UNIVERSITY OF DELAWARE

Department of Chemical & Biomolecular Engineering

PROUDLY PRESENTS THE

WINTER RESEARCH REVIEW
4TH YEAR TALKS

CLAYTON HALL
JANUARY 29, 2014

UNIVERSITY *of* DELAWARE

Department of Chemical & Biomolecular Engineering

UNIVERSITY OF DELAWARE
Chemical and Biomolecular Engineering

Welcome to the Annual Winter Research Review presented by the Chemical and Biomolecular Engineering Department of the University of Delaware. We are pleased that you can join us for research presentations by our fourth-year graduate students. During the day you can also peruse the research posters of our third-year graduate students. Our graduate program encapsulates our principal missions of education and scholarship, and both types of presentations demonstrate the outstanding progress of our graduate students towards their professional independence. We hope that you will enjoy this opportunity to learn more about our department and research programs, as well as to meet the students and faculty.

Thank you for attending and enjoy the day!

Abraham M. Lenhoff
Allan P. Colburn Professor and Chair
Department of Chemical and Biomolecular Engineering

Amalie Tuerk
President of Colburn Club
The Graduate Student Organization

Colburn Club is the graduate student organization in the Chemical and Biomolecular Engineering Department, which is comprised of representatives from each year as well as a number of members filling specialized roles. The primary functions of the club are to organize research reviews and social events for the department, in addition to serving as one line of contact between the students and the faculty. We hope you enjoy this event and can join us again in the future.

The Colburn Club

www/che.udel.edu/cc

Alphabetical List of Talks

James M. Angelo, *Advisor: Abraham M. Lenhoff*
"Mechanisms of Protein Sorption and Transport in Polysaccharidic Layers within Ion Exchange Chromatography Media"
Committee: Norman J. Wagner and Christopher J. Roberts

Alex Apostolidis, *Advisor: Antony N. Beris*
"Hybrid 1D/3D simulations of the Human Arterial Network"
Committee: Eric M. Furst, Babatunde A. Ogunnaike, Prasad S. Dhurjati and David Johnson

Jonathan Bauer, *Advisor: Eric M. Furst*
"Directed Self-Assembly in Toggled Magnetic Fields"
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Daniel Blackstock, *Advisor: Wilfred Chen*
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Committee: Maciek R. Antoniewicz and Wilfred Chen

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Committee: Raul F. Lobo, Yushan Yan and Michael Tsapatsis

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Zachary S. Whiteman, *Advisor: Babatunde A. Ogunnaike*
"Design, Analysis, Operation, and Advanced Control of Hybrid Renewable Energy Systems"
Committee: Michael T. Klein and Ajay K. Prasad

Ke Xiong, *Advisor: Jingguang G. Chen*
"Selectively Activating the C=O Bond of Furfural Using Metal Carbide and Bimetallic Catalysts"
Committee: Dionisios G. Vlachos and Michael T. Klein

Bryan Yonemoto, *Advisor: Feng Jiao*
"Porous Electrode Materials for Energy Storage"
Committee: Raul F. Lobo and Yushan Yan

Jie Zheng, *Advisor: Yushan Yan*
"PtRu Coated CuNWs as an Efficient Catalyst for Methanol Oxidation Reaction"
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Chemical & Biomolecular Engineering

Winter Research Review
John M. Clayton Hall
January 29, 2014

8:30-9:00 **Breakfast (Clayton Hall lobby)**

9:00-9:10 **Welcome (Room 101 B)**
Professor Abraham M. Lenhoff, Department Chair

Session 1 (Room 101 B) (9:10 a.m. – 10:30 a.m.)

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10:50-11:10 **Angela L. Holmberg**
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Winter Research Review (cont'd.)

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Poster Presenters

Jennifer Au	**"**^{13}C Metabolic Flux Analysis of the *Clostridium acetobutylicum* Stress Response" ***Advisor: Maciek Antoniewicz***
Gregory Barnett	**"**Improved Understanding of an IgG1 Aggregation Mechanism" ***Advisor: Christopher J. Roberts***
Qi Chen	"Engineering 3-Dimensional Protein Scaffolds for Biocatalysts Assembly" ***Advisor: Wilfred Chen***
Daniel Cook	"Cellular Network Model of Liver Regeneration Reveals Potential Mechanisms of Regeneration Suppression" ***Advisors: Babatunde Ogunnaike, Rajanikanth Vadigepalli***
Colin Cwalina	"Shear Thickening Fluid (STF) - Nanocomposites for Hypervelocity Impact Resistance" ***Advisor: Norman J. Wagner***
Jingsi Gao	**"**Silica Particle Structure And Dispersion in Ionic Liquids" ***Advisor: Norman J. Wagner***
Daniel Greene	**"**Characterization of Protein Dense Phases**"** ***Advisors: Abraham M. Lenhoff, Norman J. Wagner and Stanley I. Sandler***
Bahar Ipek	"Hydrogen Adsorption on Cu(I)-Zeolites" ***Advisor: Raul F. Lobo***
Lilian Lam Josephson	**"**Microviscosity of Therapeutic Protein Solutions Using Particle Tracking Microrheology" ***Advisor: Eric Furst***
Tyler R. Josephson	**"**Solvation and Hydrogen Bonding Effects on the Reactivity of Biomass Derivatives" ***Advisor: Dionisios Vlachos***
Jason Loiland	**"**Low Temperature Catalytic NO Oxidation over Microporous Materials" ***Advisor: Raul F. Lobo***
Robert Lovelett	**"**Production of Thin Film Cu(Inga)Se2 via Rapid Thermal Processing" ***Advisors: Babatunde A. Ogunnaike and Robert W. Birkmire***

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Poster Presenters Continued

Eyas Mahmoud	"Renewable Production of Phthalic Anhydride from Biomass-Derived Furan and Maleic Anhydride" ***Advisor: Raul F. Lobo***
Elizabeth G. Mahoney	**"**Rational Design of Electrocatalysts for Fuel Oxidation in Alkaline Environments" ***Advisors: Jingguang Chen and Yushan Yan***
Ryan Murphy	"Block CoPolymer Micelle Dynamics" ***Advisors: Thomas H. Epps, III and Millicent O. Sullivan***
Myat Myint	**"**Controlling Reaction Pathways of C3 Oxygenates using Non-precious Bimetallic Catalysts" ***Advisors: Jingguang G. Chen and Yushan Yan***
Jonathan Rosen	"Nanoporous Silver as a Highly Selective and Efficient Electrocatalyst for Carbon Dioxide Reduction" ***Advisor: Feng Jiao***
Lisa Sawicki	**"**A Controlled, Dynamic Hydrogel Model Of Breast Cancer Recurrence" ***Advisor: April Kloxin***
Jarrid Wittkopf	"High-Performance Dealloyed PtCu/CuNW Oxygen Reduction Reaction Catalyst for Proton Exchange Membrane Fuel Cells" ***Advisor: Yushan Yan***
Mariah Woodroof	**"**In-situ Measurement and Comparison of Exchange Current Densities for Proton and Hydroxide Exchange Fuel Cells" ***Advisor: Yushan Yan***

Mechanisms of Protein Sorption and Transport in Polysaccharidic Layers within Ion Exchange Chromatography Media

James M. Angelo
Advisor: Abraham M. Lenhoff
Committee Members: Norman J. Wagner & Christopher J. Roberts

High loading capacity and rapid separation of proteins are strongly desired traits of ion exchange materials utilized in the downstream purification of biopharmaceutical agents. Ion exchange adsorbents containing covalently attached or grafted polymer layers have recently become more commonly used in preparative chromatography, which display these enhanced functional characteristics.

