UNIVERSITY OF DELAWARE
ENGINEERING

DEPARTMENT OF CHEMICAL AND BIOMOLECULAR ENGINEERING

WINTER RESEARCH REVIEW

4TH YEAR TALKS

WEDNESDAY, JANUARY 25, 2023

CLAYTON HALL CONFERENCE CENTER

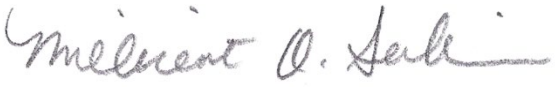
ABSTRACTS AND SCHEDULE GUIDE

COLBURN LAB • 150 ACADEMY STREET • NEWARK DE 19716

WELCOME TO OUR ANNUAL WINTER RESEARCH REVIEW.

Today's program of research presentations by our fourth-year graduate students provides a wonderful opportunity to learn about the scientific discoveries and training pathways 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 the department's mission towards 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. We are pleased that you can join us!



Millicent Sullivan
Alvin B. and Julie O. Stiles Professor and Department Chair
Department of Chemical and Biomolecular Engineering

Kenneth Cranke-Moscowitz
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

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ROOM 101B

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Enabling Polyolefin Hydroconversion by Developing Catalysts and Mechanistic Frameworks

Brandon C. Vance
Advisor: Dionisios G. Vlachos
Committee Members: Raul Lobo and Feng Jiao

Human civilization is reliant on a linear (take, make, and waste) economy that is harmful to the natural environment. Plastic products are mainly derived from fossil-fuels with ~1% produced from renewable bio-sources. In the USA, 90% of the 36 Mt of plastic waste produced in 2018 was disposed using dead-end methods, such as landfills, incineration, or environmental pollution. Furthermore, recycling plastics waste (PW) using conventional mechanical methods degrades their physical properties, eventually requiring disposal. Generation of new PW management strategies using chemical methods are urgently needed.

Polyolefins (POs), such as polyethylene (PE) and polypropylene (PP), comprise the largest fraction (66%) of plastics production and are difficult to chemically activate due to the C-H and C-C bond stability. High temperature (400-800 °C) pyrolytic methods have been demonstrated to deconstruct POs, but are energy intensive, generate large product distributions (C_1-C_{50+}), and have limited selectivity control. Hydrocracking and hydrogenolysis processes, commonly termed catalytic hydroconversion, were demonstrated in the late 1990's to reduce the reaction temperature (350-400 °C) and narrow the product distribution (C_1-C_{10}). Despite these improvements, catalytic hydroconversion of POs still require harsh reaction conditions, have limited flexibility in the product slate, and little is known about the deconstruction mechanism of polymeric substrates.

Herein, this work has developed a slate of hydrocracking and hydrogenolysis catalysts for the reutilization of PO feedstocks at mild reaction conditions (250-300 °C and 20-40 bar H_2). We have demonstrated mechanical blends of platinum tungstated zirconia and HY zeolite (PtWZr+HY) for the production of gasoline- (C_3-C_8) and jet fuel-ranged (C_9-C_{16}) hydrocarbons that can be directly inserted into the existing petroleum refinery infrastructure. Furthermore, we have established Ni/SiO_2 and Ni/Al_2O_3 as the first PO hydrogenolysis catalysts utilizing cheap, earth-abundant metals (EAMs), to produce wax and lubricant-ranged (C_{14}-C_{30}) alkanes.

Key mechanistic features have been elucidated for both PO hydroconversion chemistries. Strong adsorption of POs to the catalytic surface induces unique reaction behavior and products. In hydrocracking, strong polymer adsorption results in two reaction regimes: 1) isomerization of the polymer backbone; 2) cracking reactions that reduce the polymer molecular weight and generate hydrocarbon products. The depth of backbone branching can be tuned by controlling the ratio of the metal and Brønsted acid sites on the hydrocracking catalyst. In hydrogenolysis, strong adsorption results in long surface residence times that invoke cascade cracking reactions to generate excessive quantities of undesired methane. We have proposed a reaction mechanism to describe the hydrogenolysis behavior, which was verified using stochastic simulations.

Collectively this work demonstrates the feasibility catalytic hydroconversion for PO waste reutilization. The new generation of hydrocracking and hydrogenolysis catalysts and processes developed here are less energy-intensive with easily tunable product distributions. Our fundamental insights have built mechanistic frameworks that serve as blueprints, guiding future engineers to rationally design efficient hydroconversion catalysts and processes.

Microwave-assisted depolymerization & upcycling of plastic waste over heterogeneous catalysts

Esun Selvam
Advisor: Dionisios G. Vlachos
Committee Members: Raul F. Lobo and Yushan Yan

The accumulation of plastic waste in the environment is rising and poses a significant environmental and health threat. Polyolefins and PET account for a significant fraction of the waste due to their extensive use in single-use plastics.[1] The inadequacy of mechanical recycling to effectively handle these materials has led to a surge in chemical depolymerization and upcycling technologies such as pyrolysis, solvolysis, hydrogenolysis, and hydrocracking.[2, 3] However, the high energy demands associated with these processes can lead to significant carbon dioxide production. Furthermore, many of these processes currently employ catalysts that are either expensive or not selective to products of high value, and there is a need for better alternatives to make these processes more sustainable.

In this work, we demonstrate that coupling microwave (MW) heating with suitable heterogeneous catalysts in appropriate reactor configurations can result in rapid depolymerization of polymers such as PET and polyethylene, allowing to overcome the energy-related challenge of conventional heating (CH), at the same time achieving high selectivities to valuable products. First, we demonstrate that tuning the morphology of ZnO materials can result in high activity for microwave-assisted glycolysis of PET, achieving complete conversion and >95% yields of bis(2-hydroxyethyl) terephthalate (BHET), its monomer, in minutes. We then illustrate how reactor design and tuning acidity/porosity of the solid acids can selectivity produce olefins (>88%) via MW-slurry pyrolysis of polyethylene.[4] Lastly, we compare the performances of our MW-slurry pyrolysis with CH-pyrolysis and demonstrate how the volumetric heating of MWs can improve performance and reduce coke formation.

References

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2. G. Lopez, M. Artetxe, M. Amutio, J. Bilbao and M. Olazar, *Renewable and Sustainable Energy Reviews*, 2017, **73**, 346-368.
3. P. A. Kots, B. C. Vance and D. G. Vlachos, *React. Chem. Eng.*, 2022, **7**, 41-54.
4. E. Selvam, P. A. Kots, B. Hernandez, A. Malhotra, W. Chen, J. M. Catala-Civera, J. Santamaria, M. Ierapetritou and D. G. Vlachos, *Chemical Engineering Journal*, 2023, 454, 140332.

Propylene Esterification Coupled to Oxidative Dehydrogenation of Propane: Process Intensification through Catalyst Design

Quentin Kim
Advisor: Dr. Marat Orazov
Committee Members: Dr. Raul Lobo and Dr. Dionisios Vlachos

Propane has become more abundant in the US due to recent increases in natural gas production. However, propane is challenging to store and transport from remote locations and requires demanding reactions before it can be utilized as an industrial building block. Thus, methods to activate propane to convert it to a more useful feedstock are in high demand. Oxidative dehydrogenation (ODH) of propane can generate propylene while avoiding the high temperatures, thermodynamic limitations, and catalyst deactivation issues that plague the industrially practiced non-oxidative dehydrogenation (PDH). Current ODH catalysts and processes cannot reach high propane conversions while maintaining propylene selectivity comparable to that of PDH. As a result, ODH processes face a tradeoff between expensive and energy intensive propane/propylene separations at low propane conversions or overoxidation to CO_x at high propane conversions. To overcome these limitations, we propose a reaction scheme in which propylene is esterified with benzoic acid as it is produced by an encapsulated ODH catalyst. The ester intermediate is protected from overoxidation, and its separation from unreacted propane and benzoic acid is facile. Such a scheme enables higher selectivity in ODH without the difficult propane/propylene separation.

To protect propylene from overoxidation, its partial pressure must remain significantly lower than that of propane. The colocalization of ODH and esterification catalysts in the same catalyst bed is required to enable moderate single-pass propane conversion. However, the unrestricted vanadium-based ODH catalyst we have developed for low temperature propane ODH can also oxidize benzoic acid at the reaction conditions. To limit the transport of benzoic acid to the ODH catalyst, we design ODH catalysts encapsulated within zeolitic frameworks. 8-ring zeolites such as CHA, LTA, or PHI have small pore diameters that can exclude benzoic acid without significantly affecting the transport of propane and propylene. The encapsulation is complicated by the solubility of vanadium species in traditional hydrothermal zeolite synthesis conditions, so the encapsulation procedure must avoid hydrothermal syntheses or protect vanadium species to preserve catalyst activity. In this presentation, we will show our work on the preparation and validation of the encapsulated catalysts.

