Sep 29, 2008 10:45 AM 1011 EB1	**Dr. Melissa Moss** University of South Carolina

Soluble amyloid-beta aggregation intermediates in Alzheimer's disease

Alzheimer's disease (AD), the leading cause of dementia in the elderly, is characterized by the presence of amyloid plaques in the brain parenchyma and cerebrovasculature. These deposits are comprised primarily of fibril formed via self-association of the amyloid-β protein (Aβ). Initial aggregation of Aβ monomer occurs via a rate-limiting nucleation step. Following nucleus formation, rapid growth ensues and proceeds through soluble intermediates. Increasing evidence suggests a role for Aβ assembly in the progression of AD, and what has become known as the 'amyloid cascade hypothesis' continues to gain support.

We employ a quartz crystal microbalance (QCM) to analyze the real-time growth of Aβ1-40 aggregation intermediates immobilized on the crystal surface. Calculated kinetic constants suggest that aggregation intermediates may support only 'docking' and not 'locking' of added monomer for the formation of stable structures. We also employ an endothelial cell culture assay, designed to mimic physiological responses observed in the cerebrovasculature of AD brain, to show that isolated soluble Aβ1-40 aggregation intermediates selectively stimulate physiological response.

Ultimately, the identification and characterization of compounds that halt the formation of physiologically active Aβ aggregates will be important to the development of therapeutic agents for AD. Future work will identify structure-function relationships to elucidate key structural features and functional groups for effective small molecule compounds.

Oct 6, 2008 10:35 AM EB1, Room 1011	**Dr. Phillip R. Westmoreland** University of Massachusetts Amherst / National Science Foundation

"Measuring and Predicting Reaction Kinetics for Clean Use of Biofuels"

Fuels from renewable biomass already make up part of our energy picture, and that must surely increase. However, relative to petroleum-based fuels, they are thought to generate increased aldehyde and NOx pollutants due to their high content of oxygen and sometimes nitrogen. We are working to explore, explain, and help solve these challenges. Our two major directions are measuring kinetics with flame molecular-beam mass spectrometry (MBMS) and predicting kinetics using theory, computational quantum chemistry, and our new Reactive Molecular Dynamics methods.

We recently built a pioneering MBMS apparatus based on synchrotron VUV-photoionization [Taatjes et al., Science, 308, 1887 (2005)] and have used it to study flames of hydrocarbons, alcohols, aldehydes, ketones, esters, and most recently morpholine. From the data, we have predicted and inferred reaction pathways and the key elementary-reaction kinetics. Another useful approach is using our Reactive Molecular Dynamics algorithm and RMDff force field, developed for my group's polymer research.

This new molecular-simulation method promises to yield powerful, quantitative insights into reactions that convert biomass into fuels, as it has for polymer decomposition. We hope to make the method still more accurate by computing energies with a new, rapid, electronic-structure-based method we have termed BEBOP (bond energies from bond-order populations). When implemented on parallel supercomputers, these methods will open the door to computational experiments for obtaining many types of reaction kinetics.

Oct 13, 2008 10:35 AM Room 1011, EB1	**Dr. Sean Palecek** University of Wisconsin

Regulating human embryonic stem cell differentiation via chemical and mechanical cues

Embryonic stem cells (ESCs) hold tremendous promise in tissue engineering and regenerative medicine applications because of their unique combination of two properties, pluripotency and an extremely high proliferative capacity. Theoretically, almost unlimited supplies of cells and tissues could be generated from a single clonal source if we can regulate ESC growth and differentiation. Hurdles facing utilization of ESCs in regenerative medicine include a lack of effective systems that permit robust, large scale culture and expansion of undifferentiated cells and a lack of reliable methods to differentiate ESCs to desired developmental lineages. Several critical factors regulate whether a human ESC (hESC) chooses to self-renew or differentiate. Soluble signals bind receptors and stimulate chemical pathways that lead to global changes in gene transcription and cell differentiation state. Likewise, immobilized extracellular matrix cues synergize with soluble signals to control cell signaling and differentiation. Cell-cell communication is also an important consideration in hESC culture; at low cell densities cell growth rates diminish while at high cell densities spontaneous differentiation occurs. Finally, mechanical signals have recently been shown to affect self-renewal and differentiation. I will discuss examples that illustrate how each of these microenvironmental stimuli can be incorporated in culture systems to expand or differentiate hESCs along desired lineages.

