Applied Surface Science Division
Room: 13 - Session AS+BI-MoA

Practical Surface Analysis: Complex, Organic and Bio-systems

Moderators: Scott Lea, Pacific Northwest National Laboratory, Paulina Rakowska, National Physical Laboratory, UK

2:00pm **AS+BI-MoA2 Environmental Charge Compensation - Near Ambient Pressure XPS as a Tool for Surface Chemical Analysis of Iinsulators without Charging Effects**, ***Paul Dietrich***, *A. Thissen*, SPECS Surface Nano Analysis GmbH, Germany, *S. Bahr*, Enviro Analytical Instruments GmbH, Germany

Since many decades XPS (or ESCA) is the well-accepted standard method for

non-destructive chemical analysis of solid surfaces. To fulfill this task existing ESCA tools

combine reliable quantitative chemical analysis with comfortable sample handling concepts,

integrated into fully automated compact designs.

Generically insulators will positively charge in XPS due to the irradiation with X-rays and

the emission of photoelectrons. Without compensation this effect leads to strong continuous

shifts and asymmetric line shapes of the emission lines in the spectra. To perform an exact

characterization and quantification of strongly insulating materials different concepts of

charge compensation or neutralization have been developed over the last decades. A short

overview is given starting from low energy electrons offered from so-called "flood guns" or

other sources, via compensation by a combination of electrons and ions to rare methods like

illumination with visible light during the analysis and compensation by the produced

electron-hole pairs. The opportunities and challenges of the different methods are compared.

The development of XPS method towards environmental or (near) ambient pressure

working conditions has revolutionized this method regarding applications. In-situ and

in-operando measurements in pressure of up to and above 25mbar are easily possible, even

with laboratory based systems and using EnviroESCA even in a standard analytical tool.

During the last months, measurements on insulators have shown, that they can be measured

with exception in surrounding pressures of a couple of mbar without any charging. This new

technique of charge neutralization is neamed Environmental Charge Compensation (ECC).

This presentation summarizes results of measurements on insulating polymer samples,

showing the resulting spectroscopic resolution for C1s and O1s emission lines. A

comparison for PET and PTFE to other neutralization techniques is given. In addition

measurements on bulk insulators from polymeric materials, ceramics, food samples,

aqueous solutions, stones, soil and even zeolites are shown, that cannot easily be obtained in

UHV based XPS systems.

Furthermore the effect is described in detail, including the influence of pressure and gas composition on the charge neutralization. An outlook is presented towards completely new

resulting fields of application of XPS, when combined with ECC.

2:20pm **AS+BI-MoA3 Does Time Play a Role in Glyoxal and Hydrogen Peroxide Photochemical Aging?**, ***Fei Zhang***, *X.F. Yu, X. Sui*, Pacific Northwest National Laboratory, *J.M. Chen*, Fudan University, *Z.H. Zhu, X.Y. Yu*, Pacific Northwest National Laboratory

