JMU REU Research Project Descriptions

We offer a diversity of research opportunities, which are conducted solely by undergraduate students, in collaboration with faculty. While faculty expertise spans all sub-disciplines of chemistry, strength and synergy lie in the areas of synthesis, materials, and biophysical chemistry. These strengths are highlighted in the research summaries below. Due to the space, not all faculty involved in our REU are listed. The details of all research projects may be found on the Departmental website (http://www.jmu.edu/chemistry/people/).

*** = faculty member who has previously mentored D/HH student(s)*

Ashleigh Baber (Materials) Role of Surface Modifications on Molecular Binding and Transformation.

Take home: We are interested in tuning oxide/metal and bimetallic surfaces to control chemical selectivity, and relating reactivity changes to the nanoscale structure of model heterogeneous catalysts.

Surface science studies take a simplified look at complex heterogeneous catalysts to better identify active sites and reaction pathways. Our group investigates how molecules interact with each other on metallic surfaces, as well as how low concentration defect sites, which are important in high surface area catalysts, influence molecular binding under ultrahigh vacuum conditions. We aim to understand the fundamental interaction between molecules and surfaces to design better heterogeneous catalysts. **Intellectual merit:** The atomic-scale structure-activity relationships of model catalysts can be applied to the design of highly selective catalysts on the industrial scale.

Christopher E. Berndsen (Biochemistry) Structure and mechanism of starch degrading protein complexes**

Take home: We study how enzymes and pseudoenzymes work together to degrade starch in a controlled fashion.

While many proteins function in starch degradation, their specific roles and interactions between these enzymes to produce controlled and responsive starch degradation are often unclear. Moreover, there are several pseudoenzymes that when deleted produce starch-excess phenotypes for no apparent reason. The Berndsen lab uses an “atoms to actions” approach using a combination of computational, structural, biochemical, and organismal experiments to describe the structure and mechanism of these complexes. Current work is focused on characterizing BAM9 which we propose is the first known pseudoamylase and serves to regulate alpha amylase activity in response to stress. **Intellectual merit:** These studies describe how plants shape and reshape the essential molecule starch in response to night and environmental signals.

Kevin L. Caran (Synthesis/Materials) Bioactivity and Foam-Forming Ability**

Take-home: We aim to develop a thorough understanding of the relationship between amphiphile/polymer architecture and colloidal, antibacterial and water purification activity.

Students use the tools of organic synthesis to make and purify novel compounds in an effort to develop self-assembled soft materials (colloids) with well-defined properties. Subsequently a wide variety of tools and analytical methods are used to measure the properties and to understand the modes of self-assembly of the colloidal aggregates formed by these novel compounds. Students work to design and synthesize amphiphiles with non-traditional architecture, including those with two to six cationic headgroups and one or more non-polar tails. After synthesis and colloidal analysis, antibacterial activity is measured against a range of Gram-positive and Gram-negative bacteria in collaboration with Dr. Kyle Seifert and his students. In addition, we have recently prepared and studied novel organic polymers with structures designed to impede the formation of pathogenic bacterial biofilms. We have also demonstrated these polymers’ ability to selectively remove anionic organic impurities from water, in collaboration with Dr. Barbara Reisner. **Intellectual merit:** We design, synthesize, and study novel amphiphiles and polymers in an effort to develop potent antiseptics and materials that are inhospitable to pathogenic bacteria.

Lindsay Caesar (Analytical/Natural Products) Understanding bioactive natural products in their ecological contexts

Take-home: We aim to understand the ecological role of natural products to gain insight into their biological activities with the goal of discovering new molecules to combat disease.

Thousands of years of evolutionary selection have turned bacteria, fungi, and plants into expert synthetic chemists capable of biosynthesizing intricate natural products with powerful bioactivities fine-tuned to suit their ecological needs. These natural products have become an invaluable source of inspiration for drug discovery, and nearly two-thirds of today's pharmaceutical drugs are directly from or inspired by Nature. We utilize mass spectrometry to understand the biosynthetic regulation of natural products produced by bacteria and fungi with the goal of discovering antimicrobial agents active against both bacterial and fungal infection. Current laboratory initiatives include exploring the cave and bat microbiome for antifungal molecules that can help combat the devastating "White-Nose Syndrome" that has killed millions of bats in the last decade, as well as developing ecologically-inspired culture conditions for hyper-diverse fungi to activate silent biosynthetic pathways that may encode new molecules. **Intellectual merit:** By studying natural products-producing organisms in the ecological-contexts in which they evolved, we gain insight into their biological activities, helping to prioritize discovery of novel bioactive molecules with use in human society.