Applying cyclic biaxial mechanical strain, along with appropriate chemical self-renewal factors, to undifferentiated hESCs stimulates their self-renewal. Mechanical strain induces expression of TGFƒÒ superfamily ligands, which appear to act through a paracrine or autocrine signaling mechanism to maintain hESCs in a self-renewing state at high densities. We have developed materials that confine hESC colonies to specific sizes and shapes to assess how colony morphology affects self-renewal and directed differentiation toward therapeutically-relevant lineages, including cardiac myocytes. Finally, the temporal presentation of soluble differentiation factors (e.g. retinoic acid and bone morphogenic proteins) can be utilized to obtain pure populations of stratified epithelial progenitors, which can then differentiate to terminal cells such as epidermal keratinocytes.

Oct 27, 2008 10:45 AM 1011 EB1	**Dr. Tom Kuech** University of Wisconsin

Surfactants in Heteroepitaxy

The heteroepitaxial growth of semiconductors, particularly compound semiconductors, results from the interplay of thermodynamic and kinetic effects that are strongly influenced by the film strain and the specific nature of the surface chemical and transport properties. The film morphology, defect and film properties can all be controlled by these surface reactions. There have been many approaches to controlling the surface chemistry in order to achieve unique or improved properties.

In particular, the use of a surfactant during growth has been explored to modify strained-layer heteroepitaxial growth. For example, several studies using surfactants during the growth of SiGe have shown striking results. Antimony, bismuth and arsenic segregate to the growth front and alter the surface energy and surface kinetic processes of the growing strained SiGe layer. The use of these surfactants can lead to an increase in the pseudomorphic thickness of the SiGe layer and facilitate layer-by-layer growth.

There have been extensions of these studies to other systems. In the GaN-based systems, the addition of Bi or Sb can alter the appearance of specific surface crystallographic facets during growth and the surface morphology. In other systems, the presence of surfactants can disrupt the formation of ordered alloy structures. This talk discusses the range of surfactant-related effects important in heteroepitaxial growth and will focus on the underlying mechanisms affecting such changes in solid-state growth behavior.

Nov 3, 2008 10:45 AM 1011 EB1	**Dr. Darrin Pochan** University of Delaware

Construction of Nanostructures and Materials through Peptide or Charged Block Copolymer Self-assembly

Bionanotechnology, the emerging field of using biomolecular and biotechnological tools for nanostructure or nanotechnology development, provides exceptional opportunity in the design of new materials. Self-assembly of molecules is an attractive materials construction strategy due to its simplicity in application. By considering peptidic or charged synthetic polymer molecules in the bottom-up materials self-assembly design process, one can take advantage of inherently biomolecular attributes; intramolecular folding events, secondary structure, and electrostatic interactions; in addition to more traditional self-assembling molecular attributes such as amphiphilicty, to define hierarchical material structure and consequent properties.

First, design strategies for materials self-assembly based on small (less than 24 amino acids) beta-hairpin peptides will be discussed. Self-assembly of the peptides is predicated on an intramolecular folding event caused by desired solution properties. Importantly, kinetics of self-assembly can be tuned in order to control gelation time allowing for cell encapsulation. The final gel behaves as a shear thinning, but immediately rehealing, solid that is potentially useful for cell injection therapies.

Second, synthetic block copolymers with charged corona blocks can be assembled in dilute solution containing multivalent organic counterions to produce novel micelle structures such as toroids or helical cylinders. Micelle structure can be tuned between toroids, cylinders, and disks simply by using different concentrations or molecular volumes of organic counterion the kinetic pathway of assembly. The kinetics of block copolymer assembly can be specifically controlled to form hierarchically structured morphologies not possible through traditional block copolymer self-assembly.

Nov 10, 2008 10:45 AM 135 BTEC	**Dr. Steven Cramer** Rensselaer Polytechnic Institute

Intelligent Design of Chemically Selective Displacers and Multimodal Chromatographic Systems Using Protein Libraries, NMR, SPR and Multi-Scale Simulations

The design of novel multimodal chromatographic and chemically selective displacement systems requires a fundamental understanding of the binding of the ligands involved in these processes to protein surfaces. In this presentation a variety of experimental and theoretical approaches are employed to provide insight into the binding mechanisms involved in these processes and to exploit them for the design of chromatographic systems with unique selectivities.

