UNIVERSITY OF DELAWARE
ENGINEERING

DEPARTMENT OF CHEMICAL & BIOMOLECULAR ENGINEERING

PROUDLY PRESENTS THE

4TH YEAR & 3RD YEAR PRESENTATIONS
WINTER RESEARCH REVIEW

CLAYTON HALL | JANUARY 31, 2019
Welcome to our Annual Winter Research Review. We are pleased that you can join us. The focus of today’s program—research presentations by our fourth-year graduate students—provide one of the best opportunities to learn about the research of our senior graduate students and their faculty advisors. Throughout the day you can also visit research posters presented by our third-year students.

Our graduate program is one of the central foundations of our principal missions of scholarship and education. We hope that you will enjoy this opportunity to learn more about our department and its activities, as well as to meet the students and faculty.

Eric M. Furst  
Professor and Department Chair  
Department of Chemical and Biomolecular Engineering

Nathaniel Hamaker  
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

Casper Brady, Advisor: Bingjun Xu
“A Sulfur Resilient Nickel Based Catalyst for Internal Reforming of Jet Fuels in Solid Oxide Fuel Cells”
Committee: Raul F. Lobo, Feng Jiao, and Yushan Yan

Kamil Charubin, Advisor: E. Terry Papoutsakis
“Synthetic Clostridium Co-culture Enabling CO₂ fixation, Superior Metabolite Yields, and Expanded Metabolism”
Committee: Wilfred Chen and Maciek R. Antoniewicz

Kimberly A. Dennis, Advisor: Eric M. Furst
“High-Pressure Linear Viscoelasticity Measurements of Polymer Solutions and Gels”
Committee: Christopher J. Kloxin and Norman J. Wagner

Pierre Desir, Advisor: Dionisios G. Vlachos
“Two-phase Microreactor Design for the Reactive Extraction of Biomass Derivatives”
Committee: Raul F. Lobo and Antony N. Beris

Lucas C. Dunshee, Advisors: Millicent O. Sullivan and Kristi L. Kiick
“Self-assembly of Elastin-b-Collagen-Like Conjugates Mediated by Triple Helical Parameters”
Committee: Christopher J. Kloxin and Wilfred Chen

Eden M. Ford, Advisor: April M. Kloxin
“Directing Stem Cell Behavior Through the Incorporation of Hierarchical Structure within Hydrogel Biomaterials”
Committee: Christopher J. Kloxin and Millicent O. Sullivan

Jiayi Fu, Advisor: Dionisios G. Vlachos
“Selective Hydrodeoxygenation of Furfuryl Alcohol on Doped Metal Oxide Catalysts”
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Julie B. Hipp, Advisor: Norman J. Wagner
“Shear-Induced Microstructural Evolution and Implications for the Rheo-Electric Behavior of Carbon Blacks Suspensions Used in Energy Storage Applications”
Committee: Yushan Yan, Eric M. Furst, and Paul D. Butler

Jeffrey S. Horner, Advisors: Antony N. Beris and Norman J. Wagner
“Inhomogeneous Constitutive Modeling of Transient Blood Rheology”
Committee: Eric M. Furst and Donna S. Woulfe

Victoria M. Hunt, Advisors: Kelvin H. Lee and Wilfred Chen
“Development of a Novel RNA-sensing Spatiotemporal Gene Regulation Program for Mammalian Systems”
Committee: E. Terry Papoutsakis and Millicent O. Sullivan

Matthew Jouny, Advisor: Feng Jiao
“Selective Conversion of CO₂ to Multi-Carbon Chemicals Through Two-Step Electrolysis”
Committee: Bingjun Xu and Yushan Yan

Ohnmar Khanal, Advisor: Abraham M. Lenhoff
“Adsorption and Transport of Proteins in Depth Filtration and Ion Exchange Chromatography”
Committee: Norman J. Wagner and Kelvin H. Lee
Alphabetical List of Talks—Continued

Hojin Kim, Advisor: Eric M. Furst
“Hypersonic Bandgaps of Anisotropic Colloidal Crystals”
Committee: Christopher J. Kloxin, Raul F. Lobo, and George Fytas

Joshua Lansford, Advisor: Dionisios G. Vlachos
“Forward and Inverse Surrogate Modeling for Catalyst Characterization from Complex Vibrational Spectroscopy”
Committee: Antony N. Beris, Arthi Jayaraman, Markos Katsoulakis, and Michael T. Klein

Paige J. LeValley, Advisor: April M. Kloxin
“Design of Injectable Stimuli-responsive Hydrogels towards Controlled Protein Delivery”
Committee: Christopher J. Kloxin, Millicent O. Sullivan, and Kristi L. Kiick

Rachel M. Lieser, Advisors: Wilfred Chen and Millicent O. Sullivan
“Controlled EGFR Ligand Display on Cancer Suicide Enzymes via UAA Engineering for Enhanced Intracellular Delivery in Breast Cancer Cells”
Committee: April M. Kloxin and Kelvin H. Lee

Jonathan Lym, Advisor: Dionisios G. Vlachos
“Lattice Convolutional Neural Network for Modelling Adsorbate Coverage Effects”
Committee: Raul F. Lobo and Michael T. Klein

Alexander A. Mitkas, Advisor: Wilfred Chen
“Developing a High Affinity, Dynamic Scaffold Toolkit for Intracellular Spatial Organization of Proteins”
Committee: E. Terry Papoutsakis and Maciek R. Antoniewicz

Jannat Nayem, Advisors: Norman J. Wagner and Yun Liu
“Investigating Structure and Dynamics of Therapeutic Monoclonal Antibodies in Solution”
Committee: Abraham M. Lenhoff, Christopher J. Roberts, and Antonio Faraone

Angela M. Norton, Advisor: Dionisios G. Vlachos
“Lubricant Base Oil Production from Renewable Feedstocks”
Committee: Raul F. Lobo and Bingjun Xu

Eleanor H. Oates, Advisor: Maciek R. Antoniewicz
“Metabolic Cross-feeding Interactions between Adipocytes and Hepatocytes in an Engineered Mammalian Co-culture System”
Committee: Wilfred Chen and Kelvin H. Lee

David D. Phan, Advisor: Michael E. Mackay
“Rheological and Heat Transfer Effects in Fused Filament Fabrication Additive Manufacturing”
Committee: Antony N. Beris, Arthi Jayaraman, and Christopher J. Kloxin

Caitlin V. Wood, Advisors: Eric M. Furst and Christopher J. Roberts
“Competing Aggregation Pathways and Kinetics of Particle Formation for Therapeutic Proteins Mediated by Air-Water Interfaces”
Committee: Abraham M. Lenhoff, Millicent O. Sullivan, and Vladimir I. Razinkov
8:30-9:00  Breakfast (Clayton Hall lobby)

9:00-9:10  Welcome / Opening Remarks (Room 101 B)
          Professor Eric M. Furst, Department Chair

9:10-9:30  Elevator Pitches

Session 1  Room 101 B  9:30 a.m. – 10:50 a.m.