The complex networks of natural carbohydrates that polysaccharides such as cellulose and dextran provide incorporate easily accessible microstructures with substantial binding capacities for biomolecules. Stationary phase selection in industrial downstream applications is frequently performed in an empirical fashion, where optimization may be more conveniently achieved through the use of predictive modeling of protein transport. Before a predictive model may be formulated for these types of materials, an in-depth mechanistic understanding of protein binding characteristics and pore structure within the resin particles themselves must first be developed.

The anion and cation exchange moieties of commercially available cellulosic and dextran-grafted agarose materials were characterized by their adsorption capacity, uptake rates, protein retention and elution profiles at differing total ionic strengths and pH conditions. Batch experiments (adsorption isotherms and batch uptake kinetics) were performed along column level experiments (isocratic retention and column elution) to assess the binding characteristics of several model proteins. Additional mechanistic insight was sought using microscopic techniques to gain a physical understanding of protein uptake and elution profiles as well as multicomponent displacement.

A structural characterization helped determine the nature of the porous architecture within the modified materials using inverse size exclusion chromatography and electron microscopy techniques. Comparison between polymer-modified and non-modified materials was established to gauge the significance of pore structure in dictating functional and mechanical characteristics of these stationary phases.

Hybrid 1D/3D simulations of the Human Arterial Network

Alex Apostolidis
Advisor: Antony Beris
Committee Members: Eric Furst, Babatunde Ogunnaike, Dhurjati Prasad, David Johnson

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This research has been undertaken as a continuation of our efforts to develop a sophisticated model capable of predicting accurately the time-dependent blood pressure and flow profiles in the human arterial network. Even when one is interested in a 3D simulation of a specific vascular geometry, the complexity of the human system and the interconnectivity of all the vessels within it dictate the implementation of some type of simplified model for the rest of the network, if in vivo conditions are to be simulated. Thus, our approach so far has been to construct a hybrid model [1], involving a combination of a 1D and a 3D simulation.

In our earlier investigations we had studied the effects of non-Newtonian characteristics of human blood on steady state, shear flow conditions. Under these conditions, we systematically proved that the Casson constitutive model describes best the rheology of blood, while we also developed parametric equations for the dependence of the model parameters, yield stress and model viscosity, on the physiological parameters, the hematocrit, temperature and fibrinogen concentration. In addition to the 1D modeling, preliminary results on the simulation of steady state flow in a major artery, the left coronary artery (LCA), had been obtained.

We have extended our work to time-dependent conditions. Our analysis shows that a modified version of the "Delaware model" [2] is capable of predicting the viscoelastic and thixotropic properties of blood. The proposed model is in good agreement with the experimental data of Bureau *et al*. [3], on a simple triangular step shear rate flow. Two variables of the proposed model, the viscosity and yield stress, were pre-determined from our steady state model, thus emphasizing the importance of accurately predicting the steady state shear conditions. Finally, we have performed time-dependent simulations of the flow in the LCA. A faithful mesh representation of the vascular geometry is used, and the boundary conditions for the simulation are obtained from the updated 1D network model.

[1]. Johnson, D. A., U. P. Naik, and A. N. Beris, "Efficient implementation of the proper outlet flow conditions in blood flow simulations through asymmetric arterial bifurcations," International Journal for Numerical Methods in Fluids, **66**, 1383-1408 (2011).
[2]. Mujumdar, A., A. N. Beris, and A. B. Metzner, "Transient phenomena in thixotropic systems," J. Non-Newtonian Fluid Mech. **102**, 157-178, (2002)
[3]. Bureau, M., J. C. Healy, D. Bourgoin, and M. Joly, "Rheological Hysteresis of blood at low shear rate," Rheol. Acta **17**, 612-625 (1978)

Directed self-assembly in toggled magnetic fields

Jonathan Bauer
Advisor: Eric M. Furst
Committee Members: Raul F. Lobo, Antony N. Beris, and Feng Jiao

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Self-assembly is the process by which particles spontaneously rearrange into an ordered state due to the minimization of the system's free energy. The thermodynamic forces that drive self-assembly can be modulated and *directed* through the use of external magnetic and electric fields.[1] The persistence of order on the nano- and micro-scale created by these processes has lead to the discovery of materials with novel phononic, plasmonic, or catalytic properties. In this presentation, we discuss using the technique of toggling an external magnetic field as a route for directed self-assembly.

Originally, work in magnetic field self-assembly focused on using continuous (dc) fields. Kinetics, not energetics, determines the structural evolution in a dc field, meaning that the final configuration–one of sample-spanning columns composed of magnetic particles–is the equilibrium state. However, Promislow and Gast showed that by toggling the magnetic field it is possible to minimize the suspension's energy and condense the magnetic particles into ellipsoidal aggregates.[2,3] In toggled field self-assembly, the external field is turned on and off in a square wave, allowing the particles to diffuse when the field is off and aggregate when the field is on. Swan *et al*. further showed with extraterrestrial experiments that two regimes, sample-spanning and condensed, can be established by selecting a toggle frequency that optimizes the relaxation of the suspension while retaining some memory of the past structure.[4]

We have built upon this previous work by performing analogous terrestrial experiments. In these experiments, superparamagnetic spheres are suspended in water and assembled in toggled magnetic fields at varying field strengths and frequencies. We have examined the suspension macroscopically to provide a quantitative measure for the coarsening kinetics, showing that the time scale for coarsening grows exponentially with respect to frequency. Furthermore, we probed the internal structure of the aggregates with microscopy and small-angle light scattering to confirm the existence of body-centered tetragonal crystals, the predicted equilibrium phase. Overall, toggled field self-assembly provides a relatively temperature insensitive route for bypassing a kinetically arrest state en route to creating ordered materials.

References:

[1] M. Grzelczak, J. Vermant, E. M. Furst and L. M. Liz-Marzán. *ACS Nano*, 2010, **4**, 3591-3605.
[2] Promislow, J.H.E. and A. Gast. *Langmuir*, 1996, **12**, 4095-4102.
[3] Promislow, J.H.E. and A. Gast. *Physical Review E*, 1997, **56**, 642-651.
[4] Swan, J.W. *et al. PNAS*, 2012, **109**, 16023-16028.

New Class of Protein Labeled Molecular Beacons

Daniel Blackstock
Advisor: Wilfred Chen
Committee Members: April Kloxin and David Colby

Numerous viral infections and life threatening diseases are characterized by a specific mRNA expression pattern, making it a useful target for diagnostics and drug therapies. Molecular beacons (MBs) are nucleic acid probes which have proven to be reliable, fast acting, and highly specific tools for disease detection. By combining fusion proteins with MBs, we have constructed a new class of protein labeled MBs. Ultimately, the innovative approach offers a modular assembly process, permitting the attachment of various proteins of interest to a MB. Also, by using a dual protein-MB platform, specific nucleotide binding-dependent protein-protein interactions can be achieved.

Phase Behavior of Polystyrene/Poly(3-hexylthiophene) Blends for Organic Photovoltaics

Jillian Emerson
Advisors: Thomas H. Epps, III and Eric M. Furst
Committee Members: April M. Kloxin and Norman J. Wagner

Organic photovoltaics (OPV)s require bicontinuous, interpenetrating networks of donor and acceptor materials to provide large interfacial area and continuous conducting pathways to achieve the highest efficiency. Current OPVs are made of blends of poly(3-hexylthiophene) (P3HT), an electron donor material, with [6,6]-phenyl-C61-butyric acid methyl ester (PCBM), an electron acceptor material. These devices often lack continuous domains and are significantly affected by processing conditions, leading to reduced efficiency and reproducibility issues. Polymer blends are a promising material for OPVs, as they can self-assemble reproducibly into bicontinuous domains via spinodal decomposition. Furthermore, polymer blends provide additional handles to tune device composition through material substitution. Controlling the morphology of conjugated polymer blends is vital to producing more efficient OPV devices, however little is known about the phase behavior and morphological evolution during casting in these systems. In this work, we determined the Flory-Huggins solvent–polymer and polymer–polymer interaction parameters for a model system of P3HT and polystyrene (PS) through solvent vapor swelling of thin polymer films. From these interaction parameters, we constructed a polymer/polymer/solvent phase diagram. The resulting phase diagram was validated experimentally with solution-based transmission measurements of PS/P3HT in *o*-xylene, which was used as the casting solvent. To relate the thermodynamic behavior of these blends to the final morphology, we studied the evolution of film morphology during casting with *in situ* stroboscopic illumination. This work highlights methods to determine the phase behavior in polymer/polymer/solvent blends and understand the effect of processing on film morphology.

