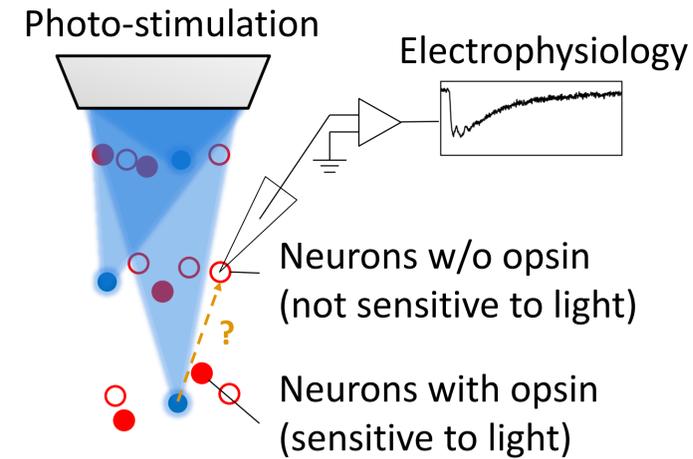# Three-dimensional Multi-site Random Access Photo-stimulation (3D-MAP)

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MOTIVATION

Photo-stimulation

Electrophysiology

Neurons w/o opsin (not sensitive to light)
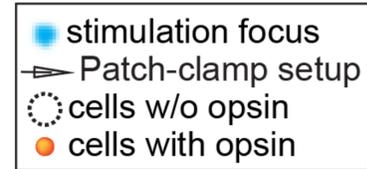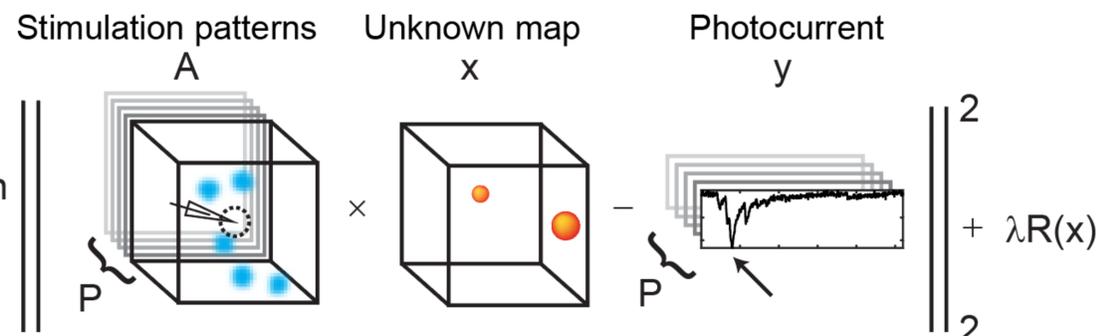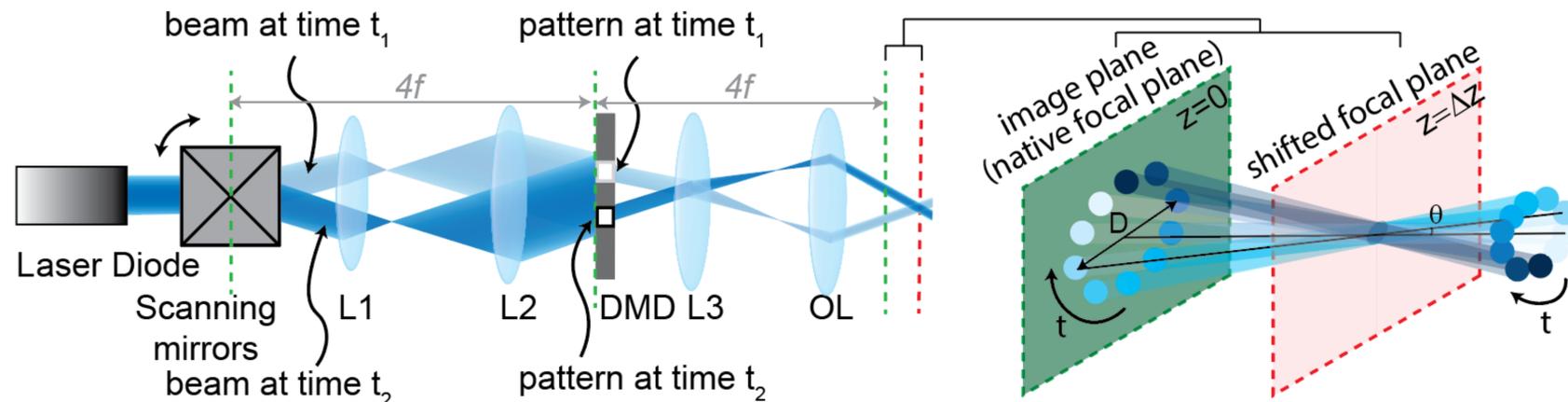
Neurons with opsin (sensitive to light)

Optogenetics enables optical control of brain circuits to study brain functions.

