

2017 CRL Student Summer Poster Symposium

Thursday, July 27, 2017

2:45pm - 3:45pm

Session B

51. Localization of ADF in auditory stereocilia to investigate its role in stereocilia length maintenance and hearing loss.

Nevin Anderson

Department of Biology, IUPUI

Actin-based protrusions, known as stereocilia, located in the organ of Corti are responsible for transmitting signals to the brain in order to process sound. The lengths of these stereocilia are precisely regulated so that signals are transmitted properly. Actin depolymerizing factor (ADF) and cofilin-1 (CFL1) are important in the severing and maintenance properties of the stereocilia. The specific localization of these proteins is still unclear and could prove fundamental in the relationship between stereocilia function and formation. For example, ADF^{-/-} null mice show defects in the maintenance of stereocilia length of shorter rows and have accelerated hearing loss. Cochlea taken from B6 mice and ADF knockouts were stained using a previously uncharacterized monoclonal antibody. The results of the immunofluorescence yielded evidence for localization at the taper region or base/rootlets of stereocilia and some evidence for tip localization. Further investigation is required to test the specificity of this antibody for ADF/CFL1 using tissue lacking both proteins as a negative control. Furthermore, ADF localization to rootlets was unexpected and raises new questions about the role of ADF. ADF could maintain and shape the formation of rootlets or the taper region which is essential for proper hearing and appropriate deflection of stereocilia throughout the mechanotransduction process.

Mentors: Jamis McGrath, Department of Biology, IUPUI; Benjamin J. Perrin, Department of Biology, IUPUI

52. The Effects of Increasing EGCG Dosage on Skeletal Parameters in Ts65Dn and Control Mice

Raza Jamal, Jonathan LaCombe, Roshni Patel, Matthew Blackwell, Sricharan Kanthala, Randall Roper
Department of Biology, Indiana University-Purdue University Indianapolis

Down Syndrome (DS) is a result of the triplication of chromosome 21 and causes cognitive deficits, reduced bone strength, and deficits in bone structure. Many phenotypes associated with DS in humans including the skeletal deformations have been recapitulated in the Ts65Dn mouse model. This mouse model is a segmental trisomy and contains half of the gene orthologs seen in human trisomy 21. Previous studies have shown that the skeletal deficits observed in DS are a result of the abnormal expression of Dyrk1a which is found in three copies of individuals with DS and Ts65Dn mice. Previous studies in mice have also shown that genetic reduction of Dyrk1a and hypothesized Dyrk1a inhibitors can improve some cognitive defects and some bone deficits associated with DS. One such inhibitor is Epigallocatechin-3-gallate (EGCG). We have examined Ts65Dn and euploid (normal) mice treated with 9mg/kg/day, 20mg/kg/day, 50mg/kg/day, and 200mg/kg/day EGCG. Trabecular and cortical bone parameters such as bone mineral density, trabecular number, and trabecular separation were compared across the various dosages. Trabecular separation, thickness, number, and percent bone volume were improved in Ts65Dn mice given 9mg/kg/day EGCG. We hypothesized that EGCG treatment would have a positive effect on trabecular and cortical bone parameters in Ts65Dn mice given 20 mg/kg/day EGCG for 7 weeks. Initial analysis of cortical bone indicates that increasing dosage of EGCG had an overall negative impact on cortical bone by reducing cortical surface area. Cortical thickness and cortical area in euploid and trisomic mice showed a negative trend for 50mg/kg/day and 200mg/day. Increasing the dosage of EGCG and treating for a longer period of time showed a trend of lower percent bone volume, but did not affect other trabecular parameters. These data suggest that increased EGCG dosage may negatively affect cortical bone more than trabecular bone structure. Because of the high availability of EGCG and some studies supporting EGCG treatment to improve cognitive deficits associated with DS, individuals with DS that receive EGCG should be closely monitored for adverse effects on skeletal structure.

Mentor: Randall Roper, Department of Biology, Indiana University-Purdue University

53. Characterization of Hedgehog Signaling in Adult Feeding Centers of the Hypothalamus

Logan S. Whitehouse¹, Staci Engle¹, Ruchi Bansal¹, Troy Masters¹, Nicolas F. Berbari¹

¹Department of Biology, School of Science, Indiana University Purdue University, Indianapolis, Indiana

Primary cilia are microtubule-based cellular appendages known to serve as signaling centers in development and adult tissue homeostasis. Diseases, known as ciliopathies, associated with cilia malfunction result in debilitating phenotypes including retinal degeneration, diabetes, and obesity. One such ciliopathy, Bardet-Biedl Syndrome (BBS), presents with hyperphagia associated obesity in patients and mouse models. One signaling pathway that cilia coordinate is the hedgehog pathway, which is critical for processes such as neural tube patterning and limb development. Little is known about the role of cilia-mediated hedgehog signaling in adult tissues, including in the brain. Here we use a hedgehog pathway reporter allele in control and BBS mutant mice to assess activity in the adult hypothalamus early postnatally, prior to the onset of obesity and once obese. Preliminary results, demonstrate an increase of hedgehog activity in the ventral medial hypothalamus of *Bbs4* mutants compared to wildtypes sibling controls. We also observe a decrease in LacZ reporter in the arcuate nucleus. Future studies looking at understanding the role of hedgehog pathway signaling in the adult hypothalamus may reveal previously unrecognized roles in adult energy homeostasis.

Mentors: Nicolas Berbari, Department of Biology, IUPUI School of Science, IUPUI

54. Duality of Cortical Representation

Daniel Kessler¹ and Samuel Weir²

Case Western Reserve University¹Indiana University –Purdue University Indianapolis: Purdue School of Science²

The brain is able to differentiate between stimuli to determine which one elicited a reward. Furthermore, it holds this information in working memory to reach a decision. We do not know how the brain differentiates between neural signals and stores information in working memory coincidentally to make a binary choice in the case of a delayed reward. The tasks of holding memories and differentiating stimuli are mutually exclusive and constitute functional duality. We want to find what mechanism mediates this duality in the brain. We explore possible mechanisms to solve this problem by reproducing two models of the phenomenon. One model focuses on winner-take-all competition between neuron clusters due to inhibitory neurons, leading to a binary decision. The other focuses on how the strengthening of synaptic connections between neurons in the presence of a reward causes clustering of neurons. Within these models, we are building matrices representing the connectivity of the neural networks to understand the similarities and differences between them. We analyze the connectivity matrices of the networks to understand how standard STDP leads to cluster formation. This will help us understand more about how the brain uses memory of past rewards to reach decisions.

55. Nociceptin Modulates the Anxiolytic Effects of Ethanol Inside the Central Amygdala

Anissa Cervantes¹

¹Clinical and Translational Sciences Institute, IUPUI Center for Research and Learning

The central amygdala (CeA) is a mediator for many anxiety and alcohol related behaviors. Past research in our laboratory has shown that alcohol directly injected into the CeA is anxiolytic. During alcohol addiction, many pro or antistress neuropeptide systems in the CeA become dysregulated. One neuropeptide particularly abundant in the CeA is nociceptin which has been shown to diminish the influence of ethanol on GABAergic and glutamatergic activity on CeA neurons in vitro. The current study investigated whether bilateral microinfusions of nociceptin into the CeA would alter the anxiolytic effects of subsequent ethanol microinfusions into the CeA. Each test rat was outfitted with a pair of cannulas directly into the CeA and then received a bilateral pre-treatment infusion of either artificial cerebrospinal fluid (aCSF) or 0.5nM nociceptin, followed by a post-treatment infusion of either aCSF or ethanol. Each rat experienced once one of the four following test conditions over the course of four daily sessions: aCSF/aCSF, aCSF/EtOH, nociceptin/aCSF, and nociceptin/EtOH. Following the second set of microinfusions, each test rat was then placed in an arena with a social partner, and its resulting social interaction behavior was recorded for five minutes a session. As nociceptin blocks the effects of ethanol in vitro, it is hypothesized that the nociceptin pretreatments will diminish the anxiolytic effects of the ethanol in the CeA. Future experimentation would investigate the exact molecular mechanism of nociceptin in the CeA.

