YOON LAB
MICHIGAN ENGINEERING

BuzsákiLab

How to Use µLED Optoelectrodes: Surgery, Data Collection and µLED Control

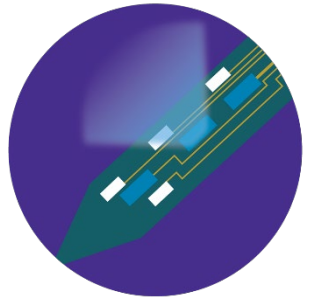
Mihály (**Misi**) Vöröslakos

NYU Langone Medical Center / University of Michigan

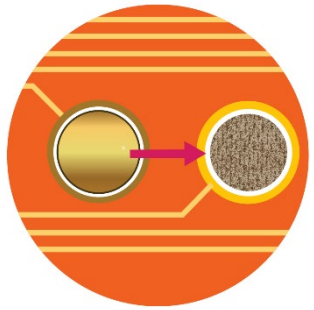
Plexon webinar series

2020. 07. 15.

NeuroNex MINT workshop[1]



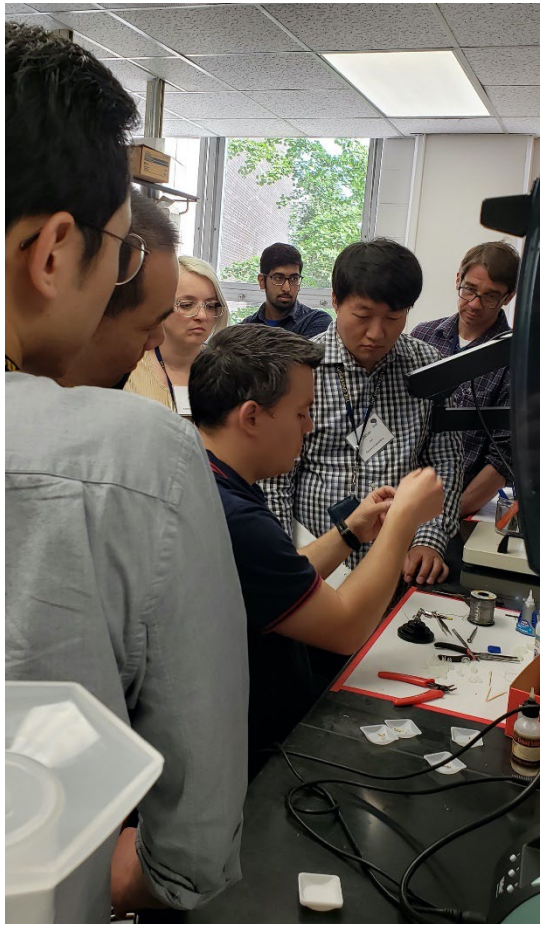
- **Optogenetic Experimentation Using a µLED Optoelectrode**
- Lesson goals:
  - *Prerequisites: stereotactic surgery*
  - Hands-on optoelectrode preparation for chronic surgery (designing and using microdrives)
  - Methods with optoelectrodes, including cell-type identification and noise/artifact reduction
  - Hands-on surgical experience using a chronic uLED array with simultaneous multi-channel stimulation and recording

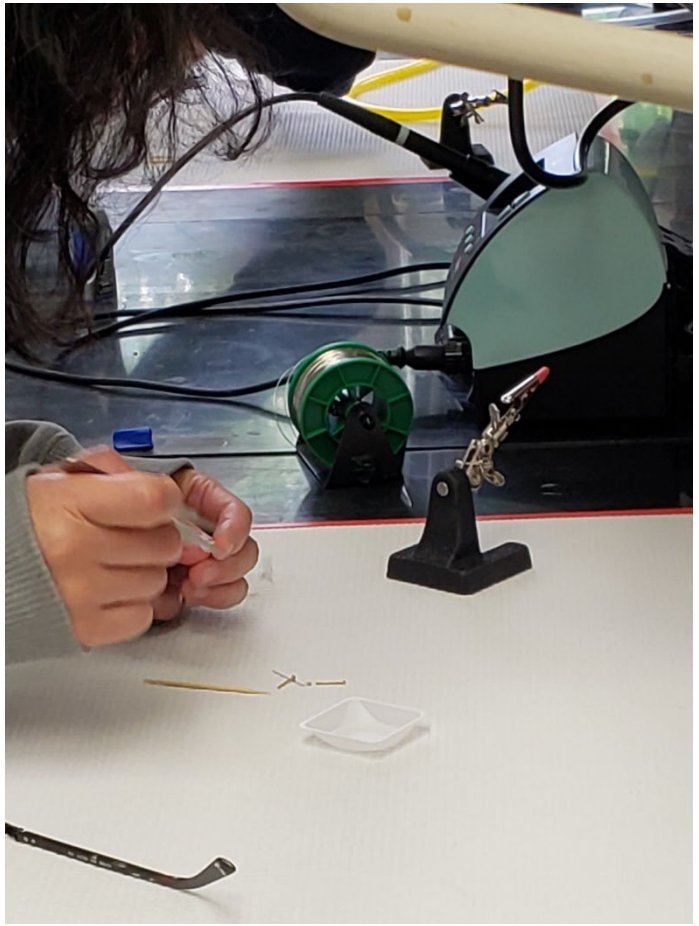


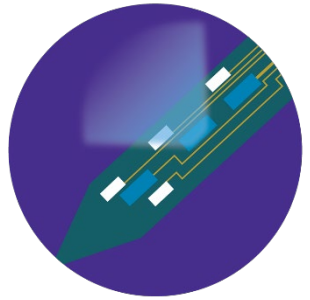
[1]https://mint.engin.umich.edu/workshop/

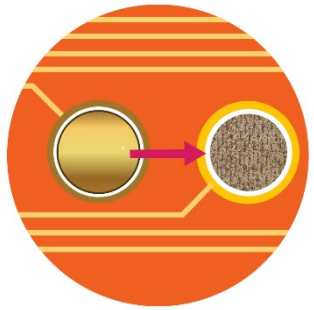
NeuroNex MINT workshop[1]

