51ST ANNUAL

Naff

SYMPOSIUM

Poster Abstracts

Forces, Flashes, and Pores:

Single-Molecule Windows into Biochemistry

April 2, 2026

College of Arts and Sciences
Department of Chemistry

Author Index

Poster #	Name	Poster #	Name
1	**Odianosen Ewah** University of Kentucky	15	**Shuvo Deb Nath** University of Kentucky
2	**Geethanjali Ekanayake** University of Kentucky	16	**Emmanuel Adejumo** University of Kentucky
3	**Nikhil Kumar** University of Louisville	17	**Virangi Hewage** University of Kentucky
4	**Claire Ray** University of Kentucky	18	**Lutfun Nahar** University of Kentucky
5	**Jessica Bone** University of Kentucky	19	**Sara Palacio** University of Kentucky
6	**Josiane Tessmann** University of Kentucky	20	**Scout Grimes** University of Kentucky
7	**Endras Fadhilah** University of Kentucky	21	**Tiffany Odita** University of Kentucky
8	**Sahar Bayat** University of Kentucky	22	**Adeyemi Abiodun** University of Kentucky
9	**Chibuike Chukwu** University of Kentucky	23	**Sara Brewer** University of Kentucky
10	**Rabia Tahir** Kent State University	24	**Ravichandra Davargaon** University of Kentucky
11	**Erika Elias Ferreira** University of Kentucky	25	**Kayla Daugherty** University of Kentucky
12	**Qianye Yin** University of Kentucky	26	**Ugochukwu Odagwe** University of Kentucky
13	**Hasanul Kabir Rafi** University of Kentucky	27	**Janan Alfehaid** Kent State University
14	**Megan Brown** University of Kentucky		

College of Arts and Sciences
Department of Chemistry

1

Development of Deep Eutectic Solvent (DES)-Resistant Polymeric Membrane Technology for Sustainable Lignin Recovery in Paper and Bioethanol Industries

Odianosen Ewah, Chemical Engineering, University of Kentucky
Advisor: Dr. Isabel Escobar, University of Kentucky

Deep Eutectic Solvents (DESs) have emerged as green alternatives to conventional chemical methods, offering advantages such as low toxicity, biodegradability, and energy-efficient processing. However, the successful implementation of DES-based technologies requires robust separation methods for recovering these solvents after use. This challenge is compounded by the solvent's potential to degrade many polymeric materials, necessitating the development of solvent-resistant membranes. As shown in Figure 1, our research employs a comprehensive approach to developing DES-resistant membranes, beginning with theoretical polymer screening using Relative Energy Difference (RED) calculations, followed by experimental validation to ensure solvent resistance. Polyvinylidene Fluoride (PVDF) membranes, selected through this screening process, were subjected to adsorption experiments to evaluate DES-membrane interactions. The adsorption kinetics were modeled using pseudo-firs t-order and pseudo-second-order equations, while isotherm behavior was analyzed through Langmuir and Freundlich models to elucidate equilibrium dynamics. Preliminary findings underscore the importance of polymer compatibility with DESs in preserving membrane integrity and performance. The adsorption studies aim to identify optimal membrane conditions for efficient DES recovery without compromising membrane durability. This research contributes to the broader effort of reducing CO_2 emissions by advancing DES-based technologies for sustainable industrial processes.

College of Arts and Sciences
Department of Chemistry

2

Invivo Reactivity and Extraction of Gadolinium Based Contrast Agents from Urine

Geethanjali Ekanayake, Chemistry, University of Kentucky
Advisor: Dr. David Atwood, University of Kentucky

Since 1988, Gadolinium Based Contrast Agents (GBCA) are the MRI scanning agents to contrast the body tissues. Gd3+ is highly toxic, to mitigate the toxicity of the elemental gadolinium most GBCA comprised of carboxyamino chelated compounds. Possible reactivity and stability of the GBCAs are tested which are present in human blood plasma and urine. Biomolecules like amino acids, metal ions such as Ca2+,Fe3+,Cu2+ and Zn2+ have possible reactivity with Gd3+ compounds. Preferrable candidate is the oxalates ranges from 1-5 μM in blood plasma tends to react with the GBCAs due to the high affinity of lanthanides to bind with the oxalates. Since Gadolinium affinity towards oxalates forms the nanoparticles inside the human body and get accumulated in the brain tissues, cause long term health implications. Gadabutrol (Gadavist), (Dotarem), (Eovist) and (Elucirem) are the most common GBCAs are in use at UK Healthcare. In this study the GBCAs react with the oxalic acid observed the formation of gadolinium oxalate in real time. By varying the molar concentrations of the GBCA and the oxalic acid the precipitation Kobserv/precipitate was calculated. In this study, the characterization of Gadolinium oxalate formation by reacting Oxalic acid with GBCA was confirmed through characterization techniques like IR and TGA. Future directions of the project refer to characterization techniques like XPS, TEM and SEM, compared with the original Gd2(C2O4)3.

College of Arts and Sciences
Department of Chemistry

3

Thermodynamic Profiling of the Plasma Proteome for Early Multicancer Detection Using Microscale Differential Scanning Calorimetry

Nikhil Kumar, Oncology and Hematology, University of Louisville
Advisor: Dr. Nichola Garbett, University of Louisville

Early-stage cancer detection remains limited by diagnostic approaches that are invasive, costly, and insensitive to subtle biochemical changes preceding clinical symptoms. Cancer induces systemic perturbations in the plasma proteome, altering protein composition, stability, and intermolecular interactions. Differential Scanning Calorimetry (DSC) enables label-free probing of these effects, as plasma thermograms reflect the collective denaturation behavior of abundant proteins such as albumin and immunoglobulins, encoding disease-specific signatures.