Mentor: Zachary Rodd, Department of Psychiatry, IU School of Medicine

56. Synthetic and structural biology of molecular machines involved in gene regulation

Jackson C. Gleaves¹ and Yuichiro Takagi²

¹College of Arts and Sciences, Indiana University; Department of Biochemistry and Molecular Biology, Indiana University School of Medicine

Mediator is a large multiprotein complex essential for gene expression in eukaryotes. In humans, Mediator is composed of 34 subunits with a molecular mass over 1.6 MD. It is organized into 4 sub-complexes, termed Head, Middle, Tail, and CDK8 module. Mutations in several human Mediator subunits have been linked to neurological disorders and cancers, exemplifying the importance of proper Mediator function for human health. These diseases include Uterine Leiomyomas, Opitz-Kaveggia syndrome, Lujan-Fryns syndrome, and Ohdo syndrome. It is important to understand how Mediator functions to regulate gene transcription in humans as well as how mutations in mediator will lead to disease states. Interestingly, over 90% of these disease-associated mutations found in Mediator are mapped onto the gene encoding hMed12 protein, which is one of the subunits of the CDK8 module. The goal of my project is to understand how hMed12 disease-associated mutations affect assembly and functions of the human CDK8 module, leading toward understanding disease mechanisms. The approach is to generate mutation-containing human CDK8 modules in vitro and test them to see how these mutations might impact assembly of the complex –the CDK8 module is composed of hMed12, hMed13, hCDK8, and Cyclin C –as well as function of the complex. So far, DNA constructs harboring the mutations leading to the diseases previously mentioned have been successfully generated. The next step will be to utilize mutant Med12 DNA to generate the mutant human CDK8 modules for structural and functional studies, which will help fulfill the goal of understanding the disease mechanism.

Mentor: Yuichiro Takagi, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, IUPUI

57. Orai1 Dependent Calcium Activity in Activated CD4+ lymphocytes from Peripheral Rat Blood following Acute Kidney Injury (AKI)

Elizabeth A. Cannon¹, Purvi Mehrotra², David P. Basile²

¹Department of Biological Science, University of Notre Dame; ²Department of Cellular and Integrative Physiology, IU School of Medicine

T cells have been implicated in the pathogenesis of Acute Kidney Injury (AKI). Previous studies from our lab have shown AKI and high-salt diet increases a specific T helper subset, Th17, characterized by the secretion of IL-17 cytokine. In addition, AKI primed T cells, when exposed to elevated sodium and angiotensin II (AngII) in vitro, secrete increased levels of IL-17, while T cells from control sham-operated rats do not. Multiple studies suggest a critical role for the CRAC of Orai1-mediated calcium release in T cell function. However, its role in AKI primed Th17 activation is unclear. We hypothesize that AKI induces elevated Orai1 channel activity, which mediates enhanced IL-17 activity in T cells. Calcium levels were measured using Fura-2 dye in T cells isolated from peripheral blood of post-ischemic rats or sham operated rats. To determine the role of Orai1, T cells were treated with inhibitors specific to Orai1 function [100mM: YM 58483; 50uM: AnCoA4]. Increased calcium levels were observed in response to elevated sodium [170mM] +AngII [10⁻⁷M] in AKI primed T cells, which was significantly reduced when treated with YM 58483 or AnCoA4. Interestingly, the majority [~40%] of AKI primed CD4⁺ T cells exhibited an increased calcium influx in response to elevated sodium+AngII. In contrast, T cells from sham operated rats showed little to no calcium influx in response to elevated sodium+AngII. Taken together, these data suggest that increased IL-17 responses in lymphocytes following AKI are dependent on Orai1-mediated calcium influx.

Mentor: David P. Basile, Department of Cellular and Integrative Physiology, IU School of Medicine, IUPUI

58. LITERATURE BASED DISCOVERY OF BLOOD AND SALIVA BIOMARKERS FOR PERIODONTITIS

Kiashia D Sloan-Stubbs (Dr. Mythily Srinivasan)

Department of Oral Pathology, Medicine and Radiology, School of Dentistry, Indiana University Purdue University at Indianapolis, IN.

Periodontitis is an inflammation of tissues surrounding the teeth. The disease is often diagnosed after tissue destruction has occurred. Research suggests that enzymes, proteins, and bacteria in saliva and blood can be used as biomarkers for early detection of periodontitis. The purpose of this research is to compare and contrast saliva and blood for clinical applications in detecting periodontitis. Literature based discovery (LBD) is the use of publications and papers to detect new connections and relationships between already existing data and knowledge. Using the LBD method, the PUBMED (<https://www.ncbi.nlm.nih.gov/pubmed>) database was searched with the key words periodontitis, saliva and/or blood and biomarker. The biomarker evaluated, the method used to measure and statistical significance reported in each article were recorded. During the last six weeks, a total of 50 articles were retrieved. Twenty-one studies evaluated periodontitis biomarkers in blood, twenty-six in saliva, and three reported evaluations in both blood and saliva. The most common test used was the enzyme-linked immunosorbent assay test (ELISA). The most common method used to determine statistical significance was the Mann-Whitney U test. Twelve different proteins were investigated as biomarkers for periodontitis in the 50 articles retrieved. The cytokine interleukin-1 Beta (IL-1 β) was the most common biomarker investigated both in saliva and blood for periodontitis. In many ways, blood and saliva are alike. Blood and saliva are complex body fluids that share nearly 40% of proteins. While, blood collection is invasive, expensive, and uncomfortable, saliva collection is easy, inexpensive and painless. From the literature-based research, it is possible to conclude that specific proteins could represent as potential biomarkers for periodontitis. It is also possible to conclude that saliva is as good as blood in detecting the same. However, these observations should be taken with some reservations since the results are only from 50 articles.

59. Expression and Characterization of a Periplasmic Nitrate Reductase Chaperone Protein, NapD

Ian Burke¹, Breeanna Mintmier¹, Jennifer McGarry¹, and Partha Basu¹

¹Department of Chemistry and Chemical Biology Indiana University-Purdue University Indianapolis

Molybdopterin enzymes are a class of molybdenum containing enzymes that are present in all phyla of life and participate in the global cycling of nitrogen, sulfur, carbon, arsenic, and selenium. This class of enzymes are separated into three families and this work focuses on the DMSO reductase family; specifically, an enzyme known as periplasmic nitrate reductase (Nap). This enzyme reduces nitrate into nitrite. The reduction of nitrate is key to life and the global nitrogen cycle due to the presence of nitrogen in both organic and inorganic molecules that allow organisms, varying from prokaryotic to eukaryotic, to function. The periplasmic nitrate reductase complex is comprised of multiple proteins that provide various functions to achieve the goal of nitrate reduction. This research aims to focus on NapD, a subunit of the Nap enzyme that acts as a chaperone protein and is located in the cytoplasm. NapD has been shown to bind with the catalytic subunit, NapA, through the twin-arginine protein transport pathway (TAT) and thus proves to be an integral part of the Nap enzyme. A thorough characterization of NapD is needed to understand its functional role, which may help understand the maturation process of related redox enzymes. Mentor: Partha Basu, Department of Chemistry and Chemical Biology, School of Science, IUPUI

60. THE EFFECTS OF E-CIGARETTE LIQUID/VAPOR ON HUMAN GINGIVAL FIBROBLASTS: CELL PROLIFERATION AND TOXICITY

Aundria Liggins¹, Crystal Peters², Theresa Nelson², Saleh Mohammed Alhijji³ and (L. Jack Windsor³)

³Department of Biomedical and Applied Sciences, Indiana University School of Dentistry, Indianapolis, IN 46202

The use of electronic cigarettes (EC) worldwide has exploded. However, there is limited data on the effects of the EC liquids (e-juices) on cells in the oral cavity that are the first ones exposed to the vaporized e-juices. There are multiple brands of e-juices available with different concentrations of nicotine or with no nicotine. These e-juices also contain propylene glycol, vegetable glycerin, natural and artificial flavorings. Therefore, the purpose of this study was to evaluate one brand of e-juice currently marketed in Indiana with and without nicotine on human gingival fibroblasts (HGF) to determine cell toxicity and its effects on cell proliferation in the liquid form and captured components after vaporization. The e-juice chosen was Space Jam, which is a top seller in the Indianapolis vapor shops. HGFs were grown in cell culture media with serum and then plated in twelve well plates (50,000 cells per well). After allowing 24 hours for cell attachment, the media was removed and media with and without liquid e-juice and captured vaporized were added at different concentrations. After 3 days, assays for cell proliferation and cell toxicity were performed. Results from the assays showed that liquid e-juices with or without nicotine were toxic and affected cell growth at 10% (V/V) only. Similar results were observed from the vaporized e-juice with and without nicotine. The overall conclusion is that the concentrations tested that the other components in the e-juice whether vaporized or not at 10% affects human gingival fibroblasts.

