Friday Morning, November 8, 2002

Applied Surface Science
Room: C-106 - Session AS+MM+BI-FrM

BioMEMS and Medical Devices
Moderator: K. Healy, University of California, Berkeley

8:20am **AS+MM+BI-FrM1 Characterization of Implant Surfaces**, ***M. Grunze***, University of Heidelberg, Germany **INVITED**

In this talk I will describe my personal recollection of the development of polymer coating (Polyzene FÂ®) for cardiovascular stents from concept to market. The idea was to develop a "stealth" surface coating for metallic stents which reduces inflammation, thrombosis and restenosis of the blood vessels. My talk discusses the design strategies of the polymer, development of the coating process and the necessary Surface Science characterization, protein, cell and bacteria adhesion experiments, the technical certification process, in vivo experiments in animal models, and the problems and successes in starting a new company to market the product. At this time the story is open-ended, since the results of ongoing long term dinical studies were not available at the time this abstract was written.

9:00am **AS+MM+BI-FrM3 Probing the Orientation of Surface-Immobilized IgG by ToF-SIMS**, ***H. Wang***, *D.G. Castner, B.D. Ratner, S. Jiang*, University of Washington

The orientation of a surface-immobilized IgG is crucial for its ability to detect antigen in biosensors. To probe the orientation of a surface-immobilized IgG, two factors are important. One is a powerful surface analysis technique while the other is a well-controlled surface for specific protein orientation. Static time-of-flight secondary ion mass spectrometry (ToF-SIMS) is well suited for this purpose since the sampling depth of ToF-SIMS (1-1.5 nm) is less than the typical dimension of most proteins (4-10 nm). At the same time, IgG orientation can be controlled by appropriately adjusting microenvironments (e.g., surface charges and solution properties). In this work, we apply ToF-SIMS combined with principle components analysis (PCA) to study the orientation of anti-hCG (human chorionic gonadotropin) on two controlled surfaces using its Fab and Fc fragments as references. The controlled surfaces are achieved using self-assembled monolayers (SAMs) with different terminal groups. Results show that the combined ToF-SIMS and PCA technique is able to probe the difference in orientations for ani-hCG adsorbed on different surfaces. In addition, ToF-SIMS results are compared with those from the protein structure. Consistency of these results indicates the reliability of this method.

9:20am **AS+MM+BI-FrM4 TOF-SIMS Analysis to Monitor Coating Processes in Organic and Biological Surfaces**, ***R. Chatterjee***, *B. Lakshmi, M.J. Pellerite*, 3M

Time of Flight Secondary Ion Mass Spectrometry (TOF-SIMS) has proved to be very useful in molecular surface characterization of organic coatings, polymeric systems and biological surfaces. This paper will focus on the application of TOF-SIMS in identifying reaction processes involved in formation of bio-reactive surfaces and organic coatings. In SIMS, absolute quantitative analysis becomes difficult because the ion yield is highly dependent on the morphology and the physical and chemical nature of the surface. Different examples will be used to illustrate how with the use of suitable control experiments, relative quantitative analysis can provide direction in the development of surface modification and surface coating processes. Relative quantitation of TOF-SIMS data was applied to monitor the reaction of aminoacids to different bioreactive surfaces. TOF-SIMS was used to identify presence of different proteins in a multistep sandwich assay. In thin organic coatings, the degree of cure of the silane end group was correlated to the coating durability. Relative quantitation was applied to determine the degree of cure, specify process conditions needed for suitable curing, identify a suitable catalyst to reduce curing times and determine whether lack of cure is the cause of failure. The rate of cure of mono-, bis- and trifunctional silanes, and their effect on the coating durability was investigated.

