Abstracts

Naff Symposium

Poster Session

Don & Cathy Jacobs Science Building, 2nd Floor

April 21, 2023

3:00pm

College of Arts and Sciences

Department of Chemistry

Author Index of Abstracts

SONOCHEMICAL INTERCALATION OF POTASSIUM INTO CARBON ALLOTROPES

Authors

Kathryn Pitton, Chemistry, University of Kentucky
Dr. Beth Guiton, Chemistry, University of Kentucky

Abstract

Graphite intercalation compounds (GICs), most commonly graphite intercalated with alkali metals to produce highly ordered materials, have been well studied as lithium-ion batteries (LIB) components, reducing agents, catalysts, and coupling reagents.1–4 Unfortunately, most intercalation compound syntheses require high heat and pressure for extended periods. It has been reported that ultrasound treatment rapidly produces high-quality KC8 in bulk at ambient temperature and pressure.5 This sonication intercalation method can be expanded to alternative layered carbon allotropes such as nanodiamond-derived carbon nano-onions (NCNOs) and multi-walled carbon nanotubes (MWCNTs), both of which have had varying successes of intercalation and doping of alkali metals and heteroatoms via alternative synthesis routes.6–8 Herein, we report an extension of rapid sonochemical intercalation to NCNOs and MWCNTs under mild conditions. These materials are imaged via transmission electron microscopy (TEM) and scanning transmission electron microscopy (STEM) equipped with energy dispersive X-ray spectroscopy (EDS) and analyzed via powder X-ray diffraction (PXRD) to examine the alkali metal configuration with respect to the discontinuity/defect sites of graphitic shells of NCNOs and MWCNTs.

ELUCIDATING THE ROLE OF ZINC IN SALMON SPERM NUCLEAR DNA PACKAGING

Authors

Md Abu Monsur, Chemistry, University of Kentucky
Dr. Jason DeRouchey, Chemistry, University of Kentucky

Abstract

In sperm chromatin, highly basic, positively charged proteins called protamine are used to condense DNA tightly to a final volume roughly 1/20th that of a somatic nucleus. Zinc is present in high concentrations in the seminal fluid and has been shown to play an important role in many sperm functions including sperm chromatin stability, sperm motility, and capacitation. Here, we aim to systematically investigate the role of zinc, and other divalent cations, on the DNA packaging inside sperm nuclei. Divalent cations, such as Zn, are known to effectively screen electrostatic interactions but typically are not able to induce DNA condensation on their own. Counterions having a net charge of +3 or higher are required to overcome the inherently large repulsion between DNA helices and mediate DNA condensation. Using small-angle X-ray scattering (SAXS), we observe that the addition of low concentrations of zinc to isolated salmon sperm nuclei results in tighter DNA packaging. This enhanced DNA packaging is also observed in salmon sperm nuclei with other divalent cations including transition metals, alkaline earth metals, and alkylamines. Experiments with reconstituted protamine/DNA also show the presence of divalents like zinc enhances in vitro condensation through a cooperative attractive interaction. At higher divalent concentrations, we observe a crossover behavior resulting in lower DNA packaging density at high salt concentrations. Lastly, we use ICP-MS to quantify the naturally occurring concentrations of Zinc and other metals in salmon sperm nuclei. Our measurements indicate the use of both protamine and divalent metals may be essential for optimized stabilization of the DNA in sperm chromatin.

SYNTHESIZING A SINGLE-ATOM CATALYST FOR USE IN CLEAN ENERGY CONVERSION TECHNOLOGIES

Authors

Jenna Rector, Chemistry, University of Kentucky
Dr. Doo Young Kim, Chemistry, University of Kentucky

Abstract

The electrocatalyst is pivotal in determining the cost and efficiency of clean energy conversion technologies. Current noble-metal catalysts have certain limitations preventing them from being implemented on a global scale. First, these catalysts are not cost effective due to low metal utilization. Second, they involve a large wastage of metal due to the oxidation and dissolving of bulk metal during electrolysis. Third, the surface-level attachment of nanoparticles to the carbon support is unstable shown by the removal of the nanoparticle during electrolysis. We propose to combat these limitations by synthesizing a single-atom catalyst using common transition metals to replace noble-metal catalysts. In our experiment, we used bottom-up synthesis and two different heat stabilization techniques to synthesize the single-atom catalyst. Then we analyzed the structure and identity of our catalyst using XRD, STEM, TGA, and Raman spectroscopy. Our analyses confirmed the proposed catalyst structure, and thus we began to test the catalyst in two major electrochemical reactions: oxygen reduction and carbon dioxide reduction. While we are still gathering data, our results show promise of an effective and economically competitive catalyst to be used in a variety of clean energy conversion technologies.

THE 12->7 CIRCTAU RNA ENCODES TWO PROTEINS THAT AFFECT NEUROFIBRILLARY TANGLE FORMATION AND OXIDATIVE PHOSPHORYLATION

Authors

Justin Welden, Molecular and Cellular Biochemistry, University of Kentucky
Dr. Stefan Stamm, Molecular and Cellular Biochemistry, University of Kentucky

Abstract

The human microtubule associated protein tau (MAPT) is central to Alzheimer's disease, as it forms neurofibrillary tangles. MAPT-pre-mRNA generates two circular RNAs (circRNAs) through a backsplicing mechanism. Both circRNAs can be translated into proteins when the circRNA undergoes adenosine to inosine epigenetic RNA editing (PMID:36533443). One of these circRNAs, generated by backsplicing of exon 12 to 7 contains one open reading frame (ORF1) with one start codon that lacks a stop codon. Since the 12->7 tau circRNA contains 681 nt, i.e. exactly 227 amino acids, its translation leads to multimers of the microtubule binding repeat regions R1-R4. The encoded proteins promote neurofibrillary tangle formation in vitro. We found that in addition to this ORF1, the 12->7 circRNA contains another shorter ORF2 of 321nt encoding a protein of 107 amino acids (12kDa). This protein is highly basic with an isoelectric point of 12.30. Using reporter systems, we found that this 'tau new ORF' protein is expressed and localized in the cytosol. Seahorse analysis shows that it reduces oxygen consumption by about 40%. Our data are the first reports that circRNAs can encode more than one protein by using different reading frames and that one of these proteins interferes with mitochondrial functions.