- **Optogenetic Experimentation Using a µLED Optoelectrode**



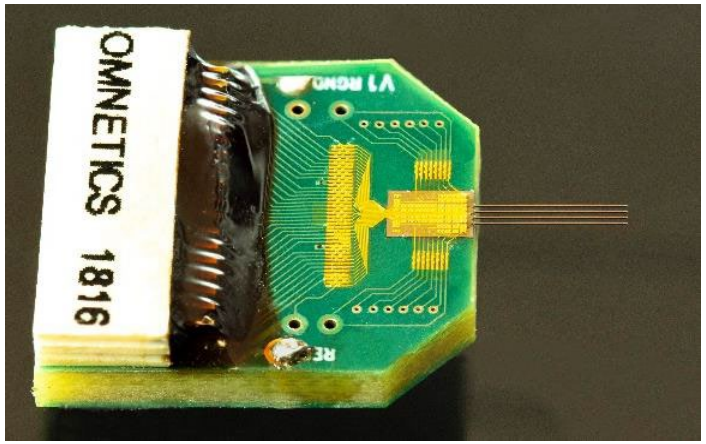




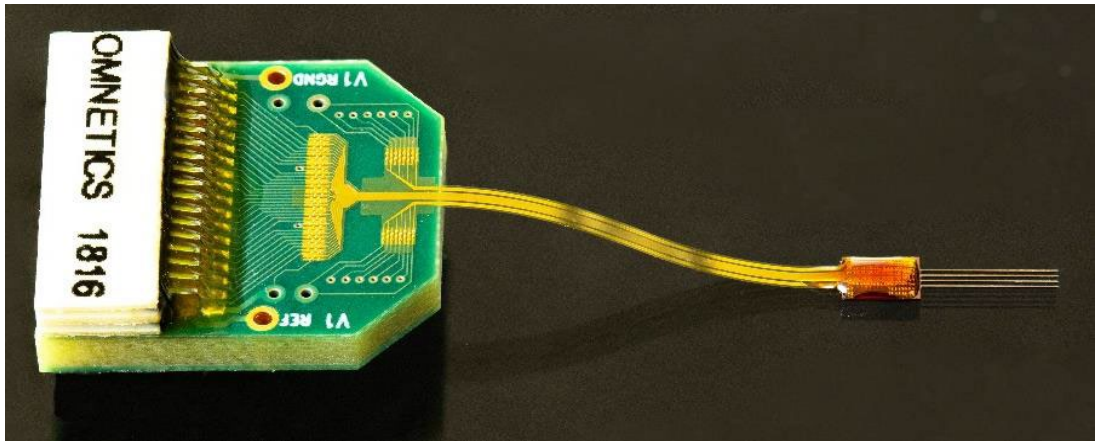


µLED Optoelectrodes

Acute

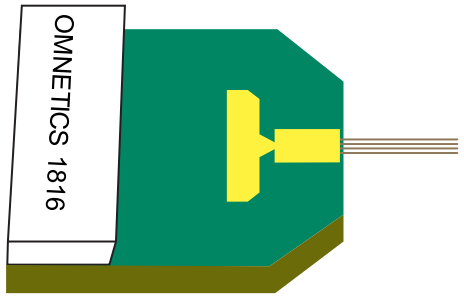
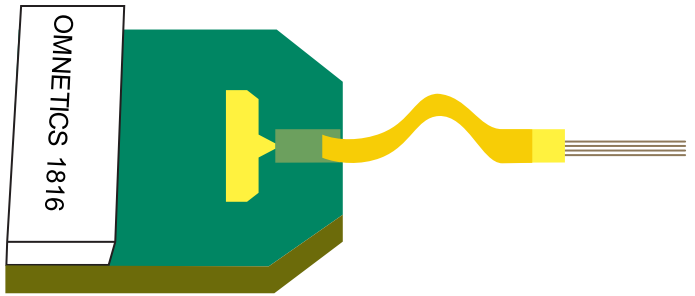


Chronic



Pictures source: http://mint.engin.umich.edu/wp-content/uploads/sites/327/2020/05/OPTOELECTRODE_NEURAL_PROBE_12uLED_32ELECTRODE.pdf

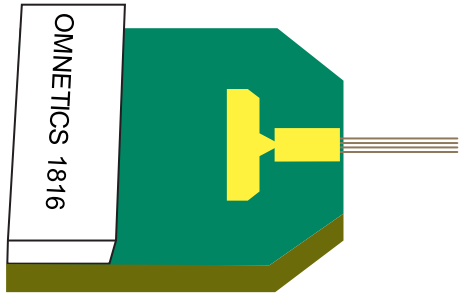
µLED Optoelectrodes

Acute		Chronic
		
n = 32 (8 sites/shank)	**Number of recording channels**	n = 32 (8 sites/shank)
n = 12 (3 LEDs/shank)	**Number of µLEDs**	n = 12 (3 LEDs/shank)
5 mm	**Length of shanks**	5 mm
No flexible cable	**Length of flexible cable**	22 mm

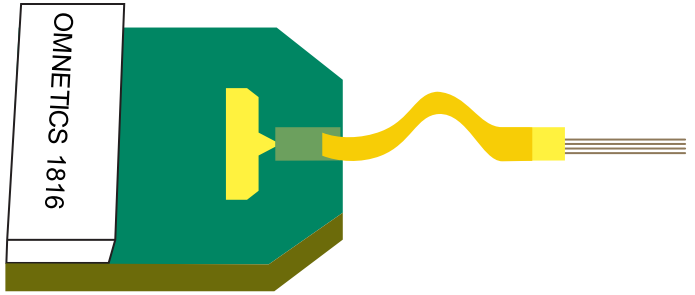
Data sheet is availabe at http://mint.engin.umich.edu/wp-content/uploads/sites/327/2020/05/OPTOELECTRODE_NEURAL_PROBE_12uLED_32ELECTRODE.pdf

µLED Optoelectrodes

Acute



Chronic



Recording of neuronal signal

Any extracellular electrophysiology system

Driving *µ*LED's during experiment

Function generator, current source, OSC1Lite from MINT program

Probe holding mechanism

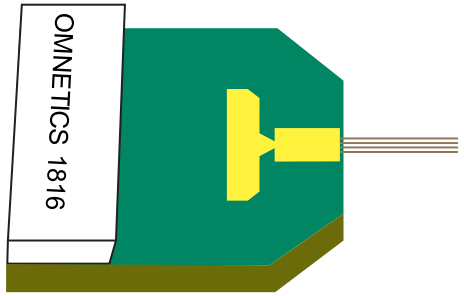
Metal bars glued to PCB

3D-printed holder

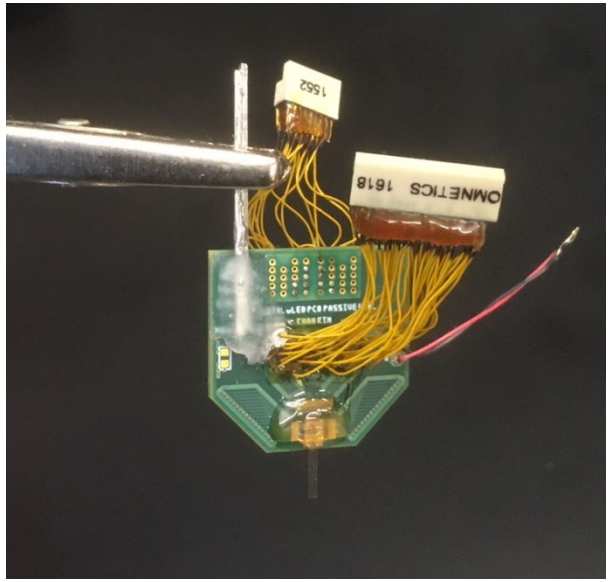
Micro-drive

How to hold an optoelectrode/silicon probe?

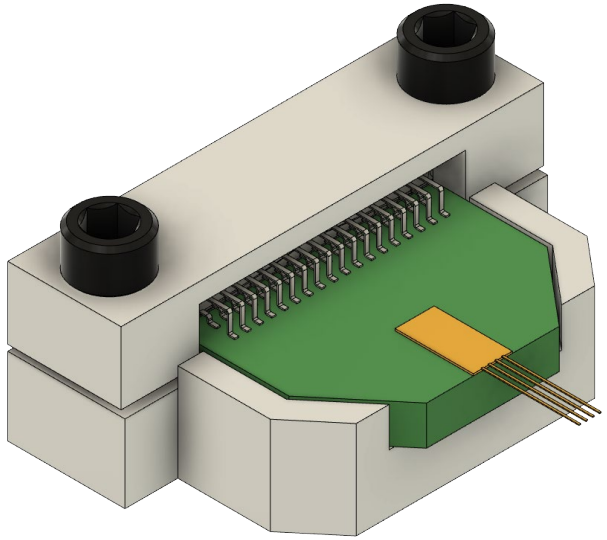
Acute



Metal bars glued to PCB



3D-printed holder



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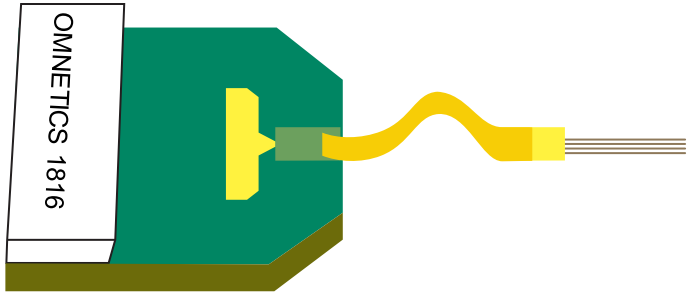
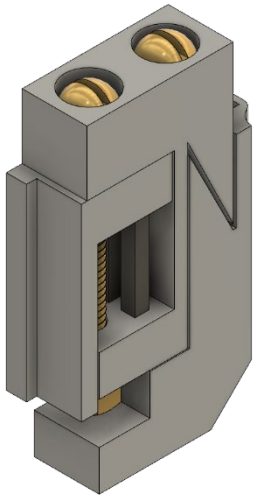
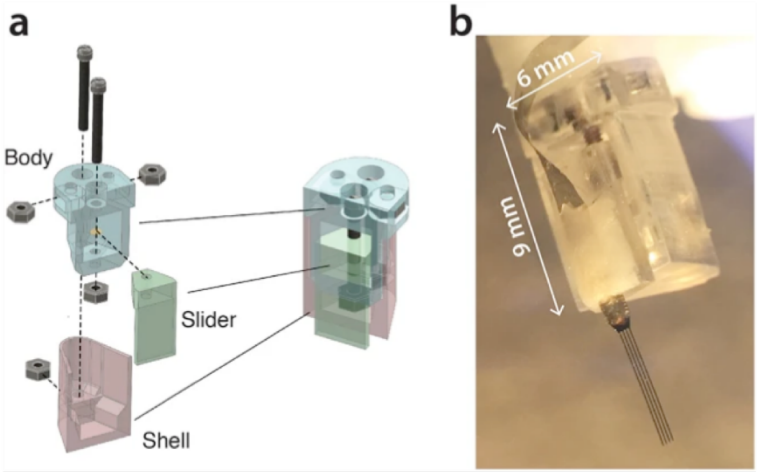


Micro-drive



How to hold an optoelectrode/silicon probe?



