Recent Advances in SIMS
Room Great Lakes B - Session RA+BS+FM+SS-TuM2

Beams, Theory Optimization and Methods
Moderator: Gregory Fisher, Physical Electronics USA

10:00am RA+BS+FM+SS-TuM2-1 Chemical Structure of Organic Molecules Sputtered with Cluster Ions, *Jiro Matsuo,* Kyoto University, Japan **INVITED**
Much attention is now devoted to the study of gas cluster ion beams (GCIB), not only for fundamental research, but also for practical applications, such as organic depth profiling and 3-dimensional molecular analysis in XPS or SIMS. Extremely high energy density and multiple collisions are responsible for "cluster effects", which play an important role during their sputtering process of organic molecules. It has been demonstrated that large cluster ion beams have a great potential to sputter organic molecules without any residual damage on the surface, because cluster ion beams are equivalently low energy ion beams. It has also been reported that cluster ions can enhance the yields of secondary ions, and this provides a unique opportunity for SIMS with organic materials. However, there is no report on molecular structure of sputtered species from organic materials. We have concerned that organic molecules sputtered with large cluster ions are destroy, or not. Secondary molecular ion yields are usually very low(<1E-4), and most of sputtered species are neutral, which is hardly measured. Therefore, SIMS spectra never tell us molecular structure of sputtered species. Capturing of neutral species and electrospray ionization mass spectrometry (ESI-MS) technique were utilized to explore molecular structure of sputtered neutral species.Fundamental phenomena of cluster ion collision with organic molecules will be discussed in conjunction with possible applications.

10:40am RA+BS+FM+SS-TuM2-5 Cluster-Induced Desorption/Ionization of Polystyrene – Detailed Information on Material Properties Based on a Soft Desorption Process, *P. Schneider, F. Verloh,* Justus Liebig University Giessen, Germany*; **Michael Dürr,*** Justuts Liebig University Giessen, Germany
Polymer materials are of growing importance for a variety of applications in the field of optical electronics, including organic light emitting diodes and solar cells. As the detailed molecular properties of the polymer molecules determine the electrical and optical properties of these devices, sample characterization is a crucial step for both research and production purposes, thus making a powerful analytical tool mandatory. Secondary-ion mass spectrometry (SIMS) is a widespread method for the characterization of solid samples of polymers and organic materials in general, however, it typically comes with significant fragmentation induced by the primary ions [1]. While this can be of advantage, e.g., for identification of larger molecules or for depth profiling of polymer samples, characterization of sample properties like the mass distribution of the smaller molecules requires a non-destructive approach.

Desorption/Ionization induced by Neutral SO_2 Clusters (DINeC) is such a soft desorption method [2,3]. In this contribution, we investigate in detail cluster-induced desorption of non-polar polystyrene oligomers. Clear peak progressions corresponding to intact polystyrene molecules are observed in the mass spectra and no fragmentation was detected; efficient desorption was deduced from quartz crystal microbalance measurements. Molecular dynamics simulations further show that desorption proceeds via dissolvation in the polar cluster fragments even in the case of the non-polar polystyrene molecules. Experimentally, a reduced desorption efficiency for samples composed of molecules with higher chain length is observed. This is in contrast to the results of the molecular dynamics simulations, which indicate that, in a simple model, the desorption efficiency is largely independent of the chain length of the molecules. Backed by additional experiments with samples containing different distributions of chain length, the reduced desorption efficiency for longer molecules is attributed to an increasing entanglement of the polystyrene molecules with increasing chain length [4].

References:

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[4] P. Schneider, et al., J. Am. Soc. Mass Spectrom. 33, 832 (2022).

11:00am RA+BS+FM+SS-TuM2-7 Ibeam: Large Argon Cluster Ion Beams as a Versatile Vacuum-Based Tool for the Fabrication of Protein Thin Films, *Vincent Delmez, B. Tomasetti, C. Poleunis,* Université Catholique de Louvain, Belgium*; C. Lauzin, C. Dupont-Gillain,* université Catholique de Louvain, Belgium*; A. Delcorte,* Université Catholique de Louvain, Belgium
The controlled immobilization of proteins at interfaces is a powerful tool for the synthesis and preparation of biofunctional materials. To this purpose, vacuum-based approaches such as soft-landing offer a valuable alternative to the traditional adsorption-based methods performed in solution and expand the scope of possible applications. By diverting a ToF-SIMS from its analytical function, we developed an alternative soft-landing technique, relying on the soft sputtering of biomolecules by large cluster ion beams (Fig. 1). Practically, a pool of proteins (the target) is bombarded by large Ar clusters, and the ejecta is collected on a solid surface (the collector). All ejected particles are collected regardless of their charge state, hence improving the deposition rate with respect to existing soft-landing methods. Small peptides, angiotensin and bradykinin, were used to optimize the transfer. ToF-SIMS analysis revealed the presence of intact protein molecules on the collector, and showed that lowering the energy per atom in the cluster projectiles promotes the deposition of intact molecules versus fragmented ones. ToF-SIMS was also used to *in-situ*measure the deposited protein thickness, as a procedure based on the attenuation of the substrate signal intensity was developed for thickness determination. The latter was used to demonstrate that our deposition method allows a precise control on the transferred quantity, from (sub)mono- to multilayers, with theoretically no thickness limitation. The deposition rate as well as the homogeneity of the deposited films could be largely improved by varying the clusters' impinging angle with respect to the target surface, from 15° to 45°. We then used this cluster-assisted deposition method, coined iBeam, to investigate the transfer of larger enzymes. Lysozyme was used as a model. SDS-PAGE electrophoresis confirmed the presence of intact lysozyme on the collector, while positive enzymatic activity assay demonstrated the preservation of the three-dimensional structure of the transferred proteins. Our current experiments indicate that even larger proteins, e.g. trypsin, 24kDa, can be successfully transferred (Fig. 2). iBeam deposition can be achieved on any vacuum compatible collector material, and offers possibilities to build complex multilayers that are out of reach of existing protein immobilization techniques.

11:20am RA+BS+FM+SS-TuM2-9 Optimisation of MeV TOF SIMS Technique for Hybrid Targets Imaging and Inorganic Material Depth Profiling, *M. Barac,* Ruder Boskovic Institute, Jozef Stefan International Postgraduate School (Slovenia), Croatia*; M. Brajkovic, **Zdravko Siketic**,* Ruder Boskovic Institute, Croatia*; J. Kovac,* Jozef Stefan Institute, Slovenia*; I. Bogdanovic Radovic,* Ruder Boskovic Institute, Croatia*; I. Srut Rakic,* Institute of Physics, Croatia*; J. Ekar,* Jozef Stefan Institute, Slovenia
MeV TOF SIMS is a variation of the standard technique TOF SIMS, in which primary ions with energies of ~MeV/amu accelerated by a particle accelerator are used for ion/molecule desorption. Since the electronic stopping in this energy range is much more pronounced than the nuclear stopping, the energy transfer to the target constituents is much "softer" (e.g. vibrational molecular modes are excited). In this way, a higher yield of molecular secondary ions and less fragmentation are achieved compared to monoatomic keV SIMS. MeV SIMS is mainly used for chemical imaging of organic molecules with masses up to 1000 Da, with applications in biomedical research, forensics, cultural heritage, etc.

