22nd MERCURY Conference on Computational Chemistry

University of California, Merced

July 14 – 19, 2024
Merced, CA

WELCOME

Welcome to the 22nd Mercury Conference on Computational Chemistry!

This conference is organized by the MERCURY (Molecular Education and Research Consortium in Undergraduate Computational ChemistRY) group, an organization of investigators at predominately undergraduate institutions, funded by a National Science Foundation NSF-MRI grant. The 2024 meeting features an outstanding group of speakers and more than 70 student poster presentations. Undergraduate students will have opportunities to learn about the breadth of research being conducted in the field, and students and faculty will be able to meet and discuss their work with other computational chemists.

This year's conference is sponsored and hosted by the UC Merced Graduate Division, School of Natural Sciences, and Department of Chemistry & Biochemistry. Graduate Dean Hrant Hratchian joins our UC Merced chemical theory and computation faculty colleagues in welcoming you to our campus! You can learn more about their research and graduate education at UC Merced by visiting https://graduatedivision.ucmerced.edu and https://cccat.ucmerced.edu.

We are also continuing MERCURY's partnership with the Molecular Sciences Software Institute (MolSSI). This year, the MolSSI workshop will provide more than 50 students with an exceptional opportunity to develop programming and collaborative software development skills.

We are grateful for our sponsors, who have made this meeting possible. Please, visit the sponsorship page to see a listing and links to all of the sponsors at https://graduatedivision.ucmerced.edu/mercuryconsortiumconference2024.

After the conference, we will ask for your feedback via a web survey to help us improve the conference. We hope you will take the time to respond to the survey. If you have any questions or problems, please contact:

Important Contacts

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Korynn Maravilla, Community Engagement Coordinator – 209.631.5057
Alex Navarro, Events Specialist – 209.261.2989

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MERCURY CAMPUS MAP

1. Campus Entrance
2. Parking – Bellevue Lot
3. Housing – Tenaya Building
4. Dining M/T/TH/F – Pavilion Dining Center
5. Dining W – Yablokoff Wallace Dining Center (YWDC)
6. MolSSI Workshop (July 15th & 16th) – Granite Pass 110
7. Opening Reception (July 17th) – Conference Center
8. Outdoor Game Night (July 17th) – University Plaza Lawn
9. MERCURY Conference (July 18th & 19th) – ACS 120
10. Poster Sessions (July 18th) – KL 355
11. Night at the Movies (July 18th) – ACS 120

MERCURY Consortium Members

2001
George Shields – Furman University
Maria Gomez – Mount Holyoke College
Carol Parish – University of Richmond

2008
Maria Nagan – SUNY, Stony Brook
Kelling Donald – University of Richmond
Adam Van Wynsberghe – Hamilton College

2012
Kelly Anderson – Roanoke College
Sudeep Bhattacharyay – U. of Wisconsin-Eau Claire
Jim Phillips – U. of Wisconsin-Eau Claire
Aimée Tomlinson – U. of North Georgia

2016
Chrystal Bruce – John Carroll University
Bill Miller – Truman State University
Joshua Schrier – Fordham University
Ashley Ringer McDonald – Cal Poly San Luis Obispo
Juan Navea – Skidmore College
Isaiah Sumner – James Madison University
George Barnes – Illinois State University

2018
Heidi P. Hendrickson – Lafayette College
Kedan He – Eastern Connecticut State University
Aurelia Ball – Skidmore College
Joseph Baker – The College of New Jersey

2019
Robert Berger – Western Washington University
Clyde Daly – Haverford College
Casey Londergan – Haverford College
Tyler Luchko – California State University Northridge
Lindsey Madison – Colby College
Simba Nkomo – Oxford College Emory
Paul Nerenberg – Claremont McKenna College
Caitlin Scott – California State University LA

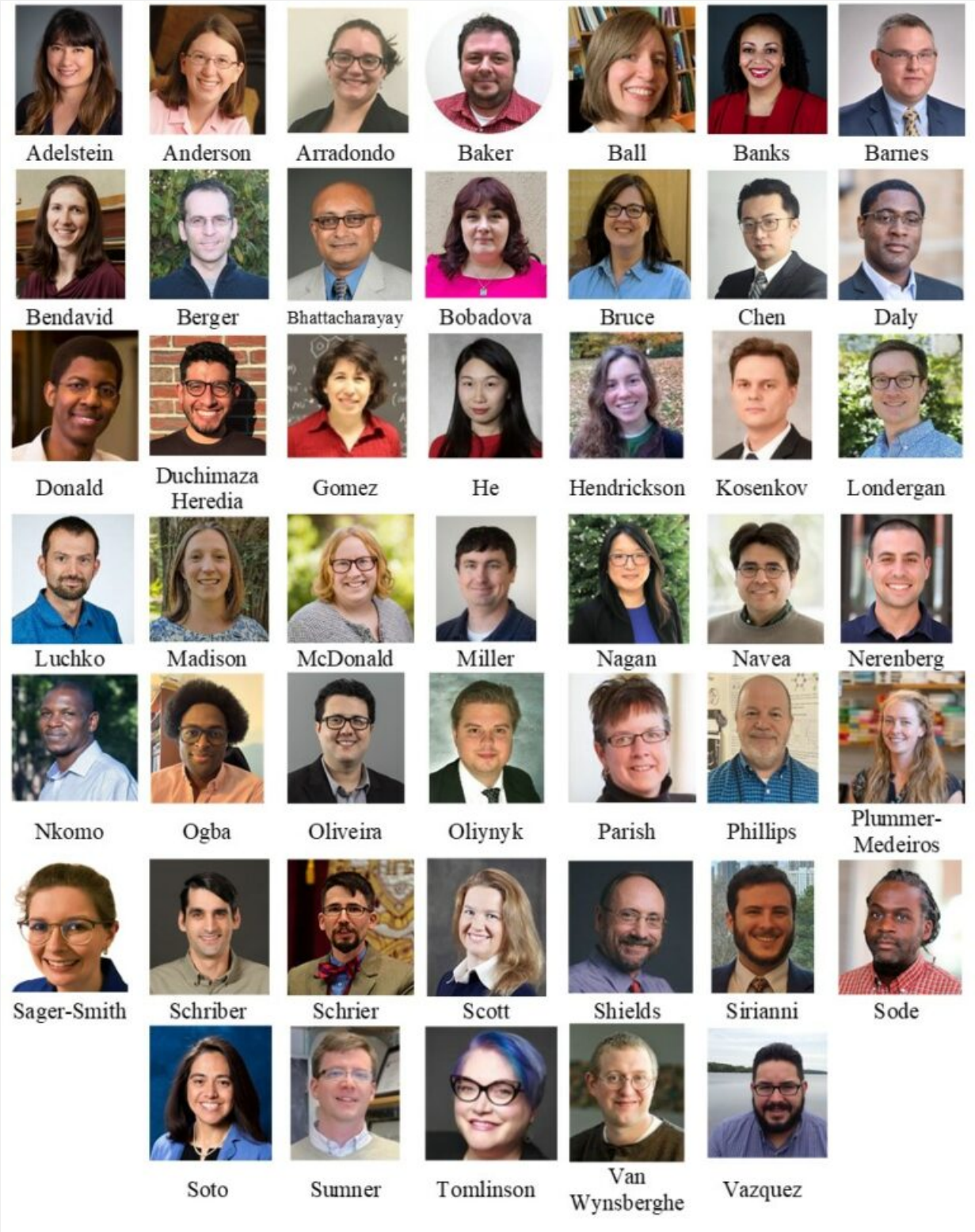
Olaseni Sode – California State University LA
Patricia Soto – Creighton University

2022
Nicole Adelstein – San Francisco State University
Lori Banks – Prairie View A&M University
Leah I. Bendavid – Vassar College
Petia Bobadova – Appalachian State University
Juan Duchimaza Heredia – Emmanuel College
Ashlee M. Plummer-Medeiros – Bryn Mawr College
Maduka Ogba – Chapman University
Luiz Oliveira – Mount Vernon Nazarene University
Leeann Sager-Smith – St. Mary's College
Jeff Schriber – Iona College
Dom Sirianni – Daemen College
Frank Vazquez – St. John's University

2024
Thais Scott – Bowdoin College

Others
Steve Young, SlyMedia and Redline Performance Solutions, HPC System administrator and research support specialist

MERCURY CONFERENCE MEMBERSHIP



MolSSI Workshops

Molecular Sciences Software Institute (MolSSI) is pleased to announce a workshop for MERCURY attendees to learn skills relevant for computational molecular science research. During the workshop participants will have the opportunity to write programs and work in a collaborative software development environment. The topic for this year's MolSSI workshop is cheminformatics, including molecular representations, molecular descriptors, and building models. Students attending the workshop will learn to use the python cheminformatics library RDKit and build models using scikitlearn. Prior experience with Python programming is assumed, equivalent to the MolSSI Python Scripting workshop.

MolSSI Guest Instructor

Dr. Jessica Nash (The Molecular Sciences Software Institute) will lead you through hands-on exercises and calculations.

Speaker	Institution	Contact
	**Dr. Jessica Nash** The Molecular Sciences Software Institute	jnash@vt.edu

MOLSSI SCHEDULE

Sunday, July 14, 2024

10:00 am – 6:00 pm	MolSSI Check – In Location: Tenaya Room 190
11:00 am – 3:00 pm	Lunch Service Hours Location: Pavilion Dining Center
4:00 – 9:00 pm	Dinner Service Hours Location: Pavilion Dining Center

Monday, July 15, 2024

MolSSI Workshop Day 1 Sessions
Location: Granite Pass 110

7:00 – 9:00 am	Breakfast – [Service Hours 7:00 – 10:30 am] – Pavilion Dining Location: Pavilion Dining Center
9:30 – 10:45 am	Python Primer and Introduction to molecular representations
10:45 – 11:00 am	Break
11:00 am – 12:00 pm	Introduction to RDKit molecules
12:00 – 1:30 pm	Lunch – [Service Hours 11:00 am – 3:00 pm] Location: Pavilion Dining Center
1:30 – 2:15 pm	Cheminformatics: Molecular Similarity Measures
2:15 – 3:00 pm	Cheminformatics: Molecular Descriptors
3:00 – 3:30 pm	Coffee & Snack Break
3:30 – 4:45 pm	Fitting a Linear Model with SciKit Learn
6:00 – 7:30 pm	Dinner – [Service Hours 4:00 – 9:00 pm] Location: Pavilion Dining Center

Tuesday, July 16, 2024

MolSSI Workshop Day 2 Sessions
Location: Granite Pass 110

7:00 – 9:00 am	Breakfast – [Service Hours 7:00 – 10:30 am] Location: Pavilion Dining Center
9:00 – 10:30 am	Python Data Science Libraries: Pandas and Seaborn
10:30 – 10:45 am	Break
10:45 – 11:45 am	Exploring Data using Data Science Libraries
11:45 am – 1:00 pm	Lunch – [Service Hours 11:00 am – 3:00 pm] Location: Pavilion Dining Center
1:00 – 3:00 pm	Model Fitting with SciKit Learn: Part 2
3:00 – 3:30 pm	Coffee & Snack Break
3:30 – 3:45 pm	Closing
4:00 – 9:00 pm	Dinner Service Hours

MERCURY CONFERENCE SCHEDULE

Lunch Service Hours [11:00 am – 3:00 pm]

Wednesday, July 17, 2024

8:00 am – 6:00 pm	Pick Your Own CA Adventure Day
11:00 am – 3:00 pm	Lunch Available Location: YWDC
6:30 – 8:30 pm	MERCURY Opening Dinner Location: Lakireddy Grand Ballroom (Conference Center)
7:30 – 8:30 pm	MERCURY Faculty PI Meeting Location: Conference Center – 110
8:30 – 10:30 pm	Faculty Dessert Social Location: Conference Center Patio
8:30 – 10:30 pm	Student Activity & Dessert Location: University Plaza Lawn
10:30 pm	Day Ends

Thursday, July 18, 2024

MERCURY CONFERENCE Meeting
Day 1 Sessions
Location: Arts and Computational Sciences Building (ACS) 120

7:00 – 8:30 am	Breakfast – [Service Hours 7:00 – 10:30 am] Location: Pavilion Dining Center
8:30 – 8:45 am	Opening Remarks Location: ACS 120
8:45 – 9:45 am	Daniel Crawford *The Mysteries of Chirality, Solvation, and Optical Activity* Location: ACS 120

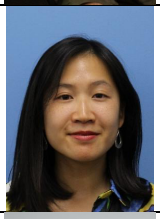
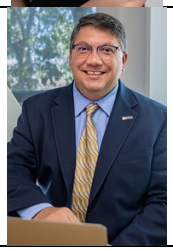
9:45 – 10:45 am	Aurora Pribam-Jones *Stretching, Squeezing, Heating, Cooling: Using the Adiabatic Connection to Learn About Electronic Interaction* Location: ACS 120
10:45 – 11:00 am	Coffee Break Location: ACS 120
11:00 am – 12:30 pm	Student Lightening Talks Location: ACS 120
12:30 – 12:45 pm	Group Picture Location: [TBD]
12:45 – 2:00 pm	Lunch – [Service Hours 11:00 am – 3:00 pm] Location: Pavilion Dining Center
2:00 – 3:00 pm	Poster Session 1 Location: Kolligian Library (KL) – 355
3:00 – 4:00 pm	Poster Session 2 Location: KL 355
4:00 – 4:30 pm	Hydration Break Location: Walk back to ACS 120
4:30 – 5:30 pm	Dean Tantillo *Dynamic Effects on Organic Reactivity – Pathways to and from Discomfort* Location: ACS 120
6:00 – 8:00 pm	Dinner – [Service Hours 4:00 – 9:00 pm] Location: Pavilion Dining Center
8:00 – 10:30 pm	Student Activity – Night at the Movies Location: ACS 120 **Doors open 8pm, movie starts 8:30pm
10:30 pm	Day Ends

Friday, July 19, 2024

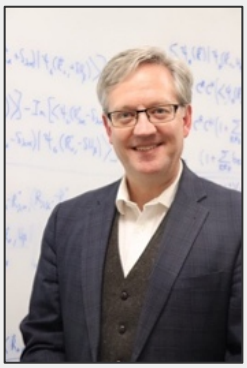
MERCURY CONFERENCE Meeting
Day 2 Sessions
Location: Arts and Computational Sciences Building (ACS) 120

7:00 – 9:00 am	Breakfast – [Service Hours 7:00 – 10:30 am] Location: Pavilion Dining Center
9:00 – 10:00 am	Mai-Anh Ha *Mechanistic Implications of the Heterogeneous Surface in Renewable Energy* Location: ACS 120
10:00 – 11:00 am	Caitlin C. Bannan *Modeling Small Drug Molecules and The Winding Career Path that Got Me Here* Location: ACS 120
11:00 – 11:30 am	Coffee Break Location: ACS 120
11:30 am – 12:30 pm	Hrant P. Hratchian *Modeling Electron Detachment Spectroscopy With Self-Consistent Field Methods* Location: ACS 120
12:30 – 1:30 pm	Lunch – [Service Hours 11:00 am – 3:00 pm] Location: Pavilion Dining Center
12:30 – 2:30 pm	Conference Check-Out Location: Tenaya 190

Conference Keynote Speakers

Speaker	Name/Title	Institution/Contact
	**Daniel Crawford** Professor Director, The Molecular Sciences Software Institute Ethyl Chair of Chemistry Deputy Editor, Journal of Physical Chemistry A	Virginia Tech Department of Chemistry crawdad@vt.edu
	**Aurora Pribam-Jones** Assistant Professor	University of California Merced Chemistry & Biochemistry apribam-jones@ucmerced.edu
	**Dean Tantillo** Professor	University of California Davis Dept of Chemistry dtantillo@ucdavis.edu
	**Mai-Anh Ha** Researcher III Computational Science	National Renewable Energy Laboratory
	**Caitlin C. Bannan** Lead Scientific Software Developer	OpenEye Scientific Software [email]
	**Hrant Hratchian** Professor, Vice Provost, Graduate Dean	University of California Merced Dept of Chemistry & Biochemistry and Graduate Division hhratchian@ucmerced.edu

SPEAKER ABSTRACTS



The Mysteries of Chirality, Solvation, and Optical Activity

Daniel Crawford
Professor, Director, Editor
Department of Chemistry
Virginia Tech University

The determination of the "handedness'" of chiral compounds remains a fascinating and critical challenge in which theory and computation play a vital role. In the effort to assign the absolute stereochemical configurations of chiral isolates, quantum chemical models have the potential to provide experimentalists with robust predictions of the requisite spectroscopic signatures, such as specific rotation, circular dichroism rotatory strengths, Raman scattering circular intensity differences, and more.

However, such properties are among the most challenging to simulate because of their delicate dependence on a variety of intrinsic and extrinsic factors. Solvent effects, for example, not only dramatically expand the complexity of the simulation, but can sometimes even alter the sign of the chiral response. In this lecture, I will discuss recent efforts in my group toward the goal of developing reliable theoretical predictions of chiroptical properties, including the exploration of reduced-scaling methods, a variety of implicit and explicit solvation models, and even explicitly time-dependent quantum dynamics.

Stretching, Squeezing, Heating, Cooling: Using the Adiabatic Connection to Learn About Electronic Interaction

Aurora Pribam-Jones
Assistant Professor
Chemistry and Biochemistry
UC Merced

In this talk, I will provide a brief overview of thermal and ensemble density functional theories, starting from the ground-state version of DFT and noting how the theories are similar and where they must be different. I will then focus on the interplay between ensemble weightings, interaction strength, and density dependence in density functional theories, particularly in how they influence the adiabatic connection and its connection to fundamental properties of matter and their limits. I'll close with some stories about how we use these tools to analyze the way electrons interact in different situations and tie these ideas back to the pursuit of fusion as an energy source and how to flip DFT on its head for a new perspective.

Introductory/pedagogical: DFT, Thermal DFT, Ensemble DFT

More recent work: DFT and Hartree-Fock, Thermal DFT, Ensemble DFT.

Dynamic Effects on Organic Reactivity – Pathways to and from Discomfort

Dean Tantilllo
Professor
Department of Chemsitry
University of California, Davis

Computational studies highlighting the importance of accounting for dynamic effects on organic reactivity will be discussed, along with descriptions of the factors that led me – as an organic chemist – to pursue these projects.

Discomfort.JPOC21

Entropy.JACS22

BeyondTST.AdvPOC21

Mechanistic Implications of the Heterogeneous Surface in Renewable Energy

Mai-Anh Ha
Researcher III
Computational Science
National Renewable Energy Laboratory

Platinum Group Metals (PGM) such as Pt- and Ir-based catalysts remain the baseline catalysts for fuel cells and electrolyzers, often offering the greatest balance of activity and durability with >60% efficiency; these catalysts are also prohibitively expensive with Ir being even more precious than Pt, costing up to 5x more than Pt at >$$160/g. Fundamental understanding of how intrinsic material properties arise from the frequently non-equilibrium surface morphology of catalyst materials can allow us to identify how to optimize both well-known and developing materials. In particular, theoretical understanding of mechanistic trends can allow for the nuanced development of low PGM or earth-abundant catalysts to replace typical PGMs. The interplay of facet dependence and redox conditions leading to mixed-metal and mixed metal-oxides combined with the many possible adsorption configurations of reaction intermediates can result in unique catalytic properties such as lowered activation barriers and bonding motifs. Rather than catalytic properties being defined by a single intermediate evolving under one mechanistic pathway, the statistical ensemble of accessible intermediates more accurately reflects a material's catalytic properties to evolve products along multiple pathways. As theory approaches more realistic surface heterostructures and captures the multiplicity of adsorption configurations and sites, it can complement, inform, and even predict macroscopic properties observed in experiment: case studies include Borated-Pt7 for selective dehydrogenation[1,2], Pt-Ni nanomaterials[3,4], and Ir/IrO2 architectures[5,6], and NiO/doped-NiO alternatives.

References: [1] Ha, M.-A.; Baxter, E. T.; Cass, A. C.; Anderson, S. L. ; Alexandrova, A. N. J. Am. Chem. Soc., 2017, 139, pp. 11568–11575 [2] Baxter, E. T.*; Ha, M.-A.*; Cass, A. C.; Alexandrova, A. N.; Anderson, S. L. ACS Catalysis, 2017, 7, pp. 3322-335.. [3] Alia, S. M.; Ngo, C.; Shulda, S.; Ha, M.-A.; Dameron, A.; Weker, J. N.; Neyerlin, K. C.; Kocha, S. S.; Pylypenko, S.; Pivovar, B. S. ACS Omega, 2017, 2, pp. 1408-1418. [4] Alia, S. M.*; Ha, M.-A.*; Ngo, C.; Anderson G. C.; Ghoshal, S.; Pylypenko, S. ACS Cat., 2020, 10, pp. 9953-9966. [5] Alia, S. M.*; Ha, M.-A.*; Anderson G. C.; Ngo, C.; Pylypenko, S.; Larsen, R. J. Electrochem. Soc., 2019, 166, pp. F1243-1252 [6] Ha, M.-A.; Larsen, R.; J. Electrochem. Soc., 2021, 168, pp. 024506.

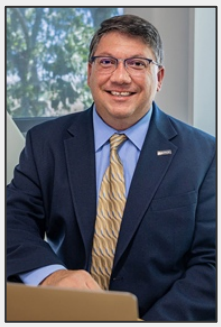
Modeling Small Drug Molecules and The Winding Career Path That Got Me Here

Caitlin C. Bannan
Lead Scientific Software Developer
OpenEye, Cadence Design Systems

Today, I am a Lead Scientific Software Developer at OpenEye, Cadence Design Systems. However, if you told me that in 2012 when I finished my BS in chemistry, I wouldn't have believed you. In this presentation, I will share my winding career path including an early dream of teaching high school science, work in inorganic and radiochemistry laboratories, to the decision to pursue a PhD in computational chemistry, and how that got me to OpenEye [1]. This journey will include my graduate research at the University of California, Irvine with David Mobley, and the Open Force Field Consortium (OpenFF) [2]. OpenFF's close connections with the pharmaceutical industry helped shape my goal to pursue a career in industry after school. In my job now, I have had the opportunity to build and manage quantum chemical (QC) workflows on Orion, OpenEye's cloud platform for drug discovery [3] and contribute to important research into small molecule crystal structure prediction [4]. Throughout this presentation I'll include an overview of the scientific research I've contributed too. This will include my work on cheminformatics fits into force field development and how my work on small molecule crystal structure prediction and QC calculations impacts the drug discovery pipeline.

Citation and context for each reference:

1. Ruggiu, F., Bannan, C. & Bootsma, A. Early Career Perspectives from Large Pharma, Software, and Start-up Companies. J. Chem. Inf. Model. 62, 2631–2638 (2022). Doi: 10.1021/acs.jcim.1c01416 This is a summary of different computational jobs written by members of the JCIM early career board. Our aim was to help provide the perspective on different industries that we wished we'd had when looking for work after our PhDs.
2. Mobley, D. L. et al. Escaping Atom Types in Force Fields Using Direct Chemical Perception. J. Chem. Theory Comput. 14, 6076–6092 (2018). doi: 10.1021/acs.jctc.8b00640 This is an overview paper of Open Force Field's work. It contains a lot of details about force fields, most of which is more detailed than I will get into in this presentation.
3. Sørensen, J. et al. Orion ® A Cloud-Native Molecular Design Platform. in Computational Drug Discovery (eds. Poongavanam, V. & Ramaswamy, V.) 579–615 (Wiley, 2024). doi:10.1002/9783527840748.ch24. This is OpenEye's contribution to the book Computational Drug Discovery. This work focuses on the impact of cloud computing in the pharmaceutical industry. It is more detail than I would cover in this presentation.
4. Bannan, C et al. Crystal Structure Prediction of Drug Molecules in the Cloud: A Collaborative Blind Challenge Study. Under Review White paper with the same methods as the one under review: Using Computational Crystal Structure Prediction (CSP) to Optimize Small Molecule Drug Formulation The white paper includes a good high level view of OpenEye's approach to computational small molecule crystal structure prediction. I can share the link to the paper when it is published, but will be more technical.



