Program

The Brown University Student Chapters of AWM and SIAM

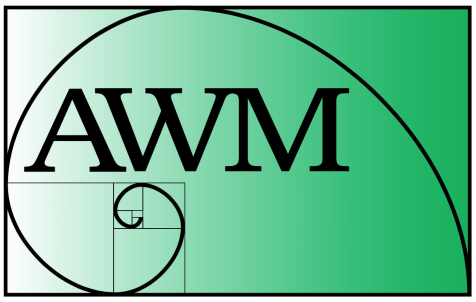
PRESENT

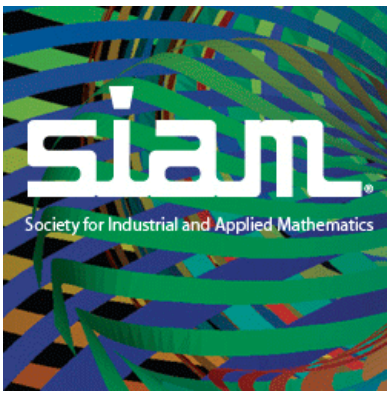
Fourth Annual REU/Internship Panel and Poster Session

Brown University

Providence, RI

November 7, 2017





This event is supported by the Division of Applied Mathematics and the NSF Research Training Group (RTG): Integrating Dynamics and Stochastics, DMS-1148284.

This event is hosted by the Brown University Student Chapters of AWM and SIAM.

Contents

Schedule

Event	Time	Location
REU/Internship Panel	4:00 pm - 5:00 pm	170 Hope St., Room 108
Poster Session	5:00 pm - 6:00 pm	170 Hope St., Rooms 108, 118, and Second Floor Common Space
Refreshments	5:00 pm - 6:00 pm	170 Hope St., Room 118 and Second Floor Common Space

1 Panel Session

The REU/Internship panel will be at 4:00 pm in Room 108 of 170 Hope St. During the panel portion of the event, students are encouraged to ask questions regarding research experiences for undergraduates (REUs) and summer internship opportunities. The panel consists of undergraduates with a range of experiences in both REUs and internships, as well as a professor who has run multiple summer REUs. The panelists are listed below.

- *Layla Abdullah*, Health & Human Biology
- *Rajita Chandrak*, APMA & Economics
- *Gillian Lee*, APMA & Economics
- *Michael Li*, APMA
- *Professor Björn Sandstede*, APMA
- *Kelly Williams*, Biomedical Engineering

After the panel is finished at 5:00 pm, the poster session will begin. The posters will be displayed in 170 Hope St, rooms 108, 118, and the second floor common space. A map of the posters can be found in Section 2, in which each poster location is marked with a number associated with an abstract in Section 3.