Aqueous surfaces consisting of glyoxal and hydrogen peroxide (H_2O_2) after photochemical aging have been studied in a microfluidic reactor (System for Analysis at the Liquid Vacuum Interface, SALVI) by in situ liquid Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS). Positive and negative ion mode mass spectra provide complementary information of the surface reactions. Compared with previous results using bulk solutions, our unique liquid surface molecular imaging approach makes it possible to observe glyoxal hydration (i.e., first and secondary products, hydrates), oxidation products (i.e., glyoxylic acid, oxalic acid, formic acid, malonic acid, tartaric acid), oligomers (i.e., $C_7H_{11}O_9^+$, $C_6H_5O_{10}^-$), water clusters (i.e., $(H_2O)_nH^+$, n< 43, $(H_2O)_nOH^-$, n< 44), and cluster ions (i.e.,$C_6H_{17}O_{12}^+$, $C_7H_9O_{11}^-$) with submicrometer spatial resolution. Spectral principal component analysis (PCA) is used to determine similarities and differences among photochemical aging samples ranging from 15 minutes to 8 hours. The oxidation products such as glyoxylic acid, glycolic acid, and tartaric acid tend to peak at around between 30 min and 1 h. UV aging; while oligomers and large water clusters (i.e., $(H_2O)_{22}OH^-$, $(H_2O)_{23}OH^-$,$(H_2O)_{24}OH^-$) form significantly at about 3 h. The oligomer formation reaches its maximum at 4 h., and reduces afterwards. Large water clusters (n> 15) become more significant as photochemical aging progresses, indicating more hydrophobicity at the aqueous surface as predicted by molecular dynamic simulation in earlier works. SIMS three-dimensional (3D) chemical mapping enables visualization of the surface mixing state at the molecular level. We have presented the temporal progression of the 3D surface mixing state of various products from glyoxal and hydrogen peroxide oxidation for the first time. Such physical measurements pave a new way to investigate complex surface reaction mechanisms as an important source of aqueous secondary organic aerosol (SOA) formation in atmospheric chemistry.

2:40pm **AS+BI-MoA4 Study of Drug Uptake and Action on Metabolic Processes at the Single-Cell Level using the 3D OrbiSIMS**, ***Ian S. Gilmore***, *M.K. Passarelli, M. Lorenz*, National Physical Laboratory, UK, *C.F. Newman, P.S. Marshall, A. West*, GlaxoSmithKline, UK, *P.D. Rakowska, R. Havelund, C.T. Dollery*, National Physical Laboratory, UK

A major quest for the pharmaceutical industry is the reduction of late-stage drug failure. Measurements that can identify future failure at the early stages of drug development are therefore of great importance. This requires label-free imaging of the distribution of pharmaceutical compounds and metabolites with subcellular resolution. We have previously shown [1] that ToF-SIMS can provide useful sub-cellular resolution images but analysis is limited by insufficient mass accuracy, mass resolving power for accurate identification of metabolites and sensitivity.

We have recently led the development of a powerful new hybrid instrument, the 3D OrbiSIMS [2], combining an Orbitrap™-based Thermo Scientific™ Q Exactive™ HF instrument and a dedicated ToF-SIMS 5. The instrument is equipped with high-resolution ion beams including a new micrometre resolution argon cluster ion beam for biomolecular imaging and 3D analysis of organics and an ultra-high resolution Bi cluster focussed ion beam with < 200 nm resolution.

In this study, we demonstrate the unparalleled ability for 2D and 3D metabolite imaging with sub-cellular resolution. We show significant variability of drug uptake at the single cell level and demonstrate direct evidence of up regulation of metabolites. This can only be revealed with a single-cell study. Furthermore, we demonstrate a new method for in situ matrix deposition for 3D imaging that significantly increases sensitivity. This is especially important for current drug candidates with Log P values ≤ 3 (Lipinski rule of five), which are known to have low molecular secondary ion yields. [3]

[1] M.K. Passarelli et al, Analytical chemistry 87 (13), 2015, 6696

[2] M.K. Passarelli et al, submitted, 2017

[3] J.L. Vorng et al, Analytical Chemistry 88 (22), 2016, 11028

3:00pm **AS+BI-MoA5 TOF-SIMS Cluster Beam Depth Profiling and 3D Imaging of Oral Drug Delivery Films**, ***Greg Gillen***, *S. Muramoto, J. Staymates, E. Robinson*, NIST

