11TH ANNUAL

CHEMISTRY RESEARCH SYMPOSIUM

CLEMSON UNIVERSITY

Message from the Chair

Dear Faculty, Staff, Students and Honored Guests,

Welcome to the 11th Chemistry Research Symposium, which highlights research performed at Clemson by our students and at other institutions by our honored guests. All of these students have worked very hard to highlight the variety and importance of research being done in chemistry. Interact with the poster authors and experience the enthusiasm and dedication they have for their work. Enthusiasm is contagious, and we hope that you will be inspired by your conversations with them to want to know more. Science isn't hard work for the curious, but it does provide education and training for a wide variety of careers and vocations, and chemistry, as the central science, provides a jumping off point to a world full of opportunities.

We hope you enjoy your time with us!

Dr. Daniel Whitehead
Department Chair
College of Science Dean's Professor
Department of Chemistry
Clemson University

Keynote Speaker

Biosensing with Square-Dancing DNA Bowties

Prof. Christopher J. Easley

Department of Chemistry and Biochemistry, Auburn University, Auburn, AL

Biomarker quantification plays a vital role in human health management, disease diagnosis, and biomedical studies on patients, animals, or cell and tissue culture models. The ideal biosensor is capable of robust measurement even in complex media like blood or serum. A familiar example of a successful technology in point-of-care (POC) biosensing is used by hundreds of millions of diabetics and others daily, the glucometer, based fundamentally on electrochemical measurement. However, this device and many others are specialized to one or a few targeted biomarkers or analytes. There remains a need for a flexible, generalizable, biosensing platform in which a single signal transduction mechanism can be adapted to measure a wide range of analytes. Inspired by this problem, our group has developed several biosensors based on DNA monolayer structures at gold electrode surfaces. In contrast to DNA aptamer-based sensors, our latest method relies on DNA as a structural element, and we take advantage of chemical synthesis to make analyte-DNA bioconjugates. With these modular, DNA “bowtie” sensors, signal from square-wave voltammetry can be correlated to the structure’s movements via tethered diffusion and, therefore, the amount of surface-bound antibody. In this seminar, I will discuss the development of these bowtie sensors, the various chemical modifications we have made, and the binding model that we have developed to describe the operation of the sensors. Using the same core DNA structure and electrochemical signaling mechanism, bowtie sensors have been developed for quantification of a wide range of clinically important molecules such as antibodies, peptides, proteins, drugs, and small molecule hormones like testosterone, estradiol, and cortisol. Considering their ease-of-use and relatively fast readout, this system is poised to make an important impact in biosensing for disease diagnosis, health monitoring, and fundamental biological studies.

https://www.auburn.edu/cosam/faculty/chemistry/easley/
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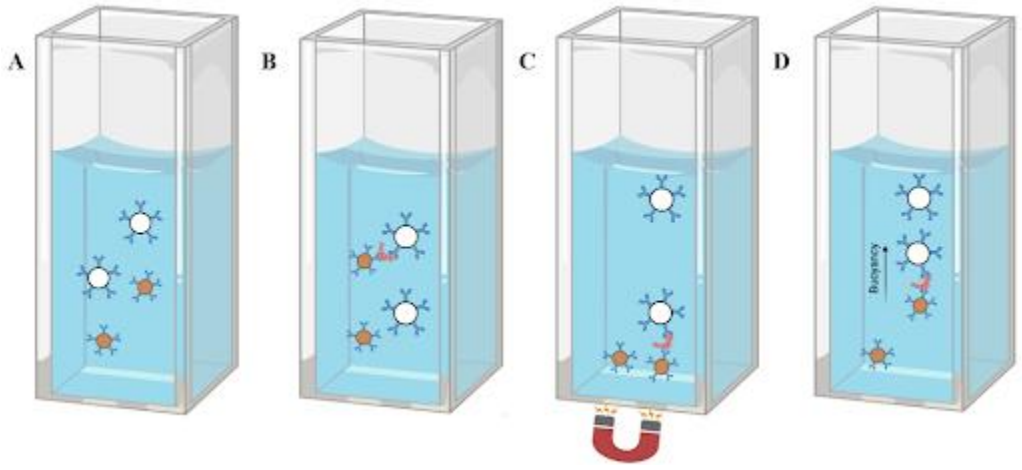
Ultrasensitive, Portable, and Rapid Buoyant-Analyte-Magnetic (BAM) Assays for Detection of SARS-CoV-2 Nucleocapsid Protein

Jeffrey Anker, Zahra Karimpour, Chuanlei Wang, Arwa Sohail, Nicholas Erwin, Ella Jenkins, Bri Walsh, Abby Alot, Aditya Thota, Elizabeth Livesay, Tim Clayton

Department of Chemistry Clemson University

We are developing a rapid screening test that can detect the presence and concentration (fg/mL) of SARS-CoV-2 in a patient's saliva using buoyant and magnetic microbeads. These microbeads are functionalized with antibodies targeting and binding to the SARS-CoV-2 nucleocapsid protein in a patient's saliva, forming buoyant-and-magnetic (BAM) complexes. The BAM complex consists of a buoyant microbubble and a magnetic microbead bound to a single viral protein through antibodies. The naked eye can see these BAM complexes, but video analysis through MATLAB has allowed us to track the individual motion of the individual BAM complexes. We are further advancing the assay by incorporating DNA-mediated strand displacement to selectively disrupt bead linkages, enabling controlled release of buoyant beads and enhanced assay specification. Once improved, this test has many applications within the mobile integrated healthcare (MIH) field. Within the MIH field, this test can deliver ultrasensitive, on-site results within 5 minutes without any complex equipment, providing a robust and quickly executable point-of-care test for COVID-19.

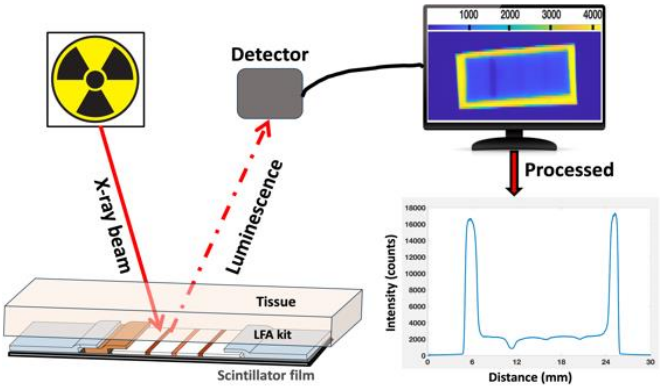


Noninvasive Through-Tissue Readout of Lateral Flow Assays via X-ray Excited Luminescence Chemical Imaging

Yu Ding (1), K.Bradley Kelly (2), Morgan N. Reel (1), Matthew J.Case (3)and Jeffery Anker (1)

(1) Department of Chemistry, Clemson University; (2) Science Department, Hreer Upstate High School; (3) Department of Radiation of Oncology, Emory University.

Lateral flow assays (LFAs) are simple point-of-care devices which can be exposed to a bodily fluid and rapidly generate a line if an analyte is present. They are widely used in pregnancy tests and for the detection of infectious diseases; they are also used to detect C-reactive protein, which is a synovial fluid biomarker for prosthetic joint infection. Implanting a lateral flow assay (or a smaller version) in a tissue of interest (e.g., a joint to detect infection, or a tumor to study progression) has not previously been explored, likely because one would need to initiate the assay on demand and, more importantly, read a small optically absorbing test line through tissue. We address this challenge using X-ray Excited Luminescence Chemical Imaging (XELCI), a non-invasive imaging technique that provides high spatial resolution through thick tissue. A polycapillary lens is used to focus the X-ray beam, allowing it to penetrate tissue with minimal scattering and irradiate a scintillator layer composed of scintillator particles. Upon X-ray excitation, the scintillator emits luminescence that is differentially absorbed by the LFA test lines depending on their intensity. After preparing dilutions of C-reactive protein and running LFA test kits at different concentrations, variations in test line intensity are obtained, which modulate the transmitted luminescence signal. The emitted light is collected using an in-house machined acrylic light guide and directed to a splitter, which separates the signal into two spectral channels detected by photomultiplier tubes at 620 nm and 700 nm. The photomultiplier tube signals are recorded using a data acquisition system, and images are reconstructed during acquisition. XELCI is further used to image LFAs through 6 mm of porcine tissue, and the resulting raw data are analyzed to quantify the intensities of the test and control lines. This study serves as a proof-of-principle demonstration that XELCI can be used to non-invasively read lateral flow assay test lines through biological tissue, supporting the feasibility of implantable LFA-based biosensing.



Poster #3

X-Ray Visualized Implanted Sensors to Detect Infection

Elizabeth Williams (1), Amelia Cavin (1), Olivia Costello (1), Nicole Cerrito (2) Abigail Sease (3), Taryn Wilkinson (3), Yu Ding (3), Jeffrey Anker (3)

(1) Department of Bioengineering, Clemson University; (2) Department of Biochemistry and Genetics, Clemson University; (3) Department of Chemistry, Clemson University

A central goal of biomedical research is to understand how local biochemical environments reflect infection states, yet clinically viable noninvasive monitoring methods remain limited. We present X-ray Visualized Implanted Sensors (X-VIS), a passive platform that enables radiographic measurement of local pH using standard clinical X-ray imaging. Synovial fluid pH decreases significantly during joint infection (6.98 ± 0.48 vs. 7.82 ± 0.29), motivating development of a radiographically readable pH sensor for early, painless, and low-cost detection of hip implant infection. Preliminary studies extend this approach to endotracheal and chest tubes.

Ventilator-associated pneumonia (VAP) affects 5–40% of intubated patients, increases hospital costs by approximately $47,000 per patient, and raises mortality by 14%. Diagnosis relies on nonspecific clinical criteria and cultures requiring 18–24 hours, with delayed treatment associated with a 34.3% increase in mortality. X-VIS offers a novel, noninvasive strategy for localized biochemical sensing that may accelerate infection detection and improve clinical outcomes across indwelling medical devices.

Poster #4

High spatial resolution imaging of oxygen through tissue using X-ray excited luminescent chemical imaging

Authors: Vigjna Abbaraju (1), Yibing Zhang (2),
Changqing Li (2), Jonathan Massera (3), Sriparna Bhattacharya (4), Jeffrey N. Anker (1,5)

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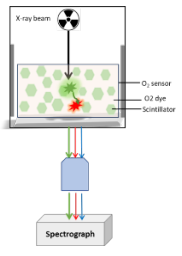
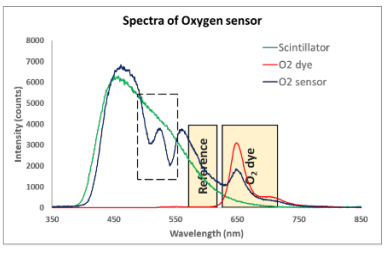
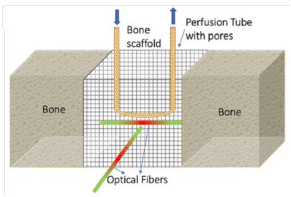
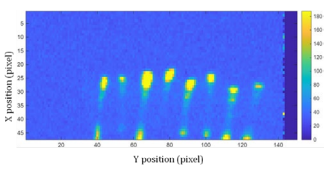
We are developing an approach to measure oxygen concentrations in bone scaffolds at submillimeter resolution using a combination of X-ray excited optical luminescence and oxygen-sensitive fluorescent indicators. Bone scaffolds are potentially useful for treating large bone defects after traumatic injuries or bone cancer. The approach works well in vitro while for small defects, translation to large in vivo models is hindered because cores usually lack an oxygen supply and become necrotic leading to failure from mechanical fatigue or infection. Researchers have suggested many ways to provide oxygen to the core, but it is difficult to measure local oxygen concentrations to assess how they work in vivo. Invasive biopsies, or optical fibers can affect the measurement and provide point readouts, while non-invasive oxygen indicator dyes are difficult to visualize through tissue and provide low spatial resolution due to optical scattering and absorption. X-ray excited luminescent chemical imaging (XELCI) can potentially address these issues by examining implanted sensor fibers using focused X-ray beams. We fabricated an X-ray luminescent oxygen sensor film (LSO-PtTFPP) to integrate into a bone scaffold to monitor oxygen gradients in real time during the cell growth using XELCI. The sensor consists of a scintillator (Lu2SiO5:Ce) to generate radioluminescence locally and an oxygen indicator (PtTFPP) that absorbs a portion of this luminescence and emit oxygen-dependent phosphorescence. Our results indicate a >6-fold increase in intensity from 21 kPa to 0 kPa oxygen levels. We further demonstrated oxygen imaging through ex-vivo bone tissue and bone scaffold.









Developing buoyant-analyte-magnetic (BAM) assays for diagnostic applications

Zahra Karimpourkalou, Chuanlie Wang, Kirsten Viola, William Klein, Walter Johnson, Tzuen-Rong (Jeremy) Tzeung, Jeffrey Anker

The detection of low-abundance biomarkers and pathogens in clinical samples is critical for early diagnosis and treatment, yet current diagnostic technologies are often complex, expensive, or lack sufficient sensitivity. To address these limitations, we are developing a Buoyant-Analyte-Magnetic (BAM) assay, a bead-based immunoassay platform that is simple, portable, and highly sensitive. This assay utilizes buoyant microbubbles and magnetic beads, each functionalized with specific antibodies, to form sandwich complexes in the presence of target analytes. These complexes can be tracked visually as they separate from unbound particles under the influence of buoyant and magnetic forces, allowing for straightforward quantification using a camera-based setup.

We are applying this platform to two major diagnostic challenges. First, we are detecting and quantifying amyloid beta oligomers (ABOs) in cerebrospinal fluid (CSF) and plasma as potential biomarkers for Alzheimer's disease. ABOs are found at extremely low concentrations in patient samples and are believed to play a role in disease progression[1,2]. The BAM assay demonstrated the ability to detect ABOs at concentrations as low as 1 femtomolar using only 20 µL of CSF in a 40-minute test. The system benefits from efficient analyte capture via buoyant microbubble motion and effective separation using orthogonal buoyant and magnetic forces.

Second, we are developing a rapid and sensitive BAM assay for the detection of *Neisseria gonorrhoeae* in urine samples, a common sexually transmitted infection with increasing prevalence[3]. Current detection methods such as nucleic acid amplification tests are not ideal for point-of-care use due to their complexity and time requirements. Our BAM assay demonstrates a limit of detection (LOD) of 544 CFU/mL, with a total assay time of 15 minutes using 100 µL of urine. The microbubble-based capture enhances mass transfer, enabling rapid analyte binding and improving assay performance in low-resource settings.

Together, these applications demonstrate the versatility of the BAM platform for diagnosing both neurodegenerative diseases and infectious pathogens, combining sensitivity, speed, affordability, and ease of use, making it highly suitable for future point-of-care diagnostic tools.

References:

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2. Mankhong,S.;Kim,S.;Lee,S.;Kwak,H.-B.;Park,D.-H.;Joa,K.-L.;Kang,J.-H.Developmentof Alzheimer's Disease Biomarkers: From CSF- to Blood-Based Biomarkers. *Biomedicines* **2022**, *10* (4), 850.
3. Miller, K. E. Diagnosis and Treatment of Neisseria Gonorrhoeae Infec1ons. **2006**, *73* (10).

Ultrasound Excited Luminescence Chemical Imaging for Implant Infection

Sriparna Bhattacharya (1), Gretchen Schober (2), Unaiza Uzair (2), Morgan Reel (2), Vigjna Abbaraju (2), Herbert Behlow (1), Apparao M. Rao (1), Jeffrey N. Anker (2)

(1) Department of Physics and Astronomy, Clemson Nanomaterials Institute, Clemson University;
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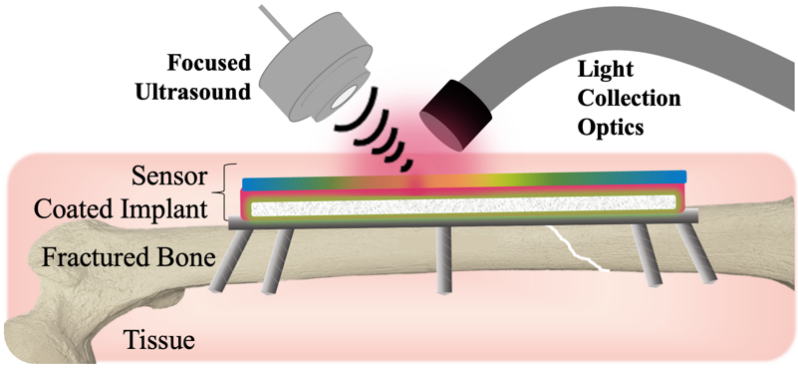
There are 2 million annual fracture fixation surgeries currently reported in the US alone. These orthopedic implants have extended and improved patient quality of life, although infection remains a grave concern in about 5% of cases. Indeed, over half of healthcare-associated infections are attributed to orthopedic and other medical implants, on which bacteria can colonize and form biofilms. These biofilms are highly resistant to antibiotics and the host's immune system due to forming dormant regions, antibiotic penetration, and changes in local biochemical environment (e.g., pH, and oxygen), which can influence antibiotic efficiency. Treating the infection often requires device removal, with replacement after the infection has cleared. Elucidating the local biochemical changes could be a way to develop biofilm-targeting strategies, and potentially to detect infections early and monitor treatment through eradication. However, detecting the local environment and imaging changes during bacterial growth requires placing and reading sensors at the implant surface beneath the biofilm. To study the local biochemistry on orthopedic devices during infection, we coated metal plates with pH indicator dyes and phosphors that could be excited using ultrasound. The phosphors serve as a local light source for chemical sensing at the surface. The ultrasound luminescence spot is scanned across the surface to image the pH indicator film absorption, compared to a reference region on the plate with no dye. Although the light scatters as it propagates through the tissue, becoming a large diffuse spot (>1 cm in diameter) when imaged through 1 cm of tissue, the intensity depends upon the local absorption in the pH-indicator film where the spot is formed. Our ultrasound-luminescence chemical imaging (ULCI) sensor comprises a mechanoluminescent film ($SrAl_2O_4$:Eu, Dy microphosphors encapsulated in a biocompatible polymer film) and a pH indicator dye, and is excited with a ~3 mm beam from an inexpensive transducer usually used in mist makers. The ULCI uses a portable and inexpensive method that could image pH-dependent changes in the luminescence spectra through a light scattering media. These findings highlight the potential use of ultrasound-modulated chemical imaging systems for non-invasive, effective imaging of implant-associated infections.

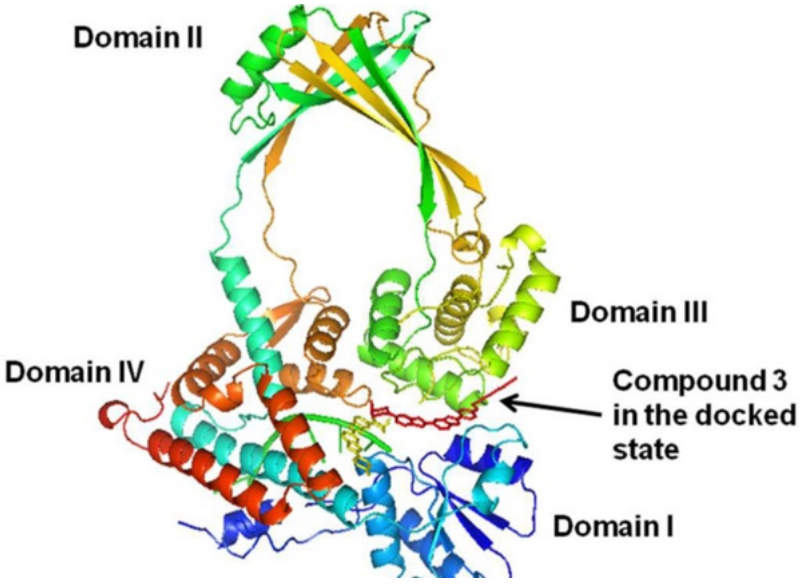


Selective Inhibition of *Escherichia coli* RNA and DNA Topoisomerase I via Structural Modifications of Alkynyl Bisbenzimidazole Derivatives

Olaoluwa Olatomiwa Oladumiye and Dev P. Arya

Laboratory of Medicinal Chemistry, Clemson University, SC 29634, USA

Topoisomerase I is an enzyme that regulates DNA topology by introducing or relaxing supercoils. These functions can be modulated for antibacterial or anticancer properties. In recent years, antibacterial medications have focused on small molecules that specifically target bacterial enzymes in an effort to combat bacterial resistance. These small molecules of interest like Hoechst dyes are benzimidazole-based compounds that have been used since the 1970s for nucleic acid staining and they are classified as non-intercalating agents due to their preferential ability to locate themselves within the minor groove of adenine-thymine (A-T)-rich, forming hydrogen bonds with the carbonyl oxygen of thymine and also the nitrogen of adenine, which makes them suitable for staining both live and fixed cells. Despite these well-established properties, their biological activities remained underexplored. Recently, our group investigated the biological activities of alkynyl bisbenzimidazoles against the enzyme topoisomerase, exhibiting selectivity and potency against *E. coli* DNA topoisomerase I over other enzymes tested. They have also been reported to be active against gram-negative and gram-positive bacteria. Herein, we show the synthesis of the substitution of *N*-methylpiperazine with different substituent groups on alkynyl bisbenzimidazoles, such as Morpholine, Pyridine and Cis-2,6-dimethylpiperazine, to evaluate their binding activities to B-DNA. We also show how the biophysical properties of these newly synthesized alkynyl bisbenzimidazoles with nucleic acids translate to an understanding of their inhibition prowess towards *E. coli* DNA topoisomerase I.

