PROBING NEURAL CIRCUITS WITH SHAPED LIGHT

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KEY WORDS: Adaptive optics, wavefront shaping, in vivo imaging, brain, neural imaging, fluorescence microscopy, two-photon fluorescence microscopy, Bessel beam

ABSTRACT: To understand computation in the brain, one needs to understand the input-output relationships for neural circuits and the anatomical and functional relationships between individual neurons therein. Optical microscopy has emerged as an ideal tool in this quest, as it is capable of recording the activity of neurons distributed over millimeter dimensions with sub-micron spatial resolution. I will describe how we use concepts in astronomy and optics to develop next-generation microscopy methods for imaging neural circuits at higher resolution, greater depth, and faster speed. By shaping the wavefront of the light, we have achieved synapse-level spatial resolution through the entire depth of primary visual cortex, optimized microendoscopes for imaging deeply buried nuclei, and developed a video-rate (30 Hz) volumetric imaging method. We apply these methods to understanding neural circuits, using the mouse primary visual cortex as our model system.

(A) Adaptive optics was used to correct brain-induced aberrations and (B) recovered synapse-resolving image resolution at depth in mouse brain in vivo. (C) A minimally invasive microendoscopy system (D) was used to measure the calcium activity of neurons in lateral hypothalamus (5 mm depth) of the mouse brain in vivo. (E) Conventional two-photon volume imaging using Gaussian focus requires taking multiple frames, whereas (F) an axially elongated Bessel focus can scan a volume in one frame at 30 Hz while maintaining synapse-resolving resolution. Scale bars: B, 5µm; C, 1 mm; D, E, F, 20 µm;