Fundamentals
Room Great Lakes B - Session FM-ThA1
High Resolution and MS/MS Methods II

Moderators: Evan Groopman, National Institute of Standards and Technology (NIST), **Christine Kern**, Justus Liebig University Giessen

2:00pm **FM-ThA1-1 Orbitrap™ MS/MS and TOF MS/MS: A Comparison of Two New Approaches for Peak Identification in Organic SIMS Applications**, *J. Zakel,* ***Derk Rading****, S. Kayser, A. Pirkl, W. Paul, R. Moellers,* IONTOF GmbH, Germany

Time-of-flight SIMS is an excellent technique for the characterization of organic surfaces and layered systems due to its high pixel repetition rate, high sensitivity, and its high lateral resolution.However, the interpretation of organic spectra with unambiguous peak assignment can be quite challenging and requires a reasonably experienced user. To facilitate data interpretation, instrument manufacturers and scientists have pursued various avenues and developed custom solutions, such as new mass analyzers with improved mass resolution and mass accuracy, spectra libraries, and software packages for multivariate statistical analysis.

However, the number of remaining possibilities for a given peak originating from molecular surfaces and especially biological samples may still be too high for unambiguous peak assignment. In these cases, MS/MS capabilities are helpful to further increase confidence in the peak identification. Since the MS/MS fragment ion spectrum is almost independent of the ionization process of the precursor ion, one can benefit from the large number of reference spectra collected in different libraries. For a comprehensive comparison, it is desirable to generate MS/MS spectra with high mass resolution and high mass accuracy.

To provide MS/MS functionality for our SIMS systems, we have developed two different solutions over the last few years. The first instrument combines an advanced TOF-SIMS system with an Orbitrap™ mass analyzer (QExactive™ HF from Thermo Fisher Scientific™). This Hybrid SIMS [1] instrument provides extremely high mass resolution (> 240,000) and very high mass accuracy (< 1 ppm) for MS and MS/MS spectra. The second solution (TOF MS/MS) uses a linear time-of-flight mass analyser to analyse the MS/MS fragment spectrum.

In this contribution we will compare the two different MS/MS approaches. Based on data obtained from different analyte classes on the two high-end systems, characteristics and key parameters will be discussed. The detailed comparison will demonstrate the analytical possibilities of MS/MS in general and furthermore compare the advantages and disadvantages of the different solutions. Also the compatibility with respect to reference library queries will be discussed.

References

[1] Passarelli et al., Nature Methods, 14, 1175–1183 (2017).

Keywords: SIMS, Orbitrap™, MS/MS

2:20pm **FM-ThA1-3 Characterization of Surface Bonding and Molecular Structure from Click-Chemistry to Biogenesis Using Tandem Mass Spectrometry Imaging**, ***Gregory L. Fisher****,* Physical Electronics

A TOF-TOF imaging mass spectrometer allows TOF-SIMS (MS^1) imaging and tandem MS (MS^2) imaging to be achieved in a lossless fashion [1,2]. Secondary ions for MS^1 and MS^2 analysis are produced from the same surface area by a primary ion nanoprobe. Monolayer film samples may be characterized without undesired erosion or degradation; even sub-monolayer 2D films are readily characterized. Kilo-electron volt collision-induced dissociation (keV-CID) enables compositional identification and structural elucidation of precursor ion moieties. This analytical capability has been brought to bear for straightforward molecular identification as well as multifaceted studies involving surface modification, polymers, composites, catalysis, forensic and failure analysis, biology and pharmaceuticals. TOF-SIMS tandem MS imaging was employed to unravel the click-chemistry of sub-monolayer films [3] and shed new light to unlock the mystery of molecular biogenesis [4,5].

[1] G.L. Fisher, et al, *Anal. Chem*. **88** (2016) 6433-6440.

[2] G.L. Fisher, et al, *Microscop. Microanal*. **23** (2017) 843-848.

[3] S. Oh, et al, *Chem. Mater*. **32** (2020) 8512-8521.

[4] T. Fu, et al, *Anal. Chem*. **90** (2018) 7535-7543.

[5] T. Fu, et al, *Nat. Sci. Rep*. **9** (2018) 1928-1938.

2:40pm **FM-ThA1-5 How to Measure and Image Large Biomolecules by Using Ar-GCIB and Bi-Cluster ToF-SIMS: Delayed Extraction, External Calibrants and Enzyme-Amplified Signal Enhancement**, ***Tae Geol Lee****,* Korea Research Institute of Standards and Science (KRISS), University of Science and Technology (UST), Republic of Korea*; H. Shon, H. Na,* Korea Research Institute of Standards and Science (KRISS), Republic of Korea*; M. Thi Le,* Korea Research Institute of Standards and Science (KRISS), University of Science and Technology (UST), Republic of Korea*; J. Son,* Korea Research Institute of Standards and Science (KRISS), Republic of Korea*; J. Moon,* Korea Research Institute of Bioscience and Biotechnology (KRIBB), Republic of Korea **INVITED**

Time-of-flight secondary ion mass spectrometry (ToF-SIMS) is a powerful tool due to its sensitivity, chemical specificity, and high spatial resolution in visualizing chemical information in cells and tissues. However, the sensitive and specific imaging of large molecules such as peptides, proteins, and mRNA, a task that has been, to date, are still challenging.

Here, we will show our strategies to measure and image large biomolecules by using Ar-gas cluster ion beam (GCIB) together with delayed extraction and external calibration [1,2], and by using Bi-cluster ion beam together with enzyme-amplified signal enhancement [3,4].

3:20pm **FM-ThA1-9 Additional Dimension to the *m/z* Scale: Separation of Structural Isomers Using Orbisims**, ***Gustavo F. Trindade****, J. Vorng,* National Physical Laboratory, UK*; A. Pirkl,* IONTOF GmbH, Germany*; I. Gilmore,* National Physical Laboratory, UK

In 2017, the OrbiSIMS instrument was introduced [1]. It features a dual analyser configuration with a Time-of-Flight (ToF) mass spectrometer (MS) and an Orbitrap MS, which confer advantages of speed and high-performance mass spectrometry, respectively. The ability to combine the MS performance usually found in a state-of-the-art proteomics and metabolomics MS with 3D imaging at the microscale and from nanolayers of <10 nm of material has proved popular in a broad field of application from organic electronics to drug discovery. In 2021, we conducted a systematic study of two key parameters, the target potential, V_T, and the collision cell pressure, P, in the transfer optics on the transmitted secondary ion intensities [2]. We revealed a sometimes complex behaviour, indicating the possibility for additional separation of ions based on their shape, stability and kinetics of formation. We showed that the V_T for maximum transmission of secondary ions will not be the same for all molecules and that sometimes multiple maxima exist. Here, we present recent progress towards understanding the origin of multiple V_T maxima and how we are leveraging this phenomenon to separate structural isomers.

[1] M. K. Passarelli *et al.*, "The 3D OrbiSIMS—label-free metabolic imaging with subcellular lateral resolution and high mass-resolving power," *Nat. Methods*, no. november, p. nmeth.4504, 2017, doi: 10.1038/nmeth.4504.

[2] L. Matjacic *et al.*, "OrbiSIMS metrology part I: Optimisation of the target potential and collision cell pressure," *Surf. Interface Anal.*, no. November 2021, pp. 1–10, 2021, doi: 10.1002/sia.7058.

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