Dynamic Electrification of Dry Reforming of Methane with *In situ* Catalyst Regeneration

Kewei Yu
Advisor: Dionisios G. Vlachos
Committee Members: Raul F. Lobo, Yushan Yan

Process heat is the driving force for chemical industries. Synthesis of important chemicals such as ammonia, hydrogen, syngas, etc., consume the majority of chemicals energy and emits significant amount of CO_2 from conventional fossil fuel burning reactors. With the rapid decarbonization of power generation and consumption, process electrification for chemical manufacturing is urgently called for. Electrified reactors exhibit multiple benefits such as short startup time, low temperature gradients, cooler gas phase temperatures, and higher energy efficiencies. However, most electrified processes have been studied under steady-state conditions. Investigation of reactors operating under dynamic conditions is needed to harness additional benefits stemming from process electrification.

Here, we develop a Rapid Pulse Joule Heating (RPH) reactor with an *in situ* Raman probe to electrify highly endothermic, high-temperature chemical reactions. We demonstrate the approach for the thermochemical dry reforming of methane (DRM), as a carbon-negative process potentially driven by renewable electricity. With a low-thermal inertia design, we achieve a typical catalyst ramping rate of ~14000 °C/s. By using $PtNi/SiO_2$ as the catalyst, we demonstrate that the dynamic electrification strategy can not only improve productivity by almost 2 times (compared with steady-state operation), but also exhibit excellent catalyst stability by suppressing coke formation, particle sintering, and catalyst phase segregation, which are the leading causes for DRM catalyst deactivation. We believed that the developed principles could potentially be extended to other heterogeneous endothermic reactions, such as methane steaming reforming and light alkane dehydrogenation.

Deconvoluting CO_2 Electrolyzer Energetic Efficiency Losses via Five-electrode Setup

Kentaro U. Hansen
Advisor: Dr. Feng Jiao
Committee Members: Dr. Yushan Yan, Dr. Marat Orazov

CO_2 electrolysis is a promising carbon utilization technology as it provides a means to link renewable electricity to the production of fuels and chemical feedstocks such as ethylene and carbon monoxide directly from water and captured CO_2. However, energetic efficiency still requires a significant improvement for widespread commercialization. Current research efforts primarily focus on improving individual components (catalysts, membranes, cathode/anode support material) while achieving better performance on a full device level remains challenging because the full cell performance under working conditions is also impacted by factors beyond individual component properties. In particular, the interpretation of full cell efficiency, routinely measured via measuring full cell potential, is challenging because it is an aggregate metric of all of the efficiency losses distributed across an electrochemical cell spanning the cathode, membrane, anode and their interfaces. Therefore, a diagnostic tool to pinpoint major sources of voltage losses is desirable for better understanding the distribution of energetic losses which may accelerate the rational design of more efficient CO_2 electrolyzers.

In this talk I will present a novel technique for the complete deconvolution of the cell voltage and internal resistances through a five-electrode setup. Unlike similar methods, three additional reference electrodes are introduced with two directly attached to the membrane. This enables the technique to be applied to low temperature electrochemical cells that do not have a liquid electrolyte gap, such as state of art CO_2 electrolysis cells and hydrogen fuel cells. Importantly, the technique has been optimized such that it can implemented without modifications to electrochemical cell endplates to improve accessibility of the technique.

As a case study, I identify that the cathode/membrane ionic interface is the major bottleneck for energetic efficiency in a standard CO_2 electrolysis cell operating with dilute supporting electrolyte, contributing 720 mV voltage loss at 600 mA cm^{-2}. This single efficiency loss is larger in magnitude than all of the efficiency losses distributed throughout entire water electrolysis and hydrogen fuel cell configurations. Fortunately, this loss can be mitigated by coating the catalyst directly onto the membrane via hot pressing to lower ionic resistances, reducing this voltage loss to 80 mV at the same current density. The improved design enables us to achieve a full cell performance of 3.55 V and >95% CO Faradaic efficiency at 800 mA cm^{-2} representing the highest performance for CO_2 electrolysis with a dilute bicarbonate electrolyte. In addition, I will present examples of how insights provided by the five-electrode technique may guide the general optimization of membrane-based electrochemical cells and preliminary work exploring the viability of the catalyst coating method for other commercial membranes and larger active areas from 5 cm^2, to a more industrially relevant 100 cm^2.

Anode-Fed Hydroxide Exchange Membrane Electrolyzers for CO_2-Tolerant Green Hydrogen Generation

Alexandra Oliveira
Advisor: Prof. Yushan Yan
Committee Members: Prof. Feng Jiao, Prof. Marat Orazov

Hydroxide exchange membrane electrolyzers (HEMELs) can produce green hydrogen with high voltage efficiencies at low capital cost. The solid electrolyte membranes in these devices reduce the ohmic resistances in comparison to liquid electrolytes and avoid the use of corrosive potassium hydroxide salt solutions. Furthermore, the basic environment of HEMELs allows for the use of inexpensive and stable earth metal catalysts. In a HEMEL, it is critical that liquid water reaches active sites at the hydrogen-evolving cathode, where it is consumed, so the intuitive mode of operation is to feed water to the cathode. However, due to the diffusion of water through the membrane, HEMELs allow for the flexibility to operate with water fed to the anode, which facilitates the pressurization and separation of the dry hydrogen product. An added benefit of the anode feed is that the ionic potential gradient drives hydroxide and any other anions toward the anode, possibly reducing the penetration of anion contaminants into the MEA.

Research has shown that anion contamination of hydroxide exchange membranes can lead to significant performance losses in HEM fuel cells when their air feed contains CO_2.[1,2] In this study, we examine the contamination effect on HEMELs by dissolved CO_2 in the electrolyte, which reacts to form carbonate (CO_3^{2-}) and bicarbonate (HCO_3^{2-}) anions. The presence of these anion contaminants can lower the ionic conductivity of the cell. In addition, during operation, these anions will be pushed by an ionic potential gradient to the anode and accumulate there. This creates a significant pH gradient between cathode and anode that can lead to Nernstian thermodynamic losses which further lower performance.[3]

More specifically, we use 1-D CO_2 transport modeling and experiments to show how altering the water feed method allows for CO_2-tolerant HEMEL operation in several different electrolytes. The model predicts that an anode-fed HEMEL can more easily purge CO_2 without contaminating as much of the HEM or inducing as high of a pH gradient due to more rapid self-purging of anions. We also find experimentally that HEMELs with anode-fed DI water are more tolerant of forced CO_2 contamination than those with cathode-fed DI water, which is likely one of the major reasons for superior anode-feed performance. Furthermore, the anion self-purging shows that electrolyzer operation in tap water (containing fluoride, chloride, and nitrates) is possible when employing an anode feed.

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(2) Shi, L.; Setzler, B. P.; Hu, K.; Weiss, C. M.; Matz, S. M.; Xue, Y.; Xu, Z.; Zhuang, Z.; Gottesfeld, S.; Yan, Y. Editors' Choice-Uncovering the Role of Alkaline Pretreatment for Hydroxide Exchange Membrane Fuel Cells. *J Electrochem Soc* **2020**, *167*, 144506.

(3) Setzler, B. P.; Shi, L.; Wang, T.; Yan, Y. (Invited) Modeling of Carbon Dioxide Exposure and Mitigation in Hydroxide Exchange Membrane Fuel Cells. In *ECS Meeting Abstracts*; IOP Publishing, 2019; Vol. MA2019-01, pp 1824–1824.

One-Pot Conversion of Acetone to Lactic Acid via Tandem Reactions

Nikolas Angyal
Advisor: Marat Orazov
Committee Members: Raul Lobo, Dionisios Vlachos

Lactic acid is an important commodity chemical whose market size is projected to continue growing. It has traditional uses in the food, pharmaceutical, and cosmetic industries. Increasingly, lactic acid is used as a building block to produce polylactic acid (PLA) and other polyesters. PLA has received significant attention as an alternative polymer due to its promising physical and chemical properties and its inherent biodegradability and ease of recycling. The use of alcohol esters of lactic acid as green solvents is also appealing. These growing markets drive the demand for lactic acid. Currently, almost all the lactic acid produced industrially is obtained via bacterial fermentation of sugars or starches. While sugars are a renewable carbon feedstock, there are a few challenges with scaling up fermentation to meet the growing demand. To maintain productive cell populations, fermentation requires neutralization of the acid during production (typically with $Ca(OH)_2$), followed by acidification of the calcium lactate (typically with H_2SO_4) after the removal of the cells. This stoichiometric use of acids and bases results in additional reagent costs and the production of a waste salt (typically $CaSO_4$). Even with continuous neutralization, the fermentation process yields relatively low concentrations of lactic acid; as a result, the purification steps needed to concentrate the product are energy intensive. The price of sugars and the intrinsic constraints of fermentation significantly contribute to the final cost of lactic acid. To meet the growing demand and to increase the economic appeal of adopting biodegradable products derived from lactic acid, there is an interest in developing alternative, inexpensive chemical routes to lactic acid from sugars or other feedstocks.

