Faculty of Medicine Multidisciplinary Research Program in Medicine Evaluation Report

2023 Program

THE UNIVERSITY OF BRITISH COLUMBIA

Faculty of Medicine Multidisciplinary Research Program in Medicine Evaluation Report

Prepared on November 7th, 2023

for Faculty of Medicine Office of Research

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Program Overview

Program Description

The Faculty of Medicine Multidisciplinary Research Program in Medicine (FoM MRPM) provides undergraduate students with an opportunity to explore their interest in interdisciplinary and multidisciplinary research by undertaking a summer project supervised by a cross-faculty pair of researchers based on the success of the University of British Columbia at Okanagan's Multidisciplinary Undergraduate Research Projects in Health (MURPH) program.

The goal of the program is to pair researchers across faculties with undergraduate and MD students for the purposes of conducting multidisciplinary/interdisciplinary research. With this goal in mind, successful primary supervisors from the Faculty of Medicine (FoM) and co-supervisors from across UBC are matched with two non-MD undergraduate students and an optional MD student for their research project. Undergraduate and MD students conducted 16- or 8- weeks of full-time research, respectively over the summer of 2023. A Postgraduate Student Advisor was assigned by the supervisors to spearhead training and oversight on the project and gain valuable supervisory experience.

Objectives

As with our past years' objectives, this program primarily aims to provide unique funding opportunities to collaborate across disciplines, in-line with overall FoM strategic plan, and to provide training and professional development to UBC undergraduate students. Specifically, these student learning objectives include:

- Networking and collaborating with supervisors and students across typically siloed disciplines
- Fostering scientific communication skills including opportunities to give a research conference presentation
- Developing concrete research skills that will have a meaningful impact on future student success and further important research goals

"The program is essential in keeping undergraduate and medical students part of the lab and is vital for education/training."

"This program not only supports important research in medicine but provides undergraduates with an incredibly valuable learning experience."

-MRPM Supervisors

Approach

Application Process

Supervisors and students applied for the MRPM program separately with staggered deadlines. Supervisors first submitted project applications by January 27th, 2023. For the summer 2023 round,10 projects were funded (see Table 1 for application vs funded project numbers). Supervisor applications required a FoM-appointed primary supervisor to collaborate with a non-FoM co-supervisor and choose a

postgraduate student advisor to help supervise the project. Along with contact details, supervisors were required to write a project summary and benefit to the student statement for review. These statements were packaged and sent for adjudication to a panel of researchers to score (see Table 2 for adjudicator scoresheet). Project applications were ranked based on adjudicator scores and the top projects were chosen for funding. Project information was then added to the website and to the student application form for students to apply directly to funded projects.

Student applications closed March 24th, 2023. We received 75 student applications. Along with contact details, students were required to give a student statement as to why they wanted to be considered for this program/project and uploaded a current, anonymized CV. Students were deemed eligible if they were a current UBC student in Year 2+ for non-MD students and in Year 1 for MD students. Students were also asked to self-identify as an Indigenous student or a student with a disability to be automatically entered to receive the Faculty of Medicine Multidisciplinary Research Award for Excellence. Project supervisors were given an anonymized list of eligible students (and their student statements and CVs) to interview. Supervisors rank ordered their top five students non-MD students and top 3 MD students from the list and were assigned 2 non-MD students and 1 MD student (optional) based on all other rankings with 24 students being funded. Students were notified in mid-April, 2023. Non-MD students started the program as early as May 1st, 2023 and MD students started the program as early as June 5th, 2023.

Table 1. Total number of project and student applications and funded awardees for the 2023 MRPM Research Projects

	Applications	Funded
Supervisor	**14**	**10**
Student	**75**	**24**

"Students gain valuable independent learning and critical thinking skills, outside the formal framework of their undergraduate/medical programs."

"We thrive on the energy that students bring, and the increased productivity to activities such as recruitment, data collection and analysis."

"This is an amazing program creating fertile and supportive environments to learn how fun, rewarding and meaningful a career in research can be."

-MRPM Supervisors

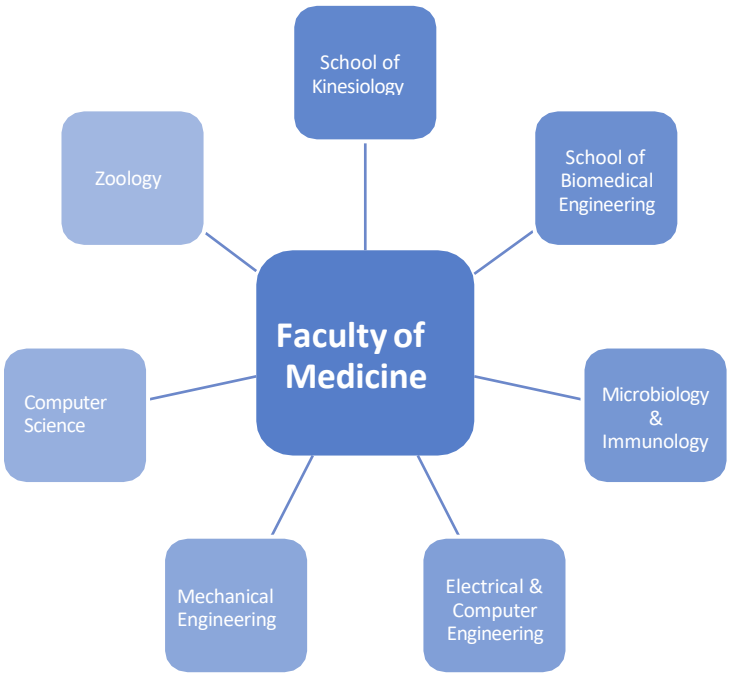
Table 2. Adjudicator scoresheet.

Criterion	Points	Notes
Project Summary The project must be based on a clear and testable research question(s) or hypothesis. Projects not meeting this requirement are not eligible for the FoM MRPM.	**60 points**	This section should address the scientific merit and feasibility of the proposed project. Considerations when scoring this section include: • Clear interdisciplinary/multidisciplinary focus • Clear rationale for the proposed research approach and methodology, including the context within the relevant field of research. • Clear and testable research question or hypothesis. • Feasibility of the research approach including the project timeline. • Expected project outcomes.
Benefit to the Student Students should benefit from their involvement and come away with new knowledge, new skills, and a better understanding of what interdisciplinary/multidisciplinary research entails.	**40 points**	This section must address how involvement in this project will help the student gain an understanding of how high-quality research is conducted. This includes addressing the opportunities to learn new skills (or develop existing skills) in the context of the following learning objectives (**as applicable – not all will be applicable to all projects**). As a result of their FoM MRPM experience the student will gain an understanding of: • How to generate testable research questions and/or hypotheses • How to critically evaluate & analyze existing literature/data • The principles of experimental design • The ethical principles of research • How to critically analyze data; appropriate statistical analyses • Effective scientific communication (such as • presentations, manuscripts, guidelines, patient learning materials, etc.) • Specific techniques/skills required for the project (of lesser importance in scoring than the above learning objectives) Additional considerations when scoring this section: • The student's learning objectives and role are clearly defined. • The fulfillment of additional learning objectives (not discussed above) related to the conduct of medical research. • Student has the opportunity to interact with and learn from other researchers (will help the student gain a broader understanding of what research entails). • The project has strong research and educational merit. • The project can be completed in the time available.