This work explores the idea of using primary ions with energies in the range of 100 keV - 5 MeV for SIMS, where due to similar contributions of nuclear and electronic stopping power both, inorganic species, as well as larger biomolecules, can be desorbed simultaneously from the sample. Thus, LE (Low Energy) MeV SIMS is an option to analyse hybrid (organic/inorganic) samples. The dependence of the secondary ion yield on the primary ion energy of leucine and various inorganic targets was studied first. The ability to image hybrid organic/inorganic samples was demonstrated on target having a lateral distribution of Cr and leucine. It was demonstrated that the contrast between the organic and inorganic regions decreases almost completely as the energy of the primary ion beam energy was lowered from several MeV to a few hundred keV. In addition, LE MeV SIMS ability for depth profiling in a dual beam mode with Ar gun was also explored. LE MeV SIMS depth profiling of a Cr- ITO bilayer sample in a dual beam mode was investigated, and the obtained depth profile was compared with the profile obtained with a well-established keV SIMS with Bi_3^+ ion beam. The depth profiles showed solid chemical sensitivity to inorganic secondary ions and satisfactory depth resolution.

The systematic study of MeV TOF SIMS in the low energy range will open new possibilities for the fundamental understanding of the effects of primary ion stopping power on the detection of secondary ions of organic and inorganic species. LE MeV SIMS can also be considered as the method of choice for imaging and depth profiling of inorganic materials in the laboratories performing standard Ion Beam Analysis, but without commercially available SIMS instruments, providing additional information on the depth profile and chemical composition of the sample.

11:40am **RA+BS+FM+SS-TuM2-11** **Reactive Molecular Dynamics Simulations of Lysozyme Desorption Under Ar Cluster Impact**, **Samuel Bertolini**, *A. Delcorte,* Université Catholique de Louvain, Belgium

Using large gas cluster ion beams (Ar^+_{3000}), it is possible to successfully desorb and transfer intact nonvolatile (bio)molecules such as lysozyme (14kDa) onto a collector surface [1]. Nevertheless, from the cluster impact up to the complete desorption of the protein, the cluster supplies energy to the protein. The collision can potentially induce fragmentation and/or denaturation of the lysozyme. To shed light on the Ar cluster-induced desorption mechanism of lysozymes, molecular dynamics (MD) simulations were performed using reactive force fields (ReaxFF) [2]. The ReaxFF calculates the energy of the system associated with the bond order of each atom, permitting reaction on-the-fly. Compared to previous modelling of large molecule desorption by Ar clusters which involved simple hydrocarbon polymers [3], these new simulations offer a realistic view of the protein behavior, accounting for all the specific interactions which stabilize its three-dimensional structure (hydrogen bonds, disulfide bridges). Prior to the bombardment simulations, some of the necessary interactions were parametrized based on density functional theory (DFT) calculations, using a set of small molecules. Then, one or more lysozymes were adsorbed and relaxed at room temperature on a gold surface with a (543) orientation. The gold surface contains several step defects, allowing stronger and more realistic adsorption of a protein on the surface. The relaxed surfaces were finally bombarded by Ar clusters with a 45° incidence angle. The simulations investigate different cluster sizes (from 1000 to 5000 atoms) and energies per atom (from 0.5 to 5 eV), and how those parameters affect desorption as well as the concomitant chemical reactions and/or protein unfolding events. This allows us to better understand the final structure of the desorbed proteins as a function of the interaction parameters and, in turn, the results of the experiments.

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12:00pm **RA+BS+FM+SS-TuM2-13 Hybrid SIMS: New Adaptive Ion Injection System (AIIS) for Improved Repeatability of Quantitative Orbitrap™ SIMS Measurements**, **Sven Kayser**, *J. Zakel, D. Rading, A. Pirkl, H. Arlinghaus,* IONTOF GmbH, Germany; *A. Franquet, V. Spampinato,* IMEC, Belgium

To boost the performances of the next generation transistors, new materials and device architectures have been investigated in the semiconductor industries[1]. In this context, strained-Ge and SiGe channel FET's have received high interest due to their excellent hole mobility[2] and recently obtained results have encouraged the semiconductor device industry to incorporate them in its latest FinFET technology[3,4]. As a consequence, characterization techniques have to provide chemical information and high sensitivity with a spatial resolution compatible with the device structure of down to 10 nm.

During the last years we demonstrated that the improved mass resolution of the Hybrid SIMS[5] instrument, which integrated the Orbitrap™ mass analyzer into a SIMS instrument, has been extremely beneficial for advanced semiconductor structure analysis. Especially the application of the so-called Self-Focusing SIMS (SF-SIMS)[6,7] approach opened up new possibilities for the analysis of next generation devices.

Despite the very encouraging first results it also become clear that, depending on the individual analytical conditions, the Orbitrap™ mass analyzer can suffer from oversteering and saturation effects. These effects limited the repeatability, absolute quantification and matching to other analytical techniques. To overcome this limitation, we developed a unique adaptive injection system for the Orbitrap™ mass analyzer. The new system automatically adapts the number of injections (i.e., Orbitrap™ sprctra per frame) or number of pixels within the field of view to avoid oversteering and saturation effects in real time.

In this presentation we will explain the working principle, apply new adaptive ion injection system to different sample systems and report the advances for the measurement repeatability, the quantification and the matching to other analytical techniques.

References:

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[6]A. Franquet et al., *Applied Surface Science***365**, 143-152 (2016).
[7]A. Franquet et al., *J. Vac. Sci. Technol.* B **34**(3), May/Jun (2016).

Beyond SIMS
Room Great Lakes A2-A3 - Session BS+FM+SS-TuA1

Cells and Tissue II

Moderators: Peter Sjövall, RISE Research Institutes of Sweden, **Michael J. Taylor**, Pacific Northwest National Laboratory

4:00pm **BS+FM+SS-TuA1-13 Answering Biomedical Questions Using Integrative ToF-SIMS Imaging**, *Sebastiaan Van Nuffel,* Maastricht University, Netherlands   **INVITED**
For the past two decades, cell and tissue imaging using Time-of-Flight secondary Ion Mass Spectrometry (ToF-SIMS) has successfully answered various biological and clinical questions over the past two decades. Because it can visualize the spatial distribution of small molecules (< 2000 Da) in 2D with a spatial resolution comparable to that of a light microscope, it can be used to simultaneously investigate the elemental composition, the metabolome and the lipidome of tissue sections as well as their interaction with non-native compounds such as drugs or toxins. However, it remains a niche technique and there are several issues still hampering its widespread application.

First of all, the data generated is very complex, because the secondary ions of the different compounds present in the sample are all formed together after the impact of the primary ion, which is why SIMS is typically combined with a 'panoramic' detector with high transmission such as a ToF mass analyzer. This property allows for label-free detection, but is a double-edged sword because it also means that a typical ToF-SIMS mass spectrum can be considered a summation of the spectra of the individual compounds present. Multivariate analysis and more advanced machine learning approaches have been successfully used for image segmentation and can help identify positive correlations between various mass peaks. However, spatial colocation does not necessarily mean that these mass peaks all originate from one compound, particularly in the case of complex biological systems. In addition, the secondary ion intensity and fragments produced using desorption-ionization techniques such as ToF-SIMS are highly dependent on the chemical environment of the compounds. This so-called 'matrix effect' has made it very difficult to fingerprint and library approaches have proven largely ineffectual for ToF-SIMS. Luckily, the creation of ToF-SIMS instruments with MS/MS capabilities makes unambiguous identification finally possible. Another issue is the fact that it is difficult to detect large molecules such as intact proteins with a typical ToF-SIMS instrument. It is therefore necessary to integrate ToF-SIMS with other imaging techniques such as other mass spectrometry imaging methods and immunohistochemistry.