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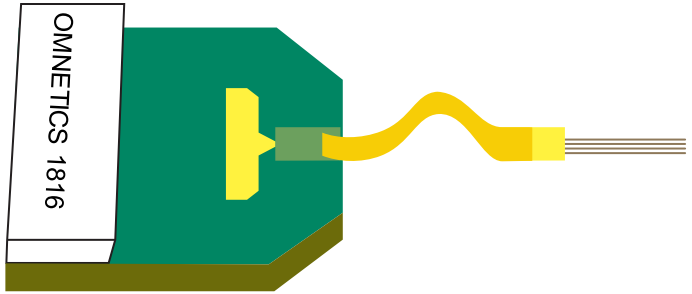
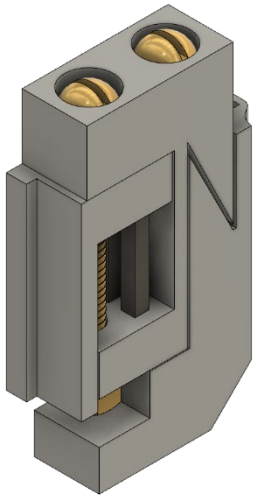


Micro-drive



Recoverable micro-drive system

- Allows probe recovery after long-term recording
- Improves recovery time and probe reusability
  - **Save time and money for researchers**

Recoverable micro-drive system

Recoverable micro-drive system

- Allows probe recovery after long-term recording
- Improves recovery time and probe reusability
  - **Save time and money for researchers**

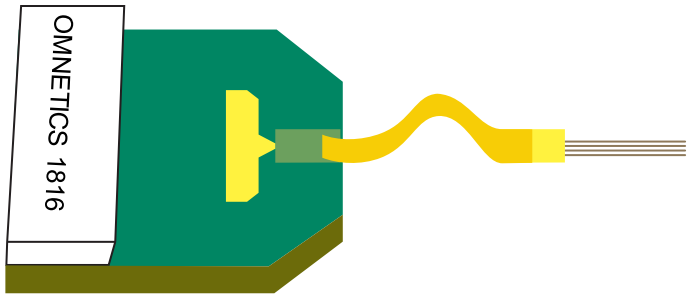
Recoverable micro-drive features

- Travel distance: 4.8 mm
- Shell base: 3.2 x 7.5 mm (WxL)
- Weight: 2g

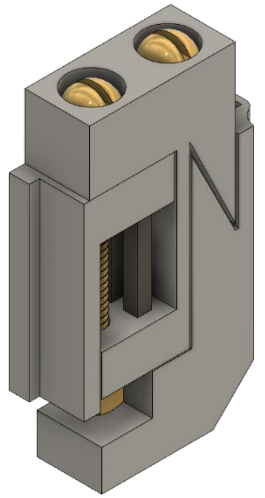
Using a recoverable micro-drive

- Build a micro-drive
- Attach probe to micro-drive
- Implant device

Chronic



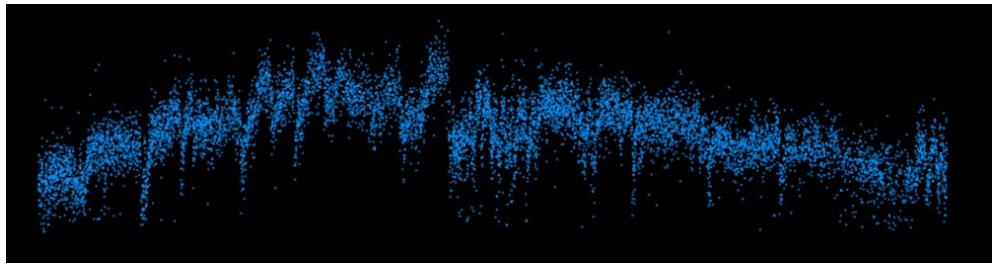
Micro-drive



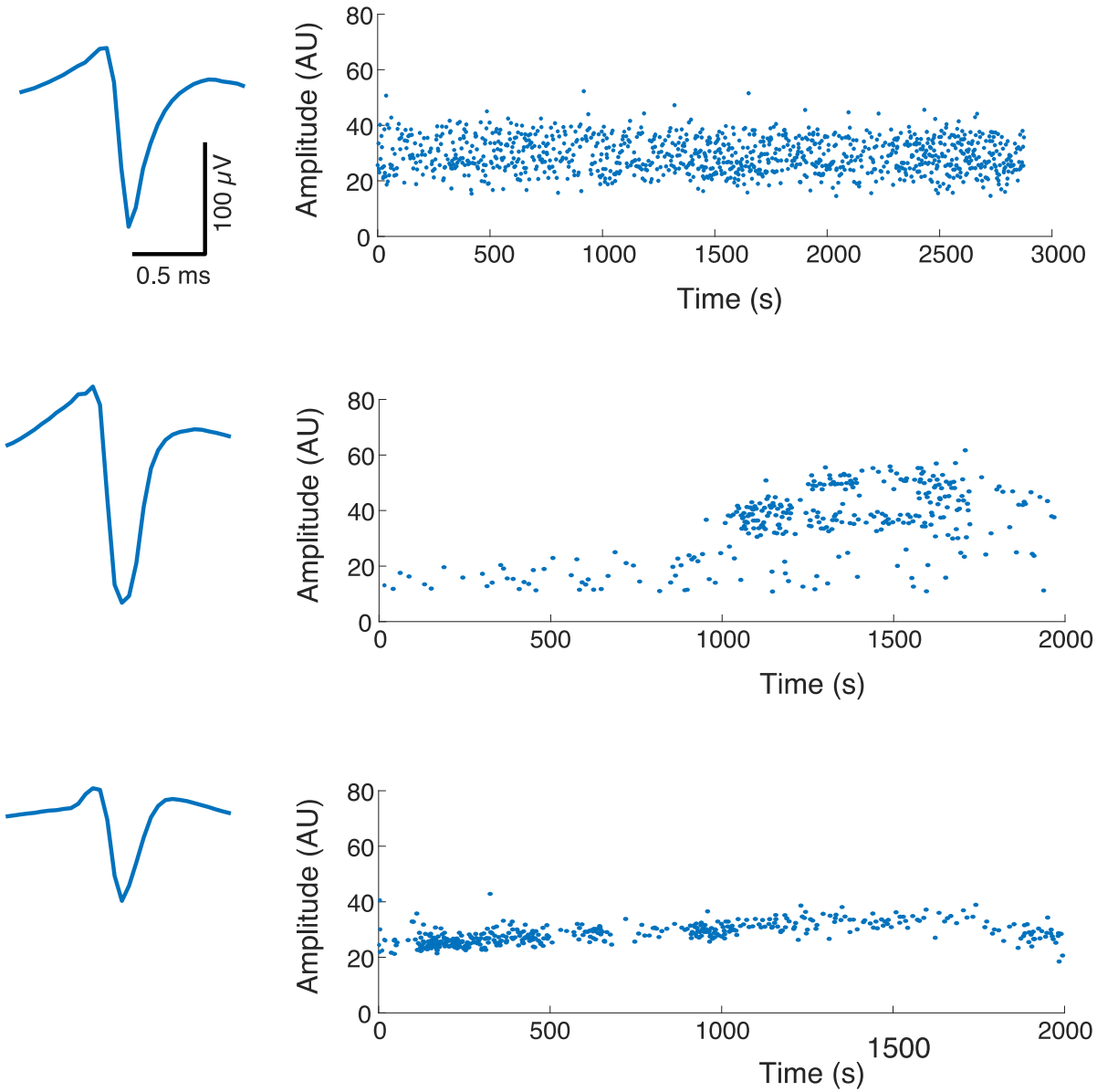
STL files, instructions, videos are availabe at https://github.com/YoonGroupUmich/Microdrive

