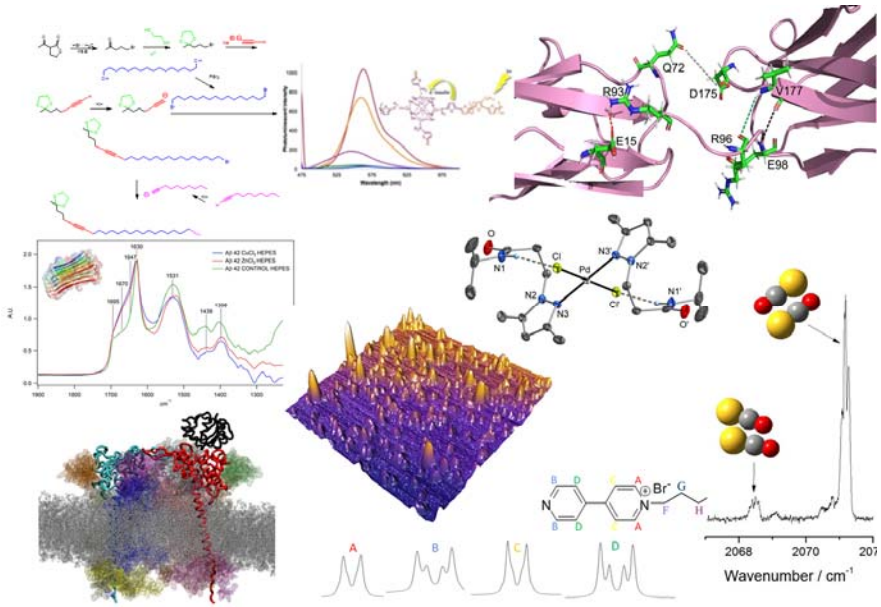
JAMES MADISON UNIVERSITY®

DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY



43RD ANNUAL SPRING UNDERGRADUATE RESEARCH SYMPOSIUM

THURSDAY APRIL 12, 2018

ORAL SESSION I: 2:00 – 3:45 PM (ISAT 259)
POSTER SESSION: 4:00 – 5:00 PM (PCB LOBBY)

FRIDAY APRIL 13, 2018

ORAL SESSION II: 1:45 – 3:30 PM (ISAT 259)
SPECIAL ANNOUNCEMENTS: 3:40PM (ISAT 159)
KEYNOTE ADDRESS: 3:45 – 4:45 PM (ISAT 159)

See back cover for image description.

43rd Annual Department of Chemistry and Biochemistry
Spring Undergraduate Research Symposium

Keynote Speaker

Dr. William Gemmill, PhD
(JMU Class of 2002)
Eminess Technologies, Inc.
Monroe, NC

William R. Gemmill has served as the R&D Manager for Eminess Technologies since 2013 were he is responsible for the development of new technologies and commercialization of new products. His career spans over twelve years of industry experience formulating cleaning and etching chemistries for the semiconductor industry and more recently polishing slurry formulations for both the semiconductor and precision optics industries. William received his B.S. in Chemistry from James Madison University in 2002 where he performed undergraduate research in Solid State Chemistry and Analytical Chemistry under the direction of Prof. Barbara Reisner and Prof. Daniel Downey, respectively. Following his time at JMU, William attended the University of South Carolina and received his Ph.D. in 2006 under the supervision of Prof. Hans-Conrad zur Loye in Inorganic Chemistry. William's graduate studies focused on the crystal growth and structural characterization of complex metal oxides of the platinum group metals. After graduate school, William began his industrial career at J.T. Baker Chemical in Phillipsburg, NJ as a research chemist developing wet cleans and photoresist strippers for the advanced semiconductor industry. In 2013 he joined his current employer, Eminess Technologies, where he has led R&D efforts and new technology acquisition supporting all aspects of their business. William has co-authored over 30 peer-reviewed publications and holds three patents.

Past Keynote Speakers

Each year we feature a keynote speaker for the Department's annual Spring Undergraduate Research Symposium. We are honored to have had speakers who are alumni of the department and are willing to come back and share with our students their experiences of "life after JMU". We thank each of these speakers and look forward to future alumni participation in Spring Symposium.

YEAR	JMU CLASS	SPEAKER	AFFILIATION
2018	2002	**Dr. William Gemmill**	*Eminess Technologies, Inc.*
2017	2004	**Dr. Zeric Hulvey**	*United States Department of Energy*
2016	2007	**Dr. Reid Gadziala**	*Cleveland Clinic*
2015	1994	**Dr. Michael Leopold**	*University of Richmond*
2014	1996	**Dr. Dana McGraw Dattelbaum**	*Los Alamos National Laboratory*
2013	1999	**Dr. Christy Vestal Martin**	*Vorbeck Materials*
2012	1994 N/A	**Dr. Melissa C. Rhoten** **Dr. Orde Q. Monro**	*Longwood University* *University of KwaZulu-Natal*
2011	1992	**Dr. Morgan S. Sibbald**	*The Sherwin-Williams Company*
2010	1988	**Dr. Kevin Morris**	*Carthage College*
2009	1988	**Dr. Chris E. Holmes**	*The University of Vermont College of Medicine*
2008	1995	**Dr. Jonathan Dattlebaum**	*University of Richmond*
2007	1987	**Dr. Elizabeth Perry (M.D.)**	*Signature Healthcare, Inc.*
2006	1967	**Dr. Carolyn Abitbol (M.D.)**	*University of Miami (FL) School of Medicine*
2005	1975 1976	**Dr. Daniel Downey** **Dr. Gary Rice**	*James Madison University* *College of William and Mary*
2004	1987	**Dr. James (Dusty) Baber**	*National Institutes of Health*
2003	1984	**Dr. Fred King**	*West Virginia University*
2002	1977	**Dr. Roger Bertholf**	*University of Florida School of Medicine*
2001	1979	**Mrs. Katheryn Lam**	*International Business Machines*
1999	1987	**Dr. Jose Madalengoitia**	*University of Vermont*
1997	1986	**Dr. Fred R. Kinder**	*Novartis Research Institute*
1996	1976	**Dr. Terry O. Trask**	*DuPont Chemicals*
1995	1973	**Dr. Carl Lentz**	*Eastman Fine Chemicals*
1994	1990	**Dr. Michele A. Kelly**	*University of Maryland Baltimore County*
1993	1985	**Dr. Cynthia K. Fallon**	*DuPont Chemicals*
1992	1983	**Dr. Laurie Locascio**	*National Institute of Standards and Technology*
1991	1983	**Dr. Noreen Naiman**	*North Carolina School of Science and Mathematics*
1990	1982	**Dr. Matthew T. Stershic**	*Atomchem North Amercia*
1989	1982	**Dr. Michael Kinter**	*Cleveland Clinic Lerner Research Institure*
1988	N/A	**Dr. Thomas J. Meyer**	*Los Alamos National Laboratory*
1987	1980	**Dr. Steven Davis**	*Naval Research Laboratory*
1986	1980	**Dr. Steven A. Hackney**	*Michigan Technological University*
1983	1978	**Dr. Richard B. Lam**	
1982	1975	**Dr. Daniel Downey**	*West Virginia University*
1981	1959	**Mr. Ronald E. Ney**	*Environmental Protection Agency*
1980	N/A	**Dr. Stanley G. Sunderwirth**	*Metropolitan State College (Denver, CO)*
1979	1973	**Dr. Carl Lentz**	*Eastman Fine Chemicals*

Oral Session I: Thursday April 12, 2018 *(ISAT 259)*		
2:00 pm	Austin Kilgore, Amber Harris, Kyle Wallenstrom, Annie Lin and Dr. Debbie Mohler	Synthesis of Antisense Nucleic Acid Monomers
2:15 pm	Allyn G. Letourneau and Dr. Nathan T. Wright	Structural Characterization of Titin Zlg9 and Zlg10
2:30 pm	Katherine Elliott and Dr. Isaiah Sumner	A Computational Study of the Role of Asparagine 79 in Ubc13
2:45 pm	Maxwell Gillum, Jeremy A. Wilke, Maria C. DePonte, Ashleigh E. Baber and Dr. Ashleigh Baber	Olefin Chemistry on Au(111)-Based Catalysts
3:00 pm	Daniel R. Marzolf, Matthew O'Malley, Coleman Swaim and Dr. Oleksandr Kokhan	Mimicking Natural Photosynthesis: Ultrafast Charge Transfer in PpcA-Ru(bpy)3 Complexes
3:15 pm	Kearney M. Foss, Jordyn Palla, Karen Fortmann and Dr. Christine A. Hughey	Targeted and Untargeted Metabolomics Profiling of Beer as a Function of Yeast Strain and Fermentation Time
3:30 pm	Killian G. Hull and Dr. Paul L. Raston	Far-Infrared Synchrotron Spectroscopy of Formic Acid