Incorporating the Wood-Ljungdahl CO_2 Fixation Pathway in *Clostridium acetobutylicum*

Alan G. Fast
Advisor: Eleftherios T. Papoutsakis
Committee Members: Maciek Antoniewicz and Wilfred Chen

The ability to express the genes necessary for instating a functional Wood-Ljungdahl (WL) pathway into *C. acetobutylicum* constitutes a major advance in that the WL pathway has never before been instated into a heterologous organism. In the specific case of *C. acetobutylicum,* it would allow one to grow this organism to high cell densities and then switch the available carbon substrate from a sugar to CO_2/H_2, CO/CO_2, or a mixotrophic culture with both sugars and gases, thereby enabling the production of carboxylic acids and solvents from syngas in a flexible and scalable fermentation system. From the perspective of biological fundamentals, the ability to install this complex, primordial pathway into a heterologous host would constitute a major advance in cell/metabolic engineering that would open new horizons for pathway engineering and synthetic approaches in the genus *Clostridium.* Comparative genetic analysis of three sequenced acetogens, *C. ljungdahlii*, *C. carboxidivorans*, and *C. difficile*, showed that the WL pathway genes of these clostridial acetogens are concentrated in a highly conserved, 18 kilobase region on their respective genomes. By examining the *C. acetobutylicum* genomes, we focused on expressing 11 core genes coding for enzymes and accessory proteins. To achieve this goal, we developed a system of two co-existing plasmids combined with a method to integrate some of these genes, starting with the formate dehydrogenase gene, into the chromosome.

The use of ^{13}C-bicarbonate and ^{13}C-formate labeling showed that the Eastern branch of the WL pathway is active in the recombinant strain; however, the bifunctional carbon monoxide dehydrogenase/acetyl-CoA synthase (ACS/CODH) that is responsible for linking the two branches of the pathway is not functioning as expected. To determine the cause of the non-functioning ACS/CODH, expression of these proteins is being examined at the mRNA and protein levels using RT-PCR and western blot. Additionally, we are able to measure *in vitro* activity for a number of enzymes in the WL pathway including the formate dehydrogenase, carbon monoxide dehydrogenase, and methylene-tetrahydrofolate reductase. We will present the chromosomal integration method, the step-by-step verification of the expression and functionality of the cloned genes/proteins, and the culture experiments to test the functional installation of the WL pathway in *C. acetobutylicum*.

Na Diffusion in Mo Thin films for Improving $Cu(In,Ga)Se_2$ Solar Cell Efficiency

Robert Forest
Advisors: Jingguang Chen and Robert Birkmire
Committee Members: Raul Lobo and Feng Jiao

$Cu(In,Ga)Se_2$ (CIGS) is a promising semiconductor material for manufacturing low cost photovoltaics.[1] The presence of sodium (Na) in CIGS is well known to increase the open-circuit voltage and solar cell efficiency[2], but this effect is poorly understood. Na can be added to CIGS from a variety of sources, but the simplest method is to allow Na to diffuse out of a soda-lime glass (SLG) substrate through a layer of molybdenum (Mo), which serves as an electrical contact to the solar cell. The downside of this technique is that it can result in spatially non-uniform cells over larger areas, although it is still favored due to its simplicity and low cost. To better understand how Na from soda-lime glass is incorporated into CIGS, this study investigates the mechanism for the transport of Na from a SLG substrate through the Mo electrical contact.

X-ray photoelectron spectroscopy (XPS) was used to measure the accumulation of Na on the surface of Mo from the diffusion out of soda-lime glass during heating at various temperatures. It was found that samples with a greater amount of oxygen on the surface accumulate more Na. Transport of Na through Mo was modeled using the analysis of Hwang and Balluffi for diffusion through the grain boundaries of a thin film.[3] The grain boundary diffusion coefficient was estimated at several temperatures by fitting this model to the experimental XPS data. The diffusion coefficient increases with temperature while following an Arrhenius type relationship. The apparent activation energy for the diffusion coefficient is higher than expected for physical grain boundary diffusion in Mo but is similar to the dissociation of the Mo-O bond. These results suggest that oxygen residing in the grain boundaries and on the surface of Mo is involved in the diffusion of Na through Mo.

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Structure, Dynamics and Rheology of Colloidal Suspensions and Protein Solutions with Complex Competing Interactions

P. Douglas Godfrin
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Committee Members: Christopher J. Roberts, Eric M. Furst and Paul Butler

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Clustered fluids are a unique structural state formed by a delicate balance of short-ranged attraction (SA), which drives aggregation, and weak long-ranged repulsion (LR) that stabilizes aggregates to a finite size.[1] These types of clusters are reversible, and have a preferred finite size and a finite lifetime. Although they are a general occurrence in SALR colloidal systems, they are most prominent in concentrated protein solutions. In particular, the formation of clusters in concentrated solutions of lysozyme and monoclonal antibodies (mAbs) has been recently shown to substantially increase solution viscosity. In the case of pharmaceuticals, high viscosities produce a significant challenge in manufacturing and administering products. Therefore, it is of great industrial and scientific interest to understand the relationship between solution conditions and solution structure. The primary goal of this project is to reveal the underline physical mechanisms of anomalous viscosity increases in both model and pharmaceutical protein solutions and their relations with solution structure (cluster formation).

As a means of predicting the conditions of cluster formation, we have successfully combined liquid-state theory and Monte Carlo (MC) simulations to expose a general phase space of clustered states. We show that cluster formation in an SALR system is accurately represented by the two phase region of a reference potential consisting of the attractive portion of the given SALR potential.[2] Further, we examine the experimentally relevant properties of clustered states investigated in our simulations. Specifically, in contrast to the literature results, we found that the formation of a low-q peak in the structure factor is insufficient for defining a cluster fluid.[3] Rather, a low-q peak with a magnitude above 2.7 or an increasing magnitude with volume fraction signifies the presence of clustered states.

We use lysozyme as a model protein and treat it within the framework of colloid science to extract the effective interactions and phase behavior using liquid state theories. Using a multi-faceted approach, including microrheology, small angle neutron scattering (SANS), neutron spin echo (NSE), rheology, and MC simulations, the large viscosity increase of lysozyme solutions is found to correspond with the formation of dynamic cluster states and percolated networks. Within the cluster regime, the viscosity is found to correlate well with the estimated cluster size.[4] The same set of techniques is then used to compare two nearly identical mAbs with markedly different viscosities at high concentration. We find the enhanced viscosity of mAb1 over mAb2 to result from dynamic dimer formation, which is mediated but not fully disrupted by the addition of salt.[5] These results are possible by combining the experimental and simulation techniques utilized here, which are uniquely capable of producing accurate structural and dynamic measurements under highly concentrated conditions.

