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Optical Tools for Unraveling Whole-brain Neuronal Circuit Dynamics Underlying Behavior

Abstract: The combination of optogenetics and high speed functional imaging are providing new opportunities to understand how the collective dynamics of neurons in functional networks leads to behavior.

While traditional imaging modalities based on two-photon imaging have relied on the manipulations of light in the spatial domain, multi-photon microscopy via femtosecond optical pulses can also provide a new degree of freedom via the pulse spectrum that can be used to "sculpt" the spatial localization of light within the sample. This has been exemplified in the technique of temporal of focusing through which a decoupling of the axial from the lateral confinement of light can be achieved. Using this technique in combination with genetically encoded calcium (Ca^{2+}) indicators we have demonstrated near-simultaneous recording of whole-brain neuronal activity in *C. elegans* at single cell resolution. More recently we developed a variant light sculpting microscopy that has enabled unbiased single- and dual-plane high-speed (up to 160 Hz) Ca^{2+} imaging in the mouse cortex as well as in vivo volumetric calcium imaging of a mouse cortical column (0.5 mm×0.5 mm×0.5 mm) at single-cell resolution and fast volume rates (3–6 Hz). This has enabled *in vivo* recording of calcium dynamics of several thousand neurons across cortical layers and in the hippocampus of awake behaving mice.

Light-field microscopy in combination with 3D deconvolution and other more sophisticated mathematical signal demixing strategies is another highly scalable approach for high-speed volumetric Ca^{2+} imaging. Using this technique termed Seeded Iterative Demixing (SID), we have recently demonstrated video-rate recoding of neuronal activity within a volume of 0.6mm×0.6 mm×0.2 mm located as deep as 380μm in the scattering mouse as well as whole-brain imaging of larval zebrafish during sensory stimulation. These tools combined with high speed optogenetic control of neuronal circuits, advanced statistics tools and mathematical modeling and will be crucial to move from an anatomical wiring map towards a dynamic map of neuronal circuits.

Bio: Dr. Vaziri is the Associate Director of the Kavli Neuronal Systems Institute, and serves as an Associate Professor at The Rockefeller University where he studies how large-scale dynamics of neuronal networks are related to brain functions and behavior. To do so, he develops new high-speed optical techniques that push the boundaries on spatial and temporal resolution, as well as volume size and depth for recording dynamic interactions of neuronal populations in awake behaving animals. He holds a Ph.D. in Physics from the University of Vienna, completed postdoctoral training at the National Institute of Standards and Technology and the University of Maryland. He subsequently worked a research scientist at HHMI Janelia Research Campus.