2 Map of Poster Session

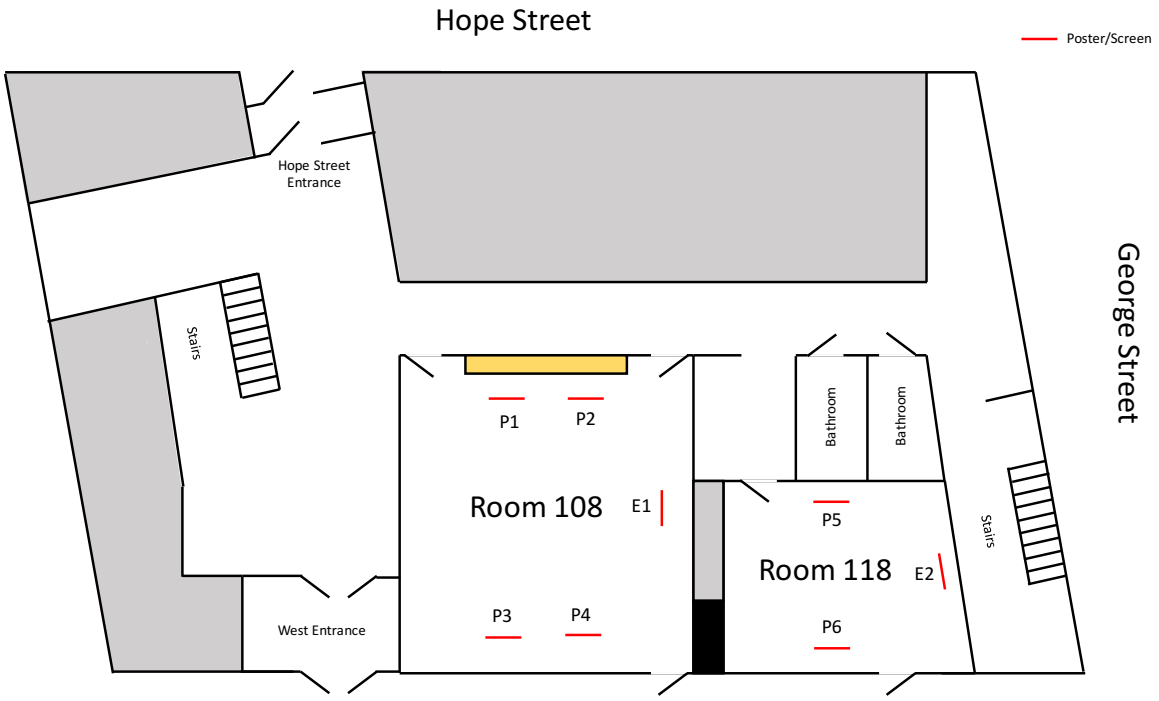


Figure 1: 170 Hope Street, First Floor

Room 108

P1: **Nitric-Oxide Based Modulation of Cell Binding**, *Kelly Williams*

P2: **Regulation of Mutant p53: The Role of the Mdm2-Mdm4 Complex in Murine Tumorigenesis**, *Tara Srinivas*

P3: **Detecting Bovine Lameness Using Three-Dimensional Limb Movement Variable Analysis**, *Ari Goldbloom-Helzner*

P4: **Perceptions of Discharge Readiness by Maternal Immigrant Status in NICU Mothers**, *Layla Abdullah*

E1: **Spatial point analysis of segregated communities and greenhouse gas sources in New York**, *Rajita Chandak*

Room 118

P5: **A Computational Approach to Modeling Dopaminergic Neurons with Application to Parkinson's Disease**, *Elizabeth Gilchrist*

P6: **Algorithms for Finding Substructure in Galaxy Clusters**, *Natalie Delworth*

