1

Layered Superconducting Ground Plane Design that Reduces Losses and Applies Magnetic Field to a Quantum Amplifier

Motz, Sarah
Department of Physics and Astronomy
University of Pittsburgh

Quantum computers have the potential to greatly surpass the power of classical computers and store memory in quantum bits (qubits). The Josephson Parametric Converter (JPC), a type of quantum amplifier, cooled near absolute zero in a dilution refrigerator is useful to measure the state of the qubit. Signals sent from the qubit are amplified by the JPC, which requires a magnetic field to function and lies above a silver ground plane. However, the external field source sacrifices space in the refrigerator and the silver ground plane dissipates energy. To solve these problems, incisions are cut into a superconducting ground plane to focus the magnetic field into the JPC, which reduces losses and serves as a source of magnetic field because the ground plane itself forms a loop-like path. When current is applied, magnetic field is generated inside the loop and allows on-chip field manipulation. The design is currently being fabricated.

2

Mass Spectrometry Analysis of Toxic Substances in Dietary Supplements

Stubbert, Lauren[1], Henderson, James[1], Hao, Weier[1], Miller, Logan[1], Pamuku, Matt[2], and Kingston, H. M. "Skip"[1]
Department of Chemistry and Biochemistry
[1]Department of Chemistry and Biochemistry, Duquesne University, Pittsburgh, PA
[2]Applied Isotope Technologies Company, Pittsburgh, PA

Dietary supplements have become increasingly popular to counteract the diminishing levels of nutrients found naturally in foods. They are not regulated by the FDA since they are regarded to come from a natural source. Supplements are therefore not held to the same stringent standards as pharmaceuticals. Since Physicians are increasingly recommending supplements to patients there is a clear need to analyze their quality.
One substance analyzed was trivalent chromium [Cr(III)] which boosts the body's metabolism and therefore promotes weight loss. Due to this desirable property, Cr(III) is found in many dietary supplements. Cr(III) is the desired form of Cr to use for human consumption however it is easily oxidized to hexavalent chromium [Cr(VI)], which is carcinogenic.
The supplements were analyzed for Persistent Organic Pollutants (POPs) such as DDT, naphthalene, and pyrene, amongst many others. Both POPs and Cr(VI) were found in the analyzed samples highlighting the need to apply more stringent standards.

3

Investigation Into The Mechanism of Bifunctional Catalyst Using Template-Stripped Metal Thin Films

Thomas Jr., ,Craig ; McKone, James
Department of Chemical and Petroleum Engineering
University of Pittsburgh

Precious metals like platinum and gold are widely used as catalysts for redox reactions in electrochemical devices like fuel cells. Moreover, there are several known cases where a mixture of two precious metals tends to outperform each individual metal, implying some emergent chemical property leading to higher catalytic activity. The mechanism of these bimetallic catalysts is still an area of debate and discovery. We have worked to use semiconductor nanofabrication techniques to deposit well-defined patterns of platinum and gold onto glass and silicon substrates. We have further used a technique called template stripping to obtain bimetallic catalyst surfaces with near atomic smoothness. By using a range of analytical tools including cyclic voltammetry and atomic force microscopy, and by controlling the dimensions of catalyst patterns with lithography, we have developed the ability to characterize the composition and activity of these bimetallic catalysts with exceptionally high precision.

4

Evaluation of Various eDNA Barcode Primers for Ray-finned Fishes Using Tissue-sample Standards and eDNA Water Samples

Wetzel, Haley; Trevelline, Brian; Hoenig, Brandon; and Porter, Brady
Department of Biological Sciences, Duquesne University, Pittsburgh, PA.

Electrified benthic trawling is the standard for conducting fish surveys in large rivers, but this method is highly labor intensive and can cause mortality to the sampled fishes. Here we developed and tested PCR primers for their potential use as mini-barcodes to identify an entire community of ray-finned fishes from the environmental DNA (eDNA) they slough off in a water sample. This amplicon mixture was submitted to the Illumina MySEQ platform and the resulting sequences were identified to species by BLAST. We tested six PCR primer combinations with a equal concentrations of DNA extracted from tissue of nineteen different fish species and human to find the optimal primer combination. We test this method on eDNA filtered from water samples taken from the Ohio River to evaluate its utility to identify the species composition of a natural fish community.

5

Synthesis of 5-substituted pyrrolo[2,3-*d*]pyrimidines with pyridine glutamate side chains as potential chemotherapeutic agents

Henry, Madison[1]; Doshi, Arpit[2] ; Gangjee, Aleem[2]
[1] Bayer School of Natural and Environmental Sciences
[2] Division of Medicinal Chemistry, Graduate School of Pharmaceutical Sciences
Duquesne University

Pemetrexed (PMX), the current standard drug used in the treatment of non-small cell lung cancer and malignant mesothelioma, suffers from dose limiting toxicity. PMX is transported by the reduced folate carrier (RFC), that is present in both normal and tumor tissues. In normal body tissue, folate receptors α and β (FRα and FRβ) and the proton-coupled folate transporter (PCFT) show limited expression unlike the ubiquitously expressed RFC. FR's are overexpressed in malignancies enabling accessibility to tumors but not to normal tissues. PCFT optimally functions at a pH of 5.5-6.9 (present in solid tumors) and is nonfunctional at physiological pH (7.2-7.4). Thus selectively targeting tumor transport via FRs and/or PCFT over RFC provides a higher safety margin. We designed and synthesized 5-substituted pyrrolo[2,3-*d*]pyrimidines with four and five carbon bridges with pyridine regioisomers in the side chain. The synthesis involved Dess-Martin periodane oxidation, Sonagashira coupling, amide coupling, alpha bromination, and basic hydrolysis.

6

Fragmentation and Other Gas-Phase Reactions of Anions Created from Complexes Containing Uranyl Ion and Formate and Acetate Ligands

Bubas, Amanda; Van Stipdonk, Michael J.
Department of Chemistry and Biochemistry
Duquesne University

Gaining a better understanding of species-specific reactivity of uranium and the actinides remains an important goal, whether to assist development of new nuclear fuel processing techniques or to understand the role of f-electrons in chemical bonding. Electrospray ionization (ESI) can be used to make a wide range of interesting and relevant species for studies of intrinsic (i.e. without influence of solvent) structure and reactivity by mass spectrometry. In this study, complex anions containing UO_2^{2+} and formate and acetate were prepared by ESI, and the fragmentation and ion-molecule reactions of specific ions with H_2O and O_2 was investigated using multiple-stage ion trap mass spectrometry. Precursor complexes undergo easy decarboxylation of formate ligand to create uranyl hydrides, and elimination of aldehydes (formaldehyde when two formate ligands are present, and acetaldehyde for two acetate ligands) to make interesting oxide products. These species then react with H_2O and O_2 to make hydroxides and superoxides.

7

Derivatization to Enhance Detection and Quantification of Emerging Threat Compounds Using Mass Spectrometry

Graça, Connor*, Van Stipdonk, Michael[+], Metzler, Luke[+]
*Duquesne University, Bayer School of Natural and Environmental Sciences, Forensic Science and Law Program
[+]Duquesne University, Bayer School of Natural and Environmental Sciences, Department of Chemistry and Biochemistry

Mass spectrometry remains one of the most sensitive and selective measurement and analysis tools for small molecules such as explosive compounds. Currently, one emerging class of explosive compounds that is of concern is using common cooking spices, which can be used both as explosive material and as components of explosive mixtures that increase surface area. One challenge is to devise and implement methods to sample and ionize these species for analysis by mass and ion mobility spectrometry. In this study, we are focusing on aldehydes, which are found in spices and flavorings such as cinnamon, cumin and vanilla. In this preliminary study, an extraction protocol was developed to produce aldehyde compounds for derivatization. Aldehydes were then converted to imines by condensation reaction with a range of amines. The derivatization improves the analysis of the aldehyde targets by both electrospray ionization mass spectrometry and gas-chromatography/mass spectrometry with electron impact ionization.

8

The Effects of Macromolecular Crowding on Human Aldose Reductase

Roman, Brynn; Seybert, David W.
Department of Chemistry and Biochemistry
Duquesne University

Enzymes are typically studied in dilute solutions under conditions which do not accurately simulate the inside of a cell. Since the intracellular matrix is crowded with macromolecules, it is essential that enzymes are studied in crowded solutions to better understand how they function in vivo. Aldose reductase (AR) is an NADPH dependent enzyme that is part of the polyol pathway which converts glucose to fructose and is thought to cause secondary complications in diabetes. AR catalyzes the reduction of glucose to sorbitol and under conditions of hyperglycemia, sorbitol accumulation can lead to cataracts, nephropathy, and neuropathy, making inhibitors of AR attractive drug candidates in treatment of these complications. In these experiments reaction rates were measured by recording changes in NADPH concentration at 340 nm. Addition of the crowding agent bovine serum albumin (BSA) at varying concentrations resulted in changes of the kinetic properties of the enzyme.

9

Macromolecular Crowding Effects on Lactate Dehydrogenase Isozymes

Shaik, Sadiq; Seybert, David W.
BSNES Department of Chemistry and Biochemistry
Duquesne University

The current project focuses on the steady-state enzyme kinetics of porcine heart LDH (LDH-1) and rabbit skeletal muscle LDH (LDH-5) in a crowded macromolecular environment. Lactate dehydrogenase (LDH) is a cytosolic enzyme that catalyzes the reduction of pyruvate to L-lactate with the concomitant oxidation of NADH to NAD^+ as the final step in mammalian anaerobic glycolysis. Bovine serum albumin (BSA), a soluble globular protein, was used as the primary model crowder. Using NADH as variable substrate and in the absence of crowder, LDH-5 exhibited positive cooperativity with a Hill coefficient of 2.5 while LDH-1 exhibited a Hill coefficient of 1.7. Slight positive cooperativity was observed with respect to pyruvate for LDH-1. Addition of increasing concentrations of BSA resulted in progressively decreasing Hill coefficients. Additionally, kinetic parameters were compared between the two LDH isozymes. Our next goal is to characterize the L-lactate and NAD^+ reverse reaction in crowded conditions using LDH-1.

10

Frictional Properties of Single and Mixed Monolayers of Octadecanoic Acid and Octacosanoic Acid.

Palmer, Jacob[1], Lim, Min Soo[1]; Gawalt, Ellen[2]
Department of Chemistry, Slippery Rock University, Slippery Rock, PA [1]
Department of Chemistry and Biochemistry, Duquesne University, Pittsburgh, PA[2]

The desire to miniaturize devices requires development of molecularly thin lubricant layers at the interfaces of the mechanically interacting components. It also demands a complete understanding on how the structure and chemical nature of the thin layer influences the lubricity of the films. A self-assembled monolayer (SAM) is a good candidate for such studies. A SAM is a two-dimensional molecular array that is spontaneously organized by adsorption of amphiphilic organic molecules on a solid surface. In this study, single and mixed monolayers of octadecanoic acid (C18) and octacosanoic acid (C28) were formed on sapphire substrates. Mixed monolayers consisted of proportions of 75%:25%, 50%:50%, and 25%:75 % of C18 and C28. Diffuse reflectance infrared Fourier transform spectroscopy (DRIFT) was employed to determine the order and binding nature of the monolayers. Friction force that is present on each monolayer was measured by an atomic force microscope (AFM).

11

Frictional Properties of Self-assembled Monolayers of Octadecanoic Acid and Perfluorooctadecanoic Acid

Fletcher, Cammi[1], Lim, Min Soo[1]; Gawalt, Ellen[2]
Department of Chemistry, Slippery Rock University, Slippery Rock, PA [1]
Department of Chemistry and Biochemistry, Duquesne University, Pittsburgh, PA[2]

The continuing desire to miniaturize devices has brought about interest in developing molecularly thin lubricant layers. The structures and chemical functionalities of the lubricant molecules play a significant role for the lubricity of the molecularly thin layer. This project focuses on how the fluorination of lubricant molecules would influence the frictional properties of the thin layer. Self-assembled monolayers (SAMs) of octadecanoic acid and perfluorooctadecanic acid were formed on a single crystalline sapphire surface by solution deposition method. The order and binding nature of the monolayers were determined by Diffuse reflectance infrared Fourier transform spectroscopy (DRIFT). Atomic force microscopy (AFM) was employed to measure the friction force of the two monolayers and visualize surface topography. DRIFT spectra confirmed the formation of highly ordered monolayers with mixed mono- and bidentate binding. Friction force measurements on the two monolayers exhibited that the fully fluorinated film was less frictional than the fully hydrogenated one.

12

A Neural Network for online spike sorting

[1]Issar, Deepa; [2,3]Williamson, Ryan; [3]Cowley, Ben; [3]Yu, Byron; [1,2]Smith, Matthew
[1]Bioengineering, [2]Ophthalmology, University of Pittsburgh
[3]Carnegie Mellon University

Brain computer interfaces (BCIs) can be used as both research tools and devices to improve patient control of prosthetics. BCIs record action potentials (spikes) from the brain, interpret these signals in real-time, and output information that can be used to control an external prosthetic or provide feedback. Unlike most cases of neural data analysis, BCIs do not use a spike sorting procedure to isolate spikes from background noise in the brain because current spike sorting methods are offline, time intensive, and require some manual intervention. As a result, BCIs must decode a noisy signal, which impedes performance. A real-time (online) spike sorter for BCIs needs to be computationally efficient and accurate. To address this need, we trained a neural network to isolate spikes from noise. Our neural network spike sorter works in real-time and has the promise to improve BCI performance and online decoding ability.

13

High-Temperature, Solid-State Synthesis and Characterization of the Diamond-like Semiconductor Cu_2MnGeS_4

Cribbs, Marvene M.; Glenn, Jennifer R.; Stoyko, Stanislav S.; Aitken, Jennifer A.
Department of Chemistry and Biochemistry, Duquesne University, 600 Forbes Ave Pittsburgh PA 15282

Nonlinear optical (NLO) crystals are used to shift the coherent, monochromatic light of lasers to other desirable wavelengths for military, medical, and industrial applications. Currently used IR-NLO materials, such as $AgGaS_2$ and $AgGaSe_2$, exhibit drawbacks including low laser-induced damage thresholds (LIDTs), multiphoton absorption, and difficult crystal growth. One avenue for new materials are quaternary DLSs. These offer a compositional flexibility that allows for the tuning of properties, such as bandgap. Although numerous quaternary DLSs have been prepared, NLO studies have only been completed on several compounds because high-quality samples are needed. This project has explored various synthetic conditions to produce materials suitable for measurements. In particular, Cu_2MnGeS_4 was prepared in pure form and the phase purity was assessed using X-ray powder diffraction along with diffuse reflectance UV/Vis/NIR spectroscopy. Scanning electron microscopy was utilized to study the morphology and energy dispersive spectroscopy was used to assess the composition of the crystals.

14

Biophysical characterization of interactions between a uridylated histone mRNA degradation intermediate and SLBP

Sarah Harris[1,2]; Patrick E. Lackey[2]; Mihaela-Rita Mihailescu[1]
Department of Chemistry and Biochemistry, Duquesne University
Division of Biological, Chemical, and Environmental Sciences, Westminster College

Histone mRNAs are a tightly cell-cycled regulated group of mRNAs that are strongly expressed at the beginning of S-phase and rapidly degraded when DNA replication ends. This cell cycle regulation is controlled by histone mRNA's unique 3' end; instead of the traditional poly(A) tail, histone mRNA instead ends with a 3' stem-loop. This stem-loop is an important factor in controlling the expression and degradation of histone mRNA during S-phase, along with two key protein binding partners: the stem-loop binding protein (SLBP) and the human 3' exonuclease (3'hEXO). At the beginning of degradation, 3'hEXO trims 2-7 nucleotides from the 3' end. These nucleotides are then often replaced by a short uridylation that preserve the length and, in some cases, structure of the stem-loop. Using biophysical methods, we worked to characterize the structure of one of these uridylated intermediates and its interactions with SLBP in comparison to SLBP's interactions with the wild-type RNA.

15

Title: "DIKB DRIVE and Portal Applications; Creating Tools for Adverse PDDI Prevention"

Authors: Katherine Milliken, Dr. Harry Hochheiser, Yifan Ning, Samuel Rosko, Dr. Richard Boyce
Dept. of Biomedical Informatics
University of Pittsburgh

Interactions between prescribed medications are common. A recent study in one hospital found potential drug-drug interactions (PDDI) in 51% and 63% of patients on admission and on discharge, respectively (Magro, 2012). Uncoordinated pharmaceutical knowledge bases allow PDDIs to go unnoticed. Pharmaceutical interaction databases, such as the Drug Interaction Knowledge Base (DIKB), can help reduce adverse PDDI consequences. The "DRIVE" project utilizes the DIKB to interpret the high volume of DDI publications. By calculating the adequacy of information with respect to DIKB criteria, we filter for useful publications. The Portal displays the subsequent DIKB information dynamically. We developed graphic user interfaces (GUIs) for the DIKB Portal and DRIVE projects through html, CSS, and javascript libraries. The GUIs incorporate the existing infrastructure of the DIKB while maintaining accessibility to healthcare professionals. By easing the collection and interpretation of PDDI information, we hope that the projects will benefit clinicians and promote patient safety.

16

Utilization of polymer microspheres for controlled release of ciprofloxacin and stem cell conditioned media

Greco, Ande, Bruk, Liza, Fedorchak, Morgan
Department of Ophthalmology
University of Pittsburgh

Controlled release of drugs and other molecules for the treatment of disease or for tissue regeneration is a common approach to improve outcomes by decreasing dosing frequency or enhancing bioavailability. Degradable polymeric microspheres are often utilized to encapsulate these molecules because they offer a high degree of versatility. In particular, drug release can be controlled by optimizing particle size and morphology. Subsequent modification of certain fabrication parameters, such as homogenization speed to alter particle size, can tailor release rate of the encapsulated substance to desired therapeutic levels and durations. For this project, we are using these principles to investigate two important classes of encapsulated molecules: small molecule drugs and proteins. Optimizing encapsulation and release of these two types of agents will provide a greater level of understanding of the material/agent interaction and how it can be exploited to achieve desired *in vivo* pharmacokinetics.

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17

Development of a Heuristic Pathway Search for Efficient Extension of a Pancreatic Cancer Model involving Tumor-Associated Macrophages

Patel, Mit
Miskov-Zivanov, Natasa
Department of Electrical and Computer Engineering
University of Pittsburgh

In this work, we are developing methods to automatically assemble intra-and inter-cellular models, and we are applying these methods to study the progression of pancreatic cancer *in silico*. We started with an initial baseline model that was created by manually identifying key components and interactions within and between tumor-associated macrophages and pancreatic cancer cells. Next, we extended the baseline model with interactions that were extracted from literature by automated reading engines and assigned confidence scores by epistemic values. Limitations set by underlying graph theory, however, restrict the approaches that can be utilized to efficiently extend the baseline model, as the number of potential extensions increases with the number of interactions extracted by reading. Therefore, our objective is to design and implement a practical approach to more efficiently and accurately extend the model with the automated reading outputs, while preserving or improving the biological validity and relevance of the model.

18

Effects of Macromolecular Crowding on Steady State Kinetics of Mammalian Malate Dehydrogenase

Wilber, Kimberly; Seybert, David W.
Department of Chemistry and Biochemistry
Duquesne University Pittsburgh, PA

Traditionally, *in vitro* steady state enzyme kinetics have been studied in dilute solutions. Intrinsically, however, the cytosol of a cell and the interior of organelles have a crowded macromolecular matrix. Therefore, macromolecular crowding must be intensively studied to better understand its effect on enzymatic reactions as they occur in a simulated intracellular milieu. The model system we are studying is mitochondrial malate dehydrogenase (MDH), a citric acid cycle enzyme that catalyzes the interconversion of malate and oxaloacetate (OAA) with the concomitant reduction of NAD^+ and oxidation of NADH, respectively. The primary model macromolecular crowding agent employed is bovine serum albumin (BSA), at concentrations up to 10% (w/v). Our main goal was to determine whether crowding affects substrate inhibition by oxaloacetate. We have verified previous literature reports of significant substrate inhibition by OAA, and then focused on determining any steady-state kinetic changes upon addition of increasing concentrations of crowder.

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Analysis of Blood Spatter on Different Stain Resistant Sprays

Wilson, Kylie; Ferrara, Lyndsie, M.S.; Wetzel, Stephanie, Ph.D.
Forensic Science and Law Program
Duquesne University, Pittsburgh, PA 15282, USA.

Bloodstain pattern analysis (BPA) is an important aspect of forensic science that is utilized in the reconstruction of events at a crime scene. Although BPA provides valuable reconstruction information, minimal research has examined the effect porous surfaces have on blood spatter patterns. The purpose of this research was to analyze impact bloodstain patterns on fabrics treated with various types of stain resistant sprays. The fabric analyzed was a cotton/polyester blend pillow case. A rat trap was used to create the blood spatter. Four different stain resistant sprays were compared against an unsprayed fabric and a butcher paper control. The results showed Scotchgard® and Guardsman sprayed fabrics did not absorb blood spatter, whereas Faultless® and Kiwi® sprayed fabrics allowed for significant absorbance. Each spray contributed to vastly different bloodstain patterns, and understanding these differences can help in correct interpretation of bloodstain patterns at a crime scene.

20

Purification of NADPH-cytochrome P-450 reductase from pig liver microsomes

Gillis, Samantha K.; Seybert, David W.
Department of Chemistry, Millersville University of Pennsylvania
Department of Chemistry and Biochemistry, Duquesne University

NADPH-cytochrome P-450 reductase is a membrane bound protein found in the liver of mammals. It catalyzes electron transfer from NADPH to cytochromes P-450, and is responsible for the oxidative metabolism of endogenous and exogenous compounds. Based upon this enzyme's molecular structure and mechanism of electron transfer, we anticipated that the activity of this enzyme will be sensitive to macromolecular crowding. Microsomes, fragments of the endoplasmic reticulum, were prepared from the centrifugation of homogenized pig liver to be used for the purification of NADPH-cytochrome P-450 reductase. Three steps were completed to purify the protein starting with the solubilization of microsomes using ionic and nonionic detergents. Next, two chromatographic processes were used: a DEAE-cellulose anion-exchange column followed by a 2', 5'-ADP-Sepharose

affinity column. The results of the purification of the enzyme as well as the initial results of macromolecular crowding experiments with this enzyme will be presented.