9:30-9:50  Rachel M. Lieser
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10:50-11:50 Poster Session

11:50-1:10  Lunch (Room 101 A) and Featured Speaker, April M. Kloxin
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5:15      End
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John M. Clayton Hall - [https://conferences.udel.edu/newark-campus/](https://conferences.udel.edu/newark-campus/)
Poster Presenters

Jacob Anibal  
“The Effect of Metal on Electrochemical Benzaldehyde Reduction”  
*Advisor: Bingjun Xu*

Elvis Ebikade  
“Kinetic Studies of Acid Hydrolysis of Food Waste-Derived Saccharides”  
*Advisor: Dionisios G. Vlachos*

Nathaniel Hamaker  
“Development and Application of a Novel Site-specific Integration Reporter System in CHO Cells”  
*Advisor: Kelvin H. Lee*

Emily Jeng  
“Design and Development of a CO₂ to CO Flow Cell Electrolyzer”  
*Advisor: Feng Jiao*

Priyanka Ketkar  
“Tapered Block Polymer Electrolytes for Lithium-ion Batteries”  
*Advisor: Thomas H. Epps, III*

Muyuan Li  
“An Active Site Investigation of Ethane Activation on Zinc-Containing Zeolites”  
*Advisors: Raul F. Lobo and Craig M. Brown*

Arnav Malkani  
“Operando Spectroscopic Investigations of Copper Catalysts for Electrochemical CO₂ and CO Reduction”  
*Advisor: Bingjun Xu*

Douglas Nmagu  
“Evaluation of HDACi’s for Titer Enhancing Bioprocesses on a High Producing Reference CHO Cell Line”  
*Advisor: Kelvin H. Lee*

Natalia Rodriguez Quiroz  
“A Fundamental Study on the Effects of Metal Salts on Cellulose Hydrolysis”  
*Advisor: Dionisios G. Vlachos*

Summer Tein  
“Development of Rheo-MAGIK SANS: Characterization of Complex Fluid Interfaces through Interfacial Rheology and Structural Analysis”  
*Advisor: Norman J. Wagner*

Yifan Wang  
“First-principles Modeling of Single Atom Catalysis: CO Oxidation Over Atomically Dispersed Pt on Ceria”  
*Advisor: Dionisios G. Vlachos*

Michiel Wessels  
“Investigating the Effect of Polymer Architecture on the Assembly of Block Polymers in Solution”  
*Advisor: Arthi Jayaraman*
Poster Presenters Continued

Gerhard Wittreich  “Mechanistic and Kinetic Study of Ethane Oxidative Dehydrogenation”  
Advisor: Dionisios G. Vlachos

Daniel Yur  “Targeted siRNA Delivery With Modular Hepatitis B Virus-like Particles”  
Advisors: Wilfred Chen and Millicent O. Sullivan
A Sulfur Resilient Nickel Based Catalyst for Internal Reforming of Jet Fuels in Solid Oxide Fuel Cells

Casper Brady
Advisor: Bingjun Xu
Committee Members: Raul F. Lobo, Feng Jiao and Yushan Yan

Aeronautic auxiliary power units (APUs) are small heat engines that provide power to auxiliary airplane systems via combustion of jet fuel when the main turbines are not engaged. Recent improvements in solid oxide fuel cells (SOFCs) have made them attractive as potentially more efficient alternatives to combustion powered APUs in both the military and civilian sectors. For many years the real-world utilization of SOFCs has been limited by the extreme temperatures required for their operation (800-1000 °C). However, the recent development of proton conducting SOFCs coupled with internal steam reforming has significantly decreased operating temperatures (<500 °C). Typical steam reforming catalysts and SOFC hydrogen oxidation electrocatalysts (Ni, Pt, Rh, etc.) are very sensitive to sulfur and can completely deactivate even at trace sulfur concentrations (<5 ppm). Most commercial jet fuel contains at least 40 ppm of sulfur in the form of organosulfur compounds which react to form hydrogen sulfide during steam reforming. Thus, implementation of SOFCs as APUs requires the development of sulfur resilient steam reforming catalysts and hydrogen oxidation electrocatalysts. Herein we present our work designing a low-cost, nickel-based sulfur resilient catalyst for the steam reforming of jet fuel.
Synthetic *Clostridium* co-culture enabling CO$_2$ fixation, superior metabolite yields, and expanded metabolism

Kamil Charubin
Advisor: E. Terry Papoutsakis
Committee Members: Wilfred Chen and Maciek Antoniewicz

In microbial fermentations, at least 33% of the sugar substrate is lost as CO$_2$ during pyruvate decarboxylation to acetyl-CoA, with the corresponding electrons lost in the form of H$_2$. Previous attempts to reduce this carbon and electron loss focused on engineering of a single organism. In nature, most microorganisms live in complex communities where syntrophic interactions result in superior resource utilization. Here, we show that a synthetic syntrophy consisting of the solventogen *Clostridium acetobutylicum*, which converts simple and complex carbohydrates into a variety of chemicals, and the acetogen *C. ljungdahlii* which fixes CO$_2$, achieved carbon recoveries into C2-C4 alcohols almost to the limit of electron availability, with minimal H$_2$ and CO$_2$ release. The syntrophic co-culture produced robust metabolic outcomes over a broad range of starting population ratios of the two organisms. We show that direct cell-to-cell interactions and material exchange among the two microbes enabled unforeseen rearrangements in the metabolism of the individual species that resulted in the production of non-native metabolites, namely isopropanol and 2,3-butanediol. This was accomplished by pathway-specific alterations of gene expression brought about by one organism on the other, and vice versa. While some of these gene-expression alterations can be explained by the exchange of metabolites that induce specific gene expression patterns, others, as demonstrated by a co-culture separated using permeable membrane system, cannot. The latter, for now, would be attributed to complex direct physical interactions among the two organisms, thus providing a glimpse of the potential microbial complexity of simple or multicomponent microbiomes. Such direct material-transfer phenomena have not been documented in the literature. Furthermore, our study shows that syntrophic cultures offer a flexible platform for metabolite production with superior carbon recovery that can also be applied to electron-enhanced fermentations enabling even higher carbon recoveries.