Q&A from last week's webinar:

- Are the chronic probes drivable / movable once implanted?
  - Yes, if you implant a probe attached to a microdrive
    - **For more details, see: Vandecasteele et. al., 2012**
- What kind of anesthesia would work best for the recording?
  - Urethane (non-survival)
  - Ketamine – Xylazine
- What is the stability like for acute recording?
  - There can be some drift, but you can minimize it with:
    - Inserting the probe slowly (for more details, see: Fiáth et. al., 2019 -> insertion speed of 2 µm/s)
    - Once at target location, wait at least 30 minutes before recording is obtained (if possible)
  - Postprocessing options
    - KiloSort2 can handle drifts very well



Drift during acute recording



Vöröslakos unpublished data

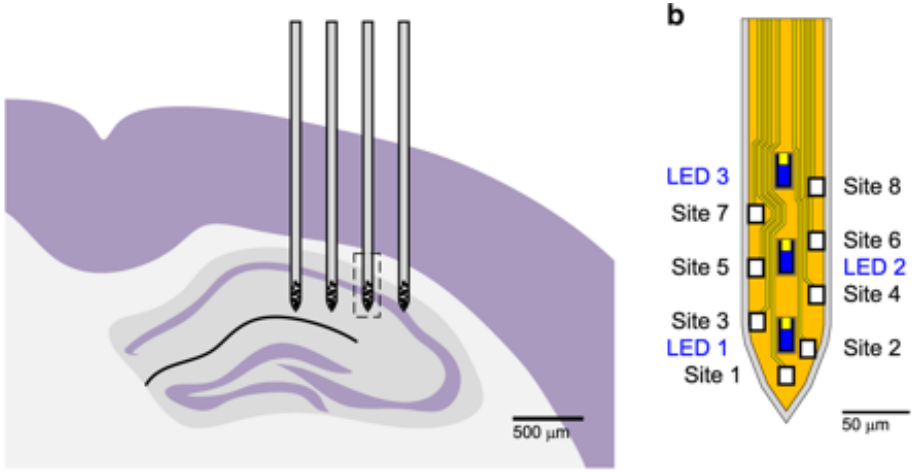
Acute recording with an optoelectrode

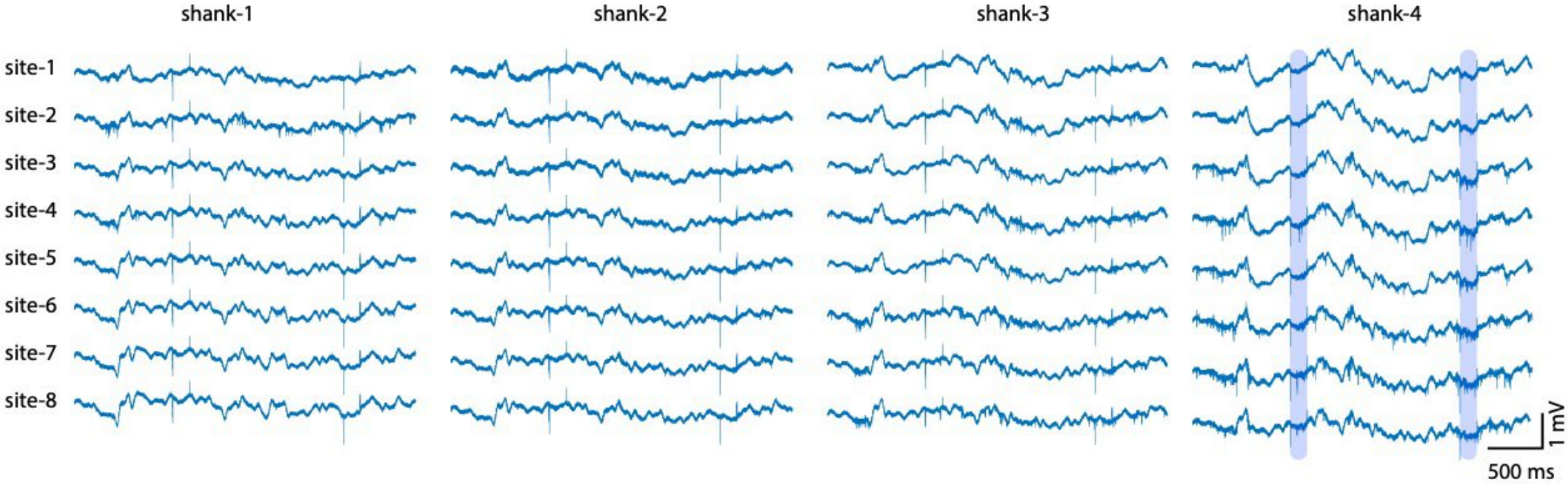
Recording

- C57BL/6J mouse injected with AAV5-CaMKIIa-hChR2
- Isoflurane anesthesia
- Recording from hippocampus

Stimulation

- Sh-4/LED-1, 30 μA, 100 ms





(7th times used in acute animals)

Vöröslakos unpublished data

Acute recording with an optoelectrode

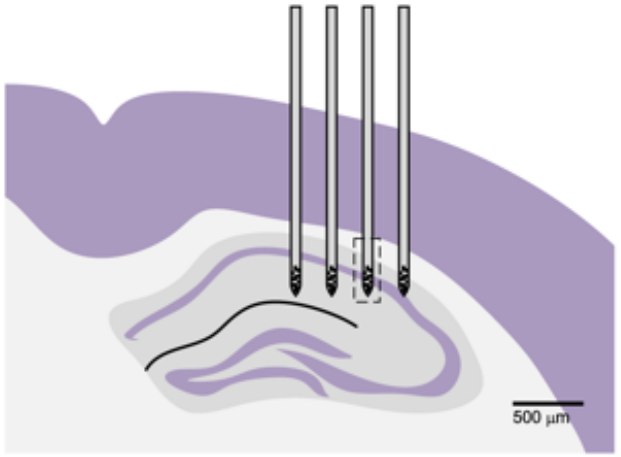
Kim et. al., 2020

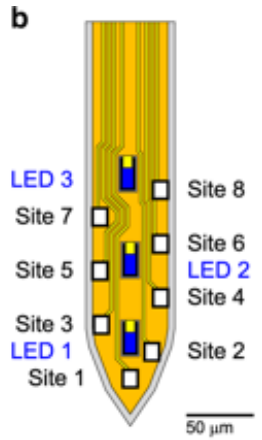
Recording

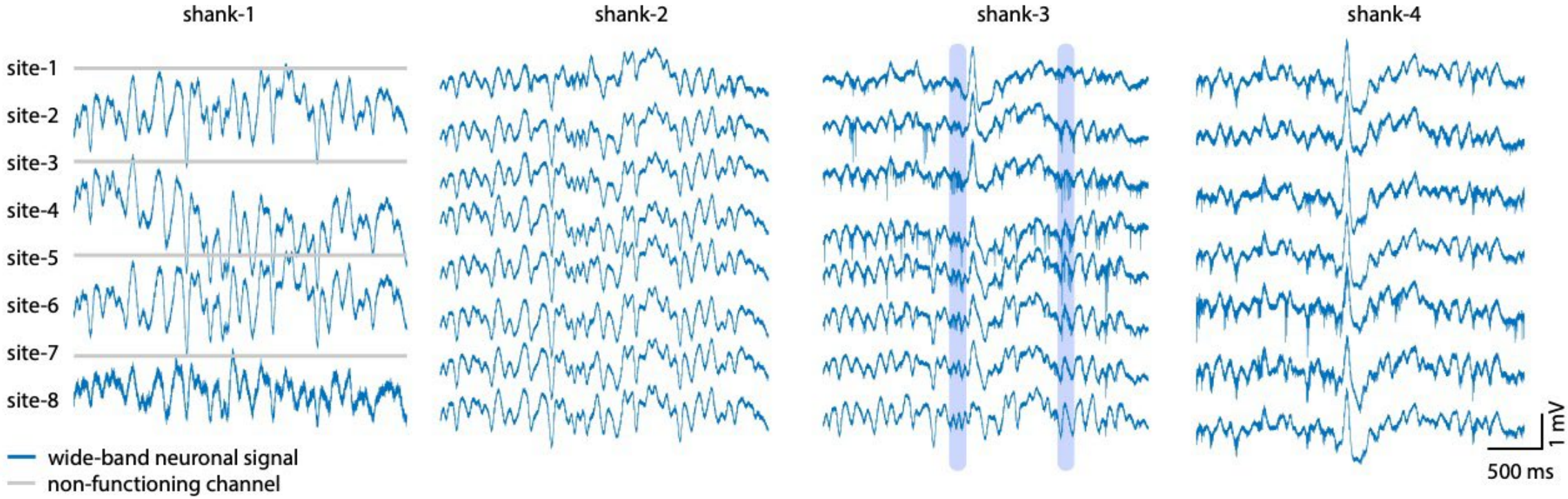
- Transgenic mouse
- Isoflurane anesthesia
- Recording from hippocampus