4

FTLD MUTATIONS CONTRIBUTE TO TAUPATHIES VIA TAU CIRCULAR RNAS

Authors

Giorgi Margvelani, Molecular and Cellular Biochemistry, University of Kentucky
Dr. Stefan Stamm, Molecular and Cellular Biochemistry, University of Kentucky

Abstract

Alzheimer's disease is characterized by neurofibrillary tangles (NFT) composed of microtubule associated protein tau (MAPT). The human MAPT gene generates two circular RNAs via back splicing of exon 12 to either exon 10 or exon 7 [Welden et al. 2019]. The circRNAs are translated after undergoing adenosine to inosine RNA editing mediated by ADAR1 and ADAR2 enzymes [Welden et al. 2022] generating multimers of the tau protein. The generated circular tau proteins promote NFT formation in vitro and cause tau aggregation in reporter cells. The NFT formation seen in AD is recapitulated by hereditary FTLD (Frontotemporal lobar degeneration). 47 of the 53 mutations causing FTLD are in the region generating circRNAs. Using cotransfection assays, we tested the mutation's influence on circRNA-protein structure and expression, as well as their interaction with eukaryotic initiation factor 4B. We identified several FTLD mutations that change the size and expression levels of proteins encoded by tau circular RNA and found that these proteins promote the formation of neurofibrillary tangles. In addition, several mutations have reduced binding affinity to eIF4B. Our data indicate that proteins made from MAPT circular RNAs contribute to tauopathies, including AD, by causing tau protein aggregation and possibly interfering with translation

IMPORTANCE OF ASP 124 FOR SUBUNIT A-B INTERACTIONS IN E. COLI ATP SYNTHASE

Authors

Cullen Martin, Chemistry, Berea College
Dr. Rashmi Shrestha, Chemistry, Berea College

Abstract

Adenosine Triphosphate (ATP), the energy currency of life, is synthesized by a multi-subunit protein complex ATP synthase. It is a ubiquitous bioenergetic enzyme found in all life forms and is thus an emerging antibacterial drug target for novel antibiotics. ATP synthase consists of a membrane-extrinsic F1 motor and a membrane-embedded F0 motor. Recent advancements in the cryo-electron microscopy (cryo-EM) of the ATP synthase of Escherichia coli (E. coli) provide a new context for its' structure. Cryo-EM structures show there may be some yet unknown interactions in the ATP synthase enzyme that could be crucial for developing future antibiotics. The complete deletion of the periplasmic loop within the subunit a of the F0 motor abolished the ATP synthesis and hydrolysis activity, indicating its importance. Additionally, structural analyses of the cryo-EM models showed that the loop residue Asp124 forms hydrogen bonds with Gln10 of subunit b and His15 of subunit a. To investigate the importance of this interaction in relation to enzyme function, we mutated Asp 124 to polar and non-polar residues and used in-vitro assays of ATP synthase functions. This study may provide insight into the importance of Asp 124 for the structural assembly of subunit a and its contribution to subunit a-b interaction.

INDIRECT DETERMINATION OF OH RADICALS IN THE OZONOLYSIS OF CATECHOL

Authors

Josiel Barrios Cossio, Chemistry, University of Kentucky
Dr. Marcelo Guzman, Chemistry, University of Kentucky

Abstract

Catechol is a model dihydroxybenzene compound naturally and anthropogenically emitted to the environment, causing pollution and capable of generating hydroxyl radicals by electron transfer to ozone. In the troposphere, OH radicals are a primary oxidant, reacting instantaneously and unselectively with the surrounding molecules. Photolysis of ozone had been identified as one of the primary sources of OH radical in the tropospheric gas phase, but the reactions of dihydroxybenzenes with ozone could be another source of OH in water. Here we aim to quantify OH radicals produced by the ozonolysis of catechol in water using electrochemical principles during studies in water at pH 1-8. A 5 mL 1 mM catechol is exposed to a flow of 0.1 L/min of 300 ppbv to 150 ppmv ozone until half of the catechol has been reacted. Multiple species are examined as OH radical scavengers, and their reaction products are characterized to confirm the validity of the method. Relevant kinetic and thermodynamic parameters needed to interpret the processing of oxygenated aromatic hydrocarbons in clouds will be presented.