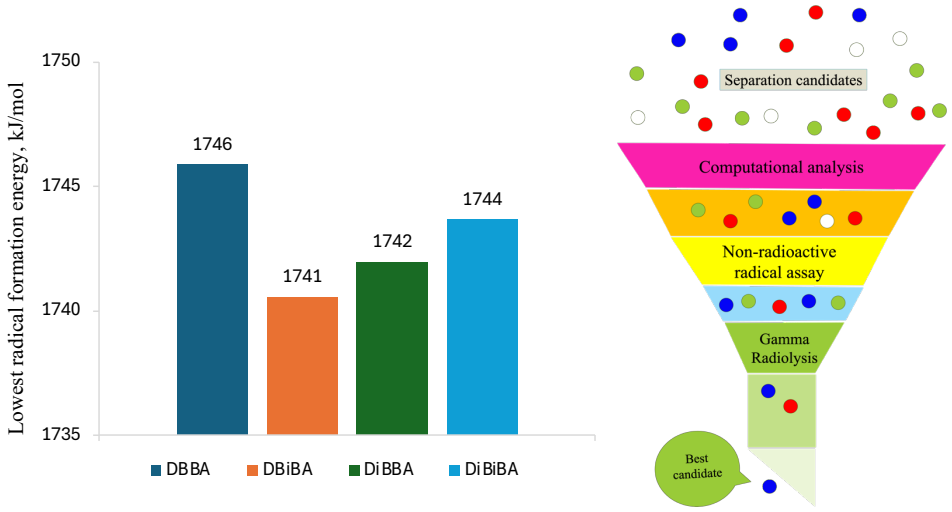


Quantum Chemical Calculation Insights into the Radiolytic Stability of Monoamide Complexants for Nuclear Separations

Fatema Tuz Zohara (1), Justin J. Talbot(1), and Julia L. Brumaghim(1)

(1) Department of Chemistry, Clemson University, Clemson, SC 29634-0973, USA

Managing nuclear waste presents a significant obstacle to advancing atomic power in the United States. Developing effective separation processes requires organic complexants that can degrade under radiolytic conditions. Monoamide extractants show promise as potential substitutes for tributyl phosphate (TBP) in nuclear separation processes such as PUREX and THOREX. Linear and branched monoamides can extract uranium and plutonium, where branching is important in selectively extracting U over Pu. However, only a few monoamides have been investigated for their radiolytic stability, hampering their adoption on an industrial scale. Traditional methods for assessing radiolytic stability, such as gamma radiolysis, are expensive and have low throughput. To address this issue, we used density functional theory (DFT) calculations to develop initial screening tools for monoamide complexant stability. Energy minimization of the selected parent monoamide species, DBBA, DB*i*BA, D*i*BBA, D*i*B*i*BA, DEHBA, and DEH*i*BA, and the formation energies of potential radical products resulting from H-atom abstraction were computed to identify their stability. Initially, benchmarking was performed by calculating the root mean square deviation (RMSD) of 49 DFT functionals against the RIMP2 results using the QChem software package. Radical formation energies of the sampled configurations were calculated using the method with the smallest RMSD error, wB97X, with the svp basis set. DFT results indicate branching affects the stability of monoamides, and DEHBA is less stable than DEH*i*BA, consistent with experimental gamma-radiolysis data. Similarly, the variety of degradation products observed experimentally corresponds to the radicals formed from hydrogen atom abstraction determined by DFT calculations. This approach allows prioritizing the most stable complexants for gamma radiolytic studies, ultimately accelerating development of more efficient and scalable nuclear waste separation processes.

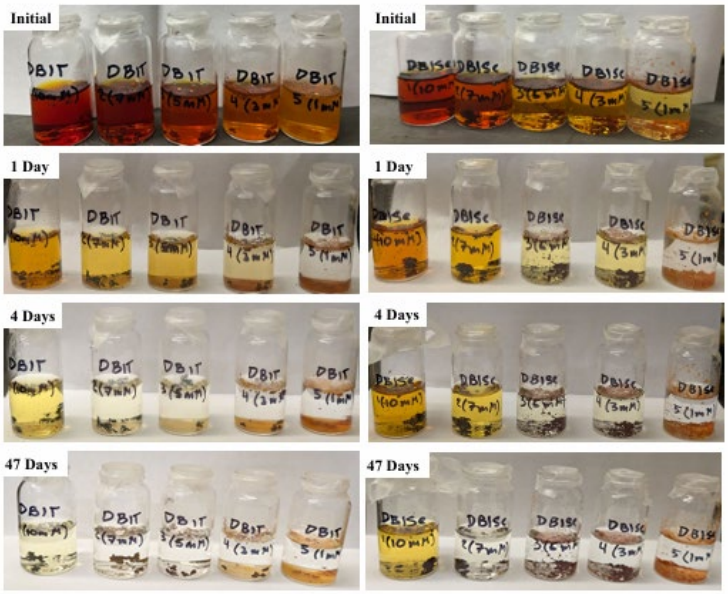


Exploiting halogen bonding properties of thione and selone *N*-heterocycles to sequester iodine

Julia L. Brumaghim (1), Abigail G. McNamee (1), Ainsley Harman (1), Kaylee E. Board (1), Louis M. Fisher (1), Colin D. McMillen (1), William T. Pennington (1)

(1) Department of Chemistry, Clemson University

Halogen bonding with *N*-heterocyclic thiones and selones has many potential applications, including iodine sequestration. Radioactive iodine is a byproduct of U-235 fission, with I-135, I-131, and I-129 (half-lives of 6.6 h, 8 days, and 15.7 million years respectively) isotopes being generated. Radioactive iodine poses challenges for nuclear power plants to meet regulatory requirements, nuclear separation solvents to be recycled, and environmental stewardship as the long-lived I-129 from legacy nuclear waste accumulates in the biosphere. Iodine possesses complex chemistry, occurs in many forms, and readily moves through the environment, complicating removal strategies. *N,N*-(dibenzyl)imidazole thione (DBIT) and selone (DBISe) were investigated for their potential to capture iodine and iodine-containing species from vapor phase and aqueous solution. Results from studies of room-temperature vapor phase capture of I_2 by DBIT and DBISe show that they capture 550 and 495% by weight, respectively, significantly higher than some literature reports. Solid-liquid extractions using Lugol's solution have proven promising with DBIT and DBISe extracting triiodide anion from aqueous solution and remaining bound to the triiodide anion for over a month. The broad impact of the work will aid in nuclear waste management efforts and understanding fundamental principles of how thione and selone *N*-heterocycles interact with iodine.



Understanding Interactions between Micro- and Nanoplastics with Metabolites at the Molecular Level

Sekinah O. Dauda, Rajan Rai and Leah B. Casabianca

Department of Chemistry, Clemson University, Clemson, SC

The ubiquitous nature of plastics can be liked to their fascinating properties, making them easily engineered for different purposes, especially for commercial and personal purposes. In the environment, plastics are exposed to stress resulting in micro and nanoplastics. Due to their high surface area acquired from the fragmentation, once plastic nanoparticles enter a biological system, biomolecules like metabolites can be adsorbed on their surface area. Metabolites in particular are often used as biomarkers to detect dysfunction which is a hallmark of diseased state. It is important to know how the interaction between nanoparticles and metabolites can potentially influence the results of biomedical analysis. Nuclear Magnetic Resonance (NMR) techniques were employed to study the interaction between surface functionalized nanoscale plastics and different metabolites that are important in biomedical analysis. In particular, WaterLOGSY and STD NMR techniques were employed to screen the metabolites to inform about nanoplastics binders, while competition Saturation Transfer Difference (STD NMR) was used to quantify the interaction of binding and provide competition information on how the presence of more than one metabolite can affect the binding abilities and the binding sites of the nanoparticle surface. This study aims to develop robust techniques for screening and characterizing interaction between small metabolites and nanoscale plastic at the molecular level. This is a fundamental step towards understanding how metabolic assays may be influenced by the presence of nanoscale plastics.

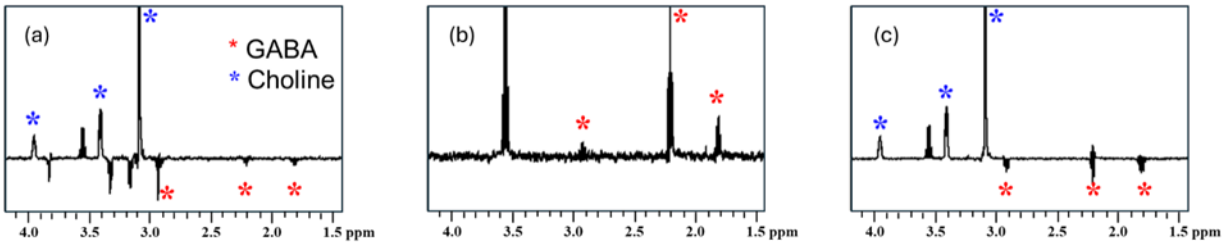


Figure 1. Evidence for competition between gamma-aminobutyric acid (GABA) and choline for binding to polystyrene nanoparticles (PSNP). WaterLOGSY NMR spectra of (a) metabolite mixture, containing GABA, creatine, choline, and taurine + PSNP (b) GABA + PSNP (c) GABA + choline + PSNP. Positive signals indicate binding molecules, while negative signals indicate non-binders.

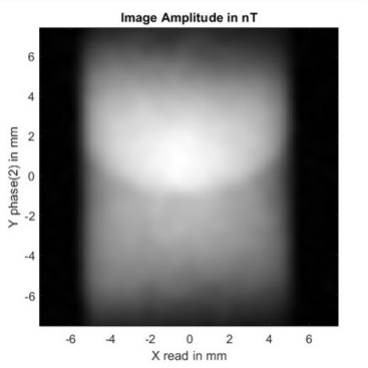
Poster #11

An Educational Approach to Connecting Chemistry and Healthcare Using Magnetic Resonance Imaging

Emily G. Cushman, Leah B. Casabianca

Department of Chemistry, Clemson University

It is hypothesized that Magnetic Resonance Imaging is an ideal tool for demonstrations and experiments to teach students about the connection between chemistry and healthcare. To test this hypothesis, we created a presentation, demonstration and simulation to educate students on the specific chemical physics of MRI. This lesson was taught to a group of high school students who are specifically interested in careers in science and/or healthcare. The high school students come from various backgrounds and locations in South Carolina. With the experiment, demonstration and simulation, students practiced critical thinking and decision-making skills crucial for high education and the healthcare field.



Applications of Structures for Lossless Ion Manipulations (SLIM): A High-Resolution Ion Mobility Technique

Heidi Sabatini, Terra Pettit-Bacovin, Ralph Aderorho, Cole L. Frank, Breland M. Jones, Emmaleigh Efird, Makenna Hoover, Selena Kingsley, Christopher Chouinard

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Ion mobility–mass spectrometry (IM-MS) is a powerful analytical technique that separates gas-phase ions by size, shape, and charge as they move through a neutral buffer gas under the influence of an electric field. This separation occurs on the millisecond timescale and provides an additional dimension of structural information complementary to MS, increasing confidence in compound identification and characterization. Furthermore, high-resolution ion mobility (HRIM) techniques, such as structures for lossless ion manipulations (SLIM), are now able to provide resolving powers in excess of 200. Long serpentine pathways with 90° turns enable these HRIM separations, while keeping the instrument footprint small. However, the detection of low molecular weight compounds has remained a challenge with this 90° turn system, so a rounded turn SLIM design that significantly improves analysis of low mass ions was created. This novel rounded turn system combines helium buffer gas with an increased SLIM RF and optimized electrode placements to allow increased transmission of low mass ions.

In this work, we demonstrate our ability to develop multidimensional methods for PFAS compounds, steroids, and explosives using structures for lossless ion manipulations (SLIM). These projects highlight the ability of IM-MS to differentiate and characterize isomeric compounds in complex environmental samples, with an emphasis on long-pathlength separations for class-based resolutions and enhanced sensitivity of closely related isomers by the new rounded-turn SLIM system.

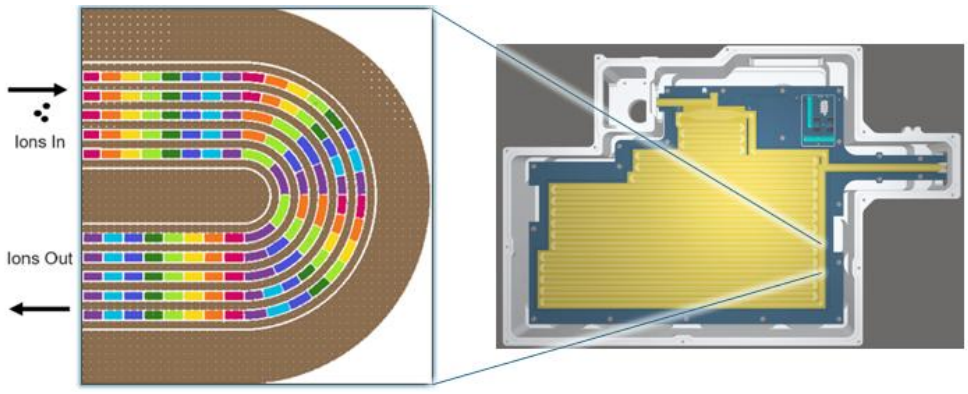
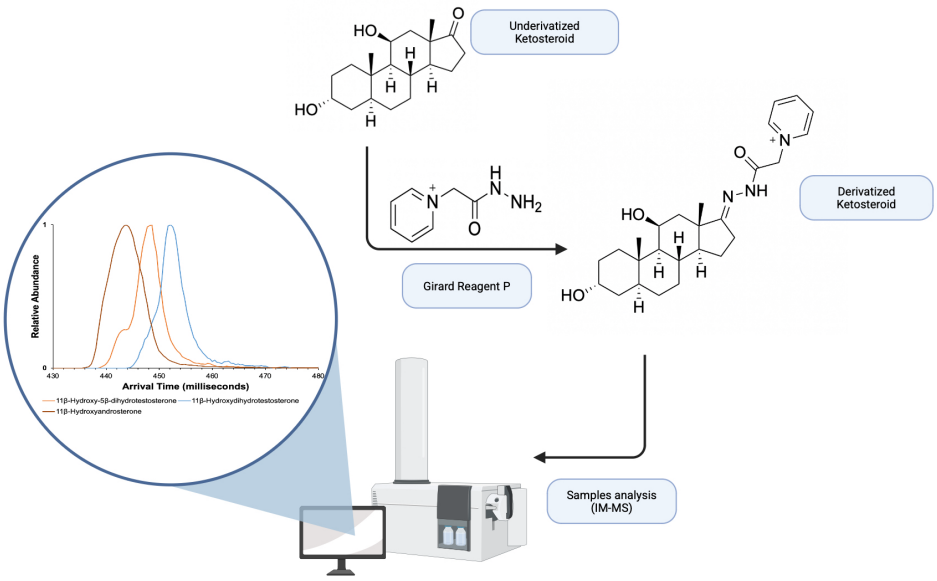


Figure 1. Schematic of the rounded turn MOBILion TW-SLIM system. This instrument features a 13 m SLIM design maintained at 3.0 Torr helium.

Targeted Carbonyl Derivatization to Enhance Ion Mobility-Mass Spectrometry Separations of Ketosteroid Isomers

Sabrina Fernandez (1), Bradley Garrison (1), Heidi Sabatini (1), Christopher Chouinard (1)
(1) Department of Chemistry and Clemson University, Clemson, SC

Ion mobility-mass spectrometry (IM-MS) is a powerful technique for rapid gas-phase separation of small molecules based on size, shape, and charge. However, steroids remain challenging to resolve due to their closely related isomeric and stereoisomeric structures. Even with high-resolution IM platforms, many ketosteroid isomers differing only in the position of a carbonyl group or hydroxyl stereochemistry exhibit nearly identical collision cross sections (CCS), limiting baseline resolution. Targeted chemical derivatization has emerged as an effective strategy to enhance IM separations by modifying molecular geometry and charge distribution prior to analysis. Building on prior work demonstrating improved IM-MS analysis of steroid hormones using carbonyldiimidazole (CDI) and Girard's Reagent P, this study investigates carbonyl-selective derivatization of ketosteroids using Girard's Reagents P, T, and D, as well as additional hydrazone-forming reagents. Ketosteroids derivatized with Girard's Reagent P exhibited measurable shifts in drift time and CCS relative to underivatized species, indicating that carbonyl modification significantly influences gas-phase ion structure. Distinct changes in mobility behavior and fragmentation patterns were observed across the tested ketosteroids, with several compounds producing multiple mobility features for a single derivatized m/z, suggesting the presence of distinct conformers or multiple reaction products. Comparison of low-resolution drift tube IM with high-resolution Structures for Lossless Ion Manipulations (SLIM) IM demonstrated enhanced separation of overlapping mobility features under SLIM conditions. Collectively, these results establish targeted carbonyl derivatization as an effective strategy for expanding IM-MS separation capabilities for ketosteroids and motivate evaluation of additional carbonyl-selective reagents to further improve isomer distinction and assess performance in biological matrices.



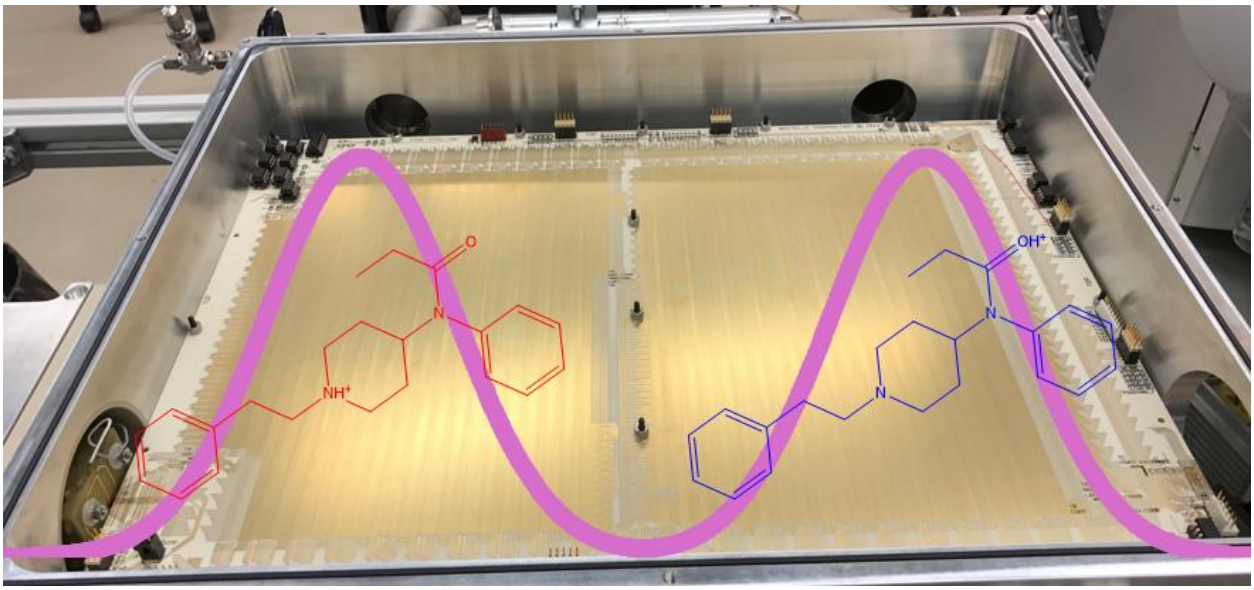
Poster #14

Analysis of Illicit Substances with Ion Mobility-Mass Spectrometry

Bradley B. Garrison (1), Ralph Aderorho (1), Copeland R. Johnson (1), Drew B. Whitman (1), Shadrack W. Lucas (1), Christopher D. Chouinard* (1,2)

(1) Department of Chemistry, Clemson University, Clemson, SC, USA; (2) Robert H. Brooks Sports Science Institute, Clemson University, Clemson, SC, USA

Illicit drugs including new psychoactive substances (NPS) have contributed to the growing drug problem in the United States and abroad. With over 1,400 NPS reported by the United Nations Office on Drugs and Crime, there is a significant analytical challenge to characterizing the constantly evolving recreational drug supply. Ion mobility-mass spectrometry (IM-MS) has emerged as a promising technique for rapid analysis of NPS, combining the ability to make high-resolution mass measurements with structure-dependent separations for molecular elucidation. This presentation will highlight recent advances in NPS analysis from our group including: (1) measurement of synthetic cannabinoid and xylazine metabolites; (2) quantification of fentanyl in human urine using cation adduction methods; (3) determination of fentanyl protonation site isomers ("protomers") and effects experimental variables; and (4) application of dielectric barrier discharge ionization (DBDI) to nitazenes and benzodiazepines.

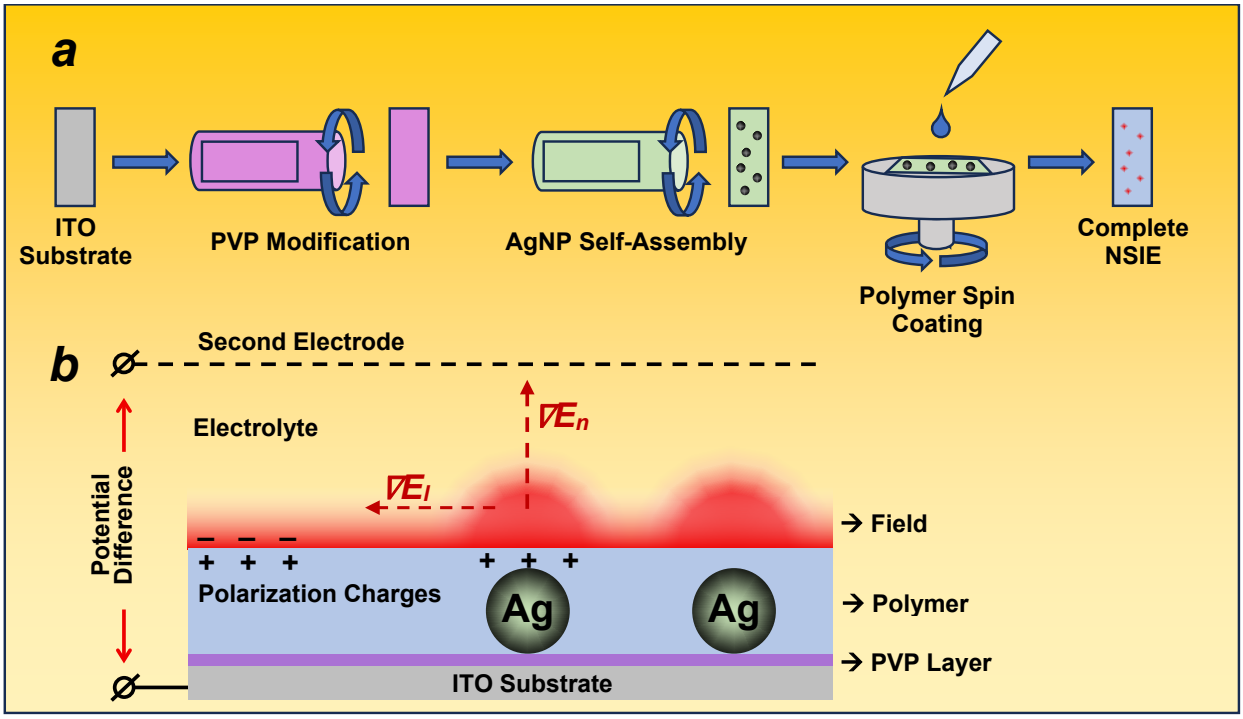


Experimental and Computational Analysis of the Electric Field Distribution at the surface of Nanostructured Insulated Electrodes

Thomas Burgess (1) and George Chumanov (1)

(1) Clemson University Department of Chemistry

Nanostructured insulated electrodes (NSIE) designed to produce a highly nonuniform electric field at their surface were fabricated. The NSIE consist of an electrically conductive substrate decorated with an array of metallic nanoparticles all completely coated in a smooth insulating polymer film, preventing electrochemical reactions. The electric field at the NSIE surface is locally enhanced due to the embedded metallic nanoparticles (NPs), as compared to the interparticle areas, thus producing a field gradient lateral to the NSIE surface. Multiple NSIE were fabricated in which the size of embedded NPs, chemical composition of the polymer film, and thickness of the polymer film were varied in order to study the effect of each parameter on the electric field gradient. The field gradient was characterized by electric force microscopy experiments and finite element computational modeling. The electric field enhancement due to the embedded nanoparticles on the order of 10^5 V/m, thus producing a lateral field gradient exceeding 10^{11} V/m^2 along the NSIE surface. NSIE will be used to direct the dielectrophoretic assembly of nanoparticle clusters upon the polymer surface for surface enhanced Raman scattering (SERS), as well as the assembly and dispersion of cells/biomolecules.

