PRISM 2020 Project Abstracts

Faculty Mentor – Dr. Dale Beach

Exposing the Hidden Genetic Character of Non-Model Organisms

The expanse of living organisms populating the earth is undeniably linked by the DNA content within the cell. All organisms utilize the same 4 letter alphabet of DNA to encode the molecule blueprints of life. Molecular Biology techniques and DNA sequencing methods allow us to decode DNA and use this information to better understand the physiology and function of the cell as well as establish unique "serial codes" to categorize organisms. For non-model organisms (those rarely used in laboratory studies), targeted DNA sequencing determines genetic variation and unique cellular properties. For example, genetic sequences from the pathogenic bacteria, *Salmonella*, collected from a henhouse or natural stream can identify genes for antibiotic resistance or traits linked to human infection. Alternatively, similar techniques can compare enzyme sequences from brewing yeast or wild fungi to establish specific genetic characteristics for industrial or taxonomic uses. Our group uses molecular techniques to purify and sequence DNA from naturally isolated organisms for identification and determination of genetic characteristics. Ongoing projects that students may work on include novel isolates of the fungal genus *Pilobolus*, the bacterial genus *Salmonella*, or an uncharacterized commercial yeast used for brewing. In each case, organisms are collected for study via whole genome analysis and single gene sequencing methods. Computational analysis of the sequence information facilitates comparisons within a known species and to other species in the genus. In general, research projects determine DNA sequence information to establish the genetic variation and characteristics within the genomes of newly-identified, non-model organisms.

Faculty Mentor – Dr. Robert Blaisdell

The effects of mouth guard use for sport performance enhancement on indices of neuromuscular force and power

Athletes in various sports have been required to wear mouth guards as prevention implements to protect against sport-related mouth injuries. In recent years the use of mouth guards for sport performance enhancement has been gaining support, but findings are still unclear and need further research. These findings have reported that the mouth guards have had positive effects on power output, in addition to aerobic power, but not strength. Proposed mechanisms responsible for these positive effects is that the mouth guard acts as a buffer between the maxilla and mandible allowing for a greater contraction of the muscles in this joint. This case of concurrent activation potentiation occurs when muscles that are not directly involved in the movement responsible for muscle contraction during a dynamic sport-related movement contract and facilitate a stronger action potential in the overall force production within or during the movement. Differences between first and fourth place in some sports have been measured as little as 1.5% between competitors, further illustrating the

importance to fully investigate any possible enhancement in instantaneous peak power and subsequent repeated bursts.

The purpose of this study will be to delineate differences and possible effects of mouth guard use for sport performance enhancement on measures of neuromuscular force and power production, specifically investigating rate of force development and impulse during multiple sport performance testing indices.

Faculty Mentor – Dr. Ben Campbell

Layers of Conceptualization: Secondary Science Teachers' Planning and Instruction of a Chemistry Topic

Conceptualizing a scientific phenomenon is often a difficult and multifaceted undertaking. Science teachers must not only acquire sophisticated conceptualizations of natural phenomena, but they must also develop effective instructional activities for facilitating students in constructing their own accurate conceptualizations. One challenge for understanding many phenomena is recognizing that they can be conceived at varying levels. For instance, a chemical reaction can be conceptualized at three levels: the macro (what the transformation of matter actually looks like), the micro (how atoms are being rearranged as bonds are broken and/or formed), and the representational (how reaction equations are written). Picturing these three layers as the vertices of a triangle, Johnstone (1991) claimed, "So much of teaching takes place *within* the triangle where the three levels interact in varying proportions and the teacher may be unaware of the demands being made upon pupils" (p. 78, emphasis in original).

For PRISM 2020, I would like to work with one or more students on a science education research project to gain insight into how high school teachers conceptualize phenomena such as chemical reactions while they are planning units of instruction, and how their plans are realized during actual classroom instruction. To conduct this research, we would first attain the appropriate permissions and IRB approval, then we would recruit practicing teachers as participants. Data sources could include textbooks, classroom observations, teacher interviews, and teachers' planning tools. The data acquired from this process will provide opportunities to answer a variety of student research questions.

