THE DEVLIEG FOUNDATION

ANNUAL REPORT

2021-2022

Michigan Technological University

1885

UNDERGRADUATE RESEARCH INTERNSHIP PROGRAM

Undergraduate Research Internship Program awards (URIPs) are open to all Michigan Tech undergraduates who are interested in engaging in a research experience in a faculty member's laboratory. Award recipients conduct a research project under the guidance of a Michigan Tech faculty mentor during the academic year, giving them first-hand access to the science and engineering processes that drive discovery.

For this cycle, three Michigan Tech students conducted research with support from The DeVlieg Foundation. This smaller number was unique for the 2021-22 academic year; 11 awards were made for research that is ongoing this academic year (2022-23) with Foundation support.

Along with their fellow undergraduate researchers across a variety of programs, URIP recipients are encouraged to present either at a relevant conference to their field or at the spring Undergraduate Research Symposium organized through the Pavlis Honors College. We have highlighted their projects in the following pages.

CALEIGH DUNN

BIOMEDICAL ENGINEERING '22

Improving North American Right Whale Satellite Tags Using a Degradable Tip

Introduction

North American Right Whales (NARW) are considered one of the most endangered whale species with less than 400 right whales remaining in the oceans. NOAA monitors the migration and movements of baleen whales using satellite telemetry tags. The currently used tags feature a sharp tip designed to cut through the blubber during deployment, which can lead to the development of persistent wounds due to the shear forces generated at the tissue-tag interface as the whale swims. The development of a self-blunting tip for the current tag design can improve tag biocompatibility and reduce the development of persistent wounds.

Materials and Methods

Through machining and hand-sharpening, a reproducible sharpened edge was created out of 316L stainless steel (thickness = 0.048 inches) to simulate the sharp edges of the consolidated tag tip. The sharpened coupons were then heat treated at 650°C for six hours to create a sensitized surface. Degradation experiments were run on the heat-treated 316L samples and non-heat-treated controls. Briefly, the sharpened sample edges were submerged in a simulated seawater solution (3.5 wt% NaCl in deionized water) for 48 hours under agitation at room temperature. Degradation was assessed through visual analysis of the edge using metallography and through a colorimetric iron assay (Sigma-Aldrich) to measure the concentration of iron ions present in solution post-degradation. The effect of case hardening on degradation is currently being investigated by heat treating sharpened 316L samples at 950°C for 6, 8, and 12 hours with the sharp edge coated with graphite and cast-iron chips. Degradation experiments will be conducted using simulated seawater and cell culture media. The cytotoxicity of serial dilutions of the degradation products will be assessed through live-dead assays and MTT proliferation assays with standard immortalized (L929) and primary humpback fibroblasts in culture.

Results and Discussion

After 48 hours in simulated seawater, the concentration of iron ions was significantly greater for 6-hour heat treated samples versus controls (average iron ion concentration post-degradation at 3.66±0.1nM, and 0.87±0.2nM respectively). This indicates that the six-hour heat treatment at 650°C accelerated corrosion of 316L stainless steel sharpened edges. This accelerated corrosion was likely due to the sensitization of the 316L stainless steel in which the chromium atoms present in the stainless steel form chromium carbide precipitates at the grain boundaries. This diffusion results in a chromium-depleted region around the grain boundaries which leaves the material susceptible to intergranular corrosion. Visual analysis did not show any obvious changes to the radius of curvature of the sharpened edge. The expected outcomes of the degradation behavior of case-hardened 316L steel are that the increase in carbon diffused into the edge of the sample will result in localized accelerated corrosion at the sharp edge. It is expected that degradation will continue to be accelerated in oceanwater and in cell culture media due to the presence of chloride ions in both solutions. It is expected that the degradation products of the corroded 316L will likely not result in a significant change in cell viability.