Modeling electron detachment spectroscopy with self-consistent field methods

Hrant P. Hratchian
Professor, Vice Provost, Graduate Dean
Department of Chemistry & Biochemistry
University of California, Merced

Photodetachment spectroscopy is a highly effective experimental tool for exploring structure. Critically, assignment of these spectra requires corroborating theoretical and computational analysis. In this talk, I will describe some of the theory and methods advancements my group has made to expand the computational toolbox for modeling anion photoelectron spectroscopy. I will also describe our group's efforts to develop new efficient methods for treating complicated electronic structures and qualitatively identifying the nature of detached electrons.

STUDENT ABSTRACTS

Poster Session 1 – Abstracts 1 – 36

Enhancing Hydrophobic Interactions in Sorafenib for Improved Binding Affinity to Target Enzymes in Modern Enzyme-Substrate Modeling Software

Kien Ngo (Dickinson College) & Hovhannes J. Gukasyan, PhD (University of Southern California)

Sorafenib is a pivotal targeted therapy in treating late-stage kidney, liver, and thyroid cancers, acting through the inhibition of c-Raf-1, a serine/threonine Raf kinase, effectively suppressing tumor-promoting gene transcription. While it stands as a primary treatment option for hepatocellular carcinoma, its commendable 10-month median overall survival is counterbalanced by substantial side effects and the common development of drug resistance. Consequently, the research focus has been directed toward the development of Sorafenib analogs with improved efficacy and safety. The emergence of modern and advanced molecular docking software has expedited the screening process by detecting cavities and simulating molecular interactions. Our research strategically employed CB-Dock 2.0 (Liu et al. 2022); an automated docking tool designed to calculate Vina scores—a weighted sum of molecular interactions—with lower scores indicative of stronger binding. We modified Sorafenib analog side chains to increase hydrophobic interactions with amino acid residues composing the c-Raf-1 cavity and generated Vina score using crystal structure of c-Raf-1 (3OMV) (Hatzivassiliou et al. 2010) and the crystal structure of the general kinase domain 4ASD (McTigue et al. 2012), yielding a Vina score 3 kJ/mol lower than the original. More significantly, the modified drug adhered to all of Lipinski's Rule of Five, suggesting a potential for oral bioavailability. There was an observed direct correlation between Vina scores from post-model and published IC_{50} values (Lowinger et al. 2002), suggesting the potential for a mathematical formula linking these parameters. Our next step involves refining and empirically validating this formula with our redesigned drug candidate.

Madison Martin

In atomic and molecular cluster systems, there are often steep potential energy barriers that are difficult to overcome in computer simulations. It is of interest to explore new computational methods to improve the efficiency of overcoming these barriers. In my work, I am studying the Ar_{13} cluster described by a pairwise additive Leonard-Jones potential, with parameters appropriate for argon. This system was chosen because it undergoes a sharp solid-to-liquid phase transition. I wrote a flexible computer program using Python for Monte Carlo simulations of clusters and applied it to the 13 argon atom cluster. I included a repulsive sphere to suppress evaporation. Then, I investigated parallel tempering as a means for facilitating overcoming the potential energy barriers in 3-dimensional space. Theoretically, you can use a 4th dimension to get around barriers in 3-dimensional space, which is the next strategy I will be exploring.

Investigation of the role of the N-terminus of YebS on lipid-protein interactions

Abigail Champlin[1] and Ashlee M. Plummer-Medeiros[1]

[1] Bryn Mawr College

Gram-negative bacteria contain both an inner and outer membrane and bacterial growth relies on the efficient transport of phospholipids to the outer membrane. In *Escherichia coli* there are two known protein complexes involved in lipid transfer (*i.e.,* PqiABC and YebST). This research will be focused on the YebST complex: YebS is an inner membrane protein while YebT, also known as LetB, is the periplasmic bridging protein which physically connects the two membranes. The goal of this research is to investigate possible interactions between YebS and phospholipids at an atomic level through molecular dynamics (MD) simulations using the predicted structure of YebS from AlphaFold. YebS has an unstructured N-terminal extension that is approximately 27 amino acids. MD simulations of YebS in a phospholipid bilayer have shown that the N-terminal extension adsorbs to the cytosolic region of YebS and potentially contacts the phospholipid bilayer. Additionally, these simulations have revealed that the interactions between the N-terminal extension and the cytosolic regions of YebS, as well as the phospholipid bilayer, are variable between replicates. Additional simulation systems will be built to further investigate the interactions between the YebS N-terminal extension, the phospholipid membrane, and the cytosolic regions of YebS.

Investigation of electrostatic interactions of membrane proteins and lipids

Sachiko Bower, Suli Kamholtz-Roberts, Ashlee Plummer-Medeiros (Bryn Mawr College)

YebS is a protein found embedded in the inner membrane of *E. coli* and other Gram negative bacteria, that is associated with the transport of phospholipids from the inner to the outer membrane. The details of YebS-phospholipid interactions that are involved with lipid trafficking have not been widely studied, and the structure of YebS remains unsolved. This project will investigate the roles of highly conserved polar and charged residues within the transmembrane domains of YebS, which may contribute to the substrate binding site. Using an AlphaFold predicted structure of the protein, simulation systems will be constructed to investigate these key interactions of YebS with membrane phospholipids. Lipid-protein interactions will be characterized by lipid residence time, bond distance, lipid specificity, and type of interaction, using computational analyses. Bulk and bound lipids will be characterized by order parameters and lipid tilt angles. In addition to the analysis of wild type YebS, simulations with proteins modified at the aforementioned residues will be constructed to observe lipid interactions without key amino acids present. This computational work will be complemented with a biochemical transfer assay in which YebS will be reconstituted into synthetic vesicles, which mimic the bacterial membranes, and the lipid transfer between vesicles will be measured to determine the role it plays in lipid trafficking. Mutated YebS proteins will be reconstituted into this assay to confirm predictions from simulations. This determination of the mechanism of substrate selection will assist in the characterization of protein function that are critical to bacterial survival, contributing to the field's understanding of bacterial life.

Computational Study of Substituents on Neighboring Group Stabilized Oxenium Ions

Melinda Amick, Brandon E. Haines

Westmont College, Santa Barbara, CA 93108

Aryloxenium ions (or aryloxylium ions) are hypovalent oxygen cations that are a potential source of electrophilic oxygen. They are stabilized through resonance with an adjacent aromatic ring which leads to mixtures of O- and C-functionalization products. A promising alternative approach to stabilizing the aryloxenium ions is through coordination a Lewis basic neighboring group. This computational study systematically investigates the effect of a diverse set of electronic substituents on i) the aryloxenium ring and ii) a pyridine neighboring group (NG) on the formation and stability of the NG-coordinated aryloxenium ion. Data were collected at the B2PLYPD3/def2-TZVPP//B3LYP/6-31G(d) level of theory with a PCM solvent model. For most of the substituents, the NG-coordinated aryloxenium ion is more stable than the uncoordinated (or resonance stabilized) aryloxenium ion with modest variation in the energetics. Electron donating groups in the *para*-position of the aryloxenium ions tended to stabilize the uncoordinated aryloxenium more than other positions. In addition, electron withdrawing groups in the *ortho*-position of the pyridine NG tended to weaken the stability of the NG-coordinated aryloxenium ion the most. These findings increase our knowledge of the role of substituents in affecting the stability of aryloxenium ions. Applications of these findings to the C–H insertion reactivity of oxenium ions will also be addressed.

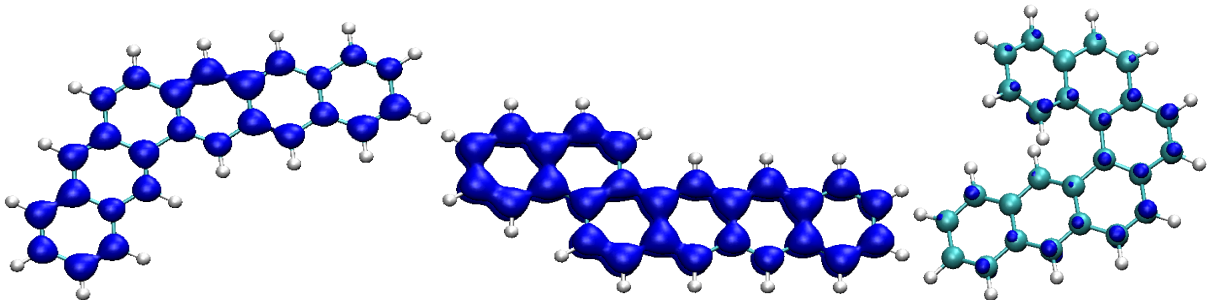
A Theoretical Study of Singlet Fission Properties of Acene Isomers

Liam Bowman and Dr. Jeffrey Schriber
Iona University
MERCURY 2024

Abstract

A major problem that not only the United States, but the world faces is that of renewable energy. Energy sources like coal, oil and gas are harmful to the environment and non-renewable, and one of the most promising of those alternatives is solar energy. Solar energy is currently not efficient enough to completely replace non-renewable energy sources, and our goal is to better understand the properties of materials that can make solar energy harvesting more efficient.

The focus of this research is on molecules that potentially undergo singlet fission, an electron excitation phenomenon. Singlet fission is often exhibited in large, conjugated hydrocarbons, including acenes. Acenes, particularly tetracene, pentacene, and hexacene serve as model compounds for understanding singlet fission processes by theoretical means. What has not been investigated as much are structural isomers of these acenes, specifically hexacene, a chain of 6 benzene rings. In linear hexacene, the stability of the molecule and the singlet fission properties are greatly influenced by the aromaticity of the molecule and by the biradicaloid character that is present. In our study, we create seven distinct isomers where we systematically introduce different numbers of turns and directions of these turns. We investigate how these structural changes effect stability of the ground state, the singlet triplet gap, and the biradicaloid character. Calculations are run using ACI-DSRG-MRPT2 and ωB97x, MP2, and various coupled cluster approximations to compare the singlet triplet gap to that of hexacene. To be an efficient replacement for the current solar cell material the singlet triplet gap needs to be within an optimal window. With the singlet triplet gap in this window then a single excitation can yield the most electrical energy making the solar cells as efficient as possible. One possible drawback of using these hexacene isomers is their emergent radicaloid character. These molecules' unpaired electrons could cause the molecules to be too unstable for practical use. Overall, the goal is to find either some particular isomers or some trend in topology that can point to a way to find more energetically desirable molecules for these solar cells. We find that the multireference methods predict a linear ground state, and that introducing turns increased energy without greatly affecting the radicaloid character. Calculations are run using the Psi4 and Forte software packages.



Unpaired Electron Densities for three example hexacene isomers.

Variational Preparation of Quantum State in a Superconducting Quantum Processor

Crystal Yeung[1], Benjamin Kuchma[2], Sean van Geldern[2], Chen Wang[2]
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Quantum computers have the potential to perform certain types of calculations significantly faster than classical computers. For example, in the fields of chemistry and molecular simulation, quantum computers can be utilized to find the eigenvalues of molecular Hamiltonian systems. The variational quantum eigensolver (VQE) is a leading method to find these eigenvalues by repeatedly preparing and measuring quantum states to find a way to minimize the measured energy. The control variational quantum eigensolver (ctrl-VQE) approach provides potential improvement over the standard VQE method by reducing decoherence errors in state preparation. Ctrl-VQE opts to variationally shape an arbitrary state preparation pulse to prepare quantum states. The advantage of ctrl-VQE lies in the increased speed of computing chemical simulations by switching to short arbitrary pulses instead of relying upon a quantum circuit-based approach. Through the usage of Qutip, a Python package, the creation of these cavity states is simulated and then compared to a physical superconducting qubit and microwave setup. Eventually, a full physical simulation of a hydrogen molecule will be possible. Further applications may expand to the simulation of other such molecules.

Greta Hightower

Abstract

Title: A Computational Hydropathy Analysis of Gram-negative bacterial Outer Membrane Protein (OMP) BamA and its mutants

Outer Membrane Proteins (OMPs) located in Gram-negative bacteria are of therapeutic interest. BamA is a transmembrane OMP of the β-barrel assembly machinery, the BAM complex. The BAM complex (consisting of four lipoproteins and BamA) is critical for vital cellular functions and is responsible for the integration and folding of the OMPs. BamA is an evolutionarily conserved central component of the BAM complex. It consists of 16 antiparallel β strands (385 amino acids in length), and past mutagenesis studies (hydrophilic to hydrophobic mutations and deletion mutants) on BamA and its mutants in Escherichia coli (*E. coli*) have identified key residues and/or regions critical for protein stability and bacterial growth. The hydropathy index is a valuable analytical tool for comprehending a protein's microenvironment and discerning subtle changes in its mutant's primary amino acid sequence, influencing the protein's three-dimensional topography, chemical properties, and biochemical activity. In this study, Molecular Dynamics (MD) simulations were employed to investigate the wild-type and six mutants of BamA, examining the hydropathy profile of each amino acid within each system. Our findings delineate the structural details and atomistic-level characteristics of the protein, revealing chemical changes in the microenvironment surrounding the mutation site(s). This insight offers a rationale for the potential causes of bacterial inactivity observed in the BamA mutants.

Using Machine Learning to Create a Potential Energy Surface for a Yttrium-Doped Barium Zirconate System with Oxygen Vacancies

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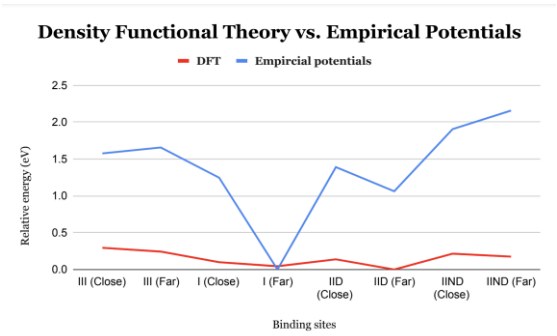
Yttrium doped barium zirconate is one of the most promising solid state proton conductors. One possible way of increasing the proton conduction in yttrium doped barium zirconate is to introduce oxygen vacancies. These positive defects tend to localize near the dopant proton trap and in principle repel proton ions. Making the yttrium less of a trap could further speed proton conduction. While yttrium doped barium zirconate systems can be modelled effectively using ab initio methods, maintaining a small realistic percentage of oxygen vacancy defects necessitates using a larger simulation box. To test the proton conduction in this distorted lattice, rapid calculation of the potential energy is needed. While a least squares fit of *ab initio* energies to an empirical potential fit the individual energy points well [1], further optimization found a changed global minimum as seen in Figure 1(a). The proton minima prior to oxygen vacancy disruption are shown in Figure 1(b). This contribution uses the machine learning implementation in the Vienna Ab Initio Simulations Package (VASP) [2] to create a force field or potential energy using our database of structures and energies and new points generated using molecular dynamics. The force field will initially be trained and tested with proton sites and low energy paths for proton conduction in yttrium doped barium zirconate. Based on the revelations from this simpler case, the training set will either be expanded with or replaced by ab initio data for proton sites and minimum energy paths in the larger yttrium doped barium zirconate system with one oxygen vacancy. Having a PES for this system will allow future calculations to determine how these oxygen vacancies impact proton conduction.

a)



b)

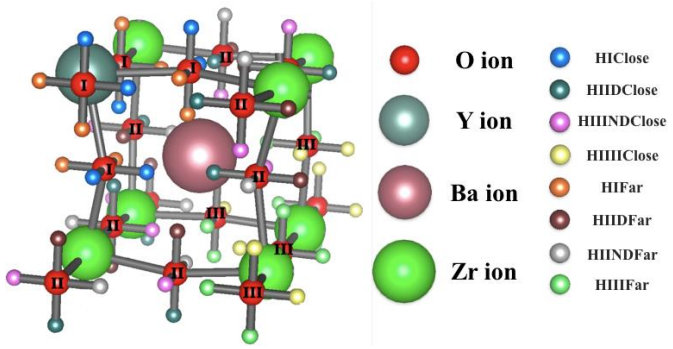


Figure 1. (a) shows the ab initio (DFT) energies calculated using VASP in red as well as the empirical potential energies after optimization. While the energies with optimized empirical parameters fit the VASP model well. Potential energy surface optimization shows changes in energies leading to a different global minimum. (b) shows the proton binding site locations without an oxygen vacancy.

[1] Personal communication with Shiuri Li from our research team.
[2] G. Kresse and J. Hafner, Phys. Rev. B 47 , 558 (1993); ibid. 49 , 14 251 (1994); G. Kresse and J. FurthmÃ¼ller, Comput. Mat. Sci. 6 , 15 (1996); G. Kresse and J. FurthmÃ¼ller, Phys. Rev. B 54 , 11 169 (1996).

Towards Practical Induced Subgraph Isomorphism with Multi-layer Gaussian Boson Sampling

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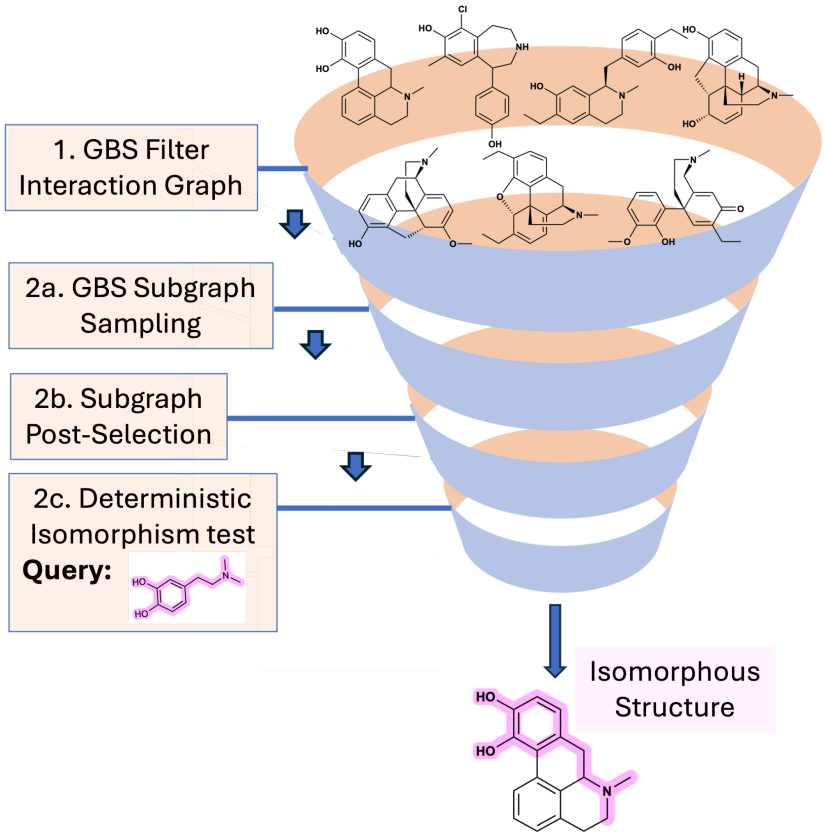
We introduce a multilayer Gaussian boson sampling methodology to tackle the induced subgraph isomorphism problem common to a wide range of applications, including molecular search, molecular docking, and retrosynthesis prediction. The proposed methodology is implementable on bosonic quantum devices using $O(n)$ photonic modes, where n is the number of nodes in each of the input graphs. Sampling can be performed with high-fidelity photon-number-resolving detectors, or cost-effective threshold detectors that work at room temperature, offering both practicality and efficiency.



Computational studies of the interactions between gold nanoparticles and cationic short-chain peptides

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Department of Chemistry and Biochemistry, California State University, Fresno

This research seeks to investigate the interactions between gold nanoparticles (AuNPs) and combinations of selected cationic amino acids: arginine (R) and lysine (K). All peptides investigated contain 1-2 of these amino acids connected to cysteine. The cysteine is used to provide a sulfur atom as it is known that sulfur and gold atoms form a strong covalent bond and it has also been suggested that van der Waals forces further enhance this bond. This research aims to understand how the interactions between AuNPs and the sulfur atom on the cysteine (C) residue are influenced by amino acids with cationic side chains by examining the effect of the sequence and the identity of the specific cationic amino acid. The methods initially used to examine such interactions were accomplished by geometry optimization using Hartree-Fock with the CRENBS basis set. Preliminary results suggest that the AuNP reacts too strongly with the peptides (sequences KKC, RKC, KRC) and will require stabilization with citrate or additional peptides as is the case in the experimental work on these systems. For sequences KKC and RKC the most common occurrences are destruction of the peptide backbone, CO_2 formation, episulfide formation, and interactions between the AuNP and nitrogen and oxygen. For KRC, the most common occurrence is CO_2 formation and destruction of the cysteine. Ongoing work using classical dynamics to provide initial minimization of the structures under more realistic conditions will provide additional insight into the structure of these nanoparticle and peptide systems.

Computational Modeling of a Series of Asymmetric Bis(BF_2) BODIPYs: BOPYPYs

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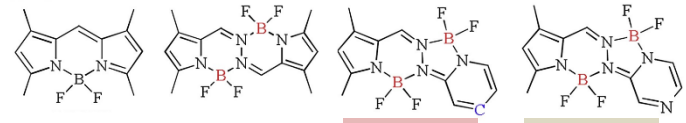
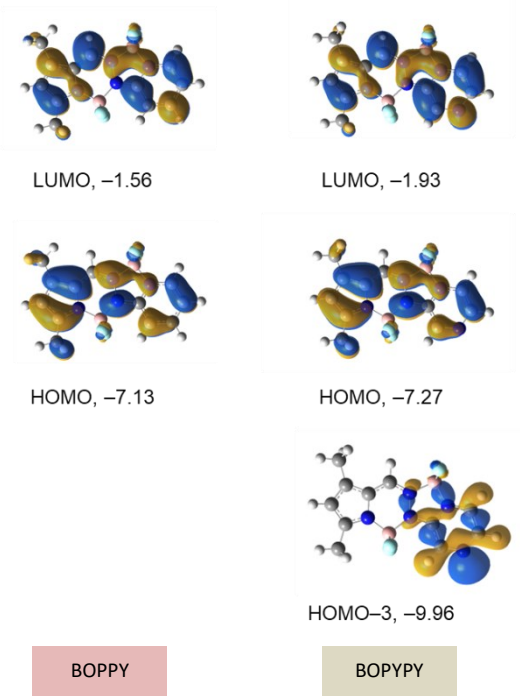
Among many heterocyclic chromophores with expansive biomedical and industrial applications, BODIPY dyes have received special focus in the field due to their advantageous photostability and relatively easy synthesis, structural modification, and tunable photophysical properties. BODIPYs have found diverse implementations, ranging from their use as photosensitizers in photodynamic therapy and biochemical labeling to optical devices and solar cells. BODIPY derivates bearing two BF_2 groups, such as the symmetric BOPHY, exhibit high fluorescence quantum yields and elevated photostability due to their rigid planar structures. Yet, some also exhibit self-quenching effects and limited solubility, resulting in reduced fluorescence quantum yields. Asymmetric derivatives such as BOPPY and BOPYPY were synthesized to address this issue.



