Talking to the Brain: Electrophysiology and Opto-Neuromodulation at Cellular Resolution

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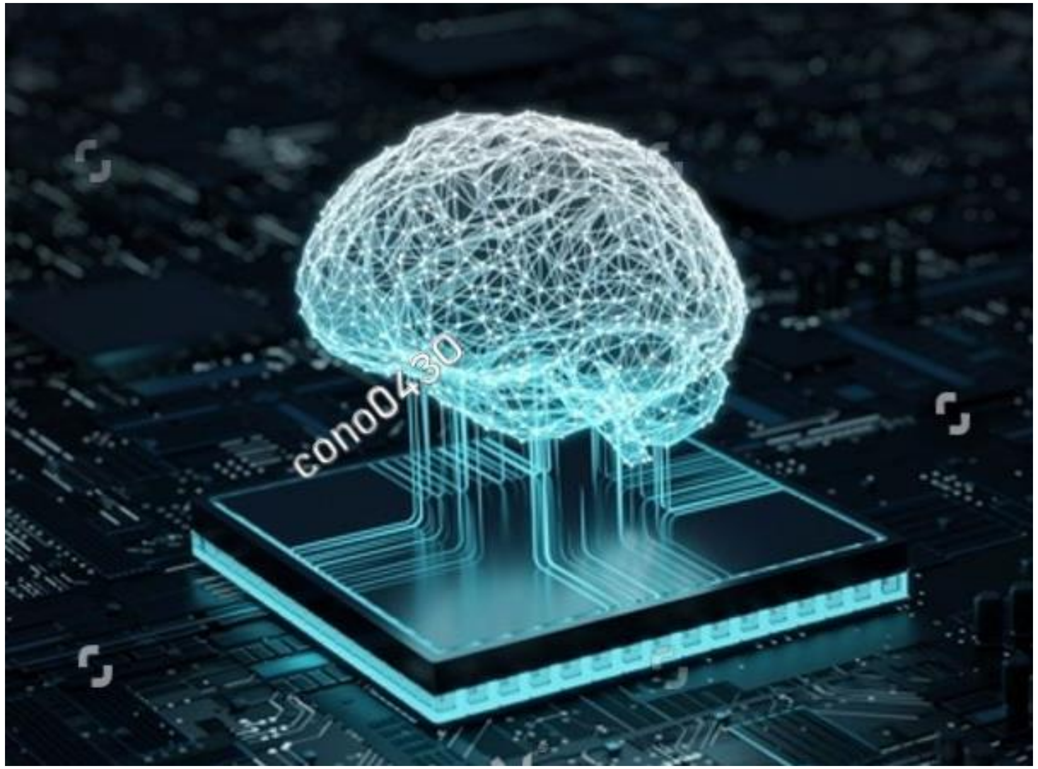
E. Yoon is one of co-founders and shareholders of NeuroLight Technologies.

Hello, Brain!

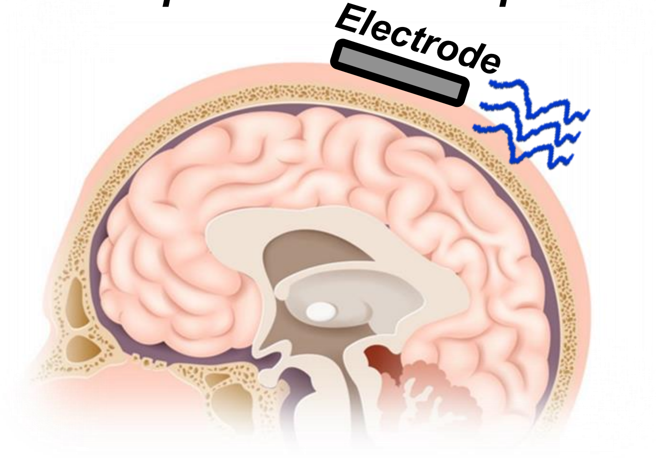


Listening to Brain: Electrical Neuro-Recording

More neuronal information

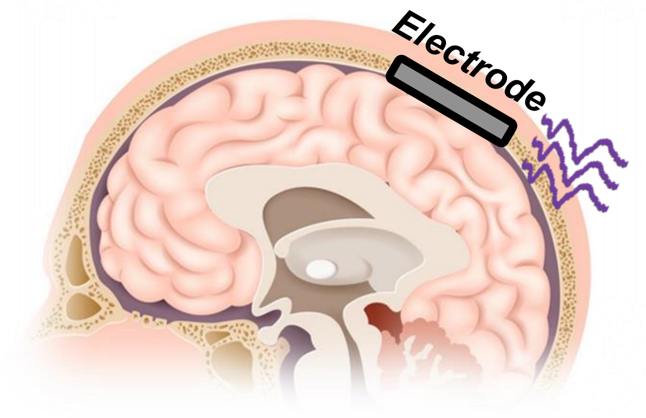
EEG

Superimposed slow & large potential on scalp



ECoG

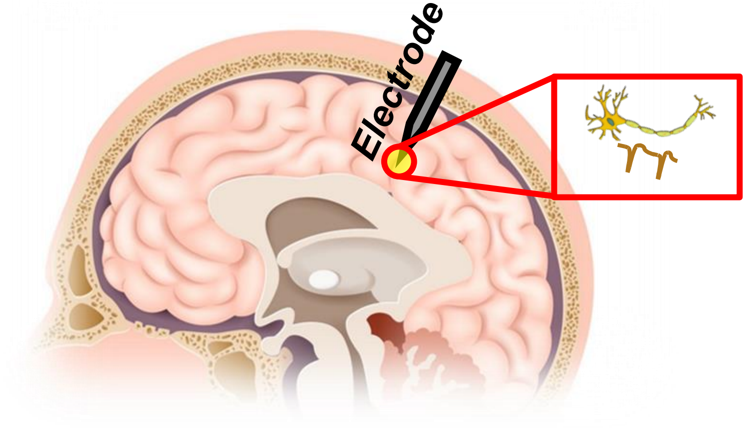
Superimposed slow & large potential on cortex



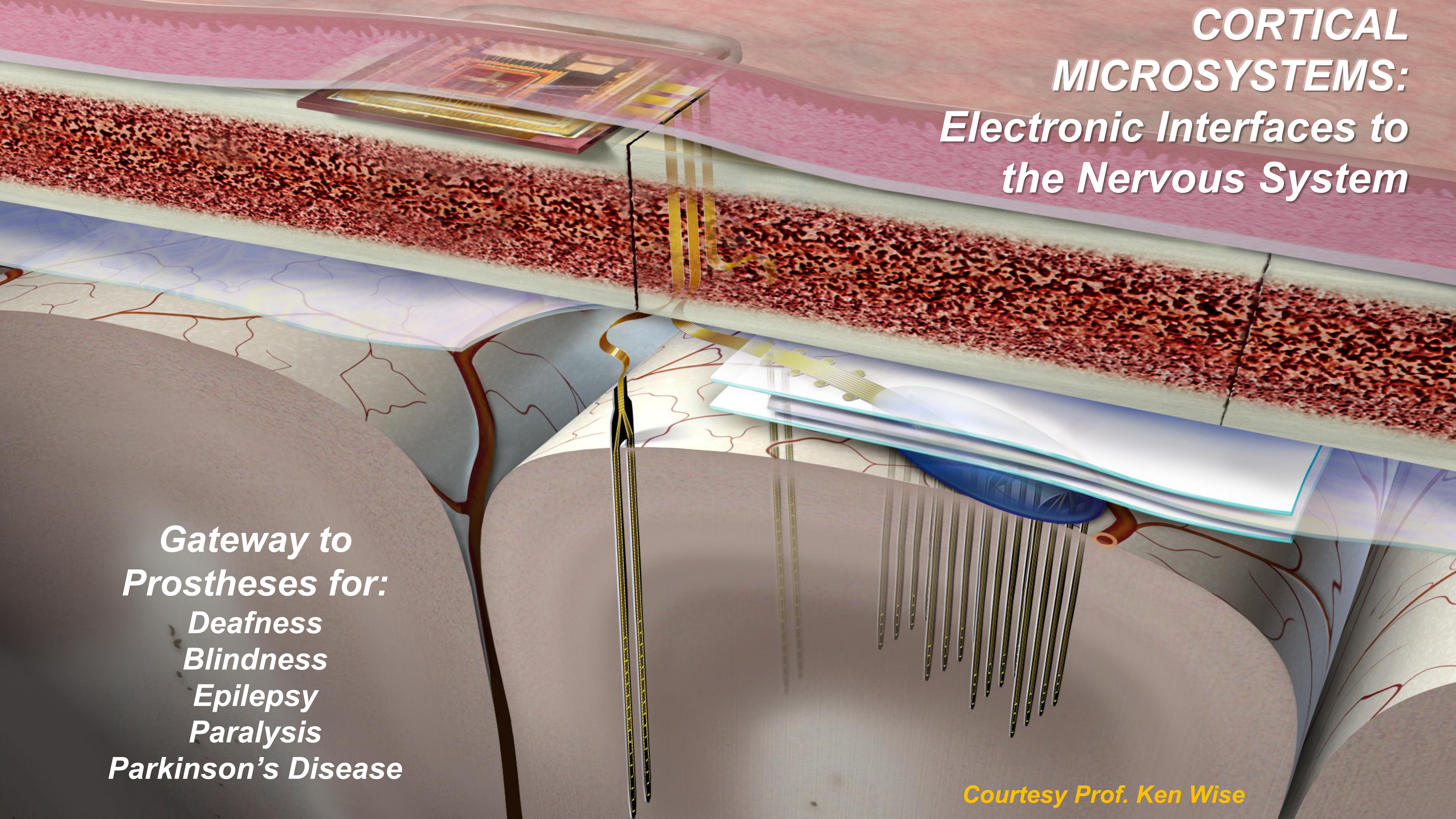
Deep-brain (Subcortex)

Near neuron potential

→ Fast & tiny single-cell activity

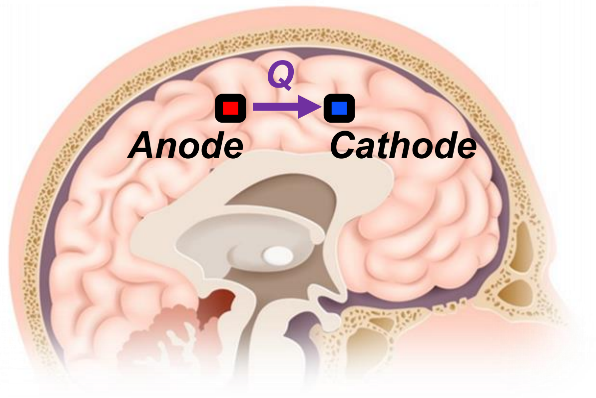


Less invasive surgery


CORTICAL
MICROSYSTEMS:
Electronic Interfaces to
the Nervous System
Gateway to
Prostheses for:
Deafness
Blindness
Epilepsy
Paralysis
Parkinson’s Disease
Courtesy Prof. Ken Wise