We propose a simple, one-pot chemical synthesis of lactic acid starting from acetone, which is inexpensive and available at large scale. This process involves a tandem oxidation of acetone to methyl glyoxal by SeO_2 and isomerization of methyl glyoxal to lactic acid by a microporous stannosilicate. The use of Se complexes for ketone oxidation is well known, including the oxidation of acetone to methyl glyoxal. However, high yields of such products are difficult to achieve due to their high reactivity. The mild conditions of the Se-mediated oxidation and its remarkable selectivity at low conversions enable a facile pairing with a Lewis-acid-catalyzed isomerization of methyl glyoxal to produce high yields of stable lactic acid. In this work, we studied a variety of catalysts, solvents, reaction conditions, and system designs to optimize this novel tandem process.

The Role of Metal Core on the WO_x/M (M = Pt, Ru, Pd, Ni) Inverse Catalysts

Jiahua Zhou
Advisor: Dion Vlachos
Committee Members: Raul Lobo, Feng Jiao

Metal-metal oxide (M-MO_x) catalysts are widely used in biomass transformation owing to providing multifunctional and tunable active sites and their superior activity and selectivity. Typical examples include metal particles (e.g., Pt, Ir, Rh) covered with reducible oxides (e.g., WO_x, MoO_x, ReO_x). However, these catalysts are structurally complex, multifunctional, and dynamic. The lack of a fundamental understanding of the catalyst active sites hinders rational design of these catalysts. In recent work, we showed that the reduction of WO_x is promoted by Pt and hydrogen spillover from the Pt surface to the WO_x surface enables the formation of Brønsted acid sites at first and redox centers at longer times. Building on this finding, we elucidated that the density of Brønsted acid sites over $PtWO_x$/C inverse catalyst can be modulated by adjusting the pretreatment and reaction conditions such as annealing, reduction, and hydrogen co-feeding. These findings were culminated by combining DFT calculations, kinetics of probe reactions, and spectroscopic studies. However, understanding the role of metal core (precious and base metals) on the properties of WO_x is still needed to establish unambiguous structure-activity relationships.

Herein, we synthesize a diverse library of MWO_x/C inverse catalysts with varying metal cores (M = Pt, Ru, Pd, Ni) to develop a fundamental understanding of the effect of the metal on the catalyst properties and performance. Combining *in situ* characterization (AP-XPS), probe chemistry, H_2-TPR and the CO chemisorption, we demonstrated that the W coverage is linearly correlated with the W surface density on metal cores. The wetness of WO_x and metals follow the trend that Pt < Ru ~ Pd < Ni due to the electronic interaction between WO_x and metals. Expectedly, the H_2-TPR and XPS results indicates that electronic interaction between WO_x and metals (reduced) follow the trend: Ni > Ru > Pt ~ Pd. The electronic interaction of WO_x-M further affects the deprotonation energy of -OH on WO_x, resulting in different BAS strengths, evidenced by t-BuOH dehydration reactivity. The work not only provides novel insights into the synergy of precious and base metal cores with metal oxide WO_x overlayers but also opens an opportunity to develop approaches to further tune inverse catalysts.

From C5 Sugars to Valuable Chemicals Through Catalysis

Mi Jen Kuo
Advisor: Dr. Raul F. Lobo
Committee Members: Dr. Christopher Kloxin, Dr. Marianthi Ierapetritou, Dr. Hari Sunkara

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4,4'-dimethylbiphenyl (DMBP) has been identified as one of the most valuable chemical platforms to the production of polymers, plasticizers, and metal-organic frameworks. A pathway to produce DMBP is the multistep conversion of benzene or toluene, reported by ExxonMobil in 2015. In this process, however, the formation of a mixture of DMBP isomers is unavoidable and difficult to separate. It would be desirable to have a biomass-derived substitute that could turn non-edible sugars into advanced materials. Here we report a two-step pathway to produce DMBP selectively using biomass-derived molecular precursors such as a 2-methylfuran (MF) and ethylene. This two-step process consists of i. the oxidative coupling of 2-methylfuran (MF) — a readily available species derived from xylose via furfural — to afford 5,5'-dimethylbifuran (DMBF), and ii. the tandem Diels-Alder (DA) and dehydration reactions of DMBF with ethylene (C_2H_4) to form DMBP. Since C_2H_4 can be sourced by the dehydration of bioethanol, the proposed reactions offer a completely renewable pathway for DMBP production. For the oxidative coupling of MF to DMBF on Pd catalysts in the presence of TFA, the site-time-yield (STY) of the reaction (6.99 h^{-1}) is improved by a factor of ~20, compared with the previously reported STY value (0.35 h^{-1}). High O_2 pressure and high TFA concentration are important to improve the DMBF formation rate. However, the mechanism of the oxidative coupling including the role of TFA are not fully understood and need further investigation. The formed DMBF undergoes P-SiO_2 catalyzed DA-dehydration reactions with C_2H_4 to generate DMBP (83% yield), with a carbon balance of ~93%. The high conversion and selectivity are because of P-SiO_2 moderate Brønsted acidity, which selectively catalyzes the dehydration of furan-ethylene cycloadducts without substantial coke formation. The P-SiO_2 catalyst also shows high recyclability under these reaction conditions.

A novel way to synthesize a diol molecule that can work as a substitute for the disputed bisphenol-A (BPA) is also proposed. Furfuryl acetate, which can be obtained by the esterification of biomass-derived furfuryl alcohol, can undergo oxidative coupling to afford bi(furfuryl acetate) as the intermediate. Hydrogenation of the intermediate can be performed to yield the final product bis(tetrahydrofurfuryl acetate) using Pd/Silica heterogeneous catalyst at mild conditions. Bis(tetrahydrofurfuryl alcohol), the hydrolyzed form of the final product, has a similar structure with BPA. The pathway provides a completely renewable route to synthesize the diol compound. Moreover, the molecule is expected to have low toxicity; this makes an excellent replacement for BPA, which is a known endocrine disruptor.

Development and Application of Bio-based Polymers for the Selective Separation and Purification of High Commercial Value Chemicals Extracted from Food Waste, Plants, and Non-Food Biomass

Yagya Gupta
Advisor: Dionisios G. Vlachos
Committee Members: Yushan Yan, Abraham M. Lenhoff, Souryadeep Bhattacharyya

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The profound challenge of food waste (FW) is evidenced by the fact that approximately a third of global food production (*i.e.*, 1.3 billion tons) ends up as waste. Traditional FW treatment methods, such as disposal into landfills and composting, are environmentally unfriendly. Intensive exploration of other methods that selectively convert the diverse components of FW to high commercial value chemicals is a key to alleviating this challenge. Extraction of antioxidant and antimicrobial activity-providing chemicals (flavonoids, phenolic acids, etc.) from FW feedstocks is one such economically lucrative option to valorize FW. However, separation and purification of these high commercial-value chemicals is challenging owing to their similar chemical nature, high boiling points, and low concentrations in FW. To the best of our knowledge, currently, there is no method to separate and purify phenolic compounds post-extraction from FW or non-food biomass. Our study directly addresses this issue by proposing a scalable and extensible methodology for conducting selective separation of the target molecules using molecular imprinted polymers. Synthesis of polymers with imprinted functionality has been identified as one of the most important steps in optimizing the selectivity and performance of the material. Thus, computational methods were used to screen 28 monomers to study their interaction with the target molecule. Experimental investigations revealed that itaconic acid, crosslinked with ethylene glycol dimethacrylate using chlorogenic acid as the template provides the highest separation factor (a factor of ~2 higher than the literature standard, acrylamide). The performance of the polymer at separating structurally similar compounds (p-coumaric acid, caffeic acid, ferulic acid) was tested in four different extraction solvents (dimethyl formamide, ethanol, water, and a mixture of ethanol and water). Complementing IR studies were done to understand the interactions between the polymer, target molecule, and the solvent for extraction. The application of the polymer for the separation of polyphenols extracted from real food waste was demonstrated. As a result, a stage-wise adsorption method is proposed to separate and purify these valuable compounds. In contrast to the current industrial purification methodology that produces mixtures, the proposed technology provides at least eleven times the higher economic value and 95% lesser carbon emissions based on lab-scale techno-economic analysis.