E2: **Dark Matter Mapping by Weak Gravitational Lensing**, *Harry Chalfin*

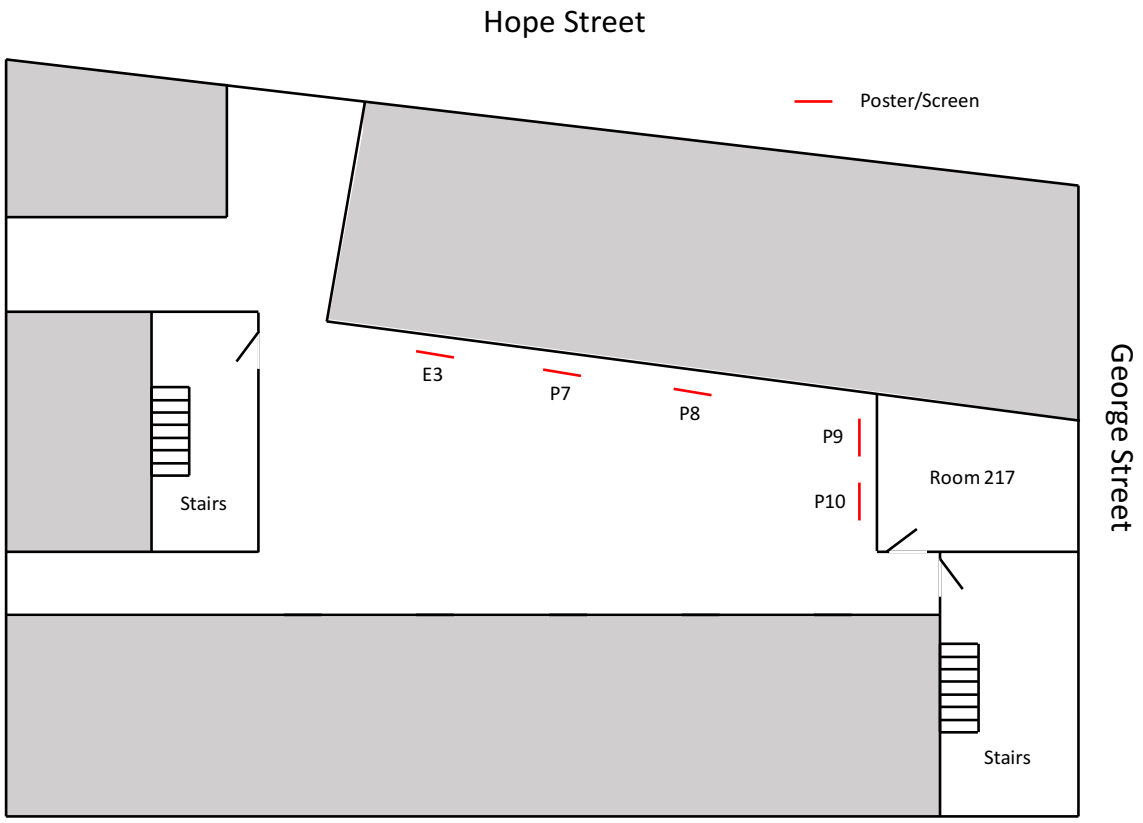


Figure 2: 170 Hope Street, Second Floor

E3: **Metabolomics Analysis Links Metabolic Syndrome in a Swine Model to Cardiac-Specific Effects of Glycolysis and Glycogen**, *Nivedita Sriram*

P7: **A Mathematical Model of the Effects of Neurostimulation Treatments on Neuronal Electrodynamics**, *Kaia Lindberg and Abigail Small*

P8: **Repurposing anthelmintic drugs for treatment of methicillin-resistant Staphylococcus aureus infections**, *Katerina Tori*

P9: **Cryptanalysis of File-Injection Attacks on Oblivious Search**, *Laura Blackstone*

P10: **An Interdisciplinary Approach to Computational Neurostimulation**, *Madison Guitard*

3 Poster Abstracts

Room 108 **Poster Number: P1**

Nitric-Oxide Based Modulation of Cell Binding

Kelly Williams, *Biomedical Engineering*

Co-authors: Bobby Leitmann, Katie Homeyer, Marcus Goudie, Hitesh Handa, Luke J. Mortensen

Introduction: Mesenchymal stem cells (MSCs) show promise in therapeutic applications, because of their ability to target injured tissues and decrease inflammation through multiple pathways. MSCs can also differentiate into bone, cartilage, and fat cells, which would make them an ideal treatment for bone diseases like osteoporosis, osteogenesis imperfecta or hypophosphatasia (HPP), diseases that result in reduced bone strength and abnormal bone development. However, MSCs are primarily adhesive cells, and under normal physiological conditions express many integrins whose cognate receptors are widely expressed in vascular endothelium. Therefore, developing effective intravenous treatments with MSCs has proved difficult, due to poor engraftment at the target site caused by the majority of the infused MSC dose accumulating in other organs. This project aims to increase the efficacy of MSC treatment by using nitric oxide signaling to reduce MSC adhesion to non-activated endothelium, with the purpose of minimizing MSC entrapment in off target organs. Exposure to elevated levels of nitric oxide has been suggested to reduce adhesion in MSCs by down-regulating the expression of the integrin vascular cell adhesion molecule-1 (VCAM-1). The nitric oxide donor S-nitroso-N-acetylpenicillamine (SNAP) has been selected because exposure to physiologically relevant levels of both heat and buffered saline trigger its release of nitric oxide. If successful, this modulation of MSC adhesion using SNAP will eventually contribute to an MSC therapy for HPP.