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Designing Renewable, Nanostructured Block Copolymers from Lignin

Angela L. Holmberg
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Consumer demand for styrenic polymers exceeds 26 million metric tons each year, of which at least 7 million metric tons comprise random and block copolymers (BCP)s. However, styrene is a nonrenewable, carcinogenic, and volatile organic compound, so development of green, cheap, and sustainable styrene alternatives is desirable. Lignin, nature's most abundant aromatic polymer, is a leading candidate for sourcing styrene alternatives. More than 70 million metric tons of lignin are harvested annually as pulp and paper mill waste and can be converted into various small molecules including vanillin, guaiacols, catechols, cresols, and other phenolic compounds. In this work, we establish a method for functionalizing lignin-based phenolic compounds and polymerizing them in a controlled manner for BCP applications. As one example, we prepare homopolymers of vanillin methacrylate, a functionalized lignin model compound, *via* reversible addition–fragmentation chain transfer (RAFT) polymerization. Subsequent chain-extension of the vanillin-based homopolymers with lauryl methacrylate, a possible derivative of used cooking oil, yields biobased BCPs. Resultant homopolymers and BCPs are characterized by differential scanning calorimetry, thermogravimetric analysis, small-angle X-ray scattering, and transmission electron microscopy. The results indicate that these lignin-based homopolymers and BCPs have promising properties in comparison to polystyrene. Eventually, this work will segue into the *de novo* design and generation of libraries of renewable polymers with tunable properties.

Probing Cathode Electrochemistry in Lithium-Air Batteries

Gregory S. Hutchings
Advisor: Feng Jiao
Committee Members: Raul F. Lobo and Yushan Yan

As a next-generation lithium battery technology, non-aqueous lithium-air ($Li\text{-}O_2$) batteries offer the potential of an order of magnitude increase in specific energy over currently-available, commercialized cells. The reason for this increase is that storage of Li^+ is not limited by insertion into relatively heavy intercalation materials; instead, oxygen from the atmosphere is reacted with Li^+ at the cathode interface to form Li_2O_2. Most practical applications demand long-term reversibility, with a minimum of undesired side products which arise from catalyzed electrolyte decomposition and degradation of carbon-based cathode components by reaction with the O_2^- radical. While porous metal and metal oxide structures may be adequate reaction substrates, a fundamental understanding of the behavior of these materials under reactive conditions is required. Precious metal cathode structures are known to be active for redox at the cathode,[1] but inexpensive transition metals and oxides can fill this role instead, and nanostructures of these materials have been shown to improve cycle life and reduce cell overpotentials. The goal of this work is to determine the properties of these cathode materials which optimize performance in the non-aqueous $Li\text{-}O_2$ system, and use this knowledge to synthesize new materials and cathode structures.

Attaining a thorough understanding of the behavior of cathode materials in operating $Li\text{-}O_2$ cells is critical for future development, and new tools are needed. Nanostructured manganese oxides, especially $\alpha\text{-}MnO_2$, have shown promising activity as cathode materials and are under active investigation.[2] With a novel in situ X-ray absorption spectroscopy configuration, we have been able to observe oxidation state and coordination environment changes for several of these synthesized oxides at discrete points in electrochemical cycling. Combined with ex situ electron microscopy and other structural characterization techniques, structural changes can then be related to electrochemical performance to determine which qualities are most desirable for future cathode design.

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High-Performance Electrodes for Hydroxide Exchange Membrane Fuel Cells

Robert B. Kaspar
Advisor: Yushan Yan
Committee Members: Thomas H. Epps, III and Antony N. Beris

Hydroxide exchange membrane fuel cells (HEMFCs) are an attractive alternative to conventional proton exchange membrane fuel cells (PEMFCs) because they are compatible with non-precious-metal catalysts. However, HEMFC performance is lower than the PEMFC benchmark, in part because HEMFCs continue to borrow electrode architectures originally developed for PEMFCs. In PEMFCs, water is produced at the cathode, so hydrophobic gas diffusion layers (GDLs) are employed to control flooding. But hydrophobic GDLs may not be necessary for HEMFC cathodes, in which water is consumed instead of produced, reversing the direction of water transport in the cell. Membrane-electrode assemblies can be improved by tailoring electrode design to reflect the unique kinetics and water transport behavior of HEMFCs. We demonstrate competitive cell performance with peak power densities above 500 mW/cm^2 at 60 °C.

At present, HEMFC lifetime is limited by chemical degradation of the electrolyte (hydroxide ion conductor). Our electrolyte is a polymer functionalized with pendant hydrophilic phosphonium salts. Synthesizing this material in house allows us to control electrode wetting and performance by varying the degree of functionalization, a critical parameter for ionic conductivity and water uptake of the resultant functional polymer. Compared to ammonium-based competitors, our phosphonium-based electrolyte shows promising *in-situ* durability.

Using Protein Semi-Synthesis to Enhance the Interface between Biology and Electrochemistry for Enzymatic Fuel Cells and Sensors

Heejae Kim
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Committee Members: Kelvin Lee and Yushan Yan

Harvesting electrochemical energy using redox enzymes is a hallmark of numerous metabolic processes that are essential to all living organisms. However, despite their high turnover rates and unique substrate specificities, redox enzymes are under-utilized in synthetic settings due to incompatibilities with conventional techniques. Recent advances in protein engineering allow us to both genetically and semi-synthetically modify biocatalysts to improve communication at the interface between enzymes and non-natural components. For example, devices such as enzymatic fuel cells and biosensors lose much of their effectiveness due to inefficient electron transfer between the active center of the redox enzymes and the electrode. It is often shown that signal loss can be mitigated using immobilization techniques, such as chemical modifications targeting random surface residues, encapsulation, or entrapment methods. However, such techniques often negatively affect enzymatic activity, making biological methods that properly expose the active center more desirable.

In this presentation, glucose oxidase (GOx) was displayed on yeast surfaces and fused to a gold binding peptide to bring the GOx in close proximity to the electrode to enhance the electron transport between the active center and the electrode. The increased potential in current production due to the enhanced attachment of GOx to the electrode surface and semi-synthetic strategies for tethering mediators in between GOx and the electrode to further aid electron transport will be discussed. Furthermore, extending this protein semi-synthesis approach with a different protein architecture, the hydrogel, will also be discussed.

CHO-Specific Recombinant Protein Glycosylation Reaction Networks

Benjamin Kremkow
Advisor: Kelvin Lee
Committee Members: Maciek Antoniewicz, Babatunde Ogunnaike

Worldwide recombinant therapeutic protein sales totaled $US 125 billion in 2012[1] and the majority of these proteins are produced in Chinese hamster ovary (CHO) cells. Many of these therapeutic proteins undergo post-translational modifications, the most prevalent of which is glycosylation. Control over glycosylation is desirable as the glycan structure affects the pharmacokinetics, efficacy, and immunogenicity of the therapeutic protein following administration. Manipulation of CHO cells to maintain optimal protein production and consistent glycan structures is difficult, as these attributes depend on culture conditions and genetic modifications, which influence the availability of nucleotide sugar substrates and the activity of nucleotide sugar enzymes. To experimentally demonstrate this, a glycosylation assay protocol has been established and verified. Production of a glycosylated, recombinant protein in CHO cells, and subsequent protein purification have been demonstrated, and a glycosylation assay protocol has been established and used to identify this protein's baseline glycan structure composition.

Glycosylation reaction network maps illustrate the pathways through which different glycans are produced, the enzymes that are involved, and the sugar nucleotides that are required. Current glycosylation reaction networks are detailed, but unlike kinetic glycosylation models, they have not been demonstrated specifically for CHO. This research aims to develop a web - based CHO glycosylation reaction network map tool to investigate CHO cell-specific glycosylation pathways. A database composed of CHO glycosylation-related genes has been created and validated from the CHO-K1 genome[2]. These enzymes are being assembled into reaction and stoichiometric matrices to be used in coding the glycosylation reaction network maps. The proposed reaction network map will incorporate and improve upon the usefulness of current reaction networks, while enabling CHO-specific results.

