Applied Surface Science
Room 206 - Session AS+BI+NS-MoM

Nanoscale Analysis: Biomaterial and Other Applications

Moderator: A.M. Belu, Medtronic, Inc.

8:20am **AS+BI+NS-MoM1 The Development of NSOM for Live Cell Applications**, ***R.C. Dunn***, *O. Mooren,* University of Kansas **INVITED**

Near-field scanning optical microscopy (NSOM) is a scanning probe technique that enables optical measurements to be conducted with nanometric spatial resolution. This technique offers single molecule detection limits, high spatial resolution, and simultaneous force and optical mapping of sample properties. As such, it has found applications in many areas including the study of thin films, polymers, and solid-state materials. Perhaps its greatest potential, however, lies in the biological sciences, where fluorescence techniques are well developed for tagging specific proteins or structures or following dynamic processes such as calcium signaling. To date, NSOM measurements on viable cells remains problematic due to the forces involved in maintaining the tip close to the sample. Our laboratory has been actively developing new methods for conducting NSOM measurements that are amenable with soft and fragile samples such as living cells. We recently reported a new NSOM tip design built around a conventional atomic force microscopy tip that can be used to make high resolution fluorescence measurements on living cells. The development of these techniques and their application to the study of lipid rafts and nuclear pore complexes in the nuclear envelope will be discussed.

9:00am **AS+BI+NS-MoM3 Local Mobility in Membranes: Atomic Force Microscopy and Fluorescence Correlation Spectroscopy**, ***A.R. Burns***, *D.J. Frankel,* Sandia National Laboratories

The lateral organization and dynamics of lipids and proteins in membranes are critical to cellular signaling processes. Fluorescence imaging and atomic force microscopy (AFM) are both effective ways to map the location and structure of membrane components and domains (e.g., lipid rafts) in supported membranes. Since dynamical processes like translational diffusion of lipids and proteins are dependent on the local membrane structure and molecular interactions, it would be advantageous to correlate dynamics with detailed topography mapped out with AFM. We do this by performing fluorescence correlation spectroscopy (FCS) at specific sites imaged by simultaneous AFM and submicron confocal fluorescence microscopy. We have thus examined the relative partitioning and diffusion coefficients for both tail and head labeled GM1 ganglioside, as well as for head and tail labeled phospholipids, in phase separated domains. Our results indicate significant mobility changes in the micron-scale domains due to differences in lipid packing and ordering. We also observe a large reduction in the mobility of GM1 when bound to cholera toxin B fragments. The effects of membrane proteins will be discussed as well. This research was supported in part by the Division of Materials Science and Engineering, Office of Basic Energy Sciences, U.S. Department of Energy. Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the U.S. Department of Energy under Contract DE-AC04-94AL85000.

9:20am **AS+BI+NS-MoM4 Molecular Orientation Imaging with sub 10-nm Resolution by Vector Piezoresponse Force Microscopy**, ***B.J. Rodriguez,*** North Carolina State University*; S. Jesse, A.P. Baddorf,* Oak Ridge National Laboratory*; A. Gruverman,* North Carolina State University*; S.V. Kalinin,* Oak Ridge National Laboratory

Functional properties of calcified and connective tissues are determined by the relative ordering and orientation of a relatively small number of biopolymers, such as collagen. Here we present a new approach for local molecular orientation imaging in biological systems by Vector Piezoresponse Force Microscopy (Vector PFM). Vector PFM is capable of determining the local electromechanical activity and orientation in piezoelectric materials with a spatial resolution below 10 nm. The applicability of Vector PFM to biological systems is demonstrated for objects from butterfly wings to bones. Electromechanical characterization of enamel and dentin layers in human tooth is demonstrated. The vector electromechanical response of a bundle of collagen molecules in human tooth dentin has been visualized with 5 nanometer resolution. A method for imaging the local orientation of biomolecules from Vector PFM data has been illustrated using collagen molecules embedded in a hydroxyapatite matrix. As another example, 2D piezoelectric properties and local elasticity of a butterfly wing are measured with nanoscale resolution and interpreted in terms of the relative orientation of chitin molecules in the wing scales. The ubiquitous presence of electro-activity in biopolymers, such as chitin, keratin, collagen, and cellulose, suggests that Vector PFM has exceptional potential for orientation imaging of biological materials on the sub-10 nanometer length scale. Research was sponsored by the U.S. Department of Energy, under contract DE-AC05-00OR22725 with UT-Battelle, LLC and by the National Science Foundation grant DMR-0072998 (AG). Research partially performed as a Eugene P. Wigner Fellow (SVK).

9:40am **AS+BI+NS-MoM5 Nanoscale Raman and Fluorescence Microscopy of Carbon Nanotubes**, ***A. Hartschuh***, *H. Qian, A.J. Meixner,* University of Tuebingen, Germany*; N. Anderson, L. Novotny,* University of Rochester **INVITED**

Spectroscopic methods with high spatial resolution are essential for understanding the physical and chemical properties of nanoscale materials including biological proteins, quantum structures and nanocomposite materials. Optical techniques are of special interest because the energy of light quanta is in the range of electronic and vibrational transitions. Advances in near-field optics open up new means to overcome the diffraction limit and extend the range of optical measurements to the length scales of most nanosystems. Recently, a near-field optical technique based on local field enhancement has been demonstrated which allows to perform spectroscopic measurements with 20 nm spatial resolution.@footnote 1,2@ The method makes use of the strongly enhanced electric field close to a sharp metal tip under laser illumination. In this approach the metal tip is held a few nanometers above the sample surface so that a highly localized interaction between the enhanced field and the sample is achieved. Raster scanning the sample then allows for simultaneous optical and topographic imaging. Single-walled carbon nanotubes (SWCNTs) have been the focus of intense interest due to a large variety of potential nanotechnological applications. We demonstrate near-field Raman and fluorescence imaging of the same individual single-walled carbon nanotube and show that a spatial resolution of less than 20 nm can be achieved. The high-resolution capability and chemical specificity of the presented method is used to study local variations in the optical spectra of SWCNTs which would be hidden in farfield measurements. The technique has great potential for becoming a routine tool for the chemical analysis of surfaces at high spatial resolution. @FootnoteText@ @footnote 1@ E. J. Sanchez et. al, Phys. Rev. Lett. 82, 4014 (1999).@footnote 2@ A. Hartschuh et. al, Phys. Rev. Lett. 90, 095503 (2003).

10:20am **AS+BI+NS-MoM7 Scanning Atom Probe Study of Fragmentation of Organic Molecules**, ***O. Nishikawa***, *M. Taniguchi,* Kanazawa Institute of Technology, Japan

Fragmentation of two organic molecules, crystal violet [(C@sub25@N@sub3@H@sub30@)@super+@Cl@super-@: 408 amu] and tetra-n-butyl-ammonium hydroxide [N(C@sub4@H@sub9@)@sub4@@super+@OH@super-@: 259 amu], was studied at atomic level by mass analyzing the dissociated fragments with the scanning atom probe (SAP). In the SAP analysis the molecules and their fragments are field evaporated as positive ions and detected one by one. Since the field evaporation is a static process, it does not disorder surface structure breaking atomic bonds by external energy. Accordingly, evaporated positive ions reflect the binding state in the molecules. For example, the radical of polythiophene, SC@sub4@H@sub2@, is field evaporated as doubly charged ions indicating that the atoms forming the radical are strongly bound. A thin layer of crystal violet was deposited on a tungsten substrate. Since the crystal violet is non conductive, the molecules are field evaporated applying a DC high voltage to the tungsten substrate and irradiating the specimen with a pulsed laser beam, 2nd harmonic of YAG laser, 532 nm. Although non-dissociated molecule ions are detected, most molecules are dissociated showing the ions such as C@sub13@H@sub2@, C@sub13@NH@sub4@ and C@sub8@NH@subn@. The detected fragments suggest that no double bonds are broken. When the molecule layer was deposited on a titanium oxide layer, all molecules were dissociated possibly due to the photo-catalytic function of titanium oxide. The most abundant fragment is C@sub4@NH@subn@. The ratio of the number of carbon atoms to that of nitrogen atom was found to be nearly 8:1 as expected. Although the dissociation of tetra-n-butyl-ammonium hydroxide molecules at the boundary with the tungsten substrate is noticeable, the dissociation is insignificant at non-boundary areas. It was also found that hydroxide of the molecules is dissociated and oxygen atoms are bound with tungsten. This may suggest that tungsten also have catalytic function.

10:40am **AS+BI+NS-MoM8 Surface Potential Mapping of DNA-protein Complex at Molecular Level**, ***E. Mikamo***, *F. Yamada, T. Matsumoto, T. Kawai,* Osaka University, Japan

Atomic force microscopy (AFM) is a valuable method for the study of biomolecules such as DNA, RNA and proteins at real-space. The biomolecules have generally been adsorbed on the insulating substrate as mica to observe by AFM. However, it is very hard to measure the local electric properties of the insulating substrate and the conductive substrate has been commonly used. Recently our group demonstrated the measurement of electric properties of DNA and Au nanoparticles on mica and sapphire substrate. This result encouraged us to measure the complex of biomolecules on the insulating substrate at molecular level. We report here surface potential and capacitance measurement of DNA, protein and DNA-protein complex on the insulating substrate. The experiments are based on frequency mode non-contact AFM (FM-ncAFM). The FM-ncAFM is able to detect the high-sensitive local electrostatic forces and prevent the charge injection caused by tip-sample contact. We observed the surface potential mapping and topographic image simultaneously. The topographic images clearly showed DNA and protein as line and dot structure. The surface potential of corresponded structures is observed as bright contrast. Our results indicate that surface potential of DNA, protein and DNA-protein complex is higher than insulating substrate surface. The potential images resolve the double strand DNA, thin structure less than 2 nm, and protein at single molecular revel. To estimate the capacitance of individual molecules, we measured d(@DELTA@F) per dV images. The measurement of surface potential and capacitance indicate that this technique is able to discriminate the individual molecules on an insulating substrate. This work was supported by grants from the New Energy and Industrial Technology Development Organization (NEDO).

11:00am **AS+BI+NS-MoM9 The Importance of Aberration Corrected SEM and TEM to the Semiconductor Industry**, ***A.C. Diebold***, SEMATECH & AMRC, US; *B. Foran,* ATDF & AMRC; *M.J. Yacaman, B.A. Korgel,* University of Texas & AMRC **INVITED**

Microscopy continues to be a critical need for the semiconductor industry. Feature sizes continue to shrink with logic having a two-year cycle for introduction of each new technology generation. Over the next fifteen years, the gate length of transistors will rapidly shrink to less than 10 nm. The interconnect technology connecting the transistors will keep pace with this size reduction. Research and development needs occur well ahead of manufacturing needs. Thus, there already is a need for microscopy capable of imaging and characterizing the interfaces, film layers and structures for future devices. Recent advances in electron optics technology have corrected for chromatic and spherical aberrations that have long limited resolution in scanning electron microscopy (SEM) and tranmission electron microscopy (TEM). Commercially available advances include monochromators to reduce the energy spread of the electron source and lens correctors to reduce spherical aberration. Resolution of state of the art scanning TEM and High resolution TEM has been proven below 0.1 nm. Aberration correction technology is also now commercially available for SEM and allowing resolution to 0.6 nm. In this paper we discuss the advances in imaging that aberration corrected lenses have enabled along with semiconductor industry applications. We will discuss near-term applications such as the characterization of interfaces in the transistor gate stack and measurement of strain in the transistor channel, and then also discuss long-term research applications such as nanowires and nanodots. Abberation correction will not solve all microscopy problems, and we will discuss specific cases such as sample or analytical limitations that can obviate any benefit of aberration correction technology.

11:40am **AS+BI+NS-MoM11 Scanning Tunneling Microscope Assisted with Inner-Shell Excitation by Hard X-ray Micro-Beam**, ***A. Saito***, Riken Harima Inst., Japan; *J. Maruyama, K. Manabe,* Osaka Univ., Japan; *K. Kitamoto,* Riken Harima Inst., Japan; *K. Takahashi,* Osaka Univ., Japan; *Y. Tanaka,* Riken Harima Inst., Japan; *M. Yabashi, M. Ishii,* Japan Synchrotron Radiation Res. Inst.; *M. Akai-Kasaya,* Osaka Univ., Japan; *S. Shin, T. Ishikawa,* Riken Harima Inst., Japan; *Y. Kuwahara, M. Aono,* Osaka Univ., Japan

A scanning tunneling microscope (STM) system was developed for in-situ experiments under the irradiation of highly brilliant hard x-rays of synchrotron radiation (SR). It appears attractive to excite the core electrons of specific level under the STM observation, because it may enable to analyze the elements or control the local reaction with the spatial resolution of STM. To surmount a small probability of the core-excitation by hard X-rays, SR of the highest brilliance at the SPring-8 was used. To prevail the difficulties produced by the highly brilliant SR (damage around the STM scanner, thermal and electrical noise, and instability of the system such as thermal drift), the beam size was limited to @phi@10 μm. The small beam size serves also to obtain a high signal to noise ratio and high spatial resolution by restraining the electrons emitted from a wide area. The in-situ STM observation was enabled by developing an accurate "three-body (invisible micro-beam, tip-end, and sample surface)" alignment system in ultrahigh vacuum. Despite a noisy condition of SR facility and radiation load around the probe tip, STM images were successfully obtained with atomic resolution. The analysis of the clean Si(111) surface revealed that the thermal expansion affects to the behavior of the tip much strongly than reported in the past reports. Next, the tip-current spectra were obtained on Ge nano-islands on the clean Si(111) surface, by changing the incident photon energy across the Ge absorption edge. A current modification was detected at the absorption edge, with a spatial resolution of the order of 10 nm. This system will serve to observation or manipulation with atomic resolution, which is based on the interaction between the surface atoms and the hard X-ray photons.

Biomaterial Interfaces
Room 313 - Session BI-MoM
BioMaterials and Neutrons (BioMaN) I

Moderator: M. Grunze, Universität Heidelberg, Germany

8:20am **BI-MoM1 Neutron Scattering Tutorial**, ***J.K. Zhao***, Oak Ridge National Laboratory

We will give an introduction to the neutron scattering techniques relevant to the current session. Topics will include Reflectometry, Small Angle Neutron Scattering and Inelastic Scattering. We will briefly describe these methods and introduce various technical terms that will be used by the subsequent talks. These subsequent presentations will concentrate on scientific achievements or potentials of neutron scattering in biomaterials. We will also distribute handouts as technical references during session.

8:40am **BI-MoM2 Compositional Depth Profiles of Biomaterial Interfaces by Specular Neutron Reflection**, ***C.F. Majkrzak***, *S.K. Krueger, U. Perez-Salas, N.F. Berk,* National Institute of Standards and Technology

We present the results of recent studies which illustrate the power of specular neutron reflectivity and diffraction for determining the compositional depth profiles of thin films and multilayered structures of interest in biology and biotechnology. Research discussed includes: probing the interactions of melittin (a model peptide for antibiotics and membrane proteins) with hybrid bilayers; the structural characterization of a polyelectrolyte/terpolymer/phospholipid sandwich; the orientation of adsorbed biomineralization proteins; and the location of cholesterol within lipid membranes. Using specular neutron reflection from single-repeat lamellar assemblies or diffraction from periodic multilayers as probes, cross sectional composition depth profiles, with spatial resolutions of the order of a nanometer and Angstrom, respectively, can now be obtained. We demonstrate, in the context of the aforementioned work, how the neutron's sensitivity to different isotopes, in particular hydrogen and deuterium, enables detailed structural information -- for example, the water concentration profile across the thickness of a film -- to be revealed through selective substitution in organic materials. We also show how the high transmission of neutrons through inorganic single crystals, e.g., silicon, sapphire, and quartz, allows such crystals to serve as both substrate for the film of interest as well as fronting medium for the incident and specularly reflected neutron beams. This in turn makes it possible to study the film in intimate contact with a fluid reservoir -- which may be, for instance, part of a functioning electrochemical cell. Finally, the uniqueness of a depth profile obtained from neutron reflection data is considered, together with the degree of uncertainty in the density and the spatial resolution.

9:00am **BI-MoM3 Neutron Scattering and Diffraction for Molecular-Scale Characterization of Biomimetic Membranes**, ***M. Loesche***, Johns Hopkins University and CNBT at the NIST Center for Neutron Research

Nanotechnology and molecular bioengineering are making ever deepening inroads into our daily lives. Physicochemical and biotechnological achievements in the design of physiologically active supramolecular assemblies have brought about an urgent need for new means of characterizing them at the molecular and submolecular levels. Because surfaces and interfaces play a pivotal role in this field, surface-sensitive neutron and x-ray scattering techniques have become particularly important for characterization. The CNBT consortium, located at the NCNR, is a biophysics partnership that utilizes neutron scattering, tightly

interfaced with MD simulations, for advanced research in membrane biology and biotechnology. A new neutron spectrometer – the Advanced Neutron Reflectometer and Diffractometer, AND/R – has been commissioned which is optimized for surface-sensitive neutron scattering. In this talk, I will discuss current highlights of research performed on the AND/R, including investigations of peptidemembrane interactions and the molecular-scale characterization of model bilayer membranes tethered to solid supports.

9:20am **BI-MoM4 Towards a Deeper Understanding of Protein Resistance: Characterizing Water/Surface and Protein/Surface Interactions by In Situ Neutron Reflectometry**, ***R. Dahint***, Universität Heidelberg, Germany; *M. Skoda, F. Schreiber,* Universität Tübingen, Germany; *M. Himmelhaus, M. Grunze,* Universität Heidelberg, Germany

Materials which are resistant towards adsorption of proteins from biological media are of crucial importance in biotechnology and biomedical applications. The most outstanding protein resistant properties are exhibited by surfaces containing poly- (PEG) and oligo(ethylene glycols) (OEG), (-O-CH@sub 2@-CH@sub 2@-)@sub n@. For surface-grafted PEG, protein resistance is associated with an unfavorable change in the free energy when a protein approaches the surface and thereby compresses and dehydrates the polymer chains. However, this mechanism cannot explain the inertness of rigid, and thus conformationally restricted, OEG terminated alkanethiolate self-assembled monolayers (SAMs). Proposed models suggest the importance of water/SAM interactions at the surface or relate protein resistance to repulsive electrostatic forces. Due to its capability to characterize biological interfaces in situ, neutron reflectometry provides a unique tool to address fundamental questions of protein repulsion. We have studied the importance of interfacial water layers between inert SAMs and the bulk water phase to repel proteins. Temperature dependent studies on the OEG/water interface reveal, that a previously observed, density reduced water phase in the vicinity of the SAM cannot account for the protein resistant properties of the films. Moreover, neutron reflectometry has been used to investigate protein/surface interactions employing biomolecules in their native state and natural environment. Room temperature measurements on protein resistant films of OEG in contact with bovine serum albumin (BSA) solutions reveal the presence of an extended protein depletion layer between the SAM and the bulk protein solution. The results are compared to the strength and range of repulsive forces measured by AFM.

9:40am **BI-MoM5 Soft Interfaces on the Nanometer Scale - How Neutrons Contribute to a Deeper Understanding on the Supramolecular Level**, ***R. Steitz***, Hahn-Meitner-Institut, Germany; *C. Czeslik,* Universität Dortmund, Germany; *H. Haas,* MediGene AG, Germany; *P. Riccio,* Università degli Studi della Basilicata, Italy **INVITED**

Current problems in soft matter and biomaterial science often require insight on the nanometer scale. In this contribution we will show how neutron reflectivity contributes to a deeper understanding of systems that are also of biological interest. Topics of increasing complexity and biological relevance will be discussed: Chapter one will focus on the properties of ultrathin polyelectrolyte coatings at a solid-liquid interface.@footnote 1@ Chapter two will show how these polymer coatings can be utilized as soft cushions for lipid membranes that form in situ by vesicle fusion from the liquid phase (under physiological conditions), or as switchable binding sites for proteins that penetrate from the aqueous solution.@footnote 2@ Number three will demonstrate the successful in situ assembly of myelin model membranes at a polymer-liquid interface, while number four will focus on the molecular organization within such membranes@footnote 3@ and their respective degradation upon reduced humidity. @FootnoteText@ @Footnote 1@ R. Steitz, V. Leiner, R. Siebrecht and R. v. Klitzing, Colloids and Surfaces A. 163, 63-70 (2000). @Footnote 2@ C. Czeslik, G. Jackler, R. Steitz and H.-H. von Grünberg, J. Phys. Chem. B 108, 13395 (2004). @Footnote 3@ H. Haas, M. Torielli, R. Steitz, P. Cavatorta, R. Sorbi, P. Riccio, A. Gliozzi, Thin Solid Films, 329, 627 (1998).

10:20am **BI-MoM7 Design & Structural Characterization of Amphiphilic 4-Helix Bundle Peptides Vectorially-Oriented at Soft Interfaces**, ***J.K. Blasie***, *J. Strzalka, S. Ye, T. Xu, E. Nordgren,* University of Pennsylvania; *S. Satija,* National Institute of Standards and Technology; *I. Kuzmenko, T. Gog,* Argonne National Laboratory **INVITED**

Amphiphilic 4-helix bundle peptides have been designed to incorporate both biological and non-biological cofactors. An ensemble of these peptide-cofactor complexes, vectorially oriented at a soft interface between polar and non-polar media, can provide for the translation of their designed molecular function into a macroscopic material property of the interface. Such amphiphilic 4-helix bundle peptides can also serve as model integral membrane proteins for vectorial incorporation into a lipid bilayer providing a molecular laboratory for the detailed study of structure-function correlations. For example, the mechanism by which anesthetic binding to a designed cavity within its hydrophilic domain modulates the ion channel activity of its hydrophobic domain. Detailed structural studies of these amphiphilic peptides within such non-crystalline ensembles can be performed utilizing an essential combination of x-ray scattering, neutron scattering, and molecular dynamics simulation techniques.

11:00am **BI-MoM9 Structural Analysis of Phospholipid Membranes and Toxin Assault**, ***T.L. Kuhl***, *C.E. Miller, T. Gog, K. Kjaer, J. Majewski,* University of California, Davis **INVITED**

In nature, membranes perform several functions of the living cell from selective transport and recognition, to simple sequestration. In general, the membrane consists of a single bilayer or in special cases, such as the lung surfactants, a single monolayer. Using powerful new neutron and x-ray sources, the techniques of reflectivity and grazing incidence diffraction permit us to obtain structural information on single lipid monolayers and supported bilayers in an aqueous environment. Recently, we demonstrated that 18 keV x-rays can be used to study lipid bilayers at the solid-liquid interface by x-ray reflectivity. We establish that this is a powerful technique for investigating biological systems in a previously inaccessible manner. Our measurements enabled the density distribution of single phospholipid bilayer membranes in bulk water to be measured with unprecedented precision enabling subtle variations in leaflet segregation to be resolved. Recent results on membrane perturbation by toxin binding will also be highlighted. In this case, scattering techniques enable us to distinguish binding and subsequent penetration of lipid layers upon toxin activation.

Biomaterial Interfaces
Room 313 - Session BI-MoA

Biomaterials and Neutrons (BioMaN) II
Moderator: M. Grunze, Universität Heidelberg, Germany

2:00pm **BI-MoA1 Effective Protein-Protein Interaction and Clustering Phenomenon in Solution Studied by Small-Angle Neutron Scattering**, ***S.-H. Chen,*** Massachusetts Institute of Technology **INVITED**

The bottleneck of protein crystallography is the lack of systematic methods to obtain protein crystals, which is partly due to imprecise understanding of the physical chemistry conditions that control the growth of protein crystals. A general knowledge and comprehension of the effective protein-protein interaction potential in solution and the resulting phase behavior thus becomes essential. It has been shown that the crystallization curves of some globular proteins appear to coincide with the phase diagrams of a hard sphere system interacting with a short range attraction.@footnote 1,2,3@ Moreover, the study of the intensity distribution, I(Q), of some proteins measured with small angle neutron and X-ray scattering also suggests presence of a short-range attractive interaction between protein molecules besides the electrostatic repulsion induced by the residual charges in protein molecules.@footnote 4,5,6@ The so-called DLVO potential, which has been successfully applied in many colloidal systems, meets some successes when applied to protein solutions,@footnote 3,4,13@ but is still not enough to explain all the phenomena.@footnote 4,7,8,9@ Due to the complexity (anisotropic property, irregular shape, distributed charge patches, etc.), the full understanding of the properties of the effective interaction between protein molecules in solutions remains a challenge.@footnote 8@ Recent measurements of small angle neutron scattering (SANS) intensity distribution, in protein solutions by my group at MIT and others show some interesting results.@footnote 6,10,14@ First, besides the first diffraction peak, arising from the nearest neighbor inter-particle correlation in the liquid, there is an extra peak appearing at a much smaller scattering wave vector Q, due to the formation of well-ordered clusters inside the solutions. The appearance of this cluster peak is explained as due to the competition between the short-range attraction and the intermediate-range electrostatic repulsion in the effective protein-protein interaction potential in solution.@footnote 5,11,12@ Secondly, a rising intensity as Q approaching zero is observed in both liquid-like and solid-like samples, which can be shown to be due to the presence of another weak, very long-range attractive interaction term, in addition to the already proven short-range attraction and intermediate-range electrostatic HYPERLINK "mailto:repulsion.@footnote"repulsion.@footnote 12,14@ In this lecture, I shall show the results of a systematic SANS investigation of the clustering phenomenon and the newly found increasing low-Q intensity and its relation to the long-range interaction term. @FootnoteText@ @footnote 1@ D. Rosenbaum et al., Phys. Rev. Lett. 76, 150 (1996). @footnote 2@ M. H. J. Hagen et al., J. Chem. Phys. 101, 4093 (1994). @footnote 3@ G. Pellicane et al., J. Phys.: Condens. Matter 16, S4923 (2004). @footnote 4@ A. Tardieu et al., J. Cryst. Growth 196, 193 (1999). @footnote 5@ A. Stradner, et al., Nature 432, 492 (2004). @footnote 6@ B. Lonetti, E. Fratini and P. Baglioni., Phys. Chem. Chem. Phys. 6, 1388 (2004). @footnote 7@ M. L. Broide et al., Phys. Rev. E 53, 6325 (1996). @footnote 8@ R. Piazza, Curr. Opin. Colloidal Interface Sci. 8, 515 (2004). @footnote 9@ A. Striolo et al., J. Chem. Phys. 116, 7733 (2002). @footnote 10@ P. Baglioni, E. Fratini, B. Lonetti and S.H. Chen., J. Phys.: Condens. Matter 16, S5003 (2004). @footnote 11@ F. Sciortino et al., Phys. Rev. Lett. 93, 055701 (2004). @footnote 12@ Y. Liu, W.R. Chen and S.H. Chen., J. Chem. Phys. 122, 044507 (2005). @footnote 13@ C. F. Wu and S.H. Chen., J. Chem. Phys. 87, 6199, (1987). @footnote 14@ Y. Liu, E. Fratini, P. Baglioni, W.R. Chen and S.H. Chen (submitted to Phys. Rev. Lett.).

