Monday Afternoon, November 4, 2002

Nanometer Structures
Room: C-207 - Session NS+BI-MoA

Nanobiology
Moderator: V. Vogel, University of Washington

2:20pm **NS+BI-MoA2 Molecular Shuttles Based on Motor Proteins: Transporters for Nanotechnology**, ***H. Hess***, *J. Clemmens,* University of Washington, *C.M. Matzke, G.D. Bachand, B.C. Bunker,* Sandia National Laboratories, *J. Howard,* Max-Planck-Institute of Molecular Cell Biology and Genetics, Germany, *V. Vogel*, University of Washington

Active transport in cells, utilizing molecular motors like kinesin and myosin, provides the inspiration for the integration of active transport into synthetic devices. Hybrid devices, employing motor proteins in a synthetic environment, are the first prototypes of molecular shuttles - an active nanoscale transport system. The key problems for the construction of a molecular shuttle are guiding the direction of the motion, controlling the speed, and loading and unloading of cargo. Various techniques, relying on surface topography and chemistry as well as flow fields and electric fields, have been developed by us[1] and others[2] to guide the movement of molecular shuttles on surfaces. The control of ATP concentration, acting as fuel supply, can serve as a means to control the speed of movement. The loading process requires the coupling of cargo to the shuttle, ideally by a strong and specific link. Applications of molecular shuttles can be envisioned e.g. in the field of Nano-Electro-Mechanical-Systems (NEMS), where scaling laws favor active transport over fluid flow, and in the bottom-up assembly of novel materials. Recently, we demonstrated that the shuttles can be employed as self-propelled nanoscale probes to image surface topography.[3] The construction of an image relies on the tracking of the random movement of a large number of independent probes, a concept which is fundamentally different from e.g. the deterministic movement of a single tip in scanning probe microscopy. An aspect of our research is that devices using molecular shuttles can be based on mechanisms which are unique to the microscopic world. An example of this is the possible application of a Brownian ratchet for directional sorting.[4]

[1] Hess, H., et al., Nano Letters, 2001. 1(5): p. 235.
[2] Hess, H. and Vogel, V., Rev. Mol. Biotechn., 2001. 82: p. 67.
[3] Hess, H., et al, Nano Letters, 2002. 2(2): p. 113.
[4] Hess, H., et al., Appl. Phys. A, 2002. 75: p. 309.

2:40pm **NS+BI-MoA3 Nanomechanics of an Intrinsically Unstructured Protein**, *R. Mukhopadhyay*, ***J.H. Hoh***, Johns Hopkins School of Medicine **INVITED**

Microtubule-associated proteins (MAPs) are a class of proteins that bind to the surface of microtubules. These proteins are known to stabilize microtubules against depolymerization, and there evidence to suggest that MAPs play a role in maintaining spacing between adjacent microtubules and may play a role in cellular mechanics. MAPs are composed of two domains: the microtubule binding domain and the projection domains. Biophysical studies of the projection domain suggest that it is highly unstructured. We have recently developed a system to study the molecular mechanics of the projection domain of MAPs. In this system MAPs are end-grafted by their positively charged microtubule binding domains to a negatively charged surface. The properties of the projection domain are then probed by direct atomic force microscope (AFM) force measurements. These measurements show a long-range repulsive force that extends more than 100 nm from the surface, and is consistent with a polymer brush like interaction. A unique thrombin cleavage site at the boundary between the microtubule binding domain and the projection domain allows the projection domain to be proteolytically removed. This results in a total loss of the long-range repulsive force. The force is also sensitive to ionic strength, suggesting that, consistent with its sequence, the projection domain behaves as a polyelectrolyte. The polyelectrolyte nature of the projection domain and the large number of phosphorylation sites suggests a mechanism for regulating the mechanical properties of the protein. This notion is supported force measurements on phosphorylated and dephosphorylated MAPs. Thus phosphorylation of the MAP projection domain offers a biochemical mechanism for modulating the molecular mechanics of MAPS and the intermolecular forces between microtubules.

3:20pm **NS+BI-MoA5 Nanostructures for Analysis of individual Biomolecules**, ***H.G. Craighead***, *S.W. Turner, M. Foquet, J. Korlach, W. Zipfel, M. Levene, W.W. Webb*, Cornell University

We have used nanofabrication methods to create fine-scale fluid channels and optical devices for nano-scale spatial confinement of optical excitation for use in the analysis of individual biomolecules. Functional fluid systems with dimensions down to ~35 nm have been etched and created by use of sacrificial layer techniques. Narrow fluid channels have been used for DNA fragment sizing by single molecule analysis and used for fluorescence correlation spectroscopy with improved signal-to-noise ratios. Related lithographic approaches have been used to create regions of optical excitation, confined in all 3 dimensions, using metallic nano-constrictions or "zero mode waveguides" in which electromagnetic waves are exponentially attenuated. These devices enable practical studies of dynamic biochemical processes at the single molecule level. An example of such a process is the observation of the activity of a single DNA polymerase molecule during the replication of a DNA molecule. We have been able to optically observe the incorporation of individual bases in the DNA replication process. With optically differentiated base types, this could lead to high speed sequencing of single DNA molecules. These approaches may allow highly parallel observation and analysis of biochemical activity at the single molecule level. This work has been supported by The National Institutes of Health, the National Science Foundation through the NBTC and the Department of Energy. Fabrication of devices was done at the Cornell Nanofabrication Facility.