21

Exploratory Synthesis of Lead-Containing Chalcogenides with Potential in Thermoelectric Applications

Moore, Shannon M.; Stoyko, Stanislav S.; Aitken, Jennifer A.
Department of Chemistry and Biochemistry
Duquesne University, 600 Forbes Ave. Pittsburgh, PA 15282

Chalcogenide semiconductors with narrow band gaps, $E_g \leq 1$ eV, have great potential for applications in thermoelectric devices used in power-generation for deep-space exploration and solid-state refrigeration. Promising thermoelectric materials must have a large ZT (figure of merit) value; therefore, high electrical conductivity and Seebeck coefficients are desired along with low thermal conductivity. Doped Bi_2Te_3 and PbTe are currently used in thermoelectric devices. Yet, improved materials with higher ZT values are needed for additional application, such as automotive waste-heat recovery and large-scale heating and cooling applications. This work focuses on the exploratory high-temperature, solid-state synthesis of new Pb-M'-M''-Se (where M' and M'' are post-transition metals) compounds with potential in thermoelectric applications. Thus far, three new compounds have been discovered and the crystal structures were solved and refined using single crystal X-ray diffraction. Scanning electron microscopy coupled with energy dispersive spectroscopy was used to investigate surface morphology and semi-quantitative elemental analysis, respectively.

22

Synthesis of Naranjamide Analogues for Structure Activity Relationship Studies

Scrivener, Sarah G.; Ahmed, Tanvir; Tidgewell, Kevin
Division of Medicinal Chemistry, Graduate School of Pharmaceutical Sciences
Duquesne University

Marine cyanobacteria produce a variety of secondary metabolites of diverse structural motifs, which are found to have potent bioactivities such as cytotoxicity, antibacterial, and anti-parasitic. These metabolites are sources of novel leads for drug discovery, and thus cyanobacteria have been the subject of research since the late 1970's. Utilizing chromatography, NMR and mass spectroscopy, our lab recently identified a novel anti-parasitic compound, Naranjamide, from samples collected in Panama. Naranjamide shows efficacy against the parasites that cause malaria (*P. falciparum*) and Chagas' disease (*T. cruz*i) *in vitro*. This project involves the synthesis of analogues with sequential replacement of the amino acid side chains in Naranjamide. We hope to observe corresponding changes in functionality, which will indicate the side chain interactions necessary for the anti-parasitic activity of the molecule. The design, synthesis, and structural assignment of analogues will be presented.

23

Impact of α-synucleinopathy on hippocampal synaptic markers in an animal model of Lewy body disorders

Dumm, Benjamin; Nouraei, Negin; Mason, Daniel M; Miner, Kristin M; Carcella, Michael A; Bhatia, Tarun N; Soni, Dishaben; Shon, Minkang; Johnson, David A; Luk, Kelvin C; Leak, Rehanna K
Graduate School of Pharmaceutical Sciences
Duquesne University

Lewy bodies are dense aggregates of misfolded α-synuclein that form in the brains of patients with Parkinson's disease (PD) or dementia with Lewy bodies (DLB). Loss of synapses is evident at early stages of PD/DLB but it is not known if this is the result of Lewy pathology. We tested the hypothesis that α-synuclein fibril injections into the hippocampus seed Lewy pathology in this structure and elicit loss of synaptic markers. As expected, fibril injections led to a robust increase in Lewy-like pathology in the hippocampus, similar to PD and DLB. Unexpectedly, there was an increase in the synaptic marker synaptophysin in the CA2/CA3 fields in the temporal pole of the hippocampus at three months post-infusion. However, there was a trend towards loss of synapsin I/II in the temporal portions of CA2/CA3 (two-tailed p=0.055). These changes were not accompanied by cell loss or behavioral deficits, suggesting that this model mimics the earliest stages of PD/DLB with

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N-acetyl-cysteine reduces Lewy pathology in some but not all brain regions in experimental Parkinson's disease

Miner, Kristin M; Mason, Daniel M; Hutchison, Daniel F; Luk, Kelvin C; Leak, Rehana K
Graduate School of Pharmaceutical Sciences
Duquesne University

Lewy body disorders are characterized by the spread of protein aggregations across the brain. We have shown that infusions of the fibrillar form of alpha-synuclein into the mouse olfactory bulb (OB) and anterior olfactory nucleus (AON) elicit the spread of Lewy-like pathology into deeper brain structures. Here we test the hypothesis that the antioxidant N-acetyl cysteine (NAC) prevents the spread of alpha-synucleinopathy from olfactory structures into the limbic telencephalon. Mice were fed NAC-containing food or regular food for three months following infusions of vehicle or fibrils into the OB/AON. NAC significantly reduced the development of Lewy-like pathology in the AON and hippocampus as expected, but not in the entorhinal or piriform cortices. Thus, NAC may mitigate protein aggregations in some, but not all types of neurons, perhaps because of topographic differences in the mechanisms underlying the development of protein aggregations.

potential disruption of synaptic structure.

25

Norepinephrine induces secretion of skin peptides in salamanders

Patrice Clemenza, Jakobi Deslouches, Kenzie Pereira, and Sarah Woodley
Department of Biological Sciences, Duquesne University

Amphibian skin is embedded with glands that secrete peptides onto the skin surface. These secreted peptides protect amphibians from infectious diseases. Because methods for collecting salamander skin secretions are poorly understood, our objective was to investigate methods for inducing peptide secretions. Treatments included immersion in: buffer control (CB), CB + norepinephrine hydrochloride, CB+ acetylcholine chloride, CB + manual induction, and 7% ether. We purified the peptides with solid phase extraction and measured peptide yield with a BCA assay. Our results indicated that CB + norepinephrine hydrochloride induced the highest peptide yield. To further test whether norepinephrine induces peptide secretion, a second experiment tested additional doses of norepinephrine in additional species. Together, our results indicate that norepinephrine is an effective method of collecting salamander skin peptides. By optimizing our method, we can now test whether skin peptides have antimicrobial properties against amphibian pathogens as well as disease-causing agents in humans.

26

Supporting Pharmaceutical Product Development using Response Surfaces: Development of an Immediate-Release Carbamazepine Tablet

Rish, Adam; Steinbach, Doug; Anderson, Carl A. Ph.D; Drennen, James K. Ph.D
Pharmaceutical Sciences
Duquesne University

Dissolution performance of Carbamazepine (CBZ; active pharmaceutical ingredient - API) tablets can be heavily influenced by the relative presence of functional excipients, crospovidone (cPVP; disintegrant) and low molecular weight hydroxyl-propyl-cellulose (HPC-SSL; dry binder), and manufacturing parameters. These excipients were homogeneously combined with CBZ and microcrystalline cellulose (MCC) powders according to a 3x3 full factorial mixture-design of experiments (range of cPVP: 1.25-6.0% w/w; range of HPC-SSL: 5.0-11.0% w/w; CBZ: 50%; MCC: filled to sufficient quantity). Each blend was compacted into tablets using the Presster™ (MCC; East Hanover, NJ) tablet press simulator to 3 nominal porosities (8, 11, 14%). Tablets were dissolved using a USP type II dissolution apparatus. Samples were automatically drawn over time and quantified for API content using a UV-vis spectrometer (Disek Inc.; New Brunswick, NJ) equipped with quartz flow through cells. Response surfaces were generated by modeling the dissolution performance as a function of the critical product/process parameters.

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Using Convolutional Neural Networks in Order to Predict Ligand Properties

Dunstan, Christopher; Ragoza, Matthew; Hochuli, Joshua; Idrobo, Elisa; Sunseri, Jocelyn; Koes, David Ryan; Read, Murray; Cole, Jason
Department of Computational and Systems Biology
University of Pittsburgh

Machine learning techniques can be applied to drug discovery in order to reduce the cost of assays. Deep learning techniques, such as convolutional neural networks, may be able to predict the melting point and crystallinity of a ligand. We use the deep learning framework caffe as a basis for our neural network. The custom MolGridDataLayer in the caffe framework, reads in a specialized binary gninatypes file that contains spatial information of each atom in every ligand. Multiple datasets with varying molecules and sizes are used for prediction. Our neural network is trained used three fold cross validation. Moreover, our neural network is optimized using Stochastic Gradient Descent. Our neural network's performance is compared to a linear model that uses fingerprints of each molecule. Their performances are measured through root mean squared deviation(RMSD) and correlation coefficient values. We apply many different changes

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A Two-Dimensional Numerical Model of a Microchannel Reactor for Fischer-Tropsch Synthesis

Ayisi Louis, Basha Omar, Arias Fabiana and Morsi Badie
Reactor and Process Engineering Laboratory (RAPEL)
Department of Chemical and Petroleum Engineering
University of Pittsburgh
Pittsburgh, PA 16261

A two-dimensional (2-D), pseudo-homogenous model has been developed to describe the steady-state hydrodynamic and mass transfer behaviors in a Micro-Channel Reactor (MCR) for a Low-Temperature Fischer-Tropsch (F-T) synthesis process. The model accounts for both axial and lateral dispersion in the MCR and includes the widely accepted semi-empirical Langmuir-Hinshelwood reaction kinetics (proposed by Yates and Satterfield (1991)) for the gas-phase reaction of the syngas feed (H_2 + CO) occurring on the surface of a spherical cobalt catalyst particle. The model was then used to predict the axial and lateral variations of the product concentration profiles and CO conversion. Also, the effects of the lateral and axial dispersion on the pressure drop, mass transfer, and hydrodynamics within the MCR were investigated. We believe this simple 2-D model could be used for proper optimization of the MCR performance in terms of

to our neural network to improve it's performance.

29

Title: Development of a Detailed Clinical Model for Assessing Nausea

Authors: Frimpong, Kojo and Lee, Young Ji PhD, RN
Department of Biomedical Informatics and School of Nursing, University of Pittsburgh, PA

Symptom assessment is essential in the field of nursing as it directly affects patients' quality of life. However, there is no standard tool for consistently assessing symptoms in patients. The aim of this project was to develop a detailed clinical model (DCM) for the nursing assessment of nausea in patients. Initially, we reviewed literature and identified 13 different assessment tools that assessed nausea in patients. However, the assessment tools only assessed two attributes of nausea (distress and severity) whereas we identified nausea possess nine attributes. Consequently, we developed a DCM that assesses nine attributes associated with nausea. Furthermore, we identified value sets that described the attributes in detail and mapped both the attributes and their value sets to the International Classification of Nursing Practice (ICNP) 2017 release version. We discovered that six out of the nine attributes sets (~67%) and approximately 30% of the value sets mapped to the ICNP.

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Convergent Evolution of *Burkholderia cepacia* complex bacteria in Cystic Fibrosis Patients

Karl Keat
Microbiology and Molecular Genetics
University of Pittsburgh

The *Burkholderia cepacia* complex (BCC) is a diverse group of bacteria which act as opportunistic pathogens which predominantly infect cystic fibrosis patients. It has been observed that following infection, the bacteria adaptively evolve within the patients, which is correlated with a deterioration of their condition. A better understanding of the pathways which are common targets of evolution could aid in the development of new treatment strategies and therapeutics for infected patients. This study computationally compared the mutations which accumulated in *Burkholderia* in several patients. This allowed for the observation of convergent evolution and the identification of traits under heavy selection. It is hypothesized that there will be heavy selection on mutations altering biofilm formation, among other traits, based on the crucial role of biofilms in antibiotic and immune resistance.

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Electronic and Optical Refinement of a Wavelength Meter

Kline, Jake; Ireland, Timothy; Tiber, Gage; Corcovilos, Theodore A.
Bayer School of Natural and Environmental Sciences
Duquesne University

In Dr. Corcovilos's laboratory, one of the ongoing projects is to create a wavelength meter, a device that can measure the wavelength of a laser to a part per million degree. The wavelength of an unknown laser can be found through comparison to a laser in which the wavelength is already known. Both beams are sent through a Michelson interferometer and the number of times each beam destructively interferes is counted. Using a proportion and the counts obtained from experimentation, the unknown wavelength can be calculated. To ensure accurate counting of the interference fringes, it is imperative that the beam stays perfectly still. This requires perfect alignment of the beams as well as a smooth change in path length to cause interference. I will further discuss the multiple improvements made to optimize the design and how the wavelength meter will play a role in future projects.

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Stabilization of the Readouts for a Homemade Fluorometer to Detect Lead in Drinking Water

Spencer Graves, Gage Tiber, Theodore A. Corcovilos

Lead in drinking water affects millions of people around the world, causing severe health problems. We have developed a device that is small, portable and economical allowing water samples to be tested on site instead of a lab. The device uses a chemical developed at Duquesne called Leadglow that changes the sample's fluorescence depending on its lead concentration. The device flashes a known amount of light onto the sample. The sample's florescence is then measured using Arduino code and then displayed on a LCD screen. We have improved the design of the device's optical and electrical systems. Previously, data taken showed that the readouts from the device varied with time for a single sample. A photodiode added next to the device's light source serves as feedback to regulate the light's intensity. Data shows the changes keep the readout relatively constant after multiple measurements, which makes the device more reliable.

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The Effects of Macromolecular Crowding on the Kinetics of Dihydrofolate Reduactase

Sheehy,Taylor L.; Seybert, David W.
BSNES Department of Chemistry and Biochemistry
Duquesne University

Dihydrofolate reductase (DHFR) catalyzes the reduction of dihydrofolate (DHF) to tetrahydrofolate (THF) through a hydride transfer from NADPH in all dividing cells. Tetrahydrofolate is essential for DNA synthesis, which makes DHFR a main target in pharmaceutical development. DHFR's importance for *in vitro* screening of antifolates as potential therapeutic agents in chemotherapy, rheumatoid arthritis treatment, and antibacterial drugs makes it essential to better define its activity in the cell. Biochemical studies have shown that 5-40% of a cell's interior volume is crowded by macromolecules, which lead to thermodynamic and kinetic deviations from dilute solutions. *In vitro* studies have been conducted to simulate crowding effects on bovine and human dihydrofolate reductase using bovine serum albumin (BSA), ovalbumin and Ficoll-70 as model crowding agents. DHFR shows remarkable sensitivity to crowding effects as reflected by substantial changes in the enzyme's steady state kinetics at low concentrations of model crowder.

34

Toward Atomistic Simulations of Pathways and Rate Constants for Protein-Peptide Unbinding Processes

Fink, Elissa; Pratt, Adam J.; Chong, Lillian T.
Department of Chemistry and Department of Computational & Systems Biology
University of Pittsburgh

Long-timescale processes such as protein folding, binding, and unbinding, are not only fundamental to biology, but of great interest to biomedical research. Many of these processes occur on longer timescales than what is currently accessible by computational resources, or that require tremendous computational resources and time. Here, we applied the weighted ensemble path sampling strategy on a computing cluster of GPUs to enhance the sampling of both binding and unbinding pathways involving the p53 peptide and the MDM2 protein at the atomistic level. The latter will be the first (to our knowledge) atomistic simulations of protein-peptide unbinding kinetics. Our simulation strategy will be a general one that can be applied to other protein-peptide binding/unbinding processes.

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Biophysical investigation of G-Quadruplex MAP1B mRNA interactions with the FMRP and FUS RNA binding proteins

Cooke, Madeline; Mihailescu, Mihaela-Rita
Department of Chemistry and Biochemistry
Duquesne University

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease with no effective treatment currently available. Although it is known that the fused in sarcoma (FUS) protein is mutated in individuals affected with ALS, the exact pathogenic mechanism of this protein has not yet been elucidated. Mutant FUS contains a motif rich in glycine and arginine residues, termed an RGG box domain, which is known to bind to G-Quadruplex structures. Similarly, the fragile X mental retardation protein (FMRP) comprises an RGG box domain, which has been shown to bind to an mRNA target sequence in microtubule associated protein 1B (MAP1B). In vivo data suggest that FMRP and FUS regulate the MAP1B mRNA translation. Thus, in this study the binding interactions of FUS and FMRP with the mRNA target sequence in MAP1B mRNA were investigated via biophysical techniques including UV-Vis spectroscopy, electrophoretic mobility shift assays and CD spectroscopy.

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Promotion of STEAM in Adolescents Through Interactive Learning

Martin, Stephanie T.[1]; Samuel, Andre[2]; Floss, Carrianne[2]
Department of Chemistry and Biochemistry
[1]Duquesne University
[2]The Citizen Science Lab

Hands-on learning in the areas of science, technology, engineering, arts and mathematics (STEAM) helps to promote better understanding of content as well as higher interest and confidence in these areas of study. The more exposure students receive, the greater the chance they will pursue a career in STEAM. To test these effects of interactive learning, both quantitative and qualitative data were taken from students ranging from grades 4-9 during a hands-on zoology camp at The Citizen Science Lab. Each day, students participated in a Mentimeter pre-quiz and post-quiz, which tested the extent of students' zoology knowledge. Analysis of the correct responses showed the amount of information absorbed each day with a final survey about their experience at the end of the camp. The quantitative data revealed the trend of improvement in the post-quiz responses compared to pre-quiz responses while the qualitative data showed a greater interest and confidence in STEAM.

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Validation of a Design of Experiments applied to Microemulsions as Nanonutraceutical Formulations

Shychuck, Emma; Herneisey, Michele; Lambert, Eric; Janjic, Jelena.
Department of Pharmaceutics
Duquesne University

Resveratrol, a natural product found in fruits and many plants, is a popular nutraceutical. Due to its poor solubility, microemulsions are an attractive strategy for enhanced efficacy in inflammatory conditions. We present a novel approach to rationally design a manufacturing process and formulation of nanonutraceuticals using statistical Design of Experiments (DOE). The four factor, two level DOE consisted of 12 microemulsions that were manufactured using a low energy water titration method and studied the effect of stirring rate, water addition rate, oil content, and propylene glycol content on physical stability. Emulsions were subjected to accelerated stress conditions to evaluate physical stability by monitoring droplet size and size distribution. Standard least squares regression methods were applied to model the data. Seven supplementary microemulsions, similarly manufactured, were evaluated to validate the goodness of fit of the models. This research is aimed to inspire others to adopt DoE for nanonutraceutical formulation development.

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Modification of the Surface of Stainless Steel 316L

Allego, Emily K.; Reger, Nina A.; Blystone, Ashley; Gawalt, Ellen S.
Department of Chemistry and Biochemistry
Duquesne University

Stainless steel 316L, used in various industrial and medical applications, is a low carbon steel that is susceptible to corrosion. Corrosion of the metal can lead to structural failures and an increase in repair and replacement costs. Self-assembled monolayers (SAMs) can be used to decrease the rate of corrosion through providing a protective barrier to cover the surface of the metal. 11-phosphonoundecyl acrylate was used to form a stable and ordered SAM. Surface initiated polymerization of the acrylate tail group was employed to increase the strength of the SAM and increase corrosion resistance. Diffuse reflectance infrared Fourier transform spectroscopy and matrix-assisted laser desorption ionization time of flight were utilized to analyze the binding and presence of the SAMs formed. Cyclic voltammetry will be used to measure the ability of the polymerized SAM to inhibit corrosion.
~~PUT IN ALLEGO – COULD NOT OPEN~~

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Towards a bacteria retardant implant surface

Schultz, A.; Reger, N.; Gawalt, E.
Department of Chemistry and Biochemistry
Duquesne University

Annually, 20% of orthopedic implants become infected. This infection is difficult to treat due to the formation of biofilms which do not respond well to traditional antibiotics. An alternative approach is to modify the surface of the implant with a nitric oxide (NO) releasing molecule. NO triggers a dispersal event of the biofilm, rendering the bacteria susceptible to antibiotics. In this work, self-assembled monolayers (SAMs) were formed on the surface of titanium aluminum vanadium (Ti-6Al-4V) and the SAMs were used as linkers to immobilize spermine *N*-diazeniumdiolate (NONOate), which releases NO under physiological conditions. The Griess Assay was used to quantify the amount of NO released from the surface. Turbidity tests were performed against *E. coli* to determine the bacterial inhibition. The ability of the substrates to work in concert with tetracycline was also tested. Future work includes turbidity studies with the dual modification of NO and antibiotics.

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The Surface Modification of Titanium: Towards A Peptide Coated Surface

Leung, Emily1; Blystone, Ashley1; Gawalt, Ellen S.1,2
1Department of Chemistry and Biochemistry, Duquesne University
2McGowan Institute for Regenerative Medicine, University of Pittsburgh, Pittsburgh, PA

Titanium metal is a commonly used implant material which can fail due to aseptic loosening, which is the absence of proper bonding between the implant material and the remaining bone at the site of implantation. Immobilizing osteoinductive molecules to the surface may help combat aseptic loosening. In this work, self-assembled monolayers (SAMs) of 12-mercaptododecylphosphonic acid were formed on the surface of titanium. Diffuse reflectance infrared Fourier transform spectroscopy was used to evaluate the formation of the SAMs on the titanium surface. These SAMs would present a thiol at the interface allowing for the potential anchoring of bioactive molecules through disulfide bond formation. A disulfide bond was formed using the model compound stearyl mercaptan. Disulfide bond formation was quantified using a colorimetric assay (Ellman's reagent). In future work, the methods developed here would be utilized in the linking of a cell adhesion peptide.

