Hypothesis or Research Question(s): We hypothesize the optical stimulation of axons coupled with biomaterials-based implants provide high density and linear axonal growth after spinal cord injury.

PROJECT BACKGROUND & SUMMARY

About ~80,000 Canadians live with spinal cord injury (SCI). There is no cure for SCI and it generally results in the loss of sensation, mobility and organ function at and below the level of lesion. SCI typically severs thousands of nerve cell processes, called axons, that do not naturally regrow. Interventions are needed to promote nerve fibre (axon) growth, remove scar tissue formation and guide axon growth across mm-long lesions.

Since its invention in 2005, optogenetics, which genetically sensitizes nerve cells, called neurons, to light, has become a powerful tool in animal brain research to understand complex nerve cell connections, aka neural circuits, via optical stimulation. However, while shown promising, its potential for axon growth has yet to be fully harnessed primarily due to technological limitations in chronic light delivery to mobile organs. We are developing flexible neural probes coupled with electronic components for chronic light and/or drug delivery to the spinal cord. We will perform a comprehensive study to assess the effects of light and scar removal on motor function recovery and axon growth in rodent SCI models. The study will then be extended to mm-long lesions where, in addition to inducing axon growth and mitigating the scar tissue, it is also necessary to provide directionality for the axons. The neural probes will be coupled with axon guidance scaffolds being engineered in the lab to assess functional recovery and axon growth across the lesion.

Exploiting optogenetics enables targeting specific neurons. Stimulating or inhibiting different neuronal cell types via optogenetics will aid in the future discovery of functional repair mechanisms to eventually develop a therapy for SCI. Coupled with drug delivery and axon guidance scaffolds in our animal studies may provide improved motor function after spinal cord injury.

Represented by our scientifically diverse team, this proposal builds on the promise of optical stimulation coupled with established promising techniques for SCI repair through a multidisciplinary approach to combine techniques in bioengineering, materials science, electronics and neuroscience.

BENEFIT TO THE STUDENTS

Having multiple components in the project, the students will benefit from independent yet highly collaborative projects. It is the intention of the PIs for all the student to lead their own sub-project while working together toward the overall goal. The students will mainly be directly advised by two graduate students who will provide a high level of experience and education for the students leading the project. The PIs of the project will remain involved and available for guidance and support throughout.

The proposed project primarily brings together the fields of bioelectronics, biomaterials and neuroscience. The already multidisciplinary lab environments offered by the PIs of this project coupled with the complementary expertise of the graduate student mentors/PIs provides the appropriate resources and learning environment for such a multidisciplinary project.

One student will be primarily involved in developing neural probes for light delivery. This sub-project will have a heavy focus on bioelectronics and some of the intended learning outcomes include printed circuit board design and development, programming microchips as well as characterizing the electrical and optical properties of the probes. This project would particularly be suitable for students interested in bioelectronics, neuromodulation and programming.

Another student will primarily focus on the engineering component of the project in advancing a 3D printer system to develop hierarchically ordered axon guidance scaffolds. The primary expertise gained by the student leading this sub-project will be implant design and development as well as materials characterization techniques such as measuring morphological changes and mechanical properties. The student of this project is most interested in biomaterials and tissue engineering fields.

Another student will primarily work on in vivo studies to perform post-mortem tissue analysis of rodents used for implantation. Specifics include tissue blocking, sectioning, staining and imaging. The student will gain valuable skills on how to operate state-of-the-art equipment and learn how to perform critical experiments necessary particularly for those interested in biology, medicine and neuroscience.

All the involved students will have ample opportunities to learn from the PIs, each other and other lab members and be exposed to different components of the project. There will be at least weekly meetings between the corresponding graduate student and each student to guide and support the students on the project. There will be clear milestones decided by the lead graduate students with consultation with the PIs that will be communicated to each student. The milestones may be changed upon mutual agreement as the projects unfold.

The intention is for the students to benefit from the multidisciplinary environment of the two involved labs as well as the collaborative project to be motivated to continue multidisciplinary research and become our future scientific leaders on innovative and translational interventions.