Supervisors

10 FoM supervisors and 10 non-FoM co- supervisors were a part of the 2023 FoM MRPM. Primary supervisors were required to hold a FoM appointment. Co-supervisors were required to hold appointments outside of the FoM (see Figure 1 for co-supervisor disciplines). There were no restrictions on the co-supervisor's Faculty or Department except that they could not be primarily appointed by the FoM. The only exception was that co-supervisors could be appointed through the School of Biomedical Engineering. This was to encourage collaborations across faculties and departments and facilitate multidisciplinary/interdisciplinary research. These co-supervisors were from the School of Kinesiology, Department of Microbiology and Immunology, Department of Electrical and Computer Engineering, etc. (see Figure 1 for full list of co-supervisor disciplines).

Figure 1. Disciplines involved in the 2023 FoM MRPM



Undergraduate Students

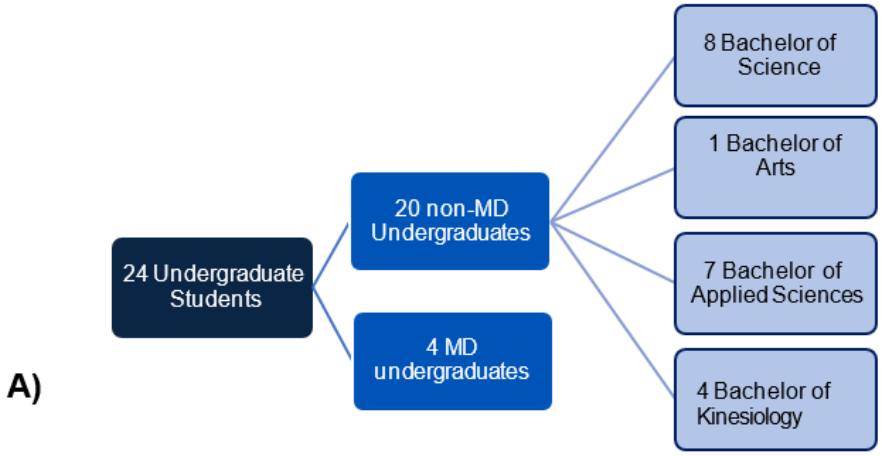
A total of 24 students were appointed to the FoM MRPM program for summer 2023. Two upper year non-MD undergraduates (years 2+ of their program) were assigned to each of the 10 funded research projects and four first-year MD students were assigned to four research projects (based on supervisor interest; see Figure 2A for program breakdown). We also asked additional self-identifying demographic information to better understand our student awardees. Of the 24 student awardees, 13 identified with she/her/hers pronouns and 11 students identified with he/him/his pronouns (Figure 2B). Additionally, 1 student self-identified as a person with a disability (Figure 2C), and 15 self-identified as a visible minority in Canada (Figure 2D).

"Thank you so much for giving me this opportunity to gain a deeper understanding of interdisciplinary research and the power I have to develop solutions to the large problems we have in the world. It has been incredibly valuable for me to be paired with such knowledgeable mentors in the lab I work in and I am thankful to have learned so much from them."

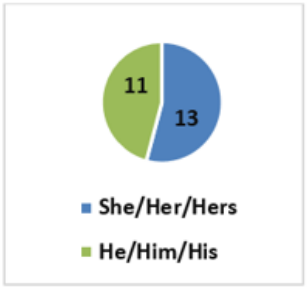
"Thank you for providing opportunities for undergraduate students to explore academic research. I am very grateful for the experience provided by the external donors of the FoM MRPM and I feel that it has positively impacted me and has made me more certain about my future goals in research."

-MRPM Students

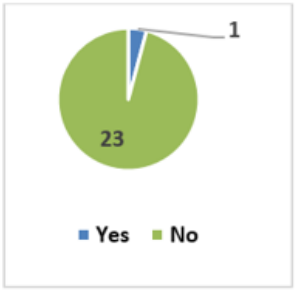
Figure 2. A) Number and program of student awardees. B)-D) Student demographic information



A)



B) Student preferred pronoun



C) *"Do you identify as a person with a disability as described in the Accessible Canada Act?"*

D) *"Do you identify as a member of a visible minority in Canada?"*

Funding

Funding was provided for research projects in the form of student stipends. Non-MD Undergraduates received at least $8,400 for 16- weeks of full-time research. Of this total, $6,000 was provided by the FoM with supervisors contributing at least $2,400. MD students received $3,200, all of which was provided by the FoM. The total funding amount for this program was $189,685 (see Table 3 for breakdown). Funding was derived from a combination of FoM endowments and supervisor contributions.

Table 3. Funding breakdown for the 2023 MRPM

Total Program Funding	Total Internal Funding	Total Supervisor Contributions
$189,685	$135,200	$54,485

"Thank you for providing this opportunity for our group to establish new research collaborations. The MRPM was a catalyst for us to explore new interdisciplinary projects."

"The funding to this program allowed us to work on an important project and provide a rich learning experience to undergraduate students - we are very appreciative!"

-MRPM Supervisors

Workshops

Workshop Overview

Workshop 1

The theme of this workshop was multidisciplinary research. During the first part of this workshop, students introduced themselves and their research project to the group to get to know each other and the scope of research being done for the project. We were also honored to have Dr. Ilker Hacihaliloglu, Assistant Professor Radiology, Faculty of Medicine at UBC, give an inspiring talk on multidisciplinary research. Finally, we had a question and answer session with the Postgraduate Student Advisors to share their graduate school, career, and research experiences with the MRPM students.

Workshop 2

The theme of the second workshop was research communication. Here, Dr. Kaylee Byers from SciCATS, gave a workshop on effective research communication to students. Dr. Byer's workshop also included tips on creating a poster presentation in preparation for student research project presentations. Finally, we provided information on the upcoming third workshop, the student research conference.

Workshop 3

The third workshop was the student research conference. Students built a one-slide poster-like PowerPoint presentation and gave 5-minute presentations on the results of their summer research project to the group with up to 2-minutes of questions from their peers. Students evaluated each other's

presentation and the highest scoring presentation won best presentation and received a certificate of award (see Appendix 1 for winning presentation).

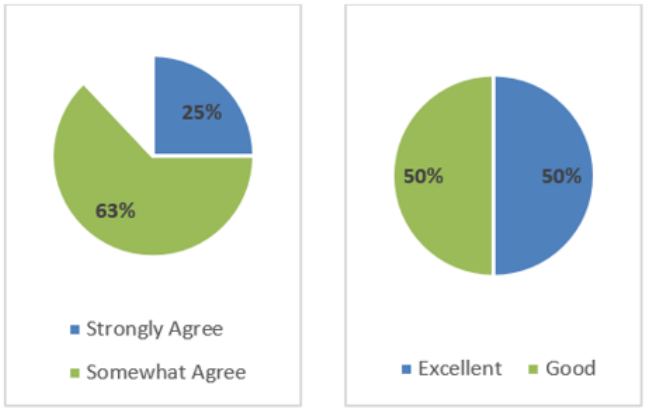
Workshop Evaluation

To improve future workshops and evaluate the success of the current workshop series we disseminated evaluation surveys for student feedback following each workshop. Students were required to attend these three workshops and so besides one or two absent due to illness or previous plans, all students were in attendance either virtually or in- person. Students rated their experience with the individual workshops and with the workshops overall. We had positive feedback from all three workshops, with students rating their satisfaction with all three workshops as good to excellent (see Table 4).

