Research Article

Rapid Communications in Mass Spectrometry

Received: 4 December 2015 Revised: 3 February 2016 Accepted: 3 February 2016

Rapid Commun. Mass Spectrom. **2016**, *30*, 1031–1036
(wileyonlinelibrary.com) DOI: 10.1002/rcm.7533

Towards matrix-free femtosecond-laser desorption mass spectrometry for *in situ* space research

Pavel Moreno-García[1]*, Valentine Grimaudo[1], Andreas Riedo[2], Marek Tulej[2], Peter Wurz[2] and Peter Broekmann[1]

[1]Department of Chemistry and Biochemistry, Interfacial Electrochemistry Group, University of Bern, Freiestrasse 3, 3012 Bern, Switzerland
[2]Physics Institute, Space Research and Planetary Sciences, University of Bern, Sidlerstrasse 5, 3012 Bern, Switzerland

RATIONALE: There is an increasing interest in the quest for low molecular weight biomarkers that can be studied on extra-terrestrial objects by direct laser desorption mass spectrometry (LD-MS). Although molecular structure investigations have recently been carried out by direct LD-MS approaches, there is still a lack of suitable instruments for implementation on a spacecraft due to weight, size and power consumption demands. In this contribution we demonstrate the feasibility of LD-MS structural analysis of molecular species by a miniature laser desorption–ionization mass spectrometer (instrument name LMS) originally designed for *in situ* elemental and isotope analysis of solids in space research.

METHODS: Direct LD-MS studies with molecular resolution were carried out by means of a Laser Ablation/Ionization Mass Spectrometry (LIMS) technique. Two polymer samples served as model systems: neutral polyethylene glycol (PEG) and cationic polymerizates of imidazole and epichlorohydrin (IMEP). Optimal conditions for molecular fragmentation could be identified for both polymers by tuning the laser energy and the instrument-sample distance.

RESULTS: PEG and IMEP polymers show sufficient stability over a relatively wide laser energy range. Under mild LD conditions only moderate fragmentation of the polymers takes place so that valuable structural characterization based on fragment ions can be achieved. As the applied laser pulse energy rises, the abundance of fragment ions increases, reaches a plateau and subsequently drops down due to more severe fragmentation and atomization of the polymers. At this final stage, usually referred to as laser ablation, only elemental/isotope analysis can be achieved.

CONCLUSIONS: Our investigations demonstrate the versatility of the LMS instrument that can be tuned to favourable laser desorption conditions that successfully meet molecule-specific requirements and deliver abundant fragment ion signals with detailed structural information. Overall, the results show promise for use in similar studies on planetary surfaces beyond Earth where no or minimal sample preparation is essential.

The analysis of organic species in solid materials by mass spectrometry (MS) has become increasingly important in various fields of research, including developments in biomaterials,[1] mineralogy,[2] archaeology,[3] astrobiology,[4–7] electronics,[8] metallomics,[9] molecular imaging,[10] and tribochemistry.[11] In addition to Thermal Desorption Photoionization MS (TDPI-MS),[12] Glow Discharge MS (GD-MS),[13] Laser Ablation Inductively Coupled Plasma MS (LA-ICP-MS),[14,15] and Secondary Ion MS (SIMS),[16,17] analytical methods based on soft Laser Desorption/Ionization MS (LD-MS)[18,19] are at the forefront of these developing technologies. In addition to the established Matrix-Assisted Laser Desorption/Ionization MS (MALDI-MS)[20] technique, alternative matrix-free LD methods requiring less elaborate sample preparation strategies have been developed for the analysis of low mass molecules, e.g., Laser Desorption Post-Ionization MS (LDPI-MS),[21–25] Desorption Electrospray Ionization MS (DESI-MS),[26–29] and Surface-Assisted Laser Desorption/Ionization MS (SALDI-MS).[30]

Furthermore, direct LD studies of organic molecules have successfully been carried out without the assistance of a matrix or substrate pretreatment.[3,11,31–35] These investigations are particularly encouraging for *in situ* space research where minimal or no sample preparation procedures and no spatial disruption of the analyte prior to the analysis are of prime importance.[36–38] In this context, special attention is currently being devoted to the quest for low molecular weight biomarkers of extinct or extant life on planetary objects beyond Earth.[6,39–42] Nonetheless, the few direct LDI studies reported so far have employed equipment that is not suitable for implementation on spacecraft, where requirements concerning weight, size and power consumption are very strict. Over the last 15 years, however, laser ablation/ionization mass spectrometry (LIMS) has re-emerged as an analytical technique suitable not only for laboratory, but also for space applications.[43–46] Its improved performance results from using state-of-the-art ultra-short femtosecond (fs) laser sources,[47–51] improved vacuum technology and fast