Dissolvable oral thin film (OTF) drug delivery systems are gaining increased interest as convenient alternatives to more conventional tablets and capsules

for drug delivery applications. The OTF's are typically made by mixing an active pharmaceutical ingredient (API) into a dissolvable polymer that is administered to the patient by placing under the tongue or against the inside of the cheek. Direct adsorption of the API into the systemic circulation bypasses gastrointestinal delivery and can provide higher levels of bioavailability and a more rapid release profile in appropriate medications. One critical challenge with further development of OTF drug delivery systems is the lack of appropriate measurement tools for the characterization of API concentration, phase and dose uniformity throughout the depth of the polymer film (typically ~100 um in thickness). Furthermore, OTF's are currently manufactured as bulk sheets with fixed levels of API. This is a significant roadblock to realization of OTF's for personalized medicine where there is a growing interest in manufacturing of OTF's with individualized and patient-specific API dosages. One promising method of production of such films that is currently being explored in our laboratory is the used of drop on demand inkjet printing to precisely deposit individualized API doses onto prefabricated films.

In this work, we explore the utility of Time of Flight Secondary Ion Mass Spectrometry (TOF-SIMS) using gaseous cluster ion beam (GCIB) depth profiling for the characterization of the lateral and in-depth distribution of API's in model OTF films. Three types of films were examined; (1) model thin films of pullulan, (2) model thin films of pullulan that had been dosed using drop on demand inkjet printing with various concentrations of relevant API's and (3), commercially available OTF films (single and multilayer films) containing the anti-opioid medications buprenorphine and naloxone which are widely used medications for treatment of opioid dependency. Cluster SIMS depth profiling was able to resolve compositional differences throughout the depth of each of these films (>70 um in thickness) and localize the individual API's. Furthermore, the ability to characterize the lateral and in depth distribution of API's in individual inkjet droplets will be demonstrated as well as the use of inkjet printing to prepare in situ concentration standards for evaluation of dosage variability. Finally, we also demonstrate the use THz Raman imaging for chemical identification of the API and possible phase changes due to the use of inkjet-printed formulations.

3:20pm **AS+BI-MoA6 Characterisation of Bioelectronic Material Surfaces using Surface Spectroscopies**, ***Sarah Coultas***, Kratos Analytical Limited, UK, *W. Boxford*, Kratos Analytical Ltd, UK, *C.J. Blomfield*, Kratos Analytical Limited, UK, *M. Firlak, J. Hardy*, Lancaster University, UK

Electromagnetic fields affect a variety of tissues (e.g. bone, muscle, nerve and skin) and play important roles in a multitude of biological processes. This has inspired the development of electrically conducting devices for biomedical applications, including: biosensors, drug delivery devices, cardiac/neural electrodes, and tissue scaffolds. It is noteworthy that there are a number of clinically approved devices capable of electrical stimulation of the body, all of which are designed for long term implantation. The first examples were developed in Sweden and include bionic eyes, ears and electrodes for deep brain stimulation (DBS). Recently there has been considerable industrial interest in the development and commercialisation of bioelectronic medicines. Bioelectronics is an emerging area of technology that promises broad impact in healthcare.

The detailed analysis of biomaterials and biomedical devices offers valuable insight into the underlying function of the products. The materials are composites of electroactive polymers (e.g. polypyrrole) and biopolymers (e.g. polysaccharides and proteins) that can be used for various applications (e.g. drug delivery, tissue scaffolds).

Here we demonstrate the application of surface spectroscopies, including XPS and UPS, to characterise bioelectronic materials in various morphologies (e.g. films and foams). We utilise a range of approaches to fully characterise the materials, including investigating any variations in composition either laterally or with depth. We also explore the usefulness of surface cleaning using Argon clusters.

