Biomaterial Interfaces Division
Room: 108 - Session BI-ThM

Biomedical Materials
Moderator: S.L. McArthur, Swinburne University of Technology, Australia

8:20am **BI-ThM2 Surface Characterization: A Critical Component in Understanding the Biocompatibility of Biomaterials**, ***L. Salvati***, *S. Vass*, DePuy Orthopaedics **INVITED**

A biomaterial is defined as "any synthetic material or device–e.g. implant or prosthesis-intended to treat, enhance or replace an aging or malfunctioning native tissue, organ or function in the body" David Williams, states that ***"Biocompatibility is largely about the chemical interactions that take place between the materials and the body fluids, and the physiological responses to these reactions."*** These reactions are dominated by the initial *events at* the molecular level, the interface, thus it is not hard to see the relationship between the implant surface properties and it's in vivo. It is clear that the performance of a biomaterial is directly linked to the surface chemistry, composition and topography of the device. However, despite the preponderance of evidence, biomedical device companies as a whole do not utilize surafce analytical methods nearly enough. Why is that?

In orthopaedics, most of the implants are fabricated from metals which directly contact biological fluids that are typically complex aqueous mixtures. Consequently corrosion and/or corrosion prevention are important considerations in device manufacturing. For the most part, orthopaedics manufacturers utilize the same passivation methodologies used to impart corrosion resistance to stainless materials. Numerous researchers have characterized the impact of acid passivation on stainless materials, but little has been done to study the effect of these treatments on the CoCr alloys. One of the topics in this presentation deals with the effects of passivation on CoCr alloys. Specifically, the presentation will correlate specific surface treatments with surface chemistry and ultimately to metal ion release. The study will also address questions relating to the use of Citric acid as a green replacement for nitric acid passivation. There is no argument that the process is much greener, but there are plenty of questions as to its effectiveness. Considering that the "changes" imparted by the passivation solutions effect the outer most 10-100A, the only means to characterize the affects of passivation requires surface analysis methodologies. The importance of surface analysis methods, especially XPS, will be highlighted by this example.

In addition to the discussion of metal alloy passivation, this presentation will also deal with other surface related issues that could impact the biocompatibility of biomaterials. The talk will show the potential impact of packaging materials and cleaning processes on the surface chemistry and composition of biomaterials.

9:00am **BI-ThM4 XPS Sputter Depth Profiling of Organic Materials Using a Coronene Ion Source**, ***S.J. Hutton***, *C.J. Blomfield, A.J. Roberts, S.C. Page, S.J. Coultas*, Kratos Analytical Ltd, UK, *C.E. Moffitt, D.J. Surman*, Kratos Analytical Inc

Controlled release of active pharmaceutical molecules from biocompatible polymers over defined time periods is an area of intense study. Present applications include drug eluting stents and other drug delivery systems. One of the most important parameters which govern drug dosing is the drug concentration depth profile in the supporting polymer matrix. In a previous study we have shown that combining X-ray photoelectron spectroscopy (XPS) with a coronene ion source is a very powerful tool for investigating the drug distribution with depth of a model system [1].

The use of cluster ion sources for sputter depth profiling of thin film or multilayer organic materials during XPS analysis has become routine. A wide range of organic systems are amenable to profiling and there is a good understanding of the experimental parameters which contribute to successful analysis. Here we report on extending the aforementioned study to materials which closely resemble real world samples intended for use in vivo.

[1] A. Rafati, M.C. Davies, A.G. Shard, S. Hutton, G. Mishra, M.R. Alexander, *J. Controlled Release*, **2009**, *138*, 40–44

9:40am **BI-ThM6 Amino-rich Plasma Polymer Films Prepared by RF Magnetron Sputtering**, *J. Hanuš, G. Ceccone*, ***F.J. Rossi***, European Commission, JRC. Institute for Health and Consumer Protection, Italy

RF magnetron sputtering of nylon 6.6 was used for the deposition of nitrogen rich films. Deposition was followed by N_2 H_2 plasma post-treatment to enhance primary amine concentration on the surface. Maximal reached NH_2 concentration was 11 % with aminoselectivity 13.5 %. The films exhibited small negative z-potential at basic pH with isoelectric point ~ pH 4.5. Bio properties of the films were tested by QCM in terms of ability to adsorb different proteins and their antigens. The interaction between the film and the buffer solution was also studied and compared to other films such as poly-acrylic acid and PEO plasma polymers. The results show that these films are stable and can be used as a platform where positively charged surfaces are needed

10:40am **BI-ThM9 Surface Analysis in Biotech & Pharma: A Surfeit of Frontiers**, ***E. Johnston***, Genzyme **INVITED**

Surface and interfacial analytical tools continue to provide new value and find unexpected new uses in the biotech and medical device industries. Some uses are investigational in nature and help solve critical problems within manufacturing and quality control. Other applications fall squarely within the realm of R&D - tilting the balance between feasibility of a product or obsolescence of a project, or providing fresh insight into the nature of biomaterial/biological interactions. By way of example, a study will be presented illustrating how TOF-SIMS was used to image a phosphate-binding drug particle in the complex matrix of the rat gastrointestinal tract. Sample preparation was challenging due to the highly hydrated nature of the tissue material. The results yielded surprising information about the ions that bind to this cationically charged particle and opened new avenues for inquiry and study.