Stimulation

- Sh-3/LED-2, 2.8V, 50 ms







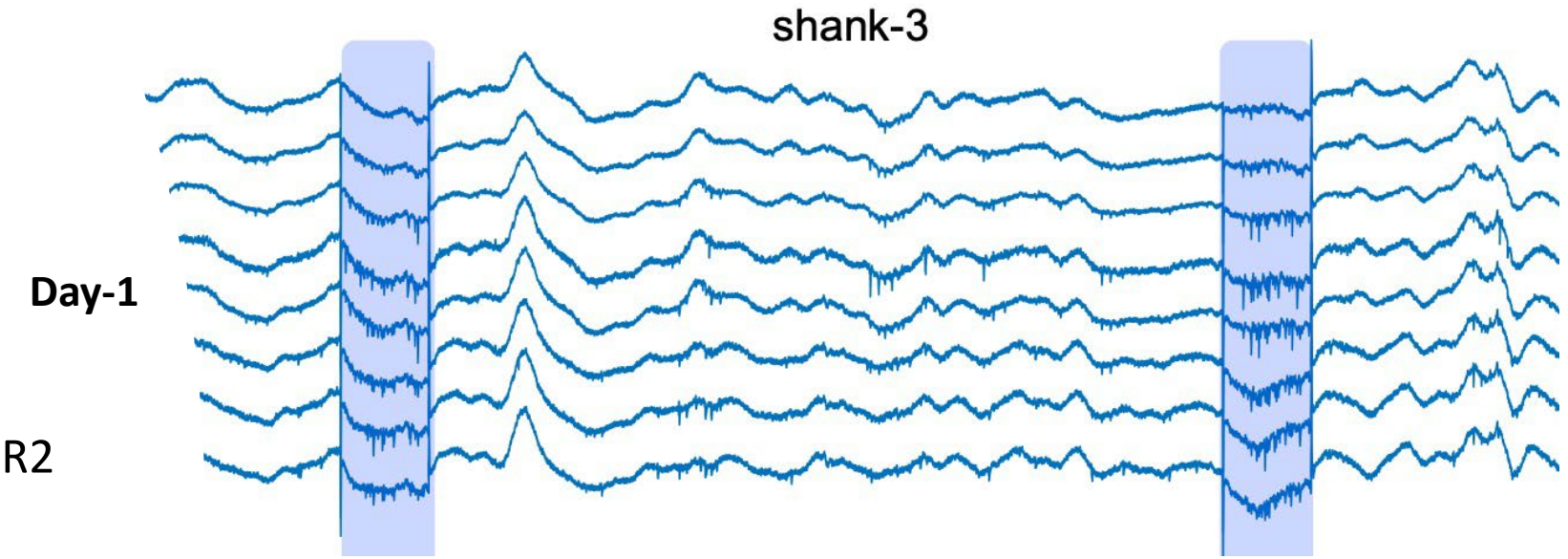
Chronic recording with an optoelectrode

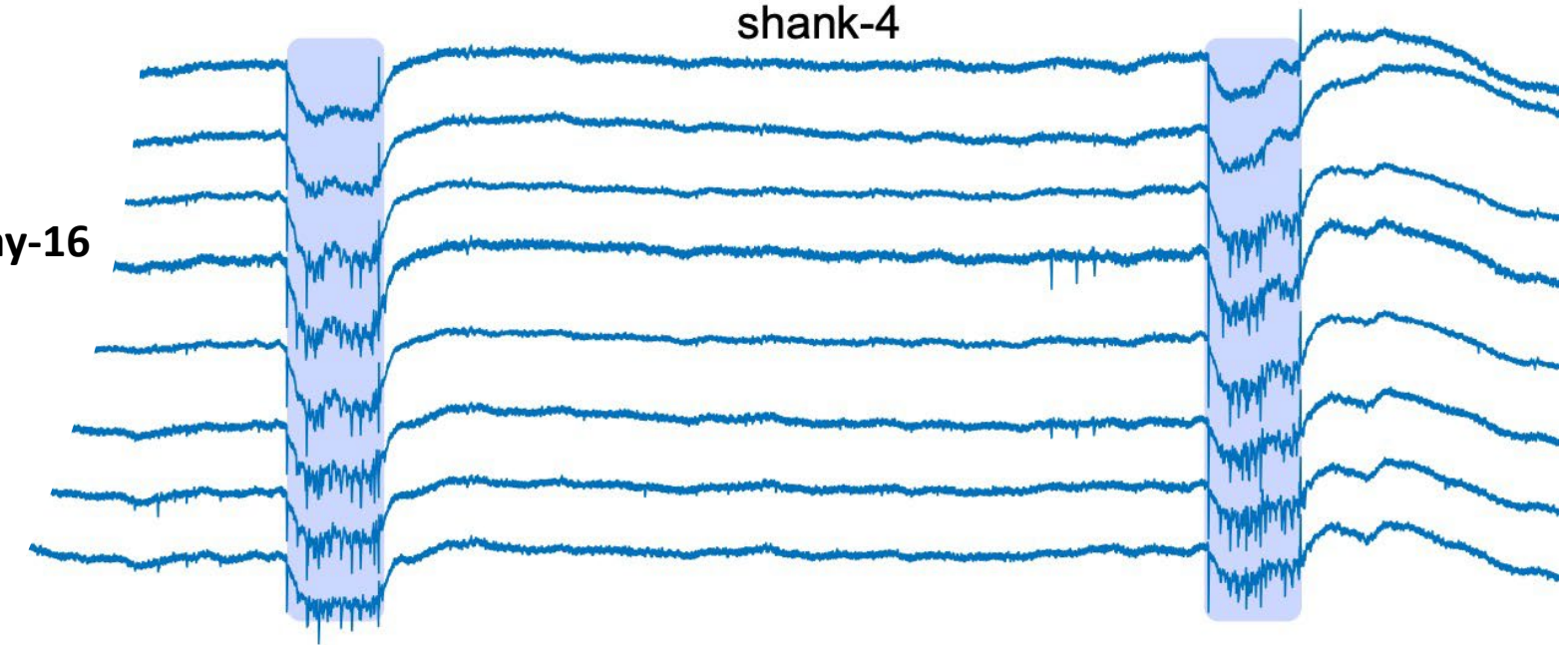
Recording

- C57BL/6J mouse
- injected with AAV5-CaMKIIa-hChR2
- Recording from hippocampus

Stimulation

- **Day-1**
  Sh-3/LED-2, 30 μ A, 100 ms
- **Day-16**
  Sh-4/LED-1, 60 μA, 100 ms