(Student presenters underlined)

Poster Session: Thursday April 12, 2018, 4:00 – 5:00 pm *(PCB lobby)*	
Nithesh P. Chandrasekharan, Dr. Jonathan Monroe and Dr. Christopher E. Berndsen	Structural comparison of the Arabidopsis thaliana family of β-amylases
Emily Smith, Dylan Hoang, Daniel Cromwell, Linette M. Watkins	Altering the Specificity Properties of 2-(2'-hydroxyphenyl)benzenesulfinate desulfinase from N. asteroides A3H1
Marissa St.George and Dr.Linette M. Watkins	Comparing E. coli expression and enzyme kinetics of wildtype and codon optimized 2-(2'-hydroxyphenyl)benzenesulfinate desulfinase (DszB) fromNocardia asteroides A3H1 and Rhodococcus erythropolis IGTS8
Keyon Carter, Elijah Johnson, Taylor Light, Dr. Gina MacDonald	Spectroscopic studies of buffer and metal ion effects on amyloid-β peptide structure and aggregation
Erin C. Krist, Eli T. Roberts, Kenna L. Salvatore, and Dr. Barbara A. Reisner	New Alkali Metal and Transition Metal Compounds Incorporating Hydrotris(dimethyltriazolyl)borate Ligands
Tyler M. Palombo and Dr.Donna Amenta	The Preparation of Palladium Complexes of N-Pyrazolylpropanamide Derivatives
Spencer Grewe and Dr. Oleksandr Kokhan	Long-Range Regulation of Cytochrome c Binding to Mitochondrial bc1 Complex
Jenny Skubal, Dr. Yanjie Zhang and Dr. Gina MacDonald	Studying Hofmeister Ion Induced Effects in Model Lipid Drug Delivery Systems
Ryan T. Kelly and Dr. Christopher E. Berndsen	Novel Fluorescent Assay of Ubiquitin-like Protein Adenylation
Mariya M Pozhilenko, Will H Vakay and Dr. Yanjie Zhang	Partial Molar Volumes and Volume of Mixing of Salts and Osmolytes
Ian R. Roy, Camden K. Sutton, and Dr. Christopher E. Berndsen	Simulation and analysis of the structural effects of human Tetherin mutations
Amber L. Harris, Annie Lin and Dr. Debbie Mohler	Overcoming Degradation: A Novel Synthetic Strategy for Antisense Oligonucleotide Analogs
Sara J. Hildebrand, Dr. Donna S. Amenta and Dr. John W. Gilje	Synthesis and Study of N-Triazolylpropanamide Derivatives and Their Reactions with Palladium(II) and Ruthenium(III) Complexes
Ty Faulkner, Isaac Miller and Dr.Paul Raston	Infrared Spectroscopic Investigation of Carbonyl Sulfide Hydration in Superfluid Helium Nanodroplets
Olivia Swahn, Dr.Daniel Downey, and William Latham	Measurement and Evaluation of Nutrient Loading and Discharge for Several Virginia Lakes
Olivia K. Lawson and Dr. Scott Lewis	Synthetic studies of the brown tree snake pheromone 6,24-tritriacontene-2-one
Michael Khafaji Zadeh, Justin Nguyen, Tyler Miller, Rachel Brown, Stephanie Sharpes, Reafa Hossain, Dr. Kyle Seifert and Dr. Kevin Caran	The Synthesis of Tetracationic Amphiphilic Viologens
Casey Noll and Dr. Isaiah Sumner	A Computational Study of the Interactions Between the Histone Acetyltransferase, Gcn5, and a Histone Tail
Adam Fischel, Kortnie Holton, Jonathan M. Schmitz and Dr.Linette Watkins	Comparison between forms of immobilization on the specificity and stability of choline oxidase
Dariia Yehorova and Dr. Richard D. Foust,	Changes in Iron, Manganese, Copper, Zinc and Arsenic Levels Resulting From the Application of Poultry Manure to Agricultural Soils
Reafa A. Hossain, Roma L. Broadberry and Dr. Christopher E. Berndsen	A Fluorometric Assay to Monitor the Activity of the E1 enzyme
Natalie L Simmons, Daniel Marzolf, and Dr. Oleksandr Kokhan	Effect of Mutations and Labeling on Structural Stability of PpcA-Ru(bpy)3 Complexes

Rebekah Soliday, Dr. Paul Raston and Dr. Isaiah Sumner	Computational analysis of ro-vibrations in vinyl alcohol and the formation of 2-chloroethanol
Jordyn M. Palla, Kearney M. Foss, Dr. Christine A. Hughey and Karen Fortmann	Optimization of a HILIC LC/TOF-MS Method to Quantify Amino Acids and Nucleosides in Beer
Tyler J Brittain, Matt O'Malley and Dr. Oleksandr Kokhan	Expression and preliminary characterization of GSU0105, a novel 3 heme c-type cytochrome from Geobacter sulfurreducens
Coleman Swaim, P. Raj. Pokkuluri and Oleksandr Kokhan	Engineering a Cytochrome with Tunable Bandgap Potentials
Sophie Cheng and Dr. Yanjie Zhang	Effects of Salt and Alcohol on Triblock Copolymer Phase Transition Behaviors

(Student presenters underlined)

Oral Session II: Friday April 13, 2018 *(ISAT 259)*		
1:45 pm	Michael Khafaji Zadeh, Justin Nguyen, Tyler Miller, Rachel Brown, Stephanie Sharpes, Reafa Hossain, Dr. Kyle Seifert and Dr. Kevin Caran	Tetracationic Amphiphilic Viologens: Trends in Antibacterial Activity
2:00 pm	R. Hunter Wilson and Dr. Isaiah Sumner	Examining Enzyme Infrastructure: Energetic Trade-Offs in a Histone Acetyltransferase, Gcn5
2:15 pm	Jeremy Wilke, David T. Boyle, Maxwell Gillum, Maria C. DePonte and Dr. Ashleigh Baber	Hydrogen/Deuterium Exchange in Ethanol/D_2O on Au(111)
2:30 pm	Melanie Odenkirk, Erika Hutchinson, Jeff Jones and Dr. Chrisi Hughey	Investigating the reproducibility of a MLR model to predict negative electrospray ionization efficiency using different instrumentation and solution conditions
2:45 pm	Taylor L. Albertelli, Heather Manring, Stuart Campbell, Maegen A. Ackermann and Dr. Nathan Wright	Desmoplakin AC Mutations' Affect on Structure and Stability of its NH2-Terminus
3:00 pm	Jake A. Whitley, Daniel R. Marzolf, Oleksandr Kokhan, and Dr. Nathan T. Wright	Experimental and Computational Studies of Obscurin's Flexibility
3:15 pm	Isatu Kamara and Dr. Thomas C. DeVore	Synthesis and Analysis of Sodium Copper Oxalate Dihydrate

Special Announcements *(ISAT 159)*	
3:40pm	Announcement of Chemistry and Biochemistry Student Award Winners

Keynote Address: Friday April 13, 2018 *(ISAT 159)*		
3:45 - 4:45 pm	Dr. William Gemmill JMU Class of 2002	Formulation design and product development of next-generation polishing slurries for the semiconductor and precision optics industries

Keynote Address

Friday, April 13, 2018 at 3:45pm
ISAT Room 159

Formulation design and product development of next-generation polishing slurries for the semiconductor and precision optics industries

Dr. William Gemmill, PhD
(JMU Class of 2002)
Eminess Technologies, Inc.
Monroe, NC

Semiconductors and advanced optical components are ubiquitous in today's society. The most common end use of these components is the modern smartphone that contains hundreds of parts ranging from scratch resistant glass to multiple application specific integrated circuits. The manufacturing processes involved are almost always complex operations utilizing cutting-edge chemistry, physics, and engineering to achieve cost-effective results. The process of polishing semiconductor substrates and precision glass is arguably the most critical step in the manufacture of these components and this presentation will cover two types of polishing slurries that together contribute to a polishing market that exceeds USD 2 billion.

