# UNIVERSITY OF NOTRE DAME

# Colleges of Science & Engineering Joint Annual Meeting

**3rd Annual COSE-JAM for Graduate Students & Postdoctoral Fellows**

**Friday – December 13, 2019**

**Jordan Hall**

# PROGRAM SCHEDULE

*Morning Session (8:45-12:15pm):*  25 podium presentations in Jordan auditoriums (101 & 105)
(continental breakfast/snacks/drinks in Galleria; 10:30-10:45 mid-morning break)


*Lunch (12-1:30pm):*  Jordan Galleria – participants, discussants, moderators, co-authors, etc.


*Lunchtime Panel Discussion (12:30-1:20pm):*  101 Jordan – Non-Traditional Career Pathways

"MATTTS – Matts Adjusting To The Times"

Discussants – Professors Matt Champion, Matt Leevy, and Matt Ravosa

Moderator – Mike Hildreth, COS Associate Dean of Research & Graduate Studies


*Afternoon Session (1:30-4:30pm):*  55 poster presentations in Jordan Galleria
(light snacks/soft drinks in Galleria)

*Afternoon Session (1:30-4:30pm):*  Representatives will be available in Jordan Galleria for
consultation – Graduate Career Services, Office of Grants and Fellowships,
Office for Postdoctoral Scholars, and IDEA Center


*Afternoon Social (3:30-6:00pm):*  Jordan Galleria – opportunities for formal and informal
peer-to-peer interactions (snacks/soft drinks/beer/wine)

# PANEL DISCUSSANTS (lunchtime at 12:30-1:20pm – 101 Jordan)

**Michael Hildreth**, Ph.D., is Associate Dean of Research and Graduate Studies in the College of Science.  Dr. Hildreth is also a Professor in the Department of Physics.

Prof. Hildreth's primary physics interest is in discovering and understanding the mechanism or mechanisms responsible for Electroweak Symmetry Breaking. Simply put, this would answer questions like: "why is there mass?"  Prof. Hildreth is a part of the CMS Experiment at CERN's Large Hadron Collider (LHC) in Geneva, Switzerland, where he and the rest of the Notre Dame High Energy Physics group played key roles in the recent discovery of a Higgs boson.  His group is involved in measuring Higgs properties, specifically the coupling of the Higgs boson to top quarks. These measurements are essential in determining if the Higgs we see is really the source of Electroweak Symmetry Breaking and the origin of particle masses, or whether new physics is required.  He is also working on searches for new physics beyond the Standard Model of particle physics, specifically looking for new physics in final states involving high energy photons and, separately, high energy tau leptons.

Hildreth is currently leading the CMS group responsible for modeling the interaction of particles with the material of the detector elements. This is essential for understanding the response of the detector to the signals for all of the various physical processes one wishes to study at the collider.

Since 2012, Prof. Hildreth has led a multi-university team that is exploring the programmatic and technical intricacies of knowledge preservation in science.  The DAta and Software Preservation for Open Science (DASPOS) team consists of physicists, computer scientists, and digital librarians from Notre Dame, University of Chicago, University of Illinois Urbana-Champagne, University of Nebraska Lincoln, New York University, and the University of Washington.  This is a multi-disciplinary effort designed to explore the knowledge preservation needs of various disciplines and to construct a prototype data and software preservation architecture that can be used as a template for knowledge preservation efforts in different fields of science.

Prof. Hildreth is also involved in an accelerator instrumentation project the KEK laboratory in Tsukuba, Japan. He leads a primarily undergraduate group of students who are building laser interferometer systems to monitor the mechanical stability of accelerator components at the 10 nanometer level. The primary goal of this research is to demonstrate that a precision energy spectrometer based on beam position monitors can attain the necessary resolution.

Hildreth is a graduate of Princeton University, and holds a Ph.D. from Stanford University.

**Matthew M. Champion**, Ph.D., is an Associate Professor of Chemistry and Biochemistry.

The Champion Lab is interested in developing and exploiting novel approaches to identify and characterize the components of secreted proteins from virulent microorganisms. They heavily utilize the 'awesome power of genetics' coupled with state-of-the art quantitative proteomics to enrich, identify and quantify the proteins responsible for biological phenotypes. They have ongoing projects in pathogenic mycobacteria, protein translation in *E. coli* through the PTRN, and quantitative protein secretion measured using capillary electrophoresis. This framework is highly extensible to the analysis of other pathogen and protein secretion systems, and has uncovered novel genes, pathways, and crosstalk among secretion systems.

Dr. Champion received a BS in Microbiology from the University of Iowa and a PhD degree in Biochemistry from Texas A&M University.

**W. Matthew Leevy**, Ph.D., is Associate Research Professor of Biological Sciences as well as the Director of the IDEA Center Innovation Lab.

The Leevy Lab integrates design, fabrication, and makerspace assets to drive the creation of parts and assemblies for commercialization, research, and education. Matt also serves as a capstone thesis adviser and mentor within the ESTEEM Graduate Program. Lastly, Dr. Leevy leads an independent laboratory of talented staff, post-docs, and undergraduates with research centered at the interface of 3D printing technology and biomedical imaging, with funding through industry partnerships. During the past four years, Matt's lab has generated numerous manuscripts and patent submissions that have served as cornerstones for the creation of two successful small-business startups: In Vivo Concepts LLC (1st Source Award, 2014), and Benefactory Manufacturing and Design LLC. Matt is also a retired Army Reserve Captain with 22 years of total service. As a whole, Matt operates a vibrant, collaborative, and entrepreneurial laboratory, with broad experience in imaging technologies, object fabrication, and business creation.

Dr. Leevy has a BS in Bioengineering from the University of Illinois at Urbana-Champaign and a PhD degree in Biophysics from Washington University.

**Matthew J. Ravosa**, Ph.D., is a Professor of Biological Sciences as well as Concurrent Professor of Aerospace and Mechanical Engineering, and Anthropology.

The Ravosa Lab is interested in major adaptive and structural transformations in mammalian musculoskeletal form during development and across higher-level clades. With an eye to both the evolutionary and translational implications, they have investigated the plasticity, mechanobiology, pathobiology, ecomorphology, aging, and performance of the mammalian musculoskeletal system, skull and feeding system. Research on biomechanics, ontogeny, and evolution has marshalled a broad range of modern engineering, cell biological, molecular, and imaging techniques as well as unique experimental and transgenic animal models to investigate outstanding questions regarding the complex underpinnings of patterns of phenotypic variation in vertebrates.

Dr. Ravosa holds a BA in Interdepartmental Studies from the University of Rochester as well as MA and PhD degrees in Biological Anthropology and Anatomy from Northwestern University. He was a NIH/NRSA-supported postdoctoral fellow in experimental biology at Duke University Medical Center.

# MORNING PODIUM SESSION (8:45am-12:15pm – 101 & 105 Jordan)

**Jordan 101** (moderator: Susan Lad)

8:30 – *Upload Presentations*

9:00 – **Rebecca Anderson**: Understanding Differences in Morphology in the Three-Spine Stickleback Fish

9:15 – **Fernando Alamos Domeyko**: Asperity Creep Behavior in Contact with a Rigid Flat Surface

9:30 – **Samantha Golomb**: Multi-Modal Single Cell Analysis Reveals Age-Induced Reshaping of Brain Immune Homeostasis

9:45 – **Emily Bacher**: Shedding New Light on Squaraines: Utilizing Squaraine Dyes as Building Blocks in Organic Synthesis

10:00 – **Martin Fevre**: Dynamics and Control of Underactuated Biped Robots

10:15 – **Emily Nett**: Food Mechanical Properties and Masticatory Behavior in Llamas

10:30 – *Break*

10:45 – **Francisco Fields**: Algorithmic Assessment of Missense Mutation Severity in the Von-Hippel Lindau Protein

11:00 – **Alexandra Niclou**: Seasonal Patterns of BAT Activity Imply Energetic Buffering and Greater Metabolism of Carbohydrates Associated with Human Cold Acclimatization

11:15 – **Ernesto Cortes-Morales**: Strategies for the Calculation of the Viscosity using Molecular Dynamics

11:30 – **Katherine Crank**: Quantitative Microbial Risk Assessment of Swimming in Sewage Impacted Waters using CrAssphage and Pepper Mild Mottle Virus in a Customizable Model

11:45 – **Robert Stanley**: Determining the Defensive Mechanisms in Green Ash (*Fraxinus pennsylvanica*) Resistant to Emerald Ash Borer (*Agrilus planipennis*)

12:00 – **Susan Lad**: Bone Remodeling and Cyclical Loading in the Maxilla of White Rabbits (*Oryctolagus cuniculus*)

**Jordan 105**  (moderator: Abigail Weaver)

8:15 – *Upload Presentations*

8:45 – **Yueh-Fu Wu & Annamarie Bryant**:  A CLIP-170-Induced +TIP Network Superstructure has Characteristics in Cells Consistent with a Liquid Condensate

9:00 – **Alexandra Chirakos**:  ESX-1 Secreted Substrates Control Gene Expression in Pathogenic *Mycobacteria*

9:15 – **Bradley Ellis**:  Adipose Stem Cell Secretome Markedly Improves Rodent Heart and Human iPSC-derived Cardiomyocyte Functional Recovery from Cardioplegic Transport Solution Exposure

9:30 – **Martin Imre**:  Spectrum-Preserving Sparsification for Visualization of Big Graphs

9:45 – **Gulberk Ozcebe**:  Effects of Heart ECM Age on Maturity, Senescence and Function of Human iPSC-Derived Cardiomyocytes

10:00 – **Qingfei Wang**:  Single-Cell Profiling Guided Combinatorial Immunotherapy for Fast-Evolving CDK4/6 Inhibitor Resistant HER2-Positive Breast Cancer

10:15 – **Abigail Weaver**:  Understanding Polymicrobial Infections in Prosthetic Joints

10:30 – *Break*

10:45 – **Hannah Wesselman**:  Estrogen Modulation of Fate Choice during Kidney Development

11:00 – **Camden Hoover**:  Loss of APC Induces Paclitaxel Resistance through Alterations in Cell Cycle Proteins

11:15 – **Gokhan Bahcecioglu**:  Aged ECM Promotes Invasion and EMT-Like Behavior in Breast Epithelial Cells

11:30 – **Casey Stefanski**:  Elucidating the Role of APC Resulting in Doxorubicin Resistance in Breast Cancer

11:45 – **Gozde Basara**:  Electrically Conductive 3D Printed MXene-Hydrogel Composite Constructs for Tissue Engineered Human Cardiac Patches

12:00 – **Elizabeth Harper**:  Age-Related Changes in the Microenvironment Enhance Ovarian Cancer Metastasis

# AFTERNOON POSTER SESSION (1:30-4:30pm – Jordan Galleria)

<u>Alvarez-Barrios through McCown present for questions 1:30-3pm</u>

**Wendy Alvarez Barrios**:  Biological Insights on Tumor Cell Behavior in Response to Physical Stimuli during Circulation and Metastatic Mechanical Arrest

**Marissa Andersen:**  A Novel Urinary Catheter Material that Prevents Fibrinogen Deposition and Investigation of Polymicrobial Biofilms

**Kurtis Breger**:  Elucidating the Kinetic Mechanism of Human METTL16

**Annamarie Bryant & Yueh-Fu Wu**:  A CLIP-170-Induced +TIP Network Superstructure has Characteristics in Cells Consistent with a Liquid Condensate

**Loan Bui**:  Engineering Bioactive Nanoparticles to Rejuvenate Endothelial Progenitor Cells

**Brooke Chambers**:  KCTD15 Regulates Nephron Segment Differentiation by Repressing TFAP2A Activity

**Joe Chambers**:  Chemical Genetic Screen Reveals Novel Roles for Ppargc1a in Cilia Development and Disease

**Farya Chattergoon**:  Src and CDK4/6 Inhibition Induces a Synergistic Vulnerability in Rb-Deficient TNBC

**Rachel Cronin**:  Uncovering Functional Relationships between ESX-1 Substrates in *Mycobacterium marinum*

**Nagehan Demirci**:  Local Investigation of the Complex Morphology of the Adult Human Brain

**Caitlin Donahue**:  Development of Optogenetic Tools to Investigate the Role of Intracellular pH in Cancer

**Fei Fan**:  Synthesis and Photopatterning of Norbornene Modified Hyaluronic Acid Hydrogel

**Christopher Gager**:  Host Factors Associated with Pathogen Persistence during Catheter-Associated Urinary Tract Infections

**Taylor Gambon**:  Effects of User Intent Changes on Onboard Sensor Measurements during Exoskeleton-Assisted Walking

**Justin Greaves**:  Persistence and Transport of Fecal Pollution Indicators in Environmental Waters

**Ian Guldner**:  Metastasis-Associated Myeloid Cells Drive Immune Suppression in Brain Metastatic Niche through Cx3cr1-Cxcl10 Axis

**Karlyn Harrod**:  Data Assimilation on Lumped Parameter Models for Congenital Group I Pulmonary Hypertension

**Aurel Holzschuh**:  Highly Multiplexed Amplicon Sequencing to Understand Malaria Transmission in Zanzibar

**Gabriel Iturralde Duenas**:  Actuated Three Dimensional Dual-SLIP of Sloped Terrain Human Walking

**Charlotte Kunkler**:  Stability of an RNA•DNA-DNA Triple Helix Depends on Base Triple Composition and Length of the RNA Third Strand

**John Lawrence**:  Trigger Rate Monitoring Tools for CMS

**Xue Li**:  A Scalable Explicit Finite Element Solver for Cardiovascular Models with Uncertain Material Properties

**Jorge Lopez**:  Dynamic Coupling as a Measure of the Transition from Slow to Self-Selected Speed Walking Mechanics

**Varun Mannam**:  Fluorescence Microscopy Lifetime Estimation from Intensity using Convolutional Neural Networks (CNNs)

**Armando Magallanes Marrufo**:  Characterizing the Role of Fibrinogen Modulating Macrophage Response to Catheter-Associated Urinary Tract Infections

**Daniel Martin**:  Exploring the Physics of the TIRAS Plasma Electrochemical System

**Phillip McCown**:  Secondary Structural Model of Human MALAT1 Reveals Multiple Structure-Function Relationships

**Kristopher Murray**:  Can Threshold Choices Influence Observed Microtubule Aging?

**Xiangyu Ni**:  Modeling and Damage Detection for Tree Model using Fractional-Order Calculus

**Kathleen Nicholson**:  Using New ESX-1 Substrates to Delineate Lytic Activities of the ESX-1 System in *Mycobacterium marinum*

**Emily Nonnamaker**:  A Role for Bacteria in Reproductive Signaling?

**Bhavana Palakurthi**:  Sensitizing Primary Breast Cancer to Anti-PD1 Immunotherapy through CD103+ Dendritic Cells using Metronomic Chemotherapy

**Lauren Partin**:  Modeling Noise Patterns from MRI Reconstruction Algorithms

**Jaynise Pérez Valentín**:  Air-Sea Interactions during Monsoon Season in the Bay of Bengal

**Ryan Posh**:  Exploring Hybrid Volitional Control of Robotic Lower-Limb Prostheses

**Marya Poterek**:  Modeling Measles Importation into the United States using International Measles Incidence and Air Passenger Travel Data

**Kevin Sanchez**:  Discovery and Characterization of a New Regulator of the Mycobacterial ESX-1 System

**Daniel Schor**:  Individual Variation in the Scope of Attention and Why It Might be Limited

**Amal Sebastian**:  Atmospheric Pressure Plasma: An Alternative Tool for the Synthesis of Efficient Photocatalytic Materials

**Elise Snyder**:  Predicting eDNA Transport and Degradation in Flowing Waters: Application of a Conservation Tool using Integrated Experimental, Field, and Modeling Approaches

**Shannon Speir**:  Controls on Nitrate Export during Storms in Two Contrasting Agricultural Watersheds

**Robert Stanley**:  Determining the Defensive Mechanisms in Green Ash (*Fraxinus pennsylvanica*) Resistant to Emerald Ash Borer (*Agrilus planipennis*)

**Brooke Stemple**: Impacts of Geological Carbon Sequestration on Subsurface Microbial Communities

**Shannon Stoffel**: NMR Relaxation Dispersion Reveals Macrocycle Breathing Dynamics in a Cyclodextrin-Based Rotaxane

**Taylor Tobin**: Observational and Theoretical Studies of SiO Maser Polarization toward Late-Type Evolved Stars: Insights from EVPA Reversal Features

**Matt Trentman**: Watershed Scale Land Use Change Increases Stream Metabolic Function in an Agricultural Stream

**Nazli Turan**: Development and Characterization of a Small-Scale Helical Surface Dielectric Barrier Discharge for Studying Plasma-Surface Interactions

**Anna Vincent**: Comparing the Effects of Winter Cover Crops on Nutrient and E. coli Loss in Great Lakes Watersheds of Contrasting Land Use

**Shuolun Wang**: Numerical Investigation of Biomechanically-Coupled Growth in Brain Gyrification

**Lauren Ward**: Impact of Neutron Induced Fission on r-process Nucleosynthesis Calculations

**Hannah Wesselman**: Estrogen Modulation of Fate Choice during Kidney Development

**Annaliese Wieler**: Attributing the Efficacy of a Spatial Repellant to Entomological Parameters

**Zhenyu Wu**: Comparative Fate of CrAssphage with Culturable and Molecular Fecal Pollution Indicators during Activated Sludge Wastewater Treatment

**Jiapeng Xu**: Event-Triggered Minimax State Estimation with a Relative Entropy Constraint

**Jinyu Yang**: Time-Resolved Characterization of a Free Plasma Jet Formed using a Piezoelectric Transformer

# ABSTRACTS

**(alphabetical by presenter)**

**Oral Presentation:**

**Asperity Creep Behavior in Contact with a Rigid Flat Surface**

Fernando J. Alamos Domeyko[1], David B. Go[1,2], Chal Park[3], Martin Philo[4], Anthony Clinton[4], Hyunok Kim[5] and Steven R. Schmid[1]

[1]Dept. of Aerospace & Mechanical Engineering, University of Notre Dame, Notre Dame, IN
[2]Dept. of Chemical and Biomolecular Engineering, University of Notre Dame, Notre Dame, IN
[3]Dept. of Materials Science and Engineering, University of Michigan, Ann Arbor, MI
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[5]EWI, Columbus, OH

High-temperature gas pressure forming (HTGF) has been demonstrated for the production of a wide range of aerospace structures. However, one of the pressing concerns is the ability to quantitatively model the HTGF process in order to effectively design tooling. One of the primary issues is the ability to quantitatively predict the accuracy of the HTGF process so that tooling designs can be validated before they are produced/purchased and placed into production. This can be quite challenging. Defects such as excessive tolerances, folds, poor surface finish, and others are difficult to predict, and discovering and mitigating them is exacerbated by the long production time and material costs. Current finite element method simulations for HTGF ignore the evolutionary nature of friction models and proper constitutive behavior. The presence of creep strain leads to junction growth and saturated contact areas at longer time scales than conventional metal forming; therefore, friction models that ignore creep-induced strains will underpredict asperity contact and friction levels. There is a significant knowledge gap that needs to be filled on the transient effects of the contact area due to creep material behavior. Most efforts have only analyzed the Hertz contact for creeping solids using a sphere in contact with a rigid flat surface, and the effect of creep on contact between rough surfaces is still not completely understood. In this work, a new micro-contact model of a single asperity and a rough random surface in contact with a rigid flat surface is created to predict asperity flattening under creep behavior.