Materials and Methods: MSCs were grown in vitro in standard culture conditions. MSCs at a passage number between 2-4 were counted and seeded to a 24 well plate for treatment at a density of 10,000 cells per well. Desiccated SNAP was weighed and dissolved in PBS to create a stock SNAP solution with concentration 10 mM. The stock solution was diluted to the appropriate concentration for each treatment, and the SNAP treatment was added to the well plate. Each SNAP treatment concentration was performed in triplicate. MSCs were incubated at 37^{o} C and 5.0% CO2 throughout treatment period. Images were taken beginning immediately after treatment at predetermined time intervals (0-82 hours). Percent adherence was quantified by counting both the number of adherent and non-adherent cells in Fiji using the MiToBo cell counting plugin, and adherence was averaged for the three replicates of each SNAP treatment concentration for each time point. Results and Discussion: SNAP concentrations of 0.5 mM, 0.75 mM, and 1.0 mM caused a significant decrease in MSC adhesion compared to the control.

Conclusions: Treating MSCs with SNAP significantly reduces MSC adhesion. Future work includes studying cell viability, testing MSC adhesion under static flow conditions, and performing gene expression assays to analyze VCAM-1 levels present. Acknowledgements: This material is based on work supported by the National Science Foundation Research Experiences for Undergraduates (REU) site program under Grant No. 1659525.

Room 108 **Poster Number: P2**

Regulation of Mutant p53: The Role of the Mdm2-Mdm4 Complex in Murine Tumorigenesis

Tara Srinivas, *Neuroscience*

Co-authors: Tamara Terzian, PhD; Molly Plehaty; Nema Sobhani; Wanida Stevens; Brendan Podell, PhD; and Brandon Lee

The interaction between p53 and its inhibitors, Mdm2 and Mdm4, is well-documented. However, the regulation of oncogenic mutant p53, which is found in more than 50% of all cancers, remains unclear. Using a mouse model carrying a hot-spot p53 missense mutation, we elucidate the role of Mdm4 and the Mdm2-Mdm4 complex in controlling mutant p53 activity. Immunohistochemistry for p53, Ki-67, caspase-3, and senescence-associated β-gal were performed and positive cells quantified. Survival curves were generated for models expressing mutant p53, mutant p53 lacking Mdm2 or Mdm4, and mutant p53 lacking both inhibitors (TTN). Tumors from these mice were characterized by type, onset, number, and emergence of metastatic lesions.

Immunoassays revealed elevated mutant p53 levels in the absence of Mdm2 or Mdm4, and even higher levels in TTN mice. WT tissues were negative for p53 staining. Proliferation was significantly lower in TTN mice than in mice lacking either Mdm2 or Mdm4. TTN mice survived longer but developed more tumors and metastases than single-gene deleted mice. No apoptosis was detected. These findings suggest that Mdm4 indeed serves as an inhibitor of mutant and WT p53. Increased stabilization of mutant p53 in TTN mice compared to single-gene deleted mice suggests that Mdm2 and Mdm4 cooperatively inhibit mutant p53. However, the lower proliferation index in TTN mice compared to Mdm4-null mice demonstrates that accumulation of mutant p53 does not necessarily correlate with tumorigenesis. These observations may indicate the presence of a novel mutant p53 inhibitor, which could lead to the development of targeted cancer therapies.