This work was supported by the National Science Foundation grant (Award No. CBET-1511660), NSF IGERT fellowship (Award No. 1144726), the Army Research Office (Award No. W911NF-17-1-0343), and the Department of Energy (Award No. DE-SC0019155).
Enhanced oil recovery (EOR) fluids are polymer solutions and gels that are designed to transport and suspend solids, reduce friction, and prevent fluid loss. EOR fluid performance depends on its viscosity and elastic modulus, yet these rheological properties are difficult to measure at the high temperatures and pressures EOR fluids experience under operating conditions. In order to address this need, we developed a passive microrheology experiment capable of measuring the linear viscoelasticity of EOR fluids at pressures up to 200 MPa. The apparatus incorporates a sealed steel alloy sample chamber with dual sapphire windows into a diffusion-wave spectroscopy (light-scattering) experiment. The measured light intensity correlation arising from the Brownian motion of polystyrene probe particles dispersed in the sample is interpreted using the Generalized Stokes-Einstein Relation (GSER) to determine the material creep compliance. We validate this high-pressure microrheology instrument by measuring the increase in viscosity of 1-propanol aqueous solutions and extend the measurement to EOR fluids containing poly(vinyl) alcohol polymer and borate as a physical crosslinker. We investigate the effect of pressure on the crosslink density and rheological properties at frequencies up to 1 MHz and pressures to 200 MPa. As pressure increases, the storage modulus decreases, confirming the hypothesis that the equilibrium of the borate crosslinker shifts to the unassociated state. A transient network model is proposed for viscous and elastic moduli to quantify the decrease in crosslink density with increasing pressure.
Two-phase Microreactor Design for the Reactive Extraction of Biomass Derivatives

Pierre Desir
Advisor: Dionisios G. Vlachos
Committee Members: Raul F. Lobo and Antony N. Beris

For the past several decades, various efforts have been made in using lignocellulosic biomass as a renewable source of energy and a potential substitute for petroleum based fuels and chemicals. In particular, biomass derived carbohydrates can undergo acid-catalyzed dehydration reactions in water to produce furanic compounds such as 5-hydroxymethyl furfural (HMF), which is considered a top value commodity chemical for the production of fuels, fuel additives, and plastics. Nonetheless, the process involves many side reactions that often require the addition of an organic solvent to the system in order to extract HMF from the aqueous phase and prevent its further degradation. While these biphasic systems fall short in the case of conventional batch reactors that require a frequent recycling of the organic phase and large volumes of the organic solvent, continuous flow microreactors enable the formation of intricate and tunable two-phase flow patterns with large specific interfacial areas that provide mass transfer rates that are 2 – 3 orders of magnitude greater than their batch counterparts for rapid extraction of HMF with improved yield, selectivity, and process economics by means of process intensification.

In this work, we study and characterize the hydrodynamic and mass transfer properties of two-phase flow patterns in a biphasic microreactor. We conducted experiments for the extraction of HMF with various organic solvents and also performed the reactive extraction using various carbohydrate substrates and catalysts. For this particular case, we will present a study of the reactive extraction of HMF in a water/ethyl acetate capillary biphasic microreactor using fructose as the substrate and an HCl and KCl buffer solution as the catalyst. A hybrid first-principles and data-driven kinetic model of the reaction network in combination with a mass transfer model was also used to evaluate the optimal reaction and operation conditions that maximize HMF yield.
Self-assembly of Elastin-b-Collagen-Like Conjugates Mediated by Triple Helical Parameters

Lucas C. Dunshee
Advisors: Millicent O. Sullivan and Kristi L. Kiick
Committee Members: Christopher J. Kloxin and Wilfred Chen

Physiochemical irregularities within extracellular matrix (ECM) proteins such as collagen can lead to a wide range of connective tissue disorders including osteogenesis imperfecta and osteoarthritis.[1] Current pharmaceutical regimens to treat such diseases suffer from off-target effects, suggesting that new approaches for targeted delivery are necessary. In the last decade, ECM-inspired polypeptide materials have garnered significant interest for their ability to selectively mimic specific matrix components such as collagens and elastins, offering new opportunities to control drug delivery within specific tissues. For example, triple helix forming collagen-like peptides (CLPs) comprising (Gly-Pro-Hyp)n amino acid repeats can hybridize with high efficiency to denatured collagen proteins in the body via thermal annealing of peptide and protein single strands into a stable triple helix.[2] Additionally, elastin-like peptides (ELPs) that consist of (Val-Pro-Gly-XAAGly)n (where XAA is any amino acid with the exception of proline) amino acid repeats possess a lower critical solution temperature in which aggregation occurs upon heating above this temperature, making ELPs ideal candidates for on demand drug delivery behavior. Recently, our group has reported on the design of hybrid peptides with linked CLPs and ELPs, and the assembly of thermoresponsive, elastin-b-collagen-like peptide nanovesicles that are capable of dissociating at high temperature (70°C).[3] These nanovesicles offer intriguing potential in drug delivery applications due to their dual thermoresponsivity and inherent ability to bind to degraded collagen protein. However, in order to make an ELP-CLP nanoparticle with optimal drug delivery properties such as physiologically relevant hybridization to degraded collagen protein, the critical parameters of their self-assembly must first be understood, specifically with respect to the CLP domain. To test the effects of the triple helical (CLP) melting temperature on temperature-dependent nanovesicle assembly and dissociation behavior a small library of ELP-CLP conjugates was made with varying numbers of CLP (GXAA-ZAAA) repeats and varied CLP sequences. These conjugates were characterized for their thermoresponsivity and their ability to form self-assembled structures. The melting temperature, repeat length, and overall hydrophilicity of the CLP domain were found to be of critical importance to nanoparticle formation.

