WiSE Undergraduate Summer Research Mini-Conference

Friday, July 24th 2020

9:30 am – 12:00 pm

Schedule

9:30 – 9:35	Introductory Remarks
9:35 – 9:50	Sarah Schaefer *Professor Cristina Zavaleta*
9:50 – 10:05	Collette Gordon *Professor Megan Fieser*
10:05 – 10:20	Lydia Cardwell *Professor Maral Mousavi*
10:20 – 10:35	Angie Shao *Professor Gary Rosen*
10:35 – 10:45	**Break**
10:45 – 11:00	Ruby Sekhon *Professor Jaykanth Ravichandran*
11:00 – 11:15	Dottie Yu *Professor Leonardo Morsut* *Professor Paul Bogdan*
11:15 – 11:30	Louise Lu *Professor David Z. D'Argenio*
11:30 – 11:45	Adriane Tam *Professor Travis Williams*
11:45 – 12:00	Closing Remarks

Searching for Gold: Using Nanoparticles for Improved Cancer Cell Detection

Sarah Schaefer, Professor Cristina Zavaleta

When it comes to cancer research, there has been an overwhelming need to improve cancer diagnostics and treatments. A promising method of making such improvements involves cancer imaging, specifically establishing nanoparticle contrast agents capable of achieving multiplexed imaging. Such nanoparticles would have biomarkers on their surface that bind to molecules known to be overexpressed on cancer cells. For example, these nanoparticles could target the epidermal growth factor receptor (EGFR), which is commonly associated with breast cancer. In addition to biomarkers, these nanoparticles would also have reporter molecules that enable multimodal imaging via methods including fluorescence, Raman spectroscopy, or even CT imaging. Thus far, multimodal nanoparticles are still in development. This research has specifically focused on utilizing surface-enhanced Raman spectroscopy (SERS) with nanoparticles. Surface-enhanced Raman spectroscopy depends on the adsorption of a Raman reporter molecule to a metallic surface, like that of a gold nanoparticle. This adsorption then intensifies the narrow SERS peaks associated with that specific Raman reporter, making SERS gold nanoparticles ideal for multiplexed imaging. This research has primarily involved extensive literature research into current SERS nanoparticle fabrication methods in Dr. Zavaleta's lab and the value of SERS imaging to future multiplexing capabilities, as well as additional types of SERS nanoparticles that are not currently being made in Dr. Zavaleta's lab. This literature research has brought about a potential future research project – creating a single gold nanoparticle capable of both fluorescent and SERS imaging. Creating this kind of nanoparticle would bring the medical imaging field one step closer to the ideal multiplexed nanoparticle contrast agent.

Magnifying Plastics

Collette Gordon, Professor Megan Fieser

As our society faces a global pandemic, plastic pollution now, more than ever is a pressing issue that we need to solve in our community and globe. The accumulation of plastics in the streets, landfill, oceans, and globe call for a more sustainable plastic that can reduce our plastic footprint. However, sustainable plastic is not enough. Improved plastic collection and recycling, increased public awareness of plastic pollution, and solutions to plastic pollution are vital steps that need to be taken.

My research in the Fieser Lab has helped address these challenges both in and out of the laboratory. I have recently been focused on synthesizing f rare-earth metal catalysts are aimed to facilitate the synthesis of a wide range of degradable plastics with different properties. My work to synthesize ketoimine ligands to stabilize these complexes, as well as my future plans to synthesize the target metal complexes will be discussed

Due to the current research conditions for undergraduates, I have devoted my time to the design a website that will educate the public about plastic pollution, recycling guidelines, and education on how to know if a product is a good replacement. Initially, my research focused on compiling as much information as possible, which then will be consolidated to clear messages to be communicated on the website. I aim to communicate about plastic packaging today, including current plastic products on the market, the applicability to our daily lives, potential health threats, and governmental action that has been taken against them. Along with a strong platform of plastic