BODIPY BOPHY BOPPY BOPYPY

Herein, we report the results of a joint research project in which a series of asymmetric bis-BF_2 tetrafluorobenzo-[α]-fused BOPYPY dyes, synthesized by our collaborators, were modeled computationally to analyze and attempt to explain the experimentally observed regioselectivity toward nucleophilic substitution and the significant differences in the photophysical properties of the synthesized compounds. We analyze the effect of the substituents on the molecular properties of the series of compounds and we discuss the proposed explanation for the observed regioselectivity. We also present our hypothesis that could explain the lower fluorescence ability of BOPYPYs compared to previously synthesized compounds, BOPPYs.



Comprehensive Analysis of Solution Optimized Fentanyl and its Analogs in the Human μ-Opioid Receptor

Errin L. Reed, Kimberlyn McKnight, Audrey Ryu, George C. Shields
Department of Chemistry, Furman University, Greenville, SC 29613

Opioids are widely administered to treat acute and chronic pain; however, the abuse of prescription and illicit opioids is a major health crisis in the United States. The current concern is that the clinical efficacy of these drugs is limited by the capacity to develop tolerance and addiction. Yet, opioids are continued to be prescribed for their unrivaled ability to moderate severe pain. Fentanyl and its analogs are capable of binding at different receptor sites, which enables different receptor conformations and production of negative side effects. This study aims to fill the gap in the understanding of how known flexible opioid ligands, like fentanyl and its analogs, are arranged in solution to bind tightly into the human μ-opioid receptor (hMOR) and why fentanyl has different physiological effects. Therefore, we hypothesize fentanyl and its analogs will stabilize different conformations of the receptor in solution, such that the overall binding energy of the hMOR-ligand complex is optimized. Solution phase structures were optimized using the ωB97X-D density functional with the 6-31++G** basis set, and entropies were generated for each structure. DLPNO-CCSD(T)/cc-pVnZ (n=D,T,Q) model chemistry with a complete basis set extrapolation resulted in accurate relative Gibbs free energies at the DLPNO-CCSD(T)/CBS/SMD//ωB97X-D/6-31++G**/SMD level of theory. All structures were computed using the SMD implicit solvation model at 310.15 K to simulate biological conditions. Results of this study will illustrate how fentanyl and its derivatives are arranged in solution and their ability to stabilize the receptor in different conformations unique from pain modulation pathways. Future work includes employing Quantum Mechanics/Molecular Mechanics (QM/MM) to combine traditional methods of Molecular Dynamics simulations with highly accurate quantum calculations for specific parameters set in the binding pocket of the hMOR.

Computational Analysis of Information Transfer in Prostaglandin E_2 Receptors Using Molecular Dynamics Simulations

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[2]*Department of Chemistry, Lawrence University, Appleton, Wisconsin 54911, United States*

G-protein coupled receptors (GPCRs) are eukaryotic integral membrane proteins that regulate signal transduction pathways associated with human health and diseases, making them common drug targets. Activation by extracellular signals, e.g., ligand binding, induces conformational changes in GPCRs, triggering intracellular signaling cascades. In this work, computational chemistry is used to investigate information transfer between GPCRs and their coupled G-proteins. In particular, the interactions between G-protein alpha subunits ($G_{\alpha s}$, $G_{\alpha i}$, $G_{\alpha q}$) and four GPCRs in the E-prostanoid family: EP1, EP2, EP3, and EP4 are being investigated. Long timescale molecular dynamics (MD) simulations of EP receptors bound to each G-protein alpha subunit were carried out using AlphaFold and cryo-EM structural models. These simulations were prepared using LEaP, and were carried out using AMBER 22. Analysis of MD simulations using graph theory approaches provides essential information at the molecular level regarding protein-protein interactions, which will contribute to further advances in therapeutic development.

Don’t be so stiff: The role of histatin-5 in CS20 pilus dynamics

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Enterotoxigenic *Escherichia coli* (ETEC) is a bacterium that can lead to serious illness such as diarrheal disease, and a significant increase in mortality. For ETEC to reliably bind and infect a host, they utilize long protein filament appendages called pili. CS20, a specific type of pilus found on ETEC, is the primary focus of our current study. Specifically, we are investigating the interaction of a small antimicrobial peptide, histatin-5, with CS20 to determine its effect on CS20 biophysical properties. Experimentally it is known that histatin-5 causes CS20 pili to bundle together and become stiffer, however the molecular-scale origins of how this occurs is unknown. We address this question through molecular modeling and simulation. In our molecular models, we introduce multiple histatin-5 peptides into the accessible core of the CS20 helical filament to study the impact of the peptide on CS20 dynamics. The dynamics of the CS20/histatin-5 system are explored through molecular dynamics (MD) simulations and Steered Molecular Dynamics (SMD) using the AMBER software. Our simulations examine pilus extension in an aqueous environment, providing insights into how histatin-5 alters the dynamics of CS20 uncoiling under tensile force. Specifically, our SMD simulations help us determine what level of force CS20 is able to withstand in the presence of histatin-5. Future efforts will include applying our methodology to determine the dependence of filament stiffness on the presence of multiple histatin-5 (or histatin-5-like) peptides for a wider range of bacterial adhesion pili.

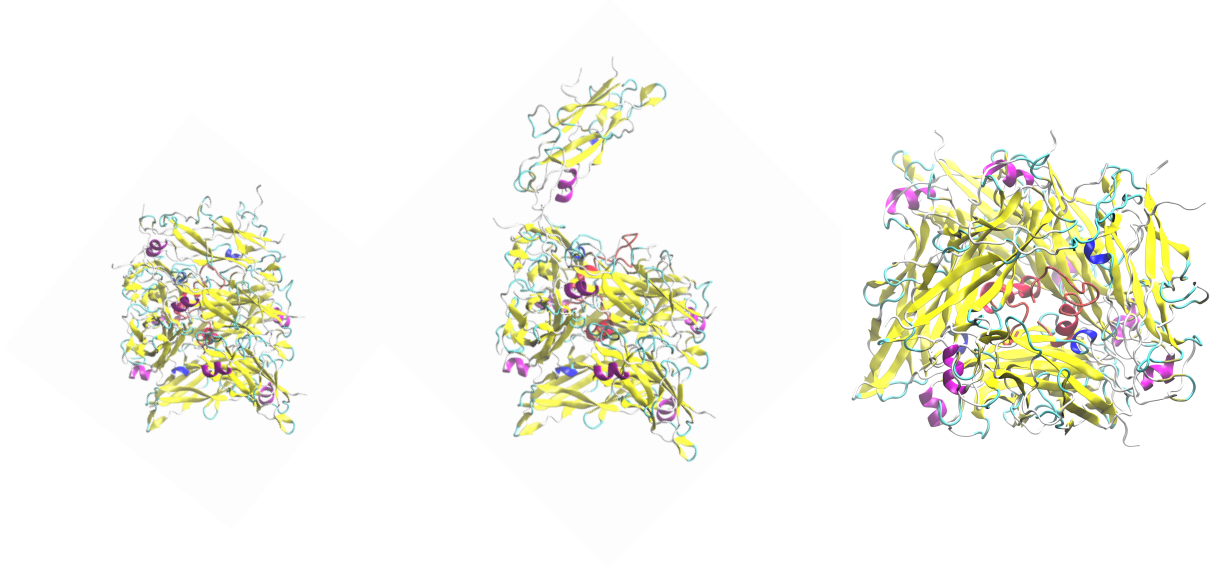

Figure: (Left) CS20 pilus filament model before steered MD. (Middle) CS20 pilus filament model after steered MD. (Right) View down center of CS20 pilus model showing histatin-5 peptides in central channel (red).

Investigating Ionomer-Electrolyte Interactions on the Catalytic Surface

Nina Borodin, Mai-Anh Ha
National Renewable Energy Laboratory

Hydrogen production is an important part of the clean energy transition. Anion exchange membrane (AEM) electrolysis can reduce hydrogen production cost and enable the use of earth abundant metals catalysts and other membrane electrode assembly components. However, these earth abundant metal catalysts may be sensitive to poisoning and degradation due to high pH conditions or ionomer interactions. The ionomer Nafion is commonly used in alkaline-based electrolyzers but its interactions with mixed-metal oxide catalysts are not well understood. Plane-wave density functional theory calculations are performed to gain insight into the binding strength of the Nafion functional group to Co_{sub}-NiO or Fe_{sub}-NiO catalysts. The adsorption energies and bader charge analysis of O*, OH*, SO_3*, and co-adsorbed SO_3* and OH* are evaluated to understand possible poisoning of active sites and the viability of mixed-metal oxide catalysts.

Phosphorylation influences the conformational dynamics of the disordered RNA Polymerase II C-terminal domain

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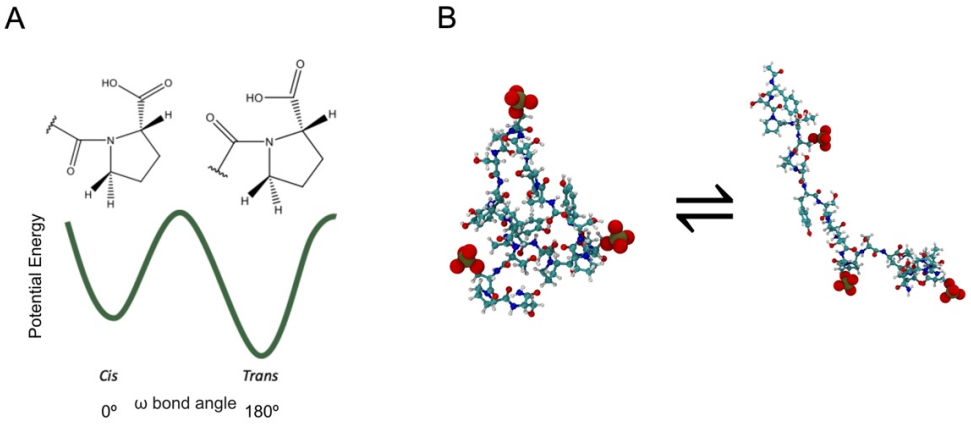
*Pennsylvania State University

Intrinsically disordered proteins (IDPs) play significant roles in cellular signaling due to their indiscriminate binding, rapid association kinetics, and propensity for post-translational modification of other biological structures. IDPs often harbor multiple diverse binding motifs, acting as "hubs" that integrate signals across various pathways, influencing complex processes such as RNA transcription. RNA polymerase II (Pol II) orchestrates DNA transcription into mRNA precursors, with its largest subunit featuring a disordered C-terminal domain (CTD) composed of a repeated heptad motif (TSPTSPS). Post-translational modifications of the CTD, notably serine phosphorylation, are key regulatory mechanisms of Pol II activity. Unlike most proteinogenic amino acids that predominantly adopt the energetically favorable -*trans* conformation, proline exhibits significant proportions in the -*cis* form. Interactions involving proline-rich motifs often exhibit conformational specificity dictated by the -*cis* or -*trans* isomer. However, observing the -*cis* conformation is difficult experimentally and computationally; NMR spectroscopy cannot directly observe proline residues since they lack an amide bond, and computational methods struggle to capture the transition between states since isomerization typically occurs on the timescale of seconds. To overcome the free energy barrier computationally, we employ Gaussian Accelerated Molecular Dynamics (GaMD) to artificially increase energy in the system. This study investigates proline residue omega angles of the Pol II structure obtained through simulations to discern their -*cis* or -*trans* configurations and compares residue contacts in phosphorylated versus unphosphorylated structures. Our findings reveal that serine phosphorylation induces a local turn, increasing the -*cis* state of the neighboring proline and leading to expansion of the CTD conformational ensemble. Understanding the conformational dynamics of IDPs and the impact of phosphorylation on Pol II's regulatory mechanisms provides crucial insights into the processes mediated by intrinsically disordered proteins.

Figure: A) Potential energy graph showing barrier height for isomerization. B) Conformations of CTD visualized.



GōMartini with a Twist: Coarse-Grained Modeling of Adhesion Pili

Rocky Lu, Joseph L. Baker
Department of Chemistry, School of Science, The College of New Jersey, Ewing, NJ, 08628

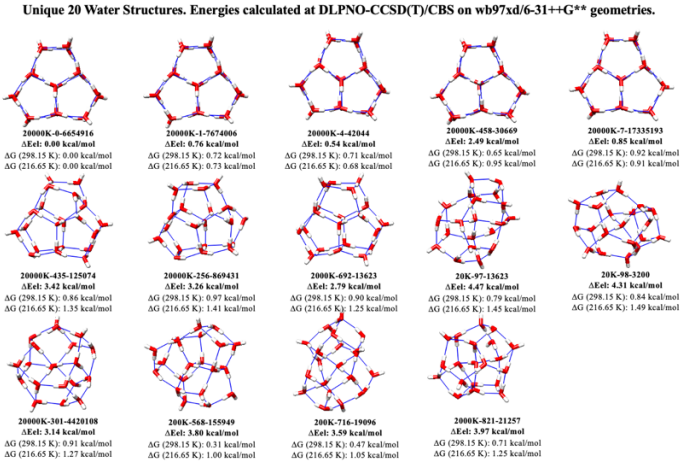
Bacterial adhesion pili are elongated protein structures extending from the bacterial surface, and are crucial for mediating initial contact and attachment to host cells or surfaces. These filamentous appendages can vary greatly in length, often ranging from hundreds of nanometers to more than a micrometer, which allows them to facilitate efficient adhesion and colonization. While all-atom molecular simulations have revealed many atomistic scale insights about small segments of adhesion pili, conducting such simulations becomes computationally prohibitive when dealing with more extended systems. Coarse-grained simulation approaches bridge that gap by grouping atoms into coarse-grained sites and thereby reducing the complexity of the simulated model. Here, we present an approach utilizing the GōMartini 3 model on a number of enterotoxigenic *Escherichia coli* (*ETEC*) and endospore appendages (Enas) pili. Our aim is to leverage coarse-grained simulations to enable investigations into the nanomechanics of adhesion pili over extended length and time scales that are not accessible at atomistic resolution.

Thermodynamic Analysis of Large Atmospheric Water Clusters (20-30)

Audrey Ryu, Ben Petty, Vance Fowler, George C. Shields*

**Department of Chemistry, Furman University, Greenville, South Carolina 19613, United States*

Large water clusters have been studied extensively to understand their influence on the countless water-involved systems not only on Earth but throughout the universe. While water appears to be a simple molecule, it possesses many complex qualities that are still poorly understood. For example, the structure that water takes on as a liquid is a subject of high debate, and deriving experimental methods to study it is extremely difficult. Hence, computational methods have been used to research the behavior of water via thermodynamic study. Literature concerning large water clusters (20-40 waters) exists in respectable amounts but is nowhere near as thorough and precise as that which covers smaller clusters. Thus, we aim to study large clusters with more accurate basis theory, then use results to determine low-energy structure trends and Boltzmann populations that exist within these systems. Millions of initial cluster configurations were generated using the OGOLEM generic algorithm-based program with the Tip4p model. This large pool size was then reduced to 1000 of the lowest energy structures for each $(H_2O)_n$ cluster for n=20-30. These structures were then subjected to geometry optimization with the ωB97X-D density functional (DFT) using the /6-31++G** basis set. All structures within 8 kcal mol^{-1} of the DFT electronic energy and Gibbs free energy (ΔG°_T) minimums were used for a high-level set of DLPNO-CCSD(T) calculations with the cc-pVDZ, cc-pVTZ, and cc-pVQZ basis sets. Additionally, augmented cc-pVnZ basis sets were used on Oxygen atoms to further refine CCSD(T)/CBS electronic energies for the final set of low-energy structures that were <1.5 kcal/mol using the cc-pVnZ basis sets. The CCSD(T) electronic energies were combined with Gibbs free energy corrections obtained from the DFT calculations to determine the most favorable structures at 217 K and 298 K (atmospheric and room temperature, respectively). Results will be presented that include how the presence or absence of a centrally solvated water molecule, as well as prism-like structures, impact the trends in ΔG° as a function of temperature.



Unlocking the secrets of interstellar hitchhikers: The F-Ena pilus enables spore-forming bacteria adhesion

Kiara Robles, Joseph L. Baker
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Spore-forming bacteria species are incredibly resistant to harsh conditions such as vacuums, environments that are anhydrous, radiation, high heat, and even chemical denaturants. Their great resilience implicates them in food and medical instrument contamination, and even as interplanetary “space travelers.” The ability of these organisms to survive under such stresses can be attributed to their capacity to form spores, become dormant during long spans of time, and then re-emerge when conditions are more viable. Additionally, spore-forming bacteria are also exceptional at binding to surfaces due to their fibrous endospore appendages (Enas). In this study, we focus on the F-Ena pilus. The F-ena pilus is built of proteins arranged into interlocking trimer layers stacked vertically on top of each other, and the pilus is also known to connect to a long collagen-like fibril with the adhesion protein BclA at its tip. While the structure of this system has been well-characterized, the dynamic behavior of the F-Ena pilus under tensile force is not well known. We use molecular dynamics simulations and steered molecular dynamics to explore F-Ena pilus dynamics. Our initial work demonstrates how the system behaves under tensile force, and will lead to the design of strategies to disrupt spore adhesion to surfaces and provide insights into the basic biophysics behind the ability of spore bacteria to thrive in many environments.

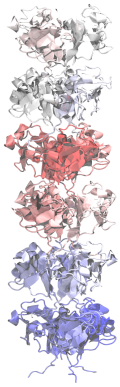

Figure 1 (Left): Model of F-Ena Pilus structure prior to steered MD.

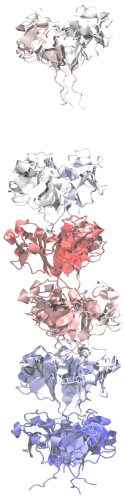

Figure 2 (Middle):Model of F-Ena Pilus structure after steered MD.

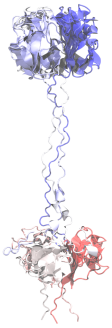

Figure 3 (Right): Model of 3 F-Ena subunits attached to BclA protein via collagen fibril stock.

Relax! Exploring Bacterial Pilus Resistance to Stressors

Nicole Rojas, Joseph L. Baker
Department of Chemistry, School of Science, The College of New Jersey, Ewing, NJ, 08628

CFA/I is an adhesion pilus that protrudes from the surface of enterotoxigenic *Escherichia coli* (ETEC) and aids in anchoring the bacteria to the host's gastrointestinal lining. F-Ena and L-Ena are pili found on spore forming bacteria that anchor and contaminate food and sterile surfaces. These bacterial pili are well known to exhibit resistance to degradation against high temperature, chemical denaturation, and remain robust against dehydrated environments. However, the molecular scale interactions which lead to these properties are less well known. In our work, we are investigating the structural integrity of CFA/I, F-Ena, and L-Ena systems using molecular dynamics simulations. We have investigated a model of the CFA/I pilus and pilin subunit solvated in 8 M urea, a frequently used chemical denaturant, and also in water, as a control group. Similarly, we have created multimeric and monomeric models of the Ena systems solvated in water, as a control group, and also in vacuum, which simulates a desiccated environment. Our simulations provide insight about the stability of each of these proteins under a range of environmental stresses.

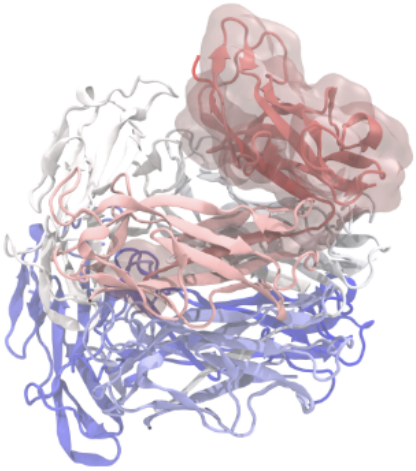

Figure 1. (Left) Model of CFA/I filament with monomeric structure highlighted

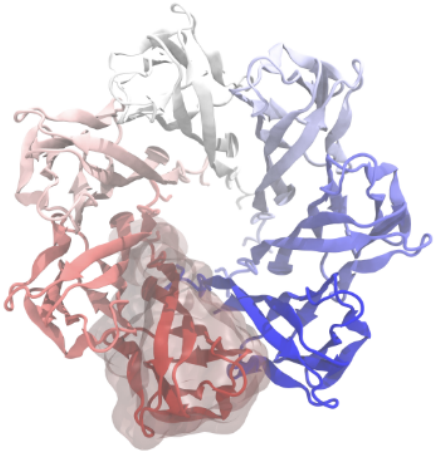

Figure 2. (Right) Model of L Ena filament with monomeric structure highlighted

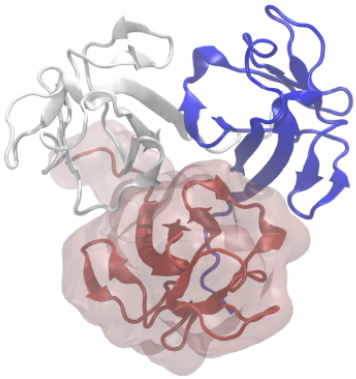

Figure 3. (Center) Model of F Ena filament with monomeric structure highlighted

A dance of two pili: Characterizing features of the binding interface between Histatin-5 and the CS20 pilus

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Enterotoxigenic *Escherichia coli* (ETEC) is responsible for causing gastrointestinal issues and mortality in children from majority world countries. ETEC capacity for persistent infection stems from pili, long filamentous protein chains that extend out from the bacterial surface, which enable both ETEC mobility and adhesion. In this study, we use a combination of protein-protein docking and molecular simulations to investigate how the histatin-5 peptide induces CS20 pilus bundling. While this phenomenon has been observed experimentally, the molecular-scale description of histatin-5 induced pilus bundling is not well understood. Our simulations demonstrate that histatin-5 remains bound and crosslinked between parallel CS20 pili (Figure 1), but binding is not as stable in single CS20 models.

To further investigate the interactions between histatin-5 and CS20, various analysis tools and enhanced sampling methods were implemented. Gaussian Accelerated Molecular Dynamics (GAMD) was used to study the intrinsically disordered nature of histatin-5 in water and to compare its conformational landscape in different environments. ClusPro was used to dock histatin-5 to multiple regions of interest on CS20 on the inner and outer parts of the pilus, and the cluster score was compared to assess the most probable models. Additionally, we are exploring the use of a coarse-grained model to simulate CS20 in a histatin-5 solution to identify additional interaction sites of interest. Overall, our approach provides molecular-scale insights about the histatin-5/CS20 binding interface that are currently inaccessible using other methods.

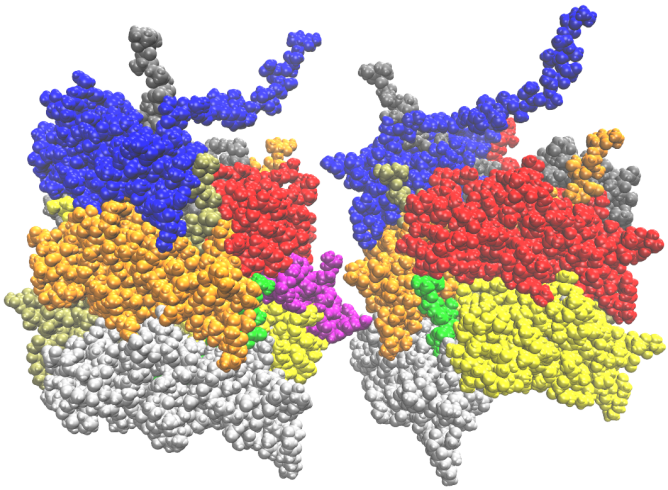

Figure 1. Histatin-5 (purple) interacting with two CS20 pili consisting of seven subunits each.