Christine A. Hughey (Analytical/Food Chemistry) Use of metabolomic tools to study the effects of processing on food stability & flavor development**

Take-home: We study how processing and/or brewing conditions effect the flavor and stability of food and alcoholic beverages.

The Hughey lab uses targeted and untargeted mass spectrometric-based techniques to monitor how compounds in food and alcoholic beverages change as a result of processing. Most our work centers around beer brewing. Beers studied are produced in the Madison Academic Brewery housed within the Department of Engineering at JMU. Volatile flavor compounds are monitored with solid phase microextreaction (SPME) GC/MS; while non-volatile compounds are monitored with LC/MS. Targeted metabolomics uses known *Saccharomyces Cerevisiae* biochemical pathways to monitor the nonvolatile metabolites that produce volatile flavor compounds. Untargeted metabolomics, including the use of molecular networking, wholistically looks at differentially expressed compounds at each stage of brewing and fermentation. The integration off GC/MS and LC/MS with targeted and untargeted metabolomic techniques provides an unprecedented, molecular-level look into the "processomics" of small molecules throughout brewing and fermentation so that brewers can better control processing and/or brewing conditions to yield the desired final product. **Intellectual merit:** The integration of GC/MS and LC/MS affords a molecular level view of flavor development from nonvolatile precursors. This allows producers to control processing and/or brewing conditions to yield the desired final product.

Gina MacDonald (Biochemistry) Spectroscopic studies of molecular-induced changes in protein structure and aggregation**

Take home: We identify environmental modulators of protein aggregation

Identifying environmental factors associated with neurodegenerative diseases has remained elusive as it has been difficult to unambiguously identify specific causes of uncontrolled protein and/or peptide aggregation. An abundance of studies have implicated environmental conditions such as metal ions and pollutants in the pathogenesis of neurological diseases. Numerous other studies that suggest other amino acids, vitamins and other molecules found in food may decrease the aggregation of proteins. Most of these studies monitor stability and aggregation after destabilization of the proteins, most commonly by heating proteins and/or altering solution pH. Previous studies in our laboratory have focused on how salts alter the solvation and aggregation of caffeine, peptides and proteins. Current work in our lab is aimed at identifying molecules that influence alter protein structure, stability and aggregation in the absence of destabilizing conditions. Circular Dichroism and infrared spectroscopies are used to study multiple model proteins in efforts to identify molecules that may be of interest for additional studies. **Intellectual Merit**: The effect of solvent components on proteins cannot yet be predicted, and often works counter-intuitively. Searching for and delineating these rules can help optimize and control protein activity. This has applications in biotechnology and medicine.

Debra Mohler (Synthesis) Oligonucleotide analogs as tools to control gene expression

Take-home: We focus on the synthesis and evaluation of novel oligonucleotide analogs without sugar phosphate backbones.

Antisense oligonucleotides have shown promise for their ability to modulate gene expression in a very selective manner, due to the innate sequence specificity of base-pairing. However, the sugar-phosphate backbones of DNA and RNA pose challenges such as low membrane permeability and modest stability in

vivo (particularly for RNA). We are developing oligonucleotide analogs based on a variety of organic polymer backbones that can be prepared in a one-step procedure via a templated polymerization of monomers containing DNA and RNA bases. We recently completed the synthesis of one set of monomers and are currently focused on the templated polymerization. Afterwards, the synthetic oligomers will be characterized spectroscopically, biochemically, and biologically; and new ones will be prepared as tools to validate gene expression or to target sequences for a number of processes involving undesirable gene expression. **Intellectual merit:** These studies are expected to lead to synthetic antisense oligomers that can be prepared easily and have better biological profiles than natural oligomers, accelerating fundamental research on gene function.

Debo Ogunjirin (Medicinal Chemistry, Gallaudet University) Developing Molecules to block PLK1**

Take home: We study how to design new compounds that will interact selectively with a specific protein involved in many cancers

Dr. Ogunjirin's research endeavors focus on the development and refinement of research protocols, particularly in the synthesis and evaluation of new analogs for nicotinic acetylcholine receptors (nAChRs) and PLK1, a kinase involved in cell division checkpoints. Through the use of organic synthesis, followed by screening using a fluorescent polarization assay, our lab designs new molecules that competitively inhibit protein-target interactions. In addition to his research in pharmaceutical sciences, Dr. Ogunjirin is deeply committed to mentoring underrepresented groups in STEM, especially Deaf students. **Intellectual merit:** Through the development of potential new anti-cancer drugs, we explore the molecular mechanism of disease.