HUNTER MALINOWSKI

COMPUTER SCIENCE & PSYCHOLOGY

Assessing the Effectiveness of the XAI Discovery Platform and Visual Explanations on User Understanding of AI Systems

Introduction

Artificial Intelligence (AI) and Machine Learning (ML) are playing an increasingly important role in our lives, including determining what we see on the internet, how the government interacts with us, and how companies assess risk regarding potential customers. Although AI has the potential to enhance our lives, there is a risk that it will also reinforce existing inequalities and prevent access to resources in unjust ways. Current AI systems are becoming increasingly complex, which has led to the development of eXplainable AI (XAI), aiming to explain AI systems to various stakeholders. In this study, we aim to find out if explanatory saliency maps, in conjunction with The Discovery System, will lead users to have a better understanding of AI systems.

Materials and Methods

Thus far, the development of the visual explanations has been the main focus of interest and presented quite a challenge due to the inconsistencies between different programming languages and libraries. When we reach the user-testing phase, we will conduct an online study to test the effectiveness of the saliency maps on the Discovery Platform. Participants will be recruited from Michigan Technological University and receive no compensation. The study will include a training portion, followed by questions to determine understanding and retention, followed by an assessment of usability. It will be a between-subjects design, with the control group receiving the platform without the addition of the visual explanations.

Results and Discussion

The study will have two main benefits. First, it will demonstrate whether enabling a user to explore patterns within an interactive browser can be an effective way of enhancing transparency and understanding. Second, it will demonstrate whether a commonly used visualization technique will lead to enhanced effectiveness over and above the interactivity. Although our study will use a commonly used imagery database, this can have important implications for other domains (credit ratings, loan recommendations, facial recognition) and for justice, equity, and fairness. Furthermore, it will provide practical approaches for enhancing overall usability and usefulness for developers and users of other AI systems.

LAUREN SPAHN

CHEMICAL ENGINEERING '22

Lauren conducted research under Dr. Rebecca Ong related to lignin separation for PU foams. In lieu of presenting at the Undergraduate Research Symposium (below), Lauren presented at the American Institute of Chemical Engineers (AIChE) Undergraduate Student Poster Session.

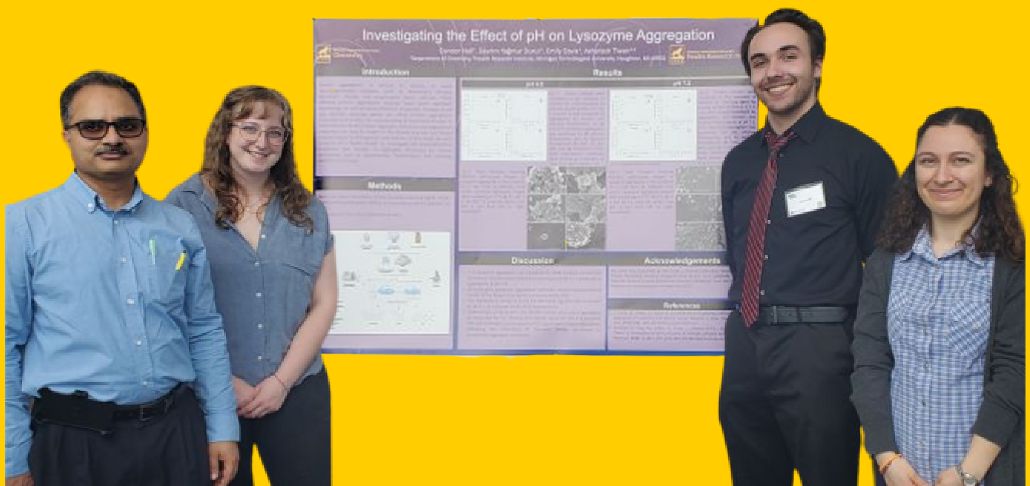
Pictured left, Lauren won an award: 2nd place in the category of Materials Engineering and Sciences IV.

Spahn L‡*, Andeme Ela RC**, Ong RG. Optimization of Lignin Precipitation with Functional Group Control for Use in Bio-Based Polyurethane Foams. AIChE Undergraduate Poster Session – Materials Engineering and Sciences IV Division.