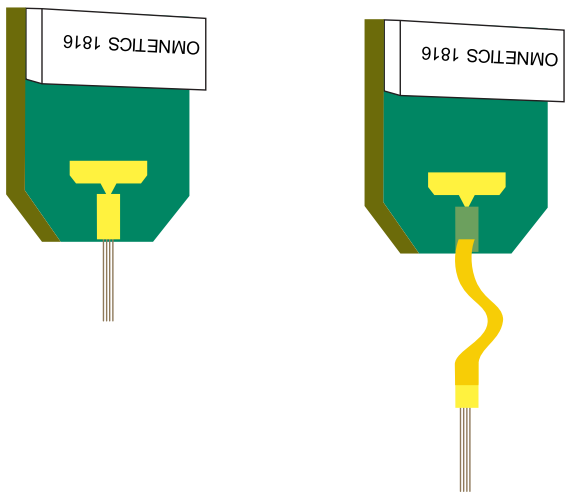




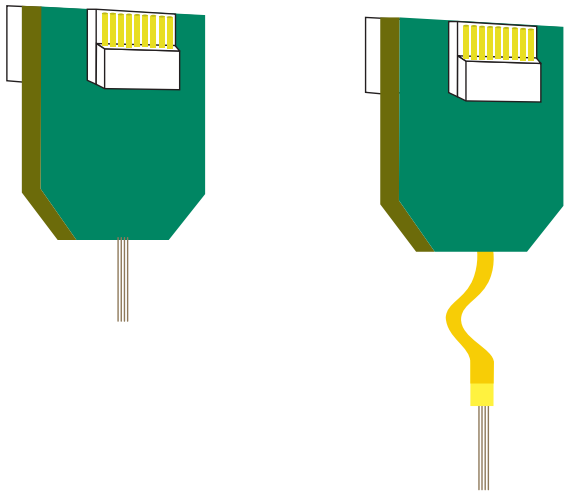
Vöröslakos unpublished data

µLED Optoelectrodes – recording and stimulation

Recording



Light stimulation



Any extracellular electrophysiology system

- Intan USB Eval Board[1]
- Plexon Omniplex system
- Tucker Davis PZ5 Digital system
- Many more...

Current mode

- OSC1Lite[2]
- Intan RHS2000

Voltage mode

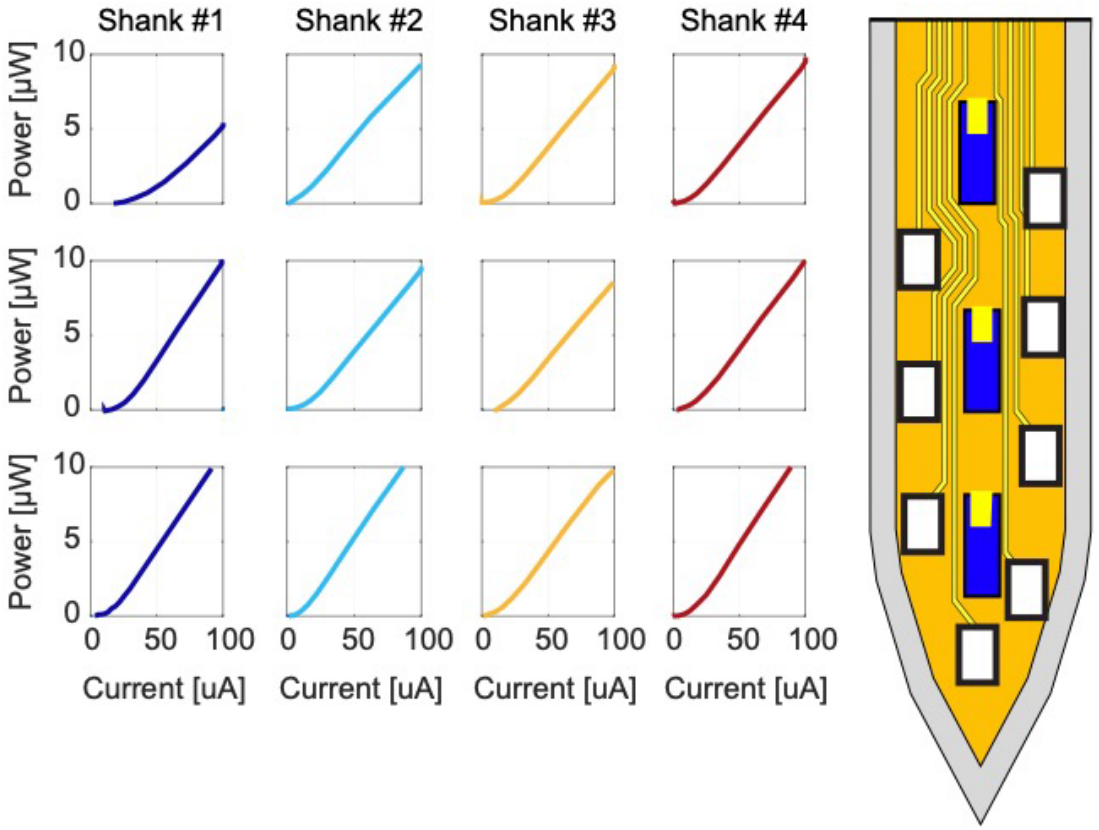
- Function generator

[1]All presented data were collected with Intan USB Eval Board. [2]Available at https://github.com/YoonGroupUmich/osc1lite

