## 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].

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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.

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## 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.

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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.

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## 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 $\mu$m x 250 $\mu$m) 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

## 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].

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

11:00am **RA+BS+FM+SS-TuM2-7 Ibeam: Large Argon Cluster Ion Beams as a Versatile Vacuum-Based Tool for the Fabrication of Protein Thin Films**, ***Vincent Delmez,*** *B. Tomasetti, C. Poleunis,* Université Catholique de Louvain, Belgium; *C. Lauzin, C. Dupont-Gillain,* université Catholique de Louvain, Belgium; *A. Delcorte,* Université Catholique de Louvain, Belgium

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

11:20am **RA+BS+FM+SS-TuM2-9 Optimisation of MeV TOF SIMS Technique for Hybrid Targets Imaging and Inorganic Material Depth Profiling**, *M. Barac,* Ruder Boskovic Institute, Jozef Stefan International Postgraduate School (Slovenia), Croatia; *M. Brajkovic,* ***Zdravko Siketic,*** Ruder Boskovic Institute, Croatia; *J. Kovac,* Jozef Stefan Institute, Slovenia; *I. Bogdanovic Radovic,* Ruder Boskovic Institute, Croatia; *I. Srut Rakic,* Institute of Physics, Croatia; *J. Ekar,* Jozef Stefan Institute, Slovenia

MeV TOF SIMS is a variation of the standard technique TOF SIMS, in which primary ions with energies of ~MeV/amu accelerated by a particle accelerator are used for ion/molecule desorption. Since the electronic stopping in this energy range is much more pronounced than the nuclear stopping, the energy transfer to the target constituents is much "softer" (e.g. vibrational molecular modes are excited). In this way, a higher yield of molecular secondary ions and less fragmentation are achieved compared to monoatomic keV SIMS. MeV SIMS is mainly used for chemical imaging of organic molecules with masses up to 1000 Da, with applications in biomedical research, forensics, cultural heritage, etc.

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

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

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

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

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

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

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

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

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

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## 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.

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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.

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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.

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## 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.

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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.

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## 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™ 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.

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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.

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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.

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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].

Authors thank The National Centre for Research and Development, Poland for funding the project PL-TW/VII/4/2020 in years 2020-2022.

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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.

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## 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.

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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.

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## 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.

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**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.

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5. *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.

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**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

## 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.

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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 bone 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: $D_{bovine,FD}=(2.09\pm2.39)\cdot10^{-9}$ $cm^2s^{-1}$); slow diffusion: $D_{bovine,SD}=(1.52\pm1.80)\cdot10^{-10}$ $cm^2s^{-1}$; total area: $D_{bovine,TA}= (1.94\pm2.40)\cdot10^{-9}$ $cm^2s^{-1}$]. 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 [$D_{rat,FD}=(7.64\pm1.70)\cdot10^{-10}$ $cm^2s^{-1}$); $D_{rat,SD}=(5.47\pm1.17)\cdot10^{-10}$ $cm^2s^{-1}$); $D_{rat,TA}= (7.50\pm1.62)\cdot10^{-10}$ $cm^2s^{-1}$]. 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.

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[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.

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[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)

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## 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.

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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.

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## 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 $Ar_{500\text{-}5000}^+$, 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.

## 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

## 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

# Author Index

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