Invited speaker Dr. Sebastiaan Van Nuffel will present various examples of his past and ongoing research to demonstrate the power of ToF-SIMS MS/MS and its integration with advanced data analysis techniques such as machine learning. He will also discuss his ongoing research efforts developing methods in order to establish a spatially resolved multi-omics atlas.

4:40pm **BS+FM+SS-TuA1-17 In Situ Matrix Enhanced Secondary Ion Mass Spectrometry for Tissue Analysis**, *Thomas Daphnis*, B. Tomasetti, D. Vincent, A. Delcorte, C. Dupont, UCLouvain, Belgium
During the last decade, mass spectrometry imaging (MSI) has gained substantial interest thanks to impressive instrumental development. MSI can achieve simultaneous detection of hundreds of biomolecules including lipids, proteins but also drugs and xenobiotics directly in tissues and cells. The main advantages of MSI compared to classical imaging techniques are the great lateral resolution and the ability to perform analysis with no prior labelling of the biomolecules of interest. MSI finds therefore applications in the biological and pharmaceutical fields as well as many others [1].

In spite of the recent progress, the sensitivity to molecular species often remains a limiting factor for high resolution 2D and 3D molecular analysis of biological tissues in cluster secondary ion mass spectrometry (SIMS). Recently, in-situ matrix enhanced SIMS, where an acidic MALDI-type matrix is applied to the sample via large gas cluster ion-induced sputtering from a matrix "target" towards the tissue sample surface inside the ToF-SIMS, was proposed to alleviate this shortcoming [2,3]. Here, the interest of the method is demonstrated for a series of matrices and samples including lipid references and tissue sections.

First, seven MALDI matrices were selected and the ability to transfer them was demonstrated using an Ar_{3000}^+ ion beam. Then, the different matrices were transferred onto a phosphatidylcholine (PC) mix layer spin-coated on silicon (PC is an abundant lipid class of cellular membranes). Matrices

CHCA, DHB and SA proved to enhance intact lipid ion signals up to one order of magnitude. Interestingly, the matrices not only increase the signals of protonated species $[PC+H]^+$ but also the signal of adducts $[PC+Na/K]^+$. Therefore, the acidic matrix deposition effect is twofold: it brings extra protons to analyte molecules but also provides a favouring environment for their ionisation.

Finally, these three matrices were transferred on real mouse brain tissue sections. As similar tissues have been extensively studied in the MSI community, peak identification was facilitated. The measured lipids ion yields were compared as a function of sample pre-treatment. Our results show that the matrix transfer of CHCA and DHB was highly beneficial to intact lipids detection in these tissue sections. Indeed, some peaks were revealed by the matrix while the signals of others were increased by 10-fold. Moreover, signal enhancement was observed for both Bi_5^+ and Ar_{3000}^+ as analysis beams.

References
[1] M. Noun et al., Microscopy and Microanalysis, pp. 1-26, 2021;[2] K. Moshkunov et al., Analyst 146, pp. 6506-6519, 2021;[3] M. Lorenz et al., Anal. Chem. 93, pp. 3436-3444, 2021.

5:00pm **BS+FM+SS-TuA1-19 Evaluating Topical Product Sensitivity and Distribution Using a Multi-Modal Imaging Approach**, *Jean-Luc Vorng*, D. Tsikritsis, National Physical Laboratory, UK*; P. Zarmpi, V. Tyagi,* University of Bath, U.K.*; A. Dexter, I. Gilmore, N. Belsey,* National Physical Laboratory, UK*; R. Guy,* University of Bath, U.K.
There is a need to characterise non-invasively both the epidermal bioavailability of a topically applied drug and to distinguish correctly between formulations that are bioequivalent, i.e., to measure if a generic formulation performs the same as the branded product. In this study, Time-of-Flight Secondary Ion Mass Spectrometry (TOF-SIMS) was used to detect, characterise, and image the distribution of 4-cyanophenol a drug permeation enhancer[1] within a pig skin tissue homogenate and pig skin tissue sections[2].

Due to its high sensitivity and the capability to provide chemical mapping of the sample, SIMS enables a step-by-step approach to the problem starting from the screening of the product to investigating the limit of detection within a biological matrix. In this study, we have investigated the distribution of 4-cyanophenol in skin using a multi-modal imaging approach. Correlative mass spectrometry imaging (MSI) measurements with non-invasive Raman spectroscopy on the same sample provides superior chemical specificity and permits the distribution of the compound to be accurately characterised using spatial registration[3]. Finally the OrbiSIMS has been used to investigate the contribution of endogenous species that might interfere with the signal of interest in TOF-SIMS[4]

In this work, the compound of interest has been successfully detected as an intact molecular ion and a linear response of intensity as a function of concentration has been obtained. Finally, the distribution 4-cyanophenol within a pig skin tissue section was mapped and a strong correlation between SIMS and Raman spectroscopy was demonstrated.

References
(1)*Romonchuk et Al. Skin Pharmacol Physiol, 23(3),* **2010**, 152–163

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Beyond SIMS
Room Great Lakes B - Session BS+FM+SS-TuA2

Cells and Tissue III

Moderators: Peter Sjövall, RISE Research Institutes of Sweden, **Michael J. Taylor**, Pacific Northwest National Laboratory

4:00pm **BS+FM+SS-TuA2-13 Nanoprojectile-SIMS in the Event-by-Event Bombardment-Detection Mode**, *M. Eller,* California State University, Northridge*; S. Verkhoturov, D. Verkhoturov,* **Emile A. Schweikert,** Texas A&M University
This sims technique differs from the usual approach in three ways: the nature of the bombarding ion, the mode of bombardment and that of data acquisition/processing. Bombardment is with nanoprojectiles, NP, i.e. gold nanoparticles (Au_{400}^{4+}, n/q=100; Au_{2800}^{8+}, n/q=350). A single NP impact causes emission from surface spots of 10-20 nm in diameter and up to 10

nm in depth. Bombardment-SI detection is done in the event-by-event mode, i.e. SIs form a single NP impact are detected via time-of-flight and recorded separately.The process is repeated at a rate of 1 kHz. Bombardment is stochastic over a surface of 100 to 250 μm in diameter and typically lasts for a few thousand s, amounting to testing 1 to 5% of the surface exposed to bombardment.The result is a listing of a few M mass spectra. Assuming that all impacts are equivalent the data set can be examined for correlations. Indeed, the SIs from one impact arise from collocated molecules. They reveal homogeneity at the nanoscale, which translates into the ability to identify rare defects. The approach outlined here is also uniquely suitedfor characterizing isolated nano-objects of dimensions a small as a few tens of nm. Direct or grazing impacts can readily be sorted based on the characteristics of the SIs. Results reported here have been obtained with a custom-built instrument featuring a gold liquid metal ion source and a 100 kV acceleration stage. As indicated, SI detection is via ToF either in the customary reflection mode or in transmission where specimens are deposited on a 1-2L graphene support. "Decision limit" detection is in the attomol range. The SI output is 5-10 times enhanced in the transmission mode. We show on molecular assemblies, polymer blends and membranes the ability to test molecular alignments, homogeneity and to identify defects occurring at the level of one in 10^4 to 10^5 nanospots. For nano-objects with large surface to volume ratios we demonstrate assays on individual items, the ability to count objects, as well as distinguishing functionalities and loading on asymmetric particles. On dimensions below 20 nm, non equivalency of impacts prevails, yet it is still possible to distinguish organic modifiers on a nano-object from ejecta arising from the substrate. In summary, nanoprojectile-sims has the ability to identify rare defects in synthesized films or biological membranes and is uniquely suited for molecular assays on individual nano-objects.