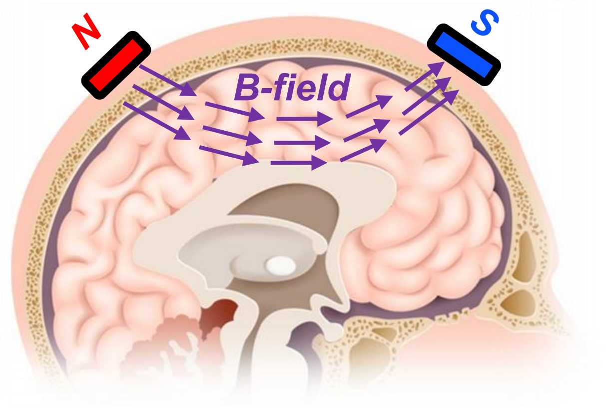
Talking to Brain: Neuromodulation

Electrical stimulation



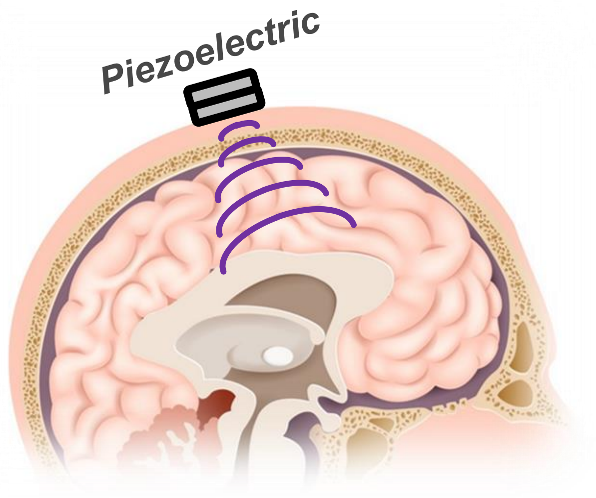
Localization O
Single-cell targeting X
High intensity O
Low artifact X
Tissue safety X

Magnetic stimulation



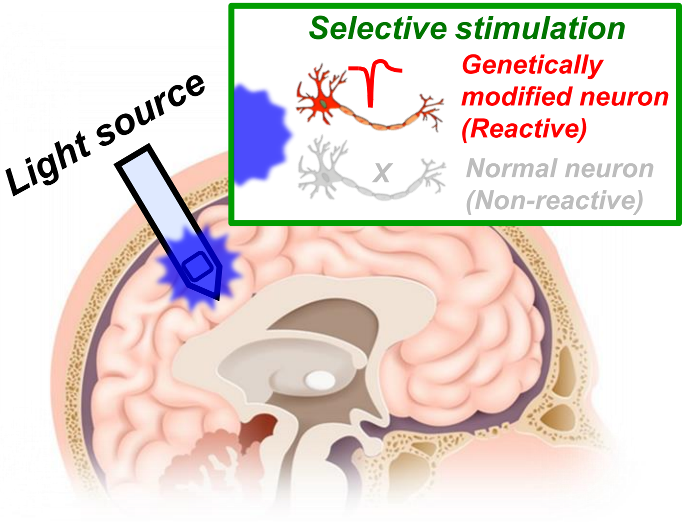
Localization X
Single-cell targeting X
High intensity X
Low artifact O
Tissue safety O

Ultrasonic stimulation



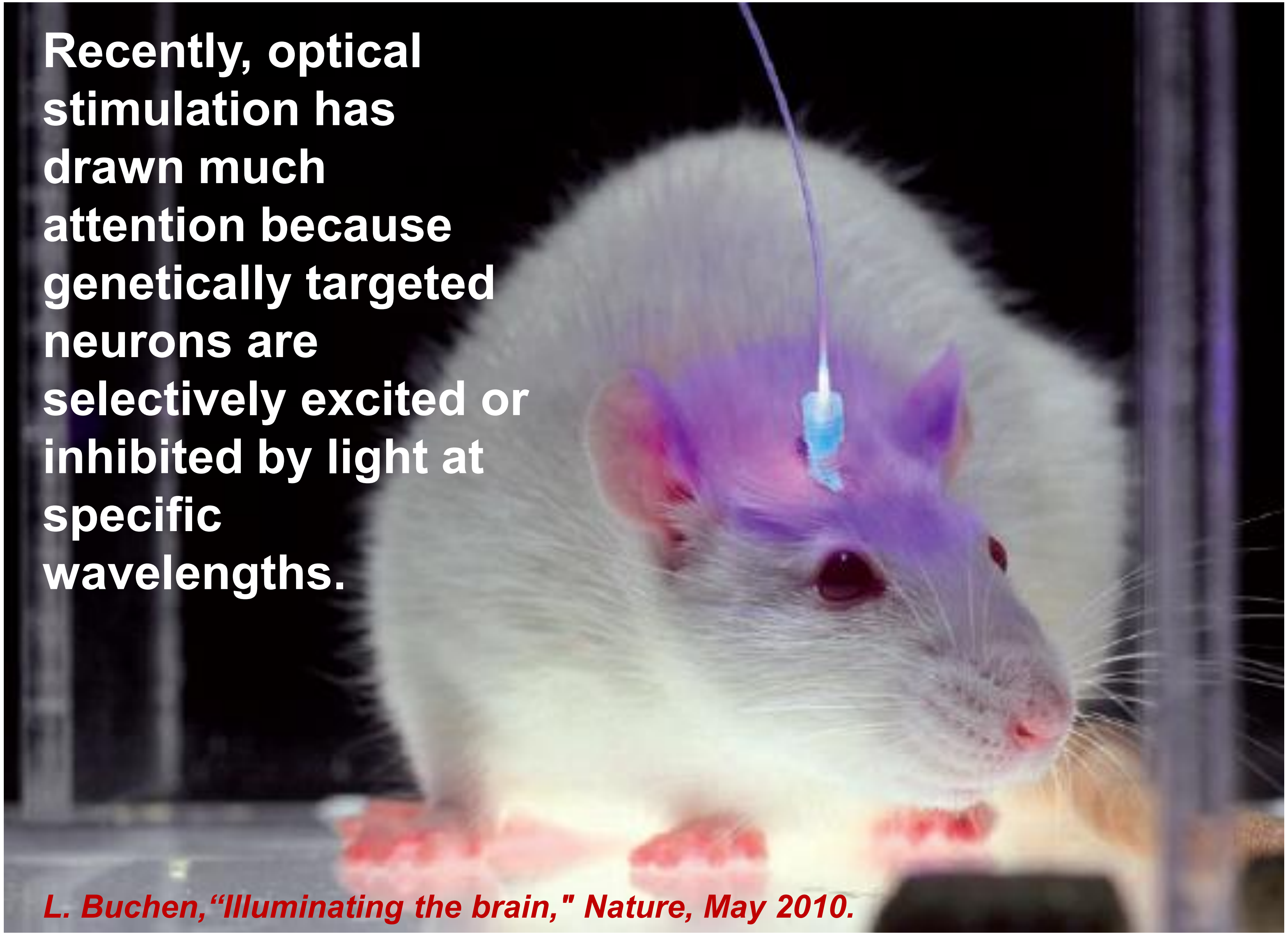
Localization X
Single-cell targeting X
High intensity X
Low artifact O
Tissue safety O

Optical stimulation



Localization O
Single-cell targeting O
High intensity O
Low artifact O
Tissue safety O

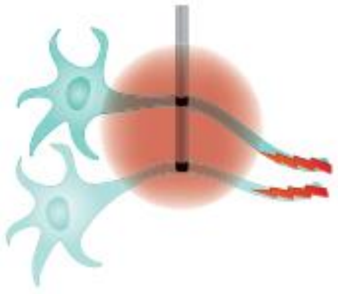
Talking to Brain: OPTICAL MODULATION



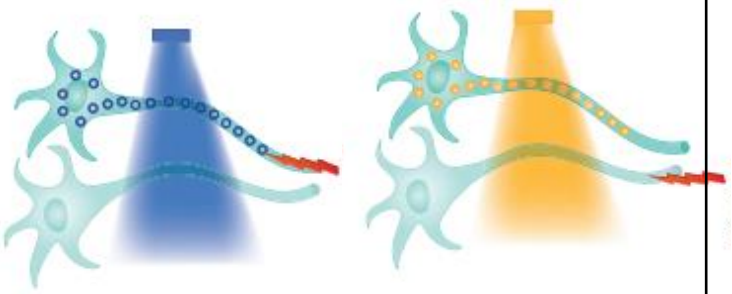
Recently, optical stimulation has drawn much attention because genetically targeted neurons are selectively excited or inhibited by light at specific wavelengths.

