Wednesday Afternoon, December 5, 2018

Biomaterial Surfaces & Interfaces
Room Naupaka Salon 6-7 - Session BI-WeE

Biomolecule/Material Interactions and Medical Applications

Moderator: Buddy D. Ratner, University of Washington

5:40pm **BI-WeE-1 Engineered Biointerfaces – Organisation and Functionalisation of Proteins at Surfaces***, **Jenny Malmstrom**,* University of Auckland, New Zealand **INVITED**

In my research group, we are interested in the interface between materials and biological systems – such as proteins and cells. Structured or organised surfaces with nanoscale features are important in a range of fields ranging from energy and computing to controlling cellular adhesion or differentiation. The precise organisation of proteins at surfaces is one route to creating such engineered interfaces. Proteins exist with an enormous structural and chemical versatility and lend themselves well to be functionalized with different moieties. The ability to rationally engineer proteins enables the use of proteins as carefully designed nanometer sized building blocks.

I will present work from our group focussed on using protein-protein interactions to build up higher order protein structures, and our efforts to organize and functionalise these structures. Proteins like Lsmα and peroxiredoxin self-assemble into robust doughnuts whose pore size can be tuned specifically to encapsulate metal complexes or nanoparticles and then assemble further into stacks to create magnetic, electrical or optical nanorods. We are harnessing this potential to create functional arrays of these self-assembling protein rings. We have explored ways of arranging these protein rings, for example through templating using a self-assembling block copolymer, or through specific binding to a patterned surface. Furthermore, the protein core has been used to template the synthesis of small (~4 nm) iron oxide nanoparticles. Throughout all of this work, imaging is an important characterisation tool and I will show how we use AFM (including magnetic force microscopy) and other techniques to understand our systems.

Building on this work, I will also present how we are developing some of these thin block copolymer films as biointerfaces, with the aim to control both protein and cellular interactions at the interface.

6:20pm **BI-WeE-3 Tunable Thermal Transport and Reversible Thermal Conductivity Switching in Topologically Networked Bio-Inspired Materials***, J Tomko,* University of Virginia*; A Pena-Francesh, H Jun,* Pennsylvania State University*; M Tyagi,* National Institute of Standards and Technology*; B Allen, M Demirel,* Pennsylvania State University*; **Patrick Hopkins**,* University of Virginia

The dynamic control of thermal transport properties in solids must contend with the fact that phonons are inherently broadband. Thus, efforts to create reversible thermal conductivity switches have resulted in only modest on/off ratios, since only a relatively narrow portion of the phononic spectrum is impacted. Here, we report on the ability to modulate the thermal conductivity of topologically networked materials by nearly a factor of four following hydration, through manipulation of the displacement amplitude of atomic vibrations. By varying the network topology, or crosslinked structure, of squid ring teeth-based bio-polymers through tandem-repetition of DNA sequences, we show that this thermal switching ratio can be directly programmed. This on/off ratio in thermal conductivity switching is over a factor of three larger than the current state-of-the-art thermal switch, offering the possibility of engineering thermally conductive biological materials with dynamic responsivity to heat. More details of this work can be found in the recently published paper, Tomko, J.A., Pena-Francesch, A., Jung, H., Tyagi, M., Allen, B.D., Demirel, M.C., Hopkins, P.E., "Tunable Thermal Transport and Reversible Thermal Conductivity Switching in Topologically-Networked Bio-Inspired Materials," *Nature Nanotechnology* **DOI: 10.1038/s41565-018-0227-7**.