AIChE Annual Student Conference. Boston, MA. November 8, 2021

Symposium

After taking a virtual hiatus, the Undergraduate Research Symposium returned in March 2022. The purpose of the symposium is to highlight the cutting-edge research conducted on Michigan Tech's campus by some of our best and brightest undergraduates. Presenting students represent a wide array of scientific and engineering disciplines across campus and highlight the diversity of research areas being explored, including the above two with URIP support from The DeVlieg Foundation.



GRADUATE SUMMER RESEARCH FELLOWSHIPS

In addition to promoting undergraduate students beginning their journey in academic research, The DeVlieg Foundation's generous support has provided opportunities for graduate students pursuing research in engineering, wildlife, and biology. Applications are evaluated by a panel of faculty representing each of Michigan Tech's colleges - a group who understand the impact and significance of the proposed research.

This year, your gift was combined with partial matching funds from the Graduate School to make an additional award to an outstanding applicant. As a result, three summer research award recipients were selected:
Brennan Vogl, Emily Shaw, and Samuel Hervey.

BRENNAN VOGL

BIOMEDICAL ENGINEERING

I am a second-year PhD student in the Biomedical Engineering department. I started my undergraduate degree at Michigan Tech in 2016; I enjoyed my time here so much I decided to come back to become a PhD student in the Biofluids lab in 2021. My field of research is cardiovascular hemodynamics - the study of how blood flows through the cardiovascular system. I work with physicians to investigate how cardiovascular diseases (aortic stenosis, hypertension, mitral regurgitation, etc.) can alter the blood flow of the heart.

I am immensely grateful for the support provided by The DeVlieg Foundation and Graduate Dean Awards Advisory panel. With their help, I was able to spend the summer investigating changes to left atrial flow dynamics in patients with atrial fibrillation (AF) and who have received treatment for AF. I am hopeful that this research will provide a basic engineering framework to conduct computational simulations of AF and improve the clinical knowledge to provide the best therapy possible for patients with AF.

The DeVlieg Foundation Fellowship awarded to Brennan had tremendous impact on our research work this summer. We managed to develop a computational framework to study the flow dynamics pertinent to atrial fibrillation starting from patient-specific data to the generation of the digital models, to the completion of the flow simulation ending in the analysis of the data and correlating them with clinical outcomes. The DeVlieg Foundation award allowed Brennan to focus on the study related to atrial fibrillation, particularly the left atrial appendage closure problem. We successfully generated preliminary data for an ongoing grant, and had abstracts accepted in two major clinical and engineering conferences: Transcatheter Cardiovascular Therapies (TCT 2022) and Biomedical Engineering Society (BMES 2022), respectively. This award has given us the opportunity to lay the foundation for larger studies in collaboration with multiple clinical sites such as Mayo Clinic, Aarhus University Medical Center and Copenhagen University Hospital.

-Dr Hoda Hatoum

Introduction

Atrial fibrillation (AF) is the most common arrythmia that can cause cardioembolic events. Blood stagnation or stasis that occurs in the atrium is associated with thrombus development, and often occurs in the left atrial appendage (LAA) (Figure 1A). A common prevention method for LAA related cardioembolic stroke, is occlusion of the appendage using the WATCHMAN device (Boston Scientific Corporation, St. Paul, Minnesota) (Figure 1B). Although this device has shown improved long-term outcomes, studies have also shown that 3.74% of patient's develop device related thrombosis (DRT)1. This can potentially lead to strokes. The factors leading to DRT are still unclear despite several clinical studies investigating potential predictors for DRT2. The aim of this study is to evaluate the hemodynamic profiles of the left atrium (LA) in patients who have received a WATCHMAN device, and to identify potential predictors for DRT. We hypothesize that DRT is more likely to occur in patients where the LA hemodynamic profiles drastically change between pre- and post-implantation, and when the LAA is not fully occluded by the device.