¹Indiana University, Bloomington, IN, ²Indiana University-Purdue University Indianapolis, Indianapolis, IN,

61. Identification of Novel Direct Binding Partners of Hypoxia-Induced Isoform of Mdm2

Sujal K. Patel, Lindsey D. Mayo

IUPUI School of Science; Department of Pediatrics, IU School of Medicine

The murine double minute 2 (Mdm2) is an oncoprotein is detectable in 40-90% of human cancers, and is correlated with high-grade metastatic tumors and poor patient outcomes. Mdm2 regulates the tumor suppressor p53 protein through post-translational modifications, resulting in p53 degradation. p53 acts as a genomic watchdog through its contribution in providing surveillance to maintain DNA integrity and protect cells from malignant transformation and therefore it is called the “Guardian of the Genome.” There are many other functions of Mdm2 besides the degradation of p53, and our lab focuses in this area. We want to explore new functions of Mdm2 using PCR, which is an accurate and reproducible method in molecular biology to amplify single copy of a DNA and generating thousands to millions copies of specific DNA. Produced DNA fragments are then separated based on their size and visualized using gel electrophoresis. Implementation of these two methods should reveal alternative binding partners of Mdm2 under conditions of hypoxia. During the progression of every solid tumor, cells experience a hypoxic environment at a certain point due to limited oxygen availability and nutrient diffusion. The protein product of the von Hippel-Lindau gene, pVHL, is an important regulator of hypoxia. According to preliminary studies, the participation of pVHL in a new pathway that may lead to the transcription of several antiangiogenic target genes and alter the transcription of Mdm2, resulting in either decreased mRNA and protein or an alternatively spliced mRNA resulting in a protein isoform of Mdm2 with altered functions.

Mentor: Lindsey D. Mayo, Department of Pediatrics, IU School of Medicine

62. Telomere Dysfunction and Mitochondrial DNA in Women with BRCA1/2 Mutation

Kanokwan Jiffy Bishop, Rie Matern, Hiromi Tanaka

Department of Medical and Molecular Genetics, IU School of Medicine

About 1 in 8 U.S. women will develop invasive breast cancer over the course of her lifetime. BRCA1 and BRCA2 (Breast Cancer genes 1 and 2) are the best-known genes linked to breast cancer risk. Multiple studies of BRCA1/2 mutation carriers suggest that the “one-hit” effects occur even before loss of the wild-type allele and precede development of cancer (so called “haploinsufficiency”). We and others have hypothesized that telomere and mitochondria dysfunction may account for the unstable phenotype in heterozygous BRCA1/2 mutation carriers. To test and further understand the BRCA1/2 haploinsufficiency, this study aimed to quantify telomere length, mitochondrial DNA (mtDNA) copy number, and plasma telomeric cfDNA levels and determine their associations in women carrying BRCA1/2 mutation. The results from these cases (N=25) were compared to their age-matched controls (N=36). First, we found that leukocyte mtDNA copy number was associated with BMI, however there is no association between mtDNA copy number and BRCA mutations. Second, leukocyte telomere length was significantly shorter in women with BRCA1/2 mutation. This finding supports the hypothesis that BRCA1/2 germline mutation carriers result in shorter overall telomere length in leukocyte at baseline. Finally, our preliminary data showed that plasma telomeric cfDNA levels were significantly lower in BRCA mutation carriers than non-carriers. These findings reinforce that telomere damage may be implanted in germ/stem-like cells because of genetic predisposition of BRCA1/2. Further, we propose that the plasma telomeric cfDNA levels may be a potential biomarker for discriminating women with BRCA1/2 mutation from age-matched controls.

Mentor: Hiromi Tanaka, Department of Medical and Molecular Genetics, IU School of Medicine, IUPUI

63. Expression of Mutant p53 Gene into Ovarian Cancer Cell Line

Aishat C. Audu¹, Yong-hyun Shin¹, Sanghoon Kwon¹, Solji Hyeon¹, Jaeyeon Kim¹
¹Department of Biochemistry and Molecular Biology, Indiana University School of Medicine

High-grade serous carcinoma (HGSC), the deadliest subtype of ovarian cancer, is characterized by widespread metastasis of tumors throughout the peritoneal cavity. Better understanding of p53, a key tumor suppressor protein mutated in 96-98% of patients with HGSC, could lead to earlier diagnosis and treatment. We have developed two mouse models that both show similar progression of HGSC to the clinical progression: Dicer1-Pten double-knockout (DKO) mice and p53R172H-Dicer1-Pten triple knockout (TKO) mice. Interestingly, the TKO mice die three months earlier than DKO mice. This suggests p53R172H accelerates ovarian cancer in mice. We seek to understand the role of mutant p53 in HGSC progression and mortality. To achieve this, we are cloning p53R172H into a retroviral plasmid vector, transducing this vector into mammalian cells, and assessing mutant p53 protein expression. In previous studies we have established the p53R172H retroviral clone. This summer, we directly transduced p53R172H into DKO cell lines. Our immediate goal was to create a stable DKO cell line that will exclusively produce p53R172H. To achieve this, a puromycin resistant gene was added to the p53R172H retroviral vector and the transduced DKO cell lines were treated with puromycin, effectively killing cells that did not integrate the p53R172H gene into their genome. Transduction efficacy was confirmed via fluorescence of the green fluorescence protein (GFP). Further studies will observe mutant p53's impact on DKO cell tumorigenic activity via proliferation, migration and invasion assays.

Mentors: Jaeyeon Kim, Ph.D., Department of Biochemistry and Molecular Biology, IU School of Medicine; Yong-hyun Shin, Ph.D., Department of Biochemistry and Molecular Biology, IU School of Medicine

64. Clcn7G215R Missense Mutation Leads to Defective Cytoskeletal Reorganization and Decreases Bone Resorption in ADO2 Mice

Gabriel Coleman*, Rita Gerard-O'Riley, Dena Acton, Dana Oakes, Shahed Sbeta, Michael Econs, Imranul Alam.

Division of Endocrinology – IU School of Medicine Indiana University-Purdue University Indianapolis

Autosomal Dominant Osteopetrosis Type II (ADO2) is an incurable osteoclastic disorder that is caused by mutations in the Chloride Voltage-Gated Channel 7 (Clcn7). ADO2 is characterized by osteosclerosis, commonly resulting in multiple fractures of the long bones and vertebrae, osteonecrosis of the jaw and in severe cases can lead to bone marrow failure. In vitro, ADO2 osteoclasts sustain an underdeveloped sealing zone (F-actin ring) and demonstrate reduced migration when compared to wild-type (WT) controls. Several studies have demonstrated that ADO2 osteoclasts express dysfunctional structural proteins that are required for adhesion of the osteoclast to the extracellular bone matrix. We hypothesize that the Clcn7 missense mutation gives rise to defective cytoskeletal organization and leads to reduced osteoclast function. To elucidate the connection between integrin activation and the broader osteoclast phenotype, we analyzed the gene expression of bone marrow derived osteoclasts from WT and ADO2 mice. Using osteoclasts in various developmental stages, we observed decreased expression in c-Src, Pyk2, and Itgb3 which are necessary for proper intracellular cytoskeletal/microtubule organization in osteoclasts. These results provide evidence that dysfunctional cytoskeletal mechanisms may play a role in the manifestation of ADO2.

65. Mechanism of osteoclast differentiation induced by apoptotic osteocytes

Sinai Valdez¹, Hannah M. Davis², and Lilian I. Plotkin^{2, 3}

¹Department of Biology, Indiana University-Purdue University Indianapolis School of Science; ²Department of Anatomy & Cell Biology, Indiana University School of Medicine, Indianapolis, IN; ³Roudebush Veterans Administration Medical Center, Indianapolis, IN

Osteocytes are embedded in fully formed bone, these cells are the key in controlling the function of bone-forming and reabsorbing cells. From previous work a very specific gap junction proteins called connexin43 was observed to be a very important component of the signaling pathway controlling osteocyte survival. Since aging decreases connexin43 then the deletion of this protein was found to mimics the skeletal phenotype of old mice. This experiment was design to examine the particular link between osteocyte apoptosis and osteoclast differentiation. As well as to determine the molecular signals responsible for mediating these effects in mice lacking osteocytic Cx43 and in old mice. In order to address this problem a molecule called HMGB1, a pro-inflammatory cytokine, which has shown to mediate osteoclast recruitment/differentiation was used on osteoclasts. To test the effects of HMGB1 osteoclasts were scored that were treated with conditioned media collected from MLO-Y4 osteocytic cells treated with anit-HMGB1. This concluded that osteocytes treated with anti-HMGB1 decreased the number of osteoclasts. Additionally, treating the osteoclasts with anti-HMGB1 had no effect on the number of osteoclasts, which tells us the osteoclast-derived HMGB1 is no required for osteoclast differentiation, but osteocyte-derived HMGB1 stimulates osteoclast formation. The data collected so far further confirms the role of apoptotic osteocyte-derived HMGB1 in stimulating osteoclast differentiation. These findings further demonstrate the link between osteocyte apoptosis and osteoclasts recruitment/differentiation.

