SIMS School: IUVSTA Short Courses
Room Great Lakes A2-A3 - Session SC-SuP

SIMS School - IUVSTA Short Courses

11:30am **SC-SuP-1 Fundamentals of SIMS - Views from Ground Zero and Beyond***, **Arnaud Delcorte**,* Université Catholique de Louvain, Belgium **INVITED**

An initial particle impact event – "big bang" in the universe of the SIMS aficionados – induces the generation of free and stable ions from solid samples, the signature of which eventually forms a *secondary ion mass spectrum.* The once hypothetical representations and/or qualitative models of this founding event have given way to more quantitative predictions in the last two decades (even for complex samples, e.g. the sputtering yields of argon clusters in organics), owing largely to the progress of molecular dynamics computer simulations. In this short course, the basics of kiloelectronvolt cluster impacts in atomic and molecular solids are reviewed using the magnifying lens of the microscopic models. For instance, (large) cluster and molecular impacts differ radically from single atom impacts in that they systematically induce collective motions in the solid (pressure waves, correlated atomic and molecular motions, crater formation as opposed to "linear cascades"), which make their action resemble (tiny) meteorite collisions. The mechanisms of projectile penetration, energy deposition, atomic motion and damage in the solid, determined in the first few picoseconds of the impact event are described. Beyond the "ground zero" of the cluster impact, the emission of atoms, fragments and molecules are discussed, with an emphasis on the conditions of intact molecular emission and their links to the molecule internal energy uptake and the projectile properties. Finally, the questions of ionization and matrix effects – annoying but central to SIMS – are considered and unresolved fundamental issues are delineated.

12:30pm **SC-SuP-7 SIMS Analysis of Biological Materials***, **Michael J. Taylor**,* Pacific Northwest National Laboratory **INVITED**

1:30pm **SC-SuP-13 SIMS Inorganic Depth Profiling***, **Jerry Hunter**,* University of Wisconsin **INVITED**

3:00pm **SC-SuP-22 Multivariate Analysis Methods for Secondary Ion Mass Spectrometry and Related Techniques***, **Jean-Paul Barnes**,* CEA-Leti, France **INVITED**

The complexity of secondary ion mass spectrometry data can make interpretation difficult and time consuming in many cases. In order to make sense of data sets, many researchers choose to apply multivariate analysis (MVA) methods or more recently machine learning approaches. This short course will give an overview, and the basic principles of the most commonly used multivariate and machine learning methods used for SIMS data, but also for other similar analytical techniques or techniques that are often correlated with SIMS data.

Using such methods may on the one hand seem daunting at first, or on the other hand tempting as a quick-fix to interpret a data set. This course will attempt to demystify the available methods and how to tackle the data acquisition and pre-processing steps in order to obtain reliable multivariate analysis results. We will address practical examples of how to plan a SIMS experiment for multivariate analysis and what can go wrong when trying to use multivariate analysis on data sets that were not initially designed for this purpose.

For example, among the multivariate analysis methods, principal component analysis (PCA) is one of the most employed approaches. This method allows the orthogonal directions (combination of mass channels) of maximum variance in a dataset to be found. This can then be used to identify the chemistry present in a data set and identify areas of different composition in an image, depth profile or group together spectra from different samples that have similar chemistry. Practical examples will be given of how multivariate analysis can be used to solve problems in both a research and an industrial context. In terms of perspectives, the potential of new and emerging algorithms to be applied to SIMS data will be discussed.

4:00pm **SC-SuP-28 SIMS Analysis of Organic Materials with Industrial Applications***, **Michaeleen Pacholski**,* Dow Chemical Company **INVITED**

SIMS analysis is a valuable tool in a large analytical group.In this presentation examples from an industrial lab will be shown highlighting how SIMS fits in to solving the analytical puzzles presented.These will include projects using multiple analytical techniques, projects focusing on adhesion (or lack thereof), combining XPS and SIMS data to understand concentrations, multilayer sample analysis, etc.Since GCIB (gas cluster ion beam) sources are now widely available, SIMS not only aids in surface analysis, but also contributes to our understanding of interfaces through depth profiling.Additionally, tips for setting yourself up for success, from sample preparation to reporting results will be shared.

Plenary Session
Room Great Lakes B - Session PS1-MoM

Plenary Session I

Moderator: Jerry Hunter, University of Wisconsin

8:40am **PS1-MoM-2 Plenary Lecture: Oxygen Isotope Analysis in Carbonates: Accuracy vs. Precision***, **John Valley**, N. Kita, K. Kitajima,* University of Wisconsin-Madison **INVITED**

Carbonate minerals form at a wide range of temperature and pressure, are common on Earth, and found elsewhere in the Solar System. Oxygen isotope ratios ($\delta^{18}O$) in carbonates are a powerful tool to understand the thermal and fluid history of igneous and metamorphic rocks [7], and sedimentary processes including the formation of diagenetic cements ([1] Fig. 1b-d), speleothems, mollusks, foraminifera ([4] Fig. 2b-e), fish otoliths ([2] Fig. 3) and pearls. Most of these samples are zoned at µm-scale and conventional analysis by acid dissolution and gas-source mass spectrometry (GSMS) results in averaged compositions and lost information. Applications such as paleoclimatology, reservoir studies of sedimentary basins and diffusion/kinetics of mineral reaction require SIMS.

SIMS analysis (1-10 µm beam) can be correlated with microscopy (Fig. 1b, 2b-d) and other in situ techniques in images or by QGIS to reveal otherwise unknown correlations and detail. Small pits (<2 µm) are visible with UV optics on IMS-1280. Spot-to-spot precision is improved to 0.2‰ (2SD) in 10 µm spots by appropriate sample preparation, attention to “down-hole” sputtering effects, and frequent standardization, and in smaller spots with a FC amplifier and 10^{12} ohm resistor. However, chemically matched carbonate reference materials (RMs) are necessary for accurate calibration to the international VSMOW or VPDB scales. A suite of 30 inorganic Ca-Mg-Fe carbonate mineral RMs demonstrates that IMF (bias) for $\delta^{18}O$ varies predictably by up to 19‰ at WiscSIMS (IMS-1280) (Fig. 1a); correlated analysis of cations by EPMA allows accurate calibration ±~0.5‰.

In contrast to inorganic carbonates, biocarbonates can have complex textures and contain additional components not amenable to EPMA including water and organics, making calibration by inorganic RMs questionable. SIMS analyses are often offset to lower values than GSMS data. Values of $\Delta^{18}O$(GSMS-SIMS) correlate with $^{16}O^{1}H/^{16}O$ (SIMS) in young biocarbonates ([5] Fig. 2a). Many biocarbonates have relatively constant OH/O and can be corrected with a constant offset [8], but samples with variable OH/O ([2] Fig. 3) should be interpreted with caution.

[1] Denny AC et al. (2020) Chem Geol, 531: 1-20

[2] Helser T et al. (2018) Rapid Comm Mass Spectrometry. 32: 1781-1790

[3] Kita NT, et al. (2011) SIMS XVII Proceedings, 43: 427-431

[4] Kozdon R et al. (2013 Paleoceanography 28:1-12

[5] Orland IJ et al. (2015) AGU Fall Meeting, Abstr. # PP52B-03

[6] Śliwiński MG et al. (2018) Geostand Geoanal Res, 42: 49-76

[7] Valley JW and Kita NT (2009) MAC Short Course. 41: 19-63

[8] Wycech J et al. (2018) Chem. Geol. 483:119-130

SIMS Solutions in Materials and Life Sciences
Room Great Lakes B - Session SS-MoM2

Industrial Applications I

Moderators: Derk Rading, IONTOF GmbH, **Alan Spool**, Western Digital Corporation

10:00am **SS-MoM2-10 The Characteristics of Multi-material Depth Profiles with Low-Energy Atomic and Diatomic Ion Beams and Cluster Ion Beams of Ar and O_2***, **Albert Fahey**, M. Zhang,* Corning Inc. **INVITED**

The newest IONTOF instruments feature several sputter sources that can be used for depth profiling.One of the sources, an O_2-Gas Cluster source, is not commonly used.However, we have found it invaluable when sputtering into insulating materials, like glass, where it is important to preserve the fidelity of the profiles of alkali and other mobile species.Data will be shown illustrating the value of different ion beams for measurements of a variety of species, even at trace levels.

Depth profiles of sputtered coatings are performed commonly, but can be problematic for a variety of reasons, not only due to sputtering artefacts.Use of low energy ion beams and cluster ion beams allows improved resolution and sensitivity.In addition, ToF-SIMS depth profiles can show previously unnoticed contaminants both in the bulk of each layer as well as between layers.Contaminants can be significant if they affect interlayer adhesion and other properties.Some examples will be shown and discussed.

10:40am **SS-MoM2-14 Analysis of Alkali and Trace Species in Silicate Glasses***, **Timothy Dimond**, A. Fahey, C. Mahoney, C. Cushman,* Corning Inc.

Data artifacts associated with insulating materials can present significant challenges for analysis by SIMS. In particular, alkali species can be elusive especially when the use of some common techniques, like O_2^+ sputtering, for promoting ionization have been employed. A societal move towards an interactive glass display world requires chemical alteration by surface treatments and coatings on commonly insulating materials and the need to be able to characterize those surfaces. Several commercially available tools for mitigating charging issues such as the use of an electron gun, gas flooding, and some novel sputtering beams conclude to some best practices for producing viable data when working with insulating materials, in particular silicate glasses and oxide thin films. Some practical explanations of these tools being used to generate HR imaging, quantitative depth profiles, and other practical data will be discussed to promote their efficacy in a growing interactive glass display industry. Our results show the use of oxygen Gas Cluster Ion Beam (GCIB) and Cs sputtering to enable ideal conditions for most positive mode analyses in silicates and other oxides.

11:00am **SS-MoM2-16 TOF-SIMS Surface Hydroxyl Measurements on Multicomponent Glasses***, **Cody Cushman**, N. Smith, J. Banerjee, C. Mahoney, A. Fahey, T. Dimond,* Corning Incorporated*; M. Linford,* Brigham Young University

Surface hydroxyls (primarily Si-OH) are thought to govern surface mediated properties and processes on multicomponent glass surfaces including particulate adhesion, surface contamination, and water adsorption. While ToF-SIMS protocols for measuring surface hydroxyls have been previously reported, they have seldom been applied to multicomponent glass surfaces. In this presentation, we will discuss ToF-SIMS surface hydroxyl measurements as applied to calcium aluminosilicate glass, including measurement reproducibility, fundamental measurement limitations, and the influence of hydrocarbon surface contamination on these measurements. Further development of ToF-SIMS surface hydroxyl measurements will ultimately provide a powerful tool for understanding the fundamental surface science of glasses and oxides.

11:20am **SS-MoM2-18 Dynamic SIMS Imaging of Impurities in Cold Spray Copper Coating***, **Jonas Hedberg**,* Surface Science Western, Western University, London, Ontario, Canada*; F. Filice, X. Li,* Department of Chemistry, Western University, London, Ontario, Canada*; S. Ramamurthy,* Surface Science Western, Western University, London, Ontario, Canada*; J. Noël,* Department of Chemistry, Western University, London, Ontario, Canada*; M. Behazin, P. Keech,* Nuclear Waste Management Organization, Toronto, Ontario, Canada

The Nuclear Waste Management Organization (NWMO) in Canada is developing and implementing a strategy for safe disposal of used nuclear fuel. The proposed multi-barrier system includes metallic used fuel containers surrounded by highly compacted bentonite buffer boxes. These containers will be emplaced in a deep geologic repository located at a depth of about 500 m in a suitable host rock. The current NWMO UFC design specifies a 3 mm copper (Cu) corrosion barrier, applied by electrodeposition and cold spray (CS) technologies onto a low alloy steel inner vessel. The cold spray coating will be applied on-site after the used fuel bundles are placed inside the container and the lid is welded shut.

Cold spray coating is produced by impingement of Cu power at a high velocity on the container surface. Adhesion is through the plastic deformation of Cu particles. The Cu powders used for CS coating can contain both metallic (Fe, Bi, Pb, Sn, Zn, and Ag) and non-metallic (O, S, C, N, and P) impurities. Even when present in trace quantities, some of the impurities may precipitate within the grain boundaries and affect the corrosion behavior of Cu coating. Hence, a major objective of this study is to determine the corrosion behavior of CS Cu coating containing known amounts of various impurities and determine acceptable tolerances for the CS Cu coatings.

Cold spray Cu coatings containing known amounts of O, S, and Fe, were applied on steel plates. Dynamic secondary ion mass spectrometry (DSIMS) was used to analyze the coated samples because the impurities were present at very low levels (~100 to 700 ppm). The DSIMS results showed that all CS Cu samples exhibited oxygen enrichment at the Cu particle boundaries, regardless of oxygen content of the Cu power used for CS Cu coating. The DSIMS images were complemented with accelerated corrosion measurements, which indicated that increased oxygen content in Cu increased the tendency for corrosion under aggressive conditions.

DSIMS images for sulfur were mainly focused on the results from 34S due to the possible overlaps with molecular ions of oxygen (16O2) for the 32S mass. Sulfur images showed stronger signals from the samples with added sulfur as well as the standard CS Cu without any impurities. However, further work is needed to determine the distribution of S within CS Cu coatings and its effect on Cu corrosion behavior.

In summary, DSIMS imaging is a valuable tool in assessing the presence and the distribution of trace amounts of impurities in CS Cu coating. SIMS images were also useful in understanding the observed corrosion behavior of CS Cu.

11:40am **SS-MoM2-20 Surface Characterization of High Entropy Alloys with Sea Water and Sulfuric Acid Corrosion Test Using Hard X-Ray Photoelectron Spectroscopy and Time-of-Flight Secondary Ion Mass Spectroscopy***, **Hsun-Yun Chang,*** ULVAC-PHI, Inc., Taiwan*; W. Lin,* Department of Photonics, National Sun Yat-sen University, Taiwan*; G. Fisher,* Physical Electronics*; S. Iida,* ULVAC-PHI, Inc., Japan

High entropy alloys (HEAs) are known to be composed of five or more principle elements with concentration commonly in equal or near-equal atomic percent. The application of HEAs has substantially gained attention in recent years due to greater fracture resistance, tensile strength and corrosion resistance than conventional alloys. Researchers have developed HEAs with various components in order to strengthen the desirable mechanical or other properties for industrial applications, such as nuclear and aerospace fields. Corrosion resistance is one of important properties to design novel HEA materials, because the cost of corrosion is known to decrease the gross domestic product (GDP) and has no good to economic benefit of industries. With the entropy increase of a larger number of elements in the mix, HEAs shows a stable solid solution phase with no intermetallic phases. The random arrangement of multiple elements results in a particular locally-disordered chemical environment, which leads to unique corrosion-resistance properties. To investigate the corrosion behavior of designed HEA materials, surface characterization on the corrosion area of HEAs is necessary. In this work, hard X-ray photoelectron spectroscopy (HAXPES) and time-of-flight secondary ion mass spectroscopy (ToF-SIMS) are utilized to examine the corrosion behaviors of a commercial AlFeCoCrNi (AFCCN) HEA under sea water or sulfuric acid treatment. Using HAXPES analysis, the greater energy range (Cr Kα 5414.8 eV) allows us to study the chemical state of alloys without Auger peaks interference in conventional XPS. Also its deeper detection depth (~30 nm) enables us to examine the thicker surface oxidized/passivated layer of corrosion area without the concern of sputter damage. Using ToF-SIMS analysis, the chemical imaging and the surface morphology of HEAs corroded area can be observed. With the information of chemical state quantification and chemical imaging, the combination of HAXPES and ToF-SIMS analyses facilitates better understanding on the variation of HEAs surface before and after corrosion.

12:00pm **SS-MoM2-22 Understanding the Retention and Distribution of Anti-Microbial Compounds on Solid Surfaces***, **Michael Clark, Jr.,*** Dow, Core R&D Analytical Science*; D. Miller, A. Jayaraman,* Dow, Core R&D Formulation, Automation & Material Science*; A. Karikari, C. Schultz,* Dow Home and Personal Care*; B. Cressman,* Dow, Core R&D Analytical Science

Disinfection of surfaces has been of great interest over the past two years due to the onset of the coronavirus disease (COVID-19) pandemic.Most commercial surface disinfectant products contain a cationic surfactant as their active ingredient along with other formulation components. This presentation will focus on the application of X-ray photoelectron spectroscopy and secondary ion mass spectrometry technologies to understand how the application method and formulation modifications influence the retention and distribution of the active ingredients across glass surfaces. Such information will aid in the design of commercial disinfectants.

SIMS Solutions in Materials and Life Sciences
Room Great Lakes C - Session SS-MoM3

Energy Storage I

Moderator: Andrew Giordani, Procter & Gamble Company

10:00am **SS-MoM3-1 SIMS Study of Interfacial Degradation in Lithium Thiophosphate-Based Composite Cathodes for All-Solid-State Lithium-ion Batteries*, Felix Walther,*** *J. Sann, J. Janek, M. Rohnke,* Institute of Physical Chemistry, Justus Liebig University Giessen, Germany

All-solid-state lithium-ion batteries (ASSBs) have gained strong attention in recent years, as they are considered one of the most promising candidates for future energy storage devices. By replacing the liquid electrolyte in conventional lithium-ion batteries (LIBs) with a solid, lithium metal could be enabled as anode material, which in turn could lead to higher energy densities compared to conventional LIBs. At the same time, safety aspects could be improved, since flammable organic electrolytes are avoided, making ASSBs highly attractive for the mobility sector. Particularly lithium thiophosphate-based solid electrolytes are considered promising, as such materials typically exhibit a high ionic partial conductivity and advantageous mechanical properties (i.e., malleability) for large-scale industrial processing. However, several problems remain to be solved before this technology can be transferred to practical application. On the positive electrode side, interfacial reactions of the cathode active material with the thiophosphate solid electrolyte are one of the main reasons for strong capacity loss and poor long-term stability. Although it is known that coatings on the cathode active material have a positive effect on such interfacial reactions, the underlaying mechanisms (with and without coating) are still largely unknown.

In this work, we show that the combination of the complementary methods ToF-SIMS and XPS is very powerful to study degradation phenomena in $LiNi_xCo_yMn_zO_2$- and lithium thiophosphate-based composite cathodes [1-3]. ToF-SIMS in particular plays a key role in this context, as it can provide detailed insights beyond the detection limit of XPS. Next to surface analysis and depth profiling, ToF-SIMS analysis was performed on FIB crater sidewalls to verify the results obtained and to identify the individual strengths/weaknesses of the respective type of measurement for this analytical task. Overall, we were able to distinguish between various reaction zones within the composite cathode by imaging mass spectrometry and could provide detailed information on the respective degradation products. Based on this knowledge, we studied the positive effect of a protective coating and were able to correlate the enhanced ASSB cell performance with the reduction of specific degradation products. These results can help to further optimize protection concepts for composite cathodes, which is an essential step on the way to long-term stable ASSBs.

[1] F. Walther et al. *Chem. Mater.* **2019**, *31* (10), 3745–3755.
[2] F. Walther et al. *Chem. Mater.* **2020**, *32* (14), 6123–6136.
[3] F. Walther et al. *Chem. Mater.* **2021**, *33* (6), 2110–2125.

10:20am **SS-MoM3-3 The Effect of Electric Double Layer on Formation of Solid-Electrolyte Interphase in Li Ion Batteries*, Zihua Zhu,*** *C. Wang,* PNNL

The solid–electrolyte interphase (SEI) dictates the performance of most Li Ion batteries, but the understanding of its formation mechanism is limited by the lack of in situ experimental tools. Recent years, it has been reported that the batteries with more fluorine components in SEI can perform better than the batteries with less fluorine components in SEI. Therefore, an interesting question is how to increase fluorine in SEI. One way is using high concentration electrolytes, in which the anions contain fluorine. The other way is using fluorine-containing electrolytes. In this work, we used unique in situ liquid SIMS to show an electric double layer can form before formation of SEI, even using a high concentration electrolyte. Formation of such an electric double layer repulses anions away from the electrode surface, leading to a fluorine depleted SEI. Therefore, using fluorine-containing electrolytes should be a better idea because electrolyte molecules are neutral and will not be repulsed away from electrode surface after formation of an electric double layer. Such a result strong supports the recent development of fluorine-containing electrolytes.

10:40am **SS-MoM3-5 Novel Strategy for the Cycling Analysis of Polymer-Based Electrolyte for All-Solid-State Lithium Ion Batteries Using ToF-SIMS***, C. Mawélé Loudy,* Université de Pau et des Pays de l'Adour, France*; G. Godillot, C. Navarro,* ARKEMA France, Groupement de Recherches de Lacq, France*; A. Bonnet,* ARKEMA France, Usine de Pierre Bénite, France*; L. Rubatat, J. Allouche, H. Martinez,* ***Cécile Courrèges***, Université de Pau et des Pays de l'Adour, France

Among the wide family of all-solid-state batteries (ASSBs) technology, polymer-based electrolytes have emerged as good candidates for the design of electrolytes for electrical cars and electronic devices.[1]In contrary to liquid electrolytes, polymer-based electrolytes exhibit less reactions with electrodes and are non-flammable. In addition, polymer-based electrolytes are likely to decrease or suppress lithium dendrites growth while maintaining good adhesion properties due to their film-forming properties. However successful comprehension of ASSBs using lithium as anode still requires further study and investigation into the lithium metal-solid electrolyte interface. It is well known that the high reactivity of lithium, the reaction products and the resulting interface when it comes into contact with most solid electrolytes (SEs) can have detrimental effects on cell performance.[2]In this context, Time-of-flight secondary-ion mass spectrometry can be used as a powerful tool to better understand the formation of interface since it can provide chemical information with high resolution in 2D as well as 3D analysis of both the surface and the bulk of the battery.[3]

In fact, depth profiling done on such sample provides information about the stability of the Li-SE interface and the microstructure. In addition to the individual study of the various components of the cell, the bulk and interfaces within the cell can be investigated with more precision when combined with a depth measurement technique such as a chromatic confocal sensor. Additionally, in situ voltage cycling system has been designed in collaboration with Physical Electronics, which will allow the chemical analysis of the battery in its original configuration.

References:

1 R. Chen, Q. Li, X. Yu, L. Chen and H. Li, *Chem. Rev.*, 2020, **120**, 6820–6877.

2 M. Golozar, R. Gauvin and K. Zaghib, *Inorganics*, 2021, **9**, 85.

3 S.-K. Otto, L. M. Riegger, T. Fuchs, S. Kayser, P. Schweitzer, S. Burkhardt, A. Henss and J. Janek, *Advanced Materials Interfaces*, 2022, **9**, 2102387.

11:00am **SS-MoM3-7 Investigation of the Li^+/H^+ Exchange Process on Washed Cathode Active Material Using ToF-SIMS*, Anja Henss,*** Justus-Liebig University, Heinrich Buff Ring 17, Germany

Energy transition and increasing electrification of transport are placing ever higher demands on the performance of lithium-ion batteries (LIB). For this reason, intensive research and development is being carried out for high-performance and competitive LIBs. [1] [file:///E:/JLUbox/Reisen/SIMS%20Minneapolis/Abstract_AH.docx#_ENREF_1] High-voltage, nickel-rich cathode active materials (CAMs) are particularly promising for electromobility, but their performance is highly dependent on the processing steps. In industry, CAMs are washed immediately after synthesis, which has several advantages: Removal of surface contaminants, prevention of gelation of slurries and reduced gas formation during cycling when surface species react off. However, washing also brings disadvantages: thermal stability seems to decrease, which is related to Ni content, and nickel-containing NCMs seem to be particularly affected. In addition, cycle performance seems to change and capacity deteriorates.[2] [file:///E:/JLUbox/Reisen/SIMS%20Minneapolis/Abstract_AH.docx#_ENREF_2] Unfortunately, current mechanistic understanding is relatively limited; we know that protons are deposited in near-surface layers during washing or high relative humidity, and lithium leaves the material to form LiOH. However, it is unknown how many protons are exchanged, what the kinetics of this process is, and how it can be controlled.

Therefore, we performed a comprehensive ToF-SIMS study to localize the protons in the NCM and to investigate the kinetics of the Li^+/H^+ exchange process. For this purpose, in a first step single crystalline NCM particles were synthesized (in micrometer range) and washed in D_2O for different time periods. The washed and unwashed NCM particles were pressed onto Al foil and investigated by FIB-SIMS. Therefore, a FIB crater was prepared at a small angle and subsequently analyzed by SIMS. In the sample with the longest washing time, an increased signal intensity of deuterated fragments could be localized in the outer regions of the particles. In addition, a 2D model system with a thin layer of NCM deposited on MgO substrate was used to study the kinetics of the exchange process. The results are discussed in context with other characterization techniques that show the structural change induced by washing and electrochemical performance data.

1. J. Janek and W.G. Zeier: A solid future for battery development. *Nature Energy* **1**, 1167 (2016).

2. D. Pritzl et al: Washing of nickel-rich cathode materials for lithium-ion batteries: towards a mechanistic understanding. *Journal of The Electrochemical Society* **166**, A4056 (2019

11:20am **SS-MoM3-9 In Situ Investigation of Lithium Metal–Solid Electrolyte Anode Interfaces with ToF-SIMS**, ***Svenja-Katharina Otto***, *L. Riegger,* Justus-Liebig-Universität Giessen, Germany; *S. Kayser,* IONTOF GmbH, Germany; *A. Henss, J. Janek,* Justus-Liebig-Universität Giessen, Germany

Solid-state batteries (SSB) with lithium metal anodes (LMAs) are explored as a promising approach for next-generation batteries with high energy densities. However, the implementation faces severe challenges partly caused by the high reactivity of lithium metal. Most electrolyte materials are unstable in direct contact with the LMA and interphases which are detrimental for the battery properties form. In order to overcome interphase formation, exact knowledge about the forming reaction products and their microstructure is needed.

In this context, we studied lithium|solid electrolyte (Li|SE) interfaces with ToF-SIMS to complement the commonly used X-ray photoelectron spectroscopy (XPS) and transmission electron microscopy (TEM) characterization.[1] In situ electrochemical deposition or lithium vapor deposition are used to prepare the interfaces. Classification of the interface type and characterization of the 3D structure of the formed interphases are possible by depth profiling through micrometer-thick lithium layers on the SE substrate. We combine ToF-SIMS with complementary XPS analyses to confirm the structural information and with atomic force microscopy (AFM) to obtain roughness and thickness information. As an example, the thickness of the forming Li_2S-rich interphase layer between the argyrodite-type LPSCl and lithium is determined. In addition, the influence of different in situ preparation methods of the Li|SE contact is investigated.[1] Also, we show the characterization of recently developed materials like the Li_7SiPS_8 (LiSiPS) solid electrolyte.[2]

[1] Svenja-K. Otto et al. *Adv. Mater. Interfaces* **2022**, doi.org/10.1002/admi.202102387.

[2] Luise M. Riegger et al. *Chem. Mater.* **2022**, doi.org/10.1021/acs.chemmater.1c04302.

SIMS Solutions in Materials and Life Sciences
Room Great Lakes B - Session SS-MoA1

Bio Materials

Moderator: Gregory Fisher, Physical Electronics USA

4:00pm **SS-MoA1-13 Spatially Mapping Single Cells in Diseased Tissue with Multiplexed Ion Beam Imaging***, **Jay Tarolli**,* Ionpath **INVITED**

The multiplexed ion beam imaging (MIBI) platform was designed to bridge the gap between imaging mass spectrometry and the clinical lab, delivering high throughput, subcellular spatial resolution imaging for 40+ protein markers per sample. Time-of-flight secondary ion mass spectrometry (ToF-SIMS) can be a powerful tool for tissue imaging. However, its applications in tissue imaging are often limited by its usability, acquisition time, and complex mass spectra, the latter making data analysis and interpretation difficult. MIBI has overcome these limitations with a high resolution, high throughput ToF-SIMS system to quickly analyze proteins of interest which are labeled using conjugated antibodies. Specifically, heavy metal atoms, which become the reporter ions measured, are conjugated to antibodies that target the proteins of interest and stain the tissue using a protocol much like that for other multiplexed imaging techniques, such as immunohistochemistry and multiplexed immunofluorescence. Antibody clones, which are known to be successful in other pathology research and clinical settings, can often be used to further facilitate the adoption of the MIBI platform in these settings.

The MIBIscope utilizes a high density Xe plasma ion source to enable rapid imaging of tissue with ToF-SIMS, acquiring an 800 µm x 800 µm ROI in as little as 35 minutes. By targeting protein species with labeled antibodies, the resulting mass spectra are less complicated and since the target analyte is not being fragmented, and the image data has higher signal to noise. An increase in throughput, simpler data analysis, and a sample prep procedure consistent with other common techniques have all allowed the MIBI platform to enter applications spaces that traditionally have been unobtainable for ToF-SIMS.

4:40pm **SS-MoA1-17 Single Cell Metabolomics using the 3D OrbiSIMS for Novel Biomaterials Development***, **Morgan Alexander**,* University of Nottingham, UK

Metabolomics provides the chemical readout that is closest of all the omics to the phenotype of cells. We believe that this level of insight is necessary to interpret the effect of the environmental cues provided to cells by manmade biomaterials.[1]

ToF SIMS struggles with its poor mass resolving power in complex biological systems when faced with myriad possible peak assignments for each secondary ion peak.[2] The 3D OrbiSIMS approach addresses that by combining an OrbiTrap with a time-of-flight SIMS instrument to undertake direct analysis of solid samples.[3]

Application examples from the field of novel biomaterials development will be provided that take advantage of the unique capability of this instrument, focussing on its ability to detect and identify small molecules with a high degree of certainty. Markers of immune cell polarisation for next generation implant materials have been found by assessing single macrophage cells rather than the 6 million cells required previously by LC-MS.[4] Small molecules in complex bacterial biofilms are of interest in understanding the response to novel materials that resist bacterial colonisation and infection.[5]The utility of recently development software to allow chemical filtering to predict molecular formula from SIMS using existing databases[6] is illustrated by reanalysis of the data from Zhang et al, to exemplify the massive increase in the proportion of the spectrum assigned using this automation of data interpretation for OrbiSIMS.[7]

These recent developments enable metabolomic analysis by OrbiSIMS to achieve a label-free, unbiased insight into cellular phenotype at the resolution of single mammalian cells in culture, but ultimately on explanted devices to interpret their responses to different biomaterials.

1. *Single-cell metabolomics hits its stride* **Nature Methods** Caroline Seydel
2. *Mass Spectrometry and Informatics: Distribution of Molecules in the PubChem Database and General Requirements for Mass Accuracy in Surface Analysis* **Anal Chem** 2011, Green et al
3. *The 3D OrbiSIMS - Label-free metabolic imaging with subcellular lateral resolution and high mass-resolving power*. **Nature Methods**2017**,** Passarelli et al.
4. *Single cell metabolomics of macrophages using 3D OrbiSIMS: correlations with phenotype* Suvannapruk et al. under review 2022
5. *Cryo-OrbiSIMS for 3D Molecular Imaging of a Bacterial Biofilm in Its Native State*. **Anal Chem**2020**,** Zhang et al.
6. *Molecular formula prediction for chemical filtering of 3D OrbiSIMS Datasets* **Anal Chem** 2022 Edney et al.
7. *Towards comprehensive analysis of the 3D chemical makeup of Pseudomonas aeruginosa biofilms*Kotowska et al. under review 2022.