Room 108 **Poster Number: P3**

Detecting Bovine Lameness Using Three-Dimensional Limb Movement Variable Analysis

Ari Goldbloom-Helzner, *Applied Mathematics*

Co-authors: William Dula (*Morehouse College*), Kayla Makela (*Michigan State University*), Jason Glover (*University of Maryland, Baltimore County*)

Bovine lameness is a common issue among commercial dairy farms, resulting in decreased productivity and consumption. In order to treat bovine lameness effectively, it is necessary that dairy farmers detect this lameness early. In this report and recent previous work, lameness has been determined using three-dimensional limb movement measurements related to a cow's gait. Previously, a statistical model was generated using the software SAS® with its LOGISTIC and TRANSREG procedures. The model produces a binary classification: lame or sound. Current implementation requires running several SAS® procedures manually and therefore is not amenable to a large scale application. In this work, we implement regression algorithms in R to mirror the TRANSREG procedure and thus speed up exploration of a large number of candidate models to maximize goodness of fit criteria such as the area under the Receiver Operating Characteristic curve (AUC). The predictive models are also evaluated using quantities

such as sensitivity (true positive rate) and specificity (true negative rate) which are quite important from the dairy industry's point of view. We also consider multinomial logistic models to divide the lame cows further into severely lame and mildly lame. These results can ultimately be used in the commercial dairy industry for early lameness detection.

Room 108 **Poster Number: P4**

Perceptions of Discharge Readiness by Maternal Immigrant Status in NICU Mothers

Layla Abdulla, *Health and Human Biology*

Co-author: Dr. Betty Vohr, *Women & Infants Hospital, Alpert Medical School*

Objective: Evaluate the effect of maternal immigrant status on perceptions of discharge readiness in mothers of preterm infants (gestational age < 37 weeks) and identify the impact of primary language, birthplace, and years in US. We hypothesized that immigrant mothers would perceive less discharge readiness in comparison to native mothers.

Study Design: Immigrant (172 (23%)) and native (560 (77%)) mothers of preterm infants cared for in the NICU for > 5 days between 2012 and 2015 completed the Fragile Infant Parent Readiness Evaluation (FIPRE), a discharge readiness questionnaire. Group comparisons were made based on immigrant status. Regression models were run to examine the effect of immigrant status, primary language, birthplace, and years in US on discharge readiness.

Results: Immigrant mothers were more likely to be older, gravida > 1, non-white, non-English speaking, have less than high school education, and Medicaid. They were less likely to have a history of child protective services, substance abuse, and adverse mental health. Infants of immigrant mothers were more likely to receive breast milk at discharge. Immigrant mothers were more likely to score unfavorably on infant well-being, maternal well-being, maternal comfort, and time impact. Immigrant mother, NICU days, non-English speaking, and social risk factors predicted unfavorable FIPRE scores while Medicaid predicted less unfavorable FIPRE scores. Among immigrant mothers, increased years in US predicted more unfavorable FIPRE scores.

Conclusions: Nearly a quarter of mothers were immigrants. They perceived less discharge readiness which highlights the need for culturally competent care and enhanced discharge readiness services specifically tailored to help this vulnerable population.

Room 108 **Poster Number: E1**

Spatial point analysis of segregated communities and greenhouse gas sources in New York

Rajita Chandak, *Applied Mathematics & Economics*

Co-author: Professor Ben Nolting *(California State University, Chico)*

In this research project, we hypothesized that sources of pollution are more likely to be built in highly segregated communities because segregated communities lack the social power to resist the establishment of these sources and disadvantaged racial minorities could be forced to live near existing sources. To test this, we designed a way to quantify segregation across a range of spatial scales using spatial pattern analysis tools: Ripley's K function and the pair correlation

function. We designed a coding framework to efficiently calculate these functions from 2010 census data. Previous studies typically only identify segregation at a single spatial scale, so our approach presents a novel way to understand this phenomenon. Using these results together with EPA data on Greenhouse Gas emissions, we examined the relationship between segregation and the location of pollution sources. Preliminary results show that areas with higher levels of racial segregation were more likely to contain major GHG emission sources. Our computational design also allows us to quantify the relationship between racial groups and pollution sources across a continuum of spatial scales, and preliminary results show that disadvantaged racial groups are more likely to be clustered near pollution sources.