4:20pm BS+FM+SS-TuA2-15 2D/3D Ion Imaging Methods using CAMECA Dynamic SIMS Instruments, *Laura Créon, S. Choi, P. Peres, S. Miwa, J. Ren, R. Liu,* CAMECA, France

Ion imaging using dynamic SIMS is one important technique for materials characterization. To perform surface imaging within a sample, the spatial position of each secondary ion must be mapped to the sample surface. Two ion imaging methods are available in CAMECA IMS 7f-Auto magnetic sector instruments: the ion *microscope* mode where spatial resolution is determined by stigmatic ion optics, and the ion *microprobe* (or scanning) mode, based on primary beam rastering across the surface, where spatial resolution is determined by the primary beam size.

The ion microscopemode allows for high sputtering rates and direct imaging using high beam current, but the instrumental transmission must be reduced and a dedicated 2D detector is required.

For the scanning ion mode, images are acquired on a standard Electron Multiplier (EM) detector with high flexibility for the image field of view (few μm^2 up to 500x500 μm^2), independently of the mass resolving power. On the IMS 7f-Auto, a lateral resolution down to sub-μm can be achieved using this mode.

It is possible to obtain 3D volume reconstruction as well as retrospective depth profiling from 2D ion image stacks recorded sequentially while sputtering in-depth.

For pure scanning probe mode, as a small beam size is required, the beam current and sputter rate are low thus limiting the achievable eroded depth within typical analysis duration.

For optimized 3D imaging capabilities in scanning mode, IMS 7f-Auto data acquisition software includes a "Sputtering between cycles" option which allows high current beam sputtering between consecutive imaging cycles. This enables 3D imaging of deep areas while keeping reasonable analysis duration.

Another method for 3D imaging consists in combining the microscope mode with scanning mode ("scanning microscope" mode), using high current primary beam and EM detector, which has advantages for the detection of atmospheric gas elements.

Different analytical protocols for 3D imaging will be described and data for different applications will be presented.

4:40pm BS+FM+SS-TuA2-17 High-Resolution Peak Analysis in TOF SIMS: Resolving Satellite Peaks and sub-Peak Structures, *Amy Walker, L. Gelb,* University of Texas at Dallas

We present progress in the quantitative extraction of chemical information from imaging TOF SIMS data using advanced statistical methods. The detectors used in many TOF SIMS instruments undercount ions due to saturation effects; if two or more ions arrive within a very short interval (the "dead time") only the first to arrive is recorded. This changes both the total number of ions collected and their statistical distribution.We introduce a new maximum-likelihood analysis thatincorporates the detector behavior in the likelihood function, such that a parametric spectrum model can be fit directly to as-measured data. In numerical testing, this approach is shown to be the most precise and lowest-bias option when compared with both weighted and unweighted least-squares fitting of data corrected for dead-time effects. We apply the maximum-likelihood method to fit two experimental data sets: a positive-ion spectrum from amultilayer MoS$_2$ sample and a positive-ion spectrum from a TiZrNi bulk metallic glasss ample. The precision of extracted isotope masses and relative abundances obtained is close to the best-case predictions from the numerical simulations despite the use of inexact peak shape functions and other approximations.

We then determine the degree to which sub-peak structure at a single unit mass can be resolved. Synthetic data are generated with multiple overlapping peaks of different intensities and separations. The data quality (number of counts) required to reliably distinguish the two-peak structure from a single peak is determined as a function of these parameters.These results are then analyzed in order to establish limits on when sub-peak resolution can reasonably be attempted.

5:00pm BS+FM+SS-TuA2-19 Innovative Approach to Safeguard Saffron Authenticity Using TOF-SIMS and Multivariate Analysis, *Alice Bejjani, O. el Ayoubi,* Lebanese Atomic Energy Commission, National Council for Scientific Research, Lebanon*; E. de Angelis, R. Pilolli, L. Monaci,* Institute of Science of Food Production, National Research Council of Italy

Saffron is a highly appreciated spice known for its aroma, color, flavor and for also its medical benefits. Therefore, it is used in food preparation, dye production and in herbal and pharmaceutical formulations. Due to the high costs and labor required for plantation and production, saffron is considered one of the most expensive products across the world and is consequently commonly adulterated. Saffron adulterations include the addition of less expensive agricultural products or synthetic components with similar color and morphology. It has been demonstrated that safflower petals and turmeric powders which are among the most frequent adulterants in saffron cannot be detected, up to 20% (w/w), by the ISO normative [1]. This work aimed to develop a rapid and sensitive method based on the Time of flight secondary ion Mass Spectrometry to discriminate between authentic and adulterated saffron with either Safflower or Turmeric at 5, 10 and 20 % (w/w). Mass spectral signatures of pure saffron, safflower and turmeric powders were acquired for the first time. Samples of adulterated saffron with safflower were easily identified via the presence of safflower unique fragments. Supervised principal component analysis was needed to differentiate between the different types of samples. The source of variations between the samples was determined and discussed.

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Beyond SIMS
Room Great Lakes Promenade & A1 - Session BS-TuP

Beyond SIMS Poster Session

BS-TuP-1 Exploring the Role of Fe-C-Al Sites for the Low Temperature CO Oxidation over Fe-oxide/Al2O3 via ToF-SIMS, *Byeong Jun Cha,* Korea Basic Science Institute, Republic of Korea; *Y. Kim,* Sungkyunkwan University (SKKU), Republic of Korea; *C. Choi, M. Choi,* Korea Basic Science Institute, Republic of Korea

Development of low temperature operating catalysts has been one of the challenges in exhaust gas catalysis since the most commonly used Pt-group catalysts are generally active above 150 °C causing 'cold-start emission'. Fe-oxide nanoparticle catalysts have been studied extensively due to their high low-temperature activity and thermal stability, and many experimental/theoretical studies have been conducted to unveil the relationship between the structure and activity of the Fe-oxide nanocatalysts. In the present work, ToF-SIMS technique, which has not been used widely on iron oxide nanocatalysts, was utilized to elucidate the structure-activity relations on Fe-oxide/Al_2O_3 for the low temperature (~50 °C) CO oxidation. The combined results of various surface analyzing tools including ToF-SIMS showed a scaling relationship of ternary interfacial sites of Fe-C-Al with the CO oxidation activity below 50 °C, indicating that the Fe-C-Al species facilitate low temperature CO oxidation. This work shows that ToF-SIMS can provide valuable information on the structure-activity relations in heterogenous catalysts.

BS-TuP-3 Evaluation of Multi-Depth Modifications of Metal-Oxide Nanotubes, *Swathi Naidu Vakamulla Raghu,* University of Siegen, Germany

Metal-oxide (MO) surfaces have successfully been modified to elicit surface functionality different than the parent material via facile application of self-assembled monolayers (SAM). Previously reported MO surfaces demonstrate superhydrophobicitywhen functionalized with phosphonic acid carbohydrate molecules.[1] In this work, we shed light on the role of SAM facilitated hydrophobic-effect as a result of application technique, i.e., immersion in bulk solution (BI) and micro-contact printing (µCP).These modifiedZrNTs were evaluated along their tube length in the depth-profiling mode using time-of-flight secondary ions mass spectrometry (ToF-SIMS). Using the depth profile mode, we were successfully able to ascertain the presence of targeted molecules at various depths inside the nanotubes. These results were used to provide in proof the possibility to develop multi-depth and multi-functional modifications within nanotubes as shown in Fig. 1a. Herein, the nanotube walls could effectively be functionalized at different depths via wet-chemistry and soft-lithography techniques devoid of clean-room fabrication.[2]In combination, with the developed synthesis and characterization strategies of ZrNT, we are able to demonstrate an enhanced functionality in addition to tailor-made storage capabilities of such nanotubular surfaces. The nanotube reservoirs were evaluated for volumetric storage via simulated dye-release behaviour as seen in Fig. 1b. Such nanotubular reservoirs developed on the implant surface would be capable of facilitating developmental strategies towards controlled multi-drug release models that can even elicit sequential release of drugs to limit clotting, inhibit infection and ultimately promote healing.