5:00pm **SS-MoA1-19 Investigation of Changes in the Cell Envelope of E. *coli* Mutants with a Deficient Conjugation Efficiency Using TOF-Sims.***, **Alfred Fransson**, K. Nilsson, M. Palm, A. Farewell, J. Fletcher,* University of Gothenburg, Sweden

The spread of antibiotic resistance is an increasingly difficult problem to deal with as more bacterial infections survive treatments with commercial antibiotics. One of the main routes for the spreading of resistance among bacterial population is horizontal gene transfer, mainly through conjugation where mobile genetic elements are transferred from a donor cell to a recipient cell through a conjugative pilus. One way to deal with the increasing levels of antibiotic resistance in bacteria is to develop new antibiotics for which resistance has not yet emerged, which can be both laborious and not always a lucrative market. An alternative is to inhibit the conjugation itself so that the rate at which new resistance genes spread between populations is reduced and the usefulness of existing and new antibiotics is extended. A previous study done in our lab used a high-throughput screen to identify chromosomal Escherichia coli genes in the donor cells that were important for conjugation of the F-plasmid and could be potential targets to reduce conjugation. Among these hits were several genes that are involved in the cell envelope through stress response pathways, biogenesis, outer membrane protein assembly and homeostasis, which formed an interest into the role and importance of the cell envelope for conjugation(1). Using a J105 ToF–SIMS instrument (Ionoptika Ltd) fitted with a 40 keV GCIB of (CO2)6k+(2,3), our group have previously investigated fabF and lpp E. coli deletion mutants and identified changes in lipid composition and by performing depth profiling to detected changes not specific to the surface of the cell envelope(4,5). Here we present recent data on how different sample preparations affect the cells as some of these mutants have compromised cell envelopes and it's important that we are able to preserve the samples before the SIMS analysis. In addition to how conjugative F-plasmid affects the cells on its own without any genetic deletions.

(1) Alalam, H.; Graf, F. E.; Palm, M.; Abadikhah, M.; Zackrisson, M.; Bostrom, J.; Fransson, A.; Hadjineophytou, C.; Persson, L.; Stenberg, S.; Mattsson, M.; Ghiaci, P.; Sunnerhagen, P.; Warringer, J.; Farewell, A. Msystems 2020, 5.

(2) Fletcher, J. S.; Rabbani, S.; Henderson, A.; Blenkinsopp, P.; Thompson, S. P.; Lockyer, N. P.; Vickerman, J. C. Anal. Chem. 2008, 80, 9058-9064.

(3) Angerer, T. B.; Blenkinsopp, P.; Fletcher, J. S. Int. J. Mass Spectrom. 2015, 337, 591-598.

(4) Nilsson, K. D.; Palm, M.; Hood, J.; Sheriff, J.; Farewell, A.; Fletcher, J. S. Anal. Chem. 2019, 91, 11355-11361.

(5) Nilsson, K. D.; Granden, J.; Farewell, A.; Fletcher, J. S. Surf. Interface Anal. 2021, 53, 1006-1012.

5:20pm **SS-MoA1-21 Collimated Beam Imaging with MeV TOF-SIMS***, **Marko Brajkovic**, I. Bogdanovic Radovic, M. Barac, Z. Siketic,* Ruder Boskovic Institute, Croatia

In MeV TOF-SIMS, heavy primary ions with higher energy produce higher secondary ion yield of heavy molecules, an important parameter for molecular imaging. These primary ions (such as 14 MeV copper ions) cannot be focused with magnetic lenses available at the RBI accelerator facility. For this reason, a new setup is developed that uses a simple round aperture with a 5 – 10 um opening to collimate the primary beam independently on primary ion mass. As the beam current is significantly reduced after collimation with the aperture, a common beam pulsing method for triggering the TOF measurement could not be utilized. Instead, two different options for the start signal for a continuous primary beam are available: for thin samples, a particle detector placed behind the target that detects primary ions that pass through the target, and for any target thickness an electron multiplier that detects secondary electrons created in the interaction of the primary ions with a 5 nm thick carbon foil placed over the aperture. The samples interesting for forensic (ink deposited on a paper and fingermark) and biological (section of brain tissue) applications of MeV TOF-SIMS were analyzed to show the imaging capabilities of the presented setup.

SIMS Solutions in Materials and Life Sciences
Room Great Lakes C - Session SS-MoA2

Energy Storage II

Moderator: Andrew Giordani, Procter & Gamble Company

2:20pm **SS-MoA2-3 Study of Lithium-Ion Battery Degradation from the Subsurface of Electrodes***, X. Yao,* Advanced Technology Institute, University of Surrey, UK*; **Tomáš Šamořil**, J. Dluhoš,* TESCAN ORSAY HOLDING, Czechia*; J. Watts,* Department of Mechanical Engineering Sciences, University of Surrey, UK*; Z. Du,* Energy and Transportation Science Division, Oak Ridge National Laboratory*; B. Song,* Neutron Scattering Division, Oak Ridge National Laboratory*; R. Silva,* Advanced Technology Institute, University of Surrey, UK*; T. Sui,* Department of Mechanical Engineering Sciences, University of Surrey, UK*; Y. Zhao,* National Physical Laboratory, UK*; D. Miller,* TESCAN USA

In recent years, considerable attention is paid to the improvement of Li-ion batteries (LIBs), currently used as powerful electrical energy storage in a wide spectrum of devices. Their life span related to capacity fade is mainly influenced by the degradation of electrodes associated with the deactivation of active materials and irreversible parasitic reactions. The selection of a suitable analytical technique for LIBs degradation study is very limited by the requirement to provide information about the chemical composition including light elements such as lithium with high surface sensitivity.

Within this contribution, a Scanning Electron Microscope equipped with a Focused Ion Beam (FIB-SEM) uniquely combined with a compact Time-of-Flight Secondary Ion Mass Spectrometer (ToF-SIMS) [1,2] was applied for the high-spatial-resolution study of chemical composition in the cross-sectional interface (see Fig. 1) of pristine and cycled LIB electrodes to identify degradation mechanisms [3]. The ability to correlate SEM observation with ToF-SIMS and other analytical techniques such as Energy Dispersive X-Ray Spectroscopy (EDS) [4] and Raman spectroscopy [5] on the same FIB-SEM system allows extended and correlated analytical capabilities that provide a deeper understanding of degradation processes in LIBs material from the mechanical, chemical, and electrochemical point of view.

[1] J.A. Whitby, et. al., Advances in Mat. Sci. and Eng., (2012), 1-13.

[2] D. Alberts, et. al., Instr. Sci. & Technol. 42, (2014), 432-445.

[3] Yao, et. al., Energy Environ. Mater., (2022), 662-669.

[4] T. Sui, et. al., Nano Energy 17, (2015), 254-260.

[5] D.J. Miller, et. al., Microsc. Microanal. 25, (2019), 862-863.

2:40pm **SS-MoA2-5 Quantification of Transport Function in Solid Ionic Conductors from Concentration Depth Profiles***, **Martin Schäfer**, J. Wiemer, J. Bernzen, V. Gunawan, K. Rein,* Philipps Universität, Germany*; K. Weitzel,* Philipps-Universität Marburg, Germany

One of the powerful applications of SIMS pertains to the quantification of concentration depth profiles as resulting from transport processes. Classical examples can be found in tracer diffusion or ion exchange experiments. A more recent application is the Charge Attachment Induced Transport (CAIT) technique, where a charge carrier beam is directed to a sample surface while the back side of the sample is in contact with a single grounded electrode [1,2]. The charge carriers softly attach to the surface and charge it up to a well-defined electric potential. Attachment of the charge carriers causes gradients of concentration and electric potential which induces the transport of charge carriers in the material. If the ion species attached is chemically different from the native carrier a concentration depth profile arises, where e.g. external K^+ ions may replace native Na^+ ions in a unidirectional transport process [3]. Complementary information can be gained by thermal electropoling experiments, where depletion zones emptied of all alkali ions (and an equal amount of electrons) can be generated [4]. Finally native alkali ions can be replaced by protons over several 100 nm by a modified field assisted ion exchange experiment [5].

All the concentration depth profiles can be quantified by means of time of flight secondary ion mass spectrometry (ToF-SIMS). The analysis of such profiles allows not only to quantify the diffusion coefficients of competing transport channels of solid ionic conductors [6]. It also allows for the first time to gain understanding of the potential energy landscape of ions in such materials [7-9].

[1]M. Schäfer, K.-M. Weitzel, PCCP, 13 20112–20122, (2011).

[2] J. Martin, M. Gräf, T. Kramer, C. Jooss, M.-J. Choe, K. Thornton and K.-M. Weitzel. PCCP.,19, 9762-9769, (2017).

[3] L. Rossrucker, P.V. Menezes, J. Zakel, M. Schäfer, B. Roling and K.-M. Weitzel, ZPC, **226**, 341- 53, (2012).

[4]K. Rein, M. Schäfer, and K.-M. Weitzel, IEEE Transactions on dielectrics and electrical insulation, p. 1422, (2020).

[5] T. Ishiyama, J. Nishii, T. Yamashita, H. Kawazoe, T. Omata, J. Mater. Chem. A, 2, 3940, (2014); and unpublished work from the authors lab.

[6] J. Martin, S. Mehrwald, M. Schäfer, T. Kramer, C. Jooss, K.-M. Weitzel,Electrochimica Acta, 191, 616–623, (2016).

[7] M. Schäfer, K.-M. Weitzel, Materials Today Physics, 5, 12–19, (2018).

[8] M. Schäfer, D. Budina, K.-M. Weitzel, PCCP., 21, 26251, (2019).

[9] J. L. Wiemer, M. Schäfer, K.-M. Weitzel, J. Phys. Chem. C, 125, 4977-4985, (2021).

3:00pm **SS-MoA2-7 High Five: UHV SIMS with Plasma Primary & Simultaneous Positive and Negative Secondary Ion Detection***, S. Fearn,* Imperial College London, UK*; R. Chater,* Imperial College of Science, Technology and Medicine, UK*; **Graham Cooke**,* Hiden Analytical Ltd., UK*; N. Smith,* Oregon Physics

High Five is a recently completed SIMS instrument at Imperial College London that provides dynamic secondary ion mass spectrometry (SIMS) measurements at multi-scale lengths from nm's to several 100microns using a novel gas plasma focused ion-beam source and column from Oregon-Physics.The SIMS detector configuration is unique as both positive and negative SIMS compositional information is recorded by two synchronised quadrupole mass (QMS) filter detectors.

The performance of the primary ion source on target is reported for both mass and neutral filtered oxygen and xenon ion beams at energies from 2keV to 30keV.These beams have been used for both SIMS measurements, i.e. both mass spectra and SIMS imaging for depth profiling.SIMS results in High-Five are obtained from either surfaces that are 'as-prepared' or by sputter-polishing processes 'in-situ' using high-current well focused ion-beams from the plasma source.

Performance results for simultaneous positive and negative secondary ion detection from High-Five are illustrated using air-sensitive solid-state lithium electrode and electrolyte material from an active research program in the Materials Department, Imperial College London.

In High-Five, the primary ion source can be configured to produce an electron beam for both non-destructive feature selection and surface processing.The performance of the primary source for this mode is reported and illustrated with imaging of complex oxides used in fuel cell electrode and electrolysers.These materials are readily amorphized & reduced with ion beam bombardment.Suitable site locations for SIMS are found using imaging for lattice orientation contrast prior to SIMS analysis.

3:20pm **SS-MoA2-9 Indigenous Organic Molecular Biosignatures are Detectable via ToF-SIMS of a Kerogen-rich Jurassic Clay***, M. Pasterski,* University of Illinois Chicago*; M. Lorenz, A. Ievlev,* Oak Ridge National Laboratory*; R. Wickramasinghe, **Luke Hanley**, F. Kenig,* University of Illinois Chicago

Organic molecular biosignatures (OMBs) detected within Mars Sample Return (MSR) samples could provide strong evidence for the existence of extraterrestrial life[1]. The utility of any OMB depends on its character, which can be: indigenous or syngenetic; non-indigenous or incorporated during sub-surface fluid migration; or contaminant. OMB character can be determined via its spatial distribution within a host rock [2, 3], but gas chromatography - mass spectrometry (GC-MS) does not readily preserve spatial information. ToF-SIMS imaging is effective at determining the spatial distribution of OMBs in various sediments [4, 5]. Ancient indigenous sterane molecular ions and fragments ions of isorenieratene derivatives (all suspected OMBs) are detected using ToF-SIMS within a kerogen-rich sample, the 164 million-year-old Oxford clay. Previous work compared ToF-SIMS of the Oxford Clay with results from laser ablation photoionization mass spectrometry imaging [6]. Data from GC-MS, ToF- SIMS, energy dispersive X-ray spectroscopy (EDS), and traditional micrographic imaging were compared using statistical packages within the data analysis platforms R and Python.

Steranes are detectable in ToF-SIMS spectra via their molecular ions and reflect a subset of the complex sterane mixture that dominates the saturated/unsaturated hydrocarbons of the extractable fraction observed via GC-MS. ToF-SIMS spectra and MS images indicate that steranes are heterogeneously distributed on the micron scale. Additionally, typical fragment ions of isorenieratene derivatives appear within ToF-SIMS spectra from regions with observable sterane ions. These isorenieratenes are the dominant constituents of the extracted aromatic fraction. EDS analysis indicates that the regions containing OMBs are high in organic carbon, likely reflecting the previously observed sulfur-rich kerogen [7]. The restricted spatial distribution of the OMBs to regions containing kerogen indicates that they are indigenous to the sample.

Indigenous OMBs are detectable via ToF-SIMS in ancient, kerogen-rich samples. The presence of an OMB molecular ion strengthens the interpretation of ToF-SIMS data of complex natural material as does the spatial coincidence of kerogen and potential indigenous OMBs in ancient sediments.

1) Neveu, *et al.* (2018) *Astrobiology, 18,* 1375.

2) Brocks (2011) *Geochim. Cosmochim. Acta,* 75, 3196.

3) Medina Ferrer (2018) *Org. Geochem., 124,* 112.

4) Thiel and Sjovall (2011) *Planetary Sci., 39,* 125.

5) Siljeström, *et al.* (2017) *Org. Geochem., 109,* 14.

6) Wickramasinghe, *et al.* (2021) *Anal. Chem., 93,* 15949.

7) Kenig, *et al.* (1994) *J. Geo. Soc. Lon., 151,* 139.

SIMS Solutions in Materials and Life Sciences
Room Great Lakes C - Session SS-MoA4

Geosciences

Moderator: Mostafa Fayek, University of Manitoba

4:00pm **SS-MoA4-13 Depth Profiling of Solar Wind Helium by Secondary Neutral Mass Spectrometry***, **Hisayoshi Yurimoto,*** Hokkaido University, Japan **INVITED**

Our Sun erupts energy plasma from the solar corona. This is called solar wind. The plasma mostly consists of electron, hydrogen, and helium. A coronal mass ejection (CME) is an outburst of significant release of solar wind. As CMEs travel through interplanetary space as interplanetary CMEs (ICMEs), they often cause large geomagnetic storms on Earth when they hit the Earth's magnetosphere. We report the first quantitative measurements in laboratories, depth profiling, of ICME atoms that were collected from "the Halloween solar storms of 2003", which was the largest solar storm during the space age. The solar wind collectors from the NASA Genesis spacecraft provide a unique opportunity to study the speed distribution of ICME plasmas during these events.

We measured solar wind helium from the Genesis collector targets by depth profiling using a secondary neutral mass spectrometer called LIMAS [1, 2]. We used a focused Ga ion beam for the primary ion to sputter the targets. Sputtered neutrals were ionized by strong field using a focused femtosecond laser. The post-ionized ions were introduced into a multi-turn time-of-flight mass spectrometer. We obtained helium depth profiles from 10 µm square with detection limits of $2x10^{17}$ atoms/cm^2 (4 ppma).

The depth profile of solar wind helium has a shape of Gaussian-like with a peak at ~20 nm in depth. The Gaussian-like shape accompany a tail at deeper than ~100 nm. We find that the tail corresponds to the ICME plasma of the Halloween solar storms of 2003. The depth profiles are converted to solar wind speed distribution applying SRIM simulation. We find that the ICME plasma speeds of the Halloween solar storms of 2003 reached greater than 2000 km/s and with a total fluence more than 10 times greater than previously reported by any space-based particle instrument. Such extreme fluences mark this event as the most intense recorded measurement of interplanetary plasma during the space age. These new findings and new technique in laboratory add new unique scientific value to investigate solar and geomagnetic activities.

References: [1] Bajo et al. *Surf. Interface Anal.***51**, 35-39 (2019), [2] Nagata et al. *Applied Physics Express***12**, 085005 (2019).

4:40pm **SS-MoA4-17 SIMS Measurements of Trace Hydrogen and Fluorine in Nominally Anhydrous Minerals: Implications for Primary and Secondary Processes on the Moon***, **Jed Mosenfelder,*** University of Minnesota*; A. von der Handt,* University of British Columbia , Canada*; M. Hirschmann,* University of Minnesota

The advent of ultra-low blank, dynamic SIMS methods for measuring trace light element concentrations in geologic materials has opened up new possibilities for exploring nominally H- and F-free minerals – including plagioclase (Pl), orthopyroxene (Opx), clinopyroxene (Cpx), and olivine (Ol) – as recorders of volatile processing in planetary bodies. The role of volatile elements in the origin and differentiation of the Moon remains controversial [1,2] and amenable to study with this approach. Building on our calibration work and efforts to reduce limits of detection (LOD) [3-6], we have acquired an extensive data set on 19 Apollo samples, including ferroan anorthosite (FAN), Mg-suite, granulitic impactite, and basaltic lithologies. Methods and references are detailed in the PDF attachment.

Our results show that trace amounts of F, up to 1.2 µg/g, are ubiquitous in Pl from FAN. Granulitic impactites contain less F (up to 0.4 µg/g), while significantly greater amounts are present in some Mg-suite rocks (up to 8.2 µg/g in Opx). Significant F is also present in Cpx from a mare basalt (up to 1 µg/g). Measurements of H in these samples are more ambiguous. Most analyses reveal no H above the LOD; where present it can be explained in most cases by ionization of sub-mm to mm-sized micropores, identified in and around analysis craters by high-resolution imaging with EPMA (see attachment). Some of these micropores may have contained volatile elements exsolved from crystals during static cooling. In most cases, however, we associate the micropores with shock events. An extreme example is FAN sample 60015, with Pl analyses yielding up to 25 µg/g H_2O, 60 µg/g F, and 18 µg/g Cl. Cl is highly incompatible in Pl and likely derived from the splash melt that partially coats and infiltrates the sample. H and F may also have been introduced in this manner – possibly from an extraselenian source – or may be redistributed from the Pl crystal structure into micropores by the shock event. This interpretation contrasts with that of Hui et al. [7], who inferred that H in 60015 was structurally bound in Pl and preserved after partitioning with H in the lunar magma ocean (LMO). On one hand, our results call this hypothesis in to question. On the other hand, we can use our robust measurements of F in less shocked FAN to place constraints on F in the LMO (see attachment).

Future work is in progress to measure H, F, and Cl in additional Mg-suite samples and basalts (including high-Al, high-Ti, and KREEP varieties), including a sample recently released after 50 years of cold storage as part of the Apollo Next Generation Sample Analysis program.

5:00pm **SS-MoA4-19 Multi-Collector Configuration Considerations for Age-Dating Measurements of Particles by Large Geometry Secondary Ion Mass Spectrometry***, **Todd Williamson**, E. Groopman, D. Simons,* National Institute of Standards and Technology (NIST)

Large geometry secondary ion mass spectrometry (LG-SIMS) has been widely used for isotopic measurements of uranium particles for many years. Recently, it has been demonstrated it is possible to perform chronometry (a.k.a age-dating) measurements of single uranium-containing, micrometer-sized particles using LG-SIMS. For this chronometry measurement, the analytes measured are the ^{234}U – ^{230}Th mother-daughter chronometry pair. This measurement protocol was developed using the single, mono-collector electron multiplier (EM) configuration on a LG-SIMS instrument with the preponderance of the counting time of an analysis cycle being on the ^{230}Th to maximize measurement precision. Most LG-SIMS instruments have a multi-collector system configured with five EM detectors, which allows for simultaneous measurement of up to five isotopes, improving measurement precision and detection limits over single, mono-collector protocols. We will present results of our work adapting the mono-collector chronometry measurement protocol to the multi-collector configuration of an LG-SIMS with a focus on uranium particle measurements. The multi-collector configuration allows the simultaneous counting of both ^{230}Th and ^{234}U, with the added advantage of allowing the collection of ^{231}Pa and ^{232}Th isotopes, too. Simultaneously counting all isotopes should improve the overall measurement precision, as well as eliminate transient artifacts during the analysis that could result in inaccurate data. We will present results focusing on three aspects of this work. The first topic will discuss comparison of the multi-collector configuration to the mono-collector configuration with an emphasis on measurement precision and variability. Results for both age-dating and more conventional uranium isotopic measurements will be discussed. The second topic will discuss how increased background from peak tailing – often referred to as abundance sensitivity – can negatively impact measurement detection limits for the multi-collector configuration. The reason for abundance sensitivity potentially having negative consequences for age-dating measurements is the design constraints of multi-collector systems for LG-SIMS. The final topic will discuss the viability of ^{231}Pa measurements using the multi-collector configuration in regard to precision and detection limits which could be expected for age dating measurements using the ^{235}U – ^{231}Pa chronometer pair.

5:20pm **SS-MoA4-21 Construction of New Biomolecular Architectures Using Large Argon Clusters*, Benjamin Tomasetti,*** Université Catholique de Louvain, Belgium*; V. Delmez,* université catholique de Louvain, Belgium*; C. Lauzin,* université Catholique de Louvain, Belgium*; A. Delcorte,* Université Catholique de Louvain, Belgium

The ability to biofunctionalize surfaces with proteins is a major challenge in many fields such as biocatalysis, tissue engineering or biomedical devices. We established a new variant of soft-landing using the argon cluster source available on a time-of-flight secondary ion spectrometer (ToF-SIMS) to transfer intact biomolecules from a pure sample target onto a collector in the vacuum. Lysozyme (MW=14 kDa) was soft-landed in this way onto a Si collector and the integrity and bioactivity of the transferred molecules were demonstrated by gel electrophoresis and bioassays [1].

After establishing the successful buildup of films of different non-volatile molecules with a good thickness control, more complex architectures could be prepared. First, we demonstrated the great flexibility of the method toward the nature of the substrate. Multilayers of bradykinin were deposited on a paper surface, knowing that this type of deposition is not possible with a solution-based method (Fig.1). Second, we investigated the construction of mixed multilayers, composed of various species. A bilayer of bradykinin and Irganox 1010, built by successive transfer with 10 keV Ar_{3000}^{+}, was studied by dual-beam depth profile analysis. It revealed that the molecular layers are well-separated and that the new material is stable in time (Fig.2). The mechanical stability against external stresses was also checked with basic tests (tape test, ect.). The ability to construct such bilayers paves the way to new applications which could not be considered previously. Indeed, we are able to build alternate multilayers of proteins with comparable solubility that can neither be adsorbed from solution without mixing on the surface nor sublimated without degradation.

In order to increase the flexibility of the method in terms of geometry, choice of clusters and possible ion selection after desorption, a home-built transfer instrument using a pulsed valve for the production of large ionic clusters is currently being home-built ion our laboratory.

[1] V. Delmez et al., J. Phys. Chem. Letters, 2021, 12, 952-957.

SIMS Solutions in Materials and Life Sciences
Room Great Lakes B - Session SS+DI-MoA3

Industrial Applications II

Moderators: Cody Cushman, Corning Incorporated, **Teruaki Kikuchi**, SONY Semiconductor Manufacturing

2:00pm **SS+DI-MoA3-1 Keynote Industrial Talk: Correlative Microscopy and Data Analysis for Semiconductor Technology Applications*, Jean-Paul Barnes,*** *C. Guyot, P. Hirchenhahn, N. Gauthier, M. Moreno, T. Maindron, Y. Mazel, E. Nolot,* CEA-Leti, France*; A. Priebe,* EMPA (Swiss Federal Laboratories for Materials Science and Technology), Switzerland*; B. Gautier,* CNRS, France*; A. Tempez, S. Legendre,* HORIBA France*; G. Fisher,* Physical Electronics USA **INVITED**

The increasingly complex structures and large variety of materials used in modern nano and opto-electronic devices drives the need to develop new approaches for their characterization. To obtain the desired information it is often necessary to combine several techniques to acquire reliable information. Ideally, this should be from exactly the same spot on a specimen. This can be challenging both in terms of measurement protocols, but also in the data treatment required to correlate data sets from different techniques and/or modalities. In an applied research or industrial environment, the ability to give fast feedback is a great advantage in materials and process development. It is thus important to have access to a wide range instruments and techniques that are complementary in their capabilities. This presentation will address developments in TOF-SIMS and tandem MS analysis for applications from semiconductor technology to display technology and the importance of using several techniques such as scanning probe microscopy, X-ray tomography, TEM-EDX, XPS and plasma profiling time-of-flight mass spectrometry. The importance of sample preparation to enable multi-technique studies is also critical and several examples will be given involving focused ion beam milling, wedge crater preparation and transfer between instruments under a protected environment (vacuum or inert gas).

Part of this work, carried out on the Platform for Nanocharacterisation (PFNC), was supported by the "Recherches Technologiques de Base" program of the French National Research Agency (ANR).

2:40pm **SS+DI-MoA3-5 Basic Evaluation and Impurity Analysis in OLED Devices with New Ion Guns for Dynamic-SIMS*, Tomomi Ohashi,*** *S. Inayoshi,* ULVAC, Inc., Japan*; D. Sakai, T. Miyayama,* ULVAC PHI, Inc., Japan

ULVAC-PHI developed new ion guns that can narrow the diameter of the beam. These have been installed in our own D-SIMS equipment (ADEPT-1010). We report that the results from the basic evaluations and impurity analyses of OLED devices.

We analyzed small areas (100 μm x 250 μm) of patterned samples. Samples were Au/Pt/Ti/Si wafers as multilayer films. These were compared before and after annealing (Fig. 1①). It was observed that Au diffused toward the Pt film in the sample after annealing. The results of measuring larger areas (Fig.1②) were equivalent to the results of measuring the smaller areas. Therefore, it has been determined that measuring smaller areas were possible without being affected by the surrounding area.

It is known that the OLED device lifetime is shortened if impurities are mixed in during their production. We evaluated the intensity and the in-plane distribution of impurities in OLED devices, especially focusing on halogen elements in the organic layers. We prepared two samples. One is the sample ※1 with a short lifetime and the other is the sample ※1 with a long lifetime. The device has a light-emitting area of 2.3 mm in diameter. The luminous area was divided into five regions (top, bottom, left, right, and center), and each location was measured multiple times. Fig. 2 shows the results at the center of the sample. Fluorine was detected from devices with shorter lifetimes, but there was no difference in chlorine intensity. Similar results were obtained from other regions. To evaluate reproducibility, we compared the Coefficient of Variation (CV) of the integrated intensity values of fluorine (m/z = 19) from 250 s to 450 s. The CV of the center position was 0.090, and the overall CV ranged from 0.050 to 0.17. Although there was some variation, the reproducibility was generally good. These results suggest that one of the reasons for the shorter lifetime of OLED devices is the presence of fluorine in the organic layer.

References:[1] K. Suzuki et al. Proc. of the 33th Meeting of Japan OLED Forum, (2021), p. 13.

3:00pm **SS+DI-MoA3-7 Sample Processing by Bi-FIB for TOF-SIMS Imaging of Buried Interfaces*, Shin-ichi Iida,*** ULVAC-PHI, Inc., Japan*; G. Fisher,* Physical Electronics*; T. Miyayama,* ULVAC-PHI, Inc., Japan

Focused ion beam (FIB) is commonly used as a standard machining technique in failure analysis, quality control, reverse engineering, material research, etc., for the samples having micro- and nanostructures. FIB combined with time-of-flight secondary ion mass spectrometry (TOF-SIMS), so-called FIB-TOF, has attracted attention as a method to determine the three-dimensional (3D) chemical distributions of complex samples. In general, a highly focused Ga^{+} ion beam is used for FIB, however, the FIB-milled area is limited and it was difficult to expand the Ga-FIB to hundreds of micron length scale sample fabrication. In order to overcome the drawback, we proposed Bi-FIB approach for large scale sample cross-sectioning. Although the possibility of Bi-FIB has been reported, there were almost no performance examinations as well as practical applications. In this study, therefore, the authors summarize the comparison of milling rate and milling damage between Ga-FIB and Bi-FIB. As a result, it was found that Bi-FIB can provide higher milling rate with thinner milling damage. Finally, the Bi-FIB approach was applied to the interfacial analysis of all-solid-state battery (ASSB) material, because the functionality of ASSBs strongly depends on the solid/solid interface. With this approach, the detailed chemical distributions at the interface was discovered, leading to the better understanding of battery behaviors.

3:20pm **SS+DI-MoA3-9 HDR of SIMS Data*, Henrik Arlinghaus,*** *D. Rading, E. Niehuis,* IONTOF GmbH, Germany

The number of secondary ions generated during a ToF-SIMS experiment is dependent on numerous factors. While the operator is able to configure the instrument to optimize the yield, many factors such as the ionization probability, differences in molecular species concentrations, or the (in)homogeneity of the spatial distribution within the sample cannot be changed. Challenging samples may therefore run into the limits of the dynamic range of a modern SIMS instrument, which is around five orders of magnitude. When this is the case the operator must find a compromise which limits the noise in low intensity signals and areas while minimizing oversaturation of high intensity signals or areas.

In photography one approach to overcome similar limitations is the use of "High Dynamic Range", or HDR photography. This approach takes multiple images in short succession with varying exposure times and then fuses these together to generate a single composite image.

Previously we had demonstrated the possibility of acquiring multiple datasets during a single acquisition pseudo simultaneously, with each dataset having been acquired using different instrument parameters, while minimizing the impact of changes in the sample or the environment, using multiplexing[1]. In this paper, we continue that work by demonstrating that it is possible to generate combined profile and images for substances of interest using a HDR-like algorithm from such a dataset, reducing noise within low intensity areas, and saturation effects in high intensity areas, simplifying data interpretation.

[1]: Multiplexing ToF-SIMS acquisition modes to improve information yield

Plenary Session
Room Great Lakes B - Session PS2-TuM

Plenary Session II
Moderator: Anna Belu, Medtronic, Inc.

8:40am **PS2-TuM-2 Plenary Lecture: The Role of Surface Collisions in Native Mass Spectrometry/Structural Biology***, **Vicki Wysocki**,* Ohio State University **INVITED**

Hyperthermal collisions with surfaces for characterization of projectiles ions in MS/MS were introduced by the Cooks lab at Purdue University in the 1980s.It was clear in the early days that collisions with surfaces, more massive targets than the projectiles used for collision-induced dissociation, CID, should be valuable for dissociation of massive ions.Unfortunately, instruments of the day could not ionize and transmit high m/z ions.Over the years, The Wysocki Research Lab has exploited surface collisions in development of the mobile proton model for peptide fragmentation and, more recently for the characterization of protein and nucleoprotein complexes.As methods and instruments in the community have morphed to accommodate more massive ions, surface collisions have been integrated into a variety of instrument types (e.g., QqQ, QTOF, ICR, Orbitrap) and coupled with online separations, with ion mobility, and with other activation methods, including electron capture dissociation, ECD.The data are used throughout the stages of a biochemical/structural biology project and in ways that are complementary to other structural biology tools (X-ray crystallography, cryoEM).Examples will be provided to illustrate 1) the value of native mass spectrometry experiments that incorporate surface-induced dissociation, SID, for structural characterization and 2) the overlap/integration of the results with data from other approaches.

Fundamentals
Room Great Lakes C - Session FM+SS-TuM3
Microelectronics

Moderators: Marinus Hopstaken, IBM T.J. Watson Research Center, **Paul van der Heide**, IMEC, Belgium

10:00am **FM+SS-TuM3-1 Keynote Industrial Talk: SIMS Quantification: Do You Remember When a Factor of Two was Good Enough?***, **Charles Magee**,* 314 Pennington-Rocky Hill Road **INVITED**

Well, do you remember when a factor of two was good enough? Probably not. You would have to have been around SIMS in the early 1970's like I was to remember those days. I will give many references back to the early days when a local thermal equilibrium (LTE) model was used to obtain the first results that were accurate to within a factor of two...but only 60% of the time. And it only worked for bulk silicate matrixes!