**Keywords**: contact mechanics, creep, sheet metal forming, friction

**Poster Presentation:**

**Biological Insights on Tumor Cell Behavior in Response to Physical Stimuli during Circulation and Metastatic Mechanical Arrest**

<u>Wendy V. Alvarez Barrios</u>[a,b], Huijie Lu[c], Kyle Cowdrick[b,d,f], Michelle Galarneau[b,d,g], Melinda A. Lake[c,h], Zhou Zhao[e], Lan Jiang[a,b,i], Emily Abramczyk[a,b,j], Sara Stewart[a,b], Lin Yang[e,k], Yini Zhu[a], Danny Z. Chen[e,], David J. Hoelzle[c,h], Zhangli Peng[c,l] and Siyuan Zhang[a,b]

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h.  Department of Mechanical and Aerospace Engineering, Ohio State University, Columbus, OH
i.  University of Kentucky College of Medicine, Lexington, KY
j.  Cleveland Clinic Learner College of Medicine, Cleveland, OH
k.  Verily Life Sciences, Notre Dame, IN
l.  Richard and Loan Hill Department of Bioengineering, University of Illinois at Chicago, Chicago, IL

Mechanical arrest of circulating tumor cells (CTCs) in capillary beds is an essential step for successful metastatic colonization. During this step in the metastatic cascade, tumor cells are exposed to extreme physical insults that can critically impact their survival, and thus hinder the formation of metastatic tumors. Although much research has been conducted to characterize cell behavior in response to physical stimuli, the specific response of tumor cells to the physical stresses dominating the metastatic stage of mechanical arrest has been largely ignored. Here, we present an integrative platform to reliably reproduce the mechanical arrest of single tumor cells and quantitatively determine their response to precisely controlled shear stress in a 3-dimensional microenvironment. Our system is based on biological observations and couples a microfluidic device for the mechanical entrapment of cells with the use a computational model to determine fluid flow dynamics and cell surface tension. Using this platform, we discovered distinct morphological deformations in the mechanically arrested tumor cells that correlate with the measured magnitude of shear stress exerted. From a more in-depth biological perspective, we examined the role of PTEN, a frequently lost tumor suppressor in metastatic breast tumors, and uncovered a surprising vulnerability of PTEN null cells to shear stress, mediated by mitochondrial dynamics, which functionally, resulted in the loss of tumor cell viability. Together, our results underline the direct influence of physical forces on CTCs, particularly as exerted during mechanical entrapment. Furthermore, our observations highlight the importance of these external cues as dynamic determinants of cellular processes and ultimately of metastatic success. As a whole, our platform aims to complement traditional biological approaches by providing a starting system to perform qualitative and quantitative studies of cell behavior during mechanical arrest, discover cell phenotypes unique to this metastatic stage, and inform on the reciprocal interactions of tumor cells and physical forces critically influencing metastatic dissemination and entrapment.

**Poster Presentation:**

**A Novel Urinary Catheter Material that Prevents Fibrinogen Deposition and Investigation of Polymicrobial Biofilms**

Marissa Andersen[1], Xinyu Jin[2], Jenna Lehn[1], Haifeng Gao[2] and Ana L. Flores-Mireles[1]

[1]Department of Biological Sciences, [2]Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN

Catheter associated urinary tract infections (CAUTIs) are the leading cause of healthcare associated infections worldwide. Prevention and treatment of Enterococci, one of the most common causes of CAUTI, is challenging due to inherent resistance to antibiotics, allowing rapid dissemination in hospital settings. This makes Enterococci a priority for development of new therapies. Current therapies in development focus on reducing the incidences of CAUTIs via vaccines, immunotherapies, and modified catheter materials. Antimicrobial-coated urinary catheters are the most promising therapeutic to reduce biofilm formation, showing great results *in vitro.* Unfortunately, they have not been successful *in vivo*.

Recently, it has been shown host fibrinogen (Fg) is released and deposited on catheters following their introduction into bladders of mice and/or humans. Fg deposits on the catheter act as a scaffold for biofilm formation and source of nutrients for uropathogens. Deposition of Fg on the catheter may give an explanation as to why the antimicrobial-coated catheters have antibacterial effects *in vitro* but not *in vivo*. Thus, my project aims to reduce the accumulation of Fg on catheters, which will reduce the ability of microbes to colonize the catheter and bladder. This was tested using anti-protein binding coatings. Preliminary data shows a reduction in Fg deposition *in vitro*, suggesting that developing anti-protein binding urinary catheters may provide an effective and affordable therapy against CAUTI.

*P. mirabilis* is another pathogen responsible for CAUTIs including polymicrobial CAUTIs. The dynamics of co-infections are still not fully understood, warranting further investigation both *in vitro* and *in vivo*. The effect of host mediated responses, such as the release of Fg, on the progression of polymicrobial CAUTIs is also unknown. Here, we look at 24hr *in vivo* polymicrobial infections, and *in vitro* co-culture biofilm formation in the presence of Fg and found changes in *P. mirabilis* swarming and dispersion behavior.

**Oral Presentation:**

**Understanding Differences in Morphology in the Three-Spine Stickleback Fish**

Rebecca Anderson[1,2], Heidi Schutz[2] and Heather Jamniczky[3]

[1]Department of Biological Sciences, University of Notre Dame
[2]Department of Biology, Pacific Lutheran University
[3]Department of Biological Sciences, University of Calgary

Three-spine stickleback fish (*Gasterosteous aculeatus)* inhabit northern hemisphere coastlines. Marine and freshwater populations span a large geographic range and this species has evolved a broad morphological, physiological, behavioral, and genetic diversity. Marine sticklebacks have been shown to invade freshwater habitats, and after several generations such populations appear to become genetically and morphologically distinct from their marine ancestors. Although predation has been posited to play a role in morphological differentiation, specific patterns of variation between groups are unknown. Here, we examined freshwater and marine specimens from several populations in the Madeira Park region of mainland British Columbia as well as the Bamfield region of Vancouver Island. We sampled a total of 304 individuals from 2 regions encompassing 6 localities. Of the 304 individuals, 115 were fresh water and 189 were marine. Our study analyzed morphological changes in the pectoral and pelvic girdles across populations, habitats, and regions. Differences in predator type and predation method may impact bone shape across habitats, hence our focus on skeletal features related to predator avoidance. To this end, we measured 3D bone shape using 32 landmarks and identified patterns within and between populations using an approach that quantifies multivariate shape differences among taxa. Our results show that pectoral and pelvic girdle shape significantly differs between habitats and between regions, suggesting that ecological and geographic differences may influence morphology ($p=0.001$ in all comparisons). Freshwater sticklebacks have shorter pelvic spines, likely due to differences in how they are ingested by predators, and taller more narrow pectoral girdles, possibly related to changes in locomotor patterns to better evade predators. Bamfield sticklebacks generally have longer pelvic spines and shorter pectoral girdles than Madeira Park sticklebacks. Ongoing work is being directed at further unraveling the interesting suite of ecological, behavioral and genetic factors underlying morphological differences among stickleback populations.

**Oral Presentation:**

**Shedding New Light on Squaraines: Utilizing Squaraine Dyes as Building Blocks in Organic Synthesis**

Emily P. Bacher and Brandon L. Ashfeld

Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN

First discovered in 1965 by Treibs and Jacob, fluorescent squaraine dyes are boldly colored compounds well known for their applications in physical and analytical chemistry. Structurally, squaraine dyes contain a central, electron deficient cyclobutendione core flanked by two electron rich aromatic substituents in a 1,3-orientation, leading to a donor-acceptor-donor resonance stabilization. These unique electronic properties enable squaraine dyes to intensely absorb and emit light in the near-infrared region. Classically, these compounds have been utilized extensively in materials applications throughout physical and analytical chemistry, including biological imaging, photodynamic therapy, nonlinear optics, photovoltaics, and ion sensing. In contrast, there are surprisingly few reported studies that explore the use of squaraine dyes as synthetic building blocks, despite possessing multiple sites of potential reactivity. This research focuses on the development of functionally rich squaraine scaffolds as readily available starting materials for the construction of more architecturally complex small molecules and the exploitation of their inherent reactivity to design chemically-driven analytical protocols. To date, the applications of squaraine dyes has been successfully extended towards: (1) the development of squaraine dyes as thermo- and chemoreversible imaging agents, (2) accessing highly functionalized oxindoles and benzofuranones via a phosphine-mediated ring expansion of appropriately substituted dianiline squaraine dyes, and (3) the design of squaraine dyes as chiral transition metal ligands in enantioselective catalysis.

**Oral Presentation:**

**Aged ECM Promotes Invasion and EMT-Like Behavior in Breast Epithelial Cells**

Gokhan Bahcecioglu[1], Xiaoshan Yue[1], Erin Howe[2,3], Ian Guldner[2,3], Sharon Stack[2,4] , Siyuan Zhang[2,3] and Pinar Zorlutuna[1,2,5]

[1]Department of Aerospace and Mechanical Engineering, [2]Harper Cancer Research Institute, [3]Department of Biological Sciences, [4]Department of Chemistry and Biochemistry, [5]Bioengineering Graduate Program, University of Notre Dame, Notre Dame, IN

Cancer incidences increase exponentially with age, which has been explained with changes in cells, including accumulation of mutations and telomere shortening. However, the effect of aged ECM on tumor initiation and progression has not been explored in detail, although ECM is also altered with aging. Here, we hypothesize that the aged ECM alters the behavior of breast epithelial cells, contributing to tumor initiation and progression. This study aims at identifying the changes in ECM characteristics upon aging, and studying the effects of these changes on breast cancer development.

Decellularized breast tissues from young (3-6 months old) and aged (22-25 months old) mice were used to evaluate the normal (KTB-21) and cancerous (MDA-MB-231) breast epithelial cell behavior. KTB-21 cells formed a lower number of spheroids on the aged matrix than the young, with the spheroids being less circular ($p < 0.0001$). Circularity of the cell nuclei was smaller on the aged matrix ($p < 0.011$), indicating that the aged microenvironment leads to nuclear deformation. Further analysis using single cell RNA sequencing (scRNA-seq) revealed upregulation of genes associated with invasion/migration and epithelial to mesenchymal transition (EMT). In line with the scRNA-seq results, immunostaining showed that KTB-21 cells deposited higher levels of MMP-2 on the aged matrix than the young ($p < 0.018$). Finally, motility of the MDA-MB-231 cells was significantly greater on the aged matrix than young ($p < 0.0001$). All in all, our study shows that the aged ECM supports invasive phenotype and ECM could be a major factor inducing tumor initiation and progression.

**Oral Presentation:**

**Electrically Conductive 3D Printed MXene-Hydrogel Composite Constructs for Tissue Engineered Human Cardiac Patches**

Gozde Basara and Pinar Zorlutuna

Department of Aerospace and Mechanical Engineering, University of Notre Dame, Notre Dame, IN

Cardiovascular disease has been the leading cause of death in the world. Recent work in the realm of tissue engineering has demonstrated the therapeutic potential of cardiac patches for the treatment of myocardial infarction. It is crucial for these patches to mimic the fibrillar structure of the extracellular matrix and the electroconductive property of native human heart while the contractile behavior of cardiomyocytes (CMs) relies on these properties. MXene ($Ti_3C_2$) is an emerging material which is suitable for cardiac tissue engineering applications due to its high conductivity and non-cytotoxic properties. Using MXene, we developed a conductive cardiac patch that integrates with the electrophysiology of cardiovascular cells while also providing alignment cues via patterning. Using aerosol jet printing, MXene was deposited on circular polyethylene glycol (PEG) gels in pre-designed patterns. The cells were seeded on the MXene-PEG constructs right after printing and cultured for one week with no signs of cytotoxicity. Additionally, when MXene strips were printed with thicknesses of 20μm – 50μm cardiomyocytes attached to only MXene and aligned in the direction of the material, demonstrating the patterning potential of the MXene with a significant increase in sarcomere length and Connexin-43 expression. These collected results demonstrate the potential of utilizing MXene as a therapeutic cardiac patch for treatment of MI.

**Poster Presentation:**

**Elucidating the Kinetic Mechanism of Human METTL16**

Kurtis Breger, Agnieszka Ruszkowska and Jessica A. Brown

Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN

Over 140 RNA modifications have been discovered, yet only recently have they been studied in depth due to recent technological advancements. $N^6$-methyladenosine (m$^6$A) is an abundant RNA modification in messenger RNA (mRNA) and long non-coding RNA (lncRNA) that affects various cellular functions such as mRNA stability. Methyltransferase-like protein 16 (METTL16) is one of four catalytically active m$^6$A RNA methyltransferases in humans. Two well-known methylation targets of METTL16 are U6 spliceosomal RNA and a hairpin in the 3' untranslated region of MAT2A mRNA. However, METTL16 binds to many other RNAs, including the 3' triple helix of MALAT1. Using *in vitro* methyltransferase assays, we have started to investigate the kinetic mechanism and other fundamental properties of METTL16. Our *in vitro* methyltransferase assays consist of purified recombinant human METTL16 (1-562) in combination with the U6 RNA substrate and *S*-adenosylmethionine (SAM), the methyl donor, to initiate the reaction. Thus far, we have recapitulated the methylation of A43 in U6 RNA and determined optimal buffer conditions: 10 mM HEPES (pH 7.0), 150 mM KCl, 10 mM MgCl$_2$, and 5 mM TCEP. However, under various assay conditions, the cancer-associated MALAT1 triple helix is not a substrate of METTL16 at position A8290 and other adenosine residues seem unlikely. Single-turnover assays established a rate constant of 0.333 min$^{-1}$ (or 0.00555 s$^{-1}$). This slow rate of methylation suggests conformational rearrangements prior to catalysis or other cofactors may contribute to the methyltransferase activity of METTL16. Our next goals are to use kinetic assays and microscale thermophoresis to measure other kinetic parameters in the kinetic pathway in addition to analyzing critical residues found within the enzyme active site. Future studies will focus on METTL16 mutants, including those identified in cancer patients, to ascertain how these residues affect the kinetic mechanism of METTL16.

**Poster Presentation:**

## Engineering Bioactive Nanoparticles to Rejuvenate Endothelial Progenitor Cells

Loan Bui[1], Kellen Round[1], Madeline Owen[1], Pietro Sainaghi[1], Prakash D. Nallathamby[1], Laura S. Haneline[3] and Donny Hanjaya-Putra[1,2]

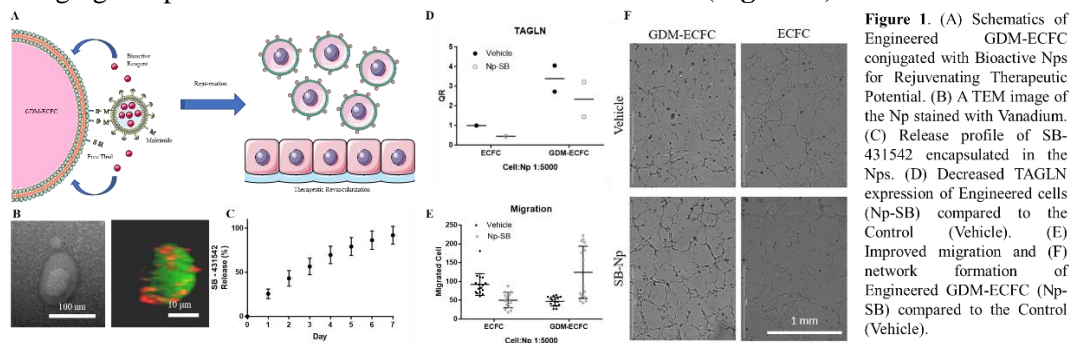[1]Bioengineering Graduate Program, Dept. Aerospace & Mechanical Engineering, Univ. Notre Dame, IN
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**Introduction:** Endothelial Colony-Forming Cells (ECFCs) are a subtype of endothelial progenitor cells (EPCs) identified from circulating adult and human cord blood which express characteristics of putative EPCs. Due to their robust clonal proliferative potential and ability to form *de novo* blood vessel *in vivo*, ECFCs have been used as cell-based therapy to treat cardiovascular diseases, as well as tissue engineering application. However, in the course of chronic diabetes, ECFCs are subject to stress-induced premature dysfunction that limits their therapeutic use. Previous studies have shown that ECFCs isolated from patients with gestational diabetes (GDM) exhibit upregulation of transgelin (TAGLN), lower cell migration, and impaired angiogenic potential. Here, we hypothesize that cell surface engineering with bioactive nanoparticles (NPs) can be used to rejuvenate GDM-ECFCs and restore their therapeutic potential.

**Materials and Methods:** We generated bioactive NPs using phospholipids to control the release rate of transforming growth factor-β (TGF-β) inhibitor SB-431542 (SB). Cell surface engineering was used to couple bioactive NPs onto the surface of GDM-ECFCs. The ability of bioactive NPs to restore cell migration and proliferation, as well as vascular tube formation was evaluated *in vitro*. Through delivery of engineered cells *in vivo*, we assess the endothelium repair and new blood vessel formation.

**Results and Discussion:** We successfully developed and characterized bioactive NPs for cell surface engineering of GDM-ECFCs (**Fig 1A-B**). By controlling the release rate of SB from the bioactive NPs (**Fig 1C**), the progenitor phenotypes of GDM-ECFCs can be restored as suggested by the decrease in TAGLN expression (**Fig 1D**). Moreover, this strategy was proven to restore cell migration and proliferation, as well as angiogenic potential of GDM-ECFCs *in vitro* and *in vivo* (**Fig 1E-F**).