2:40pm **BI-MoA3 Small-Angle Neutron Scattering: A High Resolution, Non-Destructive Probe Of Biomacromolecular Structure**, ***O. Byron,*** University of Glasgow, UK **INVITED**

Neutrons are of particular utility in the characterisation of biomaterials because of the large difference in their interaction with the @super 1@H nucleus compared with the @super 2@H nucleus. This allows contrast variation experiments to be performed in which certain components of complex biomaterials are made to be "invisible". In addition, neutrons do not damage biomaterials in the same way as their x-ray counterparts may do. Small-angle neutron scattering has been used to successfully reveal the molecular architecture of a range of biomaterials. I will describe its use in several systems and will include the following areas: Diblock copolypeptides constructed via designed molecular self-assembly; Nanomolecular architecture of biodegradable biopolymer inclusion bodies; Temperature response of dental-ceramics; Characterisation of medical biosurfaces resistant to biofouling

3:20pm **BI-MoA5 Determining the Structures of Peptides in Membranes Using Diffraction and MD Simulations**, ***S.H. White,*** University of California at Irvine **INVITED**

Quantitative structural images of peptides in oriented arrays of fluid lipid bilayers are necessary for interpreting thermodynamic measurements of peptide-bilayer energetics in molecular terms. Lamellar x-ray and neutron diffraction provide a starting point for obtaining structural images. But the high thermal motion of fluid bilayers limits "structures" to so-called bilayer profiles, representing a time-averaged projection of the unit-cell contents onto an axis normal to the bilayer plane. Specific deuteration of lipid structural groups combined with neutron diffraction difference methods allow these profiles to be decomposed into a collection of groups (phosphates, carbonyls, etc.) representing transbilayer probability distribution functions. The power of this method has been extended through the inclusion of x-ray data and a joint-refinement protocol. We have developed an x-ray method, referred to as absolute-scale refinement, that permits the determination of the disposition of peptides in fluid bilayers. These various approaches can used in concert as a powerful tool for gaining structural information. But that information is still only one-dimensional. We are now developing methods for obtaining experimentally validated three-dimensional structures by combining the diffraction methods with molecular dynamics simulations. In essence, our goal is to convert 1-D experimental data into 3-D images. Importantly, these images will be dynamic, which will permit the ensembles of peptide-lipid structures to be explored in detail. An essential issue, however, is the validation of MD simulations using diffraction data. A method of accomplishing this objective will be described. Research supported in part by grants from the National Institute of General Medical Sciences (GM46283 and GM68002) and the National Center for Research Resources (RR14812).

4:00pm **BI-MoA7 Exploring the Collective Dynamics of Lipid Membranes with Inelastic Neutron Scattering**, ***M.C. Rheinstädter,*** Institut Laue-Langevin, Grenoble, France **INVITED**

While most spectroscopic techniques, as e.g. nuclear magnetic resonance or dielectric spectroscopy, probe macroscopic responses, neutron and within some restrictions also x-ray scattering experiments give the unique access to microscopic dynamics at length scales of intermolecular or atomic distances. Only recently, it has become possible to study collective dynamics of planar lipid bilayers using neutron spectroscopy techniques.@footnote 1@ We determined the dispersion relation of the coherent fast picosecond density fluctuations on nearest neighbor distances of the phospholipid acyl chains in the gel and in the fluid phases of a DMPC bilayer. The experiments shed light on the evolution of structure and dynamics, and the relation between them, in the range of the gel-fluid main phase transition. The scattering volume restriction for inelastic neutron experiments was overcome by stacking several thousand highly aligned membrane bilayers. By combining different neutron scattering techniques, namely three-axis, backscattering and spin-echo spectroscopy, we present measurements of short and long wavelength collective fluctuations in biomimetic and biological membranes in a large range in momentum and energy transfer, covering time scales from about 0.1 ps to 150 ns and length scales from 3Å to about 1000 Å. A recent backscattering study gives information about slow molecular dynamics of lipid acyl chains and the 'membrane-water', i.e. the water molecules in between the stacked bilayers, in the nanosecond time range.@footnote 2@ The dispersion relations of the long wavelength undulation modes in lipid bilayers with nanosecond relaxation times can be determined by quasielastic reflectometry on spin-echo spectrometers and give direct access to the elasticity parameters of the membranes. @FootnoteText@ @footnote 1@ M.C. Rheinstädter, C. Ollinger, G. Fragneto, F. Demmel and T. Salditt, Phys. Rev. Lett. 93, 108107 (2004). @footnote 2@ Maikel C. Rheinstädter, Tilo Seydel, Franz Demmel and Tim Salditt, Phys. Rev. E, in print (2005), cond-mat/0501752.

4:40pm **BI-MoA9 Meeting the Challenges in Bio-Materials Research using Neutrons**, ***I. Anderson,*** Oak Ridge National Laboratory **INVITED**

When the Spallation Neutron Source, presently under construction in Oak Ridge, Tennessee, comes into operation in 2006 it will provide researchers across the world with unprecedented capabilities for the study of materials

using neutron beams. A comprehensive suite of instrumentation is under construction to address new challenges in a wide range of disciplines including physics, materials science, environment, nanotechnology, biology and medical sciences. An overview will be given of the range of applications and promising new areas of research relevant to Biomaterial Interfaces with emphasis on the new capabilities provided by SNS.

Biomaterial Interfaces
Room Exhibit Hall C&D - Session BI-MoP

Biomaterial Interfaces Poster Session

BI-MoP4 Pulsed rf Plasma Polymer Modification of Microfluidic Devices, ***Z. Segu***, Southern Illinois University; *R.B. Timmons,* University of Texas at Arlington; *G.R. Kinsel,* Southern Illinois University

There is a growing interest in the use of miniaturized systems - so-called "lab-on-a-chip" devices - for various analytical applications due to reduced solvent/reagent/sample consumption, shortened analysis time and the applicability of these devices to process / field analysis. One performance requirement for these devices often involves the ability to separate sometimes complex mixtures of analytes prior to detection. In conventional analytical instruments the separation step is most often achieved via gas or liquid chromatography using columns having a broad diversity of stationary phase chemistries. Introduction of similar diversity of chemistries into microfluidic devices can offer similar capabilities for complex analyte mixture separation while retaining the unique capabilities of the miniaturized system. In this research we explore the use of pulsed RF plasma polymer deposition for coating of channels in microfluidic devices. This approach to channel modification is attractive due to the conformal, sterile, pinhole-free, surface coverage of plasma polymer films and the wide variety of surface chemistries and functional group densities that can be achieved using RF plasma polymer deposition. In these initial studies RF plasma deposited microchannel polymer film coatings are investigated as a function of reactor power, monomer flow, monomer pressure, and positioning of the sample in the plasma reactor chamber. Resultant films are characterized by ellipsometry, SEM, FT-IR and XPS to determine various film properties including, film thickness, film uniformity and chemical functionality. These studies demonstrate the pulsed RF plasma polymer deposition can offer an effective means to incorporate a wide variety of chemical functionalities into microfluidic devices.

BI-MoP5 Pulsed RF Plasma-Modified Surfaces for On-Probe Fractionation and MALDI Mass Spectrometric Characterization of Bacterial Proteins, ***G.S. Fernando***, Southern Illinois University Carbondale (SIUC); *L.G. van Waasbergen, R.B. Timmons,* University of Texas at Arlington; *G.R. Kinsel,* Southern Illinois University Carbondale (SIUC)

Mass spectrometric characterization of bacteria is of growing importance, not only for applications in basic research but also as a means for rapid, unambiguous identification of bacterial pathogens. In this study, crude protein mixtures from cyanobacteria Synechocystis sp. strain PCC 6803 are characterized by Matrix-Assisted Laser Desorption Ionization Mass Spectrometry (MALDI-MS) following fractionation directly on the surface of pulsed RF plasma polymer modified On-Probe Affinity Capture (OPAC) MALDI probes. Pulsed RF plasma polymer deposition allows the incorporation of a wide diversity of surface chemistries and functional group densities directly on the surface of the OPAC MALDI probe, which can be subsequently used to selectively capture subpopulations of a complex protein mixture - for example, as derived from a bacterial source. OPAC protein mixture fractionation can be based on broad chemical properties (e.g. hydrophobic / hydrophilic, acid / base) or on highly bioselective interactions (e.g. metal binding properties, protein-substrate interactions). With careful optimization of the protein mixture deposition and washing procedures, fingerprint MALDI mass spectra of the bacteria proteome can be recorded which contain unique peptide and protein signature ions, not observed in the MALDI mass spectrum of the crude bacterial protein extract. The simplicity, speed and high sensitivity of the OPAC MALDI approach makes it an attractive option for bacterial proteome characterization.

BI-MoP6 Micropatterned Surface Modification of Polydimethylsiloxane via UV-Initiated Graft Polymerization of Acrylates, ***N. Patrito***, *S. Chiang, P.R. Norton,* University of Western Ontario, Canada; *N.O. Petersen,* National Institute for Nanotechnology, Canada

Polydimethylsiloxane (PDMS) is a transparent, elastic polymer that is becoming an increasingly popular substrate for the fabrication of microfluidic devices. The widespread application of PDMS-based microfluidic devices to bioanalytical research has, however, been limited by the material's extreme hydrophobicity and surface inactivity. A desire to improve the wettability and biocompatibility of PDMS has resulted in a large body of research into the surface modification of siloxane polymers. One promising method for the permanent modification of PDMS is the covalent linkage of hydrophilic polymers on its surface via UV-initiated graft polymerization (UV-GP). Combining UV-GP with photolithographic techniques, poly(acrylic acid) and poly(methacrylic acid) patterns are successfully grafted onto PDMS thin films with micron-scale fidelity. Contact angle measurements, AFM imaging, surface roughness analyses, and XPS spectra confirm the presence of the grafted layers and provide insights into their morphology and surface coverage. This report also examines the effects of the graft materials on the adhesion and proliferation of common experimental cell lines, CV-1 and A-431. AFM images illustrate the improved attachment and growth of both cell types on the PAA and PMAA patterned substrates. These observations confirm the utility of UV-GP as a means of improving PDMS biocompatibility. They also demonstrate the amenability of the UV-GP technique to precise patterning, providing researchers with an effective, efficient means of localizing bio-adhesion on a variety of substrates.

BI-MoP7 Formation of Highly Oriented Hydroxyapatite Coating by rf Thermal Plasma Spraying, ***M. Inagaki***, *Y. Yokogawa, T. Kameyama,* National Institute of Advanced Industrial Science and Technology (AIST), Japan

Hydroxyapatite (Ca@sub 10@[PO@sub 4@] @sub 6@ [OH] @sub 2@; HA) has been used for medical applications to promote the osteoconductivity of implanted materials.@footnote 1@ The HA crystal has hexagonal structure with space group of P63/m and has anisotropic properties of matter with respect to the crystallographic axis due to crystal structure of itself. Moreover, the HA crystal has two major surfaces i.e. (100) surface (a-surface) and (001) surface (c-surface) with different properties, such as protein absorption@footnote 2@ and dissolution behavior.@footnote 3@ In this study, highly oriented hydroxyapatite (HA) coatings were successfully obtained on titanium (Ti) substrates through a radio-frequency thermal plasma spraying method. XRD patterns showed that the HA coating layer had an apatite structure with (00l) preferred orientation vertical to the coating's surface. TEM observation showed that 200-800 nm-width prismatic crystals were formed in HA splats and the longitudinal axis of such prismatic crystals oriented vertical to the coating's surface. TEM images also indicate that the interface between prismatic crystals became compacted. SAD pattern show that the longitudinal axis of prismatic crystals corresponds to the (001) axis of HA. Protein absorption behavior of such a crystal oriented surface was also studied. @FootnoteText@ @footnote 1@ L. L. Hench, J. Am. Ceram. Soc., 81, (1998) 1705.@footnote 2@ T. Kawasaki, J. Chromatogr., 544, (1991) 147.@footnote 3@ H. Aoki, Surface Science, 10, (1989) 96.

BI-MoP8 Nanoscale Adhesion, Friction and Wear Studies of Biomolecules on Silicon Based Surfaces, ***D.R. Tokachichu***, *B. Bhushan, M.T. Keener, S.C. Lee,* The Ohio State University

Protein layers are deployed over the surfaces of synthetic microdevices like bioimplants and bioMEMS to facilitate biocompatibility with biological tissue. When a biosensor comes in contact with any exterior environment like tissues, or fluids with a variable pH, the biomolecules on the sensor surface may get abraded due to a change in the adhesion between the biomolecules and microdevice surface. Friction and wear properties of biomolecules (e.g. proteins) on silicon based surfaces are important because these devices come across wear and friction when they are introduced into these environments. Changes in adhesion have been studied between streptavidin and a thermally grown silica substrate in phosphate buffered saline (PBS) solution with various pH values as a function of concentration of immobilized biomolecules in solution. Wear and friction properties of streptavidin (protein) biomolecules coated on silica by direct physical adsorption and chemical linker method were studied in PBS using tapping mode AFM at a range of free amplitude voltages.

BI-MoP9 Grafting of PEG-Macromonomers to Plasma Polymers Using Ceric Ion Initiation, ***N.J. Vickers***, University of Sheffield, UK, United Kingdom; *A.G. Shard, S. Mac Neil,* University of Sheffield, UK

Bioadhesion, the adsorption of proteins, cells, or bacteria to a surface can be extremely detrimental to the performance of medical devices. Prevention of non-specific adsorption is therefore a key characteristic for many biomaterial applications and applying a non-fouling surface treatment can improve the performance of some medical devices. Poly(ethylene glycol) [PEG] is currently the most effective chemical modifier at reducing bioadhesion. Plasma polymers provide a thin, conformal base on which to graft. It is proposed that grafting PEG onto plasma polymers will confer non-fouling properties. Ceric ion initiation is commonly employed to graft polymers to natural polysaccharides e.g.

starch. The initiation is thought to proceed through oxidation of hydroxyl groups. We have investigated ceric ion initiated grafting of PEG-macromonomers to several plasma polymers. Radio frequency glow discharge plasma polymerisation of isopropanol was carried out to obtain functional surfaces containing alcohol groups. Octadiene plasma polymer surfaces were made as a control hydrocarbon. Aqueous solutions of PEG-macromonomers and cerium ammonium nitrate were combined and plasma polymer samples introduced. Characterisation was carried out via X-ray photoelectron spectroscopy [XPS]. The influence of reagent concentration, chemical nature of the plasma polymer and grafting time were investigated. The success of ceric initiated grafting was demonstrated by the presence of a chemically shifted peak in the C1s narrow scan at 286.5eV binding energy. The intensity of this peak can be directly correlated with the amount of grafted material. Both time of reaction and concentration of initator have been shown to influence the polymer graft density, whilst the plasma polymer chemistry is of paramount importance. Currently work is underway to investigate the non-fouling properties of the PEG-grafted surfaces using protein adsorption methods.

BI-MoP10 SAM-Modification of Biomaterial Surfaces as an Antimicrobial Therapy, ***R.J. Emerson***, *E.R. Soto-Villatoro, W.G. McGimpsey, T.A. Camesano,* Worcester Polytechnic Institute

Microbial infections of medical implants occur in more than 2 million surgical cases each year in the United States, increasing patient morbidity, mortality, cost and recovery time. While many methods exist to treat these infections, surgical excision of the infected device is the only certain cure. Clinically, it is of interest to determine the factors affecting microbial adhesion, the precursor to infection, and to formulate adhesion-resistant materials that are effective over protracted time periods. Self-assembled monolayers (SAMs) with a variety of terminal groups were developed and screened for antimicrobial activity. SAM molecules were bound to the surface using non-covalent metal-ligand bonds. The terminal groups of the surfaces included alkanethiols (C11 and C12), isophthalic acid (IPA), silver-containing isophthalic acid (IAG), bovine serum albumin (BSA), and tri-ethylene glycol (TEG). This methodology represents an advantage over physisorbed coatings and antimicrobial-impregnated implants, which may only prevent infection for short time periods, if at all. To screen the surfaces, single, viable bacterial cells (Staphylococcus epidermidis, Clinical isolates) were chemisorbed to the silicon cantilever of an atomic force microscope (AFM) probe, and brought into contact with the SAM surfaces. Force profiles were measured for approach and retraction interactions. IPA and IAG coatings showed promising results, since they demonstrated the lowest adhesion forces for the S. epidermidis probe.

BI-MoP11 The Effect of Solid Surface Tension on Biofilm Adhesion, ***R.A. Brizzolara***, *R.M. Lennen,* NSWC, Carderock Division

The effect of material properties on the biofouling of a surface is of great practical importance. Biofouling is a chronic and costly problem in the maritime industry as well as being a significant issue for the medical community. This study investigates the effect of solid surface tension on microbial biofilm adhesion and accumulation. The experimental approach was designed to isolate the effects of solid surface tension on the biofilm from the effects of other material properties such as elastic modulus and surface topography, as well as to isolate biofilm accumulation from biofilm adhesion. Covalently bound monolayers of organosilanes were prepared on native titanium oxide surfaces. The solid surface tension was varied through the choice of the terminal group, using hexadecyltrichlorosilane, 1H,1H,2H,2H-perfluorooctyltrichlorosilane and 3-chloropropyltrichlorosilane precursors. This resulted in surfaces with a wide range of solid surface tensions, while retaining the original topography and modulus. Monolayer deposition was verified using contact angle/solid surface tension measurements and x-ray photoelectron spectroscopy (XPS). Biofilm accumulation and adhesion measurements were performed by growing Pseudomonas fluorescens biofilms under gentle agitation (~120 RPM shaker) and performing a Bradford protein assay before and after exposing the coupons to hydrodynamic shear stresses of 3.7 N m-1 in a turbulent flow cell. It is expected that the results of this study will assist in the design of advanced coatings and surfaces by defining the optimum solid surface tension for reduced biofouling. This work was funded by the NSWC, Carderock Division In-House Laboratory Independent Research (ILIR) program.

BI-MoP13 Controlled Release of Calixarenes from Chitosan Hydrogel Coated Polymeric Surfaces as Antimicrobial Treatment of Staphylococcal Infections, *M. Vinante, C. Pederzolli, L. Pasquardini, L. Lunelli,* ***R. Canteri***, *M. Anderle,* ITC-irst, Italy*; C. Potrich, G. Viero, M. Dalla Serra,* CNR ITC, Italy*; G. Prevost, O. Joubert,* Institut de Bactériologie de la Faculté de Médecine, France

The proliferation of pathogenic microorganisms on biomaterial surfaces is one of the most widespread causes of failure of biomedical devices such as catheters, medical implants, vascular graft and joint prostheses. Staphylococcus species (e.g. aureus and epidermidis) are one of the major pathogens isolated in hospitals and are responsible for numerous nosocomial infections. Common virulence factors of these pathogenic staphylococcal strains are a group of secreted leucotoxins, which belong to the family of @beta@-barrel pore-forming toxins. They form poorly selective holes into the membrane of attacked cells, causing their lysis. We developed a local drug delivery system composed of chitosan hydrogel deposited on polymeric surfaces and loaded with hydrophilic agents, calixarenes. These molecules have been demonstrated to have an inhibitory effect on leucotoxins during pore-formation (reduction of 50% of hemolytic activity of 12 nM HlgA/HlgB on HRBC using 6 µmM of 4-sulfonic-calix(6)arene). Two different strategies of hydrogel formation are evaluated, one based upon ionic interactions between positively charged groups of chitosan chains and negative charges of calixarene molecules; the latter utilizing an homofunctional derivative polyethylene glycole as cross-linking agent (e.g. ButyrALD-PEG-ButyrALD) in order to form a permanent network with enhanced mechanical properties. These two kinds of interactions were also employed to stabilize the hydrogel film to the substrate. Data on the physical-chemical and morphological properties of the chitosan deposited hydrogel and the kinetics of calixarene release will be presented. @FootnoteText@ @footnote 1@Work supported by the P.A.T. Trento- Italy- Fondo Unico (project StaWars).

BI-MoP14 The Effect of Covalent Tethering on the Function of a Quaternary Ammonium Antimicrobial Compound, *R.A. Brizzolara,* ***D.M. Stamper***, *R.M. Lennen,* NSWC, Carderock Division

In the development of antimicrobial coatings and materials, biocidal molecules can be incorporated into a coating either as free molecules, or by covalently tethering the molecules to the coating or surface. Covalently tethering a biocidal moiety to a coating or surface has the benefit of reducing leaching of the biocide into the environment. However, the effects of covalent tethering on the biocidal activity of the molecule need to be more fully characterized. This paper reports on experiments to determine the effects of surface-immobilization on the activity of an antimicrobial molecule. Monolayers of a covalently bound organosilane containing a quaternary ammonium functional group (QAS) were used as the test platform. QAS monolayers were bound to silica surfaces and characterized by x-ray photoelectron spectroscopy (XPS). Viability of Staphylococcus aureus exposed to QAS-derivatized surfaces was measured by dilution plate counting. Control substrates derivitized with an amino-terminated silane were also included in the analysis. Flat surfaces derivatized with QAS did not possess antimicrobial activity. Results will be presented that differentiate between 1. loss of biocidal activity as a result of covalent tethering of QAS molecules versus 2. insufficient dose of antimicrobial molecules per S. aureus cell, as the cause of lack of antimicrobial activity of QAS-derivatized surfaces. It is expected this work will contribute to the development of materials and coatings with inherent antimicrobial properties and to reduced use of decontaminating solutions containing toxic chemicals. This work was funded by the NSWC, Carderock Division In-House Laboratory Independent Research (ILIR) program.

BI-MoP15 Protein Adsorption on Poly(Ethylene Glycol)-Modified Surfaces under Flow Conditions in Microfluidics Systems, ***C.J. Chun***, *K. Lenghaus,* University of Central Florida*; D.C. Henry,* Clemson University*; L. Riedel, A. Bhalkikar, J.J. Hickman,* University of Central Florida

In the last decade microfabrication technology has been used to create new microfluidics systems, bioanalytical and medical devices. The handling of relatively small amounts of analytes, at significantly lower concentrations, combined with the fact that the surface-to-volume ratio increases in direct proportion to the device size decreasing, could create potential problems in device utilization. The problem being that, the analytes or target molecules may be completely non-specifically adsorbed on the surfaces of the microdevices before they reach the detector. Thus, the basic understanding of an adsorption behavior of biomolecules@footnote 1@ on the surfaces of these systems is critical for their use in microfluidics as well as bioanalytical devices. To investigate the situation we have developed assays@footnote 2@ to evaluate protein

adsorption under flow and static conditions at submonolayer coverages on poly(ethylene glycol) (PEG)-modified surfaces, which are well known to resist protein adsorption.@footnote 3@ In this study, protein adsorption onto PEG-modified microcapillary surfaces, under flow conditions, has been determined at different flow rates as well as various protein concentrations. Alkaline phosphatase and horseradish peroxidase were used to evaluate proteins adsorption behavior, which although low, was still significant. The flow rate was also seen to affect the protein adsorption on the PEG-modified-surfaces. Simulation studies of the protein adsorption behavior are also being used to help in the development of new biocompatible microfluidics systems.@footnote 4@. @FootnoteText@ @footnote 1@K. Nakanishi, T. Sakiyama, and K. Imamura, J.Biosci.Bioeng., 91, 233 (2001). @footnote 2@K. Lenghaus, J.W. Dale, J.C. Henderson, D.C. Henry, E.R. Loghin, and J.J. Hickman, Langmuir, 19, 5971 (2003). @footnote 3@M. Zhang, T. Desai, and M. Ferrari, Biomaterials, 19, 953 (1998). @footnote 4@J. Jenkins, B. Prabhakarpandian, K. Lenghaus, J.J. Hickman, and S. Sundaram, Anal.Biochem., 331, 207 (2004).

BI-MoP16 Materials Characterization for Blood-Flow Dynamics and Platelet-Adhesion Simulation of Hematocompatible Plasma-Polymerized Tetraglyme Surfaces, ***E. Hanley***, *J.L. Shohet, J.L. Lauer, R.M. Albrecht, S. Esnault, J.S. Malter, R.H. Blick, H.S. Kim,* University of Wisconsin-Madison*; U. von Andrian,* Harvard Medical School*; S.B. Shohet,* University of California, San Francisco

The realization of small-scale biomedical devices will be closely related to the non-fouling/biocompatible properties of the exposed surfaces and the uniformity of the surface treatment throughout the device. Thrombus formation and embolization are significant problems for blood-contacting biomedical devices which often begin with platelet adhesion. In this work, we explore plasma polymerization (PP) to improve the hematocompatibility of silicon-based surfaces and the process conditions necessary to develop a uniform PP coating on the lumenal surface of artificial blood vessels. To minimize these effects, plasma-polymerized tetraglyme was deposited on flat Si@sub 3@N@sub 4@ and SiO@sub 2@ samples to produce a PEO-like surface coating. The dynamics of platelets can be modeled using a numerical simulation of adhesive particles interacting with an adhesive surface.@footnote 1@ Experimentally, emitted light from the plasma during the PP process was fed into a monochromator. Coating thickness and chemical composition of the surfaces was measured using ellipsometry and XPS, respectively. Contact-angle measurements were carried out on the PP surfaces. An atomic force microscope was used to determine the surface topology of the coated PP surface. To test platelet adhesion, the PP surfaces were exposed to heparinized human blood. After blood exposure, a scanning electron microscope was utilized to assess the density of adhering platelets on the PP surfaces. The plasma-treated surfaces showed fewer blood adherents than the untreated surfaces. The simulation can include the surface topology as measured by the AFM. By suitably modifying the plasma parameters, the plasma-polymerization treatment can be optimized with the eventual goal of producing biocompatible, small-diameter (< 5 mm ID) artificial blood vessels that contain integrated sensor systems. @FootnoteText@ @footnote 1@M.R. King and D.A. Hammer, Biophys. J. v.81, 799-813 (2001).

BI-MoP17 Studies of Protein Interactions with CaP Surfaces Using XPS and ToF-SIMS, *C. Mendoza-Barrera, H.E. Canavan, R. Michel,* ***D.G. Castner***, University of Washington

Proteins directly control the nucleation and growth of biominerals, but the details of molecular recognition at the protein-biomineral interface remain poorly understood. The elucidation of recognition mechanisms at this interface may provide design principles for advanced materials development in bone replacement. In this work, we characterize the interactions of proteins with the principal calcium phosphate components of bone. Using X-ray diffraction (XRD), we characterized the purity and phases of hydroxyapatite (HAp), dibasic calcium phosphate dihydrate (DCPD), dibasic calcium phosphate (DCP), @beta@ tribasic calcium phosphate (@beta@-TCP) and monbasic calcium phosphate (MCP). Next, adsorption isotherms of different proteins (e.g. BSA and fibrinogen) were performed on each calcium phosphate substrate. In this way, the solution concentrations necessary to produce sub-monolayer and monolayer thicknesses of each protei n was determined via X-ray photoelectron spectroscopy (XPS). As the conformation of proteins is greatly influenced by their density on a surface, we next used time-of-flight secondary ion mass spectrometry (ToF-SIMS) to compare the comformation of different protein layers adsorbed on the different calcium phosphate substrates. Finally, we discuss the effect of protein identity, conformation, and the character of the calcium phosphate substrate have on protein adsorption.

BI-MoP18 Syntheses of Polymer-Protein Composites by Plasma-Spinning Deposition, ***R. Ohta***, *N. Saito, O. Takai,* Nagoya University, Japan

Blood and/or tissue contacting biomaterials as catheters, artificial blood vessels and artificial valves are desired to have higher biocompatibilities in the medical field. Therefore, polymer-protein composites, which are expected to have excellent biocompatible surfaces, have been attracting attentions of many researchers. In this research, we aimed to synthesize polymer-protein composites by plasma-spinning deposition (PSD). In the PSD, the polymer composites were synthesized from precursor solutions. The precursor solutions were filled in a metallic capillary tube. Plasma were produced by applying voltages to the capillary tube. The polymer composites were synthesized on substrates from the precursors, which passed through the plasma. Two different processes were examined to synthesize the polymer-protein composites: (i) PSD of the polymer-protein composites from mixed solvents of the precursor polymers and proteins, and (ii) immobilization of proteins to the polymers synthesized by the PSD. Polyethylene terephthalate (PET), polyurethane (PU) and polyacrylonitrile (PAN) were used as precursor polymers. Proteins as fibrinogen, heparin and albumin were contained into the polymer composites. The PSD process was optimized by varying the concentrations of the polymers and proteins in the precursor solutions and by controlling the plasma states during the PSD. The chemical structures of the polymer-protein composites were analyzed by spectroscopic methods as X-ray photoelectron spectroscopy (XPS), Fourier transform infrared spectroscopy (FT-IR), Raman spectroscopy (RS), etc. The surface characteristics of the polymer-protein composites were investigated by scanning electron microscope (SEM), atomic force microscope (AFM), etc.

