Doctoral thesis/dissertation Digest Form

Title of Doctoral Thesis: Neuroengineering a brain-implantable imaging device and photostimulator toward a closed-loop system for seizure control
てんかん発作制御のための閉ループシステムに向けた脳内埋植撮像デバイスと光刺激デバイスの開発

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The study of the brain offers profound insights into human existence and holds potential for treating neuropsychological disorders such as temporal lobe epilepsy, which affects over 50 million people worldwide. In response, global initiatives like the BRAIN Initiative, Human Brain Project, and Brain/MINDS project aim to unravel the brain's complexities and develop advanced tools to explore and modulate brain function. Thus, to address current limitations in neurotechnology, we developed a biophotonic system for neuronal imaging and stimulation, applying it to disorders such as seizures.

First, we implemented current *in vivo* imaging techniques to explore their strengths and weaknesses. We examined two-photon (2P) microscopy, fiber photometry, and miniaturized microendoscopy for studying vision, anxiety, and epilepsy. Then, we developed brain-implantable needle-type devices that complement these established methods. Our system enables lightweight (0.02 g) multi-layer (0.9 mm vertical length) imaging and manipulation of neurons. The devices have a compact form factor, require minimal optoelectrical components, and are easy to implement. The system consists of two implantable devices, namely the imaging device and the photostimulation device.

The imaging device utilized a CMOS active pixel array with a yellow thin-film absorption filter and blue μLEDs for G-CaMP6 calcium imaging. Upgrades to the pixel architecture improved sensitivity, reduced noise, and enabled detection of weak light signals. Seizure induction in transgenic mice revealed differential calcium activity across hippocampal layers and was analyzed using machine learning models. The photostimulation device was implanted in the medial septum and delivered red optogenetic stimulation. We found that 20 Hz activation of cholinergic neurons proved effective in reducing seizure behavior. Integrating all the components of the system into a closed-loop system holds potential for real-time seizure detection and control using neuronal imaging and stimulation.