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CLAYTON HALL | JANUARY 25, 2023

ROOM 120

SCHEDULE OF TALKS

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SESSION I — 9:20 AM – 1:00 PM — ROOM 120

9:20 – 9:40 AM

Yuqing Luo
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Advisor: Marianthi Ierapetritou / Committee Members: Raul Lobo and Dionisios Vlachos

9:40 – 10:00 AM

Oluwadare Badejo
"Modeling Supply Chain Under Disruption and Uncertainty"
Advisor: Marianthi Ierapetritou / Committee Members: Antony Beris and Babatunde Ogunnaike

10:00 – 10:20 AM

Huayu Tian
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Advisor: Marianthi Ierapetritou / Committee Members: Ravendra Singh, R. Bertrum Diemer, Wilfred Chen, and Thomas Epps, III

10:40 – 11:40 AM — **POSTER SESSION**

11:40 AM – 1:00 PM — **LUNCH** (Room 101A) **and Featured Speaker, Aditya Kunjapur**

UNIVERSITY OF DELAWARE
ENGINEERING

CLAYTON HALL | JANUARY 25, 2023

ROOM 120

SCHEDULE OF TALKS

SESSION II	1:10 PM – 4:00 PM	ROOM 120

1:10 – 1:30 PM	**Vinson Liao** "Deducing Subnanometer Cluster Size and Shape Distributions of Heterogeneous Supported Catalysts" Advisor: Dionisios Vlachos / Committee Members: Antony Beris and Raul Lobo
1:30 PM – 1:50 PM	**Shizhao Lu** "Molecular Modeling, Simulation, and Machine Learning of Polymer Nanocomposites Containing Nanorod Fillers" Advisor: Arthi Jayaraman / Committee Members: April Kloxin, Eric Furst and Austin Brockmeier
1:50 – 2:10 PM	**Piaoping Yang** "Insights into the Activity of Fe-N-C catalysts for Catalytic Transfer Hydrogenation of Furfural" Advisor: Dionisios G. Vlachos / Committee Members: Marianthi Ierapetritou and Raul Lobo
2:10 – 2:30 PM	**Sanjana Srinivas** "Spin-crossing in heterogeneous ethane dehydrogenation by atomically dispersed Co/SiO_2" Advisor: Dionisios Vlachos / Committee Members: Raul Lobo and Antony Beris
2:30 – 2:50 PM	**BREAK**
2:50 – 3:10 pm	**Terrance Shoemaker** "Assessing Impact of Hinge Flexibility on Predicted Antibody Interactions" Advisor: Christopher Roberts / Committee Members: Eric Furst and Abraham Lenhoff
3:10 – 3:30 pm	**Chaoying Ding (Collaborator: Christopher Gerberich)** "Hybrid Model Development for Parameter Estimation and Process Optimization of Hydrophobic Interaction Chromatography" Advisor: Marianthi Ierapetritou / Committee Member: Abraham Lenhoff
3:30 – 3:50 pm	**Jayanth Venkatarama Reddy** "Modeling the effect of bioreactor pH on Chinese Hamster Ovary (CHO) cell metabolism and site-specific N-linked glycosylation of VRC01" Advisor: Eleftherios Papoutsakis and Marianthi Ierapetritou / Committee Members: Kelvin Lee and Abraham Lenhoff
4:00 PM	**END**
4:00 – 5:00 PM	**FREEFORM INDUSTRY SESSION (101A)**

Neural Network Surrogate Constraints for Flexible Biorefinery Design

Yuqing Luo
Advisor: Prof. Marianthi G. Ierapetritou
Committee Members: Prof. Raul F. Lobo and Prof. Dionisios G. Vlachos

The growing concerns over global warming motivate the research on replacing oil-based feedstocks with biomass raw materials for chemical and fuel production. However, biomass raw materials contain various components (e.g., cellulose, hemicellulose, and lignin) that cannot be converted efficiently with a single technology. Hence, the integrated biorefinery is proposed to combine different reactions and fully utilize all biomass components. The development of biomass conversion technologies involves design and optimization on multiple levels. Bayesian optimization could be applied to explore reaction conditions with minimum cost and emission, and stochastic programming with rolling horizon optimization has been utilized to design a biomass supply chain with modular conversion units. The design and operation of biorefineries will also be affected by various uncertainties, including prices, supply, demand, and yields.[1] Surrogate-embedded optimization has been applied to many process system design problems to simplify the problem formulation and reduce the computational complexity when detailed simulation results are part of the constraints or objective function.[2]

In this work, we utilized superstructure optimization to rationally select feedstock and conversion pathways under different market situations. The two-stage stochastic programming problem is formulated to analyze uncertain scenarios of price and biomass supply variability since the historical data could be converted to empirical probability distributions. On the other hand, the flexibility index is used to quantify the biorefinery's ability to handle the demand and yield fluctuations within an uncertain range, as empirical observations of them are scarce in the early stage.[3] Since a multi-level optimization problem has to be solved before obtaining the flexibility index, data-driven surrogate models (e.g., support vector regression, Lasso regression, and artificial neural network) have been fitted to replace this function in the optimization problem. The neural network with rectified linear unit (ReLU) activation function is established as the appropriate surrogate model because it closely approximates the flexibility index while retaining the mixed-integer linear characteristics of the overall design formulation.[4] Moreover, the stochastic programming quantifies the biorefinery's life cycle assessment (LCA) uncertainty by the empirical LCA result distribution from each scenario using historical price/demand/supply uncertainty information. This method provides a more accurate representation of LCA uncertainty than the traditional Pedigree-based analysis that only relies on data quality indicators.

References:

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Modeling Supply Chain Under Disruption and Uncertainty

Oluwadare Badejo
Advisor: Marianthi Ierapetritou
Committee Members: Antony Beris, Babatunde Ogunnaike

Networks within the supply chain (SC) have grown in importance and complexity, making them difficult to manage due to the wide variety of potential threats and uncertainties. There are two main ways to mitigate the effects of SC interruptions: proactive and reactive approaches. The former strategies provide alternative ways to build robust and resilient structures, while the latter ensures SC recovery[1,2]. Strategic decisions govern SC topology, whereas tactical decisions are made within the restrictions of strategic decisions. SC dynamics are generally not considered in existing work on tactical SC under disruption. As a result, disruptions are not considered together with durations and recovery procedures[1].

In this work, we develop a SC model that incorporates both proactive and reactive measures to address disruptions while considering process uncertainties. We adopted a discrete time-expanded model to solve the SC problem and consider the disruption dynamics using the rolling horizon framework. In the proposed SC model, a graph network represents the SC, where the nodes consisting of suppliers, manufacturing sites, warehouses, and customers interact using the arcs. The arcs determine the flow of materials between the nodes. Independent disruptions can occur at the nodes and/or arcs, and the time of disruption is quantified using the geometric distribution. In the advent of disruption, we have adopted adjusting routing plans, maintaining optimal inventory levels, and capacity flexibility to ensure high service level is maintained at low cost. A deterministic and two-stage stochastic models are used with objective of minimizing operating cost and expected cost, respectively[3,4]. To illustrate the proposed approach, we used a motivating example to illustrate the effect of arcs and node disruption in decision-making and a realistic case study to demonstrate the proposed framework's computational efficiency. The results suggested that the effect of node disruption is more predominant because the initial network configuration limits the flexibility at the nodes[3]. The results obtained offers a balance between the service level and the total cost of operating the SC. In addition, we compared the decisions made by the stochastic model to those made by the deterministic model, and the findings indicate that the stochastic model was better able to manage the variability in the demands and disturbances[4].

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A Surrogate-Based Framework for Feasibility Analysis and Optimization of Expensive Simulations

Huayu Tian
Advisor: Marianthi Ierapetritou
Committee Members: Ravendra Singh, R. Bertrum Diemer, Wilfred Chen, Thomas H. Epps, III

Simulation-based optimization has been widely studied in the field of operations research for optimization of complex systems. Compared to the optimization of systems consisting of algebraic mathematical models, numerous challenges exist for simulation-based optimization. First, the simulation is only available as a black box for the evaluation of objective functions and constraints. Second, many simulations are computationally expensive to run, limiting the number of simulations that can be performed in search of the optimal solution. Third, the derivative information is usually unavailable or hard to estimate due to the computational burden and output noise. Thus, it becomes challenging to utilize the conventional approaches such as derivative-based methods and random search methods for optimization of such systems. Surrogate models have been considered to approximate expensive function evaluations using suitable design of experiments [1]. In addition, adaptive sampling techniques have been investigated to refine the surrogate model in a search towards the optimum [2]. The surrogate-based optimization framework has been extended to feasibility analysis, with the modified adaptive sampling method to refine the feasible region boundary [3].

Most surrogate-based approaches for feasibility analysis are limited to the construction of a regression model for the feasibility function, not taking advantage of the fact that the feasibility problem is essentially a classification problem in nature. Therefore, in this work, we consider the feasibility problem as a classification problem, and investigate the ability of classification models, specifically support vector machines (SVM), to accurately characterize the design space boundary. Adaptive sampling strategy based on SVM refinement near feasible region boundary is developed. SVM is incorporated as a constraint for the optimization problem to locate the optimum within the feasible region. A global exploration stage is also introduced to improve global coverage of samples. Finally, switching strategies are developed to determine the stopping criteria for feasibility characterization, optimization, and global exploration. We illustrate the efficiency of the proposed framework on a series of test problems to explore the computational complexity along with the accuracy and compare it with existing regression-based approaches. Finally, the proposed framework is implemented on a realistic case study describing the production of solid-based drugs using wet granulation, aimed to reduce the operation cost, improve product quality, and increase process flexibility and robustness.