Table 4. Evaluation breakdown by workshop

Workshops	Percentage of students agreeing that the topic chosen was a good topic for the workshop	Percentage of students agreeing that the overall satisfaction with the workshop was good to excellent
Workshop 1: Multidisciplinary Research & Graduate School Q & A	**72%**	**89%**
Workshop 2: Research Communication Workshop	**100%**	**92%**
Workshop 3: Student Research Conference	**100%**	**87%**

Figure 3. A)-B) Student responses to prompts shown in figure



A) *"Including all three workshops in the summer research program was helpful or informative"*

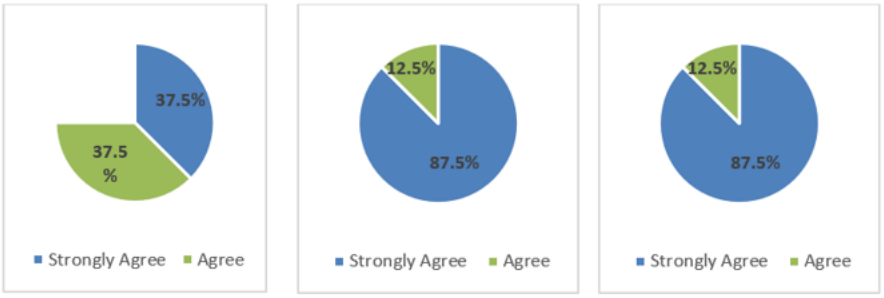
B) *"Overall satisfaction with all three workshops was good or excellent"*

Program Evaluation

Supervisor Feedback

Supervisors and undergraduate students evaluated this year's program and provided feedback for improvement. We received mostly positive feedback with all strongly agreeing that this will generate future research and that they believe this has the potential to be included in a publication. Also, 75% say this has the potential to positively impact policy, clinical practice, and/or healthcare delivery (Figure 4A). Furthermore, all supervisors said this was a positive experience (Figure 4B) and plan on applying in future years (Figure 4C).

Figure 4. Supervisor responses to the prompts in figure



A) *"The results have the potential to positively influence policy, clinical practice and/or health care"*

B) *"My overall FoM MRPM experience was positive"*

C) *"I plan to apply to the FoM MRPM in future years"*

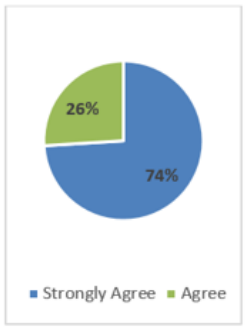
Undergraduate Student Feedback

Students also evaluated the program and provided feedback. We again received mostly positive feedback with 100% of students saying that this will generate future research and/or positively influence policy, medical education, clinical practice and/or health care delivery (Figure 5A), 95% of students agreed that they were given the opportunity to interact with and learn from other researchers in addition to their supervisor (Figure 5B), 100% of students rated their overall FoM MRPM experience as positive (Figure 5C), and 95% would recommend the FoM MRPM to other students (Figure 5D). Furthermore, this program has facilitated ongoing research opportunities for students with 79% of students agreeing that they will continue working on this project after the FoM MRPM funding ends (Figure 5E) and 89% of students agreed that participating in the FoM MRPM provided insight into potential career goals (Figure 5F).

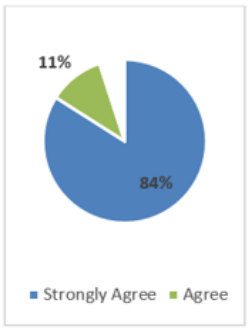
"Thank you for giving undergraduate students like me the opportunity to carry out such interesting and rewarding projects with world-class researchers over the summer. I have learned lots and also had great fun throughout the entire process."

-MRPM Student

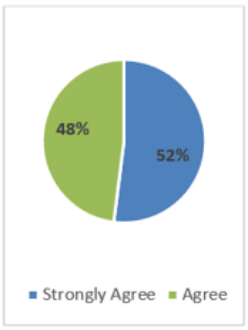
Figure 5. Student responses to the prompts in figure



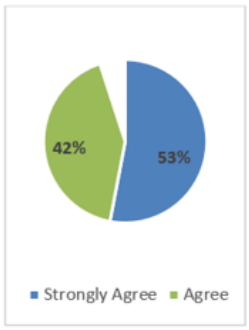
A) *"The study will generate future research and/or positively influence policy, medical education, clinical practice and/or health care delivery"*



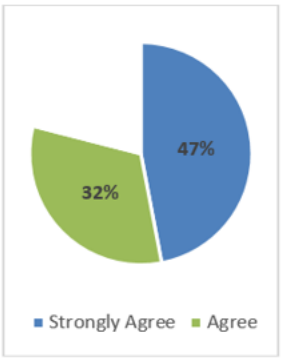
B) *"I was given the opportunity to interact with and learn from other researchers in addition to my supervisor"*



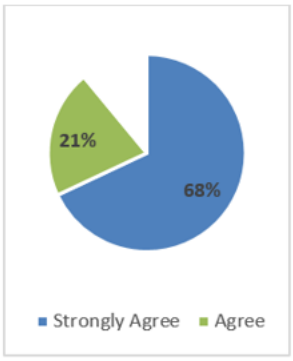
C) *"My overall FoM MRPM experience was positive"*



D) *"I would recommend the FoM MRPM to other students"*



E) *"I will continue working on this project after my FoM MRPM funding ends"*



F) *"Participating in the FoM MRPM provided insight into potential career goals"*

"This type of scholarship is so critical to catch and encourage budding scholars at a young age."

"The student involvement was important as they were the key connections between the two research labs. The students bring in their own expertise, gain new skills, and help us build a vibrant research culture."

"This is a great program. Huge cost savings to PI and applicants are always bright and motivated."

-MRPM Supervisors

Appendix 1: Example winning poster Student Research Conference

Exploring techniques used to elicit and record optimal pudendal nerve somatosensory evoked potentials in able-bodied controls

Jason Anasori*[1,5], Lauren A Platz*[2,5], Meghan Henry*[3,5], Alison MM Williams[1,5], Lukas D Linde[4,5], John LK Kramer[4,5], Tania Lam[1,5]
[1]School of Kinesiology, UBC; [2]Department of Biology, UBC; [3]Faculty of Medicine, UBC; [4]Department of Anesthesiology, Pharmacology & Therapeutics, UBC; [5]International Collaboration on Repair Discoveries (ICORD)

Introduction

- The pudendal nerve innervates pelvic floor muscles controlling urinary, genital, and bowel functions
- Somatosensory evoked potentials (SEP) may be used to evaluate the integrity of ascending sensory pathways in people with neurological injuries
- The optimal techniques to conduct pudendal nerve SEP has yet to be established.