**Figure 1**. (A) Schematics of Engineered GDM-ECFC conjugated with Bioactive Nps for Rejuvenating Therapeutic Potential. (B) A TEM image of the Np stained with Vanadium. (C) Release profile of SB-431542 encapsulated in the Nps. (D) Decreased TAGLN expression of Engineered cells (Np-SB) compared to the Control (Vehicle). (E) Improved migration and (F) network formation of Engineered GDM-ECFC (Np-SB) compared to the Control (Vehicle).

**Conclusions:** This research developed multilamellar lipid-based nanoparticles that were directly attached to the endothelial progenitor cell surface. The nanoparticles were biocompatible and allowed to control the release of encapsulated SB. The nanoparticles conjugated onto the cell surface can provide a pseudo-autocrine effect to rejuvenate GDM-ECFCs and improve their therapeutic potential. Collectively, cell surface engineering with bioactive NPs represents a powerful tool to rejuvenate progenitor cells for a wide range of translational applications.

**Poster Presentation:**

## KCTD15 Regulates Nephron Segment Differentiation by Repressing TFAP2A Activity

Brooke E. Chambers, Eleanor G. Clark, Allison E. Gatz and Rebecca A. Wingert

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A functional vertebrate kidney relies on structural units called nephrons, which are epithelial tubules that contain a sequence of segments each expressing a distinct repertoire of solute transporters. To date, the transcriptional codes driving regional specification, solute transporter program activation, and terminal differentiation of segment populations remains poorly understood. We demonstrate for the first time that the KCTD15 paralogs, *kctd15a* and *kctd15b*, function in concert to restrict distal early (DE)/thick ascending limb (TAL) segment lineage assignment in the developing zebrafish pronephros by repressing Tfap2a activity. During renal ontogeny, expression of these factors co-localized with *tfap2a* in distal tubule precursors. *kctd15* loss primed nephron cells to adopt distal fates by driving expansions in *slc12a1*, *kcnj1a.1*, and *stc1* marker expression. These phenotypes were resultant of Tfap2a hyperactivity, where *kctd15a/b*-deficient embryos exhibited increased abundance of this transcription factor. Interestingly, *tfap2a* can reciprocally promote *kctd15* transcription, unveiling a circuit of autoregulation operating in nephron tubule progenitors. Concomitant *kctd15b* knockdown with *tfap2a* overexpression produced genetic synergy and uncontrolled DE/TAL differentiation. Our data indicates nephron segmentation is determined by a transcription factor-repressor feedback module that employs tight regulation of Tfap2a-Kctd15 kinetics during kidney development.

**Poster Presentation:**

**Chemical Genetic Screen Reveals Novel Roles for Ppargc1a in Cilia Development and Disease**

Joseph M. Chambers, Shahram Jevin Poureetezadi, Amanda Addiego and Rebecca A. Wingert

Department of Biological Sciences, University of Notre Dame, Notre Dame IN

Cilia are microtubule-based organelles that function in a multitude of physiological contexts to perform chemosensing, mechanosensing, or fluid propulsion. The process of ciliogenesis is highly regulated and disruptions result in disease states termed ciliopathies. The genetic and molecular events that lead to dysfunctional ciliated cells are not fully understood. Here, we show novel roles for *peroxisome proliferator-activated receptor gamma 1 alpha* (*ppargc1a*) during ciliogenesis in mono- and multiciliated cells (MCCs) as well as discernment of renal tubule MCC fate choice during embryogenesis. We discovered that *ppargc1a* performs both roles by affecting prostaglandin levels, where cilia formation and renal MCC fate were restored with prostaglandin $E_2$ ($PGE_2$) treatment. Genetic disruption of *ppargc1a* specifically reduced *prostaglandin-endoperoxide synthase 1* (*ptgs1, or cox1*) expression and suboptimal knockdown of both genes revealed a synergistic effect. Further, *ptgs1* overexpression rescued ciliogenesis and renal MCCs in *ppargc1a* deficient embryos. These findings position Ppargc1a as an essential genetic regulator of prostaglandin synthesis during ciliated cell ontogeny.

**Poster Presentation:**

**Src and CDK4/6 Inhibition Induces a Synergistic Vulnerability in Rb-Deficient TNBC**

Farya Chattergoon[1,2], Jenna Koeing[1], Yingjia Ni[1,2], Erin N Howe[1,2] and Siyuan Zhang[1,2]

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[2]Harper Cancer Research Institute, University of Notre Dame, Notre Dame, IN

Dsyregulation of the cell cycle is a hallmark of cancer. The traditional dogma of the G1/S transition mechanism centers on the cyclin D-CDK4/6-Rb axis. In many aggressive cancers, including triple-negative breast cancer (TNBC), Rb is mutated or lost. Yet, how the G1/S transition is regulated in Rb-deficient cancers has not been fully defined. As kinases play a central role in cell cycle regulation, we hypothesize alternative kinase-mediated pathways synergize with CDK4/6 in regulating G1/S cell cycle transition in the Rb-deficient context. To explore essential G1/S regulatory kinases alternative to CDK4/6, we performed a pooled kinome CRISPR knockout screen in Rb-deficient TNBC cells under the treatment of CDK4/6 inhibitor (CDK4/6i). Screen hits were identified using Model-based Analysis of Genome-wide CRISPR-Cas9 Knockout (MAGeCK) for the underrepresented sgRNAs in the CDK4/6i treated cells compared with control cells. These underrepresented sgRNAs after the treatment corresponded to "drop-out" kinase hits, which potentially are essential for cell cycle regulation.  Using The Cancer Genome Atlas (TCGA) database, the hits were then ranked based on the prevalence of up-regulation in clinical relevance for TNBC and SRC is among the top six drop-out hits. Inhibition of SRC using Dasatinib, an FDA approved inhibitor for cancer therapy, synergize with CDK4/6i and a decrease in cell proliferation in a panel of Rb-deficient TNBC cell lines. Future studies will use genetic knockouts of SRC to decipher the mechanism between SRC and CDK4/6 inhibition synergy. In vivo studies using Rag1-/- mice with an Rb-deficient TNBC cell line and drug treatment will be performed to show the efficacy of the combination treatment *in vivo*. Overall, these top six hits will be further studied to determine how they collectively contribute with CDK4/6 to regulate the G1/S transition in the Rb-deficient context, with potential translational relevance.

**Oral Presentation:**

## ESX-1 Secreted Substrates Control Gene Expression in Pathogenic *Mycobacteria*

Alexandra Chirakos and Patricia A. Champion

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The ESX-1 (ESAT-6-system-1) secretion system is required for the virulence of mycobacterial pathogens. Both *Mycobacterium tuberculosis,* the cause of human tuberculosis, and *Mycobacterium marinum* the cause of tuberculosis-like disease in poikilothermic fish, use the ESX-1 system to secrete protein virulence factors that promote bacterial survival in the host. We demonstrated that gene expression is controlled in response to the presence or absence of the ESX-1 translocon. It is well established that substrate gene expression is regulated in response to the assembly or activity of secretion systems in Gram-negative bacteria. However, the mechanism underlying ESX-1-dependent control of gene expression is unknown. We identified two secreted ESX-1 associated proteins (Esp's), EspE and EspF, which negatively impact expression of the *whiB6* gene. WhiB6 is a redox-responsive transcription factor that regulates gene expression, including those encoding ESX-1 substrates. We show that deletion of the *espF* and *espE* genes resulted in a significant increase in transcription of the *whiB6* gene. The corresponding increase in WhiB6 protein resulted in upregulation of genes encoding other ESX-1 secreted substrates, leading to an accumulation of those substrates in the bacterial cytoplasm. Conversely, we found that the overexpression of EspE was sufficient to reduce expression of the *whiB6* gene, and genes encoding additional ESX-1 substrates. Our findings support a model in which at least two ESX-1 secreted substrates function to fine-tune the levels of other ESX-1 substrates in response to the assembly of the secretory apparatus. This represents a new paradigm of secretion dependent regulation.

**Oral Presentation:**


**Strategies for the Calculation of the Viscosity using Molecular Dynamics**

Ernesto Cortes-Morales and Jonathan Whitmer

Department of Chemical and Biomolecular Engineering, University of Notre Dame, Notre Dame, IN

In this talk I present a strategy model for the calculation of transport properties for complex molecules through Molecular Dynamics simulations. In particular, we take the Green-Kubo (GK) equation to calculate the viscosity for N independents trajectories from short-time simulations, that was already used by Zhang, et al [JCTC 2015, 11, 3537-3546]. The enhancement of the calculation of the viscosity using our method, though, comes by sampling important structural Collective Variables (CV) obtained from the system, which allow to characterize hidden slow relaxation states that are common in complex systems, such as self-assembly polymers, biomolecules, etc. This can be made by performing a sampling of the free energy surface, which helps to weight over the short-time viscosity in order to obtain an accurate value of the average. We choose a Lennard-Jones mono-disperse system as a test model for the calculation of the viscosity, and the Thermodynamic Integration from liquid to the Einstein crystal state is used as a sampling method to obtain the free energy and calculate the average of the viscosity over the ensemble. Finally, preliminary studies of the viscosity for a bi-disperse Lennard-Jones system in the vicinity of the glass-transition temperature are presented.

**Oral Presentation:**

**Quantitative Microbial Risk Assessment of Swimming in Sewage Impacted Waters using CrAssphage and Pepper Mild Mottle Virus in a Customizable Model**

Katherine Crank and Kyle Bibby

Department of Civil and Environmental Engineering and Earth Sciences, University of Notre Dame, Notre Dame, IN

Gastrointestinal disease resulting from exposure to sewage-impacted results in greater than 800,000 deaths globally per year[1] and viruses account for the majority of infections from exposure to sewage-impacted water.[2,3] Fecal indicator bacteria currently employed for microbial water quality management are poor representatives of viruses. Viral water quality indicators have recently been proposed based on the human gut bacteriophage crAssphage and the food virus pepper mild mottle virus (PMMoV) due to their high abundance in wastewater and association to human waste. We developed a model relating crAssphage and PMMoV abundance to risk of swimmer illness in a recreational water contaminated with fresh, untreated domestic wastewater using a quantitative microbial risk assessment (QMRA) framework. The developed model demonstrated that both crAssphage and PMMoV have the potential to lower acceptable regulatory disease thresholds to approximately 1 illness per 1000 swimmers. The model was built using R and is freely available via a web-based user interface. Building upon these prior developments, we have added differential decay of wastewater pathogens and indicators to account for sewage aging in the environment. Preliminary results indicate that original concentrations of pathogens in wastewater play a larger role in risk variability than decay. As risk-based regulatory approaches become more prominent, quantitative microbial risk assessment can prove to be a valuable tool in wastewater treatment plants process control tool kit.[4] This study reaffirms the importance of monitoring viral water quality to adequately protect public health, suggests the high potential of both crAssphage and PMMoV for this application, and establishes a basis to relate viral indicator abundance with probability of illness due to viral pathogens.

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2.      Boehm, A. B.; Soller, J. A.; Shanks, O. C., Human-associated fecal quantitative polymerase chain reaction measurements and simulated risk of gastrointestinal illness in recreational waters contaminated with raw sewage. *Environmental Science & Technology Letters* **2015,** *2*, (10), 270-275.
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**Poster Presentation:**

**Uncovering Functional Relationships between ESX-1 Substrates in *Mycobacterium marinum***

Rachel Cronin, Micah J. Ferrell, Clare Cahir and Patricia A. Champion

Department of Biological Sciences, University of Notre Dame, Notre Dame, IN

*Mycobacterium tuberculosis*, the causative agent of human tuberculosis, infects approximately 10 million people every year. *M. tuberculosis* requires the ESX-1 protein secretion system for survival in the host. ESX-1 actively transports protein substrates, which may either contribute to the secretory apparatus, or damage the phagosomal membrane. ESX-1-dependent phagosomal lysis is essential for bacterial survival; mycobacteria lacking an ESX-1 system are retained in the phagosome and attenuated. Although individual ESX-1 substrates are required for pathogenesis, the function of any individual substrate is unknown in part because it is thought that knocking out any individual substrate gene leads to the same phenotype: loss of secretion and attenuation. However, using *Mycobacterium marinum,* an established model for *M. tuberculosis* ESX-1 secretion, we find that deletion of ESX-1 substrate genes results in a range of intermediate secretion and virulence phenotypes. We are using genetic interaction analysis in *M. marinum* to understand the genetic and functional interactions between all known ESX-1 substrates. We have generated a collection of *M. marinum* strains with pairwise deletions between known ESX-1 substrate genes. Our characterization thus far has identified positive and negative interactions between ESX-1 substrates; some combinations restore secretion, while others reduce secretion relative to the consequences of mutating individual genes. We have also identified epistatic relationships which may indicate an order of secretion for ESX-1 substrates. Together, this study will allow us to better understand the molecular mechanisms of mycobacterial secretion systems and the individual contributions of individual ESX-1 substrates to mycobacterial secretion and pathogenesis.

**Poster Presentation:**

**Local Investigation of the Complex Morphology of the Adult Human Brain**

Nagehan Demirci and Maria Holland

Department of Aerospace and Mechanical Engineering, University of Notre Dame, Notre Dame, IN

The adult human brain has a distinctive structure and morphology which allows researchers from diverse disciplines to investigate the functional, pathological and neurodevelopmental differences among individuals. The complex surface topology of the highly convoluted (folded) cortex, ie., the outermost layer of the brain, is comprised of asymmetrical gyral crests and sulci valleys which emerge in the third gestation of the prenatal period. Quantification of this complexity is essential for our understanding of the functional and morphological development of the brain. Here we quantify the convoluted morphology of the cortex based on surface curvatures at ~150.000 vertices in each hemisphere. We considered the maximum and minimum principal curvatures, k1 and k2 respectively, as well as other curvature measures defined in terms of k1 and k2.  As principal curvatures do not fully describe the 3D surface morphology, we employed the intrinsic Gaussian curvature, extrinsic mean curvature and dimensionless shape index (SI) in this study. The outer surface of the cortex was extracted from the publicly available magnetic resonance imaging (MRI) data using the open-source software Freesurfer. Following the cortical sheet reconstruction, the aforementioned shape measures and their relation to cortical thickness were examined vertex-wise. Further, it was shown that the dimensionless shape-index offers some additional insight in delineating the sulcal and gyral regions in the cortex. This quantitative data could be used as potential diagnostic markers for various neurodegenerative diseases, neurological disorders, and/or atypical development of the human cerebral cortex.

**Poster Presentation:**

**Development of Optogenetic Tools to Investigate the Role of Intracellular pH in Cancer**

Caitlin E. T. Donahue and Katharine A. White

Department of Chemistry and Biochemistry, Harper Cancer Research Institute, University of Notre Dame, Notre Dame, IN

Intracellular pH (pHi) is highly regulated within normal cells and is maintained between 7.0-7.2. Transient changes in pHi have been linked to a variety of pH-dependent cell behaviors such as progression through the cell cycle, migration, division, and differentiation. However, in disease states such as cancer, pHi dynamics can become dysregulated. Cancer cells often have a higher intracellular pH (pHi of 7.3-7.6) compared to normal cells. This increased pHi is linked to cancer cell behaviors such as increased invasion, metastasis, proliferation, metabolic adaptation, and evasion of apoptosis. However, studies linking increased pHi to these cancer cell behaviors were performed at the population level using non-specific tools to manipulate pHi. In this work, we present a novel technique to raise intracellular pH within a single cell that is reversible and non-invasive to the cells of interest. This technique allows us to investigate the role of increased pHi on cell behaviors such as cytoskeleton remodeling, migration, and drug resistance. In this work, we use Archaerhodopsin (ArchT), a light-activated outward proton pump, to spatiotemporally raise pHi within single cells. This allows us to manipulate and monitor pHi dynamics in real-time. Preliminary data shows that ArchT can be used to induce pHi increases over a two-minute time-period and that individual cells can respond to this increase in pHi by undergoing local membrane ruffling. This tool allows us to investigate previously intractable questions in the field regarding the relationship between increased pHi and cytoskeleton remodeling, migration, and drug resistance. This technique will allow us to investigate single-cell pHi dynamics and determine how single-cell behavior is integrated to produce global cancer cell phenotypes.

**Oral Presentation:**

**Adipose Stem Cell Secretome Markedly Improves Rodent Heart and Human iPSC-derived Cardiomyocyte Functional Recovery from Cardioplegic Transport Solution Exposure**

Bradley Ellis[1,2], Dmitry O. Traktuev[3,4], Stephanie Merfeld-Clauss[3,4], Isik Can[2], Meijing Wang[5], Ray Bergeron[3], Keith L. March[3,4] and Pinar Zorlutuna[1,2]

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Heart transplantation is a life-saving therapy for end-stage organ failure. However, organ deteriorations due to ischemic transport time leads to a practical storage limitation of 4 hours, significantly lowering viable hearts for transplant. Approaches that ameliorate organ damage would increase available hearts. We have previously shown that the secretome of adipose-derived stem/stromal cells (ASC-S) rescues tissues from post-ischemic damage *in vivo*. We tested whether the therapeutic activity of ASC-S would extend to *ex vivo* hearts and human iPS-derived cardiomyocyte (iCM) layers exposed to conditions mimicking organ transportation, providing a potential practical approach to enhance transplantation by organ perfusion with ASC-S. iCMs were exposed to University of Wisconsin (UW) cardioplegic solution alone or with ASC-S, at 4°C or 37°C for up to 8 hours. Additionally, intact mouse hearts subjected to cold UW either alone or with ASC-S. The rate-pressure product and contraction rate of hearts, mechanical parameters, and apoptosis of iCMs were evaluated while hearts or cells recovered in control media or ASC-S. Exposure of hearts and iCM to cardioplegic solution led to deterioration of contractile activity, which worsened in iCM with lengthened exposure time; these compromises were ameliorated by ASC-S supplemented storage or recovery solutions. We then tested the hypothesis that ASC-S mediated enzymatic activity accelerating ROS clearance. Silencing superoxide dismutase 3 and catalase expression in ASC prior to secretome generation lowered the cardiomyocyte-protective effect of ASC-S. A novel organ transport model involving iCM was developed to assess improved approaches to cardiac preservation. ASC-S displays cardio-protective activity when presented to mouse hearts or iCM in conditions simulating either cardioplegia or post-implant recovery. The effect of ASC-S on the recovery of hearts and iCM function supports the possibility of doubling human cardiac storage time by ASC-S supplementation, thus expanding the pool of acceptable donor hearts.