66. Towards the preparation of cysteine-free variants of human muscle and human brain creatine kinase

Anthony J. Huls¹, Katharina Fransen² and Michael J. McLeish¹

¹Department of Chemistry and Chemical Biology, Indiana University-Purdue University Indianapolis, ²Department of Chemical Engineering and Materials Science, University of Minnesota

Creatine kinase (CK), found in all vertebrates, catalyzes the reversible interconversion of creatine and ATP forming phosphocreatine and ADP. Phosphocreatine can be viewed as a reservoir of "high energy phosphate", able provide ATP on demand. As such, it plays an integral role in cell homeostasis, particularly in cells that have sporadic high energy demands, like muscle and bone cells. There are two soluble isozymes of creatine kinase, muscle and brain, both of which form homodimers, MMCK and BBCK, respectively. While the enzyme is well characterized, X-ray structures of MM creatine kinase from the electric ray, *Torpedo californica*, show significant conformational changes during catalysis. Specifically, there are two loops that move considerable distance to cover the active site during phosphate transfer. This movement is of additional interest because residues that are quite distant in the substrate-free enzyme, also appear to play a role in substrate recognition.

It is thought that fluorescence resonance energy transfer (FRET) may prove useful in tracking movements of these loops. This technique is made possible by the use of fluorescent dyes attached to the enzyme in specific positions through reaction with cysteine residues. To ensure correct labelling, cysteine residues from the native enzyme must be removed. Preliminary studies indicated that complete replacement of all cysteines with serines yields insoluble protein. In this project, we have focused on addressing the issues caused by the insolubility. This includes the identification of the individual replacements that cause insolubility, and the use of histidine tags to improve the purification methodology for both the wild-type CK and its variants.

Mentor: Michael J. McLeish, *Department of Chemistry and Chemical Biology, IUPUI.*

67. Nanocomposite Sensors for Detecting VOCs and Development of a Model for PVDF-HFP/Carbon Black Composite Based on Percolation Theory

Paula Andrea Angarita Rivera¹; Ali Daneshkhah^{3,4}; Shitiz Vij²; Mangilal Agarwal^{2,4}

¹Department of Mathematics and Engineering, Marian University; ²Department of Mechanical Engineering, ³Department of Electrical Engineering, ⁴Integrated Nanosystems Development Institute Indiana University-Purdue University Indianapolis

Hypoglycemia (Blood glucose <70 mg/dl) as a result of diabetes is a major problem in the health industry. Two to four percent of people who suffer from diabetes die because they are unaware of their low blood sugar levels. A nanosensor system could detect the hypoglycemia in human breath. Resistive based sensors such as monolayer capped gold nanoparticle (MCGNP) and conductive polymer composites have successfully detected different health conditions. The purpose of this research is to design, fabricate, characterize and test resistive based sensors developed with nanomaterials. Integrated electrodes have been fabricated through lithography of gold over silicon dioxide on a silicon wafer. Resistive MCGNP (5.5 nm diameter) were deposited using drop casting method. The sensor was tested with low concentration of Volatile Organic Compounds (VOCs) in air carriers at the relative humidity (R.H) of 0% and 80%. Swelling of nanoparticles in interaction with VOC increases the gap between particles. The result of this swelling is a change in resistance. The sensors resistance increases with exposure to the VOC and decreases with exposure to air. The MCGNP sensor resistance changed up to 3.38% in response to the low concentration of VOC (45 ppm) in dry air. The resistance change at R.H 80% was 2.4% lower than R.H 0%. This showed 29% reduction in the sensitivity of the sensor. The sensor response time was measured and estimated to be 10 min. In addition to MCGNP sensors, Poly(vinylidene fluoride-co-hexafluoropropylene)/Carbon Black (PVDF-HFP/CB) sensors were fabricated and a resistive study was conducted. The results will be used to model the composite based on percolation theory. The parameters of percolation threshold (PC) and critical exponents (t) were measured for two different type of carbon black (Super C65 and Black pearl 2000). These parameters (PC and t) will be used to fabricate sensitive PVDF-HFP/CB sensors and provide information to simulate a sensor in different conditions.

Mentor: Ali Daneshkhah (PhD Student) and Mangilal Agarwal (Faculty)

68. A Cancellable and Privacy-Preserving Facial Biometric Authentication Scheme

Tyler Phillips
NSF REU; IUPUI

In recent years, biometric, or “who you are”, authentication has grown rapidly in acceptance and use. Biometric authentication offers users the convenience not having to carry a password, PIN, smartcard, etc. Instead, users will use their inherent biometric traits for authentication and, as a result, risk their biometric information being stolen. The security of users’ biometric information is of critical importance within a biometric authentication scheme as compromised data can reveal sensitive information: race, gender, illness, etc. A cancellable biometric scheme, the “BioCapsule” scheme, proposed by researchers from Indiana University Purdue University Indianapolis, aims to mask users’ biometric information and preserve users’ privacy. In this paper we will present a facial authentication system which employs several cutting edge techniques. We test our proposed system on several face databases, both with and without the BioCapsule scheme being embedded into our system. By comparing our results, we quantify the effects the BioCapsule scheme, and its security benefits, have on the accuracy of our facial authentication system.

69. Preserving Key Features of Online Social Network Graphs via Persistent Homology

Claire S. Lee
Indiana University-Purdue University Indianapolis

Online Social Networks (OSNs) are simple, undirected graphs used to store information in the context of social media and emails. A common issue of OSNs in regards to graph publication is balancing the utility of a graph while satisfying the criteria of differential privacy. Thus, it is necessary to preserve key characteristics in an OSN. Previous methods of sustaining significant features such as clustering coefficient, degree distribution, and other various graph metrics fail to give an accurate depiction of the original OSN without compromising differential privacy. Persistent homology provides a viable method for a comprehensive visual representation of the information stored in network graphs. By translating a network graph to a persistent homology barcode format, we will observe the correlation in key features between the two figures. This paper will analyze the persistent homology barcodes of OSNs across several social media and email platforms. Furthermore, it will test the stability of the generated persistence diagrams by adding small perturbations to the original network graph.

70. Implementation and Analysis of a Revocable Fingerprint Biometric Authentication Scheme

Mark Miller

NSF REU –IUPUI, Indiana University –Purdue University at Indianapolis

The use of biometric authentication has become very prominent in recent years and, as its adoption becomes more and more widespread, it is important that biometric authentication systems in place are secure. The security of these systems is of great importance because a user's biometric information, for the most part, is unable to be recreated or modified unlike other forms of authentication such as PIN, passwords, or even identification cards, and could be dangerous for users if their unique biometric information was stolen. Recently, a new scheme for masking a user's biometric information was created by the researchers at Indiana University -Purdue University at Indianapolis called the "Bio-Capsule" scheme. In this paper, we will present an implementation of this "Bio-Capsule" scheme on a fingerprint authentication system to mask a user's sensitive fingerprint information. In this fingerprint authentication system, the original fingerprint image is preprocessed and converted into a masked fingerprint image to obfuscate a user's biometric information. Our fingerprint authentication system was tested using several fingerprint databases, both with and without the "Bio-Capsule" scheme being embedded into our system. The False Acceptance Rates (FAR) and False Rejection Rates (FRR) from both systems will be compared to display the security and effectiveness of the "Bio-Capsule" scheme.

71. Development of a Mobile App for Pseudo Real-Time Peer-to-Peer Communication for Supply Chain Management

Ravynne Jenkins

National Science Foundation Research Experience for Undergraduates; Indiana University-Purdue University Indianapolis

Abstract—The management and visibility of supply chain events and transactions in pseudo real-time are critical for managing the substantial order volumes, consumer availability and complexity of events and transactions. The convenience and affordability of a mobile application makes it ideal for managing a massive system containing various types of peers, such as the supply chain. In this paper, we implement a framework for real-time data sharing using peer-to-peer communication in an Android mobile application, Hybrid Peer-to-Peer Physical Distribution (H3PD). This implementation uses blockchain technology, public ledgers and private ledgers to ensure the security of supply chain activities as order details are exchanged from one peer to another. We present the design of the app, methods and tools used in the development, as well as the overall functionality of HP3D.