References

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Deducing Subnanometer Cluster Size and Shape Distributions of Heterogeneous Supported Catalysts

Vinson Liao
Advisor: Dionisios G. Vlachos
Committee Members: Antony N. Beris, Raul F. Lobo

Infrared (IR) spectra of adsorbate vibrational modes are sensitive to adsorbate/metal interactions, accurate, and easily obtainable in-situ or operando. While they are the gold standards for characterizing single-crystals and large nanoparticles, analogous spectra for highly dispersed heterogeneous catalysts consisting of single-atoms and ultra-small clusters are lacking. Here, we combine data-based approaches with physics-driven surrogate models to generate synthetic IR spectra from first-principles. We bypass the vast combinatorial space of clusters by determining viable, low-energy structures using machine-learned Hamiltonians, genetic algorithm optimization, and grand canonical Monte Carlo calculations. We obtain first-principles vibrations on this tractable ensemble and generate single-cluster primary spectra analogous to pure component gas-phase IR spectra. With such spectra as standards, we predict cluster size distributions from computational and experimental data, demonstrated in the case of CO adsorption on $Pd/CeO_2(111)$ catalysts, and quantify uncertainty using Bayesian Inference. We discuss extensions for characterizing complex materials towards closing the materials gap.

Molecular modeling, simulation, and machine learning of polymer nanocomposites containing nanorod fillers

Shizhao Lu
Advisor: Prof. Arthi Jayaraman
Committee Members: Prof. April Kloxin, Prof. Eric Furst (Chemical & Biomolecular Engineering) and Prof. Austin Brockmeier (Electrical & Computer Engineering)

Polymer nanocomposites (PNCs) with nanorods as filler exhibit some unique morphologies (e.g., percolation of nanorods) that are not seen in PNCs with spherical nanoparticles, making them more useful in applications with desired conductive and transport properties. Past theoretical, computational, and experimental work have demonstrated the types of morphologies obtained with nanorods with homogeneous surface functionalization. In contrast, studies on PNCs containing nanorods with patchy/heterogeneous functionalization are lacking. In the first part of my talk, I will address this knowledge gap by conducting coarse-grained molecular dynamics (MD) simulations of PNCs with two different filler surface functionalization: homogeneously functionalized nanorods fillers and patchy functionalized nanorods fillers. [1]

Even though many simulation studies have focused on the morphology and dynamics of nanorods in polymer melt using coarse-grained models of nanorods, past studies have not demonstrated how the nanorod roughness impacts the phase behavior of nanorods in the polymer melt. In the second part of this talk, I elucidate the effect of nanorod roughness on nanorod aggregation, dispersion, and percolation in polymer nanocomposites using MD simulations. By choosing coarse-grained models that enable systematic variation of the nanorod roughness and by selecting purely repulsive pair-wise interactions for nanorods and polymer chains, I show how nanorod roughness affects the entropic driving forces for various PNC morphologies. [2]

In the field of materials science, microscopy is the first and often only accessible method for structural characterization. There is a growing interest in the development of deep learning methods that can automate the analysis and interpretation of microscopy images. Typically training of deep learning models require large numbers of images with associated structural labels, however, manual labeling of images requires domain knowledge and is prone to human error and subjectivity. To overcome these limitations, in the final part of this talk, I present a semi-supervised transfer learning approach that uses a small number of labeled microscopy images for training and performs as effectively as methods trained on significantly larger image datasets. [3]

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Insights into the Activity of Fe-N-C catalysts for Catalytic Transfer Hydrogenation of Furfural

Piaoping Yang
Advisor: Dionisios G. Vlachos
Committee Members: Marianthi G. Ierapetritou, Raul F. Lobo

The selective transformation of biomass-derived platform molecules into value-added fuels and chemicals plays an essential role in biomass upgrading. Low-cost single-atom catalysts are promising candidates due to their theoretical 100% atom efficiency, high selectivity, and tunable electronic structure. Recently, a Fe-N-C catalyst has exhibited TOF of 2271 h^{-1} for the catalytic transfer hydrogenation (CTH) of furfural (FF) to furfuryl alcohol (FA) by isopropanol (IPA) at 120 °C. However, there is limited understanding of the Fe-N_x single-site heterogeneous catalysts, with numerous mechanistic uncertainties regarding the actual reaction pathways and how they might be optimized.

In this work, we investigate the CTH of FF to FA over various Fe-N_x sites anchored on graphene by density functional theory (DFT) calculations. We first focus on the bulk Fe-N_3 site and bulk Fe-N_4 site to study CTH reaction mechanisms and the effect of the geometry of Fe-N_x sites on the activity of CTH. In the bulk Fe-N_4 site with a square-planar configuration, the Fe center cannot coordinate both IPA and FF at the same time, leading to unfavorable reaction pathways through a single transition state. In contrast, the Fe center in the bulk Fe-N_3 site is pulled out of the support plane after the IPA deprotonation, which enables the co-adsorption of FF and promotes a more favorable pathway that entails (1) deprotonation of IPA; (2) hydride transfer from deprotonated IPA to FF, the rate-limiting step; and (3) protonation of furoxy species to FA. Based on the understanding of the geometrical effect of Fe-N_x sites on the CTH reaction mechanisms and activity, we further constructed 7 edge-hosted Fe-N_3-C models by introducing various carbon divacancy defects around the Fe-N_3 site to establish a detailed structure-activity relationship of Fe-N_3 sites for the CTH reaction. We identify the more active model based on the activation energy of hydride transfer, the rate-limiting step. We found that the position of Fe relative to the plane of the support correlates with CTH activity. Specifically, the higher the position of Fe atom, the lower the energy of the transition state (TS). Furthermore, we demonstrate that the interaction between the Fe $3dz^2$ orbital and the HOMO of the hydride transfer TS is critical to the stabilization of TS. This work provides insights into the Fe-N_3 activity for CTH reaction and guidelines for designing high-performance Fe-N-C catalysts.

Spin-crossing in heterogeneous ethane dehydrogenation by atomically dispersed Co/SiO_2

Sanjana Srinivas
Advisor: Prof. Dionisios Vlachos
Committee Members: Prof. Raul Lobo, Prof. Antony Beris

Supported atomically dispersed metals and sub-nanometer metal clusters have been garnering attention on account of their efficient metal utilization and the high activity and selectivity they impart to several reactions. Of particular interest is the dehydrogenation (DH) of small alkanes to alkenes, as alkenes are used in the synthesis of several commodity chemicals and the recent shale gas boom in the US has made dehydrogenation economically viable. Common catalysts of the reaction are Pt-Sn alloys and alumina-supported chromium oxides, both of which have several shortcomings such as the high cost of Pt and the toxicity of Cr based catalysts (Cr^{6+}). The burgeoning activity in replacing supported Pt-group metal atom/sub-nanometer cluster catalysts with earth abundant metals is driven by the lower biological toxicity and cost of the latter. Experimental reports have demonstrated that highly dispersed Co(II) on am-SiO_2, both as single sites and sub-nanometer CoO_x clusters, exhibit high activity and selectivity for alkenes (>95%)[1,2], under oxidative and non-oxidative reaction conditions. In this work, we derive rate constants and use DFT calculations and microkinetic modelling to explore the theoretical efficiencies due to spin-crossing kinetics shown by Co and other earth abundant 3d metal catalysts, of varying nuclearity, for small alkane DH. We develop reaction mechanisms and rank them in kinetic importance using micro-kinetic analysis for single-site Co(II)/SiO_2 and di-nuclear $[CoO]_2/SiO_2$ active sites. The dominant reaction pathway on the mononuclear Co/SiO_2 system proceeds via a heterolytic C-H bond activation and the rate-determining step is the β-hydride elimination, which involves spin-crossing from the high-spin quartet to the low-spin doublet state. For the dinuclear active site model, we show that β-hydride elimination via spin-crossing on each Co(II) site is favorable compared to cooperative β-hydride elimination engaging neighboring Co(II) atoms. Our microkinetic analysis shows that the reaction rate on the di-nuclear site is 100 times the rate on the mononuclear site.

Next, we use insights from the single site mechanistic model to study the effect of surface heterogeneity of am-SiO_2 on the reaction mechanism. To this end, we construct an ensemble of single- site models with varying degrees of distortion quantified by the τ_4 geometric descriptor[3] and employ electronic descriptors such as the electrophilicity index to relate the active site coordination geometry with reaction barriers.

References

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3 Yang, L., Powell, D. R. & Houser, R. P., *Dalton Trans.*, 955-964, (2007).