Sapphire wafers are the most commonly used substrate for gallium nitride (GaN) light-emitting diodes (LEDs). The manufacture of sapphire wafers begins with the growth of a single crystal boule, coring of the boule to the appropriate diameter and crystal plane, slicing the core into thin blanks, grinding and lapping to achieve good surface quality and more importantly a flat wafer, and finally chemical mechanical polishing (CMP) to obtain a surface that is nearly atomically smooth and ready for epitaxial growth of nitride films. In the CMP of sapphire wafers the polishing consumables constitute a significant portion of the manufacturing cost to produce a high quality sapphire substrate. The productivity of a polishing operation is determined from multiple factors dominated by yield and throughput. The formulation design of polishing slurries that provide high throughput and lifetime will be discussed.

The use of cerium oxide abrasives by optics manufacturers dominates glass polishing and finishing. These abrasives are supplied in the form of powder or as pre-mixed slurry that may or may not contain other components designed to meet performance needs of the end user. There are countless products that span the range of purity, particle size, preparatory method, and physical and chemical properties. The volume of such offerings coupled with the wide range of characteristics can lead to the use of many different products inside of one factory. This increases risk associated with supply chain management, poor tool utilization, and operator error. The development of a versatile and easily tuned polishing slurry will be presented. Such a slurry can be readily applied to multiple polishing operations thus reducing the need to stock multiple solutions, allow for increased tool utilization, and provide the flexibility that is required of today's modern optic fabrication factory.

STUDENT ABSTRACTS

(Student presenters underlined)

Desmoplakin AC Mutations'affect on Structure and Stability of its NH2-Terminus

Taylor L. Albertelli[1], Heather Manring[2], Stuart Campbell[3], Maegen A. Ackermann[1] and Dr.Nathan Wright[1]
[1]Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807
[2]Department of Physiology and Cell Biology, Ohio State University;
[3]Department of Biomedical Engineering, Yale University

Desmoplakin is a large (260 kD) protein in the desmosome, a subcellular structure that links the cytoskeleton of one myocyte to that of its neighbor. In the heart, the desmosome works to propagate the contractile force and allows for the synchronized, strong contractions of the human heart. The N-terminal third of desmoplakin is composed of multiple tandem spectrin repeat (SR) domains, with a single SH3 domain positioned on top of one of the SR domains. Previously published studies suggest that this SH3 domain may be a hotspot for variants linked to arrhythmogenic cardiomyopathies (AC). While some of these variants are associated with decreased amounts of desmoplakin protein, their molecular mechanism of action remains undefined. Here, we examine these specific variants in silico and in vitro. CD and fluorescence analysis show that these mutations do not significantly perturb the global desmoplakin structure and stability. However, MD simulations suggest significant changes to local stabilizing interactions within the SH3 domain. Thus, these studies provide a compelling molecular mechanism of action for at least a subset of AC cases.

Hydrogen/Deuterium Exchange in Ethanol/D_2O on Au(111)

Jeremy Wilke, David T. Boyle, Maxwell Gillum, Maria C. DePonte and Dr. Ashleigh Baber
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

The exchange of hydrogen and deuterium (H/D) is important in biochemical processes such as protein folding and protein protein interactions. Surface science can simplify the study of H/D exchange between molecules. For example, H/D exchange has previously been studied on Au(111) using methanol/hydrogen and water/hydrogen systems. Both systems used molecular hydrogen which must first be dissociated and pre-adsorbed on the gold as atomic hydrogen (or deuterium). Since the dissociation of H_2 on Au(111) is an uphill process, the hydrogen must be activated prior to H/D exchange. The studies reported herein show the exchange of H/D using co-adsorbed ethanol and deuterated water, which are easily adsorbed to the Au surface. The presence of water affects the selectivity and efficiency of catalytic reactions involving ethanol, which is a direct fuel source and source of hydrogen. Understanding the interaction between ethanol and deuterated water on Au(111) will shed light on the reaction pathways in which water affects ethanol chemistry. Temperature programmed desorption (TPD) was used to study the desorption products after the co-adsorption of ethanol with water. The intermolecular hydrogen bonded interactions between co-adsorbed ethanol and deuterated water on Au(111) leads to H/D exchange without bond dissociation.

Expression and preliminary characterization of GSU0105, a novel 3 heme c-type cytochrome from Geobacter sulfurreducens

Tyler J Brittain, Matt O'Malley, and Dr. Oleksandr Kokhan
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

C-type cytochromes play an important role in respiration of dissimilatory iron-reducing bacteria. They form extended conduits for charge transfer between the cellular metabolism and external electron acceptors such as particles of iron oxide, metal ions, and humic substances. However, very little is known about biophysical, biochemical, and structural properties of this large and diverse class of proteins. Out of more than 80 c-type cytochromes in Geobacter sulfurreducens, only about 10 have been previously characterized. Here we present our results on expression and preliminary characterization of GSU0105, a novel 3-heme cytochrome. We successfully cloned the gene and achieved acceptable expression in E.coli. A sufficient amount of protein has been isolated to perform UV-Vis, LC-MS, and SAXS characterization. The results of our preliminary characterization reveal that the protein has the expected mass and typical for multiheme c-type cytochrome spectral properties. Despite a similar size (71 amino acids) and the same number of c-type hemes to the members of the cytochrome c7 family, multiple sequence alignment suggests the GSU0105 belongs to a new family of cytochromes. The protein is very prone to formation of long linear complexes likely caused by His-tags. Work is underway to create tag-free constructs in order to improve GSU0105 solubility, and therefore yield and enable crystallization trials.

Spectroscopic studies of buffer and metal ion effects on amyloid-β peptide structure and aggregation

Keyon Carter, Elijah Johnson, Taylor Light, Dr. Gina MacDonald
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

Amyloid-β peptides are found in brains obtained from Alzheimer's patients. These peptides aggregate forming insoluble Amyloid-b plaques. It is uncertain how the presence of these peptide plaques correlate with the onset of the disease, however environmental conditions are known to alter disease progression. Previous studies have proven that metal ions such as zinc and copper are co-localized within AB plaques. Recent studies suggest that these metal ions may serve a role in inducing AB peptide misfolding and aggregation. The Cu^{2+} and Zn^{2+} ions are believed to bind to the AB peptide structure and increase aggregation. The metal ion concentrations play a factor as higher metal ion concentrations correlate with a higher aggregation rate. Understanding the environmental conditions that affect AB peptide structure and aggregation will provide a greater understanding about the role of metals in disease. Current studies are aimed at understanding how metal ions influence peptide structure, solvation, and aggregation. Infrared spectroscopy was used to monitor aggregation and structural changes of control AB peptide and AB peptide in the presence of Cu^{2+} and Zn^{2+} over time. Infrared spectra show that peptide length, buffer and metal concentration influence AB peptide structure, solvation, and aggregation.

Structural comparison of the Arabidopsis thaliana family of β-amylases

Nithesh P. Chandrasekharan[1], Dr. Jonathan Monroe[2] and Dr. Christopher E. Berndsen[1]
[1]Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807
[2]Department of Biology, James Madison University

The β-amylase (BAM) family in Arabidopsis thaliana has nine members, some of which are known to hydrolyze starch to maltose. The members of this family show unique functional, regulatory, and catalytic behaviors due to changes in sequence or domain composition. However, the molecular basis for functional specificity and regulation is not always clear. Some of the inactive members of the lack the catalytic amino acids required for hydrolysis. However, this is not the case for all the enzymes such as BAM2, which appears to be allosterically regulated and requires KCl for activity. Given the lack of structural information on any member of this protein family, we homology modeled all 9 BAM proteins from Arabidopsis and performed molecular dynamics simulations to propose how these proteins may differ at a functional level. All simulations were equilibrated for at least 50 ns in explicit solvent, the equilibrated models were aligned structurally, and then analyzed to compare the structure, dynamics, and chemical properties. All 9 proteins modeled well as TIM barrel proteins with most of the structural deviations occurring in predicted loops. Comparison of the simulated dynamics shows that overall the BAM proteins show similar areas of high and low motion. Interestingly, BAM4 and BAM9 showed fluctuation profiles that were distinct from the other BAM proteins, which matches their predicted lack of catalytic activity and distinct active site sequences. BAM7 and BAM8 which also have distinct active sites however these enzymes show dynamics similar to those of the catalytically active BAM1 and BAM3 suggesting that BAM7 and BAM8 may also have activity, however the proper conditions are not known. We further modeled BAM2 as a tetramer based on recent biochemical information to identify how allostery and solution conditions may influence the activity of this protein. We identified predicted changes in the dynamics upon binding to a ligand in the starch-binding site as well as changes in hydrogen bonding within the protein in potassium. Both findings provide testable proposals for the regulation of BAM2 activity.

