Toward overcoming the blood-brain barrier with an optical fiber

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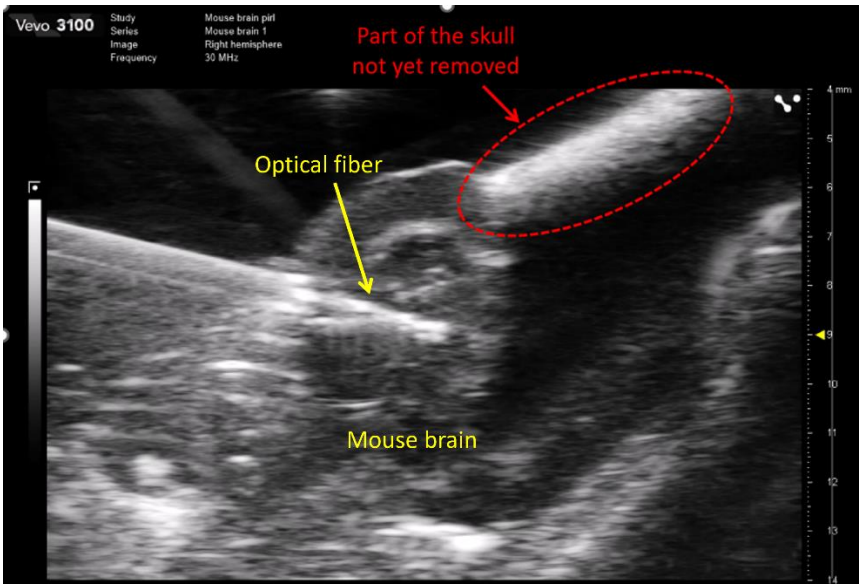
Project description: Nearly 10 million people currently live with either Parkinson's or Alzheimer's disease in the North America alone. Nonetheless, conclusive cures for these and other neurodegenerative diseases are yet to be discovered. A significant hurdle impeding the drug development efforts in this area is what is known as the blood-brain barrier (BBB), formed by endothelial cells covering the inner walls of the blood vessels in the brain. In fact, only a handful of tiny molecules weighing <400 Da, such as ethanol at 46 Da and caffein at 194 Da get to cross the above barrier. While this protects our brains from unwanted molecules and external agents under normal conditions, the existing drugs in this narrow mass range are mainly suitable to only delay the deterioration of some of the symptoms. To try complex drugs, it is imperative to find alternative pathways to overcome the BBB. Even better would be to manage to target specific sites of the brain each responsible for a different function, or where the root causes of a neural disorder such as tau and amyloid tangles and plaques are clumped up.

In our efforts to implement NIR laser pulses to develop non-invasive surgical scalpels made of optical fibers, we tackled the problem of overcoming the BBB for therapeutic drug injection. A question worth pondering here is how an optical fiber made of sapphire, about 200 μm in diameter, interacts with individual endothelial cells as the NIR pulses are delivered to the targeted area. One idea is to take advantage of the recent progress made by researchers in the field of organ-on-a-chip model development. These are microfluidic chips with human-driven cells covering their inner channel walls used mainly in drug development. What we are interested to explore is the mechanical response of these cells to the rigid fiber both in the presence and absence of laser light. The student curious about this project will be involved in designing an experiment aimed to investigating this under optical microscope. The present research is highly multidisciplinary, and so it is expected that the student will actively work to optimally take advantage of the relevant facilities available across the campus, e.g. to fabricate microfluidic chips (before trying an actual organ-on-a-chip model) and to design a platform to inspect the mentioned interaction with an optical fiber under microscope.

Required knowledge: Basic optics (e.g. fundamental reflection and refraction phenomena). Familiarity with optical fibers and pulsed laser beams will be helpful. Previous knowledge on biophysics and brain physiology and anatomy is not required but considered highly valuable for this project. Similarly, knowledge and skill in microfluidics and designing microfluidic chips will be an asset.

Learning outcomes: The curious student dedicated to this project for the duration of the program is anticipated to be able to independently study and learn about the various scientific and engineering aspects of this highly interdisciplinary research. This involves applications of pulsed lasers in surgery, microfluidics, and human brain anatomy and physiology, depending on the student's background knowledge and skills set.



Optical fiber in mouse brain. A microchannel pathway is created for drug injection. This is an ultrasound image captured during the process.

References:

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[4] C. Hajal, *et al.*, *"Engineered human blood-brain barrier microfluidic model for vascular permeability analyses"*, Nat. Protoc. 17, 95-128 (2022).