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Accounting for moisture content of powders to determine true density

Muzzio Matthew Pharm.D candidate, Valekar Pradeep Ph.D candidate, Ira S. Buckner Ph.D
School of Pharmacy and Graduate School of Pharmaceutical Sciences
Duquesne University

The purpose of this study is to determine the extent to which a powder's water content will affect the experimental value of the powder's true density and then determine an appropriate amount of time powder should be purged to account for water content. Experiments were performed over the course of two months using two chemical powders; microcrystalline cellulose (Avicel PH 102) and mannitol (Pearlitol 500) which typically have different moisture contents. Powders were stored in 33% humidity, prior to any measurements. Powders were purged for 0, 5 or 15 minutes with dry helium to remove loosely sorted moisture. After purging powders were analyzed using a stereopycnometer to determine true density. Once stereopycnometry was completed powders were removed from stereopycnometer and stored in a parafilm sealed vial then the vial was stored within vacuum chamber. Moisture contents of powders were determined and compared to thepurge time and associate true density values. Results seem to indicate that longer purge time increases experimental true density, especially for microcrystalline cellulose which is more hygroscopic.

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Interface Improvement for Generative Model Parameter Control in CellOrganizer

Ojeah, Nkechi S. [3,4], Okolo, Chinasa[5], Gagnon, Patricia[5], Kangas, Joshua D.[2], Murphy, Robert F.[2]
Department of Biomedical Informatics, University of Pittsburgh
Computational Biology Department, Carnegie Mellon University
Internship in Biomedical Research, Informatics and Computer science (iBRIC)
Lincoln University of Pennsylvania
NSF-REU in Software Engineering, Carnegie Mellon University

CellOrganizer is a tool used to learn generative cellular models from 2D and 3D fluorescence microscope images. CellOrganizer analyzes the spatial arrangement of proteins and subcellular structures to generate a statistical model of the arrangement of proteins and organelles within the cells. In order to generate these models, users are currently presented with multiple options. The goal of this work was to design, implement and test new interfaces for these options allowing users with less knowledge and experience to successfully utilize CellOrganizer. To that end, we have designed and implemented an improved interface for training models which allows various options to be hidden from the user until they make selections indicating they may need to modify those options. We have also implemented custom tools for various specialized tasks including sections and conditional tools.

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Localized Drug Delivery of Aspirin to Stent Sites Via Self Assembled Monolayers

Miskalis, Angelo J, Lovelace, Tell, Gawalt, Ellen S.
Department of Chemistry and Biochemistry
Biomedical Engineering Program
Duquesne University

Coronary Heart Disease (CHD), which is caused by plaque buildup on the arterial wall, affects over 600,000 people annually. CHD is commonly treated by the insertion of a stent. These stents are typically comprised of stainless steel 316L (SS316L). Upon insertion, the stent can damage the endothelial membrane, promoting platelet aggregation. Nonsteroidal Anti-Inflammatory Drugs (NSAIDS), such as aspirin have been utilized to prevent platelet aggregation and subsequent clotting. The direct delivery of aspirin to the site of the stent would lower the risk of internal bleeding and other side effects. The goal of the project was to immobilize aspirin to the surface of stainless steel via carbodiimide coupling using self-assembled monolayers (SAMs) as linkers. Diffuse reflectance infrared Fourier transform spectroscopy was implemented to confirm successful attachment of aspirin to the surface.

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Preparation of single crystal gamma-alumina catalyst support for Pt model catalyst

McCann, Matthew; Ayoola, Henry and Yang, Judith
Department of Chemical and Petroleum Engineering
University of Pittsburgh

We have investigated the formation of [111] oriented gamma aluminum oxide (γ-Al2O3) on single crystal [110] nickel aluminum (NiAl). γ-Al2O3 is an important catalyst support with use in fuel cells, petroleum reformers and catalytic converters. Single crystal nickel aluminum was polished through mechanical grinding techniques to ensure the surface was as flat and defect-free as possible. The NiAl was then oxidized in a tube furnace at 750°C for two hours to ensure homogenous growth of single crystal γ-Al2O3. The nickel aluminum and gamma aluminum oxide surfaces and interface were characterized by x-ray diffraction, atomic force microscopy, scanning electron microscopy, and energy dispersive x-ray spectroscopy. The resulting single crystal gamma aluminum oxide system was suitable for a cross-sectional transmission electron microscopy (TEM) sample to be prepared. The γ-Al2O3 thin films will be used as a support for Pt nanoparticle catalysts in environmental TEM experiments.

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Comparing Modeling Equations for Dissolution of Coated Theophylline Granules

Authors: Chris Winner, Henry Zhao
School of Pharmaceutical Science
Duquesne University

Drug release mechanisms such as dissolution behavior are highly associated with the patient's safety and clinical performance. The research being conducted, modeled dissolution curves based off three methods; Higuchi, Noyes-Whitney, and Weibull. Three calibration and two test batches were prepared using a fluid bed coater and differentiated by particle size and coating thickness. For Noyes-Whitney and Higuchi (first principle equations), a diffusion constant was fitted post-calibration dissolution and used for tests. For Weibull, three calibrations were used and any correlations existing regarding variables were used for tests. Analysis concluded that Weibull fit dissolution curves best due to flexibility. Since Noyes-Whitney assumes constant surface area and thickness and Higuchi assumes linear concentration gradient, Noyes-Whitney fit beginnings of dissolution curves but not ends (coated granules expand when exposed to solution). While, Higuchi fit the least due the violation of the assumption.

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Host Range Analysis of Various Bacteriophage Cocktails Against Strains of S. aureus

Cook, Justin[1]; Noel, Cierra[1]; Salvatore, Jacob[1]; Edgar, Robert[1,2]; Viator, John[1,2]
[1]Biomedical Engineering Program, Duquesne University
[2]Department of Bioengineering, Swanson School of Engineering, University of Pittsburgh

Bacteriophages are viruses that infect bacteria and utilize the cells' organelles to reproduce. The goal of this investigation was to find bacteriophage whose host range cover all *Staphylococcus aureus* strains and bacteriophage who infect only MSSA or MRSA. Methicillin-resistant *S. aureus* (MRSA) is a clinically relevant disease-causing strain while methicillin-susceptible *S. aureus* (MSSA) is a commensal bacterium found in the nose, respiratory tract, and on the skin. MRSA infections are difficult to treat due to the bacterium's resistance to the primary antibiotic methicillin. Bacteriophage offer an alternative diagnostic approach to such infections. Host range studies were performed using spot tests. The host range was tested using clinical isolates of *S. aureus*. For most isolates tested, all four cocktails were effective at eradicating the pathogen. The results are both experimentally and clinically significant as they provide support for the use of bacteriophage in diagnostic testing for *S. aureus* infections.

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Generation of Recombinant Baculovirus Using Site-Directed Mutagenesis in the Rat Serotonin Transporter

Spirik, Kassandra; Castellano, Elizabeth; Cascio, Michael
Department of Chemistry and Biochemistry
Duquesne University

The serotonin transporter (SERT) is a transmembrane protein located in neuronal cells which functions by terminating neurotransmitter action at receptor sites through the reuptake of serotonin (5-HT) from the synapse to presynaptic neurons. Dysregulation of 5-HT concentrations in the synapse is associated with several neurological conditions such as depression and anxiety. By providing more accurate modeling of SERT allostery during 5-HT transport, better drugs can be designed to treat these conditions. To do this, single point cysteine mutations were inserted into rSERT in pFastBac vector with the end goal of performing photocrosslinking studies. The single point mutation, S522C, was successfully transformed, transposed, and used to transfect insect cells which produced virus. The virus can be used to infect fresh insect cells for subsequent expression of the SERT protein. A photocrosslinker can be attached to the single cysteine mutation within the protein to be used in mass spectrometry studies.

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Testing the Efficacy of Biocides for Microbial Control in Simulated Produced Water

Nick Meray, Celcelia McGough, and John F Stolz
Center for Environmental Research and Education, Duquesne University, Pittsburgh PA
Lanxess Chemical Company, Robinson Township, PA

The extraction of natural gas and oil from tight reserves (e.g., shale) using horizontal drilling and hydraulic fracturing ("fracking") has transformed energy production in the United States. A common feature is the generation of waste fluids during the drilling, fracking, and production (e.g., produced water). The produced water is high in salts and other constituents and supports a unique microbiota. Microbial activity can lead to deleterious effects including souring (hydrogen sulfide production), scaling, and clogging (through biofilm production). Thus biocides are employed for microbial control. Previous work indicated that a biocide commonly used not only was ineffective but also stimulated growth. Further, new formulations from Lanxess were shown to be effective at high ppm levels. It was the purpose of this work to further test the efficacy of different formulations and lower (ppb) concentrations and against additional bacterial strains including sulfate reducers (e.g., SWPA, Lone Pine, and Lone Pine 1). These cultures were grown in medium with salinities

and pH similar to produced water from hydraulic fracturing of shales.

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Testing the Degradation of THC at Various Temperatures in Oral Fluid

Miranda, Colette C.; Wetzel, Stephanie J
Department of Chemistry and Biochemistry
Duquesne University

Tetrahydrocannabinol (THC) is the active ingredient in cannabis that provides a sense of euphoria in its users. In DUI cases, oral fluid is collected and tested to determine recent cannabis use. This research examined the effects of temperature and storage on THC degradation in oral fluid. Delta9-THC was used to spike pooled donor oral fluid. Then the samples were stored at various temperatures. Samples were heated at 40°C, 50°C, and 60°C for one hour and then analyzed on the GC/MS. Continued degradation of samples after being transferred to a cold room was also studied. Samples were heated at 50°C for one hour and then letting them cool in the cold room for 10 minutes, 30 minutes, 60 minutes, 4 hours, 24 hours, 48 hours, and 1 week before GC/MS analysis. All spectra were compared to the internal calibration curve to examine the amount of degradation.

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Robust Spectroscopic Method development to detect High Quality Counterfeit Drugs

Wargo, Jacob, Hossain, Nayeem, Drennen, James K., III
Graduate School of Pharmaceutical Science
Duquesne University

High quality counterfeit (HQC) products are drugs that are produced using similar formulations and manufacturing techniques to the genuine products they seek to imitate. Near Infrared spectroscopy (NIRs) is a potential analytical tool to identify these types of counterfeit products. However, to implement NIRs it is required to develop multivariate classification techniques (e.g. SIMCA). In order to develop a SIMCA model it is necessary to first designate a target class using genuine samples. This target class should be robust against raw material variabilities, which are common occurrences in manufacturing systems. The goal of this study was to build a target class that can differentiate between the genuine product and highly similar counterfeits and to test the robustness of the model. To assure the robustness of the model, chemical composition, particle size, and material vendors were varied (using 12 design points). This study found that modeling parameters are critical to the development of a robust NIRs model to detect HQC.

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A Host Range Study of Bacteriophage Against Staphylococcus aureus and Analysis of its Infectious Nature

Noel, Cierra; Jacob Salvatore, Robert Edgar, Dr. Ken Urisch, Dr. John Kellum, Dr. John Viator
Biomedical Engineering
Duquesne University

Viruses are the most common organisms present on earth and bacteriophage represent the majority of viral genetic information present in the biosphere. Lysogenic phage, often cause an increase in virulence and often allow for overgrowth of prophage containing bacteria. Staphylococcus aureus is an opportunistic pathogenic bacteria. MRSA (Methicillin-resistant Staphylococcus aureus) and MSSA (methicillin-susceptible Staphylococcus aureus) were used for determining a host range of novel bacteriophage. Additionally, prophage were found in many of the MRSA and MSSA samples. A correlation was determined between non-specific prophage and virulent factors of the staphylococcus. It is necessary to determine what bacteriophage attach to each specific strain of staphylococcus. Using photoacoustic flow cytometry, each strain of staphylococcus will be identified using a bacteriophage as a fluorescent marker on the bacteria. This will identifying the strain of bacteria in less then one day, when currently it takes over 3 days, allowing for rapid treatment options.

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Site-Directed Mutagenesis of rSERT in Preparation for Future Crosslinking Studies~~Abstract~~

Gering, Hannah; Costellano, Elizabeth; Cascio, Michael
Bayer School of Natural and Environmental Sciences
Duquesne University

The serotonin reuptake transporter (SERT) is a sodium-dependent, monoamine protein that is responsible for transporting serotonin from the synaptic cleft to the presynaptic neuron. SERT is a target for selective serotonin reuptake inhibitors (SSRIs), but SSRIs bind to other transporters and membrane proteins, causing side effects. The structure of SERT is not entirely resolved so a better understanding of SERT structure may allow designing of next generation SSRIs that bind more specifically to SERT, enhancing the benefits of the medication. Crosslinking studies can be used to gather more information about the protein structure of SERT. My work involving site-directed mutagenesis on specific locations of the rat serotonin transporter (rSERT) is in preparation for future crosslinking studies. I attempted to insert 4 different single-cysteine mutations into an rSERT DNA plasmid. 2 of these 4 mutations were successfully inserted. These can be used in the future for crosslinking.

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Preliminary Crosslinking Studies on Purified Recombinant Rat Serotonin Transporter Protein Cooper, Emily; Castellano, Elizabeth; Cascio, Michael
Department of Chemistry and Biochemistry
Duquesne University

The rat serotonin reuptake transporter is a sodium-chloride-dependent transporter that reuptakes serotonin back into the presynaptic neurons after delivering its chemical message. Due to the large size of SERT and the fluidity of the extracellular loops, the mechanism of this transport is difficult to obtain by traditional structural methods. As a complementary alternate approach, crosslinking studies were performed to determine nearby structure and interactions of the extracellular loops in which a single reactive thiol was introduced at selected sites. Here, I present my preliminary crosslinking studies with tandem mass spectrometry conducted on rSERT protein. The protein was produced and purified, crosslinked to form a disulfide attachment at the site of thiol mutation, digested to isolate peptide fragments of the rSERT protein, and analyzed with tandem mass spectrometry to determine sites of crosslinked residues in a roughly 20Å radius of location 406C in the rSERT protein in the apo conformation.

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Site-Directed Mutagenesis in the C-terminal Tail of the Rat Serotonin Transporter
Rhoa, Kathleen; Castellano, Elizabeth; Cascio, Michael
Department of Chemistry and Biochemistry
Duquesne University, Pittsburgh PA, 15282

Serotonin is a monoamine neurotransmitter located within the human brain that is responsible for maintaining positive mental health. It is released by neurons after the brain produces a chemical signal when in distress. Serotonin is later reabsorbed by a sodium chloride-dependent serotonin reuptake transporter (in humans, hSERT). Since the fluid structure of hSERT is not yet known, this study will focus on how experiments utilizing site-directed mutagenesis in X8C rat SERT (rSERT) can aid in further crosslinking studies to fully understand hSERT. Using designed primers, a point mutation (S611C) was successfully made in the poorly resolved C-terminal tail of rSERT DNA, transforming a serine to a cysteine. This mutation was confirmed with sequencing data, and will be transposed into a baculovirus for eventual overexpression. If the entirety of hSERT was confirmed, newer drugs could be designed to offer relief to people suffering from serotonin-related mental health disorders.

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GIS Mapping of Open Spaces for Community Garden Development in Pittsburgh's Low-Income Neighborhoods
Coates, Kelsey; Chitiyo, Plaxedes; Stolz, John
Bayer School of Natural and Environmental Sciences
Duquesne University

Poverty, low incomes and a lack of local grocery stores in minority neighborhoods predispose these communities to a high risk of food insecurity. Community gardens are a possible solution to this problem because they have the potential to increase access to healthy food, facilitate positive social interactions, and promote environmental protection. A study was carried out in Hazelwood, Homewood, and the Hill District neighborhoods of Pittsburgh to assess open spaces that may be viable for establishing community gardens using Geographic Information Systems (GIS). The location of grocery stores and active community gardens were mapped using GIS along with the median household income and topography of these neighborhoods. The results indicated that Hazelwood, Homewood, and the Hill District are food deserts but potential open spaces in the form of commercial areas, residential areas and parks exist where community gardens can be established and expanded, thus mitigating the risk of food insecurity.

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Biophysical Characterization of a G-Quadruplex Structure in pre-miR-125b-2
Roth, John; Mihailescu, Mihaela Rita
Department of Chemistry & Biochemistry
Duquesne University

Small, noncoding microRNAs (miRNAs) have been shown to play significant role in mRNA translation regulation. miRNA biogenesis involves a multi-step maturation pathway beginning with nuclear transcription of a typically several hundred nucleotide-long primary-miRNA which is cleaved into an approximately 80 nucleotide-long precursor-miRNA (pre-miRNA) by RNA-processing proteins. The enzyme, DICER, further processes this pre-miRNA to produce the mature, typically 22 nucleotide-long, miRNA. Recently, it has been proposed that the G-quadruplex structure present in pre-miRNAs might affect their processing into mature miRNAs. In this study, we hypothesized that pre-miR-125b-2, a guanine rich transcript, forms a G quadruplex structure which could affect its processing by DICER. To characterize this G quadruplex structure, we used biophysical methods including 1H NMR spectroscopy, CD spectroscopy, UV-Vis spectroscopy, and native PAGE. Moreover, we also analyzed the interactions of this pre-miR-125b-2 G quadruplex with G quadruplex RNA binding proteins and its DICER processing with molecular beacon assays.

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Role of Cytokines on PVR/CD155 Expression in Advanced Melanoma

Reines, Leila
Department of Immunology
Cornell University

The poliovirus receptor (PVR), also called CD155, presents itself on cancer cells as a membrane-bound receptor and the soluble form. Membrane-bound PVR serves as an adhesion molecule and as a leucocyte stimulation regulator, while the role of the soluble form is still unclear. Like the membrane form, the soluble PVR has been found increased in patients with more advanced stages of cancer. The reason why and under what mechanism this soluble form is upregulated is currently unknown, as is its impact on the patients' tumor response. We hypothesized that inflammatory cytokines released in the tumor microenvironment are involved in PVR upregulation. To further understand the PVR's role in cancer, ELISAs and flow cytometry were used to analyze the effect of cytokines in modulating PVR expression in melanoma cells. Future plans include evaluating circulating soluble PVR in patients with advanced melanoma undergoing PD-1 blockade and correlating the results with clinical outcome.

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Biophysical Characterization of FMRP RGG box binding to Drosha mRNA

McDougal, Keefe; Mihailescu, Mihaela Rita
Department of Chemistry and Biochemistry
Duquesne University

Fragile X Syndrome (FXS) is the most common inherited mental impairment disease. It is caused by a cytosine-guanine-guanine (CGG) repeat expansion mutation in the *FMR1* gene. The hypermethylation of these repeats inhibits the production of Fragile X Mental Retardation Protein (FMRP), an RNA-binding protein vital to brain development. The Arginine-Glycine-Glycine (RGG) Box Domain of FMRP is known to bind to a specific RNA secondary structure known as G-quadruplex that forms in guanine-rich RNA sequences. DROSHA is an RNAse III enzyme responsible for microRNA processing in the nucleus. The messengerRNA (mRNA) coding for DROSHA shows potential to form G-quadruplex in a G-rich sequence of its 5' untranslated region. It has been shown that FMRP regulates translation of this mRNA. We hypothesize that FMRP uses its RGG box to recognize DROSHA mRNA via this G-quadruplex structure. ^{1}H NMR and CD spectroscopies, as well as Native PAGE were employed in this investigation.

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Evolutionary Rate Covariation as a Predictive Tool to Identify α-Arrestin-Cargo Pairs

Tova Finkelstein[1], Abdullah Malik[2], Jackson Moore[3], Uthman Fadu[3], Hilary Serbin[3], Zelia Ferreria[4], Nathan Clark[4], Allyson F. O'Donnell[2]
1) Barnard College of Columbia University, New York, NY; 2) Dept. of Biological Sciences, Duquesne Univ., Pittsburgh, PA; 3) Taylor Allderdice High School, Pittsburgh, PA; 4) Dept. of Computational and Systems Biology, Univ. of Pittsburgh, Pittsburgh, PA.

Alpha-arrestins help cells survive environmental changes by controlling membrane protein movement. One hurdle to understanding α-arrestins is that few α-arrestin-cargo pairs have been identified. It is technically challenging to identify α-arrestin cargos due to their transient α-arrestin associations and the biochemical nature of cargo.
To identify α-arrestin-regulated cargos, we used Evolutionary Rate Covariation (ERC), which uses sequence-based signatures to identify genes with similar evolutionary histories. We compared ERC rates for α-arrestins with cargos across 18 yeast species. Among the top co-evolving proteins were those previously defined as α-arrestin cargos.
We are determining if the membrane proteins with the highest ERC values are α-arrestin cargos by assessing their

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Evolutionary Rate Covariation as a Predictive Tool to Identify α-Arrestin-Cargo Pairs

Tova Finkelstein[1], Abdullah Malik[2], Jackson Moore[3], Uthman Fadu[3], Hilary Serbin[3], Zelia Ferreria[4], Nathan Clark[4], Allyson F. O'Donnell[2]
1) Barnard College of Columbia University, New York, NY; 2) Dept. of Biological Sciences, Duquesne Univ., Pittsburgh, PA; 3) Taylor Allderdice High School, Pittsburgh, PA; 4) Dept. of Computational and Systems Biology, Univ. of Pittsburgh, Pittsburgh, PA.

Alpha-arrestins help cells survive environmental changes by controlling membrane protein movement. One hurdle to understanding α-arrestins is that few α-arrestin-cargo pairs have been identified. It is technically challenging to identify α-arrestin cargos due to their transient α-arrestin associations and the biochemical nature of cargo.
To identify α-arrestin-regulated cargos, we used Evolutionary Rate Covariation (ERC), which uses sequence-based signatures to identify genes with similar evolutionary histories. We compared ERC rates for α-arrestins with cargos across 18 yeast species. Among the top co-evolving proteins were those previously defined as α-arrestin cargos.
We are determining if the membrane proteins with the highest ERC values are α-arrestin cargos by assessing their

localization and relative protein abundances in wild-type cells versus those lacking the α-arrestin. We have examined over 20 predicted α-arrestin-cargos in yeast and have identified at least 6 new cargo for α-arrestins. This represents a dramatic increase in the α-arrestins regulatory network.