To enable clinical translation of proteome thermodynamic profiling, we present the development of a miniature, sensor-driven micro-DSC platform. We fabricated and evaluated two sensor geometries: a radial “spiderweb” design and a rectangular trace configuration, and characterized their resistance–temperature responses under controlled thermal ramps. Sensor stability was found to depend on heat distribution symmetry, material properties, and trace topology.

The rectangular design exhibits a predictable monotonic response, eliminating nonlinearities and electrical artifacts observed in the spiderweb architecture, and enabling reliable measurement of proteome-level thermal transitions. These results establish a foundation for portable calorimetric analysis of undiluted plasma and support future integration with machine learning for classification of disease-specific thermograms, advancing early, broad-spectrum cancer detection.

College of Arts and Sciences
Department of Chemistry

4

Development of a Preclinical Rodent Model for Oral Nicotine Pouch Delivery Systems Using Mucoadhesive Polymers

Claire Ray, Chemistry, University of Kentucky
Advisor: Dr. Chris Richards, University of Kentucky

Mucoadhesive nicotine patches (MNPs) were developed to model the sustained buccal nicotine delivery characteristic of oral nicotine pouches (ONPs), an emerging class of nicotine products with poorly understood biological effects. Prototype films were fabricated using solvent casting techniques with biocompatible polymers and systematically evaluated for key performance properties, including peelability, flexibility, swelling behavior, mucoadhesion time, and mucoadhesive strength. Optimized formulations demonstrated strong mechanical integrity, consistent handling properties, and prolonged adhesion to porcine buccal mucosa, with adhesion times reaching up to ~5 hours under simulated oral conditions. Nicotine diffusion studies conducted using synthetic membranes and porcine tissue showed sustained release profiles, with select formulations approaching the delivery kinetics observed in commercial ONPs. These results support the feasibility of MNPs as a controlled p latform for buccal nicotine delivery. Ongoing work will translate these findings into an in vivo mouse model to characterize nicotine pharmacokinetics and evaluate downstream neurobiological effects, including nicotinic acetylcholine receptor upregulation and changes in receptor stoichiometry. In parallel, bioprinted mucosal tissue models will be developed to further assess nicotine permeability and enhance translational relevance.

College of Arts and Sciences
Department of Chemistry

5

Stabilizing Iron for Use as an Electrode Material in Bioresorbable Electronics

Jessica Bone, Chemistry, University of Kentucky
Advisor: Dr. Kenneth Graham, University of Kentucky

Current research is showing tremendous advances in bioelectronic devices, such as for biomonitoring, neurostimulation, prosthetic interfaces, and drug delivery. For many applications, it would be highly beneficial to have bioresorbable devices, that is, devices that can be absorbed and eliminated from the body after the desired lifetime with no harmful side effects. To design this type of device, the metal contact, along with all other parts of the device, must be bioabsorbable. The bulk of work surrounding bioresorbable devices has centered around tungsten, molybdenum, and magnesium for use as the bioresorbable electrode material. Iron has been well studied in nanomedicine as drug carriers, but it has not been adequately evaluated for use as the metal contact in bioresorbable devices. Here, we show that iron can be used as the metal contact for cycling conjugated polymers with a non-aqueous electrolyte in acetonitrile. However, when biologically relevant aqueou s NaCl is used as the electrolyte, iron quickly oxidizes under a positive bias. A technique to control iron's degradation for implantable bioelectronic applications potentially lasting from days to month to years is needed. In this work, we investigate three different approaches to stabilize iron, including application of self-assembled monolayers (SAMs) with various binding groups and ligand tails, vapor deposited interlayers of insoluble molecular organic semiconductors, and electrodeposition of thiophene-based polymers. The effectiveness of each layer to slow irreversible oxidation reactions in biologically relevant aqueous electrolytes is first investigated through passive soaking in aqueous NaCl, where unmodified iron shows signs of degradation within hours. Effectiveness is determined through use of modified iron as the working electrode in a three-electrode electrochemical cell with aqueous NaCl as the electrolyte. Through applying a suite of characterization methods we hig hlight the challenges and potential improvements to these three approaches. Ultimately, this work provides insight into how surface modification and interlayer chemistry impact the stability, work function, and electrochemical performance of iron electrodes in aqueous electrolytes.

College of Arts and Sciences
Department of Chemistry

6

PFOS Promotes Proliferation via TRKB/EGFR–SREBP1 Activation and Lipid Metabolic Reprogramming

Josiane Tessman, Toxicology and Cancer Biology, University of Kentucky
Advisor: Dr. Yekaterina Zaytseva, University of Kentucky

PFOS is an environmental pollutant frequently detected in drinking water. Due to its high bioaccumulation potential, PFOS can accumulate and disrupt intestinal tissue function. Although PFOS exposure has been linked to adverse health outcomes, including increased cancer risk, its effects on intestinal tissues remain poorly understood. We examined the impact of PFOS on intestinal organoids and colorectal cancer (CRC) cells to elucidate the underlying mechanisms and mitigation strategies. Normal intestinal tissues and organoids, APCMin organoids, and CRC cells were used to evaluate PFOS effects. Cell proliferation was assessed using the PrestoBlue assay. RNA sequencing and kinase array analyses were performed to identify signaling pathways involved in PFOS-induced proliferation. Molecular targets were validated by RT-PCR, western blotting, and immunofluorescence, and the role of redox modulation was assessed using the antioxidant N-acetylcysteine (NAC). PFOS promo ted proliferation in APCMin organoids and CRC cells. PFOS-treated cells showed upregulation of lipid metabolism-related genes, including SREBP1, FASN, and HMGCR, along with increased cholesterol and lipid accumulation. PFOS activated SREBP1 through the TRKB/EGFR axis, and NAC attenuated this effect. Collectively, these findings suggest that PFOS enhances cell proliferation by activating TRKB/EGFR-SREBP1 signaling and promoting cholesterol and lipid accumulation, while antioxidant treatment may mitigate PFOS-driven pro-proliferative signaling.