People were not using SIMS on semiconductors in those days. I will give several early references showing profiles of ion implants in Si, but it was not until 1980 that the first paper was published that explicitly showed how to use ion implants as SIMS standards. (People were using ion implants as standards before 1980, (I was one of them!) but only in limited cases, and with no formal published equations specifying how to use them.)

But the samples for which ion implants were used as standards were for dilute concentrations in a single matrix which was uniform in depth. The rest of the talk will show how we at Eurofins EAG Laboratories tackled the problem of quantification of both major and minor elements in non-uniform, multi-element samples with abrupt or continuously graded composition changes using Point-by-point CORrected-SIMS (PCOR-SIMS). These include:SiGe, AlGaAs, B in SiO2/Si, arsenide/phosphide heterostructures, PLAD B in poly-gates, As in SiO2/Si, and GaN/AlGaN structures.

10:40am **FM+SS-TuM3-5 ToF-SIMS Characterization of Chitosan as Water Developable 193 nm Photolithography Resist for Green Micro-Nanopatterning***, P. Durin,* Univ Lyon, Ecole Centrale de Lyon, CNRS, France*; O. Sysova,* Université de Haute-Alsace, CNRS, Université de Strasbourg, France*; Y. Guan, C. Gablin,* Univ Lyon, CNRS, Université Claude Bernard Lyon 1, France*; A. Benamrouche,* Univ Lyon, Ecole Centrale de Lyon, CNRS, INSA Lyon, Université Claude Bernard Lyon 1, France*; S. Hajjar-Garreau,* Université de Haute-Alsace, CNRS, Université de Strasbourg, France*; A. Teolis, S. Trombotto,* Univ Lyon, CNRS, Université Claude Bernard Lyon 1, Université Jean Monnet, France*; T. Delair,* Univ Lyon, CNRS, , Université Claude Bernard Lyon 1, Université Jean Monnet, France*; I. Servin, R. Tiron, A. Bazin,* Univ. Grenoble Alpes, CEA, LETI, France*; D. Berling, O. Soppera,* Université de Haute-Alsace, CNRS, Université de Strasbourg, France*; T. Géhin,* Univ Lyon, Ecole Centrale de Lyon, CNRS, Université Claude Bernard Lyon 1, France*; E. Laurenceau,* Univ Lyon, Ecole Centrale de Lyon, Université Claude Bernard Lyon 1, France*; J. Leclercq, Y. Chevolot,* Univ Lyon, Ecole Centrale de Lyon, CNRS, Université Claude Bernard Lyon 1, France*; **Didier Léonard**,* Univ Lyon, CNRS, Université Claude Bernard Lyon 1, France

Lithography is one of the key steps in micro/nanofabrication. In this process, structures are written in a resist (film sensitive to electron beam or UV irradiation) that can subsequently be transferred to the substrate material (typically SiO_2 on silicon), often by etching. However, the use of toxic resists and solvents, as well as of harmful developing solutions, raises questions in terms of health, safety and environmental issues. In this context, there is a growing interest in using bio-sourced resists such as polysaccharides[1] that are water-soluble and can be processed as films with good adherence to substrates. Most of them still need to be chemically modified[1], which is outside the scope of a green resist. Chitosan appears then as an ideal candidate for replacing commercial synthetic resists, since it does not need any additional modification, and development of patterns is achievable with water or a slightly acidified solution[2].

Here, we focus on the ToF-SIMS spectra interpretation combined with multiple characterization techniques (XPS, IR,…) to understand (1) the mechanism making possible to write structures in chitosan films using UV irradiation at 193 nm; (2) the key parameters driving the plasma selectivity of the chitosan resist defined as the ratio of the resist etching rate over the substrate etching rate under given SiO_2 etching plasma conditions (selected parameters were SF_6/Ar vs CHF_3 etching plasmas as well as chitosan vs alginate films).

[1] S. Takei *et al.*, Microelectron. Eng., Volume 122, pp. 70–76, 2014

[2] M. Caillau *et al.*, Proc. SPIE - Volume 10587, pp. 105870S, 2018

11:00am **FM+SS-TuM3-7 NP-SIMS for Evaluating the Molecular Homogeneity of Photoresists***, **Michael Eller**, J. Cruz,* California State University Northridge*; D. Verkhoturov, S. Verkhoturov, E. Schweikert,* Texas A&M University

There is an urgent need to develop new semiconductor devices with critical dimensions below 20 nm. The semiconductor industry has identified extreme ultraviolet, EUV, lithography as a the most likely method to produce sub 20 nm features at scale. Chemically amplified resists, CAR, are well established materials for deep ultra-violet lithography and consist of a multi-component mixture including polymeric species, photoacid generator and base quencher. A key factor in the performance of CARs as EUV resists is local variation in resist sensitivity, due to a combination of factors including homogeneity of the resist components. Thus, there is a critical need for analytical methods capable of molecular analysis at the nanoscale to understand and optimize the performance of CARs as EUV photoresists. Here we describe a new methodology which allows for tests on molecular homogeneity at the nanoscale, with the ability to examine rare sites which deviate from the average composition. The technique uses Nano-Projectile Secondary Ion Mass Spectrometry, NP-SIMS, operating in the event-by-event bombardment detection mode. NP-SIMS has three innovative features (1) the nature of the projectile (2) the mode of data acquisition (3) the method of data analysis. Briefly, samples are analyzed with a suite of nano-projectiles (e.g. Au_{400}^{4+})separated in time and space. Each projectile generates abundant emission of analyte-specific ions. The ions emitted from each of these impacts are mass analyzed and stored as an individual mass spectrum prior to the arrival of the next projectile. Nanoscale analysis is possible because each projectile samples a nano-volume (10-15 nm in diameter). The homogeneity of a component(s) can be evaluated by examining these individual mass spectra for the co-emission of analyte-specific species. We applied this method to study how homogeneity of each component in the resist was affected by resist composition. Further, we identified rare sites which deviated significantly from the mean composition, based on the number of detected analyte molecules. These are likely due to ionic aggregations or domains with higher concentration within the top 10 nm of the film. Identifying and characterizing these rare sites is critical for understanding the fundamental and material processes occurring in these materials. This work is supported in part by the Semiconductor Research Corporation (Task ID 3032.001).

11:20am **FM+SS-TuM3-9 Dynamic SIMS Analytical Methods for Optimized Detection Limits of Atmospheric Species***, **Seoyoun Choi**, L. Créon, P. Peres,* CAMECA, France*; S. Miwa,* CAMECA, Japan*; J. Ren, R. Liu,* CAMECA, France

Information on hydrogen, carbon and oxygen impurities (atmospheric gas elements) introduced during processing and/or aging is of major importance to better understand the lifetime and failure modes of semiconductor devices.

Dynamic SIMS plays an important role in evaluating the concentration of impurities (H, C, O) in semiconductor materials because of its high sensitivity, ability for depth profiling at high throughput, and good detection limits. Dynamic SIMS imaging capabilities can also be used to investigate local non-uniformity of light elements at sub-micrometer scale. Based on a magnetic sector mass spectrometer, the CAMECA IMS 7f-Auto is a versatile magnetic sector SIMS that offers unequalled depth profiling performance.

This talk will present and discuss different analytical protocols for optimizing the detection limits of atmospheric elements.

Data obtained on the IMS 7f-Auto show that the detection limits of H, C, O in silicon can be significantly improved using a specific protocol including sample outgassing and pre-sputtering prior to analysis.

For bulk analysis, the "raster change" method is a powerful analytical method to obtain the bulk concentration of light elements. This method, based on the signals intensity variation when reducing the raster, allows to separate the net content in the sample from the instrumental background contribution, and thus provides the bulk impurity concentration.

We will show applications of the "pre-sputtering" and "raster change" dynamic SIMS methods for measuring the impurities concentration in silicon.

11:40am **FM+SS-TuM3-11 Co-Sputtering EXLIE SIMS to Achieve Non-Fully Oxidizing Conditions***, **Alexandre Merkulov**, C. Noel, A. Franquet, V. Spampinato, P. van der Heide,* IMEC, Belgium

The SIMS technique can be used to monitor in-depth distributions of dopants within the first few nanometers of the surface, provided that SIMS profiles can be measured with depth resolution better than 1 nm/decade. The application of ultra-low impact energy sputtering with Oxygen at high incidence angle in the range of 40-60 degrees is limited. Several artifacts/effects inherent to ultra-low energy sputtering within the transient were encountered:1) exponential sputter rate variation through the native oxide, empirically explaining the so-called ‘surface shift’ of depth profiles toward the surface; 2) high Boron surface peak presence on the depth profile, correlating with sputter rate variation, however, not fully cancelling the surface peak if only sputter rate variation is applied; 3) surface roughening during the sputtering through the transient and roughness development. These effects do not allow to use quantification formalism established for steady state sputtering condition in SIMS experiments. In this work, the sputter rate variation through transient until the steady state sputtering is established was studied using direct physical method such as atomic force microscopy (AFM). The part of the signal enhancement in the transient (surface peak) after taking into account the sputter rate variation can be associated with surface oxidation, thus responsible for ion yield variation through the transient. Moreover, the oxidation related to the oxygen flow in the sputtering beam can be varied using the diluted oxygen beam obtained from a certain gas mixture. Several gases were studied to form a stable plasma and to produce a high-density beam, notably N_2, Ar, Xe and O_2. The advantage of N_2 is a molecular mass close to O_2 allowing to study the sputtering cascade and surface oxidation through the native oxide. Ar and Xe have lower backscattering compared to O_2, so, higher sputter yield can be achieved. The Cameca SC-Ultra SIMS tool ion column with Wien filtering allows to sputter with pure gas species (N_2^+, Ar+, Xe^+, O_2^+) or diluted flow to study the oxidation ramp according to the oxygen percentage in the sputtering beam.A special interest will be paid to the roughness development through the transient. The AFM measurements, used for sputter yield variation study provide the surface correlation function to observe the seeding and regular surface structures formation dynamics. The main accent of this research is to provide easy data interpretation layout, produce a much-needed information on partially oxidized surface chemistry in the early state of Silicon sputtering, with the aim to improve the very shallow implants quantification.

12:00pm **FM+SS-TuM3-13 AKONIS: Automation for Easier Use of SIMS***, **Anne-Sophie Robbes**, O. Dulac, K. Soulard, S. Choi, R. Liu, B. Salle,* CAMECA, France*; M. Pietrucha,* CAMECA Instruments Inc.

The new CAMECA AKONIS SIMS tool has been developped to fill a critical gap in semiconductor fabrication processes by providing high throughput, high precision detection for implant profiles, composition analysis and interfacial data directly in the semiconductor manufacturing line. AKONIS provides a very high level of automation to ensure repeatability across tools for fab level process control and tool-to-tool matching. Building upon fifty years of experience in ion instrumentation and over thirty years of close partnerships with leading semiconductor manufacturers worldwide, AKONIS is a leap forward in high precision characterization of implants, interfaces and compositional analysis along with high repeatability metrology for the most demanding semiconductor process development and control applications. AKONIS benefits from recent development in Ultra Low Impact Energy ionic column technology (< 150 eV), coupled with a full wafer handling system including a high-resolution stage enabling measurements on pads down to 30 µm.

AKONIS implements sophisticated automation routines on the primary ion column. These allow it to run an analysis at the target current setpoint with a tightly focused beam over a broad range of energies - from 150 eV to 7 keV - for applications from ultra-thin films to deep implants. Moreover, the instrument enables running automated chain analyses, switching between different applications that may require differing instrument conditions - such as mass resolution, analysis current, or impact energy - without any need for human intervention. In addition, fitted with optical carrier enhancement (OCE) capability, the instrument is reliably and easily used for charge compensation while analyzing thin insulating films (<30nm).

We'll demonstrate how the automation, especially of the primary column, developped for AKONIS can be useful and beneficial in SIMS in general.

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:

[1] P. Schneider, et al., Anal. Chem. 92, 15604 (2020).
[2] C. R. Gebhardt, et al., Angew. Chem., Int. Ed. 48, 4162 (2009).
[3] A. Portz, et al., Biointerphases 15, 021001 (2020).
[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.

[1] V. Delmez et al., A. Deposition of Intact and Active Proteins In Vacuo Using Large Argon Cluster Ion Beams, *J. Phys. Chem. Lett.***2021**, *12*, 952–957.

[2] Weiwei Zhang and Adri C. T. van Duin, Improvement of the ReaxFF Description for Functionalized Hydrocarbon/Water Weak Interactions in the Condensed Phase. J. Phys. Chem. B 2018, 122, 14, 4083–4092.

[3] A. Delcorte, A Microscopic View of Macromolecule Transfer in the Vacuum using Gas and Bismuth Clusters. *J. Phys. Chem. C*, **2022**, *126*, 7307–7318.

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:

[1] S. Datta, *Electrochem*. Soc. Interface **22** 41 (2013).
[2] J. Mitard et al., *Jap. J. Appl. Phys.***50** 04DC17-1 (2011).
[3] M.J.H. van Dal et al., *IEEE International Electron Devices Meeting (IEDM)* 23.5.1- 23.5.4 (2012).
[4] R. Pillarisetty, *Nature***479** 324 (2011).
[5] MK Passarelli, A Pirkl, et al., *Nature Methods*, **14**, 1175–1183 (2017)
[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).

SIMS Solutions in Materials and Life Sciences
Room Great Lakes A2-A3 - Session SS-TuM1

Cells and Tissue I

Moderators: Gregory Fisher, Physical Electronics USA, **Sebastiaan Van Nuffel**, Maastricht University

10:00am **SS-TuM1-1 Biological Explorations with NanoSIMS: From Cells to Humans***, **Matthew Steinhauser,*** University of Pittsburgh **INVITED**

Measurement of metabolism within individual cells is critical for a functional understanding of heterogeneous cell populations, particularly in complex multicellular tissues. Nanoscale secondary ion mass spectrometry (NanoSIMS) probes sample surfaces at high resolution (< 50nm), yielding multiplexed quantitative images of elemental composition. Tuning of a NanoSIMS instrument to measure two different isotopic variants of a specific element effectively enables quantitative mapping of isotopic ratios. The term “multi-isotope imaging mass spectrometry - MIMS” was coined to describe the merger of stable isotope tracer methodologies with NanoSIMS. Our group and others have demonstrated the power of MIMS as a quantitative window into a wide range of biochemical pathways at subcellular and even sub-organelle resolution. MIMS has been utilized to study processes such as glucose, amino acid, lipid, and nucleic acid metabolism and cell turnover in development, homeostasis, and disease. In this presentation, I will provide an overview of our standard workflow when conducting MIMS biological experiments, incorporating considerations of tracer selection, dosing, sample processing, and NanoSIMS analytical strategies, emphasizing experiment-specific tradeoffs between measurement accuracy and analytical throughput. With a series of specific experimental examples—including studies in murine atherosclerosis, rat pulmonary hypertension, and murine tumor models—I will illustrate how MIMS can be valuable to generate new and unexpected discoveries or as a method to test specific predictions arising from orthogonal experiments. Finally, I will share early experience with human translation to underscore the immense potential of revealing aspects of human biology that are not easily accessible with any other method.

10:40am **SS-TuM1-5 Using Multimodal Mass Spectrometry Imaging to Iron Out the Mechanisms of Ferroptosis in Epithelial Ovarian Cancer***, **Michael J. Taylor**, J. Lukowski,* Pacific Northwest National Laboratory*; L. Tesfay,* University of Connecticut Health*; J. Cliff,* Pacific Northwest National Laboratory*; S. Torti,* University of Connecticut Health*; C. Anderton,* Pacific Northwest National Laboratory

Introduction: In 2023, 14,000 epithelial ovarian cancer deaths are expected to occur in the United States alone. It is an aggressive disease with a dismal five-year survival rate. In ovarian cancer, iron accumulates in tumor initiating cells making them susceptible to ferroptosis inducing agents. We have developed a method of linking iron accumulation with lipid profiles in a mouse model. High resolution secondary ion mass spectrometry (SIMS) and matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI) was performed on tissue sections to identify and correlate biologically important iron pools with lipid composition.

Methods: Mice were injected with FTT ovarian cancer tumor-initiating cells. After 7 days, Group 1 were treated with Erastin, and group 2 with a buffer solution (control). Mice were sacrificed 10 days after treatment, and tumors excised. Serial sections were taken. MPLEx followed by global-lipidomics (LTQ Velos) were performed on the first sections. The thinner sections were thaw mounted and dihydroxybenzoic acid (DHB) applied. MALDI-MSI was performed using a Bruker Scimax 7T. Imaging datasets were uploaded to METASPACE for annotation (SwissLipids). The DHB matrix was washed off (methanol, water, 2 mins). SIMS imaging (IONTOF V TOFSIMS / CAMECA NanoSIMS 50L) was used to semi-quantitatively identify iron regions.

Results: Comparison of lipid distributions between the Erastin treated and control samples revealed a chemically distinct region in Erastin samples Time-of-flight SIMS (TOF-SIMS) imaging of the washed tissue sections detected no DHB peak indicating that the washing steps removed all DHB from the tissue. High-spatial resolution SIMS imaging with the NanoSIMS identified that mineralized pockets of iron and calcium were present in the chemically distinct regions in the Erastin treated sample, whereas no iron pooling was observed in the control sample. The Iron pooling regions were used to specify regions of interest to compare lipid profile changes between iron and non-iron pooled areas. Higher relative abundance of Phosphatidylcholines was observed in non-iron pooled regions, whereas iron pooled regions were rich with sphingolipids. Liquid chromatography tandem mass spectrometry LC-MS/MS) analysis of the non-polar phase of the MPLEx bulk preparation was able to confirm lipid assignments putatively assigned in METASPACE based on MS1.

Conclusion: This preliminary study suggests thatErastin-induced ferroptosis is associated with pooling of iron and metals which correlates with changes in lipid profile composition

11:00am **SS-TuM1-7 GCIB-SIMS of Lipid Trafficking and Turn-Over in Cancer Cells and Spheroids***, K. Dimovska Nilsson, M. Leiva, G. Landberg, **John Fletcher,*** University of Gothenburg, Sweden

The tumour microenvironment is extremely heterogenous consisting of different cell types, variation in oxygen supply and different chemical species in the extra cellular milieu. Cancer cells require high amounts of lipids in order to maintain proliferation and meet this demand through *de novo* synthesis. This can result in a deficit of poly-unsaturated fatty acid (PUFA) containing lipids as many of these rely on conversion of dietary *essential* fatty acids. This weakness in the cancer cells has been suggested as a possible therapeutic target.

Imaging MS, including ToF-SIMS, studies have illustrated that while the tumour may be depleted in PUFAs the surrounding regions can actually be high in these species, especially when inflammatory cells are present in the surrounding stroma.[1]

In this study we use a J105 SIMS instrument with a 40 keV water cluster ion beam[2,3] to investigate the ability of breast cancer cells and spheroid tumour mimics to take up and process omega-3 and omega -6 fatty acids.

(1) Angerer, T. B.; Magnusson, Y.; Landberg, G.; Fletcher, J. S. *Anal. Chem.***2016**, *88*, 11946-11954.

(2) Fletcher, J. S.; Rabbani, S.; Henderson, A.; Blenkinsopp, P.; Thompson, S. P.; Lockyer, N. P.; Vickerman, J. C. *Anal. Chem.***2008**, *80*, 9058-9064.

(3) Dimovska Nilsson, K.; Karagianni, A.; Kaya, I.; Henricsson, M.; Fletcher, J. S. *Anal. Bioanal. Chem.***2021**, *413*, 4181-4194.

11:20am **SS-TuM1-9 Correlative Microscopy of SIMS, Helium Ion Microscopy and XPS***, **Jake Sheriff**, I. Fletcher,* Newcastle University, UK*; P. Cumpson,* University of New South Wales, Australia, UK

Secondary ion mass spectrometry (SIMS) is a widely used surface analytical technique to interpret surface composition. A primary beam is raster-scanned across a surface to create a total ion image from the secondary ions ejected [1]. The Ionoptika J105 is equipped with two ion beams; C60 and GCIB, the resolution of the images generated by the J105 is dictated by the spot size of these beams.

The Helium ion microscope (HIM) developed by Zeiss uses a beam of He ions to generate a secondary electron image of a surface. The use of He ions as the imaging beam allows for a spot size down to <0.5nm [2]. This has allowed the HIM to take high resolution images on a submicron scale without the need for specimen coating. At Newcastle we use a magnetic-sector analyser to allow SIMS mapping of the surface as pioneered by LIST [3], giving potentially the highest spatial resolution of any SIMS instrument.

The Axis Nova X-ray photoelectron spectrometer (XPS) is capable of parallel imaging. This is done by illuminating the sample surface with x-rays and then either electrostatically or magnetically projecting the electrons into a detector [4]. Using this type of imaging one can acquire a quantifiable image of the elemental distribution from a sample’s surface.

All of these techniques only tell a part of a surface's story. The HIM can show an accurate picture of surface morphology with nanometre resolution, while SIMS can give the composition of the surface at the submicron scale and XPS can quantify the elemental distribution. By combining these techniques one can put these parts together and gain a better understanding of the surface structure, be it a bacterial colony or a piece of Martian rock.

We have developed a methodology to be able to co-localise areas of interest when transferring samples between multiple different surface techniques. Then automatically correlate all images to form an accurate representation of a surface [5]. Correlative microscopy with SIMS, XPS, and HIM, allows an unprecedented level of surface detail to be found.

References

[1] J.C. Vickerman et al, *Surface Analysis The Principal Techniques*, 113-199, 2009

[2] D.C. Joy *Helium Ion Microscopy Principles and Applications*, 9-15, 2013

[3] T Wirtz *et alNanotechnology*26, 434001, 2015

[4] P. Van der Heide *X-ray Photoelectron Spectroscopy An introduction to Principles and Practices*, p54-56 2012

[5] J. Sheriff, *Ultramicroscopy", 228, 113322, 2021*

11:40am **SS-TuM1-11 Direct Observation of Drug Localization to Corneocytes Versus Lipid Matrix in Stratum Corneum – Differences between Caffeine and a Jasmonic Acid Derivative***, **Peter Sjövall,*** RISE Research Institutes of Sweden*; S. Gregoire,* L'Oréal Research and Innovation, France*; L. Skedung,* RISE Research Institutes of Sweden*; G. Luengo,* L'Oréal Research and Innovation, France

Understanding the penetration of molecules into stratum corneum (SC) is critical for the development of safe and effective drugs and cosmetics [1]. Proposed mechanisms describe the penetration as diffusion/migration of the active molecule either entirely in the lipid phase of the SC structure, or through the corneocyte bodies. However, experimental verification has been limited to indirect methods, or lacked the spatial resolution/sensitivity/specificity sufficient to reliably monitor the lipid phase and corneocytes separately. In this work, time-of-flight secondary ion mass spectrometry (TOF-SIMS) was used to monitor the 3D distribution of two actives with different properties in tape strips sampled after topical application of a mixture of these actives on ex vivo human skin samples. Alternating TOF-SIMS imaging of the sample surface and gradual removal of material from the same surface, by argon gas cluster ion sputtering, provides spatially resolved mass spectrometry data from the surface of the tape strip sample, through the lipid and corneocyte layers and into the tape. The results indicate that the spatial distribution of caffeine is closely associated to proteins, indicating a localization mainly in the corneocytes. In contrast, the distribution of a jasmonic acid derivative (JDA) is more inhomogeneous and indicates considerable localization to both the lipid phase and the corneocytes. Specifically, the JDA was found to be partially colocalized with C18:1 and C16:0 fatty acids at the interface between the corneocyte bodies and the underlying tape substrate. Based on previous results, we hypothesize that the C18:1 and C16:0 fatty acids represent cholesteryl esters, which are localized at the interface between the corneocyte bodies and the lipid phase of the SC structure, and that the JDA is partially localized to this interface.

(1)Sjövall, P.; Skedung, L.; Gregoire, S.; Biganska, O.; Clément, F.; Luengo, G. S. Imaging the Distribution of Skin Lipids and Topically Applied Compounds in Human Skin Using Mass Spectrometry. Sci. Rep. 2018, 8, 16683.

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*

(2)*Summerfield et al. Molecular Immunology 66 **2015**, 14–21*

(3)*Siy, P. W.et al. BioInformatics and BioEngineering. **2008**, BIBE. 2008, 8th IEEE International Conference on, IEEE: 2008; pp 1-6*

(4)*Passarelli et al. Anal. Chem. **2015**, 87, 6696-6702*

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.

[1] Sabatino, L.; Scordino, M.; Gargano, M.; Belligno, A.; Traulo, P.; Gagliano, G. HPLC/PDA/ESIMS evaluation of saffron (Crocus sativus L.) adulteration. Nat. Prod. Commun. 2011, 6, 1873–1876.

SIMS Solutions in Materials and Life Sciences
Room Great Lakes C - Session SS-TuA3

Microelectronics

Moderators: Temel Buyuklimanli, EAG Laboratories, **Jang Jung Lee**, TSMC

2:00pm **SS-TuA3-1 New Horizons for SIMS in the CMOS industry***, **Paul van der Heide**, V. Spampinato, A. Franquet,* IMEC, Belgium

The Complementary Metal Oxide Semiconductor (CMOS) industry was one of the two areas that drove the development of Secondary Ion Mass Spectrometry (SIMS) in its early years, the other being geochemistry. This arose from the unparalleled sensitivity and detection limits provided by SIMS which, in the case of the CMOS industry, introduced the possibility of deriving dopant depth distributions, albeit over spatially homogeneous regions that extended to several hundred microns. Developments in SIMS instrumentation are continuing to this day, with examples ranging from the introduction of Orbitrap™ mass analyzers in lab-based SIMS platforms to the development of inline (fab-based) SIMS platforms. The former affords a ~20x improvement in mass resolution, while the later improves time-to-data. This talk will cover some examples of how these developments are opening up new opportunities for SIMS within the CMOS industry.

2:20pm **SS-TuA3-3 Self-Focusing SIMS to Enable Boron Quantification in Small Silicon Fins***, **Valentina Spampinato**, R. Morris, W. Vandervorst, P. van der Heide, A. Franquet,* IMEC, Belgium

The continued downscaling of semiconductor devices has highlighted the importance for new metrologies to enable process control in the confined volumes and small (below 100 nm) features utilized today. Standard approaches using X-Ray Photoelectron Spectroscopy, conventional Secondary Ion Mass Spectrometry (SIMS) and Rutherford Backscattering Spectrometry lack the spatial resolution required. Alternative techniques that possess the appropriate spatial resolution e.g., Atom Probe Tomography and Transmission Electron Microscopy, are, on the other hand, time consuming and have an inherent lack of sensitivity due to the analysis volume.

In this study, the Self-Focusing (SF) SIMS concept has been successfully applied to the Boron quantification of a pattern sample composed by Silicon fins (with width size ranging from 20 to 500 nm) surrounded by SiO_2.

The spatial resolution limitation of conventional SIMS is overcome without sacrificing the excellent sensitivity by using specific cluster ions that can only originate from the Silicon fins region.

Careful study of the reference standards, such as B-doped Si and B-doped SiO_2 standards, was initially carried out in order to identify the most suitable cluster ions to use for the quantification of the Boron level. The most appropriate cluster ions were found to be BSi_2^- for the Boron and Si_3^- for the matrix.

In-situ AFM was used before and after sputtering the pattern sample, to precisely extract the sputter rate of both Si and SiO_2 regions and correctly convert the sputter time scale into depth scale.

With this approach, a Boron implant with peak concentration of ~8e^{20} at/cm^3 (average value over the different fin widths) was found, and no specific correlation with fins' size was observed. Moreover, the SF-SIMS approach was demonstrated to be in good agreement with standard SIMS approaches performed on the largest fins size, such as (1) Boron quantification after SiO_2 removal by chemical etching and (2) Boron quantification only on the fins by high lateral resolution data acquisition.

To benchmark our SF-SIMS approach, SIMS quantification was also performed on the SiO_2 region surrounding the 500 nm-wide fins and the Boron peak concentration (1.1e^{21} at/cm^3) was found to be in good agreement with SRIM simulation.

2:40pm **SS-TuA3-5 Can SIMS Still Be a Relevant and Accurate Technique for Dopant Quantification and Bulk Composition of Latest Advanced Nanoelectronic Devices?***, **Alexis Franquet**, V. Spampinato, W. Vandervorst, P. van der Heide,* IMEC, Belgium

Next generation semiconductor devices with improved performances have forced the industry to investigate and implement new materials and new devices architectures[1]. Among the different materials that have attracted interest over the past years are strained-Ge and SiGe as these are good candidates for p-FET and n-FET (Field-effect transistor) thanks to their excellent hole and electron mobilities[1]. The continuous downscaling of devices and the trend toward 3D architectures, lead to the deposition, growth and integration of the different materials in more and more confined volumes (of dimensions <10nm). Therefore, characterization methods are needed that can not only provide chemical information (for bulk composition) and high sensitivity (for dopant concentration), but also do so at a spatial resolution compatible with the devices under investigation. SIMS is a well-known surface analysis technique which enables to measure the distribution of elements and molecules in 1D (depth profiling), 2D (spatial imaging) and 3D (volumetric imaging)[2]. Since decades, SIMS was used in the Complementary Metal Oxide Semiconductor (CMOS) industry to derive dopant depth distributions thanks to its exceptional sensitivity and very low detection limits. This was until recently mostly done on blanket samples which turns to be irrelevant nowadays, as the properties of nano-volumetric devices are far away from the one of blanket samples. Although SIMS lacks the spatial resolution to directly probe devices from sub-10nm technologies, it can analyze the composition of narrow trenches (<20nm) using the concept of Self Focusing SIMS (SF-SIMS)[3].

This talk will discuss both the accuracy of Boron and Phosphorous dopant concentrations/profiles and the Ge quantification in blanket and patterned SiGe structures of dimensions far below the lateral resolution of SIMS. It will be shown how the use of concepts such as SF-SIMS and the introduction of new developments in the SIMS technique such as the Orbitrap$^{\text{TM}}$ mass analyzer allow to extend the application of SIMS in the semiconductor industry for the next decades. Several examples will be discussed, among which the quantification of the B dopant level and Ge content in complex devices made of SiGe-B epi dots (Θ<50nm) grown on 10nm wide Si:B nanowires.

[1] R. Chau, Process and Packaging Innovations for Moore's Law Continuation and Beyond, IEEE IEDM Tech. Dig. (2019) 1.1.1

[2] P.A.W. van der Heide, Secondary Ion Mass Spectrometry: An Introduction to Principles and Practices, John Wiley & Sons (2014) ISBN 978-1-118-48048-9

[3] A. Franquet, W. Vandervorst et al., Appl Surf Sci 365 (2016) 143-152

3:00pm **SS-TuA3-7 Characterization of GaN HEMT Structures by Combined SIMS & HAXPES Approach***, **Tarek Spelta**, M. Veillerot, E. Martinez, P. Fernandes Paes Pinto Rocha, L. Vauche,* CEA/LETI-University Grenoble Alpes, France*; B. Salem,* CNRS-LTM, Université Grenoble Alpes, France*; B. Hyot,* CEA/LETI-University Grenoble Alpes, France

III-N materials are gaining interest because they are widely used in high-tech industry. For instance, High Electron Mobility Transistors (HEMTs) with AlGaN/GaN structure are under development for devices in power electronics. The presence of a twodimensional electron gas (2-DEG) at the AlGaN/GaN interface allows greater electron mobility, which makes them very interesting for applications. The final properties of a device strongly depend on the quality of the interface between the GaN and the dielectric.