---

* *Correspondence to:* P. Moreno-García, Department of Chemistry and Biochemistry, Interfacial Electrochemistry Group, University of Bern, Freiestrasse 3, 3012 Bern, Switzerland.
E-mail: pavel.moreno@dcb.unibe.ch

electronics.[52–55] Because of its ultimate compactness, simplicity and robustness this is a very suitable analytical tool for elemental, isotope and molecular investigations in space research. In this contribution we demonstrate that our miniature laser mass spectrometer[43] originally designed for *in situ* chemical analysis of solids in space research can perform desorption and identification of molecular model systems under soft desorption conditions.[56] The figures of merit of LMS have been discussed in detail in previous publications and include sensitive and quantitative elemental analysis down to the 10 ppb level,[57,58] accurate isotope measurements,[58,59] 2D elemental imaging of surfaces of heterogeneous materials,[56,60] and high-resolution depth profiling at nm and sub-nm scale.[61,62] We have performed LD experiments, as a proof of concept, applying low laser pulse energies on two polymers, polyethylene glycol (PEG) and polymerizate of imidazole and epichlorohydrin (IMEP), where parameters such as laser pulse energy, number of single laser shots per composite spectrum and distance between sample and mass analyzer were tuned to establish desorption conditions with reduced molecular fragmentation. Our results confirm the suitability and extended versatility of the LMS instrument to perform not only elemental/isotope analysis with high spatial resolution, but also successful constitutional formula studies of molecules without the need for elaborate sample preparation protocols.

EXPERIMENTAL

Sample preparation

Two different polymers were investigated as model systems for the LD studies, namely polyethylene glycol (PEG) and polymerizates of imidazole and epichlorohydrin (IMEP). PEG (35 kDa, Sigma-Aldrich, Steinheim, Germany), a linear polymer serving as a proxy for complex and aliphatic molecules identified in the interstellar medium[63] and in comets,[64] was chosen as a neutral model polymer to optimize experimental conditions for the soft LD mode. In addition, IMEP (BASF, Ludwigshafen, Germany) was chosen as a second reference sample due to its more complex molecular structure and its poly-cationic nature and as a proxy for the many nitrogen-containing molecules in the interstellar medium and in comets. As shown in Fig. 1(C), the IMEP polymer contains chloride as counter ion. These polymers are easily available because they are used as additives in industrial Cu electroplating where they tend to be incorporated into the electrodeposited metal films.[61,62]

Both polymers were dissolved in a well-defined volume of methanol (Sigma-Aldrich) resulting in a stock solution with a polymer mass concentration of 10,000 ppm. Volumes of 400 µL of the PEG- and 1000 µL of the IMEP-containing solutions were stepwise dropcasted (each dose 100 µL) on two blanket Cu wafer coupons (Hionix, San Jose CA, USA, $A_{\text{PEG-sample}}$ = 117.5 mm^2 and $A_{\text{IMEP-sample}}$ = 48.9 mm^2). The methanol was evaporated in a dry Ar atmosphere. Both samples were subjected to vacuum (base pressure in the mid 10^{-8} mbar range) prior to their transfer into the main vacuum chamber of the LMS instrument to remove residual traces of the solvent.[58]

Laser ionization mass spectrometry

Laser desorption mass spectrometry measurements were conducted using a miniature (160 mm × ∅ 60 mm) reflectron-type time-of-flight (TOF) laser ablation/ionization mass spectrometer that was specifically designed for *in situ* chemical (element/isotope) analysis of solids in space research. The technical details, principles of operation and figures of merits of the instrument were discussed in detail in previous publications.[53,56–62] The desorption and

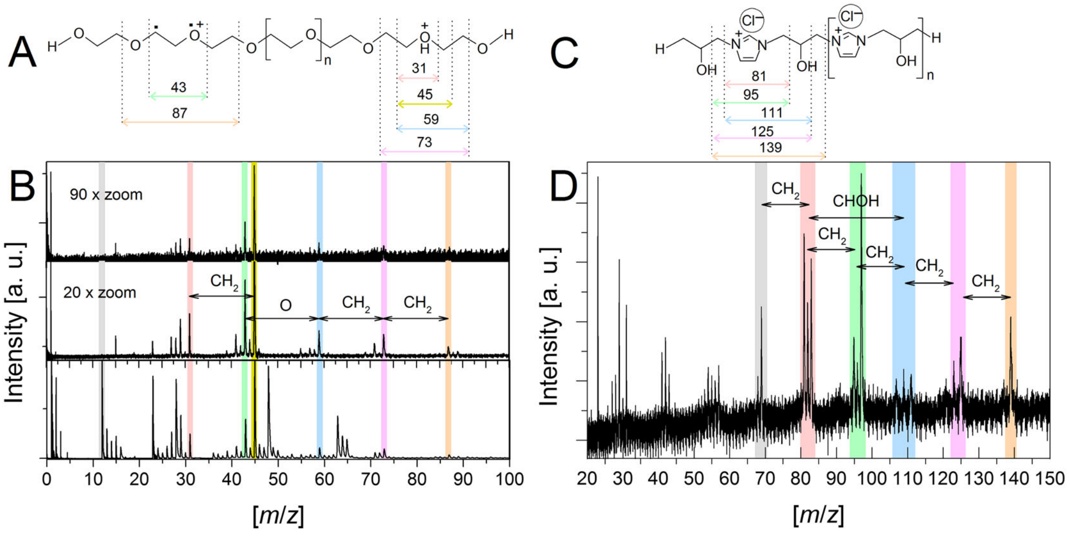

Figure 1. Molecular structures of (A) PEG and (C) IMEP. Dashed lines indicate preferential cleavage points of the parent polymer and the arrows designate the *m/z* values of the most abundant fragmentation products. These masses do not include the Cl$^-$ counter ion of IMEP in panel (C). (B) Cumulative mass spectra of PEG at three different energy-per-pulse settings (0.21 µJ, 0.32 µJ and 1.08 µJ from top to bottom). To better visualize the relevant fragments, the signals in the upper and middle panels are magnified by a factor of 90× and 20×, respectively. (D) Cumulative mass spectrum of IMEP at mild LD conditions (0.21 µJ). The intensity of the spectra is displayed in linear scale.