Assessing Impact of Hinge Flexibility on Predicted Antibody Interactions

Terrance Shoemaker
Advisor: Christopher J. Roberts
Committee Members: Eric M. Furst, Abraham M. Lenhoff

The pharmaceutical market for monoclonal antibodies (mAb) has continued to increase in recent years because of their many favorable properties such as high binding affinity, specificity, versatility, ability to invoke intended immune response etc thus allowing for treatment of a variety of diseases, including autoimmune disorders and cancers. The high versatility comes from the variable nature of the complimentary determining region, which determines the antigen epitope. These variations between mAbs can result in large changes in solution behavior. One of the largest challenges in mAb development for pharmaceutical purposes is predicting macroscopic behavior that is detrimental to its efficacy, manufacturability, delivery, or long-term storage such as viscosity, aggregation and degradation. Coarse-grained molecular (CG) simulations provide an opportunity to probe mAb behavior early in development and screen mAb candidates for these behaviors without a large computational burden. This report expands on current CG models by including flexibility of the hinge region of the mAb. The effects of flexibility on two body interactions were analyzed for a group of industrially relevant mAb candidates with known potential issues at high concentrations at low ionic strength conditions and typical formulation pH. The primary quantities used to assess the two body interactions were the second osmotic virial coefficient values and the pairwise interactions between specific amino acids. Differences between the pairwise interactions of the flexible and rigid model highlight regions that are influenced by flexibility. The largest difference between pairwise interactions were used to characterize the difference between flexible and rigid models for different mAbs. The results indicate that in a small number of cases, the difference between flexible and rigid models was significant, while for many cases it was not experimentally significant.

Hybrid Model Development for Parameter Estimation and Process Optimization of Hydrophobic Interaction Chromatography

Chaoying Ding, Christopher Gerberich (GSK, Industrial Collaborator)
Advisor: Prof. Marianthi Ierapetritou
Committee Members: Prof. Abraham Lenhoff

Preparative liquid chromatography is one of the main processes for the downstream purification in the biopharmaceutical industry. Hydrophobic interaction chromatography (HIC) is widely used in polishing steps for the separation of targeted monomeric forms of protein therapeutics from the dimeric and/or multimeric species. Despite being commonly employed as an efficient purification strategy, the mechanism for HIC adsorption is quite complex, depending on various process parameters, like pH, salt concentration, and adsorbent ligand hydrophobicity. Inspired by the quality by design (QbD) initiative [1], mechanistic modeling has become an important tool for process characterization, but it is highly dependent on the understanding of the underlying phenomena. Nonetheless, the adsorption mechanism describing HIC is still not clear, and it is very challenging to postulate appropriate mathematical equations to describe the overall process [2]. Therefore, it is essential to develop a model with high accuracy and suitable hypotheses to describe the HIC process [3].

In this work, a hybrid modeling approach is proposed to describe the HIC chromatographic process. Specifically, an equilibrium dispersive model is selected to describe the mass transfer in the liquid phase and retained in the hybrid framework since the equation is widely accepted to model the fluid behavior inside the column. One the other hand, a neural network (NN) model will be incorporated into multi-component Langmuir isotherm to help describe HIC adsorption. The combination of the mechanistic model and NN with boundary conditions constructs the basic framework of the physics-informed hybrid approach. Parameter estimation is first performed based on the experimental data from our industrial collaborator to obtain the NN weights to construct the hybrid model, followed by the experimental validation of the developed model. Moreover, a regularization strategy and robustness analysis are examined to avoid overfitting and ensure the generalizability of the modeling framework. The effect of different NN structures on the fitting results is also evaluated to acquire the model with the best performance. Process optimization is conducted using the hybrid model to find the optimal operating conditions and guide the experiments.

References

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Modeling the effect of bioreactor pH on Chinese Hamster Ovary (CHO) cell metabolism and site-specific N-linked glycosylation of VRC01

Jayanth Venkatarama Reddy
Advisor: Professor Eleftherios Terry Papoutsakis and Professor Marianthi Ierapetritou
Committee Members: Professor Kelvin Lee and Professor Abraham Lenhoff

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Optimization of Chinese Hamster Ovary (CHO) cell based monoclonal antibody production processes require optimization of media development, cell line development, bioreactor operation, process monitoring, process control and careful monitoring of product's critical quality attributes (CQA) such as N-linked glycosylation. Media optimization typically involves specifying the concentrations of more than 50 components. Optimal fed-batch bioreactor operation requires optimizing the pH, temperature, dissolved oxygen and feeding schedule. Optimizing the process performance using experiments is an expensive proposition. It has been demonstrated in the literature that models can be used to optimize the process while minimizing experimental effort. However, it is difficult to use models to optimize the overall process as the majority of models in the literature are built with the goal of specifically optimizing one of the above key aspects. There is a need to develop models incorporating all those process parameters to capture the important interactions between them.

The work here aims to overcome these drawbacks of literature models by developing a detailed model that can be used to optimize bioreactor operation while keeping track of N-linked glycosylation and change in media requirements under different pH conditions. More specifically this work targets the integration of the effect of pH on a model of CHO cell metabolism and site-specific N-linked glycosylation. VRC01 producing CHO cells were grown at pH of 6.75, 7 and 7.25 in fed-batch mode in a 1 L Eppendorf bioflo 120 bioreactor system. Cell density, viability, glucose, lactate, 18 amino acids, ammonia, titer and N-linked glycan structures were measured at each condition to develop a database for model regression. The model for metabolism was developed by integrating a combined kinetic and stoichiometric model for metabolism. The integrated model was developed by using semi-empirical kinetic expressions to determine uptake rates of a few metabolites and these uptake rates were used as constraints to generate the solution of the detailed stoichiometric model by using metabolic flux analysis. Through the experimental data it is evident that changes in pH led to depletion or accumulation of different metabolites. This leads to suboptimal media performance. The VRC01 mAb contains N-linked glycans at Fab region and the Fc region of the mAb. The glycan fractions on both sites were measured and found to be very different. The stirred tank reactor-based model for N-linked glycosylation has been modified to model the glycans at multiples sites of the mAb. This model is used to understand why there are differences in glycan fractions across sites and different bioreactor pH values. The proposed model is then used to determine the effect of pH on nutrient requirements as well as product quality, providing a platform to optimize pH and media formulation while tracking CQAs.

Data on the effect of bioreactor pH and temperature on N-linked glycosylation of Herceptin produced in CHO cells was obtained from collaborators. The model for N-linked glycosylation was also used to study the effect of bioreactor pH and temperature on the reaction rates in the glycosylation pathway.

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CLAYTON HALL | JANUARY 25, 2023

ROOM 125

SCHEDULE OF TALKS

8:00 – 9:00 AM	**BREAKFAST** (Lobby)
9:00 – 9:05 AM	**WELCOME/Opening Remarks:** Colburn Club (Room 101B)
9:05 – 9:15 AM	**REMARKS:** Dr. Millicent Sullivan (Room 101B)

SESSION I — 9:20 AM – 1:00 PM — ROOM 125

9:20 – 9:40 AM

Matthew Becker
"Development of a Purification Process by Continuous Affinity Precipitation"
Advisor: Abraham Lenhoff / Committee Members: Christopher Roberts and Kelvin Lee

9:40 – 10:00 AM

Soumitra Bhoyar
"Novel protein A ligand mitigates yield loss during high pH washes in mAb manufacture"
Advisor: Abraham Lenhoff / Committee Members: Christopher Roberts and Eric Furst

10:00 – 10:20 AM

Brian Paul
"Influence of High Hydrostatic Pressure on Salt-Induced Protein Clustering"
Advisor: Norman Wagner, Eric Furst, and Abraham Lenhoff / Committee Members: Susana Teixeira and Christopher Roberts

10:20 – 10:40 AM

Roisin Donnelly
"Temperature probed dynamics of NISTmAb RM 8670 measured by hydrogen deuterium exchange - small angle neutron scattering"
Advisor: Norman Wagner and Yun Liu / Committee Members: Kristi Kiick and Christopher Price

10:40 – 11:40 AM — **POSTER SESSION**

11:40 AM – 1:00 PM — **LUNCH** (Room 101A) **and Featured Speaker, Aditya Kunjapur**

UNIVERSITY OF DELAWARE
ENGINEERING

CLAYTON HALL | JANUARY 25, 2023

ROOM 125

SCHEDULE OF TALKS

SESSION II	1:10 PM – 4:00 PM	ROOM 125

1:10 – 1:30 PM	**Antonio Goncalves** "Assembly of a Modular and Tunable Worm-like Protein Nanostructure using a Step-wise Bottom-Up Approach" Advisor: Wilfred Chen and Millicent Sullivan / Committee Members: April Kloxin and Catherine Fromen
1:30 PM – 1:50 PM	**Yu-Tai Wong** "Exploring the Structure-Property Relationships Associated with Network Architecture in Lignin-Derivable Diacrylate Networks" Advisor: LaShanda Korley / Committee Members: Antony Beris, Thomas Epps, III, and Norman Wagner
1:50 – 2:10 PM	**Ahmad Naqi** "Dual Material Fused Filament Fabrication via Core-Shell Die Design" Advisor: Michael Mackay / Committee Members: Antony Beris and Christopher Kloxin
2:10 – 2:30 PM	**Noah Willis** "Exploration of Clostridial Co-culture Transcriptional Profiles Towards the Engineering of Microbial Syntrophy" Advisor: Eleftherios Papoutsakis / Committee Members: Wilfred Chen and Aditya Kunjapur
2:30 – 2:50 PM	**BREAK**
4:00 PM	**END of Research Review**
4:00 – 5:00 PM	**FREEFORM INDUSTRY SESSION (101A)**

Development of a Purification Process by Continuous Affinity Precipitation

Presenter: Matthew L. Becker
Advisor: Abraham M. Lenhoff
Committee: Christopher J. Roberts, Kelvin H. Lee

With contemporary titers in monoclonal antibody (mAb) expression routinely reaching over 5 g/L, affinity chromatography as the initial capture step for mAbs has continued to grow more costly. One possibility that would have costs more insensitive to titer is continuous affinity precipitation and subsequent filtration, which (compared to bind-and-elute affinity chromatography) has the added advantage of being truly continuous. Using a recently-developed multivalent nanoparticle capable of nucleating therapeutics into a micron-sized precipitate, work can proceed on developing a process based on this technology. This work includes studying the kinetics of aggregation of therapeutics as well as purification by the primarily diffusive mass transfer of impurities and wash buffers across a membrane at a very small scale. A model system using the chelator zinc chloride as precipitant is an important and economical step along the path to full process development, and results using such a model system will be discussed.