The issues to understand on this interface are the presence of deleterious Gallium oxide that lead to current leaks and the presence of undesired contaminations such as C, Cl, H, related to the manufacturing process. It is therefore necessary to characterize this interface with an analysis technique that illustrates with extreme precision the elements composition. Secondary Ion Mass Spectrometry (SIMS) appears to be particularly adapted to investigate such complex interfaces. In particular, low energy Caesium sputtering appeared to be an adequate path to depth profiling of III-N structures[1].

This research work illustrates the SIMS depth profiling of Al_2O_3/GaN stacks, where a 10 nm thick Al_2O_3 layer was deposited by ALD on top of as-epi and etched GaN surfaces. The use of two oxidant precursors such as O_3 and H_2O was investigated. The presence of Gallium oxide at the interface was investigated in the light of what was obtained for a Al_2O_3/GaO_x/GaN stack where a 4 nm-thick GaO_x layer was grown prior to alumina deposition.

Dual beam depth profiling is performed with a TOF-SIMS 5 (from IONTOF GmbH) using monoatomic Caesium sputtering beam at 500 eV, whereas the analysis is carried out using Bi_3^+ at 15 KeV. Depth profiling is also investigated through a Magnetic SIMS on SC-Ultra instrument (from CAMECA), with monoatomic Caesium beam at 250-500 eV used for both sputtering and analysis. Benefits and peculiarities of both the techniques on III-N structures are discussed. The results highlight the different Al_2O_3 structures impact oxidation and the presence of impurities at the interface.

Furthermore, these buried interfaces were explored down to 25 nm through hard X-ray photoelectron spectroscopy (HAXPES), and information about their chemical composition were provided. Finally, AFM roughness measurements before and after SIMS analysis were conducted to have morphologies information on samples.

Acknowledgments:

This work, carried out on the Nanocharacterization Platform of Minatec (PFNC), was supported by the "Recherche Technologique de Base" program.

Reference:

8. Kachan, M., et al. "O2+ versus Cs+ for[…]devices. "*Applied surface science* 231 (2004)

3:20pm **SS-TuA3-9 The Implementation of ToF-SIMS in the Development of State of the Art Ohmic Contacts to GaN**, ***Tatyana Kravchuk,*** Technion, Israel; *Z. Fogarassy,* Institute for Technical Physics and Material Science, Centre for Energy Research, Budapest, Hungary; *A. Rácz,* Institute for Technology Physics and Material Science, Centre for Energy Research, Budapest, Hungary; *A. Wójcicka, M. Borysiewicz,* Institute of Microelectronics and Photonics, Warsaw, Poland; *S. Grzanka,* Top-GaN Ltd., Warsaw, Poland; *P. Perlin,* Institute of High Pressure Physics PAS, Warsaw, Poland

For the performance and reliability of semiconductor devices stable contacts at interfaces (with low contact resistance and linear I-V behavior) are crucial. Their preparation and characterization are dominant issues in the microelectronic industry. Ohmic contacts are usually created by depositing thin metal films with a specifically chosen composition followed by annealing. The contact resistance strongly depends on the interfacequality and chemical state which makes the design and fabrication of low resistance contact structures such a challenge for microelectronics.

One of the best techniques to investigate the material processes occurring in contact structures is TOF-SIMS. The technique is able to detect all elements (even the light ones) with a high mass resolution, mass accuracy, and good signal-to-noise ratio. In a dynamic mode, TOF-SIMS has a monolayer resolution and micron depth range which makes it indispensable for the investigation of diffusion and layer intermixing, ofter arising during contact formation and aging.

Transparent or semi-transparent contacts are necessary for many applications like laser diodes or photovoltaics. The most popular choice is ITO, however alternative material systems gain interest because of sustainability and difficulties with indium sources. In this work, we investigated one of such systems which is based on zinc oxide (ZnO), which becomes conductive after doping with Al. In addition, if ZnO is in a solid solution with Mg the bandgap will widen. To investigate the interface between the ZnMgO:Al and the GaN substrate we checked a number of subcontact layers and annealing temperatures while using I-V measurements as a reference for the quality of the contact. By comparing the ToF-SIMS measurements of ohmic and non-ohmic structures we suggested the mechanism explaining the processes of contact creation. The results are supported by TEM and XRD results.

4:00pm **SS-TuA3-13 Transfer of Zirconium Oxide Nanotubes onto Zirconia-Based Ceramic Implants**, ***Swathi Naidu Vakamulla Raghu,*** University of Siegen, Germany

Nanostructured architectures, offer the possibility of creating storage units whilst improving bio-integration and functionality as a result of superior adhesion and robust reactivity due to the increased surface area.[1,2] Electrochemical anodization is an efficient way to develop large-scale nanostructures on a material's surface, unfortunately fabrication by anodization is restricted to valve-metals. Non-metals, especially biomaterials are often metal-oxides and ceramics such as in the field of dental and orthopedic applications.[3] In order to develop nanoporous or nanotubular surface structures on such surfaces, multi-step procedures can be applied, starting with metal deposition on the parent materials via vacuum assisted treatments such as ALD, e-beam sputtering, FDM, etc.[4-6] This approach poses numerous challenges, such as adhesion of deposited metal to the ceramic substrate, stability at the interface in addition to the cost-factor to name few. Herein, we demonstrate the possibility of attaching ZrNTs to ZrO_2 ceramics without the use of any intermediate treatment of the parent-ceramic. We report on the synthesis route for metal-oxide nanotubes via electro-chemical anodization of zirconium foil resulting in the formation of zirconia nanotubular (ZrNT) films, that are subsequently transferred onto pre-formed zirconia (ZrO_2) implant material. This approach involves a direct transfer of ZrNT films onto the ceramic implant via an acetone bath after a successful detachment from the foil using office-adhesive tape prior to transfer. This simple technique is not limited by geometric constraints of the parent material.

References

1.D. Losic, S. Simovic, Self-ordered nanopore and nanotube platforms for drug delivery applications, Expert Opin. Drug Deliv.2009

2.S.N.V. Raghu, G. Onyenso, S. Mohajernia, M.S. Killian, Functionalization strategies to facilitate multi-depth, multi-molecule modifications of nanostructured oxides for triggered release applications, Surf. Sci. 719.2022

3.G. Maccauro, P. Rossi, L. Raffaelli, P. Francesco, Alumina and Zirconia Ceramic for Orthopaedic and Dental Devices, Biomater. Appl. Nanomedicine.2011

4.P. Piszczek, Z. Lewandowska, A. Radtke, W. Kozak, B. Sadowska, M. Szubka, E. Talik, F. Fiori, Biocompatibility of Titania Nanotube Coatings Enriched with Silver Nanograins by Chemical Vapor Deposition

5.C.. Gent, A.N. and Lin, Model Studies of the Effect of Surface Roughness D T Ic, J. Adhes. 32,2–3,1990,113–125

6.D. Chopra, K. Gulati, S. Ivanovski, Towards clinical translation: Optimized fabrication of controlled nanostructures on implant-relevant curved zirconium surfaces, Nanomaterials. 11,2021

4:20pm **SS-TuA3-15 Quantification of Sims Measurements by Using Ion Implanted Metallic Standards**, ***Guiomar D. Soria,*** *M. González,* CIEMAT, Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas, Spain; *M. Crespillo, G. Garcia,* CMAM, Centre for Micro Analysis of Materials , Spain

Secondary ion mass spectrometry (SIMS) is a powerful analytical technique for surface characterization, allowing the identification of elements and isotopic species present in the solid composition with high sensitivity. SIMS analysis is widely used for materials with applications in microelectronics, aeronautics, and fusion, among others.

Nonetheless, it is well-known that the quantification of this method is challenging. The reason is that the signal of secondary ions sputtered from the substrate by irradiation with the primary ion beam is strongly influenced by the chemical environment of the solid. I.e., the analyte of interest will be easy/difficult to sputter and ionize depending on the type of bonding with the matrix. This fact is reflected in the measurement with greater or lesser signal intensity. This phenomenon called the "matrix effect" hinders reaching a general quantification expression for the technique, making it difficult to correlate the intensity response of the registered elements with their accurate concentration in the substrate.

In this contribution, a solution to minimize the matrix effect for SIMS analysis quantification is investigated through the production of calibrated standards. For this aim, implanted ions with known concentrations in a fusion-relevant matrix are applied and correlated with the SIMS signals. Specifically, the application of this methodology is now focused on a metallic substrate, with a particular interest in the fusion field, implanted with some elements with easy ionizability, where the parameters of concentration and depth of the ion into the substrate are controlled. Therefore, standards consisting of tungsten metal commercial matrices were prepared by ion implantation with 18 MeV iron and 10 MeV chromium ions at two different fluences (about 10^{15} and 10^{16} ions/cm^2) at room temperature. Subsequently, the implanted samples were characterized using surface and depth profile SIMS measurements for identifying the Fe and Cr ions recorded signal. The accurate value of the ion doses was obtained using Rutherford backscattering (RBS) analysis on control silicon substrates. The resulting calibration concentration curves were associated with the SIMS signals, being the tool for the quantification analyses of unknown concentrations of Fe and Cr in test substrates. Therefore, the method was validated by analysing impurities and alloying of these elements in a non-commercial tungsten matrix.

4:40pm **SS-TuA3-17 Ion Implantation Applications for In-Line SIMS Metrology**, ***Lawrence Rooney***, *S. Okada,* Nova

In the semiconductor industry, ion implantation process has expanded to a wide range of applications with doses and energies spanning several orders of magnitude.

Ion implantation is a very complicated process with many parameters and factors that affect the implant profile. For example, shadowing effects from higher aspect ratio of photoresist opening, ion channeling or de-channeling effects due to implant angle variations, and dose and implant energy accuracies are all important factors in achieving uniform device performance and good product yield. In addition, current process controls are done on test wafers with certain time intervals, where broken sample pieces are sent outside of the fab for SIMS analysis. The turnaround time is generally long, and the results often do not reflect the actual production conditions. It is known in some cases that, while the control charts are in good standing, the product has failed to meet its specification. The demand for consistent implantation material is becoming more and more important. Hence, the desire for better implant process control is sorely needed.

This paper explores how utilizing Secondary Ion Mass Spectroscopy, (SIMS) in-line to measure peak concentration, peak depth, and dose simultaneously to provide better implant process control.

5:00pm **SS-TuA3-19 Molybdenum Oxide Substrate Used in "Storing Matter" SIMS Technique – Determination of Relative Sensitivity Factors of 20 Elements***, **Piotr Konarski**, J. Ażgin,* Łukasiewicz Research Network - Tele and Radio Research Institute, Poland*; M. Kasik,* MK2 Technologies, Inc.*; H. Brongersma,* Eindhoven University of Technology, Netherlands

We present the use of molybdenum oxide substrate as a collector plate in storing matter (SM) technique applied in SIMS [1, 2] and determination of relative sensitivity factors (RSF) of this technique for a series of 20 elements from Mg to Bi.

The SM technique enables quantitative SIMS analysis by separating process of sputtering and process of secondary ion formation. The analysis is done in two steps, first the sputtered material of ion bombarded surface is deposited onto the substrate so as to obtain approximately a sub-monolayer coating. Then, the substrate with the stored material is analysed using a classical SIMS analytical method.

As substrates we use 300 nm thick molybdenum oxide MoO_{3-x} layers deposited onto titanium plates by high-vacuum evaporation of ultra-pure MoO_3. The SM experiments are carried out in Hiden SIMS Workstation apparatus equipped with a special sample manipulator enabling positioning of samples for sputter deposition process and positioning of the collector plate for SIMS analysis of the deposited material.

In SM experiments we use 5 keV, 48 nA O_2^+ beam. During sputter-deposition process this beam is scanned over 600 x 600 µm area of the sample for a time period of 540 s, equal for each analysed sample. Then the SIMS analysis of stored material is performed, and this beam is scanned over 3000 x 3000 µm area of the collector plate. Obtained results show, that most of the examined elements yield higher SM SIMS signals comparing to classical SIMS analysis of this set of elements.

The obtained results allow to calculate the RSF factors of the 20 elements deposited on MoO_{3-x} substrate. We plot the obtained RSF values versus atomic mass, and versus first ionization potential values of the examined elements and compare the plots with typical SIMS RSF factors of elements implanted into silicon matrix. We also compare the results with RSF values of another analytical technique - glow discharge mass spectrometry (GDMS) [3].

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[1] Mansilla, C., & Wirtz, T. (2010). Surface and Interface Analysis, 42(6- 7), 1135-1139.
[2] Konarski, P., Miśnik, M., Zawada, A., & Brongersma, H. H. (2014). Surface and Interface Analysis, 46(S1), 360-363.
[3] Vieth, W., & Huneke, J. C. (1991). Spectrochimica Acta Part B: Atomic Spectroscopy, 46(2), 137-153.

5:20pm **SS-TuA3-21 CsM^+ Cluster Method in Dynamic SIMS: A Versatile and Practical Approach for Thin Film Electronic Materials***, **Marinus Hopstaken**, S. Molis,* IBM T.J. Watson Research Center

Reactive Cs^+ primary beam is routinely employed in SIMS depth profiling for reasons of negative ion yield enhancement. Alternatively, positively charged Cs-cluster ions (Cs_nM^+; n= 1,2) can be analyzed, providing a versatile approach for simultaneous detection of either electro-positive (CsM^+) and electro-negative species (Cs_2M^+) [1]. Normalization of Cs_nM^+ cluster ion to their Cs_n^+ reference ions is commonly applied to reduce so-called 'matrix effects' [1]. Here, we will outline practical considerations, quantification aspects, and some artifacts in Cs_nM^+ cluster analysis. We will demonstrate this using various examples of Cs_nM^+ depth profiling of thin-film nano-structured materials for a variety of electronic (CMOS, memory) and post CMOS (III-V, quantum computing) applications.

Application of Cs_nM^+ cluster approach for dopant profiling in Si is generally compromised due to poor sensitivity [2]. In contrast, we have reported excellent sensitivity for p+ dopants (Mg, Zn) in high-mobility III-V compounds. Useful yields for Mg and Zn are found to be largely insensitive to the matrix composition for different binary and ternary III-V materials (i.e. $In_xAl_yGa_{1-x-y}As$). Quantitative analysis down to 5e15 at.cm^{-3} detection limits in III-V, using appropriate ion implant calibration standards.

Cs_nM^+ cluster approach is well suited for quantitative analysis of simple binary alloys such as $Si_{1-x}Ge_x$ and NiSi silicides [3,4]. Quantification is based on linearization of SIMS Cs_nM^+ / Cs_nSi^+ ion intensity ratios to the [M]/[Si] atomic ratio, derived by absolute external methods such as XRD, RBS, XRR). Here we extend this approach to more complex (quasi-) ternary mixtures such as group III-arsenide or phosphide compounds (e.g. $Al_xGa_{1-x}As$) and phase change materials (PCM). We generally find good linear correlation between CsM+ ion intensity ratios and their corresponding atomic ratios.

We generally employ the Cs_nM^+ cluster approach to more complex multilayer structures for the simultaneous analysis of electropositive (CsM^+) and electronegative species (Cs_2M^+), while facilitating robust and reproducible charge compensation in thin dielectric layers in a magnetic sector instrument. We will demonstrate examples across a wide range of applications (high-k / metal gate, alternate materials for memory applications, *etc*…) to demonstrate versatility and general applicability.

References:

9. B. Saha and P. Chakraborty, Energy Procedia **41**, p. 80 (2013)
10. P. Holliger *et al.*, Surface and Interface Analysis **34** (1), p. 472 (2002)
11. M. Gavelle *et al.* J. Appl. Phys. **104**, 113524 (2008)
12. M.J.P. Hopstaken et al., ECS Transactions **3** (2), p. 319 (2006)

SIMS Solutions in Materials and Life Sciences
Room Great Lakes A2-A3 - Session SS-TuA4

Cells and Tissue IV

Moderators: Gregory Fisher, Physical Electronics USA, **Sebastiaan Van Nuffel**, Maastricht University

2:00pm **SS-TuA4-1 Probing the Human Epidermis from a Materials Science Point of View***, **Xavier Delvaux**,* University of Namur, LISE Research unit, Namur Institute of Structured Matter, Belgium*; Y. Poumay,* University of Namur, Namur Research Institute for Life Sciences, Belgium*; L. Houssiau,* University of Namur, LISE Research unit, Namur Institute of Structured Matter, Belgium

The mammalian epidermis, the most topical cellular layers of the skin, may be considered as a continuously renewing and highly complex structure composed of multiple biomolecular layers. The most fundamental functions of the epidermis are to provide a barrier shielding the organism from its environment and to mitigate dehydration. This is achieved through a specific cellular death pathway known as cornification. Keratinocytes undergoing cornification produce a protein-rich cellular envelope as well as an intercellular matrix composed mainly of lipids and hydrophilic molecules, resulting in a specific histological layer referred to as the *Stratum Corneum* (SC). However, a wide range of pathologies can affect the formation of the epidermis and impair its function. In the context of dermatological research, understanding the molecular changes induced by these pathologies is paramount for their efficient treatment and prevention.

In the recent years, analytical techniques derived from the materials science field have been of increasing interest for the investigation of complex biological systems. Among those techniques, ToF-SIMS has proven to be a particularly useful tool in the field of lipidomics, as it combines a very high sensitivity with a high mass and spatial resolution. In this work, we aimed at developing a rigorous and reproducible investigation methodology of the human epidermis by applying ToF-SIMS to an in vitro epidermal model known as Reconstructed Human Epidermis (RHE). This model is composed of keratinocytes layers cultured in order to reproduce the main histological features of a real human epidermis. The ToF-SIMS characterization of these RHEs was performed under static SIMS conditions on freeze-dried cryosections and combined both high mass and lateral resolution acquisitions. Data processing was assisted by Principal Components Analysis (PCA). This approach allowed the successful decorrelation of the highly complex data sets into a few principal components (PC) carrying the essential biological information about RHE cross sections. Most notably, PCA yielded one specific PC highlighting relevant spectral features needed to distinguish the viable cells from the cornified region. Furthermore, we obtained high lateral resolution molecular maps of the major species identified by PCA. Finally, we demonstrated that this methodology was reproducible, therefore allowing the production of experimental replicates. Ultimately, these results suggest that this methodology could be of significant interest for the field of dermatology by allowing the effective characterization of molecular modifications induced by various skin pathologies.

2:20pm **SS-TuA4-3 Ambient Mass Spectrometry Imaging of Lipid Molecules from Live Cells and Tissues Using Nanomaterials***, J. Kim,* Kyungpook National University, Republic of Korea*; H. Lim,* ***DaeWon Moon,*** Daegu Gyeongbuk Institute of Science and Technology (DGIST), Republic of Korea **INVITED**

We have been developing new methods to analyze cells and tissues in ambient condition without any harsh chemical fixation or physical freezing and drying for last several years. The first approach, an atmospheric pressure mass spectrometry imaging method, is based on laser ablation in atmospheric pressure assisted by atmospheric plasma and nanomaterials such as nanoparticles and graphene to enhance laser ablation. The second one is based on secondary ion mass spectrometry (SIMS) imaging of live cells in solution capped with single layer graphene to preserve intact and hydrated biological samples even under ultrahigh vacuum for SIMS bio-imaging in solution.

Recent activities such as the extension of the molecular analysis range from lipids to proteins, applications to neuronal and cancer cell using confocal, SIMS, and SEM/HIM will be discussed.

References

[1] Jae Young Kim, EunSeokSeo, HyunminKim, Ji-WonPark, Dong-Kwon Lim, and DaeWon Moon ˝Atmospheric Pressure Mass Spectrometric Imaging of Live Hippocampal Tissue Slices with Subcellular Spatial Resolution’, Nat. Comm., 8, 2113-2125 (2017)

[2] Heejin Lim, Sun Young Lee, Yereum Park, Hyeonggyu Jin, Daeha Seo, Yun Hee Jang, Dae Won Moon, “Mass Spectrometry Imaging of Untreated Wet Cell Membranes in Solution Using Single-Layer Graphene”, Nature Methods 18, 316-320 (2021)

3:00pm **SS-TuA4-7 SiLC-MS (Single-Live-Cell Mass Spectrometry) Analysis in the Context of Drug Discovery***,* ***Carla Newman,*** GSK, UK

In the last few decades, the pharmaceutical industry has transformed people’s lives. However, the development of new drugs possesses challenges and a paradigm shift in the drug discovery workflow would be desired to reduce attrition and transform conventional drug screening assays into translatable analytical techniques for the analysis of drugs in complex environments, both in-vitro and ex-vivo.

The ability to visualise unlabelled compounds inside the cell at physiological dosages can offer valuable insight into the compound behaviour both on and off-target.

SiLC-MS is a semi-automated methodology that allows the collection of intracellular contents using a modified CQ1 imaging system developed by Yokowaga. The instrument is equipped with a confocal microscope that allows bright field imaging as well as fluorescence imaging with 4 lasers (405, 488, 561 and 640 nm). Sampling is performed using the tips developed by Professor Masujima (1-4). The tip, holding the cellular contents, is then used for static nanospray of the contents into an Orbitrap Fusion Lumos (Thermo Scientific) and the resulting data processed using Compound Discoverer (Thermo Scientific).

In this study, we show the applicability of the SiLC-MS technology to drug discovery, as it is crucial to identify compound and its metabolites when incubated in a mammalian cell at a therapeutic dose. We report on the validation studies performed using the SiLC-MS platform, in these validation studies we assess the ability to distinguish different cell types based on their metabolomic fingerprint, furthermore we have also evaluated if this assay was sensitive enough to detect drugs intracellularly.

We are currently establishing a multi-omics platform on the modified CQ1 that allows both metabolomics and transcriptomics at the single cell level. For that we have sampled the cells first for metabolomics and then for transcriptomics.

We demonstrate that dosed compound can be identified in a single cell after samplingusing the modified CQ1, endogenous metabolites can also be identified that can further the understanding of the drug’s mechanism. This technique has direct relevance for assessing compound effects on disease relevant cells and its low sample requirement makes it applicable to studying rare cell types. The use of high content imaging system enables the effect of compounds on live cells to be studied and suitable time points selected for sampling cell contents.

3:20pm **SS-TuA4-9 TOF-SIMS Study of Pharmacological Active Components in Cordyceps Sinensis***, Q. Zhan,* School of Chemical and Environment Engineering, China University of Mining and Technology , China*; M. Xia,* Institute of Geographic Sciences and Natural Resources Research, Chinese Academy of Sciences, China*; S. Sun, L. Cai,* Department of Chemistry, Tsinghua University, China*; H. Liang,* School of Chemical and Environment Engineering, China University of Mining and Technology, China*;* ***Zhanping Li,*** Key Laboratory of Organic Optoelectronics and Molecular Engineering of Ministry of Education, Department of Chemistry, Tsinghua University, China

Cordyceps sinensis is a well-known traditional Chinese medicine. This study showed TOF-SIMS was used to identify the pharmacological active substances, reveal the pharmacological active substances at different developmental stages and visualize spatial differentiation of the pharmacological active substances in Cordyceps sinensis. Base on the high mass resolution (M/ΔM) of TOF-SIMS, the positive fragment ion detected at m/z 251 might not be the molecular ion M^+ of cordycepin $C_{10}H_{13}N_5O_3$ (m/z 251). There are some “splicing” ions, which are formed between pharmacological active compounds and weakly polar compounds and/or themselves, appeared in the TOF-SIMS mass spectrum of Cordyceps sinensis. The changes of the pharmacological activesubstances of Cordyceps sinensis with time (different stages of development during growth cycle) at different parts (stroma, worm body and the base of stroma) were studied. The amino acid class showed different changes in the different parts due to the metabolic regulation in development. The changes of nucleosides are similar in the same part of Cordyceps sinensis but there are great differences betweenstroma and worm body. The content of ergosterol first rises and subsequently falls in the stroma, rises at the base of the stroma, and at the worm body first falls and subsequently rises. The visualization of spatial differentiation of ergosterol and other active components in whole Cordyceps sinensis was first realized by developing a feasible and simple “segmentation-imaging-splicing” strategy based on TOF-SIMS. Whole-body chemical mapping of Cordyceps sinensis was then accomplished by splicing these ion images with normalized size and signal intensity. Ergosterol was found more enriched in host caterpillar, especially enriched in the top of host caterpillar, than in fruiting body. Moreover, ergosterol and lipids showed obviously complementary distribution pattern in some special structures of Cordyceps sinensis.

References

[1] Committee of National Pharmacopocia. Pharmacopocia of People,s Republic of China. Beijing:

China Medicine Science and Technology Press. 2010, 106-107

[2] Li S P., Yang F Q., Karl W.K., Tsim, Journal of Pharmaceutical and Biomedical Analysis, 2006,

41, 1571-1584

[3] Guo F Q., Li A., Huanga L F., Liang Y Z., Chen B M., Journal of Pharmaceutical and Biomedical

Analysis, 2006, 40, 623–630

[4] Zhang Zhihong, Yang Lu Ming, Tai LiMei, Wu SuRui. Edi-ble Fungi of China. 2014, 33, 1-4

[5] Sprecher M.; Sprinson D B. Journal Organic Chemistry. 1963, 28, 2490-2491

[6] J.P. Yuan, J.H. Wang, X. Liu, H.C. Kuang, S.Y. Zhao, Food Chem. 2007, 105,1755–1759

Vendor Session
Room Great Lakes B - Session VS-TuA
Vendor Session

2:00pm **VS-TuA-1 Physical Electronics Vendor Presentation: Innovation and Leadership in Chemical & Molecular Analysis Instrumentation***,* ***Gregory L. Fisher,*** Physical Electronics

ULVAC-PHI and Physical Electronics (PHI) have been designing and developing surface analysis instrumentation, including Auger electron spectroscopy (AES), x-ray photoelectron spectroscopy (XPS), time-of-flight secondary ion mass spectrometry (TOF-SIMS) and dynamic SIMS (D-SIMS), for over 40 years. A guiding philosophy has been that effective and informative characterization of surface chemistry requires analyzer and probe technologies which enable the collection of signal from all parts of the sample surface in a way that enables high fidelity chemical identification and mapping. Representative examples include the pioneering developments of the cylindrical mirror analyzer (CMA) employed in our scanning Auger nanoprobe instruments and the scanning x-ray microprobe (SXM) employed in our XPS instruments. At one time, a two-stage reflectron analyzer was employed in our TOF-SIMS instrument; however, the superior angular acceptance, depth-of-field, kinetic energy focusing and spectral background characteristics of the triple electrostatic sector-based design resulted in adoption of this analyzer technology for use in our TOF-SIMS instruments. More recently, we have incorporated a lossless tandem MS analyzer technology to enable accurate peak identifications in a way that does not limit the speed, sensitivity or resolution of TOF-SIMS but, rather, expands the TOF-SIMS application space. In summary, the technology developed and employed in ULVAC-PHI instruments facilitates the analysis and characterization of topographically rough, real-world samples.

ULVAC-PHI continues to lead the research market with innovative instruments and capabilities for chemical and molecular imaging related to discovery and problem-solving applications. These developments include new ion beam technologies, automation and ease-of-use as well as new methods for 2D and 3D characterization. This talk will highlight recent developments in photoelectron and mass spectrometry instrumentation.

2:30pm **VS-TuA-4 IONTOF Vendor Presentation: Latest News and Developments from IONTOF***, **Sven Kayser**, M. Kleine-Boymann,* IONTOF GmbH, Germany

This presentation will discuss the latest news and developments from IONTOF. An overview of the technology leading M6 instrument and its derivatives, the M6 Plus and M6 Hybrid SIMS will be given along with new software features that have been released since the last International SIMS conference. Examples of how these hardware and software developments can be used in daily work will also be presented.

3:00pm **VS-TuA-7 CAMECA Vendor Presentation: Continuous Improvements in SIMS Technologies***, **Adrien Vuillaume**, O. Dulac, A. Thomen, A. Robbes, S. Choi, P. Peres, N. Lahoutifard-Henry, L. Créon,* CAMECA

CAMECA is a world leading supplier of microanalytical and metrology instrumentation for research and process control. CAMECA secondary ion mass spectrometers (SIMS) equip government and university labs as well as high-tech industrial companies around the world, with applications in different fields such as microelectronics, materials science, geosciences, and biology.

CAMECA SIMS offer **superior performances for dynamic SIMSanalyses**: extreme sensitivity, high depth and lateral resolution together with high throughput. Both elemental and isotopic information can be obtained for all species in the periodic table, with detection limits down to ppb level for many elements. Different types of dynamic SIMS output can be obtained: depth profiles, isotope ratios, quantitative imaging…

CAMECA has developed **different high-end magnetic Sector SIMS instruments** to achieve the highest performance for different applications. Among them, the NanoSIMS offers the highest performance in lateral resolution and versatility in applications.

The NanoSIMS development was initiated by Professor SLODZIAN on an original idea: the coaxial lens. The coaxial lens focuses primary beam and collects sputtered secondary ions, later sent in a double focusing Mattach-Herzog mass spectrometer. Presented at the SIMS VI in 1987, the original NanoSIMS 50 demonstrated exceptional imaging capabilities with lateral resolution down to 50 nm and sequential acquisition of 5 mass-filtered images with a high mass resolving power. Thanks to those concomitant capabilities, the NanoSIMS 50 launched in 2000 was immediately adopted by cosmochemists to image unusual isotopic signatures in submicrometric presolar material. Following the need to characterize more complex materials, the NanoSIMS 50L, for large radius, was launched in 2005 with a multicollection totalizing 7 detectors. The RF source replace the deprecated Duoplasmatron in 2013 as a source of Oxygen negative primary ions, improving the sharpness of the positive secondary ions images by a factor 4.

We will discuss (soon-to-be launched) next developments towards smaller lateral resolution and imaging capabilities on sample no longer needed to be solid nor dry.

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.

REFERENCES

[1]S.N. Vakamulla Raghu, M.S. Killian, Wetting behavior of zirconia nanotubes, RSC Adv. 11 (2021) 29585–29589. https://doi.org/10.1039/D1RA04751E.

[2]S.N.V. Raghu, G. Onyenso, S. Mohajernia, M.S. Killian, Functionalization strategies to facilitate multi-depth, multi-molecule modifications of nanostructured oxides for triggered release applications, Surf. Sci. 719 (2022) 122024. https://doi.org/10.1016/j.susc.2022.122024.

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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[1] Sheu, D. Y. (2004) *Journal of Micromechanics and Microengineering*, *15*(1), 185.
[2] Hiden Analytical, 420 Europa Boulevard, Gemini Business Park, Warrington, WA5 7UN, UK
[3] Konarski, P., Miśnik, M., & Zawada, A. (2016) *Journal of Analytical Atomic Spectrometry*, 31(11), 2192-2197.

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.

[1] Kim, Y. K.; Wang, L. S.; Landis, R.; Kim, C. S.; Vachet, R. W.; Rotello, V. M. *Nanoscale***2017**, *9* (30), 10854–10860.

[2] Zhao, Y.; Deng, G.; Liu, X.; Sun, L.; Li, H.; Cheng, Q.; Xi, K.; Xu, D. *Anal. Chim. Acta***2016**, *937*, 87–95.

[3] Choi, W.; Choudhary, N.; Han, G. H.; Park, J.; Akinwande, D.; Lee, Y. H. *Mater. Today***2017**, *20* (3), 116–130.

[4] Joh, S.; Na, H. K.; Son, J. G.; Lee, A. Y.; Ahn, C. H.; Ji, D. J.; Wi, J. S.; Jeong, M. S.; Lee, S. G.; Lee, T. G. *ACS Nano***2021**, *15* (6), 10141–10152.

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.