ionization of the analytes from the Cu wafer coupons were triggered by irradiation with an ultra-short pulsed laser system (CPA system, Clark-MXR Inc., Dexter, MI, USA, $\tau \sim 190$ fs, $\lambda = 775$ nm, laser pulse repetition rate ≤ 1 kHz). An optical system outside the vacuum chamber is used for shaping and delivery of the beam towards the mass spectrometer. A doublet lens on top of the instrument is used to focus the laser pulses through the mass analyzer onto the sample surface. The application of laser irradiances at the TW/cm^2 level (ablation mode) results in the formation of craters with a diameter of about 10 μm. The sample was positioned at a vertical separation smaller than 1 mm below the entrance electrode of the mass spectrometer on top of a high-resolution x-y-z translational stage that is controlled remotely with a position accuracy of about 2 μm.[58] The number of emitted laser pulses, the energy per pulse and the repetition rate of the laser system are adjusted via the computer interface of the laser system. Only positively charged ions can enter the mass analyzer by passing the ion optical system. The latter accelerates, focuses and confines the ions along the ion optical axis towards the field-free drift path, which guides the ions to the ion mirror, where they are reflected backwards to the detector assembly. The ions are recorded sequentially according to their TOF that is proportional to the square root of their mass-to-charge (m/z) ratio using a multi-channel plate (MCP) detector system (chevron configuration). For each laser pulse a TOF spectrum is acquired by two high-speed ADC cards (8 bit vertical resolution, each card holding two channels) at a sampling rate of up to 4 GS/s over a time period of 20 μs allowing a full mass spectrum to be recorded in the range from hydrogen to lead.[58] The acquisition and saving of the measurement data are performed on a host computer, which allows the monitoring in real time of the recorded signal during a measurement campaign. Mass spectrometric analyses of the acquired data are conducted subsequently using custom-made analysis software written in MATLAB.

Measurement procedure

To investigate in particular the evolution of molecular fragmentation upon laser irradiation several measurement campaigns were carried out on both polymer samples where the laser pulse energies were systematically varied between 0.16 μJ and 1.68 μJ. The sample surfaces were first kept at the focal point of the laser and then gradually displaced outwards in single steps of 50 μm. This approach allowed for mass spectrometric studies with high resolution of applied laser irradiances. In the case of PEG, campaigns 1–2, 3–9, 10–12 and 13–14 were conducted with pulse energies of 0.21 μJ, 0.32 μJ, 1.08 μJ and 1.68 μJ, respectively (Fig. 2(A)). For IMEP the energy per pulse was set to 0.16 μJ, 0.21 μJ, 0.32 μJ, 0.43 μJ, 0.65 μJ, 0.76 μJ and 1.08 μJ for campaigns 1–3, 4–5, 6–12, 13–14, 15–17, 18–19 and 20–21, respectively (Fig. 2(B)).

The difference between campaigns with the same energy per pulse was the increasing distance of the sample relative to the focal point, thus changing the laser irradiance on the sample. Each measurement campaign was conducted on a fresh and untreated sample position and consisted of 100 and 10 cumulative mass spectra for PEG and IMEP, respectively. Each of these mass spectra was built by signal accumulation of 2000 single laser shots.