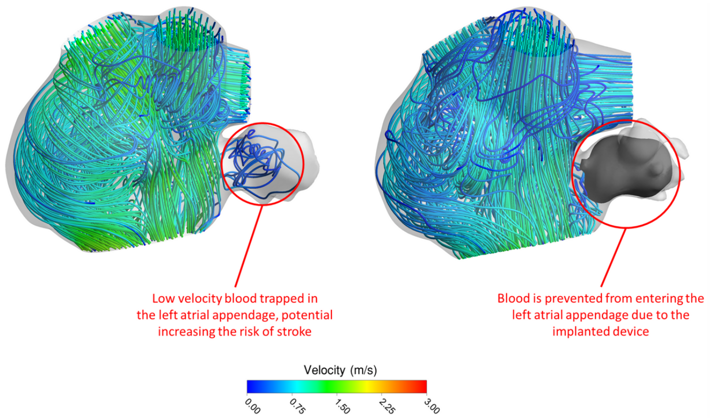


Figure 1

Materials and Methods

Contrast-enhanced computed tomography (CT) and echocardiographic (ECHO) images of patients pre and post device implantation with DRT and without (control group) were used. The datasets included full cardiac cycles, and ECHO data of the mitral valve (MV), pulmonary veins (PVs), and LA. The CT images were imported into Mimics Research 23.0 (Materialise, Belgium) and segmented to generate patient specific 3D digital models. Finite element analysis (FEA) performed by FEops (Gent, Belgium) was used to deploy the WATCHMAN in the patient digital model. The digitally implanted devices were deformed and positioned in the LAA to replicate the size and location of the device seen in each patient's post-CT images. Mitral valve velocity curves taken from ECHO, were used as boundary conditions (BCs) and the model was validated from the PVs ECHO data. Computational fluid dynamic (CFD) simulations were performed on the patient specific models (pre- and post- device implantation) using Ansys Fluent (Canonsburg, PA). The simulations used a laminar flow model with a fluid type of blood. The BCs for the PVs were set to pressure inlets with 0Pa total pressure and reverse flow was prevented. No slip boundary conditions were imposed on the LA surface and LAA occlusion device. A velocity inlet BC was used for the MV, with the velocity magnitude determined from the patient specific ECHO data. The velocity streamlines, wall shear stress (WSS), and vortex structures in the LA and LAA, before and after device implantation, are to be assessed using Ansys CFD Post (Canonsburg, PA). A schematic of the overall workflow used is shown in Figure 2 below.

Results and Discussion

LAA occlusion (LAAO) device maximum WSS was lower for the DRT patients (1Pa and 0.45Pa) than the control patients (2.5Pa and 4Pa) (Figure 3). Determining the physiological threshold of WSS on these devices is important because, low WSS levels have been associated with regions that are more prone to thrombus formation3. Interestingly, atrial WSS values remained the same between pre and post device implantation for all patients. An increase in atrial velocity from pre- to post-implantation was observed in only the control patients.