References:

J. Rivnay, et al. Review on bioelectronics: Chem. Mater. 2014, 26, 679−685

G. G. Wallace, et al. Review on bioelectronics: Nanoscale. 2012, 4, 4327–4347

J. G. Hardy, et al. Article on bioelectronic drug delivery devices: J. Mater. Chem. B, 2014, 2(39), 6809-6822.

J. G. Hardy, et al. Article on instructive bioelectronic tissue scaffolds: Macromol. Biosci., 2015, 15, 1490-1496.

4:00pm **AS+BI-MoA8 High-resolution SIMS Imaging of Subcellular Structures**, ***Mary Kraft***, *A.N. Yeager*, University of Illinois at Urbana-Champaign, *P.K. Weber*, Lawrence Livermore National Laboratory **INVITED**

In mammalian cells, lipids and cholesterol form the selectively permeable plasma membrane that separates the cell from its surroundings, and the intracellular membranes that delineate the boundaries of organelles and transport vesicles. The distributions of cholesterol and each lipid species between these organelles is correlated with health and disease. The accumulation of cholesterol and certain lipid species within lysosomes and endosomes causes defects in intracellular trafficking that can be fatal if left untreated. The ability to image the relative abundances of cholesterol and distinct lipid species within intracellular compartments could lead to a better understanding of the biological mechanisms that regulate subcellular lipid distribution. For this purpose, we have combined metabolic stable isotope incorporation with secondary ion mass spectrometry (SIMS), which is performed on a Cameca NanoSIMS 50, to image the intracellular distributions of cholesterol and sphingolipids. By using depth profiling SIMS to image the distributions of ^{18}O-cholesterol and ^{15}N-sphingolipids within a portion of a Madin-Darby Canine Kidney (MDCK) cell, we determined that these two components are enriched within separate intracellular compartments. The sizes and relative positions of the ^{15}N- and ^{18}O- enriched intracellular features that are visible in the 3-D representations of the SIMS images suggest that the ^{15}N-sphingolipids are located within transport vesicles, whereas the ^{18}O-cholesterol seem to be concentrated within lipid droplets.

4:40pm **AS+BI-MoA10 EnviroESCA – Routine Surface Chemical Analysis under Environmental Conditions For Biological Samples**, ***Andreas Thissen***, *P. Dietrich*, SPECS Surface Nano Analysis GmbH, Germany, *S. Bahr*, Enviro Analytical Instruments GmbH, Germany, *M. Kjaervik, W. Unger*, Bundesanstalt für Materialforschung und -prüfung (BAM), Germany

Since many decades XPS (or ESCA) is the well-accepted standard method for

non-destructive chemical analysis of solid surfaces. To fulfill this task existing ESCA tools

combine reliable quantitative chemical analysis with comfortable sample handling concepts,

integrated into fully automated compact designs.

Over the last years it has been possible to develop XPS systems, that can work far beyond

the standard conditions of high or ultrahigh vacuum. Near Ambient Pressure (NAP) XPS has

become a fastly growing field in research inspiring many scientist to transfer the method to

completely new fields of application. Thus, by crossing the pressure gap, new insights in

complicated materials systems have become possible using either synchrotron radiation or

laboratory X-ray monochromators as excitation sources under NAP condtions.

Based on this experience SPECS Surface Nano Analysis GmbH has developed a

revolutionary tool to realize the long existing dream in many analytical laboratories:

reproducible chemical surface analysis under any environmental condition. EnviroESCA

allows for different applications, like extremely fast solid surface analysis of degassing (but

also non-degassing) samples, ESCA analysis of liquids or liquid-solid interfaces, chemical

analysis of biological samples, materials and device analysis under working conditions.

After introduction of the technological realization a comprehensive survey of results will be

given starting from standard solid conductive samples under different pressure conditions,

bulk insulators with environmental charge compensation applied, high throughput analysis

of batches of similar objects, geological samples, chemical analysis of pharmaceuticals to

the comparative analysis of ultrapure liquid water with different aqueous solutions.

The application of Near Ambient Pressure XPS to biological specimen from plants and

animals, biofilms and bacteria, as well as food samples is a completely new field for

electron spectroscopic studies of the surface chemical composition.

An outlook is presented on the application to electrochemical and other in-operando devices.

Finally the influence of the ambient conditions on quantification in XPS will be

demonstrated and discussed.

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States and from the European Union's Horizon 2020 research and innovation programme.

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