THE UNIVERSITY OF TENNESSEE KNOXVILLE

DEPARTMENT OF CHEMISTRY

2023-2024 Seminar Abstracts

Department of Chemistry
University of Tennessee, Knoxville
1420 Circle Dr

The Department of Chemistry at the University of Tennessee, Knoxville is the oldest PhD granting department at the flagship educational institution in Tennessee. Faculty members in our department represent the traditional subdisciplines of chemistry and engage in interdisciplinary research in polymer chemistry, materials chemistry, chemical physics, bio-organic chemistry, and neutron science. We have strong collaborative ties across departments at UT and with nearby Oak Ridge National Laboratory.

In academic year 2023-2024 we are pleased to offer 14 seminar options in a variety of research areas, detailed in the following pages. Each faculty member's image in the booklet links to their page on our website, where you can learn more about their research, publications, and achievements.

To schedule a seminar please select 2-3 talks of interest and contact Jennifer Brown (jbrow209@utk.edu) to arrange scheduling. Seminars are available for both Fall 2023 and Spring 2024.

Analytical Chemistry
Ziling Xue
Thanh Do

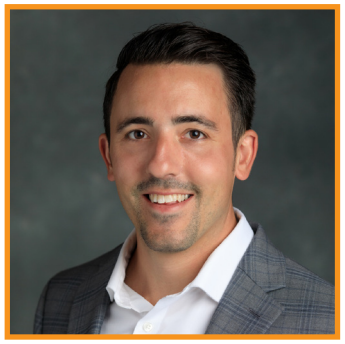
Computational & Theoretical Chemistry
Sharani Roy
Konstantinos Vogiatzis

Inorganic Chemistry
David Jenkins
Viktor Nemykin

Organic Chemistry
Joshua Baccile
Michael Best
Johnathan Brantley
Shawn Campagna

Physical Chemistry
Fred Heberle

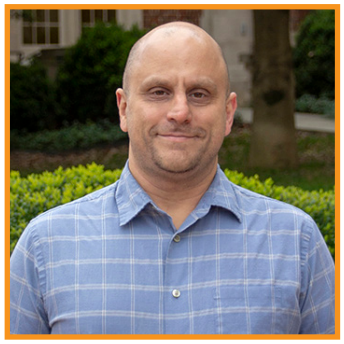
Polymer Chemistry
Mark Dadmun
Brian Long
Bin Zhao



Joshua Baccile, Organic Chemistry

Elucidating the Role of Five Carbon Metabolism in Disease

Isoprenoids are structurally diverse metabolites with an array of critical bioactivities which include cell membrane integrity (e.g., cholesterol), glycoprotein synthesis (e.g., the dolichols), steroid hormone signaling (e.g., androgens, estrogens, and cortisol), and mitochondrial health (e.g., coenzyme Q). Human isoprenoids derive from the mevalonic acid (MVA) pathway, whereas many plants and bacteria utilize the methyl erythritol phosphate MEP pathway. Both MVA and MEP pathways converge on the same two structurally related five-carbon precursors, isopentenyl pyrophosphate (IPP) and dimethylallyl pyrophosphate (DMAPP), which are chain extended to form higher order isoprenoids. Therefore, IPP and DMAPP are the central five-carbon precursors for all isoprenoids in all organisms. Beyond their role as precursors, IPP and DMAPP also directly modify other small molecules (ATP) and macromolecules (37A tRNA) in a process known as prenylation. Levels of IPP and DMAPP are directly involved in cardiovascular disease and have recently been implicated in cancer, cystic fibrosis, and nonalcoholic fatty liver disease. Despite this importance to human health, the mechanisms responsible for both the clinical effects observed by modulating the intracellular concentration of IPP and DMAPP and the distinct bioactivity of IPP and DMAPP are relatively poorly understood. This talk will be focused on our efforts to bridge this critical scientific gap through the development of a suite of IPP and DMAPP based chemical probes and methods for the metabolic labeling of isoprenoids and prenylated molecules. I will discuss our synthetic approach for access to a wide variety of IPP and DMAPP analogs. Currently, we are leveraging these compounds to do metabolic labeling studies, and to study the independent biochemical activity of IPP and DMAPP. Lastly, I will discuss the future of metabolic labeling in the prenylome, which is to develop methods to label isoprenoids and prenylated molecules in a cell-specific manner.