Key requirements for photo-stimulation:
- **Fast**
- **High resolution**
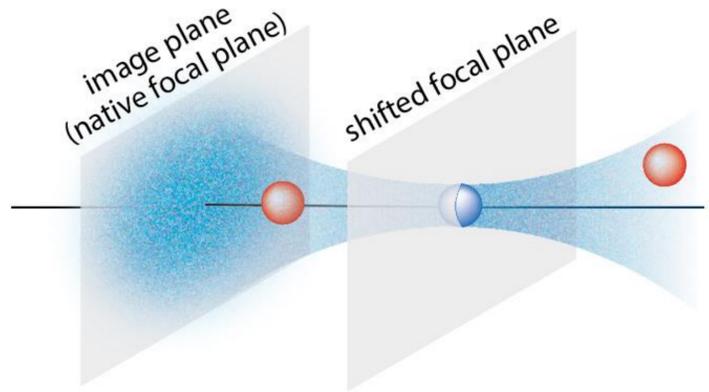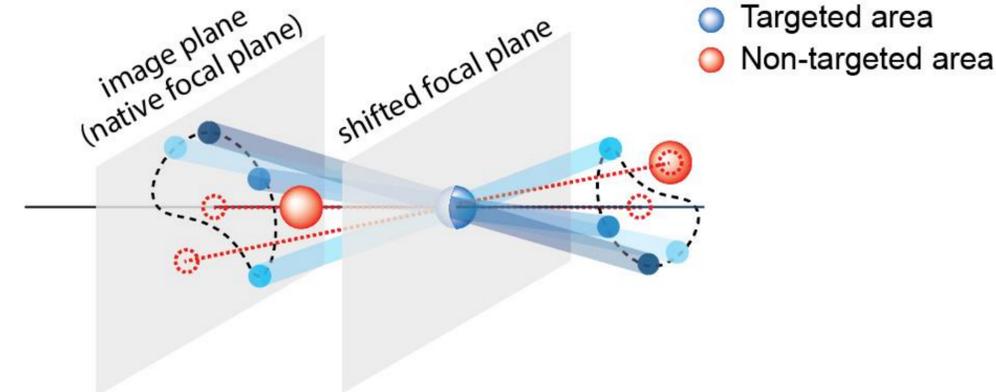- **Multi-site**
- **Accurate**

- 3D-MAP is **faster** and **more accurate** than conventional computer generated holography (CGH) because 3D-MAP has more degrees of freedom to generate special patterns that CGH cannot.

**One-photon Computer Generated Holography (<0.5kHz pattering speed)**

3D-MAP (1k-20kHz patterning speed)

image plane (native focal plane)   shifted focal plane

- Targeted area
- Non-targeted area

METHODS

- 3D-MAP generates 3D patterns by 4-D light-field control and reconstructs brain circuit maps by compressive sensing.

beam at time t_1 pattern at time t_1

4f   4f

Laser Diode

Scanning mirrors
beam at time t_2

L1   L2   DMD L3   OL

pattern at time t_2

image plane (native focal plane) z=0   shifted focal plane z=ΔZ

D   θ   t

$$\underset{x\geq0}{\mathrm{argmin}} \left\| A \times x - y \right\|_2^2 + \lambda R(x)$$

Stimulation patterns A

Unknown map x

Photocurrent y

P

- stimulation focus
- Patch-clamp setup
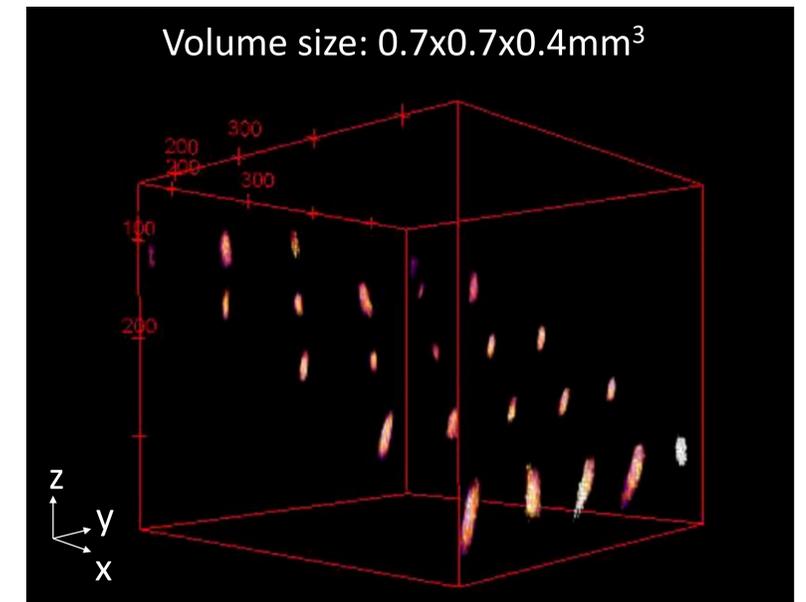- cells w/o opsin
- cells with opsin

- 3D-MAP achieves **high spatial resolution** and large accessible volume at the same time. 3D-MAP is able to generate **multiple foci simultaneously**.

3D Point-Spread Function

z
y x   10μm

Volume size: 0.7x0.7x0.4mm³
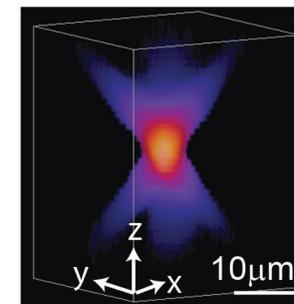
Spatial resolution:
$5.3 \times 5.3 \times 18 \ \mu m^3$

z
y
x

Ref: Xue, Y., Waller, L., Adesnik, H. & Pegard, N. bioRxiv 2020.06.28.176503 (2020) doi:10.1101/2020.06.28.176503