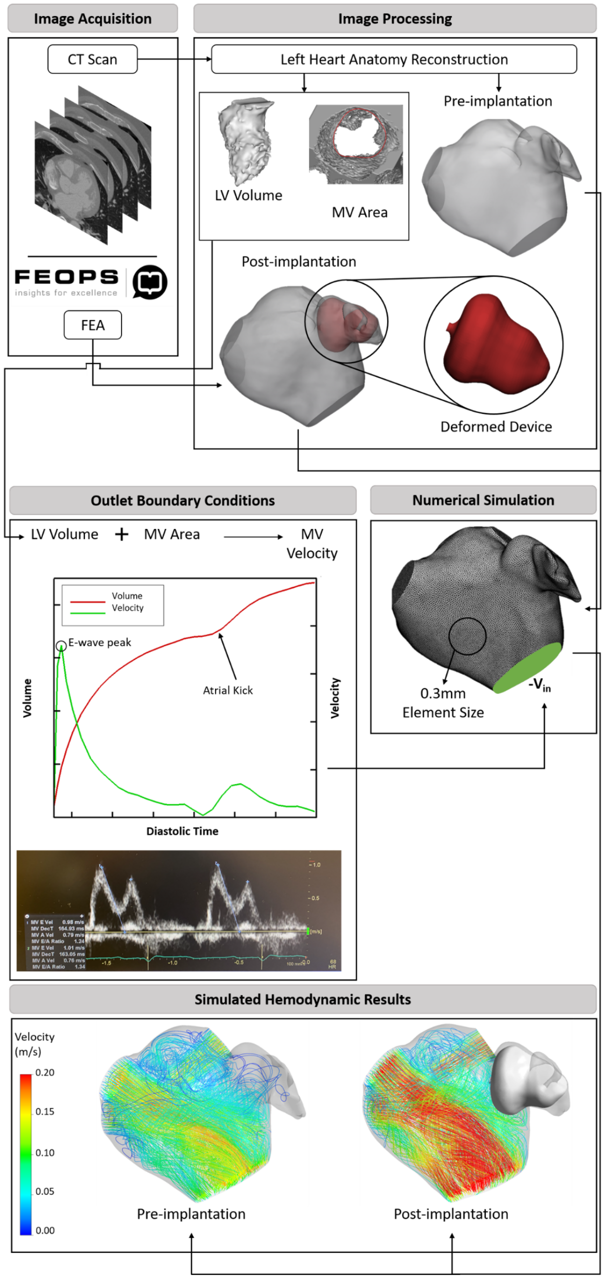


Figure 2

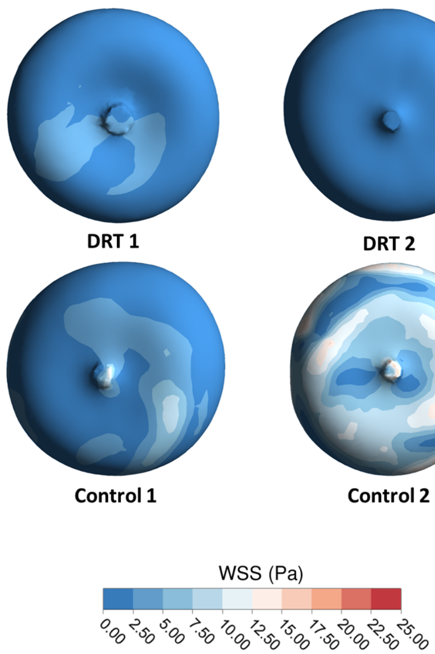


Figure 3

Conclusion

These preliminary results show the feasibility of using an FEA/CFD combined approach to model atrial hemodynamics after LAAO while emulating deployment in-vivo. The current hemodynamic parameters (WSS and atrial velocities) show a difference between patients who did and did not develop DRT. In addition, the inclusion of more parameters may elucidate new predictors for DRT. We are currently working to process more patients to further our understanding of DRT before seeking publication of this work. This work will be presented as a moderated poster at the Transcatheter Cardiovascular Therapeutics (TCT) conference and the annual Biomedical Engineering Society (BMES) conference this fall.

EMILY SHAW

ENVIRONMENTAL ENGINEERING

Emily Shaw is a settler scholar living and working within the Anishinaabe Ojibwe homelands of Northern Michigan. Currently, Emily is a PhD candidate at Michigan Technological University in environmental engineering doing research that bridges knowledge systems to understand mixture toxicity. As an indiginist researcher, her work rebuilds systems of accountability and responsibility between humans and the environment that are aligned to Anishinaabe philosophies.

Prior to graduate school, Emily earned a bachelor's degree in public affairs from Indiana University in Bloomington, IN. For four years, she was the Education and Volunteer Coordinator at Inland Seas Education Association, a non-profit in Suttons Bay, MI with a mission to inspire a lifetime of Great Lakes curiosity, stewardship, and passion in people of all ages. In the two years leading up to graduate school she spent most of her time in Antarctica washing dishes at the South Pole research station, then hiking and sailing throughout New Zealand. Now she enjoys exploring Houghton, playing roller derby, and gardening.