Studies were carried out with various combinations of protein libraries, stationary phase ligands and/or selective displacers. Protein libraries included protein charged ladders as well as homologous libraries of protein variants. Mixed mode ligands included a range of chemically diverse ligands and chemically selective displacers were selected from libraries designed for selective binding to specific protein classes.

The tools employed in this work include high throughput screening, NMR, SPR and simulations. Nuclear Magnetic Resonance was conducted on a range of protein/stationary phase ligand or displacer mixtures to verify the binding to targeted proteins and the location of the binding event on both the ligand and protein surfaces.

Surface plasmon resonance experiments were carried out to study the inherent kinetics of these processes. Molecular dynamic simulations were conducted to corroborate the NMR results and to provide further insight into the binding and preferred protein-binding orientations on the chromatographic surfaces. Finally, this data is integrated into multi-scale models to aid in the development of novel chromatographic processes with unique selectivities and high performance.

Nov 24, 2008 10:45 AM 1011 EB1	**Dr. Anne Robinson** University of Delaware

Protein Folding in the Cell: Engineering Protein Expression by Understanding Biological Interactions

Our research efforts in bioengineering are aimed at understanding and controlling macromolecular functions and cell behavior to facilitate biotechnology research, development, and production. In order to improve protein expression, we must understand the behavior of proteins and other biological macromolecules in isolation, and in the complex environment of the cell. We analyze proteins' self-interactions during folding and purification, in order to control structure, function, stability and assembly. We also study protein-protein interactions and cellular pathways, and use our knowledge to maximize the production of functional proteins.

For biotechnology, protein- and polypeptide-based therapeutic and diagnostic agents are among the most promising clinical and preclinical candidates for treatment of auto-immune diseases and numerous classes of cancer. Aggregation is a particular problem for these proteins, during both production and formulation. We have used hydrostatic pressure approaches to study the folding and aggregation pathways of these proteins, and to refold antibodies from inclusion bodies.

I will show how we have developed accurate mechanistic models for the protein expression pathways in yeast, and used the tools of systems biology to identify key steps in the stress response pathway of yeast. Finally, I will discuss our studies of integral membrane proteins, which employ a synthesis of these two approaches along with biophysical analysis of protein conformation and stability. This combination is enabling us to make major advances in large-scale production and biophysical studies of the G-protein-coupled receptors – the largest known protein superfamily, and the targets of 30-50% of drug discovery efforts.

Dec 1, 2008 10:45 AM 1011 EB1	**Dr. Matthew DeLisa** Cornell University

Quality control mechanisms that regulate protein transport

All organisms, including bacteria, localize a fraction of all of their proteins partially or completely outside of the cytoplasm. Along the way, these proteins must cross at least one hydrophobic lipid membrane. The remarkable feat of delivering proteins across tightly sealed membranes is achieved largely by complex secretion machineries known as translocons.

The bulk of protein transport across the inner cytoplasmic membrane of bacteria is facilitated by the well-known general secretory (Sec) pathway, but additional modes for transport into or across the inner membrane exist, including the revcently discovered twin-arginine translocation (Tat) pathway. During both Sec and Tat transport, a variety of quality control checkpoints ensure that only proteins that pass a stringent selection process are allowed to enter the transport cycle thereby preventing any harmful effects that might be caused by the deployment of export-incompetent proteins.

Our studies in this area focus on fundamental and applied aspects of quality control mechanisms that regulate the transport of proteins into and across biological membranes. We are currently exploiting the protein folding quality control pathways of bacteria to (1) engineer “superproteins” - high-performance proteins that ignore at least some biologically imposed restrictions on amino acid sequence and occupy regions of sequence space unexplored by proteins optimized for in vivo function; and (2) create potent new protein therapeutics and vaccines.

In parallel, we are exploiting our ever-increasing awareness of the factors influencing protein folding in bacteria to engineer “better-folding cells” by re-designing the intracellular landscape in a manner that universally improves the efficiency of the folding process.