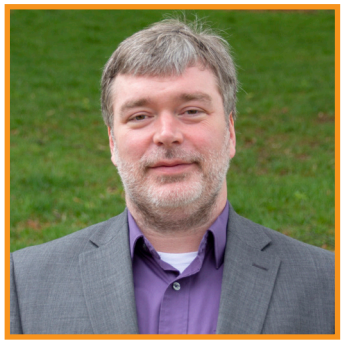
Michael Best, Organic Chemistry

Lipid Switches and Probes for Liposomal Cell Delivery and Related Biomedical Applications

Liposomal nanocarriers are effective for the encapsulation and delivery of a wide range of therapeutic cargo in a manner that improves drug pharmacokinetic properties. However, liposome therapeutic properties could be advanced by enhancing control over cell delivery as well as cargo release. This presentation will describe the development of stimuli-responsive liposomes designed to achieve both of these goals. One approach employs synthetic lipid switches engineered to modulate lipid membrane properties upon contact with disease-associated conditions, such as through programmed chemical reactions and/or conformational changes. In particular, we will focus on encapsulated cargo release triggered by the binding of chemical agents/ molecules that are commonly upregulated in diseased cells. A second strategy involves chemically triggering of cell entry. In this design, liposomes are masked as neutral carriers until they encounter stimuli that generate cationic lipids, thereby activating cell entry. The presentation will include the design and synthesis of
stimuli-responsive lipid switches, analysis of selectivity of cargo release in the presence of different stimuli, investigation of changes to liposome membrane properties, and evaluation of cellular delivery properties triggered by disease-associated stimuli.

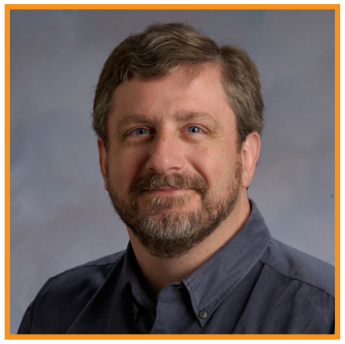
Johnathan Brantley, Organic Chemistry
Exploring New Platforms and Methods for Soft Polymer Editing

The exploration of unique architectural elements is critical for advancing our fundamental understanding of polymer structure-property relationships and accessing next-generation materials. As such, expanding the range of functional groups that can be incorporated within polymers is paramount for developing advanced soft materials. The precise installation of reactive motifs, in particular, could be leveraged to access tunable (or otherwise functional) polymers with bespoke properties. Here, we will explore a variety of novel materials that are decorated with underutilized functional groups in materials science. For example, cumulenes are valuable synthetic handles that are largely absent from macromolecular architectures. Metallocarbenes, which participate in numerous chemical transformations, are also underexplored functional groups in polymer chemistry. We found that both motifs could be incorporated into polymers with good fidelity, and the resultant materials exhibited various stimulus-responsive behaviors (e.g., network formation or CO release). We will also explore how new methodological developments can enable iterative modifications to realize functionalization and/or degradation of various polymers. For example, Suzuki chemistry can be harnessed to decorate polymers with reactive aryl aldehydes (which can undergo an array of subsequent modifications). Conversely, electrochemical editing of polymers (via radical cation pathways) can open new opportunities for polymer degradation and/or functionalization.



Shawn Campagna, Organic Chemistry
How Small Molecules Impact the World

Recent advances in liquid chromatography–mass spectrometry (LC–MS) based metabolomics and lipidomics have furthered understanding of metabolism in a variety of systems. Not only can such techniques be used to discover new molecules and measure select biomarkers for the physiological state of the system, they can also be used to probe global metabolism by providing information on the concentration of thousands of molecules (i.e. the metabolome and lipidome) from a single sample. Despite the power of these techniques, biological and technical challenges hinder the use of metabolomics to interrogate microbial communities sampled from their natural habitat as wells as to relate these results to studies performed in the lab. Herein, our efforts to circumvent these challenges and apply these emerging systems biology techniques to the study of natural microbial communities will be discussed. Using an untargeted metabolomics method employed on an UPLC-Orbitrap Exactive Plus MS, 90-180 known metabolites and ca 1500-5000 spectral features arising from water-soluble molecules with unknown structures can be detected; and an untargeted lipidomics methods using UPLC-Orbitrap Q Exactive Plus MS can be used to detect 400-600 known lipids and ca 1500-5000 spectral features arising from lipid-like molecules with unknown structures. Several vignettes discussing the application of these techniques will be discussed.