L. Buchen, "Illuminating the brain," Nature, May 2010.

Electrical stimulation

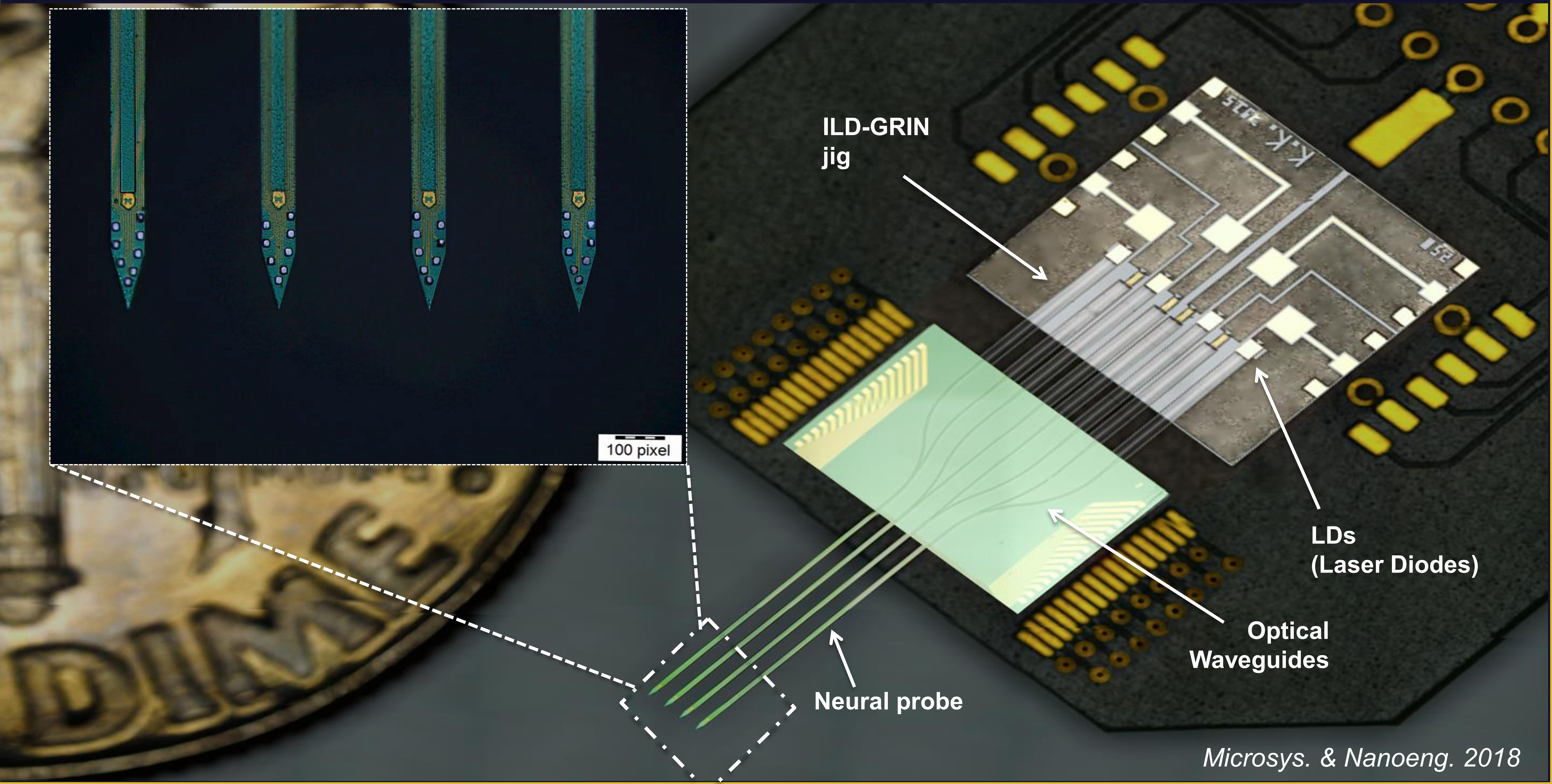


Optical stimulation



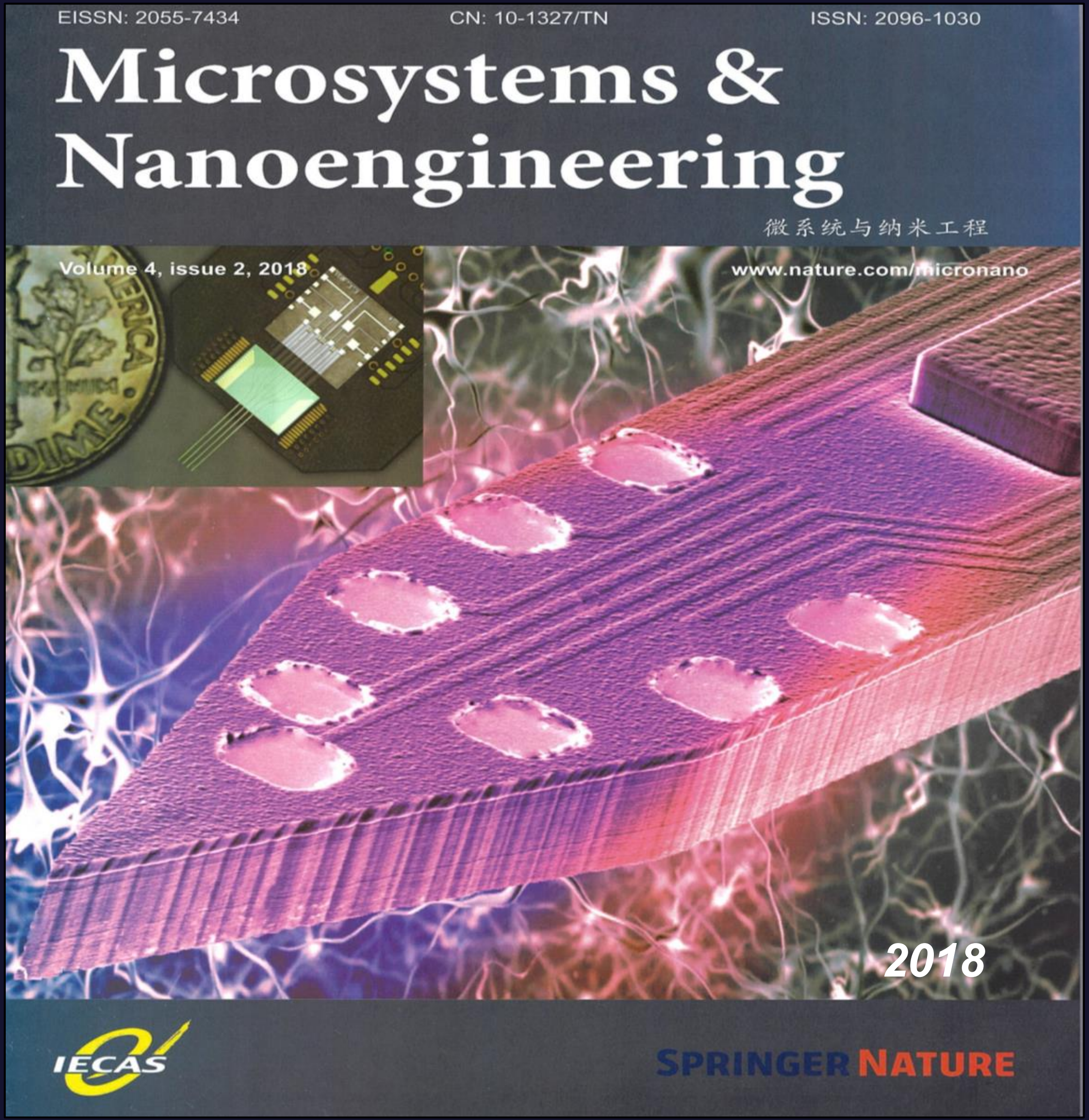
cell specific!

Fiberless Dual-Color Multi-Shank Optoelectrode



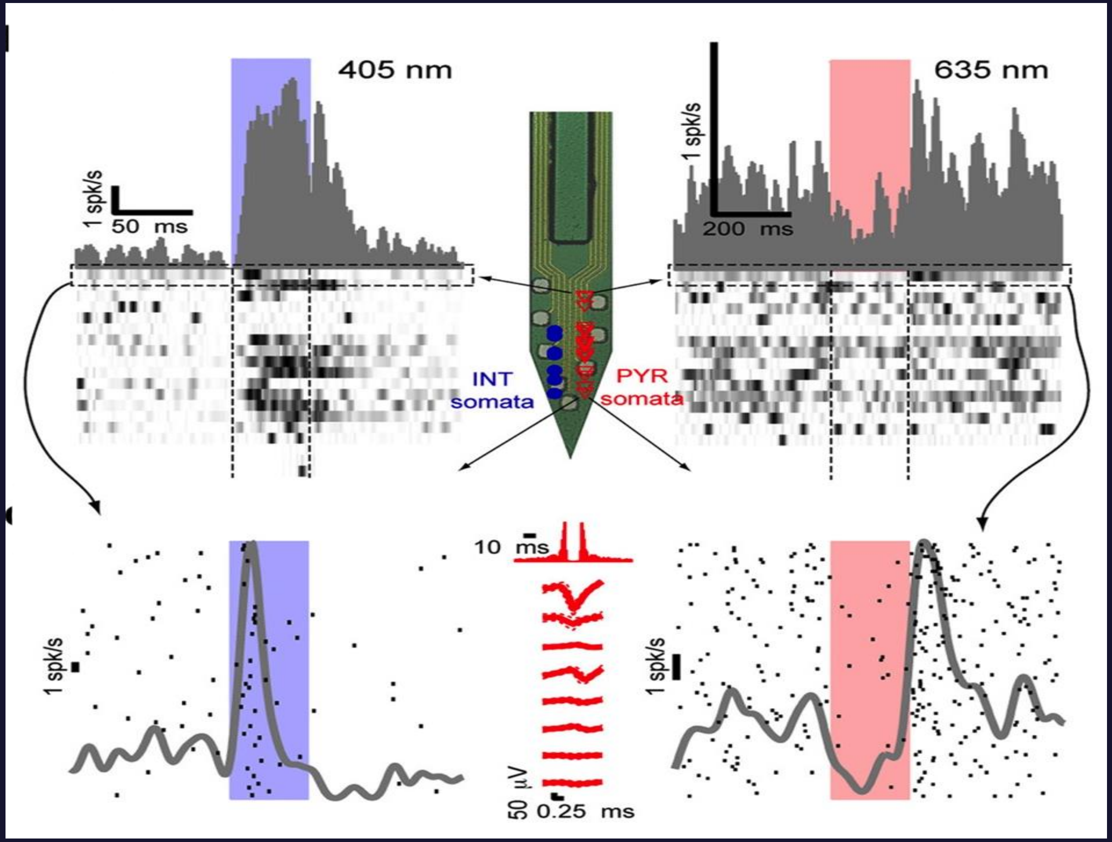
Microsys. & Nanoeng. 2018

Dual-Color Neuromodulation In-Vivo



Best Paper Award

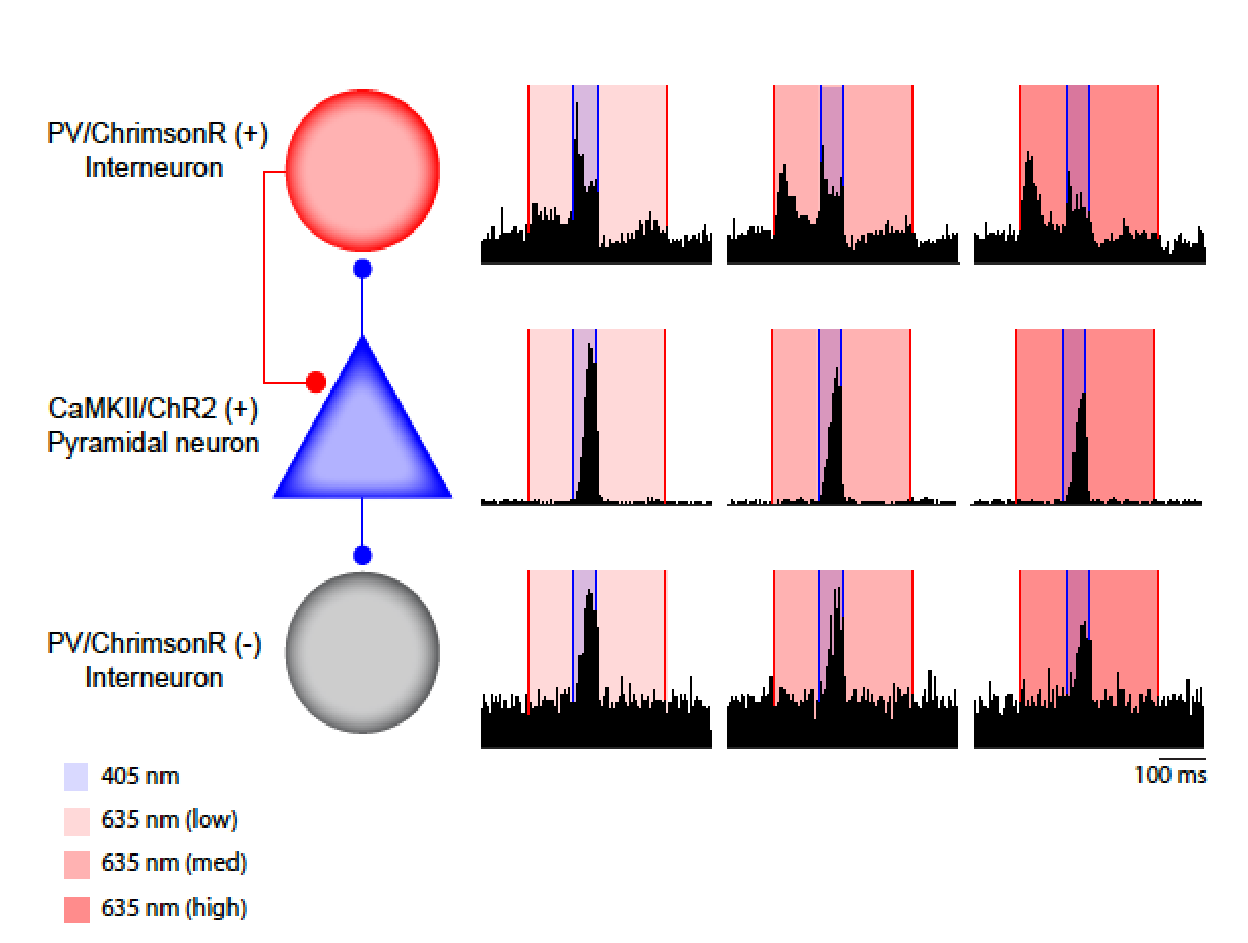
Bi-directional control (activation and silencing) of single PYR neuron