References:
3) Luo, T., Kiick, K. J.A.C.S.. 2015, 137(49), 15362-15365.
Extracellular matrix (ECM) properties, including mechanics, structure, ligand presentation, and soluble factors, play an important role in regulating cell function at early stages of bone healing. Physical and chemical properties modulate cell behavior, including cytoskeletal organization, proliferation, and migration, initiating bone repair. Engineering a synthetic matrix that presents extracellular cues in a controlled and defined manner offers an opportunity to direct bone regeneration. We hypothesize that engineering synthetic hydrogels to mimic aspects of the early stages of healthy bone healing will encourage stem cell migration to the site of injury and promote remodeling of the matrix, ultimately leading to improved bone regeneration. To test this, we have established well-defined, tunable scaffolds to recapitulate distinct features of native tissues. In particular, we aim to capture facets of the mechanical properties, biochemical content, and multiscale structure of the collagen-rich environment of the clot-like hematoma formed early in the wound healing process.

We have designed a multifunctional collagen mimetic peptide (CMP) that incorporates the Proline-Hydroxyproline-Glycine repeat found in native collagen, while charged groups promote fibrillar assembly via ionic interactions between peptide strands. Triple helical assembly of the peptide was verified through circular dichroism, and larger scale assembly of fibrils was investigated using electron microscopy. This peptide incorporates an alloxycarbonyl group that acts as a reactive handle to covalently incorporate the CMP fibrils into a larger hydrogel network. Toward studying cell response in vitro, these CMPs were covalently crosslinked within poly(ethylene glycol) (PEG)-based hydrogels containing cell-degradable motifs, and the resulting hydrogel mechanical properties were characterized with rheometry. Further, human mesenchymal stem cell (hMSC) viability was quantified after encapsulation within these unique matrices and long culture times, as well as analysis of cell response to the CMPs over time through morphological and gene expression analyses. Ongoing studies of hMSCs within these materials support their relevance for multidimensional cell culture and suggest that the presence of CMPs influences cell-matrix interactions and observed cell response.

Selective Hydrodeoxygenation of Furfuryl Alcohol on Doped Metal Oxide Catalysts

Jiayi Fu
Advisors: Dionisios G. Vlachos
Committee Members: Raul F. Lobo and Bingjun Xu

Selective hydrodeoxygenation (HDO) is a critical process for biomass valorization to fuels and chemicals. Biomass-derived molecules, such as furanics, often possess multiple reducible groups that in the presence of a hydrogen donor undergo various catalytic transformations such as hydrogenation, decarbonylation, ring opening, and HDO.\(^1\) The versatility of those complex molecules poses many challenges for designing selective catalysts targeting specific functional groups.\(^2,3\) Reducible metal oxides, such as RuO\(_x\), have been found to be active and selective towards HDO via reverse Mars van Krevelen mechanism.\(^4\) However, those oxides are not stable and undergo bulk reduction during reaction.

An alternative design approach is to incorporate transition metal dopants into moderately reducible metal oxides to promote oxygen vacancy formation and enhance HDO activity. In the present work, we prepared a series of Pt doped TiO\(_2\) catalysts for the selective HDO of furfuryl alcohol, a biomass model compound. Kinetic studies reveal that small amounts of Pt dopant consisting of single atoms and sub-nm clusters significantly enhance the HDO rate over TiO\(_2\), whereas Pt on irreducible silica shows very low activity and selectivity. Moreover, we developed a new methodology to quantify the various types of active sites for the first time for typical particle sizes by combining use of probe molecules, kinetics, modeling, and characterization.

References:

Shear-Induced Microstructural Evolution and Implications for the Rheo-Electric Behavior of Carbon Black Suspensions Used in Energy Storage Applications

Julie B. Hipp
Advisor: Norman J. Wagner
Committee Members: Yushan Yan, Eric M. Furst, and Paul D. Butler

Rising demands for the integration of renewable energy sources into the electrical grid have pushed for the continued development of efficient and economical electrochemical energy storage devices for both large- and small-scale needs. A key component of these devices is the electrode material, which primarily consists of solid active materials that are often electrically connected by a network of conductive carbon black nanoparticles. These electrode materials are frequently processed as particle suspensions and can be cast onto a surface or ultimately used as a flowable electrode slurry. In these applications, key design parameters such as the viscosity, stability, and conductivity of the electrode suspension are directly related to the microstructure, which is not only subject to change under shear, but is also strongly dependent on the shear history. Therefore, as flow plays an important role in the processing and end use of these suspensions, it is important to understand their shear-dependent microstructure and its effect on the macroscopic properties.

In this work, the relationship between the shear-dependent structural, rheological, and electrical properties of the electrically conductive carbon black nanoparticles found in electrode suspensions is studied. To probe the shear-induced microstructure and consequent macroscopic rheological response of these suspensions, a combination of Rheo-small angle neutron scattering (Rheo-SANS) and Rheo-ultra small angle neutron scattering (Rheo-USANS) measurements were performed at a range of applied shear rates. Furthermore, the shear-induced electrical properties of these suspensions were measured and directly related to the observed microstructural evolution from neutron scattering measurements. In these experiments, it is found that an apparent shear-thickening behavior and similar increase in electrical conductivity occurs at moderate shear rates that can be attributed to a transition in the microstructure from dense to open carbon black agglomerates. Below this transition, the suspensions were found to be unstable, resulting in a long lived decline in both the viscosity and conductivity due to particle sedimentation. Above this transition, a shear-thinning behavior is observed as well as a change in conductivity that can be attributed to the erosion of carbon black agglomerates with increasing shear rate. These experiments show that the shear-induced microstructure of carbon black suspensions gives rise to rich rheological and electrical behaviors that have implications for the design and improvement of electrode slurries used in electrochemical energy storage devices.
Inhomogeneous Constitutive Modeling of Transient Blood Rheology

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Blood is a complex suspension containing red blood cells, white blood cells, and platelets in an aqueous plasma with various dissolved proteins. At stasis and low shear rates, the red blood cells stack into coin stack aggregates called rouleaux. These structures give rise to various interesting rheological features including a nonzero yield stress, viscoelasticity, and thixotropy – a time dependent viscosity. Moreover, changes in the rheological properties of blood have been linked to a variety of diseases ranging from diabetes to hypertension. Thus, by understanding how the rheology of blood relates to physiology, we can potentially unlock a powerful diagnostics tool for early warning signs of such diseases. Despite the potential, understanding of blood rheology is limited due to the complexities associated with measuring blood. As blood is a living fluid, it will age once withdrawn from the body resulting in changes in the rheology [1]. Additionally, at low shear rates, a slip layer near the walls of the measurement device will develop. This phenomenon is known as syneresis and is particularly notable when rouleaux are present due to the large size of the structures as well as the significant difference between the plasma and bulk viscosities.