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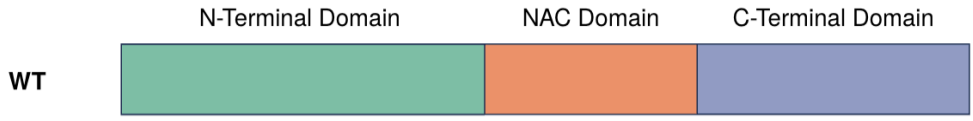
St. John's University, Department of Chemistry, Queens, NY

The Impact of Ionic Strength and pH on Alpha-synuclein Monomer Structure

Alpha-synuclein (αS) is an intrinsically disordered protein that, when improperly folded, aggregates into insoluble fibrils and aggregates known as Lewy bodies. These are associated with neurodegenerative disorders, including (but not limited to) Parkinson's disease. αS is composed of three domains: a basic and amphipathic N-terminal domain, a mostly hydrophobic central NAC domain, and a strongly acidic C-terminal domain. The N- and C-terminal domains are known to form inter-domain electrostatic contacts that modulate the protein's structure. Increasing or decreasing the ions in solution will likely interfere with the attraction these domains have to each other. We plan to use molecular dynamics (MD) to simulate the protein at low, medium, and high salt concentrations as well as acidic, neutral, and basic conditions to understand how the monomeric αS structure is affected by ionic strength and changes in pH. This will allow us to understand how protein aggregation is affected by a variety of cellular environments. Additionally, we will be testing which AMBER force fields are best able to reproduce experimental properties when used with an implicit solvent model. In determining how various conditions affect the behavior of αS, we hope to both add to our knowledge of intrinsically disordered proteins and gain important insight into the mechanisms of Parkinson's.