DEVELOPMENT OF A NOVEL DRUG FOR THE TREATMENT OF TRIPLE-NEGATIVE BREAST CANCER

Authors

Alyson Ackerman, Chemistry, University of Kentucky
Dr. Bert Lynn, Chemistry, University of Kentucky
Dr. Samuel Awuah, Chemistry, University of Kentucky

Abstract

Triple-negative Breast Cancer (TNBC) is named for the lack of three receptors found in other forms of breast cancer: HER2, estrogen, and progesterone. Current therapeutics used in breast cancer treatment have been stifled by the lack of receptors to target, limiting TNBC treatment options to radiation, mastectomy, and chemotherapy. Development of targeted therapeutics for TNBC is necessary to improving quality of care and reducing treatment side effects. In 2020, a compound named Machilin D was isolated from saururus chinensis, a plant used in Traditional Chinese Medicine. Machilin D was found to suppress breast cancer stem cells (BCSCs) and inhibit NF-kB signaling. BCSCs are similar to TNBC cells, so this compound shows great promise in TNBC-specific treatment. We have successfully synthesized this compound from isoeugenol, an inexpensive starting material. The base structure can be modified with diverse alkyl substituents, providing a vast library of compounds that can be examined for anti-cancer and anti-inflammatory properties. The current compound of interest (C300), modified with addition of an isobutyl group, showed increased efficacy in preliminary cell culture studies and was well tolerated in mice. C300 possesses two chiral centers, so current work is focused on enantiomeric separation for further in-vitro studies.

TARGET-DIRECTED ELICITATION OF SECONDARY METABOLITES IN LOBELIA CARDINALIS FOR DISCOVERY OF A-SYNUCLEIN TOXICITY INHIBITORS

Authors

Poornima Sunder, Chemistry, University of Kentucky
Dr. Bert Lynn, Chemistry, University of Kentucky

Abstract

The α-synuclein protein is an important biomarker of interest in several neurodegenerative diseases, such as familial Parkinson's Disease (PD). The accumulation and aggregation of the α-synuclein protein has been shown to play a role in the pathology of this devastating disease. In order to discover novel inhibitors of α-synuclein toxicity we expressed the A53T α-synuclein variant in cultures of several medicinal plant species that have neuroprotective activity in PD models, including the Kentucky native species Lobelia cardinalis. The transgenic (A53T) cultures are susceptible to apoptosis, but any cultures surviving and maintaining viability are of great interest due to indicating mechanisms of rapid chemical defense. In this study we compared the secondary metabolic profiles of Lobelia cardinalis transgenic (A53T) cultures with that of non-transgenic hairy root cultures. There are clear changes in expression levels of lobinaline, the major secondary metabolite of Lobelia cardinalis, as well as several putatively identified flavonoids. We tested these compounds for neuroprotective activity against MPP+ toxicity in SH-SY5Y cell cultures and discovered that pelargonidin 3,5-O-diglucoside, apigenin 7-O-diglucuronide, and lobinaline had significant protection against MPP+ toxicity with IC50 values of 1μM, 1μM, 100 μM, respectively. Our preliminary data suggests that target-directed elicitation can identify potentially neuroprotective metabolites.

MITOCHONDRIA-LABELED CAPPILARIES FROM MICE AS A UNIQUE PLATFORM TO STUDY OXIDATIVE STRESS IN NEURODEGENERATIVE DISEASES EX-VIVO

Authors

Velmurugan Gopal Viswanathan, Neuroscience, University of Kentucky
Dr. Anika Hartz, Neuroscience, University of Kentucky
Dr. Bjoern Bauer, Neuroscience, University of Kentucky
Dr. Brad Hubbard, Neuroscience, University of Kentucky
Dr. Chirayu Pandya, Neuroscience, University of Kentucky
Dr. Hemendra Vekaria, Neuroscience, University of Kentucky
Dr. Patrick G. Sullivan, Neuroscience, University of Kentucky

Abstract

Accumulating evidence from preclinical, postmortem and epidemiological studies demonstrate a strong link between neurovascular dysfunction and cognitive impairment. Indeed, blood-brain barrier damage and neurovascular deficits are major hallmarks of neurodegenerative diseases, such as Alzheimer's disease (AD), vascular contributions to cognitive impairment & dementia (VCID), stroke and traumatic brain injury (TBI). Oxidative stress plays a critical role in on-going pathology that exacerbates neurovascular dysfunction. Oxidative stress is highly associated with mitochondrial dysfunction and imbalance of reactive oxygen species (ROS). To study capillary-specific mitochondrial function and dynamics in response to oxidative stress, we developed a novel ex-vivo model using brain capillaries from transgenic mice which express photoactivatable dentdra2 green specifically in mitochondria (mtD2g). Brain capillaries were isolated from both male and female mice using a standardized protocol. Isolated capillaries were subjected to: 1. Oxidative stress using 2,2'-azobis-2-methyl-propanimidamide dihydrochloride (AAPH) a free radical generator to induce oxidative stress by lipid peroxidation. 2. Oxygen-Glucose-Deprivation/reperfusion conditions with their respective controls. Following exposure, mitochondrial function was measured as oxygens consumption rate (OCR) using the Seahorse XFe96 analyzer and mitochondrial dynamics were measured using a confocal microscope with Imaris software. Both oxidative stress and ischemia/reperfusion conditions significantly decreased OCR. Mitochondrial dynamics calculated in Z-stack demonstrated mitochondrial fission phenotype. This novel ex-vivo model will be a useful tool to test pharmacological interventions to target oxidative stress/mitochondrial dysfunction in vascular pathophysiology, as a critical endophenotype of neurodegenerative disease, such as AD.