9:40am **AS+MM+BI-FrM5 Characterization of Protein Interactions with MEMS Devices under Non-Static Conditions**, ***K. Lenghaus***, *J. Dale, D. Henry, J. Hickman*, Clemson University, *J. Jenkins, S. Sundaram*, CFD Research Corporation

The emerging field of micro electromechanical systems (MEMS), when directed to biological applications (environmental monitoring, biosensors etc.), requires an understanding of protein/surface interactions under conditions of flow at low concentrations. Previous protein studies have focussed on adsorption under static conditions and at high concentrations, which can not necessarily be extrapolated to those conditions found in Bio-MEMS under non-static or flow conditions. In an analogous system, the adsorption of proteins to surfaces in in vivo biological systems differs from other adsorption phenomena in that its consequences can be aggressively non-linear, with a biological system's response to minute deviations and changes greatly out of proportion to the magnitude of the change. Thus a relatively small fraction of aggressive sites can induce a response quite out of proportion to their numbers. To study both phenomena we have developed assays to allow enzymes to be quantified at ng/mL levels, and combined with a syringe pump we have created a simple, yet sensitive and robust test bed for protein adsorption under flow conditions. Using this approach, a PEEK capillary was found to have a small number of highly aggressive sites for protein adsorption, corresponding to 5% total surface coverage. These would serve as nucleation sites for further interactions in MEMS devices, and be difficult to detect by other methods. It was further shown that the adsorbed enzymes were in an active state, and this was used to confirm that the rate of desorption from the surface was of the order of 10-4.s-1, corresponding well with values derived from fitting the adsorption isotherm to a computational fluid dynamics model. Thus, studying enzyme adsorption can be used to give several useful insights into the adsorption/desorption behaviour of surfaces at low bulk concentrations of protein as well as generate insights for an in vivo system's protein nucleation behaviour.

10:00am **AS+MM+BI-FrM6 Selective Thermal Patterning of Self-Assembled DNA Monolayers on MEMS-based Microheater Devices**, ***T.H. Huang***, National Institute of Standards and Technology, *N. Ku*, Montgomery Blair High School, *R.E. Cavicchi, M.J. Tarlov*, National Institute of Standards and Technology

We report the selective patterning of self-assembled thiolated DNA probes on gold-coated microheater devices using temperature. The goal of our investigation is to utilize the rapid heating and cooling capabilities of MEMS-based microheaters to prepare biosensing surfaces and to monitor reactions such as DNA hybridization, melting and polymerase chain reaction (PCR). In this study, the self-assembly of thiolated-DNA probes on gold microheater array (four element array) is used as the model system. Modified DNA probes (5' end with disulfide and 3' end with fluorescein) are selectively immobilized onto the gold surface in several steps. First, a passivating layer consists of 1-mercapto-6-hexanol (MCH) is self-assembled onto the gold microheaters. The temperature for one the four heaters is elevated to ca. 200 ^{o}C to drive off the MCH. Then the thiolated DNA probes are deposited onto the freshly exposed bare gold surface. Using this method, one can use temperature to selectively deposit different DNA probes on specific heaters. The presence of the DNA probes on the surface is detected using fluorescence microscopy. In order to use the DNA-microheater surface to monitor DNA melting reactions or PCR (which require cycling to high temperatures), it is important for the probe to be thermally stable at the operating temperatures (i.e. 85 ^{o}C). We will also present results on the thermal stability of thiolated DNA monolayers on gold.

10:20am **AS+MM+BI-FrM7 Soft and Fuzzy Polymer Coatings for Microfabricated Neural Prosthetic Devices**, ***D.C. Martin***, The University of Michigan, *X. Cui*, Unilever, *R. Kim, J. Yang, Y. Xiao*, The University of Michigan **INVITED**