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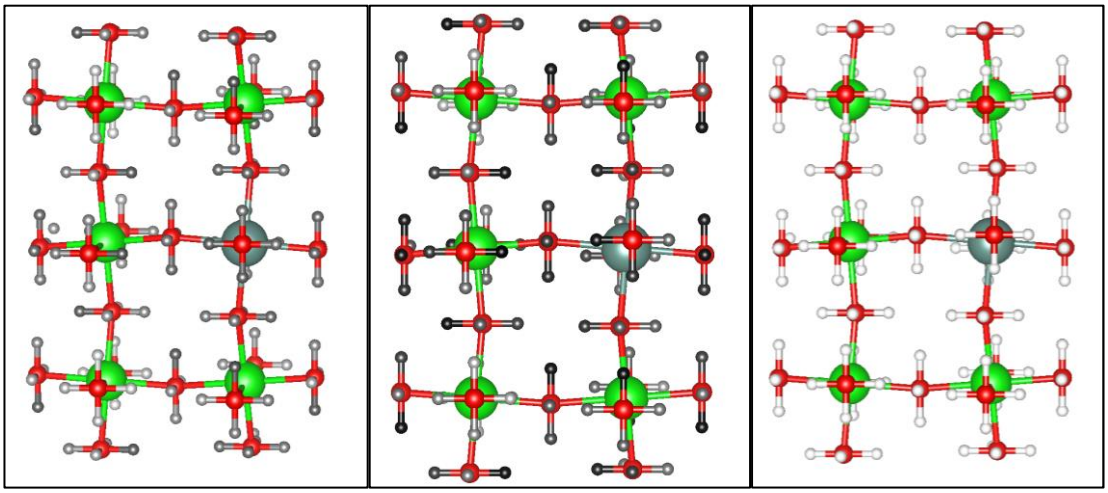
1                                                    55
MDVFMKGLSKAKEGVVAAAEKTKQGVAEAAGKTKEGVLYVGSKTKEGVVHGVATV
56                                                  110
AEKTKEQVTNVGGAVVTGVTAVAQKTVEGAGSIAAATGFVKKDQLGKNEEGAPQE
111                        140
GILEDMPVDPDNEAYEMPSEEGYQDYEPEA
```

Electric Field Manipulation of Proton Conduction Pathways in Yttrium-Doped Barium Zirconate

A. Dao, P. Chakraborty, M. A. Gomez

Department of Chemistry, Mount Holyoke College, South Hadley, MA

Centrality provides insights into proton traps and highways in proton conducting systems [1]. Applying an electric field can manipulate these pathways by adjusting energy barriers to favor a specific conduction direction. Prior studies used kinetic Monte Carlo (kMC) simulations to examine proton conduction pathways in 12.5% yttrium-doped barium zirconate [1, 2]. Results showed protons were trapped near yttrium most of the time and occasionally found longer proton pathways aided by a small applied electric field [2]. The most probable pathways aligned with high centrality regions, demonstrating a correlation between pathway probability and centrality. Building on this, centrality measures are used to highlight how electric fields shift proton traps and highways. Energy barriers in the direction of the electric field are lower while those in the opposite direction are raised. Figure 1 shows that increased field strength made several sites more prominent in centrality. Comparing new centrality images with kMC trajectories under an electric field revealed significant modulation of proton pathways. These findings highlight how electric fields choose the direction of proton conduction in otherwise isomorphic materials.



(a) (b) (c)

Figure 1 shows the centrality of the proton binding sites within the Y/$BaZrO_3$ when a potential of (a) 0 eV, (b) -2 eV, and (c) -10 eV is applied to the system.

[1] Rachel Krueger, F. G. Haibach, Dana L Fry, and Maria A Gomez "Centrality measures highlight proton traps and access points to proton highways in kinetic Monte Carlo trajectories," J. Chem. Phys. 142, 143110 (2015).
[2] Maria A. Gomez, Dana L. Fry, Marie E. Sweet, "Effects of the proton conduction limiting barriers and trajectories in BaZr0.875Y0.125O3 due to the presence of other protons," J. of the Korean Ceramic Society. 53, 5, 521 (2016).

Integration of a Second Proton in Kinetic Monte Carlo Simulations of Proton Conductivity in Doped Barium Zirconate

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Proton conductivity is essential for fuel cell electrolytes, with yttrium-doped barium zirconate (Y/BaZrO3) being one of the fastest solid-state proton conductors. Earlier studies have explored the impact of a second proton on lattice energy interactions in a smaller system [1]. The tuple energies in a larger system have been determined [2][3] but have not been implemented in a kinetic Monte Carlo simulation. This project explores the impact of a second proton on proton dynamics by incorporating tuple energies [2] into kinetic Monte Carlo simulations. Our results show that the presence of a second proton significantly alters the energy landscape, particularly affecting the size and distribution of energy barriers during transitions. The energy ranges for tuples and single protons are similar. The more negative global minimum energy of tuples indicates a more stable lattice relaxation due to both protons in comparison. Tuple barriers are more affected by individual rotations than intraoctahedral transfers. The primary hindrances for proton movement between sites are limiting barriers, whereas coupling barriers involve interactions between pathways.

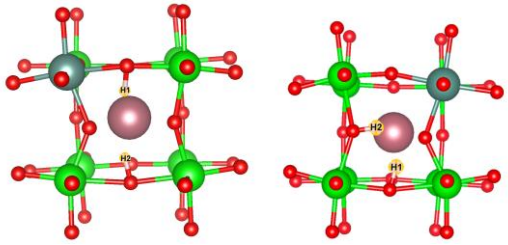

Figure 1. Shows the lowest global minima on the left and the second lowest on the right.

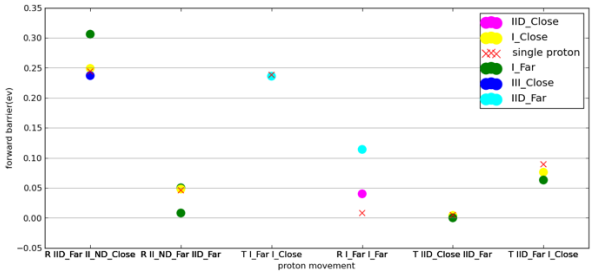

Fig 2. Shows tuple barriers compared to single proton barriers. Single proton movements are the red x. For a two-proton scenario, an unmoved proton is presented in the legend and a moving proton is presented in the x-axis

[1] Gomez, M. A., Fry, DL., Sweet, M. (2016). "Effects on the proton conduction limiting barriers and trajectories in $BaZr_{0.875}Y_{0.125}O_3$ due to the presence of other protons." Journal of the Korean Ceramic Society **53**(5): 521-528.

[2] Pan, Y, Hoang, M. T., Mansoor, S., Gomez, M. A. (2023). "Exploring Proton Pair Motion Away from the Global Proton–Tuple Energy Minimum in Yttrium-Doped Barium Zirconate." Inorganics **11**(4): 160.

[3] Du, P., Chen, Q., Fan, Z., Pan, H. Haibach, F. G., Gomez, M. A., Braun, A. (2020). "Cooperative origin of proton pair diffusivity in yttrium substituted barium zirconate." Communications Physics **3**(1).

On the Nose: Exploring the Noncovalent Driving Forces of DNA Intercalation for Ru-Based Chemotherapeutic Agents

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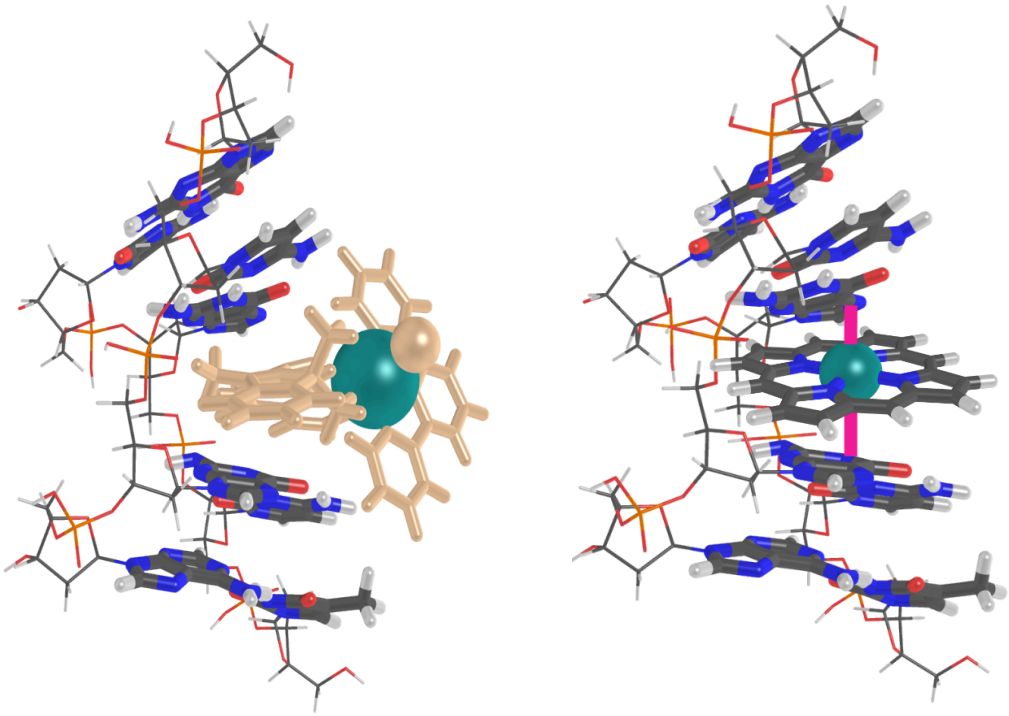
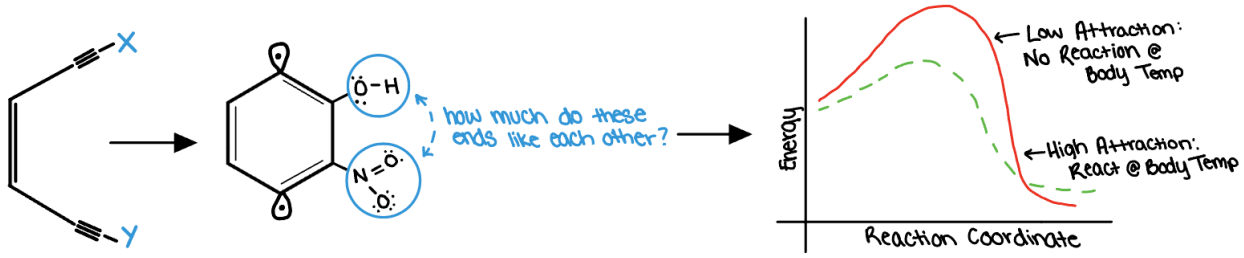
One of the leading causes of death globally, cancer is generally a disease of uncontrolled cellular division thanks to mutated DNA. Rather than treating cancer by inhibiting the enzymes necessary for DNA replication as do Pt-based chemotherapies, DNA intercalators inhibit either the unzipping of the DNA double helix by helicase or the reading of the genetic code by transcriptase by vertical insertion into DNA between adjacent nucleobase pairs. A promising family of DNA intercalators are those with a ruthenium core, who can bind irreversibly in an axial motif to the nitrogens in adjacent nucleobases when the metal is in its +2 oxidation state. Ru-based intercalators are particularly attractive as a targeted therapy because the drug can be administered as the biochemically inert Ru(III) form, which is only reduced to the active +2 oxidation state in the acidic environment of a cancerous cell. While recent progress has been made towards the design of novel Ru-based intercalators, however, the presence of bulky axial ligands has so far limited the extent that the Ru core can insert into the bulk of the DNA, preventing its therapeutic activity from being maximally effective. To better guide the design of next-generation Ru-based intercalators, therefore, here we computationally explore the noncovalent interactions driving intercalation in current generation Ru-based drugs using the functional-group and intramolecular partitions of symmetry-adapted perturbation theory (F-ISAPT). Based on the favorable and unfavorable interactions present with the ligand "nose" of current intercalators and their DNA targets, we propose a novel Ru-doped porphyrin intercalator whose flat topology should allow for optimal insertion and binding.



Could Optimal Intramolecular Interactions Drive the Bergman Cyclization for Anti-Tumor Applications?

Niya A. Enser and Dominic A. Sirianni
Department of Natural Sciences, Daemen University, Amherst, NY 14226

Radicals, which are molecules with an unpaired electron, scavenge hydrogen atoms from nearby molecules to become more chemically stable. When "free" in the body, radicals can damage DNA and induce mutations that can lead to cell death or the development of cancer. If radicals could be controllably produced *in cellulo*, however, this DNA-attacking behavior could be harnessed to induce DNA cleavage and cell death in only cancerous cells, thereby effectively halting tumor growth without the whole-body side effects normally associated with systemic chemotherapies. One possible radical-producing reaction for this purpose is the Bergman cyclization, which produces the aromatic diradical *p*-benzyne through the thermally allowed electrocyclization of (*Z*)-hexa-3-ene-1,5-diyne. While this reaction is only slightly endothermic, the high rigidity of the enediyne precursor leads to a high activation barrier that prevents the cyclization from occurring spontaneously at body temperature. Here, we explore the possibility of reducing the activation barrier to cyclization by engineering an intramolecular attraction between functional groups on the enediyne reactant's alkyne termini, thereby mechanically pulling these normally distant moieties close enough to react at body temperature. Here, we apply the functional-group and intramolecular partitions of symmetry-adapted perturbation theory (F-ISAPT) to explore the noncovalent driving force for Bergman cyclization along reaction trajectories constructed for a variety of substitution patterns with the freezing string method (FSM). We find that, especially for an enediyne terminally substituted with hydroxyl and nitro groups, Bergman cyclization is strongly driven by electrostatic attraction and the formation of an intramolecular hydrogen bond, incurring a modest decrease in overall activation barrier that could facilitate the formation of its diradical product at reduced temperatures relative to its unsubstituted parent.



Thermodynamic Investigation of the Effect of Sulfate on Atmospheric Aerosol Formation

Daniela Murillo, Vance R. Fowler, Connor J. Bready, Kelsey T. Sumter, George C. Shields*
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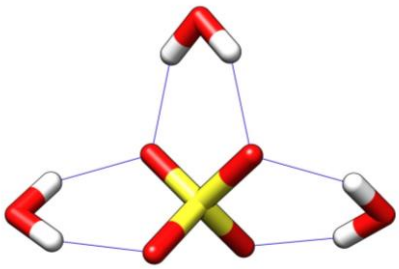
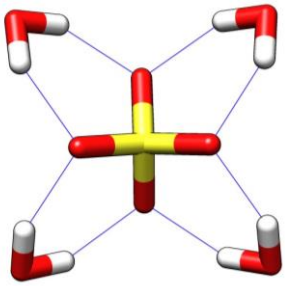
The mechanisms by which molecular species form initial prenucleation clusters remain poorly understood. This uncertainty presents a significant challenge in the study of global warming, as aerosols play a crucial role in climate dynamics by either absorbing or scattering solar radiation. While neutral species are known to be highly effective in inducing cluster formation, there is also evidence suggesting that positive and negative ions can initiate this process through ion-induced nucleation.

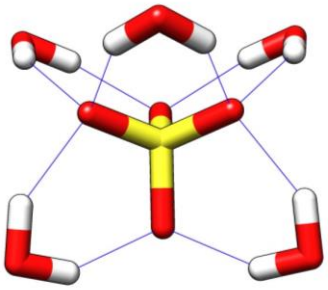
Our research focuses on hydrated sulfate ion clusters ranging from $SO_4^{2-}(H_2O)_1$ to $SO_4^{2-}(H_2O)_{20}$. To understand the formation of these sulfate-based aerosols, we calculated the structures' Gibbs free energy. We generated hundreds of thousands of initial structures using a generic algorithm-based search in OGOLEM and optimized these with either the GFN2-xTB or PM7 semiempirical methods. Next, we re-optimized the 1000 lowest energy structures from each semiempirical method using the ωB97X-D/6-31++G** level of theory. The resulting electronic energies were recalculated using the domain-based local pair natural orbital coupled cluster (DLPNO-CCSD(T)) methods with the single, double, and semi-canonical perturbative triple excitations with haug-cc-pVDZ, haug-cc-pVTZ, and haug-cc-pVQZ basis sets using Orca 5.0.1. In our investigation, we validated our results against published structures to ensure the identification of the lowest Gibbs free energy clusters. Below, we present a sample of our results, highlighting the global minima from $SO_4^{2-}(H_2O)_3$ to $SO_4^{2-}(H_2O)_6$.



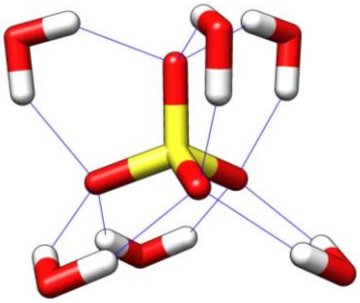
$(SO_4^{2-})_1(W)_3$



$(SO_4^{2-})_1(W)_4$



$(SO_4^{2-})_1(W)_5$



$(SO_4^{2-})_1(W)_6$

Effect of salt on a fully bound peptide SH3 domain interaction

Ally Mujica, Jorge Cardoso, Olubube Onwuzulu, Gemma Bell, Elliot J. Stollar, K. Aurelia Ball*

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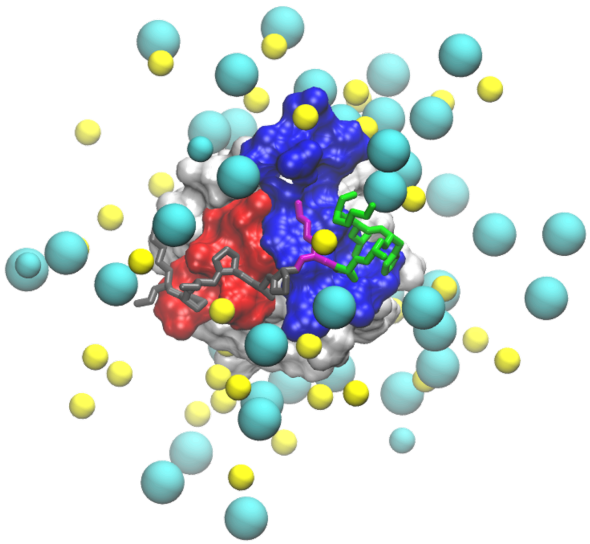
Intrinsically disordered peptides (IDPs) are peptides lacking stable structures in physiological conditions. These peptides play crucial roles in many cellular processes, mainly in cellular signaling and cellular regulation. Due to the difficulty of gathering experimental data on the dynamics of IDPs, MD simulations were used to simulate protein-protein interactions of an IDP and its binding partner. The AbpSH3 domain is a common protein interaction domain found in all eukaryotic organisms. The negatively charged SH3 domain commonly binds with the positively charged IDP ArkA, a disordered yeast peptide. Experimental data has found that the presence of salt will destabilize the bound state of the AbpSH3-ArkA complex as favorable electrostatic interactions between charged residues play an integral role in the binding. The strength of these electrostatic interactions can be influenced by the concentration and type of salt used. To further understand how salt affects the complex, molecular dynamics simulations were used to model the completely bound complex of AbpSH3-ArkA in the presence of 800 mM salt. The effects of salt on the contacts made between AbpSH3 and ArkA were compared, along with the flexibility and electrostatic interactions of the completely bound AbpSH3-ArkA complex. We concluded that minimal changes are observed in the completely bound state of AbpSH3-ArkA in the presence of salt, but that sodium ions can replace interactions that the positively charged ArkA residues have with the domain.



Investigating the impact of using Density Functional Theory (DFT) on electrophilicity predictions from machine-learning models

Camlyn Takahashi[1], Vedit Venkatesh[2], Crystal Yeung[2], Daisy Grace[3], Swetha Tadisina[2], Zheyu Cui[2], Heidi P. Hendrickson[2], Simbarashe Nkomo[1]

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[2]Department of Chemistry, Lafayette College, Easton, PA 180422
[3]Department of Environmental Health & Engineering John Hopkins University, Baltimore, MD 21218

Electrophilicity is the measure of a molecule's tendency to attract electrons. It is experimentally derived by reacting nucleophiles with electrophiles and determining rate constants. The experimental value of electrophilicity is useful in making predictions about reactivity and pharmacological properties of compounds. Electrophilicity can also be determined theoretically, using calculations of frontier molecular orbitals. In recent years, machine learning models have been developed to predict electrophilicity with various molecular descriptors. Our research focuses on Electropredictor, an ensemble model that uses machine-learning models with molecular descriptors optimized with Semi-Empirical PM3 level of theory on a set of molecules from the Mayr's Database of Reactivity Parameters. This study investigates the impact of using descriptors calculated using Density Functional Theory (DFT) on the model's prediction of electrophilicity.

The Effect of Polarizable Force Fields on CO_2 Structure, Dynamics, and Spectroscopy in Ionic Liquids

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As the amount of CO_2 in the atmosphere increases, researchers have been driven to find materials that are well suited for carbon capture. Ionic liquids (ILs) are constituted of ions yet are liquid at room temperature. Their selective absorption of CO_2 has led researchers to focus on how they might be used in direct air carbon capture. Simulations using non-polarizable force fields show that CO_2 dissolves in ILs because the CO_2 molecules are attracted to solvent cages in an IL in a way that other small gas molecules are not. We analyze the interactions between ILs and CO_2 to understand if switching between polarizable or nonpolarizable force fields will change the behavior of ILs, and the attraction of CO2 to the ion cages. Molecular dynamics simulations are performed of 1 CO_2 solvated in 256 IL pairs of [BMIM][PF6] or [BMIM][Tf2N] to compare the force field effect across ILs. Calculations of cylindrical distribution functions, orientational correlation functions, and radial distribution functions are used to quantify the interactions between ions and the CO_2 when simulated using different force fields. We find that in a polarizable system the strength of the solvent cages reorganizes more quickly, which signifies more CO_2 solvation. Further exploration into a broader range of ILs and how they act when modeled with different force fields can bring researchers closer to identifying the best properties of ILs for carbon capture.

Effect of solvents on the frequency of alkynes from MD simulations.

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Haverford College, Department of Chemistry, Haverford, PA 19041

Prior experiments on the terminal alkyne carbon-carbon triple bond stretch show that it can be used as an effective Raman probe because it exhibits strong Raman scattering that is sensitive to the local environment. These experiments show the solvation environment alters the Raman scattering frequency, but the reason for these shifts is unclear. To understand the frequency shifts of terminal alkynes, computational chemistry techniques are vital. Quantum chemistry calculations imply that alkynes in non-polar solvents like dichloromethane (DCM) produce a shift to higher frequencies while polar solvents like water and dimethylsulfoxide (DMSO) both cause a shift to lower frequencies. However, experiments show that alkynes in DCM and water have similar frequencies to each other, while the frequencies of alkynes in DMSO are much lower. This discrepancy may be because the quantum calculations only considered the interactions between a single solvent molecule and a single alkyne. To consider more complex interactions, snapshots from molecular dynamics simulations of propyne solvated in water, DMSO, and DCM were extracted. Snapshots were split into two parts. First, a quantum mechanical (QM) region where electrons are fully modeled under the Born-Oppenheimer approximation using density functional theory methods. Second, molecules in the molecular mechanical (MM) region were approximated as point charges based on the assumption that more distant molecules will have a diminishing effect on the frequency. In this work, we optimized the number of molecules included in the QM region and the size of the MM region. Calculating frequencies based on MD simulation snapshots allows computational analysis of more complex and realistic alkyne-solvent interactions. Here, we develop a QM/MM methodology for analyzing terminal alkynes in a variety of solvents. This methodology will advance building a universal spectroscopic map for the Raman active terminal alkyne carbon-carbon triple bond stretching mode.

Salt disrupts the binding pathway of an Arka-AbpSH3 peptide complex

Jorge Cardoso, Olubube Onwuzulu, Ally Mujica, Frida Angiuano, Elliot J. Stollar, K. Aurelia Ball*

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[1]University of Liverpool, Liverpool, UK

Intrinsically disordered peptides (IDPs), which lack stable structures under physiological conditions, play important roles in cellular processes such as signaling, regulation, and organization. IDPs often bind to AbpSH3 domains, common protein interaction domains found throughout all eukaryotes. ArkA, a yeast-derived IDP, commonly interacts with the AbpSH3 domain, a protein binding domain found in all Eukaryotes. The binding pathway goes through an intermediate state, known as the encounter complex, which is mediated by favorable electrostatic interactions between charged residues and non-specific hydrophobic interactions. The strength of electrostatic interactions can be influenced by salt, disrupting the formation of the encounter complex. We used molecular dynamics (MD) simulations to model the binding of the ArkA peptide to the AbpSH3 domain at low and high salt concentrations (800 mM). The observed effects of ionic strength on the flexibility, electrostatic interactions, and kinetics of the ArkA-AbpSH3 binding complex suggest that the encounter complex is the part of the binding pathway most disrupted by a high salt concentration. Investigating the role of salt in IDP binding pathways provides insight into the importance of non-specific long-range electrostatic interactions for stabilizing the formation of key binding intermediate states such as the AbpSH3-encounter complex.

Noah Pishaki
Tyler Luchko
David A Case
Steven Ayoub

Tortoise Meets Hare: Combining GB Speed and 3D-RISM Detail with HMC

The 3-dimensional reference interaction site model (3D-RISM) offers a detailed, accurate representation of solvent thermodynamics, comparable to computationally expensive explicit solvent models. However, the high computational cost of calculating atomic-scale solvent interactions in sophisticated models like 3D-RISM leads to slow sampling, making brute-force molecular dynamics (MD) infeasible. To address this, we integrated 3D-RISM with the fast generalized Born (GB) implicit solvent model using a hybrid Monte Carlo (HMC) approach. HMC generates global trial moves using MD with the GB model, leveraging its efficiency, followed by the application of the Metropolis criteria with the 3D-RISM model, thus balancing accuracy and efficiency. Our method achieved a 60% acceptance rate and a 1200x speedup compared to brute-force MD with 3D-RISM for alanine dipeptide. When applied to the host-guest binding of alpha cyclodextrin (ACD) and the beta assembly machine (BAM), it resulted in a 47% acceptance rate with water and 45% with NaCl ions at 0.3M concentration, showcasing the method's versatility. These promising results highlight the potential for significant improvements in computational efficiency while sampling with 3D-RISM using HMC. We plan to further validate this by comparing absolute binding free energy (ABFE) calculations to those performed with GB systems.

The Driving Effects of Common Atmospheric Molecules for Formation of Clusters: The Case of Sulfuric Acid, Formic Acid, Hydrochloric Acid, Ammonia, and Dimethylamine

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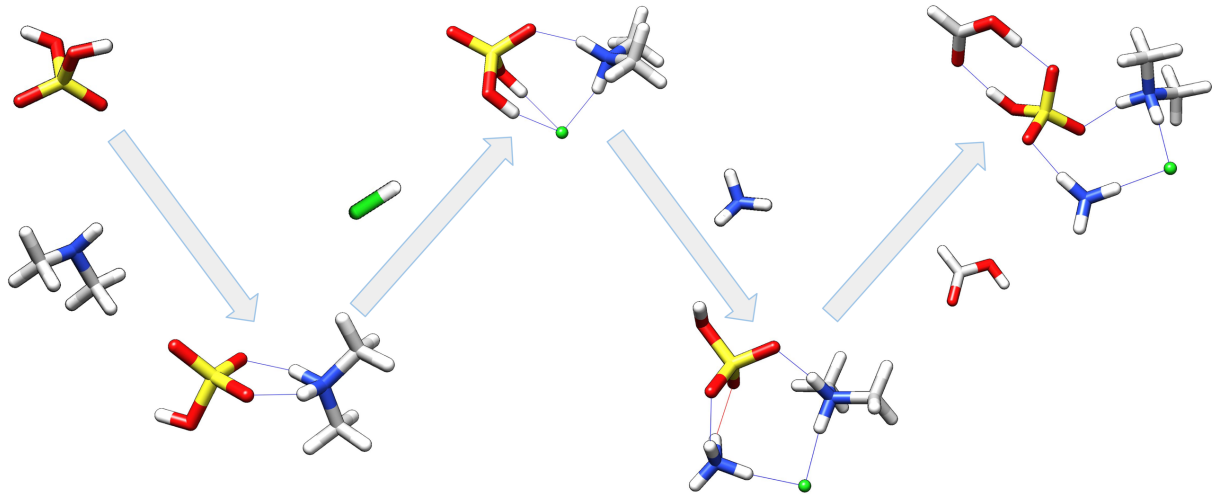