The purpose of this study was to determine the best methodology for eliciting pudendal SEPs and to compare responses between male and female participants.

Methods

- **18 participants**

- SEPs were recorded using EEG
- 600 non-painful electrical stimulations were given:
  - 6 pudendal + 1 tibial configurations in females
  - 4 pudendal + 1 tibial configurations in males

Results

There was no effect of electrode configuration on pudendal SEP amplitude

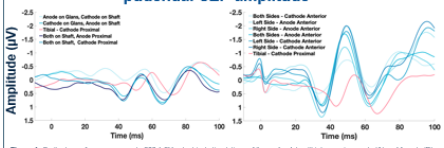


Figure 1: Cortical waveform responses to 600 1-3Hz electrical stimulations of the pudendal or tibial nerve in a male (A) and female (B) able bodied participant. Response was measured midline on the sensory cortex at Cz.

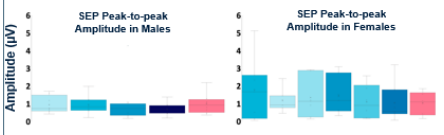


Figure 2: The average peak to peak amplitude (P40-N50) during a SEP of the tibial or pudendal nerve in male (A) and female (B) participants for each electrode configuration. No significant difference in SEP amplitude was observed for the different electrode configurations in male ($p=0.255$) or female ($p=0.555$) participants.

Pudendal SEP was tolerable across all electrode configurations

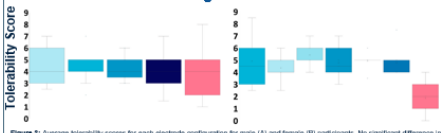
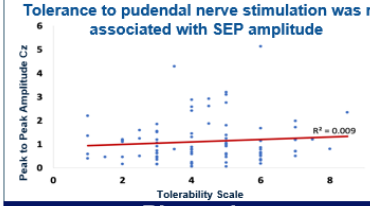


Figure 3: Average tolerability scores for each electrode configuration for male (A) and female (B) participants. No significant difference in tolerability between configurations for male ($p=0.237$) or female ($p=0.790$) participants.

Tolerance to pudendal nerve stimulation was not associated with SEP amplitude



Discussion

✓ Recorded pudendal Cz cortical SEPs

- There does not appear to be an effect of electrode configuration on SEP responses

Future Projects

★ Study these methods in people with spinal cord injuries (SCI)

★ Integrate SEP assessments to evaluate supportive therapies in SCI

Acknowledgments

We would like to thank all of the participants involved in this study for their time and efforts. This study was supported by Blusson Integrated Cures Partnership, Multidisciplinary Research Program in Medicine (MRPM) and Canadian Institute of Health Research.

FACULTY OF MEDICINE icord Rick Hansen Foundation Vancouver Coastal Health Research Institute

Appendix 2: Project Summaries

Machine learning enabled high-throughput single cell isolation for cancer genomics using inkjet printing.

What question(s) does your project aim to address?

Can the integration of computer vision and deep learning prediction into single cell inkjet printing significantly improve throughput, customizability, and speed of cell isolation methods to allow high quality cellular insights?

Project Overview

This project aims to improve and validate the Isolatrix, a single cell inkjet printer in terms of accuracy and quality of insights produced. Following standard library protocols, we follow the procedure: prepare cell suspensions, pass the cells through the inkjet printer, dispense the cells into nano wells, sequence the cells, and perform various bioinformatic analyses. The inkjet printer dispenses cells based on a neural network that predicts dispensing events that have occurred given the prior images.

One student worked primarily on bioinformatic and imaging analyses to verify the Isolatrix. This includes creating image annotation, image segmentation and image tracking software applications using Deep Learning on nozzle output images on High Performance Computing clusters. He also extracted morphological features from tracked images and ran comparisons against copy number and ploidy analyses from wells. In addition, he assessed the current strategy of prediction and summarized various instances of weaker performance. Finally, he proposed various changes to the strategy involving performant instance segmentation to correctly model the number of cells dispensed at a time.

Another student worked on improving the accuracy of the neural network in predicting cell dispensing events. This involved labelling and ensuring the accuracy of the current set of training and testing neural network images and labelling new data with different cell lines. Additionally, Taylor used some pre-trained models that are widely used for image recognition to try to create a comparison test of the Isolatrix neural network. Secondly, Taylor worked on the mechanical body of the Isolatrix. This included testing out a chip cooling assembly to prevent evaporation in the chip, redesigning the door of the Isolatrix to allow for easier loading of the machine, and testing the accuracy of the stage.

The third student's primary work was to ensure that there was enough cells to run printing tests on the Isolatrix at a regular interval. His tasks included cultivating the various cell lines that were being tested, passaging and freezing cells for future tests and preparing the suspended cell concentration for tests. He also created and wrote protocols for handling the various cell lines and how to prepare them for testing. Kipling also helped Taylor with labelling pictures of cell dispensing events to ensure that there was no errors and less labeler bias in training and test dataset.

Results/Impact

Overall, the Isolatrix has over 90% accuracy in predicting cell dispensing events, with an 86% accuracy in predicting the number of cells dispensed. It fills an entire chip of 72x72 nano wells in around 15 minutes. The instrument outputs high quality sequencing libraries as it correctly models all expected controls at expected mean depth coverage. This work will be able to accelerate the single cell analysis field by offering reduced costs and faster analyses of single cell compositions. Therefore, this allows more organizations to conduct a much closer investigation into clonal population evolution and further investigations into rare clonal sub populations in order to find potential cures and uncover the mutative factors of new emerging diseases.

Towards data-rich, accurate diagnostics at the point of need: Biofunctionalization of multiplexed silicon photonic biosensors

What question(s) does your project aim to address?

In our research, we want to know: how can we address the critical need for accurate, data-rich, quantitative diagnostics in point-of-care settings such as with first responders and in remote & rural communities using silicon photonic biosensors?

Project Overview

Silicon photonics leverages semiconductor fabrication techniques that allow silicon strips called waveguides to be micropatterned in various geometries onto small biosensor chips for very low cost at high volumes. A particular geometry we use is called a microring resonator - a small ring structure formed from these waveguides. Light of specific wavelengths resonates in these rings, creating a characteristic transmission spectrum with sharp peaks known as 'resonance peaks'. When a target molecule (such as a viral protein) binds to the surface of the microring, it leads to a change in the ring's refractive index, which, in turn, leads to a shift in those resonant peak wavelengths. This shift in wavelength can be used to detect, analyze and quantify specific binding reactions when a sample is flown over a chip. For this to work, the chip needs to be functionalized with bioreceptors specific to a given biomolecule. Functionalization refers to the process of covering the chip's surface with a series of molecules (bioreceptors) that our target proteins can attach to.

We hypothesize silicon photonic biosensor chips can be functionalized with bioreceptors through microfluidic assays for one target biomolecule and through multiplexed inkjet printing for multiple target biomolecules.

A unique aspect of silicon photonics is that it allows us to fabricate many tiny sensors onto our millimeter-scale chip that can be used to detect multiple biomarkers simultaneously. This 'multiplexing' enables the diagnosis of various conditions from one sample by linking different biomarkers to different sensors. It also improves the robustness and accuracy for single conditions like specific cancers by analyzing multiple relevant biomarkers of an individual condition.