Effects of Salt and Alcohol on Triblock Copolymer Phase Transition Behaviors

Sophie Cheng and Dr.Yanjie Zhang
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

In this paper, the effects of salt and alcohol on the aggregation of a triblock copolymer, poly (ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide) were studied by using the OptiMelt automated melting point system. It was found that NaCl promoted aggregation of the polymer and decreased the phase transition temperature of the polymer while NaSCN showed opposite behavior. Introduction of methanol into the salt-polymer mixture enhanced the effects of salts on the aggregation of the polymer.

A Computational Study of the Role of Asparagine 79 in Ubc13

Katherine Elliott and Dr. Isaiah Sumner
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

Ubiquitin (Ub) is a regulatory protein with the ability to flag proteins to be degraded. Ub is covalently attached to a lysine on the target protein by a series of reactions catalyzed by three types of enzymes: ubiquitin activating enzymes, E1; ubiquitin conjugating enzymes, E2; and ubiquitin ligases, E3. If ubiquitin is not attached properly, it can lead to various diseases, like Alzheimer, Parkinson and anemia. Our lab has recently published data on the mechanism of the E2 enzyme (Ubc13) and contrary to a popular hypothesis; our data shows that it is unlikely that the amino acid asparagine 79 in Ubc13 stabilizes a reaction intermediate. Instead, our results suggest that asparagine 79 plays an important role in maintaining the structure of Ubc13; however, this hypothesis was based on molecular dynamics simulations of a simplified model of the Ubc13~Ub system. The model system consisted of a Ubc13 bonded to a Ub and with a zwitterionic lysine residue as a substrate. This model is incomplete because it is missing the full substrate ubiquitin, an E3 ligase, and a ubiquitin conjugating enzyme variant (UeV). Therefore, we used molecular dynamics to explore the effects of these additional proteins by generating trajectories of Ubc13~Ub complexed with different combinations of E3, UeV, and full substrate Ub.

Infrared Spectroscopic Investigation of Carbonyl Sulfide Hydration in Superfluid Helium Nanodroplets

Ty Faulkner, Isaac Miller, and Paul Raston
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

Helium is unique amongst the chemical substances in that it remains liquid down to the lowest possible temperatures. Upon cooling to below 2.2 K helium becomes superfluid, possessing strange properties such as zero viscosity and frictionless flow. Superfluid helium nanodroplets have been referred to as the ultimate spectroscopic matri because of their low temperature (T = 0.4 K) and weakly interacting nature, which leads to greatly simplified spectra relative to the gas phase. They are particularly useful for synthesizing molecular complexes, and several previous investigations have focused on investigating the hydration of atmospherically important molecules, such as the hydroxyl radical. While carbonyl sulfide is the most abundant sulphur containing molecule in the atmosphere, little is known experimentally about how it interacts with water. In this study we focus on isolating OCS-(H2O)N complexes in helium nanodroplets, and on uncovering their infrared signatures with quantum cascade laser spectroscopy.

Comparison between forms of immobilization on the specificity and stability of choline oxidase

Adam Fischel, Kortnie Holton, Jonathan M. Schmitz, and Dr.Linette Watkins
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

Choline oxidase is a versatile enzyme that has uses in both industrial and medicinal settings. This enzyme has the ability to act as a biosensor and detect the presence of choline, as well as being able to produce glycine betaine, an important intermediate fro certain industrial settings. In order for choline oxidase to be feasible in industrial synthesis pathways, it must have a broad specificity while maintaining activity over a range of pH and temperature. To this end, the specificity for two different substrates, the temperature stability, and the pH stability of choline oxidase were all determined. Following this, choline oxidase was immobilized through two different methods, by attachment to CnBr-activated Sepharose beads, and by binding to a Polyethersulfone (PES) membrane. When immobilized with Sepharose beads, the temperature and pH stability increased, while reducing the enzymes specificity for choline as a substrate at the same time. More data is currently being collected for the effect of immobilization on a PES membrane.

Targeted and Untargeted Metabolomics Profiling of Beer as a Function of Yeast Strain and Fermentation Time

Kearney M. Foss, Jordyn Palla, Karen Fortmann, and Dr. Christine A. Hughey
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

Metabolomic profiling of beer by LC/MS has largely focused on the effect of hops used or compositional changes that occur during storage. Here, metabolomic differences in a pale ale that was fermented with four genetically different yeast strains, California ale, English ale, Neutral Grain, and Belgian Saison, were profiled using targeted and untargeted metabolomics. Positive and negative ion ESI LC q-TOF MS was used for untargeted profiling; while positive ion ESI HILIC LC TOF MS was used for the targeted profiling of purine bases and amino acids. Both experiments monitored compositional changes as a function of fermentation time. Metabolites found in both the final beer samples and the samples collected during 120 hours of fermentation were tentatively identified by m/z matching to a KEGG-curated Saccharomyces cerevisiae database. Database hits from the KEGG library were confirmed with authentic standards, when possible, and used in a multi-omics experiment to compare metabolite abundance in select biochemical pathways as a function of yeast strain and fermentation time. Metabolites were matched to 21 pathways with a pathway coverage of 14-60%. The identities of ~20 metabolites common across pathways (e.g., amino acids, polyamines and purines) were confirmed by matching retention times and MS/MS spectra to standards. 5-methylthioadenosine (5-MTA), which is involved in polyamine biosynthesis, was of particular interest due to its potential as a marker of oxidation during storage. Untargeted profiling of the final beer samples revealed there was a high degree of homology across the samples, with 67%-82% of all molecular features (MFs) in common. HILIC-MS measured the change in concentration of amino acids as a function of fermentation time, which supported previously reported results that wort amino acids are taken up by the yeast at different rates. Amino acids are of particular interest due to their involvement in Ehrlich pathway, which forms fusel acids and alcohols largely responsible for the taste and aroma of beer.

Comparing E. coli expression and enzyme kinetics of wildtype and codon optimized 2-(2'-hydroxyphenyl)benzenesulfinate desulfinase (DszB) fromNocardia asteroides A3H1 and Rhodococcus erythropolis IGTS8

Marissa St.George and Dr.Linette M. Watkins
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

Dibenzothiophene (DBT) and its derivatives comprise up to 60% of the organosulfur contamination of crude oil. The enzyme 2-hydroxyphenyl)benzenesulfinate desulfinase (DszB) catalyzes the carbon-sulfur bond cleavage in the final, and rate-limiting step in the biodesulfurization of DBT. The wildtype dszb genes from Nocardia asteroides A3H1 (A3H1) and Rhodococcus erythropolis IGTS8 (IGTS8) were expressed with and without chaperone proteins under different induction conditions. Yield of active enzyme was optimal when co-expressed in E. coli in the presence of GroEL and GroES. Codon optimized dszb genes were synthesized, optimizing E. coli codon usage and minimizing GC content. The codon optimized dszb genes from A3H1 and IGTS8 were expressed with and without chaperone proteins under different induction conditions. GroEL and GroES were both still required for optimal enzyme activity. Protein aggregation was observed using whole cell FT-IR spectroscopy in all cases, but was significantly larger in induced cells in the absence of chaperones.

Olefin Chemistry on Au(111)-Based Catalysts

Maxwell Z. Gillum, Jeremy A. Wilke, Maria C. DePonte and Dr. Ashleigh E. Baber
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

The partial oxidation of olefins produces industrially relevant products that are used in a multitude of chemical fields ranging from food processing to polymer production to the automotive chemistry. The use of heterogeneous metal/oxide catalysts help to increase the selectivity for these oxidation reactions. However, the reaction pathways for olefin oxidation on these surfaces are not yet well understood. To gain a comprehensive understanding of olefin intermolecular and surface interactions, temperature programmed desorption (TPD) studies were conducted using Au(111)based model catalysts. By examining and comparing how olefins, such as ethylene and propylene, interact on a clean Au(111) surface, insight can be gained on the behavior of this class of compounds on the surface. This will allow for a more direct and focused experimentation process in future research.