Recently, we have collected a number of data samples following a carefully developed handling protocol [1] for both steady and transient bulk rheology on human blood. Using these data, we have developed a model to capture the viscoelasticity and thixotropy associated with human blood rheology [2]. In this work, using newly acquired blood rheology data, we have further improved our blood flow model by including an additional viscoelastic component associated with the rouleaux. Additionally, we also introduce a model for the depletion layer at the walls of the measurement device to account for the effects of syneresis. The depletion layer is directly linked to the nondimensional structure parameter which governs the rouleaux contribution to the bulk rheology and enables an indirect tracking of the rouleaux size for different flow states. The enhanced model is compared to experimental results for steady, oscillatory, and step shear change rheological tests and significantly improves upon the previously published model predictions. Constitutive modeling of thixotropy, viscoelasticity, and slip layer formation is not only important for blood rheology but can be used for a wide range of similar concentrated colloidal suspensions. Additionally, by accurately modeling the rheology of blood, we can improve blood flow simulations throughout the circulatory system, and by linking the model parameters to the blood physiology, we can improve our understanding of how physiology and general health are linked to the flow behavior of blood.

Development of a novel RNA-sensing spatiotemporal gene regulation program for mammalian systems

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To effectively probe gene function and reprogram cell regulatory networks, it is critical to have technology platforms that provide precise and accurate targeting of genes. The use of CRISPR interference (CRISPRi) or CRISPR activation (CRISPRa) for targeted silencing or upregulation of transcription, respectively, is currently one of the most utilized technologies for predictable control over gene expression. The CRISPR system allows for sequence-specific targeting of genes but inherently lacks the ability to incorporate useful endogenous signals for spatiotemporal control of gene expression. Here we present the design and further characterization of a class of riboregulators through the incorporation of toehold riboswitches into sgRNA scaffolds. This artificial circuit is able to detect the presence of specific RNA and switch on transcriptional level gene regulation through RNA-RNA strand displacement reactions, which are governed by predictable Watson-Crick base pairing. These synthetic constructs can be programmed to process specific information within the cell including changes in native metabolism and stress responses. We demonstrate the programmability and adaptability of these engineered systems to control gene expression in mammalian systems with minimal infidelity. We envision these synthetic riboregulators can be applied in a variety of contexts within mammalian systems such as improving mammalian cell productivity and mAb product quality. This technology has the potential to function as an RNA-based master regulator for autonomous cellular control to direct specific phenotype in CHO cell cultures.
Selective Conversion of CO\textsubscript{2} to Multi-Carbon Chemicals Through Two-Step Electrolysis

Matthew Jouny  
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Committee Members: Bingjun Xu and Yushan Yan

The electrochemical conversion of CO\textsubscript{2} to value-added products is an exciting technology for the sustainable production of fuels and chemicals. Multi-carbon products such as ethylene and ethanol are particularly attractive due to their large market potential, but production directly from CO\textsubscript{2} remains challenging. Here, I will present our recent work in developing a two-stage electrolysis process that is decoupled through the carbon monoxide (CO) intermediate. We demonstrate a high-performance CO flow electrolyzer with a well-controlled electrode–electrolyte interface that can achieve a C\textsubscript{2+} selectivity of >90\% at industrially relevant reaction rates. Additionally, we show that CO electrolysis leads to enhanced acetate production relative to CO\textsubscript{2} electrolysis under identical conditions, likely due to a higher surface pH where acetate forms through nucleophilic hydroxide attack of a ketene-like intermediate. We then perform CO electrolysis in the presence of other nucleophilic species, leading to the formation of heteroatomic products, which greatly expands the scope of possible CO\textsubscript{2} electrolysis-derived chemicals.
Adsorption and transport of proteins in depth filtration and ion exchange chromatography

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Effective impurity removal and high loading capacity are desirable in bioprocessing of therapeutic proteins. Depth filtration and ion exchange chromatography are two universal purification unit operations that operate primarily based on electrostatic interactions between the adsorbent surface and the multivalent protein, whether it is a protein impurity originating from the host cell, as is in the case of depth filtration, or the product of interest, as in most cases of ion exchange chromatography. The performance of these purification steps depends upon the adsorption equilibrium between the adsorbent and the adsorbate and the transport of the adsorbate through the adsorbent. Here, we discuss the adsorption of proteins on depth filters and the competitive adsorption of mAb charge variants in ion exchange chromatography.

The adsorption of model proteins and mAbs onto depth filters and the components were correlated to measured properties such as surface area, morphology, surface charge density and composition. The polymeric resin binder was shown to be the primary contributor to the depth filter’s adsorptive functionality and the capacity for a protein that adsorb can be estimated by its monolayer coverage. In the case of ion exchange chromatography, we demonstrated that competitive adsorption among the different mAb charge variants can be leveraged in separating mAb charge variants to obtain the highest yield and purity of which we are aware for these difficult-to-separate variants. Furthermore, applying our understanding of protein surface diffusivity and binding capacity on ion exchange resins as a function of buffer ionic strength, we devised a scheme to dramatically improve the attainable transport-limited dynamic binding capacity.
Hypersonic bandgaps of anisotropic colloidal crystals

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Directed self-assembly harnesses thermodynamic transitions of colloidal nanoparticles to form periodic building blocks. The fabricated crystalline structures have the periodicity in a refractive index or elasticity; the orientational and translational arrangements give rise to unique optical or mechanical properties, like structural color and phononic bandgaps. Such properties are desirable in photonic and phononic technologies, such as hypersonic cloaking materials and metamaterials.