7:00pm **BI-WeE-5 Design Principles and Potential Applications of Cyclic Peptide Polymer-based Nanomaterials***, **Kenan Fears**,* US Naval Research Laboratory, USA

We present a new class of bioinspired nanomaterials that are stabilized by a combination of covalent and hydrogen bonds. Prior work by others has shown that cyclic peptides can self-assemble to form supramolecular assemblies through backbone-backbone hydrogen bonding. To improve upon this molecular architecture, we develop a synthesis route to polymerize cyclic peptides and form a linear polymer chain that can transition between a rigid nanorod and a "soft" unfolded conformation. For a cyclic peptide polymer containing amine-terminated side chains on each ring, we demonstrate self-assembly can be triggered in aqueous solutions by varying the pH. We measure the elastic modulus of the rigid nanorods to be ca. 50 GPa, which is comparable to our molecular dynamics (MD) prediction (ca. 64 GPa). Our results highlight the uniqueness of our molecular architecture, namely their exemplary toughness (up to 3 GJ m^{-3}), in comparison to other cyclic peptide-based assemblies. Finally, we demonstrate the potential of these novel nanomaterials for biomedical applications, such as wound healing.

7:40pm **BI-WeE-7 Metal Oxides and Bone Healing***, H Nygren,* University of Gothenburg, Göteborg, Sweden*; C Zhang,* Science for Life Laboratory, Stockholm, Sweden*; **Per Malmberg**,* Chalmers University of Technology, Sweden

Metal oxides are widely used in implant materials and trace metals are known to deeply influence bone healing. The present study was undertaken to elucidate the mechanisms of the effect of metal ions on bone healing, starting with analyses of the ability of different metal oxides to catalyze the formation of hydroxyapatite (HA) and ending with a global analysis of the transcriptome of bone tissue after implantation of metal ions.

Incubations of MnO and ZnO with cell culture medium followed by analysis with XPS, ToF-SIMS and SEM/EDX showed that these metal oxides are covered with a layer of HA within 12h. Implantation of MnO and ZnO in rat tibia stimulated the formation of callus bone. After 3w of healing of ZnO implants, the bone mineral contained high levels of Zn. This was considered a potential hazard and the use of ZnO was omitted from the study. Sham-operated tibia and bone implanted with MnO were taken to RNA-extraction and global analysis of differently expressed genes at the Science for Life Laboratory in Stockholm (head M. Uhlen). After 4 days of healing, the enrichment analysis showed upregulation of genes reflecting response to cytokines, cytokine regulation and cytokine production in the bones implanted with MnO, compared to sham. Furthermore, genes reflecting leukocyte migration, inflammation and celldeath were upregulated. Analysis of upregulated single genes shows reactions to hypoxia (RGS5), reactions to platelet Ca levels (LHFPL2), genes related to osteogenesis (FetuinB, RUFY4,NFkBIA) and osteoclast differentiation (CPMB6B). The data are still undergoing further analysis.

Manganese has been described as an essential trace metal for bone formation since the mid 1930´s when low levels of Mn in the feed was shown to cause skeletal defects in chicken, rats and rabbits. Mn has been suggested as a trace metal in bone cement based on its effect on biochemical markers of bone metabolism. Manganese is widely used in biomaterials, most extensively as a component of stainless steel.

8:00pm **BI-WeE-8 Thin Films, Coatings and Surface Solutions for Medical Devices***, **Shahram Amini**,* Johnson Matthey Inc.

As medical device manufacturers are pressed to design ever-smaller devices with increasingly long service life, optimizing the performance and profile of each component becomes more crucial. During the past few decades, various medical devices, for instance cardiac rhythm management and neurostimulation devices, have been invented and used in clinical practice to achieve electrical stimulation. These devices function via artificial stimulation of living tissue through transfer of an external electrical signal to an implantable electro-conductive microelectrode across to the membrane of the neural cells or tissue. These electrodes and their surface properties have been a focus for innovation at the Center for Coatings and Surface Solutions (CCSS) to give the next-generation devices a competitive edge via advances in coatings technology that can enable electrodes with better charge exchange capacity, thereby improving accuracy and efficacy of treatment – while also extending the devices' battery life. In developing these electrodes, the substrate, its surface, and its interface with the electrolytic physiological environment all play important roles in the stimulation process. This presentation will focus on the process development and characterization of coatings that exhibit high electrochemically-active surface areas for implantable stimulation devices. In particular, effect of various electrode surface treatment technologies on microstructural characteristics will be discussed. The results presented in this work demonstrate an unprecedented approach that has facilitated discovery of many unique features in these coatings, and the effect of electrode surface on coating surface and sub-surface features.