Novel protein A ligand mitigates yield loss during high pH washes in mAb manufacture

Soumitra Bhoyar
Advisor: Dr. Abraham M. Lenhoff
Committee Members: Dr. Christopher Roberts, Dr. Eric Furst.

Protein A (PrA) affinity chromatography is widely used in the manufacture of monoclonal antibodies (mAbs) and Fc fusion proteins due to the high affinity and selectivity of the PrA-Fc interaction. Increasingly, high pH washes are being used during PrA chromatography to improve clearance of host-cell proteins (HCPs) and reduce the propensity of mAbs to aggregate. The investigation here was prompted by a significant loss in mAb yield during high pH washes, which resulted from a dependence of both static and dynamic capacities on pH, including a significant decrease in both at high pH. We previously showed that this dependence was intrinsically linked to the Fc fragment – protein A interaction and was independent of the Fab domains. In this work, we employed a rational, site-specific mutagenesis approach to engineer novel PrA ligands based on the Z domain, with the goal of mitigating ligand-mAb dissociation at high pH. We used biolayer interferometry and chromatographic methods to evaluate the mAb binding characteristics of the engineered ligands at pH 7 and pH 9.8-10. Two out of three engineered variants showed a lower fractional yield loss at high pH than the original Z domain ligand. The above results will be presented and the mechanistic insights into protein A - Fc binding gained through them will be discussed.

Influence of High Hydrostatic Pressure on Salt-Induced Protein Clustering

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High pressure (HP) is used to increase product shelf-life or confer desired properties, particularly in food and pharmaceutical applications in which thermal processing can shift phase behavior in undesirable ways[1]. HP is also present during freezing and utilized to assist in foaming processes, yet relatively little is known about its effects on the macromolecular level. Protein clustering in the presence of salt has been well-documented as a precursor to liquid-liquid phase separation (LLPS) and macroscopic crystallization, as well as an early sign of dense phase growth[2]. Globular proteins have been previously shown to salt-out in the presence of a precipitant, exhibiting gelation and nanocrystallization on the time scale of days[3]. The present work examines early-stage salt-induced clustering of ovalbumin in an ammonium sulfate solution and the ability of pressure up to 400 MPa to drive protein dense phase behavior. High-pressure small-angle x-ray scattering (HP-SAXS) on solutions in and near the gel region reveals a contrast between pressure-driven dissociation of clusters within the gel region and pressure-enhanced clustering near the phase boundaries. In-line size exclusion chromatography (SEC-SAXS) at ambient pressure allows for a computational deconvolution of fractional oligomer populations within and outside of the gel region and illustrates how pressurization near the phase boundaries may push a solution into a new phase region. The current study provides insights into the competing mechanisms of salting out and high hydrostatic pressure as a potential route for dictating macroscopic phase behavior.

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Temperature probed dynamics of NISTmAb RM 8670 measured by hydrogen deuterium exchange - small angle neutron scattering.

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Hydrogen deuterium exchange, (HDX) is of increasing interest for characterization of protein dynamics in solution. The natural tendency for proton exchange of surface labile hydrogen atoms for deuterium can indicate which portions of the protein have been exposed to the solvent. Though this differs from the more traditional methods for approximating protein dynamics, like nuclear magnetic resonance and cryo-transmission electron microscopy, quantifying HDX has been possible in the past with mass spectrometry, (MS). HDX-MS allows for identification of site-specific deuterium incorporation. From this, it can be inferred that these sites have been exposed to the solvent, via the protein's cyclical occupation of alternate conformational states. A different approach of measuring HDX is possible with small angle neutron scatter-ing, (SANS), which is extremely sensitive to hydrogen-deuterium exchange, due to the large neutron scattering cross section of hydrogen. Unlike HDX-MS, SANS allows for the continual measurement of HDX over time. In this study, we used National Institute of Standards and Technology monoclonal antibody (NISTmAb) reference material 8670, as a precompetitive model therapeutic antibody, (IgG1), to examine how SANS can be used to measure HDX. We used SANS to monitor the HDX of NISTmAb RM 8670 over the course of many hours to identify a correlation of HDX with different excipients, such as salts from the Hofmeister series, on the rate and amount of HDX. The salts selected for this study were sodium sulphate, perchlorate, and thiocyanate, (Na2SO4, NaClO4, NaSCN). The results presented herein show that faster and greater amounts of HDX were found in NISTmAb samples containing salts NaClO4 and NaSCN, which are destabilizing according to the Hofmeister series, related with protein solubility. Conversely, NISTmAb samples containing Na_2SO4, which is considered stabilizing in the Hofmeister salts, had a slower and reduced amount of exchange. This work demonstrates that HDX-SANS is a novel and noninvasive approach to measuring the in-situ dynamics of therapeutically relevant protein, NISTmAb RM 8670, which can both qualitatively and quantitatively assess HDX. The number of deuterons incorporated into the protein as a function of time will be discussed for each NISTmAb sample containing the Hofmeister salts. This global and quantitative insight into HDX could be translated to inform the long-term conformational stability of the formulation, which could be of critical importance to the biopharmaceutical industry, to accelerate therapeutic engineering.

Assembly of a Modular and Tunable Worm-like Protein Nanostructure using a Step-wise Bottom-Up Approach

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Advisor: Dr. Wilfred Chen & Dr. Millicent Sullivan
Committee Members: Dr. April Kloxin & Dr. Catherine Fromen

Protein nanostructures have garnered interest as carriers in drug and intracellular protein delivery for their enhanced biocompatibility and stability compared to most synthetic particle systems. Studies into the design of an effective drug carrier suggest that modulating the shape of the particle is a key parameter in nanoparticle design. Where there is a balance in tuning high-aspect ratio nanoparticle's maximal lengths between lengths small enough for effective extravasation and internalization by endocytosis, and long enough for an effective circulation half-life through avoiding renal clearance and minimizing macrophage uptake. However, most high-aspect ratio protein nanostructures, like nucleoprotein-based nanorods, either form through self-assembly onto native RNA templates which limits the capacity for tuning length scales, or through a further *in vitro* disassembly and re-assembly step onto an engineered RNA template. The latter bottom-up assembly strategy instills the capacity to modify particle lengths but has been regularly shown to result in a heterogenous mixture. Furthermore, these nanostructures commonly lack the capacity for extensive and patterned surface decoration, usually limited to incorporating bioconjugation chemistries at solvent-exposed termini, or randomly reacting solvent-exposed lysine or cysteine side chains. Therefore, we have designed a step-wise bottom-up approach for generating a worm-like protein nanostructure with homogenous and tunable control of structure length and, control of the position and valency of multiple protein cargos and a Click-compatible non-standard amino acid (nsAA), using orthogonal Catcher-Tag isopeptide-ligating protein-peptide pairs in tandem with elastin-like polypeptides and the controlled incorporation of 4-azido-L-phenylalanine. With this platform we demonstrate that we can modularly control the valency of multiple protein cargos as well as their position relative to each other within the structure. And that this assembly strategy allows for the incorporation of multiple different alkyne-functionalized ligands with control of their local density and relative positions to each other by virtue of the potential multi-pot nature of this assembly approach. We anticipate that by using this assembly strategy, high-aspect ratio worm-like protein nanostructures can be assembled for any desired application due to the inherent "plug-and-play" nature of the assembly strategy with respect to protein cargos, Click-compatible nsAA positioning and particle length.