In this research, we investigated the phononic activity of self-assembled anisotropic colloidal nanoparticles. In the presence of external AC electric fields, anisotropic particles driven to circumvent kinetically-arrested randomly-packed structures to form equilibrium simple monoclinic crystals. The phononic properties of both random and crystalline arrangements are measured by Brillouin light scattering, which is based on the inelastic scattering of laser light. Crystals with the periodic elasticity destructively interfere with propagating acoustic wave and in turn, block the propagation of waves with a certain range of frequency, the so-called Bragg bandgaps. In addition, vibrational modes of elastic polymer nanoparticles interact with external acoustic waves resulting in another class of the bandgap, the hybridization bandgap, by the level repulsion of two phononic dispersion lines. The shape of dumbbell particles enables crystals to have anisotropic periodicity and therefore, they open up two discrete Bragg bandgaps depending on the direction of phonon propagation. The analysis of lattice structure confirms the fact that the Bragg bandgap originates from their structural periodicity and the bandgap positions are able to be normalized by considering the lattice constant of anisotropic monoclinic structures.

Furthermore, we describe the origin of the same hybridization bandgap positions for dumbbell-shaped nanoparticles with different geometries by analyzing eigenmodes of anisotropic nanoparticles using the finite element calculations. In all, we make use of a powerful bottom-up self-assembly technique to fabricate functional nanomaterials.
Forward and Inverse Surrogate Modeling for Catalyst Characterization from Complex Vibrational Spectroscopy

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Adsorbate vibrational excitations are a unique descriptor of adsorbate/surface interactions with the benefit of being relatively independent of temperature and pressure effects. The infrared spectra (IR) associated with activating adsorbate vibrational modes are very accurate, capture details of most vibrational modes, and can be obtained operando. Despite the possibility of obtaining detailed catalyst structural information and adsorption site preference throughout the course of a reaction from IR spectroscopy, the ability to interpret the resulting complex spectra is lacking. Current techniques depend on heuristic peak assignments and can only be done for relatively simple spectra. Quantitative assignment of adsorption sites can only be done on simple surfaces where the structure is known a-priori and requires concurrent measurements from mass spectrometry (MS) and low energy electron diffraction (LEED) studies at ultra-high-vacuum (UHV) conditions. We present a machine learning approach (using both supervised and unsupervised techniques) to determine adsorption site preference and local surface structure where complexity in the IR spectra is preferred. We combine first-principles calculations of carbon monoxide on platinum nanoparticles and a physics-based forward surrogate model to simulate IR spectra for training an inverse surrogate machine learning model. We test the machine learning model on both synthesized spectra generated from our forward surrogate model and on experimental spectra obtained under realistic reaction conditions. This work demonstrates the ability to gain relevant information from experimental data using theory and computation.
Design of injectable stimuli-responsive hydrogels towards controlled protein delivery

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Over the past decade, the use of protein therapeutics, such as growth factors or antibodies, has grown for the treatment of a variety of diseases, including cancers. Many of these therapies have improved specificity and efficacy compared to their small molecule counterparts but can suffer from poor half-lives or difficulties accessing the targeted delivery site due to steric effects. These limitations mean high doses of protein need to be delivered to achieve therapeutic efficacy, leading to increased off-target effects. To address these limitations, injectable stimuli-responsive hydrogel formulations offer a platform for the encapsulation and controlled delivery of proteins to minimize degradation in vivo and maintain high local concentrations when and where needed for improved therapeutic efficacy with minimal off-target effects. Here, we have engineered light-responsive hydrogels for the encapsulation and tailorable release of proteins. First, several different o-nitrobenzyl photolabile linkers were synthesized, where the type of photocleavable bond was varied to impart different levels of responsiveness to both water and applied light. Next, the rates of photodegradation and hydrolysis were examined to better understand the interplay of these two properties within the hydrogel microenvironment, using rheometric and swelling measurements. The different rates of photodegradation and hydrolysis of each linker subsequently were exploited toward regulating protein release. Specifically, concentric circles of hydrogels incorporating photolabile linkers with different responsiveness to water and light were formed to allow for the controlled and tunable release of model cargoes either in combination or independently. Further, toward translation in vivo, we investigated the use of upconverting nanoparticles, which convert lower energy light (e.g., near infrared (NIR)) into higher energy light (e.g., 350-450 nm), to assist in hydrogel degradation through human skin as NIR light penetrates deeper into human skin than long wavelength UV and visible light. Using such bottom-up design approaches and utilizing molecular engineering principles, we aim to design protein delivery platforms with controlled and tunable properties toward personalized medicine applications.
Controlled EGFR ligand display on cancer suicide enzymes via UAA engineering for enhanced intracellular delivery in breast cancer cells

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Therapeutic proteins are one of the fastest growing sectors on the pharmaceutical market because of their sophisticated functional properties, capacity for highly specific recognition of biological binding partners, and relevance to multiple diseases. However, despite significant investments in developing advanced protein therapeutics, delivery remains a major limitation. Most therapeutically-relevant proteins are membrane impermeable, and therefore active strategies are necessary to deliver proteins transcellularly or intracellularly, while also targeting the correct cells and subcellular compartments. As a result, the pipeline has a lack of intracellular protein drug candidates, even though intracellular proteins have predicted therapeutic applications ranging from neurological disorders to lysosomal storage disease to cancer. Engineering efforts to improve protein delivery often rely on modifying proteins through direct conjugation of biocompatible polymers or peptides that can increase protein stability, alter protein biodistribution, and/or improve cellular uptake. Conjugation is typically accomplished using reactive residues (e.g., lysines) within the protein sequence, or genetic fusion to the protein termini. While both methods have the capacity to enhance various aspects of delivery, the inability to chemically modify proteins with site-specificity often hinders pharmacological action. Additionally, such approaches do not offer control over variables such as ligand clustering, which can be an important determinant of targeting efficacy.