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High-throughput Screening for Block Copolymer Thin Film Self-assembly

Ming Luo
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Block copolymers (BCPs) have garnered significant attention in the past few decades due to their ability to self-assemble into nanoscale structures (~ 5-100 nm), making them ideal for emerging nanotechnologies, such as nanolithography, nanotemplating, nanoporous membranes, and ultra-high-density storage media.[1] Many of these applications require thin film geometries, in which the block copolymers form well-ordered nanostructures and/or precisely controlled domain orientations.[2] While the phase behavior of bulk BCPs depends primarily on the block interactions, degree of polymerization, and block volume fractions, thin film self-assembly is strongly influenced by commensurability considerations (*i.e.* film thickness) and surface interactions.[3] The goal of this research is to use gradient approach as a high-throughput screening tool to examine the effects of film thickness and surface interactions on the self-assembly of BCP thin films and to provide insights into universal manipulation of thin film nanostructures for various applications.

Previous study of cylinder-forming poly(styrene-*b*-isoprene-*b*-styrene) (SIS) thin films demonstrated the use of film thickness and monolayer substrate surface chemistry gradients to controllably obtain a hexagonally perforated lamellar (HPL) structure with intriguing 2D/3D continuity, and the through-film morphology was well characterized using ultraviolet ozone (UVO) etching, cross-sectional transmission electron microscopy (TEM) and grazing incidence small angle X-ray scattering (GISAXS) techniques.[4] In this work, we are studying the influences of tapered interfaces on the self-assembly behavior of lamellar-forming SI thin films. In tapered BCPs, we introduce a transition region between two pure blocks that tapers from one component to another, which provides an additional control over the nanostructure.[5] The tapered interface between blocks has been shown to decrease the effective χ (Flory-Huggins interaction parameter) and allows us to access the network phase in high molecular weight BCPs. To better understand the interfacial properties in tapered BCPs systems, we employed our gradient tool to quickly examine the tapered (S-SI-I and S-IS-I) and non-tapered (SI) BCPs. Self-assembly behavior in mesoscale and nanoscale are explored using optical microscope and X-ray reflectivity. Thus, we established a framework of using gradient and high-throughput methods for gaining a comprehensive picture of self-assembly to enable advanced nanotechnologies.

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Neuronal Reprogramming for an *in vitro* Model of Huntington's disease

Kyle McHugh
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Huntington's Disease (HD) is a dominantly inherited, invariably fatal neurodegenerative disease caused by a CAG repeat expansion in the huntingtin gene. The disease is characterized by extensive striatal degeneration and progressive loss of cognitive and motor function. At present there is no known therapy to halt the disease or delay onset. Existing mouse models and cell culture models fail to capture key disease characteristics because they are manipulated to overexpress truncated mutant huntingtin with a poly-CAG much longer than found in the average HD patient. An *in vitro* human model that better mimics the *in vivo* disease state would be an invaluable tool to study disease pathogenesis and screen potential therapeutics.

Recent work has shown that forced expression of particular transcription factors is sufficient to directly reprogram one cell type into another. The goal of this project is to assemble and screen a library of transcription factors to reprogram human fibroblasts or induced pluripotent stem cells from HD patients into neuronal subtypes important in HD to develop a fast, reproducible *in vitro* model that accurately captures the major phenotypic characteristics of HD.

Rational design of single-charge point mutations to reduce protein aggregation

Christopher J. O'Brien
Advisors: Christopher J. Roberts and Anne S. Robinson
Committee Members: Abraham M. Lenhoff and David W. Colby

Non-native protein aggregation is a major concern in the biotechnology industry that negatively impacts the expression and purification of therapeutic proteins and may lead to drug resistance or safety issues during administration of biomolecules to patients [1]. Understanding of non-native protein aggregation is a key area of research with the goals of engineering proteins that are resistant to aggregation and identifying conditions that reduce aggregation in biopharmaceutical production, storage, and administration. Different approaches have been used previously to improve protein stability and decrease formation of aggregates, including the "supercharging" of the surface of a protein to maximize repulsive electrostatic interactions [2].

Human gamma-D crystallin is a 20 kDa model protein in the same structural superfamily as monoclonal antibodies and antibody fragments, with aggregation pathways similar to those of therapeutic proteins. Previous studies on this system have shown that neutral point mutations can have a significant impact on its stability and intrinsic aggregation propensity [3]. The work here examines the effects of single point mutations that were predicted to minimally alter the surface charge on gamma-D crystallin while changing its aggregation propensity. These surface-charge altering amino acid substitutions were expected to modulate protein monomer interactions without having a substantial impact on folding stability. Our models suggest that these modifications alter the protein's aggregation propensity and provide insight into the effects of monomer-monomer interactions on protein aggregation. Experimental results from light scattering, size-exclusion chromatography, and denaturation studies show that even single-charge point mutations can have significant effects on aggregation rates, with negligible changes in conformational stability. Extension of the research strategies and algorithms to other aggregation-prone proteins of therapeutic value are also illustrated with single-chain antibodies.

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THE MOLECULAR BASIS FOR THE HIGH CO_2 ADSORPTION CAPACITY OF CHABAZITE ZEOLITES

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The atmospheric emission of anthropogenic carbon dioxide due to the burning of fossil fuels is one of the main causes of climate change [1]. Aqueous amine solution requires a lot of energies for the regeneration and inhibitors to control corrosion and oxidative degradation. Novel solid porous adsorbents such as zeolites and MOFs are used extensively as effective materials for the selective adsorption and separation of carbon dioxide due to their high internal surface area and micropore volume [2-4]. High silica zeolite SSZ-13 (Si/Al=6 and 12), a zeolite containing an 8-ring window and ellipsoidal cavity, was prepared by hydrothermal methods using N,N,N-Trimethyl-1-adamantanammonium ion as a structure-directing agent. Equilibrium CO_2 capacity of Na-SSZ-13/6 is 5.1 mmol CO_2 per gram of zeolite at ambient temperature and pressure, a value comparable with low silica zeolites 13X, Y, but higher than NaA because all of cation positions in smaller cages SSZ-13 are accessible to CO_2 even in the condition of less cation concentration in comparison with the others. We have investigated the site-specific adsorption properties of carbon dioxide in zeolites using Rietveld refinement method of X-ray and neutron diffraction patterns. Our refinement of neutron diffraction patterns on bare adsorbents Li-, Na-, K-SSZ-13/6(12) showed that Li+ and Na^+ are located right above the center of 6-membered ring of the hexagonal prism (site SII), and larger cation K^+ prefers to locate in the middle of 8-membered ring. Fourier map was used to elucidate the adsorption sites of CO_2 molecules in zeolite SSZ-13. The Rietveld refinement of various loading amount of molecules CO_2/8-ring on cation-exchanged SSZ-13 indicated two CO_2 adsorption sites; one locates in the center of the 8-membered ring window and the other directly interacts with extra-framework cations of the zeolite SSZ-13. The refinement of x-ray and neutron diffraction patterns of CO_2 on pure silica chabazite reveals two different adsorption sites of CO_2 in 8MR and the ellipsoid cages of chabazite framework to maximize the *van der Waals* interactions. Our study of CO_2 interactions with pure silica chabazite, Li-, Na-, and K-SSZ-13 using X-Ray and Neutron diffractions provides the better understanding of the CO_2 adsorption heats on these adsorbents in particular and other extra-framework cations 8MR zeolites in general.

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Trends in CO_2 Conversion Activity over Bimetallic Catalysts and Mo_2C

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Committee Members: Dr. Raul F. Lobo, Dr. Dionisios G. Vlachos

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Rising atmospheric concentration of CO_2 is forecasted to have potentially disastrous effects on the global climate due to its role in global warming and ocean acidification [1]. A catalytic process that utilizes CO_2 as a feedstock to make carbon monoxide, methanol, and methane is potentially more desirable than sequestration. CO is the most desired product because it can be integrated into down-stream processes to produce synthetic fuels via Fischer-Tropsch.