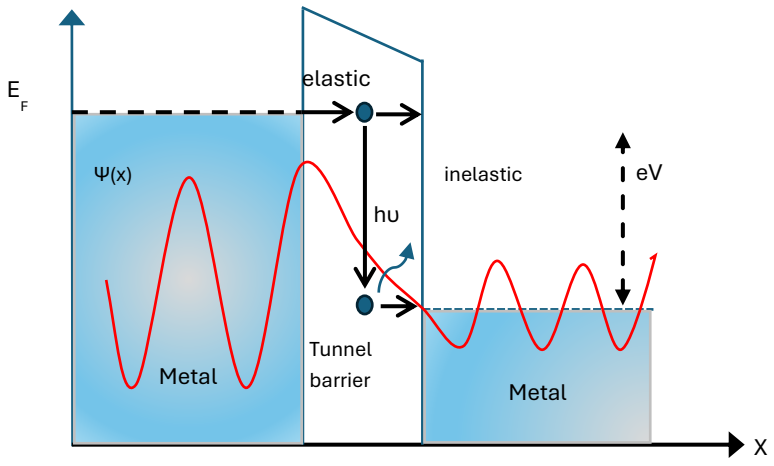


Poster #16

Plasmonic light emissions from Al/Al_2O_3-AgNP tunneling junctions

Robiul Islam, George Chumanov
Department of Chemistry, Clemson University

Light emission is a unique characteristic of tunneling junctions and has some exceptionally useful properties in chemistry and physics. These junctions with nanoparticles have high potential to be used as a sub-wavelength illumination source for near-field light microscopy, as well as scanning techniques, nano-photonics, and quantum computing. In this work, I am developing a novel method for a Metal-Insulator-Nanoparticles junction using silver nanoparticles (AgNPs) sandwiched between Indium Tin Oxide (ITO) and an Aluminum electrode. Utilizing the quantum phenomenon of electron tunneling through a dielectric barrier, plasmonic AgNPs can be excited by the tunneling electron, and the energy released by plasmonic decay can emit light in the visible range. Previously, both silver and gold thin films were used in other research for electron tunneling, yet light emission was observed from only gold deposited in the top layer of the tunnel junction. Incorporating AgNPs into the interfacial layer is a unique configuration and can open a path for further research and application opportunities in the subwavelength regime. We hypothesize that the frequency and intensity of the emitted light a functions of applied potential between the electrodes, the thickness of the dielectric layer of Al_2O_3, and the size of the silver nanoparticles. Upon the application of a potential up to 5V, light was emitted from the junction, which was captured by a CCD. This light needs to be further characterized, and the relation with applied bias needs to be established. Finally, a mechanism for the emission of light by plasmon excitation through tunneling electrons will be established, and the above hypotheses will be confirmed.



Poster #17

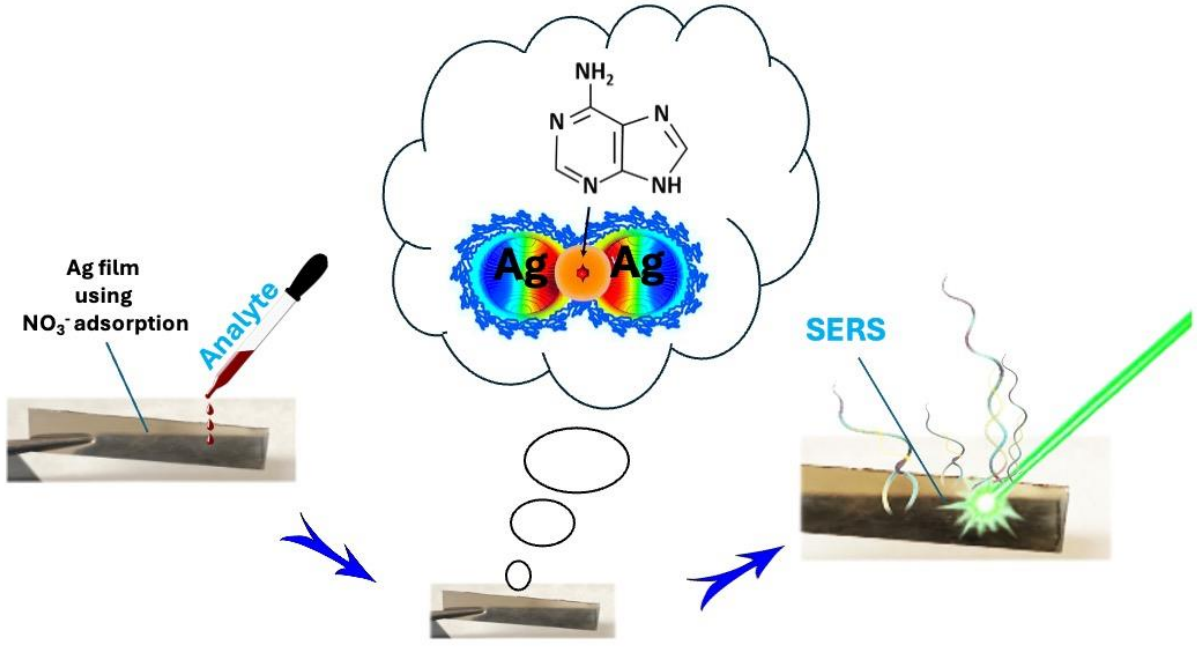
Synthesis of Silver film via Ammonia-Free Chemistry: An Easier Alternative for SERS Substrate Fabrication

Anup Adhikari (1), and George Chumanov (1)

(1) Department of Chemistry, Biosystems Research Complex, Clemson University, Clemson, SC 29634

Abstract:

This study centers on the synthesis of a silver-mirror/film via an ammonia-free chemistry to explore its potential as a silver substrate for surface-enhanced Raman scattering (SERS). The conventional Tollens' test utilizes silver nitrate, sodium hydroxide, and ammonia to generate the diamine silver(I) complex, or Tollens' reagent. Challenges with this reagent include disposal and handling hazards, as improper management can yield highly explosive silver nitride or silver fulminate. Herein, a novel nitrate-based adsorption strategy bypasses ammonia use, which no longer lead to diamine silver complex, thereby preventing formation of these explosive byproducts. On the other hand, this technique can be viable alternative for SERS substrate fabrication. As existing techniques rely on vacuum evaporation of silver or post-synthesis adhesion of silver nanoparticles for silver-based SERS substrates, this work examines a pseudo-Tollens' approach, imitating the Tollens' test without ammonia for silver SERS substrate fabrication. This silver film provides a straightforward SERS substrate fabrication method, exhibiting high sensitivity with detectable signals at analyte concentrations as low as 1 μM.



Poster #18

Investigation of polymer-metal complex based on Raman spectroscopy

Rehnuma Tabassum (1) George Chumanov (2)

Department of Chemistry, Clemson University

This project investigates the complexation formed from the interaction between Poly(4-vinylpyridine) (P4VP) and transition metal salts. The metals or salts that were selected to explore are mostly from the first transition series and they are nickel sulfate, nickel nitrate, nickel chloride, copper sulfate, copper chloride and copper nitrate. The behavior emerges mostly from the partially and exceptionally filled d-block metal centers and the quaternization of the pyridinium N atom in P4VP. Additionally, the counterions present in the salts also play a remarkable role in the interaction. Bulk complexes were prepared by mixing P4VP and metal solutions in the same solvent (methanol) and later they were analyzed through Raman spectroscopy. This fundamental based study is distinctive in such a way that till now there is little or no vibrational spectroscopy based analysis on the interaction between the P4VP and transition metal salts, specially including nickel and copper. The Raman spectroscopy can be useful over or in addition to IR spectroscopy because it possesses some advantages including working in the presence of moisture. This advantage has been utilized in the current study and the experiment has been done on the complexes in dry conditions as well as in the presence of water vapor. Significant results revealed that the complexes act differently in different surroundings as they possess different vibrational modes based on the counterion present in the system. This behavior can be indicated as 'Enhancement' which represents the resonance Raman effect. The same study was carried out as thin films in addition to bulk materials. The future application of these polymer-metal complexes lies in the modification of sensors, semiconductors and study of biomolecules.

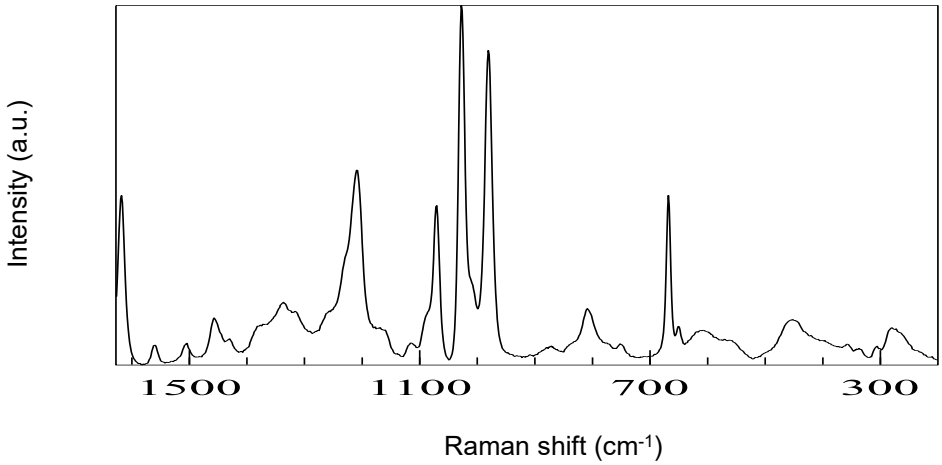


Figure: Raman spectrum of P4VP-Nickel sulfate complex

Poster #19

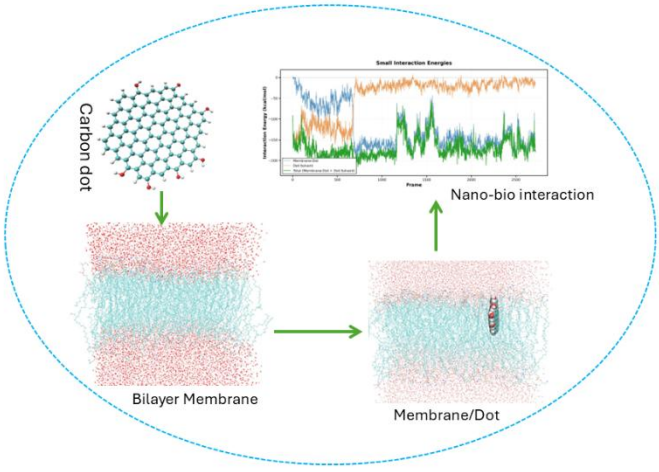
Atomistic Insights into Carbon Nanomaterial–Membrane Interactions Driving Membrane Disruption

Terkumbur E. Gber and Brian N Dominy*
Department of Chemistry, Clemson University, Clemson, SC 29634-0973, USA

Carbon nanomaterials, particularly carbon dots (CDs), have recently shown promising intrinsic antimicrobial activity and tunable biocompatibility; however, the molecular mechanisms underlying their membrane-disruptive activity remain poorly understood. In this study, we employ multiscale molecular simulations and atomistic modeling to elucidate the fundamental mechanisms by which functionalized carbon nanomaterials, hydroxyl (OH), carbonyl (C=O) and carbon dots without functionalization interact with the bilayer membrane of composition (POPE, POPG and TLCL2). This atomistic understanding of nano–bio interfacial interactions is critically needed to rationally design safe and effective nanotherapeutics. Utilizing all-atom molecular dynamics simulations with the Nanoscale Molecular Dynamics (NAMD) engine and the Chemistry at Harvard Macromolecular Mechanics (CHARMM) force field to investigate the molecular mechanisms governing carbon dot–membrane interactions with the membrane. Quantitative analysis of the membrane–nanoparticle interaction energies revealed average binding energies of −128.12, −125.05, and −117.56 kcal/mol for carbonyl, hydroxyl-functionalized-, and bare carbon dots, respectively, indicating that surface functionalization significantly enhances membrane affinity. An indication of how chemical modifications regulate adsorption, insertion depth, lipid disorder, membrane disruption, and permeability within model bilayers. Moving forward, we intend to characterize the energetics of membrane penetration by calculating the potential of mean force (PMF) to quantify pore formation, translocation barriers, and changes in membrane mechanical properties. Collectively, these findings will atomistic insight into nano–bio interfacial mechanisms, enabling the rational design of selective, biocompatible carbon nanomaterials for antimicrobial applications.

Keywords: *Nanomaterial, Molecular Dynamics, Bilayer-Membrane, NAMD*

Graphical Abstract



Poster #20

Thermodynamics of Cerium Redox Chemistry in Acidic Nitrate Solutions

Abdulrahman Abdulsemiu, Shanna L. Estes

5F-elements oxidation-reduction chemistry exhibits different behavior in acid nitrate-rich environments due to nitrate binding and formation of polynuclear species. There is no comprehensive understanding of this behavior, which prevents us from systematically probing nitrate-based reactions within the nuclear fuel cycle. Examining the influence of nitrate binding on the redox chemistry of 5F-elements will enable advanced environmental remediation, waste management, and nuclear fuel separations. This study uses differential pulse voltammetry (DPV) and cyclic voltammetry (CV) to probe the redox chemistry of cerium (Ce, a chemical surrogate for plutonium (Pu)) in 1–5 M nitric and perchloric acid solutions. The results show that, at constant acid, the redox behavior of the Ce(IV)/Ce(III) electrode potential increases with increasing nitrate concentration and decreases with constant nitrate concentration and increasing Ce concentration, suggesting quasi-reversible electron-transfer kinetics. These findings indicate that nitrate complexation enhances the stabilization of the reduced species (Ce(III)), whereas the formation of polynuclear complexes stabilizes the oxidized species (Ce(IV)). Coupling thermodynamic modeling and parameter estimation software enables the determination of the stability and stoichiometry of Ce(III) and Ce(IV)-nitrate complexes from voltammetry data, providing a unique framework for probing ligand effects on Ce and Pu chemistry in solution. These findings establish a foundation technique for the redox control of 5F-elements and contribute to a deeper understanding of the electronic structure of 5F-element ligand complexes in solution, which will facilitate predictive strategies for advanced separations and waste management.

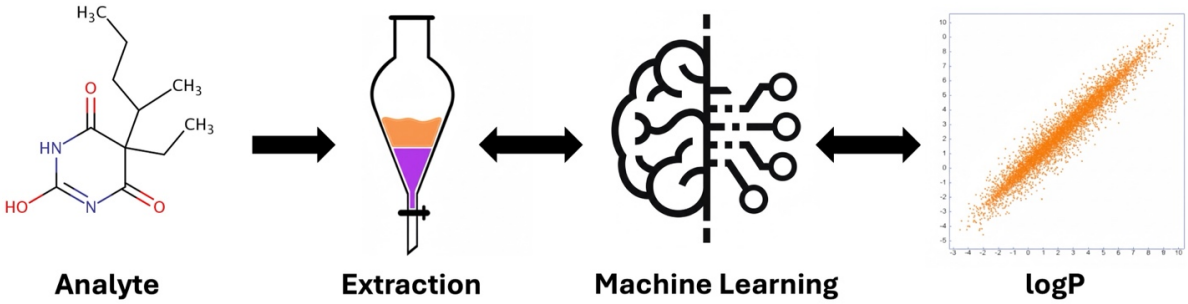
Poster #21

A Data-Driven Design of Deep Eutectic Solvents for Liquid-Liquid Extraction Beyond logP

Lukas A. Garcia, Daniel C. Whitehead, and Carlos D. Garcia*

Department of Chemistry, Clemson University, Clemson SC 29634, USA

Deep eutectic solvents (DES) have emerged as promising alternatives to conventional organic solvents in liquid-liquid extraction (LLE), yet the factors that drive successful extractions are not well defined. While the most common assumption is that the process is dominated by hydrophobic partitioning (logP) and although several reports point to additional advantages provided by the hydrogen-bond network in DES, there are no current guidelines to rationally guide the selection of DES for extraction processes. This work reports on the use of two machine learning models that can predict the most suitable DES composition and conditions for successful extraction of a given analyte. We began by creating a baseline classifier, a machine learning model that predicts LLE success using analytes and their logP values, as well as benchmarking other models in the literature, such as RDKit's Crippen logP. Then, a database of over one thousand unique liquid-liquid extraction experiments was manually curated from the literature, recording solvent matrices, DES compositions, and analytes. Following performance assessment, a second machine learning model was created to predict optimal system conditions for successful extraction of input analytes. We then expanded the database to include thermodynamic features, predicted interactions, and solvation parameters using COSMO-RS and other open-source software. Aiming to address current limitations in DES-based LLE, we seek to identify the most relevant variables governing the process, quantifying the computational features that could be tuned to improve these extractions. We envision these findings will speed up the solvent selection process, minimize the use of traditional organic solvents, and ultimately improve the analytical performance of current sensing approaches.



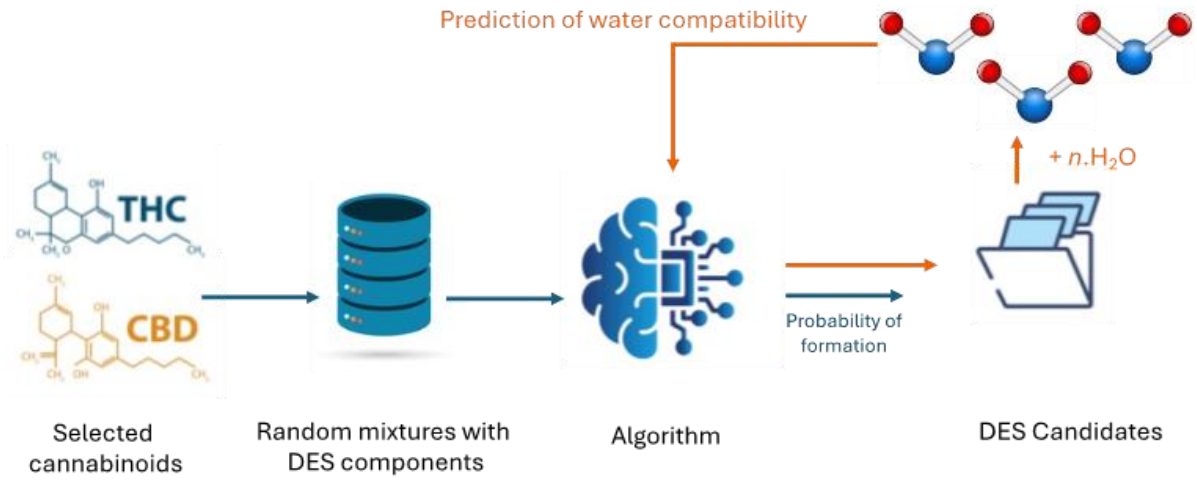
Poster #22

Deep Eutectic Solvents Incorporating Cannabinoids: The Influence of Water on Stability

Candela S. Cazzaniga, (1), Lucas B. Ayres (2), Jorge Barroso (1), and Carlos D. Garcia (1)

(1) Department of Chemistry, Clemson University; (2) Lewis-Sigler Institute for Integrative Genomics & Ludwig Institute for Cancer Research, Princeton University

The effect of the addition of water to deep eutectic solvents (DES) depends on the hydrophobicity of the hydrogen bond donors and acceptors. In one extreme are DES formed by hydrophilic HBD/HBA mixtures, which can be gradually hydrated to modulate their properties. On the other extreme, are DES formed by hydrophobic DES would only accept minute amounts of water, but still remain stable. In between, are DES formed by components with dissimilar properties (standard deviation of the logP > 3), whose behavior upon the addition of water is less clear and remains at the mercy of trial-and-error approaches. To address this knowledge gap, this report describes a machine learning approach to predict the stability of DES upon the addition of water. With the end goal of applying this knowledge to pharmacological formulations, this work focuses on DES formed with cannabidiol (CBD), ibuprofen, and choline chloride. Water stability predictions made by our model were validated by a series of complementary experimental and computational techniques. Moreover, the water stability of other cannabinoid-containing DES is presented and discussed within the context of their potential therapeutic applicability.