References:

[1] Rubin A. et al. (2007) *Geochimica et Cosmochimica*, A71(9), 2364-2382

[2] Hewins R.H. et al. (2014*)* Geochimica *et Cosmochimica*, A124, 190-222

[3] Marrochi Y. et al. (2014) *Meteoritics & Planet. Sci.*, 49(7), 1232-1249

[4] Dionnet Z. et al. (2018), *Meteoritics & Planet. Sci.*, 53(12), 2608-2623

[5] Noun M. et al. (2019) *Life*, 9(2), 44

[6] Alexander C.M.O.D. et al. (2014) *Meteoritics & Planet. Sci.*, 49(4), 503-525

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). Unfortunately, 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.

Dealing with Data and Interpretation
Room Great Lakes Promenade & A1 - Session DI-TuP

Dealing with Data and Interpretation Poster Session

DI-TuP-1 Statistical Analysis of Tof-Sims Images: Seeking Patterns in the Noise*, **Alan Spool,*** Western Digital Corporation

TOF-SIMS analysts are often asked to discern difficult to find features such as evidence for corrosion, small particles, features at the edge of our detection limits, and other hints of inhomogeneity. The human ability to recognize patterns can also lead to the discernment of non-existent features, or at least uncertainty about whether an image is truly random.A simple statistical test, comparing a calculated Poisson distribution to the actual distribution accompanied by a chi square test solves this problem.If the distributions match, the image variations are random noise.

Data that is non-random should be over dispersed.Variability within the image should produce a wider range of pixel counts, more pixels with higher counts than expected, and more with less.However, this work shows that TOF-SIMS images are often under dispersed, that is, a narrower distribution than calculated.This tends to be more of an issue with ions showing higher intensities.Dead time in the instrument tends to artificially reduce the signal overall, and it reduces the probability of pixels having higher counts more than it reduces the probability of them having lower counts, thus narrowing the distribution.It is still possible to apply the test by adjusting the data.For a Poisson distribution, the variance is equal to the mean.One can adjust the data by subtracting the difference between the variance and the mean from all of the pixel count values, thus creating a distribution where, given no other reasons for variations, the variance equals the mean.

In this work, various data sets are tested by this method and the results discussed.The use of this method turns out to be equally useful to the evaluation of image data and the evaluation of instrument artifacts.

DI-TuP-3 Characterisation of Noise in the Orbisims and Scaling Method for More Effective Multivariate Data Analysis*, **Michael R. Keenan,*** Independent*; G. Trindade,* National Physical Laboratory, UK*; A. Pirkl,* IONTOF GmbH, Germany*; J. Zhang,* National Physical Laboratory, UK*; H. Arlinghaus,* IONTOF GmbH, Germany*; L. Matjacic,* National Physical Laboratory, UK*; C. Newell,* The Francis Crick Institute, UK*; R. Havelund,* National Physical Laboratory, UK*; K. Ayzikov,* Thermo Fisher Scientific, Germany*; A. Gould,* The Francis Crick Institute, UK*; J. Bunch,* National Physical Laboratory, UK*; A. Makarov,* Thermo Fisher Scientific, Germany*; I. Gilmore,* National Physical Laboratory, UK

The most challenging measurements are often at the boundary of detection just above the noise, for example the detection of gravitational waves where an understanding of the detector noise was critical.[1] A study of the noise in a detector system is of wider importance and a better understanding can make a profound difference to measurement sensitivity, reproducibility, and the interpretation. It can have an important contribution to the variance in data that may even overbear biological sample-to-sample variance and is essential for correct use of multivariate based data analytics.

The OrbiSIMS instrument[2] features a Time-of-Flight (ToF) mass spectrometer (MS) and an Orbitrap MS, which confer advantages of speed and high mass resolution, respectively. Secondary ions are accelerated by an extraction electrode and can either pass directly through a switching electrode to the ToF MS or can be deflected to a transfer system that sends them towards the Orbitrap MS. The ToF MS uses a channel plate detector in a single ion counting mode and Poisson-distributed secondary ions are convolved with detector deadtime effects to yield binomially-distributed signal.[3] In contrast, the Orbitrap analyser uses a quasi-continuous source of secondary ions that are injected into an ion trap where they revolve around the central electrode and oscillate along spindle shaped electrodes with a frequency inversely proportional to the square root of the mass of the ion. An image charge is created in the pair of outer electrodes and is measured with time. This time-domain transient signal is converted to frequency (and hence mass) domain by a Fourier transform.

Measurement of the noise distribution of an Orbitrap analyser requires a stable source of ions. Here, we take advantage of a Bi-Nanoprobe (IONTOF GmbH) that has a very stable (< 1% RSD) 30 keV Bi_3^+ primary ion beam. We report measurements across a range of ion intensities and developed a statistical model that considers three sources of noise: “counting noise”; “transfer noise” of ions into the Orbitrap analyser; and “thermal noise” from the Orbitrap detection circuit. This model was used to develop a data scaling strategy that accounts for heteroscedasticity (non-uniform noise). We show that our scaling strategy has important implications for Principal Component Analysis (PCA), similarly to what has been developed before for the noise in ToF-SIMS.[3]

1. B. P. Abbott *et al.Phys. Rev. Lett.*, 116, 1–16, 2016

2. M. K. Passarelli *et al.Nat. Methods*, 14 1175-1183 2017

3. M. R. Keenan and V. S. Smentkowski, *Surf. Interface Anal.*, 48 218–225, 2016

DI-TuP-5 4D Surface Reconstruction to Link Microstructural Topography with Sims Information*, **Jean-Nicolas Audinot**, A. Ost,* Luxembourg Institute of Science and Technology (LIST), Luxembourg*; T. Wirtz,* luxembourg Institute of Science and Technology (LIST), Luxembourg

Surface topography is known to have a strong influence on secondary ion emission under primary ion bombardment. Topography variations induce local changes of the incidence angle of the primary ion beam, strongly affecting surface sputtering processes, and hence the sputtering yield [1]. SIMS images suffer from topographical artefacts, resulting from these local variations of the sputtering yield, which can lead to erroneous conclusions about materials’ surface concentration gradients.

In the recent years, we have developed and improved a method for 3D reconstruction of samples with complex surfaces from multi-view Secondary Electron (SE) images correlated with analytical SIMS images [2,3]. A series of SE images is taken at different angles around the sample and implemented into a photogrammetry software allowing to obtain a 3D SE surface model. Subsequently, the SIMS image is acquired in top view mode and projected onto the 3D SE reconstruction to obtain a full 4D surface model. Using a numerical processing algorithm, topographical information is extracted from the reconstruction and linked to the local intensity of the SIMS signal to better understand intrinsic properties of the material.

In this contribution, we will review the 4D methodology by showing applications from different fields (materials science and geology). The data was obtained both on commercial instruments (SIMS data from a CAMECA NanoSIMS 50L correlated with SE data obtained on a Secondary Electron Microscope) and on in-house developed instruments (SIMS and SE data from a Helium Ion Microscope equipped with a magnetic sector SIMS add-on system) [4]. 4D results are useful not only for enhanced specimen visualization, but also to study variations of the local topography to learn more about nano-scale material transformation processes and to localize and correct SIMS image artefacts.

[1] H. L. Bay & J. Bohdansky, App. physics 19, (1979), p. 421

[2] F. Vollnhals, T. Wirtz, Anal. Chem. 90 (2018), p. 11989

[3] A.D. Ost et al., Environ. Sci. Technol. 55 (2021), p. 9384

[4] T. Wirtz et al., Annu. Rev. Anal. Chem. 12 (2019), p. 523

DI-TuP-7 Comparison Study of Mouse Brain Tissue by Using ToF-SIMS with Static Limit and Hybrid SIMS Beyond Static Limit (Dynamic Mode)*, **Hyun Kyong Shon**, J. Son,* Korea Research Instutue of Standards and Science (KRISS), Republic of Korea*; J. Moon,* Korea Research Institute of Bioscience and Biotechnology(KRIBB), Republic of Korea*; J. Jim,* Korea Basic Sicence Institute(KBSI), Republic of Korea*; T. Lee,* Korea Research Instutue of Standards and Science (KRISS), Republic of Korea

The mouse brain is widely used in various studies, including studies on degenerative brain diseases such as Alzheimer’s and Parkinson disease [1-3]. In particular, several attempts have made to measure disease-related biomolecules such as metabolite, fatty acid, and lipids from tissue images of mouse brain by using cluster ion beam in time-of-flight secondary ion mass spectrometry (ToF-SIMS). To know exactly what biomolecules in the ToF-SIMS images are, ToF-SIMS equipments with MS/MS function to identify biomolecules have recently been released [4-6].

In this study, the mouse brain was sectioned approximately bregma +1 mm point in the coronal section, and mass spectra and images were obtained by using argon cluster ion beam. It is intended to compare the mass spectra from TOF-SIMS within static limit with those from Hybrid SIMS beyond static limit, i.e., dynamic mode. In particular, the outer-cortex layer, corpus callosum, caudate-putamen, and piriform region are compared in detail.

[1] W. Michno, P. M. Wehrli, K. Blennow, H. Zetterberg, J. Hanrieder, Journal of Neurochemistry, 151, 2019, 488-506.
[2] L. Carlred, V. Vuckjević, B. Johansson, M. Schalling, P. Sjövall, Biointerphases, 11, 2016, 02A312
[3] S. Solé-Domènech, P. Sjövall, V. Vukojević, R. Fernando, A. Codita, S. Salve, N. Bogdanović, A. H. Mohammed, P. Hammarström, K. P. R. Nilsson, F. M. LaFerla, S. Jacob, P. Berggren, L. Giménez-Llor, M. Schalling, L. erenius, B. Johansson, Acta Neuropathol, 125, 2013, 145-257.
[4] P. Agüi-Gonzalez, S. Jähne, N. T. N. Phan, Journal of Analytical Atomic Spectromerty, 34, 2019, 1355-1368.
[5] M. K. Passarelli, A. Pirkl, R. Mollers, D. Grinfeld, F. Kollmer, R. Havelund, C. F. Mewman, P. S. Marshall, Henrik Arlinghaus, M. R. Alexander, A. West, S. Horning, E. Niehuis, A. Kakarov, C. T. Dollery, I. S. Gilmore, Nature Methods, 14(12), 2017, 1175-1183.
[6] A. M. Kotowska, G. F. Trindade, P. M. Mendes, P. M. Williams, J. W. Aylott, A. G. Shard, M. R. Alexander, D. J. Scurr. Nature Communications, 11, 2020, 5832

DI-TuP-9 Depth Correction of 3D NanoSIMS Images Show Intracellular Lipid and Cholesterol Distributions While Capturing the Effects of Differential Sputter Rate*, **Melanie Brunet**, B. Gorman, M. Kraft,* University of Illinois Urbana-Champaign

Changes in the distributions of cholesterol and various lipid species within cells are correlated with diseases such as Niemann-Pick, influenza, SARS CoV-2, and HIV. Visualization of the spatial distribution of lipids and other biomolecules could provide new insight into their roles in cellular function and disease. Our lab has used NanoSIMS in a depth profiling mode to image metabolically incorporated, rare stable isotope-labeled cholesterol and sphingolipids within mammalian cells. This depth profiling produced a series of 2D NanoSIMS images depicting the same location on the cell but at progressively increasing depth from its surface. When SIMS depth profiling images of nonplanar samples (e.g., cells) are sequentially stacked to form a 3D image, the component-specific secondary ions detected in the same scan are positioned at the same height in the 3D image. In contrast, the molecules that produced these ions were located at different heights above the substrate. This discrepancy distorts the 3D image in the zdirection. Although 3D SIMS images may be depth corrected with strategies that require atomic force microscopy (AFM) data or the detection of additional secondary ions from the substrate, approaches for depth correction in the absence of such complementary data are desired. Thus, we developed a method to depth correct 3D NanoSIMS depth profiling images of cells that accounts for the effects of differential sputter rate. Our method reconstructs the cell's morphology at each raster plane using the secondary ion and secondary electron depth profiling images. These morphologies are used to adjust the z-positions and heights of the voxels in the component-specific 3D NanoSIMS images. To validate our method, we reconstructed cell morphologies from depth profiling images collected using focused ion beam – secondary electron microscopy (FIB-SEM) and compared them to correlated AFM data. The shape of the reconstructed morphologies agreed well with the AFM data, with an average accuracy of 90%. Intracellular features containing sphingolipids or cholesterol were better resolved in depth corrected 3D NanoSIMS images. Because this method uses only the secondary electron and secondary ion images generated during negative ion SIMS depth profiling, depth corrected 3D images for existing depth profiling SIMS datasets may now be created in the absence of correlated topography data. Application of this method to depth profiling SIMS data of cells may shed light on the mechanisms behind changes in the distributions of cholesterol and various lipid species in disease and facilitate the identification of organelles enriched with biomolecules of interest.

DI-TuP-11 Microplastic Products Discrimination with Tof-Sims Using the Clustering Self-Organizing Maps (SOM)*, **Jin Gyeong Son**, H. Shon,* Korea Research Institute of Standards and Science (KRISS), Republic of Korea*; J. Kim,* Airiss, Republic of Korea*; T. Lee,* Korea Research Institute of Standards and Science (KRISS), Republic of Korea

ToF-SIMS is a surface chemical analysis instrument that provides information at the molecular level of the surface. It has been utilized in the field of polymers to analyze composition using backbone-specific repeating units and to distinguish copolymer components.[1] However, due to the intricacy of ToF-SIMS data, it is still challenging to differentiate chemically similar types of polymers.

Principal component analysis (PCA), which has been widely used in ToF-SIMS analysis, is difficult to distinguish chemically similar data due to the manual assignment of peaks and relatively simple linear clustering or dimensionality reduction methods. Recently, there is a report that large-scale multivariate data can be classified and clustered using artificial neural networks (ANNs) for polymer analysis or protein analysis.[2,3] Here, we classified similar type of microplastic products using the self-organizing map (SOM) method, which is a type of ANNs. Through this, we were able to successfully distinguish 5 types of plastics that could not be distinguished by PCA.

[1] H.Mei, *et al*, *J. Polym. Sci.***2022**, 60, 1174-1198

[2] R. M. T. Madiona, *et al*, *Anal. Chem.* **2018**, 90, 12475−12484

[3] N. G. Welch, *et. al.Langmuir*, **2016**, 32, 8717−8728

Fundamentals

Room Great Lakes Promenade & A1 - Session FM-TuP

Fundamentals Poster Session

FM-TuP-1 To Fix or Not Fix Biofilms to Study Microbial Soil Aggregation*, Y. Zhang,* Huazhong Agricultural University, China*; J. Son,* Pacific Northwest National Laboratory*; **Xiao-Ying Yu**,* Oak Ridge National Laboratory

Bacterial biofilms are a main player in organic processing and soil aggregation. Characterization and understanding of the biofilm interactions with soil components is important to improve our knowledge in the biosphere and rhizosphere. We present two approaches to prepare biofilms suitable for high resolution mass spectral imaging using time-of-flight secondary ion mass spectrometry (ToF-SIMS). *Shewanella* MR-1 was used as the model bacteria biofilm due to their known traits in soil chemistry and microbiology. A mixture of silica, alumina, and iron oxide was used as the model soil system.

First, we took a static approach. The bacteria were inoculated in a multi-well cell culture dish at their log phase. Then soil components were added to the culturing well. The mixture of the bacteria biofilms and soil components were scratched off carefully using a pipette tip and deposited onto the clean silicon (Si) wafers before ToF-SIMS analysis. In the second approach, we used a microfluidic cell to culture biofilms. We made a modification to include a clean Si wafer as the main substrate for biofilm attachment in the microfluidic chamber. The soil component was mixed with the growth media at a ratio of 1:1 by volume as nutrients to support the biofilms' growth. A series of samples were collected to capture the temporal progression of the biofilms and the soil components in a course of several days, respectively, based on the growth curve of the strain. An IONTOF GmbH TOF-SIMS V spectrometer was used.

SIMS spectra were used to compare the effectiveness of the static and flow-cell culture methods. Characteristic fatty acids peaks such as myristic acid (m/z^- 227, $C_{14}H_{27}O_2^-$), palmitic acid (m/z^- 227, $C_{14}H_{27}O_2^-$), and arachidic acid (m/z^- 227, $C_{14}H_{27}O_2^-$) as well as an interesting biomarker riboflavin peak (m/z− 241, $C_{12}H_9N_4O_2^-$) are observed in the dynamic setup results. In contrast, the static setup does not seem to provide as much information, indicating that it is not optimal to prepare biofilm samples containing minerals for ToF-SIMS. Our results demonstrate that sample preparation is critical to study biofilms. Microfluidics is more flexible in microbial culture and media tuning; both are important in simulating a variety of conditions to understand microbes and soil interactions at the microscale. Also, characteristic signals of biofilms are not buried under the mineral components in the dynamic setup, which is imperative in understanding the role of biofilms in soil aggregation that occurs at the microbe-mineral interface.

FM-TuP-3 Matrix Enhancement in Time-of-Flight Secondary Ion Mass Spectrometry*, T. Adolphs, Y. Pohkrel, R. Peterson, H. Arlinghaus, **Bonnie J Tyler**,* University of Münster, Germany

Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS) is one of the most important techniques for chemical imaging of nanomaterials and biological samples with high lateral resolution.However, low ionization efficiency limits detection of many molecules at low concentrations or in very small volumes.One promising approach to increasing the sensitivity of the technique is by addition of a matrix that promotes ionization and desorption of important analyte molecules.This approach is known as Matrix-Enhanced Secondary-Ion Mass Spectrometry (ME-SIMS).We have investigated the effect of matrix acidity on molecular ion formation in three different biomolecules.A series of cinnamic-acid based matrices that vary in acidity was employed to systematically investigate the influence of matrix acidity on analyte ion formation.The positive ion signal for all three biomolecules showed a strong increase for more acidic matrices.The most acidic matrix was then vapor-deposited onto mouse brain sections. This led to significant enhancement of lipid signals from the brain.This work confirms that proton donation plays an important role in the formation of molecular ions in ToF-SIMS.

FM-TuP-5 Oxygen Detection Limit with Magnetic Sector Dynamic SIMS*, **Alexandre Merkulov**,* IMEC, Belgium

Information on hydrogen, carbon and oxygen impurities (atmospheric gas species) introduced during processing and/or ageing is of major importance for a better understanding of semiconductor device lifetime and failure modes.Dynamic SIMS is often used in evaluating the concentration of impurities in solids because of its high sensitivity and depth profiling capabilities with good depth resolution and high throughput. Continuous ion beam sputtering with high density primary beam providing high sensitivity and reduced background contribution from residual gases within the analytical chamber. The magnetic sector SIMS tools are supplied with UHV analysis chamber with optimized vacuum conditions, minimizing the background level created by residual gases sticking to the sample surface.

High density Cs primary ion beam is often used because of high electronegativity of most of light element species, so, the Cs surface retention increases the negative secondary ions yield. Reducing the sputtering energy leads to increased Cs surface retention, thus, the ion yield. At the same time, it might reduce the surface scattering of oxygen containing molecular species scattering from the vacuum atmosphere (gettering effect). The sputtering events density on the surface (last event of the sputtering cascade) is also a parameter to take into account for equilibrium surface concentration estimation of vacuum species elements. However, this sputtering density variation depends on primary beam density and, as a parameter of solid-ion interaction, on the sputtering yield. The angle of incidence and sputtering energy are the parameters influencing the sputter yield. The effect of sputtering energy on the light element detection limits is an aspect of current study.

The idea of varying the sputter rate during the SIMS analysis is well developed approach allowing to estimate the background from the vacuum atmosphere or surrounding environment. Extrapolating the sputter rate to the infinite value, when vacuum contamination from the chamber is negligible small compared to oxygen containing into the sample being analyzed, the detection limit can be reduced drastically. In case the signal become independent on sputter rate, the background is determined by the vacuum contamination nearby the analysis area. Moreover, the vacuum atmosphere quality and geometrical layout of analytical area influencing the gaseous species background in secondary ions spectra are the very important parameters to be investigated. The statistical analysis of big data pool on Oxygen (Hydrogen) detection limits, observed with various impact energy and very different sputter rates will be presented.

FM-TuP-7 Depth Profiling Study in TAPC Monolayer Using Laser Desorption Ionization and Home-Built Ar-GCIB*, **Ji Young Baek,*** Korea Basic Science Institute, Republic of Korea*; C. Choi,* Korea Basic Science Institute , Republic of Korea*; M. Choi,* Korea Basic Science Institute, Republic of Korea

Depth profiling ToF-SIMS analysis has widely been performed to obtain the information of multi-layered organic samples. The depth profiling of the organic sample has generally been analyzed by using a gas cluster ion beam (GCIB) as a sputter gun and a liquid metal ion beam (LMIB) as an analysis gun. However, this kind of ordinary ToF-SIMS analysis shows lots of unnecessary signals are observed in the low mass region due to the high energy of the analysis ion beam and a result of the secondary ionization process. In practice, this makes it difficult to interpret a mass spectrum and a depth profile. In order to solve the difficulties of interpretation even in the organic light-emitting diode (OLED) analysis, we used a nano second UV laser (λ = 355 nm) as an analysis mode. Because most of OLED materials contain a chromophore which absorb UV light, so it can be easily ablated and ionized by laser pulse.

Here, we performed the depth profiling analysis of 50 nm TAPC monolayer sample using laser desorption ionization (LDI) and home-built Ar-GCIB. By controlling parameters of LDI, we found an optimal analysis condition that analyzed OLED sample with less damage and by taking a GCIB as a sputter, we tried to reach below ~ 1 nm resolution as an optimal sputtering of OLED materials. The depth profile was plotted as the integral value of the parent ion peak as a function of the number of scan. The depth resolution of TAPC monolayer was about 1.78 nm per point. The depth profiling of an OLED material could be successfully and more easily analyzed using GCIB-LDI ToFMS system. The capability of this type of depth profiling analysis will be demonstrated for real organic devices in the near future.

FM-TuP-9 Novel Approaches for Measuring Cork Material: Measurements and Applications*, **Natalie Sievers,*** PNNL

The unique properties of cork materials including porosity, elasticity, friability, and complex/heterogeneous composition present interesting challenges for SIMS measurements. Several studies have been dedicated to imaging internal structures and characterizing coatings and adhesives used in bottling processes where cork is utilized. These previous studies establish that there is a need for characterizing these materials. Unlike previously utilized methods, dynamic SIMS allows better depth resolution and detection limits while maintaining a relatively small spot size. This would be advantageous when trying to quantify trace amounts of elements or understanding uniformity with depth. However, there has not been a detailed study using dynamic SIMS to determine optimal analytical conditions for characterizing such an unconventional material.

In order to understand how these, and similar materials, behave under various conditions, a methodical investigation was conducted in which several conditions are used in order to understand how cork material performs during dynamic SIMS acquisitions. Initial work shows that the types and sizes of cork materials used in wine production is highly variable and that careful consideration must be taken during sample prep. The results of this work will (1) demonstrate the ability to prepare and measure the various types of complex composite materials, (2) outline optimal analytical conditions, and (3) determine detection limits for an array of isotopes.

FM-TuP-11 AFM Observation of Topography Development on Si Surface During O_2^+ Ion Beam Sputtering as a Function of Ion Energy, Angle of Incidence and Dose*, **Masayuki Hatada,** T. Miyamoto,* Toray Research Center, Inc., Japan

Surface rippling on Si by oblique incident O_2^+ ion beam is a well-known phenomenon [1,2] but there has been no satisfactory theory of its mechanism. Recent progress in the experiment and the theory of rippling on Si surface by oblique incident Ar^+ [3] could be helpful for understanding the rippling mechanism caused by O_2^+ if we had a kind of phase diagram of surface topography as a function of ion energy, angle of incidence and dose. We observed Si(100) surface topography by atomic force microscopy (AFM) over a range of these O_2^+ ion parameters, typically down to the depth of secondary ion intensity change completion.

References:

[1] John J. Vajo, Robert E. Doty and Eun-Hee Cirlin. Influence of O_2^+ energy, flux, and fluence on the formation and growth of sputtering-induced ripple topography on silicon. Journal of Vacuum Science & Technology A 14, 2709 (1996)

[2] Prabhjeet Kaur Dhillon, Subhendu Sarkar, Alexis Franquet, Alain Moussa, Wilfried Vandervorst. Si nanoripples: A growth dynamical study. Applied Surface Science 258 (2012) 9579-9583

[3] Scott A. Norris and Michael J. Aziz. Ion-induced nanopatterning of silicon: Toward a predictive model. Applied Physics Reviews 6, 011311 (2019)

FM-TuP-13 Why Do I Always Fall to Pieces? Understanding Beam-Based Lipid Bond Breakage Through Molecular Dynamics and Density Functional Theory Calculations*, **Michael Taylor,*** The Pacific Northwest National Laboratory*; W. Kew, A. Anderson, M. Engelhard, C. Anderton,* The Pacific Northwest National Laboratory

INTRO: In-source fragmentation (ISF) is a significant problem in beam-based ionization. High degrees of ISF produces complex spectra, rich with fragment species that may be misinterpreted as intact molecules. The orientation of a surface interacting molecule is a substantial driver behind the degree of ISF. For example, in secondary ion mass spectrometry (SIMS), portions of a molecule will experience differential degrees of ion beam dosage, altering fragmentation patterns. Molecular dynamics (MD) when used in combination with density functional theory calculations (DFT) can identify the orientation and specific intramolecular bonds that are weakened in a molecule. The relative intensity of fragment can be then compared against bond energies to validate molecular orientations. For the first time, we have combined empirical data (SIMS/laser-desorption ionization; LDI) with quantum mechanical modelling data (MD/DFT) of palmitoylsphingomyelin (SM34:1) to explore how lipid orientation relates to ISF between the two methods.

METHODS: MD simulations were performed to model the interaction of SM 34:1 on gold. SM 34:1 was then drop cast at a monolayer concentration matching the maximum packing density (MD). SIMS (IONTOF V) and LDI (Bruker 15-T FTICR-MS) measurements were taken from the sample spot. Correlations between the relative intensities of fragment species and calculated bond dissociation energies for the two major lipid orientations were then compared.

RESULTS: MD simulations on gold revealed a preference for surface adsorption of the phosphocholine (PC) headgroup of SM 34:1. This was consistent with the theory of a strong charge-based surface interaction of the polar headgroup. Increasing the number of molecules modelled revealed changes in lipid orientation. A higher surface density resulted more molecules interacting via the terminal trimethylamine headgroup compared to whole headgroup. Additionally, simulations demonstrated a maximum packing density of 1.2 molecules/nm^2. MD of a single molecule revealed two major conformation, full and partial adsorption of the PC headgroup. DFT calculations revealed the electronic structure of both conformations. Corresponding beam analysis by SIMS identified abundant high m/z fragments [M - CH_3, M - N-$(CH_3)_3$, M – $C_2H_4N(CH_3)_3$] in combination with low m/z fragments, whereas LDI analysis produced cation adducts (M + Na, M + K), in combination with the fragmented PC headgroup ($C_5H_{15}PNO_4^+$) as major species. Comparison of bond dissociation energies of the PC headgroup fragments in SIMS (m/z 184, m/z 104, m/z 86, m/z 58) found a strong correlation between the summed bond and adsorption energies (R^2 = 0.94).

Recent Advances in SIMS
Room Great Lakes Promenade & A1 - Session RA6-TuP
Recent Advances in SIMS Poster Session

RA6-TuP-1 Experimental and Theoretical Analysis of Tricyclic Antidepressants Using 213 Nm Picosecond Laser Desorption Postionization Mass Spectrometry*, T. Zagorac,* University of Illinois Chicago*; H. López Pena,* Virginia Commonwealth University*; J. Gross,* University of Illinois Chicago*; K. Moore Tibbetts,* Virginia Commonwealth University*; **Luke Hanley,*** University of Illinois Chicago

Imipramine class tricyclic antidepressants have low ionization efficiencies that render them difficult to detect using secondary ion mass spectrometry

[1]. Imipramine ionization efficiency was previously studied with 800 nm, ~75 fs laser desorption photoionization mass spectrometry (fs-LDPI-MS) [2] and a significant precursor (M^+) ion was detected. Here we examine the use of 213 nm, ~30 ps-LDPI-MS for detection of imipramine, desipramine, amitriptyline and clomipramine via 7.9 eV single photon ionization. Precursor and fragment ion signal for all four compounds are compared to electron impact mass spectral libraries and ps-LDPI-MS displayed higher M^+ signal than electron impact for all four compounds. Furthermore, detection of imipramine by ps-LDPI-MS shows slightly less fragmentation than did fs-LDPI-MS [2]. A power study on the effect of desorption laser irradiance on the survival yield of the precursor ion shows that the desorption laser irradiances in the ps-LDPI-MS are significantly lower and M^+ survival yields are slightly higher than those for fs-LDPI-MS. Ionization energies of imipramine, desipramine, amitriptyline, clomipramine, and several of their major fragments are predicted using density functional theory calculations and used to explain the observed ps-LDPI-MS data. Low mass amine containing fragments are calculated to have low ionization energies, so their experimental observation might arise at least in part from dissociation during laser desorption. Results are discussed in terms of the application of 7.9 eV single photon ionization to laser secondary neutral mass spectrometry of drug compounds.

1) Vorng, J.-L.; Kotowska, A. M.; Passarelli, M. K.; West, A.; Marshall, P. S.; Havelund, R.; Seah, M. P.; Dollery, C. T.; Rakowska, P. D.; Gilmore, I. S., *Anal. Chem.* **2016,***88*, 11028.

2) Pieterse, C. L.; Rungger, I.; Gilmore, I. S.; Wickramasinghe, R. C.; Hanley, L., *J. Phys. Chem. Lett.* **2020,***11*, 8616.

RA6-TuP-3 Analysis of Organic Principal Component Distribution Using Orbitrap/TOF Hybrid SIMS*, Y. Jeong, J. Lee, H. Moon, J. Sung,* Korea Basic Science Institute, Republic of Korea*; . Suh,* Pusan National University, Republic of Korea*; **Jong Sung Jin**,* Korea Basic Science Institute, Republic of Korea

An analysis method was presented to confirm the distribution of small molecules according to the depth in the organic multilayer thin film using the newly developed Orbitrap/TOF Hybrid SIMS. With the conventional TOF-SIMS analysis method, ions such as CN^-, which correspond to the nitrogen component present in the molecule, were observed. This method has a limitation in obtaining only the information of the molecule to be analyzed accurately. Using Orbitrap/TOF Hybrid SIMS, we developed an analysis method that can obtain information on only the relevant molecules whose distribution is to be reported. In particular, by identifying each characteristic peak from the results of MVSA statistical processing, it was possible to infer different mechanisms of behavioral change depending on the molecular structure.

RA6-TuP-7 Epi SiGe Application using METRION® in-line SIMS System*, **Lawrence Rooney**, S. Okada,* Nova

The epitaxial process is a well-established deposition technique in semiconductor fabrication because it enables the ability to achieve much higher doping concentrations than can be obtained via ion implantation. As we move toward <5nm technology, a key process for enabling gate-all-around FET (GAAFET) is the stacked multi-lattice of Silicon (Si) and Silicon-germanium (SiGe) epi process for constructing the nanosheets.

Germanium (Ge) content in SiGe correlates to channel stress, and the germanium fraction (Ge%) has been increasing steadily as we move towards smaller technology nodes. When stress is high, epi layers can suffer from multiple problems such as defect formation, facet formation, non-uniform strain, etc. The challenge is greater when moving from planar to 3D structures, where uniformity of strain and control of defect density are important. Often, multiple epi layers of SiGe with varying thicknesses, Ge%, and Boron doping are deposited to optimize the device structure and process integration.

Enabling process control on the layer thickness, Ge%, and Boron doping concentration in these complicated SiGeB epi stacks is critical in high-volume manufacturing (HVM), and there is no single in-line metrology that is able to do the measurement.