College of Arts and Sciences
Department of Chemistry

7

Liquid-Phase Membrane-Enhanced Peptide Synthesis: A Pathway to Sustainable Therapeutic Production

Endras Fadhilah, Chemical and Materials Engineering, University of Kentucky
Advisor: Dr. Gosia Chwatko, University of Kentucky

Peptide therapeutics have seen rising demand in recent years, driven in part by FDA approval of GLP-1 agonists such as Mounjaro®. This growing need, alongside increasing emphasis on sustainable and green chemistry, has renewed interest in developing improved peptide synthesis methods. One promising approach is membrane-enhanced liquid-phase peptide synthesis (ME-LPPS), first introduced by the Livingston group, which integrates membrane separation to improve efficiency and sustainability. In this study, we optimized a liquid-phase method using propylene carbonate as a green solvent and polyethylene glycol (PEG) as a soluble support to maintain high peptide yield. Pressure-driven filtration experiments evaluated membrane permeability and solvent compatibility. Reaction performance in propylene carbonate was analyzed using HPLC. For Fmoc deprotection, DBU, piperazine, and piperidine were evaluated, while EDC and K-oxyma were investigated for coupling. A 10 kDa reg enerated cellulose membrane retained 94% of PEG, demonstrating effective separation. Optimal coupling conditions (2:1 EDC-HCl/K-oxyma to amino acid) achieved 91.9% conversion in 120 minutes, while 10% piperidine enabled complete Fmoc deprotection within 5 minutes. A model tripeptide (Phe-Ala-Leu) was successfully synthesized with high yield and purity, highlighting the potential of this green, membrane-enhanced approach as a sustainable alternative to traditional solid-phase synthesis.

College of Arts and Sciences
Department of Chemistry

8

Coke Formation on Bimetallic Ni-Cu Catalysts and Implications for Biomass-to-Fuel Conversion: A Joint Theoretical and Experimental Study

Sahar Bayat, Chemistry, University of Kentucky
Advisor: Dr. Chad Risko, University of Kentucky

Catalyst deactivation through coke formation remains a critical challenge in biorefinery processes involving fatty acid decarbonylation/decarboxylation to fuel-like hydrocarbons. Here, we employ density functional theory (DFT) methods combined with machine learning (ML) models to investigate the adsorption of ethylidyne (CCH_3) as a surrogate coke precursor on Ni-Cu bimetallic surfaces. We developed in silico models of fresh and regenerated Ni-Cu catalysts based on the results of surface composition measurements primarily based on X-ray photoelectron spectroscopy (XPS). For these model catalyst surfaces, we determined ethylidyne adsorption energies to establish correlations between the catalyst surface composition and the propensity towards coke formation. Our results indicate that surface Cu enrichment significantly influences thermodynamic driving forces for coke precursor stabilization. We find that site-specific adsorption energy variations correlate with sur face atomic arrangements and electronic properties, revealing how surface composition affects coking susceptibility. This in silico approach combined with experimental data provides a fundamental understanding of how bimetallic composition affects coking resistance, directly informing systematic design of improved Ni-Cu catalysts with enhanced long-term stability for biorefinery applications.

College of Arts and Sciences
Department of Chemistry

9

Application of Zinc Based Frustrated Lewis Pair for the Catalytic Activation of Small Molecules

Chibuike Chukwu, Chemistry, University of Kentucky
Advisor: Dr. Folami Ladipo, University of Kentucky

Frustrated Lewis Pair (FLP) for the Activation of Small molecules such as H2, CO2, N2O, alkenes, amines etc. has received a lot of attention in the last few years since the discovery in the early 2000s. An FLP is simply a system where a sterically hindered base is precluded from forming a dative bond with a Lewis acid. Thus, the lone pair of electrons on the base and the empty orbital on the Lewis acid are both available to activate molecules. In the current work to be presented, a zinc-based FLP system is envisioned for the activation of small molecules such as H2 and CO2. Zinc, a Lewis acid that is cheap, available, and environmentally friendly in combination with an amine-based Lewis base that is also cheap and readily synthesized, makes an interesting FLP system. The zinc-based FLP system is designed for the catalytic activation of H2 and subsequent reduction of CO2.