Long-Range Regulation of Cytochrome c Binding to Mitochondrial bc1 Complex

Spencer Grewe and Dr. Oleksandr Kokhan
Department of Chemistry and Biochemistry, James Madison University, Harrisonburg, VA 22807

The cytochrome bc1 complex is a highly conserved multisubunit protein found in the mitochondria, and is a key complex in the electron transport chain. During oxidative phosphorylation, cytochrome (cyt) c, a mobile electron carrier, binds to the cyt c1 of a bc1 complex dimer and shuttles electrons from complex III to complex IV. X-ray crystallographic studies revealed that only one molecule of cyt c binds to one bc1 complex dimer, despite two cytochrome c1 subunits available for binding, pointing toward the existence of a regulation mechanism preventing the docking of a second cyt c substrate. However, the structural basis for such a mechanism of long-range (>30Å) regulation of substrate binding is not clear from static structural studies. We employed all-atom molecular dynamics simulations to uncover a possible mechanism of regulation. Our results reveal that a finger-like domain of the vacant cyt c1 subunit undergoes a conformational change with its tip moving towards cyt c, transferring mechanical motion and causing distortion of the vacant cyt c binding site. In addition, we explored the role of naturally occurring methylated Lys-72 residue of cyt c in substrate binding.

Overcoming Degradation: A Novel Synthetic Strategy for Antisense Oligonucleotide Analogs

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Antisense oligonucleotide analogs (ASOs) are therapeutic agents that consist of short or modified DNA or RNA molecules that bind to messenger RNA (mRNA) and prohibit the synthesis of protein from translated mRNA. The potential for ASO therapeutic agents is wide, but many toxicological challenges must be overcome before ASO medication can be reliably utilized. Such challenges include poor membrane permeability, poor solubility, and rapid degradation by exonucleases. In order to negate these challenges, removing the sugar-phosphate backbone of DNA and RNA, which is responsible for the rapid degradation of ASOs in the human body, and replacing their backbone with a 7-membered carbon ring was attempted.

Synthesis and Study of N-Triazolylpropanamide Derivatives and Their Reactions with Palladium(II) and Ruthenium(III) Complexes

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Five N-triazolylpropanamide derivatives have been synthesized through base catalyzed Michael additions with Triton B as the base catalyst. The reaction of methacrylamide and 1H-1,2,3-triazole produced 1, an asymmetrically substituted triazole with a methylpropanamide moiety. The reaction of N-isopropylacrylamide and 1H-1,2,3-triazole produced two isomeric triazoles, one with the N-isopropylpropanamide substituent bonded to the exterior ring nitrogen (2), the other with the substituent bonded to the central nitrogen (3). Similarly substituted triazole isomers, 4 and 5, were obtained from the reaction of benzotriazole and N,N-dimethylacrylamide. All compounds have been characterized through NMR and IR spectroscopy. Additionally, compounds 1, 2, and 3 have been characterized through elemental analysis. Compound 1 was allowed to react with bisdichloro(1,5-cyclooctadiene)palladium(II) and ruthenium(III)nitrosylchloride mono-hydrate. Compound 2 was allowed to react with bisdichloro(1,5-cyclooctadiene)palladium(II). The products from these reactions are currently being characterized.

A Fluorometric Assay to Monitor the Activity of the E1 enzyme

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Ubiquitination is a reversible protein post-translational modification which regulates protein degradation, DNA repair, and the immune response. The process of ubiquitination requires three enzymes called the activating enzyme, the conjugating enzyme and the ligase enzyme. The catalytic mechanisms of these enzymes are poorly understood. Given the far reaching consequences of protein ubiquitination in human biology and disease elucidation of the ubiquitination mechanism would allow for the creation of potential cancer therapeutics. The activating enzyme requires ATP to activate the ubiquitin or the Ubl protein and the breakdown of ATP can be measured as an assay of enzyme activity. We are developing a new assay which can be applied to mechanistic study of the ubiquitin transferring enzymes. The proposed fluorometric assay can be used for the real-time monitoring of ATP to AMP during activation of the E1 enzyme. The relies on the difference in affinity between ATP and AMP for terbium. Binding to ATP enhances terbium fluorescence while AMP does not bind to terbium as well and therefore cannot increase terbium fluorescence. This assay allows for the use unmodified enzymes and substrates, and circumvent the variability and low sensitivity associated with previously developed molybdenum blue assays. ATP stimulation of the fluorescence of terbium was tested against different buffers, salts, and proteins such as BSA over a large range of concentrations to determine optimal conditions for ubiquitination assays.

Far-Infrared Synchrotron Spectroscopy of Formic Acid

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Formic acid, the simplest carboxylic acid, is an important atmospheric species that is known to be responsible for a large fraction of the acidity of typical precipitation. Significant biogenic sources are from plants and soils, bacterial and human metabolism, and in the venom of ants and bees. Its biological importance and simplicity makes it a sought after astrochemical species, and both its lower energy trans- and higher energy cis- conformers have been detected in interstellar space. Here we probe the torsional potential which accommodates these two conformers by far-infrared synchrotron spectroscopy. The high brightness of the Canadian Light Source allows for the observation of new hot bands from weakly populated excited torsional states that we can then use to help refine the torsional potential. Assignment of these bands may also help in untangling more congested mid-infrared spectra.

Synthesis and Analysis of Sodium Copper Oxalate Dihydrate

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Sodium copper oxalate dihydrate also known as wheatleyite was synthesized by dissolving a mixture of 3 to 1 ration of sodium oxalate and copper oxalate in a boiling water. The blue needle crystals formed on cooling. The thermal decomposition of sodium copper oxalate dihydrate was investigated using FT-IR, TGA, DSC, and X-RAY diffraction. TGA indicated the sodium copper oxalate dihydrate lost about 47% of the total mass. X-ray diffraction and inferred spectroscopy indicated that sodium carbonate and copper formed when the decomposition was done in vacuum. DSC was done in static air to determine the enthalpy of formation for this compound

Novel Fluorescent Assay of Ubiquitin-like Protein Adenylation

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Ubiquitin fold modifier 1 (Ufm1) is a ubiquitin-like protein (Ubl) found in eukaryotic organisms which plays a crucial role in ER stress management and signal transduction. Ufm1 interacts with its E1 (Uba5) via binding to the adenylation domain of Uba5 and the Ufm1-interacting sequence in the C-terminus of Uba5. During catalysis, a metastable adenylate intermediate has been proposed to form between ubiquitin and its respective E1. To further elucidate the mechanism between Ufm1 and Uba5, we have developed an assay to probe for formation of this intermediate. In this assay, the adenylate intermediate is precipitated with trichloroacetic acid and unreacted ATP is washed away. The remaining nucleotide within the adenylate, AMP, is then derivatized via reaction with chloroacetaldehyde to form 1,N6-etheno AMP which is fluorescent. Using this assay, we show for the first time evidence of a metastable Ufm1 adenylate, and that this assay can be used to quantify the kinetics of the Uba5 reaction. This assay can be used to further elucidate the mechanism Uba5 by quantifying rates without the use of radiolabeled isotopes, which has not been done before.

Synthesis of Antisense Nucleic Acid Monomers

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Antisense oligonucleotides (ASOs) are important because of their ability to selectively hinder or silence genes. The sugar-phosphate backbone of natural oligonucleotides degrades relatively quickly within the body, which has led to the study of synthetic analogues lacking this feature. Our current approach involves the synthesis of a generic ring structure that could be attached to each nucleic acid base resulting in polymerizable monomers. Progress towards the synthesis of this glycidyl-derived backbone will be discussed.

New Alkali Metal and Transition Metal Compounds Incorporating Hydrotris(dimethyltriazolyl)borate Ligands

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In an effort to synthesize new framework materials, the coordination chemistry of the hydrotris(3,5-dimethyl-1,2,4-triazolyl)borate anion ([$BH(dmtrz)_3$]- = dmtris-) was explored. Three new materials, "A[$BH(dmtrz)_3$]" (A = Li, Na, K), were crystallized by solvent diffusion of ethyl ether into ethanol solutions of the compound. Clear colorless crystals formed. Powder X-ray diffraction data indicate that these are new materials with different unit cells. M[$BH(dmtrz)_3]_2$ (M = Mn, Fe, Co, Ni, Cu, Zn) were synthesized by a solvothermal reaction in methanol between Na[$BH(dmtrz)_3$] and $M(NO_3)_2{\cdot}nH_2O$ or $MCl_2{\cdot}nH_2O$. Crystal colors were consistent with inclusion of the transition metal: pale pink Mn^{2+}, yellow Fe^{2+}, yellow-orange $Co^{2+,}$ lavender Ni^{2+}, blue Cu^{2+}, and colorless Zn^{2+}. Single crystal X-ray diffraction data of Zn[$BH(dmtrz)_3]_2$ indicate that this is a 0-D coordination compound with a triclinic cell. Zn[BH(trz)3]2 also crystallizes as a 0-D compound. Powder X-ray diffraction (PXRD) data of the other compounds are similar and differences can be attributed to unit cell differences.