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Hunsu, Victoria
University of Pittsburgh

A machine learning method has been developed recently, and this method enables learning of genome wide regulatory models from population data. This method was applied to the data of a large research study of asthma patients and it has produced a model that classified 36 genes out of 10,375 genes as affecting asthma severity. This research was done in order to access the accuracy, usefulness and applicability of this method to disease modeling. In this research, using independent sources of information we validate the set of 36 supposedly asthma related genes. Firstly, we compare the variances of the asthma related genes and the variances of the non-asthma related genes to validate the genes. Secondly, we compare the asthma related genes to previously published results. And lastly, we explore GTex data that can validate the model. Based on preliminary results we expect that comparing the gene variances will validate our method.

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Fully Automated TIRPAS System Using Picosecond Laser

Linder, S. Eric; Goldschmidt, S. Benjamin
Biomedical Engineering
Duquesne University

Total internal reflection photoacoustic spectroscopy, or TIRPAS, is a relatively new technique that is used as a type of laser excited ultrasonic spectrometer for materials on the nanoscale. We have created an automated TIRPAS system that will gather acoustic data and save the data all within a single platform. We have achieved this by using a combination of an Arduino and LabVIEW software to control the firing of the laser, acoustic wave detection, and prism rotation. As a proof of concept, the system will gather data at several angles of incidence beyond the “critical angle”, or angle that beyond which total internal reflection photoacoustic spectroscopy occurs. This system improves previous iterations of TIRPAS by fully automating the system that reduces testing time and eliminates human error in data collection. Additionally, in this iteration of TIRPAS, a picosecond laser is used that allows for more sensitive measurements to be made from less optically opaque substances sensed in medical applications such as biomarkers in human blood.

6363

A 3D printed Particle Inflow Gun and Integrated Microfluidic System

Steiner, Kyle M.; Li, Minghua; Seadler, Alan W.; Goldschmidt, Benjamin S.
Biomedical Engineering,
Duquesne University

Particle inflow guns (PIGs), notoriously known as gene guns, employ high-velocity, DNA-coated microparticles to achieve gene transfection into a cell monolayer. Such systems tend to cost a significant amount of money, upwards of $10,000, and are created through traditional manufacturing methods. Additionally, transfection typically occurs in standard petri dishes due to inflexibility in the product offering. The aforementioned economic and design barriers have the unfortunate side effect of hindering biolistic research. We have created a particle inflow gun using off the shelf components and low cost 3D printing methods to solve these problems. Additionally, we have created an integrated method to transfect

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Optimizing Radiation Therapy for Esophageal Cancer

Watson, Leonard and Parker, Robert
Department of Computational & Systems Biology, Department of Chemical Engineering
University of Pittsburgh

The purpose of this research is to try to optimize radiation treatments for cancer specifically esophageal cancer. Esophageal cancer is the 8th most diagnosed cancer and one of the most deadly as well. By using the programming language matLab we hope to create an algorithm that optimizes the death of cancerous tumor cells. What this means is we want maximize the deaths of bad, tumor, cells while minimizing the number of good, immune, cells deaths. Doing this can prevent toxicity to the blood, autoimmune responses, and dead due to radiation poisoning and treatment. While creating the algorithm we will take into account certain physiological factors such as volume, vascular fraction and blood flow of an organ as well as cell counts and cell death and regeneration rates. This will help us fine tune

cells within a 3D printed microfluidic construct to reduce contamination and improve microscopic evaluation by standardizing the process onto a microscope slide. Consistent, automated, long term growth of transfected cell monolayers within a low-cost PIG system is possible with these improvements. The project focuses on the use of vegetable cultures transfected with green fluorescent proteins (GFP) as a proof of concept for more advanced techniques.

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Understanding the mechanisms of immunotherapy outcome in metastatic melanoma

Lopez-Rivas, Andres. Benos, Takis. Wang, Shu.
Department of Biomedical Informatics
University of Pittsburgh, iBRIC

Cancer cells use a plethora of inhibitory pathways, which are crucial for the prevention of autoimmunity, to become unrecognizable by the immune system. The blockade of PD-1 pathway, the pathway melanoma cells regularly use, has shown that it can reverse the exhausted T cell state, producing an anti-tumor response. Despite the clinical success of anti-PD-1 therapy, nearly 60% of immunotherapy patients develop resistance. We performed differential gene expression and pathway analysis on publicly available data, in which a total of 49 samples were recollected in pre-treatment melanomas, to investigate the mechanisms that lead to the development of resistance and to identify biomarkers. Antigen presentation, Th1/Th2 activation, OX40 signaling, allograft rejection and dendritic cell maturation were some of the significant pathways found. The immune pathways will be compared with our laboratory results for a deeper understanding of the tumor microenvironment changes and genetic alterations of patients that are resistant to immunotherapy.

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Community-Engaged Learning in the Undergraduate Research Program

Jordan Allen, Joshua Baktay, Marissa Behun, Ansu Benjamin, Patrice Clemenza, Kelsy Coates, Abigail Cox, Riddhi Deshpande, Tova Finklestein, Tiana Fleming Hogan, Adam Gargano, Youngrim Lee, Sarah Leep, Shannon Loftus, McKenna Lohr, Abdullah Malik, Linedia Masson, Janique Miller, Madeline Myers, Bionna Nelson, Makenzie Woltz, Paul Zakutansky, Analise Zapadka, Andrew Magyan, Allyson O'Donnell, and Sarah Woodley.
Department of Biological Sciences, Duquesne University, Pittsburgh, PA

This summer, 23 science majors participated in Duquesne's summer Undergraduate Research Program (URP) while at the same time contributing to science literacy of pre-college students. This program, known as the CIRCLE program (Connecting Interdisciplinary undergraduate Research with Community-engaged Learning Experiences), allowed URP students to practice community-engagement in order to increase students' adaptability, problem solving, discipline-specific knowledge, and sense of civic mission. Some of the undergraduate researchers crafted and shared engaging science activities with middle school-aged youth at a day camp, while others mentored high school students in the lab. Middle school-aged campers were exposed to topics in cell biology, environmental science, and neuroscience, High school students received enriching experiences by working with a near-peer mentor and role model. Through the CIRCLE program, young "scientists-in-training" develop important professional and disciplinary skills and a better understanding of civic engagement, while also increasing science literacy and enthusiasm in Pittsburgh youth.

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Eclipse Ballooning Project

Chu, Grace[1]; Madhani, Janvi[1]; Vazquez, Carlos[2]
[1]Department of Physics
[2]Department of Mechanical Engineering
University of Pittsburgh

On August 21, 2017, a total solar eclipse will pass through the United States for the first time since 1979. NASA is funding around fifty teams across the nation to launch high-altitude balloons that will livestream the eclipse from near-space and be made available online for the general public. The University of Pittsburgh ballooning team will be using this opportunity to study shadow bands—patterns of light and dark bands that undulate across the Earth's surface a few minutes before and after totality. There is speculation that this phenomenon occurs due to atmospheric turbulence. To test this hypothesis, we are designing light sensor arrays that will record data about light

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patterns both on the ground and in the upper atmosphere. Additionally, our payload train contains a 360° camera ring along with filtered and unfiltered cameras that will provide different views of the eclipse.

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Analyzing and Comparing Protein Structure and Dynamics via Computational Methods

Bouhenni, Nassima
Computational and Systems Biology
University of Pittsburgh

Intrinsically disordered proteins (IDPs) are involved in many biological processes. Due to their lack of an ordered three-dimensional structure, studying their structure and function has been challenging. However, due to recent experimental and computation efforts, a better picture of IDPs is emerging. Rather than a stable conformational state, IDPs are better represented by an ensemble of states that implicate both structure and dynamics. We study both these aspects in the context of PAF15, an IDP that regulates DNA replication and repair by binding with proliferating-cell-nuclear-antigen (PCNA). Using Charmm36m force field, we probabilistically model PAF15 temporal dynamics, and study its kinetics before and after binding to PCNA. We also compare the probability model of PAF15 with the probability space defined by the known protein structures, having the same length as PAF15, to comparatively analyze IDP structure. Finally, we develop a python-based tool to seamlessly perform the analysis, and extend it to any IDP.

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Measuring the proton radius at the Paul Scherrer Institute (PSI)

Author: Sneath, Adam
Academic Department: Physics
Duquesne University
URP Summer 2017

The Proton Radius Puzzle is a high-profile issue at the forefront of experimental nuclear physics. There is a discrepancy of seven standard deviations between the proton charge radius as measured by spectroscopic analysis of the muonic hydrogen Lamb shift, and the radius as measured by electron scattering. Resolving the discrepancy will require innovative, high precision, experimental methods or possibly even new physics. The Puzzle inspires the question of whether or not electron-proton (*ep*) and muon-proton (*μp*) interactions are inherently the same, in which case all experimental methods should measure the same radius. The MUon proton Scattering Experiment (MUSE) aims to solve this Puzzle by simultaneously extracting the radius from *ep* and *μp* scattering under identical conditions. During June '17 I traveled to PSI, in Switzerland, to participate in building and testing particle detectors during the prototyping phase of the experiment.

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Development of a microfluidic protocol for fabricating PLGA microparticles for controlled release drug delivery

Walton, Sandra[1]; Schilling, Andrea[2]; Gottardi, Riccardo[2,5]; Little, Steven R.[2,3,4,5]
Ralph E. Martin Department of Chemical Engineering - University of Arkansas[1]
Department of Chemical and Petroleum Engineering[2], Bioengineering[3], Immunology[4], and The McGowan Institute for Regenerative Medicine[5]
University of Pittsburgh

As compared to traditional emulsion-based methods, microfluidics allows for precise size control of polymeric microparticles that encapsulate drug. Microparticle size is a key factor impacting *in vivo* biodistribution and potential for cellular phagocytosis. Optimal, localized drug delivery reduces the required drug load, enhances therapeutic effects, and improves overall safety for patients. For these reasons, a microfluidic method to fabricate poly-lactic-co-glycolic acid (PLGA) microparticles was explored. Two commercial microfluidic chips (Micronit, The Netherlands) with different channel widths (500μm and 100μm) were tested. Larger channels allowed for better stabilization of flow rates providing sufficient control to make microparticles and were better cleared of residual material allowing for reuse. The capacity to encapsulate drug with this approach was verified using a corticosteroid desired for local delivery to the sinuses.

Comparable drug loading to emulsion microparticles demonstrated feasibility of creating monodispersed microparticles with this microfluidic system for controlled release drug administration.

73

A Comparative Study Using Gapped K-mer Features to Predict Enhancer Function in Random Forest and Logistic Regression Models

Higgins, Connor
Kostka, Dennis (Mentor)
Computational Biology Department
TECBIO
University of Pittsburgh

The identification of enhancer regions is an important issue within the field of regulatory genomics as they are known to strongly effect development, differentiation and disease. A wealth of experimental data now exists on known enhancers, presenting an opportunity to employ machine learning algorithms. Alignment-free ML methods often use *k*-mers as features for this purpose but run into issues with statistical noise and overfitting as the value of *k* increases. The insight to use gapped k-mers as features allows ML algorithms to control these issues, however this concept has as yet only been applied to Support Vector Machines (SVMs) [Ghandi, Mahmoud, et al. 2014]. In view of the success of gapped k-mers as applied to SVMs, we aim to design a comparative study evaluating the performance of SVMs, random forest, and L1-regularized logistic regression algorithms employing gapped k-mers. Each algorithm will be run on problems currently faced in enhancer prediction.

74

Preparation of Non-Toxic Water in Oil in Water Double Emulsions for Agricultural and Environmental Applications

Vinik, Sean
Graduate Student Mentor: Urso, Joshua
Faculty Mentor: Gilbertson, Leanne
Environmental Engineering
University of Pittsburgh

The goal of this research is to synthesize non-toxic water-in-oil-in-water (W/O/W) double emulsions that can be used to deliver agriculturally relevant active ingredient loads (e.g. agrochemicals). This is an emerging area of research given the focus of emulsion science is in the areas of petroleum, food, or pharmaceutical industries. Lab experiments aim to identify a combination of constituents that would be kinetically stable for 24-48 hours and contain microspheres with nano-scale diameters. Hydrophilic-Lipophilic-Difference theory was used to guide the design of candidate systems (e.g. relative proportion of stabilizers, water, and oil). Currently, naturally-derived oils, including corn oil and limonene, were used along with low-toxicity surfactants Span 80 and Tween 80. Results indicate that the corn oil based system meets our desired nano-size-requirement and both oil systems do not meet our stability constraint. Ongoing research aims to modify the system parameters, including investigating additional constituents, to obtain the desired W/O/W platform.

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Electronic Structure Calculations of Quaternary Diamond-Like Semiconductors

Deverant, Kristianne; MacNeil, Joseph H.; Glenn, Jennifer R.; Aitken, Jennifer A.

Department of Chemistry and Biochemistry, Duquesne University, 600 Forbes Ave. Pittsburgh, PA 15282

Quaternary diamond-lik**e semiconductors** (DLSs) are compounds that crystalize with structures related to that of diamond and have bandgaps between 0 and ~3.5 eV. The semiconducting properties and inherently non-centrosymmetric crystal structures, make DLSs important in fields such as photovoltaics, non-linear optics and thermoelectrics. In this work, density functional theory was used to compute the total density of states (DOS), partial DOS, band structure and band gap of the compounds $Li_2CdGeSe_4$ and $Li_2CdSnSe_4$. A systematic study was performed to investigate the influence of k-point density on computational cost, band-gap accuracy and DOS composition. Using electronic structure calculations to predict the functional properties of novel DLS can be computationally expensive; this study helps to understand what is really needed. Producing DLSs in the lab can be time intensive; therefore, the use of computations to predict

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Electronic Structure Calculations for Lithium- and Copper-Containing Quaternary Diamond-Like Semiconductors

Radzanowski, Anne, N.; Barton, Christopher, M.; Glenn, Jennifer, R.; MacNeil, Joseph, H.; Aitken, Jennifer, A.
Department of Chemistry and Biochemistry
Duquesne University

Quaternary diamond-like semiconductors (QDLSs) have practical applications in diverse areas, such as photovoltaics and non-linear optics. QDLSs are highly flexible in their composition, and electronic calculations allow for the prediction of trends, assisting in the targeted synthesis of novel compounds with desired properties. Electronic structure calculations have been completed for Cu_2MgGeS_4, Cu_2MgSiS_4, Cu_2CdSiS_4, $Li_2CdGeSe_4$, and $Li_2CdSnSe_4$. The density functional computational package WIEN2k was used to determine electronic band structures and partial densities of states for each of the compounds. Specific focus was placed on the differences between copper and lithium as the +1 cation. Analysis of the partial density of states revealed that copper *d* orbitals heavily influence states at the top of the valence band, whereas lithium makes no significant

compounds with desired qualities can save time and resources.

contributions near the Fermi level. The contributions of the copper *d* orbitals result in a significant narrowing of the band gap. Contributions from other elements have also been examined.

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New Route Construction Algorithm for Exploration of a City

Torres, Jaziel
Department of Biomedical Informatics — Department of Computer Science University of Puerto Rico — University of Pittsburgh

Recognizing the extensive use of recommendation systems, the problem of obtaining the best piece of information/advice that satisfies a set of conditions is important and challenging. Within the Urban Informatics our work provides a way to find and recommend a route for visiting a set of venues, selected from a diversified list of user-relevant venues. This is an instance of the constraint satisfaction problem where two venues of the same type are not visited one after the other (neighboring constraint) and the route cumulative exhibits the highest relevancy. We are investigating a different approach than the standard one based on Breath First Search (BFS) that visualizes the algorithm as a spiral traversal rather than a tree. Its basic idea is to construct the shortest cyclic path that satisfies the neighboring and relevancy constraints and passes through all venues and then selecting the first in the path.

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Separation techniques for natural products

Tucci, Halie; Iuliucci, Robbie
Chemistry Department
Washington & Jefferson College

As the need for an alternative to fossil fuels continues to increase, researchers are looking to plants for help. Endophytic fungi, which live symbiotically with the host plant, have been found to produce volatile organic compounds (VOCs), which may serve as a viable biofuel. It is critical to identify the chemical structure of VOCs to properly understand the endophyte-host phylogenesis. This discovery opens the door for the possible production of desirable biofuels. Prior to identification, the compounds must be separated, which is challenging due to their structural similarity. The focus of this study is to determine an effective method to separate natural products beginning with a simpler approach of thin layer chromatography (TLC) and moving then to high pressure liquid chromatography (HPLC) and gas chromatography with mass spectra (GC-MS). The approaches are applied to a metabolite mixture from endophytes extracted from *taxodium ascendens* (pond cypress).

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Solid-state NMR of pharmaceutical polymorphs

Stuchell, Sarah; Iuliucci, Robbie
Department of Chemistry
Washington & Jefferson College

Polymorphs of pharmaceuticals pose a problem due to differing physiochemical properties, such as solubility, stability, and even drug efficacy. Structural studies of drugs are important to identify the chemical relationship between polymorphic properties. Solid-state NMR offers various ways to analyze the structure of drug polymorphs. Because microcrystalline samples are suitable for solid-state NMR, the method is complementary to diffraction techniques. Crystal structures can also be determined by NMR crystallography assisted by magic angle turning (MAT) and anisotropy measurements. Thermal transitions of polymorph structures can be observed through variable temperature NMR. Spin-lattice relaxation is polymorph dependent, and can be used to further characterize properties of individual polymorphs. The focus of this study is to use solid-state NMR techniques to analyze and identify polymorphs of the pharmaceuticals Carbamazepine and Erlotinib. Variable temperature ^{13}C and natural abundance ^{15}N MAT spectra will be presented along with ^{13}C detected ^{1}H T_1 measurements.

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Modeling of organophosphonic acids on the 101 surface of α-quartz

Wilson, Brandon[1]; Iuliucci, Robbie J.[2]; Evanseck, Jeffrey D.[1]
[1]Center for Computational Sciences and Department of Chemistry and Biochemistry; Duquesne University, Pittsburgh, PA
[2]Department of Chemistry; Washington & Jefferson College. Washington, PA

Surface chemistry of metal oxides is modeled through the use of the gauge including projected augmented wave (GIPAW) method of predicting nuclear magnetic resonance (NMR) parameters. The $^{31}P/^{29}Si$ NMR chemical shift anisotropies can reveal the bonding motifs of organophosphonic acids adsorbed to the surface of silica. In the present study, the density functional theory (DFT) method was used with generalized gradient approximation (GGA) functionals and plane wave basis sets to optimize, and subsequently perform NMR computations on, slab models of various modes of propylphosphonic acid adsorption to the 101 surface of α-quartz. Binding energies of each mode were determined to further characterize the method of bonding. Optimal slab model parameters, including k-point mesh and thickness, were also explored. Organophosphonic acid monolayers on metal oxide surfaces, such as the system studied, can be functionalized for many applications, including as protective barriers for the prevention of the shuttle effect in Lithium-Sulfur

batteries.

81

The Effect of Various Functional Groups on the Anhydrous Proton Transport of Graphane

Livingston, Joshua R.; Bagusetty, Abhishek; Johnson, J. Karl
Department of Chemical and Petroleum Engineering
University of Pittsburgh

Proton transport phenomena has been of tremendous importance for the application of proton transport membrane (PEM) fuel cells for their efficiency and clean emissions. We are specifically focused on the applications of proton transport at interfaces for a better design of new materials for PEM cells in anhydrous conditions. Study of proton transport over the surface of hydroxylated graphane in anhydrous conditions has been performed recently using density functional theory. This suggests that other functional groups, in addition to or instead of hydroxyl groups, may have comparable proton transport properties when combined with graphane. Four functional groups were considered and simulated in a variety of patterns and combinations: carboxylic acid, sulfonic acid, primary amine, and thiol. Ab-initio molecular dynamics (AIMD) simulations were used to determine the dynamic properties. Stability of the functionalized graphane material for varying degree of hydroxylation and morphological defects will be reported.

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Roman Segarra, Kevin

Diabetic ketoacidosis (DKA) is a complication of diabetes that occurs when the body fails to use sugar as an energy source. Patients who enter to ICU with this condition are also at risk of suffering from Acute Kidney Injury (AKI). We want to find out if AKI affects the length of stay of DKA patients in the ICU. Knowing this information could help to improve the monitoring and treatment of DKA patients to prevent AKI complications and reduce the length of stay of those patients. DKA patient's data comes from the MIMIC-III database. Cox models were used to test if AKI in DKA patients is associated with longer stays in the ICU. We will use machine learning to corroborate if this was true, and what other factors contribute to longer stays in the ICU.

83

The Effect of an Anti-Inflammatory Drug-Loaded Nanoemulsion on Axonal Regeneration

Hudson, Bridget[1]; Lee, Youngrim[2,4]; Summers, Austin[5]; Stevens, Andrea[2,4]; Saleem, Muzamil[2,4]; Janjic, Jelena[3,4]; Pollock, John[2,4]
[1]Cardinal Wuerl North Catholic High School, Cranberry Township, PA
[2]Department of Biological Sciences, Duquesne University, Pittsburgh, PA
[3]Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA
[4]Chronic Pain Research Consortium, Duquesne University, Pittsburgh, PA
[5]Pittsburgh Science and Technology Academy, Pittsburgh, PA

The study of axonal regeneration is observed through a rat following a chronic constriction injury on the right sciatic nerve. Once a nerve is damaged, it begins a process of self-repair. The degeneration of the injured nerve is aided by several immune responses in the body including Schwann Cells and macrophages. The infiltrating immune cells engulf the degenerating distal axon allowing room for axonal regeneration. It is known that these immune responses cause inflammation, therefore slowing down the process of regeneration and causing neuropathic pain. The Pollock group works in collaboration with Jelena Janjic, who has developed a nanoemulsion loaded with anti-inflammatory drug, Celecoxib, which influences macrophage inflammation. To study the effect of the anti-inflammatory drug on axonal regeneration we used immunohistochemistry to visualize proteins involved in axonal regeneration. Through this process, we are able to study if the nanoemulsion increases regeneration in the damaged axon.