BI-MoP19 Alginate Adsorption to Charged Surfaces: The Importance of Protein Co-Adsorption, ***N. Chandhok***, *K.T. Queeney,* Smith College

The adhesion of extracellular bioploymers, including polysaccharides and proteins, to solid surfaces is a critical step in biofilm formation. It has been shown previously that alginate, a charged polysaccharide, will adhere to amine-terminated surfaces,@footnote 1@ and that the presence of a protein conditioning film can enhance alginate adsorption.@footnote 2@ We have used surface infrared spectroscopy to examine the adsorption behavior of alginate and find that protein co-adsorption is in fact essential for adhesion of this negatively charged polymer even to positively-charged surfaces. Specifically, the co-adsorption of protein impurities, which are present in quantities less than 50 ng/mL, is seen in all cases of alginate adsorption. When these impurities are filtered out by adsorption to high surface area MgO, no alginate adsorption is detected. Exposure of purified alginate solutions to protein conditioning films prepared from specific, known proteins is used to identify the critical polysaccharide/protein interactions that favor biofilm formation. @FootnoteText@ @footnote 1@R. Dhamodharan and T. J. McCarthy, Macromolecules 1999, 32, 4106-4112.@footnote 2@P. A. Suci and G. G. Geesey, J. Coll. Interface Sci. 1995, 172, 347-357.

BI-MoP21 Prediction of Protein-Surface Interactions by All-Atom Molecular Dynamics Simulations Using Implicit Solvation, ***Y. Sun***, *F. Wang, R.A. Latour,* Clemson University

The orientations and conformations of adsorbed proteins on biomaterials surfaces have profound influences on their bioactivities. However, it's very difficult to resolve the structures of adsorbed proteins experimentally. Empirical force field-based molecular simulation can be used to complement experimental studies to investigate protein adsorption behavior and potentially provide a more detailed understanding of molecular-level interactions. The predictive power of such an approach is largely dependent on the accuracy of the underlying force field used and the adequacy of sampling in the simulation. The objective of this study is thus to develop an empirical force field method with enhanced sampling to enable protein adsorption to be accurately simulated. We are evaluating the use of a generalized Born-based analytical continuum electrostatics (ACE) implicit solvent model for the purpose of enabling protein adsorption to be simulated with solvation effects treated implicitly. To further enhance sampling, replica-exchange molecular dynamics (REMD) is employed in combination with ACE to predict the equilibrium structures of a model protein (lysozyme) on alkanethiol self-assembled monolayer (SAM) surfaces. We have determined that ACE predicts reasonable energy-distance relationships of mid-chain peptide residues on functionalized SAM surfaces; it also predicts reasonable and stable trajectories of native lysozyme structure and significant surface-induced conformational changes

of lysozyme on SAM surfaces. Qualitative agreement between model predictions and experimental observations has been established, and further studies for model validation are planned.

BI-MoP22 Role of the Chemical and Morphological Surface Properties in Platelet Binding and Protein Adsorption to Biomaterial Surfaces, *S. Forti, M. Vinante, L. Pasquardini, L. Lunelli, L. Vanzetti, R. Canteri, C. Pederzolli,* ***M. Anderle,*** ITC-irst, Italy*; S. Pascale,* Sorin Biomedica Cardio S.p.A, Saluggia (VC), Italy*; G. Rossetti,* S. Chiara Hospital, Italy

Many existing medical implants are associated with poor interfacial biocompatibility. An example is represented by the cardiovascular devices; their implantation induces a complex blood-material interaction, often leading to thrombus formation. This work describes the characterization of the protein layer and the process of platelets adhesion on four different materials (Sorin pyrolytic carbon (PyC), two different types of polystyrene and titanium alloy) after contact with human platelet poor plasma and platelet rich plasma in static conditions. Total protein quantification on eluted samples revealed that PyC adsorbed the lowest amount of plasma proteins. Using immunofluorescence microscopy specific proteins promoting platelets adhesion were characterized on PyC and titanium alloy: fibronectin was found to be present at very low levels on both surfaces while fibrinogen and von Willebrand factor adhered to PyC in a higher proportion. Adherent platelets and shape categories distribution were quantified using scanning electron microscopy (SEM) and atomic force microscopy (AFM). PyC induced less adhesion with mostly weak activated platelets, however aggregates may be present. Titanium alloy promoted a higher adhesion, with more active platelets but less cohesive. Polystyrene materials were almost covered by spread platelets. Material surface properties were evaluated by contact angle, electron spectroscopy for chemical analysis (ESCA), secondary ion mass spectrometry (SIMS) and atomic force microscopy (AFM). The final goal will be to correlate the biological response with surface morphological and physico-chemical properties of the materials.@footnote 1@ @FootnoteText@ @footnote 1@Supported by the Provincia Autonoma di Trento, post-doc project Emosurf and by National Department of Health.

BI-MoP23 Adsorption of Human Serum Albumin on Carbon Nitride Films Studied with in-situ Ellipsometry, ***T. Berlind,*** *M. Poksinski, L. Hultman, P. Tengvall, H. Arwin,* Linköping University, Sweden

Carbon based materials have received considerable attention during the last decades due to their interesting tribological, electronic and optical properties. So far not much effort has been put into the investigation of the use of these materials in biotechnology. The objective with this study is to investigate the interaction of carbon and carbon nitride surfaces with proteins. Carbon nitride (CN@sub x@) and amorphous carbon (a-C) thin films were deposited on silicon substrates by reactive sputtering. By changing sputtering parameters the microstructure can be controlled and amorphous, graphitic and fullerene-like films were grown to a thickness of 200 nm. Prior to protein adsorption, the three structures of CN@sub x@ films and the a-C films were optically characterized with spectroscopic ellipsometry in the wavelength range 350-1700 nm and with infrared ellipsometry in the range 2-30 µm to determine their complex-valued refractive index N=n+ik. Contact angles for the films were measured with water. The films were exposed to human serum albumin and the adsorption was monitored in-situ using dynamic ellipsometry. From the ellipsometric data the adsorbed amount of proteins was quantified in terms of surface mass density using de Feijters model. The protein layer index was described with a Cauchy model. The results indicate larger adsorption of protein onto the amorphous films compared to the films with more ordered structure.

BI-MoP24 Infrared Spectra of Serum Albumin Immobilized in Porous Alumina, ***L.G. Castro,*** *S. Sarkar, D.W. Thompson, J.A. Woollam,* University of Nebraska-Lincoln

While most studies of protein-surface interactions rely on chemistry to obtain specific information about what proteins are present, infrared absorption spectra also contain protein-specific features. Reliable measurement of these spectra could, for example, help identify nonspecific binding. Here porous alumina was used as a capture matrix to increase the detectability of protein infrared spectra. Layers of porous alumina were fabricated electrochemically and fully characterized using visible and mid-infrared (mid-IR) spectroscopic ellipsometry (SE). Pore sizes and center-to-center spacings were engineered to efficiently capture human serum albumin (HSA). The layers were exposed to solutions of HSA in an acetate buffer. The incorporation of the proteins into the matrix was monitored by multiwavelength visible SE. The samples were characterized before and after protein attachment with mid-IR SE. A methodology was developed to obtain the infrared dielectric function @epsilon@ of the adsorbed proteins. Full optical modelling was essential to separate the protein peak signatures from those of the alumina. Strategies to improve capture efficiency and reduce uncertainty of the @epsilon@ spectrum are discussed.

BI-MoP25 Vacuum UV to Mid-Infrared Optical Study of Immunoglobulin G Attachment to Chemical Modifications of Chitosan, ***W.H. Nosal,*** *S. Sarkar, D.W. Thompson, A. Subramanian, J.A. Woollam,* University of Nebraska-Lincoln

Optical constants of spin-cast chitosan films were determined from vacuum-ultraviolet (VUV) to mid-infrared (130 nm to 30 microns). Both pure and chemically modified chitosan films were studied using spectroscopic ellipsometry (SE). Chemical modification by attachment to the amine group in chitosan was performed using 1,2 Epoxy-3-phenoxy-propane, commonly known as glycidyl phenyl ether (GPE), to produce a hydrophobic surface. A similar modification with succinic anhydride yields a hydrophilic surface. Quantitative lineshape analysis of the optical constant spectra was performed using Lorentzian and Gaussian line-shapes, including anisotropic response due to molecular-bond orientations in-plane and out-of-plane. Dynamic in situ visible SE has been used to study the attachment of immunoglobulin G to each modified surface type (hydrophobic/hydrophilic), followed by VUV to mid-infrared ex situ SE optical analysis. Research supported by U. S. Army contract # W911NF-04-2-0011, and the College of Engineering, University of Nebraska.

BI-MoP26 Effects of Fluorescent Dyes on the Structure of Lipid Membranes, ***J.J. Heetderks,*** *P.S. Weiss,* Penn State University

Cell membranes are complex, dynamic mixtures of lipids, proteins, and cholesterol; their precise mode of molecular organization is unknown. Transient associations of molecules form â?olipid raftsâ? in active cells that may affect membrane-associated protein activity. One model to study the lipid component of these molecular interactions is the giant unilamellar vesicle (GUV). The lipids, without contribution from membrane proteins, cytoskeletal structures, cholesterol, or outside forces, form domains in GUVs when the conditions are within an appropriate range of the multi-dimensional phase diagram of lipid composition and temperature. Fluorescently labeled phospholipids and lipid analogues are used at low concentrations to visualize the vesicles and domains, and are found to influence measured membrane properties, even at concentrations below those typically used in structural studies. Through basic membrane organization measurements, we determine the effects on the vesicle properties for which the labeling is responsible. We incorporate varying amounts of fluorescent dyes into 2-phase vesicles and find clear divisions of gel and fluid domains at room temperature. The temperature is then slowly raised while monitoring the membrane domains until the domains melt into one homogeneous phase. Preliminary results show that the incorporation of several common fluorescent labels in the membrane cause measurable changes in the demixing temperatures of the two-phase vesicles at less than one percent dye concentration.

BI-MoP27 Cell Adhesion of Plasma Polymerized Allylamine Coating on Polymeric Substrates, ***S.R. Kim,*** Chungju National University, South Korea

RF plasma enhanced chemical deposition was used to get biocompatible coating on polymeric substrates with various processing conditions, such as input power, monomer/oxygen feed ratio, modulated frequency and duty cycle. Allylamine was used as feed monomer and oxygen was used as mixing gas. Input power was varied from 50 to 300 Watt. Deposition rate was 16 nm/min. Chemical bonding information of deposited film by FTIR-ATR showed peak broadening compared to the allylamine monomer and C=N stretching peak near 2200 cm@super -1@ appeared for polymerized coating. Contact angle was changed from 88° for untreated polystyrene to 30° for treated polystyrene without oxygen input. Contact angle of plasma polymerized allylamine coating obtained with oxygen input was 8°. Untreated polystyrene film had rough surfaces and the average roughness was 10.91 nm, however, the plasma coating deposited polystyrene with introduction of oxygen, the roughness decreased to 3.91 nm and it decreased to 1.98 nm without oxygen input. ESCA showed N/C ratio of 13.4, 4.36 for samples prepared with oxygen input and without oxygen, respectively. Fibroblast cell was used and MTT assay was done. Cell viability 4 days after seeding was decreased as amount of oxygen increased.

BI-MoP28 Controlled Passive Transport through a Cellular Mimetic Membrane Consisting of a Stochastic Array of SiO2-coated Vertically Aligned Carbon Nanofibers, ***J.D. Fowlkes***, The University of Tennessee, Knoxville, US; *B.L. Fletcher, E.D. Hullander, M.L. Simpson, A.V. Melechko,* The University of Tennessee, Knoxville; *M.J. Doktycz,* Oak Ridge National Laboratory

A cell mimic device has been fabricated for the purpose of mimicking and interfacing to biological processes at the molecular scale. The design of the device addresses the challenge of fabricating and filling small physical volume enclosed membrane structures. The device has the additional advantage of being totally synthetic. The feasibility of using vertically aligned carbon nanofibers (VACNF) as the semi-permeable membrane component of the cell mimic device has been successfully verified by demonstrating the controlled and size-selective transport of nanoscale species by the VACNF membrane. To date, the controlled delivery and containment of picoliter volumes to individual cells has been achieved and the efficacy of the semi-permeable membrane component of the cell mimic to mediate passive diffusion transport has been evaluated. We report here the identification of discrete regimes of membrane transport behavior based on the ability to tailor nanoscale aspects of the membrane pore by controlled oxide deposition. VACNF based membrane elements that are stochastically prepared exhibit a strong statistical nature on the nanoscale. Stochastic features are preferable over patterned ones in terms of reduced fabrication complexity but exhibit statistical deviations that lead to properties that are difficult to predict. We have created a Monte Carlo based simulation to replicate and simulate the stochastic nature of the VACNF membrane and the passive diffusion through the membrane, respectively. The simulation was found to correlate strongly with experimental results. These predictive capabilities help facilitate device design and reduce the number of experimental characterizations. Further, the results reported here implicate stochastic, statistical nanoscale structures as realistic components in integrated devices with stringent requirements on discrete and reproducible behavior.

BI-MoP29 Calcium Ion Free Supported Lipid Bilayer Formation by Giant Vesicle Fusions, ***Y.-H. Kim***, *Md. Rahman,* The Graduate University for Advanced Studies, Japan; *R. Tero, T. Urisu,* Institute for Molecular Science , NINS, Japan

Supported membranes are the lipid bilayers supported on the solid substrate, which are commonly used as a model membrane for the in vitro study of the fundamental properties of biological membranes and various biotechnological applications. We have investigated the effect of the electrostatic attractive force between vesicles and the surface on the supported lipid bilayer formation using atomic force microscopy (AFM) and fluorescence microscopy. In most of the lipid bilayer formation by vesicle fusion, Ca@super 2+@ are added to the vesicle suspensions to induce the rupture of the vesicle. The lipid bilayer formation under the Ca@super 2+@ free is required in such cases of the study of Ca@super 2+@ effects on the membrane surface reactions. When the bare SiO@sub 2@ surface was incubated in the suspension of the negatively charged giant vesicle without Ca@super 2+@, extremely low surface coverage of lipid bilayer was observed due to the surface-vesicle charge repulsion. while, high coverage of lipid bilayer was observed when Ca@super 2+@(final concentration 5 mM) was added before incubation. The remarkable difference in the coverage of the lipid bilayer on the SiO@sub 2@ surface according to the existence of calcium ion can be explained in terms of the adsorption of giant vesicles. As to the formation of the lipid bilayer, the adsorption is the initial step, and therefore a stable and strong adsorption is necessary to form high coverage of the lipid bilayer. In case of the positively charged surface modified by Aminoproplydimethylethoxysilane, the high surface coverage of the lipid bilayer was obtained without adding Ca@super 2+@. The strong electrostatic attractive force between vesicles and the surface of opposite charge enhances the stable adsorption of negatively charged giant vesicles, which promotes the lipid bilayer formation. The control of the surface and the vesicle charge is an important factor to make a supported lipid bilayer without calcium ion.

BI-MoP30 ToF-SIMS Chemical Imaging Analysis of Micropatterned Streptavidin and Cells without Labeling, ***T.G. Lee***, Korea Research Institute of Standards and Science (KRISS), Korea; *H.K. Shon,* Korea Research Institute of Standards and Science (KRISS); *K.-B. Lee,* Korea Advanced Institute Science and Technology (KAIST); *J. Kim,* Sungkyunkwan University, Korea; *J.C. Lee,* Samsung Advanced Institute of Technology (SAIT), Korea; *I.S. Choi,* Korea Advanced Institute Science and Technology (KAIST); *D.W. Moon,* Korea Research Institute of Standards and Science (KRISS)

In this work, three different analysis ion beams (Ga@super +@, Au@super +@ and Au@sub 3@@super +@) were used to obtain label-free time-of-flight secondary ion mass spectrometry (ToF-SIMS) chemical images of microcontact printed streptavidin. The image of total ions obtained by an Au@sub 3@@super +@ primary ion beam corresponded well to the real image of micropatterned streptavidin, whereas the total-ions image by Ga@super +@ or Au@super +@ primary ion beams did not. A principal component analysis (PCA) of ToF-SIMS data was initially performed to identify characteristic secondary ions of streptavidin. Chemical images of each characteristic ion were reconstructed from raw data and used for the 2nd PCA run, which resulted in a contrasted, and corrected, image of micropatterned streptavidin by Ga@super +@ and Au@super +@ ion beams. This suggests that ToF-SIMS imaging along with multivariate data analysis would be an effectual method of obtaining label-free chemical images of patterned proteins or biomolecules. Label-free chemical images of micropatterned A431 cells were obtained by using the same procedure.

BI-MoP31 Effects of Surface Topography, Chemistry and Wettability on Osteoblast Cell Adhesion and Mineralization on Sol-Gel-Derived Titanium Alloy, ***M.C. Advincula***, *E.T. Ada, F.G. Rahemtulla,* University of Alabama at Birmingham; *R.C. Advincula,* University of Houston; *S.L. Bellis, J.E. Lemons,* University of Alabama at Birmingham

The biological events occurring at the bone-implant interface are influenced by the topography, chemistry and wettability of the implant surface.The surface properties of titanium alloy Ti6Al4V prepared by surface sol-gel processing (SSP) were investigated systematically using x-ray photoelectron spectroscopy, scanning electron microscopy, atomic force microscopy and contact angle metrology. Biocompatibility of the oxide was assessed by evaluating MC3T3 osteoblastic cell adhesion to the substrate, as well as by matrix mineralization. The sol-gel coated surface had predominantly a TiO@sub 2@ composition with abundant hydroxyl OH-groups, and was highly wettable, with increased roughness and porosity. Significantly more cells adhered to the sol-gel, as compared with passivated surfaces, at 1 and 24 hours following cell seeding, and a markedly greater number of bone nodules were observed on sol gel coatings. Favorable cellular responses were attributed to the rougher porous surface, hydrophilicity and increased hydroxyl group content of the sol gel, properties which, in turn, are known to regulate the adsorption of pro-adhesive serum proteins onto material surfaces.Collectively our results show that surface properties of titanium alloy can be modified by SSP to further enhance the bioactivity of this biomaterial.

BI-MoP33 Electrical Monitoring of Cell Interaction on a Microelectronic Interface, *H.D. Wanzenboeck,* ***K. Dominizi***, *P. Hagl, E. Bertagnolli,* Vienna University of Technology, Austria; *E. Bogner, F. Gabor, M. Wirth,* University Vienna, Austria

*****PLEASE NOTE: YOU MUST IDENTIFY A DIFFERENT PRESENTER FOR THIS ABSTRACT. YOU MAY ONLY PRESENT ONE (1) PAPER AT THE CONFERENCE*****The electrical measurement of tissue properties and of cell signals has gained increased interest for ceel-based biosensor applications in medicine, pharmacology and biology. Yet, the interaction of living cells on solid sensor surfaces has not been thoroughly investigated. For application mainly microelectronic sensors are attractive due to the small size and the low cost in mass production. The objective of this work was to investigate the interaction of living human cells with microelectronic surfaces. We have performed a comprehensive study of the cells behaviour on semiconductors, metals and dielectric materials commonly used in microelectronics. Human ephitelal cells (Caco-2) were grown in-vitro on the surface of the microelectronic substrates. In a second step we have systematically varied the geometry of the surface by etching trenches with a width from 2 up to 60 µm and a depth of 2 to 30 µm into a biocompatible substrate. The growth of ephitelial cells on flat and on ridged surfaces was compared. The response of the cell behaviour on the varying surface was investigated by optical, electronoptical, enzymatic and biochemical methods. The effects of surface alterations on the proliferation rate, the cell adhesion, the cell coverage and the differentiation of cells was investigated. Finally, a microelectrode structure with microelectrodes (2x2 µm2) smaller than a single cell was implemented on the previously

investigated surfaces. The electrical properties of the cell layer and of single cells could be evaluated by impedance spectroscopy. Differences of the impedance were monitored during progressing aging of cells. The interpretation of the interrelated analysis results shines a new light on the interaction of living cells with sensor interfaces. The feasibility to identify changes of the cell-surface interaction by electrical measurements was successfully demonstrated.

BI-MoP35 Fabrication of a Polyallylamine-Based, Label-Free Piezoelectric Biosensor Platform, ***A. Papadopoulou-Bouraoui***, *F. Bretagnol, M. Lejeune, A. Valsesia, J. Barrero-Moreno, D. Gilliland, G. Ceccone, F. Rossi,* European Commission-Joint Research Centre, Italy

The Quartz-Crystal Microbalance (QCM) is a sensitive acoustic technique allowing the measurement of resonance frequency changes occurring due to changes in the total oscillating mass of the crystal. It operates as a highly sensitive weighing device. The aim of the present study was to use active amino groups provided through plasma deposition of an allylamine polymer film (PALL) towards further antibody immobilization. Two antibody immobilization routes were investigated. The first involved the use of glutaraldehyde as a crosslinker, followed by protein A (PA) or protein G (PG) for optimal antibody orientation and consecutively highly sensitive antibody-antigen interaction. The second involved the use nanometer-sized gold (20 nm) particles in combination with PA or PG. PALL films were deposited in a capacitively coupled plasma reactor onto the SiO2 covered surface of the quartz crystal and were completely characterized before antibody immobilisation. The active amino groups were quantified through evaluation of the X-Ray Photoelectron Spectroscopy (XPS) C1S high-resolution spectra of the trifluoromethylbenzaldehyde derivative. Evaluation of the stability and reactivity of all main intermediate steps was performed using the QCM in combination with other surface characterization techniques such as the Ellipsometry, Atomic Force Microscopy (AFM), Time-of-Flight Secondary Ion Mass Spectrometry and XPS. Results from this work show the possibility of producing simple, direct piezoelectric immunoprobes through appropriate antibody orientation, using PA or PG, or surface increase, using GNP, without the need for labeled compounds. The combination of surface analytical, optical and mass balance techniques is confirming the effectiveness of these immunosensor fabrication strategies. This fully characterized biosensor platform has been tested for the detection of a food allergen, ovalbumin.

BI-MoP36 Formation of Carbohydrate Microarrays with the MAPL Technique for the Detection of Specific Interactions, ***K. Barth***, *G. Coullerez, M. Textor,* ETH Zurich, Switzerland

Carbohydrates play an important role in many biological processes, like cell-cell and cell-pathogen recognition.@footnote 1@ Because of missing analytic tools there is until now little known about the role of carbohydrates in these processes. Therefore it exists a need for methods that allow high throughput screening of these specific interactions.@footnote 2@ We have newly developed a method to covalently graft mono-, di- and trimannosides to the polycationic copolymer poly(L-lysine)-graft-poly(ethylene glycol) (PLL-[g]-PEG). With this system it is possible to tailor the density and distribution of the immobilized mannosides on the polymer backbone. While spontaneously adsorbed on negatively charged oxides surfaces (Nb @sub 2@O@sub 5@, TiO@sub 2@) the copolymers show specific lectin and bacteria recognition. Furthermore we could demonstrate the dependence of the carbohydrate surface density for the interactions between the mannoside and the multivalent model systems Concanavalin A (Con A) or Escherichia coli (E. coli). This was done with methods like Optical Waveguide Lightmode Spectroscopy where no additional labeling is required. In order to develop arrays, we propose herein to combine this chemical approach with the patterning method MAPL (Molecular assembly pattering by lift-off) developed by Falconnet et al.@footnote 3@ This technique combines photolithography and the attribute of functionalized PLL-[g]-PEG to form uniform layers on many metal oxide surfaces. We are able to control the pattern geometry and size as well as the surface density of the mannosides in the adhesive patterns. Fluorescent labeled Con A and E. coli can be easily detected and is proofing the high specificity of the developed system with a non fouling background. @FootnoteText@ @footnote 1@ Sharon et al., Sci. Am. 1993, 268, 82.@footnote 2@ Seeberger et al., ChemBioChem 2004, 5, 1375.@footnote 3@ Falconnet et al., Nano Letters, 2004, 4, 1909.

BI-MoP37 Combinatorial Characterization of Geometric Effects on the Optical Properties of Gold Nanostructures for Biosensors Optimization, ***G. Nusz***, *A. Curry, A. Wax, A. Chilkoti,* Duke University

Optimizing the performance of nanoparticle optical biosensors requires design of nanostructures that exhibit the greatest change in their extinction spectrum upon receptor-analyte binding. Previous studies have suggested that highly anisotropic nanostructures that exhibit geometric asperities are likely to provide enhanced sensitivity compared to isotropic particles. Unfortunately, the optical sensitivities for nanostructures with complex shapes must be determined experimentally because current theoretical modeling and computer simulation methods for complex geometries are computationally intensive and time-consuming. Thus, a combinatorial experimental approach that allows the rapid and high-throughput optical characterization of many structures of different size and shapes is desirable to rapidly optimize the design of such nanobiosensors. As proof-of-principle of this high-throughput optimization approach, arrays of nanostructures with varying geometries with minimal dimensions of 60 nm were fabricated on glass substrates by electron beam lithography. Scattering spectra were collected with a grating spectrometer simultaneously from several nanostructure configurations on a customized Zeiss Axiovert 200 under darkfield illumination. The characterization of the geometric dependence of the optical properties of the gold nanostructures could be experimentally determined in single snapshot mode at the individual nanoparticle level using this set-up. Studies on the optical sensitivity of these nanostructures in response to perturbation of their local refractive index are currently in progress.

BI-MoP38 Sensitivity Enhanced Biosensor by Prussian Blue Modified Electrode, ***I.J. Yi***, *J.H. Kim, C.J. Kang, Y.S. Kim,* Myongji University, Korea

We propose a sensitivity enhanced biosensor by Prussian blue (PB) modified indium tin oxide (ITO) electrode. A PB film plays a significant role of electron-transfer. Capillary electrophoresis (CE) and amperometric method were adapted to our work. Microchip was fabricated with polydimethylsiloxane (PDMS) to form microchannels and ITO patterned glass in inexpensive and simple method. The PB film was electrodeposited on the working electrode of various conditions to obtain stable PB film. Atomic force microscopy (AFM) was used to observe the changes of PB film surface. Calibrated PB film deposition voltage and time were obtained by AFM topography which shows PB surface characteristics. The optimized thickness of stable PB film was obtained when deposition voltage was about 0.1 V for 3 min. We detected various concentrations of neurotransmitters (dopamine and catechol) and hydrogen peroxide which is for detecting glucose respectively. It is observed that there was 20 times higher peak current for PB/ITO electrode than that for previously reported ECDs using bare-ITO electrode.@footnote 1@ Results are indicating rapid separation and detection of the analytes. The measured peaks of dopamine, catechol and hydrogen peroxide were proportional to their concentrations. When PB-modified electrode was used, the sensitivity was improved compared with bare-ITO electrode. It is believed that the PB film can be a viable candidate for a disposable and sensitive biosensor. @FootnoteText@ @footnote 1@Ju-Ho Kim, C. J. Kang, and Yong-Sang Kim, "A Development of a Microfabricated Disposable Microchip with a Capillary Electrophoresis and Integrated Three-Electrode Electrochemical Detection", Biosensors & Bioelectronics, vol.20, no.11, p.2314-2317, (2005).

BI-MoP39 Organosilane SAMs as a Platform to Tune the Immunosensor Performances, ***R. De Palma***, IMEC vzw, Belgium*; S. Peeters,* KULeuven, Belgium*; K. Jans, K. Bonroy,* IMEC vzw, Belgium*; S. Cappelle,* Cytec Surface Specialities, Belgium*; G. Reekmans, W. Laureyn, G. Borghs, C. Van Hoof,* IMEC vzw, Belgium*; G. Maes,* KULeuven, Belgium

A central requirement in the modification of immunosensor interfaces with biological receptors is to tether the biomolecule of interest covalently and in a well-controlled geometry. A key issue in the design of these sensors involves the development of a sensitive, specific, reproducible and tunable biological interface. Self-assembly of silanes is commonly used as an effective surface modification tool in micro-array applications. However, most silanes used for micro-array are optimized towards DNA applications. Using quartz crystal microbalance (QCM-D), we have shown that the use of these silanes for immunosensing leads to inadequate characteristics, i.e. low sensitivity and specificity. Here we report on the enhanced immunosensing performances of novel preactivated silane SAMs. These preactivated functions allow for the direct coupling of receptors, thereby increasing the amount of immobilized antibodies. Using these preactivated silanes, the antibody immobilization was found to be reproducible, straightforward and controllable and the activity of the immobilized

receptors was retained. Due to the molecular architecture of these silanes, the sensitivity, detection limit and specificity increased significantly. The degree of non-specific adsorption could be tuned by using appropriate blocking agents. Furthermore, a synthesis route was developed to create PEG-modified preactivated silanes. Deposition of these silanes in mixed silane SAMs allows for the creation of tunable immunosensing platforms. The silane-based interfaces were also compared to the well-known system of mixed thiol SAMs. The molecular architecture of all deposited silane SAMs was studied using contact angle, XPS, cyclic voltammetry, AFM and RAIRS. A strong correlation was observed between the layer characteristics and their immunosensing properties. Our approach based on preactivated silane SAMs guarantees a tunable and versatile platform for surface engineering in biosensing and micro-arrays.