packaging, I researched the plastic pollution problem in our country and globe to better understand where our plastic waste ends up. The Fieser Lab strives to communicate how our daily actions lead to plastics (both bulk items and microplastics) in our environment. In addition to my research focus on plastic pollution, I also researched solutions to plastic pollution namely recycling techniques that are used on a national level including industrial recycling, curbside recycling, and drop-off recycling. Since there is no nationwide guideline for what to recycle, we intend to make it easy to find the individual county rules in every state, ideally making it easier for the public to recycle properly. Another solution to plastic pollution is the development of plastic alternatives that can utilize naturally prevalent resources in order to create biodegradable alternatives that can be made out of materials like seaweed, fungus, and a variety of others. But while businesses have coined the use of sustainability as a marketing tactic, it is important to look out for common misconceptions of users when purchasing sustainable products. The website I am designing will include tips on how to identify flaws in sustainability marketing. A brief summary of the key points I have compiled will be discussed.

Through my summer research experience, I aimed to bridge the understanding of the general public and researchers in order to spark a necessary environmental change for our future.

Novel Gloved-Based Microtear Detection System

Lydia Cardwell, Professor Maral Mousavi

As research to alleviate the COVID-19 pandemic progresse, BSL (Biosafety Level) II- IV labs maintain an essential role in developing tests, treatments, and vaccines for the novel coronavirus. Incidents of safety measure failures in such labs have led to public concern about the security of such facilities, causing affected communities to protest the construction of laboratory sites (Eaves 2020). Additionally, systematic review has shown that worker infection in laboratories often correlates with more extreme cases and abnormal disease progression (Pedrosa 2011.) Consequences of BSL safety breaches can be far-reaching and pose a threat to public health.

Thus, the following project seeks to provide additional safeguards that integrate smoothly with existing laboratory equipment. This will be achieved via a novel sensor system that indirectly detects microtears in the gloves used by staff in BSL III labs. As remote research remains the safest option in the face of the ongoing novel coronavirus pandemic, work thus far has focused on developing a literature review and identifying a potential analyte for sensor detection. In particular, the substances used by the CDC to culture cells for the growth of SARS-CoV-2 viruses, such as DMEM (Dulbecco minimal essential medium) or Gibco antibiotic-antimycotics, have a particular potential and relevance as analytes (Harcourt et al, 2020). In the future, remote research will focus on the development of the alerting component of the system and interviews with clinicians. Ideally, future in-person work will consist of the design and testing of the necessary assays to create the sensor component.

Adaptation of the Hidden Markov Model for Alcohol Bio-sensors

Angie Shao, Professor Gary Rosen

The overall purpose of this project is to improve the performance of biological alcohol sensors used for public health research. The current prevailing method for studying alcoholism behavior is for the subject to come into labs for a physical detection using breathalyzer, or manually identify the amount of alcohol consumption. Both methods are hard to perform to great accuracy

for studies across long periods of time. Therefore, a more convenient and accurate data gathering method is needed. One of the solutions is a portable bio-sensor. Designed to be placed on the wrist or ankle, an alcohol bio-sensor can record the Transdermal Alcohol Concentration (TAC) in real time, this data can then be collected by researchers to study the overall behavior of the subject. However, the process of alcohol diffusion through sweat and body vapor is a mathematically un-invertible process due to the presence of the skin acting as filter of information. We must therefore find a way around the traditional process. This project takes advantage of machine learning, assuming that there exist a relationship between TAC and the desired Blood-breath Alcohol Concentration (BrAC), attempts to model this process by using the properties of Hidden Markov Models.

Hidden Markov Models have two main properties — hidden, and Markovian. We assume that the TAC and BrAC at each time step are solely dependent on the alcohol percentage of the previous time step — hence satisfying Markovian properties. Since the changes of alcohol percentage in the subject's body are dependent on many unidentifiable variables including but not limited to: liver's processing of alcohol, general drinking behavior, social environment etc, we must consider there is an unidentifiable general variable impacting the changes we see in TAC and BrAC. To do so, we use the property of hidden Markov models, where there exists a hidden state — the general behavior state — that impacts the states we see in observation — TAC and BrAC. Since our final goal is to model a transferable connection between TAC and BrAC, we do not need to create a detailed model of the general behavior state. Rather, we can train the model using TAC and BrAC both as our output: observation state, and present the general behavior as a probability matrix. We can then use this probability matrix to substitute into the desired function between TAC and BrAC for real life application. Doing so creates a general profile of drinking behaviors that can be improved upon with further training according to the researcher's need.