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Using experimental evolution to evaluate compensatory gene expression level changes and gene mutations in yeast arrestin knockout strains

Morrissey, Alexis
Clark, Nathan
Computational Biology Department
University of Pittsburgh

S. cerevisiae is a single-celled eukaryotic model organism known for its versatility in genetic engineering applications. In our study, we utilized a yeast strain with nine of the eleven genes encoding for arrestins knocked out in order to study these proteins. Arrestins are adaptor proteins necessary for the ubiquitination of various transmembrane proteins and play a vital role in development and stress response. Dysregulation or mutations in arrestins can cause a host of diseases in humans including inflammatory, cardiovascular, and optical diseases. We believe that a yeast strain containing a knockout of the genes encoding arrestins will compensate on a genetic level through both genomic mutations and gene expression level changes. Using RNA-Seq analysis on knockout strains, we examined the compensatory gene expression level changes that took place. Additionally, experimental evolution was performed on the strains to examine compensatory mutations that resulted in increased fitness in the knockouts.

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Quantifying Changes in the Spatiotemporal Morphology of Mitochondria in the Presence of *Listeria Monoctyogenes*

Mrosek, Miller; Chennubhotla, Chakra; Quinn, Shannon
Department of Computational and Systems Biology
University of Pittsburgh

Mitochondria play a vital role in basic cellular function. They constantly undergo fusion and fission and these cycles of fusion and fission allow the mitochondria to adapt their morphology to meet the needs of the cell. Due to the importance of healthy mitochondrial function, understanding of the underlying mechanisms behind stimuli that induce mitochondrial abnormalities is imperative. Research conducted over the past few years has shown that the pathogen *Listeria monocytogenes* alters mitochondrial dynamics by causing transient mitochondrial network fragmentation. The direct cause of this fragmentation remains unclear. The aim of our research is to quantify the fragmentation of the mitochondria upon introduction of *L. monocytogenes* to HeLa cells. We have developed metrics to quantify this fragmentation for videos containing multiple HeLa cells and are currently working on a cell segmentation pipeline.

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Synthesis and Characterization of Lithium-Containing Quaternary Sulfides

Asia J. Parker, Chris M. Barton, Jennifer A. Aitken, Ph.D.
Department of Chemistry and Biochemistry at Duquesne University

Lithium-containing quaternary sulfides are an area ripe for development, due to there being fewer of these compounds than their heavier alkali metal counterparts. Recently, significant second harmonic generation and outstanding laser-induced damage thresholds have been observed for several lithium-containing quaternary sulfides, such as Li_2CdGeS_4. Several materials are being targeted for synthesis, including heavier alkaline earth-containing analogues of compounds, which have been recently prepared by members of the Aitken research team. A series of high-temperature, solid-state reactions were carried out to target new materials by adjusting synthetic variables such as temperature, time, and stoichiometric ratios. Reaction products were characterized with X-ray powder diffraction and scanning electron microscopy/energy dispersive spectroscopy.

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Crystallography, Crystal Growth and Crystal Properties: Creating a Guided Inquiry Module for Use in a High School Outreach Program

Kodjo, Gildas; Collinger, Justin; Aitken, Jennifer A.
Department of Chemistry
Duquesne University

Crystallography is the experimental science of determining the arrangement of atoms in crystalline solids. A crystal is a solid material whose constituents are arranged in a highly ordered microscopic structure, forming an infinite lattice that extends in all directions to build up the macroscopic crystal. In this learning module, concepts and techniques related to crystallography will be introduced at the high school level. Students will grow blue copper (II) sulfate pentahydrate crystals by the fast cooling and slow evaporation methods. These are the same crystals that were used in some of the first crystallography experiments conducted in 1912. In addition, they will study diffraction of a laser through a diffraction grating simulating how crystallographers study the structure of crystals with X rays. We anticipate to create a successful lab module that schools can use to understand the concepts and techniques used in modern research laboratories, such as the Aitken laboratory.

88

Study of Strange Quarks Using Kaons

Mireille Muhoza
Physics Department
Duquesne University

Strange quarks and antiquarks contribute to the spin structure and orbital angular momentum of protons and neutrons. Previous experiments in labs such as SLAC at Stanford, DESY in Germany, and CERN in Switzerland studied the contribution of the three light quark pairs to the nucleon spin. To increase the precision on these measurements, a new Ring Imaging Cherenkov (RICH) detector is under construction for the CLAS12 detector at Thomas Jefferson National Accelerator Facility Laboratory here in the US. Our group will use semi-inclusive deep-inelastic scattering (SIDIS) of electrons on a polarized proton target to study kaons. Kaons are short lived particles built of strange quarks in their ground state. I studied the relativistic kinematical coverage of scattered electrons and kaons in the SIDIS process and their simulations in relation to the designed RICH detector to access the proposed precision measurements.

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Modeling interventions in causal networks to enrich constraint-based causal search

Dilán-Pantojas, Israel O. 1; Andrews, Bryan 2; and Cooper, Greg2
Department of Biomedical Informatics University of Puerto Rico 1, University of Pittsburgh2

From uncovering potential cell signaling pathways to modeling weather patterns, Causal Discovery tries to answer one of the fundamental questions of Scientific Research, "what are the underlying causal relations that determine how a system behaves?". This can be done by utilizing Causal Discovery algorithms such as the constraint-based search Fast Causal Inference (FCI). The goal of constraint-based algorithms such as FCI is to construct a causal network from a given dataset, whilst handling latent confounding. When approaching this task, traditional methods treat all data as observed; thus they cannot accurately represent interventional information. Consequently, because we are not able to extract all the information from observational data alone, the networks derived can be ambiguous. By modeling interventions on the observational variables within the search algorithm, we drastically improve the accuracy and richness of the generated causal network.

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Serotonin transporter

Israa Abdulmuttaleb
Elizabeth Castellano
Dr. Michael Cascio
Department of Chemistry & Biochemistry
University of Duquesne

Serotonin transporters are integral transmembrane proteins responsible for the reuptake of serotonin from the synapse to the presynaptic neuron. Dysregulation of serotonin concentrations in the synapse can lead to several psychological diseases such as depression and anxiety. The long-term issue investigated in this study is the allostery of the protein when it reuptakes serotonin back into the cell. To study this, single cysteines are introduced on the loops of the protein and after expressing the protein, a MTS-benzophenone crosslinker will form a disulfide bond to the cysteine mutation. The protein can be stabilized in different states before photoactivating the benzophenone to form a second random crosslink, and the results will be compared with each other to determine protein movement. In my initial studies, we mutated S190, and A622C using PCR mutagenesis as the first step in achieving our overall goals. This research will increase our knowledge of the structure of serotonin transporters and can potentially be used to develop better medications for people who have depression and anxiety.

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“Determination of Pesticide Residues in Herbal Supplements”

Beres, Danielle; Miranda, Colette & Wilson, Kylie; Wetzel, Stephanie
Department of Chemistry and Biochemistry at Duquesne University

Herbal supplements are often used for their putative health benefits. Though because there is limited regulation, little data about possible pesticide residue contamination is known. In this study, common herbal supplements such as Gingko Biloba, Green Tea, Gotu Kola, Ginseng Complex, and Moringa Pure were analyzed using gas chromatography- mass spectrometry (GC-MS) methods and extraction methods. The extraction method was optimized for the amount of supplement and extraction solvent. Methanol and Methylene Chloride were found to extract the most compounds. In a few supplements caffeine and food additives, for example, enhancing specialists were discovered.

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Synthesis of Novel Aminoethanol-Based Pincer Complexes for Gas Phase Studies of Structure and Reactivity

Liddell, Zayauna; Tatosian, Irena; Patterson, Khiry and Van Stipdonk, Michael
Department of Chemistry, Duquesne University

Chelating agents are ligands that form multiple coordinate bonds to a metal cation. Pincer ligands are a specific type of chelating agent that bind metal cations from three coplanar sites, and are important because they can mediate and/or catalyze a variety of chemical reactions. In this study, a group of new pincer-type complexes were synthesized and characterized in the gas phase using a linear ion trap mass spectrometer. The pincer ligands were created using condensation reactions between mono and dialdehydes and primary, secondary, and tertiary amines and coordinate group II and first row transition metal cations. The synthesis procedure will be described, as will the formation of ions by electrospray ionization and the collection of single and tandem mass spectra from the respective compounds.

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"Stabilization of He-Ne Laser Wavelength Through Circuit Mediated Power Control"

Beeson, Bryonna; Mittal, Jenna; Madelyn Hoying; Isaac Davies; Corcovilos, Theodore
Department of Physics
Duquesne University

A common problem with Michelson Wavemeters, a device used for measuring laser wavelengths, is a lack of stability with regard to wavelength. To fix this problem a circuit that controls the power input to the laser, which in turn controls the temperature, was built. By controlling the temperature, the wavelength of the laser is more stable. The circuit is controlled using a digital PID feedback method. The circuit was successful in stabilizing the laser's temperature, making the wavelength of the laser more stable.

94

Cloning of the human relaxin 2 (*RLN2*) promoter for *in vitro* expression studies to investigate susceptibility to preterm birth

Loughner, Lindsay G.; Carnahan-Craig, Sarah J.; Pollock, Taylor; Zapf, Rachel; Jensen-Seaman, Michael I.
Department of Biological Sciences
Duquesne University

Relaxin 2 (RLN2) is a peptide hormone produced primarily in the corpus luteum during pregnancy. It is involved in various aspects of the birth process, such as the loosening of pelvic ligaments, cervical ripening, and uterine quiescence. Increased levels of serum RLN2 decrease the tensile strength of fetal membranes and may cause early rupture, resulting in preterm birth. This study investigates the functional consequences of variation at a single nucleotide polymorphism (SNP) and a $(CT)_n(GT)_n$ microsatellite repeat within the promoter of *RLN2* on expression of this gene. To do this, seven different haplotypes from a diverse human panel were cloned into a luciferase reporter vector and then transfected into a human trophoblast cell line. Expression was measured by luciferase activity. The effect of SNP and microsatellite variation on transcription will be discussed, along with potential future applications.

95

Characterization of Novel Lithium-containing Quaternary Diamond-Like Semiconductors for Nonlinear Optical Properties

Kotchey, Joshua; Stoyko, Stanislav S.; Aitken, Jennifer A.
Department of Chemistry and Biochemistry
Duquesne University

Diamond-like semiconductors (DLS) have applications in thermoelectrics, solid-state electrolytes, photovoltaics, and nonlinear optics. Quaternary DLSs possess the formulas, I_2-II-IV-VI_4 and I_4-II-IV_2-VI_7 and those with I=Li and VI=S are promising candidate non-linear optical materials because they generally display wide optical bandgaps which tend to favor high laser-induced damage thresholds. The compounds in this work were prepared by stoichiometric reactions of the elements in sealed, fused-silica tubes via high-temperature, solid-state syntheses using programmable furnaces. All reaction products were analyzed by X-ray powder diffraction (XRPD) to determine the phase purity of the samples. Single crystal diffraction was used to solve and refine the structures of several new compounds. Optical diffuse reflectance UV-Vis-NIR spectroscopy was used to estimate the bandgaps of the compounds and in combination with attenuated total reflectance FT-IR spectroscopy the transparency of the new materials was assessed. Differential thermal analysis (DTA) data helped to optimize the reaction heating profile leading to more phase-pure products.

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Identifying target genes of the homeobox transcription factor Gsx1 in zebrafish

Zoë A Dobler[1], Regina L Patrick[1], and Sadie A Bergeron[1]
[1]Department of Biology, West Virginia University, Morgantown, WV, USA 26506-6057

GS homeobox 1 (Gsx1) transcription factor regulates the development of neurons for prepulse inhibition (PPI), a sensorimotor gating phenomenon disrupted in schizophrenia and ASD. However, the molecular genetic pathways underlying development and function of Gsx1-expressing neurons across the CNS are not yet fully understood. A few already identified Gsx1 target genes are implicated in proliferation, migration, and specification of neural progenitors. We hypothesize that genes implicated in neurodevelopmental disorders with PPI and other sensory processing deficits are targets of Gsx1. *In silico* analysis identified putative Gsx1 binding sites upstream of zebrafish orthologues of mammalian target genes as well as schizophrenia-related genes. We are thus examining the expression of these genes in wild type and *gsx1* mutant zebrafish by *in situ* hybridization. This work will validate that genes regulated by Gsx1 in mammals are conserved in zebrafish, and that genes implicated in schizophrenia are both direct and indirect targets of Gsx1.

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What Can You Do with a Bag of Bones: Human Skeletal Remains from Rhodes

Lohr, McKenna; Ludvico, Lisa Ph.D.
Forensic Science and Law Program
Duquesne University

When excavating a site, archaeologists place emphasis on different items. At the Flevaeis Plot in Rhodes, the emphasis was placed on ceramics instead of the human skeletal remains found, which were warehoused in plastic bags for several years. The translated archaeological report indicates two graves containing six-to-seven skeletons each with associated grave goods ranging from 3200 BCE to 650 CE, indicating potential occupation by several cultures. Osteological analysis of the remains brought to Duquesne University determined there were twelve bones total, possessing very little, if any, fusion lines, arthritis, and nutritional deficiencies – indicating healthy young adults at time of death. Based on side, size, and original grave of each bone, there are at least four individuals. A decalcification/extraction protocol from the Human Identification Center at UNT has been carried out and a mtDNA mini primer set created by AFDIL is currently being used to amplify and sequence the extracted DNA.

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Biophysical Characterization of a G-quadruplex Structure on the FMR1 Gene at Exon 12

Cannanbilla, Pranav; Demarco, Brett; Imperatore, Josh; Mihailescu, M. Rita
Department of Chemistry and Biochemistry
Duquesne ~~Unviersity~~University

Fragile X syndrome (FXS) is an inherited form of mental impairment, caused by a trinucleotide expansion within the Fmr1 gene, leading to the loss of expression of the fragile X mental retardation protein (FMRP). FMRP is a RNA-binding protein whose arginine-glycine-glycine (RGG) domain binds with high affinity and specificity to the G-rich regions of RNA that form G-quadruplex structures. The *Fmr1* mRNA can undergo alternative splicing producing several isoforms whose biological functions are not fully elucidated. The mRNA encoding for the longest FMRP, isoform 1, has a G-rich region at the junction of exon 12 and intron 13, predicted to form a G-quadruplex. Prior studies found potential down-regulation of the FMRP isoforms which contain exon 12 when fused in sarcoma (FUS), whose RGG domains also bind to G-quadruplexes, is present with the *Fmr1* mRNA. Native PAGE, circular dichroism (CD) and 1H NMR spectroscopy were used to characterize this G-quadruplex structure.

99

Natural Gas-in-Oil Foams and Natural Gas-in-Water-in-Oil Foams for Hydraulic Fracturing

Horvat, Eliza; Enick, Robert
Department of Chemical and Petroleum Engineering
University of Pittsburgh

There are some “water-sensitive” shale formations that should not be fractured with aqueous solutions because the water can reduce the permeability of the fractured rock. We therefore propose that one can use high-pressure natural gas from neighboring wells as the main component of a waterless fracturing fluid. However, the low viscosity of methane reduces fracture size. Therefore, we propose to “thicken” natural gas by generating methane-in-oil foams or methane-in-water-in-oil composite foams (which utilize very small amounts of water). It has been previously reported that gas-in-oil foams can be stabilized with oil-soluble fatty acid methyl esters, therefore glycerol monostearate was dissolved in squalane and its ability to generate foams was assessed. It was hypothesized that both an oil-soluble surfactant along with a water-soluble surfactant were needed to stabilize gas-in-water-in-oil composite foams. Several surfactants were assessed for this application, and the most promising surfactants were used to generate high-pressure methane-in-water-in-oil foams.

100

Expression of recombinant human and chimpanzee peptides for functional analysis

Majors, Jasmine N[1].; Hockman, Megan R[2].; Loughner, Lindsay G[2].; Jensen-Seaman, Michael I.[2]
[1]Pittsburgh Science and Technology Academy, Pittsburgh, PA 15213
[2]Department of Biological Sciences, Duquesne University, Pittsburgh, PA 15282

Several prominent male reproductive proteins appear to be evolving rapidly in humans and our closest relatives, including chimpanzees and gorillas, likely due to intense natural or sexual selection. In particular, among these are the extracellular semenogelin proteins (SEMG1 and SEMG2) which are the most abundant proteins in human semen. They are putatively substrates for a prostate-specific transglutaminase enzyme, TMG4. In order to determine if the numerous amino acid differences among species primate species have functional consequences, we produced recombinant peptides corresponding to parts of the SEMG1 protein in humans and chimpanzees. We then tested these peptides for their ability to act as substrates in a transglutaminase reaction.

101

An Automated Image Analysis Pipeline for Measuring Microenvironmental Heterogeneity in Colon Tumor Whole-Slide Images

Dang, Brian; Nguyen, Luong; Chennubhotla, Chakra
Department of Computational and Systems Biology University of Pittsburgh

With the robust computation capabilities of modern machines, the study seeked to create an automated image analysis pipeline in order to quantify the diversity of cell types in colon tumors and associate the metrics with prognosis. The pipeline begins with images of hematoxylin and eosin stained colon tumors from the TCGA dataset. Each whole-slide image undergoes Stony Brook University's nuclei segmentation program. Imperfect segmentation was improved by combining multiple segmentations derived from using different otsu ratios. Furthermore, a watershed segmentation was applied to segmentations exceeding a designated size. Upon completion of segmentation, features of a nucleus were extracted such as area, perimeter, and eccentricity. Using ground truths, the study employed machine learning to classify the cells as either epithelial, immune, or fibroblast. Finally, the study measured microenvironmental heterogeneity by grouping equivalent cell types together via the DBSCAN algorithm and measuring distances between the groups. Additional metrics will be developed overtime.

102

Conductive Filament Formation and Dissolution in a Polymer Electrolyte for an Optically Reconfigurable Metamaterial

Radka, Brian; Chao, Zhongmou; Fullerton, Susan
Department of Chemical and Petroleum Engineering University of Pittsburgh

A promising method for creating a reconfigurable metamaterial that could change its optical properties on demand involves assembling an ordered array of metal nanoparticles within a polymer electrolyte. By applying an external electromagnetic field, metal filaments can form and dissolve between the particles. The kinetics of the filament formation are studied in a simplified system where a silver substrate serves as one electrode and a conductive AFM tip serves as the other with a polymer electrolyte between (polyethylene glycol diacrylate (PEGDA), ionic liquid (IL), and $AgPF_6$). Conductive AFM is used to create and destroy the filaments by applying a voltage bias and AFM nano-mechanical mapping is used to quantify Young's modulus. Reducing the PEGDA:IL mass ratio from 90:10 to 50:50 decreases the average formation time from > 300 to 13.6 seconds and reduces Young's modulus from > 2 GPa to 476 Megapascals..

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Use of a SapA Protein Fusion for Pertussis Toxin Vaccine Delivery

Myers, Madeline; McCormick, Joseph
Department of Biological Sciences
Duquesne University

This study aims to develop an alternative method of vaccine delivery through the use of spore-associated proteins of *Streptomyces coelicolor* as a potential vehicle to carry the major pathogenic determinant from *B. pertussis*. The major goal of this project was to create a fusion of pertussis toxin PtxA to the C-terminus of the SapA protein. A fusion was constructed using the spore-associated protein SapA because it is secreted through the standard signal sequence-dependent pathway. Once the strain expressing the fusion has been isolated, it will be analyzed using various methods, including: SDS-PAGE and Western blot analysis using a commercial polyclonal antibody to PtxA and testing in a mouse model. In the future, the use of Sap protein fusions to passenger proteins might lead to recombinant *Streptomyces* with epitopes displayed on the spore surface creating an additional method of vaccine delivery.

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Isolation and characterization of a spore shape determination gene mutant in *Streptomyces coelicolor*

Orr Erin L[1], Kandell Garrett V[1], Bennett Jennifer A[1], McCormick Joseph R.[2]
[1]Otterbein University, Department of Biology and Earth Science, Westerville, OH
[2]Duquesne University, Department of Biological Sciences, Pittsburg, PA

Gene disruption by PCR targeting was used to isolate a deletion-insertion mutation of a gene in a cosmid from *Streptomyces.* The specific *S. coelicolor* gene analyzed is known as *ssdA*, which is a spore shape determination gene. This gene was previously identified through random transposon insertion mutagenesis and the mutant was observed to be delayed for sporulation as well as having heterogenous shaped and sized spores. The transposon insertion truncated the gene, but left a large portion intact. A complete deletion mutation was isolated by PCR- directed mutagenesis of the wild type gene on a cosmid to determine if the complete deletion resulted in a similar phenotype compared to the insertion mutation. The gene was replaced with an antibiotic marker and the mutant *S. coelicolor* strain was attained with the *ssdA* deletion. In the future, the phenotype of the deletion mutation will be compared with the original insertion truncation mutant.

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Characterization of Spore-Associated Protein A Assembly onto the Spore Surface in *Streptomyces coelicolor*

Fleming Hogan, Tiana; Ghosh, Anita; McCormick, Joseph
Department of Biological Sciences
Duquesne University

Streptomyces is a soil-dwelling bacteria that is known for its production of antibiotics. *Streptomyces coelicolor* has a complex life cycle that involves sporulating aerial hyphae. *S. coelicolor* has spore associated proteins that are secreted and localized to the spore coat. Previously, recombineering was used to fuse the gene for *E. coli ltb* to 3' end of *sapA* and conjugated into *S. coelicolor*, and a full length SapA fused to Ltb was shown to be secreted and localized to the spore surface. The goal was to learn more about SapA by characterizing different Ltb fusion mutations to better understand its incorporation in to the spore coat. Currently, we are trying to further characterize the secretion and localization pattern of the ltb to sapA fusion by performing an in frame deletion of a conserved motif (CGSGY) in the SapA protein sequence, a C-terminal truncation of 38 amino acids, and a complete deletion of the gene. With more understanding of SapA secretion and assembly onto the spore surface it could provide a future alternative vaccination mechanism.