BI-MoP40 In Situ Optical Characterization of an Electrodeposited Biopolymer Film, ***S.B. Beatty***, *J.J. Park, E.C. Dreyer, G.W. Rubloff,* University of Maryland

We have previously demonstrated spatially selective, voltage-programmable deposition of the polysaccharide chitosan onto patterned electrodes in low pH solution. We have previously shown that chitosan, an amine rich biopolymer, serves as a useful platform for coupling and conjugation of biomolecules as well as a platform for bioassays and enzymatic catalysis. We have developed an optical reflectivity technique for real-time, in-situ monitoring of the electrodeposition process, demonstrated in a combinatorial deposition cell in concert with real-time electrical (current, voltage) and environmental (pH, temperature) measurements. A beam splitter separates a HeNe laser beam into a reference beam and an incident beam onto the electrodeposition surface in solution. A chopper separates the reflected beam from the surface and the reference beam in time, while both impinge on the same reversed bias Si photodetector. The resulting signal is analyzed to extract the ratio of reflected to reference beam intensities, averaged over an appropriate portion of the chopper period, providing a real-time measure of the reflectivity. Chitosan deposition on the Au electrode decreases reflectivity by about 16% for 1 micron chitosan thickness, with noise levels suggesting a thickness sensitivity of 60nm. Film growth rates vary with current density as seen in reflectivity and confirmed by ex-situ post-process characterization using profilometry and AFM. The reflectivity indicates three stages in chitosan film growth. We plan to extend the technique for use in a confocal optical microscope so that dynamic behavior at active bioreaction sites in a microfluidic network can be monitored.

BI-MoP41 Nano-mechanical and Chemical Mapping Showing Remineralization of Incipient Carious Lesions in Human Dental Enamel, ***M.E. Dickinson,*** Hysitron, Inc.*; A.B. Mann,* Rutgers, The State University of New Jersey

Human dental enamel consists of hydroxyapatite crystals arranged in a complex nano-scale prism structure. This architecture can be altered by chemical variations originating from dietary components and their interactions within the oral cavity. Temporary localized fluctuations of pH on the enamel surface create a flux of minerals into and out of the enamel which normally remains at an overall equilibrium. However, at continually low pH a net loss of mineral from the enamel results, causing the formation of an incipient carious lesion. The lesion - a stage prior to caries formation, is reversible and with specialized care such as remineralization treatments, can become arrested. Many commercial remineralization treatments use topical solutions containing fluoride and calcium phosphates to aid in caries prevention. However, the effect of these treatments at different stages of lesion progression is poorly understood. This investigation uses nanoindentation and TOF-SIMS to create high resolution mechanical and chemical maps of the lesion cross-section at different stages of demineralization. These lesions were analyzed before and after treatment with a commercial remineralization solution to study the effectiveness of remineralization at different stages of lesion progression. The results showed that the treatment acted to remineralize the lesion body for all lesions. However, the most demineralized lesions which had a different structure (no detectable surface zone), resulted in a different, possibly fluoroapatite based material being deposited at the base of the lesion with mechanical properties much higher than that of enamel. The chemical data correlated with the mechanical data to relate the structural integrity of the enamel with the change in hardness and reduced elastic modulus. Visualizing this dependence of lesion structure for efficient remineralization allows further understanding into the effectiveness of commercial dental treatments.

Applied Surface Science
Room 206 - Session AS+BI-TuM

Surface Characterization of Organic and Biological Systems

Moderator: R.T. Haasch, University of Illinois

8:20am **AS+BI-TuM1 Synthesis and Characterization of Mixed Polymer Brush Films**, ***D.J. Dyer***, *J. Feng,* Southern Illinois University*; R.T. Haasch,* University of Illinois-Urbana Champaign*; V.-N. Wong,* Southern Illinois University **INVITED**

Chameleons respond to their environment by changing color so that they take on the characteristics of their surroundings. Smart organic films may also respond to environmental perturbations and adapt to their environment. In particular, polymer brush films have shown remarkable switching properties, especially when the films are within the ultra-thin region from 1-100 nm. These so-called polymer brushes are composed of polymers that are tethered to an inorganic substrate and may stretch out away from that substrate. Polymer brushes that are composed of more than one component are referred to as mixed, or binary brushes. Typically, the two different polymers are randomly distributed on the surface and exhibit phase-separation and interfacial morphology that is distinct from that of spin-cast blends of the same composition. This occurs because the brush chains are confined to the substrate and are forced into contact with nearby incompatible chains, whereas in a blend the polymer chains can more easily rearrange during annealing. Here we discuss the synthesis and characterization of mixed polymer brushes on silicon and gold substrates. One of the major challenges we face is the quantification of the bulk film composition as compared to the air/liquid interface. For this we use a tandem XPS/RAIRS strategy. Our paper will place an emphasis on amphiphilic systems where one polymer is hydrophilic and the other is hydrophobic. These results demonstrate that a mixed brush of polystyrene (PS) and polyacrylamide (PAAM) may switch from hydrophobic to hydrophilic in one minute at room temperature. Such rapid switching is highly unusual for mixed brushes.

9:00am **AS+BI-TuM3 Characterization of a Chemically Passivated GaAs Based Sensor Device in Air and Electrolytes**, *S.M. Luber,* Walter Schottky Institut, TU Muenchen, Germany*; D. Gassull,* TU Muenchen, Germany*; D. Schuh,* Universitaet Regensburg, Germany*; M. Tanaka,* TU Muenchen, Germany*;* ***M. Tornow****, G. Abstreiter,* Walter Schottky Institut, TU Muenchen, Germany

Functionalized field effect devices are promising candidates to act as smart substrates for sensor applications. For a use in biological systems a functional layer has to provide stability against electrochemical decomposition, and allow effective coupling of the surface potential to the conductive channel. We present a resistor device passivated with a 4'-substituted 4-mercaptobiphenyl (MBP) self-assembled monolayer (SAM) for sensing applications. Base material is a GaAs-AlGaAs heterostructure containing a quasi 2D electron gas 60nm beneath the surface. In the first part of our study we investigated the influence of the MBP-SAM on the electronic surface properties of n-doped GaAs samples employing the Kelvin probe technique. We changed the dipole moment of the MBP molecules using various substituents (-H, -OH, -CH@sub 3@) and found a linear effect on the electron affinity. In the second part we tested the stability of the resistor device based on the GaAs-AlGaAs heterostructure in aqueous solutions. Whereas a bare device degraded rapidly the coated samples showed a remarkable increase in stability. Furthermore we characterized samples coated with monolayers with CH@sub 3@ (MBP-CH@sub 3@) and OH (MBP-OH) substituents in buffered electrolyte solutions with varying pH. For the MBP-OH coated sample, a change in pH induced a change in the resistance of the device. Interestingly, the sample grafted with an MBP-CH@sub 3@ SAM also showed a clear response on pH which can be attributed to the adsorption of OH@super -@ ions on CH@sub 3@ groups.

9:20am **AS+BI-TuM4 Ion Beam Alignment of Nematic Liquid Crystal on PPV-layer**, ***S. Pylypenko***, *K. Artyushkova, J.E. Fulghum,* The University of New Mexico*; O. Buluy, T. Prokopenko, Y. Reznikov,* Institute of Physics of National Academy of Sciences, Ukraine

The development of LCD technologies requires homogeneous alignment of liquid crystals (LCs). The traditional rubbing procedure, consisting of unidirectional brushing of the aligning substrates, is quite reliable but has some drawbacks, including the production of electrostatic charges and dust during the rubbing. Ion and plasma-beam alignment are among the more promising candidates to replace the rubbing procedure. Ion beam alignment is based on an angularly selective destruction and rearrangement of the surface material as a result of ion bombardment, creating orientational order on the initially isotropic surface. Here we report on effective alignment of LCs on an ion-bombarded PPV layer. Glass substrates covered with a thin layer of PPV were irradiated using 2KeV Ar@super +@ ions for varying times. The irradiated substrates were used to assemble planar cells, and the gap was filled with nematic LC 5CB. The measured value of the anchoring energy of ~ 3 10@super -3@ erg cm-2 appeared to be one to two orders of magnitude less than the typical value produced by plasma/ion-alignment. We found enhancement of the stability of the PPV layer in the irradiated area. The strong interaction of 5CB molecules with the PPV surface caused dissolution of the PPV by the LC, and the PPV-layer was not affected by LC in the irradiated region. Three-dimensional characterization of the polymer by X-ray Photoelectron spectroscopy (XPS), Angle Resolved XPS (ARXPS), and Confocal Microscopy (CM) utilizing multivariate analysis (MVA) techniques were carried out to study the mechanism of PPV alignment after ion-beam bombardment. Our results demonstrate that ion-beam treatment provides uniform alignment of liquid crystals characterized by a weak anchoring.

9:40am **AS+BI-TuM5 Plasma Beam Alignment for Liquid-Crystal Displays**, ***Y.-F. Chang***, *C.-H. Lin, C.-W. Chen,* Industrial Technology Research Institute, Taiwan

Surface alignment of liquid crystals is an important issue in practical applications of liquid crystal (LC) cells on TFT-LCD process. The most common technique of LC alignment is an unidirectional rubbing on special polymer films which deposited on an conductive substrate such as ITO (Indium-Tin Oxide). The rubbing process has many disadvantages even though it has been widely used in the actual production of LCD. Thus, rub-free methods for LC alignment are strongly required in the next generation LCD technology. A number of non-contact LC alignment methods have been proposed in attempting to replace the rubbing process. And the well-known technique is ion beam irradiation proposed by IBM group. Another non-mechanical alignment technique, named photoalignment method, in which the UV light irradiation caused surface anisotropy of the bounding plates was studied for many years. The method was relatively simple, but the corresponding drawbacks such as weak anchoring energy as well as poor photo and thermal stability, may limit the application of this technology. In this research, a plasma beam alignment technique, in which the aligning substrate was treated with a flux of plasma that was extracted and accelerated electrostatically, was applied on the PI and diamond-like carbon (DLC) film. It is also a non-contact alignment process. The plasma flux was generated with a DC plasma source known as the anode layer thruster (ALT). The discharge channel was used to produce the sheet-like fluxes. The test panels (100 mm X 50mm) were fabricated with various plasma-beam processing parameters, w/o further passivation processes to study the alignment qualities including the pretilt angle, anchoring energy, VHR and Rdc as a function of these processing parameters. In addition, the measuring methods of these alignment qualities were also investigated in this study.

10:00am **AS+BI-TuM6 Measuring the Thickness of Organic/Polymer/Bio Films on Glass Substrates using Spectroscopic Ellipsometry**, ***H.G. Tompkins***, *T. Tiwald, C. Bungay,* J. A. Woollam Co., Inc.*; A.E. Hooper,* Motorola, Inc.

In this work we discuss a method of determining film thickness for film/substrate combination where the index of refraction of the film and substrate in the transparent spectral regions are almost identical. Common examples of this situation are organic/polymer/biological films on glass substrates. IR ellipsometry is used and we use weight gain to provide some necessary additional information for determining the optical functions for the film material. The spectral regions of strong molecular vibrations are then used for determining film thickness.

10:20am **AS+BI-TuM7 Applications of Surface Analysis in the Medical Device Industry**, ***A.M. Belu,*** Medtronic, Inc.

The surface is an important zone as it is the interface between a material of interest and the environment with which it interacts. For biomaterials and drug delivery systems, knowledge of interface chemistry is important for understanding how a material will interact with the biological environment of the body. For other materials, particularly those that are employed in the manufacture of medical devices, evaluation of the surface is important to further understand issues with welding, adhesion, contamination, discoloration, etc. This talk will highlight the power of surface analysis methods and how they are employed in the medical device industry. The analytical methods include TOF-SIMS and ESCA which allow chemical characterization of the uppermost ~75Å of a material. Scanning probe

microscopy (SPM) and laser profilometry are used to gain topographical information and to measure roughness of surfaces. A field emission scanning electron microscope (FE-SEM) allows high resolution imaging of surfaces with resolution capabilities to 1 nanometer. A low vacuum SEM further allows characterization of non-conductive, wet, and organic samples. SEM also has the capabilities for elemental identification and semi-quantitative analysis using an x-ray detector (EDS). Examples will be presented to demonstrate a range of surface analysis applications, from fundamental studies of biomaterials, to solving industrial problems. The power as well as the problems of data acquisition and interpretation will be highlighted with regards to each technique. Further, a comparison of all techniques will be made to help elucidate which method or methods are best for specific problems. Examples will include imaging the distribution of drug in a polymer coating (such as on stents), identifying contamination on medical devices (such as detergent residue on leads), evaluation of particles and defects, and characterization of surface chemical modification.

10:40am **AS+BI-TuM8 Microelectronic Multielectrode Interface for Evaluation of Living Cells**, ***H.D. Wanzenboeck***, *P. Hagl, K. Dominizi, E. Bertagnolli,* Vienna University of Technology, Austria; *E. Bogner, M. Wirth, F. Gabor,* University Vienna, Austria

*****PLEASE NOTE: YOU MUST IDENTIFY A DIFFERENT PRESENTER FOR THIS ABSTRACT. YOU MAY ONLY PRESENT ONE (1) PAPER AT THE CONFERENCE.*****Tests on living cells are crucial in biomedical research, biotechnology , pharmacological diagnostics and medicine, but applied methods are often labor-intensive. Microelectronic technology has available sensitive techniques for automatized, continuous measurement and data interpretation. These advantages are not made use of due to the complex nature of the interface between the biological and microelectronic world. This work describes the fabrication and fundamental application of a functionalized biomaterial interface. For an interface to biological substances the choice of suitable substrate materials is decisive. A biological layer of human ephitelial cells (Caco-2) was grown in-vitro on the interface. The biocompatibility of inorganic and organic materials typically used in microelectronics was exploited. Metals, dielectrics and semiconductors were evaluated qualitatively by optical imaging and by scanning electron microscopy at variable pressure. A quantitative evaluation was performed with biochemical tests on cell proliferation and differentiation. Fundamental aspects of bio-interface engineering are investigated by interface analysis methods. In a second step 3-dimensionally patterned surfaces were explored as interface to the biological world. By microstructuring a miniaturisation of typical structures in the range of 20 µm down to 1 µm - smaller than the diameter of a living Caco2 cell - was performed. A functional microelectrode array proved to be an excellent bio-interface to living cells. The growth and behaviour of a Caco-2 cell layer on this array of multiple microelectrodes was studied by optical and electrical measurements. The electrical measurement through a single Caco-2 cell was recorded as impedance spectrum. The results contribute to the further understanding of the interactions between living cells and microelectronic biosensors. This work provides fundamentals to unite microelectronic engineering with in-vitro biological studies.

11:00am **AS+BI-TuM9 Chemical Imaging of Biological Cells and Tissues using TOF-SIMS**, ***P. Sjovall,*** SP Swedish National Testing and Research Institute, Sweden **INVITED**

Although time-of-flight secondary ion mass spectrometry (TOF-SIMS) has been used for chemical imaging of cells and tissues for almost 10 years, recent advances (notably the new primary cluster ion sources) have the potential to lead to a new breakthrough in this area. To realize this, however, additional research is required, addressing issues like (i) sample integrity, (ii) lateral resolution / detection efficiency, and (iii) sample complexity. We have used TOF-SIMS to record the spatial distribution of lipids in freeze-dried mouse brain sections and in surface-adhering polymorphonuclear leukocytes (PMNLs). The mouse brain sections (14 µm thick, cryosectioned, placed on a glass or Si substrate and freeze-dried inside the TOF-SIMS instrument or in a separate vacuum chamber) were analyzed using Au@sub n@@super +@ and Bi@sub n@@super +@ primary ions. It is demonstrated that TOF-SIMS analysis can provide detailed images showing the distribution of a number of lipids on the tissue surface at lateral resolutions down to < 1 µm.@footnote 1@ It is also shown that migration of lipids may be a problem under certain sample preparation and analysis conditions. The PMNLs were analyzed using a chemical imprinting technique, in which the outermost molecular layers of the cells are transferred to a substrate surface by pressing the substrate against the cell sample. The advantage of this method is that the substrate surface can be selected and/or functionalized in a manner that optimizes the subsequent imaging TOF-SIMS analysis. For the PMNLs, chemical imprints were made on Ag substrates in order to improve the detection yield and specificity of the lipids using Ga@super +@ primary ions (taking advantage of the Ag cationization). The resulting images show a complementary localization of cholesterol (plasma membrane) and phosphocholine (nuclear membrane).@footnote 2@ @FootnoteText@ @footnote 1@ Anal. Chem. 2004, 76, 4271@footnote 2@ Anal. Chem. 2003, 75, 3429.

11:40am **AS+BI-TuM11 Studying the Effect of Spacer Thiol Chemistry, Orientation and Surface Coverage on the Hybridization Properties of Mixed DNA SAMs on Gold**, ***C.-Y. Lee,*** University of Washington; *P. Gong,* Colorado State University; *H.E. Canavan, L.J. Gamble,* University of Washington; *D.W. Grainger,* Colorado State University; *D.G. Castner,* University of Washington

Although it is desirable to capture DNA targets without purification from complex milieu (e.g., serum, tissue lysate) for microarray applications, this goal is often hindered by non-specific attachment of DNA and proteins. Minimizing nonspecific adsorption to biosensors and microarrays requires a non-fouling background. Furthermore, the coverage and orientation of DNA probes should be optimized for the capture of low concentrations of DNA via hybridization. To achieve each of these goals, we evaluated the effect that two spacer thiols [11-mercapto-1-undecanol (MCU) and 11-mercapto-undecyl tetra ethylene glycol (OEG)] have on surfaces prepared using singled-stranded DNA containing a thiol anchor group (SH-ssDNA). These mixed DNA self-assembled monolayers (SAMs) have been studied with X-ray photoelectron spectroscopy (XPS), near-edge X-ray absorption fine structure spectroscopy (NEXAFS), @super 32@P-radiolabeling, and surface plasmon resonance (SPR). Although XPS and radiolabeling indicate that SH-ssDNA surface coverage steadily decreases with longer exposure to the backfill molecules, NEXAFS indicates that polarization dependence peaks at short MCU and OEG exposure times (< 1h), after which polarization dependence decreases due to the loss of DNA from the surface. A comparison of hybridization responses from these probe surfaces was made using SPR by exposing the surfaces to complementary DNA in various concentrations of serum. SPR results indicate that although surfaces with MCU and OEG thiol spacers showed resistance towards non-specific DNA binding in pure buffer, hybridization efficiency is hindered by non-specific serum protein adsorption even at minimal serum concentration of 1%. Finally, differences in the hybridization property and protein resistance of the SH-ssDNA/MCU and SH-ssDNA/OEG mixed monolayer surfaces will be discussed.

Plasma Science and Technology
Room 302 - Session PS+BI-TuM

Plasmas in Bioscience

Moderator: P. Favia, University of Bari, IMIP-CNR, Plasma Solution Srl, Italy

8:20am **PS+BI-TuM1 Plasma Polymerisation of Ethanethiol**, ***S.L. McArthur,*** *G. Mishra, A.G. Shard,* University of Sheffield, UK

The past years have seen significant development and use of functional polymer surfaces for bio-medical applications. Plasma polymerisation has proved to be one technique to generate functional surface in a single step process. Spontaneously reactive thiol surfaces produced by various wet chemistry routes have been extensively characterised as models to study surface-ligand interactions. This project aims to develop thiol functionalized surfaces utilizing plasma polymerisation of ethanethiol and with 1, 7 Octadiene as a diluent monomer. The deposited film properties were determined by X-Ray photoelectron spectroscopy and a fluorine marker was used to label any functional thiol groups present. It was observed that plasma polymerisation of ethanethiol at low discharge power resulted in a sulphur rich stable coatings and by increasing the power the coating resembled monomer composition in terms of atomic percentages, but none of the used conditions generated any detectable thiol groups. Mixing 1-7 Octadiene in a ratio of 1:1(v/v) in the gaseous feed resulted in an interesting change at high powers in the film properties with generation of 3-4% detectable active thiol groups without affecting the stability of the film. It is believed that the introduction of a diluent monomer at high powers has reduced the amount of available sulphur for crosslinking which dominates the deposition mechanism at low powers and has created a reaction pathway which favours the generation of thiol groups at the surfaces.

8:40am **PS+BI-TuM2 A Novel, Single-Step Method for the Preparation of Chemical Gradient Surfaces Using Non-Uniform Plasma-Deposition**, ***T.R. Gengenbach***, *P.G. Hartley, H. Thissen, K.M. McLean, L. Meagher, G. Johnson,* CSIRO Molecular Science, Australia

Gradient surfaces are characterised by a gradual and systematic variation of one or more chemical and physical properties along a specific direction. They are of increasing importance in combinatorial chemistry and materials science where they are being used to generate libraries of widely varying surface properties to study interfacial phenomena. In biomaterials research gradient surfaces can be employed to rapidly explore multi-variable parameter space, either to investigate how relevant variables (e.g. surface chemistry, wettability, charge) affect biocompatibility, or alternatively, to accelerate the optimisation of coupling strategies for covalent attachment of secondary layers. Radio frequency glow discharge plasma polymer coatings form robust thin films which contour and adhere strongly to the surfaces of polymeric and other materials. Their ability to modify surface properties, either by enhancing biocompatibility, or by introducing defined chemical functionalities at interfaces for the subsequent coupling of bioactive molecules, have seen their widespread application in the field of biomaterials research. We have developed a novel method to deposit plasma polymer coatings with systematically varying properties along the surface. In a standard plasma reactor with capacitively coupled electrodes the substrate to be coated is placed on a large flat horizontal base electrode (earthed); the second, specially shaped top electrode (active) is lowered to within millimetres of the substrate surface. The resulting plasma discharge is spatially non-uniform and produces surfaces with a strong gradient of chemical/physical properties. By controlling the shape of the top electrode we have also prepared patterned surfaces with well defined regions of widely different properties (e.g. density of specific functional groups). These gradient surfaces have been evaluated with respect to the biological response, such as protein adsorption and cell attachment.

9:00am **PS+BI-TuM3 Mechanistic Musings on Plasma-Enhanced CVD of Polymeric Materials**, ***E.R. Fisher,*** Colorado State University **INVITED**

Plasma-enhanced chemical vapor deposition (PECVD) is a valuable technique for deposition of polymeric materials with wide ranging applications, including micropatterns for fabrication of multianalyte biosensors, diagnostic tests, DNA microchips, and genomic arrays. One ongoing issue with PECVD processes is controlling and tailoring the molecular level chemistry, both in the gas-phase and at the gas-surface interface such that predictable and reproducible film chemistries can be created. One method for controlling the overall deposition is to use pulsed, downstream or remote deposition processes. Moreover, understanding surface interactions of plasma species provides critical molecular level information about PECVD processes. The imaging of radicals interacting with surfaces (IRIS) technique examines interactions of radicals during plasma deposition using laser-induced fluorescence (LIF) to provide spatially-resolved 2D images of radical species involved in film formation. IRIS allows for direct determination of radical-surface interactions during plasma processing. IRIS data for species in plasma polymerization and plasma modification systems will be presented, along with addition film and gas-phase composition data. IRIS results that will be discussed include data on fluorocarbon radicals (CF and CF@sub 2@), main group hydrides (SiH, OH, NH, and CH), and nitrogen-containing molecules (NH, NH@sub 2@, CN) in relationship to various plasma polymerization systems of interest to the microelectronics and coating industries. Correlation of gas-phase data, surface analysis, and plasma-surface interface reactions will also be presented to provide more comprehensive mechanisms for overall plasma polymerization processes. Examples will also be provided from polymer film and fiber modification systems.

9:40am **PS+BI-TuM5 Application of Plasma Discharges in the Biomedical Field: Biological Decontamination and Sterilization of Surfaces**, ***F. Rossi,*** European Commission-Joint Research Centre, Italy **INVITED**

Every year, thousands of patients die from nosocomial infections got in hospital after surgical intervention. Those infections are directly linked to bacterial contamination of medical devices surfaces that are used during operation. Moreover, interaction of specific biomolecules like phospholipids or lipopolysaccharides (LPS) or certain proteins with organisms can be a major cause of diseases. Prominent examples are pyrogenes - lipopolysacharides (LPS) and lipoteichoic acids (LTA) -, which cause fever in human body and are potentially lethal after contact with blood. In some cases the secondary or tertiary structure of proteins is responsible for their biological properties. Important example is PrP (prion) which becomes pathogenic after a change of its structure. The contaminated surface (e.g. medical devices, accessories, work surface or tissue) cannot be decontaminated with current sterilisation practices without inducing major damage to the substrate or tissue itself, because of the high temperature used, or chemical reaction with the surface. In the present work, the inactivation or modification of biologically potentially harmful molecules is addressed in a combined approach using low pressure plasma discharges with non toxic gas mixtures. The emerging species fluxes of these plasmas are measured. Different characteristic biomolecules (LPS, LTA, proteins etc. as well as whole micro-organism cells) are exposed to the plasmas and the changes induced are monitored in-situ using infrared spectroscopy as well as ex-situ using biochemical and structural analysis as a function of the gas mixture and plasma parameters. Different potential mechanisms (etching, UV radiation, chemical reactions) are presented. The gained knowledge on the interaction of plasma discharges with pathogenic biomolecules and microorganisms allows a targeted development of decontamination strategies for very resistant species. The potential applications are in the field of surface decontamination and sterilisation of medical objects and opens large possibilities of applications in the field of security.

10:20am **PS+BI-TuM7 Biological Response to Plasma Processed Materials**, ***L.C. Lopez,*** University of Bari, Italy*; R. Gristina,* CNR-IMIP Bari, Italy*; L. Detomaso, P. Favia, R. d'Agostino,* University of Bari, Italy **INVITED**

The demand of biomedical implants significantly increases every year and several approaches have been investigated to develop surfaces which are recognized by specific proteins of the biological milieu, ranging from template materials, to surfaces that mimic receptor sites, to biologically inspired materials. Other surface modifications approaches deal, instead, with the immobilization of biomolecules (heparine, carbohydrates, peptides, enzymes, etc.) on biomedical surfaces, to induce the growth of cells, to act as sensors in immunodiagnostics or to exhibit blood compatibility. Low temperature plasma modification processes represent an appealing tool, versatile and environmental friendly, to selectively modify materials to be used for medical devices. Surface properties of biomaterials (chemical, biological, tribological) can be selectively plasma driven to achieve specific biological response, leaving the bulk features unaltered.@footnote 1@ Furthermore, a promising strategy to control the interaction between biomaterials and biological environments, applies to binding of biomolecules to plasma modified polymers by a stable bond with surface functional groups (OH, COOH, NH@sub2@, etc.).@footnote 2@ RGD-containing peptides and galactose immobilization on plasma processed substrates, recently investigated in our group, clearly highlighted a strict correlation between specific cellular behaviour and immobilised molecules. These results plainly indicate that coupling plasma modification processes with precise biomolecules immobilization pathways may represent a successful approach to address biocompatibility and biorecognition requirements of biomaterials. @FootnoteText@ @footnote 1@ B.D. Ratner in: Plasma Processing of Polymers, R. d'Agostino, P. Favia, F. Fracassi ed., Kluwer Acad. Publ., NATO ASI Series, E: Appl. Sci., Vol. 346, 1997.@footnote 2@ L. C. Lopez, R. Gristina, G. Ceccone, F. Rossi, P. Favia, R. d'Agostino Surface and Coatings Technology, 2005, in press.