Previous work has demonstrated the ability to insert biorthogonal reactive residues into proteins through unnatural amino acid (UAA) incorporation, enabling protein conjugation with simple ‘click’ chemistries. Here, we describe a strategy to site-specifically conjugate delivery moieties to therapeutic proteins through UAA incorporation, in order to explore the effect of epidermal growth factor receptor (EGFR)-targeted ligand valency and spacing on internalization of proteins in EGFR-overexpressing inflammatory breast cancer (IBC) cells. Results demonstrate the importance of controlling ligand display on proteins for robust active targeting. In particular, high EGFR ligand valency and clustering was associated with enhanced IBC internalization with the highest performing construct resulting in a ~40-fold improvement in internalization compared to untargeted protein and ~5-fold higher delivery in IBC cells compared to healthy breast epithelial cells. Furthermore, this system has been adapted for delivery of a cancer suicide enzyme to enable IBC-targeted cell death through prodrug activation. These results demonstrate the benefits of UAA incorporation for controlling targeting peptide presentation and maximizing cargo protein activity, with key benefits relevant to prodrug therapeutics and a wide range of other intracellular protein therapies.
Lattice Convolutional Neural Network for Modelling Adsorbate Coverage Effects

Jonathan Lym
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Studying coverage effects are important for kinetic modeling techniques such as microkinetic modeling (MKM) and kinetic Monte Carlo (KMC) as the local environment can alter the stability of key intermediates and reaction pathways. For most systems, coverage effects are unfeasible to study via exhaustive density functional theory (DFT) due to the large configurational degrees of freedom. To overcome DFT’s limitations, surrogate models are trained with a finite set of DFT data and then the model is used to quickly predict the energies of different configurations. The cluster expansion is the most popular surrogate model for coverage effects, but it suffers from slow convergence due to: distortions around ideal lattice positions; its linear form whereas adsorbate interactions may be nonlinear; and a tendency to choose smaller clusters that may not fully capture the local environment around sites.

In this study, we develop a novel lattice graph convolutional neural network (LGCNN) that addresses the cluster expansion’s limitations and show superior performance compared to state-of-the-art methods such as the cluster expansion (CE) assisted by the genetic algorithm and a crystal graph convolutional neural network (CGCNN). Furthermore, we find the LGCNN outperforms other methods even using less than half of the training data. We provide rationale for the higher accuracy of LGCNN via visualization of the hidden representation of the adsorbate lattice system, and demonstrate its ability to deconvolute system formation energy into individual site formation energy.
Developing a high affinity, dynamic scaffold toolkit for intracellular spatial organization of proteins

Alexander A. Mitkas
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It is common practice in modern biotechnology to introduce nonnative enzymatic pathways in platform organisms such as *E. coli* to produce biochemical molecules ranging from specialty chemicals to biofuels. Traditionally, product titer is maximized by fine-tuning the nonnative enzymes’ activity and expression levels; however, in many instances the work can be time consuming and fruitless. Enzyme clustering is an alternative approach that has demonstrably helped increase nonnative pathway titers. However, without dynamic control of when the enzyme cluster forms, unwanted metabolic imbalances within the cell can occur.

To address the issues with these optimization techniques and provide an alternative way to improve nonnative pathway productivity, a high affinity, dynamic scaffold toolkit for intracellular spatial organization of proteins was designed. The toolkit building blocks are small RNAs and protein components taken from the CRISPR/Cas Type I systems. These Cas proteins bind to the small RNAs with high affinity and sequence specificity. Scaffold assembly is facilitated by adding short complementary regions in the RNA strands. Scaffold disassembly is coupled to the expression a third small trigger RNA which will occur when certain intracellular conditions are satisfied. The mechanism that drives the disassembly is toehold-mediated strand displacement (TMSD) which allows for displacing one DNA or RNA strand in favor of a new trigger strand. The displacement is facilitated by the presence of an unhybridized 6-18 nucleotide long toehold region at the end of one of the initially hybridized strands. The toehold region provides a foothold onto which the trigger strand can begin to hybridize on. Eventually, the trigger strand will completely hybridize with the toehold strand, essentially kicking out the second strand. TMSD is an excellent candidate for facilitating the dynamic disassembly of the scaffold because its kinetics occurs in the order of minutes to hours.

Using the split luciferase reporter system, an increase in the luminescence of the system has been demonstrated to occur only when all the correct components of the scaffold are simultaneously expressed. The scaffold assembly (and luminescence increase) only occurs when appropriate complementary regions are added to the small RNAs. Furthermore, constitutive and conditional scaffold disassembly has been demonstrated in the presence of a trigger strand. Ultimately, the scaffold will also be applied to increase the productivity and specificity of a nonnative pathway. The implementation of the scaffold toolkit will allow for intracellular dynamic process control while also providing an alternative approach for increasing nonnative pathway productivity.
Monoclonal antibodies (mAbs) constitute a $105 Billion global market by providing unique therapeutic functionalities that hold great promises for personalized medicine. More than ten new mAb-based drugs were approved by FDA in 2017, bringing the total to 76, with these drugs addressing diseases ranging from rheumatoid arthritis to high-risk neuroblastoma to multiple sclerosis. Manufacturing challenges and pharmacokinetics are often limiting the development of new mAb therapeutics. While the characterization of primary through quaternary structure is crucial for understanding their biochemical functionalities and efficacy, the quaternary structure and dynamics of therapeutic proteins in the solid state and in solution is crucial for understanding their stability in manufacturing, formulation, long-time storage, and during delivery. This work focuses on understanding the quaternary solution structure, protein-protein interactions (PPIs), and dynamics of the NIST standard reference mAb, NISTmAb RM 8671, in comparison to three industrial mAbs. The solution structure and interactions in buffer are characterized using small angle neutron scattering (SANS), while the dynamics in buffer are measured via neutron spin echo (NSE) and dynamic light scattering (DLS). The effects of concentration, temperature, sugar, and salt conditions on the conformation, interaction, and dynamics are explored for NISTmAb. The PPIs in solution exhibit strong temperature dependence for the concentrated samples driven by the competition of the charge repulsion and attraction. The diffusion interaction parameter, $K_D$, determined by DLS as a function of temperature further corroborates the temperature dependence of the PPIs observed by SANS. Measurements of the effective short time dynamics, $D_{eff}$, on timescales shorter than the structural relaxation but longer than the momentum and viscous relaxation time, as a function of concentration, temperature, sugar, and salt conditions are performed by NSE. Analysis of the $D_{eff}$ at the aforementioned conditions shows similar dependence across the reference and industrial mAbs. In addition to determining the relationship between translational dynamics and solution macroscopic behavior such as viscosity, another focus of this work is to understand the relation between the internal motions and the flexibility of mAbs as this is hypothesized to affect solution-state formulation stability. All atom MD simulations of NISTmAb is compared against NSE experiments and our analysis demonstrates the presence of some internal motions that contribute to the total effective diffusion coefficient. Further investigations are proposed to connect this motion to long-term mAb stability.
Innovations in transportation and industrial production have led to an increased demand in lubricants. Increases in worldwide demand warrant continued development of lubricants that are high performing and result in minimal harmful impacts on the environment. Currently, lubricant base oils are derived from petroleum, a nonrenewable feedstock that contributes to greenhouse gas emissions. Bio-derived, renewable feedstocks are a potential alternative, but often times result in the formation of lubricants with poor cold flow properties. These cold flow properties can be improved, however, by adding branches to the base oil’s hydrocarbon backbone. In the present work, we propose a straightforward synthesis for the production of highly branched, renewable base oils. Our starting materials are derived from fatty acids found in vegetable oil and furans found in biomass. The reaction scheme involves carbon-carbon coupling reactions followed by hydrodeoxygenation (HDO) to produce lubricant base oils. We select reaction conditions to enhance the yield of intermediates and products and use a combination of spectroscopic methods to characterize our products. In conclusion, this work demonstrates a potential strategy for the synthesis of high-quality lubricant base oils from renewable feedstocks.
Metabolic cross-feeding interactions between adipocytes and hepatocytes in an engineered mammalian co-culture system