The reduction of CO_2 by hydrogen has been conducted on supported catalysts in a batch reactor at 573 K. Catalysts synthesized on a reducible support (CeO_2) showed higher activity than on an irreducible support (γ-Al_2O_3). The active metal also played an important role in controlling the selective reduction of CO_2 to CO instead of CH_4. Extended X-ray absorption fine structure (EXAFS) and transmission electron microscopy (TEM) confirmed the formation of uniform, bimetallic particles. Among the monometallic and bimetallic catalysts evaluated in a batch reactor, PdNi/CeO_2 was found to be the most active bimetallic catalyst, but formed the greatest amount of CH_4. PtCo/CeO_2 showed the highest selectivity to CO with very low selectivity to CH_4. The selectivity of each catalyst correlated with the d-band center value of each bimetallic surface. Among the catalysts investigated, bimetallics with values of d-band center farther from the Fermi level produced more CO and less CH_4 than catalysts with values closer to the Fermi level.

Batch reactor experiments were verified in a flow reactor under corresponding conditions. Results in the flow reactor were consistent with the batch reactor, with Pt–Co showing the highest selectivity to CO and Pd–Ni the lowest. Establishing a selectivity trend for CO_2 activation provides a facile means to choose effective catalysts from the large database of d-band center values for a variety of monometallic and bimetallic catalysts. These general trends observed from different supports and active metal components indicated that Mo_2C and metal-modified Mo_2C may be active for CO_2 reduction by hydrogen.

The reactivity of CO_2 over Mo_2C is somewhat analogous to the oxidation storage capacity seen in ceria; however, in this case, Mo_2C cycles between an active carbide and an inactive oxy-carbide. Therefore, it is advantageous to modify Mo_2C with a metal that can dissociate the product, CH_4 and thereby recarburize the catalyst to maintain the active phase. Operando XANES experiments were used to study the oxidation state of Mo in Mo_2C. These experiments suggested that an oxidation-carburization cycle contributed to the high activity of Mo_2C based catalysts and that Mo_2C was maintained in a carburized state during CO_2 reduction by hydrogen.

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Modeling, Estimation and Online control of glycosylation in monoclonal antibodies (MAbs) produced in Chinese Hamster Ovary (CHO) Cells

Devesh Radhakrishnan
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Committee Members: Prasad Dhurjati, Maciek Antoniewicz

Monoclonal antibodies (MAbs), a class of commercially valuable biopharmaceuticals with annual drug sales exceeding $43 billion in 2010[1], are used for treating a wide range of diseases such as cancer and rheumatoid arthritis. A vast majority of MAbs are expressed in mammalian cell lines such as Chinese Hamster Ovary (CHO) cells to enable post-translational modifications that generate human-like protein structures. One such post-translational modification which results in structural and pharmacological changes in the protein is glycosylation, involving the addition of a sugar moiety (glycan) to the protein backbone. The attachment of different glycans to the MAb yields a heterogeneous distribution of glycoforms and this glycosylation profile affects the immunogenicity, stability and half-life of the MAb, and hence the product quality. Maintaining the desired product quality in the presence of variations in process conditions has been difficult for drug manufacturers for a variety of reasons, the most important being that (i) product quality is monitored using infrequent and time-consuming measurements that are performed off-line; and (ii) even when these measurements become available, effective techniques for using them to control product quality do not yet exist. Regulatory agencies are encouraging manufacturers to monitor and control the quality of the product during the course of manufacturing, but achieving these goals will require fundamental understanding of the process of glycosylation and the factors influencing the glycosylation profile. The overall objective of this project is to develop and implement effective techniques for online monitoring and control of glycosylation in MAbs produced in CHO cells.

To control glycosylation effectively, it is important first to identify and quantify the factors that affect it. Previous studies[2] have demonstrated that the glycosylation profile in MAbs is influenced by several process variables spanning multiple scales – from temperature, media supplements, etc. at the macro-scale in the bioreactor, to factors at the micro- and meso-scales at the cellular and organelle levels. We aim to develop a multi-scale model to establish a quantitative relationship between different bioreactor conditions and the observed glycosylation profile. In addition, effective control requires frequent measurements of the glycoform profile, which is currently impossible because existing glycosylation assays are elaborate and require several days to yield results. We plan to design and implement a novel state estimator that will employ the multi-scale model to provide more frequent estimates of the glycosylation profile in between samples of real time data and update model predictions whenever the infrequent measurements are available from the assay. The state estimator and the multi-scale model will eventually be used in a hierarchical multi-loop control scheme to control the final glycosylation profile in the product by manipulating operating conditions in the bioreactor.

This presentation will focus on the development of the multi-scale model and its validation with experimental data. Additionally, experimental data demonstrating the effect of media supplements on the glycosylation profile will also be highlighted.

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Promoting ligamentogenic differentiation of mesenchymal stem cells in controlled microenvironments

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The bone-ligament interface is a complex structure that transmits forces through zones of bone, fibrocartilage, and ligament[1]. Human mesenchymal stem cells (hMSCs) offer potential as a single, autologous cell source for restoration of the bone-ligament interface after ligament reconstruction due to their ability to differentiate into osteoblasts[2], chondrocytes[3], and ligament/tendon fibroblasts[4]. However, conditions leading to ligamentogenic differentiation of hMSCs are not yet well-established. In this work, we aim to develop *in vitro* culture conditions that promote the ligamentogenic differentiation of hMSCs. We hypothesize that a combination of microenvironment cues found during ligament development, including growth factor and integrin binding, play a key role in this differentiation lineage. Towards this, we have isolated and characterized hMSCs from bone marrow and screened the effects of soluble and tethered microenvironment cues on their ligamentogenic differentiation. Specifically, hMSCs have been cultured with bone morphogenic protein-12 (BMP-12) and bone morphogenic protein-13 (BMP-13), and the effect of these soluble cues on ligament-related gene expression and protein production has been assessed. Further, we have synthesized poly(ethylene glycol) hydrogels with thiol-norbornene photopolymerization[5] as a blank slate culture system through which presentation of biochemical cues can be controlled. Using these hydrogels, we have examined the effects of fibronectin-related and collagen-related integrin-binding sequences on hMSC gene expression. We aim to use the results of these studies towards the development of a multiphased biomaterial for hMSC delivery for bone-ligament interface regeneration.

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Histone-Mimetic Polyplexes for Targeted Intracellular Delivery during Gene Transfer

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The field of gene therapy has garnered significant interest over the past two decades as a method for revolutionizing the treatment of various diseases such as Alzheimer's, Parkinson's, and many types of cancer. In recent years, non-viral methods of delivery have received particular attention because of their low toxicity, biocompatibility, and improved controllability as compared to viral vectors. However, inefficient trafficking to the nucleus is a common cause of limited DNA delivery. Improving the efficacy of non-viral vectors necessitates thorough understanding of their endocytic uptake and subcellular trafficking behavior. Additionally, cellular division is also widely known to improve transfection efficiency; however, the detailed mechanisms controlling this effect are unknown. Nature's own mechanisms for gene packaging and transfer have stimulated strong interest in histone proteins. Building on histone biology and recognizing the need for improved control of cellular delivery, we have developed a gene transfer method that utilizes native, histone-based processing pathways.