Biomaterial Interfaces
Room 311 - Session BI1-TuA

Sensors/Diagnostics
Moderator: M.J. Tarlov, National Institute of Standards and Technology

2:00pm **BI1-TuA1 Fluorescent Conjugated Polyelectrolytes: Superquenching, Biosensing and Biocidal Activity**, ***D.G. Whitten,*** University of New Mexico **INVITED**

The talk will focus on the photophysics of fluorescent conjugated polyelectrolytes and their very high sensitivity (superquenching) to quenching by small molecules that can associate with the polymers and interact via energy or electron transfer. Superquenching occurs for the polymers in solution and also when they self-assemble on microspheres or nanoparticles. The application of superquenching to biosensing has provided a means for high sensitivity detection of enzyme activity, proteins and nucleic acid hybridization. It has also been found that these polymers have biocidal activity towards bacteria and bacterial spores. The origin of the light-induced biocidal activity will be discussed.

2:40pm **BI1-TuA3 Toward Improved Biosensors: Studies of Protein Immobilization on Polymerized Planar Supported Lipid Bilayers**, ***J. Joubert,*** *E.H. Elandaloussi, S.S. Saavedra,* University of Arizona

Planar supported phospholipid bilayers maintain high resistance to nonspecific protein adsorption, which is a useful attribute for biosensor surfaces. However, their instability to drying is a factor reducing their commercial implementation. By crosslinking polymerizable lipid monomers (e.g., bis-sorbylphosphatidylcholine, bis-SorbPC) bilayer stability can be increased while maintaining biofouling (i.e., nonspecific protein adsorption) resistance. Further, the properties of this poly(bis-SorbPC) platform can be modified to study nonspecific and specific interactions with proteins for biosensing applications. One modification for studying nonspecific interactions involves adding various percentages and types of nonpolymerizable lipid to the bilayer before polymerization and drying to introduce a varying number and size of defect sites with differing polarities (hydrophobic for exposed lower lipid leaflet and hydrophilic for exposed glass) in a controlled manner. Studies of nonspecific protein binding to this variety of defects in these bilayers can aid in understanding fouling and subsequent failure of biosensors. Another set of modifications for analyzing specific protein interactions is aimed at immobilizing analyte-specific receptor proteins onto the bilayer and analyzing the degree to which sensing activity is retained. These modifications include doping into the bilayer a polymerizable lipid with a reactive (e.g., primary amine) headgroup for protein receptor attachment or microcontact printing the protein receptor onto the polymerized bilayer. This talk will discuss development of such methodologies to attach proteins to poly(lipid) bilayers to study protein-lipid and protein-protein interactions on such surfaces.

3:00pm **BI1-TuA4 Gallium Nitride-based BioFETs for Label-free Biosensing**, ***K. McCoy,*** University of Florida*; J.C. Sullivan, J.C. Culbertson, E. Snow,* Naval Research Laboratory*; S.J. Pearton,* University of Florida*; L.J. Whitman,* Naval Research Laboratory

Biologically modified field effect transistors (BioFETs) have the potential to directly detect biochemical interactions in aqueous solutions for a myriad of applications. In order for these devices to be useful, they must satisfy three major criteria. The bioFET must be stable in aqueous solutions across a range of pH and salt concentrations, be sensitive to biochemical interactions on the surface of the device, and be able to probe specific biochemical interactions. BioFETs that we are developing based on AlGaN/GaN quantum well devices can potentially satisfy all of these requirements. These charge-sensitive devices are being functionalized with receptors to stochastically sense the binding of target molecules in aqueous samples. The sensing is based on device geometries whereby the stochastic binding of individual biomolecules above a device will cause a change in conductance. It has already been demonstrated that these AlGaN/GaN quantum well devices can sense small changes in pH of electrolyte solutions. It is our goal to functionalize the surface in such a manner that the sensitivity of the device is not severely reduced. We are evaluating two reaction schemes to accomplish this task. The first involves modifying the surface with a SAM, then attaching a polymer to that SAM which can couple to biological probes. The second method employs a proprietary scheme to functionalize the surface with a layer of avidin that can then be coupled to biotinylated probes. The reaction schemes have been characterized in both UHV (XPS) and solution (cyclic voltammetry, fluorescence microscopy). The effect of these schemes on the electrical properties of the devices will be discussed, along with our progress toward determining the ultimate sensitivity of this biosensor system.

3:20pm **BI1-TuA5 Increasing Immunosensor Responses: from Antibody Fragments and 3D Substrates to Functionalized Nanoparticles**, ***K. Bonroy,*** IMEC and K.U. Leuven, Belgium*; F. Frederix,* IMEC, Belgium*; P. Cliquet,* R.U. Gent, Belgium*; G. Reekmans, H. Jans, T. Ghoos, R. De Palma, W. Laureyn,* IMEC, Belgium*; B. Goddeeris,* K.U. Leuven and R.U. Gent, Belgium*; P. Declerck,* K.U. Leuven, Belgium*; G. Borghs,* IMEC, Belgium

Researchers are continuously seeking for new transduction principles and biosensor interfaces. Both the transducer and biochemical interface contribute to the sensor signal. However, over the years it became clear that a lot of these approaches lack sensitivity for some applications. In this paper we report on several modifications at the (bio)chemical interface in order to increase/tune the immunosensor signal. Two important routes were investigated; the increase of the amount of active/well-oriented receptormolecules on the surface and the use of functional nanoparticles for signal amplification. In this paper we present some of our approaches to control the amount of immobilized molecules and to mitigate non specific adsorption of proteins. Different mixed thiol SAMs, indirect assay formats, immobilization methods, 3D nanoparticle films, 3D porous gold surfaces, and size-reduced receptormolecules such as ScFvs and Fab antibody fragments were optimized, characterized and their influences on the sensor response were evaluated. We will show that some of these modifications at the level of the interface can generate a considerable increase in the response of immunosensors such as SPR, QCM and electrochemical sensors. In addition, we also optimized some of the above-mentioned enhancement approaches towards one application i.e. antibiotic detection. Therefore, a new antibiotic modified disulfide was synthesized and evaluated on gold substrates and nanoparticles. The characterization and optimization was performed using XPS, SPR, IR, CA, CV and TEM. The antibiotic tailored surfaces and nanoparticles were also evaluated in the final biosensing application. In conclusion, we will show that (bio)chemical modifications of the immunosensor interface can be used to manipulate and control the final sensor signal. In addition, we will show that interface modifications could offer a platform from which application-specific sensitivity problems can partially be addressed.

3:40pm **BI1-TuA6 Fluidic Force Discrimination Assays in Complex Media**, ***S.P. Mulvaney,*** *A.A. Glaser, M. Malito, C.R. Tamanaha, J.C. Rife, L.J. Whitman,* Naval Research Laboratory

We are developing a highly sensitive and selective biosensor system that uses giant magnetoresistive sensors arrayed in a Bead ARray Counter (BARC) microchip to directly detect magnetic microbead labels. The beads are used both to label biorecognition events in a binding assay and to reduce background through a process known as fluidic force discrimination (FFD). FFD is a controlled bead removal procedure that leverages the strength of biomolecular recognition against fluidic forces to selectively remove nonspecifically bound beads and beads labeling nonspecifically bound analyte. FFD not only reduces the background label density, thereby improving the analytical sensitivity of the binding assay, but also lowers the occurrence of false positives. Highly sensitive DNA assays (<10 fM) and immunoassays (<1 ng/mL) have been demonstrated in less than 30 minutes at room temperature, without amplification or concentration steps (i.e. PCR). Successful assays have also been run in serum, plasma, whole blood, and complex environmental matrices. We'll discuss mitigation steps (i.e. addition of chelating agents, filtration, etc.) required to achieve detection in complex media as well the overall impact on detection levels. We'll also examine the ability to minimize sample handling by incorporating simple processing capabilities into the microfluidics cartridge. @FootnoteText@ S.P.M., A.A.G., and M.M. are employees of Nova Research Inc., Alexandria, Va.

Biomaterial Interfaces
Room 312 - Session BI2-TuA

Surface Modification
Moderator: A. Chilkoti, Duke University

2:00pm **BI2-TuA1 Dynamic Ellipsometric Studies of Protein Adsorption to Modified Chitosan Surfaces**, ***S. Sarkar,*** *L.G. Castro, D.W. Thompson, J.A. Woollam, A. Subramanian,* University of Nebraska, Lincoln

Protein adsorption is a ubiquitous phenomenon whose effects are widespread and observable in fields as diverse as biofouling, molecular recognition and metabolic pathway activation (biocompatibility) and even

qualitative and quantitative detection methods (ELISA). Protein interaction with materials and at interfaces is an area of ongoing study; however, little is understood of the immediate response of proteins to an exposed surface. Chemically modified chitosan films were used to investigate the adsorption of human serum albumin (HSA), immunoglobulin G, and fibrinogen. Diepoxides were reacted with amine groups present on chitosan and then five atomic geometries (n-butyl amine, 2-(t-Butylamino)ethanol, n-octyl amine, 2,4,6 Tris(dimthylaminomethyl) and t-butyl amine) and an anti-HSA molecule were attached to free epoxide ends to create surfaces preferential to albumin adsorption. Dynamic ellipsometric studies were carried out on the resulting surfaces to investigate protein adsorption phenomena. We have been successful in observing real time protein adsorption. In most cases protein adsorption had reached a saturation point after one-hour with the highest rate of adsorption occurring in the first ten minutes.

2:40pm **BI2-TuA3 The Generation of Protonated Amine Groups in Plasma Co-Polymers of Acrylic Acid and Allylamine for the Co-Culture of Keratinocytes and Melanocytes**, ***A.J. Beck***, *P. Eves,* University of Sheffield, UK*; J.D. Whittle,* Plasso Technology Ltd, UK*; N.A. Bullett,* Celltran Ltd, UK*; S. Mac Neil, S.L. McArthur, A.G. Shard,* University of Sheffield, UK

Plasma polymers prepared from acrylic acid, allylamine and mixtures of the two strongly interacting vapors were characterized using X-ray photoelectron spectroscopy (XPS) and near edge X-ray fine structure (NEXAFS). Plasma polymers prepared from pure acrylic acid and allylamine contained groups retained from the monomer with additional groups formed in the plasma. For the plasma copolymers, the XPS N 1s data and NEXAFS N k-edge provided evidence of protonated amines. The mixture of monomer vapors, in the absence of a plasma, consists of acrylic acid, allylamine and the product of their reaction: allylammonium acrylate salt. More protonated amines were detected in plasma copolymers prepared at low powers suggesting that they were largely retained from the monomer mixture rather than being formed in the plasma. The protonated amines in the monomer mixture undergo less dehydrogenation to nitrile groups in the plasma than the amines from the pure allylamine. This novel use of protecting groups for amines in low power plasmas has the potential to be extended to other desirable groups which tend to be diminished due to fragmentation even in very low power systems. We have demonstrated that plasma co-polymers of acrylic acid and allylamine contain protonated amine groups with carboxylates as the counter anion. It is postulated that such zwitterionic plasma polymers will have interesting surface charge properties in aqueous solution and it may be possible to control the isoelectric point of the surface by varying the plasma conditions and ratio of allylamine to acrylic acid vapors. These surfaces have been shown to facilitate co-culture of keratinocytes and melanocytes.

3:00pm **BI2-TuA4 Pulsed RF Plasma Polymerisation of N-isopropylacrylamide (NIPAAm)**, ***R. Talib***, *A.G. Shard, S.L. McArthur,* University of Sheffield, UK

There is a growing interest in the development of responsive polymer coatings for applications as diverse as tissue engineering and microfluidic devices. Plasma polymerization affords a convenient, one step route to generate such coatings. Previous studies have shown that continuous wave (CW) plasma polymerization of N-isopropylacrylamide (NIPAAm) is able to produce thermally responsive coatings on a variety of substrates. These CW studies have demonstrated that control of the deposition power and temperature is critical for the retention of functionality, but that too little power or too lower temperature will result in unstable coatings. In this study we investigate the use of pulsed power cycles as a means for both improving coating stability and controlling the thermal response of the coatings. We have investigated the influence of power, on- and off-times and reactor temperature on the coating chemistry, stability and thermal response. The role of the plasma parameters has been monitored using a capacitive probe. The probe enables accurate measurement of the duty cycle and clearly demonstrates that in certain regimes both the power and ratio of on/off time set by the pulse generator can result in significant delays in the striking of the plasma. In some instances, we demonstrate that the plasma actually fails to ignite during the majority of individual pulses. Accurate measurement of duty cycles enables direct comparison of coatings produced under pulsed power with those produces with equivalent CW powers. X-ray photoelectron spectroscopy (XPS), secondary ion mass spectroscopy (SIMS) and captive bubble have been used to measure the resulting coating properties and compare the mechanisms of NIPAAm polymerization under CW and pulsed plasma conditions.

3:20pm **BI2-TuA5 Using Plasma Deposits to Promote Cell Population of the Porous Interior of 3D Tissue Engineering Scaffolds**, *J.J.A. Barry, M.M.C.G. Silva, K.M. Shakesheff, S.M. Howdle,* ***M.R. Alexander***, University of Nottingham, UK

Cell attachment and proliferation on poly(D,L-lactic acid) (PLA) tissue engineering scaffolds is low, this is generally regarded to be due to the hydrophobicity of the polymer surface. This study reports the first successful deposition of allyl amine plasma polymer throughout the porous network of a 3D scaffold to improve cell adhesion. This is compared and contrasted with the plasma grafting of allyl amine to the PLA. XPS analysis of sectioned scaffolds is used to demonstrate the penetration of nitrogen species to the inner surfaces. The nitrogen concentration at the exterior and interior scaffold surface was greater for the plasma deposits than the grafted surfaces. The variation in nitrogen concentration indicated a variation in thickness through the scaffold due to diffusion limited deposition in the interior pores. The chemistry was characterised using high resolution C1s and N1s core level with reference to literature NEXAFS and derivatisation studies. In vitro evaluation of biocompatibility was carried out by studying 3T3 fibroblast attachment, morphology and metabolic activity on the scaffolds. Cell activity and attachment was found to be greater for the plasma deposits than the plasma grafted PLA scaffolds and greater for both than the as-fabricated PDLLA scaffolds. It is concluded that plasma deposition is a viable method of increasing cell attachment throughout porous PLA and other scaffolds without changing the bulk characteristics of the polymer.

3:40pm **BI2-TuA6 Designing Interfaces for Biomolecular Interactions using Plasma Polymerization Techniques**, ***R. Foerch***, Max Planck Institute for Polymer Research, Germany

Recent advances in the synthesis and characterisation of plasma polymerized thin organic coatings has enabled new insights into the design of interfaces for specific interactions with biological molecules. Optical techniques such as surface plasmon resonance and waveguide mode spectroscopy have been used to monitor in real-time the reactions of proteins, antibodies and DNA at the interface of different plasma polymerised films. Combining these techniques with AFM, FTIR and XPS analysis has demonstrated a tremendous flexibility in surface design, plasma polymer structure and surface reactivity. The chemical composition, the macromolecular structure and the ability to form a 3-dimensional interface open up new concepts for the design of biomaterial surfaces. The interactions of proteins, antibodies and DNA can be correlated to plasma deposition conditions and subsequently the chemical and physical properties of the deposited layers.

Nanometer-Scale Science and Technology
Room 210 - Session NS+BI-TuA

Molecular and Biological Applications of Nanostructures

Moderator: M.C. Hersam, Northwestern University

2:00pm **NS+BI-TuA1 Nano-Patterned Surfaces Induce Bio-Molecules Oriented Immobilization**, ***A. Valsesia***, *P. Colpo, T. Meziani, P. Lisboa,* EC-JRC-IHCP Italy*; M. Lejeune, F. Rossi,* EC-JRC-IHCP Italy, Italy

The immobilization of biomolecules in domains with the typical size of the nano-meter or few tenth of nano-meters is one of the most challenging issues of the actual research in the field of biosensors and biochips. In particular the ability to create nanopatterned bio-active surfaces should be addressed to improve the performances of biosensing devices and to study new fundamental problems. From the technological point of view the nano-patterned surfaces can improve or modulate the absorption of proteins, minimize their non-specific absorption, increase the active surface density. In the last few years nano-soft lithography, dip-pen lithography, nano-fountain pen lithography and colloidal lithography were able to produce nano-patterned surfaces with fouling-antifouling contrast. The selective immobilization of the biomolecules on the fouling regions was demonstrated as well as the reduction of the nonspecific absorption in the antifouling matrix. In this work we developed a nano-patterning method which combines the spontaneous formation of molecular monolayers (SAM) and plasma based colloidal lithography. By this approach we have shown that the nano-patterning resolution is not limited in principle and can be accurately controlled by the plasma processing parameters. The techniques was employed for the creation of chemical nano-patterned surfaces with 100 nm motives with a hexagonal 2-D crystalline structure, characterized by COOH terminated SAM nano-spots in a CH3 terminated thiols matrix. By combining the information arising from

the different characterization techniques, it was possible to demonstrate the creation of a chemical contrast with a resolution of 100 nm, without a meaningful change in the morphological properties of the surface. An effective orientation of the biomolecules immobilized on these nano-patterned surfaces was demonstrated by AFM measurements and confirmed using an ELISA antibody immobilization protocol.

2:20pm **NS+BI-TuA2 Surface Nanopatterning for the Control of Cell Behavior**, ***C.M. Dekeyser***, *J. Marchand-Brynaert, A.M. Jonas, Ch.C. Dupont-Gillain, P.G. Rouxhet,* Université Catholique de Louvain, Belgium

Cell adhesion is mediated by proteins of the extracellular matrix, called adhesion proteins. RGD (arginine-glycine-aspartic acid) is the most widely spread peptide sequence responsible for these recognition events. It has been shown that a surface covered by adhesion proteins or grafted with the RGD sequence can induce different cell behaviors, depending on the distribution of the ligands. The aim of the work is to get a better insight into the influence on cell behavior of the distribution of ligands at the nanometer scale. This involves four aspects: creating a nanostructured surface, grafting a RGD ligand or adsorbing an adhesion protein according to defined motifs, passivating the rest of the surface with respect to protein adsorption and evaluating the cell behavior. The nanopatterns are created by means of electron-beam lithography. The challenge here is to draw small motifs (100 nm) on an area (500*500 µm@super 2@), large enough to allow cell adhesion to be studied. This was realized by juxtaposition of patterns (143*143 µm@super 2@) on which electron-beam lithography allowed continuous and regular lines to be drawn. In order to minimize non specific protein adsorption, the passivation of the surface is realized by self-assembly of oligo(ethylene glycol)-terminated silanes on silicon. The influence of various parameters has been examined in order to optimize the treatment in terms of cleanliness, thickness and density (AFM, X-ray reflectometry, XPS) of the obtained layer. Adsorption of different proteins is used to evaluate the inertness of the background and the selective adsorption on the patterns. RGD immobilization is realized by photografting an azide which bears an active ester able to react with the NH@sub 2@ groups of the ligand. The influence of the nanopatterned surfaces on the adhesion and spreading of neural cells will be examined.

2:40pm **NS+BI-TuA3 Enzymatic Nanofabrication: Step-wise Synthesis of DNA Scaffolds on Nanopatterned Oligonucleotide Templates**, ***D. Chow***, *W.-K. Lee, S. Zauscher, A. Chilkoti,* Duke University

Nucleic acid nanopatterns can serve as a template for step-wise synthesis for a variety of complex molecular nanostructures and have significant potential in materials science, molecular electronics, and biosensing. However, most nanofabrication techniques of nucleic acid scaffolds require DNA to be synthesized separately prior to self-assembly or manipulation at the nanoscale. Enzymes that can polymerize DNA are potentially useful molecular tools for the in situ synthesis of DNA scaffolds. Although these proteins are well studied and commercially available, they have not been previously exploited for enzymatic nanofabrication. This study demonstrates that terminal deoxynucleotidyl transferase repetitively adds mononucleotides to the 3' end of oligonucleotides on gold substrate nanopatterned by e-beam lithography. Without complex multi-step chemistry or biochemistry, the step-wise synthesis of DNA scaffolds leads to significant extension of DNA. This strategy can be modified to create more complex DNA nanostructures by simply replacing natural mononucleotides with unnatural ones, which serve as specific recognition sites along the single-stranded DNA. This enzyme-mediated nanofabrication methodology offers a new route to selectively dock nanoscale components of interest along the vertical direction with nanometer-level precision, and also provides a foundation for fabrication of hybrid molecular ensembles of biotic and abiotic components.

3:00pm **NS+BI-TuA4 Surface Modification and Morphological Stabilization of Silver Nanoparticles**, ***V.H. Perez-Luna***, *A. Dalwadi, S. Lee,* Illinois Institute of Technology

Metallic nanoparticles exhibit unique optical properties due to the oscillation of surface plasmons when excited by visible light. These optical properties are shape dependent and different modes of excitation can occur for anisomeric nanoparticles (e.g. due to transversal and longitudinal oscillation of surface plasmons). Thus, the optical properties of these systems can be changed without modifying their chemical composition. A wide variety of methods for the synthesis of anisomeric metallic nanoparticles (e.g.; triangular slabs, multipods, nanorods) have been developed over the last couple of decades. However, technological applications of these systems have not been extensively implemented in spite of their great potential for surface enhanced emission of fluorescence and Raman scattering. One of the biggest obstacles is the inherent morphological instability of these systems and processing difficulties that may lead to irreversible aggregation. Surface modification of gold and silver nanoparticles with alkane thiol based self-assembled monolayers could help circumvent these problems and allow for technological applications with great potential in biodetection assays. Experimental studies will be presented illustrating the improved morphological stability and tailored properties of surface modified nanoparticles. Experimental evidence of the strong influence exerted by metallic surfaces on emission of fluorescence will be presented. The potential of surface modified Ag and Au nanorods will be discussed with particular emphasis on biological detection assays.

3:20pm **NS+BI-TuA5 Functionalization and Electrical Characterization of Vertically Aligned Carbon Nanofibers**, ***K.-Y. Tse***, *S.E. Baker, E.A. Hindin, T.L. Clare, R.J. Hamers,* University of Wisconsin-Madison

Vertically Aligned Carbon Nanofibers (VACNFs) represent a new form of carbon with potential applications ranging from biosensing to energy storage. We have explored the electrical properties of bare and chemically-functionalized VACNFs in electrolyte solutions using electrical impedance spectroscopy and cyclic voltammetry. Electrical measurements show that the capacitance of the nanofiber forests is directly proportional to the average nanofiber length, demonstrating that the entire fiber surface is electrically active. A comparison of nanofiber forests with planar electrodes shows that the forests have approximately 7 times higher effective surface area. Measurements of DNA hybridization with DNA-modified VACNFs show a similar ratio, showing that the nanofibers have good biological accessibility. We will discuss the factors that control the electrical properties of nanofibers in electrolyte solutions, the effects of nanofiber aggregation, and prospects for the application of nanofibers for biosensing.

3:40pm **NS+BI-TuA6 Single Porphyrin Molecules as Information Storage Elements**, ***H. Kim***, *Y. Kuk,* Center for Science in Nanometer Scale (CSNS), Korea

Redox behaviors of porphyrin molecules have been widely studied for the possible application to molecular-based information storage for two main reasons; i) they form stable radicals whose redox potentials can be tuned by the synthetic design and chelating metal ions. ii) Assembled on the substrate adequately, they exhibit considerably long charge retention times. Recently, it was shown that they can survive silicon device processing,@footnote 1@ which provides a new possibility to molecular electronics. It was, however, confirmed only for a close-packed monolayer of porphyrins to act as information storage. We separated porphyin molecules both from each other and from the substrate by making a mixed self-assembled monolayer of alkanethiol-derivatized porphyrins and alkanethiols on a Au(111) surface. Alkanethiol monolayers can act as an organic insulating layer whose resistance shows approximately exponential dependence on the chain length and the HOMO-LUMO gap is about 9eV. These properties allow us to investigate more intrinsic behaviors of organic molecules attached to alkanethiol monolayers on surface. By means of scanning tunneling microscopy and spectroscopy, we identified the porphyrin groups on the insulating alkanethiol monolayer and resolved the redox states and the charge retention time of a single porphyrin molecule. @FootnoteText@ @footnote 1@ Molecular memories that survive silicon device processing and real-world operation, Z. Liu et al., Science 302, 1543 (2003).

Biomaterial Interfaces
Room 311 - Session BI1-WeM

Protein-Surface Interactions
Moderator: M. Textor, ETH Zurich, Switzerland

8:40am **BI1-WeM2 Functionalization of Diamond and Silicon Surfaces with Molecular Monolayers to Control Protein-Surface Interactions**, *T. Lasseter Clare, B. Clare, N. Abbott, B.M. Nichols,* ***R.J. Hamers,*** University of Wisconsin-Madison

We have investigated the chemical functionalization of diamond and silicon surfaces with short ethylene glycol (EG) oligomers to control the the nonspecific adsorption of proteins to these surfaces. EG oligomers bearing a terminal vinyl group were linked to H-terminated surfaces of diamond and silicon using illumination with ultraviolet light at 254 nm. The resulting layers were characterized by XPS, and the effects of EG oligomers on binding of avidin, casein, fibrinogen, and BSA were qualitatively investigated using on-chip fluorescence measurements. To avoid issues related to fluorescence quenching and facilitate quantitative comparison on different materials, we measured avidin adsorption using an elution method. These experiments show that EG-modified surfaces of nanocrysalline diamond, single-crystal silicon, and polycrystalline gold films all resist binding of avidin to nearly the same extent. One of the attractive features of diamond is its extraordinary chemical stability. In a comparison of EG-modified surfaces of diamond, silicon, and gold, we find that gold and silicon samples undergo a significant degradation over a time period of approximately 1 week, while EG-diamond samples undergo no detectable change. These results are corraborated with XPS measurements that show silicon and gold undergo partial loss of their functionalization layers, while EG-diamond shows no measurable change. The effects of surface roughness were investigated by comparing EG-modified surfaces of nanocrystalline, polished, and cleaved single-crystal diamond. The influence of monolayer termination and other factors will also be presented. Overall, these measurements show that photochemical modification of Si and diamond with vinyl-terminated EG oligomers is a very effective way to reduce nonspecific adsorption. They also provide new molecular insights into the factors the control protein adsorption at surfaces.

9:00am **BI1-WeM3 The QCM-D Technique for Control of Protein Binding on Nanoscale LSPR Active Substrates**, ***F. Höök,*** Lund University, Sweden **INVITED**

In the search for surface modifications that minimizes the influence on the structure and function of adsorbed proteins, supported phospholipid bilayers (SPBs) have been proven inert towards protein adsorption from as complex mixtures as serum. Since they at the same time fulfils the requirements set on specific coupling of both water-soluble and membrane bound proteins, have made them attractive in various biosensor applications and as coatings for biomaterials. However, so far limited progress has been made with respect to SPB formation on nanoscale solid supports. By utilizing insights gained from quartz crystal microbalance with dissipation (QCM-D) monitoring of protein/lipid interactions on either Au or SiO2, we have established a surface-modification protocol that enables localized rupture of phospholipid vesicles on SiO2 in the bottom of nanometric holes in a thin Au film. The hole-induced localization of the localized surface plasmon resonance (LSPR) field to the voids of the holes is demonstrated to provide a novel concept for studies of protein-binding reactions confined exclusively to SPB-patches supported on SiO2.@footnote 1@ In particular, we emphasize the possibility to in this way perform label-free studies of lipid-membrane mediated reaction kinetics, including the compatibility of the assay with array-based recording, with signals originating from bound protein in the sub-zeptomole regime. Extensions of this concept includes the use of the conductive LSPR hole substrate (i) as one of the electrodes of the QCM-D sensors, enabling simultaneous QCM-D and LSPR readouts of reactions occurring on, for example, either Au or SiO2, and (ii) for studies of protein binding to individual colloidal particles that match the size of the holes. @FootnoteText@ @footnote 1@Svedhem S, Pfeiffer I, Larsson C, Wingren C, Borrebaeck C, Höök F. ChemBioChem 2003:339-343. @footnote 2@Dahlin A, Zach M, Rindzevicius T, Kall M, Sutherland DS, Hook F. JACS 2005, 127:5043-5048.

