HectoSTAR microLED Optoelectrodes for Large-Scale High-Precision *in vivo* Opto-Electrophysiology

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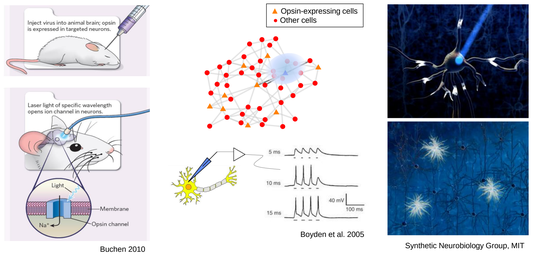
Why microLEDs?

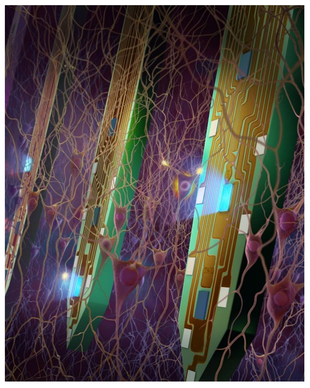


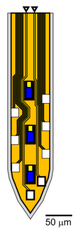
Buchen 2010

Boyden et al. 2005

Synthetic Neurobiology Group, MIT

Optogenetics allows fast, cell-type-specific manipulation of neuronal activities. A combination of this technique with *in vivo* extracellular electrophysiology via μLEDs can lead to discovery of fundamental cellular communication mechanisms in the brain:





These optoelectrodes are microfabricated, silicon-based implantable multi-electrode arrays (neural probes) with monolithically integrated, cell-sized LEDs and electrodes. These devices enable highly selective optical stimulation of ChR2-expressing neurons and simultaneous electrical recording of the resulting neuronal signals with little to no stimulation artifact. Here, we present a device that further extends the capability of the microLED optoelectrodes. The device can provide optical stimuli to more than one hundred stimulation sites located amidst its neuronal signal recording electrodes and thus enables targeting of neurons at local and long ranging scales. To emphasize the device's capability to deliver optical stimulation to more than hundred (hecto-) stimulation targets at the anatomical resolution, we named the device hectoSTAR microLED optoelectrode.

HectoSTAR microLED Optoelectrodes

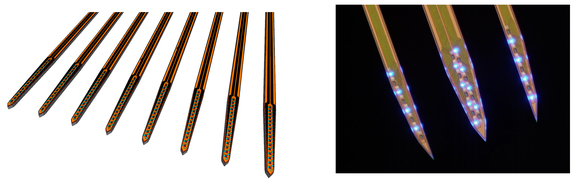
256 Platinum Iridium Electrodes
128 Blue microLEDs

The HectoSTAR optoelectrode was designed according to a few guidelines that can maximize the utility of the device:

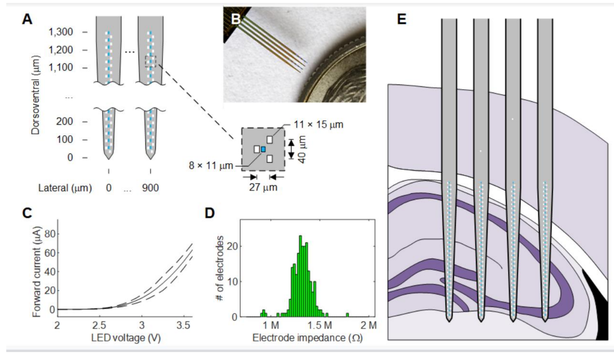
1. **The optoelectrode was required to record from as many neurons as possible from a wide brain area.**
2. **The activity of a neuron within the recorded region should be recorded from preferably more than one electrode. A hypothetical neuronal layer within the region should be able to be selectively stimulated from either above the layer, within the layer, or below the layer using an LED, without having to move the optoelectrode.**
3. **The cross-sectional area of each shank of the optoelectrode should be made as small as possible in order to minimize the acute damage induced in the tissue during insertion.**

The hectoSTAR microLED optoelectrode was fabricated in a four-shank configuration, where 64 electrodes and 32 LEDs are placed on each of the shanks. A considerably large section of a brain (either coronal or sagittal, depending on the application), whose area is as large as 1.17 mm^2 (900 × 1,300 um), can be studied in one insertion of the optoelectrode:

- **The vertical and the horizontal coverage is large enough to cover the whole CA3 and a part of CA1 in a mouse's dorsal hippocampus (see right, E).**
- **For example, For example, the signal propagation and the dynamics of long-term potentiation via Schaffer's collateral can be studied with a single insertion.**
- **The tight electrode configuration allows multiple electrodes to simultaneously pick up the activities of a neuron and assist spike sorting.**
- **The microLEDs (8 × 15 um) are located at the center of the shank, allowing a precise, co-localized optical stimulation of the neurons whose activities are being monitored by the electrodes.**

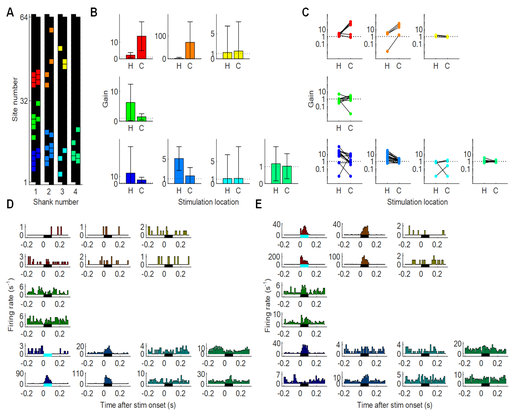


8-shank HectoSTAR Optoelectrode and example microLED illumination



A HectoSTAR shank, microLED and electrode dimensions. **B** Fabricated 4-shank HectoSTAR. **C** microLED IV characteristics **D** electrode impedance histogram. **E** The locations of the electrodes and the LEDs on a hypothetical hectoSTAR optoelectrode implanted inside the dorsal hippocampus of a mouse brain. The solid purple line indicates the pyramidal layer in the hippocampus.

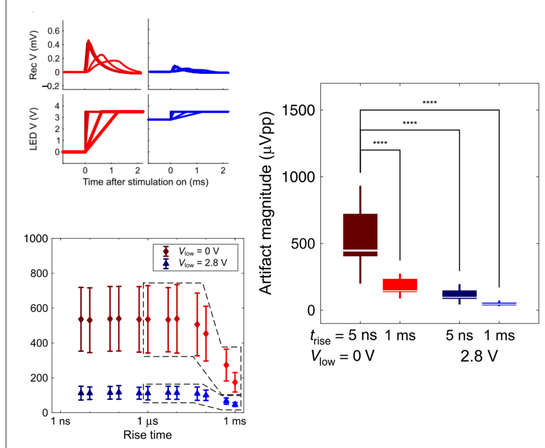
Local and Long Range Circuit Analysis



A Locations of groups of neurons whose collective and individual activity patterns are shown in parts B through E. Neurons whose action potentials were recorded the largest from an electrode are indicated with the same color as the electrode. B Firing rate gain of each neuron in each neuronal group whose location is shown in part A during hippocampal and cortical optical stimulation. Boxes indicate the mean and error bars indicate one standard deviation. Patterns similar to those shown in Fig 5C and 5D are visible. C Change in the firing rate gain of each neuron in each neuronal group. Closer analysis reveals responses of a few individual neurons acting differently from the other neurons in the same group. D-E Peristimulus time histograms (PSTHs) of a few selected neurons from each group during (D) hippocampal stimulation and (E) cortical stimulation. The solid line underneath each histogram indicates the duration (with its length) and the location (with its color; light blue color indicates the presence of the LED in the vicinity) of the optical stimulation. The activity of a hippocampal neuron (whose PSTH is shown on both part D and E on the first column from the left, the second row from the bottom) is inhibited during hippocampal optical stimulation and strongly enhanced during cortical stimulation, suggesting both an inhibitory intra-hippocampal connection and an excitatory cortical-hippocampal connection.

Artifact Free Stimulation

The HectoSTAR Optoelectrodes were fabricated with high boron doping density and an extra metal layer between recording and stimulation interconnects, yielding virtually no stimulation artifact (less than 50 uV pk-pk) (see below).



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F. Wu, et al., "Monolithically Integrated mLEDs on Silicon Neural Probes for High-Resolution Optogenetic Studies in Behaving Animals," *Neuron*, vol. 88, no. 6, pp. 1136 – 1148, Dec. 2015

Kim, K., Vöröslakos, M., Seymour, J.P. *et al.* Artifact-free and high-temporal-resolution in vivo opto-electrophysiology with microLED optoelectrodes. *Nat Commun* 11, 2063 (2020)

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