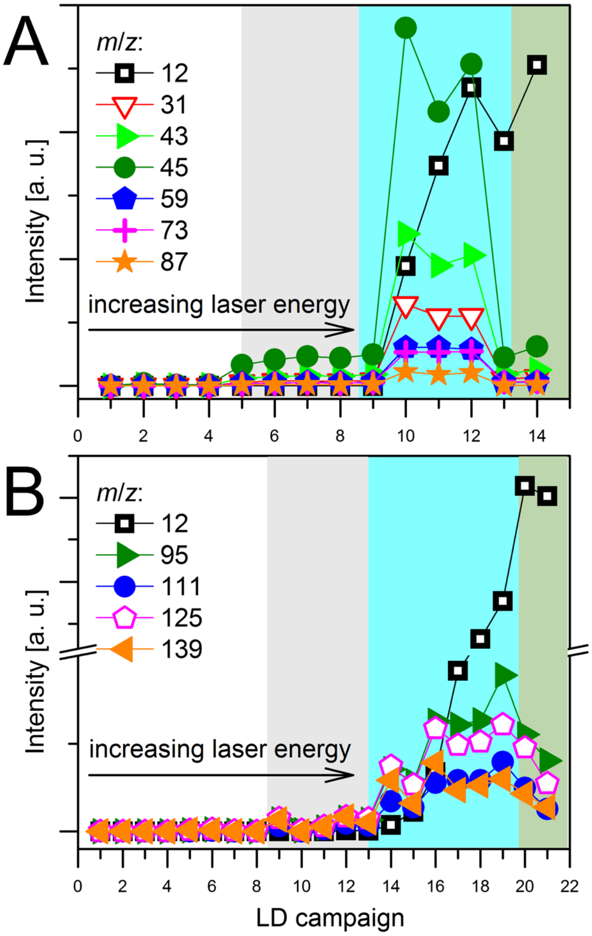

Figure 2. Signal intensity of selected fragment ions as a function of laser desorption campaign for (A) PEG and (B) IMEP. The x axis in the plot indicates the campaign number, not the applied laser energy. The laser energy that corresponds to every campaign is quoted in the main text. The signal intensity is plotted in linear scale.

RESULTS AND DISCUSSION

Figures 1(A) and 1(C) show the molecular structures of both model polymers. The expected fragment ions and their corresponding masses are indicated on these structures, and they will be discussed in the context of the measured mass spectra in more detail.

Previous investigations using the LMS instrument in laser ablation mode (at high applied laser irradiances, TW/cm^2) have determined the accurate quantitative elemental composition of Cu films electrodeposited in the presence of both model polymers (Figs. 1(A) and 1(C)) which tend to get partially embedded into the deposit upon growth.[61,62] Aiming at performing structural analysis, in this work we used significantly lower laser irradiances – close to the desorption threshold – to prevent strong fragmentation and atomization of the analytes. This was achieved by using an ultra-short fs-laser as clean desorption/ionization source for the sample material.

Figure 1(B) shows measurements of the PEG reference sample at three distinct irradiance conditions. The sample mass spectra were built from 100 files (each an accumulation of 2000 single laser shot mass spectra) for three different laser pulse energy values (0.21 μJ, 0.32 μJ and 1.08 μJ from top to bottom). At laser pulse energies just above the desorption threshold (0.21 μJ), only a few fragment ions were detected with significant signals (upper panel in Fig. 1(B)).

The peak at m/z 45 is the most intense feature in the mass spectrum (highlighted yellow in Figs. 1(A) and 1(B)) and it can be assigned to a protonated monomer species $[M + H]^+$, which forms through two symmetric C–C bond cleavages in the parent PEG polymer chain at the α positions next to the oxygen atoms. Further but less abundant fragment ions are observed at m/z 31, 43, 59, 73 and 87, and these can be, respectively, attributed to $[CH_2O+H]^+$, $[CHCH_2O]^+$, $[CH_2OCH_2CH_2+H]^+$, $[CH_2CH_2OCH_2CH_2+H]^+$ and $[OCHCH_2OCH_2CH_2]^+$.

Experiments carried out at lower laser pulse energies showed no laser-desorbed ions in the measurable mass range. However, this observation does not exclude the desorption of neutral species, which have a lower desorption threshold,[65] and do not enter the instrument operated in positive ion mode. At moderate laser pulse energies (0.32 μJ) the above-mentioned features increase in intensity and a few more fragments appear, as illustrated in the middle panel of Fig. 1(B). By further increasing the laser pulse energy we fully enter into laser ablation, causing destruction of molecules up to complete atomization of the removed material. Under these conditions the $^{12}C^+$ signal overwhelms all others indicating major fragmentation and atomization of the analyte. Moreover, under these conditions, additional molecules and clusters are generated in the ablation plume, whose signals become dominant and decrease the resolution of the overall spectrum (Fig. 1(B), lower panel).

Figure 1(D) shows measurements of the IMEP polymer. The mass spectrum is obtained at the lowest applied energy per pulse (0.21 μJ). All other acquisition conditions were the same as in Fig. 1(B). A peak at the mass of the monomer with its Cl^- counter ion (m/z 160) was not observed, nor was there any evidence for the Cl isotopes. We assume that even the lowest energy necessary to desorb the analyte is high enough to remove the Cl^- anion from the IMEP backbone. Therefore, the main fragments observed other than the positively charged monomer (m/z 125) were those ions comprising the heteroatomic ring ($C_3N_2H_3$, m/z 67, denoted hereinafter Im): $[CH_2Im]^+$, $[CH_2ImCH_2]^+$, $[ImCH_2CHOH]^+$ and $[CH_2ImCH_2CHOHCH_2]^+$. Less intense peaks were also observed at lower masses, and these might represent protonated aliphatic fragments. Suggested fragment ions and corresponding features in the mass spectra are highlighted by the same colour code in both the polymer structures and the mass spectra in Fig. 1.

At the lowest applied laser pulse energies, the rate of the desorption process was not uniform and not every laser pulse removed detectable material from the sample by means of continuous desorption of the analyte, which is typical for laser desorption near the threshold energy.[65] This is why we represent the mass spectra in a cumulative fashion. This approach provides solid data sets for further interpretation.