Neurocircuit Connections

Independent control of PYR and PV neurons in a local circuit with high temporal resolution

D. English, G. Buzsaki



Microsys. & Nanoeng. 2018

Monolithic Integration of μLEDs on Shanks

Advantages:

- ***Fiberless*** external connection

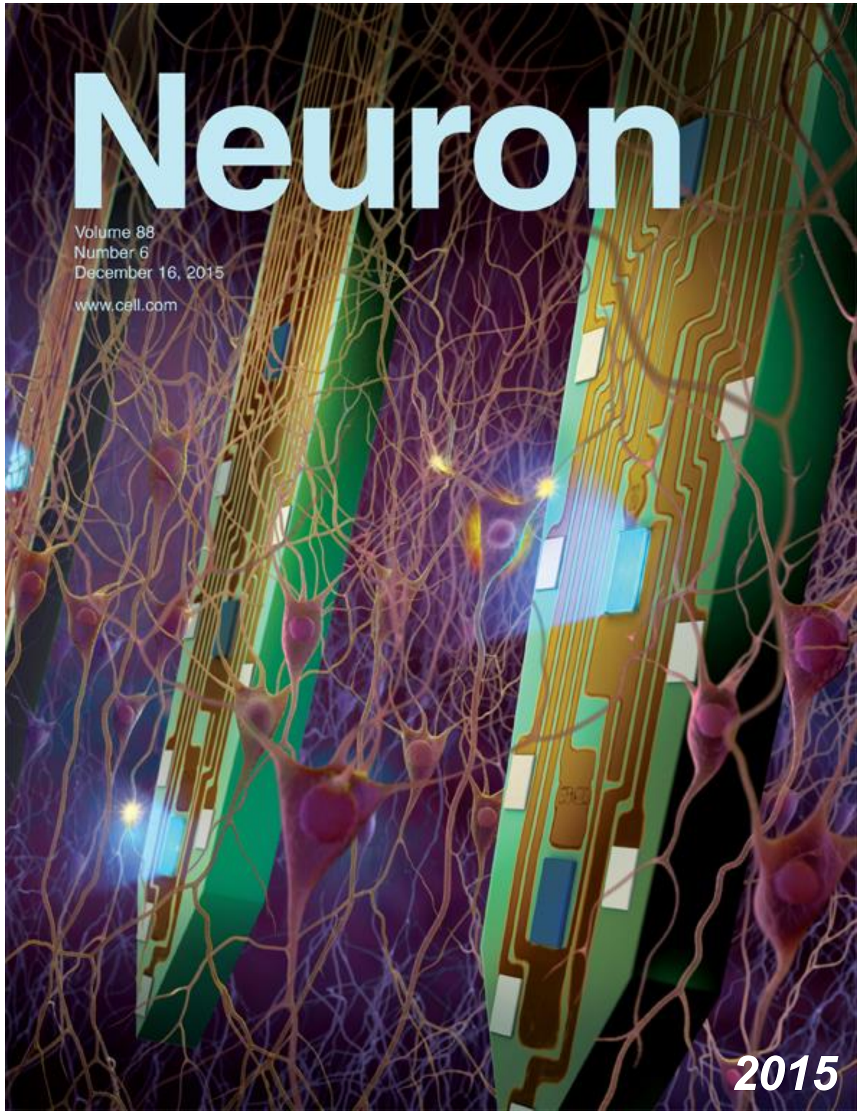
- ***No Optical Couplers***

- ***Subcellular*** stimulation resolution

  μLED emission area:
  10 μm x 15 μm

- ***High scalability***

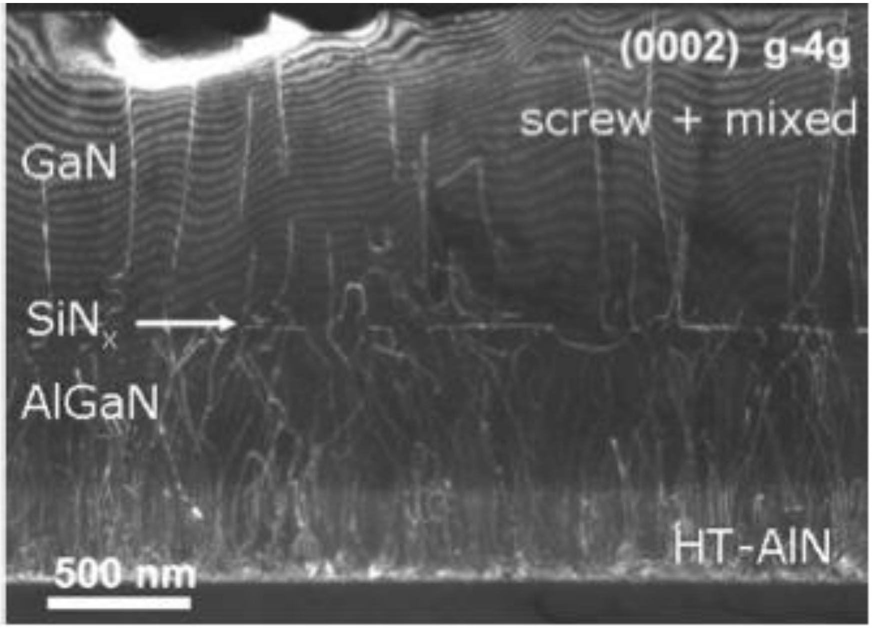
- Minimal surface topology



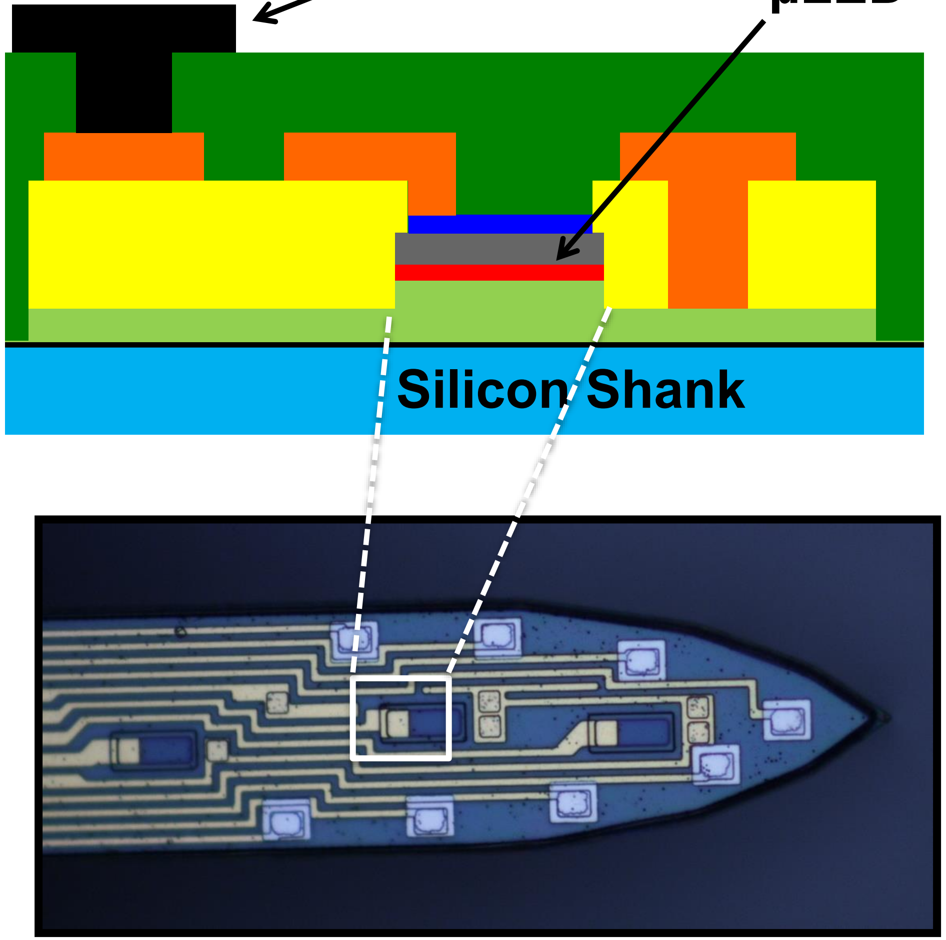
12! = 480 million possible spiking sequences: artificial generation of spatial memory