**Poster Presentation:**

## Synthesis and Photopatterning of Norbornene Modified Hyaluronic Acid Hydrogel

Fei Fan[1], Junyu Zhao[1], Laura Alderfer[1], Loan Bui[1] and Donny Hanjaya-Putra[1,2]

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The extracellular matrix (ECM) provides complex and dynamic supports of surrounding cells. Hydrogels are tissue-like biomaterials with highly biocompatibility and mechanical tunability, which have been widely applied for cell encapsulation and tissue engineering. To mimic the natural behavior of extracellular matrix, a series of chemical and engineering approaches are developed to fabricate tunable hydrogels with multiple properties.

The photopatterning of hydrogels is an alternative and potentially simpler approach that permits gel formation and provides both spatial and temporal control[1]. The thiol-Michael chemistry have emerged as powerful tools in small molecule synthesis as well as polymer synthesis and hydrogel formation[2]. Of those thiol-Michael reactions, the radical mediated thiol-norbornene click reaction presents highly specificity which permits precisely tailoring biochemical and mechanical properties of hydrogels by UV light. Herein, we present the synthesis of norbornene modified hyaluronic acid (NorHA) through esterification and photopatterning of NorHA hydrogel with mono-thiol dyes through thiol-norbornene chemistry.



a. synthesis of NorHA
b. fabrication of NorHA hydrogel
c. photopatterning of NorHA hydrogel
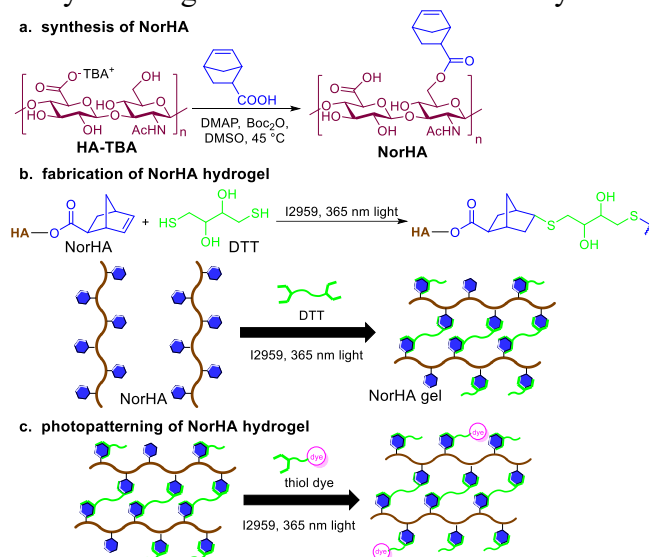
[1] Lampi M. C., Guvendiren M., Burdick J. A., and Reinhart-King C. A. Photopatterned hydrogels to investigate the endothelial cell response to matrix stiffness heterogeneity. *ACS Biomater. Sci. Eng.*, **2017**, 3, 3007-3016.

[2] Spicer C. D., Pashuck E. T., and Stevens M. M. Achieving controlled biomolecule–biomaterial conjugation. *Chem. Rev.*, **2018**, 118, 7702-7743.

**Oral Presentation:**

## Dynamics and Control of Underactuated Biped Robots

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In the past few decades, robotics research has sought to engineer versatile walking biped robots that can move efficiently alongside humans in unstructured environments. In the future, applications for such robots may include in-home assistance of the elderly and people with disabilities, parcel delivery, warehouse logistics, military assistance, security, construction, and even space exploration. Moreover, the study of bipedal locomotion has the potential to inform the design of powered prostheses, exoskeletons, and other bio-inspired robotic devices to assist in rehabilitation. Even state-of-the-art applications, however, are incapable of coping with unforeseen perturbations when the magnitude or frequency of the disturbances becomes too high. These practical challenges still limit the ability of efficient biped robots to achieve their envisioned potential in today's society. This oral presentation will showcase the robotics research done in the Locomotion & Biomechanics Lab at the University of Notre Dame that intends to address these limitations. More specifically, this presentation will introduce a novel method for biped robots to switch their walking gaits after experiencing unexpected disturbances. This method was shown to give robots the ability to transition among walking gaits just like humans switch gaits to robustly and efficiently navigate man-made environments and uneven natural terrain.

**Oral Presentation:**

**Algorithmic Assessment of Missense Mutation Severity in the Von-Hippel Lindau Protein**

Francisco R. Fields[1,2], Niraja Suresh[1,2], Morgan Hiller[1,2], Stefan D. Freed[1,2,3], Kasturi Haldar[1,2] and Shaun W. Lee [1,2,3,4]

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Von Hippel-Lindau disease (VHL) is an autosomal dominant rare disease that causes the formation of angiogenic tumors. When functional, pVHL acts as an E3 ubiquitin ligase that negatively regulates hypoxia inducible factor (HIF). Genetic mutations that perturb the structure of pVHL result in dysregulation of HIF, causing a wide array of tumor pathologies including retinal angioma, pheochromocytoma, central nervous system hemangioblastoma, and clear cell renal carcinoma. These VHL-related cancers occur throughout the lifetime of the patient, requiring frequent intervention procedures, such as surgery, to remove the tumors. Although VHL is classified as a rare disease (1 in 39,000 to 1 in 91,000 affected) there is a large heterogeneity in mutations listed for observed pathologies. Understanding how these specific mutations correlate with the myriad of observed pathologies for VHL could provide clinicians insight into the potential severity and onset of disease. Using a set of 285 ClinVar mutations in VHL, we developed a multiparametric scoring algorithm to evaluate the overall clinical severity of missense mutations in pVHL. The mutations were assessed according to eight weighted parameters as a comprehensive evaluation of protein misfolding and malfunction. Higher mutations scores were strongly associated with pathogenicity. Our approach represents a novel *in silico* method by which VHL-specific mutations can be assessed for their severity and effect on the biophysical functions of the VHL protein.

**Poster Presentation:**

**Host Factors Associated with Pathogen Persistence during Catheter-Associated Urinary Tract Infections**

Christopher Gager and Ana L. Flores-Mireles

Department of Biological Sciences, University of Notre Dame, Notre Dame, IN

Catheter-associated urinary tract infections (CAUTIs) are the most common healthcare-associated infections in the world. Enterococci represent the most common pathogens responsible for CAUTIs, and exhibit a wide spectrum of antibiotic resistance, making its prevention and treatment extremely difficult. In the Flores-Mireles lab, we focus in understanding *E. faecalis* pathogenesis strategies during CAUTI. Urinary catheterization facilitates *E. faecalis* colonization and persistence in the bladder and dissemination to multiple organs, including the kidneys, spleen, and heart. In the absence of the catheter, the pathogen is cleared out of the bladder. The main question we are examining is how urinary catheterization promotes bacterial colonization and persistence. We have found that catheterization leads to bladder inflammation, edema, infiltration by neutrophils, and inflammatory cytokine induction. Despite the immune response the bacteria is able to thrive in this environment. Therefore my project focus in characterizing the inflammatory response and identify the host factors that support pathogen persistence in CAUTIs, which in consequence leads to dissemination. We have shown that the fibrinogen, a coagulation cascade member, is important for healing the urothelial damage caused by the catheter; however, fibrinogen accumulation becomes detrimental for the host and instrumental in the persistence of *E. faecalis* infection. Fibrinogen is only produced in the liver and recruited in the bladder upon catheterization via cytokine signaling. Therefore we are 1) characterizing the temporal cytokine response profile during catheterization and catheterization and *E. faecalis* infection, 2) their role in fibrinogen accumulation and immune cell recruitment in the bladder. Additionally, we are also examining the neutrophil response to catheterization and *E. faecalis* infection. By characterizing the role fibrinogen, cytokines, and neutrophils exhibit in *E. faecalis* CAUTIs, we will develop a further understanding of what host factors promote pathogen persistence in this infection model.

**Poster Presentation:**

**Effects of User Intent Changes on Onboard Sensor Measurements during Exoskeleton-Assisted Walking**

Taylor Gambon and James P. Schmiedeler

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Robotic exoskeletons are a promising technology for rehabilitation and locomotion following neurological injury or muscular weakness, but their adoption outside the physical therapy clinic has been limited by relatively primitive methods for identifying and incorporating the user's gait intentions. Intentions can have various resolutions, from high-level goals (speed up/slow down) to mid-level actions (increase/decrease stride length) to low-level joint behaviors (increased flexion). Sensors onboard the exoskeleton sense the human only indirectly, via the human-robot interface, but offer advantages over more direct methods in terms of measurement consistency. In this study, exoskeleton users, both able-bodied and having spinal cord injury, were asked to perform goal-level changes in their intended gait speed in order to characterize joint- and action-level responses. Trials were completed for both a trajectory-free and a trajectory-based control mode and with either crutches or a walker. Experimental results confirm statistically significant differences between the pre- and post-command joint-level measures of position and motor currents. The coordination of these joint-level changes resulted in significant differences in the action-level measures of stride length and stride time. In most cases, users were able to realize their intended gait speed change by as much as 0.30 m/s (48% of the nominal gait speed) for the trajectory-free control mode and as much as 0.19 m/s (39% of the nominal gait speed) for the trajectory-based control mode. Overall, the findings suggest that intent detection is possible for both able-bodied and non-able-bodied users with onboard sensors alone but demonstrates that the intent signals depend on exoskeleton control settings, user ability, and temporal considerations.

**Oral Presentation:**

**Multi-Modal Single Cell Analysis Reveals Age-Induced Reshaping of Brain Immune Homeostasis**

Samantha Golomb and Siyuan Zhang

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The central nervous system (CNS) contains a diverse array of immune cell types. Immune cells in the brain, despite their disparate roles, collectively contribute to brain tissue homeostasis and disease progression[1]. Importantly, brain immune homeostasis is influenced by the aging process[1,2]. Yet, characteristics of the brain immune environment due to aging have not been systematically delineated. In this study, using Cellular Indexing of Transcriptomes and Epitopes by sequencing (CITE-seq),  we analyzed compositional and transcriptional changes of brain immune cells in aged mice. Among several changes, we noted particularly significant changes with potential functional implications that are inflammatory in nature. Aged mouse brains had a 5.4 fold increase in infiltrating CD8+ T lymphocytes relative to young mice. Additionally, aged brains had a higher abundance CNS-resident, border associated myeloid cells (BAMs) with a disease-associated gene signature characterized by high MHCII, Il1b and Ccr2 expression, as opposed to young brains mostly comprising homeostasis-associated BAMs. Enabled by a high resolution molecular phenotyping, our study revealed distinct changes in the brain immune homeostasis of aged mice, suggesting that factors of ageing prime for a higher propensity for neuroinflammation in the aged brain.

**Poster Presentation:**

## Persistence and Transport of Fecal Pollution Indicators in Environmental Waters

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Fecal indicator bacteria (FIB) are typically used to monitor microbial water quality but they are poor representatives of viruses due to differences in persistence and transport in the environment. Viral indicators such as crAssphage and pepper mild mottle virus (PMMoV) have been proposed as alternatives to FIB. Assessing the persistence and transport of fecal-associated viral indicators under realistic environmental conditions is essential to evaluate their suitability to represent pathogenic virus fate in the environment. In this study, we examined the persistence of five viral fecal indicators and pathogens (somatic coliphage, crAssphage, adenovirus, human polyomavirus, and PMMoV) and three bacterial indicators (human Bacteroides HF183/BacR287 and the culturable FIB E. coli and enterococci). We also examined the transport of FIB in relation to HF183, CPQ56 and PMMoV in an artificial stream. Overall, our results showed that viral indicators had slower decay rates than bacterial indicators and that viral indicators were less susceptible to UV than bacterial indicators. Notably, PMMoV had much slower decay rates than all other targets tested. The decay characteristics calculated for each fecal pollution indicator confirm that bacterial indicators inadequately represent viral fate during aging of sewage contaminated water. Our results also showed that culturable indicators E. coli and enterococci had differing transport characteristics than the molecular indicators CPQ56, PMMoV and HF183. These results will inform the development of enhanced viral water quality monitoring tools and risk modeling.

**Poster Presentation:**

**Metastasis-Associated Myeloid Cells Drive Immune Suppression in Brain Metastatic Niche through Cx3cr1-Cxcl10 Axis**

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Brain metastasis develops in an immunologically-unique brain metastatic niche. Microglia, the CNS-resident myeloid cell, and bone marrow-derived myeloid cells (BMDM) cooperatively regulate brain immunity during neuroinflammatory events through actions including phagocytosis, cytokine secretion, and immune cell recruitment and modulation. The roles of these myeloid subsets in shaping the metastatic niche to regulate brain metastasis outgrowth have not been fully revealed. Here, applying multimodal single cell analyses coupled with genetic mouse models, we elucidated a heterogeneous but spatially-defined brain myeloid cell response during brain metastasis outgrowth. Through genetic perturbations of myeloid subsets *in vivo*, we found Ccr2$^+$ BMDM minimally influenced brain metastasis while microglia promoted brain metastasis outgrowth. Additionally, brain metastasis-associated myeloid cells (Br.MAM) identified by scRNA-seq exhibited a global downregulation of *Cx3cr1*. Mechanistically, knocking out *Cx3cr1* in Br.MAM increased brain metastasis incidence and led to an enriched interferon response signature and *Cxcl10* upregulation in Br.MAM. Significantly, co-injection of rCxcl10 with tumor cells increased brain metastasis size and brain-infiltrating CD86$^+$ Br.MAM, which displayed numerous immunosuppressive pathway signatures and genes, including *Visr* (VISTA) and *Cd274* (PD-L1). Inhibiting VISTA and PD-L1 signaling axes by neutralizing antibodies resulted in partial relief of immune suppression and reduced brain metastasis burden. Our results demonstrate a microglia subset fosters a brain metastasis-promoting immunosuppressive niche through a *Cx3cr1-Cxcl10* axis.

**Oral Presentation:**


**Age-Related Changes in the Microenvironment Enhance Ovarian Cancer Metastasis**

Elizabeth Harper[1,3], Elizabeth Loughran[1,3], Emma Sheedy[2], Annemarie Leonard[1], Tyvette Hilliard[1], Yueying Liu[1], Jeff Johnson[1], Marwa Asem[1,3], Jing Yang[1], Zonggao Shi[1] and M. Sharon Stack[1]

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Aging is one of the biggest risk factors for the development of ovarian cancer (OvCa), the deadliest cancer of the female reproductive system. Half of OvCa diagnoses are in women over the age of 63. Despite this, age is understudied in the OvCa field. Using a C57Bl/6 mouse model of aging, young (Y) mice ranging from 3-6 months of age, and aged (A) mice ranging from 20-23 months of age were used to study the role of aging on metastasis. Fluorescently tagged C57Bl/6 syngeneic ID8 p53$^{-/-}$ mouse OvCa surface epithelial cells were injected intraperitoneally in Y and A mice and disease progression was evaluated for 5.5 weeks. Organ-specific tumor burden was quantified with ImageJ, revealing increased tumor burden in aged mice compared to their young counterparts. These results were reproduced in the FVB mouse model using syngeneic oviductal epithelial cells. Analysis of these tumors by Collagen Hybridizing Peptide (CHP) shows an increase of collagen remodeling in aged tumors. In addition, Second Harmonic Generation Microscopy (SHG) was used to visualize age-related changes in collagen at common metastatic sites from Y and A C57Bl/6 mice. Distinct structural differences were shown in omental collagen in the Y vs A cohorts, and validated with Scanning Electron Microscopy (SEM). Y and A collagen was digested by MMP-1, showing differences in enzymatic degradation measured by hydroxyproline release. Using Boyden invasion chambers, human OvCa cells showed increased invasion through A collagen compared to Y, despite no significant changes in cell adhesion or proliferation. In conclusion, aging induces changes in the structure and MMP susceptibility of peritoneal and omental collagen, which contribute to OvCa metastasis.

**Poster Presentation:**

**Data Assimilation on Lumped Parameter Models for Congenital Group I Pulmonary Hypertension**

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Diastolic dysfunction is a common pathology occurring in about one third of the patients affected by heart failure. This condition is not associated with a marked decrease in cardiac output or systemic pressure and therefore is more difficult to diagnose then its systolic counterpart. Compromised relaxation or increased stiffness of the left ventricle in absence of mitral valve stenosis induces an increase in the upstream pulmonary pressures, usually referred to as secondary or group II (2013 Nice classification) pulmonary hypertension. This may determine an increase in the right ventricular afterload leading to right ventricular failure. Elevated pulmonary pressures are therefore an important clinical indicator of diastolic heart failure (sometimes referred to as heart failure with preserved ejection fraction), showing significant correlation with the associated mortality, but accurate measurements of this quantity are typically obtained through invasive catheterization. In this study, we use the hemodynamic consistency of a differential circulation model to predict pulmonary pressures in adult patients from other, possibly non-invasive, clinical data. We investigate several aspects of the problem, from the well-posedness of a modeling approach for this type of disease, to the identifiability of its parameters, to the accuracy of the predicted pulmonary pressures. We also find that a classifier using the assimilated model parameters as features is able to detect pulmonary hypertension with high accuracy. For a cohort of 82 patients suffering from various degree of heart failure severity we show that systolic, diastolic and wedge pulmonary pressures can be estimated on average within 8, 6 and 6 mmHg, respectively, where increasing data availability leads to improved prediction.

**Poster Presentation:**

**Highly Multiplexed Amplicon Sequencing to Understand Malaria Transmission in Zanzibar**

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Over the past 15 years, the Zanzibar archipelago has achieved substantial reductions in the burden of malaria, which have been attributed to the introduction of a package of interventions including artemisinin-based combination therapy (ACT), the free provision and distribution of long lasting insecticidal nets (LLIN) and indoor residual spraying (IRS). Stagnation in the reduction started in 2007. Since then, malaria incidence has remained on a low but fairly constant level. In the course of a rolling cross-sectional study we found that the majority of infections were low-density and below the detection limit of conventional rapid diagnostic tests (RDT). Amongst 6'281 samples screened by qPCR, 148 (2.3%) were tested positive. The persistent reservoir of low-density malaria infections on the islands presents a challenge to malaria control. Assessment of the level and existence of ongoing local transmission is highly dependent on both the classification of cases as local or imported and on the reconstruction of transmission chains based on epidemiological information. Genetic sequence information based on highly polymorphic molecular markers could potentially differentiate between locally circulating strains of parasite and strains which are imported and clarify the relatedness between clinical cases and the asymptomatic cases surrounding them. Typing of a large number of loci in low density infections and with little template material available remains a challenge. In order to overcome these limitations, we are developing a novel, highly multiplexed amplicon sequencing genotyping method based on amplification of each locus in microdroplets. We aim to apply this method to the samples collected in Zanzibar to understand malaria transmission dynamics.