72. Using Twitter Streaming API to Gauge the Effects of Air Quality on Climate Change Sentiments.

Joevita Weah

NSF REU; Depauw University Indiana University-Purdue University Indianapolis

Evidence has shown that climate change is a growing problem of the 21st century, however many individuals do not fully support this assessment as being true. Understanding an individual's feelings towards climate change may aid in better educating the public in improved mitigation strategies for the future. In this paper, we examined the impact of health factors, such as air quality and asthma, on an individual's sentiment towards climate change. Microblogging social media services, such as Twitter, allow users to express varying levels of emotions, through emoticon usage, retweeting, replying, sharing, and other actions. To analyze sentiments, we gathered data from Twitter in the form of tweets that mentioned 'climate change' and assigned each tweet a sentiment score. We categorized sentiments as positive, negative or neutral. Using a Self Organizing Map (SOM), we clustered related features with varying sentiments. Our approach defined features as toxins, prevalence of asthma, and sentiment. We compared different features related to air quality and asthma, as well as how these features related to sentiment scores. To further analyze the health and Twitter data, we looked at the features by state. This then allowed us to compare the data and assess how health quality at the state level correlates with an individual's sentiments on social media.

73. Using Cancellable Electrocardiographic Templates to Authenticate and Encrypt Users

Brandon Johnson (Rollins College) and Dr. Xukai Zou(IUPUI)

Biometric authentication offers a unique method of verifying a user's identity through the analysis of physiological characteristics. There has been a recent proliferation of devices that use biometric information as means to authenticate users, such as iris scanners, fingerprint readers and electrocardiogram (ECG) readers. ECG measures the electrical activity produced by a heart and is unique to every person. The continuous nature of a heartbeat allows for ECG biometric authentication to retain user access to a device for the duration of device operation. This property allows for an increase in convenience, but also lends itself to the vulnerability of user biometric information being uncovered if attacked. Analysis of stolen ECG data could reveal sensitive user information such as an illness. This paper explores the viability of using a revocable encryption mechanism, developed by researchers from Indiana University -Purdue University Indianapolis, as a means of preserving the privacy of a user's ECG characteristics. This encryption mechanism is known as the "BioCapsule" scheme. Using "The PTB Diagnostic ECG Database," we assess the encryption performance of the BioCapsule through the implementation of various tests.

74. Misinformation Trends in Social Media and the Global Terrorism Database

Ivana Terziyska (Cornell University) and Xiao Luo (IUPUI)

NSF REU; Indiana University-Purdue University Indianapolis

Social media plays an important role in shaping an audience's beliefs and sentiments regarding current issues. Up to 65% of adults obtain their news from social media, and "fake news" articles are just as likely to go viral as accurate accounts, greatly impacting general perception and understanding. A comparison between significant features of objectively accurate, holistic datasets and user features of social media data would give insight into the spread of misinformation as well as ways to inform users and prevent it. We use the Global Terrorism Database (GTD), a focus of previous comparisons to diverse datasets, to highlight trends in terrorism, an extensive issue that is frequently referred to in media and data obtained using the Twitter API to assess features of social media data pertinent to relevant queries. We present a connection between terrorism as recorded in the GTD and terrorism as spoken about in tweets to determine discrepancies in the trends and features of both data sets. We also further extract user features, such as location, sentiment, popularity, and keywords used about recent fake news articles to determine which features are most likely to account for discussion and propagation of misinformation. Depending on user sentiment, features are extracted to classify users who spread misinformation as well as how they view it. We create a self-organizing map (SOM) of each dataset to identify clusters present both in the GTD and Twitter data to link our findings to broader conclusions about media bias and the spread of misinformation.

75. Study, Methodology and Analysis for Tracking Qbot Family of Botnets

Nash M. Fry

NSF REU; Indiana University-Purdue University Indianapolis

Botnets are an immediate and serious threat to current internet infrastructure and network security. Botnets are a network comprised of computers which have been infected with a malicious program. This malicious program allows an attacker, or "botmaster", to control an infected computer, or "bot". In order for a botmaster to control their bot network, bots must find and connect to a command and control (C2) server for critical commands. In this paper, we will discuss the methodology for finding and tracking the Qbot family of botnets. The methodology for tracking and analysis is broken down into three specific steps: (1) list of IPs/Ports/Hostnames of suspected command and control (C2) servers that exhibit specific properties that we have identified are collected using third party applications. (2) Using the collected information, we then use a custom script that acts as a fake bot that connects to and communicates with the suspected command and control (C2) servers. (3) Finally, we use information collected from our fake bot connection and communications to analyze and monitor the C2 server and its activities to better understand how C2 servers communicate with their bots in a botnet.

76. Alternative Synthesis of Gold Nanoprisms

Manpreet Kaur¹; Takshila Liyanage²; Ashur Rael²; Rajesh Sardar^{2,3}

¹DePauw University; ²Department of Chemistry; ³Integrated Nanosystems Development Institute Indiana University-Purdue University Indianapolis

Gold nanoprisms are typically created through a reaction that occurs with Trioctylamine (or Triethylamine), Triethylphosphine gold (I) chloride, and Polymethylhydrosiloxane. We are looking at different methods of trying to synthesize gold nanoprisms using Oleylamine instead of the commonly used Trioctylamine or Triethylamine. Additionally we substituted H₂AuCl₄ for Triethylphosphine gold (I) chloride. Lastly, we utilized a monomer unit of Polymethylhydrosiloxane. When changing one variable such as the stabilizing ligand, the type of gold salt, or the reducing agent we kept the others constant. We looked at different methods to determine what structure of the variables was playing a significant role in the synthesis of gold nanoprisms. By determining this we can see how the gold nanoprisms are created and further improve the process of creating gold nanoprisms. The Triethylphosphine gold (I) chloride that is used is important to create nanoprisms as when H₂AuCl₄ was used other nanostructures were created. Oleylamine can be used as a substitute for Triethylamine, which indicates that the three carbon chain structure does not impact the gold nanoprism structure as much as the amine group does.

Mentors: Takshila Liyanage (Graduate Student), Ashur Rael (Graduate Student), Rajesh Sardar (Faculty)

We would like to thank National Science Foundation for their support through the Research Experience for Undergraduate Students (REU) program (Award #1659688). Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation.

77. Metallic and Nonmetallicnanoparticle toxicity

Marcelius Lewis¹, Dr. Yogesh Joglekar²⁻³

¹Department of Communication/Business,Duquesne University, ²Department of Physics, ³Integrated Nanosystems Development Institute Indiana University-Perdue University Indianapolis

As research and development in nanotechnology increases, its potential application in various fieldsknownno bounds. Here at the Integrated Nanosystems DevelopmentInstitute (INDI)I am reviewing researchliterature on nanoparticle toxicity. Nanoparticles are tested for genotoxicity, cell toxicity, and immunotoxicity.Tetrazolium-based assays such as MTT and Cometare usedassessing the cell viability.From this,my maingoal wasto find the parallels between the toxicity effects of metallic and nonmetallic nanomaterials. Recent research finds that smaller zinc oxide nanoparticles produced the mosttoxicity mainly in lung cells. Carbonyl iron and silica nanoparticles,which are nonmetallic nanoparticles,did produce inflammatory cytokine production; only in macrophages.

Mentor: Yogesh NJoglekar Ph.D (faculty)

We would like to thank National Science Foundation for their support through the Research Experience for Undergraduate Students.(REU) program (Award #1659688)

78. Thermal annealing study of Polyvinylidene Fluoride (PVDF) Crystalline Thin Films

Adolfo Isaac Alvarado-Rivera¹; AaronMosey²⁻³; Dr. Ruihua Cheng²⁻³

¹Valencia College; ²Department of Physics, ³Integrated Nanosystems Development InstituteIndianaUniversity-Purdue University Indianapolis

Nanoscale organic ferroelectric materials, specifically Polyvinylidene Fluoride (PVDF) thin films have been studied extensively for their unique properties and have a wide range of applications. Understanding the crystallization of PVDF thin films through thermal annealing process is crucial for the optimization of ferroelectric properties. At the Integrated Nano-systems Development Institute (INDI), the effect of annealing temperatures on end-state crystalline structure of Polyvinylidene Fluoride (PVDF) thin films was examined. Preparation of the PVDF thin film was done by dissolve PVDF matrix in acetone. After the matrix dissolved and cooled, the Langmuir-Schaefer technique was used to apply successive monolayersonto glass substrates. The samples were then annealed at temperatures ranging from 120o C to 160oC. The varying temperatures affect the crystallization process in PVDF thus effecting the ferroelectric properties. Characterization of phase change and crystallization was done by x-ray diffraction (XRD) and scanning electron microscopy (SEM). Preliminary XRD results showed that the annealing process is dependent on both time and temperature, showing that longer time scale had higher order crystallization.

We would like to thank National Science Foundation for their support through the Research Experience for Undergraduate Students (REU) program (Award # 1659688). Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarilyreflect the views of the National Science Foundation.

