.[35,36]

As it can be seen, beyond caffeine, only little information is given by a few occurring signals. These can mainly be related to fatty acids.[35] In the spectrum in Fig. 4(b), an additional measurement with REMPI-mode is shown. The mass

extraction was adjusted beyond caffeine at *ca.* 200 *m/z*. REMPI serves additional information in the mass range beyond 200 *m/z*. Which compounds are responsible for these signals is not clear yet, but the degradation of larger structures, *i.e.*, lignins, cellulose, tannins, melanoidins, and also from chlorogenic acids might be possible. The signals at 310 *m/z*, 294 *m/z* and 312 *m/z*, 296 *m/z* can be attributed to kahweol and cafestol (double dehydrogenated and dehydrated at masses 294 *m/z* and 296 *m/z*), respectively. This was confirmed for kahweol by the pure substance. Even with a soft ionization technique such as REMPI, some molecules tend to fragment, particularly high functionalized ones. Masses lower than 200 *m/z* also appear in the REMPI spectra. This behavior is not fully understood yet. Some molecules may fragment in the first drift stage and will be extracted afterward.

The combination of both ionization techniques is shown in the last spectrum in Fig. 4(c). With this combination, more information is obtained in a single experiment without extensively mixing SPI and REMPI signals. This mode of operation is not only time- but also cost-effective, as 79 kg of coffee were roasted in a single roasting batch. As the three spectra in Fig. 4 are from three independent measurements, slight changes in relative signal intensities are given. REMPI ionization efficiency is considerably higher than SPI in most cases. Therefore, REMPI is better used for low concentrated components (if they can be ionized) and SPI for high concentrations. In the ESI in Fig. S2,[†] the capability and reproducibility of the system for on-line coffee roast gas monitoring is shown for selected time traces of several masses and roasts.

Furthermore, the system was used in an industry roasting facility connected to a rotary drum roster (*Neptune 3000*). In 3 days, over 130 roasts were monitored and only one major maintenance was necessary, as the sampling probe had to be flushed with pressurized air for cleaning. By further improvement of the sampling system, continuous monitoring of several hundred or over one thousand roasts should be unproblematic and only requiring minimal maintenance. In the ESI in Fig. S3,[†] a comparison indicating the robustness of the measurement system can be seen. The comparison shows the monitored spectra for two different roast recipes, which are one hundred measurements apart.

Example II: e-cigarette vapor monitoring

Another example of highly dynamic concentration changes and the need for on-line analysis is the monitoring of e-cigarette (e-cig) vapors. According to standard puffing regimes, a single puff can only last for 2 s.[37] Accordingly, direct monitoring of e-cig vapor, requires a highly time-resolved measurement system. In an e-cig, the contained liquid is converted into a vapor *via* a heating element. The liquid consists mainly of the humectants glycerol and propylene glycol. Nicotine and water are also added. This matrix can account for more than 99%.[38] To this matrix, some flavors are added to achieve a specific taste, *e.g.*, watermelon, tobacco, or cherry. Direct analysis without any separation technique makes the monitoring of e-cig vapor challenging. When the aim is to analyze the output of humectants together with flavor compounds, an on-line technique like tofMS can be very useful. Dynamically, high changing numbers of ions do not disturb the ionization process as it is likely possible for atmospheric pressure ionization sources. Consequently, mass spectrometric analysis is negligibly affected from ion suppression or matrix effects in vacuum photoionization. Therefore, as shown in the coffee example, vacuum ionization is a very suitable approach, while SPI is used to monitor "bulk" components, REMPI can be used for ionizable flavor compounds with aromatic moieties. In Fig. 5, the use of simultaneous SPI/REMPI oa-tofMS is shown together with spectra for the SPI- and REMPI-mode for a (55 ml/in 3 s) puff from an e-cig with cherry flavor. In Fig. 5(a), a spectrum for the SPI-mode is shown. The signals can be assigned to glycerol (main signals: 74, 60, 61, 62, 44 *m/z*), propylene glycol (main signals: 76, 61, 45 *m/z*), and nicotine (signals: 162, 84 *m/z*). This assignment is known from a previous study.[39]