Monolithic Integration of μLED-on-Silicon

η_r ~33% on Si; >70% on sapphire

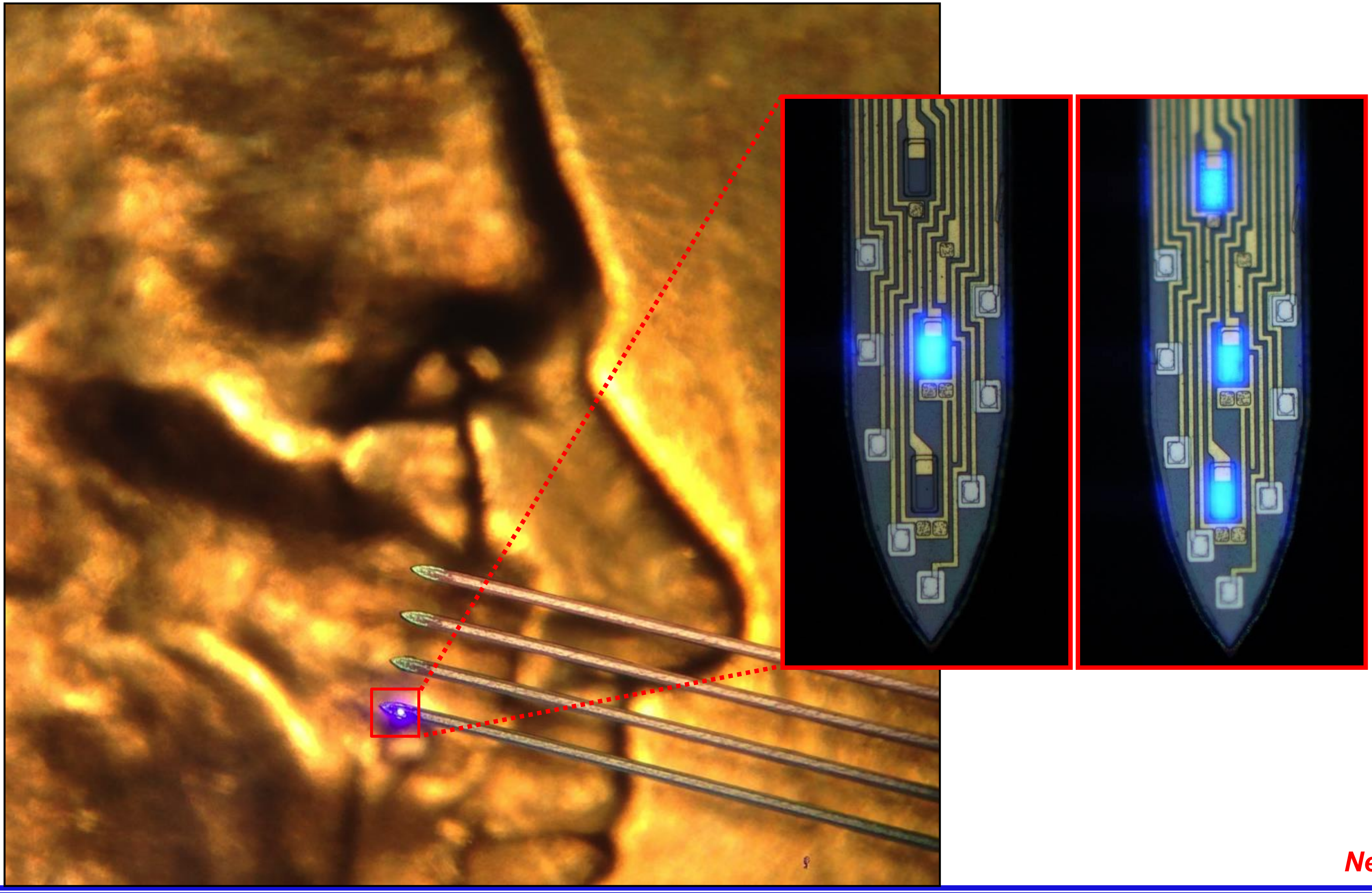


Zhu, Proc. SPIE, 2009



Wafer thinning by dry etching to release the final probe structure

FIBERLESS OPTICAL STIMULATION: Lighting the μLEDs



Neuron 2015

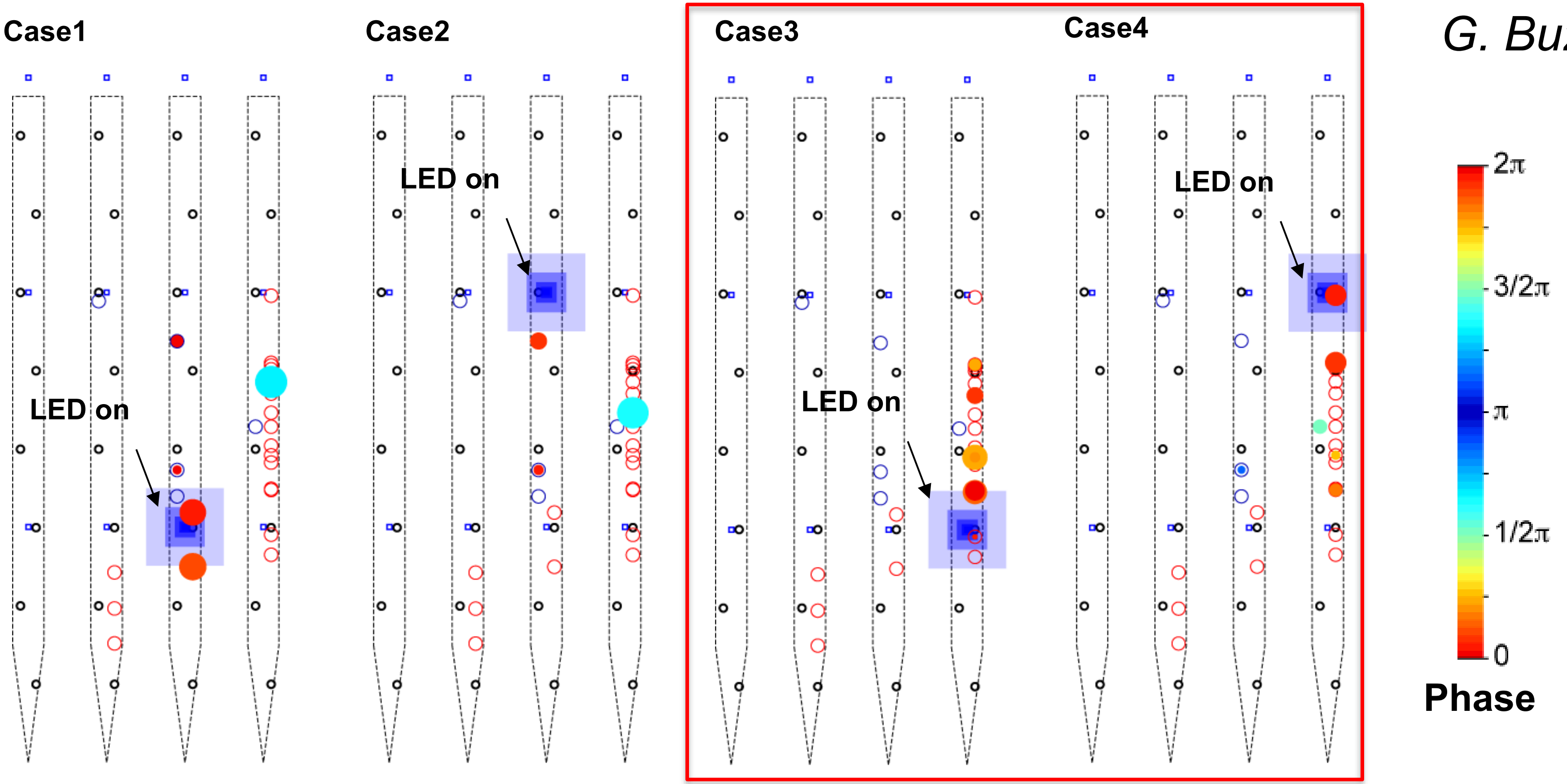
A Lightshow for the Brain

Neuron 2015, 2017
Science 2022

Low Power Cellular Mapping

Stimulation using 0.8μW (4.9mW/mm^2) light output

E. Stark,
G. Buzsaki



Open circles = spontaneous activity; Filled circles = induced activity

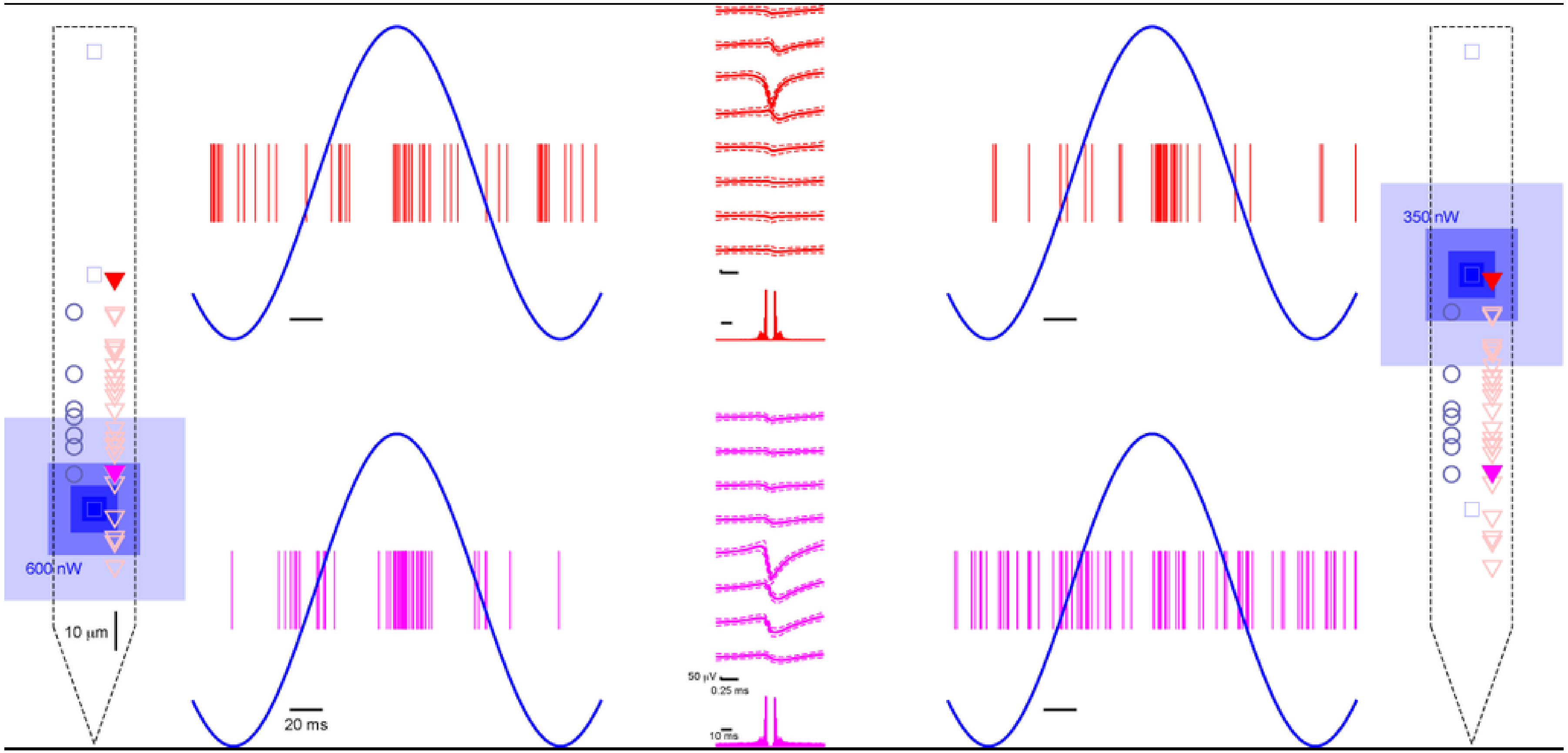
- Different μLEDs (60μm pitch) on the same shank activates different neurons.
- Indirect circuit activation can be observed by anti-phase-locked activities.