79. Time-dependent PT-Symmetric Electronics

Zachary Cochran

IUPUI School of Science, Physics Department

A relatively new topic in physics is the concept of coupled gain and loss systems to simulate the behavior of quantum-mechanical systems modeled by non-Hermitian Hamiltonians that are parity-time (PT) symmetric. Much work has been done on these so-called “PT-Symmetric systems,” particularly in coupled laser systems, but recently PT-symmetric electronics has arisen as a new area of research, presenting the opportunity to study these systems with standard electrical components. In particular, Floquet PT-symmetric systems – systems whose Hamiltonians are periodic with time – are an exceptionally new topic, and easily achieved in electronics. In this research, I describe the true behavior of a non-ideal LC circuit and a method for reducing or negating the effects of the internal resistance in the inductor to create a “pseudo-ideal” LCR circuit via an equivalent gain component. I then show in a time-independent case how when two of these pseudo-ideal LCR circuits are coupled – one with amplification and the other with equivalent decay – two regions of operation emerge, depending on the parameter choices: either the system oscillates with two real eigenfrequencies simultaneously, indicating PT-symmetric behavior (the “Exact Region”); or they oscillate with exponential gain to a saturation point, indicative of the “PT-Broken Region,” where they cease to behave like a quantum-mechanical system. Finally, I explore the behavior of the Floquet system theoretically via Floquet analysis and perturbation theory, and then experimentally by then converting the static, time-independent system to the Floquet case by making the gain/loss parameters dependent with time by using voltage-controlled resistors.

Mentors: Dr. Yogesh Joglekar

80. Analyzing the effectiveness of Citizen Science within the Safe Urban Gardening Initiative in communicating risk and initiating change

Taylor Pemberton¹; Gabriel Filippelli²

Department of Psychology, Purdue School of Science¹; Department of Earth Sciences, Purdue School of Science

Recent studies show that high levels of lead in soil produce lasting cognitive effects when exposed to young children. Lead poisoning is identified as a leading childhood disease, but is preventable through taking proper action. Community engagement is a key factor in dealing with environmental concerns, such as lead poisoning. The Safe Urban Gardening Initiative was launched in 2014 to provide lead testing services for soils and recommendations for reducing risks of exposure to lead-contaminated soils, a common situation in older cities like Indianapolis. This citizen-science program provided instructions for people to take samples in their yards and to deliver the samples to the IUPUI lab for analysis, and delivered individualized reports for those people with results and recommendations to reduce lead levels. To date, approximately 2,500 samples have been analyzed from over 900 locations. In this current study, a survey was developed to determine the effectiveness of the delivery of lead level results, to see if community members have taken action to reduce lead levels in soil and ultimately prevent lead poisoning in young children. Our anticipation is that survey respondents will prefer different methods of delivery of lead level results (i.e. via email, website). Responses should show that this project increased awareness of environmental health concerns and initiated efforts to reduce levels of lead in soil. Future studies should explore other effective methods for educating community members of the risks of lead poisoning.

Mentors: Gabriel Filippelli, Department of Earth Sciences, Purdue School of Science, IUPUI

81. Computer simulation studies: Are vitamin E and PUFA driven together by cholesterol?

Samuel Canner^{1,2}, Xiaoling Leng¹, Dr. Stephen R. Wassall¹

¹Department of Physics, Indiana University-Purdue University, Indianapolis, IN 462022; Department of Computer Science, Indiana University-Purdue University, Indianapolis, IN 46202

Indiana University-Purdue University Indianapolis Vitamin E (α -tocopherol) is the principal antioxidant in cell membranes and is believed to protect PUFA (polyunsaturated fatty acids) from oxidation. Since α -tocopherol is in low concentration in membranes, generally less than 0.1 molar percent, co-localization with PUFA would be advantageous. We hypothesize that more abundant cholesterol drives α -tocopherol and PUFA together. To test our hypothesis, we performed computer simulations. All-atom, umbrella sampling molecular dynamics (MD) simulations that we initially ran on SOPC (a monounsaturated lipid) membranes containing 100 lipid molecules demonstrated that the presence of cholesterol reduces affinity for α -tocopherol. We are now running coarse-grained MD simulations to model a membrane containing a mixture of 1000 lipid molecules comprised of DPSPM (a saturated lipid), PDPC (a PUFA-containing lipid), cholesterol, and α -tocopherol (in a 7:7:7:1 ratio, respectively). DPSPM has high affinity for cholesterol, so we will see whether α -tocopherol is driven towards PUFA. The results of these studies will be presented.

82. Comparison of Gunshot Residue (GSR) Dispersal Patterns Deposited by a Firearm with and without a Silencer Attached and the Affect a Silencer has on Muzzle-to-Target Range Determination

Robert A. Johnson¹

¹Department of Forensic & Investigative Sciences, School of Science, IUPUI

Gunshot residue (GSR) patterns, created by a firearm discharge, are used by forensic scientists to determine a muzzle-to-target range. It is suspected that the addition of a silencer to a firearm will change the GSR pattern deposited. It is important to understand any differences that may be caused by the addition of a silencer in the event that a firearm with an attached silencer is used in a crime but the silencer is not recovered. This research shows the affect a silencer has on the GSR patterns of a 9 mm Glock model 17 pistol. The method used for the examination consisted of five parts: 1) the creation of test panels, 2) microscopic and macroscopic examination, 3) measuring of GSR pattern diameter, 4) chemical processing for nitrites and measuring of nitrite pattern diameter, and 5) chemical processing for vaporous lead. These methods are currently used by forensic scientists to determine a muzzle-to-target range. Distinct differences were observed when using the silencer and they include the variation in deposit densities, the absence of stellate tearing at contact, and inconsistent reproducibility of patterns. Conversely, no significant change in the diameter of the GSR patterns existed between panels created with and without a silencer. Results show that it may be possible to determine a muzzle-to-target range for crimes committed using a firearm with an attached silencer. However, this conclusion depends of the presence of features that could indicate a silencer may have been used.

Mentors: Mentor: Tim Spears, Department of Forensic & Investigative Sciences, School of Science, IUPUI, and Indianapolis-Marion County Forensic Services Agency

83. A Paired Geochemical and Molecular Study of Anoxygenic Photosynthesis in Modern Lake Sediments

Shruthi Garugu, Amanda Evans, Amandeep Kaur and Omer Sajid

Department of Neuroscience, Purdue School of Science; Department of Geography, IU School of Liberal Arts,
Department of Biology and Department of Geology, School of Science

This study was designed to analyze the past environmental conditions of Lime Blue Lake (Washington, USA) over the last 1500 years. This lake is today permanently anoxic and has free dissolved sulfide in the bottom waters. This oxygen-free environment is analogous to the low oxygen conditions of Earth 3 billion years ago. Sulfide in Lime Blue is particularly beneficial to anaerobic phototrophic bacteria prospering in this lake, making it crucial to study the conditions which allow these organisms to fix carbon dioxide through anoxygenic photosynthesis. We are studying the history of anoxygenic photosynthesis in this lake by examining the biological records recorded in the sediments. Sediment for this study comes from a surface core collected at this lake, which is stored at -80 C. Samples will be subdivided for use in a range of analysis, including DNA extraction, to test for relative abundance of phototrophic organisms, pigments, biomarkers, pyrite and other reactive iron minerals to determine water column redox state and its change over time. We are also analyzing the stable isotopes of carbon ($\delta^{13}\text{C}$) and nitrogen ($\delta^{15}\text{N}$) using isotope ratio mass spectrometry. This will allow us to determine the sign of life from known broad range of isotope values. By analyzing results from chemical and biological analysis, this research will provide information regarding the vertical and temporal distribution of the anaerobes located in the water column of this lake. This in turn will aid in determining the environmental conditions and redox states of early, anoxic Earth.

Principal mentor: William Patrick Gilhooly III- Assistant Professor, School of Science, Earth Sciences Department
Co-mentor: Alice Bosco Santos- Postdoctoral Scholar, School of Sciences, Earth Sciences Department
Co-mentor: Christine Johanna Picard- Assistant Professor, School Sciences, Department of Biology and Forensic and Investigative Sciences Program
Co-mentor: Charity Owings- Ph.D. in Forensic Entomology

84. Comparing Scaling Laws for Two- and Three-Dimensional Fractal-Like Tree Networks

Ryan Geib¹ and Trent Stutzman²

University of Rhode Island¹, Indiana University South Bend² Indiana University- Purdue University Indianapolis

The scaling laws of transport properties in two dimensions for fractal-like tree networks are important for understanding the mechanism of transport in such networks, as well as the nature of two-dimensional transport. In this paper, analyze the properties of electric and heat conductivity, convective heat transfer, and laminar and turbulent flow for the networks; adapt the laws that govern three-dimensional transport to two dimensions; and derive the scaling laws associated with these properties. Building off of work done by P. Xu and B. Yu from 2006, we derived two-dimensional formulae for different properties of fractal-like tree networks, including total area, total electric resistance, and total flow resistance, among others. The formulae derived were generally the same as the three-dimensional case, with the exception of the power of, the ratio of successive branch diameters, being reduced by one or two. These formulae were used to derive the scaling power laws for electric and heat conductivity, convective heat transfer, and laminar and turbulent flow for two-dimensional fractal-like tree networks with branching number $n=2$, both in general and under area- and volume-preserving conditions. Lastly, the behavior of the two-dimensional network is critically compared to the three-dimensional case.