Fig. 5
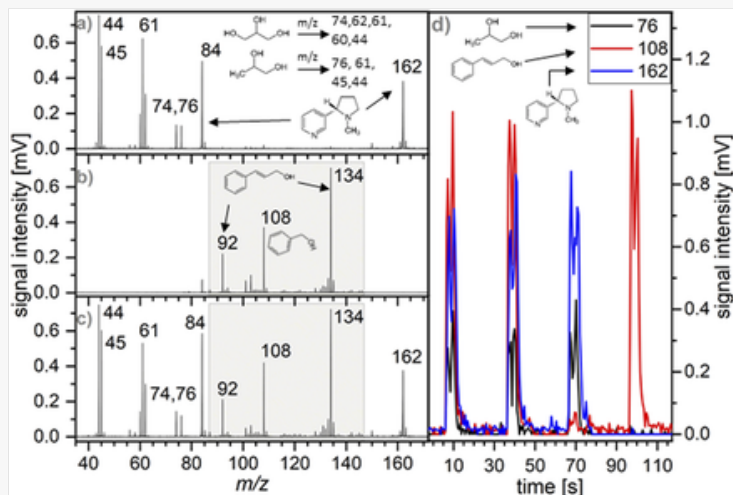
Monitoring of e-cigarette (e-cig) vapor. (a) Average spectrum for one puff in SPI-mode. (b) Average spectrum for one puff in REMPI-mode extracted mass range between 90 and 150 m/z. (c) Spectrum for one puff in SPI-REMPI-mode. (d) Puff-resolved monitoring of propylene glycol (76 m/z), benzyl alcohol (108 m/z), and nicotine (162 m/z). The first two puffs are measured in SPI/REMPI-mode, the third in SPI-mode, and the fourth in REMPI-mode. The example shows the capability of the system for measuring high and low concentrated analytes in a single run, directly without any dilution or pre-separation.

Due to the high ratio of alcohol moieties to carbon number of the humectants, extensive fragmentation occurs even with a soft ionization method, such as SPI. Furthermore, additional signals, which could be attributed to flavor components in the e-cig vapor, are displayed at low S/N ratio (*e.g.*, S/N = 13.5 at m/z = 108). Therefore, only in SPI (lamp) mode, puff-resolved monitoring of the flavor compounds is not well feasible as signals are near the detection limit. Fig. 5(b) shows a spectrum from another puff in REMPI-mode. In this measurement, the delay times in REMPI-mode were set to extract a range of about 90 to 150 m/z. This range includes some flavor components of the e-cig vapor. As shown before, many signals with a low S/N ratio are visible in SPI mode. In REMPI mode, due to the more efficient ionization, the S/N ratio of the masses 92, 108, and 134 m/z (S/N = 230 at m/z = 108are highly enhanced. The mass signals observed at m/z = 134 and 92 can be assigned to molecular and fragment ions of cinnamyl alcohol, respectively, the mass signal at m/z = 108 being assigned to a molecular ion of benzyl alcohol, which were confirmed by GC. The repetition rate of the laser was set to 500 Hz. Higher laser repetition rates are possible but not necessary as S/N-ratios are sufficient enough and one gas filling of the laser holds longer (*ca.* 100 million shots each filling). Using the SPI/REMPI combination mode, as shown in Fig. 5(c), bulk components and flavor substances can be monitored in the same run. This aspect can also be seen in Fig. 5(d), where exemplarily the time traces of the masses 76 m/z (propylene glycol), 108 m/z (benzyl alcohol), and 162 m/z (nicotine) are shown. The first two puffs are measured in SPI/REMPI mode. The following two puffs are measured in SPI and REMPI-mode, respectively. This example shows the availability of the system for measuring highly dynamic processes and brings both ionization techniques together in an appropriate way. In this example, low efficient ionization with the deuterium lamp is not a drawback as highly concentrated analytes can be monitored without heading in issues by overproduction of ions in the ionization chamber, which consequently leads to a saturation of the detector. In combination with efficient laser-based ionization, a high dynamic range can be achieved.

Separation of SPI and REMPI signals

The first examples are well suited for the joint storage of signals from both ionization processes. By further development of the system, it was equipped with a second data acquisition card, which enhances the applicability of the system. SPI spectra can be recorded without overlapping REMPI signals, and the full m/z-range can be covered with

REMPI. This aspect enhances the capability toward better suitability for GC or other separation methods. This 2-in-1 approach is also beneficial in terms of analysis time, data alignment, and measurement condition changes.

The separation of recorded signals is achieved as indicated in Fig. 1(d). For demonstration, the system was coupled to a GC and a solution extracted from coffee using hexane was injected. The data recording frequency used is at 5 Hz. Fig. 6 shows the SPI total ion current (TIC) of channel 1 (a) and REMPI TIC signal of channel 2 (b) for two measurements (M1 and M2), respectively. Furthermore, the REMPI sensitivity is modified over the monitored m/z-range by changed delay times. This is done in measurement two (M2). The goal was to lower the highly abundant signal of 150 m/z and to skip a second non-diagnostic mass range of roughly 200 to 250 m/z. The skipped delay times saved in the protocol were utilized for enhancing the signal intensities in the range from m/z = 290 to 340, with important contribution of kahweol and cafestol. The SPI data remained unchanged in both the experiments (even) when the delay time in REMPI was changed. The spectra in Fig. 6(b1), (b2) and (b3) show the modified sensitivity for the GC run. The signal intensities observed at m/z = 150 and 230 decreased significantly, while the signal intensity at m/z = 178 remained unchanged. The variation in the delay time protocol doubles the sensitivity for detecting the dehydrated diterpenoids kahweol and cafestol at 294 m/z and 296 m/z (both H_2 abstracted). The difference can be seen in Fig. 6(b4) and (b5).