Mark Dadmun, Polymer Chemistry

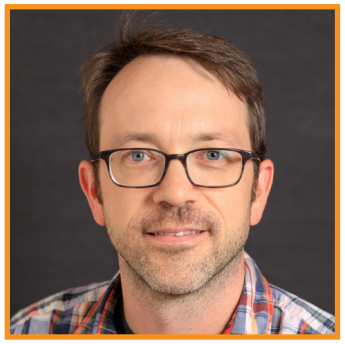
New Polymeric Materials to Expand Opportunities for 3D Printing

3D Printing has emerged as an interesting fabrication technique for models, prototypes, and complex structures. However, producing complex geometries with isotropic, robust mechanical properties by 3D Printing remains a key target in expanding additive manufacturing towards the production of large scale commercially relevant structures. Due to the large size of polymer chains and the complex thermal environment experienced by the printed filament in fused deposition modeling (FDM), entanglement of polymers between layers is incomplete, resulting in weak inter-layer interfaces and unsatisfactory Z-strength. In this presentation, I will discuss work in our group that seeks to address these shortcomings, by developing novel polymer materials for FDM that revolve around the introduction of low molecular weight surface segregating additives to the filament. We have recently expanded this concept to reactive additives, where these reactive additives can now form inter-layer crosslinks by rational introduction of UV photo-initiators and fiber-optic based UV illumination during printing. In situ reactive processing of the printed layers results in drastic increases in the interlayer strength to create essentially isotropic materials.

Thanh Do, Physical/Analytical Chemistry

Taming Conformational Heterogeneity on Ion Race Tracks

About 85% of the human proteome is undruggable by traditional small molecules. The potential drugs must be large and flexible enough to engage large, groove-shaped binding sites, or to bind at the interface between two proteins. Cyclosporines, a class of N-methylated macrocyclic peptides, have challenged the traditional view of structure-based drug design. Although cyclosporine A (CycA) has revolutionized the field of organ transplantation since 1983, attempts to design drugs similar to it for different targets have been unsuccessful, indicating a knowledge gap in the roles of N-methylation and the functions of conformational heterogeneity in cyclosporine chemistry. Cyclosporines are flexible due to N-methylation, and each cis/trans amide isomerization can alter the molecule's conformations and physicochemical properties. CycA can bind to multiple targets (two are known so far) with different bound states, indicating that the bound states depend on the target. Previous studies have shown that the bound states (to known targets) exist as minor conformers in solution. This suggests that cyclosporines may bind to their targets via a reversed induced-fit model, where the ligand alters its conformation to accommodate the binding sites. Therefore, the number of targets that cyclosporines can bind to is likely proportional to the number of possible conformers it can adopt. Thus, to fully understand the biochemical properties of cyclosporines, my lab has worked to accurately probe both major and minor conformers of CycA and CycA analogs, using a wide range of techniques, including both experimental (X-ray/neutron crystallography, ion mobility mass spectrometry, 2D-NMR, ion spectroscopy), and computational approaches. We discovered an intricate conformational network and dynamics modulated by divalent ions.



Fred Heberle, Physical Chemistry

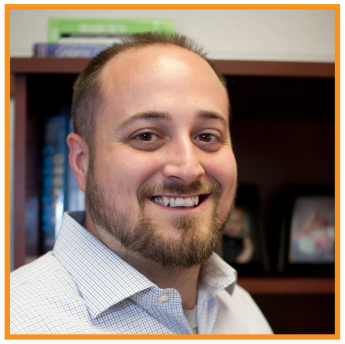
A Raft on Stormy Seas: Using Physical Chemistry to Unlock the Mysteries of Cell Membranes

The cellular plasma membrane (PM) is an enormously complex mixture, containing hundreds of chemically distinct lipids and potentially thousands of unique proteins. It is increasingly clear that the three-dimensional organization of these components has profound functional consequences for the life of a cell. In the outer leaflet of the PM bilayer, sphingolipids and cholesterol are thought to assemble into ordered yet fluid domains, with diverse evidence supporting participation of these “rafts” in membrane processes including protein sorting and signaling. Cells also actively maintain an asymmetric distribution of different lipid types between the inner and outer PM leaflets, resulting in transmembrane differences in fluidity and charge density. Despite intense interest, the fundamental mechanisms controlling raft composition, size and morphology, as well as interleaflet coupling of domains, remain elusive. Much can be learned by studying simplified model membranes, where precise control of composition is possible. Mixtures with as few as three representative lipids can reproduce many salient features of the PM outer leaflet including coexistence of ordered and disordered fluid domains. Organizing this information into phase diagrams reveals a nearly universal propensity for liquid-liquid phase separation in PM-like lipid mixtures, and provides crucial information and constraints for further investigation of transverse and lateral membrane structure. In this talk, I will describe how an experimental approach grounded in the physical chemistry of mixtures can reveal the organizing principles of complex biomimetic membranes.neo ludus quae ingenium ea patria.