Figure 2 shows the dependence of the integrated intensities for selected PEG and IMEP fragment ions as a function of the applied laser pulse energy. The plot clearly illustrates the existence of characteristic thresholds in the applied laser pulse energy for the desorption of the two monomer units (m/z 45 and m/z 125 for PEG and IMEP, respectively) and their fragments.[65] Generally, the dependence of the intensity on the laser energy can be subdivided into four sections which are highlighted white, grey, cyan and green in Fig. 2: (i) at low pulse energies, below the desorption threshold, there is no measurable intensity at all; (ii) at mild pulse energies, just above the desorption threshold, the abundance of relevant fragment ions marginally increases whereas the $^{12}C^+$ intensity remains at zero; (iii) passing a certain level of the applied pulse energy leads to a drastic increase in the intensities of polymer-related fragment ions and $^{12}C^+$, the intensities reach fragment-specific plateaux; and (iv) applying even higher laser pulse energies leads to a decrease in the intensities of fragment ions whereas the $^{12}C^+$ intensity continues to increase. The latter observation is indicative of the more severe fragmentation and atomization of the model polymers at the highest pulse energies.

It should be noted that the characteristic thresholds in the applied pulse energy for the desorption of fragment ions are polymer-specific quantities, which are higher in the case of the neutral PEG and significantly lower for the charged IMEP polymer.

As expected from matrix-free laser desorption, both polymers fragment to some extent even under the mildest experimental conditions (in terms of laser energy) and desorption of positive ions from the analyte can be observed. However, our results clearly demonstrate that useful molecular and structural information can be obtained from these measurements. This result shows promise for the future identification of low molecular mass organic molecules serving as biomarkers beyond Earth, e.g., amino acids.[6] These results also show improved performance compared with previous desorption studies on glycine.[56]

CONCLUSIONS

The increasing interest in the detection of bio-markers in space research is driving the current development of dedicated instruments for space investigations based on LD-MS. The LD measurements discussed in this report and conducted on two different model polymers, PEG and IMEP, demonstrate the versatility of our miniature laser mass spectrometer designed for *in situ* space research. Under optimal laser desorption conditions, mass spectra with detailed structural information of the model polymers can be obtained allowing for the clear identification of the parent monomer molecules. Overall, the results show promise for similar studies being performed on planetary surfaces beyond Earth where no or minimal sample preparation is a requirement for operation. The performance of this laser mass spectrometer should be improved by the implementation of a UV fs-laser source, which would enhance the ionization efficiency and reduce fractionation effects.[66] This instrument is currently being developed.

Acknowledgement

Financial support of this work by the Swiss National Science Foundation (SNSF) is gratefully acknowledged.

REFERENCES

[1] A. Vertes, V. Hitchins, K. S. Phillips. Analytical challenges of microbial biofilms on medical devices. *Anal. Chem.* **2012**, *84*, 3858.

[2] S. S. Dimov, S. L. Chryssoulis, R. H. Lipson. Quantitative elemental analysis for rhodium and palladium in minerals by time-of-flight resonance ionization mass spectrometry. *Anal. Chem.* **2003**, *75*, 6723.

[3] E. Ribechini, J. Pérez-Arantegui, M. P. Colombini. Positive and negative-mode laser desorption/ionization-mass spectrometry (LDI-MS) for the detection of indigoids in archaeological purple. *J. Mass Spectrom.* **2013**, *48*, 384.

[4] J. Chela-Flores, A. Cicuttin, M. L. Crespo, C. Tuniz. Biogeochemical fingerprints of life: earlier analogies with polar ecosystems suggest feasible instrumentation for probing the Galilean moons. *Int. J. Astrobiol.* **2015**, *14*, 427.

[5] Z. Martins, M. C. Price, N. Goldman, M. A. Sephton, M. J. Burchell. Shock synthesis of amino acids from impacting cometary and icy planet surface analogues. *Nat. Geosci.* **2013**, *6*, 1045.

[6] J. W. Aerts, W. F. M. Röling, A. Elsaesser, P. Ehrenfreund. Biota and biomolecules in extreme environments on Earth: implications for life detection on Mars. *Life* **2014**, *4*, 535.

[7] P. Ehrenfreund, W. F. M. Röling, C. S. Thiel, R. Quinn, M. A. Sephton, C. Stoker, J. M. Kotler, S. O. L. Direito, Z. Martins, G. E. Orzechowska, R. D. Kidd, C. A. van Sluis, B. H. Foing. Astrobiology and habitability studies in preparation for future Mars missions: trends from investigating minerals, organics and biota. *Int. J. Astrobiol.* **2011**, *10*, 239.

[8] T. Kudo, M. Macht, M. Kuroda. Laser desorption ionization-time-of-flight mass analysis of perfluoropolyether monolayer directly from hard disk medium surface. *Anal. Chem.* **2011**, *83*, 5563.

[9] J. S. Becker, A. Matusch, C. Depboylu, J. Dobrowolska, M. V. Zoriy. Quantitative imaging of selenium, copper, and zinc in thin sections of biological tissues (slugs – genus arion) measured by laser ablation inductively coupled plasma mass spectrometry. *Anal. Chem.* **2007**, *79*, 6074.