106

Elucidating translational regulatory pathways during early embryonic development

Okerstrom, Kieran and Lee, Miler
Department of Biological Sciences
University of Pittsburgh

During early embryogenesis, gene expression is controlled by a carefully timed concert of genetic and epigenetic factors. While effective translational regulation of mRNA is crucial for development, the mechanisms of regulation are not fully understood. In previous work, it was found that some mRNAs contain regulatory sequence patterns in their untranslated regions; however, it remains unclear whether these sequence patterns are relevant to early embryonic development. Our research project identifies sequence patterns that may confer regulatory effects during the maternal-to-zygotic transition, which is an early stage of embryonic development. To do so, gene expression was analyzed at various developmental time points, and the nucleotide contents of those genes were analyzed to search for patterns which have been found in other mRNAs. The elucidated translational regulatory mechanisms may be relevant to the maintenance of pluripotency in stem cells, which have been shown to have similar regulatory mechanisms as a developing embryo.

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3D-BrainView: A Visualization of the Human Brain

Nicole Matamala and Art Wetzel
TECBio REU and Pittsburgh Supercomputing Center
Carnegie Mellon University

Automation of brain tumor segmentation from MRI images, along with significant tracking of tumor growth, would aid a radiologist in diagnosing a patient, ideally with higher precision, accuracy, and speed. Such a computer program, created alongside the radiologist, surgeon, and/or physician, would revolutionize the medical community and the standard for diagnosing brain tumors and/or other abnormalities. With this future goal in mind, the 3D-BrainView (or 3BV) program is to convert a 2 – dimensional MRI image series into an interactive 3 – dimensional model, where internal cranial structures are spatially arranged and all MRI images are embedded. For a specified MRI series, each of the internal cranial structures are computationally segmented, compartmentalized, and labeled in a 3D model, where time taken is dependent on the size of the series. As of now, 3BV creates an accurate surface model from a single MRI series.

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TO BUILD A VIRAL CAPSID AND COMPLEXITY INVOLVED IN PATHWAY FROM PRE-EQUILIBRIUM TO EQULIBRIUM ASSEMBLY SYSTEMS

OKETUNJI OLUWAFERANMI DAVID[1]
SCHWARTZ RUSSELL[2]* (RESEARCH MENTOR)
[1] Department of Chemistry, Lincoln University of Pennsylvania
[2*] Russell Schwartz
Professor of Biological Sciences and Computational Biology
co-Director, Carnegie Mellon/University of Pittsburgh
Joint Ph.D. Program in Computational Biology
Carnegie Mellon University

~~**Abstract**~~

As computational and mathematical skills become increasingly pivotal to analysis of complex reaction systems, it will become ever more important to identify the assumptions our models must make and using simulation and comparison to indirect experimental measures (such as light scattering experiments), the goal is to understand the kinds of assembly pathways available to different viruses. We use two model types for this study: ordinary differential equation models, which allow us to compare the accuracy of capsid models under different degrees of simplification precisely and deterministically, and stochastic discrete event simulations, which allow us to sample use of reaction intermediates across a wide parameter space allowing for an extremely large number of possible reaction pathways. We are also interested in investigating amyloid aggregation which also involves protein subunits. Amyloid diseases include Huntington's disease and Alzheimer's.

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The Influence of Race on MBC outcomes in Women with Her 2 positive Metastatic Breast Cancer (Her 2+MBC)

Authors: Rosenzweig, Margaret; Khan, Amin
Department: School of Nursing
University: University of Pittsburgh

Background: With the changing paradigm of MBC as a chronic, treatable disease, particularly in Her2+ MBC, it is important to assess the influence of race on survival outcomes among women with not curable, but highly treatable disease.

Methods: We retrospectively compared the cohort of Black patients with matched (2:1) White patients for: age (within 5 years), ER status, and date of metastatic diagnosis within 3 specific time spans (1999-2005, 2006-2011, and 2012-2017).

Results: There were n=24 Black patients with Her 2 positive MBC matched to n=48 White Her 2+ MBC patients. Overall survival after MBC until death (or censored at June 30, 2017) for Black patients was 33.8 months and 48.2 months for White patients.

Discussion: Although the sample of black women with Her 2 + MBC was small, the aspect of race alone profoundly influences MBC survival. A prospective analysis of Black women with MBC must be further examined.

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Exploring the Potential Bistability of CaMKII using Rule-Based Modeling

Grundy, McKenzie K.; Kaya, Cihan; Faeder, James R.
Department of Computational and Systems Biology
University of Pittsburgh School of Medicine

Calcium/calmodulin-dependent protein kinase II (CaMKII) is a dodecameric holoenzyme found in high abundance in the synapses of the brain. There is strong evidence that CaMKII plays a significant role in the process of memory and learning, and might also function as a molecular switch underlying long-term memory. A better understanding of the molecular mechanisms of CaMKII activation might lead to development of therapeutic treatments for memory-related diseases. However, conventional ordinary differential equation (ODE) based modeling methods struggle to fully capture the complexities of CaMKII activation. Recent studies have shown that the number of subunits can fluctuate and affect its activation kinetics. Here, we used the rule-based modeling software, BioNetGen, to simulate the activation of CaMKII and search for bistability within the system. Models of CaMKII were created with a different number of subunits in each. The parameters of the system were varied in each of the models and then examined for regions of bistability.

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Temperature and Wavelength Laser Stabilization Circuit Using Arduino Microcontroller

Mittal, Jahnavee [1], Hoying, Madelyn [1], Beeson, Bryonna [2], Davies, Isaac [1], Corcovilos A. Theodore [1]
[1] Department of Physics at Duquesne University
[2] SEED program Shaler High School

To find the wavelength of an unknown laser, one can compare a reference laser's wavelength to that of the unknown laser. But, the reference laser's wavelength must be stable to within a part-per-million for use in spectroscopy. The dominant source of long-term instability in the wavelength is caused by temperature drifts and thermal expansion of the laser cavity. In order to improve wavelength stability, a successful circuit was built using an Arduino PID microcontroller. This circuit measures the polarization of the laser's light, which is related to wavelength, and uses the signal to feedback to the temperature of the laser. We describe the circuit in detail and discuss the optimization of the measurement system.

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Stabilizing a reference laser for a modified Michelson interferometer

Hoying, Madelyn; Mittal, Jahnavee; Beeson, Bryonna; Corcovilos, Theodore Department of Physics Duquesne University

Controlling the wavelength of a laser to high precision has a wide range of applications in spectroscopy and metrology. With a simple ratio, a stabilized laser can be used to determine the wavelength of an unknown laser to that same precision. The helium-neon reference laser for a modified Michelson interferometer was successfully stabilized using a digital proportional-integral-derivative (PID) controller implemented using an Arduino microcontroller. Our PID controller uses three variable parameters to provide a feedback mechanism that controls a heater inside the laser. By controlling the temperature of the laser, we can vary the length of the laser cavity and the wavelength of the emitted light. The polarization of the laser was measured as a proxy for the wavelength, and when the polarization changed, the PID controller changed the output of the heater to return the polarization and therefore the wavelength back to its original value.

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Finding sparse universal hitting sets for long k-mers

Fiyinfoluwa Gbosibo[1,2], Dan DeBlasio[3], Guillaume Marçais[3] Carl Kingsford[3]

[1] Internship in Biomedical Research, Informatics, and Computer Science (iBRIC), University of Pittsburgh

[2]Math and Computer Science Department, Lincoln University

[3]Computational Biology Department, Carnegie Mellon University

A universal hitting set is a collection of k-mers (strings of length k) such that each substring of a certain length in a sequence will always contain at least one element of the hitting set. The use of a small universal hitting set is helpful in reducing complexity of assembly problems. DOCKS (Design Of Compact K-mer Sets) by Orenstein et al, is a method of selecting such universal hitting sets but currently, these sets cannot be produced for a large enough k to be used in major applications. The goal of this project is to find sets with increasing k while keeping the performance as close as possible to DOCKS. We begin by expanding the sets naively, appending all possible strings to the elements in the set. We then remove a subset that only appeared windows with other elements in the set. Using these methods it is possible to increase the k-mer length of the universal sets and achieve performance similar to DOCKS.

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Transmembrane Domain Interactions Play a Role in the Lhs1-dependent Degradation of αENaC

Deshpande, Riddhi; Buck, Teresa; Guerriero, Chris; Brodsky, Jeffrey. Department of Biological Sciences, University of Pittsburgh

The epithelial sodium channel (ENaC) is a heterotrimeric protein that is responsible for reabsorbing sodium in the kidney and regulating blood pressure. It consists of α, β, and γ subunits that each contain intracellular N- and C- termini, a large extracellular loop, and two transmembrane domains. Misfolded ENaC subunits are degraded by a process called endoplasmic reticulum associated degradation (ERAD). Previous work has shown that ERAD of αENaC is dependent on the ER lumenal chaperone, Lhs1, and that the αENaC transmembrane domains are recognized by Lhs1. To investigate the mechanism by which Lhs1 recognizes transmembrane segments, we studied another Lhs1-dependent ERAD substrate, Chimera A. Chimera A also contains two transmembrane segments. A series of Chimera A constructs with model transmembrane segments of varying hydrophobicity were expressed in Lhs1 deletion yeast and cycloheximide chases were performed. We found that insertion of “ideal” model transmembrane domains blocked Lhs1 dependent ERAD, confirming that transmembrane domain properties are important for Lhs1-dependent ERAD. Understanding the mechanisms of ENaC quality control will be useful in developing treatments for diseases that result from defects in ENaC folding and degradation.

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Synergetic effects of protein kinase D inhibitors on prostate cancer cells

Colón-Marrero, Stephanie[1], Prasad, Sahdeo[2], Wang, QJ[2]

[1]Department of Biology, University of Puerto Rico Rio Piedras Campus, San Juan, Puerto Rico

[2] Department of Pharmacology and Chemical Biology, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261, USA.

Protein kinase D (PKD) is increasingly associated with biological processes implicated in cancer development. Studies have suggested PKD isoforms (PKD1-2-3) as potential chemotherapeutic targets against prostate cancer. Our laboratory has discovered several first-in-class potent and selective PKD small-molecule inhibitors, however their therapeutic efficacy in prostate cancer has not been fully evaluated. This study seeks to exploit the therapeutic potential of combining PKD-inhibitors with chemotherapeutic agents for prostate cancer treatment. Drug combinations may increase efficacy and reduce toxicity of chemotherapeutic drugs. We used FDA-approved docetaxel, doxorubicin, carboplatin, paclitaxel and MLN8237, in combination of PKD-inhibitor – CRT0066101 to study their anticancer effect in PC3-ML prostate cancer cells. Doxorubicin proved most effective by being cytotoxic. These findings will lay the foundation for testing drug combinations in prostate cancer metastasis mouse model that is being developed in our laboratory. It will also serve to advance our understanding on synergetic actions of PKD-inhibitors in cancer therapy.

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The use of hydroponic systems to bioaccumulate PFAS into plants from water as a means of purification

Tyra Robinson[1], Carla Ng[1 2], David Sanchez[2], Dan Chi[2], Manoochehr Khazaee[1]

1. Department of Chemical and Petroleum Engineering
2. Department of Civil and Environmental Engineering
University of Pittsburgh, Pittsburgh, PA, USA

Per- and polyfluorinated alkyl substances, or PFAS, are man-made chemicals that have become an emerging drinking water contaminant. The most persistent of these substances are short-chained perfluorinated alkyl acids because they do not bind well to soil and are water soluble thus they are extremely resistant to all known degradation processes. However, because of these properties, they can accumulate in plants which, through hydroponic systems, could be used to remove these chemicals from water. Furthermore, through pyrolysis/carbonization, the PFAS in the plants could be destroyed while simultaneously producing valuable carbon products (e.g., biochar for soil amendment). In this study, we found which plants can accumulate the highest concentrations of PFAS and which of those are the best input materials for biochar, hydrochar and activated carbon. The responses of these plants in a hydroponic environment when exposed to different concentrations of PFBA, a short-chained perfluorinated acid, were then studied.

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Predicting Activity of Tissue Specific Enhancers Using a Deep Learning Framework

Patiño Calero, Michelle; Chikina, Maria Department of Computational and Systems Biology University of Pittsburgh School of Medicine

A mammalian genome is mainly comprised of non-coding sequence that contains regulatory regions that orchestrate the complex gene expression patterns necessary for multi-cellular processes. Despite progress in experimental techniques to assay these regions, the relationship between primary sequence and function is poorly understood. Recent deep learning models have been shown to predict some functional features of non-coding sequence. In this work we evaluated if a similar framework could be used to predict activity of tissue specific enhancers as directly measured with enhancer RNAs. Building on a previously developed deep learning framework, DeepSEA, we trained a model to predict enhancer activity profiles from 1,036 biological samples of different tissues, developmental stages, and disease states. Our results demonstrated a proof-of-principle that shows the possibility of learning these signatures directly from sequence with a limited dataset. We experimented with model parameters and data augmentation strategies to identify promising avenues for model improvement.

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Use of natural language processing to highlight key information in electronic medical records and reduce cognitive burden on clinical providers

Obregon, Laura; Hochheiser, Harry
Department of Biomedical Informatics
University of Pittsburgh

Data from Electronic Medical Record systems (EMR) has potential to ensure timely and quality care delivery. EMRs are dense to read and may lead to cognitive burden on the clinician, consequently missing important clinical data that may signal future patient health problems. We aim to develop a strategy for identifying and highlighting factors in clinical notes to reduce the cognitive load and ultimately increase the efficiency of the clinician.
The Natural Language Toolkit (NLTK) and regular expression (re) libraries in Python were used to highlight information relevant to clinical care. Sample notes were tokenized, parts-of-speech tagged, and noun phrases extracted through chunking of manually selected sentence structures. Ontology driven concept extraction was performed by mapping noun phrases to terms from SNOMED-CT, with using the Python library PyMedTermino. Terms extracted from PyMedTermino will be reviewed to extract a preferred SNOMED-CT concept for each text span, then reviewed for accuracy and completeness.

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Software Development for a Ring Imaging CHerenkov (RICH) Detector

Aaron, Elise; Goodwill, Justin; Muhoza, Mireille; Smoot, Waymond; Benmokhtar, Fatiha, Ph.D.
Department of Physics
Duquesne University

The “up” and “down” quarks are believed to give the proton its intrinsic properties; however, the Standard Model of particle physics does not fully account for the spin property of the proton as observed by experiments. We would like to know what other factors might be contributing to this spin. One plausible candidate is the “strange” quark. A Ring Imaging CHerenkov (RICH) detector, under construction at Jefferson National Accelerator Facility (JLab), has been designed to identify strange-containing kaons as products of proton collisions. The aim of this project was to develop software tools for the retrieval and analysis of RICH data. Several key elements have been added to an intuitive graphical user interface (GUI) which will be used for visual monitoring of the RICH. Preliminary detector runs will also be performed and presented at JLab during late July.

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The role of the retinoic acid pathway for tumor immunogenicity in IDH mutant chondrosarcomas

Authors: Camacho-Horvitz, Isabela; Lee, Donna; James, Reyanna; Liu, Lijun; Watters, Becky; Rao, Aparna; Weiss, Kurt; Amankulor, Nduka; Duensing, Anette
Academic Department: Cancer Biology, UPMC Hillman Cancer Center
University: Wesleyan University

Chondrosarcomas are malignant bone tumors that produce cartilage. Approximately 65% of chondrosarcomas have a mutation in the isocitrate dehydrogenase (IDH) gene, causing the production of 2-hydroxyglutarate (2HG) instead of alpha-ketoglutarate (α-KG). These are also prominent in gliomas and affect the function of natural killer (NK) cells by epigenetically silencing NKG2D ligands, UL16 binding protein (ULBP) 1 and 3. Preliminary studies have also shown that retinol-binding protein 1 (RBP1), a critical factor in the retinoic acid (RA) pathway is downregulated. Treating with RA may prove to be effective in promoting tumor suppression and immune activation. Evaluation of publicly available chondrosarcoma data sets was performed to identify other genetic similarities between gliomas and chondrosarcomas. Immunoblotting, qRT-PCR, and NK-cell killing assays were done to test the efficacy of RA in inhibiting cell proliferation and restoring immunogenicity. Further invivo studies will help determine the efficacy of RA as a new potential treatment for chondrosarcoma.

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Analysis of Photo-Anode Multipliers (MA-PMTs) for a Ring Imaging Cherenkov (RICH) detector

Smoot, Waymond; Goodwill, Justin; Muhoza, Mireille; Aaron, Elise; Dr. Benmokhtar
Physics Department
Duquesne University

Future experiments at the Thomas Jefferson ~~Laboraroty~~ Laboratory require the addition of new a RICH detector to the CLAS12 spectrometer. RICH will be used to discriminate between sub-atomic charged particles called pions and kaons by analyzing the Cerenkov light that is emitted by this particle jets when they are moving faster than the speed of light in a radiator material. Cherenkov radiation will be caught by approximately 400 Hamamatsu H12700 MA-PMTs. These MA-PMTs are connected to flash analog-to-digital converters. The output from these FADCs is being analyzed. I am analyzing test data that is being taken at Jefferson Lab by developing C++ codes and using the ROOT program. The process will include finding the mean values of both the pedestal generated by the electronic noise and single photoelectron spectrum. This is then transcribed onto a .txt file, while graphs are made of the gain of each pixel within the PMTs vs their channel numbers for different experimental conditions: High voltages, thresholds and more. This study will help understand the PMTs better and how to organize them in a triangular array inside the RICH detector.

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Medical image segmentation, geometry preparation and 3D printing for in-vitro flow visualization in patient-specific left atrial geometries

Oladosu, Michael; Menon, Prahlad
Biomedical Engineering Department
Duquesne University

DICOM cardiac computed tomography (CCT) image were segmented in 3D in order to derive patient-specific left atrial (LA) surface geometries, from pulmonary veins to the mitral valve hinge plane. 3D LA surface models are employed by The MeDCaVE lab at Duquesne University for computational fluid dynamics (CFD) as well as 3D printing for integration in a mock-circulatory flow loop environment which facilitates the visualization of hemodynamics in conditions seen in atrial fibrillation (AF) - a cardiac rhythm abnormality affecting ~2% of US population. DICOM image volumes were first converted to Visualization Tool Kit (VTK) files in ITK-SNAP - an open source image-processing software - for visualization in Paraview (Kitware, Inc.), from which crude surface models of the LA were generated using an iso-contouring approach. Finally, surfaces were iteratively refined by clipping and smoothing in Geomagic Studio (Geomagic Inc.) in order to isolate the LA and LA appendage.

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Genomic Discrimination of Sporadic Type 1 and 2 Papillary Renal Cancers

Gil, Louis
Computer science
Universidad de Puerto Rico

Papillary renal cell carcinomas are rare forms of kidney cancer which have been subclassified into type 1 (PP1) and Type 2 (PP2) based on minor phenotypic differences as well as long term outcome. In an attempt to improve the discrimination of these 2 classes of phenotypically similar tumors, genomic profiling has been employed with variable success. In this study, we used exome sequences for 6 PP1 and 6 PP2 tumors derived from frozen, micro-dissected specimens including DNA from matched blood control specimens. We used a variant calling pipeline to identify deleterious germline and somatic variants (SNV, Indels, CNV) for each tumor. Our hypothesis is that a distinct signature of genomic variants can be used to identify and discriminate between these tumor classes. The DNA exome variants were subjected to a pathway analysis to determine the mechanisms underlying and discriminating between Pap1 and Pap2 classes of RCC.

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Reassessing Biodigestor Technology for Renewable Natural Gas Production

Christensen, Alexander and Stolz, John F.
Center for Environmental Research and Education, Duquesne University, Pittsburgh PA

The production of natural gas through biomass transformation (e.g., RNG), holds great promise as an alternative to unconventional shale gas extraction. A previous study done the by CERE (Gehrig et al., 2014) determined that 1.18-8.83 cubic feet per year could be generated just on the amount of waste produced by the cows and pigs raised annually in the United States. The purpose of this study was to update the values for potential methane production from anaerobic biodigesters based on more recent Methane Conversion Factors (MCFs) from operating multistage anaerobic biodigesters in the Quasar Energy Group. The new range was found to be 9.24-14.54 trillion cubic feet per year. This increase is believed to be from increased efficiency and methane yields of multistage anaerobic digesters. This study also found a range of 159-250 billion cubic feet per year of potential methane production in the state of Pennsylvania alone. These ranges compare quite favorably to the 19.56 trillion cubic feet per year of methane from hydraulic fracturing in the United States. Including other feedstocks, including municipal waste and compostable materials, the amount of biogas (RNG) potentially produced from biodigesters could meet our current needs for natural gas.

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Differential production of cyclic-di-GMP in a bacterial community leads to the evolution of a unique multicellular trait

~~Authors~~ Ansu Benjamin, Sarah Adrian, Collin Kessler, Wook Kim

Bacteria are traditionally described as a unicellular organism, but they spend most of their lives in densely structured communities known as biofilms. Biofilms are central to infectious diseases as they are very difficult to eradicate. Cyclic-di-GMP is an intracellular compound produced by all bacteria, and its level dictates whether an individual will grow as a free living cell or form a biofilm. Here, we describe how cyclic-di-GMP production is genetically modulated as bacteria repeatedly and bi-directionally evolve between two distinct phenotypic states. Our work demonstrates how cyclic-di-GMP's role could extend beyond the physiology of a single cell to a multicellular trait whereby different genotypes divide labor to collectively conquer new territory.