8:20pm **BI-WeE-9 Effects of Metal Implants on Bone Healing Analysed by Transcriptomics**, ***Håkan Nygren***, University of Gothenburg, Göteborg, Sweden; *C Zhang, M Arif, M Uhlen,* Science for Life Laboratory, Stockholm, Sweden

Bone fractures affect hundreds of millions people worldwide and are a leading cause of long-term pain and disability. Fractured bone normally heals *ad integrum* through a process undergoing characteristic stages of blood coagulation, inflammation, formation of soft and hard callus and, finally, remodeling to its original structure. In approximately 10% of femur-neck fractures, healing meets with failure, or delay. Common causes of failure to heal are critical size defects, infection, or mobility of the fracture parts. Internal stabilisation of fractures with metal implants is an efficient aid of fracture healing. Tissue engineering of bone healing is efficiently made by implanting metal species like Mg, Sr, Zn and Mn. These metals often have a capacity to catalyze formation of hydroxyapatite in bone tissue (Nygren, Pacsurf 2016) suggesting a possible common pathway for the well documented effect of trace metals on bone healing. In this study we analysed the transcriptomics of fracture healing with and without implanted Mg and Mn after 4 and 7 Days of healing, before mineralization and after completion of the callus bone.

Proteins coded by the most differentially expressed genes during normal fracture healing after 4 Days of healing where regulators of platelet degranulation, upregulators of TGF-beta, regulators of Beta-1 Integrin, IL10 receptor antagonist and ROBO proteins guiding cell movement in embryos.

Proteins most differentially expressed after 7 Days of healing were an enzyme hydrolysing lysine, inhibitors of inflammation, NFkappaB, microtubule associated scaffold protein, angogenic proteins and BMP-2 signalling proteins.

Venn diagrams comparing the up-regulated genes after healing with Mg and Mn after 4 Days of healing showed no overlap between the activated genes in these Groups. After 7 Days of healing, there was an 80% overlap between genes upregulated by Mg and Mn. The data suggest that pathways of bone healing at metal implants differs after 4 Days of healing, before the start of mineralisation, but are more congruent after 7 Days of healing when the callus bone is mineralised and remodelling starts.

8:40pm **BI-WeE-10 Synthesis and Characterization of Reactively Sputtered Platinum Group Metal Oxides for Stimulating and Recording Applications**, *G Taylor, N Page, A Marti, R Paladines,* Rowan University; *A Fones,* Johnson Matthey Inc., UK; *S Tint,* Johnson Matthey Inc.; *H Hamilton,* Johnson Matthey Inc., UK; *S Amini,* Johnson Matthey Inc.; ***Jeffrey Hettinger***, Rowan University

A range of materials have been examined as coatings over the past several decades to improve the performance of implantable devices used in neurostimulation and recording applications. Iridium oxide (IrO_2) has been widely investigated due to its biocompatibility and high charge storage capacity. Modification of the synthesis conditions, as one means of improving the coating performance, led to reports of surface platelets forming at high deposition pressures. This study complements earlier research by extending the range of deposition parameters for the IrO_2 system and investigates the ruthenium oxide (RuO_2) system under the same experimental conditions. The results show that the platelet microstructure in tetragonal IrO_2 is due to the formation of a specific orientation of crystallite. In contrast to previous reports that platelet formation coincided with a decrease in coating performance, it will be shown that the presence of platelets can improve the electrochemical performance of the coatings as measured by cyclic voltammetry in a phosphate buffered saline electrolyte. Furthermore, the platelet microstructure, and thereby the effective surface area, can be systematically controlled by adjusting deposition parameters, including temperature and oxygen partial pressure, used during the reactive sputtering. No such platelet formation has yet been observed in the RuO_2 system.

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