9:40am **BI1-WeM5 In Deuterated Water the Unspecific Adsorption of Proteins Is Significantly Slowed Down: Results of an SPR-study using Model Organic Surfaces**, ***Chr. Grunwald,*** Ruhr-University, Germany; *J. Kuhlmann,* Max-Planck-Institute for Molecular Physiology, Germany; *Ch. Woell,* Ruhr-University, Germany

The control of unspecific adsorption of proteins to natural and technical surfaces plays an important role in biology and also for many applications. Organic model surfaces e.g. self-assembled monolayers, are often used to identify fundamental surface and/or protein properties that rule protein adsorption.@footnote 1@ Some techniques involved in biointerface research require the use of heavy water, e.g. neutron scattering techniques.@footnote 2@ Also in NMR studies D@sub 2@O is the solvent of choice when focusing on biomolecular and hydration dynamics. So far several studies have been concerned with the characterization of the unspecific adsorption of proteins from normal water buffers.@footnote 3@ In the present work we report a comparison of the unspecific protein adsorption from normal and heavy water buffers. Previously it has been assumed that the surface kinetic of the unspecific adsorption is unaffected by the substitution of water by D@sub 2@O.@footnote 2@ However, for the four proteins investigated here this assumption does not hold. The ratio k@sub H@/k@sub D@ of the adsorption rate constants of the different buffer conditions describe the strength of the isotope effect. We have measured ratios between 1.0 and 2.6 indicating that the adsorption kinetics are strongly affected by a H@sub 2@O-D@sub 2@O-substitution. @FootnoteText@ @footnote 1@Herrwerth, S.; Eck, W.; Reinhardt, S.; Grunze, M. Journal of the American Chemical Society 2003, 125, 9359-9366.@footnote 2@Schwendel, D.; Hayashi, T.; Dahint, R.; Pertsin, A.; Grunze, M.; Steitz, R.; Schreiber, F. Langmuir 2003, 19, 2284-2293.@footnote 3@Ostuni, E.; Grzybowski, B. A.; Mrksich, M.; Roberts, C. S.; Whitesides, G. M. Langmuir 2003, 19, 1861-1872.

10:00am **BI1-WeM6 The Development of Molecular Simulation Capabilities as a Tool to Understand Protein Adsorption Behavior at the Molecular Level**, *F. Wang, Y. Sun, S.J. Stuart,* ***R.A. Latour,*** Clemson University

Although important, the molecular mechanisms involved in protein adsorption processes are still not well understood. Empirical force field-based molecular simulation methods have been successfully developed to enable molecular mechanisms to be studied for other applications, such as protein folding and ligand-receptor binding; these methods have similar potential to help elucidate the molecular mechanisms for protein adsorption. Two of the most important problems that must be addressed before methods can be developed for this application are the force field problem and the sampling problem. The force field problem relates to the design of the energy function and its parameters that control how atoms interact with one another during a simulation. The sampling problem relates to the need to sample molecular events over timeframes that extend far beyond those that are capable of being reached using standard molecular dynamics methods. The objective of our research is to develop computational methods to address both of these issues, with an initial focus on the development of methods to calculate the free energy of peptide adsorption. In conventional simulations, peptides become stuck in low-energy conformations and this prevents adsorption free energy from being accurately calculated. We are therefore developing biased-sampling methods to enable adequate conformational space to be sampled in peptide-surface simulations so that adsorption free energy can be properly calculated. With this capability, the accuracy of a protein adsorption force field can be evaluated, modified, and validated by comparison between calculated adsorption free energy and experimentally measured values.

10:20am **BI1-WeM7 Model Dielectric Functions for Adsorbed Protein Layers**, ***H. Arwin,*** Linköping University, Sweden; *J.A. Woollam, D.W. Thompson,* University of Nebraska, Lincoln

A detailed knowledge about protein-surface interactions is of crucial importance for development of biomaterials, bioanalytical tools and biosensors as well as for understanding the mechanisms in protein-cell interactions. Ellipsometry is extensively used in these areas due to its nm-resolution in layer thickness and capability for in situ studies at solid-liquid interfaces. The outputs from an ellipsometer study are typically quantification of adsorbed surface mass and/or dynamics of protein adsorption. Recently also infrared ellipsometry has become available and optical signatures like amide bands in surface-bound proteins can be quantified. However, for layers of nm thickness, the analysis is not straight forward and it can be hard to separate thickness and refractive index of the protein layer, especially with single wavelength ellipsometry data.

Spectroscopic ellipsometry can in some cases resolve this but very few studies are reported. Another major advantage if spectroscopic data are available is the possibility to model, i.e. to parameterize the wavelength dispersion of the refractive index. This also leads to noise reduction. In this report a model dielectric function (MDF) concept for protein layers is proposed. Notice that the square root of the MDF equals the refractive index. The MDF is based on a Cauchy dispersion to which Lorentzian and/or Gaussian resonances are added to account for electronic and vibrational excitations in ultraviolet/visible and infrared spectral regions, respectively. The use of the proposed MDF is exemplified on fibrinogen adsorbed on gold. With variable angle spectroscopic ellipsometry, data were recorded in the spectral region 0.2 to 30 µm (300-5000 cm@super-1@) before and after protein adsorption. In the analysis the fibrinogen layer thickness is obtained as well as the refractive index (the square root of an MDF) and the amide bands I, II and A are resolved. A generalization to protein layers in general will be discussed.

10:40am **BI1-WeM8 Protein Nanopatterning onto Nanostructured Polymer Surfaces**, ***C. Satriano***, *G.M.L. Messina, G. Marletta,* University of Catania, Italy

The preferential adsorption of human fibronectin, lactoferrin, serum albumin and lysozime has been investigated onto nanostructured polysiloxane surfaces obtained by a colloidal crystal-based technique in combination with cold plasma treatment. In particular, 2D arrays of nanopores, having typical dimensions of about 55 nm of diameter and about 3 nm and 1 nm respectively for the rim height and the pore depth were fabricated. Polystyrene nanoparticles were used to imprint regularly-spaced nanopores within a bilayer formed by an untreated polysiloxane film onto a plasma-modified one. The internal area of the pores consisted of hydrophilic O@sub 2@-plasma treated polysiloxane, while the external surface was the hydrophobic untreated polymer. The spatially-resolved features of adsorbed proteins were investigated by means of Atomic Force Microscopy. The in situ adsorption process on homogeneously modified surfaces has been investigated by means of Quartz Crystal Microbalance with Dissipation Monitoring, while X-ray Photoelectron Spectroscopy was employed to evaluate ex-situ the coverage and thickness of the protein adlayers for the two types of surfaces. The results showed that the relevant chemical factors are the surface free energy and the chemical termination of the different surfaces. In particular, human fibronectin and lactoferrin showed a preferential adsorption outside of the hydrophilic nanopores, while lysozime and human serum albumin seem prefer the nanopore area. The results suggest that it could be possible to achieve the separation of protein mixtures by a spatially resolved adsorption.

11:00am **BI1-WeM9 Immobilization of Protein Nano-Clusters on Polymeric Nano-Craters**, *A. Valsesia,* ***P. Colpo***, EC-JRC-IHCP Italy*; M. Lejeune,* EC-JRC-IHCP Italy, Italy*; F. Bretagnol, T. Meziani,* EC-JRC-IHCP Italy*; F. Rossi,* EC-JRC-IHCP Italy, Italy

The reduction of the typical length scale in the creation of patterned surfaces is of high interest in the field of bio-interacting materials and more particularly for biosensors design. For instance, the creation of sub-micrometric or nano-metric patterns is important for the miniaturization of the actual protein and DNA micro-spotting technology, or for the minimization of the non-specific absorption in biosensors, or to increase the orientation capability of immunosensors. To generate these patterned surfaces at the submicron level, the use of classical optical lithography methods becomes complex, since they are reaching the diffraction limits when the feature sizes are lower than 200 nm. Among the alternative techniques of lithography such as E-beam, nano-sphere lithography is a reliable method to produce nano-topography over large area surfaces. In this work we developed a reliable technique to produce polymeric nano-craters with bio-specific carboxylic functionalities and with controlled surface density and distribution, surrounded by an homogeneous matrix of anti fouling polymer. The process has been carried out combining plasma deposition and etching techniques with colloidal masking. The plasma etching process parameters have to be accurately studied in order to create the nano-structures without affecting their chemical properties. The micro-structural characterization of the nano-structured films was carried out by the combination of Ellipsometry, FT-IR spectroscopy and Atomic Force Microscopy (AFM). The surface chemical contrast at the nano-scale was characterized by using Chemical Force Microscopy. The creation of nano-patterned surfaces with controlled topography and chemistry at the sub-micron scale was demonstrated. In particular a contrast in the wettability between the two nano-regions was observed. The preferential absorption of the biomolecules inside the fouling nano-craters was demonstrated by Confocal Fluorescence Microscopy measurements.

11:20am **BI1-WeM10 Binding of the Streptococcal C5a Peptidase to Immobilized Fibronectin**, ***J.R. Hull***, University of Washington*; G. Tamura,* The University of Washington Dept. of Pediatrics*; D.G. Castner,* University of Washington

Group B Streptococci (GBS) are a leading cause of sepsis and meningitis in newborns, and an emerging cause of serious bacterial infections in immunocompromised adults and the elderly. The streptococcal C5a peptidase (ScpB) of GBS is found in virtually all clinical isolates of GBS. ScpB inhibits neutrophil chemotaxis by enzymatically cleaving the complement component C5a. ScpB is a known Fibronectin (Fn) adhesin; however, it only binds to immobilized Fn and not soluble Fn. Therefore, it is unknown whether or not ScpB binds to a conformational determinate of Fn or multiple adjacent Fn molecules. For this study, surface plasmon resonance (SPR) was used to determine the affinity of ScpB for immobilized Fn. The measured affinity is in the nM range, which is biologically significant. ScpB was tethered to an atomic force microscope (AFM) tip via the bifunctional cross linker pyridyldithio poly(ethylene glycol) succinimidylpropionate (NHS-PEG-PDP). Each step of the tip functionalization was verified by X-ray photoelectron spectroscopy, static secondary ion mass spectrometry, and infrared spectroscopy. Adsorbed Fn was imaged via intermittent contact AFM with the ScpB modified tip at varying surface concentrations. Then force-distance curves were used to measure the interactions between ScpB and adsorbed Fn.

11:40am **BI1-WeM11 Enzyme Adsorption as a Model System to Probe Adsorption-Induced Changes in Protein Bioactivity**, ***K.P. Fears***, *Y. Sun, R.A. Latour,* Clemson University

Although the control of the bioactivity of adsorbed proteins is recognized to be critical for the control of cellular response, little is known about the actual molecular mechanisms involved. Molecular simulation provides great potential to elucidate these mechanisms and to be developed as a tool for surface design to control the orientation, conformation, and bioactivity of adsorbed proteins. The development of accurate molecular simulation methods, however, is critically dependent on the development of experimental methods that can be used to isolate specific molecular events using protein-surface systems that are sufficiently simple to enable them to be represented in molecular simulations. The objective of this research is to experimentally develop model enzyme adsorption systems for this purpose. Homogenous alkanethiol self-assembled monolayers with various end group functionalities are being used in conjunction with surface plasmon resonance spectroscopy to measure the effect of adsorption on protein bioactivity using a set of small enzymes (e.g, lysozyme, trypsin) with known molecular structure, bioactive site, substrate, and native-state bioactivity. An adsorbed trypsin layer on a positively charged surface was measured to be approximately 96% active, only 5% active on a hydrophobic surface, and have no detected activity on a negatively charged surface. It is hypothesized that orientational and conformational effects are primarily responsible for the differences between the charged surfaces and the hydrophobic surface, respectively. Circular dichroism studies are planned to measure the secondary structures of the adsorbed proteins to support this hypothesis.

Biomaterial Interfaces
Room 312 - Session BI2-WeM
Biomembranes and Spectroscopy

Moderator: J. Hickman

8:20am **BI2-WeM1 Fabrication of Well Structures with Electrode by Synchrotron Radiation Etching and Formation of Lipid Bilayer Giga-Ohm Seals**, ***Md. Rahman***, The Graduate University for Advanced Studies, Japan*; R. Tero,* NINS, Japan*; Y.-H. Kim,* The Graduate University for Advanced Studies, Japan*; T. Yano, M. Aoyama,* NINS, Japan*; R. Sasaki, H. Nagai, M. Yoshida,* AISHIN SEIKI Co., Ltd., Japan*; T. Urisu,* NINS, Japan

Supported membrane is a lipid bilayer supported on solid surfaces, and is useful as an artificial cell membrane for the study of biological reactions of membrane proteins. We are developing supported membrane biosensors for the purpose of developing the new research tool of the cell membrane surface reactions. These devices are interesting also from the view point of the application to the large scale screening method for the new medicine development. We have established a technique to fabricate a well-type microelectrode with about 1 µm diameter on the surface of a SiO@sub 2@/CoSi@sub 2@/Si substrate. The SiO@sub 2@/CoSi@sub 2@/Si was covered by Co contact mask by sputtering deposition. The circle pattern was made on the Co mask using the femto-second laser ablation. The

SiO@sub 2@ was etched by synchrotron radiation (SR) etching. SR was used because of its unique features such as high spatial resolution, extremely high material selectivity between CoSi@sub 2@ and SiO@sub 2@, low damage, and clean etching atmosphere. AFM images of the SiO@sub 2@ surface after the removal of the Co mask with 0.1 M HNO@sub 3@ aq. showed that the surface was very flat (R@sub a@=0.8 nm). Ag (50 nm) was deposited by electroplating on the CoSi@sub 2@ which is exposed at the bottom of the etched well. Then the surface of the Ag was coated with AgCl also by electroplating. A single planar lipid bilayer (DPPC : POPS = 90:10) was deposited on these microelectrodes by the rapture of giant unilamellar vesicles. From the I-V characteristics of the membrane, the resistance of the lipid bilayer was 1.2 G@ohm@. This value was larger enough for the single channel current measurement. The measured capacitance was 10.7 pF, which is larger than that estimated from the total electrode area. This may be due to that the charge is accumulated at the larger area of the lipid bilayer than the area of just the electrode holes by the current through the thin (1 nm) water layer under the lipid bilayer.

8:40am **BI2-WeM2 Probing Lipid Membrane Responses to Surface Morphology**, ***S.D. Gillmor***, *J.J. Heetderks, X. Wang, Q. Du, P.S. Weiss,* The Pennsylvania State University

The outer cellular membrane is a mixture of protein receptors, lipids and cholesterol whose organization is incompletely understood. Many cell membranes have complex interactions with the underlying basement membrane, and our investigations focus on lipid deformation due to adhesion to this support. We model the complex basement membrane structure chemically and topographically, through lithographically defined features for control over substrate morphology, and through chemical modification of the surface. Initially using simplified, lipid-only giant unilamellar vesicles (GUVs) as models, we probe the membrane behavior in response to surface topography. Biotin-labeled lipids allow us to tether the vesicles to the surface and to investigate the role of adhesion proteins in the deformation during the vesicle-surface interactions. From confocal microscopy, we image the profile of the vesicle on both planar and topographically patterned substrates. From our model system, we measure the lipid membrane deformation due to the topography, and we compare these findings with the line tension characterization in the literature.@footnote 1@ We model and categorize these responses in our simple system using phase field formulation and compare these findings to cell responses on topographically patterned surfaces. @FootnoteText@ @footnote 1@ Baumgart, Hess and Webb, (2003) Nature 425, 821.

9:00am **BI2-WeM3 Computer Simulation of Water-Mediated Force between Supported Phospholipid Membranes**, *A. Pertsin,* University of Heidelberg, Germany; ***M. Grunze***, University of Maine and University of Heidelberg, Germany

The grand canonical Monte Carlo technique is used to calculate the water-mediated force operating between two supported 1,2-dilauroyl-DL-phosphatidylethanolamine (DLPE) membranes in the short separation range. The intra- and intermolecular interactions in the system are described with a combination of an AMBER-based force field for DLPE and a TIP4P model for water. The long range contributions to the electrostatic interaction energy are treated in the dipole-dipole group-based approximation. The total water mediated force is analyzed in terms its hydration component and the component due to the direct interaction between the membranes. The latter is, in addition, partitioned into the electrostatic, van der Waals, and steric repulsion contributions to give an idea of their relative significance in the water-mediated interaction of the membranes.

9:20am **BI2-WeM4 Phospholipid Bilayers Nanomechanics**, *G. Oncins, S. Garcia-Manyes,* ***F. Sanz***, University of Barcelona, Spain

Mechanical properties of several phosphocholine supported planar bilayers deposited on mica have been tested in liquid environment by lateral force microscopy (LFM) and force spectroscopy. The presence of these bilayers has been detected topographically using atomic force microscopy (AFM). To test how the presence of NaCl affects the frictional properties of phospholipid bilayers, samples in saline media ranging from 0 M to 0.1 M NaCl were prepared. Changes in the lateral force vs. vertical force curves were recorded as a function of NaCl concentration and related with structural changes induced in the phosphatidylcholine bilayers by the presence of electrolyte ions. Three friction regimes are observed as the vertical force exerted by the tip on the bilayer increases. In order to relate the friction response with the structure of the bilayer, topographic images were recorded simultaneously to friction data. Ions in solution have proved to be able to screen charges present in phosphatidylcholine polar heads, leading to more compact bilayers.@footnote 1@ As a consequence, the vertical force at which the bilayer breaks while performing friction experiments increases with NaCl concentration.@footnote 2@ In addition, images show that low NaCl concentration bilayers recover more easily due to the low cohesion between phospholipid molecules. The vertical mechanical resistance of phosphatidylcholine bilayers has been tested with force curves,@footnote 3@ showing a discontinuity when the bilayer breaks under the pressure exerted by the tip. As expected, the force at which this breakthrough takes place increases with NaCl concentration, pointing out an increase of vertical and lateral mechanical stability induced by ions. @FootnoteText@ @footnote 1@Pandit,S.A.; Bostick, D.; Berkowitz, M. L. Biophys. J., 2003, 84, 3743.@footnote 2@Oncins,G.; Garcia-Manyes, S.; Sanz,F.; (sent 1st revision to Langmuir)@footnote 3@Garcia-Manyes,S.; Oncins,G.; Sanz,F.; (sent 1st revision to Biophys.J.).

9:40am **BI2-WeM5 Fabrication of Nanobiological Materials through Molecular Self-assembly**, ***S. Zhang***, Massachusetts Institute of Technology **INVITED**

Two complementary strategies can be employed in the fabrication of molecular biomaterials. In the 'top-down' approach, biomaterials are generated by stripping down a complex entity into its component parts. This contrasts with the 'bottom-up' approach, in which materials are assembled molecule by molecule and in some cases even atom by atom to produce novel supramolecular architectures. The latter approach is likely to become an integral part of nanomaterials manufacture and requires a deep understanding of individual molecular building blocks, their structures, assembling properties and dynamic behaviors. Two key elements in molecular fabrication are chemical complementarity and structural compatibility, both of which confer the weak and noncovalent interactions that bind building blocks together during self-assembly. Significant advances have been achieved at the interface of biology and materials science, including the fabrication of nanofiber materials for 3-D cell cultures, tissue engineering and regenerative medicine, the peptide detergents for stabilizing, and crystallizing membrane proteins as well as nanocoating molecular for cell organizations. Molecular fabrications of nanobiomateirals have fostered diverse scientific discoveries and technological innovations. Shuguang Zhang made a serendipitous discovery of self-assembling peptides from studying yeast protein, zuotin. He subsequently conceptualized, developed and commercialized diverse self-assembling peptide materials including peptide nanofibers, functional peptide ink, peptide molecular switches and antennae, peptide surfactants/detergents. These self-assembling peptides materials have a broad spectrum of uses, ranging from nanofiber scaffold hydrogel for 3-D tissue cell culture, tissue repair, tissue engineering and regenerative medicine; biochips for direct printing, anchoring and patterning molecules and cells; and peptides for solubilizing, stabilizing and crystallizing membrane proteins. Using systematic and molecular engineering approach, he and his students, postdocs and colleagues opened a new avenue to fabricate novel nanobiological materials from bottom up through molecular self-assembly.

10:20am **BI2-WeM7 1-dimensionally Crosslinked Intra- and Interleaflet Bilayers for Cell Surface Studies**, ***R. Michel***, *M. Halter, G. Sather, E. Naeemi, D.G. Castner,* University of Washington

Although supported lipid bilayers are increasingly used as model systems for biological coatings, they lack the high stability desired for use in ambient or ultrahigh-vacuum environment. Poly(hydroxyethyl methacrylate) (pHEMA) is a hydrogel used in many biomedical applications, most commonly in ophthalmic applications. By tethering lipid bilayers to a pHEMA support, we better mimic the natural environment of the implant. In this work, a twofold approach was employed to stabilize the supported lipid film to the pHEMA. The intra-leaflet stabilization is achieved by cross-linking part of the lipids via the hydrophobic tail using SH-dipalmitoylphosphatidylcholine (DPPC) /acryloyloxy-phosphatidylcholine. To stabilize the leaflet to the surface, dimyristoylphosphatidylethanolamine (DMPE) lipids are mixed with the intra-leaflet crosslinked lipids. The DMPE lipids are crosslinked to the pHEMA substrate via 1.1' carbonyldimidazole (CDI) activation of the pHEMA surface and attachment of the polar head group. Using X-ray photoelectron spectroscopy (XPS), time-of-flight secondary ion mass spectrometry (ToF-SIMS), and fluorescence microscopy, we characterized the purity, composition, and degree of crosslinking of the bilayers. We find that use of these inter- and intra-leaflet crosslinking agents allow us to tailor the fluidity and rigidity of the supported lipid bilayers, which opens up new possibilities for protein incorporation and activity in these lipid bilayers.

10:40am **BI2-WeM8 A Method to Quantify and Evaluate the Efficiency of Nanometer-Sized Lipid Vesicle Modifications***, I. Pfeiffer,* Chalmers University of Technology, Sweden*; F. Höök,* Lund University, Sweden

We recently demonstrated a DNA-hybridization-based concept for site-selective and sequence-specific sorting of lipid vesicles on DNA arrays.@footnote1@ By utilizing bivalent cholesterol-based coupling of oligonecleotides to lipid membranes, we showed that the coupling was irreversible in a broad concentration range on planar supported phospholipids bilayers (SPBs) and that exchange between differently modified vesicles in a suspension was sufficiently low to provide efficient sorting. In order to evaluate in further detail the efficiency of this and other lipid vesicle modification protocols, we present in this work a generic method that provides a simple means of quantifying the modification in terms of number of molecules per lipid vesicle. By exposing an SPB to a mixture of cholesterol-modified DNA and lipid vesicles, the amount of free DNA, i.e. DNA not anchored to the lipid vesicles, can be estimated by recording the initial rate of binding to the supported membrane. By comparing the so obtained response with a calibration curve based on the initial rate of binding from suspensions of free DNA, it was demonstrated that the efficiency of the bivalent coupling was 100% in the range of <1 to 35 oligonucleotides per vesicle - thus demonstrating a high stability and efficiency of this particular coupling. The generic value of the method for other types of modifications was demonstrated using cholera toxin binding to GM1 modified lipid vesicles, and given that a solid support can be made inert to colloidal particles, the method holds great promise to be generic for any type of modification scheme. @FootnoteText@ @footnote1@Pfeiffer, I.; Hook, F. Journal of the American Chemical Society 2004, 126, 10224-10225.

11:00am **BI2-WeM9 Mapping Protein Dynamics in Living Cells using Two-Photon Image Correlation Spectroscopy***, P. Wiseman,* McGill University, Canada **INVITED**

We will present recent advances in image correlation methods and their application for measurements in living cells. The talk will focus on the development of image correlation spectroscopy (ICS) as an imaging extension of fluorescence correlation spectroscopy (FCS). The ICS technique is ideally suited to measure transport and clustering of fluorescently tagged proteins in cellular membranes where transport is slow and static proteins abound. The image correlation methods are based on the measurement of fluorescence intensity fluctuations as a function of space and time in cells collected as image time series using a laser scanning microscope (either confocal or two-photon). Spatial and temporal variants of the basic ICS method will be introduced and the power of these approaches to measure both aggregation and transport of cell surface proteins will be explained with the aid of computer simulations to demonstrate the measurement detection limits. The use of two-photon microscopy to perform image cross-correlation spectroscopy (ICCS) studies will also be discussed. ICCS allows direct measurement of the interactions of two co-localized proteins labeled with fluorophores having different emission wavelengths even in a high density environment. The transport properties of the co-localized proteins are also measured simultaneously by ICCS. Recent applications of the ICS and ICCS methods for characterizing the transport and clustering of GFP labeled alpha-actinin adhesion proteins in living fibroblasts will be presented. Image correlation studies which demonstrate simultaneous measurement of diffusing and flowing populations of alpha-actinin clusters, and correlated transport between the alpha-5 integrin and intracellular alpha-actinin in CHO fibroblasts at 37C will be shown. We will show spatially resolved vector maps of directed flow of proteins in living cells as measured using our new spatio-temporal ICS method.

11:40am **BI2-WeM11 Microspectroscopic Probing of Intracellular Structures by Observation of Infrared Linear Dichroism in Single Cells in a Micro-Fluidic Cuvette***, M. Schmidt,* University of Maine*; M. Rumpler, N. Gierlinger,* Max-Planck-Institut für Kolloid- und Grenzflächenforschung, Germany*; U. Schade,* BESSY GmbH, Germany*; T. Rogge,* Forschungszentrum Karlsruhe GmbH, Germany*; P. Fratzl,* Max-Planck-Institut für Kolloid- und Grenzflächenforschung, Germany*; M. Grunze,* University of Maine and Universität Heidelberg, Germany

Cellular properties and functions are closely related to cell structure. Probing intracellular structures and their dynamic nature is essential for the understanding of the functional characteristics of cells. Infrared (IR) microspectroscopy is an attractive tool for the investigation of biological materials and systems.@footnote 1@ Combining@footnote 2@ this technique with polarization modulation@footnote 3,4@ (PM) and employing synchrotron IR radiation allows us to perform polarization-dependent measurements with high spatial and temporal resolution. Thus, we are able to measure IR linear dichroism (LD) and hence determine preferred molecular orientation of distinct biochemical species in individual cells. Ultimately, observing single living cells in their native environment seems desirable when studying cell structure and function. Therefore, we developed an IR cuvette which facilitates the investigation of individual cells in aqueous solution. This custom-built, demountable and temperature-controllable micro-fluidic cuvette was microfabricated in order to meet the requirements of low pathlength (8 µm) and low volume (1 µL). Our goal is to gain insights into the formation and organization of the cytoskeleton in the context of cell adhesion. Using substrates with well defined surface properties and geometries we seek to control and model cell adhesion. Importantly, IR LD serves as an intrinsic marker for the preferred molecular orientation of the fibrous cytoskeletal proteins. Introduction of external stimuli such as chemicals, mechanical stress and substrate surface variation can be used to study the dynamic response and structural changes inside the cells. @FootnoteText@ @footnote 1@H.Y.N. Holman et al., J. Biomed. Opt. 7, 417 (2002).@footnote 2@Y. Shigematsu et al., Rev. Sci. Instrum. 72, 3927 (2001).@footnote 3@L.A. Nafie and M. Diem, Appl. Spectrosc. 33, 130 (1979).@footnote 4@T. Buffeteau et al., J. Chim. Phys. 90, 1467 (1993).

Biomaterial Interfaces
Room 311 - Session BI1-WeA

Protein-Surface Interactions
Moderator: J.Y. Wong, Boston University

2:00pm **BI1-WeA1 Time of Flight Secondary Ion Mass Spectrometry (ToF-SIMS) of Short Peptides-Noble Metal Surface Interactions Analyzed by Principal Component Analysis (PCA)**, ***N. Suzuki***, *L.J. Gamble, D.G. Castner, M. Sarikaya, F.S. Ohuchi,* University of Washington

Recent progress in the adaptation of combinatorial biology selection protocols to materials science has created a new class of polypeptides with specific affinity to inorganics. Here, we have used short peptide chains whose sequence consists of MHGKTQATSGTIQS in single- and triple-repeat forms, and have assessed quantitatively their binding specificity to Au, Ag and Pd surfaces by Time of Flight Secondary Ion Mass Spectroscopy (ToF-SIMS). Due to high mass resolutions, ToF-SIMS is capable of providing information about specific amino acidsâ?"surface interactions as well as their mutual interactions at the surface, but numerous mass fragments from the amino acids complete the analysis. We have therefore adopted Principal Component Analysis (PCA) to the static ToF-SIMS spectra, from which characteristic information related to binding specificity was obtained by reducing the dimension of data sets. The score plot in the PCA analysis has revealed that the effect of alkali ions from buffer solution significantly alters the fragmentation patters. Once, the grouping based on alkali ions content is carried out, the loading plot within the same group suggests that the strength of a localized amino acid sequence, MHGK, observed from the triple repeated chain differentiates the binding characteristics specific to a certain type of inorganics. In addition, the inherent binding site of this peptide toward inorganics is determined from loading plots. This technique is capable of analyzing the complex, multivariate ToF-SIMS spectra from the adsorbed polypeptide films and compared to univariate methods providing unique insight about the sample.