This paper describes how in-line Secondary Ion Mass Spectrometry (SIMS) could be a solution to this problem by providing material composition profiles as a function of depth – resulting in thickness, Ge% and Boron concentration data from each nanosheet.

RA6-TuP-9 Detection of Contaminants in Positive and Negative Ion Mode Using in-Line SIMS with an Oxygen Primary Ion Beam*, **Julia Hoffman**, S. Okada,* Nova

Utilizing Secondary Ion Mass Spectrometry (SIMS) for in-line metrology is a newly emerging method of process control that requires contamination-free measurements, enabling SIMS on product wafers. SIMS measurements of negative ions are usually associated with a Cesium primary ion beam. Unfortunately, when Cesium is present in Silicon, it forms trap states in the Si band gap, which can cause serious leakage issues for Si-base transistors. Therefore, Cesium is considered a very damaging contaminant in semiconductor devices.

To enable contaminant-free inline SIMS a choice of Oxygen ion source is a preferable choice since it is generally benign and not considered a contaminant. This kind of source is typically used for positive secondary ion measurements. By switching the secondary spectrometer polarity between positive and negative ion modes, an Oxygen primary ion source can be used successfully to measure both positive and negative

species.

While an Oxygen primary ion source may not provide the same sensitivity to negative secondary ions as a Cesium primary ion beam, the ability to directly measure a range of species without the risk of contamination creates a wide field for in-line SIMS applications.

In this paper, the use of an Oxygen primary ion source for positive and negative secondary ion detection is being investigated on an in-line SIMS tool. We evaluate sensitivity levels of detecting contaminants like O, F^-, Cl^- in positive and negative ion mode with an Oxygen primary beam, as well as the use of proxy species or alternate isotopes for improved results.

SIMS Solutions in Materials and Life Sciences
Room Great Lakes Promenade & A1 - Session SS-TuP

SIMS Solutions in Materials and Life Sciences Poster Session

SS-TuP-1 Cluster-Induced Desorption/Ionization Mass Spectrometry of Highlighter Ink: Unambiguous Identification of Dyes and Degradation Processes Based on Fragmentation-Free Desorption*, K. Bomhardt, P. Schneider, M. Rohnke,* Justus Liebig University Giessen, Germany*; C. Gebhardt,* Bruker Daltonik GmbH, Germany*; **Michael Dürr**,* Justus Liebig University Giessen, Germany

Ink which was either written or printed on paper may serve as an illustrative example for a complex mixture of chemical compounds to be analyzed by mass spectrometry directly on the original substrate without further processing steps. In particular, identification of different types of aging of the dyes used in the ink by means of a well-defined correlation between the aging process and the associated decomposition products requires a soft desorption method which does not introduce additional fragments as the latter cannot be distinguished from the products of the degradation process and hinder the discrimination of the different processes.

Here we show that Desorption/Ionization induced by Neutral SO_2 Clusters (DINeC) is such a soft desorption method which can be combined with mass spectrometry (MS) as an analytical tool to solve this task [1]. DINeC features matrix-free, soft desorption/ionization which comes together with simple preparation of the samples, e.g., by means of drop casting.

For the investigation of highlighter ink, a dot of ink was simply drawn on either paper or a piece of Si-wafer and directly analyzed by means of DINeC-MS. Five different inks were investigated; in the respective spectra three major peaks were observed with varying relative intensity depending on the color of the ink. Decomposition of the dyes either by thermal treatment or by UV irradiation leads to corresponding fragment peaks. Based on the different fragment peaks,the different degradation processes can be clearly distinguished. In addition, due to the high surface sensitivity of DINeC-MS [2], different layers of inks, which were applied subsequently on top of each other, could be distinguished. Both, the possibility to discriminate between different degradation processes by means of DINeC-MS as well as to distinguish different sequences of application in multilayers of ink, are of potential interest for applications in forensic science.

References:

[1] K. Bomhardt, et al., Analyst 147, 333 (2022).

[2] A. Portz, et al., Biointerphases 13, 03B405-1 (2018).

SS-TuP-3 3d Tof-Sims Imaging of Ciprofloxacin in Biofilms at Physiologically Relevant Concentrations with Cell Level Spatial Resolution*, A. Akbari, R. Peterson, H. Arlinghaus,* ***Bonnie J Tyler,*** University of Münster, Germany

High spatial resolution mass spectrometry imaging has been identified as a key technology needed to improve understanding of the chemical language that influences antibiotic resistance within biofilms.Time-of-flight secondary ion mass spectrometry (ToF-SIMS) offers the unique ability for label-free 3D imaging of organic molecules with sub-micrometer spatial resolution and high sensitivity.Several studies of biofilms have been done with the help of ToF-SIMS, but none of those studies have shown 3D imaging of antibiotics in native-state hydrated biofilms with cell-level resolution.Because ToF-SIMS measurements must be performed in a high-vacuum environment, cryogenic preparation and analysis are necessary to preserve the native structure and antibiotic spatial distribution during ToF-SIMS measurements. In this study, we have investigated the penetration of the antibiotic ciprofloxacin into *Bacillus subtilis* biofilms using sub-micrometer resolution 3D imaging ToF-SIMS.*B. subtilis* biofilms were exposed to physiologically relevant levels of ciprofloxacin.The treated biofilms were then plunge-frozen in liquid propane and analyzed with ToF-SIMS using cryogenic conditions.Multivariate analysis techniques, including Multivariate Curve Resolution (MCR) and inverse Maximum Signal Factors (iMSF) denoising were used to aid analysis of the data and facilitate high spatial resolution 3D imaging of the biofilm, providing individually resolved cells and spatially resolved ciprofloxacin at “real life” concentrations.

SS-TuP-5 Orbisims Imaging of the Developing *Drosophila* Brain*,* ***Yuhong Jin****, C. Newell,* The Francis Crick Institute, UK*; I. Gilmore,* National Physical Laboratory, UK*; A. Gould,* The Francis Crick Institute, UK

During development, human and other mammalian fetuses often face stresses such as nutrient restriction and hypoxia. Critical to surviving these stresses is the ability to maintain growth of the brain, which often comes at the expense of the growth of other organs. This organ selective growth phenomenon is known as brain sparing and, although documented in humans many years ago, the underlying molecular mechanisms remain unclear (Gruenwald, 1963 PMID: 14081642; Dobbing, 1971 PMID: 5166176). Our lab developed the fruit fly *Drosophila melanogaster* as a powerful genetic model organism for studying brain sparing. Using the *Drosophila* model, we have shown that metabolic communication between neural stem cells (neuroblasts), glia and neurons within the niche is important for brain sparing during nutrient restriction and hypoxia (Cheng et al., 2011 PMID: 21816278; Bailey et al., 2015 PMID: 26451484; Lanet et al., 2013 PMID:23478023)

To construct a single-cell resolution atlas of metabolite distributions in the normal and spared *Drosophila* brain we are using OrbiSIMS mass spectrometry imaging. OrbiSIMS was developed at the National Physical Laboratory and combines high lateral resolution with high mass resolution to enable chemical imaging at cellular resolution (Passarelli et al., 2017 PMID: 29131162). Here we use OrbiSIMS analysis of brain sections to map the distribution patterns of more than 100 identified lipid and signalling metabolites. Comparisons between normal and spared *Drosophila* brains are beginning to reveal, at near single-cell resolution, how the stresses of nutrient restriction and hypoxia can lead to specific changes in the metabolite distribution atlas.

SS-TuP-9 Advance Understanding of Soil Organic Matter-Mineral Interactions Using Time-of-Flight Secondary Ion Mass Spectrometry*,* ***Zihua Zhu****, P. Jiang, X. Zhang, Q. Zhao,* Pacific Northwest National Laboratory*; M. Bowman,* PNNL*; E. Graham, X. Chen,* Pacific Northwest National Laboratory

Carbon cycling in current Earth System models (ESMs) are based on traditional ex-situ bulk analysis data of soil organic matters (SOM), leading to large uncertainties and bias in predictions by treating SOM-mineral interactions as a “black-box”. SOM-mineral association is essential for stabilizing soil nutrients that influences carbon and nitrogen biogeochemical cycling in soil. The poor understanding of the complex SOM-mineral interactions, constrained by the information content in traditional bulk analyses, has been limiting the further improvement of carbon and nutrient cycling modeling from the ecosystem to global scales. SOM-mineral interactions occur majorly at various surfaces, which is at a nanoscale or even molecular scale. Therefore, a state-of-the-art surface analysis tool with molecular recognition capability is highly desirable. In this work, time-of-flight secondary ion mass spectrometry was used to characterize the SOM composition and identify their co-existence with various mineral particles. Meanwhile, AI and machine learning methods were used to leverage these experimental data, along with massive data available in various projects (such as 1000 Soil project in Environmental Molecular Sciences Laboratory) and other open-source community database, to generate reaction parameters that take into account the SOM-mineral interactions derived from those micro-scale measurements and will be incorporated into ESMs, ultimately reducing the uncertainty and bias in predicted carbon emission/sequestration.

SS-TuP-11 Massive Cluster SIMS for Analysis of Nanoparticles and Their Interfaces*,* ***Michael Eller,*** California State University Northridge*; J. Sandoval, S. Verkhoturov, E. Schweikert,* Texas A&M University

Nanoprojectile Secondary Ion Mass Spectrometry, NP-SIMS, is a promising technique for molecular analysis at the nanoscale. In this methodology, termed the event-by-event bombardment detection mode, individual nanoprojectiles impact the surface one-by-one and the resulting secondary ions are mass analyzed by time-of-flight mass spectrometry prior to the arrival of the subsequent projectile. Analysis of co-emitted ions from each impact allows for the inspection of co-localized moieties within the ejected volume (10-15 nm). Surfaces were probed stochastically with a suite of individual gold nanoparticles (520 keV Au_{400}^{4+}) separated in time and space. In this study, we examined a mixture of three nanoparticles with identical metal cores, differing only by their functionalization. The particles were deposited as a sub-single layer onto a cleaned silicon surface. Using the NP-SIMS, we evaluated the extent of mixing between particles and quantified the abundance of each particle on the surface. We found that the relative concentration of each particle was approximately 33%, which is in good agreement with the sample preparation. Our results show that despite the relatively large sampling volume of each projectile, measurements on the 3-5 nm particles can differentiated from one another based on the impact parameter between the projectile and the surface nanoparticle. Since the impact parameter affects the number and type of emitted secondary ions, examining the secondary ions from each impact allows for impacts which occur on the particle core to be distinguished from those on the particle-particle and particle-substrate interfaces. We found that direct impacts were characterized by the emission/detection of multiple Au_n^- ions while ultra-peripheral impacts were identified by the detection of multiple of $Si_xO_y^-$ ions. Peripheral impacts, which sample the particle-substrate interface, are characterized by the co-emission of Au_n^- ions and $Si_xO_y^-$ ions. Due to the differences in the length of the ligands, peripheral measurements occurring closer to the core were more likely to contain decanethiol, while peripheral impacts occurring farther from the particle core were more likely to contain hexadecanethiol. Differentiating and isolating these measurements, allows for mass spectrometry evaluation of interfaces among nano-objects and between nano-objects and their support. This work was supported by the National Science Foundation grant CHE-1308312.

SS-TuP-13 Measurement of Metabolite Relative Ion Yields from Frozen-hydrated and Freeze-dried Tissue and Application of Cryo-OrbiSIMS to Tissue Imaging*,* ***Anya C.S. Eyres,*** NiCE-MSI, National Physical Laboratory , UK*; J. Zhang,* NiCE-MSI, National Physical Laboratory, UK*; C. Newell, Y. Jin,* The Francis Crick Institute, UK*; C. Nikula,* NiCE-MSI, National Physical Laboratory, UK*; A. Gould,* The Francis Crick Institute, UK*; J. Bunch,* NiCE-MSI, National Physical Laboratory, Imperial College London, Rosalind Franklin Institute, UK*; I. Gilmore,* NiCE-MSI, National Physical Laboratory, UK

The OrbiSIMS combines high-resolution imaging using a focused gas cluster ion beam with an Orbitrap mass spectrometer to enable sub-cellular resolution imaging with high-mass resolving power (*1*). We recently introduced the cryo-OrbiSIMS (*2*)(*3*) for native-state imaging in ultra-high vacuum. To preserve the native biological state and prevent sample damage, it is crucial to form ice rapidly and prevent surface ice from forming water condensation. We present a protocol for the cryo-preparation of tissue sections for consecutive frozen-hydrated and freeze-dried analysis.

Using this protocol, we measure the relative ion yields, *R*, for metabolites of importance in cancer biology in frozen-hydrated tissue compared with freeze-dried tissue. To ensure equivalence of molar amounts the secondary ion signal was integrated over a fixed area for the entire thickness of tissue. We show that the positive polarity metabolite (36 metabolites) ion yields for a frozen-hydrated liver tissue are enhanced between 1 and 5 orders of magnitude compared with the freeze-dried equivalent. In an earlier cryo-OrbiSIMS study (*2*) of a *Pseudomonas aeruginosa* biofilmwe found that the ion yield ratio, *R*, inversely correlated with the Log *P* of the molecule. We find the same relationship here. Molecules with a low Log *P* value are more polar and consequently can be expected to be protonated from the water matrix (*4*). This is important since we have previously shown that the SIMS ion yield of polar molecules is low (*5*), limiting applications in cancer biology and drug disposition studies. For negative ions, no correlation is found with the molecule log *P*, as expected. Cryo-OrbiSIMS tissue imaging examples will be provided.

13. *et al.*, The 3D OrbiSIMS—label-free metabolic imaging with subcellular lateral resolution and high mass-resolving power. *Nature Methods***14**, 1175-1183 (2017).
14. *et al.*, Cryo-OrbiSIMS for 3D Molecular Imaging of a Bacterial Biofilm in Its Native State. *Analytical Chemistry***92**, 9008-9015 (2020).
15. *Angewandte Chemie International Edition* **59**, 18194-18200 (2020).
16. *Rapid Commun Mass Spectrom* **20**, 1327-1334 (2006).
17. *et al.*, Semi-empirical rules to determine drug sensitivity and ionization efficiency in SIMS using a model tissue sample. *Analytical Chemistry***88**, (2016).

SS-TuP-15 OrbiSIMS Localises Interfacial Degradation in Blue Phosphorescent OLEDs*, G. Trindade,* National Physical Laboratory, UK*; S. Sul,* Samsung Electronics Co., Ltd., UK*; J. Kim,* Samsung Electronics, Ltd., UK*; R. Haveland,* National Physical Laboratory, UK*; S. Park,* Samsung Electronics Co., Ltd., UK*;* ***Lidija Matjacic****, I. Gilmore,* National Physical Laboratory, UK

Developments in lifetime of red and green OLEDs have come a long way to sufficient stability, comparable to conventional LEDs. However, degradation pathways in blue phosphorescent OLEDs are not yet fully understood, which limits its lifetime and OLED applications in full colour displays and lightning. The understanding of degradation mechanisms in blue OLEDs to improve device lifetime is a topic of high importance in industry and academia [1]–[3]. OLED failure, if not process-related, arises mostly from chemical instability. However, the challenges of sampling from nanoscale organic layers and interfaces with enough analytical information has hampered identification of degradation products and mechanisms. Here, we present a high-resolution diagnostic method of OLED degradation using an Orbitrap mass spectrometer equipped with a gas cluster ion beam to gently desorb nanometre levels of materials, providing unambiguous molecular information with 7-nm depth resolution. We measured blue phosphorescent OLED devices and showed that dominant chemical degradation occurred at the interface between electron transport and emission layers (EML/ETL), where exciton distribution was maximised. We also show an approximately two orders of magnitude increase in lifetime of a device with slightly modified host material, which presented negligible EML/ETL interfacial degradation. Our results provide insight for material and device architecture development.

[1] S. Kim *et al.*, “Degradation of blue-phosphorescent organic light-emitting devices involves exciton-induced generation of polaron pair within emitting layers,” *Nat. Commun.*, vol. 9, no. 1, 2018, doi: 10.1038/s41467-018-03602-4.

[2] H. Aziz and Z. D. Popovic, “Degradation phenomena in small-molecule organic light-emitting devices,” *Chemistry of Materials*, vol. 16, no. 23. 2004, doi: 10.1021/cm040081o.

[3] S. Sudheendran Swayamprabha *et al.*, “Approaches for Long Lifetime Organic Light Emitting Diodes,” *Advanced Science*, vol. 8, no. 1. 2021, doi: 10.1002/advs.202002254.

SS-TuP-17 Secondary Ion Mass Spectrometry Imaging of Wet/Live Cell Membranes in Solution Using Single-Layer Graphene*,* ***Heejin Lim****,* Center for Scientific Instrumentation, Korea Basic Science Institute (KBSI), Republic of Korea*; S. Lee, Y. Park, H. Jin, D. Seo, Y. Jang, D. Moon,* DGIST, Republic of Korea

Nanoscale characterization techniques based on accelerated electrons and ions require an ultra-high vacuum environment. Therefore, it is not viable to perform an analysis in a solution environment; Biological samples should be frozen or chemically fixed and dehydrated by harsh and laborious procedures, which could disturb the native state, localization, and chemistry of biomolecules. Single-layer graphene techniques have enabled transmission electron microscopy and scanning electron microscopy imaging of materials and cells in solution. Here, we report on how atomic and molecular secondary ions, including cholesterol and fatty acids, can be sputtered through single-layer graphene so that secondary ion mass spectrometry (SIMS) imaging of wet/live cell membranes in a solution can be performed at subcellular spatial resolution. We observed intrinsic molecular distributions of lipids, such as cholesterol, phosphoethanolamine, and various fatty acids, in wet/live cell membranes without any labeling. Cell viability assay, optical imaging, and time-lapse SIMS imaging showed that graphene-covered cells cultured on a wet substrate with a cell culture media reservoir were not dead and their cellular membranes were not disintegrated during SIMS imaging in an ultra-high vacuum environment. Ab-initio molecular dynamic (AIMD) calculations and ion dose dependence studies suggest that sputtering through single-layer graphene occurs through a transient hole generated in the graphene layer. Cholesterol imaging shows that methyl-β-cyclodextrin (MβCD) preferentially extracts cholesterol molecules from the cholesterol-enriched regions in cell membranes. Our work will provide a new in-vitro mass spectrometric imaging platform in an ultra-high vacuum environment for wet/live cells and materials in solution for various research in basic biology, biomedical science, electrochemistry, and materials science.

SS-TuP-19 Mass Spectrometry Imaging of Lipid Changes on 6-Hydroxydopamine-Induced Parkinson’S Disease Mouse Model Using TOF-SIMS*,* ***Sun Young Lee****, H. Shon, J. Son, T. Lee,* Korea Research Institute of Standards and Science (KRISS), Republic of Korea

Parkinson's disease (PD) is one of the three major senile diseases, along with dementia and stroke that affect the nervous system.Parkinson's disease (PD) is characterized by the loss of dopaminergic neurons from the substantia nigra (SN) that project to the dorsal striatum (caudate-putamen).[1] We tried mass spectrometry imaging (MSI) on the disease-related candidate lipid profile by comparing the difference between the brain lesion region and the normal region using a one-sided 6-hydroxydopamine injection model in Parkinson's disease using flight time secondary ion mass spectrometry (ToF-SIMS). As a result of the analysis, the change in the surrounding area was more pronounced than the SN area where the actual drug was injected. In addition, it was confirmed that the signal strength of the piriform region and the entorhinal area involved in olfactory sense and memory were different. In particular, the fact that the signal strength of the disease-causing right hemisphere in this area has decreased, which is consistent with the problem of olfactory abnormalities experienced by 70-90% of Parkinson's patients.[2,3] The study of Parkinson's disease through this model was meaningful to determine the nerve cell death-induced lipid changes through MSI analysis.

SS-TuP-21 ToF- and Orbitrap-SIMS Analysis of Hybrid Solid Electrolytes - Comparing Fragment Patterns and Ionization Efficiency of PEO:LiTFSI*,* ***Timo Weintraut****, J. Becker, A. Henss,* Institute of Physical Chemistry, Justus Liebig University Giessen, Germany

Fundamentals
Room Great Lakes B - Session FM-WeM1

Fundamentals - Secondary Ion Formation I

Moderator: Andrew Giordani, Procter & Gamble Company

8:40am **FM-WeM1-1 Improving Uranium Particle Analysis by SIMS using O_3^-**, ***Evan Groopman***, *T. Williamson, D. Simons,* National Institute of Standards and Technology (NIST) **INVITED**

We have investigated the use of negative molecular oxygen primary ion beams (i.e., O_2^- and O_3^-) to determine the benefits of using such beams for U particle SIMS analyses. Typically, O^- is the most practical negative primary ion species for both age dating and uranium isotopic analysis with the conventional duoplasmatron ion source. Molecular O_2^- and O_3^- are produced in greater abundance in newer RF plasma sources, making them viable primary beam species for these analyses. We used two particulate samples of known mass, IRMM CRM 2329P and inkjet printed deposits, to compare the useful yields of U^+, UO^+, and UO_2^+ ions under Köhler bombardment from O^-, O_2^- and O_3^-. We also investigated the effects of substrate chemistry and primary species on the Th/U relative sensitivity factor by measuring particles of NIST CRM U900 on graphite and silicon. We determined that by using an O_3^- beam, the ionization yield of uranium can be increased by a factor of approximately two over an O^- beam, up to 4.7%, a substantial improvement which positively impacts measurement precision and detection limits. We also found that O_3^- reduced instrumental mass fractionation and matrix/substrate effects relative to the other negative ion beams. Particle measurements using O_3^- were improved in every respect compared to conventional O^- beam analyses. With the use of increasingly common RF oxygen sources, the precision of U particle measurements can be improved by using O_3^- primary ions without the need for additional changes to standard operating procedures.

9:20am **FM-WeM1-5 Surface Properties of Ionic Liquids: A Mass Spectrometric View Based on Soft Cluster-Induced Desorption**, ***Karolin Bomhardt***, *P. Schneider, T. Glaser, M. Dürr,* Justus-Liebig-University Giessen, Germany

Ionic liquids (IL) feature a large technological potential, e.g., in catalysis or as designer solvents; with respect to their bulk properties, they have been intensively investigated. However, since in most applications the interaction proceeds via the surface of the IL, e.g., in the case of catalytic reactions, the surface properties are of equal or even higher interest.

Here we show the application of Desorption/Ionization Induced by Neutral SO_2 Clusters (DINeC) [1] in combination with mass spectrometry (MS) for the investigation of the molecular composition of the surface of IL. Clear and fragmentation-free spectra of the cations and anions present in the sample are obtained after DINeC from bulk and thin film samples of IL. Based on both softness [2] and surface sensitivity [3] of DINeC-MS, accumulation of either cations or anions was discriminated on the surface of bulk IL, depending on the molecular structure of the IL components. In particular, cations with long alkyl chains were found to aggregate on the surface, but this tendency is the more reduced the larger the respective anion is; in the case of larger anions and smaller cations, the effect is found to be even reversed.

For thin layers of IL, the ratio between cations and anions as detected in the mass spectra is further influenced by the surface of the substrate; structural inhomogeneities such as the formation of islands of bulk material as well as the dynamical behavior of the thin film layer are deduced from the temporal evolution of the mass spectra and the relative intensities of cations and anions.

References:

[1] C. R. Gebhardt, et al., Angew. Chem., Int. Ed. 48, 4162 (2009).

[2] M. Baur, et al., Rapid Commun. Mass Spectrom. 28, 290 (2014).

[3] A. Portz, et al., Biointerphases 15, 021001 (2020).

Fundamentals
Room Great Lakes B - Session FM-WeM3

Fundamentals - Secondary Ion Formation II

Moderator: Andrew Giordani, Procter & Gamble Company

10:20am **FM-WeM3-11 Ion Suppression Effect of Atrazine in SIMS and MALDI Imaging in Earthworm Samples and its Correlation to Gas Phase Basicity**, *T. Weintraut, S. Heiles, A. Henss,* ***Marcus Rohnke,*** Justus Liebig University Giessen, Germany

Rationale: In mass spectrometry imaging (MSI), ion suppression can lead to misinterpretation of results. Especially phospholipids, most of which exhibit high gas-phase basicities, are known to suppress the ionization rates of metabolite and drug molecules out of tissues. Thus, for a distinct MSI anaylsis of a selected tissue type, it is essential to reveal and cope with these ion suppression effects. Motivated by unexpected analyte distributions within environmentally relevant tissue sections, we systemtatically investigated the apparent suppression of an herbicide signal in earthworm samples with ToF-SIMS and MALDI-MSI. We hypothise that the gas-phase basicity correlates with ion suppression effects.

Methods: The accumulation of the herbicide atrazine in earthworms was investigated with ToF-SIMS and MALDI-MSI and subsequently compared with untreated samples spiked with the herbicide. Furthermore, the relationship of signal intensity and gas-phase basicity in binary mixtures of lipids and herbicide was evaluated and applied for measurements with atrazine. Finally, atrazine standards with varying concentrations of a homogenized earthworm suspension were analysed in ToF-SIMS and MALDI-MSI.

Results: ToF-SIMS measurements of the earthworm sections revealed pronounced ion suppression of protonated atrazine in most sample areas. MALDI-MSI showed similar ion suppression, but in comparison more areas with atrazine could be detected. For binary lipid-atrazine mixtures, the logarithmic intensity ratios of the two protonated components followed a linear relationship when plotted as a function of the corresponding gas phase basicity. A possible range for the gas-phase basicity of atrazine (GB_{ATR}=930-985 kJ/mol) was determined. Measurements of the atrazine standards with varying earthworm content showed no clear dependence on concentration.

Conclusions: The presence and elevated concentration of phospholipids in ToF-SIMS and MALDI-MSI analysis of earthworm samples leads to ion suppression of the protonated atrazine signal. The determined possible range for the gas-phase basicity of atrazine (GB_{ATR}=930-985 kJ/mol) lies significantly lower than the known gas-phase basicity of one of the major lipid components, phosphatidylcholine (GB_{PC}=1044.7 kJ/mol).[1] Therefore, competition for protons in the desorption process of both MSI techniques is most likely the cause for the observed ion suppression of atrazine.

[1] Miller ZM, Zhang JD, Donald WA, Prell JS. Gas-Phase Protonation Thermodynamics of Biological Lipids: Experiment, Theory, and Implications. Anal Chem. 2020;92(15):10365-10374. doi:10.1021/acs.analchem.0c00613.

10:40am **FM-WeM3-13 Ion Emission of Molecules from Graphene and Carbon Nanotube Substrates via Large Cluster Impacts: Mechanisms of Ionization**, ***Stanislav Verkhoturov***, *D. Verkhoturov,* Department of Chemistry, Texas A&M University; *M. Gołuński, S. Hrabar, Z. Postawa,* Department of Physics, Jagiellonian University, Kraków, Poland; *A. Kolmakov,* National Institute of Standards and Technology, Gaithersburg; *E. Schweikert,* Department of Chemistry, Texas A&M University

We study here the ion emission of molecules stimulated by impacts of cluster ions of C_{60} and Au_{400} (~1 keV/projectile atom) from Graphene and Carbon Nanotube substrates. Figure 1 (supplemental document) shows the sketch of bombardment/emission directions. The analytes are: a) sub-single molecular layer of Phe molecules deposited on 2L graphene; b) sub-single layer of Phe molecules on multi-wall carbon nanotubes; c) a polymer layer of PMMA (~1 mm) covered by a single-layer ^{13}C graphene.

Two custom-built Cluster ToF SIMS devices with similar parameters were used. The experiments were run in the event-by-event bombardment/detection mode; thus, the regime of bombardment is super-static [1]. The primary cluster ions used were 50 keV C_{60}^{2+}, and 520 keV Au_{400}^{4+}.

For the cases a) and b) (C_{60} impacts), the mechanism of ejection is described with the "trampoline" model [2]. The proposed mechanisms of molecule ionization are electron tunneling and direct proton transfer exchange. For both mechanisms, the presence of graphene support plays an important role as an electron donor.

The configuration c) is different. The emission of molecular ions is suppressed by a single layer of graphene (C_{60} impacts). MD simulations show that this is not a case of low ionization probability for this sample configuration but in fact graphene suppresses the ejection of molecules. The compression of matter in the excitation volume around the impact is not sufficient to destroy the graphene.

However, impacts of 520 keV Au_{400}^{4+} stimulate abundant emission of molecular ions (configuration c). We will discuss new mechanisms of ejection/ionization for the case of 520 keV Au_{400}^{4+} impacts. We posit that these mechanisms involve an electromagnetic interaction of Au_{400} projectile with graphene (case c).

[1] M. Eller et al. Anal. Chem. 88 (2016)

[2] S.V. Verkhoturov et al. J. Chem. Phys. 150 (2019)

Acknowledgement: NSF Grant CHE-1308312, NIH Grant R01 GM123757-01,

Polish National Science Center 2019/33/B/ST4/01778, PLGrid Infrastructure Grant

11:00am **FM-WeM3-15 Oxygen Enhancement of Sputtered Ion Yields: Anomalous Behavior of Electropositive Impurities (Al and B) in Cu(O) Matrices**, ***Peter Williams***, *K. Franzreb,* Arizona State University

Oxygen enhancement of sputtered ion yields continues to be one of the most useful, yet least understood, phenomena in SIMS.In an earlier study [] we noted that the yield of an Al implant in silicon was almost unaffected by the oxygen content of the sample, whether delivered by an oxygen primary ion beam or by oxygen gas flooding or both.Here we extend this study to single crystal copper and aluminum substrates.With the oxygen content of the targets calibrated using an implanted 18O internal standard, we observed that the yields of both Al+ and B+ from implants in Cu were minimally -- or not at all -- enhanced by changing O levels.As a check, oxygen enhancement of Al+ ion yields from an Al metal target behaved “normally”, i.e. could be enhanced by almost 3 orders of magnitude by increasing oxygen content.Cu+ sputtered from a Cu target started to be enhanced at O/Cu levels ~ 0.1.In contrast, Cu+ from a Cu implant in Al responded to added O at levels of a few % and in fact paralleled the behavior of Al+/Al at a factor of ~5 lower yield.Currently we rationalize these behaviors in terms of:

a) enhanced ion yields of both Al and impurities in the maximally ionic Al(O) lattice;

b) gettering of trace amounts of O in Cu by B and Al to form nanoprecipitates of Al2O3 and B2O3 (and similarly of O in Si by trace Al) that result in ion yields of B+ and Al+ similar to the bulk oxides, and

c) incorporation of trace Cu in Al(O) into cation sites in the aluminum oxide lattice and/or in Al2O3 precipitates that give yield enhancement similar to that of Al+ (although lower in absolute magnitude due to the higher ionization potential of Cu).

11:20am **FM-WeM3-17 Strategy for the Construction of Accurate 3D NanoSIMS Depth Profiling Images of Cells Despite Lateral Variations in Sputter Rate**, *M. Brunet, B. Gorman,* ***Mary Kraft,*** University of Illinois Urbana-Champaign

We present a new strategy that enables the construction of accurate three-dimensional (3D) NanoSIMS depth profiling images of cells in the presence of lateral variations in sputter rate and the absence of correlated topography data. We use the secondary electrons that were collected in parallel with the negatively charged secondary ions during NanoSIMS depth profiling to reconstruct the cell’s morphology at the time each depth profiling image was acquired. Next, we adjust each of these morphology reconstructions so that the height at every x, y location decreases with increasing image plane. Finally, we shift each voxel in the component-specific 3D NanoSIMS images to the z-position of the corresponding pixel in the morphology reconstruction for the same image plane. We validated this strategy by comparing the morphology reconstruction created using the first secondary electron depth profiling image acquired from a cell with focused ion beam - secondary electron microscopy (FIB-SEM) to AFMmeasurements of the cell taken before depth profiling. The shape, curvature, and relative height of the reconstructed morphology agreed well with the AFM data. Use of this approach to depth correct 3D NanoSIMS depth profiling images of ^{18}O-cholesterol and ^{15}N-sphingolipids that were metabolically incorporated into a mammalian cell yielded more accurate representations of the cholesterol and sphingolipid distributions within the cell. Depth correction also improved the clarity of the component-specific 3D images, allowing transport vesicles and organellar membranes containing ^{18}O-cholesterol and ^{15}N-sphingolipids to be more clearly visualized. This strategy opens the door to constructing relatively accurate 3D NanoSIMS images that show the distributions of molecules of interest within cells without requiring a constant sputter rate or correlated topography measurements.