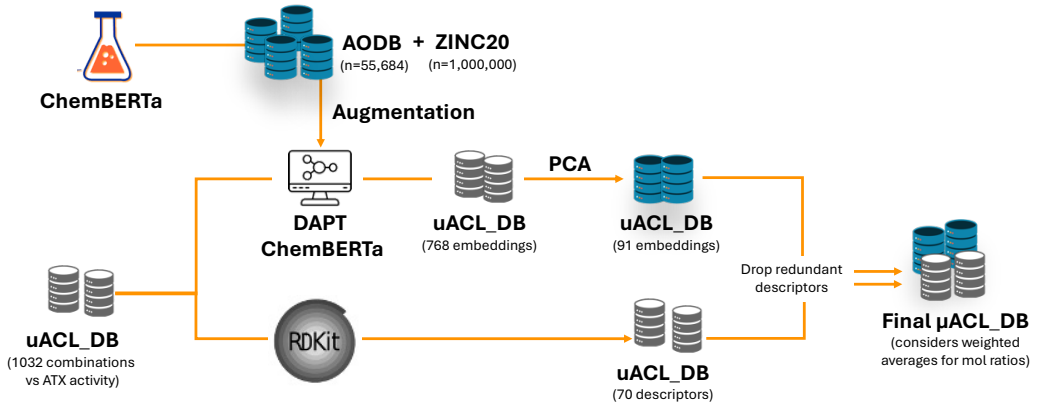
Poster #23

Transfer Learning with Domain-Adaptive ChemBERTa to Model Antioxidant Behavior and Oxidative Stability in Oleic Acid

Emmanuel D. Dike, Jorge Barroso, and Carlos D. Garcia*

Department of Chemistry, Clemson University, Clemson SC 29634, USA

Understanding antioxidant behavior, particularly in mixtures, remains a fundamental challenge in lipid oxidation research. Although combining antioxidants is a widely used and proven strategy to enhance oxidative stability, accurately predicting the resultant synergistic, additive, or antagonistic behavior remains difficult. In this study, we develop a comprehensive experimental-machine learning framework that integrates controlled antioxidant oxidative analysis with molecular descriptors, ChemBERTa embeddings, and mechanistic feature engineering to accurately model antioxidant interactions. Our architecture combines three complementary datasets that enable chemical generalization of antioxidant interactions. First, we employ a large-scale comprehensive antioxidant database (55684), which supported the domain-adaptive pre-training (DAPT) of ChemBERTa, enabling the model to learn chemically enriched embeddings specific to antioxidant chemistry. Second, a curated database (1032) containing binary mixtures of antioxidants reported in the literature is used to train a classifier model that identifies the informative molecular descriptors and DAPT-derived embeddings dimensions relating to antioxidative behavior. Furthermore, these learned informative descriptors were subsequently transferred to a third dataset obtained from a controlled Rancimat experimental analysis of (360) binary mixtures in oleic acid, to build a regressor for predicting the combination index (CI), which served as the quantitative metric defining antioxidant behavior in oleic acid. Results obtained across all model development tasks from this approach demonstrate strong predictive performance and substantial interpretability through SHAP analysis, thereby providing chemical insights into antioxidant behavior. Overall, the findings from this work offer a transferable and chemically hybrid framework that can be leveraged across diverse lipid matrices and antioxidant combinations for future predictions.



Poster #24

Machine Learning-Based Inference of Oxidative Stability of Vegetable Oils

Emmanuel D. Dike (1), Lucas B. Ayres (2), Jorge Barroso (1), Justin Furgala (1), Daniel C. Whitehead (1) and Carlos D. Garcia (1)*

(1) Department of Chemistry, Clemson University, Clemson SC 29634, USA, (2) Lewis-Sigler Institute for Integrative Genomics & Ludwig Institute for Cancer Research, Princeton University, Princeton, NJ, USA

The induction period (IP, obtained via standard conditions and a commercial instrument) is nowadays one of the most common tools to assess oxidative stability in lipid samples. Despite its advantages and widespread use in industry, the development of algorithms to predict IP values has been (thus far) impaired by the scarcity of data linking the composition of the sample with the corresponding IP value. Addressing this need and considering the persistent difficulties in bridging experimental and theoretical approaches related to edible fats, this poster reports on the development of a machine learning approach based on extreme gradient boosting (XGBoost) that was trained using a biodiesel database and then fine-tuned using a vegetable oils database, in both cases linking composition their corresponding oxidative stability. The resulting model was able to predict stability of vegetable oils with a mean average error of only 1.37 h, one of the lowest ever reported. Beyond demonstrating the ability of our model to provide meaningful predictions, this report highlights the importance of incorporating oxidation-related chemical descriptors and the utility of using associated databases and transfer learning to support the development of accurate machine learning models.

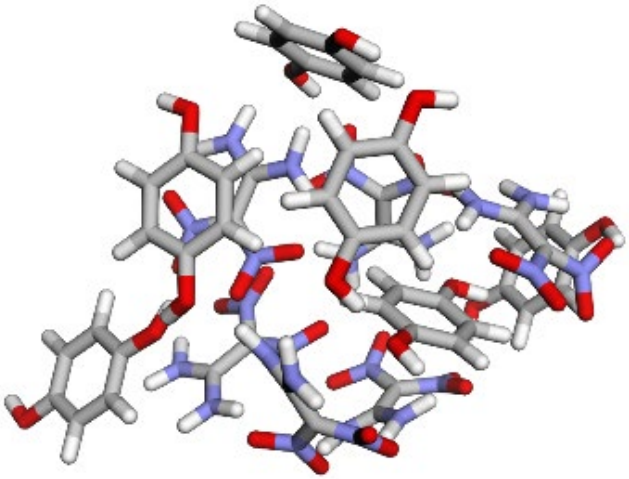
Poster #25

The Fox and the Hound: Utilizing AI to Tailor Reactivity of Energetic Eutectic Materials

Connor J. Parker (1), Lucas B. Ayres (2), Jorge Barroso (1), and Carlos D. Garcia (1)*

(1) Department of Chemistry, Clemson University, Clemson SC 29634, USA, (2) Lewis-Sigler Institute for Integrative Genomics & Ludwig Institute for Cancer Research, Princeton University, Princeton, NJ, USA

Recent global conflicts have underscored the need for adaptable, high-performance energetic materials for use in explosives, propellant manufacturing, and inventory management. The challenge in this pursuit lies in the design and procurement of energetically dense materials that are both insensitive to external stimuli while remaining environmentally benign. This trichotomy of performance, safety, and environmental impact presents a unique research opportunity that directly imacts both tactical flexibility and strategic deterence. Addressing this need, this poster reports on the incorporation of an extreme gradient boosting (XGBoost) machine learning approach to identify and characterize high-energy, insensitive explosive (HIE) deep eutectic solvents (DES). As a point of reference, 1,1-diamino-2,2-dinitroethylene, also called FOX-7, was investigated as the HIE component of interest in our eutectic modeling. The resulting predictions highlighted a dynamic range of binary compositions illustrating extreme depression of FOX-7's melting point at high degrees of probablistic success (>70%), suggesting subsequent xTB and density functional theory computations to identify the underlying thermophysical parameters and potential impact of hydrogen bonding on potential explosive capability.



Poster #26

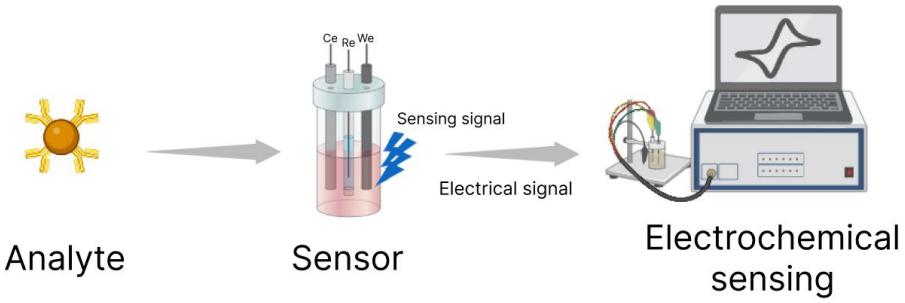
Stencil-Printed Multisensor Device for Electrochemical Antibiotic Susceptibility Testing of Bacteria

Bruna Bragantin (1,2,3), Renato S. Lima (1,2), and Carlos D. Garcia (3)

(1) Brazilian National Laboratory of Nanotechnology, Brazilian National Center for Research in Energy and Materials, Campinas-SP, Brazil; (2) School of Chemical, State University of Campinas, Campinas-SP, Brazil. (3) Department of Chemistry, Clemson University, Clemson, SC, 29634, USA

This work presents a stencil-printed multisensor device designed to provide a low-cost, simple, and scalable approach for electrode fabrication. The proposed method enables large-scale production of electrochemical sensors while maintaining high reproducibility and manufacturing efficiency. The carbon-based (C-based) multisensory platform was developed as a compact and sustainable device, combining environmental responsibility with cost-effectiveness. By employing eco-friendly materials and fabrication processes, the proposed system represents a promising alternative for portable and high-throughput sensing applications. As a future application, this platform is intended for monitoring bacterial antibiotic susceptibility of bacteria, targeting antimicrobial resistance, one of the most critical global public health challenges.

Electrochemistry sensing



Electrochemiluminescence reaction

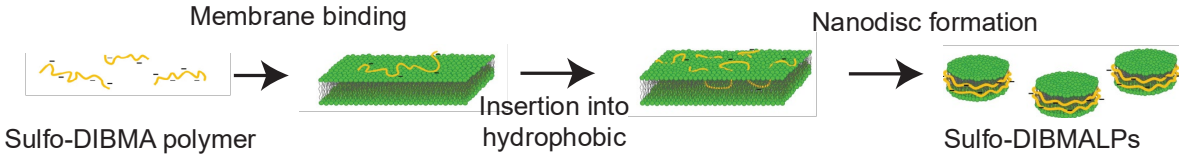
Poster #27

Non-Detergent Based Techniques for Studies of Membrane Proteins in Native Bilayer

Abideen O. Ayangbemi (1) and David R. Jacobson (1)

(1) Department of Chemistry, Clemson University

Membrane proteins make up > 60% of targets for therapeutics. Despite their importance, they remain an understudied class of biomolecules and there is a dearth of information on how they unfold in their native environment. Atomic force microscopy (AFM)-based force spectroscopy has emerged as a technique to study membrane proteins by attaching a single membrane protein molecule to the tip of a cantilever and applying force to unfold the protein. Details about the unfolding pathways, unfolding force, and energetics can be discerned from the force-extension curves obtained. AFM-based techniques to study membrane proteins involve the use of detergents during extraction and the differences in unfolding or refolding energetics and dynamics in synthetic bilayer compared to native bilayer is not well known. Here, we employ a polymer, sulfo-DIBMA, to extract OmpG directly from *E. coli* membrane. Sulfo-DIBMA interacts with the membrane, inserting itself into the hydrophobic region to carve out OmpG-containing nanodiscs, which were purified by size-exclusion chromatography and characterized via light scattering and electron microscopy. These nanodiscs are to be adhered to mica surfaces and unfolded via force spectroscopy. The force-extension curves obtained will be compared with those obtained from unfolding OmpG via detergent-based techniques. Accurate calibration of the AFM cantilever spring constant is essential for quantitative force measurements in single-molecule force spectroscopy, yet the influence of medium, air versus water, on calibration accuracy and precision has not been systematically evaluated. Here, we develop a Langevin simulation framework to compare thermal noise calibration in air and water under controlled conditions. We simulate trajectories across damping regimes and compute their power spectral densities (PSDs). From these, we recover spring constants by non-linear fitting to the theoretical PSD to determine the robustness of calibration in each medium.



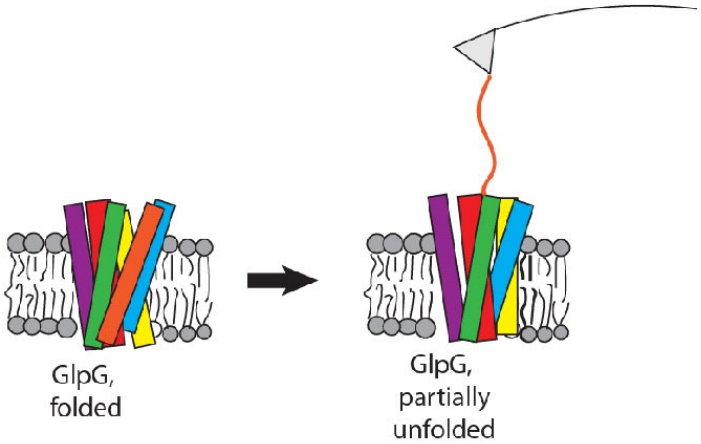
Poster #28

Investigation of Unfolding Process of E. coli Serine Rhomboid Protease (GlpG) using Atomic Force Microscopy (AFM)

Alex Lybrand (1), David R. Jacobson (1)

(1) Department of Chemistry, Clemson University

Membrane proteins are the target of roughly 50% of pharmaceuticals, and their misfolding is the cause of serious health conditions such as cystic fibrosis and Creutzfeldt-Jakob disease. As such, a better understanding of membrane protein structure and folding is necessary—often requiring protein denaturation into an unfolded state. In recent decades, single-molecule force spectroscopy (SMFS) has emerged as an alternative to chemical protein denaturation, allowing for reversible protein folding and unfolding with piconewton (pN) force quantification. These qualities are suited to studies of membrane proteins, whose membrane insertion and structure in lipid bilayers are difficult to characterize with irreversible chemical denaturation. The magnetic tweezers (MT) utilize a magnetized bead to physically denature an attached protein at constant force. The atomic force microscope (AFM) uses a metal-coated silicon nitride cantilever that undergoes deflection as it applies force on a stable secondary protein structure and relaxation once the secondary structure unfolds, resulting in a variable force upon the protein. Previous SMFS studies on the membrane proteins bacteriorhodopsin (bR) via AFM and serine rhomboid protease (GlpG) via MT reveal more unfolding intermediates for bR than for GlpG. However, it is unclear if these differences observed are attributable to the differences in SMFS method employed or to variations in the protein's structure itself. To determine whether the aforementioned discrepancy stems from the SMFS method used or from structural characteristics of GlpG itself, AFM of GlpG in a surface-supported lipid bilayer will be performed.



Poster #29

Understanding the Single-Molecule Unfolding Pattern of Arginine Vasopressin Receptor 2

Researcher: Christopher Hatchell

Advisor: Dr. Jacobson (Physical Chemistry)

Date: 21st February 2026

Misfolding of G-protein Coupled Receptors (GPCRs) cause many diseases including hypothyroidism, color blindness, and nephrogenic diabetes insipidus (NDI), which makes these proteins good targets for drugs and pharmaceutical chaperones. The defective GPCR in the case of NDI has been identified as arginine vasopressin receptor 2 (AVPR2). Here we use Atomic Force Microscopy (AFM)-based single-molecule force spectroscopy (SMFS) to enable characterization of individual AVPR2 molecules through application of mechanical force. By optimizing SMFS pulling experiments using site-specific attachment chemistry, we have been able to successfully obtain numerous Force-Extension Curves (FECs) of AVPR2 unfolding. After analyzing the FECs, we found an overall unfolding length that corresponds to the contour length change expected with numerous intermediates spaced throughout. As such we concluded to move to a “zig-zag” pulling procedure to capture richer data per attachment and identify the number and structural location of the intermediates. The zig-zag procedure applies tension to the protein and then relaxes at a set interval. This back and forth allows the protein to unfold and refold numerous times over the course of an SMFS pulling experiment. In addition to this updated pulling procedure, we plan to apply high time resolution cantilevers to pinpoint short lived intermediates. Once we have obtained equilibrium force information for these intermediates, we can construct a free-energy landscape for unfolding and refolding. Finally, we want to compare correctly folded AVPR2 protein as well as misfolded AVPR2 protein to determine the connection between disease-causing mutations and thermodynamic stability of the protein.

Poster #30

Silanes to Silatranes

Tommy Courtney (1), Christopher Hatchell (1), Xuliana O (1), and David R. Jacobson (1)

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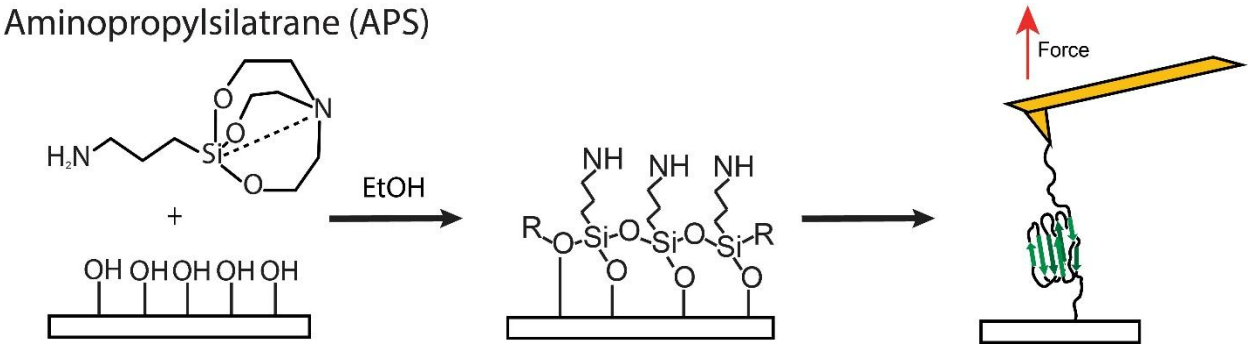
Atomic Force Microscopy (AFM) based single-molecule force spectroscopy (SMFS) studies allow for insight into protein unfolding and energetics. To perform these experiments on soluble and membrane proteins, stable and reproducible functionalization methods for surfaces and cantilevers are essential. Classical approaches utilizing silanes run into a variety of stability and storage issues due to their tendency to crosslink, ultimately limiting their usability. In this work we present an ethanol-based Aminopropyl-silatrane (APS) functionalization protocol. Due to its superior chemical stability from its cage-like structure, APS outperforms silane-based functionalization methods and provides a reliable functionalization process that yields consistent single molecule SMFS data. Given the cost of AFM cantilevers, reliable cleaning and re-functionalization protocols are also important for maximizing their lifespan. Accordingly, we also present an easily accessible reliable cleaning method using a benchtop UV ozone cleaner and a series of rinses in easily accessible solvents.

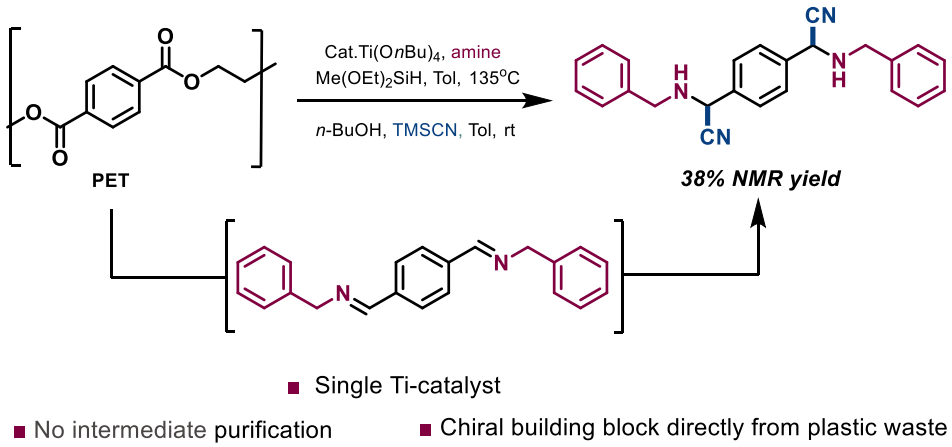


Enantioselective Deoxygenative Upcycling of PET via Titanium Multicatalysis

Samirah Muhammad (1), Danny Yang (2)

(1) Department of Chemistry One; (2) Department of Chemistry

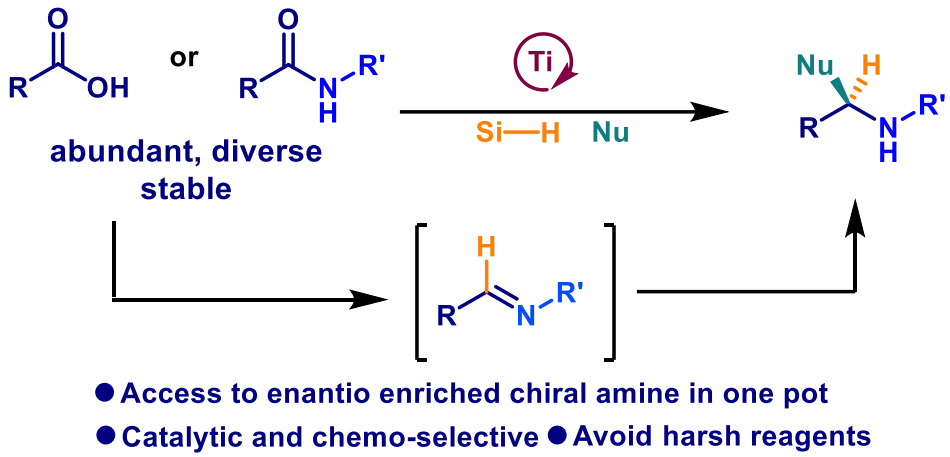
Chemical upcycling, wherein plastics are depolymerized into simple monomers, is an emerging approach to addressing the plastic waste challenge. Despite numerous efforts, upcycling plastic waste to directly generate enantio-enriched chiral building blocks, which could be used to build new materials, remains rare. To address this challenge, we developed a method that combines a titanium multi-catalytic system with chemical upcycling to catalyze the direct chemical depolymerization and functionalization of polyethylene terephthalate (PET), to generate enantiomerically enriched chiral amines. We envisioned that titanium would catalyze the depolymerization of PET into a bis-amide, then the partial reduction into a bis-imine, then finally the enantioselective nucleophilic attack generating the desired chiral amine. We have successfully developed a method that directly catalyzes the conversion of PET into first a bis-imine product which then undergoes nucleophilic attack to generate a bis-aminonitrile production 38% NMR yield. We are currently working on producing the enantioselective variant of this product.