Wide Band Gap Semiconductors

Ruby Sekhon, Shantanu Singh, Professor Jayakanth Ravichandran

High power electronic devices are ubiquitous from cell phones to electric vehicles. Silicon is the most common semiconductor found in electronics because it is relatively cheap and abundant. However, it has many limitations, such as low band gap and low power figure of merit. There is a dearth of alternatives, which includes silicon carbide (SiC) and gallium nitride (GaN). Therefore, it is desirable to explore novel materials candidates for high power electronics.

Researchers have done extensive research on oxides and nitrides, but many chalcogenides – materials made of sulphur, selenium, or tellurium– have been left largely unexplored due to their tendency to be more unstable. However, chalcogenides can offer some benefits –such as, they tend to have a high electron mobility, they can operate at high temperatures, and they are often easier to be p-doped– that cannot be found in other alternatives to silicon. As a result, the Laboratory for Complex Materials and Devices is focusing on investigating chalcogenides that could improve on the current state of high power electronics.

In order to identify materials that have a high potential of being successful, a list of materials was made based on some calculations. Baliga's Figure of Merit is a formula that allows us to identify materials that would have the least conduction loss. Based on this figure of merit, we can identify a short list of materials that can be tested in the lab in order to experimentally identify whether they could show benefits when used in the place of silicon in high power electronics. However, Baliga's Figure of Merit can be difficult to use with many materials that do not have a

known value for the dielectric constant. As a result, the dielectric constant is determined using the summation of the polarizabilities of the ions that make up each material. Then, the Clausius-Mosotti relation can be used to calculate the dielectric constant.

With these calculation, we anticipate identifying materials for faster and smaller power electronic devices tbat can revolutionize the world of electronics.

Evomorph: *in silico* Tissue Development Optimization

Dottie Yu, Professor Leonardo Morsut, Professor Paul Bogdan

Embryonic development is an early phase that all mammalian organisms go through in which a single fertilized cell develops and differentiates into a complex multicellular life form. This development depends on critical cell-cell communication pathways, which are encoded by the organism's cellular genome. Understanding these pathways is critical to the field of synthetic development, which seeks to build smart synthetic tissues in lab and thus holds immense regenerative medicine applications. In synthetic development labs, these cell-cell communication pathways and their underlying genetic circuitry are engineered to elicit a host of user-defined intracellular morphological responses including both physical and transcriptional changes; for instance, several former experiments (Toda et al 2018, Lam & Morsut 2020) have manipulated Notch, a contact-dependent (juxtacrine) pathway to build complex synthetic structures capable of regeneration, self-organization, and response to injury. In this light, synthetic tissue development holds tremendous potential for regenerative medicine applications. However, due to our limited understanding of embryonic development and pattern formation, current methods rely on trial and error to engineer the genetic circuitry yielding a desired synthetic structure. Here we introduce a computational program capable of systematically optimizing the genetic programming to yield the desired tissue structure, avoiding the need for trial and error. This machine-learning program, named Evomorph, optimizes tissue development systematically and rationally through black-box optimization. Currently, we are testing Evomorph with a *in silico* trial structure: a 2-dimensional "checkerboard"-like multicellular structure encoded by a lateral inhibition circuit, chosen for its convenience, simplicity, and appearance in nature. In an initial 1-dimensional parameter scan of the beta parameter, which encodes the sensitivity of the cells in the *in silico* lateral inhibition structure to Delta ligand levels, we ran 100 lateral inhibition simulations with varying beta levels between 0 and 4000 units for 15000 monte carlo steps, allowing their *in silico* development into phenotypically mature structures. We found that higher beta levels correlated to lower phenotypic fitness. In the future, we hope to run higher dimension parameter scans on the lateral inhibition structure. Furthermore, we are interested in optimizing more complex structures, such as a 3-dimensional elongating tube structure also previously built through *in vitro* and *in silico* trial-and-error experiments (Lam & Morsut 2020). One other future direction is to test other optimizers, such as the more flexible and versatile Distributed Evolutionary Algorithms in Python (DEAP) optimization package. Ultimately, our goal is to create a novel program that foregoes the need for trial-and-error tissue development, brings scientists closer to understanding the genetic networks underlying morphogenesis and patterning, all in order to advance the nascent and high potential field of synthetic tissue development.