11:40am **FM-WeM3-19 Cs^+ SIMS using a Low Temperature Ion Source (LoTIS)**, ***Brenton Knuffman***, *A. Schwarzkopf, A. Steele,* zeroK NanoTech

We present SIMS instruments featuring the Cs^+ Low Temperature Ion Source (LoTIS). When compared with other cesium ion sources LoTIS can deliver much smaller spot sizes (1 pA into ~2.5 nm), or substantially more current into moderate spot sizes (~100 pA into 50 nm). LoTIS offers high sputter rates, high yields of secondary ions, and a wide range of beam currents from pA to many nA.

The talk will center on our new Secondary Ion Mass Spectrometry (SIMS) system called SIMS:ZERO. It is currently the highest-resolution SIMS instrument in the world and was built in collaboration with the Luxembourg Institute of Science and Technology (LIST). SIMS:ZERO is capable of high-resolution focused ion beam operations while also providing SIMS data. Its spectrometer has a mass-resolving power of ~400 at full transmission, making it suitable for general materials analysis or as a replacement for EDX. We will also show how the capabilities of a FIB allow for in-situ preparation of extremely smooth sample surfaces for SIMS analysis, and how these contribute to data quality. A soon-to-be-added continuous focal plane detector will further enhance the utility of SIMS:ZERO in the analysis of complex, multi-element samples.

Data from several demonstration targets will be presented. These include a Rb-doped CIGS solar cell, localization of tiny TnO nanoparticles, and deconstruction of silica-encased diatoms.

12:00pm **FM-WeM3-21 Development and Characterization of a Drug Dosed Biomimetic Reference Material for a Sims Vamas Inter-Laboratory Study to Study Sensitivity and Linearity**, ***Jean-Luc Vorng***, *A. Eyres,* National Physical Laboratory, U.K.*; C. Newman, A. West,* GlaxoSmithKline, UK*; I. Gilmore,* National Physical Laboratory, UK

The application of SIMS to biological materials has expanded substantially in the last decade (1). There have been important advances in technology including the use of a wide range of gas cluster ion beams for analysis using argon (2), water / CO_2 mixtures (3) and water (4). In addition, new analysers have been developed for improved biological analysis including the J105 (5) (Ionoptika, UK) and the OrbiSIMS (6,7) (Hybrid-SIMS, IONTOF GmbH, Germany) amongst others. SIMS now allows molecular imaging of complex biological samples ranging from cells to tissues. To improve repeatability and determine reproducibility between laboratories with varying instrument configurations there is a need to define and establish a biologically relevant biomimetic sample for pharmaceutical and small molecule analysis.

In this study, we present a step-by-step approach for sample preparation of a biomimetic reference material composed of doped tissue homogenate from rat liver using a protocol developed by GlaxoSmithKline for MALDI MS (8). The resulting material was characterised using ToF-SIMS (Bi_3^+ analysis beam) and OrbiSIMS (Ar_{2500}^+) depth profiling. The spiking of different drugs in the resulting material is used to study the influence of matrix effects on detection sensitivity (9), limit of detection and calibration for quantification. This study evaluates the possibility of using this reference material for a future VAMAS interlaboratory comparison suitable for dual beam and single beam analysis instruments.

Reference:

(1): D. Schaumlöffel J. Anal. At. Spectrom. ***2020****,35, 1045-1046*

*(2)***:** M. Fuji et *al*. Rapid Commun Mass Spectrom. **2014**, 30;28(8):917-20

(3): M. Lagator et *al*. Surf Interface Anal. **2022**,54:349–355

(4): S.Sheraz et *al*. Anal. Chem. **2019,** 91, 14, 9058–9068

(5): S. Rabbani et *al*. Surf. Interface Anal. **2011**,43, 380–384

(6): M.K. Passarelli et al. Anal. Chem. ***2015****, 87, 6696-6702*

(7): M.K. Passarelli et *al*. Nature Methods. **2017**, 14, 1175–1183

(8): J. A. Barry et *al*, Bioanalysis. **2019**,11(11):1099-1116

(9): J-L. Vorng et al Anal. Chem.**2016**, 88, 22, 11028–11036

Recent Advances in SIMS
Room Great Lakes C - Session RA-WeM2

Cluster and Novel Ion Sources

Moderators: Arnaud Delcorte, Université Catholique de Louvain, **Christine Mahoney**, Corning Research and Development Corporation

8:40am **RA-WeM2-1 Study of Mixed-gas Cluster Ion Beam for TOF SIMS***,* ***Myoung Choul Choi,*** Korea Basic Science Institute, Republic of Korea

Time-of-Flight Secondary ion mass spectrometry (ToF-SIMS) offers new possibilities for surface analysis of various organic samples such as materials science, material defect analysis, semiconductor analysis, and biological analysis. Advances in ToF-SIMS are based on developing novel first-order cluster ion beams for molecular analysis. Au3+ and Bi3+ cluster ions increased the secondary ion yield of high-mass molecular samples by 100-1000 fold compared with conventional atomic ion beams [1]. In particular, Ar cluster ion beams are being studied for both sputtering and analysis.[2] Despite several advantages of Ar gas clusters, the secondary ion yield of molecules sputtered by GCIB decreases with increasing cluster size. In addition, although there is a problem in that spatial resolution is low due to a relatively large beam size compared to a liquid metal ion beam, improvement of the gas cluster ion beam to minimize sample damage in the primary ion beam analysis has been continuously required. Recently, although the Ar mixed gas and CO2 have improved, the change in the characteristics of the cluster ion beam concerning the Ar and CO2 mixing ratio has not been studied in detail. If the gas cluster ion beam can be controlled by the ratio of the gas mixture, more effective cluster ion beam improvement will be possible.

Over the past few years, the Korea Basic Science Institute (KBSI) has been developing cluster ion guns and ToF-SIMS for three-dimensional (3D) mass imaging analysis of organic materials and bio samples [3].

In this study, the characteristic change of the cluster ion beam according to the ratio of Ar and CO2 mixed gas was measured.[4] Also, to improve the ToF-SIMS analysis, we propose the Ar and CO2 mixed gas ratio of the GCIB source. This mixed gas method can improve the efficiency of secondary ions and increase spatial and depth resolution compared to pure Ar gas.

Reference

[1] J.S. Fletcher, J.C. Vickerman, N. Winograd, Label free biochemical 2D and 3D imaging using secondary ion mass spectrometry, Curr. Opin. Chem. Biol. 15.5 (2011) 733–740.

[2] I. Yamada, J. Matsuo, Z. Insepov, D. Takeuchi, M. Akizuki, and N. Toyod, J. Vac. Sci. Technol. A, 14(3), 1996, 781

[3]S.J. Lee, C.M. Choi, B.K. Min, J.Y. Baek, J.Y. Eo, M.C. Choi, Development of an argon gas cluster ion beam for ToF-SIMS analysis, Bull. Korean Chem. Soc. 40.9 (2019) 877–881.

[4] Sang Ju Lee, Aram Hong, Jinwan Cho, Chang Min Choi, Ji Young Baek, Jae Yeong Eo, Byeong Jun Cha, Woo Jun Byeon, Jin Young We, Sangwon Hyun, Minwoo Jeon, Choelho Jeon, Dong Jin Ku, Myoung Choul Choi*, Applied Surface Science, 572, 2022, 151467

9:00am **RA-WeM2-3 Properties of Vacuum Electrospray Droplet Ion Beams Produced by Capillaries with Different Inner Diameters***,* ***Satoshi Ninomiya,*** *S. Tsuneki,* University of Yamanashi, Japan*; L. Chen,* University of Yamanashi, Malaysia*; K. Hiraoka,* University of Yamanashi, Japan

We have been studying a vacuum electrospray droplet ion (V-EDI) beam gun as a new massive cluster ion beam for secondary ion mass spectrometry (SIMS). In the previous studies, the V-EDI gun was installed in a time-of-flight SIMS (TOF-SIMS) system, and the secondary ion spectra produced by the V-EDI beams were measured for several biomolecular samples[1-3]. The fragment ion generation was strongly suppressed and the protonated intact molecules were observed with high intensities. However, the basic characteristics of the V-EDI beams are not enough revealed. In this study, the properties of V-EDI beams produced by capillaries with different inner diameters will be investigated.

The moderately focused (~0.5 mm) V-EDI beams which were generated by vacuum electrospray of a 0.01 M trifluoroacetic acid aqueous ethanol solution (water/ethanol=4:1) were raster-scanned over an area of typically 4.5x4.0 mm^2 at a scan speed of 0.1 Hz for short (300~1000 s) or long (2000~50000 s) time. For sputtering yield evaluation, primary 8 kV V-EDI beams produced from capillaries with different inner diameters (5, 10 and 15 μm) were irradiated uniformly on polymer or plasticizer film (~100 nm) samples prepared by spin-coating. The irradiated samples were analyzed with atomic force microscopy (AFM) and spectroscopic ellipsometry. The microscopic images of the films irradiated for short periods were observed with AFM, and the sputtering volumes per primary ion were calculated from the diameter and depth of the impact crater. The thicknesses of the films irradiated for long periods were observed with spectroscopic ellipsometry, and the sputtering volumes per primary ion were calculated from the difference in film thickness between irradiated area and non-irradiated area.

The sputtering volume per primary ion depended strongly on the inner diameter of each capillary. The sputtering volumes of the V-EDI beam generated by the capillary with an inner diameter of 5 μm were smaller than those by other capillaries (i.d. 10 and 15 μm). The differences in sputtering volume are assumed to be originated from the droplet ion size included in the V-EDI beams obtained from capillaries with different inner diameters.

References

[1] S. Ninomiya, Y. Sakai, R. Watanabe, M. Sogou, T. Miyayama, D. Sakai, K. Watanabe, L.C. Chen, K. Hiraoka, *Rapid Commun. Mass Spectrom*. **30**, 2279 (2016).

[2] S. Ninomiya, L.C. Chen, K. Hiraoka, *J. Vac. Sci. Technol. B***36**, 03F134 (2018).

[3] S. Ninomiya, Y. Sakai, L.C. Chen, K. Hiraoka, *Mass Spectrometry***7**, A0069 (2018).

9:20am **RA-WeM2-5 Effects of Reactive Gas Cluster Ion Beams on Yields and Matrix Effects in SIMS***,* ***Matija Lagator,*** *I. Berrueta Razo ,* The University of Manchester, UK*; N. Lockyer,* University of Manchester, UK

Two of the greatest challenges in SIMS research are low ionization yields and matrix effects. Polyatomic water beams demonstrate that primary ion beam chemistry can increase yields while reducing matrix effects. We report a study demonstrating that carrier gas chemistry alters the SIMS characteristics of water cluster beam. The study aims to test if carbon dioxide reacts with water clusters thus increasing the likelihood of clusters acting as proton donors.

By applying water clusters with a reactive (CO_2 containing) carrier gas to drug standards we were able to measure the effect on the secondary ion yield. We show that compared to an inert (Ar) carrier gas, the yield observed with reactive water clusters is up to 50 times higher (Figure 1). This implies a change in primary cluster composition as a result of using a reactive carrier gas.

Matrix affects arise from the often unpredictable interaction of surface species which results in an ionization suppression/enhancement effect. Complex sample environments present a greater obstacle due to a myriad of potential chemical interactions. We show that by applying the newly developed chemically reactive water cluster beam, it is possible to reduce the matrix effects achieving a higher level of quantification over a range of drug concentrations (Fig. 2).

Together these observations indicate a novel methodology promoting the application of SIMS in a more sensitive and more quantitative manner to complex samples.

9:40am **RA-WeM2-7 Development of a High Throughput Microscope-Mode Secondary Ion Imaging Mass Spectrometer***,* ***Maria Elena Castellani,*** *N. Smith, Y. Jia, M. Burt,* Oxford University, UK*; J. Bunch,* National Physical Laboratory, U.K.*; Z. Takats,* Imperial College London, UK*; M. Brouard,* Oxford University, UK*; F. Green,* Rosalind Franklin Institute, UK

Secondary ion mass spectrometry (SIMS) is a surface analysis mass spectrometric technique that analyses solid samples by collecting the secondary ions produced by impact between the sample and a primary ion beam. When using stigmatic optics and a position-sensitive detector, microscope mode SIMS imaging can acquire spatially resolved images with high speed and throughput.

We hereby describe the conceptualisation, development and testing of a high-throughput microscope-mode SIMS imaging instrument that combines a highly defocussed microprobe mode SIMS C_{60} primary ion beam with novel extraction optics, pulsed extraction of the secondary ions, and a multichannel-plate/phosphor screen assembly. Exploiting a Pixel Imaging Mass Spectrometry (PImMS) camera, we recorded the spatially resolved mass spectrum images in seconds.

Mass and spatial resolution were tested through metal grid samples, comparing the findings with previous ones obtained with another microscope-mode imaging mass spectrometer. Hence, microscope-mode SIMS imaging appears as a promising technique for the rapid simultaneous analysis of multiple composite samples.

SIMS Solutions in Materials and Life Sciences
Room Great Lakes C - Session SS+RA-WeM4

High Resolution and MS/MS Methods I

Moderators: Gregory Fisher, Physical Electronics USA, **Andrew Giordani**, Procter & Gamble Company

10:20am **SS+RA-WeM4-11 A Novel Method for Measuring Young's Modulus Using Water Cluster SIMS***, **Naoko Sano**, A. Bellew,* Ionoptika Ltd., UK

Many techniques are available to measure mechanical properties such as material hardness, for example, nanoindentation. However, certain materials or structures provide challenges to measuring the actual hardness, such as when an underlying material is much softer than the one above, *e.g.*, an ice cube sitting on water.

Water Cluster SIMS is a powerful technique for analysing organic and biological samples. The enhanced sensitivity provided by the water cluster beam enables ultra-clear 2D and 3D analysis of high-mass compounds. In this work, we will explore a novel use of Water Cluster SIMS – for measuring the modulus of elasticity by the dissociation of water cluster ions.

It has been observed in SIMS spectra that water cluster ions colliding with a surface dissociate into smaller ions with the formula $[(H_2O)_n+H]^+$, where $2 \leq n \leq 100$. Additionally, the dissociation rate appears to depend on the surface's physical properties and the energy of the ion beam.

Initial results have demonstrated a relationship between Young's modulus and the observed ion intensity. The ability to measure the mechanical properties of a surface in situ whilst performing SIMS measurements would be especially beneficial for thin multilayer films and those materials where other measurements have failed.

10:40am **SS+RA-WeM4-13 Toward the Analysis of Hydrated Biological Specimens Using Atom Probe Tomography***, **Daniel Perea**,* Pacific Northwest National Laboratory **INVITED**

Within the field of materials science, the adage that *structure determines properties* is foundational to the field, while a similar adage underpins the field of structural biology where *form follows function*. This concept is beautifully exemplified by proteins, where function from providing structural support, motility, transport, and enzymatic activity, is as varied as their unique amino acid sequence and resultant complex physical 3-D structure. Currently, the application of individual or combinations of established analytical techniques such as cryo electron microscopy, nuclear magnetic resonance spectroscopy, mass spectrometry, and X-ray crystallography are commonly used determine protein structure from ensembles of isolated proteins or protein crystals. However, the need to make measurements from ensembles of isolated proteins or crystals means that information is lost, for example, ionic gradients with respect to the native aqueous environment. Here I will explore the question*, can the analytical technique Atom Probe Tomography (APT), which produces 3D atom-by-atom composition point cloud maps, be applied to map macromolecular structure and ionic gradients of hydrated biological materials*? Recent work by our group has established the ability of APT to map gradients over nanoscale distances within an embedded protein specimen. More recently, established approaches for the preparation, handling, and transfer of cryogenically frozen hydrated specimens provides a route for the site-specific targeting of hydrated biological samples for cryo-APT analysis, including regions containing proteins cryogenically embedded in water ice. In this talk, I will discuss recent progress toward this end, which importantly includes the development of machine learning models aimed at mapping macromolecular structure from the 3-D point cloud composition maps.

11:20am **SS+RA-WeM4-17 Identification of Organic Molecules Produced from a Surface using Laser and QIT-ToF-SIMS***, **Chang Min Choi**, J. Baek, J. Eo, M. Choi,* Korea Basic Science Institute, Republic of Korea

Over the past few decades, time-of-flight secondary ion mass spectrometry (ToF-SIMS) has been continuously developed and used as a powerful instrument for a surface analysis[1]. Since the gas cluster ion beam (GCIB) developed, ToF-SIMS has helped us to detect a bigger organic ion from biological samples including tissues, cells, and so on[2-3]. Even though it has great advantages using GCIB for observing a secondary molecular ion, simple ToF mass spectra often have a difficulty assigning a peak which might exist candidates having a similar mass. Recently, some ToF-SIMS developers have been trying to add tandem mass spectrometric function for the accurate molecular identification[4].

We also wanted to resolve the aforementioned problem and developed a quadrupole ion trap time-of-flight secondary ion mass spectrometer (QIT-ToF-SIMS). Secondary molecular ions are generated from a sample surface with 20 keV toluene ion projectile produced by a UV pulse[5]. The generated secondary ions from a surface are transferred to a QIT though an extraction electrode and a set of electrostatic lens. After ion accumulation in QIT, the stored waveform inverse Fourier transform (SWIFT) pulse are applied to the QIT for the selection of an interested molecular ion. A nano second (ns) laser pulse is irradiated onto the selected secondary ion in the QIT for the photo-induced dissociation (PID). The PID-resulting ions are detected by reflectron ToF-MS. The electronic absorption probability is obtained by recording photodepletion of the secondary molecular ion as a function of the laser wavelength.

In this work, different molecular ions with similar mass are separated by photodepletion spectra. This would help us not only eliminate candidates with a confusion come from a similar mass but also research photophysical and photochemical properties of secondary molecular ions sputtered from surface. Furthermore, we anticipate PID study for a secondary ion open a chance to see a surface in a new perspective.

References

[1] N. Winograd, *Anal. Chem.***2015**, *87*, 328-333.

[2] A. S. Mohammadi, N. T. n. Phan, J. S. Flecher, A. G. Ewing, *Anal. Bioanal. Chem.***2016**, *408*, 6857-6868.

[3] H. Tian, L. J. Sparvero, A. A. Amoscato, A. Bloom, H. Bayır, V. E. Kagan, N. Winograd, *Anal. Chem.***2017**, *89*, 4611-4619.

[4] M. K. Passarelli, A. Pirkl, R. Moellers, D. Grinfeld, F. Kollmer, R. Havelund, C. F. Newman, P. S. Marshall, H. Arlinghaus, M. R. Alexander, A. West, S. Horning, E. Niehuis, A. Makarov, C. T. Dollery, I. S. Gilmore, *Nat. Methods***2017**, *14*, 1175-1183.

[5] C. M. Choi, S. J. Lee, J. Y. Baek, J. J. Kim, M. C. Choi, *Appl. Surf. Sci.***2018**, *458*, 805-809.

11:40am **SS+RA-WeM4-19 Cryo-ToF-SIMS and OrbiSIMS investigations of Sr^{2+} Diffusion in Bone Marrow***, **Christine Kern**, A. Pauli, R. Jamous, T. El Khassawna, M. Rohnke,* Justus Liebig University Giessen, Germany

Osteoporosis, a systemic bone disease, is characterized by increased fracture risk and delayed, incomplete fracture healing. To improve fracture healing, next generation biomaterials are functionalized with drug release systems. Here, we are interested in the local release of healing-promoting agents, such as Sr^{2+} ions. In previous work, we studied Sr^{2+} release from functionalised bone cements and its dispersion in the mineralised areas of rat bone by time-of-flight secondary ion mass spectrometry (ToF-SIMS).[1, 2] In this work, we investigate Sr^{2+} transport within the more complex, highly viscous bone marrow. As analytical tools for tracking and spatially resolving the Sr^{2+} diffusion within bone marrow we apply 2D and 3D ToF-SIMS and orbitrap secondary ion mass spectrometry (OrbiSIMS). In a first approach, a ToF-SIMS depth profiling protocol under cryogenic conditions was specifically developed for determination of diffusion coefficients in bovine bone marrow. The validity of our experimental approach is shown within a time-dependent experimental series. Average diffusion coefficients of Sr^{2+} in different bovine bone marrow areas were obtained [fast diffusion: $D_{\mathrm{bovine,FD}}=(2.09\pm2.39)\cdot10^{-9}\ \mathrm{cm^2s^{-1}}$); slow diffusion: $D_{\mathrm{bovine,SD}}=(1.52\pm1.80)\cdot10^{-10}\ \mathrm{cm^2s^{-1}}$; total area: $D_{\mathrm{bovine,TA}}= (1.94\pm2.40)\cdot10^{-9}\ \mathrm{cm^2s^{-1}}$]. In a subsequent proof-of-concept study, the developed protocol was successfully applied to the determination of Sr^{2+} diffusion in bone marrow of osteoporotic rats [$D_{\mathrm{rat,FD}}=(7.64\pm1.70)\cdot10^{-10}\ \mathrm{cm^2s^{-1}}$); $D_{\mathrm{rat,SD}}=(5.47\pm1.17)\cdot10^{-10}\ \mathrm{cm^2s^{-1}}$); $D_{\mathrm{rat,TA}}= (7.50\pm1.62)\cdot10^{-10}\ \mathrm{cm^2s^{-1}}$]. For both bovine and rat bone marrow, high-resolution 2D and 3D mass spectrometric imaging analysis as well as OrbiSIMS spectral analysis revealed a correlation of slower Sr^{2+} diffusion in bone marrow areas with high intensity of lipid/fatty acid signals and fast Sr^{2+} diffusion in areas with less intensity of lipid signals. The mass spectrometric results are correlated with histological stainings. Overall, our results provide important insights about Sr^{2+} diffusion in bone marrow and show that both cryo-ToF-SIMS and cryo-OrbiSIMS are useful tools for the investigation of rapid diffusion in water-containing highly viscous media.

[1] M. Rohnke, et al., Strontium release from Sr2+-loaded bone cements and dispersion in healthy and osteoporotic rat bone, J. Controlled Release 262 (2017) 159
[2] C. Kern, et al., Investigation of strontium transport and strontium quantification in cortical rat bone by time-of-flight secondary ion mass spectrometry, J. R. Soc. Interface 16 (2019) 20180638

12:00pm **SS+RA-WeM4-21 Diagenetic Degradation of Organic Molecules in Fossils Characterized by ToF-SIMS***, **Peter Sjövall,*** RISE Research Institutes of Sweden*; M. Jarenmark, J. Lindgren,* Lund University, Sweden

Fossils constitute the only source of information that we have of the evolution of life on Earth prior to the emergence of humans. This knowledge is constantly increasing as new fossils are discovered and studied by an increasing number of advanced analytical techniques [1]. For example, organic residues in >50 million-year-old fossils have been found to contain molecular species that can be attributed to endogenous biomolecules of the once living animal, including the pigments eumelanin and heme, whereas claims of preserved proteins are more controversial. An important advantage of ToF-SIMS over conventional mass-spectrometric techniques is the possibility to associate molecular information directly with specific microstructures on a fossil surface, thereby providing additional confidence in the biomolecular assignments. However, the complexity of organic residues often limits the amount of molecular information that can be obtained from ToF-SIMS analysis, and diagenetic degradation adds additional uncertainties to the biomolecular identification. In this work, we subjected eumelanin and two abundant structural proteins, collagen and elastin, to extended treatments at high temperatures and pressures to simulate diagenetic maturation. The samples were analysed by ToF-SIMS and complementary techniques to monitor induced molecular transformations, and the results were then compared against data acquired from a selection of exceptionally preserved fossils. For eumelanin, the resilient properties of this macromolecule were demonstrated by only minor changes to the spectra even after harsh experimental maturation, as expected from the well-documented preservation of this pigment in the fossil record [2]. In contrast, the results for the proteins showed considerable spectral changes upon high T/P treatment, including decreasing signal intensities of typical amino-acid-specific ions and increasing intensities of ions consistent with N-containing heterocyclic compounds, in agreement with recent suggestions [3] that “N-heterocycles” represent degraded proteinaceous matter in fossils. Our results indicate that biomolecules undergo transformations during diagenesis that lead to the formation of more stable molecular structures, which in the studied fossil may or may not preserve information about their original identity.

[1] Lindgren et al., Soft-tissue evidence for homeothermy and crypsis in a Jurassic ichthyosaur, Nature 564, 359-365 (2018)

[2] Jarenmark et al., Chemical Evaluation of eumelanin maturation by ToF-SIMS and alkaline peroxide oxidation HPLC analysis, Int. J. Mol. Sci., 22, 161 (2021)

[3] Wiemann et al., Nat. Commun. 9:4741 (2018)

Dealing with Data and Interpretation
Room Great Lakes B - Session DI-ThM1

Data and Data Processing

Moderators: Christine Mahoney, Corning Research and Development Corporation, **Bonnie J. Tyler**, University of Münster

8:40am **DI-ThM1-1 Denoising of Tof-Sims Images via Inverse Maximum Signal Factors Analysis***, **Bonnie J. Tyler**, H. Arlinghaus,* University of Münster, Germany

One of the long-term objectives of ToF-SIMS research has been the high resolution 2D and 3D imaging of pharmaceuticals and biomolecules in tissues and biofilms at physiologically relevant concentrations.Although much progress has been made through advances in instrument design and development of cluster ion sources, the technique continues to be limited due to low signal-to-noise ratio for many important systems.Improving signal-to-noise, and thereby image contrast, is one of the key challenges needed to expand the useful applications of ToF-SIMS.Various multivariate analysis (MVA) methods have proven to be effective for improving image contrast in ToF-SIMS.However, the distribution of important but low intensity ions can be obscured in the MVA analysis leading to a loss of chemically specific information.In this work we propose inverse maximum signal factors (iMSF) denoising as an alternative approach to both denoising and multivariate analysis for ToF-SIMS imaging.This approach differs from the standard MVA techniques in that the output is denoised images for each original mass peak rather than the frequently difficult to interpret scores and loadings. Five tests have been developed to optimize and validate the resulting denoised images.The algorithm has been tested on a range of simulated data with different levels of noise, correlated noise, varying numbers of underlying components and non-linear effects.In the simulations, excellent correlation between the true images and the denoised images was observed for peaks with an original signal-to-noise ratio as low as 0.1 as long as there was sufficient intensity in the sum of selected peaks.Applications of this approach for 2D imaging of glycolipid accumulation in Fabry mouse kidney, 3D imaging of antibiotics in frozen/hydrated biofilms and MALDI-MSI imaging of mouse brain will be presented.A signal-to-noise improvement of as much as two orders-of-magnitude was achieved for very low intensity peaks.MSF denoising is a powerful addition to the suite of image processing techniques available for studying mass spectrometry images.

9:00am **DI-ThM1-3 High-Speed 3D ToF-SIMS Analysis of Unknown Samples***, A. Bellew, N. Sano, A. Stickland, P. Blenkinsopp,* Ionoptika Ltd, UK*; K. McHardy, **Michal Ryszka**,* Ionoptika Ltd., UK

ToF SIMS allows for high-resolution 3D tomography, where each voxel contains a mass spectrum. With spatial resolutions of hundreds of nanometres and depth resolutions of just a handful of nanometres, we should expect ToF SIMS to be used in every analysis lab worldwide. It is not the case, of course.

Up to now, 3D ToF SIMS images were a “nice to have” - the cherry on top once the analysis was complete. Something for the journal cover or some pretty marketing material, but often no more than that. However, it is not for lack of desire but rather a lack of computing power. These authors believe 3D analysis should be part and parcel of the ToF SIMS workflow.

The J105 SIMS collects 200,000 bins per spectrum, up to 32 bits each. A good quality 3D image contains at least 128x128x128 pixels – more than 2 million voxels. This amounts to more than a terabyte of uncompressed data! Existing methods would require a high-powered server to load this data to make each mass image accessible to the user in a reasonable time frame.

We present here for the first time a new software tool for high-speed inspection and analysis of large 3D data sets that requires very little computing power and can operate on a mid-range laptop computer. Coupled with Ionoptika’s smart compression solution, Analyse3D can display 3D images of a single peak in mere seconds. All peaks in the data set may thus be imaged and compared in 3D quickly and easily.

We shall demonstrate the capabilities of this new tool on OLED devices, multi-layer coatings, ion implantation samples, and more.

All the features you expect from 2D analysis, but with the flexibility of 3D. Analyse3D™ completely changes the way we look at ToF SIMS data.

9:20am **DI-ThM1-5 Towards Comprehensive Analysis of Complex Biological Samples in 3D OrbiSIMS***, **Anna Kotowska**, M. Edney,* University of Nottingham, UK*; A. Shard,* National Physical Laboratory, UK*; J. Aylott, M. Alexander, D. Scurr,* University of Nottingham, UK

In contrast to biological imaging methods such as fluorescence microscopy, SIMS has the capability to map several groups of compounds simultaneously in an untargeted way, without labelling. Particularly, reduced fragmentation offered by the GCIB primary beam and high mass resolving power of the Orbitrap™ analyser enable detailed characterisation of biological samples[1]. Lipids, metabolites and proteins, which previously would have been undistinguishable in complex samples due to the limited mass resolving power of ToF-SIMS, can be assigned in the spectra. However, this advantage of the 3D OrbiSIMS cannot be fully utilised because of large volume (tens of thousands of peaks) and complexity (diverse chemistry) of real biological samples.

Here, we have developed a chemical filtering process by the application of molecular formula prediction (MFP) and the level of molecule saturation (double bond equivalent) to separate multidimensional SIMS data[2]. This approach is particularly advantageous in 3D OrbiSIMS data, which contains mixtures of molecular ions as well as several fragment ions per molecule. Furthermore, we integrated the LIPIDMAPS® database and generated a protein fragment database to facilitate chemical filtering and assignment of these molecules. Our chemical filtering method has been successfully applied to challenging biological samples, assigning salts, lipids and protein fragments in human serum[2], mapping different lipid classes throughout human skin[3] and tracking lipids, polysaccharides, glycolipids and protein fragments in a bacterial biofilm[4].

This work describes the interpretation of complex biological datasets using the chemical filtering approach. Particularly, it focuses on the chemical filtering and assignment of poorly ionisable molecules (e.g. protein fragments), which are likely to be missed in statistical analysis. In addition to filtering protein fragments, this method enables rapid assignment and classification of protein ions. This approach can enable progress in predicting which fragments will be seen in the 3D OrbiSIMS spectrum and identify proteins in an analogous way as the proteomics community has developed for liquid chromatography MS.