- Single Ti-catalyst
- No intermediate purification
- Chiral building block directly from plastic waste

Direct Deoxy-Imination of Carboxylic Acid Derivatives via Titanium Multi-Catalysis and Asymmetric Deoxy-Fluoroalkylation of Amide using Transimination Strategy

Interconversion of carbonyl compounds for generating diverse chiral products has been an important endeavor in synthetic organic chemistry. In this regard, carboxylic acids and amides are ideal feedstock chemicals due to their structural diversity, bench stability, anon-toxicity, and they are abundant in bioactive compounds. Although deoxygenation of carboxylic acids and amides are known, catalytic methods that generate enantio-enriched products through deoxy-functionalization are underdeveloped. This gap is mainly due to the difficulty in achieving partial reduction of carboxylic acids and amides. Such a process is desirable because it provides synthetic flexibility to access diverse chiral amine-containing drugs and natural products. In this talk, we will present our efforts to generalize the titanium multi-catalysis to develop direct deoxy-imination of carboxylic acids, enabling chemo-selective reduction of amide, and asymmetric deoxy-fluoro alkylation of amides via transamination, which could help establish a new method for late-stage deoxy-functionalization of complex molecules.



Asymmetric Deoxy-Fluoroalkylation of Amides Enabled by Transimination

Jason A. Wilt, Samirah Muhammad, Yasoda Rajapaksha, Erin Batchelor, Danny Yang, Ethan Apsley, Jacob Moore, and Byoungmoo Kim*

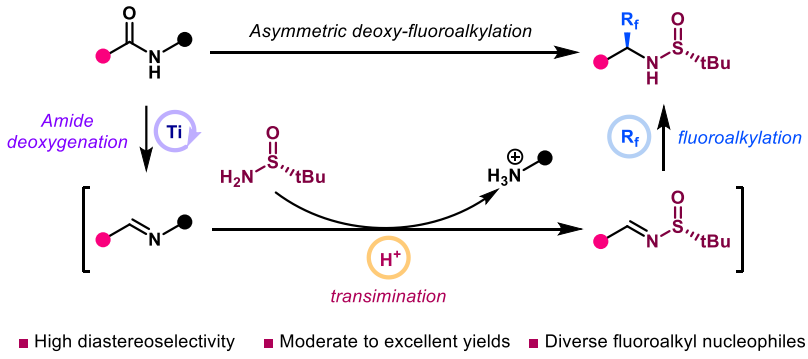
Name of Institution: Clemson University

Research Advisor: Prof. Byoungmoo Kim

Undergraduate studies began in: 2015

Graduate studies began in: 2019

Amides are the most-common functional group synthesized in medicinal chemistry laboratories. They are biocompatible, bench-stable, simple to synthesize, and are inert towards reactions that consume aldehydes, ketones, and esters. Due to these attractive features, the use of amides as a pivot point for constructing diverse amines has been a major synthetic chemistry goal for decades. While amide partial reduction has enabled chemo- and enantioselective amine construction since 2008, installation of CF_3 via these methods has lagged behind, with few reports of limited substrate scope, reliance on expensive reagents, and only yielding racemic products. This sharply contrasts with the growing prevalence of α-CF_3 amine moieties in bioactive compounds. This paradox stems from low CF_3^- nucleophilicity and low electrophilicity of N-alkyl/benzyl imines currently accessible via amide partial reduction. To address this formidable challenge, after quantitative partial reduction of amide into imine using our Ti^{IV} catalysis, we devised a novel transimination approach to convert the initial N-benzyl imine into a chiral sulfinimine that reacts easily with CF_3^-, yielding α-CF_3 amines in up to 70% isolated yield and >20:1 d.r. Furthermore, we have extended this to CF_2H and C_6F_5 nucleophiles in similar yields and up to 4.5:1 d.r., making this the first diverse asymmetric fluoroalkylation of amides.



Poster #34

SUFEX-ENABLED DIRECT DEOXY-AMINATION OF ALCOHOLS

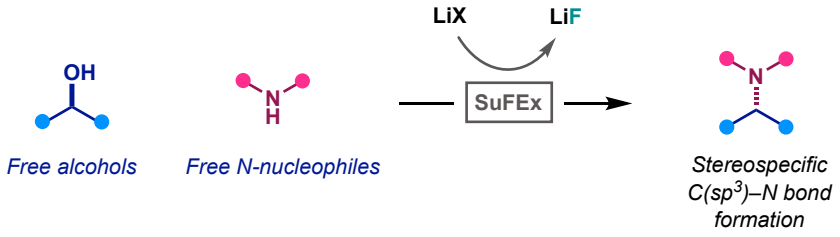
Giovani Gutierrez (1), Amaechi Odoh (1), Austin Seilkop (1), and Byoungmoo Kim (1)

(1) Department of Chemistry and Clemson University

The increasing demand for optically active and complex alkylamines in drug discovery has driven efforts to develop practical and efficient C(sp^3)–N bond-forming strategies. While alcohols are abundant and structurally diverse feedstocks, traditional N-alkylation methods often rely on hazardous reagents, exhibit poor stereocontrol, and promote overalkylation. To address these limitations, our group has developed a deoxyamination strategy that directly converts alcohol-based natural products and bioactive scaffolds into stereochemically rich alkylamines with high stereospecificity. This approach leverages sulfur(VI) fluoride exchange (SuFEx) click chemistry, which utilizes sulfonyl fluorides as key reagents for instantaneous alcohol activation. However, *in situ*-generated fluoride leads to a competing deoxy-fluorination pathway. To solve this, we discovered that lithium salts are effective fluoride traps, completely suppressing the unwanted deoxy-fluorination pathway by forming a thermodynamically stable LiF salt *in situ*. Overall, this strategy enables the direct conversion of C–O bonds in complex hydroxy-containing molecules into C(sp^3)–N bonds, affording a broad range of complex alkylamines in high yields with excellent stereospecificity (>20:1 dr) and no elimination side-products.

Our key solution: Simple lithium ion as a fluoride scavanger

Formation of LiF *in situ* suppresses deoxyfluorination and allows the use of free N-nucleophiles, enabling general deoxyamination



- Facile alcohol activation
- Diverse N-nucleophiles and alcohols
- Stereospecific and enantiodivergent

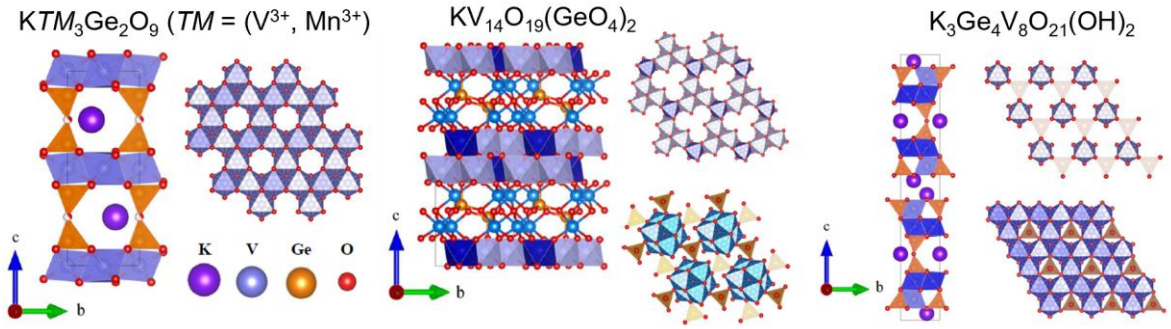
Poster #35

Structural and Magnetic Properties of First Row Transition Metal Germanates

Analeece Long (1), Matthew S. Powell (1), Colin D. McMillen (1), and Joseph W. Kolis (1)

(1) Department of Chemistry, Clemson University

Hydrothermal synthesis has widely been used to examine silicates of most open shell first row transition metals. This leads to a- natural desire to extend the chemistry to metal germanates. There are 15 times more inorganic silicates than germanates. This large of a disparity suggests that there is a wide range of rich and unexplored chemistry to be discovered. Despite the similarity in the ionic radii of these two elements (1.6Å vs 1.7Å) they can have quite different structural properties. Germanium can form tetrahedral, octahedral and five coordinate oxyanion building blocks. Germanium oxide is also readily soluble and stable in superheated water. These factors make the examination of transition metal germanates via high temperature hydrothermal reactions very promising. An interesting material in this research is KTM_3Ge_2O9 (*TM* = V^{3+}, Mn^{3+}). This structure adopts an ideal kagome lattice, with antiferromagnetic order. This is an example of the tetrahedral germanium and octahedral first row transition metals leading to a high symmetry structure with potentially frustrated magnetic behavior. The synthesis and crystal growth of these target materials also led to the discovery of several new materials as well, including $K_3Ge_4V_8O_{21}(OH)_2$ and $KV_{14}O_{19}(GeO_4)_2$. The synthesis, structures and magnetic properties of these new transition metal germanates will be presented as well as their relationship to a few naturally occurring minerals.



Geometric Magnetically Frustrated Quasi-1D Nickel Phosphate Materials with Potential Haldane-like Behavior

Emily D. Williams (1), Matthew S. Powell (1), Colin D. McMillen (1), and Joseph W. Kolis (1)

(1) Department of Chemistry, Clemson University

Novel frustrated magnetic transition metal phosphates and arsenates are being sought out for their interesting properties in magnetoelectric applications.[1-3] It is known that phosphates and arsenates can have iso-atomic structures but not iso-magnetic structures which vary widely with a misunderstanding of the mechanism as to how this happens.[4-7] This research employs a hydrothermal synthesis that mimics the earth's natural mineral formation process and eliminates many crystal lattice defects via a slow growth technically that is at moderate temperatures (500-700^{o}C) and pressures (1-2kbar).[8] The novel materials in this presentation were characterized via powder and single crystal x-ray diffraction to look at structural features such as one-dimensional chains and/or layers that have shown promising frustrated magnetic systems within the *intra*-chain and *inter*-chain magnetic coupling. The proposed future direction for this project is to further synthesize novel phosphate and arsenate structures with the addition of making new phosphate and arsenate analogs of what already has been synthesized. Currently, the novel structures are undergoing hydrothermal optimization process' to achieve enough material and notable sized crystals (1-2mm) for magnetic measurements on Clemson's Physical Properties Measurement System. This will allow preliminary data to briefly understand if the material undergoes paramagnetic transitions as well as if it has the potential to be a frustrated magnetic system. Because our materials can grow to significant sizes, the materials are also of interest for single crystal neutron diffraction that allow us to better understand the mechanism as to how the iso-atomic structures turn into the varying ranges of new magnetic structures.

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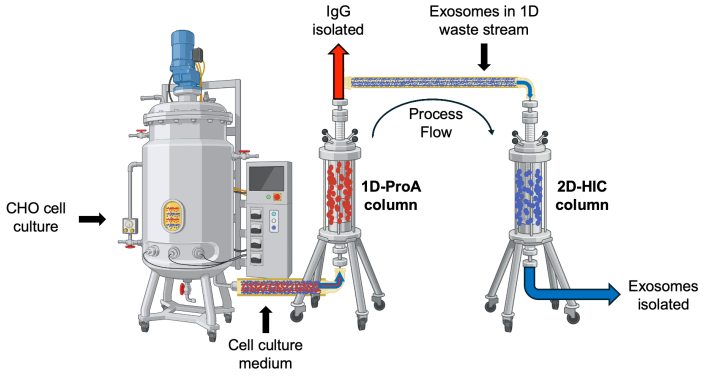
TWO-DIMENSIONAL LIQUID CHROMATOGRAPHY ISOLATION AND QUANTIFICATION OF IMMUNOGLOBULIN G AND EXOSOMES FROM CELL CULTURE MEDIUM USING CAPILLARY-CHANNELED POLYMER FIBER COLUMNS

Christopher D. Topper (1), R. Kenneth Marcus (1)

(1) Department of Chemistry, Clemson University, Clemson, SC 29634

Pharmaceutical companies are currently investigating the use of extracellular vesicles (EVs), specifically exosomes, as vectors to deliver biomolecular therapeutics in a targeted manner to damaged or diseased cells. EVs are small membrane-bound particles that are naturally released by cells into the extracellular environment. Exosomes constitute a subset of EVs characterized by a size range of 30–150 nm and membranes enriched in tetraspanin proteins. Exosomes are essential for intercellular communication, transporting proteins, mRNA, and miRNA to both nearby and distant cells, thereby directly influencing gene expression. They are produced by nearly all plant and animal cells, including those used in engineered cell lines to produce biotherapeutics. Monoclonal antibodies (mAbs) such as immunoglobulin G (IgG) are manufactured using engineered Chinese hamster ovary (CHO) cells cultured in suspension within bioreactors. The initial purification involves passing the culture medium through a Protein A (ProA) affinity chromatography column to isolate the antibodies. The waste stream from this process, however, contains valuable EVs that are ultimately discarded. Therefore, the isolation of EVs from CHO cell waste streams presents an opportunity for by-product valorization. We describe a two-dimensional liquid chromatography platform employing columns packed with capillary-channeled polymer (C-CP) fibers to isolate both IgG and exosomes from CHO cell-culture supernatant. The first dimension utilizes ProA to isolate and quantify IgG, while hydrophobic interaction chromatography (HIC) is used in the second dimension to isolate exosomes from the first-dimension effluent. Quantitative recoveries of both IgG and exosomes were observed; exosome quantification, in particular, has practical implications beyond serving as a process yield metric. Quantification of exosomes in culture medium can be used to monitor cell-culture health during bioprocessing, as exosome production is upregulated in response to stress. Thus, we demonstrate a convenient framework for characterizing CHO cell cultures in terms of both IgG and exosome production traits. The two-dimensional methodology provides practical insights into the co-production of these two disparate biotherapeutic modalities, and enables recovery of valuable EVs during the production of mAbs.



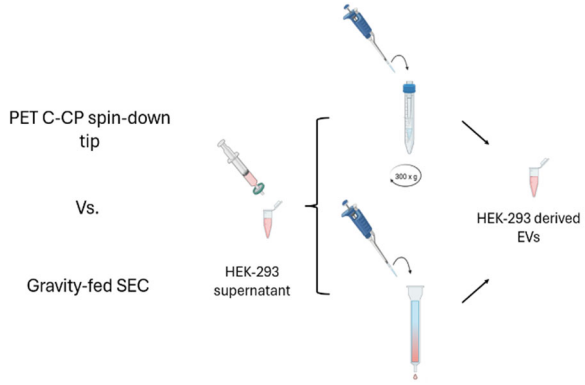
Poster #37

Comparison of HEK-293-derived extracellular vesicles (EVs) isolated via polyester (PET) capillary-channeled polymer (C-CP) fiber spin-down tips and gravity-fed size exclusion chromatography (SEC) columns

Carolina Mata (1), Christopher D. Topper (1), and R. Kenneth Marcus (1)

(1) Department of Chemistry, Biosystems Research Complex, Clemson University; (2) Department of Chemical and Biomolecular Engineering, Clemson University; (3) Department of Bioengineering, Clemson University, Clemson, SC 29634-0973, USA

A sub-population of extracellular vesicles (EVs), exosomes, mediate intracellular communication and bio transport. Their biomarker-rich lipid bilayer makes them ideal diagnostic tools and putative vectors for therapeutics. EVs derived from human embryonic kidney (HEK-293) cells are of interest for human applications due to their rapid production, scalability, and biocompatibility. Widespread applications of HEK-293-derived EVs are hindered by the complexity of the matrix, as current separation platforms fail to deliver high throughput and purities on practical time and cost scales. As separation platforms continue to evolve for the isolation of EVs, it is critical that emerging platforms yield products comparable to those of existing methods, including gravity-fed size exclusion chromatography (SEC). SEC separates EVs based on their hydrodynamic radii; however, it struggles with purity and throughput. Marcus et al. have developed polyester (PET) capillary-channeled polymer (C-CP) fiber spin-down tips that address these limitations using hydrophobic interaction chromatography (HIC). Using a HIC gradient, filtered HEK-293 supernatant is mixed 1:1 with high ionic strength solvent, influencing EV binding. Using a tabletop centrifuge, ionic species and matrix-related precipitants are eluted. A second centrifugation step occurs after the addition of a solvent with decreased ionic strength and a small amount of organic solvent, eluting nominally hydrophobic matrix-related species (i.e. proteins/lipoproteins). Finally, EVs are eluted using a solvent of low ionic strength and increased organic solvent strength. A comprehensive comparison of EV eluates from PET C-CP fiber spin-down tips and SEC cartridges was conducted to ensure that PET C-CP fiber platforms are performing on par with the commercialized method. Metrics for comparison included retention of vesicle morphology, immunoconfirmation, purity metrics, and particle quantification. Through this comparison, PET C-CP spin-down tips demonstrated a rapid and high-throughput alternative to commercial EV isolation methods on scales appropriate for diagnostic applications, with implementation in column formats directed towards therapeutic applications.



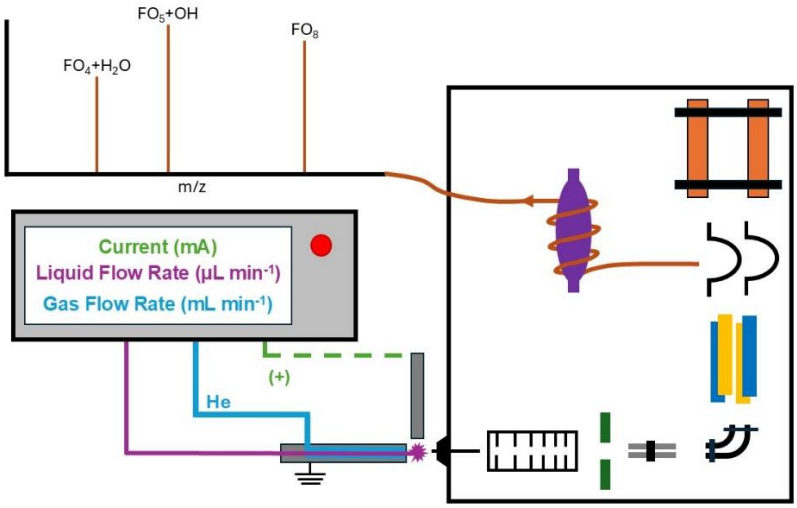
Poster #38

Detection of Anions using the Liquid Sampling – Atmospheric Pressure Glow Discharge Microplasma Ionization Source with Orbitrap and Compact Mass Spectrometry

Dehlia Lang and R. Kenneth Marcus

Department of Chemistry, Clemson University, Clemson, SC

Fluoride detection is essential across environmental monitoring, drinking water analysis, and nuclear forensics. In the context of PFAS analysis, an area of growing environmental concern, identifying fluoride anions can help estimate total fluorine content. Many communities add fluoride to the water to prevent tooth decay. However, excessive fluoride exposure can cause dental and skeletal fluorosis. In nuclear forensics, fluoride detection aids in the dating of UO_2F_2 particles, formed when uranium hexafluoride (UF_6) in enrichment processes reacts with atmospheric moisture enabling investigators to estimate contamination timelines. Traditional fluoride detection methods include gas chromatography–mass spectrometry (GC-MS), inductively coupled plasma–mass spectrometry (ICP-MS), molecular absorption spectroscopy (MAS), and fluorescence spectroscopy. While effective, these techniques often involve complex sample preparation or derivatization, limited sensitivity, challenges with negative ion mode, isobaric interferences, suboptimal detection limits, or difficulty quantifying fluoride directly. To overcome these challenges, we propose a novel approach using liquid sampling–atmospheric pressure glow discharge (LS-APGD) microplasma coupled with Orbitrap mass spectrometry. This technique generates high-resolution spectra of fluoride-containing complexes from simple salt solutions. By optimizing in-source collision-induced dissociation (CID), higher-energy collisional dissociation (HCD), and plasma conditions, we simplified these complexes to their most basic detectable forms. This approach leverages the resolving power of the Orbitrap and FTMS Booster X2T at resolutions of 70,000 or higher to minimize isobaric interferences and provide a method for the detection of fluorine in its anionic form.



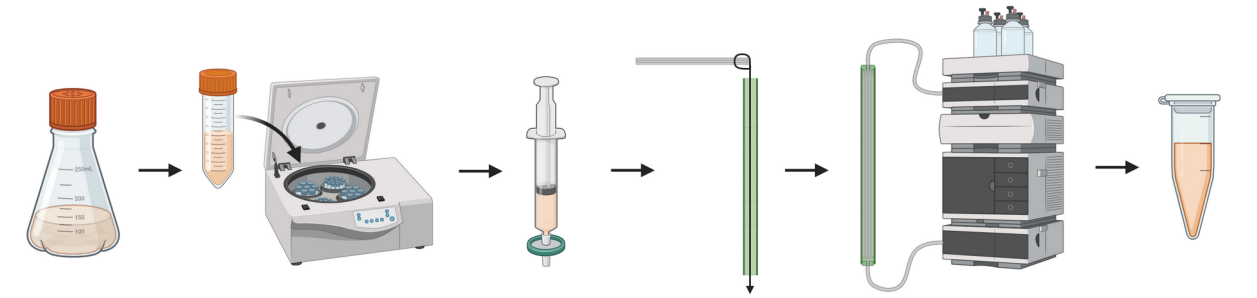
Poster #39

Monitoring HEK293 cell extracellular vesicle (EV) production via a polyester capillary-channeled polymer (C-CP) fiber column with HIC modality

William F. Pons (1), Stephanie Beitle (2), Raphael Ewonde Ewonde (1), Sarah W. Harcum (2, 3), and R. Kenneth Marcus (1)

(1) Department of Chemistry, Biosystems Research Complex, Clemson University; (2) Department of Chemical and Biomolecular Engineering, Clemson University; (3) Department of Bioengineering, Clemson University

Extracellular vesicles (EVs) are phospholipid bilayer-enveloped bionanoparticles released from all living cells, with the potential to advance diagnostic and therapeutic applications. Cell culture-derived EVs provide an abundant, scalable, and reproducible source of EVs. Human embryonic kidney (HEK293) cells, a widely-cultured cell type for recombinant protein and viral production, also release great quantities of biocompatible EVs. Monitoring the release of EVs and their concentration in supernatant from cell culture provides insights for multiple important cell growth parameters, including the effects of culture medium composition, pH, glucose, serum presence, and cellular stress. This presents a need for a simple method to monitor cell culture EV release, highly desirable for optimizing industrial cell culture growth and facilitating scalable EV collection. An EV isolation method applied to cell culture must address several primary metrics, including high throughput, rapid separations, pure and concentrated isolates, and high levels of reproducibility. Described here is a rapid isolation method using hydrophobic interaction chromatography (HIC) with polyester (PET) capillary-channeled polymer (C-CP) fiber chromatographic columns for the separation of EVs from HEK293 suspension cell culture supernatant. This method rapidly (<15 min) isolates EVs, enabling in-process concentration determination and subsequent collection for downstream characterization. The present protocol is applied to three parallel HEK293 cell cultures, monitoring the EV concentration as it relates to viable cell density (VCD) and cell viability. Effective EV isolation was verified through multiple standard characterization techniques, including light scattering and immunofluorescence detection with nano-flow cytometry, a comparison of EV absorbance-based quantification, and vesicle morphology confirmation with transmission electron microscopy (TEM).