85. Determining the Structure of ACCH Lipid Binding Domain of Amot with Nuclear Magnetic Resonance

Elyse Hoy¹, Dr. Ann Kimble-Hill², PhD

¹Franklin College, Franklin, IN and ²Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, IN

Nearly one out of eight women will be diagnosed with some form of breast cancer throughout their lifetime. Studies have shown that a majority of these and other epithelial cell cancers are linked to an increased expression of Angiotensin (Amot) family members. Amot plays a significant role in initiating and regulating cancer cell proliferation. The Amot protein has an AMOT coiled-coil homology (ACCH) domain that binds to lipids in cell membranes and causes membrane deformation and fusion events. This domain is also responsible for regulating family specific functions in cell growth and differentiation. The complex physical structure of the ACCH domain is not known, therefore determining this information will reveal specific mechanisms by which the protein binds to lipids. Therefore, this project aims to find the atomic structure of this domain. In order to do this, we will be purifying N15 labeled protein from E. coli BL21 cells. We then analyze the protein by nuclear magnetic resonance spectroscopy (NMR) to determine the 2D structure. With the NMR structure, we can compare it to previously predicted homologous models from our laboratory. Our hypothesis is that NMR analysis will enable us to extend our understanding of the mechanism that drives ACCH domain function. This information could be helpful in the future development of chemotherapy drugs that are inhibitors of Amot associated cancers.

86. Analysis of Dehydrin Requirements for Stress Response in Arabidopsis

Cecelia R. Chapin¹ Stephen Randall

¹Department of Biology, Purdue School of Science, IUPUI

Many plants produce a class of proteins called dehydrins when they are exposed to stressors such as low temperatures, drought or increased salt levels. While the accumulation of dehydrins is recognized as a defense mechanism against these stressors, little is known about their physiological mechanism conferring stress tolerance. The goal of this work includes: characterizing dehydrin expression in single and double Arabidopsis dehydrin knockouts, genotype confirmation in double dehydrin knockout mutants (cor47, erd10) via PCR and creating a triple knockout with a 3rd dehydrin (ERD10). Both seedlings and mature Arabidopsis plants were cold-treated in order to compare total dehydrin expression in the different knockout lines using a general dehydrin antibody and western blotting. Agrobacterium containing a plasmid including Cas9 and a guide RNA targeting the ERD10 dehydrin gene was used to transform the Arabidopsis double knockout. Western Blotting confirmed the knockouts and suggested no significant impact of single or double knockouts on expression of other dehydrin genes. When seedlings from the Agrobacterium-transformed Arabidopsis are ready to be planted (approx. 6 weeks), the plants will be selected for antibiotic resistance and then verified for the knockout of dehydrin genes COR47, ERD10 and ERD14. Triple knockouts will be grown and observed for impact on dehydrin expression and any changes in cold tolerance phenotype. Deeper understanding of dehydrin production in response to stressors could further the development of transgenic plants with heightened cold resistance.

Mentor: Stephen Randall, Department of Biology, Purdue School of Science, IUPUI

87. Modeling Chronic Vascular Responses Following a Major Arterial Occlusion

Emma Brewer¹, Jordan Pellett²

Rose-Hulman Institute of Technology¹, University of Wisconsin-La Crosse² Indiana University-Purdue University Indianapolis

Peripheral Arterial Disease (PAD) is a serious health concern characterized by a full or partial occlusion of a major artery in the systemic vascular system, often caused by atherosclerosis. As a result of the occlusion, the blood supply to peripheral tissues (e.g., calf and foot) is significantly reduced, causing many patients to experience severe pain and reduced mobility. While the body's natural responses compensate sufficiently for an occlusion in some patients, the majority of patients rely on surgical grafts to restore flow to distal tissues. Improved therapies to treat PAD using non-invasive techniques are needed as PAD becomes more prevalent. This study uses mathematical modeling techniques to investigate the role of different vascular segments in restoring blood flow following a major occlusion. Vascular adaptations to collateral arteries and the microcirculation distal to the occlusion have been observed to occur on both acute and chronic time scales. Here, the contributions of long-term (chronic) vascular responses, specifically arteriogenesis (increased diameter of existing vessels) and angiogenesis (new vessel formation), are investigated in a single vessel and a complex network of vessels. By coupling these chronic responses to acute vascular responses in a complex network, this model provides a framework for better understanding the time frame and significance of vascular responses that help to restore flow following an occlusion. Ultimately, the model can be used to identify the most important vessels to target for future PAD therapies.

88. The Effect of Ionic Solutions on Surface Potential of Lipid Membranes

Michele Costantino¹; Ryan Lybarger²; Horia Petrache^{2,3}

¹Department of Chemistry and Biochemistry, Indiana University South Bend; ²Department of Physics, ³Integrated Nanosystems Development Institute Indiana University-Purdue University Indianapolis

Cellular membranes provide a barrier between two environments and are composed of a variety of lipid molecules. The composition of the membrane determines its function and can be influenced by ions and molecules in the surrounding environment. Amongst the factors affected is the electric charge and the surface potential (zeta potential) of the membrane. The mechanism by which the zeta potential of membranes is affected by water-soluble ions and molecules involves, not only the net electrical charge, but also a physical property called electrical polarizability. In the lab, we use a method by which electrical polarizability is determined from measurements of index of refraction and mass density as a function of solute concentration.

This research will provide understanding in how polarizability of a molecule affects a cellular membrane by observing the zeta potential of a lipid vesicle at varying concentrations of one molecule in solution. The dioleoylphosphatidylserine (DOPS) lipid was utilized, which contains two monounsaturated hydrocarbon chains with eighteen carbons each and a negatively charged head group that consists of both an amine and carboxylic acid. The results showed that while the vesicles maintained approximately a -60 mV charge in water, addition of the calcium chloride altered the zeta potential in the positive direction as the concentration increased. It is believed that the calcium cations have a strong affinity for the lipid head group and therefore contribute substantially to the change in surface potential of the lipid vesicles.

Future research will focus on other divalent chlorides—including magnesium, manganese, and cobalt—as well as organic phosphates and phospholipids with different head groups such as dilauroylphosphatidylcholine (DLPC), a neutral lipid. This research will help us to further understand how molecules and ions in the surrounding environments affect cellular membranes in regards to zeta potential, size, and formation of multilamellar vesicles (MLVs).

Mentor: Ryan Lybarger (Graduate Student) and Horia Petrache (Faculty)

89. Distributed Drug Discovery: using modified amino acids to kill *P. aeruginosa*.

Isaac Lamb¹, Martin J. O'Donnell¹, William L. Scott¹, J. Geno Samaritoni¹

¹Indiana University-Purdue University Indianapolis Department of Chemistry
Indiana University-Purdue University Indianapolis

Drug discovery requires a highly integrated scientific process to develop new and powerful disease treatments. Unfortunately, diseases that afflict the impoverished of the world do not have medicines developed for them because the sufferers cannot afford the developed treatments. The focus of our research is to discover novel, affordable drugs for these neglected diseases by distributing the identification, synthesis, and screening of these compounds among many academic institutions. To take advantage of the educational aspects of the drug discovery process, the methods of synthesis and screening have been adapted for use in university classrooms. Our research focuses on using solid-and solution-phase chemistry to synthesize amino acid analogs that inhibit the growth of *Pseudomonas aeruginosa*, a common bacterium that is a complicating factor in the progression of cystic fibrosis. The synthesized compounds are screened in a biofilm assay to assess biological activity. The simplicity of both the chemical synthesis and biological screening provides ample opportunity for educational gains while remaining economically effective. A variety of N-acyl, urea, and oxycarbonyl modifications of our lead compound were synthesized and screened, while dipeptides formerly-synthesized as a mixture of diastereomers were separated into individual diastereomers for further testing.