Fig. 6
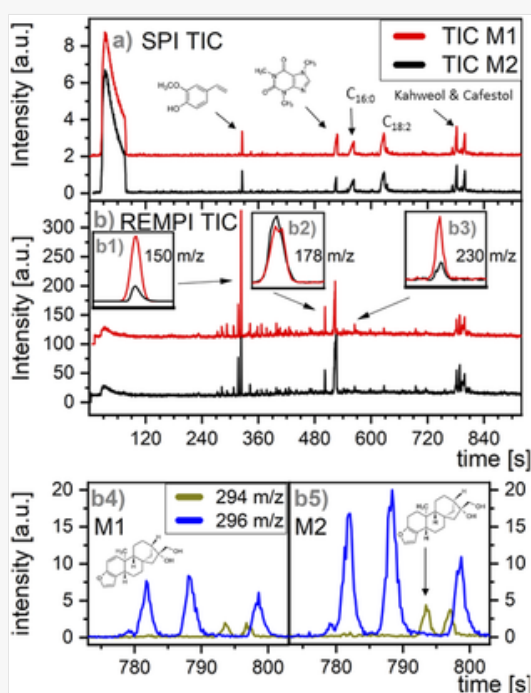
Demonstration of simultaneous SPI/REMPI measurement with GC coupling with two separate channels for data storage. The subplots (a) and (b) show the total ion current (TIC) for two independent measurements (M1 and M2). For visualization, M1 is presented with an offset. In (a), the SPI channel TIC is shown. No differences are visible for both measurements. In (b) REMPI was used in M1 for the whole m/z range in equidistant delay time steps. In M2, the delay times for the regions 150 m/z (high signal, subplot b1) and 230 m/z (no relevant information for this measurement, subplot b3). This approach largely unaffected the "middle" mass region at 178 m/z. The "saved" delay times are used for enhancing the mass region of roughly 300 m/z, for shifting the sensitivity of the system towards the signals for dehydrocafestol (296 m/z, H_2 abstraction) and dehydrokahweol (296 m/z, H_2 abstraction). The subplot (b4) shows the measurement for M1 and (b5) for M2.

The SPI data shows mainly the lipid fraction of the coffee extraction due to their high abundance in coffee and high affinity to hexane. The sensitivity of the SPI channel is relatively low. Roughly, a better efficiency of one order of magnitude would be desirable in this case. However, it is sufficient to illustrate the basic concept of the system development. Lipids are essential for coffee taste, as they help extract aroma components in the coffee beverage and are crucial for the mouthfeel and creaminess (taste descriptors) of the coffee.[40,41] The lipid fractions of the coffee varieties are very distinct and represent an essential quality criterion.[42–44] At the end of the chromatogram, two very important lipids are visible. These are the diterpenoids kahweol and cafestol. These two diterpenoids are typical coffee components and can be present at high concentrations of 0.7% to 3.5% in roasted *Arabica* coffee.[45,46] Both are known for increasing the blood levels of low-density cholesterol in unfiltered coffee. These components are also assumed to positively impact human health by lowering the risks of evolving cancer and Parkinson's disease.[40,47] Despite the

occurrence of a special form of cafestol, 16-O-methylcafestol is exploited in the quality control of Arabica coffee, as this species is mainly present in *Robusta* coffees. Food fraud by mixing cheaper *Robusta* coffee in *Arabica* coffee can be detected in this way.[42] Thus, the occurrence of these diterpenoids in the chromatogram is of high interest. Through REMPI at 248 nm, these species can also be ionized. For this reason, the sensitivity for the respective mass region is enhanced by using a higher number of averaged extractions, as can be seen in Fig. 6(b4) and (b5). Kahweol shows a higher signal. The natural abundance of both species is in the same range in the plant.[48] Therefore, kahweol seems to have a higher ionization efficiency (higher cross-section). Additionally, the simple extraction process in this work could influence the kahweol-cafestol ratio by favoring the free diterpenoid forms. This example is intended to demonstrate that the system can reliably work simultaneously with two different ionization techniques. The maximum resolving power (R) of $m/\Delta m$ = 5000 for toluene of this instrument presented here is limiting the informative value. For a GC coupling with REMPI, a change of the MS platform serves for tremendously better resolving power. This has already be proven with a vacuum ionization Orbitrap-REMPI development serving for a resolving power of up to 140 000 at a mass of 200 m/z.[49]

In this example, the sensitivity of the instrument is enhanced by a factor of two. The approach is still untargeted. In a targeted approach (single delay time), an enhancement of a factor of ten is possible.