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BS-TuP-5 In Situ Liquid Secondary Ion Mass Spectrometry - a Unique Tool for in Situ Molecular Analysis of Various Liquids and Solid-Liquid Interfaces, *Zihua Zhu,* PNNL

Secondary ion mass spectrometry (SIMS) is a powerful surface analysis tool with several unique advantages. It can provide elemental, isotopic and molecular information with excellent sensitivity and decent spatial resolution. SIMS has been extensively used in semiconductor industry and increasingly important in scientific research. However, SIMS is a high-vacuum technique, and it has been normally used for analysis of solid samples. In situ liquid SIMS, which was developed in Pacific Northwest National Laboratory about 11 years ago, can be used for molecular examination of various liquids and liquid interfaces, providing critical information that any other techniques can hardly provide. In the last several years, in situ liquid SIMS has been successfully used to resolve some interesting scientific questions in energy, biology, environment and other fields. In this presentation, the principle of in situ liquid SIMS and its major applications will be summarized.

BS-TuP-7 Surface Modification of Steel, Molybdenum and Tungsten by the Use of Two Techniques: Electron Beam Scanning and Electric Discharge Machining – SIMS and GDMS Maps, *Piotr Konarski, J. Ażgin, A. Zawada,* Łukasiewicz Research Network - Tele and Radio Research Institute, Poland; *S. Feng ,* Department of Mechanical Engineering, National Taipei University of Technology. , Taiwan; *C. Chien ,* Chien's Scientific Company, Taiwan; *D. Sheu,* Department of Mechanical Engineering, National Taipei University of Technology, Taiwan

Process of surface modification of steel (s235 and ss304), molybdenum and tungsten samples was carried out with the two techniques - by a high-energy electron beam line scanning in vacuum in a device used for electron beam welding, and by a technique of electric discharge machining (EDM) in which samples are submerged in dielectric fluid.

In the case of electron beam technique we use a beam of 18 keV energy and approx. 500 µm diameter, which is linearly scanned over the surface of the samples at a speed of 0.5 m/s. The used beam currents of 0.5, 1, 2, 5 and 10 mA correspond to the transmitted energy ranging from 10 to 200 J per 10 mm long line scan lasting 0.02 s.

In case of EDM [1] we use electrical energy to generate the spark between the tool made of copper and a workpiece so that material removal is taking place from the sample surface by local melting or vaporization. EDM pulse generator is set for discharge voltage from 80 V to 30 V with calculated charging time = 4.7∗10e-5 s and discharge time = 9.8∗10e-9 s. We use processing time from 100 to 2200 s to erode 10 mm long and 1 mm wide grooves. Deposited energy for such grooves ranges from 10 to 220 J.

For mapping of the modified samples we use two quadrupole-type mass analyser systems: SIMS and glow discharge mass spectrometry (GDMS). Using the two techniques of imaging one can acquire a quantifiable image of the elemental distribution from a sample's surface.

SIMS maps are registered due to scanning of a 100 nA, 5 keV O_2^+ beam over area of 3x3 mm, in the Hiden SIMS Workstation apparatus [2], while GDMS maps are obtained with SMWJ-01 system [3], in which the glow discharge of 0.8 mA current at a voltage of 1.2 kV DC is used. GDMS measurements are carried out by moving the sample line by line in the range of 7x7 mm above the stationary cell of the glow discharge.

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BS-TuP-9 High-throughput Therapeutic Drug Monitoring of Immunosuppressive Drugs using Tungsten Disulfide-based Laser Desorption Ionization, *Sunho Joh, H. Na, J. Son, A. Lee,* Korea Research Instutue of Standards and Science (KRISS), Republic of Korea; *C. Ahn,* Yonsei University, Korea, Korea (Democratic People's Republic of); *D. Ji,* Yonsei University, Korea; *J. Wi,* Hanbat National University, Republic of Korea; *M. Jeong,* Hanyang University, Korea; *S. Lee,* Yonsei University, Korea; *T. Lee,* Korea Research Instutue of Standards and Science (KRISS), Republic of Korea

Transition metal dichalcogenides are promising candidates for alternative matrix-assisted laser desorption and ionization (MALDI) matrices owing to their excellent physicochemical properties.[1,2] Characteristics of tungsten disulfide (WS_2) such as strong UV absorbance, direct bandgap, low thermal conductivity and high electron mobility are conducive to serve as an effective inorganic matrix; however, its application in mass spectrometry (MS) is rarely reported.[3,4] Here, we present a sensitive time-of-flight (TOF) MS platform by utilizing WS_2 nanosheet-assisted laser desorption ionization (LDI) for quantitative analysis of immunosuppressive drugs in the blood of organ transplant patients. By adopting a micro-liquid dispensing inkjet microarray system, high-throughput analysis of the patient samples with enhanced sensitivity and reproducibility was achieved. To evaluate the performance of our LDI-MS platform, up to 80 cases of patient samples

were analyzed and the results were compared with those of liquid chromatography tandem mass spectrometry (LC-MS/MS). The results obtained by inkjet-printed WS_2-assisted LDI-MS were in good agreement with those of LC-MS/MS while being rapid and cost-effective. Our advanced material and method will facilitate therapeutic monitoring of blood samples from a large number of patients for accurate immunosuppressive drug prescriptions.

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Keywords: Tungsten Disulfide, Laser desorption ionization, Therapeutic drug monitoring, Nanosheets

BS-TuP-11 Tof-Sims Imaging of Organic and Minerals Matters in Primitive Meteorites, *Manale Noun,* Lebanese Atomic Energy Commision, NCSR, Lebanon*; Y. Arribard,* Institut d'Astrophysique Spatiale, Université Paris-Saclay, France*; S. Della-Negra,* IJCLab, CNRS/IN2P3, Université Paris-Saclay, France*; R. Brunetto,* Institut d'Astrophysique Spatiale, Université Paris-Saclay, France*; D. Baklouti,* Institut d'Astrophysique Spatiale, Université Paris-Saclay, France, , France

Introduction:

The primitive organic matter of the chondrites is a witness to the early stage of the Solar System.Their investigations aid in understanding critical issues in astrochemistry and astrophysics. In this work, we present the study of organic and inorganic matters of differently altered CM chondrites (Cold Bokkeveld [1] and Paris [2,3] directly analyzed without any chemical extraction by TOF-SIMS technique [4,5].

Materials and methods:

Millimetric unpolished fragments of the two meteorites were measured using an ION-TOF V mass spectrometer. Areas of 500 µm*500 µm were analyzed using a bismuth clusters beam of 2 µm of spatial resolution. Cleaning with argon clusters was performed systematically prior to the analyses according to an established previous protocol [5].