The DeVlieg Fellowship in summer 2022 enabled Emily to push forward our research on mixture toxicity and protocols for collaboration with Tribal Nations. My research group embarked on the topic of mixture toxicity several years ago. Most of the research is still experimental, with lower organisms and simple mixtures of chemicals. Emily chose an ambitious topic: the effects of chemical mixtures of bioaccumulative toxics in fish on humans. Emily has not only tied together the national mapping and statistical analyses of toxic contaminants in fish, but has really pushed forward the theoretical framework based on her understanding of both biochemical toxicology and risk assessment. We are now preparing for publication of this work in a high-visibility journal. Through her extensive dialogues with Keweenaw Bay Indian Community (KBIC), Emily has clarified to us the perspectives and research needs of the tribe on this topic. [...] In summary, Emily's work supported by The DeVlieg Foundation has led to a major scientific advance, it has facilitated continued collaborative work with KBIC, it has opened the door for future collaborative research funding, and it has influenced the direction of research for three beginning doctoral students.

-Dr. Noel R. Urban

Bogged down by detail, toxicity resulting from exposure to chemical mixtures has long been recognized as a concern (e.g., Rall 1974); defining terms and building consensus on what are and are not reasonable assumptions continues to be immensely complicated. Such complications are present in both the scientific and policy pursuits of exploring and defining mixture and combined toxicity. In the US, for decades, EPA guidelines pertaining to chemical mixtures tried to offer unifying focus areas and terminology but are thought to have been largely ineffective (Sprinkle and Payne-Sturges 2021). A recent review shows that narrow considerations of mixtures continue; most mixture toxicity studies consider relatively few compounds from relatively few numbers of compound classes (Martin et al. 2021).

Rather than continue to consider chemical contamination as singular exposures with singular toxic effects, this work quantifies mixture and combined toxicity for humans based on simultaneous exposure to PCBs, dioxins, furans, and mercury via fish consumption. The primary hypothesis of this work is that combined toxicity more accurately represents risk than does individual contaminant or mixture toxicity. Our research questions ask why should we quantify the mixture and combined toxicity of exposure to PCBs, dioxins, furans, and mercury? and what constitutes an effective strategy for quantifying mixture and combined toxicity of chemical mixtures? Understanding the nuances of toxicity defined by different frameworks will advance the conversation about mixture and combined toxicity by sharing a comparison of toxicity frameworks for legacy contaminants.

To quantify toxicity, measured fish tissue concentrations were normalized to threshold concentrations to establish unitless descriptors of toxicity called hazard quotients (HQs; equation 1). Summed together, the individual HQs create a hazard index to represent mixture toxicity. The threshold concentrations were calculated based on reference doses (RfD) for specific toxic endpoints (Table 1), body weight (70 kg), and the EPA-defined subsistence fish consumption rate (143.3 g/day; equation 2).

$$hazard\ quotient = \frac{measured\ concentration}{threshold\ concentration} \quad \text{Equation 1}$$

$$threshold\ concentration = \frac{RfD \times body\ weight}{fish\ consumption\ rate} \quad \text{Equation 2}$$

Three different toxicity frameworks – most recent RfDs, most sensitive RfDs, and shared reproductive system RfDs – were used to compare the magnitude and relative contributions of the toxic contribution from five different compound classes. For each of the three frameworks, most of the fish samples (> 90%) had HQtotal > 1; none of these scenarios demonstrate safe fish consumption when combined toxicity is considered. Benthivorous fish are significantly more toxic than predator fish (ΣHQbenthivore = 15 and ΣHQpredator=6; $P<0.001$), and mercury toxicity is most important in predator samples while bottom-dwellers are dominated by the hydrophobic compounds. Toxicity based on the most sensitive endpoint is significantly higher for both benthivores and predators ($P<0.001$) than that based on the shared reproductive RfDs. Under the sensitive framework, predator fish are twice as toxic as benthivores, with most toxicity (86%) resulting from mercury contamination. For benthivores, the sensitive framework shows non-dioxin-like PCBs contribute 40% of mixture toxicity while mercury contributes 25%. This breakdown is markedly different from the mixture toxicity based on the most recent RfDs where dioxin-like PCBs, dioxins, and furans are responsible for 92% of toxicity in benthivores and 39% of toxicity in predators. Geographic-weighted regression (GWR) to predict lake water quality suggests some of the variance in mixture toxicity is based on lake and watershed characteristics. Understanding these relationships and the complexity of quantifying mixture toxicity will facilitate improvements in managing risks associated with fish consumption. This work emphasizes the validity of combined toxicity as a reasonable and necessary framework for establishing safe fish consumption guidelines (FCGs). Currently, FCGs as a risk mitigation strategy grossly underestimate the actual hazard associated with fish consumption.