The formation of secondary aerosols is a main source of uncertainty for the understanding of global warming. The beginning stages of secondary aerosol cluster formation starts with the formation of prenucleation complexes from precursor monomers of acids, bases, and organic molecules. The detailed interactions responsible for prenucleation and subsequent aerosol formation are difficult to decipher experimentally. We present a computational chemistry study of the interactions between three different acid molecules and two different bases. We combine a comprehensive search routine covering thousands of configurations at the semiempirical level with high level quantum chemical calculation of approximately 1000 clusters for every possible combination of clusters containing a sulfuric acid molecule, a formic acid molecule, a hydrochloric acid molecule, an ammonia molecule, a dimethylamine molecule, and 0-3 water molecules. Additionally, we have completed an exhaustive search of the DLPNO-CCSD(T)/CBS// ωB97X-D/6-31++G** Gibbs free energy surface for the system $(H_2SO_4)(HCOOH)(HCl)(NH_3)((CH_3)_2NH)(H_2O)_{0\text{-}3}$. This first detailed study of HCl interacting with two other acids and two bases reveals the subtleties that exist in the formation of prenucleation complexes for this system. When this system is compared with the previously studied cluster $(H_2SO_4)(HCOOH)(HNO_3)(NH_3)((CH_3)_2NH)(H_2O)_{0\text{-}5}$, we see that nitric acid forms stronger interactions in dry clusters. As the clusters are hydrated and grow larger, we often see the sequential energies of clusters containing hydrochloric acid become more favorable than those with nitric acid. The results of this research add to the conclusions that hydrogen bond topology and detailed structure geometries are more important than traditional acid or base strength.



The Effect of a Double Mutation on Key Negatively Charged Residues on the Bound State of the ArkA-SH3 Complex

Jaden Ali ’27, Oluebube Onwuzulu ’24, Elliot J. Stollar, K. Aurelia Ball*

Intrinsically Disordered Peptides (IDPs) are peptides that lack a defined secondary structure. IDPs often bind partner proteins to help perform various cellular processes like signaling and cytoskeletal regulation. The IDP ArkA binds to the AbpSH3 domain by transitioning through an encounter complex that is formed through non-specific electrostatic and hydrophobic interactions between ArkA (net charge of +3) and SH3 (net charge of -12). The formation of specific short range electrostatic interactions is necessary to form the fully bound state of the ArkA-SH3 complex. Previously we used Molecular Dynamics (MD) simulations to study the effects of a single negatively charged residue mutation by simulating an E14Q and E17Q mutant. These mutations were chosen because E14 and E17 interact directly with the central lysine that is critical to the binding of ArkA to SH3 and glutamine was used to maintain a similar structure while removing the negative charge. We discovered that changing glutamic acid to glutamine decreased the average number of electrostatic interactions formed between ArkA and SH3, but surrounding residues partially compensated for the loss of charge in the bound state. We also found that mutating the E17 position had a larger impact on short range electrostatic interactions than the E14 mutation. We then used MD simulations in the bound state of the double (E14Q+E17Q) mutant to study the effect of simultaneous mutations. We found that the double mutant had similar changes in interaction with ArkA as the E17Q mutation but with a larger effect and surprisingly we saw the complex completely unbind. Overall, this experiment showed that performing the double mutation had similar effects to the E17Q mutation with an increased effect, but the double mutant unbound in some of the simulations which showed a greater destabilization of the complex than the single mutations. Future research should focus on binding simulations of the double mutant to see how the binding pathway is affected by the double mutation.

STUDENT ABSTRACTS

Poster Session 2 – Abstracts 1 – 37

Theoretical study of Sulfate Aerosol Particle Formation: The Case for Sulfuric Acid-Ammonia Cluster Systems.

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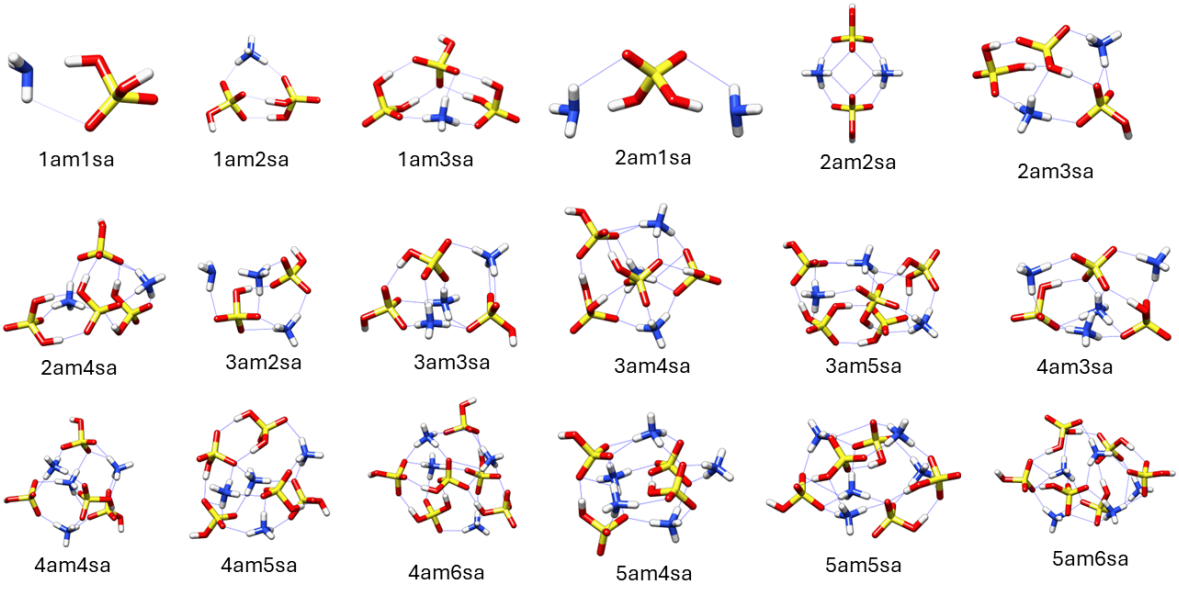
Prior studies have established the formation of stable molecular clusters as the main contributor to new particle formation (NPF) in the Atmosphere. However, the mechanism by which various precursors (sulfuric acid, ammonia, and water, bind) stabilize against evaporation and grow into stable aerosol particles remains elusive. This is owing to the existing knowledge gap between the inherent limits of theoretical and experimental methods. In this present study, we present increasingly accurate binding energies of ammonia and sulfuric acid-containing clusters ((AM)m(SA)n where m=n±2, m_{max}= 6) computed by employing higher-level Quantum Mechanics (QM) methods with large basis sets. We extracted initial geometries of (AM)m(SA)n clusters from previously published studies. These structures were then re-optimized at ωB97X-D/6-31++G** level of theory. Afterward, the electronic energies were corrected using the domain-based local pair natural orbitals coupled cluster method with singles, doubles, and semi-canonical perturbative triples (DLPNO-CCSD(T)). The electronic energies were computed using the correlation-consistent Dunning basis sets cc-pVnZ, aug-cc-pVnZ, and Haug-cc-pVnZ (where n=D, T, Q,5,6). The complete basis set limit (CBS) energies were then extrapolated using a 4-5 inverse polynomial scheme for the DTQ, TQ5, and Q56 energies (where applicable) to generate the final list of electronic energies. Finally, the CBS, aug-CBS, and haug-CBS electronic energies were combined with thermodynamic corrections for H°, S°, and G° at atmospherically relevant temperatures and 1 atm pressure to generate the final free energies. Our study presents the new lowest global minima binding free energies of (AM)m(SA)n clusters. These new energies are crucial inputs for the atmospheric cluster dynamics (ACDC) simulation which will provide us with insights into the clusters' kinetics as well as the chemical mechanism in which the clusters grow into stable sulfate aerosol particles.

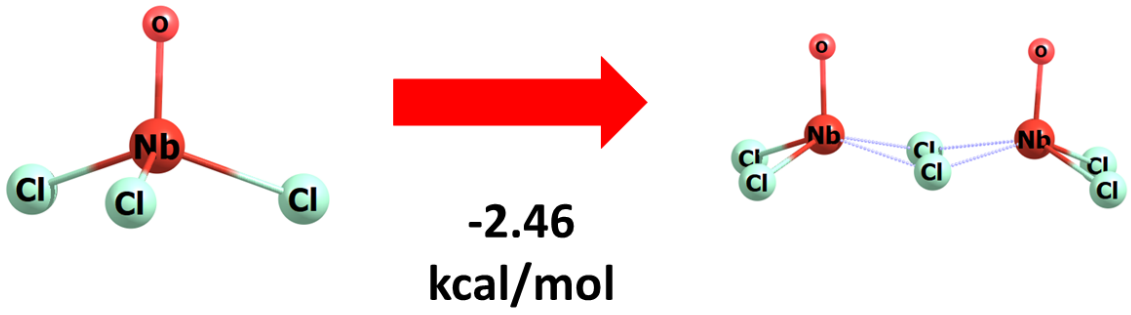


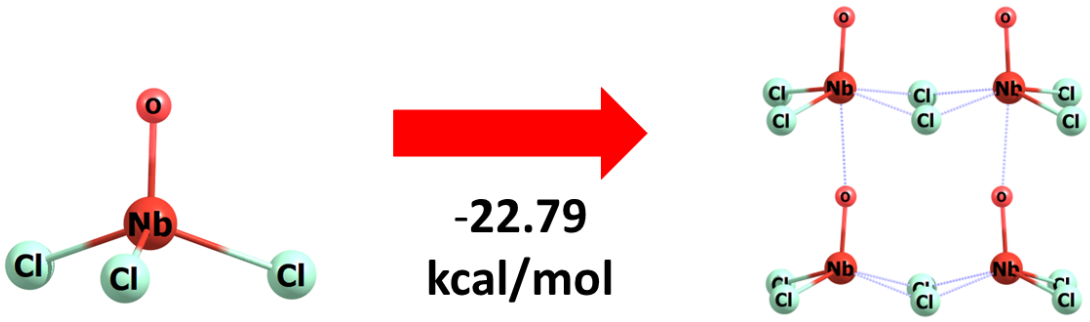
The Bonding and Stabilization of Group 5 Oxyhalide Polymers: Sigma-hole Interactions

Donovan Hoilette Jr, Gabriel Stewart, Kelling Donald*

Gottwald Center for the Sciences, University of Richmond, Richmond, Virginia

In 1959, a paper was published that reported the Nb-O-Nb fragment in the extended solid of $NbOCl_3$ as having equal Nb-O distances of 1.99 Å experimentally. However, in 2002, a paper presented differences in the bond lengths along the Nb-O-Nb axis. Crystal structures of Group 5 oxyhalides (MOX_3; M = V, Nb, and Ta; X = F, Cl, Br, and I) suggest the presence of sigma holes on the M center of the C_2v dimers. These dimers can be stacked multiple times, leading to the formation of the crystal structures. We examine the nature of these sigma holes to understand their overall impact on the extended solid. Our analysis relies on DFT calculations for structural optimizations, frequency, and bond analysis using the Gaussian software. We also investigate the effect oligomerization has on oxyhalide stability and the structural differences that occur. These types of weak O---M interactions are design elements that can be incorporated into novel materials and may already exist in other systems. A goal of this project is to identify other such cases where weak O---M bonds are supported by sigma hole interactions.





Computational Analysis of Citronellal and Butynol Dimers

William Nix[1] , *Brooks Pate*[2] , *George Shields*[1]

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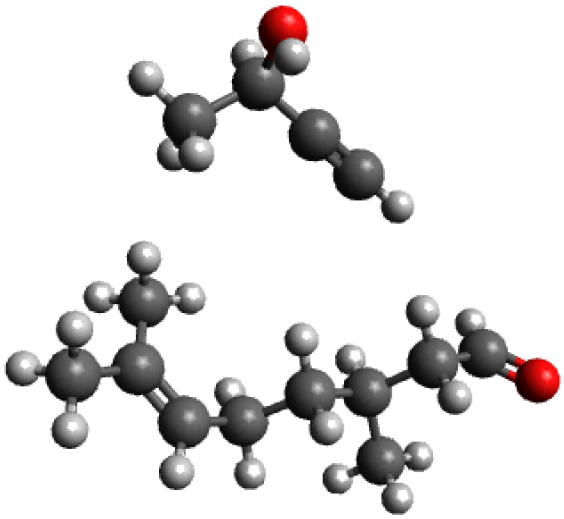
Citronellal is a monoterpenoid commonly known for its fly-repelling abilities and its presence in roses or tangerines. In previous studies, citronellal was found to have 15 primary conformations populated in the pulsed jet expansion with neon. However, the spectrum of citronellal-butynol clusters is exceptionally simple with one spectrum of the 1:1 complex dominating. It is unknown why citronellal takes one chiral form in the presence of butynol, but a hypothesis is that unique hydrogen bonding topology between the molecules could contribute to the chiral selection. Before combining the citronellal monomers and butynol together, we first had to run our R and S conformations through a genetic algorithm. Our conformations of (S)-(-)-Citronellal along with our butynol and (R)-(+)-Citronellal, were obtained by running their initial structures through the genetic algorithm CREST at the GFN2 level of theory. The structures were then repotimized using the the ωB97X-D/6-31++G** level of theory. The electronic energies were corrected using domain-based local pair natural orbital coupled-cluster with singles, doubles, and perturbative triples with a complete basis set extrapolation using the Dunning correlation consistent cc-pVDZ, cc-pVTZ, and cc-pVQZ basis sets (DLPNO-CCSD(T)/CBS), with augmented basis functions on the non-hydrogen atoms. These methods were repeated for (R)-(+)-Citronellal and butynol, and structures within 2 kcal/mol of the minimum were selected for structural analysis. The primary structures of (R)-(+)-Citronellal and (S)-(-)-Citronellal were reoptimized in the presence of butynol using the OGOLEM genetic algorithm. The structures within 2 kcal/mol of the minimum will be analyzed to determine the presence of all the low-lying conformations. When geometrically optimized with butynol, we will further be able to understand whether either citronella=butynol complex optimal or "primary" form that (S)-(-)-Citronellal or (R)-(+)-Citronellal takes.



(R)-(+)-Citronellal and Butynol GFN2 Conformation 2

Substituent Effects on the Photophysical Properties of a Series of *meso*-Pyridyl-BODIPYs: A Computational Analysis of the Experimental Data

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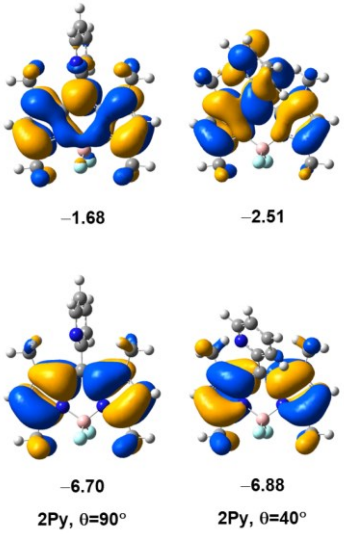
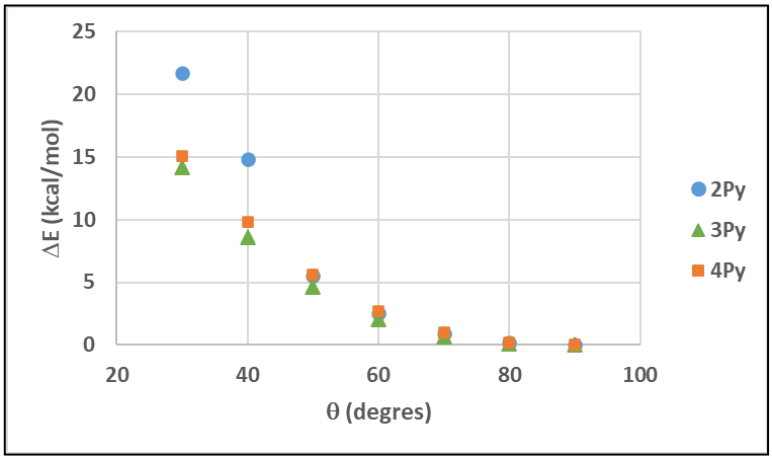
Department of Chemistry, Talladega College, Talladega, AL 35160

BODIPYs are a series of fluorescent dyes that have excellent photophysical properties, including sharp absorption and emission bands in the visible spectral region, high fluorescence quantum yields, and high molar extinction coefficients. BODIPYs could be functionalized at all the carbon atoms and at the boron center, enabling the fine tuning of their chemical and photophysical properties for a particular application. Among the various BODIPY derivatives, 8(*meso*)-pyridyl-substituted BODIPYs have received special attention and have found applications as pH sensors, metal ion sensors, mitochondria-specific probes, etc. Recently, a series of 8(*meso*)-Pyridyl-BODIPYs (2-Py, 3-Py, and 4-Py) and their 2,6-substituted derivatives were synthesized and their structure and photophysical properties were studied both experimentally and computationally. One of the main trends that was observed was that the 2-Py BODIPYs were consistently less fluorescent that their 3-Py and 4-Py analogs, regardless of the 2,6 substituent.

Herein, we extend our previous computational studies and model not only the ground but also the excited states of the entire series of previously synthesized *meso*-pyridyl-BODIPYs with the aim to explain the observed differences in the emission quantum yields. To better understand the trends and the effect of 2- and 2,6-substitution on the photophysical and electron-density related properties, we model also the ground and excited states of compounds that were not synthesized experimentally, however represent a logical part of the series (all mono- or di-substituted analogs, BODIPYs with $R_{1,2}$ = CF_3, as a strongly σ-bond electron-withdrawing group, and the *meso*-phenyl analogs of each series). We calculate a variety of molecular properties and propose that the experimentally observed low quantum yields for all 2Py compounds could be due to the very flat potential energy surfaces with respect to the rotation of the pyridyl ring in the excited states and the stability of a non-planar and significantly less fluorescent 2Py structure.





Frontier orbitals and energies of the S_1 excited state of **2Py** at different angles of Py rotation (θ).

Quantum Mechanical Investigation of Small and Intermediate Sized Ammonia-Water Clusters

Ben Petty, Sara Bourini, George C. Shields

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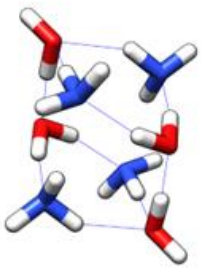
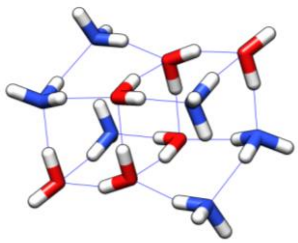
Seed particles provide surfaces or nuclei where gas molecules can condense, creating prenucleation sites that favor the initial formation of aerosols. While extensive research has investigated the prenucleation abilities of pure ammonia clusters in both gas and liquid phases, our understanding of the formation and structure of ammonia-water clusters remains lacking. This knowledge gap impedes accurate modeling of atmospheric chemistry, which is essential for research on the negative radiative forcing of large aerosols that creates a net cooling effect on the climate. Through a comprehensive study of key intermediates along the potential energy surface we have identified a limited number of stable ammonia-water clusters. These clusters were studied with a 1:1 ratio ranging in size from 1 to 6 units across a temperature range of 50 K to 298.15 K. Many thousands of initial structures were generated using a genetic algorithm and optimized initially at the GFN2 semi-empirical level of theory in OGOLEM. The optimized structures were further refined using the ωB97X-D/6-31++G** level of theory in Gaussian. Electronic energies of all structures within 8 kcal mol^{-1} or 6 kcal mol^{-1} of the density functional theory (DFT) minimum were corrected using domain-based local pair natural orbital coupled-cluster with singles, doubles, and perturbative triples (DLPNO-CCSD(T)) with complete basis set extrapolation (CBS) using Dunning's correlation consistent basis sets (DZ, TZ, QZ) in ORCA. Structural frequencies were scaled by a factor of 0.971 to partially correct for anharmonicity. The complete DLPNO-CCSD(T)/CBS//ωB97X-D/6-31++G** model chemistry results were used to calculate the relative Gibbs free energies (ΔG°) from 50 K to 298 K. The low temperature ΔG° values were used to calculate the relative Boltzmann populations of the $(NH_3)_n(H_2O)_n$ clusters for n=2-6, and will be used to compare with experimental results from molecular rotational spectroscopy conducted at the University of Virginia.



A4W4-C_i-1



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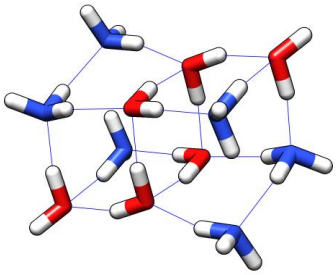


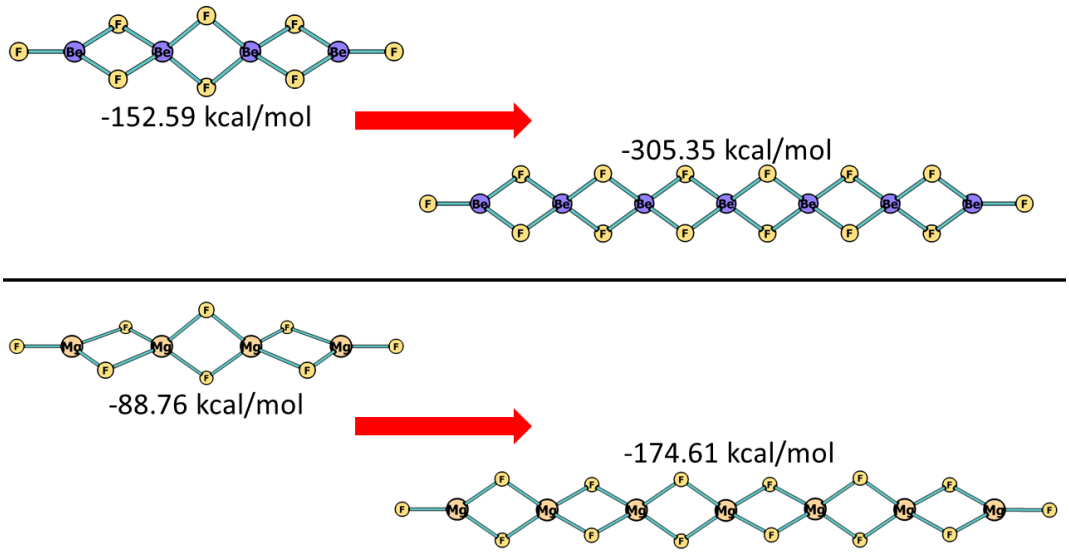
A6W6-C_i-2

Investigation into the Oligomerization Energies of BeF_2 and MgF_2 in Relation to Anomalies in HgF_2 Clusters

Ethan Leonard, Kelling J. Donald*

Department of Chemistry, University of Richmond, Richmond, Virginia

Across the groups 2 and 12 metal halide clusters, certain oligomeric energies and modes of bonding are common for their different clusters. In the case of HgF_2, the oligomerization patterns across the different oligomers up to the decamer (i.e., monomer, dimer, trimer, etc.) reveal an anomalous phase change as the number of monomers in the oligomer increases. However, a similar assessment of other systems such as $HgCl_2$ and CO_2, reveal no such phase change. A chain of each of those molecules remains completely covalent ($HgCl_2$) or completely non-covalent (CO_2) as monomers are added. In the study, we relied on the use of DFT methods in addition to optimization and frequency calculations to probe other metal halides for the presence or absence of the phase change phenomenon observed in HgF_2. In particular, the same calculations and observations regarding the oligomerization energies were carried out on $(BeF_2)_n$ and $(MgF_2)_n$, with the goal of determining whether these clusters exhibit the existence of such a phase change or if they would show a progressively covalent chain. The results suggest that the pattern in HgF_2 is a remarkably unique feature of that system.

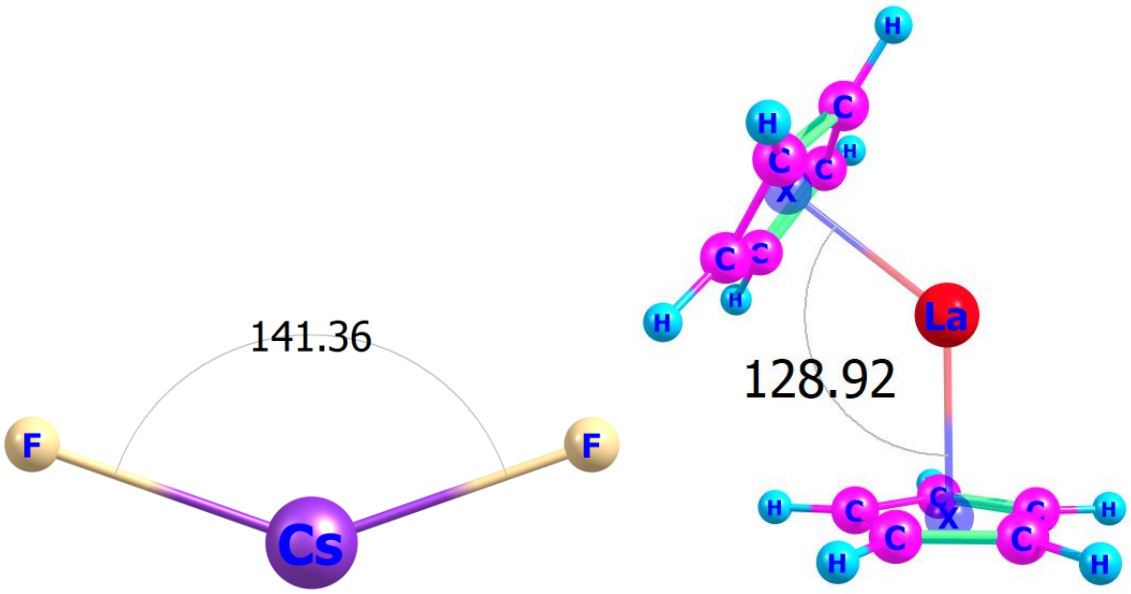


Title: Exploring the Conformational Preferences of Groups 1 – 3, and 13 Metal Halides, Metallocenes, and their Derivatives

Sabahudin Redzic and Kelling J. Donald

Department of Chemistry, University of Richmond

Group 2 metal dihalides are among the most thoroughly examined of the metal halide structures due in part to the bent and quasi-linear nature of some of these compounds. Similarly, the group 2 metallocenes exhibited both coplanar and bent geometries. A variety of bonding models sought to explain this bonding phenomenon including but not limited to orbitals theories and Walsh diagrams, polarized ion models, and the Pseudo-Jahn Teller effect. We examined the isoelectronic analogs of the group 2 metal halides and metallocenes, namely the group 1 anions, group 3 cations, and group 13 cations, to see if they exhibited similar bending patterns. Density functional theory (DFT) calculations were ran to determine equilibrium geometries. We found that, with the exception of the CsF_2, FrF_2, and group 3 dihalides, bending was nonexistent. The structures that reported bending followed existing trends with the highest degree of bending occurring to the heaviest metal difluorides.



Addressing Isomerization of Water Clusters in Diffusion Monte Carlo

Sijing Zhu and Lindsey R. Madison

Department of Chemistry, Colby College, Waterville, ME 04901

Obtaining the vibrational wavefunction from the Schrödinger equation is fundamental to understanding the structural and spectroscopic properties of a water cluster. Nevertheless, the coupling between vibrational modes render the Schrödinger equation analytically unsolvable, and the presence of multiple stable conformations (isomers) for large clusters complicates the wavefunction sampling. Diffusion Monte Carlo (DMC) is a numerical method that uses an iterative "random walk" method to sample the ground state vibrational wavefunction across multiple isomers and approximate the zero-point energy (ZPE). Our research focuses on the complicated behavior of DMC on a simple point charge / flexible water (qSPC/Fw) potential energy surface (PES), particularly in the presence of geometrically and energetically similar isomers. We observed that initializing DMC sampling across multiple isomers frequently leads to unphysical localization in a single isomer, misrepresenting the vibrational wavefunction that should spread across multiple isomers. Conversely, initializing sampling within a single isomer, intended for isomer-specific spectral analysis, can result in leakage to other isomers. These dynamics are closely related to isomerization, which occurs due to the kinetic energy of the vibrational ground state as modeled by the diffusion step in DMC. To better understand isomerization in DMC, we conducted a complete scan of the PES for the water hexamer, locating isomers and minimum energy pathways and compiling them into a transition map. To address the challenges of localization and leakage, we implemented an intermolecularly Guided DMC, which not only guides the intramolecular bond stretching and angle bending modes but also directs the sampling towards selected intermolecular geometries. We evaluated the validity of intermolecularly Guided DMC by analyzing the behavior of ZPE convergence and the fractional contribution of each isomer to the wavefunction sampling. While a multi-isomer PES, typical of systems with non-covalent interactions, requires a large sample size for DMC to accurately capture the intermolecular geometries, our intermolecular guiding approach potentially makes the sampling more computationally tractable.

Olivia DeLucia

Optimizing the Synthesis of Ferroin Catalyst-loaded Sodium Alginate (F-SA) Beads for the Belousov-Zhabotinsky (BZ) Reaction

Model nonlinear systems are useful in a wide variety of fields for furthering understanding of various physical, chemical, and biological phenomena. The Belousov-Zhabotinsky (BZ) reaction is an example of a nonlinear chemical oscillator that has been successfully used to model phenomena such as synchronization, pattern formation and biologic morphogenesis, quorum sensing, and other biological and physical occurrences. The complex mechanism of this reaction can be summarized by three main processes: consumption of bromide, autocatalysis of bromous acid, and oxidation of an organic species resulting in the reproduction of bromide. This study sought to develop a method for synthesizing ferroin catalyst-loaded sodium alginate (F-SA) beads for investigating the origins of complex oscillation behaviors, such as chimera states and mixed period states. In these states, coupled BZ oscillators exhibit partial synchronization and aperiodic behaviors. The experimental results will be used to improve existing kinetic models to capture new bead dynamics. Using a microfluidic experimental system, we investigate the effect of the alginate gelation temperature, setting time, and storage medium on the stability of the beads. Our results indicate that higher gelation temperature yielded more stable beads that increased ferroin catalyst retention. However, long-term storage of F-SA gel resulted in beads exhibiting inconsistent oscillatory behavior that degraded over time. The storage of beads in oil improved the initial concentration of encapsulated ferroin catalyst. More experiments need to be done to optimize the use of fluorinated oil.

How opioids such as fentanyl interact with the mu-opioid receptor (MOR) and the different pathways they influence.

Samrawit Menghistu,[1] Josephine Rocha,[1] Leah Juechter,[2] George C. Shields,[2] and Caitlin E. Scott[1]