3:40pm **NS+BI-MoA6 Polyelectrolyte Multilayer Self Assembled Nanoparticles for Delivery of Transforming Growth Factor Beta**, ***C. Catuogno***, *M. Tabrizian,* McGill University, Canada

Biocompatible and biodegradable nanoparticles with additional high drug encapsulation efficiency and controllable targeting would form an ideal drug delivery system. Investigation of the possibility of making such vehicles is presented in this work. Such devices could be used in combination with polymeric bone scaffolds for delivery of transforming growth factor beta (TGF-b) in order to accelerate bone cell differentiation and bone formation in vitro. The particle shell is made of natural carbohydrate polymers namely chitosan or hyaluronic acid that are commonly used in tissue engineering. Chitosan is insoluble in water or in alkaline solutions but dissolves readily in dilute solutions of most organic acids. Chitosan has gel-forming ability at low pH and swells in acidic medium or in water. These proprieties added to those of hyaluronic acid have motivated the use of both materials to control TGF-b adsorption and release from the nanoparticles. Additionally, composite materials have been shown to improve mechanical properties of scaffolds. The nanoparticles are built from a succession of polyelectrolytes using the layer-by-layer method. Colloidal iron oxide particles are adsorbed on the polymer layers and encapsulated into the nanoparticles. This aims at inducing the guidance of nanoparticles using an external magnetic field to desired site of delivery when such device is used for in situ bone generation.

4:00pm **NS+BI-MoA7 Resolving Scanning Tunneling Microscopy Features of Oligomers Adsorbed on Si(100)**, ***B. Grandidier***, *Mathieu Dubois, C. Delerue, J.P. Nys, D Stievenard,* IEMN, France, *J. Roncali*, IMMO, France

Scanning tunneling microscopy (STM) gives the possibility to observe complex organic molecules on silicon surfaces in ultra-high vacuum. Although the reactivity of the silicon surfaces often leads to the modification of the molecular electronic states, a clever synthesis of the molecules can keep their structures intact after adsorption. As a result, the molecules are imaged in their integrity and the contrast variation observed along the molecules is usually associated with the highest occupied and lowest unoccupied electronic states of the molecules. Here, we have investigated the STM imaging of conjugated oligomers on Si(100) by tight binding simulations. The molecules are physisorbed on the surface and extend over a few dimers rows. Due to coupling of the molecular states with the electronic states of the silicon surfaces, we show that the off-resonance tunneling process is the major contribution to the tunneling current in usual tunneling conditions. As a result, the potential barrier is lowered when the tip scans above a molecule and the contrast variation gives an enhancement of the Si dimer rows. Experimental STM images of conjugated oligomers confirm this theoretical prediction.

4:20pm **NS+BI-MoA8 Q-dots Patterned Surfaces for Cell Adhesion**, *A. Szucs,* ***J.P. Spatz***, University of Heidelberg, Germany

Highly luminescent semiconductor quantum nanodots (Q-dots) regularly patterned on different substrates, were synthesized and applied as binding sites for single cell receptors in order to study cell adhesion. CdS, CdSe and CdTe/ Q-dots in the size range of 2-8 nm in diameter were generated in Poly (styrene-b-2-vinyl-pyridine) (PS-P2VP)/inorganic hybrid reverse micellar system (RM). Solid Cd salts loaded polymer cores, constructed by the 2-vinyl-pyridine, were used as nanocompartments for preparation of

uniform semiconductor nanoparticles. Particle size could be controlled by varying the diameter of the RM core, via the length of the core constructing polymer, and by changing the precursor salt loading in the polymer core. Different kinetics and structures were observed inside the RM core during the particle formation by using different precursor salts (Cd(ClO4)2, Cd(OAc)2). Photo luminescent properties of semiconductor nanoparticles were investigated by different methods (UV-VIS spectrophotometry, steady-state fluorescence, color luminescence imaging). "In situ" surface patterning on different substrates (Glass, Si-wafer etc.) by self-organization of the diblock copolymer micelles on the surfaces was monitored by AFM measurements.

4:40pm **NS+BI-MoA9 Cell Adhesion to Nanostructured Interfaces**, ***J.P. Spatz***, University of Heidelberg, Germany **INVITED**

Nanostructures with micrometer or nanometer spacings have been prepared through pure self-assembly of diblock copolymer micelles (formation and compartmental localization of metallic nanodots within block copolymer micelles) or in combination with a top-down approach (electron beam lithography). Within these structures, 7 nm Au particles can be positioned with a precision of < 10 nm and large freedom in pattern choice (periodic, aperiodic, dotes, lines). Specifically, this is obtained by casting a solution of HAuCl4 loaded block copolymer micelles onto the prestructured resist film. Due to capillary effects and steric hindering, the particles are centered within the prepatterned holes and at the edges of prestructured lines. Subsequent lift-off of the resist allows the removal of all micelles with the exception of those that are in direct contact to the underlying substrate. The block copolymer is then removed by plasma etching, which strips the polymer micelle and reduces the gold salt to gold thereby leaving behind nanoscopic dots or lines of gold in a defined array. These nanostructured interfaces are used as platform for biofunctionalisation of solid interfaces. The surfaces are used as a tool to investigate cluster formation of focal adhesion associated proteins of fibroblasts. Cultured human melanocytes allowed to study the regulation of cell shape through contact with interfaces offering different topography and biochemical pattern. The cellular morphology of melanocytes is a measurable indicator for cell reaction to the cellular environment. The characteristic cellular shape of different cell cultures was quantified by different shape parameters like the number and length of dendrites. A decreased signal-to-noise ratio was found for melanocyte cells concerning the number of dendrites and orientation of dendrites if cultured on biochemically and topographically structured substrates.

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