[10] L. A. McDonnell, R. M. A. Heeren. Imaging mass spectrometry. *Mass Spectrom. Rev.* **2007**, *26*, 606.

[11] C. Gabler, E. Pittenauer, N. Dörr, G. Allmaier. Imaging of a tribolayer formed from ionic liquids by laser desorption/ionization-reflectron time-of-flight mass spectrometry. *Anal. Chem.* **2012**, *84*, 10708.

[12] E. Schramm, J. Hölzer, M. Pütz, R. Schulte-Ladbeck, R. Schultze, M. Sklorz, A. Ulrich, J. Wieser, R. Zimmermann. Real-time trace detection of security-relevant compounds in complex sample matrices by thermal desorption–single photon ionization–ion trap mass spectrometry (TD-SPI-ITMS). *Anal. Bioanal. Chem.* **2009**, *395*, 1795.

[13] J. Pisonero, N. Bordel, C. Gonzales de Vega, B. Fernández, R. Pereiro, A. Sanz-Medel. Critical evaluation of the potential of radiofrequency pulsed glow discharge–time-of-flight mass spectrometry for depth-profile analysis of innovative materials. *Anal. Bioanal. Chem.* **2013**, *405*, 5655.

[14] J. Pisonero, D. Günther. Femtosecond laser ablation inductively coupled plasma mass spectrometry: fundamentals and capabilities for depth profiling analysis. *Mass Spectrom. Rev.* **2008**, *27*, 609.

[15] J. J. González, D. D. Oropeza, H. Longerich, X. Mao, R. E. Russo. Rapid bulk analysis using femtosecond laser ablation inductively coupled plasma time-of-flight mass spectrometry. *J. Anal. At. Spectrom.* **2012**, *27*, 1405.

[16] I. S. Gilmore. SIMS of organics – Advances in 2D and 3D imaging and future outlook. *J. Vac. Sci. Technol. A* **2013**, *31*, 050819.

[17] A. Brunelle, D. Touboul, O. Laprévote. Biological tissue imaging with time-of-flight secondary ion mass spectrometry and cluster ion sources. *J. Mass Spectrom.* **2005**, *40*, 985.

[18] D. Zakett, A. E. Schoen, R. G. Cooks, P. H. Hemberger. Laser-desorption mass spectrometry/mass spectrometry and the mechanism of desorption ionization. *J. Am. Chem. Soc.* **1981**, *103*, 1295.

[19] R. J. Cotter. Lasers and mass spectrometry. *Anal. Chem.* **1984**, *56*, 485A.

[20] M. Karas, F. Hillenkamp. Laser desorption ionization of proteins with molecular masses exceeding 10,000 daltons. *Anal. Chem.* **1988**, *60*, 2299.

[21] Y. Cui, I. V. Veryovkin, M. W. Majeski, D. R. Cavazos, L. Hanley. High lateral resolution vs molecular preservation in near-IR fs-laser desorption postionization mass spectrometry. *Anal. Chem.* **2015**, *87*, 367.

[22] Y. Cui, C. Bhardwaj, S. Milasinovic, R. P. Carlson, R. J. Gordon, L. Hanley. Molecular imaging and depth profiling of biomaterials interfaces by femtosecond laser desorption postionization mass spectrometry. *ACS Appl. Mater. Interfaces* **2013**, *5*, 9269.

[23] Q. Zhan, R. Zenobi, S. J. Wright, P. R. R. Langridge-Smith. Spatially resolved in-situ analysis of polymer additives by two-step laser mass spectrometry. *Macromolecules* **1996**, *29*, 7865.

[24] S. A. Getty, W. B. Brinckerhoff, T. Cornish, S. Ecelberger, M. Floyd. Compact two-step laser time-of-flight mass spectrometer for *in situ* analyses of aromatic organics on planetary missions. *Rapid Commun. Mass Spectrom.* **2012**, *26*, 2786.

[25] Y. Chen, M. C. Sullards, T. T. Hoang, S. W. May, T. M. Orlando. Analysis of organoselenium and organic acid metabolites by laser desorption single photon ionization mass spectrometry. *Anal. Chem.* **2006**, *78*, 8386.

[26] P. M. Flanigan IV, F. Shi, J. J. Perez, S. Karki, C. Pfeiffer, C. Schafmeister, R. J. Levis. Determination of internal energy distributions of laser electrospray mass spectrometry using thermometer ions and other biomolecules. *J. Am. Soc. Mass Spectrom.* **2014**, *25*, 1572.

[27] P. Flanigan, R. Levis. Ambient femtosecond laser vaporization and nanosecond laser desorption electrospray ionization mass spectrometry. *Annu. Rev. Anal. Chem.* **2014**, *7*, 229.

[28] J. M. Wiseman, D. R. Ifa, Y. Zhu, C. B. Kissinger, N. E. Manicke, P. T. Kissinger, R. G. Cooks. Desorption electrospray ionization mass spectrometry: imaging drugs and metabolites in tissues. *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 18120.

[29] J. Pól, V. Vidová, G. Kruppa, V. Kobliha, P. Novák, K. Lemr, T. Kotiaho, R. Kostiainen, V. Havlíček, M. Volný. Automated ambient desorption – ionization platform for surface imaging integrated with a commercial Fourier transform ion cyclotron resonance mass spectrometer. *Anal. Chem.* **2009**, *81*, 8479.