Selective Stimulation at Single-Cell Resolution

- Stimulation at 0.8μW (4.9mW/mm^2)
- μLED separation: 60 μm
- PYR neuron distance: 50 μm

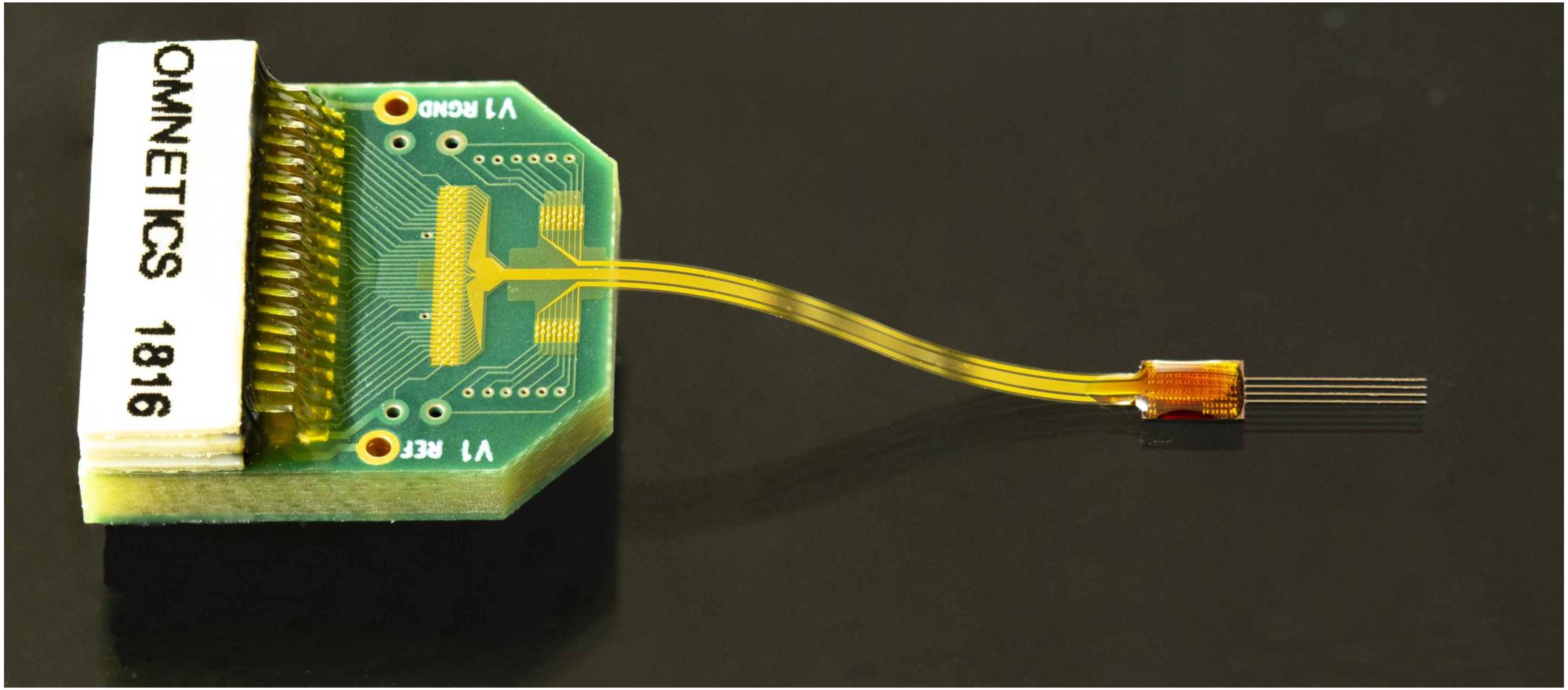

Dr. Eran Stark


Prof. György Buzsáki



MiniSTAR μLED OPTOELECTRODES

DISSEMINATION: NSF NeuroNex Hub: MINT (Multimodal Integrated Neural Technologies)

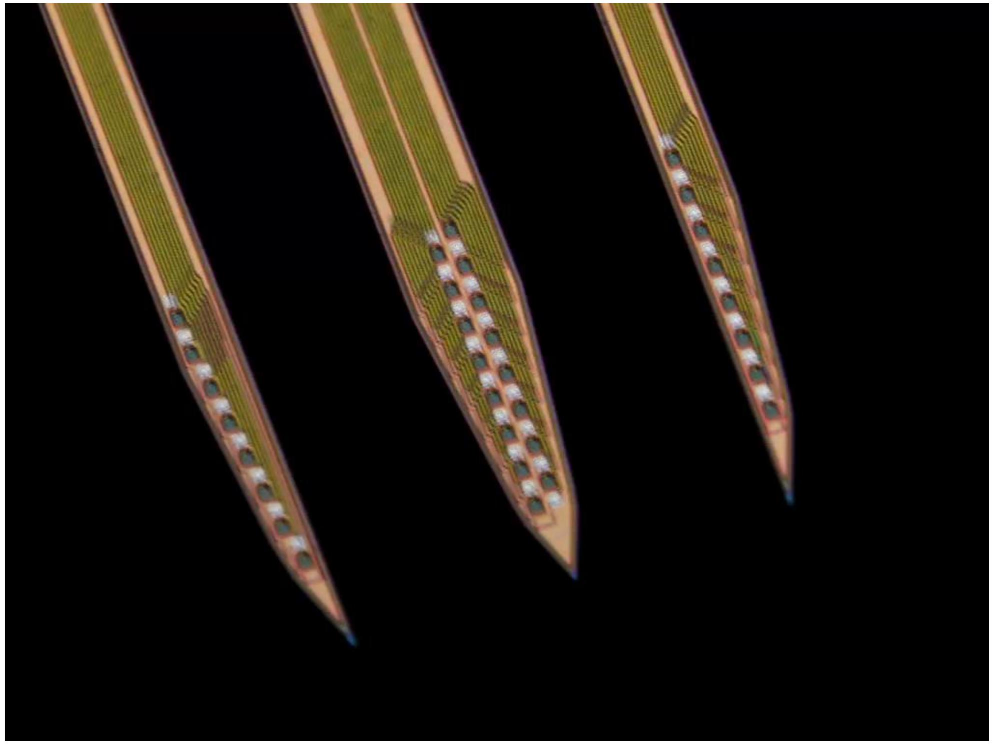


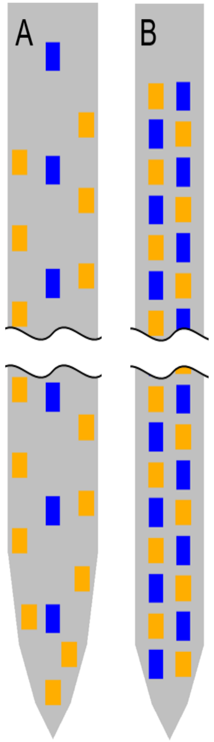
ContactMINT@umich.edu

TRANSLATION: NeuroLight Technologies, LLC

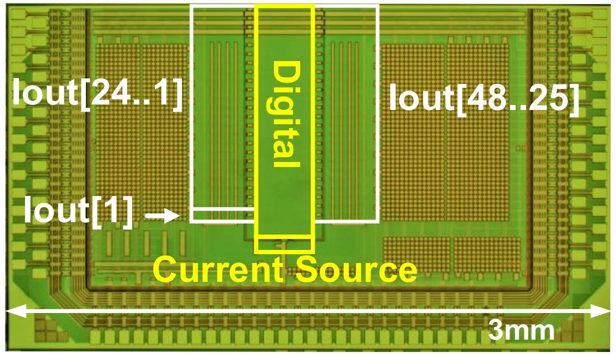
Scaling the Number of LEDs

- Scaling to a large number of optical stimulation sites and recording sites.
- > 120-ch optical stimulation control chip