The presented research involves histone-mimetic polyplexes as gene therapy packaging materials. We have shown that caveolar endocytosis of polyplexes displaying modified histone 3 (H3) tails promote nuclear accumulation and enhanced gene expression. By the use of Rab GTPase colocalization analyses, chemical endocytic inhibition assays, and subcellular fractionation experiments, we determined that H3 polyplexes utilize a solely vesicular caveolar pathway and are released into the nucleus during cell division. The results of this study have expanded our understanding of how polyplexes are trafficked to cell nuclei, and provide new evidence for the role of cell division in transfection. These findings suggest new design criteria and opportunities to strategically target non-viral gene delivery vehicles.

Reaction kinetics and reactor design for the production of HMF from monosaccharides

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Committee Members: Raul Lobo, Yushan Yan, Michael Tsapatsis

Biomass is been considered a feasible supplement for fossil fuel-based feedstocks. Two of the main components of biomass, cellulose and hemicellulose, can be broken down to individual carbohydrates, such as glucose and xylose. These monosaccharides can be converted, via acid-catalyzed dehydration, to furans such as 5-hydroxymethylfurfural (HMF) or furfural. These furans can, in turn, be converted to a wide range of feedstocks, including drop-in replacements for petroleum-based chemicals[1] and fuels[2]. However, the potential of this approach has not been realized to do the non-selective conversion of sugars to furans in aqueous solution[3]. Most processes that have been proposed for the high yield conversion of glucose or fructose, a reactive isomer of glucose, have required the use of intensified reaction systems featuring multiphasic reactors[4], mixed solvents[5], multifunctional catalysts[6]. Designing reactors featuring such complex systems requires an understanding of each functionality as well as interactions between different functionalities.

We have conducted a range of investigations to understand the effects of process variables on HMF yield from fructose in different reactor configurations. Within our research group, low temperature processes (less than 150 ^{o}C) have garnered much attention[7]. However, there have been few studies on the kinetics of fructose dehydration in that temperature range. We conduct a kinetic analysis of a large experimental data set to determine relevant kinetic parameters[8]. Furthermore, we have developed a model for fructose dehydration that includes fructose tautomerization for the first time, as well as a reduced two-step dehydration model that accurately describes the rate-limiting step of the reaction. These insights are applied in a flow reactor to maximize HMF yield. These insights are a necessary step in the modeling of biomass conversion in complex reactor configurations.

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An Engineering Control System Paradigm for Quantitative Understanding of Hemostasis

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Hemostasis, the physiological process that arrests bleeding and keeps blood within the blood vessel, consists of a complex set of reactions that achieve a delicate balance between effective hemostasis and pathological conditions such as thrombosis, one of the major causes of death in the world.[1] Because of the complexity of the interacting subsystems and the dynamics involved in the hemostatic process, how the various components work together to implement fast, effective and stable responses to vascular injury has been difficult to understand using traditional experimental methods alone. Mathematical modeling has been established as an efficient tool for organizing detailed molecular information and for obtaining quantitative insight into the system behavior of complex biological systems.[2] Nevertheless, while a significant amount of effort has been devoted to developing mathematical models for many individual subsystems of hemostasis, only a model that adequately captures the interactive nature of the subsystems will be capable of providing a meaningful representation of the complete process. To develop a faithful representation of known mechanistic details of the entire hemostatic process, however, the standard approach to modeling will produce a model containing an inordinately large number of variables and an even larger number of unknown parameters, which will hinder our ability to analyze the model and gain insight from it. Therefore, an alternative conceptual paradigm is required for developing such a holistic representation of hemostasis.

When viewed from a process engineering perspective, one observes that hemostasis involves highly sophisticated regulation that is mediated by an automatic biological control system.[3] A control system approach whereby hemostatic process subsystems are organized into functional modules, each represented as an appropriate corresponding control system component, should therefore provide a modular structure for efficiently organizing the mechanistic details associated with the complete hemostatic process. Additionally, such an approach will facilitate systematic analysis and provide deeper insight into conditions for normal and pathological function. Our goal is to develop an engineering control system paradigm for quantitatively understanding hemostasis holistically.

We will present the previously proposed[3] engineering control system block diagram as the foundational basis of the model and then focus on the development of specific models for the blocks representing platelet-associated processes. As platelets play a central role in hemostasis, a single platelet model based on mechanistic understanding of signaling pathways within platelets has been developed and validated against experimental data. Additional characteristics of the model will be discussed along with future plans for incorporating it into the overall block diagram, completing the holistic model, and using the model for systematic analysis of the overall process of hemostasis.

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Optimization and Application of Proteomic Methods for Host Cell Protein Characterization

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Therapeutic proteins are used to treat a variety of complex diseases such as oncological and immunological disorders, and their effectiveness is indicated by their global market value of $125 billion. Chinese hamster ovary (CHO) cells secrete therapeutic proteins into the extracellular media along with endogenous host cell protein (HCP) impurities, which must be removed from the therapeutic product for patient safety. Identification and characterization of these extracellular CHO HCPs can aid in rational process design, resulting in efficient development and robust biopharmaceutical manufacturing operations. Extracellular CHO HCP analysis can be achieved by proteomic techniques including gel-based and shotgun methods. Gel-based methods, such as two-dimensional electrophoresis (2-DE), generally refer to methods to separate and quantify proteins; whereas, shotgun methods generally begin with a proteolytic digestion of proteins and thus separate and quantify peptides. The goal of this research is to maximize protein recovery for both proteomic workflows and subsequently apply these optimized protocols to identify and characterize extracellular CHO HCPs across biopharmaceutical manufacturing operations.

Optimized recovery protocols that improve proteome capture are fundamental to increasing the utility of proteomic methods, and extracellular CHO HCP recovery is particularly challenging due to the relatively low protein concentration and complex media composition. We developed optimized protocols that improve proteome capture to facilitate CHO HCP analysis using either the gel-based or shotgun workflows. Precipitation protocols were optimized by design of experiment approaches, and precipitation conditions were compared by 2-DE and shotgun methods. Optimized precipitation conditions were demonstrated to differ between the two proteomic techniques. These two optimized proteomic methods were both applied to investigate extracellular CHO HCPs across cell culture and purification operations. One application of these optimized proteomic methods demonstrates protein identification over varied cell culture durations. This study identifies a variety of differentially expressed proteins, many of which are shown to correlate with cultivation duration and cellular productivity. These results generate fundamental knowledge about extracellular CHO HCPs and identify a sub-set of HCP impurities that may present manufacturing challenges due to varied expression.

Direct measurement of bond strength in colloidal depletion gels

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The presence of non-adsorbing polymer in a colloidal suspension induces an attraction between the particles that often results in gelation. Such depletion gels are found in a wide range of materials, including paints, coatings, foods, personal care products, and pharmaceuticals. The ability to characterize and measure gel properties has great industrial significance. Gel coarsening, yield stress and stability against gravitational consolidation are important for the shelf life of many products. However, predicting the macroscopic rheology of depletion gels using microscopic properties has often relied on theoretical calculations to estimate the pair interactions rather than direct measurements. Therefore, our goal has been to develop an experimental technique to precisely and quantitatively determine the interparticle forces in a depletion system.

Laser tweezers were used to measure the thermal rupture forces between two particles suspended in solvent containing depletant. Fluorescent polyhydroxystearic acid (PHSA) stabilized polymethyl methacrylate (PMMA) particles were suspended in 75% (v/v) cyclohexane and 25% (v/v) cyclohexyl bromide. The dilute PMMA suspensions also contained non-adsorbing polystyrene depletant (M_w = 900,000 g/mol) in concentrations ranging from 0.0-15.9 mg/mL. The tweezers were used to bring two particles into contact with each other and then pull them apart at load rates between 7-11 pN/s. By averaging the particle trajectories over many approach and retraction cycles, we calculate the cumulative probability distribution for the particles being bonded as a function of applied force [1]. Lastly, we compare the results with the theoretical predictions of the DLVO and Asakura-Oosawa potential for depletion interactions.