10

EFFECT OF CBD ON OXIDATIVE STRESS AND COGNITIVE IMPAIRMENT IN 5XFAD MICE

Authors

Wijitra Chumboatong, Sanders-Brown Center on Aging, University of Kentucky
Dr. Anika Hartz, Sanders-Brown Center on Aging, University of Kentucky

Abstract

Cannabidiol (CBD) is a non-psychoactive compound in Cannabis sativa with anti-oxidant and anti-inflammatory properties that has potential for the therapy of CNS disorders such as Alzheimer's disease (AD). In the present study, we tested the CBD effect on oxidative stress and cognition in a mouse AD model. Male WT and 5xFAD mice were fed purified diet containing 200 and 500 mg/kgDiet CBD for 3 and 6 months. Using the Morris water maze test, we found that 5xFAD mice displayed increased escape latencies compared to WT mice, but 5xFAD mice treated with CBD had lower escape latencies compared to untreated 5xFAD mice after six months of treatment. These data suggest that CBD treatment slowed cognitive decline in 5xFAD mice. MDA is a byproduct of lipid peroxidation and serves as an indicator of oxidative stress. We detected higher MDA levels in brain and kidney tissues from untreated 5xFAD mice compared to WT mice. In contrast, MDA levels were lower in 5xFAD mice treated with 200 mg/kg and 500 mg/kgDiet CBD compared to untreated 5xFAD mice. Our study suggests that CBD decreases oxidative stress and slows cognitive decline in 5xFAD mice.

THE EFFECT OF ZINC ON THE NEURAL ACTIVITY OF MUSCLE RECEPTOR ORGANS

Authors

Lauren Sotingeanu, Chemistry, University of Kentucky
Dr. Christopher Crutchfield, Chemistry, University of Kentucky

Abstract

Zinc (Zn) is an essential element for life that facilitates proper organ function, cell growth, and immune function in the body. In cases of excess Zn presence in the body, Zn toxicity can occur, causing symptoms from minor effects, nausea and vomiting, to more severe neurological and cardiovascular complications. Our study examines the effects of zinc chloride (ZnCl) on the nervous system. More specifically, we are studying this effect in muscle receptor organs (MROs). The MRO is a proprioceptive organ analogous to the mammalian muscle spindle. Understanding the effects of excess ZnCl on sensory neurons is essential to understanding the effects of Zn toxicity. In this study, crawfish models were used, as comparable to mammals. The MRO was stimulated by moving the joint it monitors before and during Zn exposure. The results indicated that high concentrations of ZnCl depressed neural activity, but this neural activity was able to return upon removal of the Zn. Further experimentation is needed to determine if Zn is blocking stretch-activated ion channels in the sensory endings and/or electrical conduction down the axon. This data emphasizes the importance of controlling Zn concentrations in waterways and drinking water, and also in products like sunscreen and fertilizers.

ASSESSING IMPACTS OF EIF5A HYPUSINATION ON TDP-43 PATHOLOGY, NEUROINFLAMMATION, AND BRAIN METABOLISM IN TDP-43 TRANSGENIC MICE

Authors

Rohan Desai, Chemistry, University of Kentucky
Dr. Maj-Linda B. Selenica, Chemistry, University of Kentucky

Abstract

According to the NIH, approximately 600 brain disorders impact 50 million Americans. The cytoplasmic accumulation and inclusions of TAR DNA-binding protein (TDP-43) are hallmarks of two diseases in particular: Alzheimer's Disease and Limbic-Predominant Age-Related TDP-43 Encephalopathy (LATE). Eukaryotic Translation Initiation Factor 5A (eIF5A) is the only eukaryotic protein that undergoes a post-translational modification: hypusination. This modification of lysine (K) to hypusine (hypk50) occurs through the enzymatic activity of deoxyhypusine synthase (DHS) and deoxyhypusine hydroxylase (DOHH). Our laboratory has reported that this pathway directly regulates TDP -43 accumulation in stress granules, phosphorylation and aggregation. This study investigates the effects of induced eIF5A hypusination via AAV-directed DHS/DOHH overexpression on TDP-43 pathology, neuroinflammation, and brain metabolism in a TDP-43 transgenic (TAR) mouse model. Our analysis indicated induction of eIF5A hypusination following both AAV-eIF5A and AAV-DHS/DOHH injection in cortex and hippocampus compared to empty capsid injection ($p<0.001$). Considering published effects of hypusinated eIF5A on peripheral macrophages, we investigated its effect on IBA-1 (+) microglia morphology, which showed increased numbers of ameboid profiles following both AAV-eIF5A and AAV-DHS/DOHH ($p<0.01$ vs. $p<0.001$). We also observed vast alterations in TDP-43 cytoplasmic inclusions in AAV-DHS/DOHH injected mice. TDP-43 inclusion patterns were comparable to those described in FTD/ ALS/LATE human disorders.

EXPLORING THE PATHOLOGICAL EFFECTS OF TDP-43 ON NEUROVASCULAR COUPLING AND BRAIN METABOLISM IN A TRANSGENIC MOUSE MODEL

Authors

Meghana Gazula, Biochemistry, University of Kentucky
Dr. Maj-Linda B. Selenica, Biochemistry, University of Kentucky

Abstract

TDP-43 proteinopathy is recognized as one of the contributing pathogenic factors that better correlates with early cognitive decline and severity of Alzheimer's Disease (AD) and Limbic-Predominant Age-Related TDP-43 encephalopathy (LATE). Earlier, our laboratory showed that overexpression of TDP-43 resulted in significant infiltration of mouse immunoglobulin G (IgG), CD3+, and CD4+ T cells, along with endothelial and pericyte activation, indicating blood-brain barrier (BBB) permeability. This study investigates how the progression of TDP-43 pathology affects glial activation, BBB permeability, neuronal activity, and neurovascular coupling in a TAR6/6 mouse model. TAR6 and TAR 6/6 mouse models express wild-type human TDP-43. Homozygous TAR6/6 mice manifest TDP-43 cytoplasmic inclusions and phosphorylated aggregates, impaired motor neurons, functional decline, and early mortality. Analysis showed increased TDP-43 positive cytoplasmic accumulation in TAR6/6 mice compared to heterozygous TAR6 and non-Tg littermates. TDP-43 inclusion patterns were comparable to FTD/ALS/LATE human disorders. Image analysis of NeuN staining demonstrated a significant reduction of cortical and hippocampal neuronal layers in TAR6/6 mice. Behavior testing in TAR6/6 mice also confirmed impaired motor function. Multiphoton imaging revealed that the progression of TDP-43 pathology in TAR6/6 mice significantly increased neuronal activity; however, a significant muted vascular response was recorded, suggesting an uncoupling of neurovascular signaling.