Using Minimal Model to Study the Glucose Effectiveness in Current Diagnosis Method of Type 2 Diabetes

Louise Lu, Professor David Z. D'Argenio

Type 2 diabetes is a chronic condition that affects the way human body metabolizes glucose. With type 2 diabetes, patient's body either resists the effects of insulin, or cannot produce enough insulin to maintain normal glucose levels. Glucose effectiveness (S_G) is the ability of glucose per se to stimulate its own uptake and to suppress its own production under basal/constant insulin concentrations. In an individual, glucose tolerance is a function of insulin secretion, insulin action and S_G. Under the condition of declining insulin secretion and action that usually caused by type 2 diabetes, the degree of glucose effectiveness assumes increasing significance in determining the level of glucose tolerance both in fasted and postprandial states. However, the role of glucose effectiveness in the regulation of the glucose tolerance is often ignored. Thus, my study focuses on the Minimal Model approach to quantify the glucose effectiveness in the type 2 diabetes patients versus control group with five different parameters of sex, age, weight, height and BMI.

This study collects 1280 sets of clinical data of standard intravenous glucose tolerance test (IVGTT) from multiple pharmaceutical companies and hospitals. Several computer programming tools are used to analysis the data and plot data graph. MATLAB are used to format raw data for the minimal modeling scripts and conduct the follow-up analysis of the minimal models including bar graph, linear regression and histograms. R scripts are used to recursively fit the data to minimal models.

From the hitherto results we got, it can be concluded that the correlation between BMI versus S_G and glucose tolerance are the strongest among all parameters. Meanwhile, sex also causes difference in S_G. Males tend to have lower S_G than females on average in control groups, but the difference decreases or even reverses in the type 2 diabetes group that males have slightly higher S_G than females on average. These results might suggest some improvement on the current diagnosis methods of type 2 diabetes that they should take BMI and sex into consideration while modeling the patients' glucose and insulin data.

Diazacycle Synthesis in Ruthenium Catalyzed Diamine and Diol Coupling

Adriane Tam, Anju Nalikezhathu, Professor Travis Williams

Dilazep is used as a vasodilator. Homochlorcyclizine is used as an antihistamine. Sitagliptin isused to treat diabetes. Imatinib is used to treat leukemia. These four medications represent alarge group of drugs that contain a diazacycle substructure. Piperazine, a six-membereddiazacycle, and homopiperazine, a seven-membered diazacycle, are especially ubiquitous inthe structures of many pharmaceutical drugs. The aim of our project is to develop a novelsynthetic route to access these diazacycle analogs. Our synthetic route involves a newlydeveloped amination reaction with diamines and diols. This reaction involves a base andsolvent-free ruthenium catalyst that only generates water as a byproduct, which makes it moreenvironmentally-friendly. An example of the optimized synthesis of a homopiperazine derivativeis shown in Figure 1. The focus of this work was to identify important medicinal diazacycles totarget as well as research current synthetic routes for these diazacycles. Three main databases,USC Libraries, SciFinder, and Reaxys, were used to explore the current landscape fordiazacycle synthesis. Based on this work, we have gained a better understanding of where ourproject fits into the landscape of diazacycle synthesis. Numerous strategies and various startingmaterials have been reported to synthesize piperazine and

homopiperazine. In fact, there havebeen several reported methods to synthesize piperazine and homopiperazine from diaminesand diols, which is the same starting material that we use in our project. However, most of thesepublished methods require high temperatures and harsh conditions, which shows theapplicability of our work. In addition, published methods have demonstrated that there is still aneed to efficiently synthesize homopiperazine, a seven-membered diazacycle, in good yields,which also highlights the relevance of our work. The importance of other diazacycles such as1,4-diazocane, an eight-membered diazacycle, is also indicated in the literature. Therefore, weplan to expand our substrate scope to generate other homopiperazine derivatives with differentsubstituents as well as optimize the synthesis of 6-, 7-, and 8-membered diazacycles.