**Oral Presentation:**

## Loss of APC Induces Paclitaxel Resistance through Alterations in Cell Cycle Proteins

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Adenomatous Polyposis Coli (APC) is a multi-domain tumor suppressor with multiple binding partners, including β-catenin, axin, and microtubules. APC is lost in many epithelial cancers, including up to 70% of sporadic breast cancers, with a tendency towards triple negative breast cancers (TNBCs). We previously demonstrated that APC knockdown in the human TNBC cell line, MDA-MB-157, resulted in resistance to Paclitaxel (PTX), a chemotherapeutic agent of the Taxane family that inhibits mitotic progression. In the current study, we sought to understand the mechanism of APC-mediated resistance. Given that PTX and APC impact microtubule dynamics and the G2/M phase of the cell cycle, we hypothesized that APC controls expression of cell cycle proteins, leading to PTX resistance. We examined the effect of APC loss on expression of cell cycle proteins CDK1, Cyclin B1, Cyclin A2, and P27. We observed a significant upregulation of CDK1 and p27 in APC$^{KD}$ cells, with a modest increase in Cyclin A2. Given that a Cyclin B1/CDK1 nuclear complex is necessary for G2/M transition, we focused specifically on the localization and complex of Cyclin B1 and CDK1. We identified that while the majority of CDK1 and Cyclin B1 are localized to the cytoplasm, there is a small amount in the nucleus. In addition, Cyclin B1 and CDK1 are only found in a complex in the APC$^{KD}$ cells, suggesting increased activation. Based on these findings, we sought to investigate whether PTX sensitivity would be altered in response to CDK1 inhibitor, RO-3306. We have shown that the APC$^{KD}$ cells have a decreased IC50 to RO-3306 compared to the control MDA-MB-157 cells. Future studies will use combination and sequential treatments to monitor PTX response in vitro and in vivo. Along with our molecular studies of cell cycle proteins, we have also performed an unbiased analysis of transcriptomic changes downstream of APC loss to identify potential therapeutic targets to overcome PTX resistance. In this, a group of transcripts involved in regulation of the cell cycle were identified, including FOXS1, GLI1, and NUPR1. Upon validation of results by qRT-PCR and western blot, studies in the laboratory will investigate the effect of manipulating expression of these genes in the response to PTX. Combined, these studies are elucidating the mechanisms by which loss of APC controls sensitivity to PTX in TNBC, with the long-term goal of designing treatment regimens to improve patient health and survival.

**Oral Presentation:**

**Spectrum-Preserving Sparsification for Visualization of Big Graphs**

Martin Imre and Chaoli Wang

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Graphs are ubiquitous in representing data from various fields, such as social or life sciences, geographic knowledge, and engineering problems. With the evergrowing amount of data we are able to collect, the size of these graphs increases steadily. Thus, there is a need for tools to extract key parts of large graph data. We present a novel spectrum-preserving sparsification algorithm for visualizing big graph data. Although spectral methods have many advantages, the high memory and computation costs due to the involved Laplacian eigenvalue problems could immediately hinder their applications in big graph analytics. In this paper, we introduce a practically efficient, nearly-linear time spectral sparsification algorithm for tackling real-world big graph data. Besides spectral sparsification, we further propose a node reduction scheme based on intrinsic spectral graph properties to allow more aggressive, level-of-detail simplification. To enable effective visual exploration of the resulting spectrally sparsified graphs, we implement spectral clustering and edge bundling. Our framework does not depend on a particular graph layout and can be integrated into different graph drawing algorithms. We experiment with publicly available graph data of different sizes and characteristics to demonstrate the efficiency and effectiveness of our approach. To further verify our solution, we quantitatively compare our method against different graph simplification solutions using a proxy quality metric and statistical properties of the graphs.

**Poster Presentation:**

**Actuated Three Dimensional Dual-SLIP of Sloped Terrain Human Walking**

Gabriel Iturralde Duenas and James P. Schmeideler

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The three dimensional dual spring-loaded inverted pendulum (dual_SLIP) model is a well established passive template which captures the key characteristics of human walking on flat ground by specifying a lateral plane angle at touchdown as an extension to the planar dual-SLIP. This paper adds actuation to this model by injecting energy for declines and absorbing energy in inclines in order to analyze how well it captures actual human data on slope walking. The motivation is to apply this results to improve the controls of humanoid robot walking or in intent detection in exoskeleton assisted-walking. Furthermore, decline walking has being actively studied for rehabilitation applications because muscles tend to perform negative work through eccentric contractions so as to absorb energy to maintain the forward velocity constant. Feasible gaits of the actuated 3D dual-SLIP were found by solving a constrained no linear optimization problem with direct collocation with ten control parameters. Furthermore, solution gaits range between 0.2 to 1.8 m/s and slope range between -10 to 10 degrees. The results capture some important features of human incline walking, such as the slope on stance phase, double support duration, step length, nature of ground reaction forces, exchange of kinetic and gravitational energy and CoM trajectory.

**Key Words**: human walking, 3D dual-SLIP, slope terrain, optimal control, trajectory optimization, direct collocation

**Poster Presentation:**

**Stability of an RNA•DNA-DNA Triple Helix Depends on Base Triple Composition and Length of the RNA Third Strand**

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Recent studies suggest noncoding RNAs interact with genomic DNA, forming an RNA•DNA-DNA triple helix that regulates gene expression. However, base triple composition of pyrimidine motif RNA•DNA-DNA triple helices is not well understood beyond the canonical U•A-T and C•G-C base triples. Using native gel-shift assays, the relative stability of 16 different base triples (Z•X-Y, where Z = C, U, A, G and X-Y = A-T, G-C, T-A, C-G) at a single position in an RNA•DNA-DNA triple helix was determined. The canonical U•A-T and C•G-C base triples were the most stable, while three non-canonical base triples completely disrupted triple-helix formation. We further show that our RNA•DNA-DNA triple helix can tolerate up to two consecutive non-canonical A•G-C base triples. Additionally, the RNA third strand must be at least 19 nucleotides to form an RNA•DNA-DNA triple helix but increasing the length to 27 nucleotides does not increase stability. The relative stability of 16 different base triples in DNA•DNA-DNA and RNA•RNA-RNA triple helices was distinctly different from those in RNA•DNA-DNA triple helices, showing that base triple stability depends on strand composition being DNA and/or RNA. Multiple factors influence the stability of triple helices, emphasizing the importance of experimentally validating formation of computationally predicted triple helices.

**Oral Presentation:**


**Bone Remodeling and Cyclical Loading in the Maxilla of White Rabbits (*Oryctolagus cuniculus*)**

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Processing mechanically challenging (e.g., tough or stiff) foods alters feeding behaviors in mammals, requiring larger bite forces or prolonged mastication. The bony response to high bite forces in the mammalian skull is well known, but osteogenesis due to protracted chewing (i.e., cyclical loading) is more poorly understood. Prior studies indicate greater bone formation in mandibles of rabbits raised on mechanically challenging foods, and a stronger link between bone remodeling and cyclical loading vs. high-magnitude strains. Here, we assess the relationship between cyclical loading and remodeling, the repair of microdamage due to mechanical deformation and fatigue loading. 20 male white rabbits (*Oryctolagus cuniculus*) were obtained at weaning (4 weeks) and raised on one of two diets until mature (52 weeks). Ten subjects ate pellets ($E=29MPa$, $R=1031Jm^{-2}$), and the other ten processed pellets and hay ($E=3336MPa$, $R=2760Jm^{-2}$). Mastication of hay results in higher chewing investment (475 vs. 161 chews/g) and prolonged chewing duration (568 vs. 173 sec/g). Remodeling was measured as osteon population density (OPD) and percent Haversian bone (%HAV) in 100µm coronal sections of alveolar and hard palate regions of left maxillae between $P^2$ and $P^3$. Mann-Whitney U tests revealed a significant difference ($P=0.009$) in %HAV between groups in the alveolar portion of the maxilla. All other comparisons were non-significant. This suggests that more chewing cycles results in a greater proportion of secondary bone in close proximity to the teeth. However, the high %HAV is likely not a consequence of osteon density because OPD did not differ between groups. Rather, the size of individual osteons might be the cause of the disparity in %HAV. Future analyses will investigate the relationship between osteon size and mechanical loading, bone modeling (changes in shape or amount of bone) differences between control and overuse groups, and also remodeling in other aspects of the chewing apparatus.

**Poster Presentation:**

**Trigger Rate Monitoring Tools for CMS**

John Lawrence and Kevin Lannon

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Inside the Compact Muon Solenoid (CMS), a detector designed to further our understanding of fundamental physics, collisions occur at an approximate rate of 40 MHz. This is much more data than can possibly be stored, and the CMS detector uses two trigger systems to filter out uninteresting data, allowing only the more manageable 1kHz of relevant data to be stored. The two trigger systems are the hardware base Level-1 trigger (L1) and the software base High Level Trigger (HLT). Monitoring the trigger rates is of critical importance to the operations of the CMS detector these rates can help determine the performance of the trigger and give indications of issues in other systems in the detector. Software tools that can monitor, characterize, and visualize the trigger rates have been developed for both the runtime operations and the data analysis. This presentation will discuss the functionality of these tools and further development of these tools.

**Poster Presentation:**

**A Scalable Explicit Finite Element Solver for Cardiovascular Models with Uncertain Material Properties**

Xue Li and Daniele Schiavazzi

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Simulation of cardiovascular flow under uncertainty is an extremely intensive computational task, requiring large meshes and hundreds to thousands of high-fidelity model solutions. In this context, we propose a novel approach for ensemble simulation, and demonstrate it to the segregated, explicit-in-time solution of blood flow in the thoracic aorta with random material properties, focusing on the implementation of fast matrix-vector products on CPUs and GPUs. Distributed CPU storage is achieved through METIS partitioning and using sparse compressed row storage (CRS) format with dense blocks containing multiple material property realizations for a three-d.o.f.s shell finite element. We developed an optimized Cython code for the sparse matrix-vector multiplication using MPI+openMP and compared it to the mkl_cspblas_dcsrgemv routine provided through the Intel MKL library. Our implementation achieves better performance on a wide range of mesh sizes, number of cores, and with/without multithreading. Our OpenCL-based GPU matrix-vector product achieves instead a 10-fold speed-up with respect to a naive implementation, by using separate command-queues, overlapping the CPU to GPU data transfer with GPU kernel execution, and using page-locked CPU memory. Additional improvements are obtained by direct computation of local element matrices on the GPU. Ongoing work focuses on coupling our explicit structural solver with a variational multiscale finite element fluid solver.

**Poster Presentation:**

**Dynamic Coupling as a Measure of the Transition from Slow to Self-Selected Speed Walking Mechanics**

Jorge Lopez and James P. Schmiedeler

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Walking speed is considered by some to be the 6th vital sign because it is a valid, reliable, and sensitive measure for assessing and monitoring functional status and overall health in a wide range of populations. The speed of "community ambulation," often quantified as 0.44 m/s, indicates the minimum speed required for an individual to enjoy an active lifestyle and fully participate in the community. Stroke and spinal cord injury combine to impact more than 800,000 people annually in the U.S., leaving many unable to walk above this relatively speed threshold. The kinematics and kinetics of slow walking differ dramatically from those of normal speed walking. For example, mediolateral displacement of the center of mass is much greater in slow walking, while the vertical displacement is much less. Other key differences at slow speeds include flat foot posture at touchdown as opposed to rolling on the heel in early stance, a reduction in knee flexion during this same phase of gait, the absence of ankle plantar flexion at toe off, increased energy cost, and reduction of EMG amplitudes. This work is grounded in the observation that the mechanics of slow walking are fundamentally different from those of walking at normal speeds. More specifically, the hypothesis is that sagittal plane motion favorably contributes to stabilizing the frontal plane dynamics at higher walking speeds, so the absence of this stabilizing coupling effect at slow walking speeds contributes to the different gait strategy to maintain balance. The goal of understanding these different mechanics and the transition between them is ultimately to enable superior rehabilitation outcomes and improved quality of life. In this regard, the work will investigate how ambulatory assistive devices (AADs) influence the same coupling metric via their impact on gait mechanics.

**Poster Presentation:**

## Fluorescence Microscopy Lifetime Estimation from Intensity using Convolutional Neural Networks (CNNs)

Varun Mannam, Yide Zhang, Xiaotong Yuan and Scott Howard

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Fluorescence microscopy has enabled a dramatic development in modern biology, and the output of conventional fluorescence microscopy is the intensity. However, it is hard to segment a sample with multiple cells using intensity. Specifically, fluorophores have overlap- ping emission spectra, and these cells cannot be segmented with only intensity information. Also, it is sensitive to the applied laser power, movement of the animal, and temperature. In this scenario, one can use fluorescence lifetime image (FLIM) of excited fluorophores, which enables the segmentation of the cells and also provide the vital information such as the ion concentration, the dissolved oxygen concentration, the pH, and the refractive index, which are the micro-environment in living tissues. FLIM methods are generally di- vided into two categories, namely, time-domain (TD) FLIM and frequency-domain (FD) FLIM. Time-domain consists of two methods: time-correlated signal photon counting (TC- SPC) and time-gating (TG). However, the aforementioned methods suffer from either slow in computation time since more pulses are required to extract the lifetime information or additional hardware requirement, which is used for the phase measurements of an intensity- modulated excitation and emission signal. Therefore, we present a novel convolutional neural network (CNN) based approach to estimate the lifetime image from the intensity information. In this work, we create a dataset that consists of intensity and lifetime images. We train our model by considering the composite lifetime (HSV image: where the intensity and the lifetime are mapped to the brightness and hue, respectively) as the target image. The results show that the predicted lifetime image has less noise when compared to the ground truth image.

**Poster Presentation:**

**Characterizing the Role of Fibrinogen Modulating Macrophage Response to Catheter-Associated Urinary Tract Infections**

Armando Magallanes Marrufo, Felipe Santiago-Tirado and Ana L. Flores-Mireles

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Catheter-associated urinary tract infections (CAUTIs) are urinary tract infections associated with an implantation of a urinary catheter that leads to life-threatening complications. CAUTI is a significant public health concern that must be addressed by unveiling mechanisms that pathogens utilize to evade immunosurveillance. Inflammatory response to uroepithelium damage by catheterization encompasses release of fibrinogen (Fg) into the bladder where Fg is polymerized into fibrin for tissue healing. However, deposition of Fg on catheters allows uropathogens such as *Enterococcus faecalis*, a prevalent CAUTI pathogen, to exploit accumulated Fg for further growth and dissemination. During *E. faecalis* CAUTI, macrophages are recruited to the bladder; however, despite of its recruitment, *E. faecalis* is able to thrive and persist. Therefore, it is unclear why macrophages are unable to clear the pathogen. It has been shown that macrophages can switch between pro- (M1-bactericidal activity) or anti-inflammatory (M2) behavior when interacting with either Fg or fibrin, respectively. Our hypothesis is that macrophages switch between M1 and M2 during CAUTI due to the presence of Fg/fibrin which affects the outcome of infection. An *in vivo* temporal study was performed from 1-hour post-catheterization to 14 days in the absence or presence of *E. faecalis*. Our preliminary *in vivo* studies demonstrated prevalent inducible nitric oxide synthase (iNOS, M1 marker) production in the acute inflammation phase of CAUTI while iNOS production decreases in prolonged inflammation. Additionally, we found that catheterization and infection decreased iNOS production around catheters more than catheterization alone. Furthermore, we have observed prevalent arginase-1 production (M2 marker) in the prolonged inflammation phase of CAUTI. This suggests that M1 macrophages that produce iNOS transitions to M2 anti-inflammatory phenotype where macrophages can no longer eradicate *E. faecalis*. Understanding the macrophage response will unveil a novel understanding of immune response to persistent pathogens in CAUTI necessary in developing therapeutic treatments.

**Poster Presentation:**


**Exploring the Physics of the TIRAS Plasma Electrochemical System**

Daniel Martin[1] and David B. Go[1,2]

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Department of Chemical and Biomolecular Engineering, University of Notre Dame[2]

The study of plasma-liquid interactions is an emerging field with multifarious applications, including medicine (wound healing, sterilization), environmental remediation (water purification, fracking fluid treatment), and material synthesis. These applications are driven by chemical species created in the plasma or at the plasma-liquid interface, such as OH, H2O2, and, in particular, solvated electrons ($e_{aq}^-$). These are free electrons in some polar solution, loosely confined in a sphere of polar charge, notable for their speed of reaction (ns). Previously, solvated electrons have been observed primarily through pulse radiolysis. However, recently we were able to produce them using an atmospheric pressure discharge incident on a liquid surface, and observe them using phase-locked absorption spectroscopy[1]. However, the absorption spectrum we observed appeared to be blue shifted from the recognized bulk radiolysis spectrum. This may be either the result of measurement error or the effect of ionic strength, which has been observed to cause such a shift in radiolysis measurements. In parallel with this, we predict a change in the intensity of TIRAS signal as a function of current density, which in turn is a function of ionic strength, based on our current understanding of the physics at the plasma-liquid interface. Our aim with this work, using recent improvements to the TIRAS optical setup, is to find the source of the originally observed blue shift, and subsequently measure the scaling of TIRAS intensity, corrected for any observed blue shift, with current density.

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[1] Rumbach *et al.* (2015), *Nature Communications* 6, 7248.