CYCLOMETALATED GOLD(III) DITHIOCARBAMATE COMPLEXES ELICITS POTENT ANTICANCER ACTIVITY IN CANCER CELLS

Authors

Breyanna Walker, Chemistry, University of Kentucky
Dr. Samuel Awuah, Chemistry, University of Kentucky

Abstract

The design of stable metal-based complexes is central to the development of new anticancer drugs. In this work, we report on the facile synthesis of two classes of Au(III) dithiocarbamate complexes with differing degrees of cyclometalated frameworks; Au 1-4 have a phenylpyridine Au(III) framework while Au 5-6 bear a biphenyl Au (III) framework. The impact of cyclometalation on the pharmacodynamic properties of these classes of Au(III) complexes were determined using electrochemical, spectroscopic, and biological experiments. The electrochemical behavior coupled with LCMS stability studies in L-glutathione indicates that complexes with the biphenyl backbone demonstrate enhanced stability relative to complexes with phenylpyridine backbone. It was observed that the improved stability of the biphenyl Au(III) dithiocarbamate complexes altered their cytotoxicity as they showed reduced cytotoxicity compared to phenylpyridine Au(III) dithiocarbamate complexes. This result suggests that the cytotoxicity of phenylpyridine Au(III) dithiocarbamate complexes may result from its reduction to a more cytotoxic gold(I) complex in cells whereas the more stable biphenyl Au(III) dithiocarbamate is not subject to reduction and shows minimal cytotoxicity. Furthermore, the degree of cyclometalation affected mitochondria oxygen consumption rates. Seahorse data reveals that phenylpyridine Au(III) complexes inhibit OCR significantly in a concentration dependent manner compared to the biphenyl Au(III) complexes that show no inhibition. This work provides a basis for the development of future anticancer Au(III) complexes.

GREEN SYNTHESIS AND ELECTROCATALYTIC ACTIVITY OF SEMICONDUCTING WS2 NANOSHEETS FOR HYDROGEN EVOLUTION REACTION

Authors

Nadeesha Kothalawala, Chemistry, University of Kentucky
Dr. Doo Young Kim, Chemistry, University of Kentucky

Abstract

Transition metal dichalcogenides (TMDs) are an exciting type of material that can be used as a substitute for expensive and scarce Pt-based electrocatalysts in various electrochemical reactions. TMDs are abundant, inexpensive, and can be modified by changing their phase and dimensionality. Recently, TMDs have gained much attention as electrocatalysts for hydrogen evolution reaction (HER) due to the growing demand for cost-effective sustainable green hydrogen production. However, despite extensive research efforts, many challenges still exist to overcome in developing TMD nanostructures for clean hydrogen production. There is a need to find greener and scalable synthesis protocols to obtain exfoliated TMD nanostructures without impurities.
This study presents a modified liquid-phase exfoliation method using a greener solvent mixture of water and ethanol under ultra-sonication, followed by a solvothermal process to produce crystalline highly exfoliated (monolayer) WS2 nanosheets. Through this method, mostly the semi-conducting phase of WS2 nanosheets was obtained, which showed comparable electrocatalytic HER performance to previous reports with metallic phase. This work highlights the potential of the thermodynamically stable and catalytically active semi-conducting phase of WS2 nanosheets for clean hydrogen production. Furthermore, operando Raman spectroscopy provided insights into the nature of catalytic sites on WS2 nanosheets participating in HER.

16

DNA-AGNC LOADED LIPOSOMES FOR MONITORING CEREBRAL BLOOD FLOW VELOCITY USING TWO-PHOTON FCS

Authors

Xiaojin Wang, Chemistry, University of Kentucky
Dr. Chris Richards, Chemistry, University of Kentucky

Abstract

Understanding drug and nanocarrier transport in the cerebrovascular at the level of individual capillaries is important to understanding the pharmacokinetic and hemodynamic properties of therapeutic delivery. These types of measurements are currently constrained by the available techniques that lack the spatial and temporal resolution to quantify these properties in real-time. Fluorescence correlation spectroscopy (FCS) is a technique that enables the tracking of analytes at the single-molecule level. FCS has been widely applied in solution, but applications in vivo to monitor analytes in the vasculature are challenging. Here, we utilized liposome encapsulated DNA-stabilized silver nanoclusters (DNA-AgNCs) that possess excitation in the second near-infrared window (NIR-II) and NIR-I emission as single molecule tracer molecules in the brain vasculature to achieve FCS measurements. Encapsulating DNA-AgNCs in liposomes protects them from degradation in vivo and increases their brightness, making them detectable by FCS. Combining the two-photon fluorescence imaging and FCS allowed us to simultaneously image and perform high spatial and temporal measurements on blood flow velocity in the cerebrovascular of arterioles, venules, and capillaries (<10 μm in diameter).

