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

SIMS Solutions in Materials and Life Sciences Poster Session

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

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

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

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

References:

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

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

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

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

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

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

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

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

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

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

Nanoprojectile Secondary Ion Mass Spectrometry, NP-SIMS, is a promising technique for molecular analysis at the nanoscale. In this methodology, termed the event-by-event bombardment detection mode, individual nanoprojectiles impact the surface one-by-one and the resulting secondary ions are mass analyzed by time-of-flight mass spectrometry prior to the arrival of the subsequent projectile. Analysis of co-emitted ions from each impact allows for the inspection of co-localized moieties within the ejected volume (10-15 nm). Surfaces were probed stochastically with a suite of individual gold nanoparticles (520 keV Au_{400}^{4+}) separated in time and space. In this study, we examined a mixture of three nanoparticles with identical metal cores, differing only by their functionalization. The particles were deposited as a sub-single layer onto a cleaned silicon surface. Using the NP-SIMS, we evaluated the extent of mixing between particles and quantified the abundance of each particle on the surface. We found that the relative concentration of each particle was approximately 33%, which is in good

agreement with the sample preparation. Our results show that despite the relatively large sampling volume of each projectile, measurements on the 3-5 nm particles can differentiated from one another based on the impact parameter between the projectile and the surface nanoparticle. Since the impact parameter affects the number and type of emitted secondary ions, examining the secondary ions from each impact allows for impacts which occur on the particle core to be distinguished from those on the particle-particle and particle-substrate interfaces. We found that direct impacts were characterized by the emission/detection of multiple Au_n^- ions while ultra-peripheral impacts were identified by the detection of multiple of $Si_xO_y^-$ ions. Peripheral impacts, which sample the particle-substrate interface, are characterized by the co-emission of Au_n^- ions and $Si_xO_y^-$ ions. Due to the differences in the length of the ligands, peripheral measurements occurring closer to the core were more likely to contain decanethiol, while peripheral impacts occurring farther from the particle core were more likely to contain hexadecanethiol. Differentiating and isolating these measurements, allows for mass spectrometry evaluation of interfaces among nano-objects and between nano-objects and their support. This work was supported by the National Science Foundation grant CHE-1308312.

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

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

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

1. *et al.*, The 3D OrbiSIMS—label-free metabolic imaging with subcellular lateral resolution and high mass-resolving power. *Nature Methods***14**, 1175-1183 (2017).
2. *et al.*, Cryo-OrbiSIMS for 3D Molecular Imaging of a Bacterial Biofilm in Its Native State. *Analytical Chemistry***92**, 9008-9015 (2020).
3. *Angewandte Chemie International Edition* **59**, 18194-18200 (2020).
4. *Rapid Commun Mass Spectrom* **20**, 1327-1334 (2006).
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.

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

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

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

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

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

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

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

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

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