SAMUEL HERVEY

FOREST SCIENCE

I am a PhD student in the College of Forest Resources and Environmental Science. My main research interest is wildlife conservation and how we can utilize noninvasive methods to study and inform management of wildlife. For my PhD research, I am developing multiple noninvasive genetic methods to study the health of the recently introduced wolf population on Isle Royale.

Over the summer semester and with the support of The DeVlieg Foundation, I worked to optimize a set of molecular markers that will help us track the number of wolves occupying Isle Royale, as well as the level of inbreeding within the population. With this information, we can better understand the health of the wolf population through time and assess whether interventions may be necessary. I cannot thank The DeVlieg Foundation and the Graduate Dean Awards Advisory panel enough for their support.

Sam Hervey is an exceptional PhD student and The DeVlieg Fellowship provided Sam the opportunity to focus exclusively on research throughout the summer. Given Sam's research focus he was able to advance several important Brzeski Lab research initiatives. These included developing a new assay to track Isle Royale wolf genetic health and to assess the genetic variation of Michigan's gray wolf populations more broadly. These projects are helping move wolf conservation and management forward in the region and continuing the long history of Michigan Tech being a center of excellence for wolf research.

-Dr. Kristin Brzeski

RESEARCH SUMMARY | SAMUEL HERVEY

Thanks to the support of The DeVlieg Fellowship I have been able to accomplish many research objectives, over the summer. My main research objective focused on testing a novel noninvasive method that will help track the number of wolves occupying Isle Royale as well as the level of inbreeding within the population. By understanding how many individuals are on the island and using assignment of relationships to construct a pedigree, we will be able to better understand the health of the wolf population and if future interventions may be needed.

The noninvasive method we are testing is a set of molecular markers that allow us to individually identify wolves and the relationships between them from the DNA they leave behind, in their scat. Since 2018, over 600 wolf scats have been collected on Isle Royale and have had DNA extracted allowing us the sample size needed to address both individual identification and assignment of relationships.

Because DNA extracted from scat tends to be lower in quality, we first wanted to test the molecular markers we designed on DNA coming from higher quality sources such as blood and tissue. We tested our method on high quality samples using multiple replicates to assess error. Overall, the molecular markers are performing as expected and with an error rate of 0.04%, well below other common molecular methods.

From the high quality wolf DNA we have analyzed so far, we determined there are two breeding pairs currently on Isle Royale. The first breeding pair is located on the East end of Isle Royale, and we have identified five of their offspring, while the other breeding pair is located on the West end and we have identified two of their offspring. We are excited with the initial results we gathered from high quality DNA and will be able to generate a more complete understanding of the Isle Royale wolf population once DNA from scat is included in the analysis.

Our next steps are to test the molecular markers on DNA extracted from scat samples to make sure it is performing at an acceptable level. Then we can begin analyzing the 600+ scat samples we have extracted DNA from to estimate the number of wolves currently occupying Isle Royale as well as reconstructing a pedigree to determine if any inbreeding events have occurred.

In addition to my main research objective focused on optimizing the noninvasive molecular method for Isle Royale wolves, I have also been studying the genomic health of Great Lakes wolves. To do this, over 500 wolf samples coming from Ontario, Minnesota, Wisconsin, and Michigan were compiled and used for genomic analyses. We compared a suite of genomic health metrics to understand how different states and provinces may differ. Preliminary results suggest that Ontario and Minnesota have served as source populations for Wisconsin and Michigan wolves as they have been recolonizing over the past couple of decades, but overall appear to share similar levels of genomic health metrics.

The research questions on Isle Royale and the Great Lakes regions are absolutely vital when making management decisions about wolf populations and because of the financial assistance provided by The DeVlieg Fellowship I was able to pursue these questions over the summer.