ASSESSING THE IMPACT OF ANTISENSE OLIGONUCLEOTIDE THERAPY IN A LAFORA DISEASE MOUSE MODEL

Authors

Laiken Griffith, Chemistry, University of Kentucky
Dr. Matthew Gentry, Chemistry, University of Kentucky

Abstract

Lafora Disease (LD) is glycogen storage disease that occurs in children and young adults, includes symptoms like seizures and neurodegeneration, and results in the death of the patient within about ten years of the onset of seizures. LD results from mutations in either the EPM2A or EPM2B genes that encode for the proteins laforin and malin, and is driven by the formation of insoluble glycogen, which aggregates into Lafora Bodies (LBs). This study examined an antisense oligonucleotide that targets glycogen synthase (Gys1) as a potential therapy with the goal of slowing the formation of LBs. We found that the Gys1 ASO resulted in a significant decrease in the formation of LBs, as well as fewer large LB aggregates.

TUNING THE OPTICAL PROPERTIES OF π-CONJUGATED MOLECULES THROUGH MACHINE-INFORMED DESIGN

Authors

Parker Sornberger, Chemistry, University of Kentucky
Dr. Chad Risko, Department of Chemistry & Center for Applied Energy Research, University of Kentucky

Abstract

While organic π-conjugated materials demonstrate utility in energy generation and storage, lighting, transistors, sensors, and other optical and electronic devices, designing a new molecular material with precise properties for a specific application requires the exploration of a vast chemical space. Molecular generative models show efficacy for in silico property prediction and design of drug-like molecules. Given this success, these models have a natural extension to the design of π-conjugated molecules. Here, we discuss the development of generative normalizing flow models to tune the optical properties of π-conjugated chromophores. The models are trained on the more than 25,000 chromophores and points of optoelectronic data from the Organic Crystals in Electronic and LightOriented Technologies (OCELOT) database. The generative models focus on molecules that can be of interest for singlet fission and can quickly generate structures with the aim of tuning the energy gaps between low-lying singlet and triplet excited states. The model optimizes these gaps through sampling a learned chemical space and uses pretrained message passing neural networks trained on the optoelectronic data from OCELOT to predict the gap between a molecule's low-lying singlet and triplet excited states. Results from the generative models are verified via high-throughput density functional theory (DFT) and time-dependent DFT (TDDFT) calculations to obtain their optical transitions and frontier molecular orbital energies. Though the models here focus on robustly tuning optical transitions, the methods can be transferred to optimize additional electronic properties.

NAC1 DRIVE THE DUAL ROLE OF NEUTROPHILS IN PRIMARY AND METASTATIC TNBC THROUGH MODULATION OF THE JAK/STAT3 PATHWAY

Authors

Chrispus Ngule, Toxicology and Cancer Biology, University of Kentucky
Dr. Jin-Ming Yang, Toxicology and Cancer Biology, University of Kentucky

Abstract

The interaction between cancer stem cells (CSCs) and immune cells and its role in tumor aggression remain poorly understood. Nucleus accumbens associated protein 1 (NAC1), a BTB-POZ family member, is implicated in tumor development and progression of various cancer types. Using in vitro and in vivo triple-negative breast cancer (TNBC) models, we examined the role of NAC1 in the modulation of the crosstalk between immune cells and CSCs in tumor immune microenvironment (TIME). We found increased expression of NAC1 in TNBC clinical tissues, and that NAC1 stemness regulation was dictated by neutrophil and NK cells status of the host. NAC1 knockdown in TNBC cells demonstrated reduced tumorigenicity in neutrophil and NK cells-competent mice while in NK deficient mice, NAC1 depletion promoted tumor aggression. Depletion of neutrophils in neutrophil-NK cells-competent mice decreased tumor growth of NAC1-depleted cells. Intriguingly, neutrophil depletion in same mice increase tumor growth of NAC1 -low cells, suggesting the involvement of NAC1 in enhancing tumor-immune cells interaction. Further, depletion of NAC1 in immature neutrophils decreased TNBC stemness markers expression. Moreover, NAC1 physically associates with STAT3 to enhance protein stability. Collectively, we uncovered a novel role of NAC1 in regulation of TIME. Thus, targeting NAC1 may reverse TNBC immunosuppressive phenotype.

ATOMISTIC DYNAMICS OF THE RIGID AND MOBILE AMORPHOUS FRACTIONS IN π-CONJUGATED POLYMERS

Authors

Kehinde Fagbohunge, Chemistry, University of Kentucky
Dr. Chad Risko, Department of Chemistry & Center for Applied Energy Research, University of Kentucky

Abstract

The aggregated domains in π-conjugated polymers (CPs) before and after the increase in conformational freedom during melting of the glassy state, respectively termed the rigid and mobile amorphous fractions (RAF and MAF), have been observed by temperature-modulated differential scanning calorimetry (TMDSC). While the atomistic dynamics within these regions are hypothesized to influence CP solid-state morphology (and consequently optoelectronic performance), but the exact role played by the dynamics of these regions remains unknown. In this contribution, we use molecular dynamics (MD) simulations to study a representative system of poly(3-hexylthiophene) (P3HT) comprising both amorphous and crystalline regions connected via tie chains extending from within the crystallite into the amorphous regions. This approach, which to the best of our knowledge has not yet been explored in the literature, presents an avenue to characterize the atomic-level events corresponding to the RAF and MAF transitions with an emphasis on thermomechanical stability. This suite of MD simulations contributes a holistic view of how RAF and MAF dynamics ultimately govern the stability and processing of CPs for organic optoelectronic devices.