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Chronic pain is generally defined as pain lasting three months or more beyond the time of normal tissue healing. Chronic pain is associated with multiple complications, including impaired memory, cognition, and attention; sleep disturbances; reduced physical functioning; and a decreased overall quality of life. It has been proven that the most effective treatment for chronic pain is opioids, which are drugs that bind to the mu-opioid receptor (MOR). MORs are G protein-coupled receptors (GPCRs) that play an important role in pain control. In recent years, the published high-resolution experimental structures of opioid receptors have provided a solid foundation for both experimental and computational studies. Once activated, the MOR can bind to different intracellular proteins, including the G_i protein and β-arrestin proteins. The G_i protein causes signaling pathways leading to pain relief, while the β-arrestins pathway is known for causing undesirable side effects. β-arrestins may sensitize and internalize receptors, which reduces their signaling through the G_i protein pathway. In order to understand these pathways, it is very important to develop opioids that provide the most effective pain relief while minimizing side effects. Our objective is to model how different opioids can stabilize different conformations of the MOR to explain how one ligand can elicit different signaling pathways. In this experiment, we will be looking at the fentanyl bound-MOR in complex with G_i protein, (PDB ID: 8EF5). We used Induced Fit Docking as part of the Schrodinger software to accurately predict multiple ligand binding modes. We will explain how different ligand structures lead to structural changes within the receptor. We are expecting that the higher energy fentanyl structure to dock with the MOR and stabilize a different conformation than what was captured experimentally. This can lead to greater receptor activation even at very low drug concentrations. Knowing how these reactions occur at the cellular level will eventually help us in developing better drugs as well as strategies for reducing the negative effects of effective opioids such as fentanyl. This is essential for creating opioids that may reduce pain while lowering the risk of addiction and other side effects.

Investigating Prion Protein-Lipid Interactions and Prion Protein-Fibril Binding

[1] Noah Greenwood, [2] Jace Westphal, [3]Moo Law La Soe, [1]Patricia Soto

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[2] Department of Biology, University of Nebraska Omaha, Omaha, NE

[3] Omaha North High School, Omaha, NE

Prion proteins, which are glycoproteins anchored to the plasma membrane, play a crucial role in developing fatal neurological degenerative disorders like Creutzfeldt-Jakob Disease. These proteins' misfolding, accumulation, and deposition are central to their toxicity. This misfolding, influenced by lipid composition in the plasma membrane, results in fibrillar aggregates that are pivotal in disease transmission and templated misfolding. Our project uses structural bioinformatics to understand protein-lipid and protein-fibril interactions and their role in remodeling the cell membrane surface. Simulations indicate selective binding of the protein on the membrane, with the surface re-modeling based on the interacting protein residues. Protein-fibril docking calculations suggest that the prion protein binds to the fibril via two loops, driven by hydrophobic or electrostatic interactions. We will report on how our findings are modulated by glycosylation and the intrinsically disordered N-terminus of the prion protein. Ultimately, we aim to identify molecular targets for the rational design of anti-prion drugs to develop effective treatments for these currently incurable diseases.

Mapping thermodynamics of photoexcitation and reaction pathways of phenolic carbonyls

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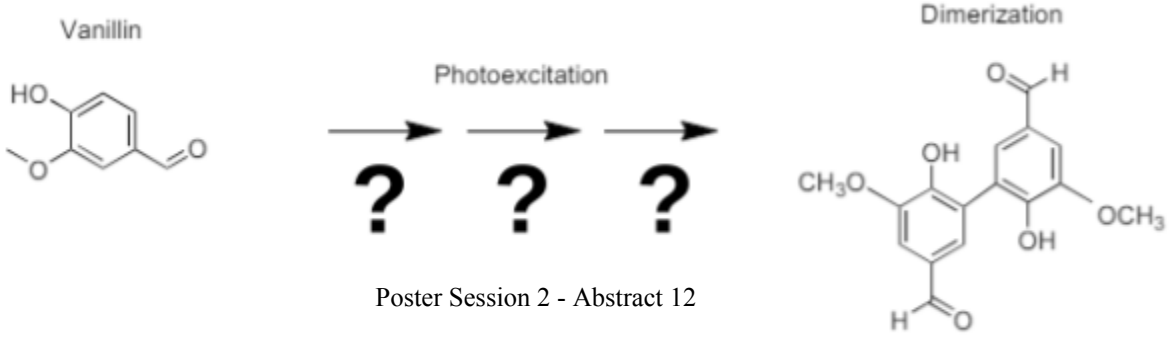
The burning of organic matter in plants, such as lignin, produces a variety of atmospherically significant compounds which are increasing in prevalence as global temperatures rise and wildfires become more frequent. Phenolic carbonyls, such as vanillin and syringaldehyde, are used as model compounds to understand their reactivity and the impact they may have on the atmosphere. Once produced, both molecules are able to undergo photoexcitation within atmospheric conditions, but the outcomes are notably different despite their related structures. Namely, vanillin is capable of dimerization, while syringaldehyde instead decomposes into substituent molecules. To understand why certain products are more likely to form and what significance those products have, electronic structure calculations (B3LYP/6-311+G(2d,p)) were used to model the possible reactivity of these atmospheric molecules. In order to develop an accurate computational model of solvent conditions, a set of simple molecules involved in the dissociation of hydrofluoric acid were used with a variety of basis sets and levels of theory. The initial data collection of electronic energy and spectroscopy of hydrofluoric acid dissociation molecules provided the groundwork to understand different computational models that could then be used to analyze the thermodynamics of atmospherically relevant phenolic carbonyls. Geometry optimization and vibrational frequency calculations done with B3LYP/6-311+G(2d,p) provided a means to compare the relative thermodynamic stability of phenolic carbonyls and the pathways forming their derivatives. These pathways include photoexcitation, oxidation, reduction, protonation, deprotonation, and hydrogen abstraction. Comparing the stability of structures resulting from different pathways helps to identify thermodynamically favorable products and explain why molecules of the same family may react differently despite matching conditions.



Structure-property models for transport in evolving polymer matrices

Erik Sapper, Miles Brockbank, Zoe Bryan, Wyatt Goldman, Liam Alsbury
California Polytechnic State University - San Luis Obispo

The transport of small molecules through polymer matrices is a key characteristic of many material systems, from drug delivery devices to latex paint film formation. While first-principles based transport and diffusion models exist, these do not readily allow for treatment of a polymer matrix that is dynamically changing. For example, the swelling or shrinking of a polymer matrix due to solvent ingress or egress or the crosslinking of the system during polymer film cure. Descriptor-based models for transport through evolving polymer matrices that will enable subsequent material system design, such coatings with controlled volatility profiles during cure, or drug delivery systems with an optimized drug release rate. This work combines thermogravimetric analysis of latex-based paint formulation components to study time and temperature dependent curing and evolution of volatiles. Early efforts at developing QSAR models for volatility of small molecules in a dynamically curing polymer matrix will be presented.

Study of the functionally of chimeric proteins using predicted structures

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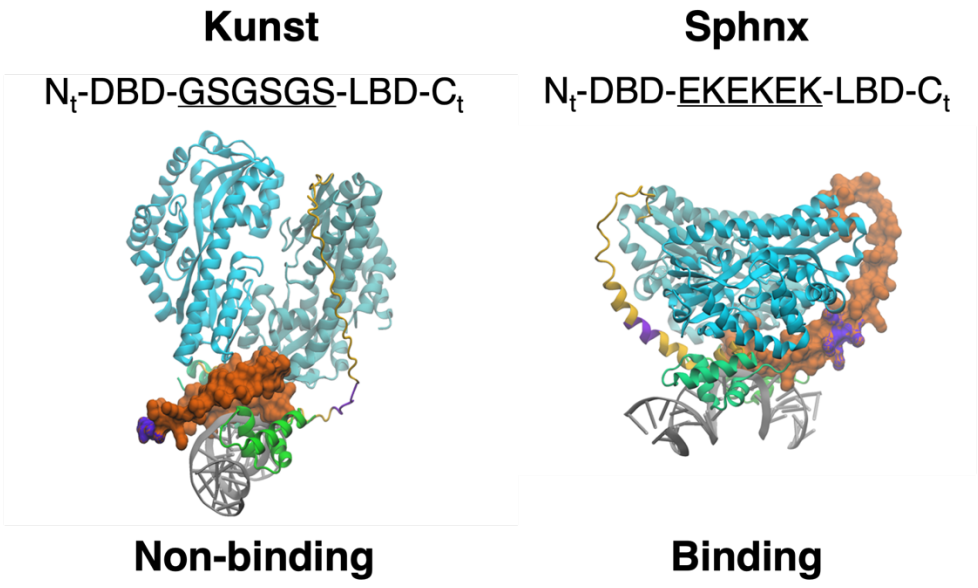
Sphnx is a new multimeric synthetic chimeric protein that has been designed to bind neuraminic acid (Neu5Ac) in a whole cell sensor. Neu5Ac can be found in the saliva of patients with oral cancer; such synthetic protein-based cell sensors could be a promising way detect early disease markers. The protein consists of a DNA binding domain (DBD), an engineered six residue linker, and a ligand binding domain (LBD). Experimental results show that Sphnx protein can bind Neu5Ac, while an almost identical control protein, Kunst, does not bind the ligand. Interestingly, the two proteins differ only by their six residue linkers: Sphnx, N_t-DBD-EKEKEK-LBD-C_t; Kunst, N_t-DBD-GSGSGS-LBD-C_t. With the use of the AlphaFold 3 web server, we were able to predict the 3D structure of both chimeric proteins, modelled both proteins as dimers along with the operator DNA double helix (5'-ATTGTGAGCGGATAACAATT-3' and its complementary sequence). Understanding why the six amino acid linker causes such a difference to functionality is key to designing new protein based sensors. By predicting structures of Sphnx and Kunst and eventually simulating them using molecular dynamics, we hope to understand which key features affect functionality to provide useful insight into new protein sensor design.



Inhibiting the Ryanodine Receptor Ca2+ release in Alzheimer's Disease: S100A1 Inhibitor Drug Discovery

Hamza Mohammed,[1] Megan E. Pelley,[2] and Dr. Caitlin Scott[1,2]
[1]Department of Chemistry and Biochemistry, California State University Los Angeles, California
[2]Department of Chemistry, Hendrix College, Conway, Arkansas

Alzheimer's disease (AD) is a neurodegenerative disease that involves dysregulated calcium signaling triggering neuroinflammation. S100A1, a homodimeric protein promotes the release of calcium from intracellular stores through excitation of the ryanodine receptor (RyR), S100A1-RyR complex with accompanied dysregulation of calcium release leads to neuroinflammatory AD-triggering cascades. The objective of the study involves the use of computational modeling to develop AD-preventative therapeutics via identifying molecular inhibitors of the S100A1-RyR interaction.
An equilibrated structure of S100A1 was developed using molecular dynamics with AMBER software and energy minimizations over 100 nanoseconds in triplicate to develop a model reflective of the human physiological state. The modeling pipeline through Schrodinger's Maestro was further validated with extensive redocking trials based on experimental data. Virtual screening of 7173 compounds was carried out for the identification of potential inhibitors.

Screening yielded three significant hits with high docking scores reflective of strong interactions at the S100A1-RyR interface. The top three scoring compounds CHEMBL3978112, CHEMBL3426696, and Batfenterol showed high binding affinities with docking scores of -8.634, -8.240, and -7.442 kcal/mol, respectively.

This work demonstrates the usefulness of structure-based screening for the identification of inhibitors of S100A1-RyR protein-protein interaction. The identified compounds are promising leads for experimental validation and potential therapeutic development for Alzheimer's disease. This study validated computational tools and ligand starting points for drug design targeting AD, offering a novel approach to address the critical need for effective Alzheimer's treatments.

Molecular Modeling of beetle antifreeze protein protects alcohol dehydrogenase in freeze-thawing conditions

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Freeze-labile enzymes are proteins sensitive to freezing temperatures. Their long-term stability poses a unique challenge as the enzymes lose their function under freeze-thawing conditions. Freezing is commonly applied to proteins to slow down the denaturation process. To protect these proteins during the freeze and thawing process, additives and co-solutes are added to the enzyme solutions; however, there is still a need to identify effective protectants since many on the market are prone to crystallization and are costly. The antifreeze proteins (AFPs) of cold-adapted organisms have the ability to inhibit ice crystal growth and provide protection. Through multiple repeated freezing and thawing cycles of ADH with added DAFP-1 demonstrated increase ADH activity. In this study, beetle antifreeze proteins (AFP) from *Dendroides canadensis* (DAFP-1) are used along with the freeze-labile enzyme alcohol dehydrogenase (ADH) to investigate its cryoprotection mechanism by structural modeling of the protein-protein interactions of ADH: DAFP-1 complexes. The webserver ClusPro performed protein-protein docking, and subsequent analysis of the top 10 complexes based on "balanced" energy scoring functions show a salt-bridge interaction between Arg25 of DAFP-1 and Glu101 of ADH. Additionally, the Visual Molecular Dynamics Hydrogen bonds plug-in identified six hydrogen bonds between the two. Thus, the molecular docking identified interactions between DAFP-1 and ADH, which provides better insight into the mechanistic role of AFP in preserving freeze-labile proteins.

Modeling Dimerization of 4-Mercaptopyridine using Thermodynamics and Vibrational Spectroscopy

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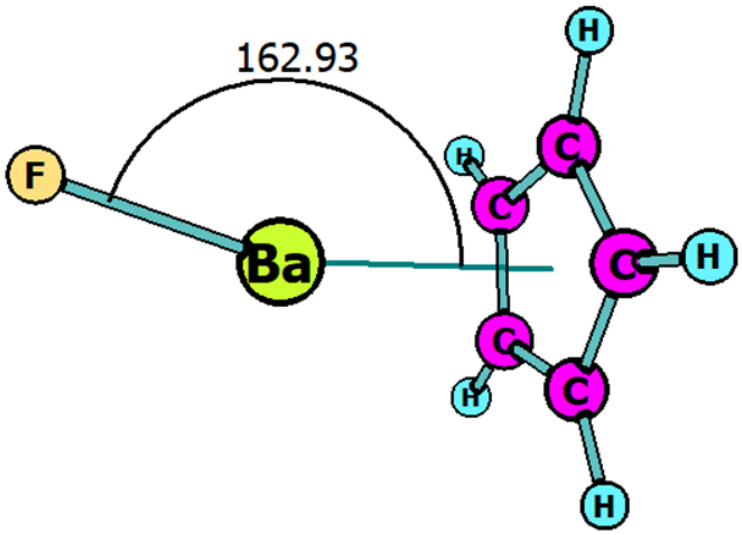
Recent experimental gold Tip-Enhanced Raman Spectroscopy (TERS), a form of vibrational spectroscopy, of the organic molecule 4-mercaptopyridine captured spectroscopic changes, indicating that an unknown reaction was taking place. Experimentally, TERS is used as a signal enhancing technique for Raman spectroscopy by utilizing the electric field and chemical enhancement of the electrons found on transition metals such as gold or silver to enhance the polarizability of an attached molecule, thus increasing the Raman sensitivity by a factor of 10^3-10^7. Due to the controlled, single-molecule experimental setup, the change in spectra over time possibly indicates dimerization. However, because there are multiple possible covalent bonds with which a dimer of 4-mercaptopyridine may be formed, the final product is unknown. Electronic structure calculations were used to determine the thermodynamics of possible dimers along with computationally predicted spectroscopic TERS signatures of the dimer so that the unknown 4-mercaptopyridine dimer may be identified from the experimental TERS spectra. To replicate the gold tip and its chemical effects that were present in the experimental procedure, the 4-mercaptopyridine was modeled attached to a 20-atom gold tetrahedron and had geometry and Raman Spectroscopy run on Gaussian 16 with B3LYP/LANL2DZ theory. This investigation into an unexpected result of TERS can help experimental researchers gain a better understanding of the limitations and side-reactions that may occur during TERS experiments.

Implications on the Bending of Cyclopentadienyl Ligands in Half-Sandwich Complexes.

Brice Di Carlo, Sabahudin Redzic, Kelling J. Donald

Gottwald Center for the Sciences, Department of Chemistry, University of Richmond, Virginia.

Abstract: Metallocenes are well-known compounds in organometallics that experience co-planar or bent configurations. It has not been fully established experimentally or computationally the extent to which half-sandwich complexes experience bending. We have investigated the bond angles of C_5H_5-M-X systems of group 2 half-sandwich complexes, and the influence of methylation on these complexes. Optimization and frequency calculations at the MP2 and wB97X-D level of theory have been used to determine the bond angles and bond lengths. We find that only certain heavy half-sandwich structures experience a substantial degree of bending with particular halogens and alkaline earth metal combinations. C_5H_5-Ba-F showed the most significant bending, all other C_5H_5-M-X complexes showed to be linear. Further investigations have been carried out to assess the energy barriers to bending in these systems. These results offer insights and predictions for future experimental investigations.



Allosteric Signal Propagation in PDZ: A Network Analysis with Rotamerically Induced Perturbations

Samvit P. Singhal, Kelly M. Thayer, and David L. Beveridge

Wesleyan University

Allostery is a special case of cooperativity in protein-ligand binding, where the binding of a molecule at one site on a protein affects the function at a different, distal site. Understanding the mechanism of thermocyclic signal transmission in the PDZ3 protein (Figure 1) is essential, as PDZ3 is a crucial component in cellular signaling and the regulation of protein-protein interactions. Moreover, we know that the thermocycle directly influences allosteric regulation in PDZ3. This knowledge has significant potential for advancing our understanding of the signaling pathways involving the p53 protein, a major factor in cancer research. This study proposes two computational methods to investigate this phenomenon.

1. Rotamerically inducing perturbations using the Ho-Agard method to heat the atoms at the active site, followed by molecular dynamics (MD) simulations to observe the equilibration process. This allows us to map how thermal energy spreads over the atoms as a function of time.
2. Creating a protein structure network (PSN) with amino acids as nodes and edges representing assumed interaction strengths. We will then perform a Markov Transient Analysis (MTA) to map the communication channels in the PSN.

In this study, we aim to characterize allosteric signalling channels between the allosteric effector and the ligand binding site in PDZ.

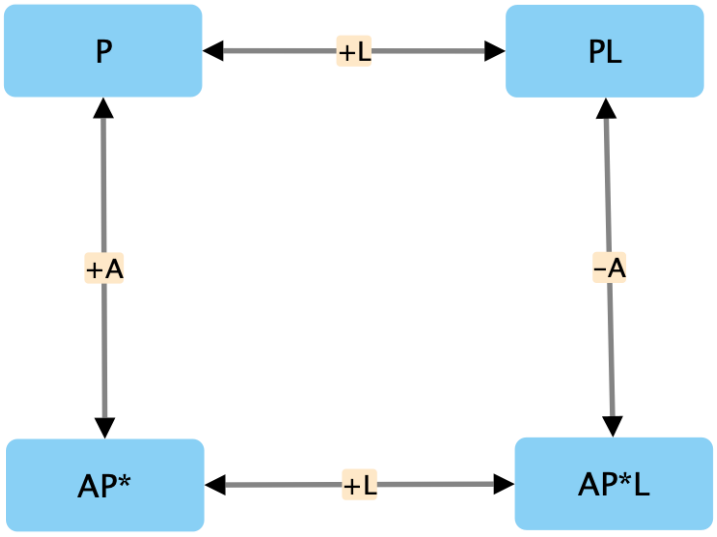


Figure 1: Thermocycle of allostery. P = protein; P = allosterically activated P; L = ligand (binding site); A = allosteric site*

Computational Study of Water Filtration through Graphynes' Pores

Alyssa McPhee, Luiz Oliveira

Department of Biology and Physical sciences, Mount Vernon Nazarene University, Mount Vernon OH.

Carbon-based nanotechnology has attracted considerable attention for industry purposes including numerous electrochemical applications, fuel cells, and water electrolyzers. Carbon has several hybridization states that create different allotropes. A common example of this is graphite, which is an sp^2 allotrope of carbon. A recent synthesis of a novel carbon allotrope, graphyne, is composed of sp- and sp^2- hybridization with uniform distributed nanopores (Figure 1) and has been discovered to have applications developed in a wide range of fields such as energy, environmental issues, and biomedicine.

The nanopores are created with chains of carbon-carbon triple bonds, and the size of the pore can be manipulated through changing the number of triple bonds (represented by *n*). This study investigates graphyne-*n* structures for n = 3, 4, and 5.

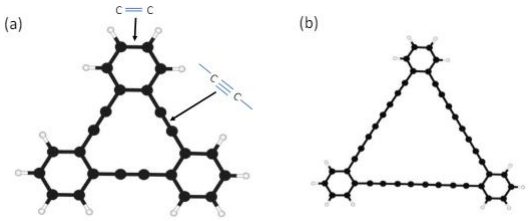


Figure 1: Examples, with a) n = 1 triple bond and b) n = 4 triple bonds on each side

A recent application for graphyne has been in the desalination process. Desalination is a viable solution to alleviate the pressing issue of water scarcity. Water scarcity is important because, even though we have abundant water resources, 98% of it is in the form of salty water we cannot drink. Current desalination methods encounter high energy usage and expensive infrastructure as obstacles.

Recent molecular dynamics (MD) simulations have demonstrated the usefulness of graphyne-n=3,4,5 for desalination. However, these simulations relied on force fields (FF) and showed a disappointing spread of results. Therefore, there is a need to go beyond FF schemes while maintaining a reasonable computational cost. To this end, we have used the DFTB method that maintains a reasonable computational cost and also provides an explicit quantum description of the electronic structure. Our MD simulations are accelerated with metadynamics (MetaD), achieving enhanced sampling through the introduction of a history-dependent bias potential, (Figure 2). We will show the filtration performance of grapyne-n structures as well as the free energy profiles of different salts across the nanopores.

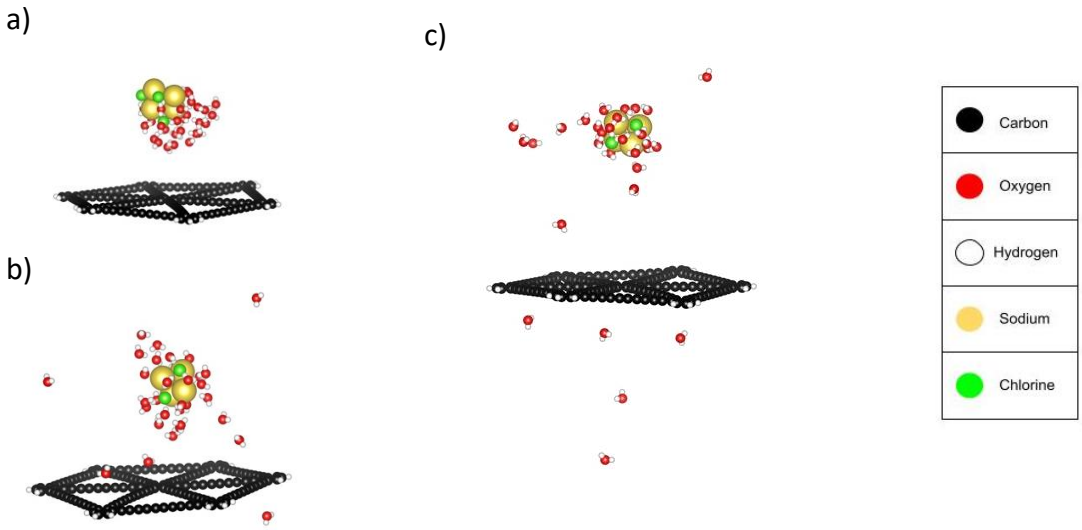


Figure 2: Snapshots of a MetaD simulation of 32 water molecules and 4 Na and 4 Cl ions through graphyne-5 at a) 0 ps, b) 20 ps, and c) 36 ps

Free energy landscape of knotted and unknotted homolog proteins

Alyssa McPhee, Cailey Bubis, Mason Lewis, Luiz Oliveira

Department of Biology and Physical sciences, Mount Vernon Nazarene University, Mt Vernon, OH

Knotted proteins have been identified in approximately 1% of the entries in the protein data bank. These proteins are generally topologically more complex than their unknotted homologs. Additionally, they have a diverse topology with different levels of complexity. Four distinct knot types have been detected in proteins: trefoil (3_1), figure-of-eight (4_1), three-twist (5_2), and stevedore (6_1) knots (Figure 1).

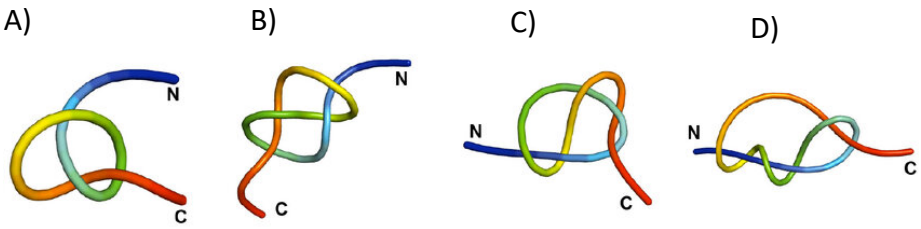


Figure 1*. Schematic representation of A) 3_1, B) 4_1, C) 5_2, D) 6_1 knots

The exact purpose of knots within proteins and their implications are unknown. However, it is theorized that their complicated topology, and thus longer folding time, contributes to impaired function. This impaired function may have a relationship with neurodegenerative diseases, which are known to be caused by protein misfolding and aggregation.

Knotted proteins consistently navigate structural constraints to form a knot from a simple native loop. The persistent appearance of this generally suboptimal structure suggests that these proteins may have some sort of stability advantage over unknotted proteins. It is hypothesized that knotted proteins, when compared to their unknotted counterparts at equivalent temperatures, will resist denaturation more effectively, and will therefore be more stable.

In this project, we seek to better understand how the presence of a molecular knot affects a protein's unfolding mechanism compared to its unknotted homolog. To accomplish this, we are studying the free energy surface (FES) of the unfolding/unknotting as a function of the fraction of native contacts. To overcome the high-energy barriers along the FES of these proteins, we use metadynamics (MetaD). Figure 2 shows the structure of the knotted protein MJ0366 (PDB ID 2EFV) and the obtained unknotted structure from our MetaD simulation.

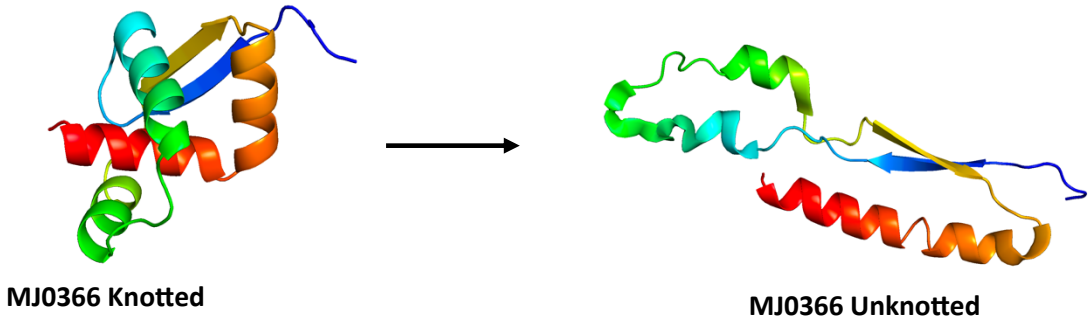


Figure 2: Unknotting of MJ0366 from *Methanocaldococcus jannaschii* (PDB ID 2EFV), a knotted protein, using MetaD.

*Adapted from Nicole C H Lim and Sophie E Jackson 2015 J. Phys.: Condens. Matter 27 354101

Molecular Dynamic Simulations of p53 Inform Machine Learning of Allosteric Reactivators

Jeremy T. Zay, Theodore B. Sternlieb, Conrad Fischl, and Kelly M. Thayer

Allosteric modulators are compounds that bind to a protein at a non-active site, causing a conformational change that affects its activity. PK11000, an allosteric modulator of interest from the literature, binds to the p53 protein with a Y220C mutation. A crucial tumor suppressor, mutations in p53 present in approximately 50% of cancers. For p53 with the Y220C mutation, the compound PK11000 was able to allosterically restore its normal function. However, PK11000 is toxic to humans, and since it binds to p53 in an unintended site, the process is poorly understood.