Microextraction-LS-APGD/Orbitrap Mass Spectrometry for Direct Isotope Ratio Analysis of Environmental Swipes

Suraj Shrestha[1], Joseph V. Goodwin[1], Cameron Stouffer[1], Benjamin T. Manard[2], and R. Kenneth Marcus[1]

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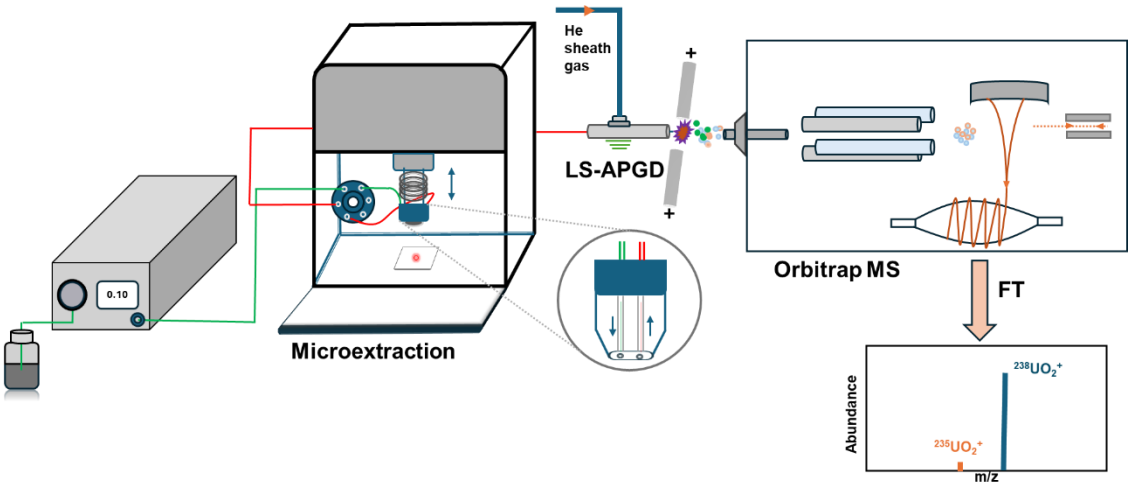
[2]Chemical Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN 37830, USA

Analysis of environmental samples (ES) provides critical information on the nature of the elements and their isotopic composition at the sample collection site. The International Atomic Energy Agency's (IAEA) nuclear safeguards monitoring program employs this sampling technique to detect undeclared activities and materials in a nuclear facility. Isotopic analysis of these swipes, however, is a laborious and time-consuming process that requires ashing the entire swipe, digestion, chemical separation, and, finally, isotope ratio analysis using a mass spectrometer. Additionally, inherent elements present in the swipe itself make trace-level analysis even more uncertain. To overcome some of these limitations, we have developed a rapid method for direct isotopic analysis of uranium in ES using the microextraction sampling technique coupled with the liquid sampling-atmospheric pressure glow discharge (LS-APGD) ionization source and a high resolution Orbitrap mass spectrometer. This novel platform offers two-fold advantages over the traditional bulk digestion method. First, direct analysis of these swipes, bypassing digestion steps, significantly improves the method's throughput, and the analysis results are indicative of the samples alone, free of the inherent components present in the swipes. Second, it leverages the high resolution capability of the Orbitrap mass spectrometer, requiring no chemical separation to overcome isobaric interferences before mass analysis. In this presentation, optimization of key microextraction and microplasma source parameters will be discussed. The accuracy and precision of the method evaluated using an isotope reference standard will be presented. Finally, its application to a real-world swipe sample will be discussed.



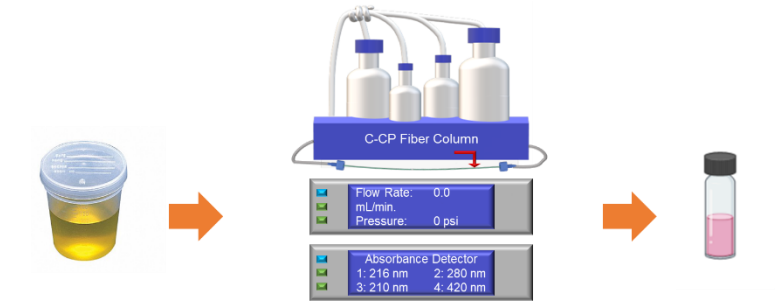
Poster #41

Evaluation Of Dynamic Loading And Recovery Of Extracellular Vesicles On Analytical-Scale Capillary-Channeled Polymer Fiber Columns Via Frontal Analysis

Md Khalid Bin Islam and R. Kenneth Marcus

Department of Chemistry, Clemson University, Clemson, SC 29634

Extracellular vesicles (EVs) are lipid-bound nano particles (50 - 1000 nm) secreted by cells and play central roles in intercellular communication under both normal and disease conditions. Exosomes, a smaller EV subpopulation typically ranging from 30 - 200 nm, are of particular interest due to their emerging utility in diagnostics and therapeutic delivery. Despite this promise, existing EV isolation techniques remain constrained by low throughput, extended processing times, and limited scalability. To address these challenges, the Marcus group has introduced a hydrophobic interaction chromatography (HIC) strategy based on capillary-channeled polymer (C-CP) fiber stationary phases, enabling rapid (<15 min) and low-cost EV purification using microbore column format (0.8 mm i.d. × 300 mm). While this format offers efficient capture, translating it to a higher-throughput operation requires further development. In the present work, C-CP fiber columns were expanded to an analytical-scale format (2.1 mm i.d. × 250 mm) and packed across different fiber packing densities. Column performance was assessed using breakthrough and frontal analysis on a high-performance liquid chromatography (HPLC) platform, revealing EV binding capacities of up to 10^{12} particles per column and a 2.4 fold improvement in capture relative to the microbore columns. Urine-derived EVs were employed to evaluate binding efficiency, recovery, throughput, and overall yield as functions of packing density. Operation at elevated flow rates and linear velocities (up to 6 mL min^{-1} and 45 mm s^{-1}) resulted in increased productivity without loss of vesicle integrity, as verified by transmission electron microscopy (TEM). These results demonstrate that increasing fiber surface area while maintaining favorable flow characteristics enables scalable, high-yield exosome isolation, with projected capacities approaching 10^{13} particles. This work advances C-CP fiber chromatography toward practical, preparative-scale EV purification workflows.



Investigating the Impact of Gd Substitution on Magnetic Interactions and Hyperthermia Efficiency in Fe_3O_4 Nanorods

Ehimen Odion,[a] Nasim Ahmed,[a] Suvra S. Laha,[b] and O. Thompson Mefford,[a]b*]

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Abstract

Magnetic nanoparticle hyperthermia relies on field-driven magnetic losses to generate localized heating under alternating magnetic fields. While both rare-earth substitution and particle anisotropy have been reported to influence specific absorption rate (SAR), their combined effect within anisotropic magnetite nanorods remains unclear, particularly under clinically relevant low-field conditions, and dopant concentration is rarely mapped to identify an optimal substitution window to distinguish enhanced magnetic interactions from magnetic dilution effects.

Here, we investigate the effect of controlled Gd^{3+} substitution (~0-2 mol%) on solvothermally synthesized Fe_3O_4 nanorods functionalized with PEG-nitroDOPA and evaluate structure, magnetic property and heating performance relationships under low-field AC conditions. X-ray diffraction confirms retention of the spinel structure across compositions, and transmission electron microscopy reveals Gd-dependent morphological evolution from well-dispersed rods at low substitution to thinner, elongated web-like assemblies at ≥1 mol% Gd. DC magnetometry shows composition-dependent magnetic behavior, including reduced saturation magnetization at higher Gd levels, while low-temperature measurements exhibit a Verwey transition near ~118 K, supporting a preserved magnetite-like phase. Hyperthermia performance, quantified using both AC magnetometry and calorimetry, showed a distinctly non-monotonic SAR trend. SAR increased from undoped rods to a maximum at intermediate Gd content (~0.75 mol%), then drops sharply at ~1 mol% Gd. This enhanced SAR is significant for reaching therapeutic temperatures more rapidly at lower dose and shorter exposure times under safe field conditions.

Overall, these results identify an optimal Gd window and show that SAR is governed by a balance of shape anisotropy, hysteresis loss and magnetic interactions rather than magnetization alone, providing mechanistic insight into how controlled rare earth substitution can be used to tune hyperthermia performance in anisotropic ferrimagnetic nanostructures.

Halogen Bonding in Cocrystals of Organoiodines with Diphenyliodonium Halide Salts and Organic Ammonium Halide Salts

***Lahiruni Pelendage, Lillian Hicks, Makenna Lankford, Meridee Ritzer, Colin D. McMillen, William T. Pennington**

Doctoral Student, Department of Chemistry, Clemson University, Undergraduate Student, Department of Chemistry, Clemson University, Undergraduate Student, Department of Chemistry, Clemson University, Undergraduate Student, Department of Chemistry, Clemson University, Assistant Professor, Department of Chemistry, Clemson University, and Professor, Department of Chemistry, Clemson University

Keywords: Halogen bonds, cocrystals, solid state X-ray, Diphenyliodonium Chloride/Bromide/Iodide Salts, Tetraalkylammonium Halide

Halogen bonding is a highly directional, tunable non-covalent interaction that occurs between the electrophilic region (sigma hole) of a halogen atom and a nucleophilic region of the same molecule or another molecule. Diphenyliodonium halide (chloride, bromide, and iodide) salts (Ph_2IX) and tetraalkylammonium halide (NR_4X) are identified as potential halogen bond acceptors to organoiodines: 1,2-diiodotetrafluorobenzene (1,2-F_4DIB), 1,3-diiodotetrafluorobenzene (1,3-F_4DIB) and 1,4-diiodotetrafluorobenzene (1,4-F_4DIB). The behavior of halogen bonds in the presence of various halide anions and the cation in the crystal structure was analyzed. The systematic comparison was made between cocrystals synthesized by solvent-based and mechanochemical methods. Obtained cocrystals were analyzed using single crystal x-ray diffraction and powder x-ray diffraction. The current study lays out a comparison of the halogen bond strengths and halogen bond motifs across different halide identities and investigates how different organoiodine donors contribute to long-range halogen bonding patterns. Interestingly, the stoichiometries of the cocrystal structures differed in both series and non-isostructural assemblies were observed. Cocrystals obtained from Ph_2IX with organoiodines exhibited a key characteristic— a halogen-bonded rhombus-shaped core. Depending on the specific organoiodine isomer and the stoichiometric ratio of the crystal structure, there are several ways in which the organoiodine and the cation are bonded to the rhombus-core. The current study highlights long-range halogen-bonding patterns alongside structural characteristics of halogen-bonded cocrystals: halogen bond strengths (distance) and melting point. Moreover, we intend to develop highly dependable crystal engineering principles through halogen bonding.

Cooperative assemblies of halogen bonds and hydrogen bonds in cocrystals of organic salts with organoiodine

Maryelle Nyeck, Meridee Ritzer, Makenna Lankford, Jade Johnson, Colin McMillen*, William Pennington*

Abstract

The halogen bond arises from the attractive interaction between an electron-deficient region on a halogen atom and an electron-rich site on another molecular entity. This noncovalent force is useful in crystal engineering and pharmaceutical design, particularly in the rational development of cocrystals with targeted properties. The electrostatic attraction that occurs in a halogen bonding interaction makes halide salts particularly interesting candidates for halogen bonding, as the anionic halogen ion provides an electron-rich and flexible acceptor site for co-crystallization with organoiodine. At the same time, cations or organoiodine molecules bearing hydroxyl groups can add further structural diversity to these cocrystal systems through hydrogen bonding interactions. The present study examines two scenarios: choline iodide/organoiodine cocrystals, where the hydroxyl group is present on the cationic species, and tetraalkylammonium iodide/iodophenol cocrystals, where the hydroxyl group is present on the organoiodine species. A great diversity of structural motifs is observed from the competitive/cooperative effects of halogen bonding and hydrogen bonding, as well as the variation in iodine/hydroxide location on the organoiodine molecules. Moreover, the study leverages several different crystal growth techniques, including solution chemistry, self-flux chemistry, and mechanochemistry, to synthesize these cocrystals. The study contributes to the application of crystal engineering principles in the design of materials with tunable structural and physicochemical properties.

Poster #45

A New Halogen Bond Donor: 1,2,3-Trifluoro-4,5,6-Triiodobenzene

Marrissa A. Raynesford (1), Meridee Ritzer (1), Colin D. McMillen (1), and William T. Pennington (1)

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Halogen bonding is well studied, yet numerous organoiodine-heterocycle systems lack structural characterization. The arrangement of electron-withdrawing fluorines around three highly polarized iodine sites in 1,2,3-trifluoro-4,5,6-triiodobenzene represents a unique organoiodine donor with no reported crystal structures in the Cambridge Structural Database. This work investigates its cocrystallization with a diverse set of nitrogen heterocycles to determine whether halogen bonding emerges and how these assemblies organize. Together, these results will establish the interaction patterns that govern these systems and enable more reliable design of future supramolecular architectures.

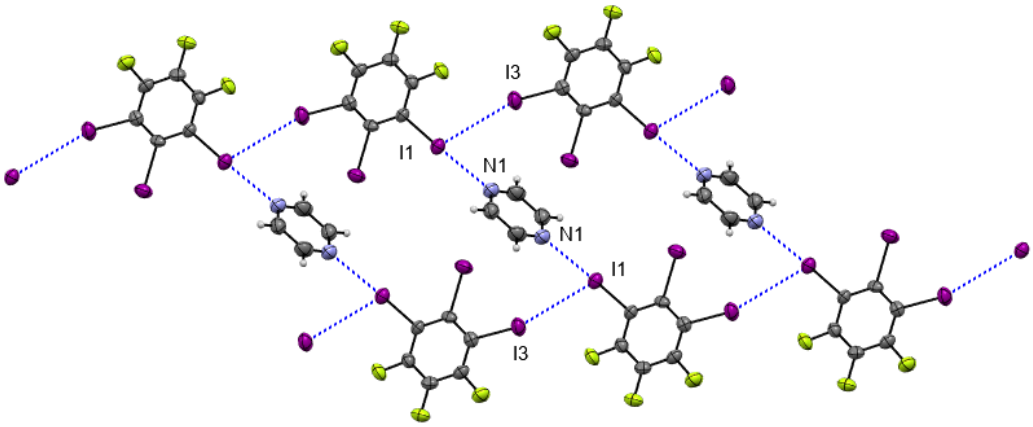


Figure 1. Novel cocrystal of 1,2,3-trifluoro-4,5,6-triiodobenzene and pyrazine

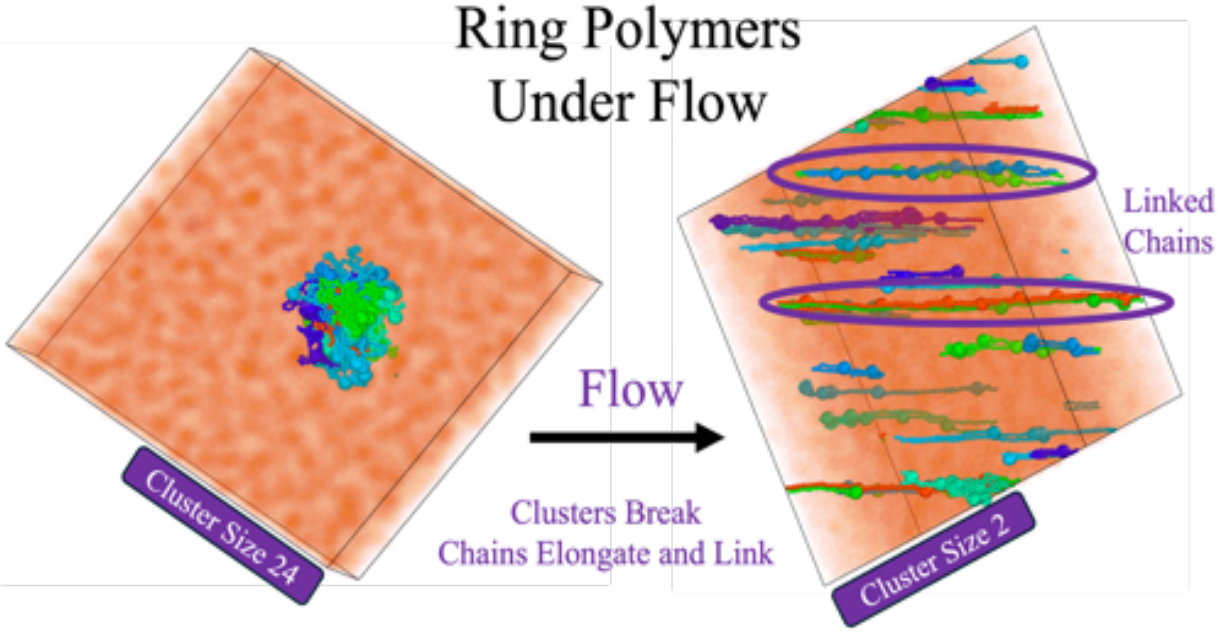
Poster #46

Flow Response of Associating Ring-Polymer Melts

John Bracewell (1), Dvora Perahia (1,2), Gary Grest (3)

(1) Department of Chemistry, Clemson University (2) Department of Physics, Clemson University (3) Sandia National Laboratories, Albuquerque, New Mexico

Associating polymers are macromolecules that bear groups that interact with higher energies than typical Van der Waals forces. Examples include π-π stacking, hydrogen bonding, and ionic clustering, which drive the formation of complex structures. These types of polymers are used in a wide range of applications, such as clean energy and biotechnology and are processed into materials under flow. Their viscoelastic response is a complex function of chemistry and connectivity. Rings are a unique class of polymers because of the lack of free ends, which affects their structure and dynamics. We use large-scale molecular dynamics simulations to study associating ring polymer melts under elongational flow, with association strengths ranging from 1 to $8k_BT$, and 5% of the beads that constitute the chains are modeled as associating groups. This range of association strength corresponds to interactions that vary from van-der-Walls forces to hydrogen bonds. We find that under flow, the rings not only stretch and align, but also form topological links that extend the polymer dimensions, and concurrently, the clusters formed by the associative groups break and reform. Both cluster dynamics and ring linking are flow rate-dependent and affect the viscosity and density of these melts under flow.



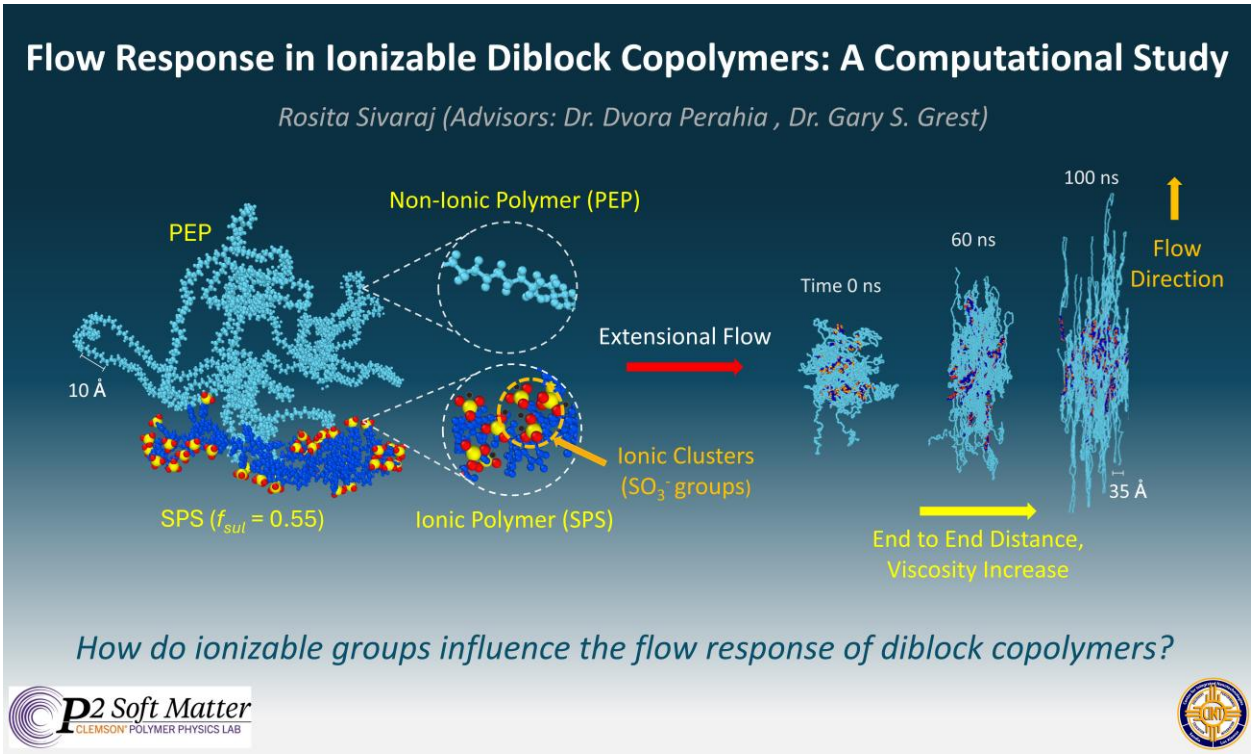
Poster #47

Flow Response in Ionizable Diblock Copolymers: A Computational Study

Rosita Sivaraj (1), Gary S. Grest (2) and Dvora Perahia (1)

(1) Department of Chemistry, Clemson University, (2) CINT, Sandia National Laboratories

Diblock copolymers are macromolecules that consist of two chemically distinctive blocks, leading to a wide variety of structures. When one of the blocks consists of ionizable groups, it becomes an ion conductor that enables a broad range of applications. These include electrochemical membranes and stretchable conductors. In both processing and practical use, these polymers are subjected to flow fields. Ionizable polymers form complex structures due to assemblies of ionic groups. Here, using molecular dynamics simulations, we study the response of sulfonated polystyrene-poly(ethylene-r-propylene) (SPS-PEP) diblock melts under flow. We find that when flow is applied, polymer chains stretch, and ionic clusters dynamically break and reform. At low flow rates, higher sulfonation promotes larger ionic clusters, whereas at high flow rates, the applied flow disrupts cluster formation. As a result, extensional viscosity increases with sulfonation but decreases with flow rate. The two blocks stretch heterogeneously, with ionic clusters in the SPS block limiting chain extension. These results provide a fundamental understanding of polymers and impact their transformations into useful materials.