2:20pm **BI1-WeA2 The Application of Magnetic Tweezers to High Throughput Screening of Peptide Libraries**, ***H. Shang***, *G.U. Lee,* Purdue University

Single molecule force measurement techniques, such as, the atomic force microscope (AFM), have provided us with the ability to directly measuring the force and displacement involved in the rupture single ligand-receptor interactions. These techniques are providing us with fundamentally new information about molecular recognition interactions, which potentially is extremely useful for designing ligands for specific receptors. Magnetic tweezers is a technique in which micron size paramagnetic particles are used to transduce pico-newton scale force to single ligand-receptor pairs. This technique has the force resolution of a single hydrogen bond and allows millions of ligand-receptor pairs to be simultaneously screened. A kinetic model is used to analyze the data and the binding affinities of different ligand-receptor pairs are revealed by statistical analysis. The advantage of using this technique over conventional assays is that force can be used to define the affinity of the bond. In this presentation, we review recent single molecule force measurements with AFM and advances that have been made in screen phage libraries using magnetic tweezers.

2:40pm **BI1-WeA3 Invited Paper**, ***M. Grinstaff***, Boston University **INVITED**

NO ABSTRACT SUBMITTED.

Biomaterial Interfaces
Room 311a - Session BI2-WeA

Cell-Surface Interactions
Moderator: J.Y. Wong, Boston University

3:20pm **BI2-WeA5 Receptor-Ligand Interactions to Promote Endothelial Cell Adhesion and Function**, ***G.A. Truskey***, *W.M. Reichert, B. Chan,* Duke University **INVITED**

Endothelial cell adhesion and proper function are crucial for the development of tissue-engineered vessels and non-thrombogenic vascular grafts. In vivo shear stresses and mechanical forces can reduce adhesion endothelial cell function. We have systematically examined factors affecting endothelial adhesion and identified. To promote rapid and firm adhesion we developed a dual ligand system using a high affinity ligand to initiate adhesion and facilitate integrin-mediated adhesion. Avidin was used as the high affinity ligand. This ligand-receptor pair enabled endothelium to resist high shear stresses encountered in vivo. An RGD group was grafted onto avidin to permit adhesion to integrins. Interestingly, the RGD-avidin bound the endothelium in solution with high affinity and served to prime adhesion once the cells attached. Functional studies indicated that this dual ligand system promoted a nonthrombogenic phenotype. Preliminary in vivo studies of endothelium attached to ePTFE grafts indicate that the dual ligand system can promote firm adhesion but mechanical trauma to the graft is a significant limitation to complete coverage of endothelium. Current work is optimizing endothelial attachment to commercially available grafts and identifying a tissue-engineering alternative for endothelialization. (supported by NIH grants RO1 HL44972 and R21 HL72189.).

4:00pm **BI2-WeA7 Interactions Between Membrane-Bound Receptors and Soluble Ligands Measured by AFM, QCM-D and SPR**, ***Y. Lam***, *S.M. Alam, S. Zauscher,* Duke University

Many proteins in the immune system are membrane bound, presented on the cell surface. Once bound to their soluble ligands, they facilitate interactions to initiate a foreign body response. To gain a deeper understanding of these interactions we initially investigated the bonds between soluble antigen and antibodies by single molecule force spectroscopy using an atomic force microscope (AFM). We immobilized monoclonal antibodies (mAb A32) specific to HIV-1 envelope glycoprotein gp120 on a substrate, and incubated this surface with gp120. This interaction between gp120 and mAb A32 causes a conformational change in gp120, exposing an epitope for a secondary mAb (17b) to bind. We measured the strength of interaction between gp120 and 17b by single molecule force spectroscopy using a cantilever tip decorated with 17b. AFM was also used to generate an energetic landscape of the binding pocket via pulling force experiments at different pulling rates. We also report on our measurements using membrane bound receptors, providing a more native environment for the system. Quartz crystal microbalance with dissipation (QCM-D) was employed to monitor the formation of protein-lipid bilayer constructs. Finally we report on measurements using surface plasmon resonance (SPR) to elucidate changes in affinity between membrane bound and immobilized soluble receptors. This detailed knowledge of receptor ligand interactions is essential to better engineer and tailor therapeutic treatments for various diseases.

4:20pm **BI2-WeA8 A Photolithographic Method for Patterning Soft Polyacrylamide to Enhance Smooth Muscle Cell Elongation**, ***J.G. Jacot***, *J.L. Jackel, S.G. Koester, J.Y. Wong,* Boston University

Vascular smooth muscle cells (VSMCs) express a contractile phenotype in vivo that is lost as cells proliferate in vitro. The manufacture of a successful tissue engineered blood vessel requires the ability of VSMCs to proliferate and populate a scaffold, then revert to a contractile state. In vivo, VSMCs are highly elongated and previous studies from our lab have shown that cell shape influences the localization of proteins such as F-actin and calponin that have a contractile function. Further studies by others found that cell constrainment can also reduce proliferation. However, all these studies investigated cells on rigid substrates, which do not mimic the mechanical environment of the arterial wall, and cannot functionally measure contractile force generation. We have developed a soft lithography technique for patterning 10-micron lanes of collagen on soft polyacrylamide hydrogels. These patterned materials allow separate control of substrate elasticity and cell shape and also allow measurement of cell-generated forces by following the displacement of embedded fluorescent marker beads. Because these materials are fully hydrated and very compliant compared to previously patterned rigid cell culture substrates, maintaining high pattern resolution is difficult. The 10-micron patterns presented here are higher resolution than previously published protein patterns on soft polyacrylamide. Passaged bovine arterial VSMCs plated on these patterned hydrogels attach and spread only on the collagen lanes and have aspect ratios 2-fold higher than unpatterned VSMCs.

4:40pm **BI2-WeA9 Identification of Residual ECM Proteins Retained at pNIPAM Surfaces using Time-of-Flight SIMS**, ***H.E. Canavan***, *M. Greenfeld, X. Cheng, D.J. Graham, B.D. Ratner, D.G. Castner,* University of Washington

Treatment of tissue culture polystyrene (TCPS) with poly(N-isopropyl acrylamide) (pNIPAM) has been developed as a technique for the harvest of intact cell layers. Recently, we demonstrated that although low-temperature liftoff removes the majority of the Extracellular Matrix (ECM) concurrently with the cells, some protein does remain at the pNIPAM surface. However, little is known about the identity of the ECM proteins

retained at the pNIPAM surface after cell liftoff. In this work, we characterized the time-of-flight secondary ion mass spectrometry (ToF-SIMS) molecular fragmentation pattern of adsorbed single protein mixtures of important ECM proteins (e.g., laminin, fibronectin, and collagen). We next performed Principal Component Analysis (PCA) to distinguish between the proteins through the identification of unique amino acid fragmentation patterns in the ToF-SIMS positive ion spectra, a technique previously developed in our group. In this way, a model ToF-SIMS projection of the ECM was constructed. We subsequently compared the ToF-SIMS fragmentation pattern of the proteinaceous layer retained on the pNIPAM surface to that of the model ECM. ToF-SIMS fragmentation patterns of bovine serum albumin and serum-containing media controls were compared as positive controls as well. Using the comparison of the model ECM to that of ECM retained on pNIPAM surfaces, we discuss the identity of the proteins retained on the substrate after low-temperature liftoff from pNIPAM surfaces. We then compare our results to those obtained from analysis of the ECM using other surface analytical techniques, including immunoassay, gel electrophoresis, and matrix-assisted laser desorption ionization (MALDI).

5:00pm **BI2-WeA10 Compartmentalized Bioreactor Mitigates Culture Shock-Engenders Bone Tissue from Isolated Bone Cells**, ***D. Ravi***, *E.A. Vogler,* Penn State University

Reducing the profound gap between the physiological environment of the bone cells and in vitro cell culture models is critical for realizing the promise of tissue-engineering strategies to replace, regenerate and restore function to bone lost as a result of disease or injury. An advanced bioreactor that mitigates culture shock or the behavioral variations associated with the transition of bone cells from the in vivo to the in vitro environment was developed and tested. The bioreactor based on the principle of simultaneous-cell-growth-and-dialysis, separates a cell growth chamber from a media reservoir by a dialysis membrane, compartmentalizing cell growth and cell nutrition functions. As a consequence of compartmentalization, the pericellular environment is unperturbed by continuous perfusion or punctuated re-feeding schedules and luxury macromolecules synthesized by cells are retained in a manner that more closely simulates the in vivo condition. The stable culture conditions afforded by the bioreactor sustained model cell lines, mouse calvaria-derived MC3T3-E1 (ATCC CRL-2593) and human fetal osteoblasts (hFOB 1.19, ATCC CRL-11372) for extended time periods (30-120 days) without the need for sub-culture. The transformation of isolated osteoblast inoculum to mineralized, collagenous tissue that simulates native osteoid was followed using optical microscopy and scanning and transmission electron microscopy. Mineralization was assessed using Von Kossa assay and SEM-EDS (Energy Dispersive Spectroscopy. Development of differentiated, collagenous bone tissue (biosynthetic osteoid) from disaggregated osteogenic cells over 120 day culture was demonstrated on both 2-D polymer substrates as well as 3-D hydroxyapatite scaffolds. The compartmentalized bioreactor substantially mitigates culture shock and shows promise as an ideal in vitro tool for evaluation of orthopedic biomaterials and development of engineered bone tissue.

Biomaterial Interfaces
Room 311 - Session BI1-ThM

BioMEMS and Microfluidics

Moderator: G.P. Lopez, University of New Mexico

8:20am **BI1-ThM1 Long Lifetime Polymer Microfluidic Devices for HPLC-MS Applications**, ***K.L. Seaward***, *D.L. Ritchey, K.P. Killeen, H. Yin, R.A. Brennen,* Agilent Laboratories

Polymer microfluidic devices have been developed for High Performance Liquid Chromatography with integrated nano-electrospray tips for interfacing to Mass Spectrometry. HPLC-MS is regarded as a preferred analytical technique for protein identification in very small (nanoliter) volumes of sample and has been used, for example, to determine protein content in blood. Commercially available microfluidic devices consist of separate parts for liquid chromatography and electrospray functionality connected with fittings. This leads to difficulties in use, compromised performance, and complicated fabrication. The devices described in this presentation are made in a biocompatible polyimide and contain sample enrichment and liquid chromatography columns plus electrospray tips. Their size is approximately 2.5cm x 6cm with 200-400 micron thickness in a multi-layered structure made by direct laser writing of patterns followed by vacuum lamination. Laser cutting of electrospray tips and incorporation of metal traces in the layer structure provide electrospray functionality. A rotary valve interface between high-pressure fluids delivered by a nanoflow pump and the microfluidic device itself provides efficient fluid switching between various ports on the device. Gas-phase plasma processes, similar to those found in microelectronic device manufacturing, are used in the fabrication process. These are critical to ensure long lifetime performance of the devices, resulting in repeatable high-pressure performance of the column structures and stable electrospray behavior. In combination with mass spectrometry, state-of-the-art attomole level detection of protein digests has been demonstrated using these microfluidic devices. The device fabrication will be outlined and recent applications to proteomics will be shown.

8:40am **BI1-ThM2 BioMEMS Chip and Package Design for Surface-Controlled Bioreaction Processes**, ***J.J. Park***, *M.A. Powers, X. Luo, R. Ghodssi, G.W. Rubloff,* University of Maryland

BioMEMS research exploiting multi-step, multi-site biomolecular reactions for metabolic engineering and other applications requires an integrated chip, packaging, and control system designs to accommodate fluidic, electrical, and optical networks. We have developed approaches for sealing and re-opening bioMEMS systems to allow reuse and post-process analysis. Photoimageable SU-8 is used on pyrex wafers to create microfluidic channels as micro-knife-edges for sealing to flexible PDMS gaskets. Electrical networks provide Au and ITO electrodes for selective assembly and functionalization of amine-rich chitosan as the platform for biomolecular reaction steps, while integrated SU-8 waveguides enable fluorescence sensing at these sites. PDMS is spun onto a Plexiglas top wafer, inverted, and placed onto the SU-8 channels. The two wafers are then compressed by bolting together a Plexiglas package comprised of top and bottom plates, along with a Plexiglas ring which carries the inputs and outputs to external control systems. The design enables optical microscopy observations from above, which confirm leak-free sealing when colored dye is transported through the microfluidic network. Chitosan polysaccharide, positively charged in low pH solution, is electrodeposited at negative electrodes in the bioMEMS system. This provides a promising avenue for extending to bioMEMS environments our prior work using patterned electrodes on chips in solution, which included selective conjugation of proteins and nucleic acids, as well as enzymatic conversion of small molecules.

9:00am **BI1-ThM3 Artificial Extracellular Matrices: Polymer Films Modified with Positive Cues to Promote Cell Adhesion and Neurite Extension**, ***G.T.R. Palmore***, *H.-K. Song, D. Hoffman-Kim,* Brown University **INVITED**

Nerve growth is modulated in vivo by positive (permissive or growth-promoting) and negative (growth-inhibitory) biochemical cues. Neurons of the peripheral nervous system (PNS) are able to regenerate after injury because of the endogenous growth-promoting environment provided by Schwann cells. Traumatic injury to the central nervous system (CNS), however, often results in irreversible loss of function because the neurons in the CNS reside in an environment that contains too many negative cues and too few positive cues. We seek to calibrate the quantity of positive cues relative to negative cues needed for CNS regeneration and thus have fabricated patterned substrates of specific dimensions for this purpose. These substrates consist of a conductive polymer matrix doped and chemically modified with biologically-active molecules in varying spatial relationships. The preparation of these substrates will be discussed, including their spectroscopic, microscopic and immunochemical characterization. In addition, results will be shown that demonstrate how these substrates promote cell adhesion and guide neurite extension of neurons in the presence of both positive and negative cues.

9:40am **BI1-ThM5 Study of Molecular Transport in Nanofluidic Channels by Integrated Multiple Internal Reflection Infrared Waveguide**, ***T.C. Gamble***, *Y.J. Oh, C.H. Chung, D.R. Petsev, S.R.J. Brueck, G.P. Lopez,* University of New Mexico*; C.F. Ivory,* Washington State University*; S.M. Han,* University of New Mexico

We have successfully integrated nanofluidic channels into Si multiple-internal-reflection (MIR) infrared waveguides for the purpose of biomolecular separation and detection. Biomolecules, electrolyte solution, and their reactions can be probed by the MIR waveguide, provided that the channel width is substantially less than the IR wavelength. In the regime where the channel width (10 to 100 nm) is comparable to the Debye length (~20 nm) of the electrolyte solution, we have investigated the electrokinetic transport of fluorescent dyes in a range of pH with the application of transverse "gate" bias in the field effect transistor (FET) configuration.* The gate bias controls the zeta potential and therefore the electroosmotic flow of dye molecules with a possibility of reversing its flow direction. Fluorescent dyes are chosen for the purpose of initial transport studies and visualization. We will also present the effect of ionic strength on the electrokinetic transport of fluorescent dye molecules. The addition of salt increases the ionic strength, but it also adds mobile ions that can move through the thermal SiO@sub 2@ layer that insulates the Si substrate from the electrolyte solution. We evaluate the use of a Si@sub 3@N@sub 4@ sub-layer as a means of preventing the leakage current due to mobile ions moving through the SiO@sub 2@. We compare our observations with fluorescence spectroscopy and current measurements. * U.S. Patent Application was filed on July 19, 2004.

10:00am **BI1-ThM6 Electrochemical Programming of Bioactive Surfaces**, ***B.C. Bunker***, *M. Farrow, K.R. Zavadil, W.G. Yelton,* Sandia National Laboratories

Self-assembled monolayers containing cyclodextrin have been used as a template for the reversible electrochemical patterning of surfaces. Electrochemical patterning occurs as a result of the oxidation and reduction of functionalized ferrocene in solution. When Fe(II) is present in the ferrocene, this neutral aromatic species is adsorbed by the cyclodextrin surface. When Fe(II) is oxidized to Fe(III), the ferrocene desorbs from the cyclodextrin. The electrochemically switchable surface is of interest in microfluidic systems when the ferrocene is functionalized to interact with specific biological species. We have succeeded in attaching biotin to the ferrocene via an ethylene glycol linkage. The biotinylated ferrocene can be made to adsorb and desorb from cyclodextrin deposited on gold electrodes. We have demonstrated that the biotin on the ferrocene is active toward the adsorption of streptavidin. With programmable streptavidin surfaces, we can create patterns with a wide range of biological species (i.e. any species that can be biotinylated). The synthesis, characterization, and electrochemical switching of the films are described, involving techniques such as cyclic voltammetry, electrochemical stripping, secondary ion mass spectroscopy, ellipsometry, and the quartz crystal microbalance. Use of the switchable films for creating programmable patterns of antibodies in sensors is described.

Biomaterial Interfaces
Room 311a - Session BI2-ThM

Sugars at Surfaces

Moderator: G.P. Lopez, University of New Mexico

10:20am **BI2-ThM7 Chemical Glycomics: Carbohydrates on Surfaces to Screen Biopolymer Interactions**, ***P.H. Seeberger***, ETH Zurich, Switzerland **INVITED**

The growing field of glycomics is suffering from the lack of molecular tools for screening, imaging, purification and other procedures that are routine in studies involving peptides and oligonucleotides. Using an automated oligosaccharide synthesizer we developed some time ago, access to defined oligosaccharides has become very rapid. These synthetic

molecules, as well as any isolated carbohydrate, can now be readily converted into a series of tools that aid biological and medical investigations. Described are: 1) Carbohydrate microarrays that require small quantities of material, are fully amenable to HTS technologies to screen carbohydrate interactions with proteins, DNA, and carbohydrates as well as cells; 2) Affinity colums, magnetic beads and carbohydrates containing biotin are used to isolate proteins interacting with oligosaccharides and glycoconjugates; 3) Carbohydrates equiped with fluorescent tags or quantum dots is used to image carbohydrates in vitro and in vivo. Application of these tools to biological problems of medical significance will be discussed. Particular emphasis will be placed on novel aminoglycoside antibiotics, HIV glycobiology and the development of fully synthetic carbohydrate vaccines.

11:00am **BI2-ThM9 Synthetic Glycopolymers as Scaffolds to Study Multivalent Carbohydrate Interaction at Surfaces***, **G. Coullerez**, K. Barth, M. Textor,* Laboratory for Surface Science and Technology, Switzerland

Carbohydrates are information-rich molecules vital in intercellular interactions. As cell surface receptors, they play a role as recognition site for interactions with other cells, viruses or bacteria. To investigate those bio-interactions sugar tools based on carbohydrate chemistry and sensitive analytical techniques are needed. Functionalized surfaces with synthetic carbohydrate-tagged polymers that display multiple copies of the binding sugar units are attractive approaches to mimic interaction at cell-surfaces. They are often multivalent providing strength and specificity. In this aim, we have developed PEG-graft polycationic copolymers tagged saccharides. While spontaneously adsorbed on negatively charged surfaces the copolymers show specific lectin and bacteria recognition. Combined with a photolithography patterning method on metal oxide surfaces (Nb@sub 2@O@sub 5@, TiO@sub 2@), the high specificity of this platform in a non-fouling background is also demonstrated. The glycopolymers can also be synthesized with atom transfer radical polymerization (ATRP) of glycosylated monomers, featuring a wide range of functionalities, molecular weight and polydispersity for specific protein or cell-targeting applications. To demonstrate the versatility of our approaches, we use in particular the well-known mannose-lectin Concanavalin A (ConA) or bacteria E. Coli specific interactions. To sense in situ/in real time and quantitatively the interfacial processes between carbohydrate-modified surfaces and proteins in solution, fluorescence microscopy and optical evanescent field based sensor are used. The carbohydrate surface density is also quantitatively investigated by chemical surface analysis methods (XPS, ToF-SIMS). First applications and case studies using synthetic glycopolymers tagged with mono- or oligosaccharide will be discussed mainly in the context carbohydrate chips for proteins and pathogens detection and delivery vectors to target specific cell receptors.

Biomaterial Interfaces
Room 311 - Session BI-ThA

Bionanotechnology
Moderator: T.P. Beebe, University of Delaware

2:00pm **BI-ThA1 Strategies to Increase the Sensitivity of Biosensors based on the Light Absorption of Immobilized Metal Nanostructures**, ***F. Frederix,*** *K. Bonroy,* IMEC, Belgium*; D. Saerens,* VUB, Belgium*; G. Maes,* KULeuven, Belgium*; S. Muyldermans,* VUB, Belgium*; G. Borghs,* IMEC, Belgium

The Transmission Plasmon Biosensor is a novel, cheap and easy-to-handle biosensing technique. It consists of immobilized metal nanoparticles that exhibit plasmon absorption peaks. This absorption is highly dependent on the size, the shape and the dielectric properties of the close environment of these nanoparticles and can therefore be used to perform biosensing. The nanoparticle films were realized using self-assembly techniques, thermal evaporation, electroless plating or soft-lithographic techniques. Mixed SAMs were used to couple antibodies to the nanoparticle films. The change in absorption properties of the nanoparticle films upon antibody-antigen binding was monitored in order to obtain quantitative information on the antibody-antigen interaction (prostate specific antigen). Besides the localised plasmon resonance sensing, we observed a novel physical phenomenon namely the intraband transition absorption enhanced sensing. Furthermore, the applied technique was identified to be a useful alternative for the most widely used clinical immunosensing technique, i.e. the ELISA technique. This promising alternative was applied onto modified microtitre plates, which allow for the implementation into an array technology. The Transmission Plasmon Biosensor fulfils therefore the needs of an ideal, multi-analyte bio(nano)sensor. However, the sensitivity could be a drawback of this sensing technique. We will show several strategies to increase the sensitivity to a diagnostically interesting concentration range (ng/mL range). These strategies will involve the use of camel antibodies to sense closer to the sensor surface (the sensitivity decreases exponentially away from the surface), the use of multiple nanoparticle films and nanoparticles with special morphologies. In addition, we will show that this sensing technique can be also applied for performing enzyme sensing and that it showed remarkable results for small molecule detection (antibiotics).

2:20pm **BI-ThA2 Impact of Composite Shell Thickness on Stability of Single Enzyme Nanoparticles**, ***A.S. Lea****, J.B. Kim, J.W. Grate,* Pacific Northwest National Laboratory

Single-enzyme nanoparticles (SENs), comprised of individual alpha-chymotrypsin molecules surrounded by a porous organic/inorganic composite network less than a few nanometers thick, have been developed. The synthetic procedure, entailing enzyme modification and two orthogonal polymerization steps, yields nanoparticles containing a single enzyme. In stability experiments, the incorporation of these enzymes into the nanostructure dramatically increased its enzymatic stability. Furthermore, the nanoscale structure around the enzyme is sufficiently thin and porous that it does not impose a significant mass transfer limitation on the substrate. We have used tapping mode AFM (TM-AFM) to characterize single enzyme nanoparticles containing alpha-chymotrypsin (SEN-CT). Compared to transmission electron microscopy (TEM), TM-AFM resulted in much quicker and more accurate characterization of SENs since they are still in a hydrated state. We can tailor the thickness of the composite shell during the orthogonal polymerization steps in the synthesis of the SENs. The measured size-distribution of the different preparations was used to relate enzyme stability to the thickness of the porous composite shell. We will discuss this relationship in detail.

2:40pm **BI-ThA3 Vertically Aligned Carbon Nanofiber Array Integrated with Active-Addressed Thin Film Transistors for Intra/Extracellular Stimulus and Measurement**, ***S.-I. Jun****, P.D. Rack,* The University of Tennessee*; T. McKnight, A.V. Melechko, M.L. Simpson,* Oak Ridge National Laboratory

Vertically aligned carbon nanofibers (VACNF) have been used as nanoscaled electrodes for electroanalysis and as nanostructured scaffolds for delivering biological material into live cells. Thin film transistors (TFTs) have long demonstrated their effectiveness for driving, switching, and read-out capabilities in many microelectronic applications. In this study, we have fabricated and characterized a 20X20 active matrix thin film transistor array with integrated vertically aligned carbon nanofibers grown from Ni catalyst by direct current plasma enhanced chemical vapor deposition (DC-PECVD). This integrated device provides great potential to perform direct cell sensing, probing, and recording with a high electrode density and active addressing. Consequently, actively addressed nanofiber arrays can offer bi-directional interfacing with tissue matrices using intercellular positioning of electrode elements as well as the potential for intracellular residence of probes within individual cells. For this device, each film in the TFT array was fabricated by an rf magnetron sputtering process with DC substrate bias at a substrate temperature below 200°C. In this presentation, we will demonstrate the process flow of the inverted metal-oxide-semiconductor field effect transistor and the nanofiber integration scheme. The electrical characteristics of the transistor will be discussed and the electrochemical characteristics of the TFT addressed array in various biological electrolyte solutions will be presented.

3:00pm **BI-ThA4 Dynamic Surface Modification and Patterning using Electrochemistry and Molecular Assembly Approach**, ***C.S. Tang****,* Swiss Federal Laboratories for Materials Testing and Research (EMPA), Switzerland*; S. Makohliso, M. Heuschkel,* Ayanda Biosystems SA*; J. Voeroes, S. Sharma,* Swiss Federal Institute of Technology (ETH)*; B. Keller,* Swiss Federal Laboratories for Materials Testing and Research (EMPA), Switzerland*; M. Textor,* Swiss Federal Institute of Technology (ETH)

Microarray technology is a powerful and versatile tool commonly used in biochemistry and molecular biology. This miniaturized and parallelized technique has contributed significantly to bioanalytical processes such as large-scale genomic sequencing. One option for additional flexibility within a microarray is the use of electrochemical tools to dynamically influence and steer formation and properties of adsorbed molecular layers at the solid-liquid interface. By controlling and manipulating the placement of polyelectrolytes and biomolecules under the influence of an electric field, we have demonstrated that an electroactive biosensing platform with specificity and high sensitivity enable rapid screening and discrimination of different biomolecules with high selectivity. Using patterned substrates consisting of conductive areas in a non-conductive background, the electrically switchable surface can be modified to reversibly adsorb and release an adlayer of protein-resistant polymer. Macromolecules or biomolecules could be subsequently adsorbed onto the polarized indium tin oxide (ITO) microelectrodes by using simple surface chemistry. As a proof of concept, labeled functionalized polymer, proteins and vesicles were immobilized onto the ITO microelectrodes to produce a highly selective and heterogeneous microarray with specific electronic addressability. Some future applications with a localized addressable electronic microarray could include microfluidics, biosensors, drug delivery and manipulation of cellular neuron network for tissue engineering.

3:20pm **BI-ThA5 Fabrication of Bioconjugated Polymeric Nanostructures and Metal Nanowires by AFM Anodization Lithography**, *W.-K. Lee, H. Ma, S. Chen, A. Chilkoti,* ***S. Zauscher****,* Duke University

Patterning of polymeric and biomolecular nanostructures on surfaces and the control of their architecture are critically important for the fabrication of biomolecular devices and sensors. Here we show for the first time how we use AFM anodization lithography to chemically modify polymer brushes directly to allow conjugation of biomolecules. Surface-confined non-fouling and protein resistant poly(oligo(ethylene glycol) methyl methacrylate) (pOEGMA) brushes were prepared on silicon substrates by surface-initiated atom transfer radical polymerization (ATRP) in a grafting-from approach. These pOEGMA brushes were then patterned directly on the nanoscale by AFM anodization lithography, generating nano-trenches with carboxylic acid functionality. Proteins were then immobilized on these nanopatterned areas by suitable coupling chemistries. We also show an intriguing approach to deposit gold onto silicon oxide patterns by field-emission from gold-coated AFM probes. We capitalize on this novel lithography approach to fabricate gold nanowires of arbitrary shape. Our unique nanofabrication approaches lead to novel types of nanostructures that can potentially be used as biosensors or as substrates for the precise presentation of biomolecular queues to cells. Furthermore, our gold nanostructures can be used for electrical connections, or as plasmonic structures for biomolecular sensing.

