Electrode stimulation-driven circuit reorganization in the adult visual cortex

Dr. Jennifer Sun

Visual Plasticity Laboratory. Dr. Y. Jennifer Sun (jennifer.sun@ucl.ac.uk), UCL Institute of Ophthalmology, 11-43 Bath St, London EC1V 9EL, UK

Research overview: Our lab is interested in understanding the working mechanisms by which electrode stimulation alters neural network in the adult visual cortex, which has the potential to be applied to enhancing learning and rehabilitation in the adult brain. To achieve this goal, we have designed a multimodal system that integrates electrode stimulation and 2-photon imaging to achieve long-term tracking of neural responses at single-neural and population level.

Research project: Intracortical microstimulation (ICMS), passing a small electrical current through electrode in a focal cortical area, is a neuroengineering technique widely known to effectively evoke neural activities and drive plasticity in the adult brain. Despite its wide application in clinics for brain-machine interface and neural prothesis, little is known about its biological underpinnings. This gap of knowledge results in inconsistent treatment outcome and makes it challenging to evaluate and optimize ICMS therapies for enhancing learning and post-injury rehabilitation.

This project aims to study how electrical stimulation enhances visual representation by evaluating the neural response changes resulted from chronic ICMS. The proposed work is built upon our recent innovation to integrate electric stimulation and 2-photon microscopy [1]. This multimodal platform combined with molecular tools enables us to visualize the long-term, large-scale changes in neural circuits and structures in the local brain of awake behaving animals. In collaboration with Dr Dadarlat in the department of Biomedical Engineering at Purdue University, we have stimulated the local visual cortex in the adult mice and recorded neural activities in different types of neurons. This project will further evaluate the calcium responses in a genetically identified neural population, and determine if their functional activities [2], with or without visual stimuli, change over weeks in response to chronic ICMS treatment. The results from this study will provide valuable information if and how ICMS modulates neural network in a cell-type specific manner, which can be used as a biomarker in designing effective therapies.

Requirements: Calcium signals has been recorded using *in vivo* 2-photon imaging in awake head-fixed mice. Student working on the functional analysis is expected to have substantial training in neural data analysis using Python / MATLAB and strong interest in learning basic biological concept of neuroplasticity.

Reference:

1. Dadarlat MC, Sun YJ, Stryker MP. Widespread activation of awake mouse cortex by electrical stimulation. International IEEE/EMBS Conference on Neural Engineering, 2019:1113-1117

2. Sun YJ*, Espinosa JS*, Hoseini MS, Stryker MP. Experience-dependent structural plasticity at pre- and postsynaptic sites of layer 2/3 cells in developing visual cortex. Proceedings of the National Academy of Sciences, 116(43), 21812-21820

Two-photon imaging analysis for blood flow and neurovascular changes in stroke model

Dr. Jennifer Sun

Visual Plasticity Laboratory. Dr. Y. Jennifer Sun (jennifer.sun @ucl.ac.uk), UCL Institute of Ophthalmology, 11-43 Bath St, London EC1V 9EL, UK

Research overview: Our lab is interested in understanding the biological basis of visual cortical plasticity in the adult brain, the ability to make long-term modification of its neural responses. To this end, we employ 2-photon imaging and systems approach to reveal the cellular and vascular remodeling during visual cortical plasticity.

Research project: After the critical period in early brain development [1], the adult cortical circuits gradually stabilize and only maintain a limited degree of plasticity. This adult plasticity is critical for perceptual learning and rehabilitation, yet its neural processing and underlying cellular and molecular mechanisms are not well understood.

The goal of this project is to study how cellular and vascular remodeling happen after ischemic stroke. We have tracked the stroke-induced vascular and blood flow changes in the mouse visual cortex, in collaboration with clinicians and researchers at UCSF Neurology Department. We focus on developing robust imaging processing toolkits [2] to analyze 2-photon imaging data and systemically characterize the changes of blood cells density, aggregate movement, and structure of vasculatures after stroke. This research line will result in a valuable toolkit that can serve as a potential biomarker for disease diagnosis and rehabilitation research. In particular, it will allow us to further investigate how blood flow changes might contribute to the impaired visual function and assess if running and other treatment improve visual cortical plasticity in the adult brain, which could help with the rehabilitation and functional recovery in stroke patients.