Gretchen Peters Crosslinker cooperativity in polyvinyl alcohol gels**

Take-home: We study changes in the morphological and material properties of PVA organogels with combinations of different boron-based crosslinkers.

Gels are useful for a wide range of applications, including environmental remediation, tissue engineering, and drug delivery. The diol-rich polymer polyvinyl alcohol (PVA) can be effectively crosslinked with boric acid (BA) or a diboronic acid to form soft materials and gels. While the complexation of PVA by BA has been extensively studied, the possibility of cooperativity between BA and diboronic acids remains largely unexplored. Our studies suggest that the introduction of a linear diboronic acid crosslinker to a PVA-BA organogel improves the physical properties (thermal stability and stiffness) of the material, while a non-linear diboronic crosslinker has little to no effect. Currently, we are investigating how structural variations in the diboronic acid crosslinkers (linker length and flexibility) impact the morphology and material properties of the PVA-BA gel. We rationalize that a well-developed understanding of these processes will allow us to develop stimuli-responsive materials with easily tunable physical and morphological properties. **Intellectual merit:** This work investigates cooperative crosslinking which is a novel mechanism that can be used to manipulate and tune the material properties of gels to suit specific applications.

Barbara A. Reisner (Inorganic Chemistry) Developing Shared Pedagogical Content Knowledge (PCK) in Inorganic Chemistry

Take home: We work collaboratively with instructors to study students' conceptions and identify their shortcomings in understanding to develop PCK and targeted interventions for teaching.

Pedagogical Content Knowledge (PCK) has been shown to help instructors promote deeper learning by their students, but there has been little work to develop shared PCK in inorganic chemistry. Through testing then deploying open-ended questions and student interviews, we identify what students know about a topic, the common diffiulties they encounter in integrating new ideas into existing knowledge, and alternate conceptions in student thinking. We will examine the explanations students construct about periodic trends, how students connect these explanations to disciplinary core ideas, and how their explanations vary across different inorganic chemistry courses and institutional contexts. From these studies, we develop (1) activities that will help students develop scientifically accurate explanations that use causal mechanistic reasoning to explain phenomena and (2) shared PCK that can be enacted by instructors. **Intellectual merit:** We uncover and analyze student conceptions to build shared PCK and develop curricular materials that can be used to improve teaching and learning.

Isaiah Sumner (Computational Chemistry) Using computation to understand the molecular basis of plasticization.**

Take Home: We use computers to understand how molecules interact and how those interactions relate to a plastic's properties

Chitosan, a polymer derived from crustacean exoskeletons, can be mixed with plasticizers, small molecules used to tune chitosan's physical properties, to synthesize environmentally friendly plastics. However, the molecular-level interactions between chitosan and the plasticizers that drive plastic formation are not well understood. We hypothesize that the number and types of interactions available between the polymer and the plasticizer change the amount of polymer-polymer interactions, which change the flexibility of the plastic – the so-called "gel model" of plasticization. We use density functional theory to model small clusters of glucosamine to examine the types of intermolecular forces present and molecular dynamics to understand larger-scale trends. These models help us understand which types of intermolecular forces are present and they help us to interpret data provided by our experimental collaborators. **Intellectual merit:** These simulations provide a molecular-level understanding of plastic formation and may lead to rational design principles.

Nathan Wright (Biochemistry) Measuring how proteins react to physical strain**

Take-home: We study how cytoskeletal proteins respond to physical force, and how this influences protein structure/function and cell motility.

Besides providing structure, the cytoskeleton senses the physical environment around the cell and converts this into a biochemical signal. Thus, the cytoskeleton enables cells to make fundamental decisions such as whether or not to divide and whether or not to migrate. Our lab has discovered that the giant cytoskeletal protein obscurin is central to controlling cell migration through at least four independent pathways. These include a kinase-dependent pathway, a RhoA-pathway, a PH-p85 pathway, and a newly-discovered pathway involving direct interactions with cell-cell junctions. At least some of these pathways are hypothesized to be controlled through modulating the tensile strain of obscurin, which is normally under significant tension in adherent cells. Using FRET-microscopy, molecular biology techniques such as western blots, and mathematical modeling of cell migration, our lab is characterizing this new obscurin migration pathway and testing whether obscurin tension controls any of these pathways. **Intellectual merit:** These studies explore mechanisms through which cells decide whether to move, and this has fundamental implications in our understanding of eukaryotic cellular homeostasis.