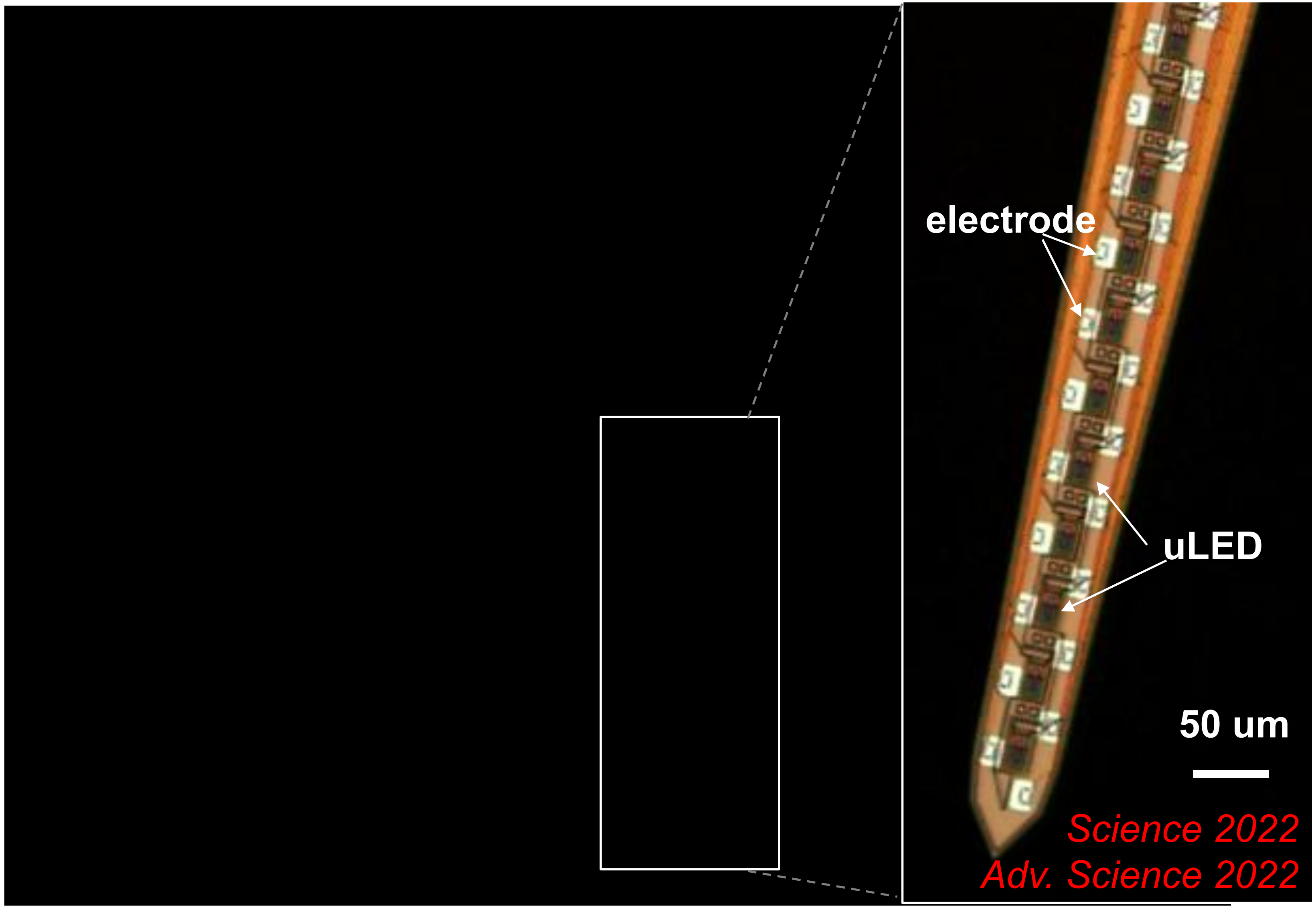
Controlled by custom driver IC



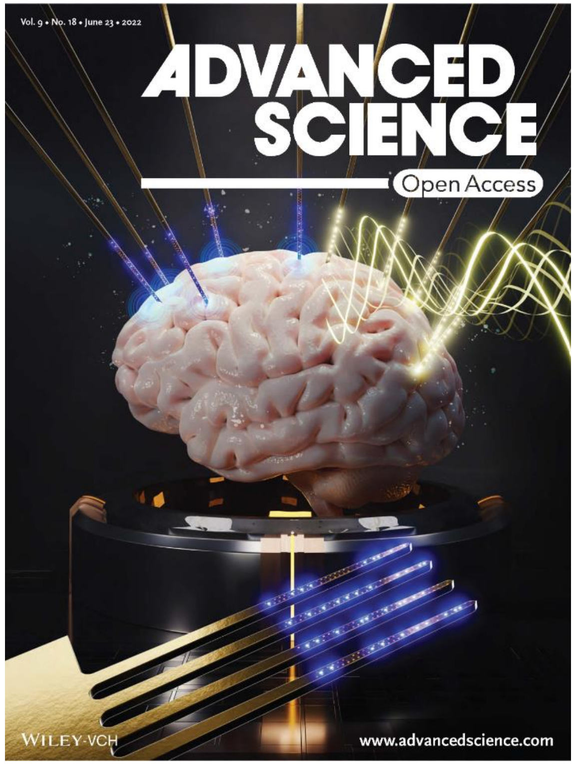
BioCAS 2017

HectoSTAR μLED OPTOELECTRODES

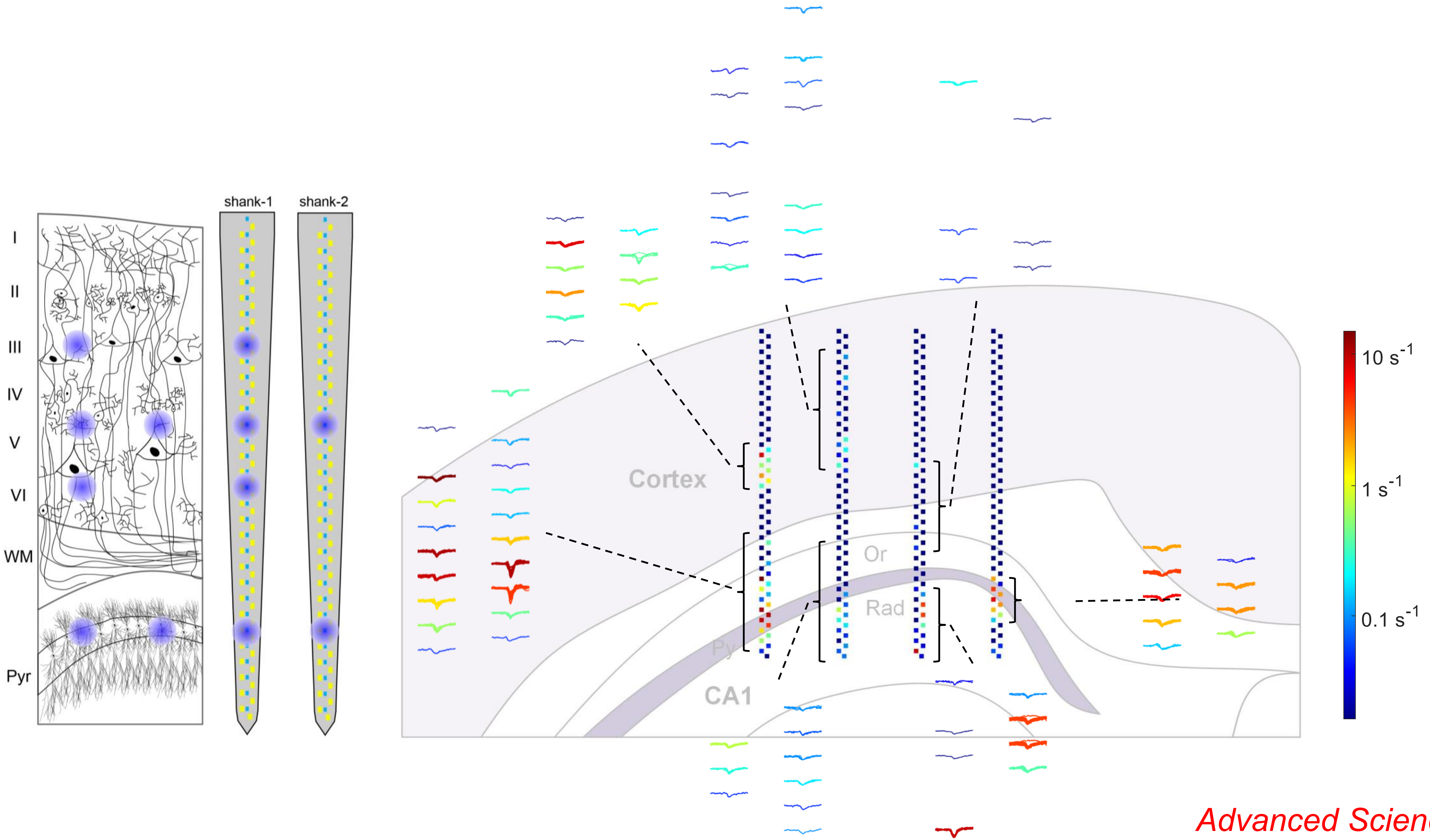
HIGH-DENSITY, LARGE-SCALE OPTICAL MODULATION



- 256 recording sites
- 128 μLEDs

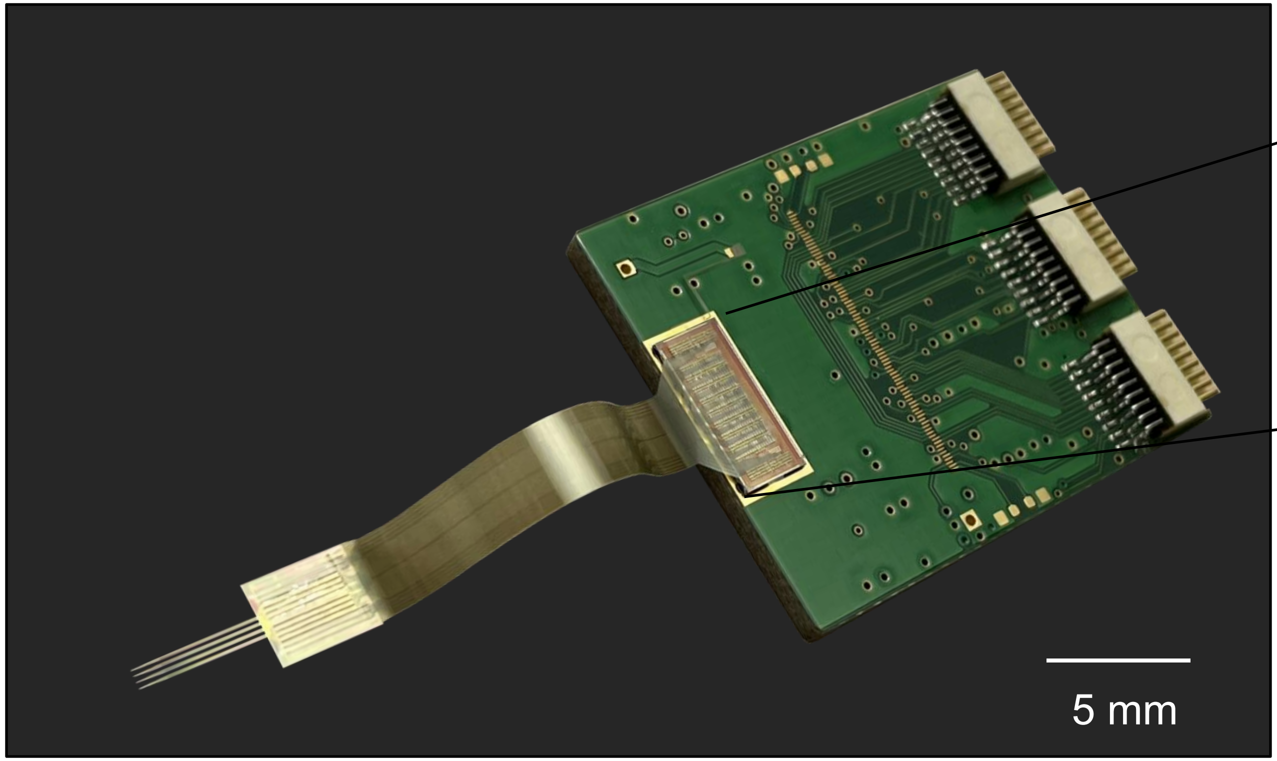


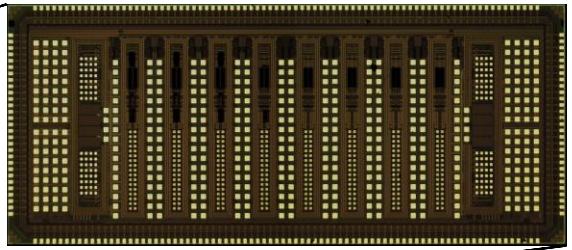
Global/Local Connection Network in Brain



Advanced Science 2022

HectoSTAR μLED OPTOELECTRODES





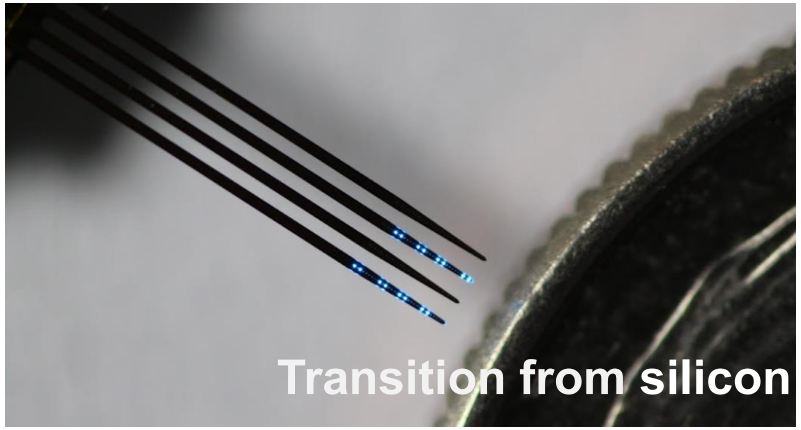
Miniaturized for chronic recording and modulation:

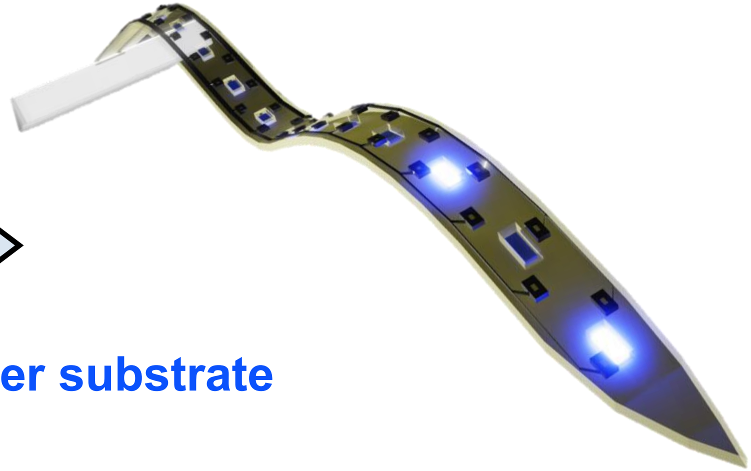
Fully multiplexed, programmable digital interface