µLED Optoelectrodes – understanding the datasheet

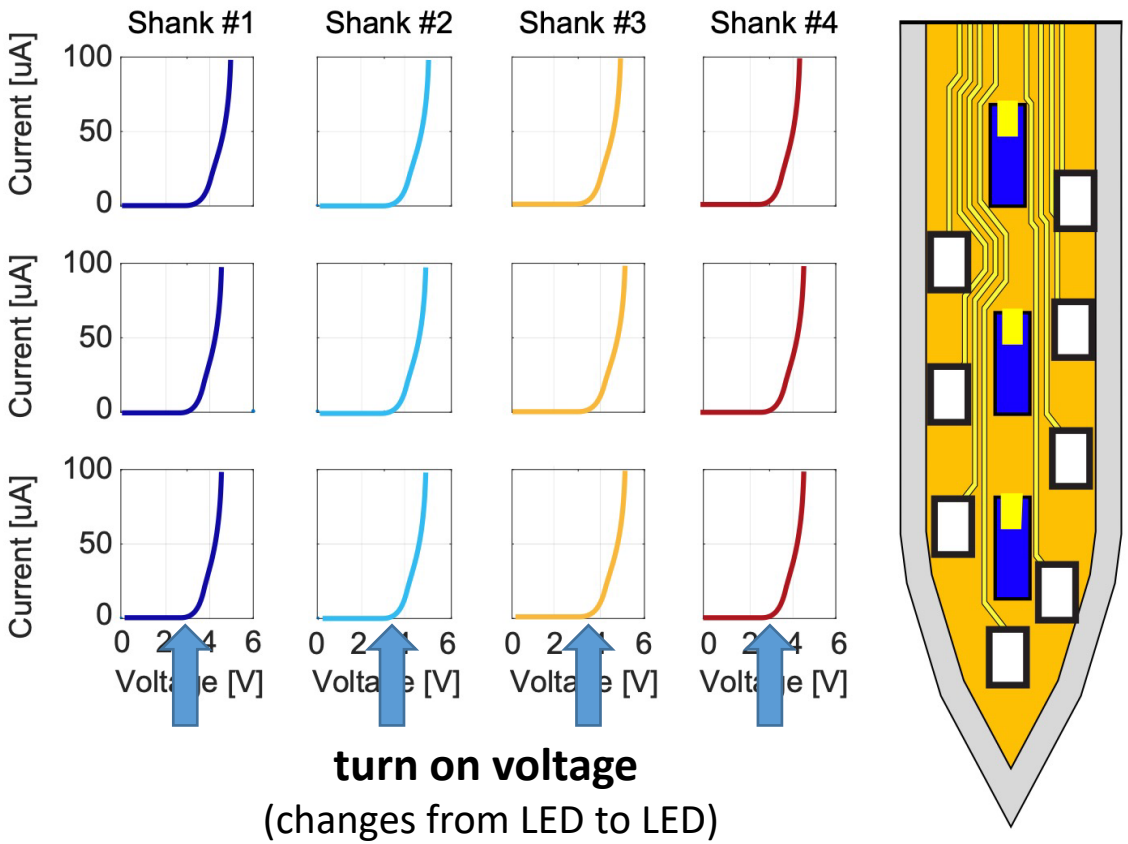
Current mode

- OSC1Lite[2]
- Intan RHS2000



Voltage mode

- Function generator
  - Apply offset voltage



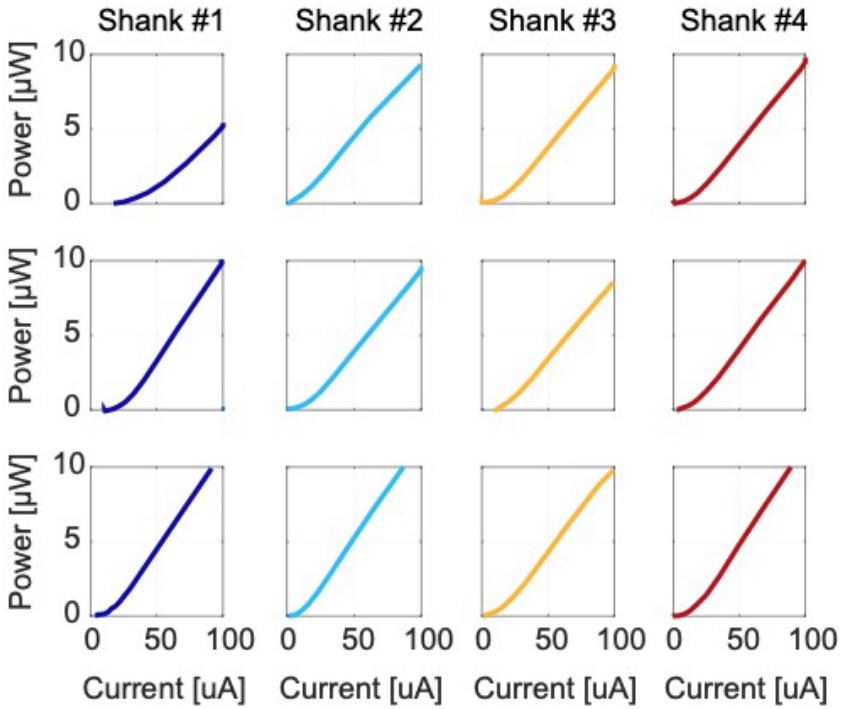
turn on voltage
(changes from LED to LED)

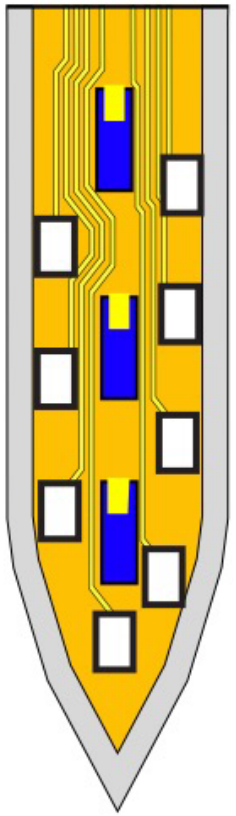
µLED Optoelectrodes – understanding the datasheet

Current mode

- OSC1Lite[2]
- Intan RHS2000

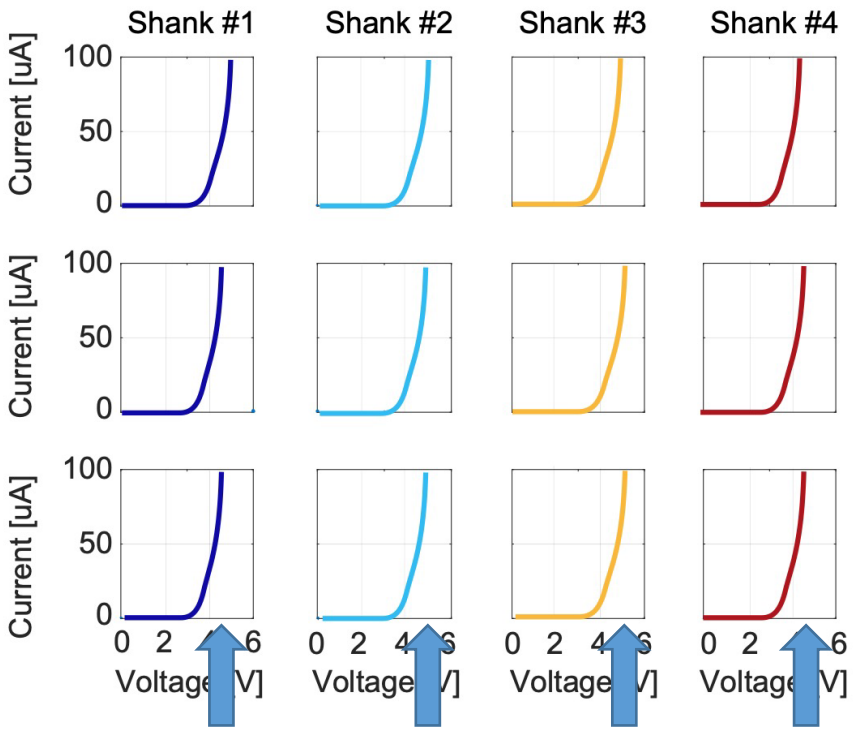
Never apply more than 100 μA

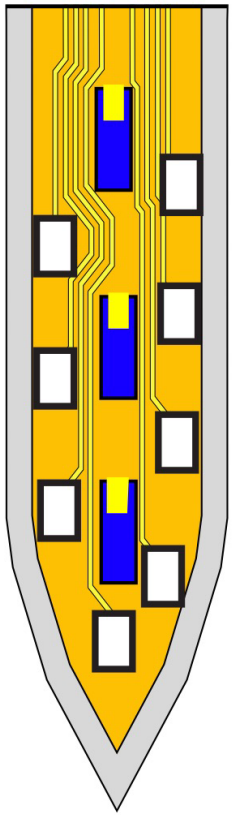




Voltage mode

- Function generator
  - Apply offset voltage
  - Set upper threshold @ 100 µA



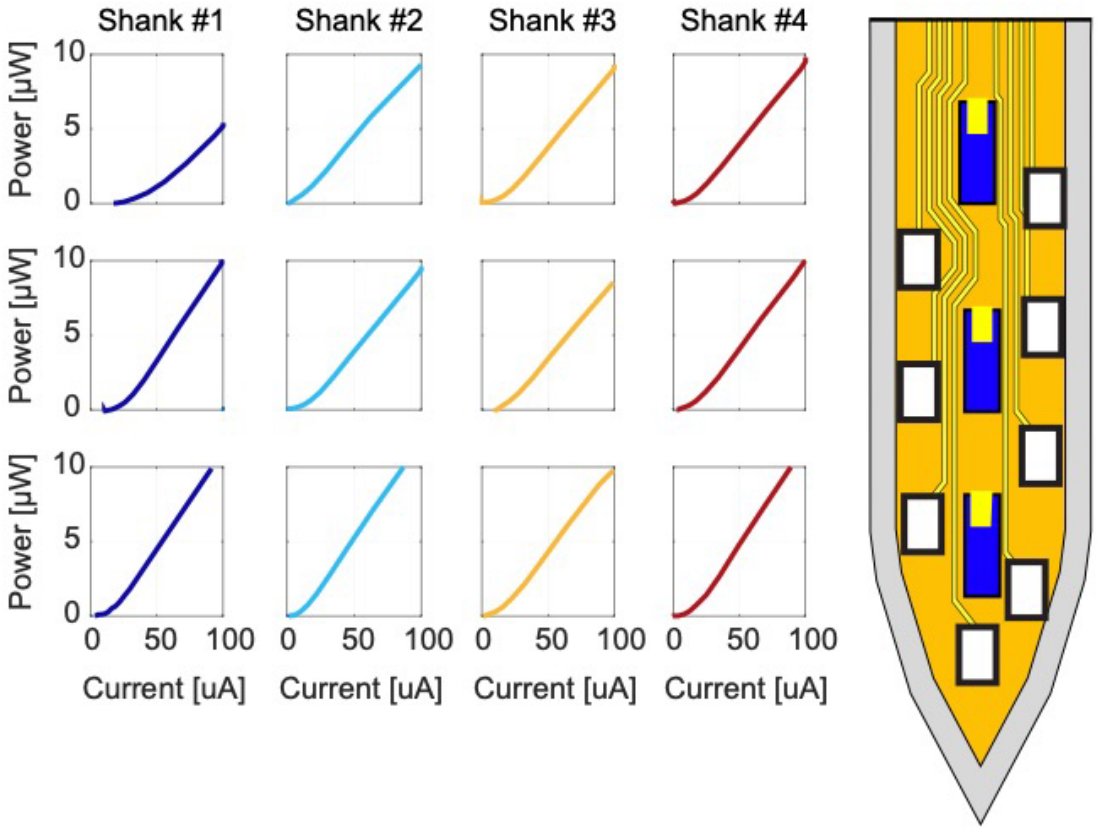


Maximum voltage
(changes from LED to LED)