Synthetic studies of the brown tree snake pheromone 6,24-tritriacontene-2-one

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The mid-20th century invasion of Guam by Boiga irregularis, the brown tree snake, has left much of the island natural fauna devastated. Various methods have been used to reduce the snake population, but to little or no avail. A recent method involves the synthesis of natural female B. irregularis pheromones for use in scent trails leading to traps that are intended to lure males. This work attempts to synthesize one of six pheromones of interest:
6,24-tritriacontene-2-one. A convergent synthesis has been proposed that brings together three independent sections to prepare the final 33 carbon methyl ketone. At this time, the synthetic studies continue to complete this methyl ketone, laying the groundwork to prepare the other five pheromones in the future.

Structural Characterization of Titin Zlg9 and Zlg10

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Titin domains Zlg9/10 bind to obscurin domains Ig58/59 during myofibrillogenisis. Mutations in the obscurin domain of this region lead to distal muscular dystrophy (DMD) in humans, primarily due to weakened binding with titin . While the cellular consequences of this interaction are well characterized, the molecular determinants governing this structure are unknown. Previous work from our lab has solved the high-resolution structure of the obscurin domains of the complex. Here, we describe the purification and complete structure characterization of titin domain Zlg10, as well as preliminary structure attributes of titin domain Zlg9/10. Although Zlg9â€™s sequence suggests it to be a model Ig domain, experiments suggest that Zlg10 plays a role in stabilizing Zlg9 in solution.

Synthesis of Antisense Oligonucleotide Analogues

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Antisense oligonucleotides (ASOs) are therapeutic agents that consist of short or modified nucleic acids, DNA or RNA, that bind to messenger RNA (mRNA) to prohibit the synthesis of target proteins. The potential for ASO therapeutic agents is wide, but many toxicological challenges, such as poor membrane permeability, poor solubility, and rapid degradation by exonucleases, must be overcome before ASO medication can be reliably utilized. In order to negate these challenges, the ASO sugar-phosphate backbone, which is responsible for its rapid degradation will be replaced by one that is hydrolytically stable. To do so, exchanging the traditional backbone for a 7-membered carbon ring was attempted.

Mimicking Natural Photosynthesis: Ultrafast Charge Transfer in PpcA-Ru(bpy)3 Complexes

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We are developing biomimetic molecular architectures for efficient solar energy conversion using artificial photosensitizers combined with natural and genetically engineered host systems capable to support long-lived charge-separated states and conduct charges away from the photosensitizers. Converting light energy into its electrochemical equivalent requires precise control and fine tuning of relevant kinetic and thermodynamic parameters, including primary charge separation. To this end, we developed a series of 22 cysteine mutants of PpcA, a 3-heme cytochrome from Geobacter sulfurreducens. These proteins were successfully expressed in E.coli and isolated for covalent labeling with Ru(bpy)2(bpy-Br). Protein purity and successful posttranslational modifications were confirmed with HPLC-MS. With time-resolved nanosecond and ultrafast transient absorbance spectroscopy we have identified 6 constructs with apparent photo-induced charge transfer time constants of 20 ps or faster, including 2 constructs with 1-2 ps time constants. The is a significant result as up to this point only natural photosynthetic systems demonstrated such a fast initial charge separation, while all artificial covalent biohybrid constructs exhibited charge transfer rates 3 or more orders of magnitude slower. To understand molecular principles responsible for such a dramatic acceleration of electron transfer rates, we used small- and wide angle X-ray scattering and currently attempting to obtain X-ray crystallographic and NMR structures of ultrafast constructs. Finally, we performed triplicate 250-300 ns all-atom molecular dynamics simulations of all 6 ultrafast constructs. Based on the obtained results we conclude that that photo-induced ultrafast charge transfer requires van der Waals contact between heme vinyl groups and photosensitizers while contacts with propionates or a small number of covalent bonds between the donors and acceptors play much less significant role.

A Computational Study of the Interactions Between the Histone Acetyltransferase, Gcn5, and a Histone Tail

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Post-translational modifications (PTMs) can have a profound effect on protein structure and function. One such PTM involves the acetylation of free lysine residues. An essential acetylation reaction involves the transfer of the acetyl group from acetyl CoA to a histone (a protein involved in DNA binding). This transfer neutralizes the positively charged lysine, which allows for the DNA to be exposed for transcription. The histone acetyltransferase our study focuses on is Gcn5. The first step in the reaction is the deprotonation of a lysine on the histone tail by a glutamate in Gcn5. This glutamate is ~15 Ã… away from the transferring acetyl group. Thus, after deprotonation, the Gcn5/histone/acetylCoA complex must reorganize and the lysine must swing back towards the active site. We use molecular dynamics (MD) simulations to probe the interactions between the histone and Gcn5 before and after lysine deprotonation to understand which contacts must be broken before the final acetylation step can occur.

Investigating the reproducibility of a MLR model to predict negative electrospray ionization efficiency using different instrumentation and solution conditions

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Numerous studies have used physiochemical properties to predict positive ion electrospray response. Less work has been done to predict negative ion response. Most notably, Kruve et al. (Anal. Chem. 2014, 86, 4822-4830) developed a multiple linear regression (MLR) model with 48 phenols and benzoic acids that correlated ionization efficiency with physiochemical properties, such as WAPS (a measure of charge delocalization in anions), pKa and degree of ionization in solution using an Agilent XCT ion trap. Here, the negative ion ESI response of 13 compounds (0.01-1000 µM) used in the original Kruve et al. MLR model was measured in triplicate flow-injection experiments on an Agilent 6460 QqQ. Response was measured in both neat MeOH and 0.1% NH4OH in 80:20 ACN:H2O (solvent used in original study). Slope over the linear dynamic range was used as a measure of compound response. A linear regression fit failed if the linearity had an R2<0.95, precision <0.35 or residuals >0.3. In addition, four or more calibration levels were required in the fit. Ionization efficiency was calculated as log IE or the slope of analyte divided by the slope of benzoic acid, as reported in the original model. Response of these compounds measured on the QqQ in our laboratory does not correlate well to the published MLR model in MeOH, but trends in the same solvent system and within similar concentration range (0.1-10 µM vs 0.22 to 24 µM) show stronger correlation to published results. That said, there are qualitative similarities in that unsubstituted compounds or compounds substituted with electron donating groups (e.g. NH2, OH) have the lowest responses and compounds substituted with multiple electron withdrawing groups (e.g., F, Br, NO2) have the highest responses.

Optimization of a HILIC LC/TOF-MS Method to Quantify Amino Acids and Nucleosides in Beer

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Amino acids and nucleosides are polar molecules that are not well retained on reverse phase LC columns due to their hydrophilic nature. Hydrophilic interaction liquid chromatography (HILIC), a variant of normal phase LC, works well with polar analytes since it employs a polar stationary phase with typical reverse-phase solvents. Over the last year, we have explored the use of two different HILIC columns to separate and quantify amino acids, purine bases, pyrimidine bases and nucleosides in beer. Specifically, a Phenomenex Kinetex HILIC column and an Agilent InfinityLab Poroshell 120 HILIC-Z column was used in Fall 2017 and Spring 2018, respectively. On both columns, the bases and nucleosides eluted in the first 2.5 minutes of the ~10 minute run. Retention was slightly better on the Kinetex column than on the HILIC-Z column. The aliphatic, aromatic and cyclic amino acids eluted in the middle of the run. Leucine and isoleucine were baseline resolved on the Kinetex column but not on the HILIC-Z column. However, the HILIC-Z column significantly out-performed the Kinetex column by providing better separation and peak shape for the acidic and basic amino acids, such as histidine, glutamine, glutamic acid and asparagine. Subsequently, the HILIC-Z column afforded the quantitation of 21 target compounds (vs. 18 on the Kinetex column). Quantitation of amino acids and nitrogen bases in beer using the HILIC-Z column will allow us to monitor how these compounds change during the fermentation and storage of beer.