Poster #48

Structure and Dynamics of Polymer Grafted Nanoparticles in Water

Abdul Nasir Abdullah[1], John M. Bracewell[1], Gary S. Grest[3], Dvora Perahia[1,2]

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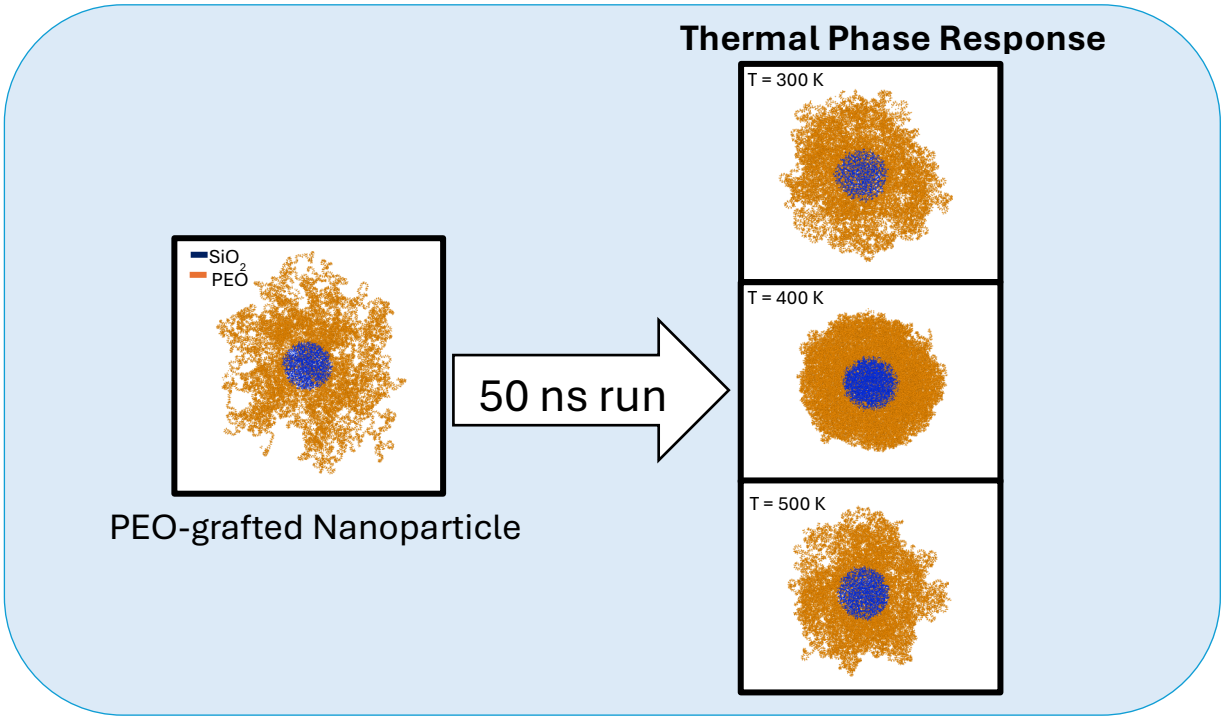
Polymer-grafted nanoparticles (NPs) are highly promising for applications ranging from drug delivery to advanced electronic materials. The polymer coating enables the tethering of specific functionality to the NPs, forming a shell that controls the interactions with the surrounding environment. Grafted polymers immersed in a good solvent form a brush-like shell whose structure depends on the polymer properties, including molecular weight, polymer-solvent interactions, grafting density, and the nature of the interface. Polyethylene oxide (PEO) is a biocompatible macromolecule suitable for drug delivery, tissue-engineering scaffolds, and medical device coatings, all of which operate in an aqueous environment. The current work aims to resolve the structure and dynamics of PEO-grafted silicon oxide nanoparticles at the nanoparticle-water interface using fully atomistic molecular dynamics simulations. We investigate the conformational properties of PEO grafted nanoparticles of 50 and 100 monomer chain length and nanoparticle size (3 nm and 5 nm) at a grafting density of 1.53 chains/nm^2. Surprisingly, unlike most polymer-grafted NPs, the PEO shell collapses with increasing temperature. This anomalous phase transition is significantly more pronounced at higher molecular weights, highlighting the unique interplay between chain length and thermal response in grafted systems.



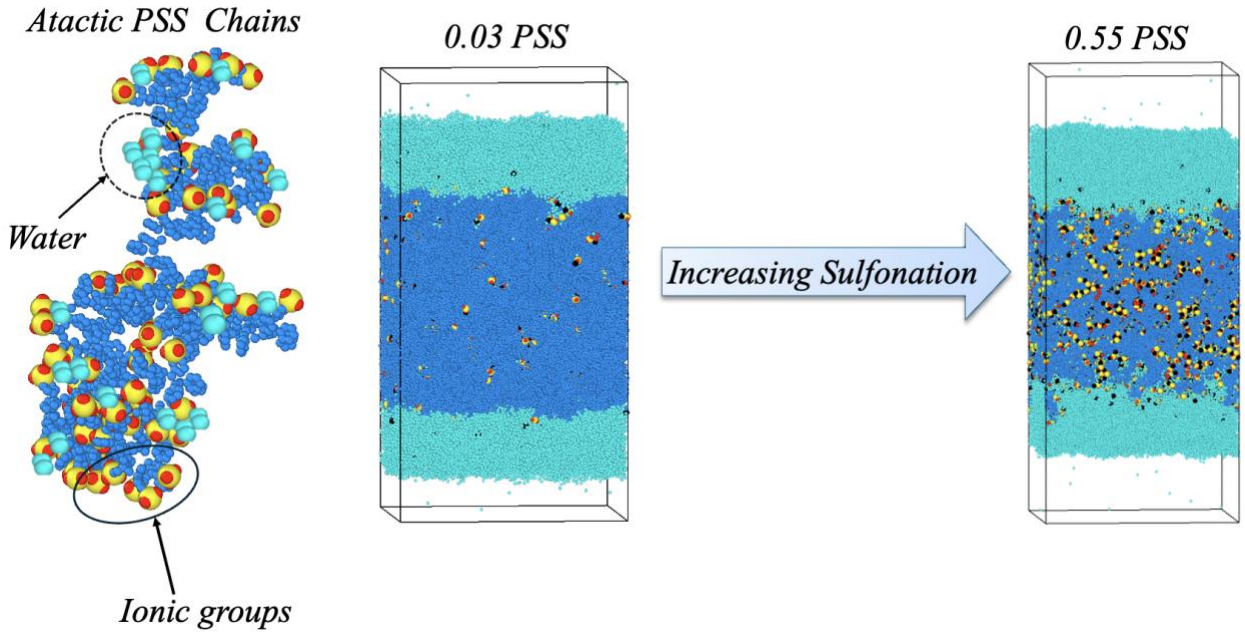
Poster #49

Ionizable Polymer Thin Films at the Interface with Water

Ernestine Akorlor [1], Dvora Perahia[1,2], Gary S. Grest[3]

[1]Department of Chemistry, Clemson University, Clemson, SC, [2]Department of Physics, Clemson University, Clemson, SC, [3]Sandia National Laboratories, Albuquerque, NM

Using molecular dynamics simulations (MDS), we investigate how the structure and dynamics of a model ionizable polymer affect water uptake, ion conductivity, and film stability at the interface of water at elevated temperatures. These polymers consist of flexible chains substituted with ionizable groups, whose structure is dominated by the assembly of these groups, resulting in interfaces that contain both hydrophilic and hydrophobic domains. These polymers serve as key components in clean energy generation, storage devices and biotechnology, where water is inherent to their function. Understanding the effects of different sulfonation levels on the water uptake and film stability at the structured interfaces of ionizable polymers remains a fundamental challenge with immense technological impact. Here, the results of a fully atomistic MD simulation of films of a model polymer, sulfonated polystyrene (PSS), with different sulfonation fractions exposed to water, are discussed. MD simulations were run using LAMMPS and GROMACS at 400 and 500 K. The results show that polymers can be divided into low- and high-sulfonated groups. At low sulfonation levels, ionic groups are sparsely distributed, forming isolated domains that limit water uptake. As the sulfonation level increases, ionic domain connectivity improves, thereby facilitating water uptake and ion conductivity. Increasing the temperature to 500K further accelerates both the water penetration and the dynamics of the polymer.



Synthesis of Nitroalkene Scaffolds for Organocatalyzed Reactions

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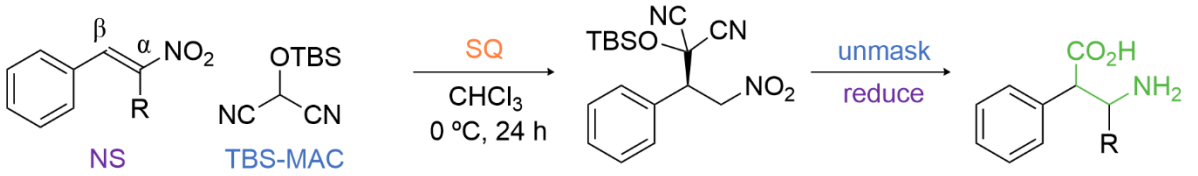
Chiral α- and β-amino acids and esters are widely found in nature and in pharmacological or biologically relevant molecules. Due to their importance, versatile and efficient syntheses of these chiral building blocks are of great interest in the pharmaceutical industry. Squaramide organocatalysts are alternatives to metal catalysts that can catalyze a wide range of reactions by taking advantage of noncovalent interactions to activate one or both substrates stereoselectively. We previously developed an enantioselective organocatalyzed reaction of masked acyl cyanides (MAC) to β-nitrostyrenes as a complementary method towards the synthesis of chiral β-amino acids and esters. Based on the high yields and high enantioselectivity of the prior reaction, we propose to extend this chemistry to α-substituted β-nitrostyrenes to probe the diastereoselectivity. Preliminary investigation using MAC addition to a cyclic α,β-nitrostyrene substrate favored one major diastereomer. We propose to study the applicability of this reaction through the synthesis of various cyclic and substituted nitroalkenes as scaffolds. These include the nitration of alkenes including cyclohexene, benzofuran, indene, 1,5-cyclooctadiene, norbornene, annulene, and 1,4-dihydronaphthalene. The future work will be to explore the conjugate addition of MAC to these scaffolds as a route to access chiral amino acids.



prior work: R = H, β-NS, chiral SQ, 81-92 %*ee*
this work: R ≠ H, α,β-NS, chiral SQ, ?? %*ee*
achiral SQ, ?? %dr

Poster #51

Surface-Mediated Redox Transformations of Plutonium in High Ionic Strength Systems

Chineyem Ebite (1,3), Valery Bliznyuk (2,3), Shanna L.Estes (1,2,3), Brian Powell(1,2,3)

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Mineral surfaces such as goethite, hematite, gibbsite, and quartz have been widely reported to promote the reduction of Pu(VI), a soluble and mobile oxidation state, to the far less soluble and strongly sorbing Pu(IV), with major implications for radionuclide retention in subsurface environments and nuclear waste repositories. Despite repeated observation of this phenomenon, the mechanism by which mineral surfaces drive plutonium reduction remains incompletely understood, particularly how surface complexation alters redox energetics sufficiently to enable electron transfer in the absence of traditional reductants. This study investigates plutonium sorption and redox behavior on iron oxyhydroxide minerals under high ionic strength conditions representative of repository brines. Batch sorption experiments were conducted across a range of pH and electrolyte concentrations to quantify plutonium uptake. Raman spectroscopy was used to monitor oxidation-state evolution through changes in Pu–O vibrational signatures, particularly the disappearance of the plutonyl symmetric stretch. Electron microscopy analyses confirm that plutonium is primarily associated with the mineral surface and does not form discrete colloidal PuO_2 precipitates under the conditions examined. A thermodynamically based double-layer surface complexation model was developed to quantitatively describe plutonium sorption and interfacial speciation, and stability constants calibrated at 0.1 M NaCl were applied to higher ionic strengths (1 and 3 M) to evaluate model transferability and to quantify the effects of double-layer compression, electrolyte competition, and chloride complexation in brine systems. Together, these studies provide a mechanistic, spectroscopically validated, and quantitatively modeled framework for predicting plutonium behavior in high-ionic-strength nuclear waste repositories.

Lithium ion-conducting triazacoronene-based neutral 2D covalent organic framework as a solid-state electrolyte

Luke Cromer

Clemson Research Symposium

Saturday, February 21st , 2026

Absract

Due to the increasing demand for energy and the transition from fossil fuels to renewable sources, there is a growing need for reliable and sustainable energy storage solutions. Lithium-ion batteries (LIBs) are among the most widely studied and commonly used technologies for efficient and portable energy storage. The development of solid-state electrolytes (SSEs) is crucial to advancing LIB technology, as commonly used liquid electrolytes raise concerns for safety and long-term performance.

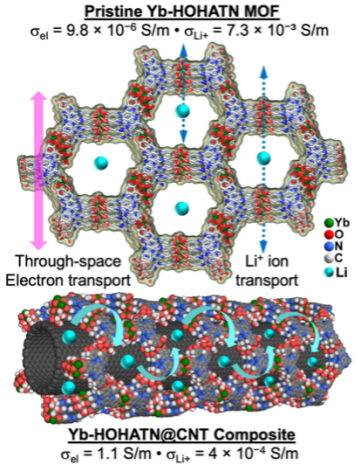
Recently, covalent organic frameworks (COFs) have emerged as promising solid-state electrolyte in LIBs due to their defined porosity, thermal stability, and diverse tunability within the framework. In this work, we present a new neutral two-dimensional hexagonal COF (HMTAC-COF1) constructed from hexamethoxy-triazocoronene (HMTAC) structural units. The framework features abundant lithophilic sites that enhance Li^+ ion mobility via accelerated ion hopping between Lewis Basic centers. Upon Li^+-doping, Li^+@HMTAC-COF1 displayed a remarkable ionic conductivity of 4.95 x 10^{-5} S/cm at 20 °C and 1.95 x 10^{-4} S/cm at 120 °C. Moreover, Li^+@HMTAC-COF1 demonstrated a high Li^+transference number (t_{Li+}) of 0.57. These results are comparable to, and in some cases outperform, similar neutral 2D-COFs in the field. When tested as an SSE in a Li|Li^+@HMTAC-COF1|$LiFePO_4$ coin cell, it displayed a promising specific capacity (178 mAh/g) with ~99% Coulombic efficiency over multiple cycles at 100 °C. These results reinforce the potential of heteroatom-rich neutral COFs to serve as advanced SSEs enabling safer, more efficient solid-state LIBs.

Dual Electronic and Li^+ Ion Conducting Ytterbium-Hexaazatrinaphthalene MOF as High Performance Anode for Li^+ Ion Batteries and Its Carbon Nanotube Composites

Mohd Azhar Hasan Ansari (1), Ashok Yadav (1), Janak Basel (2, 3), Mihir Parekh (2, 3), Jorge Barroso (1), Apparao Rao (2, 3), and Sourav Saha (1)

(1) Advanced Materials Innovation Complex, Department of Chemistry, Clemson University, Clemson, SC, United States; (2) Department of Physics and Astronomy, Clemson University, Clemson, SC, United States; (3) Clemson Nanomaterials Institute, Clemson University, Clemson, SC, United States

Mixed ionic—electronic conductors (MIECs) are critical for next-generation electrochemical technologies, yet crystalline solids with both properties remain rare. Here, we report a multifunctional metal-organic framework (MOF) built from a trigonal planar hexahydroxy-hexaazatrinaphthalene (HOHATN) ligand and Yb^{3+} nodes. Peripheral catechol groups enable MOF formation via Yb—O coordination, while core bipyridyl-N sites remain available for Li^+ binding and transport. The resulting Yb—HOHATN MOF crystallizes into a highly ordered framework with 1D channels lined with Lewis basic N sites, showing modest electronic conductivity (~10^{-6} S/m) and, after LiOTf infiltration, excellent Li^+ conductivity (7.3 × 10^{-3} S/m). To boost electronic transport, the MOF was grown on multiwalled carbon nanotubes (MWCNTs), producing Yb—HOHATN@CNT composites with much higher electronic conductivity (0.54 S/m). LiOTf-doped Yb—HOHATN@CNT-25% achieved simultaneous electronic (1.1 S/m) and ionic (4.0 × 10^{-4} S/m) conductivities, surpassing device integration thresholds. This heteroaromatic ligand-based strategy offers a new design principle for crystalline dual-conducting materials, positioning MOFs and their CNT composites as candidates for solid-state electrolytes, mixed-conducting electrodes, and ion-transport membranes. As a lithium-ion battery anode, Yb—HOHATN delivered a near-theoretical initial discharge capacity of 315 mAh g^{-1} and retained >100% capacity after 200 cycles at 0.7C. Even under fast charging up to 3C, it maintained stable performance with nearly 100% Coulombic efficiency over 600 cycles. CV and EIS confirmed rapid, reversible Li^+ insertion/extraction and reduced charge-transfer resistance with cycling, underscoring its structural robustness and high-rate capability for next-generation, fast-charging energy storage devices.



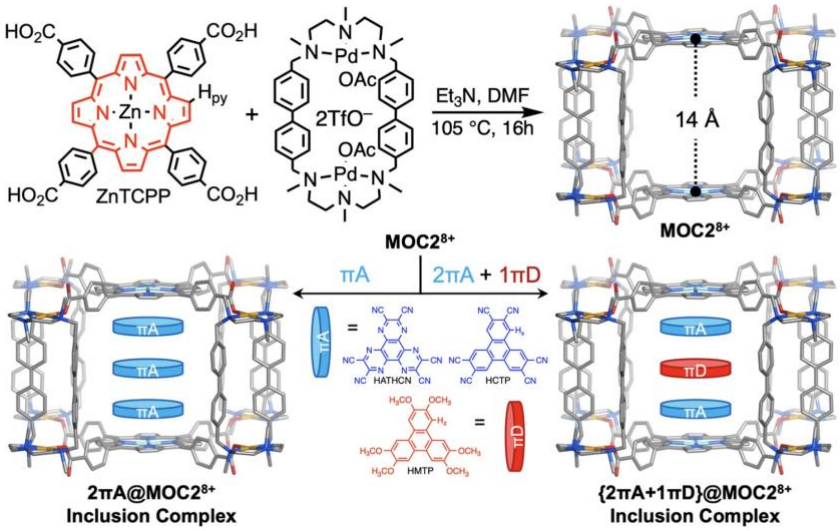
Poster #54

From an insulating Zn-porphyrin metallacage to electrically conducting inclusion complexes featuring extended π-donor/acceptor stacks

Evan Thibodeaux (1), Paola Benavides (1), Ellis Barger (1), Rakesh Sachdeva (1), Sourav Saha (1)

(1) Clemson University Department of Chemistry

π-Donor/Acceptor charge-transfer (CT) interactions between redox-complementary π-systems often give rise to non-native optical and electronic properties that are beneficial for modern electronics and energy technologies. However, the formation of extended supramolecular π-donor/acceptor stacks capable of long-range charge transport requires ingenious design strategies that can help reinforce otherwise weak π-donor/acceptor noncovalent interactions. Herein, we demonstrate that a large tetragonal prismatic metal–organic cage ($MOC2^{8+}$) having two parallel π-donor tetrakis(4-carboxyphenyl)-Zn-porphyrin (ZnTCPP) faces located ~14 Å apart can accommodate up to three redox-complementary planar aromatic guests (either three π-acceptor guests or two π-acceptors surrounding one π-donor guest) between the ZnTCPP faces, forming extended π-donor/acceptor stacks. While empty $MOC2^{8+}$ behaves as an insulator due to the lack of charge delocalization across its large cavity, its inclusion complexes saturated with π-acidic hexaazatriphenylene hexacarbonitrile (HATHCN) and hexacyanotriphenylene (HCTP) displayed noticeably higher electrical conductivity (8.7×10^{-6} and 1.3×10^{-6} S m^{-1}, respectively) owing to more facile charge transport through the π-donor/acceptor stacks composed of the π-acidic guests intercalated between the ZnTCPP faces. Thus, this work demonstrates that tetragonal prismatic metallacages with two parallel electroactive faces can facilitate the creation of extended π-donor/acceptor stacks by encapsulating redox-complementary planar guests, which in turn facilitates through-space charge delocalization, generating non-native electrical conductivity.