Faculty Mentor – Dr. Julian Dymacek

Constrained Non-negative Matrix Factorization

Our previous work (PRISM 2017) developed a novel constrained, non-negative matrix factorization algorithm and Monte Carlo Markov chain simulation to identify underlying patterns in mRNA and miRNA gene expression data. To keep up with the growing size of available data sets, we created a hybrid system (PRISM 2018), allowing for a reduction in computation time and an increase in accuracy. During PRISM 2019, we found promising results using non-biological, high-frequency data for the first time. We were unable to successfully implement constraints with this new data. Our 2020 goals are as follows:

1. implement constraints for high frequency data,
2. optimize the pattern matching algorithm,
3. and develop an intuitive, web-based interface.

We originally built this system to analyze a very specific kind of biological data, but these modifications focus on adapting our work to be user-friendly for external audiences and diverse projects. Now that we have developed a very fast system, we can work backwards to fine tune other aspects to make it more complete for analyzing patterns in general time-series data. These proposed modifications have been suggested by interested collaborators both internal and external to LU. Our work from Prism 2017 was presented at one of the top international conferences on bioinformatics and published in the peer reviewed conference proceedings as the only paper with
an undergraduate co-author. Funding from Longwood's PRISM 2020 program will help us bring our research full circle by providing a tool that is functional for the end user.

Faculty Mentor – Dr. Sujan Henkanathagadara

An Assessment of Aggressive Interactions between Native and Invasive Crayfish using a Novel Video Tracking System

Invasive crayfish are a growing threat to native species due to competition, primarily for food and shelter, and predation. Invasive crayfish tend to have higher levels of agonism towards native species and may have a significant role in replacing native crayfish. Therefore, it is important to study the interactions between native and invasive crayfish when thinking about conservation measures and management options. Previously, we have studied invasive crayfish impacts on native crayfish using field surveys and mesocosm experiments (PRISM 2016) and using lab experiments to better understand the mechanisms of impacts (CURIO 2017). We studied one-on-one crayfish interactions focusing on aggressive and submissive behavior using lab experiments. During these experiments, we developed a 2D video tracking system to collect real-time data of tagged crayfish and was successful in collecting real-time data on speed and direction of movement, total distance travelled and acceleration. We are proposing new research, where we will develop a system to track crayfish behavior in 3D space using QR code-tagged crayfish with more sophisticated tracking system. This involves initial lab experiments with individual crayfish to develop and fine-tune the tracking system and subsequently conducting experiments with interacting native and invasive crayfish. Once completed, this research would be the pioneering 3D tracking system developed to study crayfish behavior and. once published, we envision a wide application of this method for other behavioral studies. More importantly, this research would provide fine-tuned information on crayfish behavior and may help better understand the role of invasive crayfish in replacing natives congeners.

Faculty Mentor – Dr. Steven Hoehner

The Geometric Balls and Bins Problem in Low Dimensions

In the recent paper [2] (joint work with Gil Kur, MIT), we asked: Are random partial coverings of the sphere optimal in high dimensions? We call this problem the *geometric balls and bins problem (GBBP)* because it is the natural geometric analogue of the famous and fundamental "balls and bins" problem from probability. More specifically, consider the sphere of dimension $n \geq 1$, and draw

N points independently and uniformly from the sphere. For each point, consider the geodesic ball of volume of $1/N$ centered at the drawn point. In expectation, the proportion of the surface area of the sphere that the random balls capture is $1 - e^{-1} + O(N^{-1})$, which is the same value for the proportion of the occupied bins in the original balls and bins problem. In [2] we ask: Is there a (deterministic) partial covering of the sphere by N geodesic balls, each of measure $1/N$, which captures more than $1 - e^{-1}$ of the measure of the sphere?

Although random partial coverings are not optimal in dimensions 1 or 2, we conjecture in [2] that they are optimal in high dimensions. It is unknown how large the dimension needs to be for random sphere coverings to become nearly optimal. The purpose of this PRISM project is to prove that ran- dom partial sphere coverings are not optimal in dimension 3 (and perhaps, for some other low dimensions such as 4 or 5). This would show that the dimension must be at least 4 for the GBBP to hold, but more interestingly, the project may lead to an idea for how to prove (or disprove) the GBBP.

Our GBBP has attracted interest from other mathematicians; see, e.g., the blog post [1] where our question is discussed.