To develop a multiplexed sensor, we first need to validate assays against each biomarker target individually through microfluidic assay development and testing. Then, we need a system to facilitate the multiplexed functionalization of each sensor on the chip with the validated chemistries. To achieve this, we are developing an inkjet dispensing system. Ultimately, we expect that our silicon photonic biosensor technology will enable accurate and data rich diagnostic testing in a format suitable for the point-of-care.

Our team evaluates biosensor performance for a single target biomolecule using an automated fluidics setup that flows solutions into a two-channel gasket over the chip. A laser input and photodetector outputs are used to measure shifts in the resonance peaks to indicate binding events.

We've conducted ten experiments with some modifications testing the detection of SARS-CoV-2 Spike Protein to gain insight on the reproducibility of our detection assays. The general protocol involves flowing solutions over the chip with steps including Protein A which captures the tail regions of antibodies to more effectively immobilize and orient them, a blocking agent BSA which prevents non-specific binding, the anti-spike protein antibody which aims to capture and immobilize spike protein in the sample and the spike protein which we want to detect and quantify. Some variability is seen in our spike protein binding signal between different trials. We are continuing to conduct multiple replicates of this binding assay to better understand sources of variability so we can develop highly reproducible sensing chemistry to then deploy in a multiplexed inkjet system.

The multiplexed piezoelectric inkjet printer aims to dispense up to four different types of bio-receptors onto the ring resonator surfaces of the Silicon Photonic Chip. This is known as multiplexed functionalization as it transforms the Silicon Photonic sensors into biosensors while also enabling the Silicon Photonic Chip to sense up to four different types of biomolecules.

The overall printing mechanism is as follows:

1. The Arbitrary Waveform Generator generates and sends an electrical pulse to the Amplifier
2. The Amplifier amplifies the voltage of the electrical pulse by 20 times and sends it to the piezoelectric dispensing nozzle filled with bio-receptors
3. The piezoelectric dispensing nozzle receives the pulse which expands and contracts the piezoelectric crystal - dispensing a single droplet
4. A high speed camera images the droplet to ensure only one droplet is dispensed
5. The droplet falls onto the ring resonator surface - functionalizing the ring resonator
6. The Zaber Stage moves the chip to the next position and the process repeats until all ring resonators are functionalized

In order to ensure the multiplexed printer is able to functionalize the fabricated Silicon Photonic Chips, the following specifications were developed:

1. The nozzle dispenses one droplet per electrical pulse
2. The multiplexed printed droplets do not overlap
3. The multiplexed printer's resolution is near 200 um
4. The multiplexed printer can dispense up to four different types of bio-receptors in a multiplexed

In order to test the system, square grids of water droplets spaced approximately 200 um apart were printed on water sensitive paper. During testing, a high speed camera and top-view microscope camera were used to determine if the specifications were met. Additionally a relay was tested to check if the signal can selectively be sent to a single nozzle.

Results/Impact

Initial Testing of the Piezoelectric Inkjet Printer has shown the following:

1. Dispensing exactly one droplet per electrical pulse sent to the nozzle.
2. The ability to print square grids of dots that were 500 um apart (500 um resolution).
3. Demonstration of multiplexing capability using a solid state relay (voltage controlled switch)

Further testing will aim to demonstrate the goal resolution of 200 um - the approximate distance between the ring resonators on the Silicon Photonic Biosensor chip. Additionally, the introduction of multiplexing will enable the functionalization of ring resonators with different types of bio-receptors; this will enable the detection of multiple biomolecules present in a biological sample such as blood.

One of the main goals of the UBC Silicon Photonic Biosensors team is to develop a manufacturing pipeline:

1. Design and Fabrication of Silicon Photonic Sensors
2. Multiplexed functionalization of Silicon Photonic Sensors - making them biosensors
3. Integration of biosensors into portable device that intakes sample and outputs results to a nearby phone/computer

The Silicon Photonic Biosensors team aims to bring accurate and cost effective biosensors to point of care settings - the bedside of a patient, rural areas, or even emergency health services. The development of silicon photonic biosensors will help bridge the gap between lab-based and home-based testing - providing accurate, portable, data rich, and cost effective solutions.

Gender pathways into and out of biomedical engineering

What question(s) does your project aim to address?

Although an abundance of research has been conducted to look at gender differences in motivations and reasons to pursue engineering in general, there is still limited knowledge specifically relating to why students choose to pursue or leave BME and if there are any gender differences.

Our research questions are the following:

1. What reasons do students give for selecting BME at UBC and not selecting other engineering disciplines? Are the reasons for selecting BME (or not selecting other disciplines) different between women/gender minority students and men students?
2. Do BME students at UBC experience a change in their career goals over their degree? If so, why? Do women/gender minority students express more significant changes in career goals or for different reasons than men students do?
3. Do alumni of BME undergraduate at UBC enter jobs/graduate programs in BME or other engineering fields following their degree? If not, why, and what field do they enter? Do women/gender minority students leave BME/engineering for different reasons, or go to different specific fields than men students do?

Project Overview

This project aims to look at the gender differences in motivations to pursue BME, changes in career goals of BME students, and factors that may shift their goals throughout their degree. To do this, semi-structured interviews were conducted with all genders of current and alumnus of UBC's undergraduate BME program.

The research assistants (Misato and Krishma) conducted extensive literature research to determine the topic's scope and themes of research questions. Both research assistants developed an interview script from the themes identified from the literature research.

The five themes identified are as follows:

- Family Influence
- Intrinsic/Extrinsic Motivators
- Communal/Agentic Goals
- Engineering Identity
- Self-Efficacy

Qualtrics surveys were then sent to potential participants to gauge participant interest and to screen participants for interviews, ensuring a wide variety of participants. The research assistants also scheduled, conducted, and recorded the interviews together. Recorded interviews were then transcribed and coded to determine trends and themes amongst participants using thematic content analysis methods.

Results/Impact

The screening survey received over 75 responses, most of which were women. The research assistants conducted and transcribed 22 interviews. Not all the transcripts were able to be fully coded to determine conclusive trends and themes due to time constraints. However, some preliminary results were seen from the data.

Some students of all genders indicated that they enjoyed BME due to the combination of design and engineering with the ability to help people. A few women students indicated that they initially pursued an

undergraduate BME degree as a backup for medical school. This suggests that these students do not necessarily identify as engineering students and ties into our theme of engineering identity, specifically feelings of non-engineering identity. Some students indicated that low grades were a barrier for applying to other disciplines such as mechanical engineering or engineering physics due to the competitive nature of second-year placements in first-year engineering. This indicates that students may feel insecure about their academic capabilities and that grades are a strong extrinsic motivator which can lower self-efficacy. Regarding changes in career goals, many alumni indicated that the lack of career opportunities in the BME industry forced them to change career goals.

These findings involving academic capabilities and job opportunities suggest that both grades and future career prospects are large extrinsic motivators. A few women students also stated that they felt like biomedical engineers are “jacks of all trades and masters of none” and how they did not feel competent enough in their disciplines. This may suggest that women are more likely to feel less capable in biomedical engineering in contrast to the men in the discipline since it was not brought up amongst men participants.

