**Docket #:** S14-043

# Optogenetics System for High-Speed, Precise Imaging and Control of Neuronal Circuits in Live Animals

Researchers in Prof. Karl Deisseroth's laboratory have developed a highly precise, scalable optical system for imaging or controlling thousands of individual neurons in the 3D volume accessible with a single multiphoton fluorescent microscope objective. This technology utilizes custom hardware and software to multiplex spatial light modulators (SLMs) such that the speed and intensity of the imaging laser is increased without damaging the SLMs. This allows high spatial resolution (1 micron) during a behavioral task in awake, live animals. In addition, light-responsive neurons can be manipulated and imaged simultaneously to dissect effects on surrounding neural activity, reading out local dynamics in real time with neural activity imaging at greater than single cell resolution. By eliciting and emulating precise patterns of natural neural activity in large areas (tissue spanning cortical layers and multiple brain regions), this technology could be used for research into the links between neural activity and behavioral/cognitive outcomes. It could also be used to manipulate specific neurons to augment perception and provide realistic sensory feedback for neural prosthetics.

**Stage of Research**

The inventors have developed and tested key components of this system and demonstrated:

a) transition between different holograms (3D brain volumes) at 330-500 Hz with 90-100% target hologram efficiency

b) combining two SLMs could excite twice as many neurons and reduce stimulation duration to a few hundred microseconds

c) capability to stimulate at least 50 neurons/ms with true simultaneity in kilohertz ensemble activation over a 1mm$^2$ field of view

d) read/write performance across multiple cortical layers

## Applications

- **Optogenetic brain imaging and neuronal control in live animals with multiphoton fluorescence microscopy**:
  - imaging and neuronal stimulation occurs simultaneously to measure effects on surrounding neural activity
  - facilitates mapping neuronal circuits and effects on neural dynamics and behavior
  - could augment perception of animal with highly realistic patterns of activity
- **Neural prosthetics** - enhance plasticity and learning for sensory feedback

## Advantages

- **High speed, high precision imaging and control** in a living brain:
  - micron-level spatial precision/resolution of selected individual neurons
  - millisecond-level temporal precision with high refresh rate
  - selectively controls ~15,000 neurons in a 3D field of view (e.g., spanning an entire cortical column)
- **Scalable** - temporal precision and number of neurons that can be activated scales with the number of spatial light modulators added and integrated in the system

## Patents

- Published Application: WO2019183376
- Published Application: 20210063964
- Issued: 11,703,800 (USA)

## Innovators

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