COMPUTATIONAL INVESTIGATION OF THE DYNAMICS OF EXTREME CONCENTRATIONS RELEVANT FOR NONAQUEOUS REDOX-FLOW BATTERIES

Authors

Anton Perera, Chemistry, University of Kentucky
Dr. Chad Risko, Department of Chemistry & Center for Applied Energy Research, University of Kentucky

Abstract

Organic redox-active compounds have been explored for many uses including serving as redox-active molecules in redox flow batteries (RFBs) and providing overcharge protection in lithium-ion batteries (LIBs). The concentration of the redox active species and the supporting electrolyte in an RFB plays a significant role in determining the energy density of a battery. Nevertheless, at very high concentrations, the physicochemical relationship between the redox active molecule, electrolyte salt, solvent, and the electrochemical performance of an RFB had not yet been well studied. Herein we present a molecular-level understanding of the effect of concentration on physical properties leading to RFB performance complementing experimental observations. To examine this relationship, we explored the redox-active molecule 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) and TBAPF6 electrolyte salts varied across concentrations of 1 mM to over 1000 mM in acetonitrile. We observed intriguing relationships between the transport properties of these solutions that were primarily based on solvation and ion-pairing effects. Furthermore, we also provide suggestions on obtaining optimum performance as a function of concentration in similar systems based on our theoretical insight.

COMPREHENSIVE DATA INFRASTRUCTURE FOR ORGANIC REDOX FLOW BATTERIES

Authors

Rebekah Duke, Chemistry, University of Kentucky
Dr. Chad Risko, Department of Chemistry & Center for Applied Energy Research, University of Kentucky

Abstract

Efforts to reduce dependence on non-renewable natural resources like coal for power generation have resulted in increased dependence on renewable power sources like solar and wind. While the cost of energy production has decreased over recent years, concurrent energy storage technology is still expensive as it depends on lithium and other transition metals. A highly scalable and cost-effective alternative is the redox-flow battery based on organic redox-active materials. Unfortunately, the metanalyses necessary to elucidate the properties of organic redox activate material are prohibited by the inaccessibility of data scattered throughout the literature and the data's lack of uniformity. We present D3TaLES, a curated collection of computational, experimental, and literature-reported data on redox-active molecules for use in redox flow batteries. The raw data and derived properties are organized into a molecule-centric schema, and the database ontology contributes to the establishment of community reporting standards for electrochemical data. Data are readily accessed and analyzed through an easy-to-use web interface. The data infrastructure is coupled with data upload and processing tools that extract, transform, and load relevant data from raw computation or experimental data files. An intuitive web-based interface allows experimentalists to systematically encode their laboratory workflows. These processing tools along with an embedded high-throughput computational workflow enable community contributions and versatile data sharing and analysis. Ultimately, the uniform and accessible D3TaLES data have enabled machine learning and robotic experimentation towards better exploring relevant chemical space for application-suitable redox molecules.

REDOX-ACTIVE SPECIES IN VARIABLE STATES OF CHARGE IN ELECTROLYTES: A MOLECULAR DYNAMICS INVESTIGATION

Authors

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Abstract

2,2,6,6-tetramethylpiperidine N-oxyl (TEMPO) is a stable redox-active molecule that has been investigated as a component in catholyte for redox-flow batteries. Here we present a molecular dynamics (MD) investigation of TEMPO in an electrolyte comprised of tetrabutylammonium hexafluorophosphate (TBAPF6) and acetonitrile (ACN) to investigate how varying the TEMPO state of charge and concentration impact the dynamics of the complex solution. Three TEMPO:TBAPF6 millimolar (mM) concentrations of 1000:100, 100:100, and 50:1000 were examined. To examine the effect of different charging levels, 20:80, 50:50, and 80:20 TEMPO:TEMPO+ species ratios were investigated. Radial distribution functions (RDF) of the solute and solvent molecules are reported to demonstrate solute and solvent ordering, while diffusivity and viscosity calculations are reported to examine how these concentrations may influence the system used in a redox-flow battery. The insights gathered demonstrate how the solution composition can be designed to improve electrolyte systems.

APPLICATION OF LEWIS ACIDIC DEEP EUTECTIC SOLVENT IN CATALYSIS: SYNTHESIS OF UNSYMMETRICAL ETHERS VIA ALCOHOL DEHYDRATION

Authors

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Abstract

Unsymmetrical ethers are typically synthesized via the Williamson ether method, but the unwanted formation of symmetrical ethers plus the basic and harsh conditions of the route pose a synthetic challenge. Transition metal-enabled Ullmann-type synthesis, on the other hand, comes with a high economic cost. Dehydration of alcohols in the presence of base-metal catalyst has, however, recently offered the greenest approach to synthesize unsymmetrical ethers, leaving water as by-product. Ionic liquids employing base-metal catalysts, known as deep eutectic solvents (DESs), are low-price, recyclable, and offer high recovery in the synthesis of unsymmetrical ethers. In this contribution, we describe our use of deep eutectic solvent as Lewis acid homogeneous catalyst for the dehydration of primary, secondary, and tertiary alcohol substrates using aryl groups as protecting agents, to form unsymmetrical ethers. Specifically, we utilize choline chloride and zinc chloride as DES catalyst to form a new C-O bond. The use of this DES catalyst mixture provides a better approach from the green chemistry standpoint as environmentally benign, efficient and recyclable catalyst in the synthesis of unsymmetrical ethers for broader industrial applications in surfactants, liquid fuels, polymers, and pharmaceuticals, to name a few.