We hope that what we learn from our interviews can be used to create a survey that can be distributed to a larger audience and help us gain a better understanding of the reasons why our BME engineering student body went into BME or why they chose to leave post-graduation. Knowing the motivations of UBC’s biomedical engineering student body will allow us to create a more diverse engineering community.

Turning pain off - Neurophysiological markers of pain 'onsets' and 'offsets' in response to contact heat

What question(s) does your project aim to address?

We hypothesize that the BVT app will enable high inter-rater reliability of both time domain and time-frequency domain outcomes when compared across three raters.

Project Overview

We accessed three datasets; each one contained a large number of trials (between 30-95) and each trial corresponded to a participant's electrical activity (as measured by EEG) when being administered a painful stimulation (contact heat or pinprick). Christina and I recruited a third undergraduate student with the same basic knowledge of signal processing and evoked potentials as us to be the third "rater" in our project. All three raters went through every single trial and completed the following steps: 1) Extract the time domain response and rate confidence of extraction, 2) extract the wavelet-filtered time domain response and rate confidence of extraction, and lastly, 3) extract the time-frequency response without rating confidence, since it is an automated step. Finally, to evaluate the inter-rater reliability of the normal time domain and wavelet-filtered time domain responses between the three raters, the Intraclass Correlation Coefficient (ICC) was calculated for each pain marker and the outcomes were all plotted.

Results/Impact

The normal and wavelet-filtered time domain responses demonstrated statistically significant inter-rater reliability between the three raters. The time-frequency domain responses were automated, and thus, no reliability tests were required. These results indicate that BVT is a user-friendly app that allows individuals who are non-experts in the field of signal processing to extract and further analyze outcomes of complex EEG signs. Because of these findings, clinicians can use BVT to analyze pain signals in the chronic pain population, improving quality of care for patients. In the future, BVT can be used to investigate pain "offsets," which have the potential of contributing to the research on strategies to alleviate chronic pain.

Exploring techniques used to elicit and record optimal pudendal nerve somatosensory evoked potentials in able-bodied controls

What question(s) does your project aim to address?

Our objective was to determine the best methodology for eliciting pudendal SEPs and compare responses between male and female participants.

Project Overview

Our study recruited 18 able-bodied subjects ages ranging from 19 to 43 years, including 10 males and 8 females. To reduce the potential barriers to participation, we developed a visual diagram as the guide to allow participants to place the electrodes on themselves.

In the literature, we observed inconsistencies in the methodologies used by various research groups regarding the electrode configurations to stimulate the pudendal nerve. We identified six possible configurations in females and four in males and sought to determine which had the best tolerability. We also measured the responses from the tibial nerve which supplies the lower leg as the control. To control the level of stimulation, we determined each person's perceptual threshold, which is the minimum stimulus each participant could feel, and then scaled it to a current intensity equivalent to three times their perceptual threshold. The stimulation protocol consisted of 600 pulses, and we used an EEG system to detect the evoked potentials from the sensory cortex.

We were also interested to know if there was a difference in people's tolerability to different electrode configurations, so at the end of each trial, we asked participants to rate the trial on a scale of 0 to 10 on how tolerable it was.

Results/Impact

Through the analysis of cortical waveform responses to stimulations of the pudendal nerve we observed a positive peak at 40 ms and a negative trough at 50 ms aligning with previously established literature, and confirming the accuracy of our chosen electrode placements in eliciting the anticipated response. Despite the variation in electrode placement, there was no significant difference in SEP amplitude in male and female participants, or when comparing sexes. These results suggest that the electrode configurations explored in this study, although different, did not significantly influence the SEP amplitude.

We measured tolerability on a scale of 0-10 with 0 representing no discomfort and 10 being the worst pain of an individual's life. To our surprise, there was no significant difference in tolerability between the configurations for male or female participants. Participants who reported higher tolerability to the stimulations did not necessarily exhibit larger peak-to-peak amplitudes, suggesting a dissociation between the sensory perception of the stimulus and the magnitude of the neural response it elicits. The independence of these two factors raises questions about the complex interplay between sensory processing and neural activation and underscores the need for a more nuanced understanding of the neural mechanisms underlying these phenomena.

The findings presented in this study provide valuable insights into the tolerability to electrical stimulations of the pudendal nerve. Considerations for these findings include our small sample size, the variability in how participants placed electrodes on themselves, the subjectivity of tolerability as a measure and the cross sectional nature of the study design.

Looking ahead, we will be continuing this study in the fall and recruiting more able bodied participants to increase the power of our study. We will also begin the second phase of this project and start testing on our target population of spinal cord injury patients as our research aims to inform clinical assessments and therapies for patients. Spinal cord injury often results in sensory and motor deficits and electrical

stimulation has the potential in restoring sensory and motor function. The study's validation of the specific electrode placements that reliably elicit cortical responses can guide development of more effective neural stimulation strategies. One of the major challenges with spinal cord rehabilitation is restoring sensory perception. The dissociation between tolerability and neural response magnitude, as indicated in this study suggests that individuals might perceive the stimulation differently from the actual neural activity. This can guide researchers in designing stimulation parameters and therapies that improve the quality of life for individuals with spinal cord injuries. Pudendal nerve rehabilitation is vital for spinal cord injury patients as it can allow them to restore voluntary control over their pelvic floor muscles (which are essential for maintaining bladder and bowel function), sexual sensation and function, and reduce pain thereby enhancing individuals daily comfort and quality of life.

In summary, the findings of the study hold the potential to transform how researchers and clinicians approach spinal cord injury research and therapy development. By offering insights into electrode placement, stimulation strategies, sensory perception, and treatment customization, these findings pave the way for more targeted and impactful interventions in the field of spinal cord injury rehabilitation.

Blinded by Granzyme B: a key contributor in the development of age-related macular degeneration

What question(s) does your project aim to address?

This project aims to address the effect of Granzyme B (GzmB) on neovascularization, which is a diagnostic marker of AMD.

Project Overview

The main method used to investigate AMD in this project is called a choroid sprouting assay (CSA), which is a tissue culture system that allows us to model the neovascularization that occurs in AMD. In a CSA, we embed small pieces of mouse retinal tissue into a gel-like matrix and measure the growth of the tissue. The tissue growth is our estimate for neovascularization occurring in retinal tissue. Our experiment compares the retina of normal mice (wildtype mice) to mice with the GzmB gene removed (GzmB knockout mice). The wildtype mice have GzmB present in the retina, while the GzmB knockout mice have no GzmB present in the retina.

To test the effect of GzmB on neovascularization, we apply our treatment which is a substance that causes GzmB to be released from its stores. We then compare the neovascularization between 4 groups:

1. Wildtype mice control
2. Wildtype mice treated
3. GzmB knockout mice control
4. GzmB knockout mice treated

We hypothesize that the treated wildtype mice, will have more GzmB released into the tissue, which should cause more neovascularization compared to the control wildtype mice. The GzmB knockout mice should not express any GzmB and therefore we would expect a lower level of neovascularization compared to wildtype mice. Additionally, when comparing GzmB knockout mice given control versus treatment, there should be no significant difference in neovascularization as there is no GzmB present to be released even when given the treatment in these knockout mice.