The Preparation of Palladium Complexes of N-Pyrazolylpropanamide Derivatives

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The reaction of 3,5-dimethylpyrazolyl-N-isopropylpropanamide (L1) with dichloro(1,5cyclooctadiene)palladium(II) displaces cyclooctadiene forming Cl2Pd(L1)2. This complex has been characterized by NMR and IR spectroscopy, single crystal X-Ray diffraction, and elemental analysis. It is composed of a square planar Pd with trans L1 ligands attached through a pyrazolyl nitrogen and intramolecular hydrogen bonding between the amide and chloride. Similar reactions were carried out with 3,5-dimethylpyrazolylpropanamide (L2), pyrazolyl-Nisopropylpropanamide (L3), 3-(1H-benzotriazol-1-yl)-N,N-dimethylpropanamide (L4), 3methylpyrazolylpropanamide (L5), 3-(1H-benzotriazol-1-yl)-2-methylpropanamide (L6), and Npyrazolypropanamide (L7) presumably forming analogous complexes. This formulation for Cl2Pd(L3)2 and Cl2Pd(L4)2 is supported by NMR and IR spectroscopy and elemental analysis, while the formation of Cl2Pd(L2)2 is supported by NMR and IR spectroscopy. The products of the reactions of L5, L6, L7 are yellow precipitates that are insoluble in most organic solvents. The reaction product of L5 and L6 has been characterized by IR spectroscopy. The reaction product of L7 has been characterized by IR spectroscopy and elemental analysis. Single crystals have not yet been obtained for the products from L6, L7.

Partial Molar Volumes and Volume of Mixing of Salts and Osmolytes

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The goal of this project was to study ion-water interactions by volumetric analysis. Densities of a series of salts and osmolytes at varied concentrations were measured to determine the apparent molar volume of the solute, partial molar volume of solvent and solute, and volume of mixing in aqueous solutions. In general, strongly hydrated salts showed smaller limiting partial molar volume compared to weakly hydrated salts. Volume of mixing values were more negative for strongly hydrated anions suggesting that the interactions of these anions with water were more favorable. Detailed volumetric analysis of solute-water system will be presented.

Simulation and analysis of the structural effects of human Tetherin mutations

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Human Tetherin, also known as BST-2 or CD317, is a dimeric, extracellular membrane-bound protein that consists of N and C terminal membrane anchors connected by an extracellular coiled coil. BST-2 is involved in binding enveloped viruses, such as HIV, and inhibiting viral release in addition to a role in NF-kB signaling. Viral tethering by Tetherin can be disrupted by the interaction with Vpu in HIV-1 in addition to other viral proteins. The structural mechanism of Tetherin function is not clear and the effects of human tetherin mutations identified by sequencing consortiums are not known. To address this gap in the knowledge, we used the Ensembl database to construct and analyze all known human mutants to further investigate how the structure of the ectodomain influences function. We employed the YASARA program to systematically construct each mutant and run 10 to 20 ns simulations of 45 full-length Tetherin mutants embedded in the membrane and with explicit solvent. From the data, we identified islands of sequence stability within the ectodomain and mutations near these stable regions cause more dramatic changes in flexibility compared to distal mutations in simulations. These islands of stability correspond to functionally or structurally important regions identified in previous biochemical and biophysical studies. Further analysis of and comparison between the mutant models will lead to insights into the structure and function of Tetherin.
In addition to the results above, the data from these simulations have been made freely available on the Open Science Framework to promote transparency in the methods and analysis. Additionally, we developed an Rmarkdown based workflow in an effort to standardize the communication and interpretation of this large set of simulation data. These resources and workflows will facilitate future analysis and comparison of large numbers of simulations and structural models such as those from course-based research projects.

Studying Hofmeister Ion Induced Effects in Model Lipid Drug Delivery Systems
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Caffeine consists of two fused aromatic rings with four nitrogens and a variety of functional groups, and its structure is similar to many biomolecules. In previous studies, the Hofmeister anion series was shown to affect the solvation and aggregation of caffeine. In this study, the effects of the Hofmeister series are expanded to examine the cation and anion induced interactions with caffeine, lipid, and solvent. ATR-FTIR was used to monitor both Hofmeister anion and cation induced changes in the caffeine and lipid absorption spectra, as well as isolated caffeine and lipid interactions. Hofmeister ions effects on caffeine-caffeine and caffeine-lipid interactions will be discussed.

Effect of Mutations and Labeling on Structural Stability of PpcA-Ru(bpy)3 Complexes
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We are engineering biomimetic atomic structures for solar energy conversion to produce a lot with very little waste. By doing this we are using artificial photosensitizers combined with natural and hereditarily built host frameworks proficient to help seemingly perpetual charge-isolated states and direct charges from the photosensitizers. Changing over light vitality into its electrochemical comparable requires exact control and adjusting of important active motion and thermodynamic parameters, comprising of essential charge separation.
To this end, we developed a series of 22 cysteine mutants of PpcA, a 3-heme cytochrome from Geobacter sulfurreducens. Protein mutants were labeled at the engineered Cys sites with Ru(bpy)3Br. We verified correct photosensitizer attachment and the extent of labeling with Liquid chromatography- mass spectroscopy (LC-MS). The correctly labeled complexes were analyzed with Circular Dichroism (CD) spectroscopy at various temperature points between 25 and 90Â°C. Our results reveal that contrary to previous expectations from competing groups, mutations and labeling do affect stability of the formed complexes. The obtained results are discussed in context of prior extensive Small-angle X-ray scattering (SAXS) characterization and all-atom Molecular Dynamics (MD) simulations in explicit solvent.

Altering the Specificity Properties of 2-(2-hydroxyphenyl)benzenesulfinate desulfinase from N. asteroides A3H1
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Biodesulfurization is a metabolically important process that occurs naturally in bacterial cells found near oil and coal deposits. In sulfur-specific biodesulfurization, the dsz pathway, enzymes selectively remove the organic sulfur found in crude oil without disrupting the carbon backbone. The rate-limiting step within this metabolic pathway is the conversion of 2-(2-hydroxyphenyl)benzenesulfinate (HPBS) to 2-(2-hydroxybiphenyl) using HPBS desulfinase (DszB). The DszB enzyme from Nocardia asteroides A3H1 was overexpressed in E. coli, purified and characterized kinetically. Homology studies identified an active site loop with conserved amino acids that could play a role in the specificity for different organosulfur compounds found in crude oil. Point mutations were generated to study the importance of amino acids 195 and 200 on the specificity of the enzyme. Three mutant enzymes (A195R, A200R and A195/200R) prepared using codon-optimized gene constructs were co-expressed with GroESL and purified from E. coli using Ni2+-affinity chromatography. Substrate specificity experiments were performed to define the role of the active site loop on specificity. Kinetic measurements indicate a decreased specificity for HPBS. Fixed-time sulfite assays indicate an increased preference for smaller ringed substrates, demonstrating the importance of amino acids 195 and 200 and defining the specificity of the enzyme.

Computational analysis of ro-vibrations in vinyl alcohol and the formation of 2-chloroethanol
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The rotational and vibrational signatures of small molecules are of interest when attempting to identify molecules in the interstellar medium, and their reaction pathways are important when considering the plausibility of a molecule being present at all. For example, in 2001, Turner and Apponi positively identified vinyl alcohol in the molecular cloud, Saggitarius B2(N) by rotational spectroscopy, which motivated lab based research into how it is produced. Researchers continue to look for signatures of this molecule in the interstellar medium since it is an important intermediate in many organic reactions and may therefore play a role in the formation of complex organic molecules. We used computational methods to calculate ro-vibrational constants of both syn- and anti-vinyl alcohol and compared them to experiments performed using far-infrared spectroscopy. Specifically, we calculated the anharmonic vibrations using second order vibrational perturbation theory (VPT2) at the CCSD(T)/cc-pVTZ level of theory. The vibrational frequencies, rotational constants and centrifugal distortion constants are in good agreement with experiment, which should be useful in searches for anti vinyl alcohol in the atmosphere of Titan and in the interstellar medium. We also investigated several reaction pathways that lead to the formation of 2-chloroethanol, starting from known interstellar molecules. Intrinsic reaction coordinate (IRC) calculations were performed at the MP2/cc-pVTZ level of theory for both solvated and gas-phase reactions of oxirane with HCl, and ethylene glycol with HCl. The results of these calculations show that the reactions are exothermic, with barrier heights that are reduced upon solvation in water ices.