90. Understanding Medieval Midcontinent Native American Societal Migration Circa 1450 C.E. Using Isotopic Composition of Lake Core Sediment

Joseph D. Warner¹, Maxwell Wright², Shelby Gills², Elias Atallah², Kara Banks³, Justin Lazaro², Avery Prevette⁴

¹Department of Electrical and Computer Engineering, PU School of Engineering and Technology
²Department of Earth Sciences, PU School of Science
³Department of Pathology and Laboratory Medicine, IU School of Medicine
⁴Department of History, IU School of Liberal Arts

In the modern era, different broad scale weather patterns produce isotopic signatures in their precipitation. There are two primary sources of precipitation in the midcontinental United States (US), the Gulf of Mexico and the North Pacific/Arctic. These two patterns are in phase, meaning that only one is acting as a source of precipitation at a time. There is not widespread data about the paleoclimate of the Medieval Climate Anomaly (MCA; 950 – 1250 C.E.) and the Little Ice Age (LIA; 1350 – 1850 C.E.). Here, we examine paleoclimate data of the midcontinental US circa 1450. These climate patterns are hypothesized to play a significant role in the decline of Mississippian Native American civilization. With more in depth understanding of the paleoclimate of the region, we could better understand the pressures influencing this decline. This study examines the physical properties of lake sediment cores from several sites across the Midwest and High Plains of the mid-continental US. These cores are tested for grain size and isotopic composition at various depths. We use grain size as a proxy for lake level and the percentage of isotopic oxygen in carbonate from the sediment to infer the precipitation to evaporation (PE) ratio of hydrologically open lakes. We can compare this to the PE ratio of hydrologically closed lakes to infer the evaporative qualities of these sites throughout time. We utilize these results to better understand and analyze the local evaporative and broader regional precipitation characteristics of the mid-continental US around 1000 to 1500 C.E.

Mentors: Broxton Bird Department of Earth Science PU School of Science, Jeremy Wilson Department of Anthropology IU School of Liberal Arts, William Gilhooly Department of Earth Science PU School of Science

91. An Investigation of the Sedimentology of Lake Cores to Determine Hydroclimate Variability of the Mid-continental United States Circa 1000 –1450 CE

Maxwell Wright¹, Shelby Gills¹, Joseph D. Warner², Elias Atallah¹, Kara Banks³, Justin Lazaro¹, Avery Prevet⁴

1. Department of Earth Sciences, PU School of Science, 2. Department of Electrical and Computer Engineering, PU School of Engineering and Technology, 3. Department of Pathology and Laboratory Medicine, IU School of Medicine 4. Department of History, IU School of Liberal Arts

The paleoclimatology of the midcontinental United States (US) during the Medieval Climate Anomaly (MCA; 950 –1250 CE) and Little Ice Age (LIA; 1350 –1850 CE) has not been extensively detailed. However, Medieval Mississippian Native American population rise and decline between 1000 and 1450 CE is hypothesized to have been influenced by climatic variability. Here, we utilize lake sediment cores from several sites across the High Plains and Midwest to investigate spatial hydroclimate variability. Physical properties of these cores are used to infer changes in lake level, depositional energy, and the delivery of clastic material to the lake via storm runoff. We can use this data to infer local lake level with regards to continental climate pattern fluctuation. There exists a trend within the climate of the midcontinental US in which regional precipitation amounts are antiphase; meaning, drought in the western midcontinental US correlates to a wetter eastern midcontinental US. Although the pattern has been consistent in both modern times and the MCA, it was reversed during the LIA. We hypothesize that this reversal led to the eastern migration of Mississippian Native American civilizations during the MCA and the population decline during the LIA. These results can better inform us about the paleoclimate of the MCA and LIA periods which in turn can help us better understand the pressures faced by Mississippian civilizations, particularly the conditions that helped these civilizations rise and the conditions that contributed to their downfall.

Mentors: Broxton Bird Department of Earth Science PU School of Science, Jeremy Wilson Department of Anthropology IU School of Liberal Arts, William Gilhooly Department of Earth Science PU School of Science

92. Using Mathematical Modeling to Optimize Regulatory T Cell Therapies for Heart Transplant Patients

Ross Wallgren¹ and Julia Arciero¹

1 Department of Mathematical Sciences, Indiana University-Purdue University Indianapolis, Indianapolis, IN, USA

Following transplantation, organ transplant patients must remain on immunosuppressive drugs for the remainder of their lives to prevent their immune system from rejecting the organ. However, by leaving patients susceptible to infections and chronic diseases, these immunosuppressive drugs significantly reduce patient quality of life and long-term graft survival. It has been proposed that the adoptive transfer of regulatory T cells (Tregs) can be used as a therapy to prevent transplant rejection with little to no use of simultaneous immunosuppression. Tregs inhibit many of the immune cells and interactions that trigger graft destruction, and thus adoptive transfer of Tregs is hypothesized to have great potential for achieving transplant tolerance. In this work, a mathematical model of transplant rejection is adapted to simulate various dosing strategies of Treg adoptive transfer following organ transplantation. The model is used to predict the number of graft cells that remain following the administration of a single dose of Tregs on different days after transplantation. A non-monotonic relationship between graft survival and the day of Treg administration is predicted, suggesting that correct timing of Treg doses is critical for developing successful treatment strategies. The model is also used to optimize treatments consisting of two separate administrations of Tregs; the best outcome for the graft corresponded to doses given on days 2 and 11. Finally, the optimal strategy for multiple consecutive doses of Tregs is predicted by the model to be administration of Tregs on days 1-17. Overall, the insight provided by this theoretical model can be used to guide future experiments to optimize the use of adoptive regulatory T cell therapies for transplant patients.

93. Determining Presence of ACCH Binding Site of Amot using Protein Spot Blot

Peter Andrews¹, Dr. Ann Kimble-Hill¹, PhD

Indiana University, Bloomington, IN and Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, IN

Angiomotins (Amot) are a family of adapter proteins that are directly involved in signaling pathways that initiate cell differentiation and proliferation in certain breast cancer cells. The ACCH domain of the Amot protein, as a result of its coil-coil nature, allows for selective binding to phosphoinositol lipids, resulting in membrane deformation. Understanding the structure-function relationship of this domain may provide insight into methods of modulating these signaling pathways; ultimately, leading to the reduction of cancer cell proliferation, differentiation, and migration. The long-range goal of this project is to define the mechanisms whereby the Amot130 N-terminal domain (NTD) regulates the protein scaffolding and membrane trafficking activities that underlie Amot130 function. In vitro epithelial cell studies demonstrate that the presence of this domain causes association with actin, and prevents lipid binding. Amot proteins bind membranes via the Amot coiled-coil homology (ACCH) domain. However, the mechanism by which the NTD regulates this function is unknown. We hypothesized that the NTD directly binds the ACCH domain, thereby shielding residues responsible for lipid binding. To that end, we used protein spot blot to determine if the Amot 130 NTD directly binds to the ACCH domain. We expect to see NTD binding site attach to the lysates containing the ACCH domain in the spot blot. As a result of understanding this mechanism, we will be able to learn more about these protein lipid interactions in breast cancer cells. If successful, our research may lead to new drug discovery to combat breast cancer.

94. Electrochemical Paper-Based Device for Bacteria Detection

Shavonte' Crayton^{1,3}; and Frédérique Deiss^{2,3}

¹Martin University, ²Department of Chemistry and Chemical Biology; ³

Integrated Nanosystems Development Institute, Indiana University-Purdue University Indianapolis, IN, 46202, United States Foodborne bacterial infection and diseases are the most common source of illnesses and death around the world. Point-of-care devices that allow for the detection of bacteria before consumption can play a critical role in prevention of bacterial breakouts. The objective of this project is to develop a portable and low-cost paper-based device for the culture and electrochemical detection of bacteria. Paper-based devices are convenient, affordable, user-friendly, disposable and producible in many different environments and resource-limited settings. They are made of packaging tape, wax-patterned paper, and polydimethylsiloxane (PDMS) membranes. Electrochemical analyses are sensitive and quantitative. An additional advantage of electroanalytical methods includes, the absence of interferences from light, color, dust, or insoluble particulates. The current prototype presented some instabilities which were not allowing for optimal usage, such as, stability of the conductive ink, thickness of the electrodes, and resistance to changes in temperature. We first assessed the evaporation level of the devices upon one day in an incubator at 37.5 °C. We proceeded by weighing each device, before and after adding a known amount of water, and then monitoring their weight hourly. We compared devices made from two different brands of tape: Duck[®] and 3M[®], the 3M-tape devices seemed to lose less liquid than Duck-tape devices and evaporation rate was lower. We continue to explore other factors that can help optimize the stability of the devices.

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