Conclusion

The new setup of an oa-tofMS with simultaneous SPI and REMPI is used for on-line gas-phase monitoring of highly dynamic industry relevant processes, such as coffee roasting or e-cig vapor. These matrices are very challenging to study due to high water and particle loads. To demonstrate the storage of the SPI and REMPI data on two different channels, a GC measurement of a coffee hexane extract is provided. The direct combination of a pulsed vacuum laser ionization source with an oa-tofMS without any additional ion trapping or multipole components is the first of its kind, to the best of our knowledge. The integration of a laser into an existing oa-tof system is a relatively cheap and straight-forward approach of enhancing the capability of an oa-tofMS significantly. This coupling allows the monitoring of (optionally pre-selected) m/z-ranges *via* a targeted ionization scheme, REMPI. SPI is used for monitoring highly abundant analytes in the sampling matrix whereas REMPI can be used for lower concentrated analytes (if ionizable). In the ideal case, the accessible concentration range with linear response of the instrument can span seven orders of magnitude in a single measurement. By adjusting the delay time between the laser shot and the extraction pulse for guiding ions in the second drift stage, different m/z ranges are accessible in a single spectrum.

By using only one channel for data storage, it is beneficial to utilize REMPI in m/z-regions, where the information content of SPI is low. In this work, the aforementioned methodology is used to monitor coffee roast gas. SPI serves information for highly abundant species, such as, *e.g.*, small aldehydes, ketones, or caffeine. At a range of over 200 m/z, SPI only serves information for some lipids. REMPI is used at this point to enhance the amount of information the system can deliver in a single measurement. Besides the on-line information for the chemical release pattern of kahweol, there is a variety of signals from unknown analytes. The 2-in-1 approach of SPI and REMPI usage in a single measurement serves for more informational depth and is not only beneficial in environments where experiments cannot be repeated (as in industrial facilities) but, for coffee roasting, the information could also be further exploited in correlation with off-line data and model building.[33–35] The system is also used for such a highly dynamic process as monitoring e-cig vapor. SPI is once again used for the highly abundant analytes. In this case of the challenging matrix containing glycerol, propylene glycol, and nicotine. REMPI can be used for monitoring of the flavor components such as benzyl alcohol and cinnamyl alcohol. The benefit of this setup lies in both application examples in the virtual enhancement of the dynamic range of the instrument and the possibility of targeted REMPI of preselected m/z ranges. The sub-second time resolving power of the instrument is still maintained.

By adding a second data acquisition card, SPI and REMPI can be used in the full m/z range. Both ionization methods are measured simultaneously and stored separately. As REMPI is pulsed, there are no ions from REMPI in the time scale of the collection of SPI spectra. The contribution of SPI ions in the REMPI channel is, in most cases, negligible. If targeted REMPI information is needed, the delay times can be adjusted for achieving higher or lower signal-to-noise ratios for different m/z ranges. This means that more laser shots at the same spectral range and extractions into the mass separator can be used for several m/z ranges in a single spectrum. By the proper use of the combination of SPI and REMPI, sample preparation could be shortened. Highly concentrated interfering components in a matrix do not have to

be removed from a sample. Such a complementary approach is useful to avoid time-intensive, complicated extraction protocols. In industrial environments, well-controlled laboratory conditions cannot be ensured and experiments cannot be repeated. A robust on-line MS-system with multiple simultaneously working ionization modes is beneficial in terms of analysis time, data alignment (data is recorded in parallel), and measurement condition changes.

Through a long series of monitoring the coffee roast gases emitted from the industrial roasters, the system has proven itself to be highly reproducible and robust.

For higher versatility of the system, the use of EI would be very desirable. SPI and REMPI could serve molecular mass information and EI structural information in a single run. In the current setup of the instrument, EI mode could not be pulsed. Additionally, it would be wishful for SPI to be an order of magnitude more sensitive. In future work, these limitations would be the subjects to be solved to improve the variability and time-saving capabilities of the system.

Author contributions

J.H. worked out many of the technical details, carried out the experiment, collected the data and performed the data analysis, wrote the original draft. S.E. helped supervise the project, contributed with technical support, wrote software and ideas for the experiments. T.K. contributed to the design and implementation of the research, provided resources for measurements at industrial sites. C.P.R. supervised the manuscript, supervised the work, contributed with ideas. A.W. helped supervise the project. R.Z. conceived the original idea, supervised the findings of this work, provided critical feedback and made the funding acquisition.

All authors discussed the results and contributed to the final manuscript.

Conflicts of interest

■■■■

Acknowledgements

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[†] Electronic supplementary information (ESI) available. See DOI: https://doi.org/10.1039/d2an00774f

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