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

High Resolution and MS/MS Methods I

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

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

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

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

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

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

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

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

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

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

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

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

References

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

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

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

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

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

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

Osteoporosis, a systemic bone disease, is characterized by increased fracture risk and delayed, incomplete fracture healing. To improve fracture healing, next generation biomaterials are functionalized with drug release systems. Here, we are interested in the local release of healing-promoting agents, such as Sr^{2+} ions. In previous work, we studied Sr^{2+} release from functionalised bone cements and its dispersion in the mineralised areas of rat bone by time-of-flight secondary ion mass spectrometry (ToF-SIMS).[1, 2] In this work, we investigate Sr^{2+} transport within the more complex, highly viscous bone marrow. As analytical tools for tracking and spatially resolving the Sr^{2+} diffusion within bone marrow we apply 2D and 3D ToF-SIMS and orbitrap secondary ion mass spectrometry (OrbiSIMS). In a first approach, a ToF-SIMS depth profiling protocol under cryogenic conditions was specifically developed for determination of diffusion coefficients in 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.

[1] M. Rohnke, et al., Strontium release from Sr2+-loaded bone cements and dispersion in healthy and osteoporotic rat bone, J. Controlled Release 262 (2017) 159

[2] C. Kern, et al., Investigation of strontium transport and strontium quantification in cortical rat bone by time-of-flight secondary ion mass spectrometry, J. R. Soc. Interface 16 (2019) 20180638

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

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

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

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

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

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