

Optical tools for large-scale in vivo Interrogation of neuronal activity underlying behavior

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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. Using this approach in combination with genetically encoded calcium (Ca²⁺) indicators we have shown that near-simultaneous recording of whole-brain neuronal activity in *C. elegans* at single cell resolution is possible. Moreover, the combination of light sculpting microscopy with rapid volumetric scanning has allows for unbiased, high-speed and single-cell resolution volumetric calcium imaging in scattering tissues. Using this technique, we have shown that the activity of thousands of neurons in a mouse cortical column or the hippocampus can be captured in awake behaving animals.

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 Ca²⁺ 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 during free behavior. 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.

References:

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