Exploring the Structure-Property Relationships Associated with Network Architecture in Lignin-Derivable Diacrylate Networks

Yu-Tai Wong
Advisor: Prof. LaShanda Korley
Committee Members: Prof. Antony Beris, Prof. Thomas H. Epps, III, Prof. Norman Wagner

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Commercial (petroleum-based) acrylates offer widely tunable thermomechanical properties for diverse range of applications, including coatings and composites. However, there is relatively lesser understanding on structure-property relationships using bio-derivable building blocks for sustainable acrylate networks. To this end, lignin is the most abundant natural aromatic polymer, and thus materials derived from lignin are promising in the development of sustainable, performance-advanced polymers. Notably, one relatively unexplored area in lignin-derivable polymeric materials is the tailored design of crosslinked systems that incorporate not only the chemical tunability of phenolic building blocks but also architectural flexibility driven by acrylate network design. Herein, we envision a comprehensive investigation to probe structure-architecture-property relationships in lignin-derivable networks that encompasses both chemical and structural diversity. To achieve this goal, we develop a material platform varying the composition (25, 50, and 75 mol%) and type of lignin-derivable diacrylates with different aromatic content, vanillyl diacrylate (VDA) [monoaromatic] and bisguaiacol diacrylate (BGFDA) [bisaromatic], with a bio-derivable aliphatic acrylate, *n*-butyl acrylate (BA), as the reactive diluent, to investigate the role of chemical structure on thermomechanical properties and network architecture. The extent of inhomogeneity induced by the presence of unreacted groups and fluctuations in network density can impact the network architecture and is generally considered to lower material performances. We showed that networks with more diacrylate and a higher aromatic content exhibited increased inhomogeneity with lower conversions (*i.e.*, more unreacted groups) and a broadening of the tan δ peak. For example, the conversion of VDA/BA-25/75 is 92.4%, whereas for VDA/BA-75/25 is 61.6% and for BGFDA/BA-25/75 is 86.6%. Furthermore, the broadening of the tan δ peak can be deconvoluted into multiple Gaussian peaks that indicate the formation of multiple network phases, leading to complex thermal transitions. However, the incorporation of a higher diacrylate content led to networks with a significantly improved storage modulus at 25 ºC (E_{25}') due to increased crosslink density even if higher extent of inhomogeneity is presented (*e.g.,* E_{25}' ~ 3.1 GPa for VDA/BA-75/25 and ~ 1.1 GPa for VDA/BA-25/75), suggesting that thermomechanical properties are driven by diacrylate content. This fundamental understanding of the connection between molecular structure, microstructure, and mechanics will facilitate the development of design strategies for high-performance (meth)acrylate networks from lignin-derivable feedstocks.

Dual Material Fused Filament Fabrication via Core-Shell Die Design

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In this work a novel fused filament fabrication (FFF) die design, capable of extruding two thermoplastics simultaneously in a core-shell configuration, is demonstrated as a means to produce composite structures in a single step. Despite the enormous advancements in 3D printing, fabrication of FFF objects with a composite structure remains a challenge due to the difficulty in finding dies to extrude such structures. We used polyethylene terephthalate glycol (PETG) and high density polyethylene (HDPE) filaments to perform core-shell 3D printing. HDPE is one of the most commonly produced plastics but rarely used in FFF due to the severe warpage caused by volume changes upon its crystallization. Rheological and thermal analysis suggest the use of HDPE as a shell material due to its extremely short reptation time and sharp melting peak that facilitate superior surface contact and interlayer weld strength at the interface between neighboring FFF tracks. PETG is a commonly used 3D printing filament with excellent printability and sufficient zero shear viscosity to help maintain the extruded filament shape against shrinkage induced by the HDPE shell.

Impact and tensile properties of core-shell objects revealed tremendous improvements in the impact resistance and toughness especially at 30 vol % HDPE shell with 1280% and 150% enhancement in impact resistance when compared to individual components: PETG and HDPE, respectively. Scanning electron microscopy was used to analyze the fracture morphology of the tested specimens to obtain an understanding of the fracture mechanism leading to the increased impact resistance. Using this die design can help open avenues of fabricating high impact resistance materials suitable for high performance applications and using HDPE in 3D printed objects with its superior solvent resistance.

Exploration of Clostridial Co-culture Transcriptional Profiles Towards the Engineering of Microbial Syntrophy

Noah B. Willis
Advisor: Eleftherios T. Papoutsakis
Committee Members: Wilfred Chen, Aditya Kunjapur

Past breakthroughs in microbial biotechnology have relied predominantly on monocultures of wild-type or genetically engineered bacterial strains. However, most microbes evolved to function within a complex community of fellow travelers. Based on this history, we would expect bacterial species to possess cooperative mechanisms that enable them to function synergistically with other species within their community. Elucidating these mechanisms will further fundamental understanding of bacterial biology and inform the design of stable industrial processes based on synthetic, defined microbial cocultures.

Recently, our group has shown that, when cocultured, *Clostridium acetobutylicum* (*Cac*) and *Clostridium ljungdahlii* (*Clj*) improve substrate carbon and electron conversion and expand the metabolic space, producing valuable products, such as isopropanol and 2,3-butanediol, that neither species can make independently. Further exploration of this syntrophic system showed that the unique metabolic phenotype of the *Cac*-*Clj* coculture is due in large part to direct, large-scale transfer of cytoplasmic material between the two species. The mechanism by which these exchanges occur is unknown.

As a first step towards dissecting the *Cac*-*Clj* coculture phenotype, RNA sequencing (RNAseq) experiments were performed to identify genes in both organisms differentially expressed in response to the introduction of their partner. These experiments were conducted at four different timepoints across the fermentation, and in two different coculture setups. In the first coculture system, gene expression in a mixed coculture was compared to monoculture controls grown in separate bottles. In the second system, a mixed coculture system was compared to a transwell system which the two species were separated by a permeable membrane, preventing interspecies cell-to-cell contact. These experiments showed that the transcriptomes of both organisms undergo radical change when they are cocultured with one another. Genes involved in autotrophic energy metabolism, electron management, amino acid biosynthesis, cell motility, and cell wall biosynthesis were among those most affected. Many previously uncharacterized genes were also upregulated in response to direct interspecies contact, providing fertile ground for further bioinformatic and reverse genetic exploration. In addition, these results have helped inform parallel efforts to rationally engineer bacterial cocultures that combine *Clj* and either *Cac* or *Escherichia coli* for the carbon-negative production of isopropanol.

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Shelby Anderson	"Enhanced nitro-functional group stabilization in an engineered E.coli strain" **Advisor: Aditya Kunjapur**
Erha Andini	"Biomass Conversion into Neo Acids" **Advisor: Dionisios Vlachos**
Eric Chen	"Data-Driven DFT Adsorption Energy Correction" **Advisor: Dionisios Vlachos**
Luke Cherniack	"Production of Pure Products from CO2 Electrolysis" **Advisor: Feng Jiao**
Jason Conradt	"Dissipative self-assembly of paramagnetic colloids in microgravity" **Advisor: Eric Furst**
Bradie Crandall	"Scale-up of Tandem CO2 Electroreduction to Multi-carbons" **Advisor: Feng Jiao**
Kenneth Crane-Moscowitz	"Stability and Self-Assembly of Cylindrical Coiled-Coil Domains into Discrete Nanoparticles and Soluble Aggregates" **Advisors: Eric Furst, Christopher Kloxin, & Darrin Pochan**
Roman Dickey	"Whole Cell Biocatalysis for the Valorization of PET Deconstruction Products" **Advisor: Aditya Kunjapur**
Amanda Forti	"Achieving synthetic cellular communication using orthogonal amino acid biosynthesis" **Advisor: Aditya Kunjapur**
Michelle Gee	"Closed-loop modeling of central and intrinsic cardiac nervous system circuits underlying cardiovascular control" **Advisors: Abraham M. Lenhoff, Rajanikanth Vadigepalli, & Babatunde A. Ogunnaike**
Philip Gitman	"Engineering Yarrowia lipolytica for methanol assimilation" **Advisor: Mark Blenner**
Tejas Goculdas	"Highly Selective Cross Ketonization of Renewable Acids" **Advisor: Dionisios Vlachos**
Madan Gopal	"Reductive Enzyme Cascades for Valorization of PET Deconstruction Products" **Advisors: Wilfred Chen & Aditya Kunjapur**

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John Hill	"Refining the Immediate and Generational Impacts of Microbial Fusion in Synthetic Clostridial Syntrophies **Advisor: Eleftherios Papoutsakis**
Nefeli Kamarinopoulou	"Direct HCN synthesis via plasma-assisted conversion of methane and Nitrogen" **Advisor: Dionisios Vlachos**
Thomas Leibiger	"Analysis of Adeno-associated Virus Vector Quality Attributes for Gene Therapies" **Advisor: Kelvin Lee**
Christopher Mayhugh	"Engineering a Bacillus subtilis Spore Display Platform for Nitrated Antigen Delivery" **Advisor: Aditya Kunjapur**
Darien Nguyen	**"**Plasma functionalization of plastic waste and plastic waste derivatives for upcycling" **Advisor: Dionisios Vlachos**
Tessa Posey	"Coiled-Coil Peptides as Molecular Building Blocks" **Advisor: Christopher Kloxin**
Katherine Raudenbush	**"**Predicting the effect of dissolved oxygen gradients on cell culture performance in large scale bioreactors" **Advisors: Marianthi Ierapetritou & Eleftherios Papoutsakis**
Alfred Worrad	"Dynamics of Hydration in Molybdenum Oxide-Alumina Catalysts" **Advisor: Dionisios Vlachos**

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