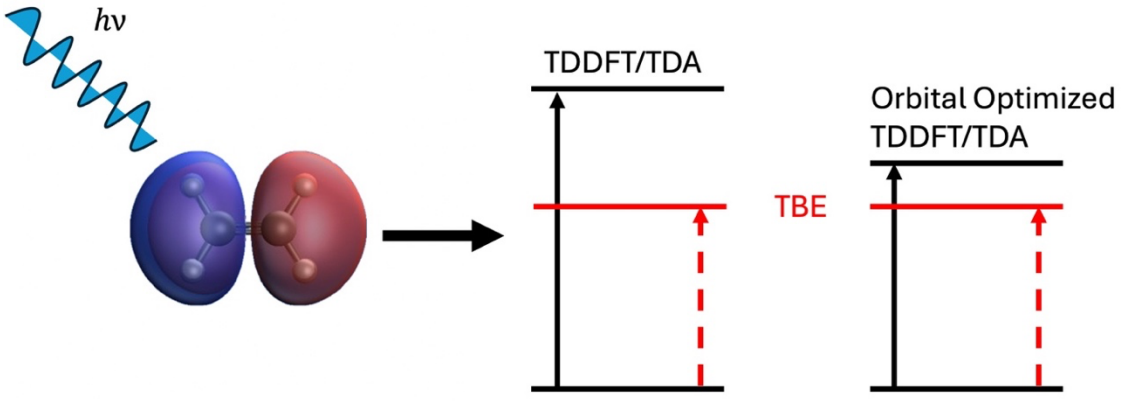


Analyzing Electronic Structure via Orbital Optimization and High-Level Correlation

John Paul Bell (1), J. Cesar Cruz (1), and Justin J. Talbot (1)

(1) Department of Chemistry, Clemson University

The sizeable computational cost of electronic structure calculations with molecular size is a barrier when simulating photochemistry. To make these calculations more tractable, less expensive methods, like density functional theory (DFT), are employed at the cost of energy accuracy. In an effort to improve the accuracy of these calculations, our group has developed an orbital optimization procedure that finds the lowest variational energy for a given electronic excitation. As a rigorous test of the robustness of this approach, 490 vertical excitations were analyzed and compared to theoretical best estimates (TBEs) taken from the QUEST database. Our results show that some functionals are significantly corrected by our minimization procedure. To further investigate the robustness of orbital optimization as a predictor of vertical photocatalytic excitation, it was tested on the complex torsion of ethylene, and the outcome was compared to results obtained using the equation-of-motion coupled-cluster method with double electron-attaching operators (EOM-DEA-CCSD). Unlike DFT, EOM-DEA-CCSD is near exact and provides direct access to restricted doubly excited states, enabling characterization of degenerate (π, π^*) orbitals generated by diradicals. The ability to capture such configurations highlights the importance of high-level correlation methods and has implications for further modification of computational approaches to orbital optimization and electronic structure modeling in conjugated systems.



Utilization of Bis(trifluoromethyl)amine for the Incorporation of –N(CF$_3$)$_2$ Groups into Organic Compounds

Marcia Reeves[1], Erik Csapo[2], Garrett Dean[1], Emma Fortuna[1], Maik Finze[2], Viacheslav A. Petrov[3], Joseph S. Thrasher[1]

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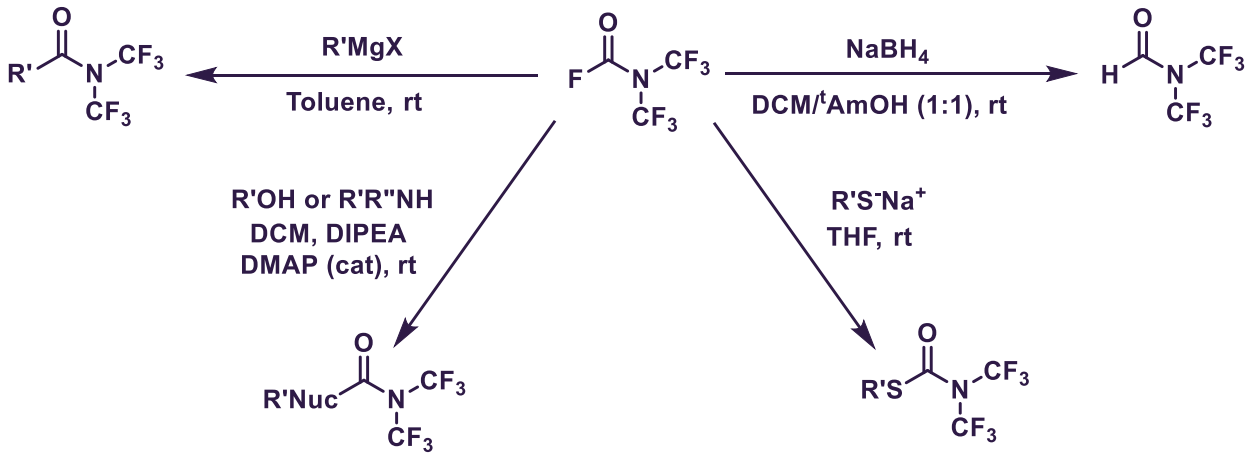
Perfluoroalkyl nitrogen groups have great potential in agrochemical and pharmaceutical research due to the bioactivity of nitrogen-containing groups; however, the chemistry of these groups has not been deeply explored. Recent advances have made some previously inaccessible moieties possible, including examples of *N*–CF$_3$ formamides. Despite this, compounds containing the bis(trifluoromethyl)amino group are exceptionally rare and rely on a stable source of the N(CF$_3$)$_2^-$ anion, such as in the recently reported copper(I) and silver(I) bis(trifluoromethyl)amido complexes. Other less stable anion sources include perfluoroazapropene, which is prone to dimerization into CF$_3$N=CF–N(CF$_3$)$_2$. While bis(trifluoromethyl)amine is known, its use has so far been limited due to its gaseous nature, extreme moisture sensitivity, and its weak basicity/nucleophilicity. This work focuses on exploring the use of bis(trifluoromethyl)amine to install the –N(CF$_3$)$_2$ group, as our group has access to approximately one kilogram (1 kg) of HN(CF$_3$)$_2$ left over from a previous project. Inspired by the recent catalyst-free syntheses of vinyl triflimides, efforts have been made towards hydroamination reactions of HN(CF$_3$)$_2$ with alkynes. Another promising direction includes the use of HN(CF$_3$)$_2$ in the repeated synthesis of bis(trifluoromethyl)carbamoyl fluoride, (CF$_3$)$_2$NC(O)F, which will be further derivatized through nucleophilic acyl substitution reactions to produce amides, carbamates, and ureas, as well as reduction to produce bis(trifluoromethyl)formamide. Additional investigations involve using the dimer, CF$_3$N=CF–N(CF$_3$)$_2$, for interesting chemistry, including reactions with thiocyanates, cyanates, and cyanides.



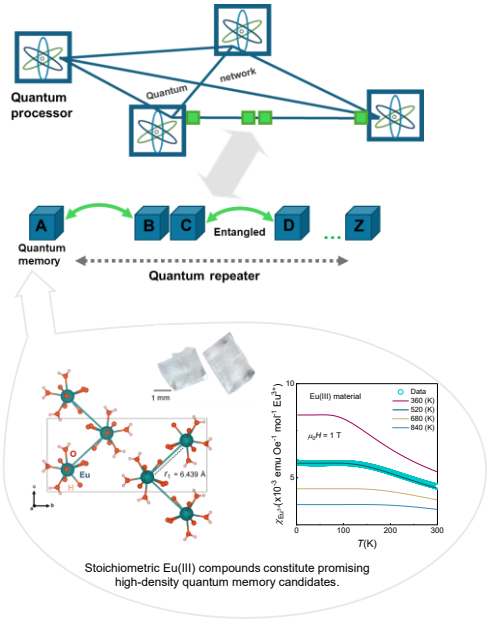
Poster #57

Tuning Emitter–Ion Spacing for Enhanced Coherence and Efficiency in Quantum Memory Candidates

Uchenna Chinaegbomkpa[1], Hugo Sanabria[2], Thao Tran Dominy[1]*

(1) Department of Chemistry, Clemson University, USA.
(2) Department of Physics and Astronomy, Clemson University, USA.

Quantum memories are fast transitioning from proof-of-concept to deployable technologies. As essential components of most quantum repeater protocols, the practical feasibility and achievable transmission rates of such networks depend critically on the coherence times and retrieval efficiencies of the memories. Recent results highlight ensemble-based memories, such as stoichiometric compositions of rare-earth ions, for their high collective efficiency, intrinsic multimode storage capacity, and clear pathways to scalability. Here, we present two Eu(III) materials designed with efforts to improve coherence times by increasing Eu-Eu distance in an extended lattice. The materials show a polar site symmetry for the Eu(III) ion allowing the observation of the $^5D_0 \rightarrow {}^7F_0$ transition needed to store photon states in quantum memories. This talk discusses the synthesis, physical and spectroscopic characterization of the materials and proposed further studies.



Poster #58

Energy Storage and Logic Circuitry in Poly(ionic Liquids)

Sourav Biswas,[a,b] Jack Austin,[a] and Marek W. Urban [a]*
[a] Department of Materials Science and Engineering
[b] Department of Chemistry
Clemson University, Clemson, SC 29634

Abstract:

Precise control over the positions of cation–anion pairs in poly(ionic liquids) (PILs) provides an opportunity for obtaining distinct electrical responses governed by polar and dipolar interactions. Adjusting the relative placement of ions along the side chains and electrical activation enable energy storage with logic circuitry. The ion pairs adopt energetically favorable non-equilibrium states, which are controlled by molecular rearrangements of dipolar aliphatic groups, aiding in simultaneous polarization-depolarization. These orchestrated events reduce local disorders and enhance structural stability, which can be finely tuned by polar and dipolar components, thereby extending the duration of electrical energy storage. Furthermore, by changing the position of the ion pair with respect to the aliphatic components of PILs, it enables the formation of multi-bit logic systems with precise control of the range of output bits, paving the way for multi-bit computing systems. These materials, with controllable ion-bit energy and easy moldability, offer promising applications in parallel computing and energy storage devices.

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Structural Diversification of Diazacyclobutenes and their Antiparasitic Activities

Authors:
Monireh Noori[1], Sabrina Pizarro[2], James C. Morris[2] and Daniel C. Whitehead[1]

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Abstract

Nitrogen-containing heterocycles with diverse ring sizes are key motifs in pharmaceutically active compounds. Our group recently developed a synthetic method that leverages the union of thioalkynes and triazolinediones to access diazacyclobutenes (DCBs) – a stable yet rarely studied class of heterocycles. Remarkably, these diazacyclobutenes have exhibited potent antiparasitic activity against *Trypanosoma brucei* – the causative organism of human sleeping sickness.

In ongoing work, we are expanding the molecular diversity of the DCB scaffold to further explore its antiparasitic potential. We have successfully oxidized the vinyl sulfide moiety of DCBs to the corresponding vinyl sulfone, which undergoes nucleophilic addition with carbon, oxygen, or nitrogen nucleophiles to furnish structurally intriguing 3,4-dihydro-1,2-diazetes.
Additionally, we have developed an efficient two-step strategy for the synthesis of 1,2-diazetidin-3-ones (aza-β-lactam scaffold) from the DCB intermediates. The transformation involves acid-promoted ring scission, followed by base-induced intramolecular nucleophilic cyclization affording the desired aza-β-lactam scaffold in good yields. This method offers straightforward access to a structurally unique and underexplored four-membered heterocycle, expanding the synthetic toolbox for strained nitrogen-containing ring systems that is of both synthetic and biological significance, given the prevalence of β-lactam functionality in many potent drug molecules, such as Penicillins.
This presentation will highlight the synthesis, structural diversification, and antiparasitic activity of DCB derivatives, underscoring their potential as novel therapeutic agents.

Targeting Plant-Like Heme Biosynthesis in *Toxoplasma gondii*: Development of Oxadiazon-Derived PPO Inhibitors as Novel Antiparasitic Agents

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Abstract

Toxoplasmosis is a zoonotic condition caused by an intracellular parasite, Toxoplasma gondii, that falls into the Apicomplexa phylum in toxonomy. This parasite is capable of infecting almost all warm-blooded animals, and studies estimate that up to one-third of the global human population may be chronically infected. Individuals with compromised immune systems are particularly vulnerable to severe, and potentially fatal, outcomes from *T. gondii* infection. Despite its prevalence, treatment options remain limited and often ineffective. This project aims to develop a novel class of potent antiparasitic compounds that specifically target *T. gondii*. We are focusing on molecules that inhibit the enzyme protoporphyrinogen oxidase (PPO), a key player in the parasite's heme biosynthesis pathway, which is essential for its infectivity. Phylogenetic studies reveal that the PPO enzyme in *T. gondii* closely resembles the PPO found in plants. Interestingly, prior research has shown that certain herbicides designed to inhibit plant PPO also display activity against the parasite's PPO. Building on this finding, our research group has been modifying the structure of oxadiazon, a known plant PPO inhibitor. To date, we have synthesized and tested over 40 analogues. Several of these compounds have shown moderate to strong inhibitory effects on *T. gondii*. By further refining the chemical structure—particularly focusing on the 1,3,4-oxadiazolin-5-one ring of the parent oxadiazon molecule—we aim to develop an optimized library of highly potent compounds, potentially leading to a promising drug candidate for treating toxoplasmosis.

Poster #61

Development of Small Molecule Derivatives for Growth Inhibition of the *Bacteroides* Genus

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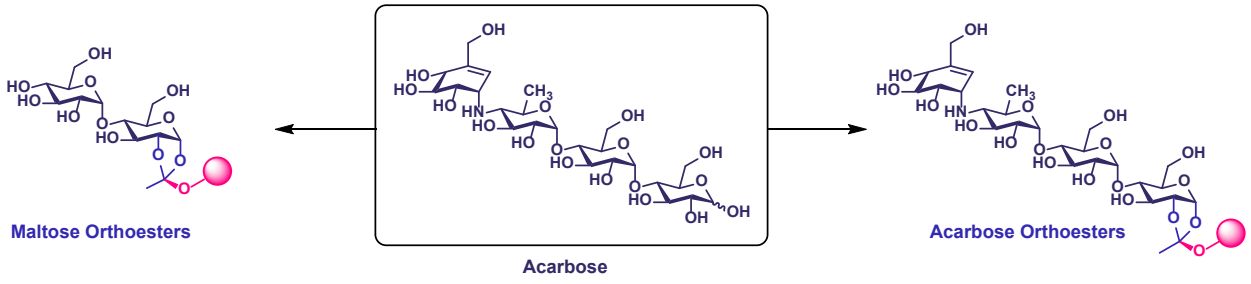
The bacteria of the human gut can greatly influence the health of an individual. Bacteria of the *Bacteroides* genus are prevalent members of the human gut microbiota, and they are often seen as harmless to human health. However, there has been an increase in evidence that overgrowth of *Bacteroides spp*. can cause major illnesses, exacerbate chronic gut-related diseases, and generate autoimmunity that may lead to Type 1 diabetes. A selective method for regulating these bacterial species would be a therapeutic benefit, but the classic strategy of using bactericidal antibiotics can be hindered by the development of antibiotic resistance. We sought out to create a non-microbicidal growth inhibition method to surpass this issue. Previous work shows that acarbose, an α-glucosidase inhibitor, can act as a non-microbicidal small molecule drug for the growth inhibition of *B. thetaiotamicron* and *B. fragilis* in the human gut. However, little is known about the mechanism of action for acarbose in this instance. Recognizing the key interactions between acarbose and these bacterial species is crucial for understanding how this medication can best be utilized to treat illnesses caused by *Bacteroides* overgrowth. Continuing these efforts, we have planned to synthesize several derivatives of acarbose to gain a better understanding of the important interactions taking place. Additionally, a high-throughput screening method has been developed to identify other derivatives of acarbose that may possess antimicrobial activity without orthogonal activity towards human enzymes as well. From these results, we will reveal fundamental features of *Bacteroides spp.* metabolism and better understand how acarbose can be used to change the microbiota.



Cycloaddition of azodicarboxylate and thioalkyne to access oxadiazinones

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Nitrogen containing heterocyclic compounds, especially oxadiazinones, have gained interest from chemists due to their diverse applications in material science, pharmaceutics, and natural product chemistry[1]. The existing methods targeted at the synthesis of oxadiazinones involved multiple steps, which renders the process time -intensive and laborious as each step requires purification. We have developed a single step method to access oxadiazinones through Lewis's acid promoted cycloaddition of azodicarboxylate and thioalkyne. Our method displayed a wide substrate scope as well as broad functional group tolerance.

References

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Poster #63

Process Optimization and Cost Reduction for Cellulose Nanocrystals for Metal Removal from Rendered Fat

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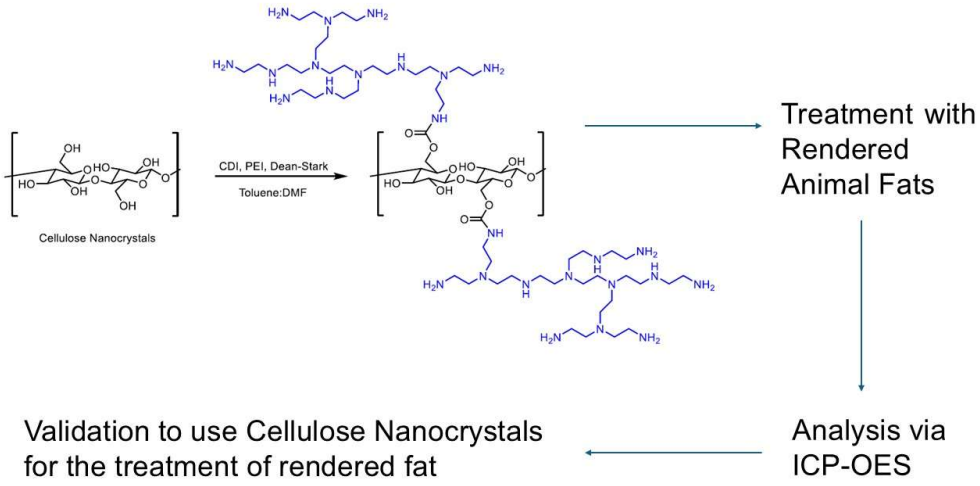
Cellulose nanocrystals (CNCs) coupled with polymers featuring a high density of amine functional groups, such as polyethylenimine (PEI), exhibit significant metal-capturing capabilities. Rendered animal fat has applications in a vast number of industries, with the potential to be used as a feedstock for the biodiesel/renewable diesel industries. Nevertheless, rendered fat samples occasionally contain concentrations of metals/inorganic contaminants above the suitable threshold for use in this application. Thus, a cost-effective solution to remove light metal/inorganic contaminants from rendered fat samples is desirable. To address this problem, a cellulose nanocrystal coupled with polyethylenimine, *i.e.*, CNC-*f*-PEI, was developed by previous members of the Whitehead lab to aid in the removal of metals/inorganics from rendered fat. This method was effective in removing approximately 95% of metals from the rendered fat; however, it proved too costly to use at an industrial scale due to the high costs of the required reagents and purification steps for the first-generation synthesis of the material. This issue was addressed by replacing the costly reagents with a cheaper coupling agent to graft the polyamine onto the cellulose nanocrystals. Further, we decided to forgo the costly dialysis purification step. The second generation material worked well for the removal of metal contaminants from rendered fat samples, with the exception of sodium cations, which contaminated the CNC-*f*-PEI material, owing to the elimination of the dialysis purification. We resolved this issue by developing a method to remove sodium and sulfur contamination from the raw CNCs prior to PEI grafting using CDI. This work allows for significantly more cost-effective second generation synthesis of CNC-*f*-PEI, which is more amenable to scale-up. Importantly, CNC-*f*-PEI material prepared using this technique retains its strong performance in the removal of metal contaminants from rendered animal fat, achieving approximately 96% removal of target contaminants.



Oxadiazon Derivatives – A Scaffold to Fight *Toxoplasma gondii* by Targeting Its Heme Biosynthesis Pathway

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Toxoplasma gondii is an intracellular human protozoan pathogen that causes the infectious disease toxoplasmosis. Approximately one-third of the human population is affected by this parasite. *Toxoplasma gondii* infections are generally asymptomatic, leading to them often being overlooked and untreated. However, if an immunocompromised individual is infected, the parasite can cause severe, life-threatening complications. Currently, there are no effective treatments for chronic infection. In a phylogenetic analysis, we previously found that plant protoporphyrinogen oxidase (PPO) is closely related to Toxoplasma PPO. Moreover, we observed that herbicidal PPO inhibitors, such as oxadiazon and oxadiargyl derivatives, are effective at suppressing parasite growth by disrupting the heme biosynthesis pathway. Based on this understanding, we synthesized a small-molecule library featuring oxadiazon and oxadiargyl derivatives to explore their structure-activity relationships (SAR). We found that several compounds showed potent inhibition against *T. gondii* PPO with better IC50 values. To further extend the SAR study, we developed a new synthetic method to systematically assess oxadiazon derivatives across a broader range of chemical modifications. Continued structural investigations will deepen our understanding of PPO inhibition, enabling the development of more effective and selective drugs for the treatment of toxoplasmosis.

Keywords: *Toxoplasma gondii* PPO, Heme biosynthesis, Oxadiazon, Toxoplasmosis.

Synthesis of nitrogen-containing heterocycles from α-iminothioimidate

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Nitrogen-containing heterocycles are commonly found in nature, appearing in plant alkaloids and amino acid derivatives. Modifications of these heterocycles have led to partially hydrogenated derivatives, which retain the fused pyrrole framework while introducing greater three-dimensional character. These modified heterocycles have emerged as important backbones in drug development with broad medical applications. Recently, our group developed a method for accessing tetrahydroindoles and their derivatives via a formal [2+2] cycloaddition between electron-rich thioalkynes and nitrogenous electrophiles, such as azodicarboxylates. Despite the available approaches for accessing these important heterocycles, there is a need for more efficient, cost-effective methods for the synthesis of nitrogen-containing heterocycles with therapeutic importance. To address these challenges, this research investigates the synthesis of substituted indoles and chiral imidazolinones with unique biological properties. In this study, we describe a one-pot synthesis of chiral imidazolinones and a preliminary study on substituted indoles.

Molecular Modelling of Some Synthesized Nitrogen-Containing Heterocyclic Scaffolds

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Nitrogen-containing compounds have gained significant importance in pharmaceutics due to their intriguing structural features. Despite the advances made in this area, targeting the synthesis of substituted diazacyclobutene (DCB) derivatives remains limited and remains a concern. Our group has successfully developed efficient strategies to access dicarbamoyl 2-iminothioimidate derivatives *via* cycloaddition followed by ring-opening of diazacyclobutenes, yielding α-iminothioimidate. This innovation not only provides easy access to the motifs but also highlights the significant antiparasitic activities against *Trypanosoma brucei*. In this study, we describe Molecular docking simulations of some synthesized scaffolds against *Trypanosoma brucei* using the α-iminothioimidate. Results revealed that most of the synthesized moieties have good binding affinities. In addition to understanding the mechanism of the synthesized compounds, DFT calculations were performed using the transition-state method at the WB97XD/def2svp level of theory. Results revealed that the reaction followed a stepwise mechanism, starting with the activation of the carbonyl group of the α-iminothioimidate *via* a proton transfer