College of Arts and Sciences
Department of Chemistry

10

Methylene Blue Flips Hierarchical Aggregation Pathways in Tau Protein

Rabia Tahir, Chemistry, Kent State University
Advisor: Dr. Hanbin Mao, Kent State University

Microtubule-associated protein Tau undergoes aberrant self-assembly into amyloid fibrils through a multistep pathway progressing from peptide-peptide interactions to liquid-liquid phase separation, and finally to condensate maturation. Central to this process are two aggregation-prone hexapeptide motifs, PHF6 (VQIVYK) and PHF6* (VQIINK), which nucleate β-structure formation within Tau filaments. Despite their importance, the geometry and sequence dependence of the earliest intermolecular interactions between these motifs remain poorly defined. Here, we combine single-molecule optical tweezers, single-droplet fusion assays, and ensemble turbidity measurements to systematically map homotypic and heterotypic interactions within or between PHF6 and PHF6* across molecular and aggregating regimes. Single-molecule force spectroscopy reveals a clear hierarchy of dimer formation, with parallel homotypic PHF6-PHF6 and PHF6*-PHF6* interactions dominating over heterotypic and antiparallel associations. Introducing methylene blue, a small-molecule modulator of Tau aggregation, enhances dimer formation across all configurations while disproportionately stabilizing heterotypic PHF6/PHF6* interfaces without altering dimer geometry. At the mesoscale, methylene blue does not increase the extent or rate of liquid-liquid phase separation but markedly accelerates condensate aging to a solid-like state, with the strongest effects observed for heterotypic assemblies. Together, these results demonstrate that methylene blue flips the hierarchical aggregation pathway of Tau by reweighting early intermolecular interactions, favoring heterotypic interfaces to transit towards solid-like condensates. These findings establish a mechanistic framework for how small molecules can invert early interaction preferences to reshape downstream phase behavior and suppress fibril formation.

College of Arts and Sciences
Department of Chemistry

11

Utilizing a Combination of Epigenetic and Lipid Metabolism Inhibitors as a Potential Therapeutic Strategy for BRAFi-resistant Colorectal Cancer

Erika Elias Ferreira, Toxicology and Cancer Biology, University of Kentucky
Advisor: Dr. Yekatarina Zaytseva, University of Kentucky
Co-authors: Josiane Webber Tessman, Mariah Geisen, Qiou Wei, Stephanie Rock

BRAF-mutant CRC, mainly driven by the BRAFV600E mutation, is associated with reduced response to chemotherapy. BRAF inhibitors (BRAFi) are FDA-approved and effective; however, resistance typically develops within 4–6 months. BRAFi resistance has been linked to upregulation of fatty acid synthase (FASN), a key enzyme in lipid metabolism. HDACs also drive epigenetic reprogramming, and screening of the APExBIO DiscoveryProbe FDA-approved drug library identified histone deacetylase inhibitors (HDACi) as highly effective in BRAFi-resistant cells. However, HDACi show limited efficacy alone or with chemotherapy in solid tumors, highlighting the need for new combinational strategies. This study evaluates the efficacy of combining HDACi with TVB2640 (FASN inhibitor) in BRAFi-resistant cells and investigates underlying mechanisms. We utilized organoids and cell lines resistant to PLX8394 (a second-generation BRAFi) and encorafenib/cetuximab (an FDA-approved treatment for BRAFV600E CRC). Cell viability was assessed by CellTiter-Glo, and synergy by SynergyFinder (Bliss model). Western blot evaluated acetylation and protein expression. The combination of romidepsin and TVB2640 significantly reduced viability, showed high synergy, and increased caspase-3/7 activity and cleaved caspase-7. Resistant cells showed higher HDAC and FASN expression, supported by clinical data. The combination altered H3K27 and H3K9 acetylation, suggesting epigenetic modulation. In summary, combining FASN and HDAC inhibitors is an effective strategy for BRAFi-resistant CRC, though further studies are needed to clarify the underlying mechanisms.

College of Arts and Sciences
Department of Chemistry

12

Quantitative Single-Molecule Analysis of Ryanodine Receptor 2 Subunit Assembly in Cardiac and Neuronal Tissues

Qianye Yin, Chemistry, University of Kentucky
Advisor: Dr. Chris Richards, University of Kentucky

We developed a method for ex vivo receptor encapsulation and single-molecule imaging techniques from neuronal and cardiac tissues, illustrating the method's broad applicability for measuring membrane receptor assembly. Ryanodine receptor 2 (RyR2) is a tetrameric Ca2+ channel governing intracellular Ca2+ dynamics, critical for muscle contra tion. Employing GFP-RyR2 knock-in mice, we isolated individual receptor proteins in tissue specific nanovesicles and performed subunit counting analyses to yield quantitative assessment of stoichiometric distributions across the different organs. With this method, we explored the potential heterogeneity of brain-derived RyR2 which has been reported to form heteromeric assemblies with other ryanodine receptor isoforms.

College of Arts and Sciences
Department of Chemistry

13

Programmable Force Routing Reveals Hairpin-mediated Modulation of G-quadruplex Conformational Landscapes

Hasanul Kabir Rafi, Chemistry, University of Kentucky
Advisor: Dr. Prakash Shrestha, University of Kentucky

DNA secondary structures such as hairpins (HP) and G-quadruplexes (GQ) regulate key genomic processes, yet their structural and functional crosstalk when coexisting in proximity remains poorly understood. Here, we present a programmable force routing enabled motif-selective single-molecule unfolding assay to allow selective probing of multiple folded structures within the same DNA strand. We incorporate short DNA handles with identical sequences into HP and GQ motifs to enable motif-specific unfolding in alternating force cycles via stochastic rebinding of each handle. Using this platform, we investigate how proximal HP and GQ motifs modulate each other's stability and dynamics. By performing the assay in different ionic conditions that favor different GQ conformations and control experiments, we find that GQ adopts an antiparallel basket-type conformation even under ionic conditions that typically stabilize hybrid forms, revealing that the local structural co ntext imposed by a neighboring hairpin can override bulk ionic preferences. In contrast, the unfolding behavior of HP remains unchanged. These findings reveal that the coexistence of secondary structures can fine-tune DNA G-quadruplex conformational landscapes, with potential implications for gene regulation. More broadly, our approach provides a versatile platform for dissecting structural and functional crosstalk in multi-domain nucleic acids and protein systems at the single-molecule level.