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Crosslinking Mass Spectrometry Study of Phosphatidic Acid Interaction with Human α-1 Glycine Receptor

Tidwell, Elizabeth D.[1], Ferraro, Nicholas[2], Cascio, Michael[2]
[1]Department of Chemistry, Hastings College, Hastings NE 68901
[2]Department of Chemistry and Biochemistry, Duquesne University, Pittsburgh PA 15282

Phosphatidic acid (PA), a negatively charged diacyl-glycerolphospholipid, has been found to be necessary for proper function of pentameric ligand gated ion channels like the human glycine receptor (GlyR). Utilizing lipid-protein photocrosslinking, the interactions between the photoactivatable PA and GlyR were studied. Wild type human α-1 GlyR was over expressed in insect cells and purified through strychnine affinity chromatography. Purified protein was reconstituted in unilamellar lipid vesicles above 12 mole percent PA, incorporating PA crosslinker, produced through choline cleavage of precursor pacFA-18:1 phosphatidyl choline. GlyR was verified by Western blotting and quantified by modified Lowry assay. Following photoactivation, crosslinked PA-GlyR was trypsinzed and mass fingerprinted. Mass shifted peptides containing PA were identified by ESI-Q-TOF MS. Sites of direct covalent attachment were refined by targeted MS/MS. Unique crosslinking events identify the location of amino acids within the membrane and possible specific GlyR-PA interactions, including binding to regions of GlyR, currently poorly resolved.

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First Principles Modeling of Gaseous Molecules Diffusing Through Graphene Pores

Celani, Caelin; Basdogan, Yasemin; Keith, John A.
Department of Chemical & Petroleum Engineering
Swanson School of Engineering, University of Pittsburgh

Many carbon-based membranes for gas separations can be made, but the degree that fundamental chemical bonding interactions in the membrane can be optimized for selective molecular separations remains an open question. For insight into this, we have computationally studied molecular diffusion of CH_4, CO_2, O_2, and N_2 through carbon membrane pore models using different levels of computational quantum chemistry theory. We study how chemical substitutions along the edge of the pore affect diffusion barriers. Our present work with a dispersion-corrected Kohn-Sham generalized gradient approximation exchange correlation functional indicates there is little interaction between a diffusing molecule and a moderately large, 54 atom pore lined with different chemical functional groups. Diffusion through a smaller pore produces more significant diffusion barriers ranging from 1–10 kcal/mol, depending on molecular orientation, pore functionality, and the diffusing molecule. Future work will consider the effects of different levels of quantum theory and different chemical functionalizations.

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"Rapid Screening of Stable Bimetallic CuZr Nanoparticles"

Mascareno, Ashley A. , Taylor, Michael G. , Yan, Zihao , Mpourmpakis, Giannis
Department of Chemical and Petroleum Engineering
University of Pittsburgh, Pittsburgh, PA 15213

Although bimetallic nanoparticles are useful for a diverse range of applications, their physical and chemical characteristics as a function of size, shape, and composition remain poorly understood, largely due to the almost infinite morphological combinations. Previously, a simple, quick nanoparticle size/shape stability (in terms of cohesive energy) model was developed, successfully capturing the monometallic nanoparticle stability trends[1]. We have recently expanded the previous monometallic stability models to capture bimetallic nanoparticle energetics. We validated our newly developed model by calculating the energetics of bimetallic CuZr nanoparticles (19-172 atoms) using Density Functional Theory calculations (CP2K code). We focused on CuZr nanoparticles due to their catalytic applications in CO_2 conversion[2]. The nanoparticles accounted represented a wide range of morphological configurations and bimetallic compositions. Interestingly, we show that our new energetic stability model accurately predicted bimetallic CuZr nanoparticle trends, potentially accelerating research into bimetallic nanoparticles.

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Methanol Reduction of Cu_2O Nanoislands on Copper thin films using *in situ* Environmental Transmission Electron Microscopy (ETEM)

David, Edwin; Andolina, Christopher; Chi, Hao; Veser, Gotz; Yang, Judith Chun-Hsu
Department of Chemical and Petroleum Engineering – PFM-REU
University of Pittsburgh

The fundamental understanding of the reduction mechanisms of metal oxides is useful for the optimization of materials in various applications including catalytic reactions and corrosion resistance. The reduction of Cu_2O has been observed in many processes but still poorly understood on the nanoscale. The copper thin films were prepared on specifically ordered NaCl substrates using an e-beam evaporator. The *in situ* reductions of cuprous oxide islands were carried out in the Hitachi H9500 Environmental-TEM in order to observe the surface dynamics down to the nanoscale under relevant gaseous and thermal conditions to determine the important factors impacting reduction on this scale such as underlying the metal surfaces, temperature, pressure, and island geometry. The copper reduction rates of the Cu_2O islands were studied on three facets Cu (100), (110), and (111). These results will be used to develop more accurate kinetic models to facilitate in designing material improvement for environmental stability.

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2D Photonic Crystal Protein Polymers for Organophosphate Gas Sensing

Gray, Vincent; Ho, Brenda; Smith, Natasha; Asher, Sanford
Department of Chemistry
University of Pittsburgh

Novel protein hydrogels and organogels were developed for organophosphate (OP) sensing. The chemical warfare agent, Sarin, is a toxic OP derivative. Organophosphorus hydrolase (OPH) enzyme reacts with the OP paraoxon. Acetylcholinesterase (AchE) enzyme binds paraoxon. Aqueous protein solutions were crosslinked with glutaraldehyde forming transparent protein hydrogels. Protein hydrogels and organogels are volume responsive toward analytes specific to each protein. 2D photonic crystals (2DPC) attached to protein hydrogels monitor volume changes. 2DPC diffract visible light into Debye rings. The Debye ring diameter is used to calculate particle spacing, which is directly related to hydrogel volume. OPH/AchE 2DPC hydrogels were tested for responsivity toward paraoxon. Fabrication of gas sensors requires low vapor pressure solvents. We showed albumin protein organogels in ethylene glycol (EG) sense basic ammonia and acidic acetic acid gases reversibly. The activity of OPH in low vapor pressure organic solvents was measured. OPH activity was higher in glycerol than EG.

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Hydrogen bonding in metal-free catalysis of the cyanation reaction

Latawiec, Elisabeth and Evanseck, Jeffrey D.
Center for Computational Sciences and Department of Chemistry and Biochemistry
Duquesne University

Metal containing Lewis acids catalyze cyanation and other important carbon-carbon bond forming reactions; however, the use of ecofriendly hydrogen-bond donor organocatalysts has been growing in recent years. Jacobsen pioneered the study of urea and thiourea complexes as efficient nonmetal catalysts, yet his interpretation and explanations failed to consider the reactions in the condensed phase. The research design was to first define the gas-phase reaction path of the cyanation reaction. Computational studies have been employed using Stewart's PM7 semi-empirical method and Truhlar's M06-2X functional with Pople's 6-31+G(d) basis set to determine the activation energies of urea-catalyzed cyanation of acetone. An ion-dipole structure was studied as an intermediate to account for hydration of the cyanide anion in solution, and its energy will be discussed. The investigation of mechanistic possibilities of urea and other nonmetal catalysts prepares a foundation for analyzing the role of the hydrogen bond in organic catalysis.

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Solvent participation in five-membered ring oxocarbenium ion nucleophilic addition reactions

Castele, Erin[1]; Woerpel, Keith[2]; Evanseck, Jeffrey D.[1]
[1]Center for Computational Sciences and Department of Chemistry and Biochemistry, Duquesne University, Pittsburgh PA; and [2]New York University, New York City, NY.

Nucleophilic additions to five-, six-, and seven-membered ring oxocarbenium ions require predictive and reliable models in order to be synthetically useful. Reactions involving oxocarbenium ions proceed with strong stereoselectivity that depends on the nature of the substituent and is not fully understood. Our methods involved Truhlar's M062X density functional with Dunning's jul-cc-pvdz correlation consistent basis set to determine the nucleophilic addition reaction path for systematically substituted five-membered cyclic oxocarbenium ions. The electrostatic model has been developed by Woerpel to explain the strong cis selectivity for oxocarbenium ions having electronegative substituents. We expand upon this understanding of selectivity by including solvent participation along the reaction coordinate, specifically in ground state stabilization through ion-dipole interactions. The effects of explicit solvent in the gas phase are necessary to understand fully the reactivity of oxocarbenium ions. Our results with five-membered ring systems provide a foundation for analysis of larger ring systems.

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EAffect of charge parameterization on ONIOM activation enthalpies

Andreola, Laura; Pathiraja, Inoka; Tamez, Angel; Firestine, Steven, M.[1]; and Evanseck, Jeffrey D.
Center for Computational Sciences and Department of Chemistry and Biochemistry; Duquesne University, Pittsburgh PA, and [1]Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI.

Non-catalyzed rate constants and enthalpies of activation for the decarboxylation of malonate have been reported by Wolfenden. The nonenzymatic decarboxylation of malonate has been studied computationally with *n* explicit water molecules employed in a hydrogen bonding "buckle" (*n*=0-3) using Truhlar's M062X density functional and Dunning's jul-cc-pvdz basis set. Our efforts have led to the identification of an "orthogonal" conformation previously not considered, which is stabilized in the ground state by explicit water hydrogen bonding to yield an activation enthalpy comparable to the experimental value. Combined Quantum Mechanical and Molecular Mechanical methods (QM/MM) were employed to decrease computational time and resources, where charge calculation schemes, such as NBO, APT, and Mulliken, were utilized to determine which method compares best to the experimental and QM calculated activation enthalpies. These methods will be employed in future work to assess enzymatic catalysis, where arylmalonate decarboxylases (AMDase) catalyze the decarboxylation of α-aryl-α-methylmalonates.

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Fortuitous boron-fluorine and formyl hydrogen eclipsing orientations in BF_3 crystal structures of Lewis acid aldehyde complexes

Mihailescu, Petru[1]; Osborne, Brittney[2]; Vernier, Brandon T.; Rohde, Jeffrey J. [3], and Evanseck, Jeffrey D.
Duquesne University Center for Computational Sciences and Department of Chemistry and Biochemistry; [1]Mount Lebanon Senior High School Pittsburgh PA; [2]Florida Memorial University; [3]Franciscan University of Steubenville

Lewis acids are widely used as catalysts in important industrial and academic organic reactions, a source of environmental pollution, and often poorly understood mechanistically. Lewis acid complexes of BF_2OCH_3 and BF_3 with dimethyl formamide (DMF) have been studied with Stewart's PM7 and Truhlar's M06-2X functional with Dunning's cc-pVTZ basis set. The "formyl" hydrogen bond has been put forth within a ground state framework as a rationale for the eclipsing conformations observed in the complex single crystal structures. This has been controversial because it does not always agree with experimental results. We describe a series of computations, where we calculate the enthalpy of formation of the aforementioned complexes and compare the results to results from X-ray crystallography. We uncover that the previously found BF_3 formyl hydrogen bond is not due to stereoelectronic forces.

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Oxaloacetate decarboxylation mechanism in solution

Cruz, Ahyssa R[1]; Tamez, Angel[1]; Kotsikorou, Evangelia[1], and Evanseck, Jeffrey D.
Duquesne University Center for Computational Sciences and Department of Chemistry and Biochemistry; [1]Department of Chemistry, University of Texas Rio Grande Valley, 1201 West University Drive Edinburg, Texas 78539-2909

A condensed phase understanding of β-keto carboxylic acid decarboxylation is not well understood. Truhlar's M06-2X functional with Pople's 6-31+G* basis set was used to carry out a conformational analysis of oxaloacetate in the gas and condensed phases. We find a cyclic arrangement of three hydrogen bonding waters, known as the "water buckle," stabilizes the "orthogonal" conformation over the 6- or 7-pseudochair conformations. Thermodynamic parameters of activation were computed for the decarboxylation of oxaloacetate in gas phase and the water buckle. The strong hydrogen bond network of the water buckle delays the departure of CO_2 in the decarboxylation mechanism. The experimental enthalpy of activation is 17.2 kcal/mol, whereas the gas phase computed value is 14.1 kcal/mol, which is expected to become aligned with the experimental value as seen in calculations with malonate. The decarboxylation of oxaloacetate in solution is crucial for understanding the mechanism of enzymatic decarboxylation of β-keto carboxylic acids.

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Computational model of CO_2 adsorption on TiO_2 (101) anatase

Mark Recznik[1], Amy N. Carlson and Jeffrey D. Evanseck
Duquesne University Center for Computational Sciences and Department of Chemistry and Biochemistry; [1]Franciscan University of Steubenville

To model the adsorption energy of a gas molecule on a crystal surface, computational chemists rely either on direct comparison with experiment or on their calculations to converge. To date, the creation of a model that accurately reproduces adsorption phenomena remains controversial, specifically in the minimum number of layers is needed to obtain a converged value. For the adsorption of CO_2 on TiO_2 (101) anatase, studies have not fully explored the system's energetic dependence on the total number of layers, n_T, or the relaxed number, n_R. We calculated the adsorption energy, E_{ads}, for this system with an increasing number of layers. As we varied n_T from two to six, we varied n_R from zero to n_T. It was found that E_{ads} converges within 0.5 kcal/mol of the converged limit when at least $n_R = 2$ and $n_T = 4$.

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Nontraditional catalytic elements for Trost semicrown aldol reaction cycle

Ahmed, Ayan N.; Vernier, Brandon, T.; Rhode, Jeffrey, J.[2]; Evanseck, Jeffrey, D.
Duquesne University Center for Computational Sciences and Department of Chemistry and Biochemistry; [2]Franciscan University of Steubenville, Steubenville OH

Semicrown ligands show promise replacing asymmetric Mukaiyama aldol reaction; however, the three-dimensional structure, mechanism, and factors that control the stereoselectivity have not yet been explained. We have determined plausible dinuclear zinc-based semi-crown ligand three-dimensional structures using the M06-2X functional paired with Dunning basis sets. Our results reveal a unique mechanistic cycle, where a C2 symmetric ligand works by employing nontraditional hydrogen bonding to predispose aldol reactants into reactive positions. We investigate the structural and energetic findings and consequences of the *alpha* and *formal* hydrogen bonds that occur separately for the electrophile and the nucleophile with the semi-crown ligand in the Mukaiyama aldol reaction. Our results contribute to the development of a rational strategy for designing catalysts for the Mukaiyama aldol reaction, which serves to be an excellent template to expand to other asymmetric processes.

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Crystal packing forces in the formation of nontraditional hydrogen bonding

Osborne, Brittney[1]; Vernier, Brandon; Mihailescu, Petru[2]; Rupprecht, Alexander; Rohde, Jeffrey, J.[3]; Evanseck, Jeffrey, D.
Duquesne University Center for Computational Sciences and Department of Chemistry and Biochemistry; [1]Florida Memorial University, 15800 NW 42nd Ave, Miami Gardens, FL 33054; [2]Mount Lebanon Senior High School Pittsburgh PA; [3]Franciscan University of Steubenville, Steubenville OH

Corey and Rohde developed a model of nontraditional hydrogen bonding between Lewis acids and dienophiles to explain the asymmetric Diels-Alder reactions reported by Koga. However, weaknesses in the explanatory power of the model have been discovered and the stereoselectivity observed by Koga has never fully been explained. Comprehending the origin of the stereoselectivity is critical to understanding control of asymmetric catalysis. We investigate crystal packing forces rather than nontraditional hydrogen bonding to explain how organic dienophiles (DMF, DMA) coordinate with Lewis acids (BX_3, X=F and Cl) to form complexes in the solid state. Single crystals were grown through vapor diffusion and analyzed through single-crystal X-ray diffraction. Structure analysis produced a 6.55% error and a hydrogen bond distance of 2.675 Å. Our x-ray structure supports strong crystal packing forces, which we term the “steric pinch” and “electronic anchor,” and a new interpretation of the data.

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Determination of novel peptide fragmentation pathway using density functional theory

Pollak, Nick, G.[1], VanStipdonk, Michael, and Evanseck, Jeffrey D.
Center for Computational Sciences and Department of Chemistry and Biochemistry
Duquesne University; [1]Lebanon Valley College 101 College Ave, Annville, PA 17003

Fragmentation of salicylaldehyde-modified alanine-glycine-glycine (Sal-AGG) to salicylaldehyde-modified glycine-glycine (Sal-GG) was discovered through the use of tandem mass spectrometry and collision-induced dissociation during previous studies by van Stipdonk *et al.* Two possible mechanisms for this fragmentation were proposed, but remain unresolved. Density functional calculations using Truhlar’s Minnesota functional M06-2x and Pople’s 6-31G* basis set were used to find the activation energies of both pathways. The lower energy pathway involved a protonated nitrogen in alanine, as well as the use of a five-membered ring intermediate. The lower energy pathway has an activation energy of 12.9 kcal/mol and is more favorable thermodynamically, thus it is considered to be the proper mechanism for this novel fragmentation.

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Conformation, Stabilization, and Decarboxylation of L-DOPA

Mary E. Burton[1], Jeffrey J. Rohde[1], Jeffrey D. Evanseck[2]
[1]Franciscan University of Steubenville, [2]Duquesne University Center for Computational Sciences: Department of Chemistry and Biochemistry

Symptoms of Parkinson’s disease can be treated with Levodopa (L-DOPA) in combination with Carbidopa, a peripheral dopa decarboxylase inhibitor. To treat the symptoms, L-DOPA undergoes decarboxylation in the brain to increase the dopamine levels. The mechanism of L-DOPA decarboxylation has not been investigated. We report a conformational analysis of L-DOPA in the gas and condensed phases. We find that a “buckle of hydration” with 3 or 5 waters using Truhlar’s M06-2X density functional with Pople’s 6-31+G(d) basis set and the Tomasi’s polarizable continuum model (PCM) provides ground state stabilization of a specific “orthogonal” conformation over other pseudochair conformations. The computed buckle follows a different hydrogen bonding pattern than that observed for ketoacids, where L-DOPA capitalizes upon three waters serving as hydrogen bond donors to buckle-in the CO_2 group from departing. This discovery could help drug manufacturers to improve the design of dopa decarboxylase substrates and inhibitors to treat the disease.

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Hydrogen bonding and structure of G-quartets

Gagliardi, Austin L; Mihailescu, R.; Evanseck, Jeffrey D.
Center for Computational Sciences and Department of Chemistry and Biochemistry
Duquesne University

Despite the significance of the G-quadruplex structure in DNA/RNA, the structure and associated energetic stability of the G-quartet formation remains largely unknown. Models of guanine tetrads have been examined with C_{4h}, C_4, C_{2h}, C_2, C_s, and C_1 symmetry and using Stewart's PM7 semiempirical method, Truhlar's M062X density functional, and Dunning's cc-PVDZ and cc-jul-PVDZ basis sets. Within each point group symmetry, the possibility of different hydrogen bonding patterns of all-Hoogsteen (HHHH), all-bifurcated (BBBB), and hybrid (HBHB) were computed. Our results show that gas phase models of the G-quartet do not have a plane of symmetry, that the BBBB complex is ~ 1 kcal/mol more stable than HBHB G-quartet, and that total hydrogen bond energy is worth ~ 90 kcal/mol. This work sets the foundation for future quadruplex studies, which could provide insight into diseases, such as ALS and fragile-X mental retardation syndrome, related to G-quadruplex presence.

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Few-Layer Transition Metal Dichalcogenide Exfoliation, Characterization and Modeling for Future Electronic Devices

Matei Jordache, Jierui Liang, Susan Fullerton
Department of Chemical and Petroleum Engineering
University of Pittsburgh

Transition metal dichalcogenides (TMDs) are a class of materials that possess unique electrical and mechanical properties when isolated to thin flakes, making them desired for advanced electronic devices. These devices offer potential advantages over traditional devices, including lower power, smaller size, and larger ON/OFF current ratio. Specifically, molybdenum disulfide (MoS2) and molybdenum ditelluride (MoTe2) are of interest. To build and characterize these devices, we must isolate thin flakes; however, this exfoliation is unpredictable. We found that annealing the tape before exfoliation will increase flake yield and thinness (~ 3-7nm). After exfoliation, we characterize the lateral size and surface roughness of the flakes using Atomic Force Microscopy (AFM). The ideal flake is rectangular, with length from 10-30 um and width from 2-3 µm. The average surface roughness measured is ~ 0.4 nm for MoS2. The devices are also being modeled in COMSOL Multiphysics to provide insight into electrical and mechanical behavior.

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Microglia impact the differentiation of neural stem/progenitor cells during a viral infection in the brain.

Woltz, Makenzie A., Chandwani, Manisha, Kulkarni, Apurva, O'Donnell, Lauren A.
Graduate School of Pharmaceutical Sciences, Mylan School of Pharmacy
Duquesne University, Pittsburgh, PA 15282

Viral infections in the central nervous system (CNS) induce a variety of neurodevelopmental disorders. Microglia reside in the CNS and are the first immune cells to respond to infection. Activated microglia secrete specific cytokines, but how these factors affect neurodevelopment is unknown. We predict that microglia release cytokines that aid in neuronal commitment of neural stem/progenitor cells (NSPCs). To test this hypothesis, primary microglia were co-cultured with virally-infected neurons to induce microglial activation. Supernatants from virally-infected co-cultures were incubated with primary NSPCs. The differentiation of NSPCs into committed cells (*e.g.* neurons, astrocytes) was assayed by flow cytometry and immunofluorescence assay. NSPCs exposed to supernatants from infected neurons/microglia produced more immature neurons, whereas supernatants from infected neurons without microglia produced more mature neurons and astrocytes. These results suggest microglia enhance neurogenesis in the presence of infected neurons. Furthermore, infected neurons may release factors independently of microglia that encourage neural cell maturation.