Requirements: The project is a collaborative project. Data collection is done at University of California San Francisco using *in vivo* 2-photon imaging in awake head-fixed mice. Student working on the imaging analysis and toolkit development is expected to have substantial training in digital imaging processing using Python / MATLAB and interested in learning basic biological concept of neuroscience.

Reference:

1. Sun YJ, Espinosa JS, Hoseini MS, Stryker MP. Experience-dependent structural plasticity at pre- and postsynaptic sites of layer 2/3 cells in developing visual cortex. Proc Natl Acad Sci U S A. 2019 Oct 22;116(43):21812-21820.

2. Shih AY, Driscoll JD, Drew PJ, Nishimura N, Schaffer CB, Kleinfeld D. Two-photon microscopy as a tool to study blood flow and neurovascular coupling in the rodent brain. J Cereb Blood Flow Metab. 2012;32(7):1277-1309.

Cell-type specific dissection of circuit remodeling during visual cortical plasticity

Dr. Jennifer Sun

Visual Plasticity Laboratory. Dr. Y. Jennifer Sun (jennifer.sun @ucl.ac.uk), UCL Institute of Ophthalmology, 11-43 Bath St, London EC1V 9EL, UK

Research overview: Our lab is interested in understanding how neuromodulation regulates information processing and neuroplasticity in the visual systems. We apply computational modelling and systems approach to reveal the biological basis of visual cortical plasticity.

Research project: The adult brain keeps a fine balance between reliability and flexibility, maintaining only a limited degree of plasticity, the ability to make long-term modification of its neural responses. Recently studies report the existence of various forms of visual plasticity in the adult human or mice brain only when visual stimulation is presented while the subject is running but not stationary. For example, after 5 days of exposure to visual stimulation for 1 hr/day during running, neurons in the mouse primary visual cortex (V1) increase their responses [1] towards stimulus presented during running. This adult plasticity is critical for perceptual learning and rehabilitation, yet its neural processing and circuit mechanism are not well understood.

The object of this project is to understand how V1 functional reorganization is achieved through the interaction of different neuronal types, especially the potential role of inhibitory neurons in regulating plasticity in the adult brain. Local GABAergic inhibitory neurons are shown to drive various forms of juvenile plasticity and exhibit structural changes earlier than excitatory neurons [2]. We hypothesize that in the adult brain, local GABAergic inhibitory neurons might also exhibit plastic changes that allow the excitatory cells to be modified. We focus on Parvalbumin-positive (PV) and Somatostatin-positive (SST) interneurons, the 2 major inhibitory sources, to characterize when and how their functional properties change in comparison to excitatory neurons. We will apply analytical approaches and computational modelling to reveal the circuit changes underlying the basis of functional reorganization during adult plasticity.

Requirements: The project is a collaborative project. Data collection is done at University of Toronto using *in vivo* calcium imaging in awake head-fixed mice [3]. Student working on the analysis and modelling of neural data is expected to have computational skills using Python / MATLAB and interested in learning biological concept of neuron networks.

Reference:

1. Kaneko, M., Fu Y., and Stryker, M.P. Locomotion induces stimulus-specific response enhancement in adult visual cortex. Journal of Neuroscience. 2017. 37:3532-3543
2. Liu BH, Li P, Sun YJ, Li YT, Zhang LI, Tao HW. Intervening inhibition underlies simple-cell receptive field structure in visual cortex. Nature Neuroscience, 2010.13:89-96
3. Dadarlat MC, Sun YJ, Stryker MP. Widespread activation of awake mouse cortex by electrical stimulation. International IEEE/EMBS Conference on Neural Engineering, 2019:1113-1117