College of Arts and Sciences
Department of Chemistry

14

Electronic and Structural Properties of the Polymer–Electrolyte Interphase in Electrochemically Doped Polymers

Megan Brown, Chemistry, University of Kentucky
Advisor: Dr. Chad Risko, University of Kentucky

Determining the complex interplay of the multitude of physicochemical processes that take place during the electrochemical doping of polymer electrodes provides opportunities to develop a framework for electrolyte and polymer design for (photo)electrochemical energy transformation and storage applications, where fine-tuning interactions at the polymer–electrolyte interphase can enhance charge-carrier and ion transport, the rates of electron transfer and catalytic efficiencies, device stability, and overall device performance. Here, we report on the investigations of the napthalenediimide–bithiophene based copolymer, N2200, using a combination of computational modeling and experimental validation to reveal how changes in polymer and electrolyte chemistry modulate the electronic and structural properties of the semiconducting electrode during electrochemical (de)doping. We find in these systems that there exists an ensemble of polarons, as opposed to single-po laron-like character often reported, whose properties vary with the nature of the local environment. Importantly, these polarons serve as reporters of the nanoscale environments in which they reside. We demonstrate how controlling the polymer and electrolyte chemistry regulates the nature of the charge carriers generated upon electrochemical doping. We couple these findings with simulations of polymer swelling of an amorphous interphase, showing that charge formation has a large impact on polymer swelling and ion penetration.

College of Arts and Sciences
Department of Chemistry

15

Impact of Self-assembled Monolayer Structure on the Stability of Electrochemical Transistors for Bioelectronic Applications

Shuvo Deb Nath, Chemistry, University of Kentucky
Advisors: Dr. Kenneth Graham, University of Kentucky, and Dr. Alexandra Paterson, University of Kentucky

Conjugated polymers, a class of organic mixed ionic–electronic conductors (OMIECs), are widely used as channel materials in organic electrochemical transistors (OECTs). These materials and devices have attracted significant attention for biosensing and bioelectronic applications; however, their stability in biological environments remains a major limitation. Enhancing the operational stability of OMIEC-based devices is therefore critical for their long-term use and commercialization. In this study, we examine different structural themes of thiol-based self-assembled monolayer (SAM) to improve the stability of OECTs by modifying the gold source and drain electrodes. A diverse set of SAMs is selected to systematically evaluate the influence of molecular structure, including aliphatic versus aromatic backbones, hydrophobic versus hydrophilic terminal groups, and fluorinated versus non-fluorinated chemistries. Devices treated with long-chain alkanethiol SAMs, such as decanethiol, exhibited the highest and most reproducible stability. Although benzenethiol-treated electrodes also yielded stable devices, their performance showed greater variability than that of long-chain alkanethiol-treated electrodes. Across both aliphatic and aromatic SAM families, increased hydrophobicity correlated with enhanced device stability. This trend was confirmed by modifying terminal functionalities from nonpolar methyl or hydrogen groups to polar alcohol or carboxylic acid groups, which consistently resulted in reduced stability. Fluorinated aliphatic SAMs produced device stability comparable to that of decanethiol, whereas fluorinated aromatic SAMs did not result in additional benefits. Overall, these results demonstrate that passivating gold electrodes with hydrophobic, long-chain alkanethiol SAMs effectively mitigates metal-induced degradation of OMIECs, thereby improving the stability of OECTs.

College of Arts and Sciences
Department of Chemistry

16

Li^+ Transport in Amorphous MoxSy-based Chalcogels for Lithium-Sulfur Batteries

Emmanuel Adejumo, Chemistry, University of Kentucky
Advisor: Dr. Chad Risko, University of Kentucky

Efficient Li^+ transport in disordered cathode hosts is critical for high-performance lithium-sulfur (Li-S) batteries. Amorphous molybdenum sulfide (a-MoxSy)-based chalcogels are promising candidates, yet the atomistic mechanisms governing ion mobility remain unresolved. Using ab initio molecular dynamics (AIMD) simulations, we investigate Li^+ diffusion across 400-1200 K. The AIMD simulations reveal that the Li^+ ions are highly mobile, whereas Mo and S remain largely immobile due to strong Mo-S bonding. Migration occurs via hopping along channels formed by sulfur-rich layers, with preferential pathways shaped by local atomic environments. Diffusion coefficients range from 10-6 to 10-4 cm2/s as a function of temperature, and the activation energies are approximately 0.2 eV, indicative of facile Li+ transport. These findings reveal how disorder and coordination govern Li^+ migration and highlight a-MoxSy-based chalcogels as tunable, high-rate cathode materia ls for next-generation Li-S batteries.

College of Arts and Sciences
Department of Chemistry

17

Mechanotransduction through LINC Protein Complex

Virangi Hewage, Chemistry, University of Kentucky
Advisor: Dr. Ryan Cheng, University of Kentucky

Mechanical stimuli in a cell are in the form of stress, pressure, tension and compression. Mechanical forces are generated by different sources in both cytoskeleton and nucleoskeleton and propagate in either way. Converting a mechanical stimuli into a biochemical signal is known to be the mechanotransduction which adjust the cellular and extracellular mechanics and cellular functions highly relies on the mechanotransduction. The Linker of Nucleoskeleton to Cytoskeleton (LINC) is a protein complex composed of two protein families, SUN and KASH spanning within the perinuclear space (PNS) of the nuclear membrane. It physically links and propagates mechanical forces from cytoskeleton to nucleoskeleton and vice versa. The structural details of different domains of LINC with its binding is vital to investigate the force propagation for nuclear integrity as well as how the nuclear integrity loss under the structural mutation while causing genetic disorders such as lami nopathies and cancer. Modeling the different domains of LINC complex through artificial intelligence and coevolution of amino acids is essential due to the lack of structural details of different domains of LINC and how each domain binds. We used umbrella sampling to characterize the both folding and pulling landscape to determine the underlying free energy profile and identify the mechanical transition states along the reaction coordinate.