Neural prosthetic devices facilitate the functional stimulation of and recording from the peripheral and central nervous systems. It is important that these implantable devices function in vivo for long periods of time. Bioactive and electrically conductive materials are deposited on the surfaces of neural microelectrode arrays through various means to build a stable interface for better biocompatibility and signal transduction. To mediate the mechanical property differences between the brain tissue and silicon device, integrate the device within tissue and minimize the host reaction, bioactive coatings were developed that can be applied over the whole surface of the silicon micro-devices. One approach that has been developed is electrospinning of protein polymers to form a porous film composed of electrospun nano-scale protein fibers with cell-binding sites exposed. Another ongoing approach has been to coat the device with bioactive hydrogel materials which change volume according to their environment, and therefore integrate the device in the tissue with minimal insertion damage. To stabilize the connection between neurons and the electrode sites and facilitate the signal transduction from electrically conductive metal electrode to the ionically conductive tissue, conductive polymers together with bioactive molecules were co-deposited on the electrode site areas by electrochemical deposition. The coatings presented a fuzzy and conductive

surface which lowered the impedance of the electrode by 1 to 2 orders of magnitude. The bioactive molecules with cell binding ability in the deposited films on the electrode sites were shown to be able to anchor neurons in both in vitro and in vivo experiments.

11:00am **AS+MM+BI-FrM9 Voltage-Dependent Assembly of the Polysaccharide Chitosan onto an Electrode Surface**, *L.-Q. Wu, A.P. Gadre, H. Yi, M.J. Kastantin, G.W. Rubloff, W.E. Bentley, G.F. Payne,* ***R. Ghodssi***, University of Maryland

We examined the assembly of a basic polysaccharide - chitosan - from solution onto electrode surfaces as a result of voltage bias on the electrode. Chitosan is positively charged and water-soluble under mildly acidic conditions, and is uncharged and insoluble under basic conditions. We observed that chitosan is deposited from acidic solution onto the surface of a negative electrode and that the thickness of the deposited layer is dependent upon the deposition time, the applied voltage, and the chitosan concentration. No deposition occurs on the positive or neutral electrode. Once deposited and neutralized, the chitosan layer can be retained on the electrode surface without the need for an applied voltage. Infrared (FTIR) and electrospray mass spectrometry (ES-MS) confirmed that the deposited material was chitosan. The voltage-controlled deposition of chitosan provides a means for anchoring biopolymer material in specific locations in bioMEMS environments, such as encapsulated microfluidic devices fabricated in our laboratory using MEMS-based polymeric materials (EPON SU-8, Polypyrrole and Polydimethylsiloxane). Furthermore, chitosan's amine functionality should enable standard coupling chemistries to be exploited to anchor additional biomolecules (e.g. DNA and proteins) to the surface of bioMEMS devices.

11:20am **AS+MM+BI-FrM10 Alternative Approaches to Microfluidic Systems Design, Construction and Operation**, ***D.J. Beebe***, University of Wisconsin, Madison **INVITED**

Many approaches to the construction of microfluidic systems have appeared in the last few years including glass and silicon etching and bonding, laser machining, micromolding and others. Here we present an alternative approach to the design, construction and operation of microfluidic systems that we call ÂµfluidicÂ tectonics (ÂµFT) that compares to injection molding in cost, but allows for a wide variety of functionality. ÂµFluidic Tectonics utilizes liquid phase photopolymerization, responsive materials and in situ fabrication to achieve elegant yet functional designs. Ultra rapid microchannel fabrication (2 minutes) is demonstrated using off the shelf components (glass microscope slides, polycarbonate top, simple UV lamps and transparency masks). The process eliminates the need for traditional bonding to achieve a closed channel and no master is required (as in elastomeric micromolding). The same basic process has been used to create filtering, flow control, readout (chemical and biological) and mixing components. Thus, the construction platform leads to highly integrated systems by using a single fabrication process and class of materials (photopolymerizable polymers). Closed loop feedback control is demonstrated without the use of electronics. A single structure created in situ from responsive materials performs the sensing and actuation functions. The responsive component senses the local chemical environment and undergoes a volume change in response to changes in the local environment. The volume change is coupled to a valve that regulates the compensating stream providing closed loop regulation. The design flexibility ÂµFT combined with the ease of fabrication and low cost (similar to injection molding) enhances the microfluidic toolbox and broadens the base of potential designers and users by simplifying the construction process and reducing the infrastructure needed to create and use microfluidic systems.

Authors Index

Bold page numbers indicate the presenter