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Design and development of locally injectable nanoemulgel for COX-2 targeted delivery to treat chronic inflammatory pain

~~Authors:~~ Loftus, Shannon[1,2,3]; Liu, Lu[2,3]; Herneisey, Michele[2,3]; Janjic, Jelena M.[2,3,4]
[1]Department of Biology, The University of Scranton, Scranton, PA
[2]Division of Pharmaceutical, Administrative, and Social Sciences, Duquesne University, Pittsburgh, PA
[3]Chronic Pain Research Consortium, Duquesne University, Pittsburgh, PA
[4]McGowan Institute for Regenerative Medicine, Pittsburgh, PA

Chronic pain is associated with an infiltration of macrophages to a site in the body and their secretion of pro-inflammatory cytokines. In diseases like rheumatoid arthritis, macrophages have a large role in the progression and severity of the disease. Problems with current free-drug treatments include unintended side effects and low efficacy per dose. Nanoemulsions provide a solution by improving the bioavailability of poorly water-soluble drugs such as celecoxib, a cyclooxygenase-2 inhibitor, while also selectively targeting macrophages. Nanoemulsions can also be theranostic (therapeutic and diagnostic) when near-infrared dyes are added to visualize the nanoemulsion's fate in body tissue. Additionally, when nanoemulsions are added to a thermoresponsive hydrogel, locally injectable drug delivery at the site of inflammation is possible. Here we develop and optimize a celecoxib-loaded nanoemulgel for macrophage COX-2 inhibition. Additionally, we show that the nanoemulgel will target macrophages with low toxicity while maintaining the integrity of the nanoemulsion droplets.

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Investigating the Analgesic Properties of PolyMorphine

Leep, Sarah[1,2]; Lax, Neil[1,2]; Yu Lei[3]; Uhrich, Kathryn[4]; Kolber, Benedict[1,2].
[1]Department of Biological Sciences
[2]Chronic Pain Consortium,
Duquesne University;
[3]Department of Genetics, Rutgers University;
[4]Department of Chemistry and Chemical Biology, Rutgers University and Department of
Chemistry University of California Riverside

Opioids are commonly used to treat chronic pain patients, however, many formulations are associated with abuse. Abuse of opioids (e.g. morphine) is driven, in part, by the short-lasting euphoric effects of mu opioid receptor (MOR) activation. Therefore, low dose long-lasting opioids must be developed. PolyMorphine, a polymer form of morphine, induces extended analgesic effects by slowly releasing individual morphine molecules over time. Thus, PolyMorphine will not have to be administered as frequently as morphine. We tested whether the analgesic effects of PolyMorphine were mediated by the MOR. To evaluate this hypothesis, we tested whether naloxone, a competitive antagonist at the MOR, would block PolyMorphine effects. After establishing an effective dose of naloxone in a free morphine experiment, we delivered one injection of PolyMorphine and daily injections of naloxone followed by von Frey behavioral testing in a mouse model of chronic pain. The results show that naloxone completely blocks PolyMorphine effects.

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Characterizing neurophysiological mechanisms of chronic bladder pain regulation through the central amygdala.

Cox, Abigail[1,2], Sadler, Katelyn[1,2], Kolber, Benedict[1,2]
[1]Department of Biological Sciences, and [2]Chronic Pain Research Consortium
Duquesne University, Pittsburgh, PA

Millions of individuals suffer from urologic chronic pelvic pain syndromes with unknown mechanisms. Recent data, however, have demonstrated that the central nucleus of the amygdala (CeA) in the brain regulates bladder nociception (i.e. pain). Specifically, the CeA in the right hemisphere functions to increase bladder nociception, while the left CeA decreases bladder nociception. It is hypothesized that the neuropeptide, calcitonin gene-related peptide (CGRP), facilitates these divergent roles. In order to test this, the nociceptive responses to painful bladder stimuli were measured in female mice before and after injecting the left or right CeA with CGRP. The preliminary results demonstrate clear trends for decreased pain-like effects after CGRP is administered to the left CeA compared to the right. The ultimate goal of this study is to characterize bladder pain processing through CGRP signaling, which will hopefully provide new insight for therapeutic treatments of urologic chronic pelvic pain syndromes.

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Interactions of the Fragile X Mental Retardation Protein with a BACE1 mRNA G-quadruplex Structure and with miR-124-3p: Implications for Translational Regulation

Zakutansky, Paul M; Mihailescu, Mihaela Rita
Department of Chemistry and Biochemistry
Duquesne University

Fragile X Syndrome is an inherited genetic disease caused by the hypermethylation of a CGG expansion repeat in the *FMR1* gene, which leads to the loss of expression of fragile X mental retardation protein (FMRP). FMRP binds to messenger RNA (mRNA) G-quadruplexes by using its arginine-glycine-glycine (RGG box) binding domain. We hypothesized that beta-secretase 1 (BACE1) mRNA sequence containing a binding site for miRNA 124-3p forms a G-quadruplex structure that will be bound with high affinity and high specificity by the FMRP RGG box. In this study we have analyzed the interactions of the BACE1 G-quadruplex with the FMRP RGG Box through biophysical methods such as ^{1}H-nuclear magnetic resonance (^{1}H NMR) spectroscopy and native polyacrylamide gel electrophoresis (PAGE), and then investigated the impact they have upon the miRNA-124-3p recognition of its target site on BACE1 mRNA.

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Phylogenetic relationships of marine cyanobacteria serving as possible targets for pain and depression

Zapadka, Analise; Lax, Neil; Tidgewell, Kevin; Kolber, Benedict
Department of Biology, Duquesne University

Chronic pain and depression affect millions of people worldwide and often occur together in a comorbid manner. Most medications used to treat these conditions separately target G-protein coupled receptors (GPCRs), suggesting that there may be receptors that could be targeted to address both pain and affective symptoms. Our lab uses a natural product approach to search for novel marine compounds that bind to GPCRs. We target and isolate peptide-like molecules from marine cyanobacteria, which have been found to produce secondary metabolites that resemble endogenous ligands to GPCRs. Several cyanobacterial samples were collected from Las Perlas, Panama and Curacao for investigation. The 16S rRNA gene for several collections was sequenced for phylogenetic analysis with the goal of finding meaningful relationships between previously discovered cyanobacterial species. By comparing ecology, morphology and phylogenetic relationships, we aim to find novel relationships between these characteristics and psychoactive potential, allowing for more directed natural drug discovery.

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Expression of a Gene Regulated by the Hypoxia Inducible Factor in Snow Leopards Indicative of High Altitude Adaptation

Nelson, Brionna; Winston, Amirah; Pulugulla, Sree; Galson, Deborah; Auron; Philip; Davis, Bryan; Janecka, Jan
Department of Biological Sciences
Duquesne University

Hypoxia, defined as low levels of oxygen, is one of the most stressful conditions for cells as it can rapidly lead to death. The primary regulator of the cellular response required to compensate for low oxygen is HIF1a. Snow leopards, *Panthera uncia*, are adapted to a hypoxic environment and occur in high-altitude mountains. In contrast, tigers, *Panthera tigris*, occupy low-elevation forests and grasslands. Snow leopards have a unique mutation EGLN1, a gene which acts as the oxygen sensor for HIF1a. We hypothesized that this has led to differences in gene expression in the Hypoxia Inducible Pathway. We extracted RNA from tissue of both species and compared relative expression for 5 genes using qPCR. VEGF, which stimulates angiogenesis leading to improved tissue perfusion and oxygen delivery, was upregulated in snow leopards. This is likely an important adaptive mechanism enabling snow leopards to maintain sufficient levels of oxygen at high altitudes.

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Fabrication of a Timed-Pressure Regulator to Enable the Study of Bladder Pain

Marissa Behun[1,2,3], Benjamin Goldschmidt[2], Benedict Kolber[1,3]
[1]Department of Biological Sciences, [2]Biomedical Engineering Program, [3]Chronic Pain Research Consortium, Duquesne University, Pittsburgh, PA

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a common, poorly treated chronic pain disorder. Many IC/BPS symptoms suggest a central nervous system component. The role for the brain in processing and modulating bladder pain is still largely unknown. *In-vivo* recordings of the left and right central amygdala using carbon-fiber electrodes were made during noxious bladder distention in *Mus musculus* (mouse). Once a neuron was detected during the recording process, urinary bladder distensions (UBD) were used to observe how the neuron responded to a noxious stimulus. Currently, UBD is done using a manual distention device. To better standardize UBD data, a timed-pressure regulator (TPR) has been designed and built. The TPR consists of a microcontroller, pinch valve, and pressure sensor that will be able to regulate the various air pressures during UBD, while also monitoring the duration of UBD. TPR instrumentation is currently undergoing testing before being implemented in the recording process.

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Determining the External Loop Conformations of the Rat Serotonin Transporter through Single Cysteine Point Mutations and Cross-Linking Mass Spectrometry (CX-MS).

Gargano, Adam[1,2] ; Castellano, Elizabeth[1,2] ; Tomcho, Kayce[1,2] ; Cascio, Michael[1,2]
[1]Department of Chemistry and Biochemistry, Duquesne University.
[2]Chronic Pain Consortium, Duquesne University

The serotonin transporter (SERT) is a transmembrane protein in neurons. It is responsible for the re-uptake of serotonin, a monoamine neurotransmitter, from the synapse to the pre-synaptic neuron. Dysregulation of serotonin in the synapse results in psychological disorders such as depression. Hypothetically, understanding the structure of SERT could lead to better drug design to fight depression. To understand the allostery and structure of the external loops of the rat serotonin transporter (rSERT), single cysteines were inserted systematically at specific points (V310C and R564C) into a cys-null background. A crosslinker can be used to form a disulfide bond to the introduced cysteine. Subsequent UV radiation resulted in non-specific crosslinks with benzophenone to the local protein. After in-gel trypsin digest, Mass Spectrometry (MS) studies can identify which amino acids were non-selectively bound by the cross-linker and therefore probe the local environments of V310C and R564C. MS results are currently pending.

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Using crosslinking mass spectrometry (CX-MS) to refine the states of the Glycine receptor with the site specific mutation K116C

Miller[1], Janique, Tomcho[2], Kayce Alexandra, and Cascio[2], Michael
Florida Memorial University, Department of Natural Sciences, Miami Gardens, FL 33054[1]
Duquesne University, Department of Chemistry and Biochemistry, Pittsburgh, PA 15282[2]

The glycine receptor (GlyR) is an ionotropic receptor primarily responsible for inhibitory neurotransmission. Upon activation, the channel opens initiating the influx of chloride ions, causing cellular hyperpolarization. Studies regarding GlyR's structure will provide insight into receptor function and aide in the development of novel therapeutics to modulate function. These studies were conducted by overexpressing human α1 GlyR into *Spodotera frugiperda* (Sf9) cells. Each analysis focuses on the introduction of a single active Cys mutation in which a crosslinker, MTS-benzophenone, attaches via disulfide linkage. The receptor is then enriched in its~~an~~ allosteric state~~s~~: resting, open, and desensitized, before photo activation and generation of intra- and intermolecular crosslinks. CX-MS was used to identify unique sites of crosslinker attachment, to examine the local topography. For this study, the focus was the K116C mutation.

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Effects of Anti-Inflammatory Drug-Loaded Nanoemulsion on Protein Expression Involved in Axonal Regeneration

Lee, Youngrim[1,3]; Hudson, Bridget[1,4]; Summers, Austin[1,5]; Stevens, Andrea[1,3]; Saleem, Muzamil[1,3]; Janjic, Jelena[2,3]; Pollock, John[1,3]
[1]Department of Biological Sciences, Duquesne University, Pittsburgh, PA
[2]School of Pharmacy, Duquesne University, Pittsburgh, PA
[3]Chronic Pain Research Consortium, Duquesne University, Pittsburgh, PA
[4]Cardinal Wuerl North Catholic High School, Cranberry Township, PA
[5]Pittsburgh Science and Technology Academy, Pittsburgh, PA

Axonal injury promotes peripheral neurons to regenerate their axons by the intrinsic growth capacity of the neuron itself and by the influence of infiltrating macrophages and Schwann cells. These cells phagocytose axonal and myelin debris from the distal axonal degeneration following injury, improving the environment for axonal regrowth. However, the ~~infiltrating~~ activated ~~macrophages~~ immune and glial cells can lead to chronic inflammation resulting in neuropathic pain. Our colleague, Dr. Jelena Janjic has developed nanoemulsion that has imaging capabilities and delivers anti-inflammatory drugs to cells involved in inflammation. Our lab has previously shown that we can track neuroinflammation in a rat model of chronic pain, the chronic constriction injury (CCI) of the sciatic nerve. When an anti-inflammatory drug-loaded nanoemulsion is present, a reduction in inflammation is shown. ~~In a rat model of chronic pain, the chronic constriction injury (CCI) of the sciatic nerve, we have previously shown that we can track neuroinflammation, showing a reduction in inflammation when nanoemulsion containing anti-inflammatory drug is present. Utilizing a chronic pain model known as chronic constriction injury (CCI) in rats, we have previously shown that we can neuroinflammation and have demonstrated a reduction in inflammation when nanoemulsion containing anti-inflammatory drug is present versus nanoemulsion containing no drug.~~ In this study, we used immunohistochemistry to investigate ~~observe the expression of proteins involved in axonal regeneration, investigating~~ whether nanoemulsion containing an anti-inflammatory drug can improve axonal regeneration, which may lead to faster recovery.

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Alterations in the Morphology of Dystrophic Neuromuscular Junctions

Department of Physical Therapy
Allen, Jordan[2];Omstead, Maddie[1]; Kostek, Matthew[1]
Duquesne University, Pittsburgh PA[1]
Hamilton College, Clinton NY[2]

The neuromuscular junction (NMJ) structure is fundamental to the function of any mammalian nervous system. In Duchenne Muscular Dystrophy (DMD) and other neurodegenerative diseases, the NMJ is damaged and undergoes morphological changes that undermine its function. Our goal was to optimize a protocol for visualizing and quantifying the NMJ in mice for use in future studies. Muscle samples (40 um) were cyrosectioned and immunostained with alpha-bungarotoxin to identify the postsynaptic membrane. Fluorescence and confocal microscopy were then used to visualize and quantify the morphology of NMJ's in dystrophic muscle tissue. Significant differences were found between diseased and healthy samples in the morphology of NMJ's. This technique will be extended to measure NMJ morphology in muscle injury and disease treatment trials.

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Discovery of norepinephrine transporter ligands from marine cyanobacteria for neurological disorders

Masson, Linedia, Parker, Stacy-Ann J., Tidgewell, Kevin
Department of Medicinal Chemistry, Graduate School of Pharmaceutical Sciences, Duquesne University, Pittsburgh, PA 15282, United States

Marine cyanobacteria produce bioactive natural products with activities ranging from cytotoxicity to neuromodulation. Despite the wide array of bioactive secondary metabolites, their use as a source for CNS modulatory activity is understudied. To alleviate this disparity, this project will explore marine cyanobacterial extracts for lead compounds targeting receptors and monoamine transporters (MATs) located in the CNS. Approximately 225 cyanobacterial fractions were screened, using a radioligand competition-binding assay, for their ability to bind to receptors and MATs. Fraction 2064E, collected in Panama, demonstrated affinity for the norepinephrine transporter (NET: Ki = 279 nM) and will be further investigated. Compounds that selectively inhibit NET terminate the uptake of norepinephrine. Increase in synaptic concentration results in psychostimulant, appetite suppressant, and antidepressant effects which could potentially treat neurological disorders. Efforts to isolate (HPLC, flash purification) and characterize (1D, 2D NMR spectroscopy, mass spectrometry) compounds from this NET active fraction will be discussed.

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A Computational Model of the Central Nucleus of the Amygdala during Bladder Pain

Joshua Baktay, Dr. Rachael Neilan, Marissa Behun, Dr. Benedict Kolber

Chronic bladder pain (CBP) activates neurons in the central nucleus of the amygdala in the brain which exhibits asymmetric behaviors across each hemisphere. To better understand CBP, an agent-based computational model was created using Netlogo software to replicate neuronal behavior observed in bladder distension experiments on mice. In the simulation agents represent individual neurons with unique firing rates updated stochastically at each time step. In total, the model represents the behaviors of four neuron types and an organism's overall perceived pain in response to different noxious stimuli. A damage accumulation feature was added to the model to track the organism's long-term pain history. The model interface provides a dynamic framework for viewing neural activity as it evolves over time and allows the user to predict different pain states by controlling model parameters. Ongoing work will account for the topology of the neural network, cell-type specificity, and three spatial dimensions.

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Alpha-Arrestin regulation of potassium channel Kir2.1 trafficking

Natalie A. Hager[‡], Collin J. Krasowski[‡], Lan Anh Le[‡], Timothy D. Mackie[§], Alexander R. Kolb[§], Patrick G. Needham[§], Alison Dempsey[‖], Christopher Szent-Gyorgyi[‖], Marcel P. Bruchez[‖], Daniel J. Bain[‡‡], Adam V. Kwiatkowski[¶], Allyson F. O'Donnell[‡,1] and Jeffrey L. Brodsky[§,1].
From the [‡]Department of Biological Sciences, Duquesne University, Pittsburgh, PA, the [§]Department of Biological Sciences, University of Pittsburgh, Pittsburgh, PA 15260, the [‖]Molecular Biosensor and Imaging Center, Carnegie Mellon University, Pittsburgh, PA 15213, the [‡‡]Department of Geology and Environmental Sciences, University of Pittsburgh, Pittsburgh, PA, 15260, and the [¶]Department of Cell Biology, University of Pittsburgh School of Medicine, Pittsburgh, PA, 15261.

To ensure optimal cell growth, protein composition at the plasma membrane (PM) is tightly regulated in response to environmental changes. To identify the factors that regulate protein trafficking we have employed the Kir2.1 potassium channel. This inward rectifying potassium channel is of the KCNJ family found in mammalian cardiomyocytes and therefore essential for maintaining potassium homeostasis. Our lab has recently found that a family of trafficking adaptors, the □-arrestins, regulates Kir2.1 localization using a yeast model system. In contrast to their well-described manner where a-arrestins act as endocytic adaptors, we demonstrate that these □-arrestins promote Kir2.1 trafficking to the cell surface, increasing Kir2.1 activity at the PM and raising intracellular potassium levels. By using cutting edge microscopy and a single chain antibody fusion to Kir2.1 we can selectively monitor Kir2.1 cell surface localization or its intracellular distribution, providing a powerful tool for delineating the intracellular sorting pathway for this transporter.

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Chronic bladder pain (CBP) activates neurons in the central nucleus of the amygdala in the the brain which exhibit different responses in each hemisphere. To better understand CBP, an agent-based computational model was developed to replicate neuronal behavior observed in laboratory experiments. Simulations of the model are performed using Netlogo software where agents represent individual neurons with unique firing rates updated stochastically at each time step. Model parameters were estimated using the results of laboratory experiments in which firing rates of four neuronal types were measured during various pain states. A damage accumulation feature was added to the model to track the organism's long-term pain history. The model interface provides a dynamic framework for viewing neural activity as it evolves over time and in response to different pain stimuli. Ongoing work includes accounting for the topology of the neural network, cell-type specificity, and expanding the model to three spatial dimensions.

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Determination of novel peptide fragmentation pathway using density functional theory

Pollak, Nick, G.[1], VanStipdonk, Michael, and Evanseck, Jeffrey D.
Center for Computational Sciences and Department of Chemistry and Biochemistry
Duquesne University; [1]Lebanon Valley College 101 College Ave, Annville, PA 17003

Fragmentation of salicylaldehyde-modified alanine-glycine-glycine (Sal-AGG) to salicylaldehyde-modified glycine-glycine (Sal-GG) was discovered through the use of tandem mass spectrometry and collision-induced dissociation during previous studies by van Stipdonk *et al.* Two possible mechanisms for this fragmentation were proposed, but remain unresolved. Density functional calculations using Truhlar's Minnesota functional M06-2x and Pople's 6-31G* basis set were used to find the activation energies of both pathways. The lower energy pathway involved a protonated nitrogen in alanine, as well as the use of a five-membered ring intermediate. The lower energy pathway has an activation energy of 12.9 kcal/mol and is more favorable thermodynamically, thus it is considered to be the proper mechanism for this novel fragmentation.

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Conformation, Stabilization, and Decarboxylation of L-DOPA

Mary E. Burton[1], Jeffrey J. Rohde[1], Jeffrey D. Evanseck[2]
[1]Franciscan University of Steubenville, [2]Duquesne University
Center for Computational Sciences: Department of Chemistry and Biochemistry

Symptoms of Parkinson's disease can be treated with Levodopa (L-DOPA) in combination with Carbidopa, a peripheral dopa decarboxylase inhibitor. To treat the symptoms, L-DOPA undergoes decarboxylation in the brain to increase the dopamine levels. The mechanism of L-DOPA decarboxylation has not been investigated. We report a conformational analysis of L-DOPA in the gas and condensed phases. We find that a "buckle of hydration" with 3 or 5 waters using Truhlar's M06-2X density functional with Pople's 6-31+G(d) basis set and the Tomasi's polarizable continuum model (PCM) provides ground state stabilization of a specific "orthogonal" conformation over other pseudochair conformations. The computed buckle follows a different hydrogen bonding pattern than that observed for ketoacids, where L-DOPA capitalizes upon three waters serving as hydrogen bond donors to buckle-in the CO_2 group from departing. This discovery could help drug manufacturers to improve the design of dopa decarboxylase substrates and inhibitors to treat the disease.

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Hydrogen bonding and structure of G-quartets

Gagliardi, Austin L; Mihailescu, R.; Evanseck, Jeffrey D.
Center for Computational Sciences and Department of Chemistry and Biochemistry
Duquesne University

Despite the significance of the G-quadruplex structure in DNA/RNA, the structure and associated energetic stability of the G-quartet formation remains largely unknown. Models of guanine tetrads have been examined with C_{4h}, C_4, C_{2h}, C_2, C_s, and C_1 symmetry and using Stewart's PM7 semiempirical method, Truhlar's M062X density functional, and Dunning's cc-PVDZ and cc-jul-PVDZ basis sets. Within each point group symmetry, the possibility of different hydrogen bonding patterns of all-Hoogsteen (HHHH), all-bifurcated (BBBB), and hybrid (HBHB) were computed. Our results show that gas phase models of the G-quartet do not have a plane of symmetry, that the BBBB complex is ~ 1 kcal/mol more stable than HBHB G-quartet, and that total hydrogen bond energy is worth ~ 90 kcal/mol. This work sets the foundation for future quadruplex studies, which could provide insight into diseases, such as ALS and fragile-X mental retardation syndrome, related to G-quadruplex presence.

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