College of Arts and Sciences
Department of Chemistry

18

Depth Profiling of Intra-Gap Defect States in Organic Semiconductors Using Gas Cluster Ion Beam (GCIB) Etching

Lutfun Nahar, Chemistry, University of Kentucky
Advisor: Dr. Kenneth Graham, University of Kentucky

Organic semiconductors (OSCs) are widely used in organic electronic devices, but their performance and stability are limited by defect states that trap charges and cause recombination. These defect states are difficult to detect because of their very low concentrations, typically parts per thousand or less relative to the concentration of states in the HOMO or LUMO band. Conventional defect detection techniques often rely on measurements of full devices, making it challenging to pinpoint the defect location. Variable energy ultraviolet photoemission spectroscopy (VE-UPS) has recently demonstrated as a promising method for probing intra-gap defect states in OSCs. However, the main limitation of VE-UPS is surface sensitivity. To resolve this issue, we couple VE-UPS with gas cluster ion beam (GCIB) etching to investigate the defects through the sample without causing damage to remaining material. Regio-regular Poly (3- hexylthiophene) (rr-P3HT) and Zinc phthalocyanine (ZnPc) were sputtered using Ar1000+ and Ar2000+ clusters at energies of 5 kV followed by XPS and VE-UPS analysis. XPS results confirmed that both materials are chemically stable under GCIB etching. VE-UPS measurements show HOMO broadening, shifts in the ionization energy and work function for rr-P3HT, but minimal formation of new intra-gap defect states while ZnPc exhibits negligible damage.

College of Arts and Sciences
Department of Chemistry

19

Glioblastoma Derived EVs that Contain 4HNE Cause Neurotoxic Inflammation

Sara Palacio, Toxicology and Cancer Biology, University of Kentucky
Advisor: Dr. Luksana Chaiswing

Glioblastoma (GBM) remains an incurable cancer, characterized by severe cognitive impairments. GBM patients exhibit high numbers of extracellular vesicles (EVs) enriched in 4HNE adductions caused by the high ROS levels in GBM, particularly after radiation (RedoxEVs). We hypothesize that GBM-EVs could be key mediators driving therapy-associated neurotoxicity in GBM.

We used radiation to increase 4HNE content. High levels of 4HNE in RedoxEVs were confirmed by western blotting, immunogold labeling and mass spectrometry. We administered NonRedoxEVs and RedoxEVs intranasally. Mice treated with RedoxEVs showed delay in object exploration and increased 4HNE adductions and CD68 expression.

To control the EVs delivery to the brain, we injected RedoxEVs intracranially. These mice exhibited cognitive deficits, DNA damage in cerebral tissue, decreased neuron markers, and elevated p50 and pro-inflammatory cytokines. Mechanistically, RedoxEVs are internalized by microglia, causing pronounced activation and release of cytokines and H_2O_2 as mediators. To assess the downstream neurotoxic effect of H_2O_2, RedoxEVs were added to a microglia-neuron co-culture. Neuron viability was reduced when exposed to microglia activated by RedoxEVs. Additionally, mice with RedoxEVs-derived cognitive deficits demonstrated elevated pro-inflammatory cytokines and CD68. Consistently, proteomics analysis revealed RedoxEVs' enrichment in NFkB pathway activators. Overall, RedoxEVs induce microglia-mediated neurotoxicity and cognitive alterations.

College of Arts and Sciences
Department of Chemistry

20

Neuron-specific LRP1 Knockout Mice Exhibit Resistance to Mitochondrial Dysfunction Following Traumatic Brain Injury

Scout Grimes, Chemistry, University of Kentucky
Advisors: Dr. Samuel Awuah, University of Kentucky, and Dr. Patrick Sullivan, University of Kentucky

Traumatic brain injury (TBI) often leads to persistent cognitive impairment, with mitochondrial dysfunction and excess reactive oxygen species (ROS) playing key roles in its pathology. We previously found that loss of Low-Density Lipoprotein Receptor-Related Protein 1 (LRP1) increases resistance to oxidative stress. Building on these findings, we tested whether neuron-specific LRP1 deletion protects against TBI using neuron-specific LRP1 knockout (NLKO) mice in a controlled cortical impact model.

NLKO mice showed preserved mitochondrial function 24 hours post-injury, as measured by oxygen consumption rates, compared to controls. Mitochondrial complex I expression decreased after injury in controls but remained stable in NLKO mice, while complex II levels were elevated in NLKO mice. Transcriptomic analysis further revealed reduced expression of mitochondrial respiration genes in injured controls but not in NLKO mice.

Using a mitochondrial reporter line, we observed that NLKO neurons maintained elongated, healthy mitochondrial morphology after injury, whereas control mitochondria were fragmented and reduced in volume.

These findings demonstrate that neuronal LRP1 deletion mitigates TBI-induced mitochondrial dysfunction and preserves mitochondrial integrity, identifying LRP1 as a potential therapeutic target for neuroprotection after brain injury.