Results and discussion:

The goal of this research is to understand the effect of the aqueous alteration process, which will lead to a better understanding of the hydrothermal processes in the parent asteroids. The SIMS imaging highlight some differences between the composition of the two meteorites. The Cold Bokkeveled sample shows that the "CN^- and CNO^-" fragments are prevalent throughout the sample and are due to organic compounds. While the Paris meteorite demonstrates that these fragments are only found throughout the matrix and are due to sodium and potassium cyanide salts, as well as nitrogen-rich organic matter. Moreover, the comparison of the "H/C" ratio to the number of carbon in the two meteorites reveals that the Cold Bokkeveld has less hydrogenated fragments and a more aromatic, olefinic and/or cross-linked structure. This relationship between aromatization and aqueous alteration is consistent with previous studies [6].

Conclusion

TOF-SIMS measurements allow to highlight the aromatization and the decrease of aliphatic chains with the increase of aqueous alteration. The application of this analytical approach to various altered chondrites levels permits more comprehension of the asteroid alteration processes.

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BS-TuP-13 Time of Flight Secondary Ion Mass Spectrometry (ToF SIMS) Analysis of Porous Transport Layers for Proton Exchange Membrane Water Electrolyzers, *Genevieve Stelmacovich, M. Walker,* Colorado School of Mines*; D. Cullen ,* Oak Ridge National Laboratory*; S. Ware, T. Schuler, G. Bender,* National Renewable Energy Laboratory*; A. Paxson ,* Plug Power*; S. Pylypenko,* Colorado School of Mines

As the United States strives to develop a hydrogen-based energy infrastructure, there is a heavy industrial focus on the optimization and scale up of reliable hydrogen production. A promising system for large-scale hydrogen production is the proton exchange membrane water electrolyzer (PEMWE). Unfortunaly, there are still major advances that need to be made with both cost efficiency and durability before PEMWE's can be used on a commercial scale. In PEMWE's, the porous transport layer (PTL) contributes to a large percentage of overall cell cost. Due to the harsh operating conditions of the anode, protective coatings are applied to the PTLs, but the use of noble metals leads to cost concerns. Additionally, the degradation of coated PTLs at various operating conditions is not well understood. As the hydrogen production industry continues to try to improve the PTL, and ensure reliable operation of the device over long-term, advanced physicochemical characterization at various stages of fabrication and testing is vital to improve durability and meet cost targets.

Currently, the state-of-the-art characterization technique to analyze PTL's and their respective protective coatings is Focused Ion Beam Scanning Electron Microscope, Scanning Transition Electron MicroscopeEnergy Dispersive X-ray Spectroscopy(FIB-SEM STEM-EDS). This technique is labor and time intensive and only targets a small area of the PTL, thus is an impractical technique to rely on for industrial testing. This talk will introduce ToF SIMS as a promising technique for the characterization of PTLs with focus on protective coatings and interface between coating and PTL. This presentation will highlight the benefits of this technique in comparison to current techniques, as well as discuss challenges with optimization of ToF SIMS for these morphologically challenging samples.

Thursday Afternoon, September 22, 2022

Beyond SIMS
Room Great Lakes C - Session BS+SS-ThA2

Polymers & Multi-Technique

Moderators: **Andrew Giordani**, Procter & Gamble Company, **Michaeleen Pacholski**, Dow Chemical Company

2:00pm **BS+SS-ThA2-1 Multidimensional Chemical Imaging of Polymeric Materials Using TOF-SIMS with GCIB Sputtering**, *Paul Vlasak*, M. Clark, R. Drumright, J. Harris, M. Pacholski, H. Ying, Dow **INVITED**
Time-of-Flight Secondary Ion Mass Spectrometry (TOF-SIMS) aided by gas cluster ion beam (GCIB) sputtering has become an important tool for studying morphology of polymer systems. While electron microscopy (EM) remains a workhorse approach, SIMS allows specific detection of low concentration components such as additives, catalysts, colorants, or crosslinkers that are not easily detected by other methods, and 3D SIMS imaging can reveal how these trace components are distributed relative to the overall morphology of multiphase systems. While SIMS cannot yet match the ultimate spatial resolution of EM methods, these results have been critical to orient the electron micrographs by identifying features directly based on mass spectrometry that would otherwise be differentiated only by single channel contrast mechanisms, often relying on heavy metal staining strategies. Because the 3D SIMS depth profiles can be acquired reasonably quickly over relatively large areas, SIMS can identify features existing on larger length scales and verify uniformity in a single analysis whereas similar information obtained by EM would require preparing and imaging many cross-sections.

This presentation will highlight an industrially important multiphase polymer system. In this example, complex coating phase morphology existing on the single micron scale shifts dramatically with changes in proportions of the raw materials or with the addition of various compatibilizers, sometimes at low concentration. These coatings derived from polyolefin dispersions (POD's) have been developed as an attractive alternative to coatings from bisphenol A based epoxies for next generation aluminum beverage can interior linings. Various compatibilizers and dispersants with polar functionalities are compounded with the nonfunctional polyolefin resins to achieve stable waterborne emulsion formulations. Key performance requirements demonstrated by POD derived coatings include superior adhesion to the aluminum surface, effective barrier properties, and preservation of the canned products' flavor. These properties, including flavor scalping, or the absorption of key flavorants from the beverage into the coating, are influenced by coating morphology.

2:40pm **BS+SS-ThA2-5 Mixed Actinide Glasses as Working Reference Materials for Spatial Analyses**, *David Willingham*, J. Matzel, P. Weber, Lawrence Livermore National Laboratory; *E. Groopman,* National Institute for Science and Technology (NIST); *D. Weisz, J. Wimpenny, J. Caseres, K. Knight,* Lawrence Livermore National Laboratory
Secondary ion mass spectrometry (SIMS) has long been applied to the analysis of isotopic heterogeneities in nuclear materials. Few other methodologies challenge the ability of SIMS to measure the isotopic composition of nuclear materials with high accuracy and precision with micrometer/nanometer spatial resolution. While a number of certified/standard reference materials exist for bulk actinide concentration and isotopic analytical techniques, there are few, if any, working reference materials available for spatially resolved analyses, such as SIMS. These working reference materials must be well-characterized for actinide concentration and isotopic composition, homogeneous at the lateral resolution appropriate for the application, and representative of the real-world elemental concentrations and isotopic compositions of the materials of interest.

For this study, two working reference materials were developed in a glassy matrix containing both uranium and plutonium. The first, UPI, was composed of 496 ppm of uranium with a ^{235}U enrichment of 92.3% and 50 ppm of plutonium with a ^{240}Pu/^{239}Pu ratio of 0.0054 ± 0.00001. The second, UPO, was about 8x less concentrated than UPI and was composed of 60 ppm of uranium with a ^{235}U enrichment of 79.6% and 8 ppm of plutonium with a ^{240}Pu/^{239}Pu ratio of 0.05541 ± 0.00001. In addition to SIMS analyses, these glasses were analyzed by traditional bulk methods to determine their elemental concentrations and isotopic compositions. These methods include chemical dissolution of the bulk glasses following the principles of Isotope Dilution Mass Spectrometry (IDMS) and Inductively Coupled Plasma – Mass Spectrometry (ICP-MS).

In addition to traditional SIMS, these mixed actinide glasses were analyzed by the Naval Ultra-Trace Isotope Laboratory's Universal Spectrometer (NAUTILUS) developed at the U.S. Naval Research Laboratory, which combined the best attributes of SIMS and Single-Stage Accelerator Mass Spectrometry (SSAMS). The NAUTILUS is comprised of a SIMS instrument that provides micrometer resolution ion imaging and high precision isotope ratio measurements couple to a SSAMS that enables the dissociation of molecular isobaric interferences common to mass spectrometry.