[30] Y.-C. Chen, J.-Y. Wu. Analysis of small organics on planar silica surfaces using surface-assisted laser desorption/ionization mass spectrometry. *Rapid Commun. Mass Spectrom.* **2001**, *15*, 1899.

[31] Q. Zhan, S. J. Wright, R. Zenobi. Laser desorption substrate effects. *J. Am. Soc. Mass Spectrom.* **1997**, *8*, 525.

[32] Z. Ma, L.-L. Qiang, Q.-L. Fan, Y.-Y. Wang, K.-Y. Pu, R. Yin, W. Huang. Direct laser desorption/ionization time-of-flight mass spectrometry of conjugated polymers. *J. Mass Spectrom.* **2007**, *42*, 20.

[33] Y. Cui, J. F. Moore, S. Milasinovic, Y. Liu, R. J. Gordon, L. Hanley. Depth profiling and imaging capabilities of an ultrashort pulse laser ablation time of flight mass spectrometer. *Rev. Sci. Instrum.* **2012**, *83*, 093702.

[34] B. Zhang, M. He, W. Hang, B. Huang. Minimizing matrix effect by femtosecond laser ablation and ionization in elemental determination. *Anal. Chem.* **2013**, *85*, 4507.

[35] Y. Gao, Y. Lin, B. Zhang, D. Zou, M. He, B. Dong, W. Hang, B. Huang. Single-cell elemental analysis via high irradiance femtosecond laser ionization time-of-flight mass spectrometry. *Anal. Chem.* **2013**, *85*, 4268.

[36] J. Parnell, D. Cullen, M. R. Sims, S. Bowden, C. S. Cockell, R. Court, P. Ehrenfreund, F. Gaubert, W. Grant, V. Parro, M. Rohmer, M. Sephton, H. Stan-Lotter, A. Steele, J. Toporski, J. Vago. Searching for life on mars: selection of molecular targets for ESA's Aurora ExoMars mission. *Astrobiology* **2007**, *7*, 578.

[37] J. Chela-Flores. Instrumentation for the search for habitable ecosystems in the future exploration of Europa and Ganymede. *Int. J. Astrobiol.* **2010**, *9*, 101.

[38] J. Chela-Flores. A case for landing on the moon's farside to test nitrogen abundances. *Int. J. Astrobiol.* **2012**, *11*, 61.

[39] X. Li, R. M. Danell, W. B. Brinckerhoff, V. T. Pinnick, F. van Amerom, R. D. Arevalo, S. A. Getty, P. R. Mahaffy, H. Steininger, F. Goesmann. Detection of trace organics in Mars analog samples containing perchlorate by laser desorption/ionization mass spectrometry. *Astrobiology* **2015**, *15*, 104.

[40] G. G. Managadze, A. A. Safronova, K. A. Luchnikov, E. A. Vorobyova, N. S. Duxbury, P. Wurz, N. G. Managazde, A. E. Chumikov, R. X. Khamizov. A novel technique and mass-spectrometric instrument for extraterrestrial microbial life detection via analyses of the elemental composition of Martian regolith and permafrost/ice sample. *Astrobiology* **2016**, submitted.

[41] R. Saladino, E. Carota, G. Botta, M. Kapralov, G. N. Timoshenko, A. Y. Rozanov, E. Krasavin, E. Di Mauro. Meteorite-catalyzed syntheses of nucleosides and of other prebiotic compounds from formamide under proton irradiation. *Proc. Natl. Acad. Sci. USA* **2015**, *112*, E2746.

[42] Y. Kebukawa, A. L. D. Kilcoyne, G. D. Cody. Exploring the potential formation of organic solids in chondrites and comets through polymerization of interstellar formaldehyde. *Astrophys. J.* **2013**, *771*:19.

[43] U. Rohner, J. A. Whitby, P. Wurz. A miniature laser ablation time-of-flight mass spectrometer for *in situ* planetary exploration. *Meas. Sci. Technol.* **2003**, *14*, 2159.

[44] W. B. Brinckerhoff, G. G. Managadze, R. W. McEntire, A. F. Cheng, W. J. Green. Laser time-of-flight mass spectrometry for space. *Rev. Sci. Instrum.* **2000**, *71*, 536.

[45] G. G. Managadze, P. Wurz, R. Z. Sagdeev, A. E. Chumikov, M. Tuley, M. Yakovleva, N. G. Managadze, A. L. Bondarenko. Study of the main geochemical characteristics of Phobos' regolith using laser time-of-flight mass spectrometry. *Sol. Syst. Res.* **2010**, *44*, 376.

[46] X. Li, W. B. Brinckerhoff, G. G. Managadze, D. E. Pugel, C. M. Corrigan, J. H. Doty. Laser ablation mass spectrometer (LAMS) as a standoff analyser in space missions for airless bodies. *Int. J. Mass Spectrom.* **2012**, *323*, 63.