Results/Impact

GzmB has been found to have a significant contribution to neovascularization. When wildtype mice were given the treatment (which releases GzmB), it significantly increased neovascularization compared to wildtype mice given control. This demonstrates that it is the release of GzmB into the retinal tissue that causes neovascularization to occur and thus supports the hypothesis that GzmB is responsible for AMD development. Both the control and treated wildtype mice had higher levels of neovascularization compared to both groups of GzmB knockout mice. This demonstrates that when you remove the gene that expresses GzmB and there is no GzmB present in the retina, there is a significant decrease in neovascularization.

GzmB greatly contributes to the progression (neovascularization) of AMD, thus mice eyes that do not express GzmB may be protected against AMD disease development. To truly understand how GzmB contributes to AMD development, our future research will focus on (1) identifying the key protein targets that GzmB degrades, (2) how GzmB release increases in the retina with age or other risk factors (such as smoking), and (3) how these processes affect photoreceptor and retinal health. We will also test the effect of (4) a synthetic inhibitor of GzmB on neovascularization in wildtype mice. We hope that by understanding the underlying mechanisms of AMD development, we can create therapies that stop the retinal changes present in AMD from occurring in patients at risk of disease development and progression. Ultimately, we hope to prevent the irreversible vision loss that occurs in AMD and restore patient vision.

Unraveling drug and virus specific biosignatures using high-content and super resolution microscopy

What question(s) does your project aim to address?

1. What is the impact of the natural, small molecules CA, Biotinylated-CA (Bio-CA), and bafilomycin A1 (BafA1) on intracellular pH in HT-1080 cells?
2. In relation to the Mitochondria and the ER, where does the HCoV-229E virus localize and how do Mitochondria-ER Contact Sites (MERCs) differ in infected HT-1080 cells compared to uninfected cells when observed through 3D STED imaging?

Project Overview

Aim 1: Examining antiviral impact on cellular pH using pH bioassay, acridine orange (AO): Danielle Gordon– Jean Lab

The work done in the Jean Lab was related to investigating the effects of natural, small molecule V-ATPase inhibitors (CA, Bio-CA and BafA1) on cellular pH using the AO bioassay.

As previously mentioned, CA is a new natural, small molecule that we hypothesize is blocking a master regulator of intracellular pH, the V-ATPase, but the MOA remains to be fully understood. In this experiment our negative control is cladoniamide D (CD) which is a metabolite of CA that is inactive against viral infection and has no effect on intracellular pH. BafA1, our positive control, is a classical V-ATPase inhibitor that inhibits viral infection but is toxic to cells over time. In addition to CA, biotinylated analogues, Bio-CA and biotinylated CD (Bio-CD) were created and tested with the purpose of identifying the cellular target of CA through a future pull-down experiment. In order to identify the cellular target of CA, it is important that the biotinylated analogues of the two compounds show similar efficacy in inhibiting acidification.

In order to investigate the effect of these compounds on the intracellular pH of HT-1080 cells, I performed a pH sensitive bioassay with the fluorescent dye, AO, which diffuses and clusters in areas of low pH. Areas of the cell that have a low pH will fluoresce orange, whereas areas with higher pH will only be labeled by the nuclear stain, Hoechst. I hypothesize that untreated cells will maintain a low pH resulting in orange fluorescence whereas the cells treated with V-ATPase inhibitors will inhibit acidification and no fluorescent signal will be detected. Throughout the course of the project, HT-1080 cells were cultivated and treated with compounds for 3 hours for both the concentration dependent and 24 hour time point AO experiments.

Aim 2: Examining intracellular viral distribution and comparing MERCs in infected and uninfected cells using 3D STED imaging: Kshemaka Gunawardena– Nabi Lab and Jean Lab (in collaboration with the Harmaneh Lab)

The work done in the Nabi Lab and Jean Lab, in collaboration with the Harmaneh Lab, was aimed at understanding how the HCoV-229E interacts with human cells and how this interaction affects the organization of MERCs.

To do this, we introduced an ER reporter protein called ERmoxGFP into HT-1080 cells, which localizes and fluoresces within the ER, allowing for visualization of the ER. This process involved selecting cells that stably expressed the ER reporter protein at high levels. These cells were subsequently infected with HCoV-229E by the Jean lab, and the infection was allowed to progress for 48 hours. For imaging purposes, cells were then stained using antibodies to label the infected cells and their mitochondria. These antibodies specifically targeted double-stranded RNA (dsRNA), a molecule produced during viral replication, and TOM20, a mitochondrial receptor protein. This approach provided us with detailed images

of infected cells and their organelles using 3D-STED microscopy. Our analysis, facilitated by MCS-detect, allowed us to quantify the contact sites between the ER and mitochondria within our cells.

Results/Impact

Aim 1: Examining antiviral impact on cellular pH using pH bioassay, AO: Danielle Gordon– Jean Lab

The 24 hour time point AO experiment shows that both CA and BafA1 inhibit acidification. More specifically, from the results of this experiment we hypothesize that CA is less toxic than BafA1 due to the reversibility of inhibition shown by CA. The reversibility of CA versus BafA1 is shown by cellular pH recovering faster from treatment with CA than BafA1, where acidification in CA starts to return substantially starting around 12 hours and acidification does not recover after 24 hours in BafA1. This discovery suggests that CA could be a more suitable antiviral candidate than BafA1. The concentration dependent AO experiment provides insight into determining what concentration of the compounds are required to inhibit acidification in HT-1080 cells. Similar to the 24 hour time point experiment, we observe that BafA1 and CA both inhibit acidification using approximately 50 nM of compound. In addition to this, CA appears to inhibit acidification more efficiently than Bio-CA, where Bio-CA requires more than 250 nM to inhibit acidification. Importantly, this research demonstrates that Bio-CA is biologically active and acts by inhibiting acidification, confirming its suitability for a pull-down experiment. Overall, CA is shown to be an excellent antiviral candidate as it has shown broad spectrum antiviral activity in addition to reversibility of its inhibitory effects on intracellular pH. We hypothesize that if CA is targeting the V-ATPase, it will be able to prevent viral infection in most human enveloped viruses of concern.

Aim 2: Examining intracellular viral distribution and comparing MERCs in infected and uninfected cells using 3D STED imaging: Kshemaka Gunawardena– Nabi Lab and Jean Lab (in collaboration with the Harmaneh Lab)

Our findings revealed that HCoV-229E predominantly localizes to the perinuclear region near the ER and within the mitochondria, as evidenced by the localization of viral dsRNA. The proximity to the ER suggests the formation of viral replication complexes, which have previously been observed to form over the course of infection. This finding not only reinforces broader knowledge on coronavirus replication but also provides a potential target for antiviral drug development. Furthermore, the association of dsRNA with mitochondria suggests a vital role for mitochondria in viral replication and hints at potential alterations in mitochondrial function during infection. This aligns with recent findings indicating that SARS-CoV-2 can induce mitochondrial dysfunction. Such knowledge can inform the development of interventions aimed at preserving mitochondrial function during viral infection, potentially leading to improved patient outcomes. In addition to this, our investigation showed that infection led to an increase in the number of MERCs. Notably, the size of these contact sites remained relatively unchanged. Understanding the role of MERCs in viral infections could pave the way for therapeutic strategies that target these contact sites to either inhibit viral replication or enhance the host's antiviral defenses.