**Poster Presentation:**

## Secondary Structural Model of Human MALAT1 Reveals Multiple Structure-Function Relationships

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Human metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) is an abundant, nuclear-localized long noncoding RNA (lncRNA) that has significant roles in cancer. While the interacting partners and evolutionary sequence conservation of MALAT1 have been examined, much of the structure of MALAT1 is unknown. Here, we propose a secondary structural model for 8425 nucleotides of human MALAT1 using three datasets that probed RNA structures *in vitro* and in various human cell lines. Our model indicates that approximately half of human MALAT1 is structured, forming 194 helices, 13 pseudoknots, five structured tetraloops, nine structured internal loops, and 13 intramolecular long-range interactions that give rise to several multiway junctions. Evolutionary conservation and covariation analyses support 153 of 194 helices in 51 mammalian MALAT1 homologs and 42 of 194 helices in 53 vertebrate MALAT1 homologs, thereby identifying an evolutionarily conserved core that likely has important functional roles in mammals and vertebrates. Additional data mining revealed that RNA modifications, somatic cancer-associated mutations, and single-nucleotide polymorphisms may induce structural rearrangements that sequester or expose binding sites for several cancer-associated microRNAs. One notable example is an $m^6A$ modification that facilitates formation of a pseudoknot, a structure that would prevent cancer-associated miRNAs, miR-101 and miR-217, from binding to MALAT1 in noncancerous cells. In HeLa cells, this $m^6A$ modification and pseudoknot are absent, suggesting that MALAT1 sponges miR-101 and miR-217 away from their cognate mRNA targets (e.g. MYC and KRAS, respectively) in cancer cells. Our findings suggest that the dynamic structure of MALAT1 underlies its biological functions, revealing new mechanistic leads into the roles of MALAT1.

**Poster Presentation:**


**Can Threshold Choices Influence Observed Microtubule Aging?**

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Microtubules, built from tubulin subunits, are biological polymers intimately involved in numerous key cellular processes.  One major aspect of MT activity that is still poorly understood is the process of dynamic instability (DI): where *in vivo* and *in vitro*, individual MT polymers undergo periods of length growth and shrinkage, with transition between these phases occurring seemingly at random through events known as rescue and catastrophe.  *In vitro* MTs have been experimental observed to undergo catastrophe events at a nonrandom rate, where the rate at which a microtubule catastrophe's increases over the lifetime of the MT.  This MT "aging" has been examined in more detail computationally, and simulations have both confirmed this effect and allowed for the development of hypotheses to explain aging in molecular detail. While aging has gained a consensus in the MT field, there are a few features of MT aging that makes it worthy of closer examination.  MT aging has only been observed to occur at one end of the MT (the "plus" end) and not the other ("minus" end), which would be unusual if it were a general feature of MT dynamics.  Experimental measurements of catastrophe are impeded by the diffraction limit of light, which prevents the measurement of shorter and newly formed (i.e. "young") MTs. The plus end of the MT undergoes faster dynamics than the minus end, which may mask minus end aging or cause a bias towards identifying catastrophe events of longer, "aged" MTs.  We are using a simplified MT simulation system that does not have microscopy-induced measurement limitations to determine if discrepancies in observed aging can be explained, in part, by measurement thresholds.

**Oral Presentation:**

## Food Mechanical Properties and Masticatory Behavior in Llamas

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Mammals typically process foods in the oral cavity much more extensively than other vertebrates. Dental morphology, jaw movements, and tongue manipulation all work to facilitate oral fragmentation of dietary items. During the oral processing of mechanically challenging foods, mammals modulate mandibular movements and bite forces via the recruitment of greater jaw-adductor muscle forces and/or protracted biting and chewing. As jaw-loading patterns are influenced by the magnitude, frequency, and duration of muscular forces during routine feeding behaviors, relatively larger jaws are thought to be more characteristic of mammals that process mechanically challenging foods. The ease of food fracture during chewing is mainly determined by the extent to which a food item is stiff and/or tough. Stiff and tough foods have been associated with increased loading magnitude and greater amounts of cyclical loading (i.e., chewing duration). Dietary properties are thought to modulate cyclical loading through changes in chewing frequency and chewing investment, however little evidence exists regarding the influence of dietary properties on these parameters in mammals. Here, we assessed chewing behavior in 7 adult llamas processing foods with a wide range of mechanical properties (grain, hay, carrots, dried corn). Each subject was filmed at 60 frames/second, with video slowed for frame-by-frame computer analysis to obtain feeding bout length and the number of chewing cycles for each food type. These parameters were used to calculate chewing frequency (chews/s), chewing investment (chews/g), and chewing duration (s/g). Chewing frequency was unrelated to food mechanical properties, while chewing investment and chewing duration were related to dietary stiffness. Although toughness is commonly linked to cyclical loading, no such relationship was observed. Thus, jaw robusticity in extinct and extant mammals appears due to greater amounts of cyclical loading with diets consisting of stiff foods, whereas jaw robusticity was previously viewed as a sole outcome of hard-object feeding.

**Poster Presentation:**

**Modeling and Damage Detection for Tree Model using Fractional-Order Calculus**

Xiangyu Ni and Bill Goodwine

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Fractional-order calculus involves differential equations whose order is no longer limited to integers. Therefore, fractional-order calculus brings many advantages over classical integer-order calculus. One of such advantages is its capability to model a large network with a concise transfer function. Using this advantage, previous work in the literature shows that the transfer function for a specific large network, the undamaged tree model, is exactly half-order. From that starting point, in this project, we focus on both the forward and the inverse problem for the damaged tree model. Specifically, for the forward problem, we analytically prove the structure of the transfer function for the damaged tree model given its damage information. In addition, that proof lays the groundwork for an algorithm to numerically compute that transfer function. Leveraging the knowledge from the forward problem, we can then do the inverse problem, whose goal is to identify the damage components inside the tree model given the measurements of its frequency-domain response.

**Poster Presentation:**

**Using New ESX-1 Substrates to Delineate Lytic Activities of the ESX-1 System in *Mycobacterium marinum***

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The ESX-1 (ESAT-6 system-1) secretion system plays a conserved role in the virulence of diverse mycobacterial pathogens including the human pathogen, *M. tuberculosis* and *M. marinum,* an environmental mycobacterial species. The ESX-1 system promotes the secretion of protein virulence factors to the extra-cytoplasmic environment. The secretion of the substrate proteins triggers the host response by lysing the phagosome during macrophage infection. Using proteomic analyses of the *M. marinum* secretome in the presence and absence of a functional ESX-1 system, we and others have hypothesized that MMAR_2894, a PE family protein, is a potential ESX-1 substrate in *M. marinum.* We used genetic and quantitative proteomic approaches to demonstrate that MMAR_2894 is secreted by the ESX-1 system, and we defined the requirement of *MMAR_2894* in ESX-1 mediated secretion and virulence. We showed that MMAR_2894 is secreted by the ESX-1 system in *M. marinum* and is itself required for the optimal secretion of the other known ESX-1 substrates. Moreover, we found that MMAR_2894 was differentially required for hemolysis and cytolysis of macrophages, two lytic activities ascribed to the *M. marinum* ESX-1 system. We have followed up these studies by testing if additional PE/PPE genes are similarly part of the ESX-1 system in *M. marinum.* Using this knowledge, we seek to understand how hemolytic and cytolytic activities are separable with regard to ESX-1 function at the molecular level.

**Oral Presentation:**

**Seasonal Patterns of BAT Activity Imply Energetic Buffering and Greater Metabolism of Carbohydrates Associated with Human Cold Acclimatization**

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Brown adipose tissue (BAT) is a metabolically costly heat-generating tissue primarily located in the shoulder region. BAT is activated under cold conditions and may play a crucial role in glucose disposal and human cold adaptation. However, little is known about the seasonality of BAT activation. This study compared summer and winter patterns in BAT activity in upstate New York. BAT was inferred by combining metabolic rate (MR, kcal/day) measurements and thermal imaging of the shoulder under room temperature (RT) and mild cold exposure (CE) in two separate but overlapping cohorts. Respiratory quotient (RQ, indicates macronutrient use) measurements were also obtained. Outside temperatures during the summer were consistently >15°C, while winter temperatures remained <10°C. The summer sample consisted of 59 participants (females n=37, ages:18-51). The winter sample consisted of 60 participants (females n=36, ages:18-63) 44 of which also participated in the summer. While not significant, results showed higher MR during winter compared to summer at RT and CE. Skin temperatures at the shoulder under both conditions were significantly higher during colder months ($p<0.05$). The reduced metabolic cost may suggest that BAT generates heat more efficiently in winter months, indicating a seasonal pattern in BAT activity. RQ was also found to be significantly greater under both RT and CE in the winter compared to summer ($p<0.05$), suggesting a greater metabolism of lipids and carbohydrates in warmer and colder months, respectively. These findings may suggest a greater use of glucose as BAT fuel for faster heat production during extended periods of cold exposure. Increased glucose disposal may result in a decreased risk of diabetes over time. The preliminary data from this study, thus, highlights the potential role of BAT in diabetes prevention therapies and further supports the implication of BAT in cold acclimatization.

**Poster Presentation:**

**A Role for Bacteria in Reproductive Signaling?**

Emily Nonnamaker and Elizabeth Archie

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In humans and other animals, individuals use chemicals to communicate information within societies. In the last few years, new evidence has emerged that these chemical cues are generated by host-associated microbial communities (i.e. microbiomes), rather than compounds directly produced by the animal itself. These bacterially-generated compounds signal animals' identities, relatedness, and even reproductive success. Such communication is thought to be especially important in primate reproduction. Indeed, the reproductive tracts of female primates contain diverse microbial communities that change across ovarian cycles. These communities have the potential to produce volatile compounds that males may use to judge female ovulation and fertility. As such, microbial communities likely serve as key intermediaries in mammalian communication, conveying information that is important to their host's evolutionary fitness. Despite the evolutionary and behavioral importance of this hypothesis, we still do not know how female scents change across ovarian cycles or whether males use this information to choose mates. Filling this gap will help reveal the complex interplay between primates, their microbiomes, and their behavior, providing a theoretical foundation for future work in humans.

**Oral Presentation:**

**Effects of Heart ECM Age on Maturity, Senescence and Function of Human iPSC-Derived Cardiomyocytes**

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Aging is one of the main risk factors for cardiovascular diseases where myocardial infarction (MI) prevalence reaches its peak, the highest of which being to 17% in males over 80 years of age[1]. Current preclinical MI models that heavily relay on young cell or animal models that lack the ability to fully recapitulate the human disease condition. As such, an engineered tissue model of the aging heart microenvironment would be essential for an increased understanding of the MI injury as well as for discovering novel solutions to ameliorate it. In this study, we combined both cell-level and extracellular matrix (ECM)-level aging towards creating an *in vitro* model of the aging heart to study the effect of ECM age on heart cells.

**Methods:** Human cardiomyocytes (iCM) were differentiated from hiPSC, and mice cardiac tissue were collected, decellularized and solubilized following established protocols[2,3]. Young (35-60days in culture) and aged (100-120days in culture) iCMs were seeded on decellularized mice heart ECMs of three different age groups (1-3-month, 6-9-month and 22-24-month-old) as well as on pure fibronectin and collagen-I as controls. After 3 weeks of culture, iCMs were assessed for aging-associated phenotype, cardiomyocyte maturity, and myocardial injury response via cell viability and staining for mitochondrial ROS accumulation and apoptosis-related proteins, Cytochrome-C and cleaved Caspase-3.

**Results and Discussion:** Young cells on adult ECM displayed improved contractile kinetics and drug response. ECM age greatly altered the aged iCM phenotype and MI response. Young ECM significantly promoted the proliferative abilities, and cardiac function, and hindered senescence-related marks of aged iCM. Furthermore, aged cells better handled MI/RI stress condition by activating less apoptotic pathways when cultured on young and adult ECMs. Overall our results suggest that cardiac aging is the cumulative result of both cellular and microenvironmental aging and ECM possesses biochemical cues to alter cell aging, function, and survival.

**References**
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2. Lian, X. *et al. Nat. Protoc.* 8, 162–175 (2013).
3. Saldin, L. T. *et al. Acta Biomater.* 49, 1–15 (2017).

**Poster Presentation:**

## Sensitizing Primary Breast Cancer to Anti-PD1 Immunotherapy through CD103+ Dendritic Cells using Metronomic Chemotherapy

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Neoadjuvant chemotherapy is the infusion of the cytotoxic drugs systemically into a cancer patient before radiation or surgery. Along with the tumor cells, chemotherapy non-specifically annihilates the cells in tumor environment, such as endothelial cells and immune cells. It is known that single agent chemotherapy induces anti-tumor immunity. However, the mechanism of neoadjuvant chemotherapy lead modulation of the primary breast tumor immune compartment and sensitization to immunotherapy is poorly understood. In this study, we examined the differential effects of clinically used maximum tolerated chemotherapy dosage (MTD) and metronomic dosage (MCT) of Doxorubicin and Cyclophosphamide on primary breast tumor. Both MTD and MCT were equally efficacious in curbing tumor growth of spontaneous tumor bearing MMTV neu and C3-1-TAg mice. By using mass cytometry, we identified that MCT preserved immune compartment while MTD depleted. Specifically the CD11b+ Conventional Dendritic cells (cDCs) were enriched with MCT treated tumors. On simultaneous cellular indexing of epitopes and transcriptomes by sequencing (CITE-Seq), CD11b+ cDCs had antigen presenting and co-stimulatory signature differentially expressed over other DC subtypes. Further, MCT priming leads to a significantly increased PD-L1 expression on myeloid cells. Combining MCT with anti-PD 1 drug substantially decreased tumor burden along with an enrichment of CD103+ CD11c+ cells in residual tumors. These findings suggest a role of MCT in instigating anti-tumor immunity and the need to combine regulator of common immune deterrents to achieve optimal anti-tumor efficacy.

**Poster Presentation:**

## Modeling Noise Patterns from MRI Reconstruction Algorithms

Lauren Partin and Daniele Schiavazzi

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4D flow MRI introduces the possibility of imaging in-vivo hemodynamics (blood velocities) and tissue composition in the same scan. Simultaneous acquisition of flow and anatomy is, however, extremely time consuming, requiring patients to spend a significant amount of time in the scanner and subsequently limiting access to MRI diagnostics. The paradigm of compressed sensing was recently introduced to design significantly faster acquisition sequences, where only a small subset of the frequency information is acquired by the MRI scanner, and a non-linear reconstruction algorithm employed, which leverages the sparsity of the images in a certain dictionary of carefully selected waveforms or atoms. Although the noise in the frequency domain of medical images is known to have independent Gaussian components, these algorithms result in a correlated, as yet undetermined noise distribution in the image space.

A random field characterization of this noise would allow one to synthetically generate velocity field realizations consistent with compressed sensing reconstructions, in order to better design post-processing tasks for relevant clinical indicators. In this context, we employ Gaussian random field models which are widely used, but whose inference from large image datasets is known to be computationally expensive. To reduce the computational complexity of these algorithms for large structured images, methods such as Nearest Neighbor Gaussian Processes (nnGP) are used to estimate random field parameters while inducing sparsity [1].

In this poster, we compare the non-linear reconstructions from various algorithms, and examine the correlation found in the resulting noise. Additionally, we show the application of nnGP to generate noise models.

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**Poster Presentation:**

**Air-Sea Interactions during Monsoon Season in the Bay of Bengal**

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Monsoon Intra-seasonal Oscillations (MISOs) are a part of the energetic boreal-summer sub-seasonal (20 to 60 day) variability in the northern Indian Ocean (IO). MISOs are characterized by negative outgoing longwave radiation (OLR) anomalies originating near the latitudes around -5 degrees, and they propagate northward into the Bay of Bengal (BOB) with a typical westward component originating in the northern BOB that brings in precipitation to the western Indian landmass.  MISO signals are characterized by alternative active (moist convection) and break/dry cycles, and the predictability of such phases are frequently noted as unreliable.  It has been pointed out that inclusion of air-sea coupling is essential for high fidelity MISO predictions, especially for propagation and precipitation intensity. A pilot experiment (June 3 to July 20, 2018) and a full experiment (June 1 to July 30 2019) were conducted as part of the Office of Naval Research initiative MISO-BOB to investigate the driving mechanisms and thermodynamic structure of MISO events. Atmospheric and Sea Surface Temperature (SST) data both taken during the field campaign as well as some provided from the Indian Meteorological Department (MD) are analyzed. Time-series anomalies of the data from the North-South and West-East locations show patterns of wet/dry phases at different frequencies which can be indicative of multiple atmospheric wave interaction, but further analysis is yet to be made.

**Poster Presentation:**

**Exploring Hybrid Volitional Control of Robotic Lower-Limb Prostheses**

Ryan Posh and James P. Schmiedeler

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Many robotic lower-limb prostheses today and their various control strategies allow the user to achieve basic functionality, such as standing, walking, and stair ambulation. Due to the nature of how these devices are controlled, however, users are limited to only basic movements and are often unable to perform certain activities. Specifically, activities that deviate from basic gait dynamics, such as marching in a marching band, standing or walking on tip-toes, reacting quickly to the environment, and others are not currently achievable in a reliable way for individuals who have experienced lower-limb amputation. These limitations motivate new control strategies that are reliable enough to achieve various walking gaits without the user falling, while also giving them more control over the limb to achieve a wider variety of tasks under their own volition (free will). This research will explore a new class of control strategies, known as Hybrid Volitional Control, that seeks to combine the advantages of robust state-based control schemes with purely user-directed volitional control schemes. Electromyography (EMG) sensors will be explored as a noninvasive approach to enable volitional alteration or augmentation of the dynamics and/or parameters associated with the robotic limb. Largely underdeveloped and underexplored, Hybrid Volitional Control could allow individuals who have experienced lower-limb amputation to regain the freedom of moving their limb in any way that they desire. This class of control strategies could be the key to further erasing the distinction between ability and disability from amputation.

**Poster Presentation:**

**Modeling Measles Importation into the United States using International Measles Incidence and Air Passenger Travel Data**

Marya Poterek, Moritz Kraemer, Alexander Watts, Kamran Khan and Alex Perkins

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Measles incidence in the United States has grown dramatically, as vaccination rates in the US are declining and transmission internationally is on the rise. Measles is a highly infectious illness that can cause severe symptoms and even death in unvaccinated individuals. Cases imported to the US are key drivers of autochthonous outbreaks that pose an increasing threat to vulnerable populations. As a result, predicting US measles outbreak activity depends crucially on predicting imported cases.

We performed a statistical analysis using a generalized linear model that connects air travel data and international measles incidence data with imported measles cases in the US. To assess the predictive capability of this model, we performed cross-validation on 80% subsets of the data. We then used the model's predictions to characterize spatiotemporal variation in imported measles cases across years and US states.

This model had good predictive abilities with respect to the presence or absence of one or more imported cases (AUC = 0.77) and the magnitude of imported cases (correlation = 0.82). Through a comparison of models averaging over either international incidence or air travel data, we found that international incidence contributes significantly to the model's ability to predict the presence of imported cases.