3:00pm **BS+SS-ThA2-7 An Overview of Automotive Coatings and the Analytical Tools that Drive Innovation**, *Sabrina Peczonczyk*, N. Hosking, C. Peters, T. Misovski, C. Seubert, M. Nichols,* Ford Motor Company
The development and implementation of high-quality, robust automotive coatings requires a critically fundamental understanding of coating properties, process conditions, and durability in automotive environments. To achieve this Ford Motor Company employs a suite of surface analytical techniques and expertise. This talk will focus on the use of Auger electron spectroscopy (AES), time-of-flight secondary ion mass spectrometry (ToF-SIMS), and x-ray photoelectron spectroscopy (XPS) for the evaluation of automotive coatings. Case studies highlighting applications in Research and Development and Corporate Support will be discussed.

Beyond SIMS
Room Great Lakes C - Session BS+SS-ThA4

Multi-Technique

Moderator: **Andrew Giordani**, Procter & Gamble Company

4:00pm **BS+SS-ThA4-13** *In Operando* **Correlated Studies in Energy Materials** *via* **Combined Afm/Tof-Sims Platform**, *Anton V. Ievlev,* Oak Ridge National Laboratory, USA
The performance of energy storage and conversion devices, including batteries, fuel cells, and photovoltaics, is defined by the delicate interplay of electrical response and charge carrier migration at the nanoscale. Although physical behavior and macroscopic functional response is well established, intrinsic chemical phenomena associated with ionic motion or localized electrochemical reactions can dramatically alter behavior and restrict utility of these materials. Over the last decade, advancements in development of novel characterization tools such as atomic force microscopy (AFM) have revolutionized our understanding of the electrical and mechanical response of materials; however, *dynamic* electrochemical behavior and ion migration remain poorly understood. Recently time-of-flight secondary ion mass spectrometry (ToF-SIMS) has proven to be effective tool for characterization of static chemical states in energy materials. However, its application to study of dynamic electrochemical processes still requires development.

Here we introduce approach based on combined AFM/ToF-SIMS platform for correlated studies of the dynamic chemical phenomena on the nanoscale in operando conditions. Being used for characterization of the perovskite materials it allowed direct observation of the ionic migration within the device in externally applied electric fields, which is important for fundamental understanding of the material functionality. Similarly, this approach allowed to study relaxation processes of the chemical phenomena in ferroelectric materials as a function of sample temperature. Altogether, developed approach enables direct characterization of interplay between chemical and functional response in energy materials and aids in the development and optimization of novel devices.

4:20pm BS+SS-ThA4-15 Adsorption Differences of Organic Molecules on the Metal Oxide Surfaces, *Aydan Yadigarli, S. Mohajernia, M. Killian,* Chemistry and Structure of new Materials, Siegen University, Germany*; M. Aktan,* Department of Materials Science and Engineering, KU Leuven, Belgium*; A. Braem,* Department Materials Science and Engineering, KU Leuven, Belgium

Tuning the surface properties of metal oxide allows to obtain an improved surface with new functionalities without compromising on the bulk properties of a substrate. Modification of oxide surfaces with self-assembled monolayer (SAM) has been introduced for advanced applications by changing the wettability, biocompatibility, adhesion, dye-sensitization, and chemical reactivity of the surface. The adsorption efficiency of SAMs on metal oxide surfaces depends on the molecular head group and inherent properties of metal oxide. Solution pH value influences the prevalent surface charging of metal oxides, which can be positive or negative depending on the isoelectric point (IEP) of the metal itself. Positively/negatively charged metal oxide surfaces lead to an attractive interaction with the negatively/positively charged functional head groups dissociated in the solution. In this study, the affinity of organic molecules with a selected range of specific head groups (carboxylic acid and amine) to metal oxides (TiO_2 and NiO) that are varying with their IEP was investigated. Compact metal oxides were formed by electrochemical anodization method and their IEP was found by zeta-potential measurement. Time of flight secondary ion mass spectrometry (ToF-SIMS) and X-ray Photoelectron spectroscopy (XPS) were used to confirm the chemically binding of the organic molecules. The coverage of the metal oxide surfaces was evaluated by contact angle measurement. The adsorption affinity of organic molecules has shown a relatable trend with the IEPs of the metal oxides.

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SIMS Solutions in Materials and Life Sciences
Room Great Lakes B - Session SS+BS+FM-ThA3

High Resolution and MS/MS Methods III
Moderator: Gregory Fisher, Physical Electronics USA

4:20pm SS+BS+FM-ThA3-15 A Fine Analysis of the Composition of Organic-inorganic Complex Layers of Cross-sections from Old Paintings by TOF-SIMS Imaging, Enlightened by MS/MS and Orbitrap, *Alain Brunelle, C. Bouvier,* LAMS, Sorbonne Université, CNRS, France*; S. Kayser, A. Pirkl, E. Niehuis,* IONTOF GmbH, Germany*; P. Walter,* LAMS, Sorbonne Université, CNRS, France

When painting, an artist works with diverse mixtures of pigments and binders, which he layers in expert gestures to achieve the intended rendering. The mastery of the binder properties allows him to exploit their possible optical effects, with layers which can be down to a few micrometers thick. Ancient paintings are several centuries old, during which the various heterogeneous mixture of inorganic and organic compounds have interacted with each other and with their environment. Sub-millimeter scale cross-sections of the painting, removed with a blade, offer simultaneous access to all the layers. Such samples are fragile, unique and should be kept as intact as possible to allow subsequent examinations using different analytical techniques.

TOF-SIMS imaging enables the localization and identification of both pigments and organic materials, providing submicron indications of their nature, origin, or state of preservation.[1] With a TOF-SIMS IV instrument, a spatial resolution down to 400 nm can be reached, while preserving mass resolution, in the so-called delayed extraction mode.[2] The identification of binders can nevertheless be ambiguous, since organic materials detected may also be degradation products or surface contaminants. Local optimization of the analysis parameters on small analyzed areas and knowledge of the expected characteristic ions for each binder type proved to be of further importance to avoid erroneous conclusions.[3] Moreover, additional analyses using much more powerful instruments, namely M6 with tandem MS analysis and M6 Hybrid SIMS with Orbitrap™ analyzer, can remove many ambiguities. This is particularly the case when high mass

resolution and accuracy are required in conjunction with maintaining lateral resolution in the micrometer range.

Examples will be given with the compositions of fine layers in ancient paintings analyzed in this way. On the one hand, the analysis of samples from the *Infant Bacchanals* (Nicolas Poussin, 1626, Museo Nazionale d'Arte Antica, Rome) has shown that a fine surface layer alters the final appearance of the painting, making it look like a tempera painting, when in fact it is an oil painting underneath. On the other hand, analyses with the modern M6 instruments of cross-sections from the *Ecce Homo* (Titian, 1547, Museo del Prado, Madrid) have provided evidence of a fine inner organic layer, likely made of egg white, and have also shown the presence of a red lake pigment.

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4:40pm SS+BS+FM-ThA3-17 How Do Water Clusters Work? Insight from Molecular Dynamics Simulations, *M. Kański, S. Hrabar, C. Chang, Zbigniew Postawa,* Jagiellonian University, Poland

The introduction of water clusters $(H_2O)_n$ to SIMS opened new possibilities in analyzing biological samples. The main advantage of the water clusters is an increase in ion yield by more than an order of magnitude compared to argon clusters of similar size and kinetic energy. The mechanism behind this effect is unknown, though. It has been theorized that a semi-aqueous environment is created in the impact site, which would promote ion creation [1].