Room 118 **Poster Number: P5**

A Computational Approach to Modeling Dopaminergic Neurons with Application to Parkinson's Disease

Elizabeth Gilchrist, *Mathematics (Roger Williams University)*

More than one million individuals suffer from Parkinson's Disease (PD) in the United States alone, and while the biomedical research community continues to progress neurotherapeutics and enhance our knowledge of the causes and pathogenesis of this disease, a comprehensive understanding of the intracellular mechanisms by which dopaminergic neurons prematurely commit to an apoptosis phenotype in PD remains elusive. To address this issue, we have developed a mathematical model of the intra-cellular signaling pathway of the key proteins in dopaminergic neurons that are directly involved in the progression of PD, including Parkin, PINK1, and alpha-synuclein. To accomplish this, we have completed an extensive search of the PD neurobiological and medical literature and constructed a systems biology based wiring diagram, which in turn was used in developing a kinetics-based system of ordinary differential equations to model this pathway. The model incorporates intracellular species recently found to be central in the pathogenesis of PD, including calcium, the IPAS pathway, and the LRRK2 enzyme which importantly phosphorylates alpha-synuclein. Further, the novelty of this work includes an approach for deducing currently unknown pathway kinetics based upon system phenotype. In particular, we view the premature commitment to a pathological apoptosis phenotype as an irreversible biological switch, and use this perspective to identify those kinetic rate values that enable the mathematical model to support this phenotype. We will present our intra-cellular signaling pathway wiring diagram, mathematical model, numerical approach for identifying kinetics, and preliminary results that showcase the capability of the model to computationally emulate PD pathogenesis. We hope that this work will ultimately help contribute to a greater understanding of the role of the intracellular components responsible for PD progression as well as uncovering potentially new treatment targets and their impact on neuronal survival.

Room 118 **Poster Number: P6**

Algorithms for Finding Substructure in Galaxy Clusters

Natalie Delworth, *Applied Math*

Co-author: Professor Eric Wilcots, *University of Wisconsin-Madison; NRAO/NAC*

In order to better understand the role of environment in determining the properties of galaxies, we present statistical approaches to identifying substructure in galaxy clusters and groups. A

subgroup is composed of a set of galaxies within a galaxy cluster that share similar attributes. To create subgroups from galaxies in a cluster, we explored several different clustering algorithms: Agglomerative Hierarchical Clustering, Spectral Clustering, and K-Means Clustering. We evaluate the strengths and weaknesses of these algorithms by applying them both to data from the Antlia Cluster, as well as to output from simulated galaxy clusters. We also examined how subgroups and the properties of the galaxies in those subgroups changed over time through analysis of data from simulations that extend over a long time scale. We synthesize these results to provide a perspective on how these analyses contribute to our understanding of galactic evolution.

Room 118 **Poster Number: E2**

Dark Matter Mapping by Weak Gravitational Lensing

Harry Chalfin, *Physics*

Co-author: Professor Ian Dell'Antonio, *Brown University Department of Physics*

Dark matter is an exotic type of matter which is not yet well-understood. Our research team investigated dark matter using a phenomenon called weak gravitational lensing – matter causes a curvature in space, so massive clumps of dark matter cause nearby light rays to bend, creating a lensing effect. We analyzed distant galaxy clusters, trying to detect the presence and abundance of dark matter in these regions of space by looking for these gravitational lenses. Since this lensing effect is usually very weak, we used statistical methods to pinpoint the lenses and hence the dark matter. We produced several dark matter maps in galaxy clusters with particularly high concentrations of dark matter, and physicists can continue to use the methods we developed to create and calibrate dark matter maps of many more galaxy clusters. We hope our work will help teach physicists something about the nature of dark matter.