College of Arts and Sciences
Department of Chemistry

21

Targeting Heme Degradation Pathway in Metastatic Triple Negative Breast Cancer (mTNBC) using Au(III)Macrocycles

Tiffany Odita, Chemistry, University of Kentucky
Advisor: Dr. Samuel Awuah, University of Kentucky

Triple-negative breast cancer (TNBC) remains one of the most aggressive subtypes of breast cancer, largely due to its high metastatic potential and lack of effective targeted treatments defined by the absence of estrogen receptor (ER), progesterone receptor (PR), and HER2 expression. Metastatic cancer cells are known to reprogram their metabolism to sustain survival and bioenergetic demands. Heme, a ubiquitous and essential cofactor, supports mitochondrial respiration and oxidative signaling, processes frequently exploited during tumor progression, yet the role of heme degradation in this context remains poorly understood.

In this study, we investigated heme oxygenase 2 (HMOX2), a constitutive enzyme responsible for heme breakdown, as a potential metabolic vulnerability in metastatic TNBC. Using Au-Macrocycles, we found that targeting HMOX2 induced cell death at an IC50 of 0.6μM and suppressed long-term proliferative capacity. We also observed decreased mammosphere formation, suggesting impaired tumorigenic growth under anchorage-independent conditions. Beyond proliferation, Au-Macrocycles significantly attenuated migration and invasion of metastatic TNBC cells and altered EMT-associated protein expression consistent with reduced metastatic capacity. Target engagement was confirmed through cellular thermal shift assays showing thermal destabilization of HMOX2, alongside concentration-dependent protein depletion following treatment.

Hence, our results identify HMOX2 driven heme metabolism as an underappreciated contributor to metastatic TNBC and suggest that targeting heme degradation may be a viable strategy for limiting metastatic progression.

College of Arts and Sciences
Department of Chemistry

22

Identification and Development of Small Molecule Probe and Inhibitors Targeting ARID4B in Cancer

Adeyemi Abiodun, Chemistry, University of Kentucky
Advisor: Dr. Samuel Awuah, University of Kentucky

ARID4B is an epigenetic regulator that functions dually as a transcriptional repressor via the SIN3A/HDAC complex and as a transcriptional coactivator. Its overexpression is strongly associated with tumor growth and poor clinical outcomes across multiple cancers, yet its molecular function remains poorly understood. With RWR18 being the only reported molecule with modest antagonistic activity against ARID4B, improved chemical tools are urgently needed.

We employed two complementary strategies: an in-silico small molecule screen against a 3D homology model of ARID4B, and covalent modification of RWR18 via incorporation of a lysine-reactive warhead to improve potency and target residence time.

In-silico screening identified AA-Br (IC50 = 51 μM, MTT assay) with confirmed ARID4B target engagement by CETSA. Covalent modification yielded AA133, which demonstrated markedly superior potency over parent RWR18 in MCF7 colony formation assays, achieving complete inhibition at 50 μM. In contrast, RWR18 compound requires up to 200 μM to achieve comparable inhibitory effects demonstrating an approximately 4-fold improvement in potency. AA133 on-target activity was confirmed by CETSA-mediated ARID4B destabilization.

Collectively, these findings provide two cytotoxic chemical tools with cellular and on-target activity to investigate the oncogenic role of ARID4B and lay the groundwork for future therapeutic development.

College of Arts and Sciences
Department of Chemistry

23

Assessing the Role of Activation of the PI3K/Akt Pathway by the Myokine Apelin During Plasma Membrane Repair

Sara Brewer, Molecular and Cellular Biochemistry, University of Kentucky
Advisor: Dr. Noah Weisleder, University of Kentucky
Co-Author: Kevin E. McElhanon

Plasma membrane repair is a fundamental process in maintaining membrane barrier function. Membrane repair deficiencies are linked to multiple disease states which can lead to muscle weakness, respiratory failure, and heart failure due to myocyte death. If membrane integrity can be increased, the severity of these pathologies could be reduced. Previous studies from our lab elucidated the importance of the PI3K/Akt signaling pathway in membrane repair. We hypothesize that activation of PI3K/Akt in deficient repair models will improve membrane repair. Apelin is a myokine ligand upstream of PI3K/Akt which may be necessary for myogenesis after injury and shows cardioprotective effects. We propose experiments to increase PI3K/Akt signaling with apelin to determine its potential benefit to membrane repair. Mouse myoblasts were treated with apelin, and membrane repair was evaluated by laser injury assay. Initial results showed that in myoblasts with no repair defect, me mbrane repair is not impeded after laser injury disruption. Immunoblot analysis reveals increased PI3K subunit p85 phosphorylation at site Tyr467 in these cells. Future directions include investigating apelin's effect on membrane repair in myoblasts from limb girdle muscular dystrophy patients. Through these experiments, apelin's activation of PI3K/Akt will be examined, evaluating its potential for treatment of muscular disorders.

College of Arts and Sciences
Department of Chemistry

24

Prediabetic Amylin Hypersecretion Impairs Brain Glucose Regulation

Ravichandra Davargaon, Pharmacology and Nutritional Sciences, University of Kentucky
Advisor: Dr. Florin Despa, University of Kentucky

Introduction: Type-2 diabetes-related hyperglycemia increases the risk for cognitive decline. Amylin is a centrally-linked pancreatic hormone that induces satiation. The beneficial metabolic effects of amylin led to regulatory approval of the amylin analog drug, pramlintide, for weight loss. Different research teams (including ours) report amylin co-aggregates with brain parenchymal and vascular β-amyloid in persons with Alzheimer's dementia. Using cancer cells, other teams reported that amylin inhibits glycolysis. The present study sought to determine changes of glucose utilization in brain tissues associated with suppressed vs. oversecreted pancreatic amylin.