We performed molecular dynamics (MD) computer simulations to study the behavior of water clusters that impact the surface of trehalose. Four water clusters consisting of 4000, 7000, 10000, and 25000 molecules had been chosen. The total kinetic energy of each projectile was the same, equal to 20 keV, so the results of the simulations could be compared with the experimental observations [1]. We observed three different projectile behaviors depending on their size (or kinetic energy per molecule). The $(H_2O)_{4000}$ cluster fragments into individual molecules during impact, as do argon clusters of similar size. Decreasing the kinetic energy per molecule (or increasing cluster size) leads to the emission of trehalose molecules enveloped in a partial water shell. The largest projectile bounces from the surface while dissolving trehalose molecules in it. During the presentation, we will discuss the importance of this shifting behavior. Finally, we will show that the amount of emitted water-trehalose complexes correlates with the ion yield observed experimentally.

[1] S. Sheraz (née Rabbani) et al., Anal. Chem. 2019, 91, 9058–9068

5:00pm SS+BS+FM-ThA3-19 *In situ* identification, imaging and depth profiling of proteins using 3D OrbiSIMS, *David Scurr,* School of Pharmacy, The University of Nottingham, UK   **INVITED**

In situ identification of proteins at surfaces has potential applications in areas crucial to health, medicine and medical device development, however, it commonly requires digestion and/or matrix application prior to mass spectrometry. Secondary ion mass spectrometry (SIMS) can potentially overcome these limitations but the analysis of proteins has previously been limited due to fragmentation resulting in only single amino acid secondary ions, devoid of primary structural information.

Employing a gas cluster ion beam (GCIB) moderates fragmentation, resulting in multi amino acid fragments in peptide spectra and molecular ions from proteins up to 12 kDa, however, this method has not been successfully applied for larger proteins. Here we use the 3D OrbiSIMS technique which combines a GCIB and an Orbitrap™ analyser, to achieve *in situ* label and matrix-free 3D mapping of undigested proteins at surfaces. We successfully applied *de novo* sequencing for identification of proteins using fragments generated by the GCIB. We analysed 16 model protein films in a range of sizes from insulin (6 kDa) to fibronectin (272 kDa), achieving amino acid sequence coverages up to 53%. The obtained spectra contain b and y ions, common to low energy collision induced ionisation (CID) and a, c and z ions characteristic to other methods of ionization such

as electron capture dissociation (ECD). Similarly, ions observed in negative polarity 3D OrbiSIMS spectra are deprotonated N terminus a, b, c ions and deprotonated C terminus y, z-H and x ions. The 3D OrbiSIMS imaging capability was demonstrated by masking a protein film with a transmission electron microscopy grid, achieving lateral resolution of 10 μm. Additionally we assigned highly specific protein ions in a monolayer biochip sample. Finally, we successfully assigned characteristic peptide sequences from collagen, keratin and corneodesmosin within the depth profile through human skin.

These findings demonstrate a breakthrough approach employing 3D OrbiSIMS to identify proteins by direct surface analysis with minimal manipulation of sample [1].

[1]. Kotowska et al., *Nature Communications*, **11** (1), 2020

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Kayser, S.: RA+BS+FM+SS-TuM2-13, **2**; SS+BS+FM-ThA3-15, 8
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Kim, Y.: BS-TuP-1, 5
Knight, K.: BS+SS-ThA2-5, 7
Konarski, P.: BS-TuP-7, **5**
Kovac, J.: RA+BS+FM+SS-TuM2-9, 1
— L —
Lauzin, C.: RA+BS+FM+SS-TuM2-7, 1
Lee, A.: BS-TuP-9, 5
Lee, S.: BS-TuP-9, 5
Lee, T.: BS-TuP-9, 5
Liu, R.: BS+FM+SS-TuA2-15, 4
— M —
Matsuo, J.: RA+BS+FM+SS-TuM2-1, **1**
Matzel, J.: BS+SS-ThA2-5, 7
Misovski, T.: BS+SS-ThA2-7, 7
Miwa, S.: BS+FM+SS-TuA2-15, 4
Mohajernia, S.: BS+SS-ThA4-15, 8
Monaci, L.: BS+FM+SS-TuA2-19, 4
— N —
Na, H.: BS-TuP-9, 5
Nichols, M.: BS+SS-ThA2-7, 7
Niehuis, E.: SS+BS+FM-ThA3-15, 8
Noun, M.: BS-TuP-11, **6**
— P —
Pacholski, M.: BS+SS-ThA2-1, 7
Paxson , A.: BS-TuP-13, 6
Peczonczyk, S.: BS+SS-ThA2-7, **7**
Peres, P.: BS+FM+SS-TuA2-15, 4
Peters, C.: BS+SS-ThA2-7, 7
Pilolli, R.: BS+FM+SS-TuA2-19, 4
Pirkl, A.: RA+BS+FM+SS-TuM2-13, 2; SS+BS+FM-ThA3-15, 8

Poleunis, C.: RA+BS+FM+SS-TuM2-7, 1
Postawa, Z.: SS+BS+FM-ThA3-17, **8**
— R —
Rading, D.: RA+BS+FM+SS-TuM2-13, 2
Ren, J.: BS+FM+SS-TuA2-15, 4
— S —
Schneider, P.: RA+BS+FM+SS-TuM2-5, 1
Schuler, T.: BS-TuP-13, 6
Schweikert, E.: BS+FM+SS-TuA2-13, **3**
Scurr, D.: SS+BS+FM-ThA3-19, **8**
Seubert, C.: BS+SS-ThA2-7, 7
Sheu, D.: BS-TuP-7, 5
Siketic, Z.: RA+BS+FM+SS-TuM2-9, **1**
Son, J.: BS-TuP-9, 5
Spampinato, V.: RA+BS+FM+SS-TuM2-13, 2
Srut Rakic, I.: RA+BS+FM+SS-TuM2-9, 1
Stelmacovich, G.: BS-TuP-13, **6**
— T —
Tomasetti, B.: BS+FM+SS-TuA1-17, 3; RA+BS+FM+SS-TuM2-7, 1
Tsikritsis, D.: BS+FM+SS-TuA1-19, 3
Tyagi, V.: BS+FM+SS-TuA1-19, 3
— V —
Vakamulla Raghu, S.: BS-TuP-3, **5**
Van Nuffel, S.: BS+FM+SS-TuA1-13, **3**
Verkhoturov, D.: BS+FM+SS-TuA2-13, 3
Verkhoturov, S.: BS+FM+SS-TuA2-13, 3
Verloh, F.: RA+BS+FM+SS-TuM2-5, 1
Vincent, D.: BS+FM+SS-TuA1-17, 3
Vlasak, P.: BS+SS-ThA2-1, **7**
Vorng, J.: BS+FM+SS-TuA1-19, **3**
— W —
Walker, A.: BS+FM+SS-TuA2-17, **4**
Walker, M.: BS-TuP-13, 6
Walter, P.: SS+BS+FM-ThA3-15, 8
Ware, S.: BS-TuP-13, 6
Weber, P.: BS+SS-ThA2-5, 7
Weisz, D.: BS+SS-ThA2-5, 7
Wi, J.: BS-TuP-9, 5
Willingham, D.: BS+SS-ThA2-5, **7**
Wimpenny, J.: BS+SS-ThA2-5, 7
— Y —
Yadigarli, A.: BS+SS-ThA4-15, **8**
Ying, H.: BS+SS-ThA2-1, 7
— Z —
Zakel, J.: RA+BS+FM+SS-TuM2-13, 2
Zarmpi, P.: BS+FM+SS-TuA1-19, 3
Zawada, A.: BS-TuP-7, 5
Zhu, Z.: BS-TuP-5, **5**