DEVELOPMENT OF NEW CHEMICAL TOOLS FOR SPECIFIC PROTEIN MODULATION USING METAL-MEDIATED LIGAND AFFINITY CHEMISTRY (MLAC)

Authors

Udara Munugoda Hewage, Chemistry, University of Kentucky
Dr. Samuel Awuah, Chemistry, University of Kentucky

Abstract

The use of transition-metal-based electrophiles to selectively modify proteins has emerged as an invaluable tool for the development of modified proteins. Metal-based electrophiles show unique biorthogonal chemistry, yet it is an underdeveloped method when it comes to their applications in protein within the cells. Our approach involves in tuning the ancillary ligands of cyclometalated gold(III) to act as a warhead, to rapidly and selectively modify only cysteine residues among the presence of the other amino acids. The observed and optimized reactivity of the cyclometalated gold(III) system enables the rational design to covalently modulate the Cereblon E3 ubiquitin ligase complex through the engagement of cysteine. This research demonstrates how structure-activity relationship studies can be used to optimize the kinetics of cysteine arylation and develop metal-mediated ligand affinity chemistry (MLAC) of native proteins along with their application in targeted protein degradation in Cereblon E3 ubiquitin ligase which has become an important new drug discovery modality in the area of therapeutic research.

MACHINE LEARNING FOR PREDICTION OF NONCOVALENT INTERMOLECULAR INTERACTIONS IN ORGANIC SEMICONDUCTORS

Authors

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Abstract

Organic semiconductors have been widely used in various optoelectronic applications such as solar cells, light-emitting diodes, and transistors. The performance of these materials depends on the non-covalent intermolecular interactions between the organic molecules. The accurate computation of these non-covalent intermolecular interactions is particularly crucial for understanding crystal packing in organic semiconductors and enhancing the design of high-performance materials. While theoretical based approaches such as symmetry-adapted perturbation theory (SAPT) are used to calculate these interactions; this calculation can be time-consuming especially for large chemical systems. This inherently slows down the exploration of the vast organic semiconductor chemical space. This study introduces a machine learning (ML) model trained on SAPT computed values to predict these non-covalent intermolecular interactions. The ML model also predicts the different components of the interaction energy, including repulsion, induction, electrostatics, and dispersion energies. Ongoing efforts involve using python coding methods to run and benchmark the SAPT calculation steps and results, and improvement of the prediction capacity of the ML model. Anticipated results from this study would provide insights into the potential of ML in predicting non-covalent intermolecular interactions in organic semiconductors, which could lead to the development of new, high-performance materials for various optoelectronic applications.

INHIBITION OF AEROBIC GLYCOLYSIS SENSITIZES TRIPLE-NEGATIVE BREAST CANCER TO AURAFORMIN

Authors

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Dr. Samuel Awuah, Chemistry, University of Kentucky

Abstract

A growing concern in cancer management is the ability of cancer to evade the cytotoxic effect of anti-cancer therapies. This drug resistance is primarily caused by altered energy pathways, a key hallmark of cancer. Cancer cells have aberrant metabolic phenotypes, such that even in the presence of oxygen, there is increased glycolysis and reduced oxidative phosphorylation (OXPHOS). These metabolic alterations ensure a rapid supply of energy and biosynthetic intermediates required for the sustained proliferation of cancer cells. Furthermore, the altered energy metabolism confers drug resistance on cancer cells, especially against OXPHOS-targeting drugs. Targeting cancer metabolism by inhibiting glycolysis and OXPHOS has emerged as a promising approach for cancer management. In this study, we demonstrated that inhibiting glycolytic pathway using 2-deoxyglucose (2DG) suppresses cancer proliferation and sensitizes triple-negative breast cancer (TNBC) to auraformin, an OXPHOS inhibitor. 2DG and auraformin combination therapy synergistically inhibited colony formation and reduced mitochondrial respiration in TNBC. The 2DG-auraformin combination therapy has a significantly higher potency than 2DG and auraformin administered as single therapies. This study highlights the importance of multi-pathway targeting in circumventing drug resistance in cancer and the efficacy of gold-based compounds in cancer management.

LEVERAGING ARTIFICIAL INTELLIGENCE IN THE CHARACTERIZATION OF NON-SMALL CELL LUNG CANCER

Authors

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Abstract

Given the importance of immunotherapy in treating tumors, this study examined the relationships between epigenetics and immune signaling molecules in non-small cell lung cancer (NSCLC). A tissue microarray of 216 NSCLC patients was immunohistochemically stained for 6 markers: EZH2, a methyltransferase and epigenetic modifier; Histone 3 Lysine 27 trimethylation (H3K27me3), the product of EZH2 methylation and a suppressor of gene expression; B2M, a presenter of endogenous antigen; HLA-DR,DQ,DP, a presenter of exogenous antigen; PD-L1 (Programmed Death Ligand) and CBS, a determinant of methyl availability. Artificial intelligence was then trained to identify malignant cells among the diverse tumor microenvironment, allowing the degree of staining in just those cells to be quantified. Results showed that H3K27me3 was associated with lower levels of PD-L1 and B2M, as would be expected given its established role as a repressor. However, there were also surprisingly positive associations between H3K27me3 and both CBS and HLA-DR,DQ,DP. Perhaps most interesting though is the lack of coordination between EZH2 and H3K27me3, since EZH2 is the canonical methyltransferase targeting H3K27. The disconsonant nature of these results suggests that gene expression in NSCLC is not well understood, and that much work remains to be done.