3:40pm **BI-ThA6 In-situ Microcontact Printing of Proteins**, ***D. Mayer****, D. Schwaab, O. Salomon, A. Offenhaeusser,* Research Center Juelich, Germany*; A. Yasuda, J. Wessels,* Sony International (Europe) GmbH, Germany

Soft lithography appears to be a promising candidate among other techniques like electron beam-, ion beam- or x-ray lithography, in order to define structures below 100 nm. In contrast to the others, soft lithography has the advantage of being a relatively simple low costs technique. In

addition, the technique can in principle be applied for large areas and therefore provides a fast lithography process. Furthermore soft lithography is fully chemical and bio-compatible. The main objective of the presented work is to establish a powerful technique in order to transfer biomolecules to functional surfaces with structure size beyond the limit of photolithography. On this account we have developed a novel in-situ approach for the patterned transfer of proteins. The proposed technique is a modification of the commonly used Microcontact Printing (@mu@CP). The main derivative is that all transfer steps are performed under physiological conditions. For testing the capabilities of in-situ Microcontact Printing we have used horse heart cytochrome c (cyt c) as model molecule. Electrochemical investigations were performed to compare the conventional and the new in-situ @mu@CP method by measuring the redox activity of cyt c transferred with different techniques. We succeeded to print proteins under conservation of their structural integrity and functionality, while the activity of molecules transferred with conventional @mu@CP is much lower. In addition we will demonstrate by means of surface scanning microscopy methods that this technique is also capable of transfer patterns with a critical dimension of 150nm.

4:00pm **BI-ThA7 Microfluidic Neuronal Culture Device for Neuroscience Research**, ***N.L. Jeon,*** University of California, Irvine **INVITED**

This presentation will describe a novel microfabricated neuronal culture device and its application in Alzheimerâ?Ts Disease and Axonal Regeneration research. The device combines microfabrication and surface micropatterning approaches to create a multi-compartment neuronal culturing platform that can be used in a number of neuroscience applications. A replica-molded PDMS is placed on a tissue culture dish (polystyrene) forming two or more fluidically isolated compartments. These compartments are separated by a physical barrier in which a number of micron-size grooves are embedded to allow growth of neurites across the barriers while maintaining fluidic isolation. Cells are plated into the somal (cell body) compartment and after 3-4 days, axons extend into the adjacent compartment via the grooves. We have successfully used this device to culture primary rat cortical and hippocampal neurons for upto 3 weeks. We demonstrate the ability to maintain fluidically isolated compartment and, thus, expose localized areas of neurons to insults applied in soluble form. We also use microfluidics-compatible surface micropatterning approach to facilitate identification and visualization of neurons. The ability to direct sites of neuronal attachment and orientation of axon outgrowth by micropatterning techniques, combined with fluidically isolated compartments within the culture area offer significant advantages over standard open culture methods and other conventional methods for manipulating distinct neuronal microenvironments.

4:40pm **BI-ThA9 Investigations About the Formation of Supported Phospholipid Bilayers on Structured Surfaces**, ***B. Seantier,*** *I. Pfeiffer, M. Zaech, D. Sutherland,* Chalmers University of Technology, Sweden

There has been a strong current interest in the interaction of lipid vesicles with different homogenous materials surfaces. A number of mechanisms have been discussed leading to the formation of Supported Phospholipid Bilayers (SPBs) (for example on flat SiO@sub 2@) or intact vesicles (for example on flat Au). In our study, we have utilized lithographically defined nanoscale patterns to investigate the role of local variations in surface topography and chemistry on vesicle-surface interaction. We have studied surfaces combining two chemistries (SiO@sub 2@ and Au) where the domain sizes are similar to or below the characteristic size of the vesicles. The mechanism of the SPB formation has been studied by varying parameters such as phospholipids composition, vesicles size and concentration, and the ionic strength of the buffer solution. Quartz Crystals sensor surfaces were structured using dispersed colloidal monolayer masks (d=100nm) and lift off pattern transfer giving pits with combinations of upper and lower surface (~20% of the total surface area) chemistries. 100 nm and 200 nm extruded vesicles of POPC and DMPC have been used to form SPBs (vesicle conc. range varied between 50 μM and 500 μM with and without CaCl@sub 2@). Parallel experiments with identical surfaces utilized Quartz Crystal Microbalance with Dissipation monitoring technique and the Atomic Force Microscopy technique providing time-lapse images of the SPBs formation. The results show a two step mechanism, different from the classical SPB formation, which cannot be explained by the superposition of the vesicle behavior on Au and SiO@sub 2@ surfaces. A complex mechanism involving trapping vesicles in holes and SPB formation at the pits is assumed. In the future perspectives, the size and the shape of the Au pits will be varied. This study should allow us to better understand the influence of the surface topography and chemistry on the SPB formation.

5:00pm **BI-ThA10 Bionanodevices Integrating Biomolecular Motors**, ***R. Tucker,*** University of Florida*; S. Ramachandran, D. Wu, T. Nitta,* University of Washington*; H. Hess,* University of Florida

Biomolecular motors have the ability to convert chemical energy into mechanical work with high efficiency, and can be used to integrate active movement and actuation into hybrid micro- and nanodevices. Recent improvements in the design of nanoscale transport systems (molecular shuttles) based on the motor protein kinesin will be discussed. We will focus in particular on the selective capture of target analytes by the transporters, and on improving the control over motor activation. An investigation into the origins of velocity dispersion of molecular shuttles traveling in channels permitted us to compare sample dispersion occurring in this novel mechanism of transporting samples with established transport methods, such as pressure-driven fluid flow or electroosmotic flow. Applications for biomolecular motor-based devices can be found in a variety of biosensing scenarios.

Biomaterial Interfaces
Room 311 - Session BI+SS-FrM

Biomaterials Surface Characterization
Moderator: S.L. McArthur, University of Sheffield, UK

8:20am **BI+SS-FrM1 Charge Injection Barriers and Gap States at the L-Cysteine/Au Interface**, ***M.M. Beerbom***, *R. Gargagliano, R. Schlaf,* University of South Florida

Protein/inorganic materials interfaces are interesting for many bio-engineering applications such as bio-sensors or molecular electronic devices. L-cysteine is particularly interesting since it can form self-assembled monolayers on gold due to its thiol-group. In our experiments we investigated the L-cysteine/Au interface using x-ray and ultraviolet photoelectron spectroscopy (XPS, UPS) in combination with a multi-step deposition procedure. PE-spectra obtained after each deposition step yielded a data set allowing the determination of charge injection barriers at the interface, as well as the characterization of the chemical interaction. The L-cysteine deposition was carried out in a glove box directly attached to the PES system enabling contamination-free measurements. Our results indicate the formation of an interface state within the HOMO-LUMO gap due to the thiol-Au interaction.@footnote 1@ This is supported by control experiments on L-cysteine/graphite interfaces, which did not show the formation of this gap state. @FootnoteText@ @footnote 1@M.M. Beerbom, R. Gargagliano and R. Schlaf: "Determination of the Electronic Structure of Self-Assembled L-cysteine/Au Interfaces Using Photoemission Spectroscopy", Langmuir Articles ASAP), (2005).

8:40am **BI+SS-FrM2 Injection into Vacuum and Alignment of Biological Molecules for Electron Diffraction**, ***D. Starodub***, *R.B. Doak, J.C.H. Spence, U. Weierstall, K. Schmidt, G. Hembree,* Arizona State University

Resolving the protein secondary structure (folding),critical for its functionality, is a demanding task, especially for the proteins, which cannot be easily crystallized. Recently it was proposed to collect diffraction patterns dynamically from an array of biological molecules embedded in submicron water droplets, consecutively traversing the intersection of a focused 50 keV electron beam and a polarized 100 W laser beam.@footnote 1@ The latter aligns the molecules due to field interaction with a dipole moment induced in the molecule with anisotropic polarizability tensor.@footnote2@ We show experimental results on generation of monodispersed microdroplets via growth of Rayleigh instability, their injection into high vacuum, evaporation and cooling. The limitations on the droplet size and temperature for a given jet source configuration are obtained. Rotational relaxation of the spherical (small protein) and rodlike (tobacco mosaic virus) biomolecules to thermal fluctuations about the equilibrium orientation is considered in viscous and free molecular flow regimes, and optimal conditions for alignment, sufficient to obtain sub-nanometer resolution in diffraction, are derived. We also consider adiabatic effects of different spatial profiles of laser beam intensity and droplet velocity on final oscillation states of a biomolecule. Supported by NSF funding SGER DBI-0429814. @FootnoteText@ @footnote1@J.C.H. Spence and R.B. Doak, Phys. Rev. Lett. 92, 198102(2004). @footnote2@J.C.H. Spence, K. Schmidt, J. Wu, G. Hembree, U. Weierstall, R.B. Doak, P. Fromme. Acta Cryst. A61, 237(2005).

9:00am **BI+SS-FrM3 Chemical Interaction Analysis of Adhesive Biomaterial-Hard Tissue Interfaces**, ***Y. Nakayama***, Toray Research Center, Inc., Japan*; Y. Yoshida, K. Suzuki,* Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Japan*; B. Van Meerbeek,* Catholic University of Leuven, Belgium

Adhesion to human hard tissue plays an important role in both dental and orthopedic therapies. Synthesized adhesive biomaterials made of polymer, as well as of functional monomer, have been developed. Among such adhesive biomaterials, those capable of forming chemical bond with hard tissue such as dentin, enamel or hydroxyapatite (HAp) are more appreciated for achieving more durable adhesion. Evidence of chemical bonding at biomaterial-hard tissue interfaces was recently reported for interfaces between polyalkenoic acid and enamel or HAp with the use of high resolution X-ray Photoelectron Spectroscopy (XPS).@footnote 1@ Preparation of ultrathin biomaterial molecular layer on enamel or HAp substrate enabled high resolution XPS spectrum to distinguish carboxylic carbons with chemical bond to HAp from those without chemical bond at the interface. Chemical interaction of carboxylic acids with HAp was analyzed and adhesion-decalcification concept (AD concept) was proposed.@footnote 2@ According to the AD concept, the less soluble the calcium salt of the acidic molecule, the more intense and stable the molecular adhesion to a hydroxyapatite-based substrate. Subsequently, adhesive performance of functional monomers, such as those containing dihydrogen phosphate or carboxylic acid, with HAp and dentin was studied.@footnote 3@ In this presentation, we will report chemical interaction analysis of functional monomer-hard tissue interfaces by utilizing high resolution XPS and relating analytical data. @FootnoteText@ REFERENCES:@footnote 1@ Y.Yoshida, B.Van Meerbeek, Y.Nakayama, J.Snauwaert, L.Hellemans, P.Lambrechts, G.Vanherle, K.Wakasa: J.Dent.Res., 79, 709 (2000).@footnote 2@ Y.Yoshida, B.Van Meerbeek, Y.Nakayama, M.Yoshioka, J.Snauwaert, Y.Abe, P.Lambrechts, G.Vanherle, M.Okazaki: J.Dent.Res., 80, 1565(2001) .@footnote 3@ Y.Yoshida, K.Nagakane, R.Fukuda, Y.Nakayama, M.Okazaki, H.Shintani, S.Inoue, Y.Tagawa, K.Suzuki, J.De Munck, B.Van Meerbeek: J.Dent.Res., 83, 454(2004) .

9:20am **BI+SS-FrM4 Evaluation of Residues on Implant Surfaces by X-ray Photoelectron Spectroscopy**, ***V. Frauchiger***, *R. Luginbuehl,* Dr. H.C. Robert Mathys Foundation

Success of modern implants does not depend on the proper material choice only, but also on the surface chemistry and the proper removal of the ubiquitous present surface contaminations. There are many contemporary analytical methods that permit the qualitative and quantitative analysis of picogram amounts, but only a few methods are suitable for a direct assessment without a special preparation of the implants or the chemical extraction of residues. We applied X-ray photoelectron spectroscopy to assess the cleanliness of osteosynthesis plates and hip endoprosthesis implants. In addition, specially designed test coupon surfaces were used to simulate different surface textures. The samples were soiled with exact amounts of two model process adjuvants (MPA). The first one was based on a mixture of organic compounds used in lubricants and cutting fluids while the second one contained inorganic particles used in blasting processes. The cleaning efficacy of an industrial cleaning process in aqueous media and with sonication was tested. Imaging XPS was applied to localize critical contamination on the surfaces and small area analysis was used to identify the organic residues. In addition to XPS, GC-MS and gravimetric analysis were carried out as complementary techniques. Principal component analysis was used to establish a sensitivity at the ng/cm@super 2@ level by calculating the ratio between the bulk implant material and the carbon or other MPA specific elements. Cleaning tests revealed that the organic residues are completely removed upon proper choice of cleaning conditions and detergents. Residual inorganic particles were found on many samples with a blasted surface texture. The particles were removed only by special treatment of the samples.

9:40am **BI+SS-FrM5 Characterisation of Analyte / Matrix Interaction for MALDI / TOF Targets Using Spatially Resolved X-ray Photoelectron Spectroscopy**, ***A.J. Roberts***, *D.J. Surman, S.J. Hutton,* Kratos Analytical Ltd, UK*; M. Resch,* SDG, Germany*; E. Raptakis, O. Belgacem,* Kratos Analytical Ltd, UK

Matrix-assisted laser desorption/ionisation (MALDI) is now an established technique for mass spectrometry of proteins and peptides. Different matrix-analyte preparation protocols have been shown to influence the desorption or ablation process resulting in either high or low metastable fragmentation. It has been speculated that following laser ablation the velocities of the analyte and matrix can be regarded as a valuable and meaningful characteristic of the MALDI process. However, the interaction and distribution of the analyte with respect to the matrix is poorly understood. Here we present a study of the distribution of a fluorinated peptide as a function of matrix material using imaging x-ray photoelectron spectroscopy (XPS). Both the lateral and depth distribution is investigated to draw conclusions on the incorporation of the analyte in the matrix.

10:00am **BI+SS-FrM6 In Situ Sum Frequency Generation Characterization of Adsorbed Alpha-helical Peptides**, ***N.T. Samuel***, University of Washington*; K. McCrea,* Polymer Technology Group*; L.J. Gamble,* University of Washington*; R.S. Ward,* Polymer Technology Group*; D.G. Castner,* University of Washington

Controlling and characterizing the structure of adsorbed biomolecules is important for applications in diagnostics, tissue engineering and nanobiotechnology. Our previous studies showed that peptides with well-defined sequences of lysine (K) and leucine (L) amino acids spontaneously adsorb onto hydrophobic substrates with an alpha-helix secondary structure. The present study characterizes the adsorption of the LK peptides onto the surface through two approaches - immersing the

hydrophobic substrate through the air-water interface (AWI) and avoiding the AWI. When the LK peptide is adsorbed avoiding the AWI a time-dependent change in the amide I intensity is observed. However, X-ray Photoelectron Spectroscopy (XPS) analysis showed no significant time dependence of the nitrogen surface composition. Similarly, the CH region of the SFG spectrum shows no time-dependence. These results indicate that the amide I SFG spectrum follows the time-dependent ordering of the peptide molecules on the hydrophobic surface. Results from site-specific labeling of the alpha-helix LK peptide molecules with deuterated leucine residues showed it was possible to follow interactions of one amino acid residue of the peptides with the surface.

10:20am **BI+SS-FrM7 Molecular Level Studies on Interfacial Protein and Peptide Structures Using SFG**, ***Z. Chen***, University of Michigan

Molecular structures of interfacial proteins and peptides play important roles in biocompatibility, anti-biofouling control, membrane protein function, and anti-microbial peptide behavior. Sum frequency generation (SFG) vibrational spectroscopy has been applied to investigate molecular structures of proteins and peptides at the solid/liquid interface in situ. A thin film model was adopted to interpret SFG spectra. Isotope labeled method was introduced in the SFG studies. SFG results demonstrate that C-H stretching and amide signals can elucidate structures of hydrophobic side chains and secondary structures of interfacial peptides and proteins respectively. Detailed correlations between SFG amide I signals and secondary structures of interfacial proteins and proteins have been deduced. Various peptides and proteins including several anti-microbial peptides, albumin, lysozyme, fibrinogen, and factor XII (FXII) have been studied. Time-dependent structural changes of adsorbed proteins at the solid/liquid interface have been monitored. In addition, SFG chiral spectra were collected from interfacial peptides and proteins, which provide additional measurements to determine structures of these proteins and peptides. We also showed that combinations of linear vibrational spectroscopy such as attenuated total reflection Fourier transform infrared spectroscopy with nonlinear vibrational spectroscopic techniques such as SFG and four-wave mixing provide more detailed structure of surfaces/interfaces than that from a single technique.

10:40am **BI+SS-FrM8 Using Ellipsometry and Textured Surfaces to Enhance Infrared Response of Adsorbed Biomaterials**, ***D.W. Thompson***, *J.A. Woollam,* University of Nebraska-Lincoln

Infrared spectra are of interest for numerous applications because of the chemical bond information present in the absorption characteristics, but obtaining meaningful infrared spectra from monolayers adsorbed to surfaces can be difficult because of the small amount of material being probed. For instance, it is often of interest to probe adsorbates on a surface after exposure to a protein solution. Use of textured (patterned) surfaces to increase the mass of material sensed is expected to enhance these spectra. Here the infrared ellipsometric enhancement is calculated for a layer of adsorbate on a number of proposed nanostructured surfaces to predict which is most advantageous for obtaining infrared spectra. The approach used here could also be applied to other adsorbates by optimizing the pattern dimensions for different sizes. It also works for visible spectroscopy as long as pattern dimensions are significantly smaller than the wavelength. The effect of using these structures (rods, wells, and trenches) is compared to the response of flat metal or dielectric surfaces over a range of incidence angles of the infrared beam. Predicted sensitivities are based on the calculated effect of adsorbate on intensities in an ellipsometric measurement. Trench structures appear to have significant advantages both in sensitivity and ability to distinguish adsorbed species orientation.

11:00am **BI+SS-FrM9 Understanding the Elasticity of Fibronectin Fibrils: A Single Molecule Force Spectroscopy Study**, ***N.I. Abu-Lail***, *T. Ohashi, R. Clark, H. Erickson, S. Zauscher,* Duke University

Although fibronectin (FN) is considered to be one of the most important components of the extracellular matrix, the detailed mechanism of the elasticity of FN fibrils is still unknown. To investigate the molecular origin of FN fibril elasticity we performed single molecule force spectroscopy (SMFS) measurements on a recombinant 1-8FN-III protein construct that contained two green fluorescent protein (GFP) domains spliced in-between the 3FN-III and 4FN-III domains. The relative strengths of both domains were investigated over a wide range of pulling rates (50 nm/s to 1745 nm/s). FN-III domains were distinguished from GFP domains based on their characteristic unfolding distance signature. We found that the mechanical stability of both domains was similar and that the unfolding forces of both domains were linearly related to the logarithm of the pulling rate. An extrapolation of the unfolding forces to small pulling rates showed that the force required to unfold the FN-III domains and GFP domains were undistinguishable and on the order of physiological forces (~10 pN). Our results, combined with earlier fluorescence resonance energy transfer (FRET) studies performed on the same recombinant proteins, suggests (1) that the FN-III domains are most likely bent and looped into a compact conformation in the cell culture and (2) stretching extends their conformation while the domains remain mostly folded.

11:20am **BI+SS-FrM10 Protein-Solvent Interactions in Surface-Grafted ELPs Measured by Single Molecule Force Spectroscopy**, ***A. Valiaev***, *D.W. Lim, S. Schmidler, A. Chilkoti, S. Zauscher,* Duke University

Stimulus-responsive biomolecules attract significant research interest due to their potential applications in areas such as drug delivery, molecular motors and nanoscale sensors. Here we present our results of the conformational and hydration behavior of surface grafted elastin-like polypeptides (ELPs), measured by single molecule force spectroscopy. ELPs are stimulus-responsive polypeptides that contain repeats of the five amino acids Val-Pro-Gly-Xaa-Gly (VPGXG), where Xaa is a guest residue, and undergo an inverse phase transition in response to an environmental stimulus, such as a change in temperature. Our results suggest that single-molecule force spectroscopy can be used to quantify the effect of the type of guest residue, pH or ionic strength on molecular conformation and elasticity. By fitting ELP force-extension data to a freely jointed chain model, using our newly developed data analysis approach, we showed that we can resolve differences in Kuhn segment lengths as small as 0.03 nm; i.e., differences that are about an order of magnitude smaller than those previously reported. The observed force-extension behavior at intermediate and large extensions supports a phenomenological model that describes ELPs as kinetically mobile and disordered macromolecules. Importantly we find that molecular elasticity upon extension arises both from a deformation of the polypeptide backbone and from hydrophobic polymer-solvent interactions. Our observations here agree with recent MD simulations which suggest that hydrophobic hydration of side-chains plays an important role for elasticity and provides the molecular basis for the inverse temperature transition behavior.

11:40am **BI+SS-FrM11 Developments of Flexible Tethers to Measure Antibody-Antigen Interactions using AFM**, ***Z. Suo***, *F. TerÃ¡n Arce, R. Avci, E. Smith, K. Thiltges, B. Spangler,* Montana State University

Functionalization of an AFM tip surface with covalently bound flexible tether molecules is of special interest because such a flexibility is necessary to measure, in a controllable fashion, the receptor-ligand binding events in the physiological environment of the biomolecules. However, the interpretation of the experimental data is often obscured by and confused with the nonspecific binding events between the substrate surface and the so functionalized AFM tip. Effective methods must be developed to eliminate and/or to identify these nonspecific binding events. To achieve these objectives we employed low densities of varying-length poly(ethylene glycol) (PEG) units grafted onto gold-coated AFM tip surfaces. These tethers were covalently linked to the antibodies of interest, in this case anti-cytochrome c. It was necessary to pacify the uncovered portions of the AFM tip in order to block the nonspecific tip-surface interactions. This was achieved by using the flowers-in-the-meadow concept: by mixing a self-assembled monolayers of small molecular size hydroxyl-terminated PEG unit (meadow) with the specifically terminated larger molecular size PEG unit (flower) as described above. AFM force-extension measurements using such a tip conducted on mica substrate covered with cytochrome c resulted in force and length distributions which are consistent with the tether lengths employed. The pH value and the ionic strength of the buffer have considerable influence on the binding events between the AFM tip and the surface covered with cytochrome c. We will present results covering these topics as well as the role of the coupling chemistry between the end terminals of a PEG molecule and the anti-cytochrome c and the AFM tip on the efficiency of antibody-antigen recognition events.

Magnetic Interfaces and Nanostructures
Room 204 - Session MI+BI-FrM

Biosensors and Biomagnetism
Moderator: D.P. Pappas, NIST-Boulder

9:00am **MI+BI-FrM3 Engineered Magnetotactic Bioreporter Bacteria@footnote 1@***, **L.J. Whitman,*** Naval Research Laboratory **INVITED**
There is an urgent need for compact, low power, broad spectrum sensors for sentinel point detection of toxins and pathogens. Although cell-based sensors have the potential to meet many of these requirements, it is a challenge to make such systems deployable because of the fragility of most cell cultures and the short lifetime of most bioreporter cells. We are addressing these issues by developing a robust, microbial sensor based on a strain of magnetotactic bacteria, Magnetospirillum magneticum AMB-1, that naturally produces an intracellular chain of magnetite nanoparticles (magnetosomes). We have produced a variety of genetically engineered AMB-1, including magnetic knockouts, with the goal of creating a reporter strain that only produces magnetosomes in the presence of specific toxic industrial chemicals. Wild-type and engineered strains have been extensively characterized by a variety of physical and chemical methods. We have determined that magnetosome production can be a rapid process, occurring in minutes, and that iron uptake correlates well with the measured magnetic moments. To rapidly determine when magnetosomes are present in the live cultures, a miniature optical system has been developed that detects differential light scattering from magnetically-aligned bacteria. Because stable populations of AMB-1 can be maintained for weeks under a range of environmental conditions, this organism appears to be a promising candidate for cell-based sentinel point detection. @FootnoteText@ @footnote 1@This work was done in close collaboration with M. B. Johnson, A. Krichevsky, J. C. Rife, M. J. Smith, C. R. Tamanaha, and R. J. Tonnuci at NRL, and B. M. Applegate, L. N. Csonka, L. K. O'Connor, and L. Perry at Purdue University. Supported by DARPA BioMagnetICs.

9:40am **MI+BI-FrM5 Synthesis and Surface Engineering of Superparamagnetic Nanoparticles***, **R. De Palma**, S. Peeters, K. Bonroy, G. Reekmans, F. Frederix, W. Laureyn, G. Borghs, C. Van Hoof,* IMEC vzw, Belgium*; G. Maes,* KULeuven, Belgium
Superparamagnetic nanoparticles with appropriate surface chemistry have been widely used for numerous applications such as MRI, hyperthermia treatment, magnetic biosensing, etc. These applications require that the nanoparticles have high magnetization values, a well-defined and controllable morphology and an overall uniform size distribution. In addition, these applications need special (bio)chemical functionalisation of the magnetic nanoparticles, specifically tuned towards their demands. Most work has been done in improving the quality of magnetic nanoparticles, but only a few scientific investigations have been carried out in engineering and improving their (bio)chemical surface characteristics. Here we present several approaches, to engineer the surface characteristics of superparamagnetic nanoparticles, without altering their magnetic and morphological characteristics. Monodisperse superparamagnetic nanoparticles with controllable size, shape and magnetic properties were synthesized based on the thermal decomposition method. The chemical functionality of these nanoparticles could be tuned by the covalent attachment of thin silane SAMs on the particle surface. An optimized procedure allowed the controllable deposition of high quality silane SAMs with different endgroups. By these means, the nanoparticles could be made water-soluble and capable to covalently couple biological receptors. Several receptors were successfully immobilized onto magnetic nanoparticles, while retaining their biological activity. The degree of receptor immobilization was determined to be 2-10 times higher, compared to 2D substrates. The synthesized magnetic nanoparticles were also coated with a thin shell of inorganic material such as Au and SiO@sub 2@ based on a novel and straightforward coating procedure. The superparamagnetic nanoparticles were characterised using TEM, XRD, FTIR, XPS, UV/vis, SQUID and Bradford.

10:20am **MI+BI-FrM7 Shaken Not Stirred, A New Approach to Biomagnetic Sensing***, **A. Hoffmann**, S.-H. Chung, K. Guslienko, S.D. Bader, C. Liu, B.D. Kay, L. Makowski, L. Chen,* Argonne National Laboratory **INVITED**
Micron and nanosized magnetic particles coated with biochemical surfactants have emerged recently as an important component for enabling many biological and medical applications. Among these biomagnetic sensors have received a lot of attention lately, due to their potential advantages of simplicity and rapidity. The most common approach to biomagnetic sensors utilizes magnetic beads, whose magnetic moment is detected by a magnetic field sensor, such as a giant magnetoresistive spin valve. In contrast we demonstrated a new substrate-free approach to biomagnetic sensing which uses the magnetic ac-susceptibility of ferromagnetic nanoparticles suspended in a liquid for the signal transduction.@footnote 1@ The magnetic relaxation of these nanoparticles is due to their Brownian rotational diffusion, which is easily modified by binding the target of interest to the particles. This scheme has several distinct advantages; (i) it requires only one binding event for successful sensing; (ii) since there is a useful signal both in the absence and presence of the target it has an inherent check for integrity; and (iii) the signal contains information about the size of the target besides the biochemical affinity, which may be used to further distinguish between several different potential targets. We are developing novel magnetic viruses for application in our sensing scheme. They provide a well-defined, mono-dispersed size distribution of the ferromagnetic particles and offer the possibility to readily engineer the desired biological recognition functionality. This work was supported by DOE, BES under contract W-31-109-ENG-38 and DARPA under contract 8C67400. @FootnoteText@ @footnote 1@ S.-H. Chung, et al., Appl. Phys. Lett. vol. 85, 2971 (2004).

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