Method: Because murine amylin is not amyloidogenic, we generated mice "humanized" for amylin expression (hAON mice). Amylin knock-out mice (hAOFF mice) and mice expressing wild-type mouse amylin (WT mice) served as controls. All mouse groups underwent four-month overnutrition to induce prediabetic amylin hypersecretion (in hAON and WT mice), followed by endpoint novel object recognition and mass spectrometry analyses of brain tissue glucose 6-phosphate (G6P) (the first intermediate of intracellular glucose metabolism) and glycolytic amino acids serine, glycine and alanine. We then assessed the ratios of serine, glycine and alanine to G6P (i.e. the glycolytic amino-acid flux).

Conclusion: Prediabetic amylin hypersecretion increases brain amylin level and exacerbates amylin receptor signaling controlling glycolysis, leading to impairments of glycolytic flux and memory.

College of Arts and Sciences
Department of Chemistry

25

Affinity Separations of Therapeutic Biocolloids with Heparinized Anodized Aluminum Oxide Membranes

Kayla Daugherty, Chemical Engineering, University of Kentucky
Advisor: Dr. Barbara Knutson, University of Kentucky

Affinity membranes are developed by the immobilization of heparin onto anodized aluminum oxide (AAO) supports via amine grafting followed by amide coupling. Optimized procedures give heparinized AAO (HEP-AAO) membranes with a stable layer of 0.899 – 1.43 mg heparin/m2 pore area based on a methylene blue assay. Following the heparinization of the membrane, the bioactivity of heparin is demonstrated through the capture and release of fibroblast growth factor 2 (FGF2), a protein for which heparin acts as a ligand. Capping of unreacted amines using citraconic anhydride is found to reduce nonspecific protein binding without loss of heparin activity. Pore accessibility towards colloidal particles is confirmed through the electrostatically-driven binding and release of 20 nm fluorescent amine-grafted silica nanoparticles. HEP-AAO with 224 nm pores captured 70% of the theoretical surface capacity of nanoparticles from a 0.2 mg/mL feed. Proof of heparinized AAO membr anes ability to function as an affinity membrane for a therapeutic biocolloid is demonstrated through the capture and release of adeno associated virus 2 (AAV-2) via tangential flow filtration. The HEP-AAO membranes captured 80% of AAV-2 present in the culture medium in a single affinity step after depth filtration and ultrafiltration, paving a path toward further optimization and process improvements for viral vector purification.

College of Arts and Sciences
Department of Chemistry

26

Intramolecular 1,2-diamination of Alkenes with Amazing Azimines

Ugochukwu Odagwe, Chemistry, University of Kentucky
Advisor: Dr. Robert Grossman, University of Kentucky

The development of synthetic methodologies for 1,2-diamines has gained substantial scientific interest in recent years. This can be attributed to the emerging and extensive utilities of 1,2-diamine containing molecular scaffolds in various fields such as medicine, catalysis and materials science. 1,2-diamination of alkenes remains an attractive route to these compounds bearing the vicinal diamino functionality. After initial proposal that the then-unknown compounds in 1963 would undergo [3+2] cycloadditions, the chemistry of azimines, a group of 1,3-dipoles with the general formula RN=N+(R)N-(R), has barely been explored. In this work, we show that ω-alkenyl alcohols, carboxylic acids or chloroformates can be easily converted to ω-alkenyl azimines, which spontaneously undergo intramolecular syn [3+2] cycloaddition to install their terminal N atoms across the double bond of the alkene. These cycloadditions lead to the formation of 1,2,3-triazolidine intermediat es which form 1,2-diamines under high-pressure hydrogenation over Raney Ni. Our work is of both intellectual and practical interest: not only does it demonstrate the utility of a neglected class of 1,3-dipoles, the amazing azimines, but it also provides a convenient synthetic pathway to 1,2-diamines.

College of Arts and Sciences
Department of Chemistry

27

Accessibility of Telomeric Overhangs to Stabilizing Small-Molecule Ligands

Janan Alfehaid, Physics, Kent State University
Advisor: Dr. Hamza Balci, Kent State University

Human chromosomes terminate in 50-300 nucleotide (nt) long single-stranded telomeric overhangs composed of repeating d(TTAGGG) sequences, which can fold into tandem G-quadruplex (GQ) structures that protect chromosome ends. Stabilization of GQs by small-molecule ligands inhibits telomerase activity, motivating extensive efforts to develop GQ-targeting anti-cancer therapeutics. However, how interactions between successive GQs and bound ligands influence small-molecule accessibility remains poorly understood. Here, we employ single-molecule fluorescence microscopy and stepwise photobleaching analysis to quantify the binding stoichiometry of a fluorescently-labeled oxazole telomestatin derivative (L1Cy5-7OTD) to telomeric overhangs capable of forming 1-6 GQs (30-162 nt long), spanning much of the physiologically relevant range. We find that longer overhangs accommodate more ligands on average but exhibit consistently lower binding stoichiometry than the theoretical maximum, saturating at six molecules even in constructs with twelve binding sites. This trend was further supported by experiments showing increased L1Cy5-70TD binding when the inter-GQ spacer was extended from 3-nt to 9-nt. This effect was independently confirmed by ensemble fluorescence enhancement experiments utilizing N-methyl mesoporphyrin IX (NMM) as a ligand. Together, these findings demonstrate how telomeric overhang architecture governs ligand accessibility and provide mechanistic insight to guide the rational design of GQ-targeting anticancer agents.

College of Arts and Sciences
Department of Chemistry