11:20am **BI-ThM11 Enhancing Monoclonal Antibody Drug Detection by Developing a Microparticle-based Immunoassay**, ***N. Mendez***, *M.E. Ruidiaz, A.B. Sanchez, B.T. Messmer, A.C. Kummel*, University of California San Diego

Monoclonal antibodies are a notable and rising class of cancer therapeutics due to their enhanced targeting and immune system stimulation properties. Dosage guidelines are typically developed with many uncertainties which may affect treatment outcome and cause unwanted side effects. The requirement for an assay that can quickly and precisely measure the concentration of the monoclonal antibody in a serum sample of a patient during therapy is needed. The present study has demonstrated that the key to detection is compensation for variation in non-specific binding of serum to the assay surface. A microparticle-based assay with peptide antigen mimetics has been developed to rapidly determine the concentration of antibody drug present in serum specimens with high sensitivity. Alemtuzumab (anti-CD52) and rituximab (anti-CD20) antigen peptides, as discovered by phage display, were synthesized on 10 um TentaGel resin beads using conventional solid phase peptide synthesis techniques. The microparticle beads were modified to allow for multiplexing and microfluidic handling via fluorescent labeling and magnetic functionalization. The antigen-displaying fluoromagnetic particles were incubated with spiked serum samples which allowed free antibody to be captured. Primary antibody detection was performed on alemtuzumab while rituximab detection was used to compensate for non-specific serum binding to the beads. After washing, the beads were incubated with a fluorescently tagged secondary antibody for detection by flow cytometry. Serum from thirty (30) individual donors with various spiked serum concentrations of antibody drug were assessed using this assay. Analysis of bead fluorescence data allows for a limit of quantitation down to 0.5ug/ml of serum antibody drug concentration. Using detection of an antibody known to be absent in serum, an accurate compensation technique for non-specific binding has been developed on multifunctional antibody assay beads in realistic samples. The developed assay is robust against donor serum variation.

11:40am **BI-ThM12 Controlling the Hydroaffinity of Silicone/Hydrophobic Acrylic Surfaces of Intraocular Lenses using Visco-Elastic Colloids and Blood Proteins**, *N.X. Herbots*, ASU / SiO2 NanoTech Inc. / SiO2 Associates, LLC, ***R.J. Culbertson***, *Q.X. Bradley, D.A. Sell, A.M. Murphy*, Arizona State U., *C.H. Sell*, Arizona Vitro-Retinal Consultants, *H.M. Kwong*, Arizona Vitro-Retinal Consultants / ASU, *T. Kutz, A.S. Benitez, M.A. Hart, B.J. Wilkens, R.B. Bennett-Kennett*, Arizona State U.

Over 15 million cataract surgeries are performed each year world wide. 2-6 % of cataract patients suffer subsequently from diabetic and other retinal issues post surgery due to aging and accidents and must undergo a secondary eye surgery. Secondary surgery performed after implantation of artificial intra-ocular lenses (IOLs) can fail due to the fogging of IOL's from condensation of bodily fluids. New, high performance accommodating silicone and hydrophobic acrylic IOL's can fog during such surgery. This work solves the problem by modifying water affinity of IOL's using a polymer emulsion, VitreOx™ [1-5] with a 100% success rate in the lab. Ten

clinical trials yielded a success rate of 80% in the year 2010-211 with failure inferred to be due to blood proteins on IOL's.

Thus, the role of hydro-affinity of blood proteins preventing coagulation, heparin, present during surgery, has to be investigated. Our results show that heparin behaves identically to H2O on hydrophobic surfaces. Heparin simply de-wets on silicone IOL's and hydrophobic acrylic lenses. It does not prevent fogging on IOL's nor interfere with our anti-fogging emulsion.

Fibrinogen is the other protein investigated because it enhances blood coagulation and is often present in trauma situations. Fibrinogen applied to IOL's in various dilutions does prevent fogging. However, it cannot be removed after application on the IOL's, thus remaining as a potent coagulant agent in the eye. Thus fibrinogen can indeed prevent fogging, but is not viable since it cannot be removed after application like VitreOx™. Fribrinogen could explain why some IOL's fog while others do not during emergency secondary eye surgery.

[1] U. S. Patent Application “Molecular Films for Hydrophobic Implant Surfaces” N. Herbots, J. D. Bradley, M.A. Hart, D.A. Sell, S. D. Whaley, Q. Xing Bradley Filed 11/9/10

[2] "Modeling Mechanisms of Water Affinity & Condensation on Si-based Surfaces via Experiments & Applications" by Q. Xing, ASU (2011).

[3] N. Herbots, Q. Xing, M. Hart, J. D. Bradley, D. A. Sell, R. J. Culbertson, B. J. Wilkens; "IBMM of OH Adsorbates and Interphases on Si-based Materials" Nucl. Instr. & Meth. B, IBMM 17 (2010), accepted.

[4] Q. Xing, M. A. Hart, R. J. Culbertson, J. D. Bradley, N. Herbots, B. J. Wilkens, D. A. Sell, C. F. Watson;"Particle-Induced X-ray Emission of Silicate Coatings on High Impact Resistance Polycarbonates". 21st ICAARI (2010), accepted

[5] Q. Xing, N. Herbots, M. Hart, J. D. Bradley, B. J. Wilkens, D. A. Sell, C. H. Sell, H. M. Kwong, R. J. Culbertson, S. D. Whaley; "Ion Beam Analysis of Silicon-Based Surfaces and Correlation with Surface Energy Measurements?. 21st ICAARI (2010), accepted.

Authors Index

Bold page numbers indicate the presenter