Faculty Mentor – Dr. Chris Labosier

Thermal Safety and Risk of Children's Outdoor Playhouses

Children are more vulnerable to heat-related illnesses as their bodies are not as efficient at evaporative cooling. At the same time, many children's outdoor play spaces are structured and designed in such a way that increases temperatures. Consequently, both their physiology and activity spaces put children at an increased risk of heat-related illnesses. Previous studies have documented the thermal dangers of enclosed vehicles, playgrounds, and bounce houses. Recently published work demonstrated the danger of children's outdoor playhouses with heat index values statistically higher inside these structures than outside. This project will continue and expand previous work by examining (a) circulation/wind flow and (b) a model child's energy balance inside multiple playhouses. Previous work has suggested that circulation is minimal, if not entirely absent, inside such structures. Consequently, thermal energy may build during the day causing temperatures inside the structures to rise. Circulation inside these structures has only been mentioned as a possible mechanism but has not been assessed and so by including a wind flow component to the assessment, this research seeks to address this gap in knowledge. Additionally, this work uses a model child's energy balance to more directly assess thermal risk. By including components of the energy balance alongside measures of a model child's physiology, this work will draw a more direct connection between conditions inside a playhouse and thermal safety for children, as opposed to heat index alone as in the previously mentioned study.

Faculty Mentor – Dr. Jeff Ledford

Non-local Kernel Approximation

This project investigates a phenomenon in approximation theory, which we will call non-local approximation. Starting with a *nice enough* kernel ϕ, one can form an interpolant of form

$$I(x) := \sum_{j=1}^{N} a_j \varphi(x - x_j),$$

where (a_j) is a sequence of coefficients and (x_j) is a sequence of nodes. By choosing the nodes carefully one can solve the interpolation problem by in- verting a matrix corresponding to the kernel. Typically, this is achieved by selecting the nodes to be inside the domain of a continuous signal and using a convenient kernel such as a spline to interpolate function values of the signal. What we will investigate is what happens when the nodes are taken to be very far from the domain of interest. There is very little in the literature on this topic. In fact, only three examples currently exist, $\varphi(x) = \sqrt{1 + x^2}$,

$\varphi(x) = (1 + x^2)^{-1}$, and $\varphi(x) = (1 + x^2)^{k-1/2}$, where *k* is a positive integer. All three of these examples rely on properties of the Taylor series of $\phi(x)$ to provide approximation results. Our investigation attempts to tease out properties of the kernel which provide good approximation rates for continuous functions.

Faculty Mentor – Dr. Dina Leech

Fish Foraging and Freshwater 'Browning': The Balance Between Visual, Chemical, and Mechanical Cues in Searching for Zooplankton Prey

In recent decades, many lakes, rivers, and estuaries have become browner in color due to increased inputs of terrestrial organic matter. These changes in water color have far reaching ecological consequences for the structure and function of aquatic ecosystems, including predator-prey interactions. Most fish species are visually orienting predators, relying on sight during daylight to best locate and capture prey. However, as light availability for foraging declines with browning, it is possible that fish rely on other sensory mechanisms, such as olfactory cues or mechanoreception. This PRISM project will investigate potential differences in the sensory strategies used by foraging larval fish as a consequence of freshwater browning.

Moreover, it builds off previous PRISM research suggesting minimal, negative effects of browning on larval fish feeding efficiency (Figure 1). Here we hypothesize that as light availability decreases with increased browning, fish will rely less on visual cues and more so on chemical and/or mechanical cues when foraging on zooplankton prey. These hypotheses will be tested in the laboratory with replicate experimental tanks of varying brown water color.

Feeding experiments in light or dark and chemical ablation of fish neuromasts with neomycin sulfate will allow all or a limited set of senses to be used by the fish. Following approved IACUC and DGIF protocols/permits, larval fish and zooplankton prey will be collected from local systems near Longwood. Efforts will focus on bluegill sunfish and largemouth bass, two prominent species in aquatic food webs.