[47] R. Hergenröder, O. Samek, V. Hommes. Femtosecond laser ablation elemental mass spectrometry. *Mass Spectrom. Rev.* **2006**, *25*, 551.

[48] X. Zeng, X. L. Mao, R. Greif, R. E. Russo. Experimental investigation of ablation efficiency and plasma expansion during femtosecond and nanosecond laser ablation of silicon. *Appl. Phys. A: Mater. Sci. Processes* **2004**, *80*, 237.

[49] R. E. Russo, X. Mao, J. J. Gonzalez, S. S. Mao. Femtosecond laser ablation ICP-MS. *J. Anal. At. Spectrom.* **2002**, *17*, 1072.

[50] D. J. Hwang, H. Jeon, C. P. Grigoropoulos, J. Yoo, R. E. Russo. Femtosecond laser ablation induced plasma characteristics from submicron craters in thin metal film. *Appl. Phys. Lett.* **2007**, *91*, 251118.

[51] R. E. Russo, X. Mao, J. J. Gonzales, J. Yoo. Femtosecond vs nanosecond laser pulse duration for LA chemical analysis. *Spectroscopy* **2013**, *28*, 24.

[52] F. Caridi, L. Torrisi, A. Borrielli, G. Mondio. Isotopic ratio measurements with laser ablation coupled to mass quadrupole spectrometry. *Radiat. Eff. Defects Solids* **2010**, *165*, 668.

[53] M. Tulej, M. Iakovleva, I. Leya, P. Wurz. A miniature mass analyser for in-situ elemental analysis of planetary material–performance studies. *Anal. Bional. Chem.* **2011**, *399*, 2185.

[54] Y. Lin, Q. Yu, W. Hang, B. Huang. Progress of laser ionization mass spectrometry for elemental analysis – A review of the past decade. *Spectrochim. Acta B* **2010**, *65*, 871.

[55] Q. Yu, L. Chen, R. Huang, W. Hang, B. Huang, J. He. Laser ionization time-of-flight mass spectrometry for direct elemental analysis. *TrAC, Trends Anal. Chem.* **2009**, *28*, 1174.

[56] M. Tulej, A. Riedo, M. B. Neuland, S. Meyer, P. Wurz, N. Thomas, V. Grimaudo, P. Moreno-García, P. Broekmann, A. Neubeck, M. Ivarsson. CAMAM: A miniature laser ablation ionisation mass spectrometer and microscope-camera system for *in situ* investigation of the composition and morphology of extraterrestrial materials. *Geostand. Geoanal. Res.* **2014**, *38*, 441.

[57] A. Riedo, A. Bieler, M. Neuland, M. Tulej, P. Wurz. Performance evaluation of a miniature laser ablation time-of-flight mass spectrometer designed for *in situ* investigations in planetary space research. *J. Mass Spectrom.* **2013**, *48*, 1.

[58] A. Riedo, M. Neuland, S. Meyer, M. Tulej, P. Wurz. Coupling of LMS with a fs-laser ablation ion source: elemental and isotope composition measurements. *J. Anal. At. Spectrom.* **2013**, *28*, 1256.

[59] A. Riedo, S. Meyer, B. Heredia, M. B. Neuland, A. Bieler, M. Tulej, I. Leya, M. Iakovleva, K. Mezger, P. Wurz. Highly accurate isotope composition measurements by a miniature laser ablation mass spectrometer designed for in situ investigations on planetary surfaces. *Planet. Space Sci.* **2013**, *87*, 1.

[60] M. B. Neuland, S. Meyer, K. Mezger, A. Riedo, M. Tulej, P. Wurz. Probing the Allende meteorite with a miniature laser-ablation mass analyser for space application. *Planet. Space Sci.* **2014**, *101*, 196.

[61] V. Grimaudo, P. Moreno-García, A. Riedo, M. B. Neuland, M. Tulej, P. Broekmann, P. Wurz. High-resolution chemical depth profiling of solid material using a miniature laser ablation/ionization mass spectrometer. *Anal. Chem.* **2015**, *87*, 2037.

[62] A. Riedo, V. Grimaudo, P. Moreno-García, M. B. Neuland, M. Tulej, P. Wurz, P. Broekmann. High depth-resolution laser ablation chemical analysis of additive-assisted Cu electroplating for microchip architectures. *J. Anal. At. Spectrom.* **2015**, *30*, 2371.

[63] E. Herbst, E. F. van Dishoeck. Complex organic interstellar molecules. *Annu. Rev. Astron. Astrophys.* **2009**, *47*, 427.

[64] M. J. Mumma, S. B. Charnley. The chemical composition of comets – emerging taxonomies and natal heritage. *Annu. Rev. Astron. Astrophys.* **2011**, *49*, 471.

[65] P. Wurz, K. R. Lykke, M. J. Pellin, D. M. Gruen, D. H. Parker. Characterization of fullerenes by laser-based mass spectrometry. *Vacuum* **1992**, *43*, 381.

[66] S. Milasinovic, Y. Cui, R. J. Gordon, L. Hanley. Internal energy of thermometer ions formed by femtosecond laser desorption: implications for mass spectrometric imaging. *J. Phys. Chem. C* **2014**, *118*, 28938.