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Design, Analysis, Operation, and Advanced Control of Hybrid Renewable Energy Systems

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The development of affordable, dependable, and low-emission sources of renewable energy is of paramount importance for a variety of reasons: the projected 60% rise in global energy demand expected over the next 30 years [1], the proven influence of greenhouse gas emissions on global climate change [2], and the diminishing availability of non-renewable energy resources, for example. However, stand-alone renewable energy systems (e.g., photovoltaics, wind turbines, and fuel cells) are more expensive alternatives to traditional, non-renewable energy systems (e.g., coal powered co-generation power plants and hydrocarbon combustion engines). In addition, the intermittency of some natural resources, such as solar irradiance and wind, renders some stand-alone renewable energy systems incapable of meeting the continuous energy demands of many stationary applications (e.g., in homes and businesses) and mobile applications (e.g., in cars and buses). Despite the shortcomings of stand-alone renewable energy systems, a hybrid renewable energy system (HRES)—a system consisting of two or more individual renewable energy systems utilized simultaneously to meet an energy demand—has the potential to be a cheaper source of renewable energy that can be used to meet continuous energy demands effectively. The overall goal of this project is to develop the principles governing the design, operation, and advanced control of HRESs that will result in cost-effective, efficient, and reliable energy solutions for stationary and mobile applications.

We propose to achieve the stated overall goal by completing the following specific tasks: 1) economic analysis and rational selection of HRESs; 2) control system design for HRESs; and 3) experimental implementation of a HRES. In this presentation, for perspective, we will first review briefly an economic analysis of HRESs as well as the design of an appropriate control system for a photovoltaic/PEM fuel cell/NiCd battery shuttle bus [3]. However, the primary focus of the presentation will be the development of an adaptive data-driven control framework capable of determining the relative strength of connection between energy sources and energy sinks in a HRES, and, from this, the most efficient use of energy generated from energy sources in a HRES. The practical applicability of the adaptive data-driven control technique developed in this project is illustrated with a non-linear stirred mixing tank process in which a hot stream flowrate, a cold stream flowrate, and a brackish stream flowrate are to be used to control the liquid level height in the tank, the temperature in the tank, and the salt concentration in the tank independently. The proposed data-driven control method is shown to be effective in correctly determining the relative strength of connection between process variables and the optimal control loop structure of the stirred mixing tank under varying operating conditions [4]. Future work on this project includes developing a generalized control solution for HRESs that incorporates the proposed data-driven control framework and experimental implementation of a designed HRES.

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Selectively Activating the C=O Bond of Furfural Using Metal Carbide and Bimetallic Catalysts

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Selectively activating the C=O bond of furfural is crucial for converting this important biomass-derived platform molecule to value-added chemicals such as 2-methylfuran and furfuryl alcohol. 2-methylfuran is a promising biofuel due to its high blending research octane number and high energy density[1] while furfuryl alcohol is widely used for making resins in industry[2]. Previously, copper chromite was used for activating the C=O bond of furfural due to its high selectivity[3]. However this catalyst is toxic and an environment-benign substitute is demanded.

Molybdenum carbide (Mo_2C) is an emerging hydro-deoxygenation (HDO) catalyst due to its high selectivity of C-O/C=O bond scission compared to C-C bond scission, though the mechanistic reason for its high HDO activity is not well understood. In this work, Mo_2C is investigated in terms of its ability for converting furfural to 2-methylfuran. Density functional theory (DFT) calculation predict a preferential bonding configuration of furfural on Mo_2C through the C=O bond which is experimentally confirmed by a surface vibrational technique. Both temperature programmed desorption (TPD) and flow reactor study detect 2-methylfuran from the reaction of furfural on Mo_2C with a high selectivity, confirming the selective HDO activity of Mo_2C.

On the other hand, Pt-based catalysts are investigated in terms of their ability for converting furfural to furfuryl alcohol. Pt has been shown to be active for this reaction but suffers from low selectivity[2]. In this work, combination of DFT modeling and surface science experiments reveal that there exist interaction between the C=O bond of furfural and Pt(111) which should be ideal for hydrogenating the C=O bond. However, the interaction could be too strong which favors the undesired decarbonylation pathway instead. PtNiPt(111) was shown to be able to weaken the interaction with the C=O bond of propanal which can help hydrogenation[4] and is therefore tested for the hydrogenation of furfural. Surface science experiments show similar results on PtNiPt(111) compared to Pt(111), suggesting the interaction between the C=O bond and PtNiPt(111) could still be too strong for the hydrogenation to happen.

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Porous Electrode Materials for Energy Storage

Bryan Yonemoto
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Committee Members: Raul Lobo, Yushan Yan

The need to store portable electrical energy has never been greater, with cell phones, laptops, electric cars, tablets, and power tools all requiring even better batteries. In the past ten years Li-ion battery chemistry has been the dominant choice for portable energy storage because it can recharge with minimal storage losses and has high energy storage per mass. A common way to improve the energy storage amount is thru nanoscaling, which results in higher fluxes and shorter diffusion lengths for Li-ions. While nanoparticles are an option, porous structures are preferred because electrical contact is easier to maintain as the particles swell and contract during cycling. In addition, if a hierarchical porous structure is made, the particles can be used as model systems to better understand the structural changes occurring during cycling. Unfortunately, the number of hierarchical structures currently available is limited, so new synthesis strategies must be employed to make the phosphates, sulfides, and oxides currently used commercially for Li-ion batteries.

To make porous materials soft or hard templating approaches are typically employed. To make phosphate materials we have used the soft template ionothermal synthesis method to make a variety of Co, Mn, and Fe structures.[1] Currently, we are focused on synthesizing and making iron sulfide structures from a hard template of KIT-6 or SBA-15. This is the first report of a porous iron sulfide material, as proven by BET and TEM. At the same time, we have been investigating 3DOM TiO_2 to understand what happens to mesoporous materials during cycling.[2] Thru this investigation we have used the hierarchical structure to identify, for the first time, significant evidence of strain for micron sized mesoporous materials during cycling.

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PtRu coated CuNWs as an efficient catalyst for methanol oxidation reaction

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Direct methanol fuel cells (DMFCs) are an attractive alternative to hydrogen-fueled proton exchange fuel cells for powering portable electronic devices because of their high energy density and ease of fuel transportation and storage. While nearly zero overpotential is observed for hydrogen oxidation reaction in acid, large overpotential exists even on the state-of-the-art PtRu/C MOR catalyst.[1] Therefore, developing catalysts with high MOR activity is of great importance.

MOR is known to be a structure sensitive reaction with Pt(110) facet showing the highest specific activity among low index surfaces.[2] One-dimensional (1D) nanostructures such as nanowires, nanotubes and nanorods often have the preferential exposure of certain facets which will enhance the MOR activity.[3] Studies have shown that platinum nanotubes (PtNTs) have higher MOR specific activity than platinum nanoparticles supported on carbon (Pt/C)[4], which might be attributed to the exposure of (110) facets of PtNTs. However, it remains unclear whether 1D PtRu nanostructures have higher MOR activity.

In our work, we synthesized one-dimensional PtRu coated Cu nanowires (PtRu/CuNWs) via partial galvanic displacement of CuNWs by Pt and Ru precursors. By varying the Pt and Ru precursor ratio, PtRu/CuNWs with different Pt:Ru ratio were obtained. Their MOR activities were evaluated by cyclic voltammetry using rotating disk electrodes. By varying the Pt:Ru ratio, we achieved higher specific and mass activity on PtRu/CuNWs compared with a commercial MOR catalyst PtRu/C (HiSPEC® 12100). The thin coating of PtRu on CuNWs reduced the amount of precious metals used, enabling the enhancement of mass activity.

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