As a result, the geographic source of imported measles cases varied considerably across years and US states, depending on which countries had high incidence in a given year. Our results emphasize the importance of the relationship between global connectedness and the spread of measles, as well as the significant influence that international measles incidence has on case importation into the US. These insights suggest that recently proposed travel screening measures could be targeted effectively based on our model's predictions.

**Poster Presentation:**

**Discovery and Characterization of a New Regulator of the Mycobacterial ESX-1 System**

Kevin G. Sanchez, Micah J. Ferrell, Alexandra E. Chirakos, Kathleen R. Nicholson, Matthew M. Champion, Robert B. Abramovitch and Patricia A. Champion

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*Mycobacterium tuberculosis* and other pathogenic mycobacteria use the ESX-1 secretion system to survive within the host macrophage. Despite its clear role in mycobacterial pathogenesis, the mechanisms regulating the ESX-1 system are unclear. Using *Mycobacterium marinum*, a mycobacterial pathogen and an established model for *M. tuberculosis* ESX-1 secretion, we found that deletion of the ESX-1 secretory machinery caused significant and widespread changes in gene expression. ESX-1-dependent changes in gene expression have since been corroborated in *M. tuberculosis.* Our prior findings demonstrated that the ESX-1 system is feedback regulated. In the absence of the ESX-1 secretory apparatus, we observed a significant down-regulation of the expression of the *whiB6* gene. Reduced levels of the WhiB6 transcription factor caused reduced expression of genes encoding ESX-1 substrates. The mechanisms connecting the ESX-1 secretory apparatus to changes in *whiB6* gene expression is unknown. We used genetic and biochemical approaches to define proteins required for ESX-1-dependent changes in *whiB6* gene expression. We identified and characterized a new transcription factor, EspM (ESX-1 associated protein, M). We demonstrated that EspM binds directly and specifically to the *whiB6* promoter through its C-terminal half. We found that EspM represses *whiB6* gene expression downstream of the ESX-1 secretory apparatus. We show that EspM is functionally conserved in between *M. marinum* and *M. tuberculosis.* Finally, we demonstrate that EspM regulates widespread gene expression in *M. marinum*. Together our results further define a new aspect of regulation of the ESX-1 system, which may connect the assembly of the secretory system to expression of ESX-1 substrates, and other genes required for survival in the host.

**Poster Presentation:**

**Individual Variation in the Scope of Attention and Why It Might be Limited**

Daniel Schor and Bradley S. Gibson

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The maintenance capacity of working memory is thought to be limited to approximately three items of information. However, it has proven difficult to estimate the maximum capacity of an individual's "scope of attention" (SoA) separate from their ability to consistently achieve this maximum due to lapses in "attention control" (AC). The present study accomplished this separation by using a maximum likelihood framework to extract latent AC and SoA constructs from a whole report version of the Visual Array task. Although significant individual variation in SoA was observed, its range was small, with 91% able to maintain a maximum of 3 or 4 items, and only 1% able to maintain a maximum of 5 or 6 items. Furthermore, moderate SoA was associated with better performance on a test of fluid intelligence than extreme SoA, suggesting that extreme SoA might give rise to greater interference when multiple rules need to be maintained.

**Poster Presentation:**

**Atmospheric Pressure Plasma: An Alternative Tool for the Synthesis of Efficient Photocatalytic Materials**

Amal Sebastian and Sylwia Ptasinska

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Photocatalytic splitting of water into hydrogen and oxygen is a method to convert solar energy into storable chemical energy directly, and it has received significant attention for its high potential for low cost and clean energy production. Developing efficient and cost-effective photocatalysts for water splitting is a growing need for solar energy research. In this work, we propose a novel method to deposit photocatalytic materials with atmospheric pressure plasma (APP). The design and experimental approach for depositing the visible light photoelectrode $TaO_xN_y$ using APP with a suitable solution precursor are explained in detail. The effect of plasma parameters on the composition of films is investigated by monitoring the surface chemistry changes with X-ray photoelectron spectroscopy. The pronounced low binding energy shoulder appearing in the Ta 4f XPS spectra upon APP treatment reveals the oxynitride formation. The observed changes in the composition of films with modulation of plasma parameters hint towards alternative processing routes to deposit photocatalytic materials efficiently.

**Poster Presentation:**

**Predicting eDNA Transport and Degradation in Flowing Waters: Application of a Conservation Tool using Integrated Experimental, Field, and Modeling Approaches**

Elise Snyder, Jennifer L. Tank and Gary Lamberti

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Aquatic species are difficult to detect at low population densities using traditional sampling methods; alternatively, detection of environmental DNA (eDNA) in freshwater systems is a pioneering technique developed to monitor rare or endangered species and combat invasive species. Traces of eDNA from an organism can remain in suspension and be collected in a water sample, revealing the presence of a target organism. While eDNA can travel long distances in fluvial systems (i.e., streams and rivers), current data come from idealized experiments in standing water, leaving significant knowledge gaps in the interpretation of eDNA in streams and rivers. The objective of this project is to mature eDNA as a conservation tool from basic to applied research, with a focus on rare species in streams and rivers, which are highly relevant at Department of Defense (DoD) sites. The project will determine the potential and limitations of eDNA detection and transport in flowing waters using a unique interdisciplinary approach coupling new molecular techniques that inform eDNA sampling, with integrative hydrologic modeling, informed by targeted experimentation involving the use of unique experimental platforms. To clearly understand and quantitatively interpret "positive detection events," three synergistic approaches will be used: (1) Molecular Ecology (technology development) to improve eDNA quantification and test novel detection platforms to build better spatio-temporal distributions of eDNA in aquatic habitats of DoD interest; (2) Stream Ecology (experiments and field sampling) to accurately quantify environmental factors that influence eDNA detection and its interpretation; and (3) Hydrology (integrative modeling) to incorporate data from (1) and (2) into predictive models of eDNA fate and transport. These findings will be translated for use by managers and stakeholders to ensure that the research outputs will provide guidelines for managers and regulators that can be applied at existing DoD installations and through eDNA programs across North America.

**Poster Presentation:**

**Controls on Nitrate Export during Storms in Two Contrasting Agricultural Watersheds**

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Streams and rivers have been identified as critical hotspots for nutrient transport. Widespread anthropogenic alterations to the landscape, including excess nutrient inputs, changing land cover, and modified hydrology, may influence transport processes. Additionally, climate change impacts on hydrology may add complexity to our current understanding of the mechanisms driving nutrient transport in aquatic ecosystems. Previous research has shown that, in many watersheds, storm-driven export makes up a large proportion of annual nutrient losses. Looking to the future, storms are expected to increase in both frequency and intensity across the US. For example, in the Midwest and Great Lakes region, more frequent, intense precipitation and changing snow patterns are predicted. We used high-frequency sensor data from two Northern Indiana agricultural watersheds understand how storm events influence nitrate export. We quantified the relationship between discharge and nitrate concentrations to improve understanding of the physicochemical controls on nitrate export, documenting patterns via both hysteresis and flushing indices. Such indices are indicative of the magnitude, timing, and source behavior of nutrient loss from the surrounding watershed. Using a 4-year dataset, we seek to quantify seasonal and annual patterns in storm nitrate yields and the effects of shifting precipitation patterns, as well as those due to changing land cover (e.g., use of winter cover crops). To our knowledge, this is the first study to examine hysteresis patterns and nitrate storm export in multiple tile-drained, agricultural watersheds using high-frequency sensor data.

**Oral Presentation/Poster Presentation:**

DETERMINING THE DEFENSIVE MECHANISMS IN GREEN ASH (*FRAXINUS PENNSYLVANICA*) RESISTANT TO EMERALD ASH BORER (*AGRILUS PLANIPENNIS*)

ROBERT K STANLEY[1], DAVID CARY[2], ALETTA DORAN[2], MARY MASON[2], JENNIFER KOCH[2], A. DANIEL JONES[3], MARGARET E. STATON[4] AND JEANNE ROMERO-SEVERSON[1]

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Emerald ash borer (EAB, *Agrilus planipennis*), an accidentally introduced Asian beetle, poses an acute threat to the native *Fraxinus* species in North America due to the trees' lack of functional resistance. A small number of green ash (<1%) termed "lingering" survive for years after all other green ash have died. Our collaborators have collected and verified these phenotypes for a structured breeding program. By using structured crosses, we can account for the confounding effects of genetic background and identify the potentially different resistance mechanisms seen in the phenotypes. These multiple resistance mechanisms can be 'stacked' or pyramided in a selective breeding program to produce trees with greater long-term resistance to EAB.

Our metabolomics analyses of these structured populations reveals significant standing genetic variation within green ash population for metabolites. In addition we have conducted analyses that show 1) uninfested families with different parents have different metabolic profiles 2) the metabolic profiles of infested vs uninfested progeny within a single family are different and 3) within families, we have the potential to distinguish between the metabolic profiles of infested progeny with highest and lowest defensive responses. Additionally, discriminate analysis reveals that while there is an overall chemical response to infestation, this is distinguishable across families.

This first set of results allows us construct predictions of phenotypes based on metabolic profiles in a study of larger green ash structured populations. If our predictions are supported, we can design a test that will allow for a strong prediction of resistance from a small tissue sample to allow for a higher throughput in the breeding program. By increasing the rate at which defensive traits in ash can be selected for in a targeted breeding program, we can produce green ash with enough resistance to restore green ash on the landscape and in our cities.

**Oral Presentation:**

**Elucidating the Role of APC Resulting in Doxorubicin Resistance in Breast Cancer**

<u>Casey Stefanski</u>[1,2], Kaitlyn Keffler[1,2], Stephanie McClintock[1,2], Lauren Milac[1,2] and Jenifer Prosperi[1,2,3]

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Chemoresistance is a leading cause of breast cancer related deaths. Therefore, understanding the molecular basis for chemoresistance is essential for novel therapeutic advancement improving patient outcome. The Adenomatous Polyposis Coli (APC) tumor suppressor is lost in up to 70% of sporadic breast cancer; however, little is known about how APC loss contributes to chemoresistance. Using mammary tumor cells isolated from the $Apc^{Min/+}$ mouse crossed to the Polyoma middle T antigen (PyMT) transgenic model, we demonstrated that APC loss decreased doxorubicin (DOX) induced apoptosis. Therefore, we investigated the mechanisms contributing to DOX resistance with APC loss to identify combination therapy options. DOX, a commonly used chemotherapeutic in breast cancer, inhibits topoisomerase IIa, resulting in double stranded DNA breaks (DSBs) and cell cycle arrest. DSB repair is mediated through HRR (homologous recombination repair) or NHEJ (nonhomologous end joining), which are regulated by the repair serine/threonine kinases: ataxia telangiectasia mutated (ATM) or ataxia telangiectasia and Rad3 related (ATR), but only NHEJ activates DNA-dependent protein kinase (DNA-PK). We hypothesized that APC loss prevents DOX-mediated apoptosis through alterations in HRR and NHEJ. To investigate the effect of APC loss on DNA damage repair pathways, we monitored damage recognition pathways after 24-hour DOX treatment. The MMTV-PyMT;$Apc^{Min/+}$ cells exhibited decreased expression of γH2AX, a marker of DNA damage, and ATM phosphorylation following DOX treatment compared to control. Decreased phosphorylation of Chk1 and Chk2 was also observed in DOX-treated MMTV-PyMT;$Apc^{Min/+}$ cells. Using the ATM inhibitor (KU55933) or the DNA-PK inhibitor (NU7441), we observed increased DOX-induced apoptosis in MMTV-PyMT;$Apc^{Min/+}$ cells. These data suggest enhanced DNA repair in MMTV-PyMT;$Apc^{Min/+}$ cells and will be confirmed by measuring repair efficiency via reporter plasmids. Taken together, APC loss mediates DOX resistance via increasing DNA repair demonstrating the potential use of combination therapy to overcome chemoresistance.

**Poster Presentation:**

**Impacts of Geological Carbon Sequestration on Subsurface Microbial Communities**

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Geological carbon sequestration (GCS) is the process of capturing $CO_2$ from industrial sources, compressing it into a supercritical fluid ($scCO_2$), and injecting it into geologic repositories such as enhanced oil recovery (EOR) or deep saline aquifers sites for long term storage. Microorganisms are effective geochemical catalysts for processes that can influence the efficacy of carbon storage, through multiple processes such as biofouling, biomineralization, and biocorrosion. A diverse microbial community thrives in the deep geologic subsurface that drives biogeochemical reactions that will impact the fate of carbon, minerals, and nutrients in these environments. Comprehensive characterization of the biogeochemistry of these complex systems is essential to ensure the adequacy of long-term GCS. Our current study investigated the microbial diversity of targeted GCS sites including a simulated GCS site located in the Gorgas Field in Alabama. We examined overall shifts in dominate microbial taxa in response to the injected $CO_2$ in the subsurface environment finding strong selection for the anaerobic, benzene-degrading genus *Sporotomaculum* in samples collected after $CO_2$ injection. Our results show dominant taxa within relevant GCS systems and highlight shifts in the microbial community composition as a result of $CO_2$ injection.

**Poster Presentation:**

## NMR Relaxation Dispersion Reveals Macrocycle Breathing Dynamics in a Cyclodextrin-Based Rotaxane

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A distinctive feature of mechanically-interlocked molecules (MIMs) is the relative motion between the mechanically-bonded components, and often it is the functional basis for artificial molecular machines and new functional materials. Optimization of machine or materials performance requires knowledge of the underlying atomic-level mechanisms that control the motion. The field of biomolecular NMR spectroscopy has developed a diverse set of pulse schemes that can characterize molecular dynamics over a broad time scale, but these techniques have not yet been used to characterize the motion within MIMs. This study reports the first observation of NMR relaxation dispersion related to MIM motion. The rotary (pirouette) motion of $\alpha$-cyclodextrin ($\alpha$CD) wheels was characterized in a complementary pair of rotaxanes with pirouetting switched ON or OFF. $^{13}$C and $^{1}$H NMR relaxation dispersion measurements reveal previously unknown exchange dynamics for the $\alpha$CD wheels in the pirouette-ON rotaxane with a rate constant of 2200 s$^{-1}$ at 298 K, and an activation barrier of $\Delta F^{\ddagger} = 43 \pm 3$ kJ/mole. The exchange dynamics disappear in the pirouette-OFF rotaxane, demonstrating their switchable nature. The $^{13}$C and $^{1}$H sites exhibiting relaxation dispersion suggest that the exchange involves "macrocycle breathing", in which a $\alpha$CD wheel fluctuates between a contracted or expanded state, the latter enabling diffusive rotary motion about the axle. The substantial insight from these NMR relaxation dispersion methods suggests similar dynamic NMR methods can illuminate the fast time scale (microsecond-to-millisecond) mechanisms of intercomponent motion in a wide range of MIMs.

**Poster Presentation:**

**Observational and Theoretical Studies of SiO Maser Polarization toward Late-Type Evolved Stars: Insights from EVPA Reversal Features**

Taylor Tobin[1], Athol Kemball[2] and Malcolm Gray[3]

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Masers provide a high-resolution probe of the near-circumstellar environment of late-type evolved stars. SiO maser polarization may be key in characterizing their magnetic fields. However, the mechanisms responsible for polarizing these SiO masers continue to be the subject of debate. Primary sources may include the local magnetic field or anisotropic pumping, while additional polarization may arise due to conversion from linear to circular modes through scattering or Faraday rotation. Reducing uncertainties in maser polarization theory is critical to our understanding of the astrophysics of these regions. The linear polarization in some masers displays a rotation of ~90° as a function of position within the feature; such features can provide robust observational constraints on SiO maser polarization theories. We analyzed a single SiO $v=1$, J=1−0 maser feature displaying a linear polarization rotation of >90° toward the Mira variable, TX Cam, as observed by the Very Long Baseline Array in five epochs. While the fractional linear polarization across the feature is consistent with the asymptotic theoretical solution for polarization induced by the local magnetic field, the polarization angle itself rotates too smoothly to arise from this mechanism alone. Possible explanations for this discrepancy include a variation in the angle between the magnetic field and the line of sight, $\theta$, along each sampled line of sight, or Faraday rotation. We provide the first quantitative estimate of the former. To investigate the latter, we developed a new theoretical formalism for radiative transport of maser polarization more general than several previous approaches, including optional Faraday rotation. Preliminary results indicate that, Faraday rotation does little to smooth the instantaneous flip expected by magnetic field polarization theories. The two studies described here provide important new constraints on maser polarization theory and open new observational and theoretical avenues for further exploration of this area of research.

**Poster Presentation:**

**Watershed Scale Land Use Change Increases Stream Metabolic Function in an Agricultural Stream**

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Stream metabolism, in the form of gross primary production (GPP) and ecosystem respiration (ER), is an important measurement of stream ecosystem function, given GPP and ER are integrative measurements of basal ecosystem activity that are highly sensitive to environmental change. In agricultural streams, GPP can be light-limited by water column turbidity associated with soil erosion, primarily when fields are bare (Oct-April). The planting of winter cover crops after the cash crop growing season has the potential to reduce water column turbidity by decreasing soil erosion. We predicted that increased vegetative cover would decrease water column turbidity, and in turn, increase GPP in streams, specifically at elevated flows. We also predicted that ER would decrease due to decreased deposition of particles high in organic matter. We tested these predictions by measuring water column turbidity, GPP, and ER for a 9 yr period (2008-2017) in the Shatto Ditch Watershed (SDW; Kosciusko Co, IN). Watershed scale cover crop implementation was initiated in the fall of 2013, allowing us to compare the effect of cover crops across a range of climatic scenarios pre (5 yrs) and post (4 yrs) cover crop implementation. We used in situ sensors to measure dissolved oxygen, temperature, turbidity, and light at 30 minute intervals at the base of the watershed, and used these data to model GPP and ER at daily intervals using a Bayesian hierarchical model. We show that cover crops decreased mean daily water column turbidity by 50%, which coincided with a 60% increase in GPP at moderate flows (40-90% of flow exceedance categories). Contrary to our prediction, ER increased at most flow periods (0-90%), in part as a result of increased autotrophic respiration. Overall, we show that changes on the landscape can affect stream function.