Overall Impact and Conclusion

The SARS-CoV-2 pandemic highlights the importance of understanding how coronaviruses interact with human cells and what viral infection and treatment does to human cells long term. Recognizing the limitations of monotherapies, which often lead to viral resistance, our findings support CA as a potential candidate that can be incorporated into multidrug regimens to combat SARS-CoV-2 infections. Our project also sheds light on the intricate interactions between HCoV-229E and HT-1080 cells, emphasizing the significance of the ER and mitochondria in viral replication and infection outcomes. Together, this knowledge has the potential to inform the development of antiviral drugs, treatment strategies, and health policies aimed at combating viral infections more effectively. Ultimately, our research is a vital step towards improving health practices and patient outcomes in the face of viral pandemics and emerging infectious diseases.

Finding breast cancer relapses in pathology reports using natural language processing

What question(s) does your project aim to address?

Metastatic disease is currently detected in about 12% of patients with breast cancer. We hypothesize that an NLP model can identify metastatic disease in pathology reports with 95% sensitivity and 90% specificity, so <5% of relapses are missed and <20% of cases have positive predictions that require review by human coders.

Project Overview

This study extracted data of relapse occurence from roughly 1,600 pathology reports detailing information about patients with a history of breast cancer. This data was then used to create a natural language processing model that would be able to automatically classify whether a pathology report has a mention of local, regional, or distant recurrence. The dataset for the model was created through manually extraction by a group of four research assistants and extracted by following an annotation schema. This annotation scheme was created based on analysis of pathology report structure, troubleshooting during data extraction, and discussions with a breast reconstruction surgeon and an oncologist.

For this project, we created the annotation scheme and annotated roughly 800 reports between Jaimie and Annah. In addition, we attended weekly meetings with the data science team to discuss potential pitfalls and issues that may arise due to the structure and information contained within the pathology reports.

Results/Impact

Once modeling has been completed for pathology reports, we hope to have a working application that is able to accurately determine whether a patient has had a relapse based on their pathology reports. Hopefully, this model can be connected to a database, which will allow for much easier data extraction and data collection for future research projects and breast cancer patient care. While all electronic health records are stored within a database, the information contained within these records are not easily accessible. Thus, our application hopes to make the information more readily available for researchers and physicians without manually going through each report to extract the data.

PhysViz: validation of a new telerehabilitation platform

What question(s) does your project aim to address?

The objective of the project was to validate the Achilles tendon strains (i.e., how much the tendon stretches) achieved during ankle flexion using the PhysViz (PV) against the 'gold standard' Biodex in three distinct patient groups (control, Achilles rupture, and Achilles tendinopathy). We hypothesized that the strains achieved during PV trials would be equivalent to those achieved during Biodex trials across all three groups.

Project Overview

The students were responsible for the same tasks during the extent of the project. These include, but are not limited to patient recruitment, data collection, data processing, and academic paper writing. There were two main data collection technologies used to inform the Achilles tendon strain of the participants – ultrasound and motion capture. Using the motion capture markers as anchors at the attachment sites of the Achilles tendon, we were able to track how much the tendon stretches on the ultrasound video and represent it as a percent of original tendon length (i.e., strain). This was done for both PV and Biodex trials of the same patient. The methodology was similar across all three patient groups with slight modifications to avoid injury.

Results/Impact

Over the course of the summer, our primary objective was to collect data pertaining to the relationship between strains measured by the PhysVis and the Biodex. The significance of this research lies in the fact that the Biodex, a sophisticated and expensive piece of equipment typically confined to research laboratories, has proven to be an invaluable tool in Achilles tendon rehabilitation.

Our project's overarching goal is to develop a portable, user-friendly version of the Biodex for use in clinical and practical settings. Initial findings from our data analysis indicate that, on average, strains experienced by injured Achilles tendons are greater than those observed in matched trials on uninjured sides. This discovery underscores the potential for improved rehabilitation protocols and treatment strategies for individuals suffering from Achilles tendon injuries.

Moving forward, our research will focus on conducting a case series to demonstrate the safety, practicality, and clinical outcomes of utilizing the portable PhysVis system in real-world scenarios. Our intention is to ensure that the device meets or exceeds the expectations of healthcare professionals and patients alike. Subsequently, we plan to seek Health Canada approval for clinical and consumer use. The potential outcomes would be an easy to use strain gage that health professionals can use to monitor a patients rehabilitation remotely without expensive and inaccessible equipment

A biomaterials-based approach for axon guidance and growth

What question(s) does your project aim to address?

Can we guide axon growth by using a porous multichannel scaffold in order to support successful recovery in SCI patients?

Project Overview

1.0 Biomaterials project:

The potential of biomaterials for nerve guidance scaffolds have been previously examined by different researchers, using various manufacturing techniques. However, the work done over the summer extensively utilized 3D printing, due to its one-step ease of use and consistency. Peter created various models differing in shapes and sizes, to figure out what parameters should be used for the printer. As well, it should be noted that extensive work was committed to include salt into the 3D print, as it would be washed away after the print to leave behind pores in the structure.

2.0 DeepLabCut project:

The next section of the project was done by Brianna to assess the efficacy of the model if it were to be implanted into an animal. The purpose of this project was to evaluate the typical single pellet reaching behavioral assay and improve its accessibility by employing DeepLabCut (DLC). DeepLabCut is a machine learning toolkit that allows researchers to markerlessly track fine movement during invivo studies. Firstly, the single pellet reaching task was streamlined by use of an automatic pellet dispenser. This way, the machine would automatically replenish the pellet when it was taken by the rat. Then, a camera set up was created using a GoPro Hero 9, 3 magnification lenses and a 3D printed camera mount. This ensures that all footage taken was of optimal quality for DLC to assess. Although DLC is an extremely useful tool with a graphical user interface, its more complex functions require a deeper understanding of python. Thus, we created a standard operating procedure of the DLC basics for biologists with no coding experience to use.

3.0 Tissue analysis techniques:

The next portion of the project was to learn and propose how the tissue would be processed after invivo studies. 2 techniques that were practiced by Brianna, cryosectioning for confocal microscopy and tissue clearing for lightsheet microscopy. Throughout the summer, many tissue samples for another lab member's project were frozen and cryosectioned by Brianna and she became proficient at the technique. Later in the summer, we investigated the other, more novel technique of clearing the spinal cord via delipidation and imaging it using a light sheet microscope.

Results/Impact

By the end of the summer, a reproducible 3D printing procedure was created to fabricate porous multichannel scaffolds. Simultaneously, the project also led to a standard operating procedure (SOP) to utilize the DLC software in order to assess motor function in rodents. Moving forward, we hope to actually implant the scaffolds in rats and examine the clinical efficacy of the procedure using DLC and the outlined tissue processing techniques. If there is potential for clinical usage, we hope that our work over the summer will be iterated upon to make a real difference in SCI treatment options.