Measurement and Evaluation of Nutrient Loading and Discharge for Several Virginia Lakes
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Nitrogen and phosphorus entering the Chesapeake Bay must be reduced to meet the requirements of the 2010 Chesapeake Bay TMDL. Lake fertilization is both an accepted management tool for fisheries enhancement and necessary when allochthones sources are limited. The problem is whether or not the addition of fertilizers to recreational fishing lakes is contributing to the nutrient loading of the Bay. This research project is conducting a comprehensive evaluation of four lakes in the watershed of the Bay: Lake Brittle, Lake Burke, Huntsman Lake and Lake Shenandoah. A fifth lake outside of the Bay watershed (Lake Keokee) is also being studied. The water chemistry of samples taken from the feeder streams, tail water, and locations within the lake is assayed and compared for the evaluation. This project involves both extensive field work for sample collection and laboratory analytical methods. Parameters include: total phosphorus, dissolved phosphorus, chlorophyll a, nitrogen nitrate, nitrogen ammonia, nitrogen TKN, pH, alkalinity, base cations, acid anions and physical measurements. Data obtained from the water chemistry analyses will be used to determine any significant release of phosphorus and nitrogen compounds due to fertilization and to better estimate the amount of fertilizer necessary for future applications to achieve the goals of fisheries management.

Engineering a Cytochrome with Tunable Bandgap Potentials

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For bio-hybrid mimics of natural photosynthetic systems to be efficient solutions to current energy challenges, the relative bandgap potentials of component energy transfer structures must be optimized. To this end, we developed and extensively characterized 12 point mutations of PpcA, a 3-heme member of the cytochrome c7Â family native toÂ Geobacter sulfurreducens.Â These mutations were engineered to influence the redox potential (Em) of the middle heme (heme III) in PpcA by using four different strategies: performing charge reversal mutations, decreasing solvent access to the heme plane with bulky residues, altering the native bis-histidine axial ligation of the heme, and by attempting to form hydrogen bonds with the propionates of the heme. The latter strategy is expected not only to increase EmÂ but also to introduce a redox Bohr effect. Out of 13 mutants, 12 were expressed inÂ E.coliÂ in sufficient quantities and show thermal stability in temperature-dependent CD experiments comparable to wild-type protein (TmÂ > 90Â°C). HPLC-ESI-MS was used to confirm both the purity and the mass of the expressed mutants.Â Small-angle X-ray scattering confirmed that the mutant proteins were folded correctly and formed the expected compact globular structures while high resolution crystallographic data that has been obtained for A23R and K14E shows unexpected structures. Optical redox titrations have shown our ability to obtain reliable and reproducible data thereby allowing us to measure the effect of the mutations on the electrochemical properties of all 3 hemes and to understand the underlying principles and viability of different approaches in tuning relative heme redox potentials. Successful development of this project may lead to biological semiconductors with much smaller footprints and selectively tunable bandgap properties.

Experimental and Computational Studies of Obscurin's Flexibility

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Obscurin is a giant modular muscle protein that functions to connect the sarcoplasmic reticulum to the contractile apparatus. Obscurin is made up of multiple Ig domains in a chain connected by short linkers. Previous structural papers show that short linkers are less flexible, yet MD papers show these linkers to be very flexible. Our research reconciles these divergent data. Here, we test the flexibility of 5 dual obscurin domain systems. Using NMR and SAXS, we show that these domains all adopt an extended architecture. However, MD and SMD data demonstrate obscurin to be significantly flexible. Therefore, we believe obscurin to be an extended, flexible protein, despite its short linkers.

Examining Enzyme Infrastructure: Energetic Trade-Offs in a Histone Acetyltransferase, Gcn5

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Epigenetic control of proteins allows for several forms of gene expression at a much more efficient cost to the cell. For example, the acetylation of histone tails can allow DNA to become exposed, allowing a gene to be transcribed. The reaction is catalyzed by the enzyme, Gcn5. Past results suggest that the reaction proceeds via a tetrahedral, oxyanion intermediate stabilized by a hydrogen bond to a backbone cysteine residue. This stabilizing element falls into an enzymatic archetype known as an oxyanion hole, yet our simulations show that the oxyanion hole in Gcn5 does not display the same canonical characteristics. To determine the nature of this non-canonical interaction, we implemented static quantum mechanics/molecular mechanics (QM/MM) electronic structure calculations, and traditional molecular dynamics (MD). We propose that the observed interaction is the result of a trade-off between the energetics of catalyzing the reaction and orienting the necessary substrates.

Changes in Iron, Manganese, Copper, Zinc and Arsenic Levels Resulting From the Application of Poultry Manure to Agricultural Soils

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Use of poultry feed additive, roxarsone (4-hydroxy-3-nitrobenzenearsonic acid) has raised public concerns for the potential of arsenic concentration increase in agricultural soils. This study focused on quantitative metal content analysis of both poultry litter and treated agricultural soil. Six applications of poultry litter were made to a 2.0 ha field located in the Shenandoah Valley of Virginia, USA, between March 2007 and April 2014. The field was used as pastureland on an active farm. As a part of the study, copper, iron, manganese, zinc and arsenic concentrations in the poultry litter were measured and the application rate of these metals was calculated. The application rates were: Cu, 0.92-1.15 kg/ha, Fe, 28.37-35.46 kg/ha, Mn, 2.23-2.76 kg/ha, Zn, 1.27-1.59 kg/ha, and As, 0.010-0.013 kg/ha. Twelve surface and subsurface soil samples were taken from the treated field in February 2016. Twelve samples were also taken from a control site adjacent to the treated field. The control site has only been used for forestry and forestry products. Cu, Fe, Mn, Zn and As concentrations in the soil samples were determined by atomic absorption spectroscopy and the results of the chemical analysis were analyzed by ANOVA. Fe and Mn were depleted from the soil in the treated field, Cu and Zn levels increased over the seven years of treatment and grazing, and arsenic levels were unchanged in both the surface and subsurface soils between the control and the study site.

The Synthesis of Tetracationic Amphiphilic Viologens

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With a rise in antibiotic resistant bacterial strains, the demand for novel antimicrobial compounds has increased. The goal of this study is to produce a series of tetracationic amphiphilic viologen derivatives and to determine their antimicrobial properties. The synthesis of these compounds consists of two steps to produce a polycationic amphiphile. Preliminary data indicates that these compounds are effective against a variety of bacteria. Ongoing experiments include melting point temperature, mass spectrometry, 13C NMR, 1H NMR, critical aggregation concentration, time kill assays, and minimum inhibitory concentration studies. Understanding factors such as the head to tail interactions, flexibility of the compound, and the length of the tails and linkers within the compound will allow for even more effective antiseptics to be synthesized. The observed trends in time kill assays and minimum inhibitory concentration in relationship to amphiphile structure will be presented.

2018 Department of Chemistry and Biochemistry Student Award Winners

Amenta Award	Leanna Carter
R.D. Cool Award	Amy Fox
J.W. Chappell Scholarship	Tabitha Hain
Palocsay Award in Undergraduate Research	Nithesh Chandrasekharan
Service Award	Kearney Foss
J. W. Chappell Award	Tyler Palombo
American Institute of Chemists	Coleman Swaim
Degesch America Award	Olivia Lawson
ACS-Award	Hunter Wilson
Casali Scholarship (May, 2017)	Tyler Palombo
CRC First Year Student Award (April 2017)	Erin Krist
Outstanding Student Researcher Award	*to be announced*

American Chemical Society Divisional Awards

ACS Analytical	Melanie Odenkirk
ACS Environmental	Olivia Swahn
ACS Inorganic	Hunter Wilson
ACS Organic	Amber Harris
ACS POLYED Organic Award	Amy Fox
ACS Physical	Ryan Kelly

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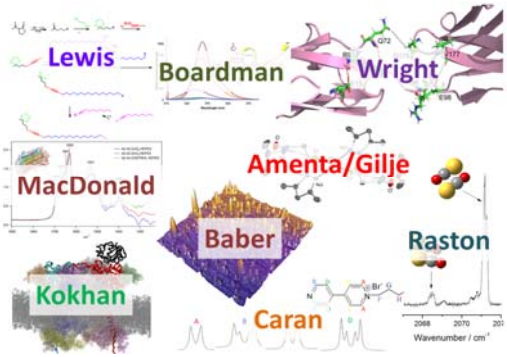

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