Understanding the Y220C mutation is a key case study for developing a pipeline for creating allosteric drugs to restore p53 native activity. In this study, we investigate the allosteric properties of p53 using molecular dynamics (MD) simulations, which provide information for machine learning (ML) approaches for the development of allosteric drugs.

Title: “Constructing a QSAR-based model to help detect GHB”

Authors: Sarah Chang, Zane Fink, Dr. Erik Sapper

Many emerging technologies are being used to combat drug-facilitated sexual assault (DFSA), ranging from fingernail polishes that change color when dipped in a spiked drink to wristbands and other wearables that can provide real-time indication of a dopant in a drink before consumption occurs. While some of these technologies rely on chemical indicators with specific affinities for particular DFSA drugs of concern, many rely on other mechanisms, which can be problematic. For example, acid-base indicators can easily lead to false positives and false negatives. Here, we propose a QSAR-based study of fluorophores as they respond to gamma-hydroxybutyrate (GHB). Fluorophores will be synthesized, binding and fluorescent activity will be recorded, and a descriptor-based model will be built to provide an in-silico design tool for improved fluorophore discovery.

Anticancer Fluorouracil: Uncatalyzed hydrolytic deamination of Cytosine to Uracil.

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Potential energy surfaces (PES) studies are invaluable for uncovering the intricate details behind the geometry of chemical reactions dynamics. 5-fluorouracil (5-FU) is an anticancer compound synthesized as Capecitabine; a pro-drug inhibiting 5-FU cytotoxicity until it reaches an enzymatic conversion by cytidine deaminase.[1,2,3] Here, the hydrolytic deamination (HD) mechanism alters cytosine with water to form uracil and ammonia. We study the HD mechanism using quantum chemistry calculations and the B3LYP density functional. Cytosine was used as a model of cytidine (1), and additional molecules including waters, zinc ions, and acetate ions were included to more appropriately mimic the active site of cytidine deaminase. Our calculations compare favorably to existing literature data for this system. The calculations provide detailed pathways for the cytidine deaminase catalyst and establish a basis to compare relative energies of the catalyzed cytosine deaminase mechanism.[4]

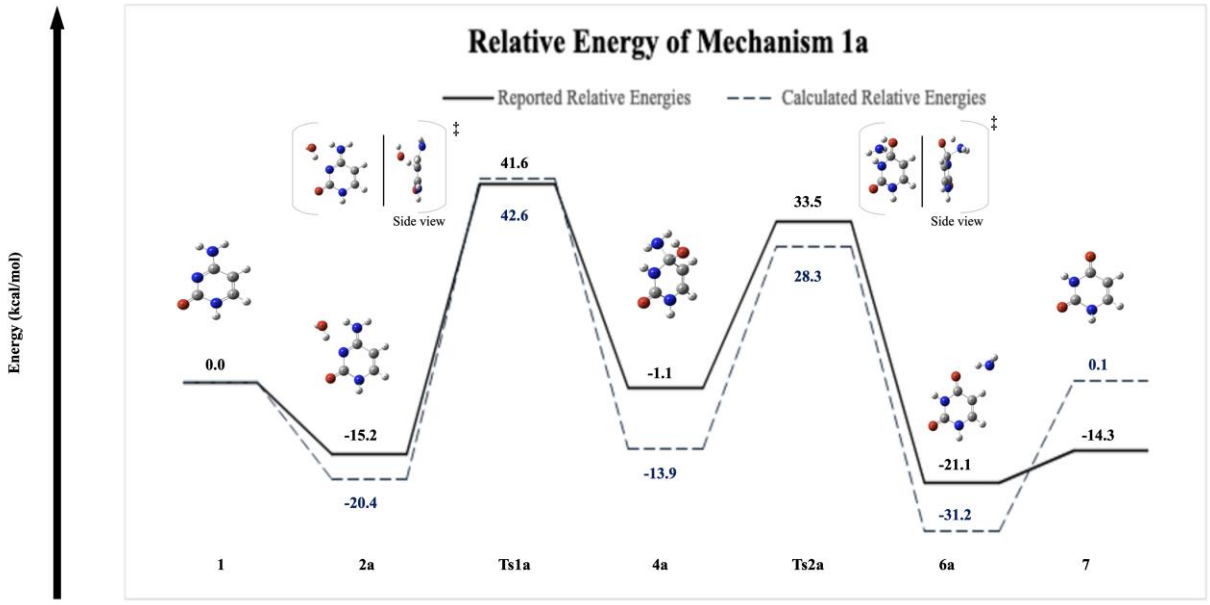

Figure 1. Uncatalyzed hydrolytic deamination, potential energy surface diagram (kcal/mol). Published data by Matsubara et al using B3LYP/6-31G** level in solid line.[4] Calculated data in dashed line HF, 321-G. Optimized geometry and bond angles.

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Tumor Suppressor Protein p53 Isoform Molecular Dynamics

Fernando Caballero & Kelly M. Thayer
Wesleyan University – Middletown, Ct

Eukaryotic proteins are translated from encoding DNA not as a single sequence but as several variants through a process known as alternative splicing. This is also the case for p53, a tumor suppressor protein that has twelve variations in different tissues of the human body. However, most current studies on p53 do not take this into consideration.

We explore the hypothesis that the difference in protein sequence may hard code differences in the way that p53 and DNA interact, affecting the role of p53 as a transcription factor. We aim to determine the dynamic differences in these variations, also known as isoforms, through molecular dynamics simulations. Furthermore, we explore the effects of mutations on the isoforms, particularly the Y220C mutation, in which Tyrosine is replaced by Cysteine in the DNA Binding Domain. This exploration is conducted from a dynamic standpoint through the use of Molecular Dynamics Markov State Models, among other methods.

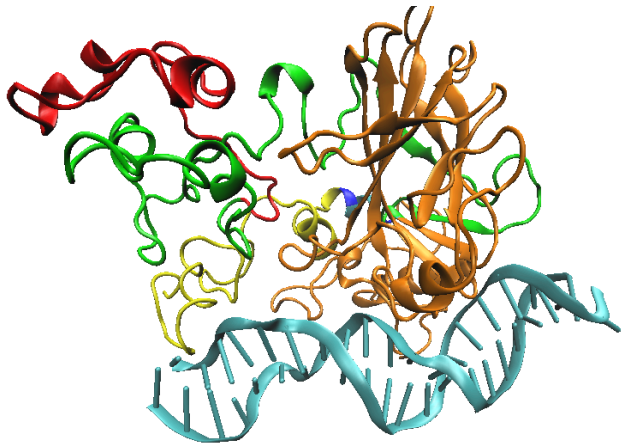

Figure 1:Full Length Y220C p53 Protein Showing Isoform Variable Regions.
Red: Isoform Variable Region 1
Green: Isoform Variable Region 2
Orange: DNA Binding Domain
Blue: Isoform Variable Region 3
Purple: Isoform Variable Region 4

Machine Learning Insight and Optimization of Keto-Enol Tautomerization

Anthony Vendome, Gerrick E. Lindberg, Frank X. Vázquez

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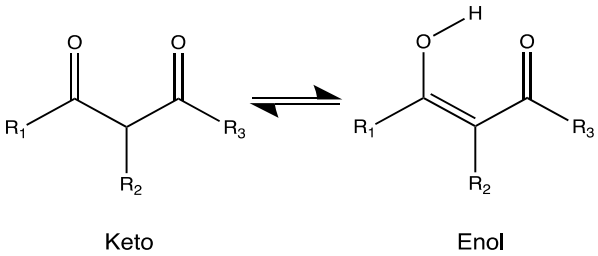
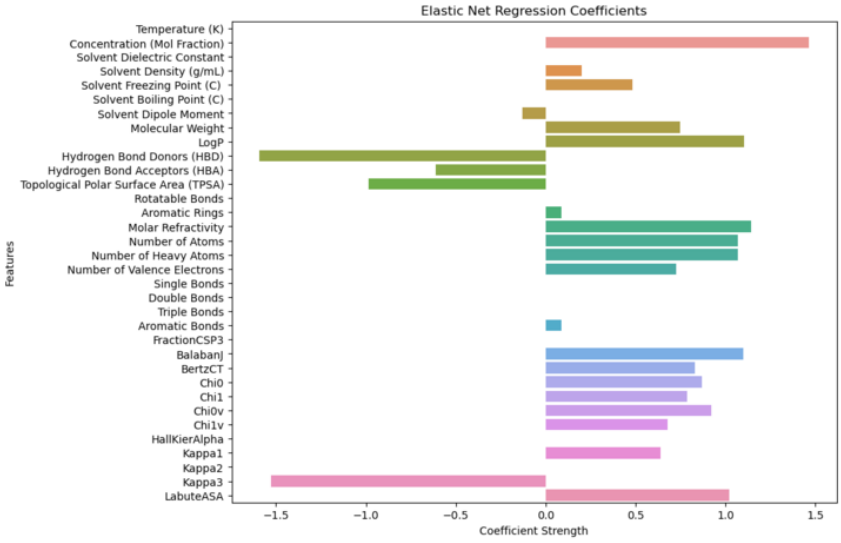
This project aims to develop a comprehensive framework to optimize chemical reaction yields using existing data, initially focusing on keto-enol tautomerization. Leveraging machine learning (ML) algorithms, we will identify key macroscopic and molecular properties that play a role in keto-enol tautomerization's reaction equilibrium and kinetics. ML methods such as LASSO, Ridge, and Elastic Net regressions will be used to predict equilibrium constants, with subsequent goals of predicting rate constants. After this model is developed for tautomerization, we hope to generalize this framework for other organic reactions. This approach aims not only to improve the yields of experimental reactions, but to offer deeper insights into mechanistic pathways of new reactions. By gaining a stronger understanding of these pathways, reaction conditions can be optimized for more favorable outcomes, such as enhancing reaction yields and improving the sustainability of chemical/pharmaceutical manufacturing.





Allosteric Signaling in p53: An Analysis of p53 Function and Dysfunction Using Molecular Dynamics Simulations

Finn Hartigan-O'Connor, Kelly M. Thayer, and David L. Beveridge Wesleyan University

Allostery is a process by which binding of an allosteric effector at one site of a protein affects the function of another, distant site. A drug binding to its target protein can affect the structure and function of the whole protein, changing its affinities and properties. The allosteric interaction we are interested in is the ability of the drug PK1100 to rescue the function of the p53 protein after a Y220C mutation. p53 is an important protein in cancer regulation, as it is involved in signaling cells to commit apoptosis in response to genetic damage. Proper p53 function requires that the protein binds DNA at a certain place. The Y220C mutation mentioned above, however, reduces p53's affinity for DNA by changing the structure and rigidity of the protein. But when PK1100 is bound to p53, although it binds distantly from the DNA-binding site, it nonetheless renews the ability of p53 to act almost as normal. This restoration of function was discovered by accident and unfortunately, PK1100 has toxic side effects and so is not a viable drug; nonetheless, our lab is attempting to find or design other drugs with similar ability to restore p53 function, and cause apoptosis of tumor cells.

In this paper, we use analysis of molecular dynamics (MD) simulations to understand how rescue of function happened with PK1100. We try to understand how mutation can affect p53's interactions with DNA, and what properties of the p53 structure allow PK1100 to reverse that change. We aimed to understand which residues of p53 are connected, so as to determine the path of change from the allosteric binding site to the active site of p53 which is used by PK1100. After exploring the physical properties of allostery in our MD simulations, we discussed what our analysis can tell us about rescuing the function of p53.

Dynamics of water on zirconia and yttria-stabilized zirconia surfaces

Daniel Daly, Luiz Oliveira

Department of Biology and Physical sciences, Mount Vernon Nazarene University, Mount Vernon OH.

We use density functional theory (DFT) calculations to obtain energetic and structural information of ZrO2 surfaces and yttria-stabilized zirconia (YSZ) surfaces on the (100), (110), and (111) crystallographic orientations in contact with an aqueous solution. Additionally, to provide information on the system's dynamics and to include temperature effects we use ab initio molecular dynamics (AIMD). Our AIMD simulations are performed at different temperatures as well as with different water surface coverages to determine the effect of chemisorbed water on the stability of the different surfaces.

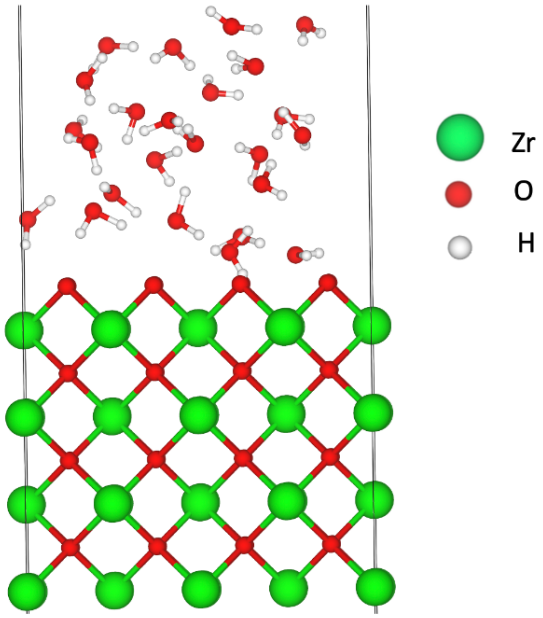


Figure 1 Molecular representation of water molecules physisorption on ZrO2(110) surface

Title: Unveiling the Function of P30646 as a Xylulose Printing: Kinase: A Biochemical Investigation

Authors: Chaunice V. Figueiredo, Jaren C. Obia, Laura A. Rusch-Salazar and Bonnie L. Hall

Institution: Grand View University

Abstract:

P30646, a protein with known structure but unknown function, was subjected to a thorough biochemical investigation to illuminate its role in cellular metabolism. Through a combination of enzymatic assays, protein structure analysis, and computational tools, such as CLEAN, BLASTp, DALI, SPRITE, and Interpro, it was discovered that P30646 might function as a xylulose kinase. After extensive research into P30646, the protein was over-expressed and purified. Enzymatic assays were used to determine the catalytic activity of P30646 in phosphorylating xylulose to produce xylulose-5- phosphate. The kinase assay showed that P30646 does act to phosphorylate xylulose.

Developing Quantum Machine Learning Algorithms to Predict Electrophilicity and Teaching High Schoolers About Quantum Information Science

Leah Boyle[1], Padmanabh Kaushik[1], Nicholas Sorak[1], Kusum Subedi[1], Swetha Tadisina[1], Vedit Venkatesh[1], Lucas Villamil[1], Nam Vu[1,2], Crystal Yeung[1], Maya Zilberstein[1], Delmar Azevedo Cabral[2], Brandon Allen[2], Pouya Khazaei[3], Andrew Projansky[4], Anthony Smaldone[2], Scott Smart[5], James Whitfield[4], Victor Batista[2], Heidi P. Hendrickson[1]

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Machine learning (ML) methods are increasingly used to predict toxicity of chemical species and are especially useful for areas such as the pharmaceutical industry, for virtual screening and de novo drug design, as well as environmental protection efforts. Although ML models are effective, they require large datasets and significant computing time. Quantum machine learning (QML) has the potential to overcome these limitations due to the smaller data sets required to train an effective model, as well as the quantum advantage in computing time. Recently, the Batista group at Yale University showed that a hybrid quantum-classical neural network for predicting drug toxicity performs as well as a classical neural network. In this work, we extend the QML approach to predict the electrophilicity in aqueous pollutants, and compare to a corresponding classical ML model.

Quantum mechanics is not often taught in high school, and even when it is, it remains a challenging subject for introductory students. Game-based approaches are often to engage introductory students to quantum mechanical concepts, however there have been few studies investigating the learning outcomes from such activities. In this study, high school students are introduced to the idea of superposition through a workshop based on a "quantum chess" game. Specifically, we present our investigation on the impact of the workshop activities on student learning outcomes and student perceptions.

MD Sector Analysis of Tumor Suppressor Protein p53

Josh P. Phythian, Chris Chiu, Kelly M. Thayer

Wesleyan University

Allosteric signaling occurs when the perturbation of one part of a protein affects another part of a protein via the active site. A mutation can act as an allosteric effector distally controlling the active site of a protein. Similarly, allosteric effectors have been shown to have deleterious effects on hotspot mutations. These effects occur via amino acid networks within proteins. However, due to the complex nature of amino acid interactions, network dynamics and protein behavior is a hard process to predict. The sector hypothesis posits that a cohesive network of amino acid residues is capable of transmitting an allosteric signal through a protein. Our model system, the p53 tumor suppressor protein is implicated in 50% or more of all human cancers. We observed *in silico* that p53 contains a network of cohesive amino acids, which can send signals over long distances within the protein. The test case of allosteric restoration by the introduction of a small molecule has been demonstrated by the compound PK1100, which is not suitable as a drug candidate. This became the proof of concept providing the basis for a reverse engineering of other molecules suitable for human cancer treatment. This study undertakes the development of MD sectors, a methodology for identifying a cohesive network for the propagation of long range allosteric signals. The implications for utilizing sectors for the development of allosteric therapeutics for currently undruggable diseases are considered.

Dalton Michael Dencklau

The Protein Data Bank (PDB) contains over 198,000 experimentally determined protein structures, approximately 4300 of which have not been assigned a specific function. One such protein is PDB ID 3r8e from *Cytophaga hutchisonii,* a potential kinase with a solved structure but no confirmed function. Utilizing modules from the Biochemistry Authentic Scientific Inquiry Laboratory (BASIL) consortium, we first used a range of *in silico* tools to analyze 3r8e. These online tools included BLASTp, Pfam, and DALI. Together the *in silico* results indicated that 3r8e could be a glucose kinase. Next, molecular docking was used to explore whether glucose was an appropriate substrate for 3r8e. Glucose and five other sugars were docked into 3r8e along with ATP. Although all the sugars could be docked, glucose had the best calculated affinity for the active site. The 3r8e protein was then overexpressed in *E.coli* and purified using nickel affinity chromatography. Protein purity was assessed using SDS PAGE analysis. The purified protein was subsequently used in coupled kinase assays to determine the specific activity of 3r8e for the six different sugar substrates. A high specific activity was seen for 3r8e with glucose as the kinase substrate. Little to no activity was seen using fructose, galactose, lactose, ribose, or sucrose. Thin layer chromatography (TLC) was used to validate phosphorylation of glucose. In summary, online tools, molecular docking, coupled assays, and TLC using purified protein demonstrate that 3r8e is a glucose kinase.

Developing a QSAR model for enzymatic polymer degradation.

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Co-Authors: Giselle, Jordan, Ryan, E. Jones, Ourcelium

Recent studies have shown that certain enzymes found in the mycelial structure of fungi can break down commercial polymers into smaller oligomers and polymer fragments. Current research at Cal Poly is exploring the long-term mycelial degradation of polymers, although this mode of enzymatic degradation is slow and not particularly suitable towards scaled up applications. Here, we propose the use of molecular descriptors and polymer QSAR approaches to discover polymer design rules that are particularly relevant for enzymatic degradation. Experimental results of early mycelial degradation studies will be presented, along with initial work in screening molecular descriptors that would be suitable for an enzymatic polymer degradation model.

Oskar Garcia

The composite cathode consisting of garnet-type solid-electrolyte $Li_7La_3Zr_2O_{12}$ (LLZO) and active material $LiCoO_2$ (LCO) is one of the most promising solutions for the cathode design of all-solid-state lithium batteries. The transport properties of Li within the LLZO-LCO composite cathode are known to be sensitively dependent on the composition and microstructural features. This study focuses on computationally refining the performance of solid-state batteries by modifying the porosity and volume fractions of the LLZO-LCO composite cathode while considering the variations in the microstructural features. Various 2D and 3D microstructures were synthesized using a stochastic stacking particle model and the corresponding effective diffusivity of Li is calculated using a numerical homogenization method, which allows for a systematic assessment of the impact of composition on lithium transport within the microstructure. By identifying the optimal ratio between LLZO and LCO phases and porosity, this research yields crucial insights for improving the performance of solid-state batteries by tailoring the composite cathode.

Figure 1: A) An example 3-dimensional microstructure with 20.3% percent vacuum (white space) and 39.25% percent LCO (yellow) and 40.45% LLZO (orange). B) The highest effective diffusivity (purple) is found when the LLZO percentage is highest. Once the vacuum percentage is 30% or higher, minimal effective diffusivity (red) is observed.

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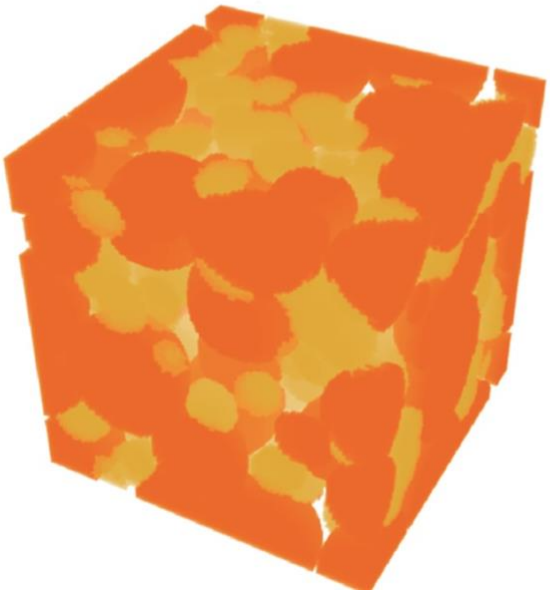
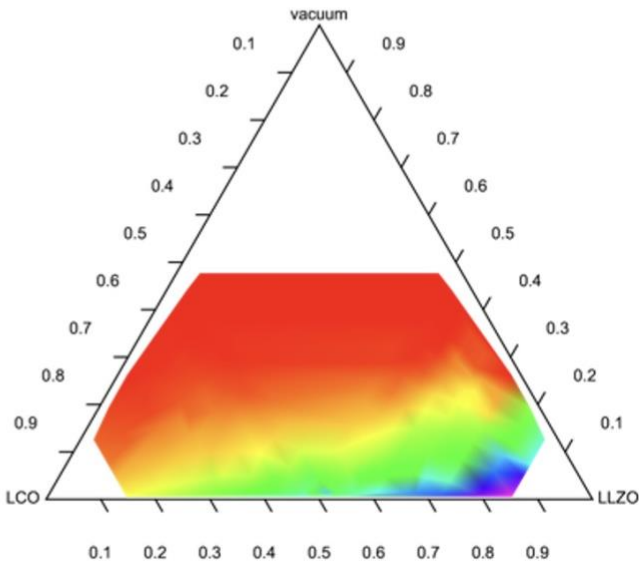
A)



B)



A physiologically-relevant computational model of rotavirus non-structural protein 4 (NSP4) in a membrane environment

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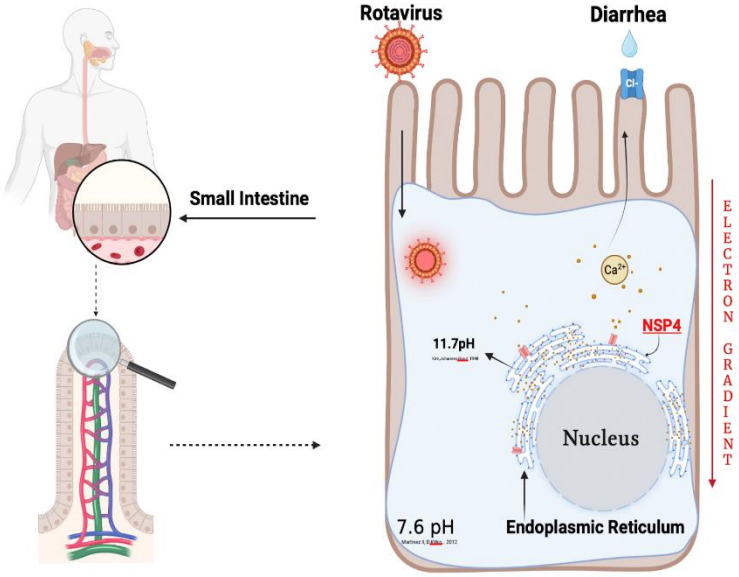
Non-structural protein 4 (NSP4) is found to interact with the endoplasmic reticulum (ER) and is involved in RV infection, causing alterations in Ca^{2+} ion concentration that lead to disease. Thus, NSP4 is vital in RV replication, morphogenesis, and pathogenesis. It is recognized that the ER plays a key role in rotavirus replication and disease by being the target of NSP4's activity. The graphical abstract shows the natural buffer conditions of the cytoplasm and ER of an enterocyte cell in the small intestine during rotavirus infection. It is shown that NSP4 alters the endoplasmic reticulum's Ca^{2+} ion concentration by releasing it from the ER lumen. This alteration in the electron gradient between the ER and cytoplasm is a major contributor to rotavirus disease. By assessing the natural conditions of cytoplasm and ER of an enterocyte during the naturally occurring infection, it is possible to understand the activity of NSP4 and to design drugs to target RV. However, due to the limitations of in vitro methods to study NSP4 structure (including cost and time), computational analysis of the protein is a viable alternative to simulate NSP4 dynamics. This project sought to assess the behavior of NSP4 folding and dynamics in a membrane model that mimics the human enterocyte ER built using CHARMM-GUI. Using the molecular dynamics simulation software GROMACS, the NSP4 monomer was studied in an ER-like membrane with Ca^{2+} and Cl^- ions in the flanking aqueous solutions. Equilibration of the system showed folding of the N-terminus toward the membrane, which is consistent with prior biochemical data. Ongoing studies seek to determine the conformation of dimeric and tetrameric forms of NSP4 in this environment.



Modeling the Complex Surfaces of Citrate-Coated Silver Nanoparticles

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Understanding the mechanisms by which silver nanoparticles (AgNPs) exert their antibacterial effects is crucial for ensuring their safe use in consumer products. While it is well known that silver ions are toxic to bacteria, the dissolution behavior of AgNPs and its dependence on environmental factors remains poorly understood. Building on previous experimental work that found a relationship between biomolecule concentration and AgNP dissolution rates, this study employs molecular dynamics simulations to investigate the surfaces of AgNPs before biological molecules are added. We focus on the commonly used citrate-coated AgNPs. In this study, we analyze the stable citrate coating in terms of the distribution of citrates across the surface. The spatial orientation of the citrates relative to the nanoparticle is also quantified. These investigations are used to determine if there are any notable trends associated with these two factors and build a clear picture of the citrate coating. We also performed seven hundred 2 ns simulations where a random surface silver atom was given a +1 charge. These simulations were used to study AgNP dissolution and determine whether the coating affects the dissolution behavior. Future work will focus on extending simulations to 100 ns and incorporating biomolecules to capture more complex surface interactions.

The Effect of Molecular Dynamics Thermostat on Simulated Ensemble Absorption Spectra: Cresyl Violet in Methanol

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In order to produce accurate simulations of absorption spectra for molecules in solution there is a need for accurate sampling of chromophore-solvent configurations; these can be generated from molecular dynamics trajectories. A key factor in controlling the sampled chromophore solvent configurations is the temperature of the trajectory. The temperature is controlled by the model of the thermostats. Three common varieties of thermostat are Berendsen, Langevin, and Nose Hoover. Nose Hoover is regarded as being more accurate in the reproduction of ensemble results, Langevin is often used where solvent interactions are of key importance, and Berendsen is typically used for quick equilibration. In a prior study performed in the Isborn group, a molecular dynamics trajectory using the Berendsen thermostat resulted in a simulated absorption spectrum for the cresyl violet chromophore in a methanol solution that was too narrow when compared to experimental results. We then hypothesized that a potential cause of the narrow spectrum was due in part to the poor description of the chromophore's temperature when using the Berendsen thermostat. In this study, we tested Nose Hoover, Berendsen, and Langevin thermostats when applied to the molecular dynamics trajectories of solvated cresyl violet. We here analyze the chromophore temperature, dynamics of hydrogen bonds, and simulated absorption spectrum.