Form 4-3

Japan-U.S. Brain Research Cooperation Program
Training Course Dispatch to the U.S. Program FY2021: Report

Field: Behavioral/Systems Neuroscience

1. Researcher

Name: Joshua Philippe Olorocisimo
Title: Doctoral student
Affiliation: Nara Institute of Science and Technology

2. Training Course name:

Epilepsy Training Program, Huguenard Lab, Stanford School of Medicine

3. Dispatch Period, from/to (yyyy/mm/dd):

2023/02/01 to 2023/03/21

4. Abstract, Results, and Research Significance (300 Words):

Over 70 million people are diagnosed with epilepsy; however, about one-third of these people have conditions resistant to drug treatment. Thus, further studies about the neuronal mechanisms that underlie this condition is needed in order to find better alternative treatments. To achieve this, I am developing brain-implantable devices for neuronal imaging and modulation. We combine CMOS nanotechnology and genetic engineering to develop a closed-loop biophotonic system using calcium imaging and optogenetics. This newly developed system can aid in the investigation of neural circuits during freely-moving behavior. Our device is one the lightest systems for animal studies due to its small size and lensless feature. A thin-film fluorescence filter is spin coated and placed onto the CMOS image sensor. The sensor rests on a thin flexible substrate made of polyimide. Micro-LED chips are attached as excitation light. The entire device is then encapsulated in a biocompatible polymer called parylene. Weighing about 0.02 g, and less than a millimeter in length and width, the system allows for multiple sites to be studied at the same time.

I targeted the hippocampus for calcium imaging and the medial septum for optogenetic stimulation. Due to the small size of the devices, the image sensor can be directly implanted into the brain resulting in a wide vertical field of view that can image multiple layers simultaneously. Thus, after seizure induction through kainic acid, I image the CA1 and dentate gyrus of the hippocampus to determine epileptiform calcium dynamics. Furthermore, I am investigating if activation of cholinergic neurons in the medial septum can suppress seizure and affect hippocampal epileptic activity. For my training, I was shown how to perform optogenetic experiments while recording a whole-cell patch clamp in brain slice cultures. Also, we performed calcium imaging *in vivo* in head-fixed mice through one-photon and two-photon microscopy.

5. Other (Research-related concerns, particular points to note):

During the training, I learned electrophysiology techniques such as patch clamp, LFP, and EEG recordings. I built electrodes for EEG and used these to record absence seizures in freely-behaving mice. In addition, I learned about mouse disease models for epilepsy and autism. Then I was shown different behavioral assays to assess pathological phenotypes in mouse behavior.

Aside from lab work, I also attended lectures and seminars on various topics in neuroscience. I participated in a class on machine learning for neural data analysis, and learned different algorithms for signal extraction, encoding, and decoding models. I attended the Mind, Brain, Computation, and Technology (MBCT) seminars and the Wu Tsai Neuro seminars during my stay in Stanford. I learned about the latest findings and techniques for neuroscience and neuroengineering. Overall, it was a great learning experience, and I am very thankful to the Japan-US Brain Research Cooperation Program for supporting my stay in Stanford University. This experience is a monumental step towards my personal and professional development as an aspiring neuroscientist.