David Jenkins, Inorganic Chemistry

NHCs Ligands Two Ways; For Oxidation Catalysis and AU Nanoparticles

N-heterocyclic carbenes (NHCs) have disrupted organometallic chemistry since their isolation in the 1990s. Their combination of impressive strong s-donor strength plus the ability to tune the sterics near a metal center has led them to replace ligands such as phosphines. Our research group exploits these properties through the synthesis of novel NHCs for two distinct applications. In the first vignette, we focus our efforts to synthesize a library of macrocyclic tetra-NHCs that are shaped like porphyrins for oxidation catalysis. In particular, we are developing the catalytic synthesis of aziridines in a C2 + N1 addition reaction. In the second application, we are harnessing their strong bonds to gold for forming self-assembled monolayers (SAMs). SAMs on gold have myriad potential applications in bio-medicine, but to be effective the organic layer must remain stable under physiological conditions. Most current technology, which is based on thiols, is unsuitable for long term usage, whereas NHC SAMs show excellent stability.



Brian Long, Polymer Chemistry

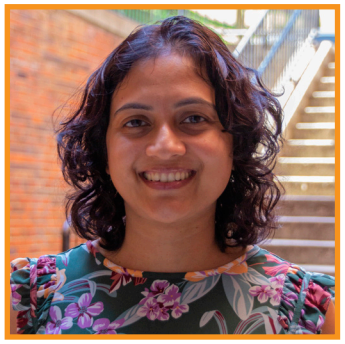
Harnessing the Power of Light and Polymers to Address Fundamental Challenges in Chemistry and Biology

The Long Research Group utilizes the tools of organic synthesis, polymer science, and organometallic chemistry to address interdisciplinary challenges within the fields of macromolecular (polymer) chemistry and catalyst design. Our research projects are often fundamental in nature, but aim to tackle research problems and topics with real-world implications extending well-beyond the academic laboratory. Over the past several years, our research group has led advancements in olefin polymerization catalyst design, ring-opening polymerization catalysis, and tailored gas separation membranes. While these research areas have been fruitful, both in terms of research progress and student training, we have recently welcomed several new research projects into our expanding research portfolio. These new projects aim to address current challenges within the field of polymerization catalysis and deepen our fundamental understanding of biological systems. More specifically, this talk will highlight our efforts to: a) harness the power of light and develop a new polymerization methodology, termed photoinduced olefin polymerization (PIOP), that may enable the 3D printing of polyolefins, and b) harness the unique properties of amphiphilic copolymers to efficiently and selectively extract integral membrane proteins from various biological systems in an effort to advance our understanding of protein structure and function.

Viktor Nemykin, Inorganic

Creating New Electron-Deficient Types of Functional Dyes that are Potentially Useful as Electron Acceptors in Solar Cells

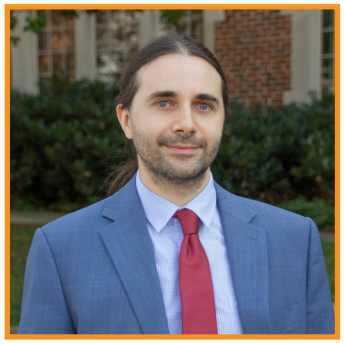
We have developed synthetic protocols for the preparation of several classes of electron-deficient functional dyes that have a first reduction potential close to the traditional fullerenes. These include (i) functionalization of BODIPY core at meso-position; (ii) creation and functionalization of BOPHY platform; (iii) selective synthesis of 2-pyridone-BODIPYs; (iv) creation of electron- deficient “Manitoba Dipyrromethene” (MB-DIPY) chromophores and (v) discovery of hybrid β-isoindigo-aza-DIPY systems.