Faculty Mentor – Dr. Erin Shanle

Modeling the pathogenicity of single nucleotide polymorphisms in DNA damage response proteins

Single nucleotide polymorphisms (SNPs) are single base pair changes in the DNA that can be associated with disease. These associations provide insight into a possible connection between the change in the DNA and a change in the function of the protein that is coded by the DNA sequence. However, it is difficult to predict how these changes affect protein function and therefore cause disease. The goal of this project is to use molecular modeling to predict the effects of SNPs on the structure of proteins that are involved in sensing and repairing DNA damage. First, a search of scientific literature will be used to identify five candidate DNA damage response proteins that have been structurally characterized and shown to be associated with cancer, a disease that results from unrepaired DNA damage. Second, publicly available databases (dbSNP and ClinVar) will be used to identify SNPs that cause single amino acid changes in the candidate proteins. Third, the amino acid changes will be modelled using the available protein structures and the root-mean-square difference (RMSD) will be calculated across the amino acids of the proteins using Pymol, SWISS-MODEL, and Molecular Dynamics. The SNPs that cause the greatest change in the structure, as indicated by the RMSD value, will be selected for further study in cells. Overall, this project will provide insight into the structural changes caused by SNPs in DNA damage response proteins thereby improving our prediction of the pathogenicity of SNPs.

Faculty Mentor - Dr. Jonathan White

Characterization of cellular targets and derivatization of a choline-appended Pt anticancer therapeutic

Cancerous cells are characterized by numerous metabolic re-programming events, and many of these phenotypes have been utilized as avenues for targeted drug therapies. In cancers, oncogenes are overexpressed that are crucial for the uptake of choline. Despite a majority of cancers expressing enhanced choline uptake, relatively little effort has explored potential avenues for “hijacking” choline metabolism for targeted therapies. Such strategies might utilize small-molecule drugs covalently tethered to a quaternary ammonium cation, mimicking the structure-function relationship of choline and enhancing cellular uptake in tumor cells.
Currently, a mainstay of small-molecule anticancer therapeutics remains the platinum-based drugs. Many cationic Pt complexes have been generated from modifying existing drugs in order to improve solubility and enhance delivery and target binding; however, none of these compounds have demonstrated superior efficacy in vivo. We have synthesized a novel, hybrid cationic Pt compound—a choline-conjugated Pt(II) compound—incorporating the potential cancer cell targeting of choline metabolites and enhanced solubility and target binding of a cationic Pt complex. This work will characterize the target binding of this compound to known cellular targets of Pt in vitro, and begin investigating its toxicity in cell cultures. We will quantify cellular toxicity using *S. cerevisiae* as a model organism and compare the activity to unmodified
Pt drugs. In addition, we will synthesize derivatives of our Pt–choline conjugate and similarly characterize their efficacy in order to better understand the structure-function relationships of Pt–choline cellular reactivity.

Faculty Mentor – Dr. Andrew Yeagley

Investigating aliphatic phosphazenes as quaternary amine cation (QAC) mimics

Our lab is interested in various medicinal chemistry projects that intersect chemistry and biology. The biological focus of our lab is primarily that of anti-bacterial treatments. More particularly, I am interested in compounds that may be alternative treatments to traditional antibiotics.
One alternative treatment that my post-doctoral lab focused on was the inhibition of bacterial biofilms. Over 80% of bacterial infections in the body are caused not by the presence of bacteria, since they are most often present constantly, but when bacteria manage to form biofilms. It is this biofilm that often provides the bacteria some safety from external pressures (such as antibiotics, our immune system, temperature, pH changes, etc.). The ability to prevent or even disperse the presence of bacterial biofilms presents an interesting alternative treatment that is less susceptible to bacterial resistance. Throughout my independent career, I have search for some lead compounds that may be of interest as biofilm inhibitors, but have skirted the attention of the primary literature. I have recently become interested in the possibility of phosphazenes. Some biofilm inhibitors are thought to work as cation counters to membrane lipids. For instance, QACS are the simplest for of such cation bearing lipid molecules and have seen some utility in mouthwash applications (see cetyl pyridinium chloride in Crest, Act, and Colgate). My post-doctoral work was involved in testing 2-aminoimidazoles for their antimicrobial and anti-biofilm activities. These molecules were thought to have basicities similar to guanidine super bases and thus likely act similar to QACs. For this project, I envision investigating if the super basic function of phosphazenes contain similar activities.