1. Passarelli, M.K. *et al.* The 3D OrbiSIMS - Label-free metabolic imaging with subcellular lateral resolution and high mass-resolving power. *Nat. Methods,* 2017
2. Edney, M.K. *et al.* Molecular Formula Prediction for Chemical Filtering of 3D OrbiSIMS Datasets. *Anal. Chem.*, 2022
3. Starr N.J. *et al.* Elucidating the molecular landscape of the stratum corneum. *PNAS*, 2022
4. Kotowska A.M. *et al.* under review 2022

9:40am **DI-ThM1-7 Time-of-Flight Sims Investigation of Isobaric Oligopeptides***, **Alessandro Auditore**,* Università di Catania, Italy*; N. Grasso,* Università di Catania*; N. Tuccitto, A. Licciardello,* Università di Catania, Italy

Mass Spectrometry methods are widely used analytical techniques for structural characterization of biological molecules. Soft ionization techniques such as ESI and MALDI allow easy determination of the molecular mass and, through the fragmentation patterns, enable the sequencing of linear biomolecules. In this framework, the capability to distinguish between isobaric species has always been a challenging analytical task[1], which is normally tackled by complex mass spectrometric approaches[2]. Often, this holds even in the case of relatively low mass systems such as oligopeptides. On the other hand, time-of-flight secondary ion mass spectrometry, due to the peculiar emission/ion formation mechanisms, often does not allow the detection of the molecular ion of proteins and peptides, while it gives rise to a rich fragmentation pattern which can be used for recognizing, for example, surface adsorbed proteins, often with the help of multivariate analysis methods[3]. Indeed, the different aminoacidic sequence in the oligopeptide chains is expected to determine a different fragmentation pattern in the spectrum. Due to the relevant number of peaks in the SIMS spectra of peptides and protein and the slight differences in intensities between different samples, the multivariate analysis approach allows an easier interpretation of the information included in the ToF-SIMS spectra.

In the present work we investigated four peptides with high similarity in the aminoacid sequence along the peptide chain. The reference peptide (TAT1) is a 12-unit sequence of six aminoacids (GRKKRRQRRRPS). The other three peptides have been obtained by inserting a bAla-H dipeptide (carnosine) in three different positions inside the TAT1 chain, leading to three isobaric molecules, namely GRKKRRQRRRPS-bAla-H (TAT1-Car), bAla-HGRKKRRQRRRPS (Car-TAT1) and GRKKRRQ-bAla-H-RRRPS (T-Car-T), not easily distinguishable each other even by means of conventional MS-MS techniques. We show that these oligopeptides can be easily distinguished by ToFSIMS if deposited onto a surface and after multivariate data analysis of the spectra. Additional information will be provided on the results obtained by deposition on different types of surfaces.

[1]Y. Zhang et al. *J. Am. Soc. Mass Spectrom.* 16 (2005) 1827–1839.

[2]N. Pappireddi et al. *J. Chem. Biol*. 20 (2019) 1210–1224.

[3]S. Muramoto et al, The J. Phys. Chem. C, 115 (2011) 24247-24255.

Recent Advances in SIMS
Room Great Lakes B - Session RA-ThM3

HR Imaging and Spectrometry

Moderators: Laura Creon, CAMECA, **Albert Fahey**, Corning Incorporated

10:20am **RA-ThM3-11 Highest Resolution Sims Imaging Performed on Focused Ion Beam - Based Platforms***, **Jean-Nicolas Audinot**, O. De Castro, P. Philipp, A. Biesemeier, H. Hoang, T. Wirtz,* Luxembourg Institute of Science and Technology (LIST), Luxembourg

FIB–SEM platforms are equipped with a Focused Ion Beam (FIB) column and a focussed electron beam column. This combination is used for a vast number of applications, including nano-patterning applications, sample preparation, imaging in various electron microscopy (EM) modes (SE, BSE, EBSD, STEM) and chemical analysis (WDS/ EDX). However, electron beam probes for EDX analysis have a large interaction volume in the sample, and EDX does not allow detection of light elements (H, Li, ...) and trace elements (<1% in at.). Ion sources have seen significant improvements in source brightness in recent years, resulting in better spatial resolution and current densities. The gas field ion source (GFIS) emitting He^+ or Ne^+ ions has a brightness of 10^9 $Acm^{-2}sr^{-1}$ and thus enables a spatial resolution of 0.3 nm or 2 nm for He^+ or Ne^+ beams, respectively[1]. Likewise, a low temperature ion source (LoTIS) working with Cs ions and reaching a brightness of 10^7 $Acm^{-2}sr^{-1}$ can produce nm-sized probe sizes while maintaining high ion currents, which is of great interest not only for their ability to mill a variety of structures, but also to provide structural and morphologic information with (sub)nm resolution[2,3].

Therefore, the prospect of connecting SIMS spectrometers to FIB-SEM platforms to combine high spatial resolution imaging with high sensitivity analytical data has emerged. To maximize the extraction and detection of secondary ions (SI), LIST developed a compact SIMS system based on a double focussing magnetic sector spectrometer that is optimized for state-of-the-art FIB platforms [2,4]. The design of the SIMS system first optimizes the SI collection by placing a small retractable extraction box as close as possible to the surface of the sample. The extracted SI are then post-accelerated and focussed into the mass spectrometer. After mass filtering, SI are detected using either a multi-collector system that allows simultaneous counting of several isotopes or using a newly developed continuous focal plane detector, which allows detection of the full mass spectrum of each sputtered voxel.

Here, we will review the performance of the FIB-SEM-SIMS platforms developed at LIST by showing applications, focusing on specific methodologies, correlative microscopy, and high-resolution 3D chemical imaging. Thus, we will show that the SIMS data correlated with other data obtained on the FIB-SEM platforms, such as SE images, can provide solutions for current and future analytical challenges.

[1] T. Wirtz et al., Annu. Rev. Anal. Chem. 12, 2019

[2] B. Knuffman, A. V. Steele, and J. J. McClelland, J. Appl. Phys. 114, 2013

[3] J. N. Audinot et al., Reports Prog. Phys. 84, 2021

10:40am **RA-ThM3-13 Integrated Spatial Multiomics using Successive $(H_2O)_n$-GCIB-SIMS and C_{60}-SIMS Imaging to Delineate Tissue Heterogeneity at Single-cell Resolution***, **Hua Tian**,* Pennsylvania State University

Tissue is highly organized with diverse cells that interact and communicate. Together with numerous biomolecules (e.g. metabolites and lipids) of cellular processes, the multilevel heterogeneities drive the biological function and disease-associated discoordination[1-2]. This spatial complexity is often ignored by traditional tissue assay. Mass spectrometry imaging holds the potential to visualize the heterogeneous cell organization and biomolecules in their context. However, it is challenging to achieve high spatial resolution and high chemical sensitivity toward different biomolecules. Moreover, the correlation of spatial omics in a single sample is impossible due to the difficulty of preserving the fast-changing metabolites.

To overcome these analytical hurdles, innovative technology and methodology are developed for omics imaging in single cells. On the same frozen-hydrated tissue, successive $(H_2O)_{n\ (n>28k)}$-GCIB-SIMS and C_{60}-SIMS imaging are employed to profile untargeted metabolites/lipids and targeted proteins by lanthanides antibodies (~ 40 in one acquisition) at 1 µm resolution. The novel ion source, $(H_2O)_{n(n>28k)}$-GCIB enhances chemical sensitivity, improves beam focus, reduces matrix effect, and extends detection ranges up to *m/z* 6000 [3-12]. Coupled with cryogenic analysis, the tissue is analyzed at near nature state, retaining the spatiotemporal distribution of metabolites and lipids. The AI-aided computational processing is used to register the omics in different cell types for further discriminant analysis.

With the new development, a number of tissues are imaged. On breast cancer tissue, the high population of macrophages (CD68) and less infiltration of immune cells (CD45, CD4) are observed, as well as the variation of the metabolic state in different cells. Several phosphatidylinositol species are concentrated in the epithelial tumor cells (pan-cytokeratin), along with desaturated lipids and GSH, indicating the mechanism of immune resistance and antioxidation for tumor survival [27]. Eight ganglioside GM3s correlate with the Ki-67 expressing cells, likely the markers of neoplastic transformation of breast tissue[37]. On liver tissue, distinct lipid clusters colocalize with periportal and pericentral proteins, and metabolic and lipidomic signature varies in distinct liver cells (*e.g.,* sinusoidal, Kupffer, hepatocytes, Ito stellate, immune cells). Similar to protein markers, further clustering analysis shows that metabolites and lipids classify the cell types for the first time. The multimodal SIMS imaging opens broad applications for exploring various biological phenomena of cellular/biomolecular interactions in health/disease.

11:00am **RA-ThM3-15 Preliminary Development of Microscope Mode Secondary Ion Mass Spectrometry Imaging***, **Felicia Green**,* Rosalind Franklin Institute, UK*; M. Castellani, A. Eyres, Y. Jia, M. Brouard,* Oxford University, UK*; J. Bunch, Z. Takats,* Rosalind Franklin Institute, UK*; S. Thompson, P. Blenkinsopp,* Ionoptika Ltd, UK

We want to achieve parallel detection of hundreds of thousands of chemical species, to enable rapid localisation of molecular interactions in tissues. Microscope-mode imaging mass spectrometry has the potential to provide rapid imaging of the many chemical constituents present at a surface in a variety of applications; it decouples acquisition time from spatial resolution and is a promising route to attaining MS images in seconds rather than days. This project aims to construct a unique stigmatic imaging secondary ion mass spectrometry (SIMS) instrument, which allows the rapid molecular mapping of biological tissues at unprecedented speed, with good mass range and mass resolution.

Here we describe the development and initial results from a secondary ion mass spectrometer coupled with microscope mode detection. Stigmatic ion microscope imaging enables us to decouple the primary ion beam focus from spatial resolution and is a promising route to attaining higher throughput for mass spectrometry imaging (MSI). Using a commercial C_{60}^+ primary ion beam source, we are able to defocus the probe beam to give uniform intensity across a 1 mm area. This allows simultaneous desorption of ions across a large field of view and with the potential to get an MSI of a 1mm area in a matter of seconds. Moreover, we can distinguish features with better than 20 µm spatial resolution. Then coupling the probe to a position sensitive detector, we are able to show the detection of a range of positive and negative secondary ions from both metals and dyes. Each of the spectra took less than a minute to acquire and although the present mass resolution is sufficient, we can see the scope for significant improvements with planned upgrades in the instrumentation. Simulations show that we have the potential of achieving >10,000 mass resolution over a 400 m/z range, and up to 2 µm spatial resolution simultaneously. As we move to complex biological samples this will become increasingly important, but will not incur any loss in speed. These initial experiments suggest a very promising set up to achieve rapid secondary ion mass spectrometry imaging with data comparable to microprobe mode SIMS.

11:20am **RA-ThM3-17 Implementation of an OTOF-SIMS on a FIB/SEM UHV Workstation for Correlative Imaging at High Spatial Resolution and High Mass Resolution***, **Jean Almoric Almoric,*** Orsay Physics, France*; T. Genieys,* CIMAP, France*; A. Houel,* Orsay Physics, France

Due to technology advances in most of the science field (microelectronics, metallurgy, life science), the need of highly resolved analysis technics is rising. In this context, the instruments used to analyze materials at nanoscale are driven by a constant optimization of their spatial resolution. The latest generation of Focused Ion Beam (FIB) using Ga^+ ion source and developed by Orsay Physics can go down to an imaging resolution of 2.5 nm [1]. Integrated into a workstation and coupled with an electron microscope (SEM), this equipment allows nano-patterning [2], implantation [3], preparation of TEM coverslips, cross sectioning and 3D tomography. In addition to conventional detectors (SE, BSE…), advanced analytical tools can be added to the workstation such as an orthogonal time-of-flight secondary ion mass spectroscopy (OTOF-SIMS).

In this work, we studied the possibilities offered by a correlative approach, combining several analysis and imaging tools (O-TOF SIMS, SEM, FIB and GIS) in a single versatile and customizable UHV platform called "NanoSpace". Chemical mapping combining a high spatial resolution (<30nm) and a high mass resolution (FWHM 4500 on ^{28}Si) was reached by pulsing the secondary ion beam instead of the primary one. The injection of reactive precursors near the surface using a gas injection system was done to increase the secondary ionization and allowed to achieve high useful yields despite the use of a primary Ga^+ ion source. This great improvement of the transmission and mass resolution was able thanks to the redesign and the optimization of the secondary ions extraction column from an O-TOF spectrometer. Correlative analysis and innovative approach had been applied to the study of different materials, in particular a nickel-based superalloys. These materials contain precipitates of a few tens of nanometers which have been chemically characterized by a semi-quantification protocol, which is not possible by SEM-EDX [4].

[1] S. Guillous et al; A new setup for localized implantation and live-characterization of keV energy multiply charged ions at the nanoscale; Review of Scientific Instruments 87, 113901 (**2016**)

[2] A. Benkouider et al; Ultimate nanopatterning of Si substrate using filtered LMAIS-focused ion beam; Thin Solid Films (**2013**)

[3] M. Lesik et al; Magnetic measurements on micrometer-sized samples under high pressure using designed NV centers; Science 366, 1359-1362 (**2019**)

[4] J. Almoric et al; Implementation of Nanoscale Secondary-Ion Mass Spectrometry Analyses: Application to Ni-Based Superalloys, Physica Status Solidi (a), 2100414 (**2022**)

11:40am **RA-ThM3-19 Polyamide Chemical Bonding with Titanium and Aluminum Probed with ToF-SIMS and XPS***, P. Hirchenhahn, **Laurent Houssiau,*** University of Namur, Belgium

Structures joining metals and polymers are increasingly demanded as they combine the high mechanical resistance of the metal with the functionality and low weight of the polymer. Laser welding turns out to be a fast and efficient method to bind directly metals to polymers with no need for adhesives or mechanical fastening, but the root cause for adhesion is still poorly understood. In this contribution, we show how titanium alloys and polyamide-6.6 (PA or Nylon™) can be easily joined by shining a laser on the metal side. The very nature of the chemical bond was then probed with ToF-SIMS and XPS [1]. The first batch of samples was made of raw materials directly welded to each other, then disassembled. The fracture was both cohesive and adhesive, so that surface analysis could be directly performed on the adhesive fracture sites. Signals from the polymer and the metals were recorded simultaneously on the Ti side, proving that a very thin layer of PA was still present after fracture. Hybrid ions containing Ti and PA elements (C,H,N,O) were observed and only two of them exhibited a sharp increase in the welded area, i.e. $CHNOTi^+$ and $CHNOTi^-$, clearly pointing at the formation of C-O-Ti bonds at the interface. The second batch of samples were made by spincoating thin PA layers on Ti plates, followed by laser welding and subsequent dissolution of the polymer with trifluoroethanol. Interestingly, a very thin polymeric film remained on the Ti substrate after dissolution on the welded area but also on the non-welded area, allowing an assessment of the heat effect on binding. A PCA analysis was ran to identify which ions intensities were most changing in the weld. Ions from the substrate decreased while ions from the polymer increased in the weld, hinting at a thicker polymer residual layer. Moreover, most hybrid ions decreased in the weld, with the exception of ions containing C,H,N,O and Ti (e.g. $CHNOTi^-$ or $CHNO_2Ti^-$), confirming the formation of C-O-Ti bonds assisted by laser heat. A mechanism is proposed, with amide groups reacting with Ti hydroxide groups to create covalent C-O-Ti bonds along with imine formation in the polymer chain. This is also supported by a weak contribution of imine groups in XPS high resolution N1s spectrum. The results will be briefly compared with a previous work [2] carried out on Al laser welded to PA, which led to a similar conclusion: the formation of C-O-Al bonds upon heating with the laser beam.

[1] P. Hirchenhahn, A. Al Sayyad, J. Bardon, P. Plapper, L. Houssiau; *Talanta***2022**, 123539

[2] P. Hirchenhahn, A. Al Sayyad, J. Bardon, P. Plapper, L. Houssiau; *ACS Omega***2021**, 6, 33482-33497

SIMS Solutions in Materials and Life Sciences
Room Great Lakes C - Session SS-ThM2

Environmental

Moderators: Felicia Green, Rosalind Franklin Institute, **Zihua Zhu**, Pacific Northwest National Laboratory

8:40am **SS-ThM2-1 Liquid ToF-SIMS Revealing the Oil, Water, and Surfactant Interfacial Evolution***, **Xiao-Ying Yu,*** Oak Ridge National Laboratory*; Y. Shen,* Ocean University of China*; J. Son, Z. Zhu,* Pacific Northwest National Laboratory

Bilgewater formed from the shipboard is regarded as a major pollutant in the marine environment. Bilgewater exists in a stable oil-in-water (O/W) emulsion form. However, little is known about the O/W liquid-liquid (l-l) interface. Traditional bulk characterization approach is not capable of capturing the chemical changes at the O/W l-l interface. Although surfactants are deemed essential in droplet formation, their roles in bilgewater stabilization are not fully revealed. We have employed novel in situ chemical imaging tools including in situ scanning electron microscopy (SEM) and in situ time-of-flight secondary ion mass spectrometry (ToF-SIMS) to study the evolving O/W interface using a NAVY bilge model for the first time. The droplet size distribution (DSD) does not change significantly without the addition of X-100 surfactants at static or rocking conditions. Both the oil components and the water clusters are shown to evolve over time at the O/W droplet interface by in situ liquid SIMS imaging. Of particular interest to droplet stabilization, the contribution of surfactants to the aged bilge droplets becomes more significant as the droplet size increases. The higher mass surfactant component does not appear on the droplet surface immediately while many lower mass surfactants are solvated inside the droplet. We have provided the first three-dimensional images of the evolving O/W interface and demonstrated that in situ surface chemical mapping is powerful to reveal the complex and dynamic l-l interface in the liquid state. Our observational insights suggest surfactants are important in mediating droplet growth and facilitating effective separation of bilgewater emulsion.

9:00am **SS-ThM2-3 Investigation of Bacteria/Model Hybrid Core-Shell Nanoparticles Interactions by an Innovative Combination of Surface Analysis and Mass Spectrometry Techni***, S. Fernández-Castillo Suárez , **Cecile Courreges**, J. Jiménez Lamana, S. Godin, S. Nolivos, R. Grimaud, J. Szpunar, J. Allouche,* Université de Pau et des Pays de l'Adour, E2S UPPA, CNRS, IPREM, France

The increasing use of nanomaterials in our lifestyles induce significant problems of pollution in the environment, particularly with respect to microbes and bacteria, which are ubiquitous in ecosystems. However, the mechanisms of interaction between bacteria and nanoparticles are still poorly studied. In particular, the physico-chemical parameters governing the complex processes of degradation of nanoparticulate organic matter and/or the mechanisms of recognition of substrate nanoparticles by bacteria are still unknown[2]. In this project, the study of these parameters is carried out through a multidisciplinary strategy involving a combination of several domains including nanoscience, analytical chemistry and microbiology. In this context, model core-shell hybrid nanoparticles based on hierarchical structure involving gold@silica@gelatin morphologies were designed. Gelatin was used as organic substrate for *Alteromonas macleodii*, the marine bacteria species selected for this study. The characterization of nanomaterials and the monitoring of enzymatic degradation processes and bacteria/nanoparticle interactions (Fig. 1), were achieved through an innovative combination of surface analysis and mass spectrometry techniques,[3,4] including Time-of-flight secondary ion mass spectrometry (ToF-SIMS Tandem MS), X-ray photoelectron spectroscopy (XPS), Auger microscopy (AES), liquid chromatography electrospray ionization mass spectrometry (LC-ESI-MS) and Single particle inductively coupled plasma mass spectrometry (SP-ICP-MS). On one hand, SP-ICP-MS and AES analyses allow the quantification of nanoparticle binding mechanisms on cells by following the gold core particles used as markers. On the other hand, ToF-SIMS Tandem MS, XPS and LC-ESI-MS techniques enable to identify peptide fragments originating from the degradation of gelatin on the surface of model nanoparticles. The results obtained and the strategy implemented thus open the way to the determination of key parameters governing the interactions between nanoparticles and bacteria, which are of primary importance in environmental degradation processes but also in the fight against pathogens.

References: [1] F. Ameen, K. Alsamhary, J.A. Alabdullatif, S. AlNadhari, Ecotoxicol. Environ. Saf. 213 (2021), 112027. [2] M. Mansor, J. Xu, Environ. Microbiol. 22(9), (2020), 3633–3649. [3] C. Courreges, M. Bonnecaze, D. Flahaut, S. Nolivos, R. Grimaud, J. Allouche, Chem. Commun. 57 (2021), 5446-5449. [4] L. Yin, Z. Zhang, Y. Liu, Y. Gao, J. Gu, Analyst 144, (2019), 824–845.

9:20am **SS-ThM2-5 Surface and Functional Characterization of Nanostructured Thin Films for Environmental Remediation***, **Enrica Maria Malannata**, A. Auditore, A. Licciardello,* Università di Catania, Italy

Nowadays the presence of pollutants in water represents an ever greater and difficult problem to solve. Efficient removal of contaminants from aqueous solutions requires advanced oxidation processes (AOPs). This can be accomplished by different methods, such as electrocatalysis, photocatalysis and photo-electrocatalysis, involving the use of materials that allow the fast removal of the pollutant with high degradation efficiency. The photo-electrocatalytic approach appears to be among the most promising processes because it combines the advantages of photocatalysis and electrocatalysis [1].

The most used material in this regard is TiO_2 which, however, shows several problems including a band gap around to 3.0-3.2 eV that does not allow the absorption of visible light.

With appropriate surface modifications such as the presence of phosphate anions, it is possible to improve the generated photocurrent [2] to obtain a best performing material in photo–electrocatalysis applications.

In this work the surface of nanostructured TiO_2-based films were chemically modified to improve its electro-, photo-electro and photocatalytic performance. In particular, mesoporous TiO_2 films were engineered using the zirconium phosphate (ZP) modification [3] in order to improve the sensitivity to sunlight, the electrical properties, and the thermal stability of the material.

We used extensively TOF-SIMS for obtaining space-resolved information on the functionalization of the mesoporous oxide, necessary for the engineering and monitoring of the material modification protocol. Moreover, TOF-SIMS allowed to monitor the photocatalytic reactions at the mesoporous oxide surface providing information on the degradation pathway under solar light irradiation. In particular the present study considered, as target molecules, both model dyes such as Rhodamine B and real-world persistent pollutants such as pesticides. Understanding the degradation pathways occurring at the photocatalyst surface, indeed, is an important step for the design of specific functionalization processes aimed to the improvement of the performances of the material.

[1] T.H. Jeon et al. ACS Catal. 8 (2018) 11542–11563.

[2] L. Jing et al. Energy Environ. Sci. 5 (2012) 6552–6558.

[3] S. Vitale et al. J. Vac. Sci. Technol. B. 34 (2016) 03H110.

SIMS Solutions in Materials and Life Sciences
Room Great Lakes C - Session SS-ThM4

Polymers

Moderators: Satoshi Ninomiya, University of Yamanashi, **Michaeleen Pacholski**, Dow Chemical Company

10:20am **SS-ThM4-11 Advances in Polymer Science by ToF-SIMS Depth Profiling***, **Tanguy Terlier**, D. Lee,* Rice University*; C. Bottoms,* University of Tennessee Knoxville*; A. Masud, A. Karim,* University of Houston*; G. Stein,* University of Tennessee Knoxville*; R. Verduzco,* Rice University **INVITED**

Over the last two decades, we have seen remarkable advances in the development and understanding of organic materials using ToF-SIMS. The introduction of polyatomic ion beam technology such as the argon gas cluster ion beam has made it possible to access quasi-intact molecular information and offered a high sputter efficiency for etching the organic films. This evolution has benefited polymer science by providing a tool to examine spatial variations in the chemistry of multicomponent polymer films. Thus, various studies have shown that it is now possible to monitor a variety of processes such as diffusion in photoresists and surface segregation in polymer blends. A key challenge is using ToF-SIMS data to extract quantitative parameters, such as diffusion constants or surface excesses, and this has motivated us to study how to quantify the depth-dependent composition of the ToF-SIMS depth profiles.

While the sputter mechanisms have been carefully studied, the quantification of the ion distribution in depth profiles remains challenging due to the ionization process and the complexity of the fragmentation mechanism.

This work will focus on different approaches to converting the profiles into quantitative information. To illustrate the challenges and the potential outcomes of the quantitative depth profiles, we have limited our investigation to the migration process with two-compound systems.

We will begin by presenting an overview of the analytical challenges in ToF-SIMS depth profiling of polymer films. We will then detail our approach for quantifying the depth-dependent composition in a polymer film, which consists of three steps: identification of characteristic molecular ions from pure material films; use of miscible blends with known composition to examine the linearity of the molecular ion ratio and measure the sputter yield for each mixture; and conversion of the ion intensity distribution into the composition as a function of depth.

With this procedure, we can elucidate the segregation behavior of bottlebrush polymer blended with linear polymer by determining the relationship between surface excesses at interfaces and properties of polymer films. We have also used this method to measure molecular diffusivities through analysis of bilayer samples and compared these observations with molecular simulations. Finally, we determined how to quantify the dopant concentration throughout a polymer film, which has permitted us to characterize the in-depth distribution of an ionic liquid in self-assembled block copolymer films.

Thus, we will demonstrate the possibilities of quantifying different types of the migration process in polymer films by ToF-SIMS.

11:00am **SS-ThM4-15 Keynote Industrial Talk: Characterizing Bonding of Perfluoropolyether Lubricants to Magnetic Recording Disks by Tof-Sims***, **Alan Spool**,* Western Digital Corporation **INVITED**

The bonding of perfluoropolyether lubricants to magnetic recording disks is one of the keys to longevity of the head disk interfaces in these devices.Bonding is defined in the industry by the degree to which the lubricant after application can be removed from the surface with a solvent rinse.The exact nature of the bonds between the lubricant and the disk is not fully understood.It may be either a result of hydrogen bonding between the alcohol end-groups on the polymer lubricants and surface moieties, or covalent bonding may occur.

In this study, the increasing difficulty in removing lubricant from the disk surface by solvent extraction is shown to directly correlate with changes in the TOF-SIMS spectra through the study of Z-Tetraol, a perfluoropolyether lubricant used in the industry for many years which has four alcohol groups, two at each end of the chain. The hypothesis that a stronger attachment to the surface would reduce the intensities of fragments whose formation would require desorption of intact or nearly intact polymer chain end-groups from the surface was confirmed by experiments in which disks with lubricant bonded to different degrees were analyzed.In addition to the identification of peaks in the complex negative ion spectra, their assignments to likely structures, and the comparisons of their intensities, disappearance cross section measurements were performed.The significance of the results with respect to ion formation mechanisms are considered.

11:40am **SS-ThM4-19 Depth Profiling in Thick Polymer Films with Ar and O_2 Gas Cluster Ion Beam Sources***, **Christine Mahoney**, K. Adib, R. Yongsunthon,* Corning Research and Development Corporation*; B. Burger,* Corning Varioptic, France

Gas cluster ion beam sources (GCIB) are a very important tools at Corning and have many uses ranging from sputter cleaning of glass surfaces to depth profiling of organic coatings.Recently, we have been utilizing both Ar GCIB and O_2 GCIB sources to probe the chemistries of both glass and polymer substrates.Here we describe our most recent work in depth-profiling of thick (>500 nm) polymeric films under different ion beam conditions. Two important polymer systems were interrogated: 1) parylene C films (~4 µm), and 2) plasma polymerized hexa(methyldisiloxane) (HMDSO), a silicone-based film with an irregular structure (~500 nm). Both films represent classes of materials that can be used for making hydrophobic conformal coatings. The literature regarding the surfaces and in-depth analysis of these materials is sparse. The overall effect of ion beam impact energy (5 keV, 10 keV and 20 keV), as well as the chemistry of the ion beam (O_2 vs Ar GCIB) on the resulting depth profiles were investigated. Furthermore, the chemistry and morphology of the sputtered crater bottoms were characterized in detail with a combination of X-Ray Photoelectron Spectroscopy (XPS) and Atomic Force Microscopy (AFM). The results highlight the importance of beam chemistry in polymeric depth profiling with GCIB.

12:00pm **SS-ThM4-21 Gas Cluster Ion Scattering: A Local Probe of the Ferroelectric to Paraelectric Transition in P(VDF-ran-TrFE) Copolymers***, M. Chundak, C. Poleunis, A. Jonas,* ***Arnaud Delcorte****,* Université Catholique de Louvain, Belgium

Secondary ion mass spectrometry (SIMS) is widely recognized for its detailed information on the chemical and molecular composition of surfaces and coatings, with submicron lateral resolution and nanoscale depth resolution. The technique reached a new pinnacle with the use of large gas cluster ion beams (GCIB), such as $Ar_{500-5000}^+$, which induce softer desorption from organic and biological samples, with important applications in bio-imaging, damageless depth-profiling and even protein soft-landing [1]. Ar-GCIB can also provide local information about the physical properties of polymer surfaces, in a variant of the technique coined gas cluster ion scattering spectrometry or GCISS. Indeed, the distribution of backscattered Ar_n^+ ($n \leq 7$) clusters observed in the positive SIMS spectra proved to depend on the surface structural and mechanical properties. For instance, GCISS was used to locally determine the glass transition temperature of (ultra)thin films of thermoplastics, thermosets and even plasma-deposited coatings [2], where classical techniques are inadequate.

For this contribution, GCISS was applied to polyvinylidene fluoride-trifluoroethylene P(VDF-*ran*-TrFE) ferroelectric copolymers with a range of compositions (Fig. 1). The Ar_n^+ ion intensities were measured upon 10 keV Ar_{3000}^+ bombardment of the films and the intensity ratios $Ar_2^+/(Ar_2^++Ar_3^+)$ and $Ar_2^+/(Ar_2^++Ar_4^+)$, representing the dissociation rate of the Ar cluster projectiles, are shown to depend on the structural changes of the polymer surfaces. These intensity ratios provide direct access to the surface transition temperature T_T (related to the bulk glass transition T_g of the material), but are also sensitive to more subtle changes such as the ferroelectric to paraelectric transition of P(VDF-*ran*-TrFE) occurring at the Curie temperature (T_c) [3]. Comparison with our DSC measurements and with mechanical measurements from the literature show that the surface Curie transition remains close to the bulk value in these copolymers. This study confirms that GCISS constitutes a versatile approach for the local measurement of physical transitions occurring in polymer thin films.

[1] A. Delcorte et al., *Large cluster ions: Soft local probes and tools for organic and bio surfaces*, Phys. Chem. Chem. Phys., 2020, 22, 17427-17447.

[2] N. Vinx et al., *Investigating the relationship between the mechanical properties of plasma polymer-like thin films and their glass transition temperature*, Soft Matter, 2021,17, 10032-10041.

[3] M. Chundak et al., *Probing the Surface Curie Temperature of Ferroelectric P(VDF-ran-TrFE) Copolymers by Argon Gas Cluster Ion Scattering*, J. Phys. Chem. C 2022, 126, 1125−1131.

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.

This work was performed under the auspices of the U.S. Department of Energy by Lawrence Livermore National Laboratory under Contract DE-AC52- 07NA27344 and was supported by the LLNL-LDRD Program under Project No. 20-SI-006.

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.

This research was conducted at the Center for Nanophase Materials Sciences, which is a DOE Office of Science User Facility and using instrumentation within ORNL's Materials Characterization Core provided by UT-Battelle, LLC under Contract No. DE-AC05-00OR22725 with the U.S. Department of Energy.

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.

References

-Monteiro M. C. O., Schmuki P., Killian M.S. Metal–Phosphate Bilayers for Anatase Surface Modification. *Appl. Mater. Interfaces*. 2018, 10, 7, 6661–6672. doi.org/10.1021/acsami.7b16069

-Tombácz E. pH-dependent surface charging of metal oxides. *Per. Pol. Chem. Eng*. 2009, 53, 2, 77–86. doi: 10.3311/pp.ch.2009-2.08

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.

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.

References

1 Bouvier *et al*. (2022) doi: 10.1002/jms.4803

2 Vanbellingen *et al*. (2015) doi: 10.102/rcm.7210

3 Bouvier *et al*. (2021) doi: 10.1021.acs.analchem.0c04471

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

The work has been supported by Polish National Science Center Grants 2019/33/B/ST4/01778. Computer simulations were performed on the PLGrid Supercomputer infrastructure and at Penn State's ICDS supercomputer system.

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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