Sharani Roy, Computational Chemistry

Bridging the Pressure Gap in Theoretical Models of Gas-Solid Adsorption

Akin to the pressure gap between laboratory surface-science experiments performed under ultrahigh vacuum and industrial surface chemistry conducted under high gas pressures, theoretical models of gas-solid interfacial chemistry are often developed for low gas concentrations yet applied to surface phenomena that occur under high gas concentrations. The primary reason for this discrepancy is the steep cost of computing chemical properties at high surface concentrations (or coverages) of the gas using electronic structure methods. To address this challenge and to study the percolation of gases just beneath the surface, i.e., into the subsurface, at high coverages, we have developed lattice-gas adsorption models that include surface as well as subsurface sites in a crystalline solid and are fully parameterized using density functional theory (DFT). We have applied the models to study the adsorption of atomic oxygen on the Ag(111) surface, first as functions of coverage and temperature using canonical Monte Carlo simulations, and next as functions of pressure and temperature using grand-canonical Monte Carlo simulations. The simulations show the conditions under which subsurface adsorption occurs and provide insight into how subsurface adsorbates might participate in catalytic partial oxidation on silver surfaces. The probable adsorption geometries predicted by Monte Carlo are further investigated by DFT to understand their electronic properties, such as the projected density of states, core- electron binding energies, and subsurface-to-surface diffusion pathways. Overall, the lattice-gas adsorption model provides a simple and transferable theoretical framework to explore the competition between surface and subsurface adsorption in gas-surface systems.



Konstantinos Vogiatzis, Computational/ Theoretical Chemistry

From Artificial Intelligence to Chemistry: Challenges and Applications

The field of chemical sciences has undergone a significant transformation in recent years with the emergence and proliferation of artificial intelligence (AI) technologies. The application of AI has brought sweeping changes across multiple chemical domains, including drug discovery, material design, and robotics for chemical applications. Critical elements of AI include the development of effective molecular representations and chemical descriptors, the systematic collection of precise and standardized data, and the optimization of models for enhanced performance. These technological advancements hold the potential to revolutionize the chemical sciences and drive progress in the development of novel materials and therapeutic agents.

In my talk, I will cover key aspects of AI and modern chemoinformatics including molecular representations and chemical descriptors, virtual screening of databases for molecular and material discovery, and machine learning for computational chemistry. Representative examples from the research activities of our group will be discussed, such us the automated search of molecules with strong CO2 binding, exploration of polymer properties, and the design of new molecular catalysts.

Ziling Xue, Analytical Chemistry

Probing Single-Molecule Magnets and Qubit Candidates for Quantum Information

Metal compounds with unpaired electrons are of intense current interest as candidates for quantum information technologies. These inorganic compounds include single-molecule magnets (SMMs), qubits (quantum bits), and Haldane topological materials. Challenges in probing magnetism of the compounds include: (1) Determination of magnetic excited levels; (2) Understanding magnetic relaxations of the compounds through spin-vibration (also known as spin-phonon) couplings. There are few techniques to directly measure large magnetic separations (>30 cm-1) between ground and excited states. We have recently used advanced spectroscopies [e.g., far-IR and Raman magneto-spectroscopies, high-field electron paramagnetic resonance (HFEPR), and inelastic neutron scattering (INS)] to determine magnetic excited levels. The spectroscopies also reveal rarely observed spin-phonon couplings. Recent studies and their potential applications as quantum materials will be discussed.

Bin Zhao, Polymer Chemistry

Macromolecular Brush Materials: From Science to Application

Macromolecular brush materials are composed of polymer chains densely grafted by one end on a solid substrate, commonly called polymer brushes, or on a polymer backbone, descriptively named molecular bottlebrushes (MBBs). Characterized by the stretched, deformed conformations of end-tethered polymer chains, these brush materials have found applications in numerous areas, including surface-responsive materials, antifouling, lubrication, drug delivery, and advanced nanocomposites. In this talk, I will first introduce the basic chemistry for the synthesis of surface brushes and bottlebrush polymers and then present three types of brush materials from our research: (a) multivalent hairy nanoparticles (NPs), (b) oil-soluble brush NP lubricants, and (c) stimuli-responsive shape-changing MBBs. By growing two distinct polymers from the surface of 20 nm NPs, we show for the first time the fabrication of multivalent brush NPs with a small but defined number of nanodomains from microphase separation of mixed brushes, which opens up a new avenue for the metamaterial fabrication. While inorganic NPs are potentially effective oil lubricant additives for friction and wear reduction, further development is hindered by their poor stability in hydrophobic oils. By synthesizing oil-soluble polymer brushes from metal oxide NPs, we demonstrate that such brush NPs exhibit superior stability in polyalphaolefin oil and significant reductions in friction and wear are achieved. In the third work, well-defined stimuli-responsive multicomponent MBBs are synthesized by “click” reactions. These brush molecules can undergo reversible shape transitions between wormlike/starlike and collapsed yet stable globular conformations in response to external stimuli.

For More Information

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