Various configurations

Support GUI

Rigid to Flexible Substrate





Transition from silicon to polymer substrate

Rigid

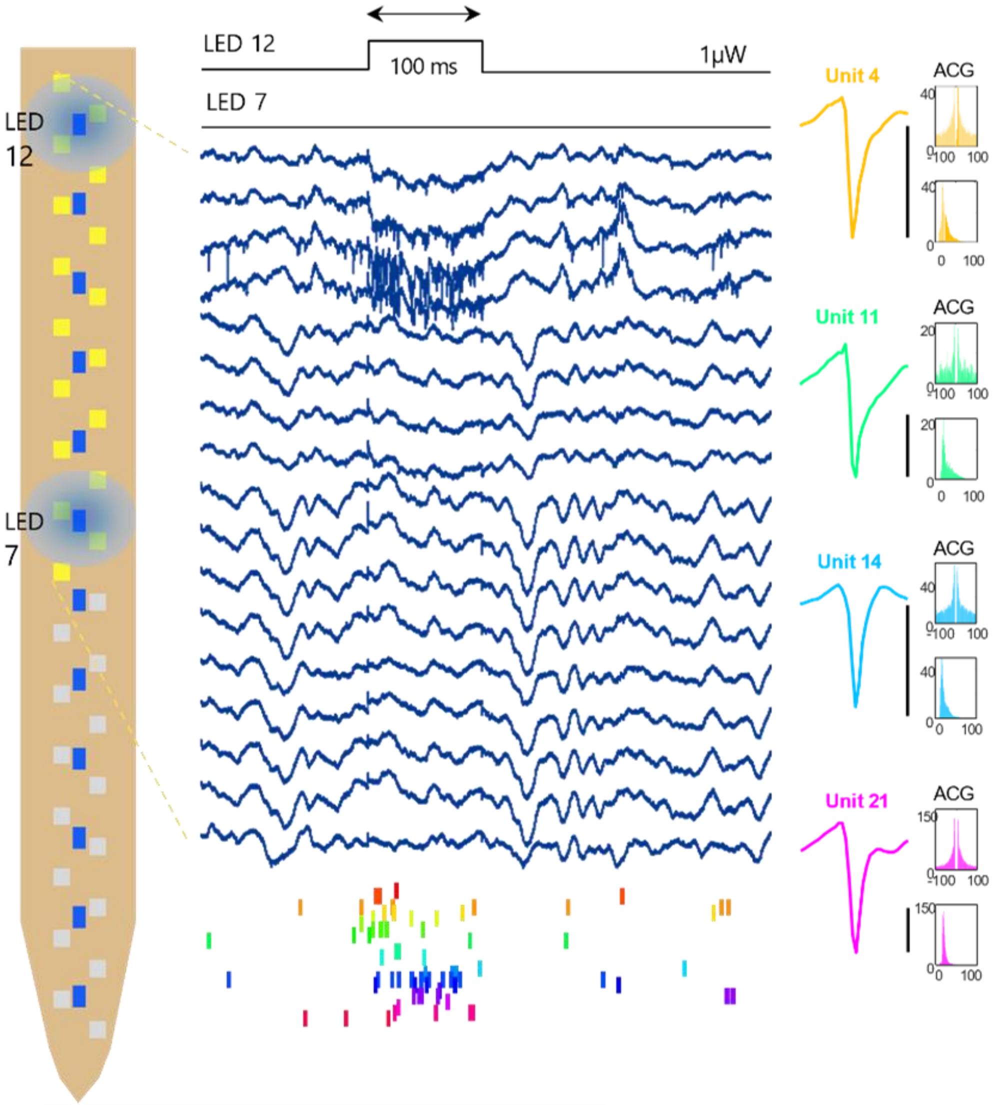
- Silicon substrate
- Monolithic integration LED/REC
- Backside grinding
- GaN on Silicon structure

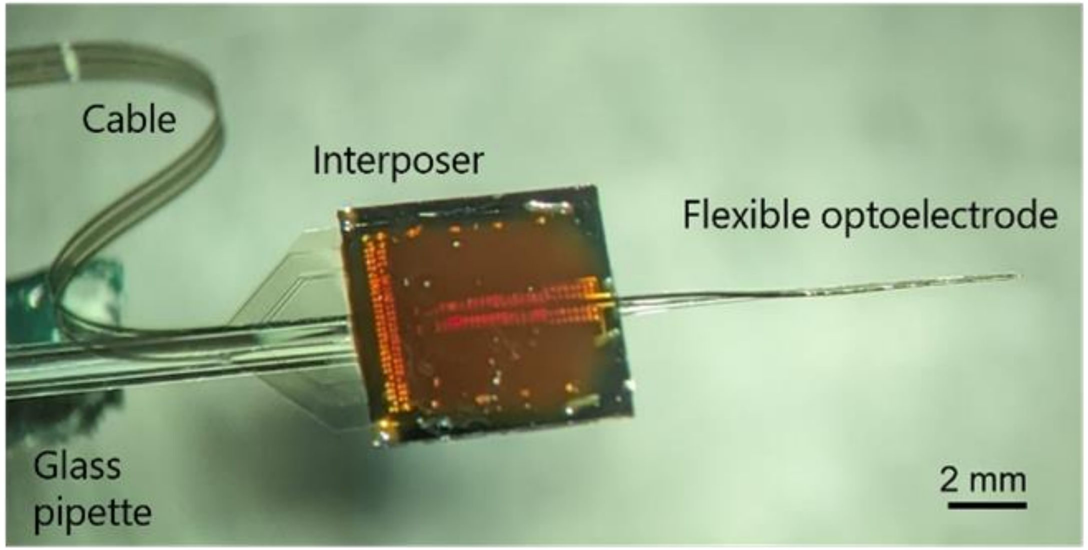
Flexible

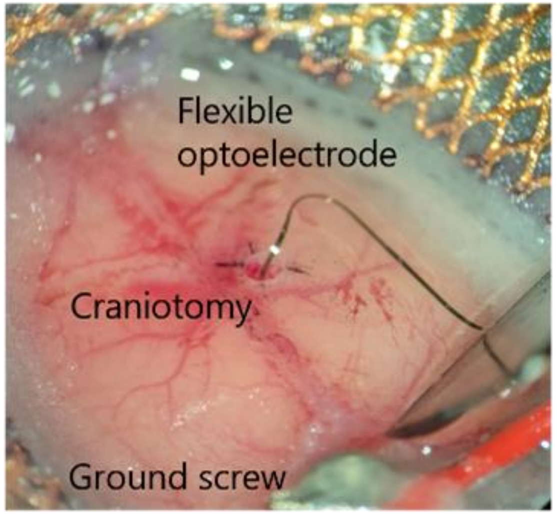
- Polymer substrate: polyimide
- Complete LED insulation
- Modular fabrication LED/REC
- Scalability ~ silicon probes

Primary design goal: device reliability for long term chronic in-vivo experiment

Chronic In-vivo Experiment – 8 Months Longevity







bioRxiv 2024

Thy1-ChR2 transgenic mouse

ACKNOWLEDGMENTS

- **Collaborators**
  - Prof. Ken Wise (U. of Michigan)
  - Prof. György Buzsáki (NYU)
  - Dr. John Seymour (now UT Houston)
  - Prof. Dan English (Virgia Tech), Prof. Sam McKenzie (UNM), Dr. Liset M de la Prida (Instituto Cajal CSIC)

Prof. Ken Wise

Prof. György Buzsáki

- **Post doctors, current and former students**
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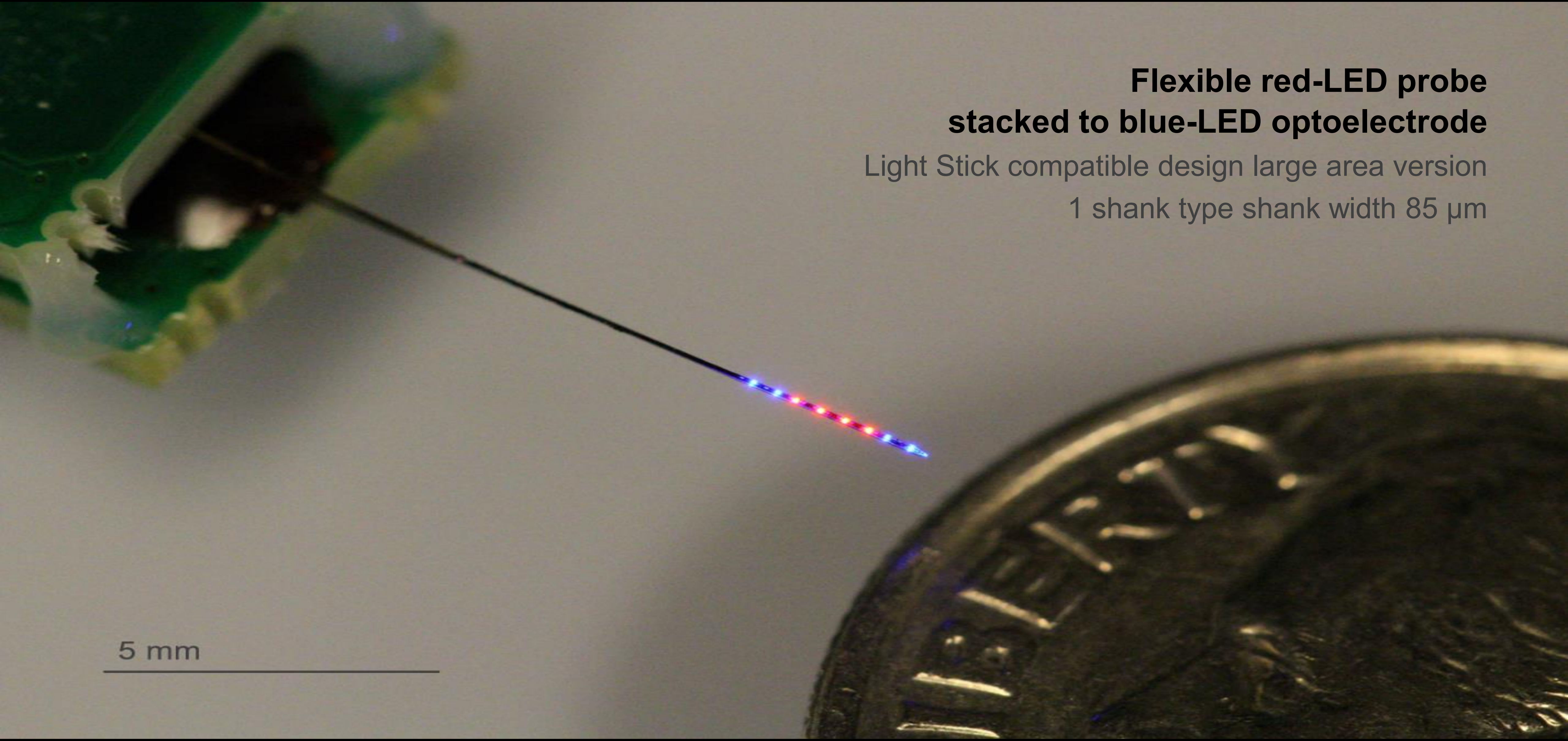
  - NSF, NIH, KIST, DARPA
  - Kavli Foundation
  - Lurie Nanofabrication Facility


Thank you

Questions?

The DuoLiTE


Flexible red-LED probe
stacked to blue-LED optoelectrode
Light Stick compatible design large area version
1 shank type shank width 85 μm
5 mm

Wireless Optogenetic Probes