**Poster Presentation:**


**Development and Characterization of a Small-Scale Helical Surface Dielectric Barrier Discharge for Studying Plasma-Surface Interactions**

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The study of plasma-surface interactions is an emerging field for a wide variety applications, including sustainable energy (catalytic $H_2$ production), environmental remediation (water purification), medicine (sterilization), and high-value manufacturing (nanomaterial synthesis). These applications are driven by species created in the plasma or at a plasma-surface interface, such as free electrons, gaseous ions, excited molecules and radicals, driving chemistry at a surface. Here, we develop a new dielectric barrier discharge (DBD) configuration to produce surface DBDs over a three-dimensional geometry. The motivation for this geometry was to embed the plasma source inside a packed bed (*e.g.*, catalyst) reactor that had tight spatial restrictions so that it could be implemented in a commercial Fourier transform infrared (FTIR) spectrometer instrument.

The design, which we term a helical DBD, was inspired by surface DBD configurations often employed in plasma actuators for fluid dynamics applications. However, rather than using a 2D surface common in plasma actuators, the helical DBD uses the 3D surface of a cylinder as its dielectric, allowing for greater plasma coverage and in this case, greater interaction with a packed bed. This study characterizes the electrical properties of the helical DBD in both free space and within a packed bed reactor. Various electrical parameters, including energy, deposited power, and plasma current are measured as a function of frequency and voltage. Visual properties are presented to show how the DBD spreads along the dielectric surface or into the packed bed. The effect of being immerged in a packed bed is quantified and the potential future prospects of this type of DBD geometry are discussed.

**Poster Presentation:**

**Comparing the Effects of Winter Cover Crops on Nutrient and *E. coli* Loss in Great Lakes Watersheds of Contrasting Land Use**

Anna E.S. Vincent, Jennifer L. Tank, Ursula H. Mahl, Ceara J. Talbot and Marrissa A. Roseman

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Fertilizer runoff is a significant source of nutrients to surface waters in agricultural watersheds. The downstream transport of excess nutrients results in myriad impacts downstream, including algal blooms, drinking water contamination, and coastal hypoxia. Additionally, pathogens, including Escherichia coli (*E. coli*), can also be exported from fields following manure application and result in recreational closures, economic losses, and health risks. Winter cover crops are a conservation practice used to reduce nutrient losses from agricultural fields to adjacent freshwaters. We employed a year-round sampling regime to assess the role of cover crops in reducing nitrate, soluble reactive phosphorus (SRP), and *E. coli* export. We compared export among 3 subwatersheds of contrasting land use in the Paw Paw River Basin (MI): an agricultural watershed dominated by row-crop agriculture, a "treatment" watershed planted in winter cover crops, and a forested watershed which served as a control. Our findings suggest that cover crops reduce nitrate export. However, trends in SRP and *E. coli* export were more variable. At the watershed outlet, nitrate export matches patterns in discharge, while peaks in SRP export are more intermittent over the study period. Heterogeneous land use and other confounding variables within the cover crop subwatershed suggest additional conservation strategies (e.g., manure management) may need to be combined with winter cover crops to further improve water quality. This project will provide insight on the role of conservation strategies in reducing nutrient and pathogen export from agricultural watersheds.

**Oral Presentation:**

## Single-Cell Profiling Guided Combinatorial Immunotherapy for Fast-Evolving CDK4/6 Inhibitor Resistant HER2-Positive Breast Cancer

Qingfei Wang[1,2], Ian Guldner[1,2], Jacqueline Lopez[3], Longhua Sun[1,2], Samantha M. Golomb[1, 2], Jack Harris[1,2], Xin Lu[1,2,4] and Siyuan Zhang[1,2,4]

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Targeted cancer therapy has pioneered the concept of precision medicine by integrating genetic profiling of each patient's tumor biopsy with rationally-designed targeted therapy. Trastuzumab (Herceptin™), a humanized monoclonal antibody targeting the extracellular domain of human epidermal growth factor receptor-2(HER2), is one of the most successful examples of targeted therapies for HER2-positive breast cancer. However, acquiring resistance to targeted cancer therapy is a significant clinical challenge. The recent development of cyclin dependent kinase(CDK) 4/6 small molecule inhibitors has provided patients with relapsed trastuzumab resistant tumors a new hope. In parallel with clinical trials that combining CDK4/6 inhibitor to treat HER2+ breast cancer, we sought to prospectively model the tumor evolution in response to this regimen in vivo and identify a clinically actionable strategy to combat potential drug-resistance. Notably, despite a promising initial response, acquired resistance emerges rapidly to the anti-Her2/Neu antibody plus CDK4/6 inhibitor Palbociclib treatment. By leveraging high-throughput single-cell profiling over the course of treatments, including treatment naive, sensitive/residual and resistant/progressive tumors, we reveal a distinct immunosuppressive immature myeloid cells (IMCs) infiltration in the resistant tumors. Guided by single-cell transcriptome analysis, we demonstrate a combination of IMC-targeting tyrosine kinase inhibitor cabozantinib and immune checkpoint blockades enhances anti-tumor immunity, and overcomes the resistance. Further, our rationally designed sequential combinatorial immunotherapy enables a sustained control of the fast-evolving CDK4/6 inhibitor-resistant tumors. Our study demonstrates a translational framework for treating rapidly evolving tumors through preclinical modeling and single-cell analyses.

**Poster Presentation:**

**Numerical Investigation of Biomechanically-Coupled Growth in Brain Gyrification**

Shuolun Wang and Maria Holland

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Brain gyrification – the process of forming the characteristic gyri (hills) and sulci (valleys) in the cortex – has been long studied by joint efforts of researchers from different backgrounds of biology, mechanics, medical images, etc. The debate of whether biology or mechanics dominates brain gyrification is ongoing. The consistent locations of the major folds across individuals are evidence of the influence of gene expression. However, smaller folds are likely to be affected by compressive mechanical forces. The cortical thickness, in particular, serves as an important biomarker for diagnosing many neurological disorders such as lissencephaly, polymicrogyria, and autism spectrum disorder is consistently found to be thicker in gyri and thinner in sulci. This fact has been well explained by pure mechanical buckling theory and with good agreement from the non-biological polymer experiments (Holland et al., 2018). Building upon this previous work, the current study focuses on a biomechanically-coupled theory to investigate the importance of interaction between biological signals and mechanical forces. We link the cortex's growth rate to various geometrical measures in the brain and introduce either positive or negative biological feedback. The theory is implemented numerically in a commercial non-linear finite element software Abaqus/Standard (2019) by writing a user-defined material subroutine. The simulations in both 2-D and 3-D settings are performed on a bi-layer system consisting of a growing cortical layer and an elastic subcortical substrate. Our results show that the thickness ratio between gyri and sulci is not solely determined by mechanics or biology but the interaction between the two. This study suggests that both biological signals and mechanics are equally important in terms of brain development and our theory should be further investigated and clarified.

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**Poster Presentation:**

**Impact of Neutron Induced Fission on *r*-process Nucleosynthesis Calculations**

Lauren Ward and Rebecca Surman

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Recent evidence indicates that the $r$ process, which is responsible for the creation of the heaviest elements in the universe, occurs at the site of a neutron star merger. Within such merger environments fission has the potential to be greatly influential on abundance yields of nucleosynthesis calculations. We perform sensitivity studies that look at how changing individual neutron induced fission rates and yields affect the abundances of such calculations. We do this for two distinct sets of theoretical nuclear data (based on FRDM 2012 and HFB-17 masses, respectively) and then relate the result to the fission barrier predictions for both models. Additionally, we perform Monte Carlo variations of all of the fission rates to determine the potential uncertainty range in these nucleosynthesis calculations given two distinct fission yield prescriptions (simple symmetric split and GEF). We find that varying the properties of neutron induced fission have a dramatic impact on $r$-processes nucleosynthesis yields and require further study.

**Oral Presentation:**


**Understanding Polymicrobial Infections in Prosthetic Joints**

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The Center for Disease Control (CDC) estimates that 332,000 and 719,000 total hip and total knee replacements are performed in the United States annually. After joint replacement, a fraction of these reconstructed joints develop microbial infections at the site where these implanted materials meet human tissue. These prosthetic joint infections (PJIs) are challenging to treat therapeutically because the infectious agents often are resistant to antibiotics and capable of abundant growth in surface-attached biofilms. Though infection rates are low, ca. 1-2%, the overall increase in sheer number of joint replacement surgeries results in an increased number of patients with risk of infection. Clinical samples from PJIs were collected and used for Whole Genome Shotgun Sequencing (WGSS), finding that infections are often polymicrobial with population compositions similar, but unique from, vaginal, skin and gut microbiomes. We found that some microbes were not easily cultured from these infections, while others, of low relative abundance by WGSS, were readily cultured. Using clinical isolates from this initial study, we find that single and mixed species cultures have varied growth responses to hyaluronic acid, an important component of joint synovial fluid that declines with age. Our studies find that this environmental change can shift the microbial composition of the infection in an aging joint.

**Oral Presentation/Poster Presentation:**

**Estrogen Modulation of Fate Choice during Kidney Development**

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Vertebrate kidney formation is a nuanced process that directs renal progenitors to form the functional units of the kidney, known as nephrons, which are comprised of specialized cell types organized into discrete functional segments. The zebrafish embryo forms two nephrons by 24 hours post fertilization (hpf) and offers a simple but tractable genetic model to study nephron patterning. A chemical screen carried out by our lab coupled with whole mount *in situ* hybridization (WISH) identified 17ß-estradiol (E2), the dominant form of estrogen in vertebrates, as a potential regulator of segmentation. Further investigation has revealed that E2 results in an expansion of the distal early (DE) and decrease of the distal late (DL) nephron segments due to alterations in cell number that were quantified with fluorescent ISH. Furthermore, E2 treated animals had expanded expression of the essential DE lineage transcription factor *irx3b* and its target, *irx1a*, suggesting E2 affects specification of DE precursors. To delineate the possible mechanism of action of E2's renal effects, we conducted a targeted chemical screen with selective estrogen receptor modulators (SERMs) that exhibit preferential binding for known E2 receptors. The *esr2* antagonist PHTPP similarly reduced the DE segment, suggesting that Esr2 may be involved in nephrogenesis. Consistent with this hypothesis, *esr2a* and *esr2b* transcripts are expressed during renal progenitor specification. To investigate which of these receptors (or both) are a major player in distal cell fate choice, we have created CRISPR/Cas9 mutants using guides designed for *esr2a* and *esr2b*, respectively. With additional genetic studies, we hope to further our understanding of the role of estrogen signaling in kidney development. Combined, these preliminary findings have relevance for understanding kidney disease models, as well as efforts to recapitulate development *in vivo* for drug discovery and regenerative therapies.

**Poster Presentation:**

**Attributing the Efficacy of a Spatial Repellant to Entomological Parameters**

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Other than vaccines, all current interventions designed to reduce vector-borne disease burden act by directly affecting life history traits, whereas other interventions, such as spatial repellents that are currently being evaluated in clinical trials, are expected to achieve their impacts through indirect effects related to movement away from a human, attraction-inhibition, and/or feeding inhibition. Quantifying changes in intervention impact through both direct and indirect effects on vector populations is critical for making projections of efficacy in contexts outside that in which trials are performed.

We used the classic Ross-Macdonald model of malaria transmission to simulate epidemiological endpoints in a cluster-randomized control trial based on simulated differences in entomological parameters between intervention and control arms. Differences in entomological parameters were modelled based on a spatial repellent intervention, which is expected to reduce both mosquito survival and blood-feeding. Given uncertainty about the effect size on epidemiological endpoints, we quantified the joint uncertainty around the effect size on model parameters related to mosquito survival and blood-feeding.

For a given change in an epidemiological endpoint caused by a spatial repellent, many combinations of degrees of increase in mosquito mortality and decrease in biting rate could be responsible for the observed change. However, the model is able to recreate the parameters used to generate the data and the relative contribution of each control method to overall incidence reduction. This model shows promise for use in future impact projections when deciding how and where to implement the spatial repellent.

**Oral Presentation/Poster Presentation:**

**A CLIP-170-Induced +TIP Network Superstructure has Characteristics in Cells Consistent with a Liquid Condensate**

Yueh-Fu O. Wu[1,2], Gail Fernandes[1], Annamarie T. Bryant[1,2], Naro Nelson[1] and Holly V. Goodson[1,2]

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Proper regulation of microtubule (MT) dynamics is critical for many cellular processes such as cell division and intracellular transport. Plus-end tracking proteins (+TIPs) dynamically track growing MTs and play a key role in MT regulation by participating in a complex web of intra- and inter- molecular interactions known as the +TIP network. Hypotheses addressing the purpose of +TIP:+TIP interactions include relieving +TIP autoinhibition and localizing MT regulators to growing MT ends. We propose a third purpose in which the +TIP network creates a dynamic scaffold surrounding the fragile MT tip, constraining its structural fluctuations, and therefore promoting MT assembly (Gupta, Bioessays. 2014). Many +TIP network proteins are multivalent with intrinsically disordered regions, suggesting that the +TIP network assembled on MT tips may constitute a liquid condensate (i.e. liquid droplet or membraneless organelle). Such a condensate could potentially form a sleeve-like structure at the tip, providing an attractive model for how the +TIP network might physically promote MT polymerization. Previous studies have shown that overexpression of the +TIP network member CLIP-170 induces large structures containing CLIP-170 and other +TIPs but are independent of known intracellular membranes. We hypothesize that these structures are a novel liquid condensate and may reflect a physiological role for the endogenous +TIP network.

Video microscopy experiments show GFP-CLIP-170 induced structures undergo fission, fusion, and elastic deformation. Fluorescence Recovery After Photobleaching (FRAP) experiments demonstrate dynamic exchange of CLIP-170 within a structure and between a structure and the cytoplasm. These properties are consistent with liquid condensates; the structures are not simply protein aggregates. Immunofluorescence experiments show the inclusion of a range of +TIPs and the exclusion of molecules found in other liquid condensates. Overall, these results suggest CLIP-170 induced structures are phase-separated liquid condensates, consistent with the idea that the endogenous +TIP network forms liquid droplets at MT tips.

**Poster Presentation:**

**Comparative Fate of CrAssphage with Culturable and Molecular Fecal Pollution Indicators during Activated Sludge Wastewater Treatment**

Zhenyu Wu and Kyle Bibby

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Wastewater treatment plants are typically monitored using fecal indicator bacteria to ensure adequate microbial water quality of the treated effluent. Fecal indicator bacteria exhibit poor correlation with virus fate and transport in the environment. Viral-based microbial source tracking methods have the potential to overcome this limitation. The recently discovered human gut bacteriophage crAssphage is highly human-specific and abundant in human fecal waste, which makes it promising as a viral human fecal indicator. In this current study, samples were taken from the primary influent, primary effluent, secondary effluent, and final effluent of a conventional activated sludge wastewater treatment plant. CrAssphage was the most abundant fecal indicator measured through the wastewater treatment process. Culturable and molecular bacterial fecal pollution indicators showed higher removal than viral fecal pollution indicators, including crAssphage, confirming the necessity of a viral-specific fecal pollution monitoring target. CrAssphage was strongly correlated with the viral human adenovirus and polyomavirus molecular indicators through the wastewater treatment process. This study offers a comparison of the fate of crAssphage with other fecal pollution indicators through an activated sludge wastewater treatment plant. The average log 10 removal through the treatment process varied widely for the measured fecal indicators, with a maximum log 10 removal of greater than 4.64 for enterococci and a minimum log 10 removal of 1.51 for HPyV. The culturable bacterial fecal indicators E. coli and enterococci had a different fate from molecular indicators, including crAssphage. Somatic coliphages, a culturable viral fecal pollution indicator, exhibited a strong or moderate correlation (Pearson's correlation coefficients (r) from 0.69 to 0.83) with all molecular indicators. The molecular bacterial fecal indicator HF183/BacR287 was strongly correlated (r from 0.83 to 0.99) with viral molecular indicators in the current study. HAdV and HPyV were strongly correlated (for both, r = 0.87) with crAssphage through the wastewater treatment process.

**Poster Presentation:**

## Event-Triggered Minimax State Estimation with a Relative Entropy Constraint

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Event-triggered state estimation, whose aim is to maintain an acceptable estimation performance at a reduced communication cost, has gained significant attention in cyber-physical systems (CPSs). Different from traditional time-triggered systems in which the sensor data are taken by the estimator at every time instant, an event-triggered estimator receives the data via a network only when a predefined event-triggered condition is satisfied. The event-triggered condition defines some importance metric of the data and provides implicit information available to the remote estimator, so that a good tradeoff between communication cost and estimation performance is achieved. On the other hand, in CPSs it is usually difficult to characterize exactly the dynamics of the physical plant considered by a mathematical model due to the complexities of systems and some uncertainty factors. In this context, it is necessary to consider system uncertainty for event-triggered state estimation problems.

We consider an event-triggered minimax state estimation problem for uncertain systems subject to a relative entropy constraint. This minimax estimation problem is formulated as an equivalent event-triggered linear exponential quadratic Gaussian problem. It is then shown that this problem can be solved via dynamic programming and a newly defined information state. As the solution to this dynamic programming problem is computationally intractable, a one-step event-triggered minimax estimation problem is further formulated and solved, where an *a posteriori* relative entropy is introduced as a measure of the discrepancy between probability measures. The resulting estimator is shown to evolve in recursive closed-form expressions. For the multi-sensor system scenario, a one-step event-triggered minimax estimator is also presented in a sequential fusion way. Finally, comparative simulation examples are provided to illustrate the performance of the proposed one-step event-triggered minimax estimators.

**Poster Presentation:**

**Time-Resolved Characterization of a Free Plasma Jet Formed using a Piezoelectric Transformer**\*

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The time-resolved characteristics of plasma generated by a piezoelectric transformer (PT) have been investigated. A PT is a non-centrosymmetric crystal that converts low-voltage AC input (*e.g.*, a high frequency sinusoidal wave) to high-voltage AC output through an electro-mechanically coupled process. The high voltage gain can be several orders of magnitude, such that a free atmospheric-pressure plasma jet (APPJ) can be formed off the surface of the PT. PTs are attractive for non-equilibrium plasma generation because of their simple operation and low power consumption. In this work, the temporal evolution of the PT-driven plasma was visualized by using an intensified CCD camera. For time-resolved plasma visualization, one period of the input voltage cycle (~14.8 µs) has been separated into 60 phases with a time interval of 250 ns, and APPJ images are taken for each phase. Results visually demonstrate the plasma jet formation within one period. Notably, the plasma formation is a discrete process, appearing at a fixed phase of the sinusoidal input, and the strongest plasma jet appears at the end of the positive cycle. Simultaneous measurements of the current, however, show that the discharge current spikes appear statistically about a microsecond earlier than the strongest plasma jet images, which indicates that the plasma produces a strong afterglow.