Second Floor **Poster Number: P7**

A Mathematical Model of the Effects of Neurostimulation Treatments on Neuronal Electrodynamics

Kaia Lindberg and Abigail Small, *Mathematics (Roger Williams University)*

Neurostimulation therapies continue to demonstrate success as a medical intervention for individuals with neurodegenerative diseases. In particular, transcranial direct current stimulation and deep brain stimulation treatments have shown to alleviate movement disorders associated with both early and late stages of Parkinson's disease (PD). Despite promising results from these neuromodulation modalities, the mechanisms by which neurostimulation alleviates PD symptoms remain elusive. Specifically, the influence of an electric current on intracellular and extracellular ion concentrations and subsequent transmembrane electric potentials is not clear. While the equations that govern these bioelectromagnetics are understood, current mathematical models of neurostimulation do not incorporate them, nor do they incorporate biologically-based cellular processes such as transmembrane ion channel gating. This project has focused on developing the first cellular-level mathematical model of neurostimulation, with the goal of better understanding its effects on the electrodynamics of a neuron. To date, we have implemented a numerical solution to the neurologically-inspired Poisson-Nernst-Planck system of partial differential equations using the finite element method, which effectively models intracellular and extracellular electric potential, neuronal transmembrane voltage, as well as

sodium, potassium, chloride, and calcium ion concentrations. In addition, we have integrated a Hodgkin-Huxley based scheme to quantify transmembrane ionic flux for all ion species. We have conducted numerous numerical experiments on two-dimensional neuronal geometries involving action potential generation and external current application. We are currently extending these simulations to three-dimensional physiologically-inspired neuron domains. Our future endeavors also include coupling our electrodynamics model with an intracellular signaling pathway model of a dopaminergic neuron. We hope that this work will ultimately help elucidate the principles by which neurostimulation alleviates PD based symptoms.

Second Floor **Poster Number: P8**

Repurposing anthelmintic drugs for treatment of methicillin-resistant Staphylococcus aureus infections

Katerina Tori, *Cell and Molecular Biology*

Co-author: Dr. Mylonakis, *Rhode Island Hospital*

Bacteria escape antibiotics by entering into non-growing dormant state without acquiring resistance mutations. These bacteria, known as persisters, exhibit minimized biosynthetic processes, such as DNA, protein, and cell wall synthesis, which are the major targets for most antibiotics currently prescribed. Evidence reports that persisters are responsible for antibiotic-tolerance of biofilms and recalcitrance of chronic infections, which are hard to cure via conventional antibiotics. Therefore, discovery of new antimicrobials effective against bacterial persisters is of clinical importance. We identify a clinically approved anthelmintic drug, bithionol, that kills methicillin-resistant Staphylococcus aureus persisters by inducing rapid membrane permeabilization. Bithionol kills both growing and persistent MRSA cells with low toxicity profiles. Our results suggest the potential usage of bithionol for treating MRSA chronic infections.

Second Floor **Poster Number: P9**

Cryptanalysis of File-Injection Attacks on Oblivious Search

Laura Blackstone, *Mathematics & Computer Science*

Co-authors: Seny Kamara (*Brown University*) and Tarik Moataz (*Brown University*)

In an age where databases can be cheaply and easily stored on 'the cloud', clients should be able to easily access their data with the confidence that it is secure. The Oblivious RAM (ORAM) method for using keywords to search over encrypted data prevents devastating access-pattern leakage, which plagues more efficient mainstream methods. Because of this, the Searchable ORAM Model is often regarded as the gold standard of security for this problem, yet no formal cryptanalysis of it exists.

This research presents known-document injection attacks on the Searchable ORAM model under several database growth patterns. The attacks aim to identify the keyword(s) associated with single-word searches performed over an email database. The existence of successful attacks demonstrates that the models' leakage is non-trivial, and can be exploited to reveal sensitive information about clients' private files and search patterns. These findings suggest that the Searchable ORAM model is not as secure as the cryptography community perceives it to be.