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Understanding the dynamic nature of metabolic interactions between different mammalian cell types is vital if we are to characterize and identify novel therapeutic targets for metabolic disorders such as obesity and diabetes. Towards this end, we have engineered a co-culture system between adipocytes (fat cells) and hepatocytes (liver cells) that can be used as a platform for investigating metabolic interactions, e.g. cross-feeding of small molecules and other nutrients. The metabolic interactions between these specific cell types are of particular interest since impaired interactions between liver and fat cells have been directly linked to a cluster of disorders including diabetes and obesity. The co-culture system that we have developed thus far provides a convenient platform for investigating how system perturbations affect adipocyte-hepatocyte metabolic interactions, as well as for fine-tuning experimental techniques so that they can be translated to future \textit{in vivo} studies.

In this contribution, we describe the specific adipocyte-hepatocyte co-culture system that we have engineered using a trans-well cultivation experimental setup, and we highlight how we have applied this setup and recently developed approaches for co-culture $^{13}$C-metabolic flux analysis (co-MFA) to analyze in detail how global regulators of mammalian metabolism (e.g. insulin and isoproterenol) impact adipocyte-hepatocyte metabolic interactions (e.g. metabolite cross-feeding) and individual cell population physiology. Towards this end, we have performed a series of co-culture experiments with global regulators of cellular metabolism added to the medium. As an example, the addition of insulin induced both cell types to transition into a “fed state metabolism”, the state in which hepatocytes and adipocytes consumed glucose and utilized it for glycogenesis (in liver cells) and lipogenesis (in fat cells). In contrast, the addition of isoproterenol promoted “fasted state metabolism”, the state in which adipocytes released metabolic precursors such as glycerol, lactate, and fatty acids that were then used by hepatocytes for energy generation and gluconeogenesis. To gain further insights into the metabolic phenotypes, we also applied advanced co-MFA methods based on $^{13}$C-tracer experiments to quantify precisely the intricate cross-cell metabolite communications that occurred in these two metabolic states.
Rheological and heat transfer effects in fused filament fabrication additive manufacturing

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Committee Members: Antony N. Beris, Arthi Jayaraman, and Christopher J. Klooxin

Additive manufacturing (AM), more commonly known as 3D printing, provides unlimited design freedom and access to geometries too complex or otherwise impossible for the more traditional means of manufacturing. Recent advances in this technique have contributed to a diverse palette of printable materials, some of which include: metals, hydrogels, ceramics, and polymers. Complementary to this is a plethora of printing methods, such as the laser sintering of powders and the controlled extrusion of thermoplastic materials. The latter is often referred to as fused filament fabrication (FFF) and is the most commercially-adopted printing technique. Despite the cost savings and design flexibility that FFF offers, products designed in this manner are mechanically weaker compared to parts made using other polymer processing operations. Our work focuses on understanding this discrepancy through the lens of rheological and heat transfer theory.

In FFF, a fiber of thermoplastic material is conveyed towards a melting zone before being pushed through a computer-controlled nozzle and deposited onto a build plate, with the process being repeated until the desired product is formed. The strength of the final product relies heavily on how well individually laid tracks of molten material “weld” together due to the diffusion of polymer chains. This diffusion process depends on the temperature the material achieves within the melting zone, making this a heat transfer problem. The complex flow geometry of the printing nozzle also presents itself as a rheological problem, thus requiring a unified rheology-heat transfer analysis to understand the strengthening mechanism. Firstly, we present a modified Cogswell rheological model, which we use to relate extrudate temperatures to entry pressures developed within the flow field. Entry pressure measurements and calculations reveal unintuitive flow behavior, which we believe is attributable to heat transfer limitations within the melt zone. We then present a dimensionless Nusselt-Graetz number analysis and indeed find that heat transfer is a significant bottleneck in manufacturing the strongest printed parts. Future work will focus on applying our models to inform the redesign of FFF-based 3D printers.
Competing aggregation pathways and kinetics of particle formation for therapeutic proteins mediated by air-water interfaces

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Committee Members: Abraham M. Lenhoff, Millicent O. Sullivan, and Vladimir I. Razinkov

Therapeutic monoclonal antibodies (MAbs) are the largest overall selling class of biologics and consist of many approved and prospective therapies that are in clinical trials. A major obstacle to MAb development is their propensity to irreversibly aggregate, compromising drug potency and patient safety. There are a variety of aggregation mechanisms that can change for the same protein depending on the drug solution and stress condition. Bulk solution aggregation has been extensively studied in a mechanistic context. Conversely, aggregation at interfaces is a known phenomenon but still lacking in mechanistic understanding. This surface-mediated aggregation results in protein films that putatively desorb into solution as particles when the interfaces are agitated and/or destroyed.

This work evaluates the combined effects of temperature and compression/dilation of air-water interfaces on aggregation rates and behavior for representative MAb formulation conditions for a model MAb. High-pressure liquid chromatography is used to monitor monomer loss over time, which is converted to a rate constant that can be fit to an Arrhenius rate equation. Results indicate that surface-mediated aggregation is pH- and temperature-dependent and continues to be important even at elevated temperatures. Turbidity and particle counting measurements are used to monitor the rapid conversion of monomer to macroscopic and sub-visible particles. Added surfactant reduces but may not always eliminate aggregation. These results will be presented and discussed in terms of applications in elucidating mechanisms of surface-mediated protein aggregation.
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