Second Floor **Poster Number: P10**

An Interdisciplinary Approach to Computational Neurostimulation

Madison Guitard, *Mathematics (Roger Williams University)*

Transcranial direct current stimulation (tDCS) is a noninvasive neurological treatment that applies low doses of electrical current directly to a patient's head surface using scalp electrodes with the goal of modifying cortical excitability, which is the propensity of neurons in the brain to fire action potentials. This treatment has shown great promise as a medical intervention for neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease. The central focus of our project is to determine and quantify the influence that individualized cranial tissue conductivities have on delivering an electric field from electrotherapies, such as tDCS, to a targeted region of the brain. Existing simulations of tDCS, as well as other modes of neurostimulation, typically choose average values for the conductivities of the scalp, skull, cerebrospinal fluid, and gray and white matter tissues, and so these simulations do not incorporate patient specific electrical conductivity variability. Therefore, it is currently unclear whether these standard values are appropriate and most effective for simulations for all patients. The goal of this research is to determine how variability in conductivity impacts tDCS simulation predictions. To achieve this goal, we are working to create a stochastic partial differential equation based mathematical model of tDCS, and assess the impact that differences in conductivities have on simulation efficacy. Our governing equations include the Laplace Equation, as well as several Dirichlet and Neumann boundary conditions that model tDCS treatment conditions. We are in the process of solving the Laplace equation in Cartesian coordinates and polar coordinates for an idealized two-dimensional geometry. We plan to then run numerical simulations in order to assess and quantify the importance of incorporating conductivity stochasticity into computational simulations of tDCS. We would like to be able to present our knowledge, and what we have learned from this research, to an audience at the conference through a poster in order to inform them of the forward movements we have made in increasing the efficiencies of neurostimulation treatments.

Second Floor **Poster Number: E3**

Metabolomics Analysis Links Metabolic Syndrome in a Swine Model to Cardiac-Specific Effects of Glycolysis and Glycogen

Nivedita Sriram, *Biochemistry*

Co-author: Dr. Anny Usheva *(Cardio Thoracic Research Department of the Rhode Island Hospital at the CORO centre)*

Metabolic syndrome (MetS) is a group of conditions including hypertension, hyperglycemia, low HDL levels, high triglyceride levels, and central obesity, that raises the risk of cardiovascular disease (CAD), diabetes, and stroke. Due to the current obesity epidemic, MetS is prevalent in the U.S with about 34% of adults affected.

To prevent said complications in such a large population alternative therapies for MetS are necessary. With this in mind we aimed to better understand the metabolomic alterations in MetS and the effects of GSK-3b inhibition on chronic ischemic cardiac tissue.

We used a porcine model of diet-induced MetS and surgically-induced CAD. Cardiac tissue from Ossabaw and Yorkshire pigs was used for extraction of polar metabolites2,3. LC/MS-MS, non-negative matrix factorization (NMF) of mass-spec data4 and thin-layer chromatography

(TLC) were used to verify the content of selected metabolites in cardiac tissue. Then, tissue lysates from pigs on lean diet (ND), pigs on hypercholesterolemic diet (MetS) and GSK-3b inhibitor treated MetS pigs were analyzed for phosphorylated glycogen synthase 1 (P-GYS1) content by Western blotting with a P-GYS1 specific antibody. Finally, immunocytochemistry was used for glycogen staining of paraffin embedded cardiac tissue from ND, MetS and GSK-3b treated pigs.

301 polar metabolites were identified by LC/MS-MS in the cardiac tissue. ND pigs showed higher content of metabolites from the glycolysis pathway and gluconeogenesis and increased glucose-6-phosphate, fructose-6-phosphate, pyruvate and lactate levels vs MetS pigs. These trends are supported by findings that several pathways are diminished in MetS vs ND. Additionally, P-GYS1 and glycogen content in cardiac tissues shows closer values in ND and GSK-3b inhibitor treated MetS pigs than in MetS pigs sans treatment.

NMF2 classified the metabolomics mass-spec data into specific signatures clearly separating MetS from the ND control. Furthermore, glycolysis is suppressed in MetS as the cardiac content of entry metabolites, glucose-6-phosphate and fructose-6-phosphate, and final products, pyruvate and lactate, are significantly diminished. Finally, in MetS, transcriptional GSK-3b activation leads to GYS1 inactivation and lessened glycogen. However, treatment of MetS pigs with GSK-3b inhibitor rescues GYS1 and glycogen production, thus showing potential as an alternative treatment for MetS.