µLED Optoelectrodes – understanding the datasheet

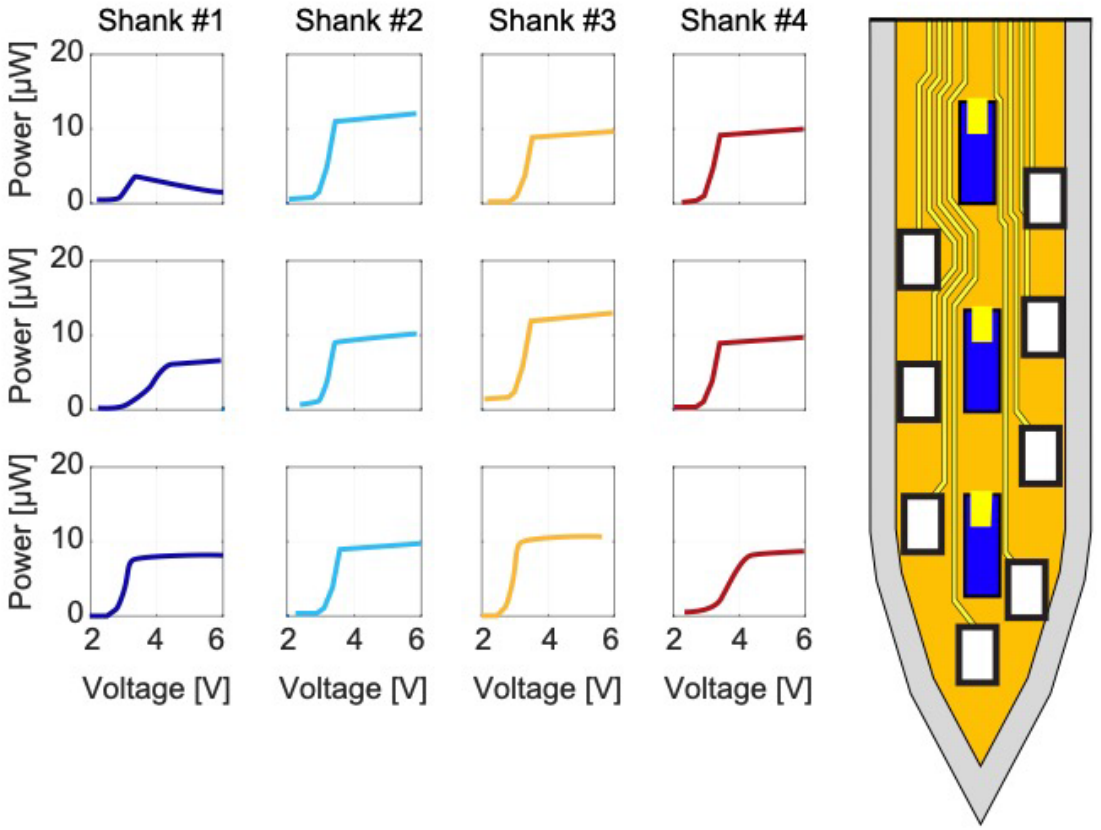
Current mode

- OSC1Lite
- Intan RHS2000



Voltage mode

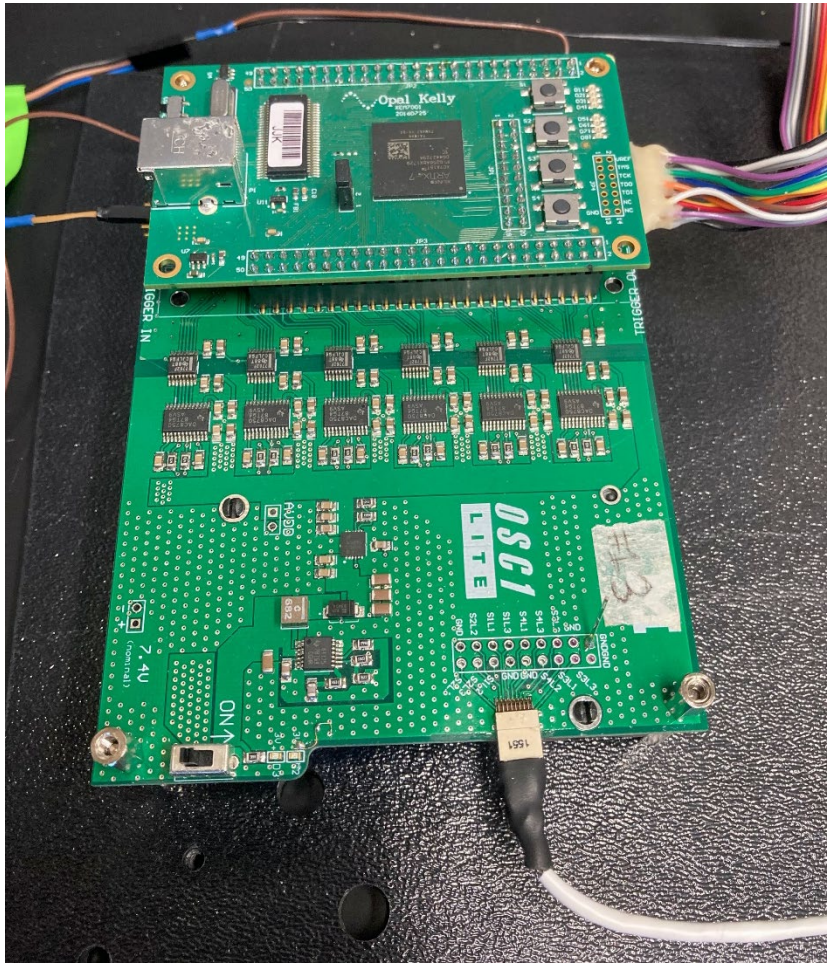
- Function generator



Controlling µLED Optoelectrodes

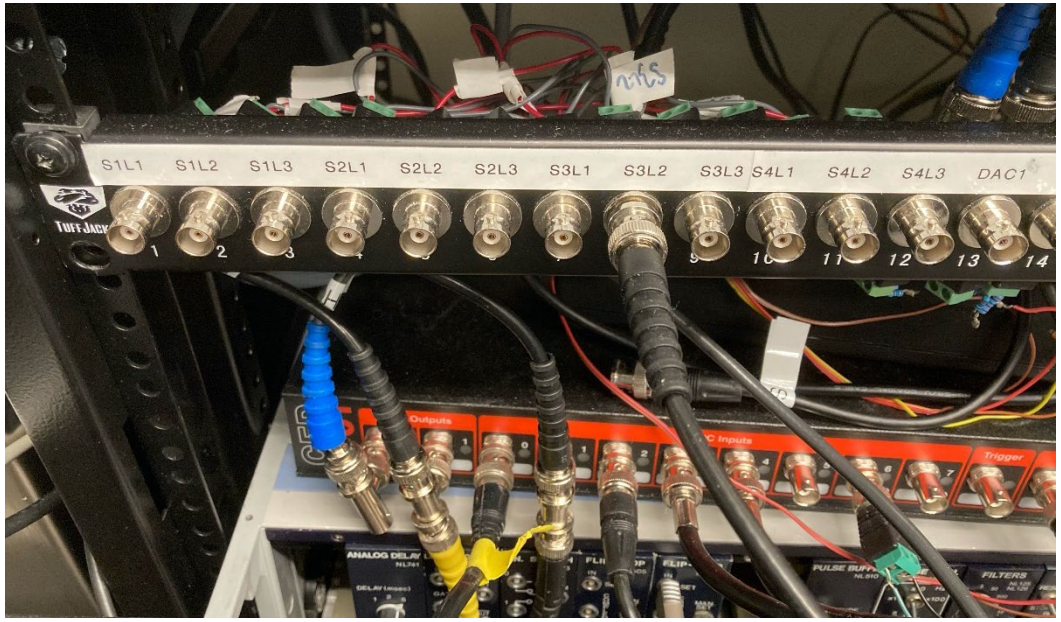
Current mode

- OSC1Lite
- Intan RHS2000



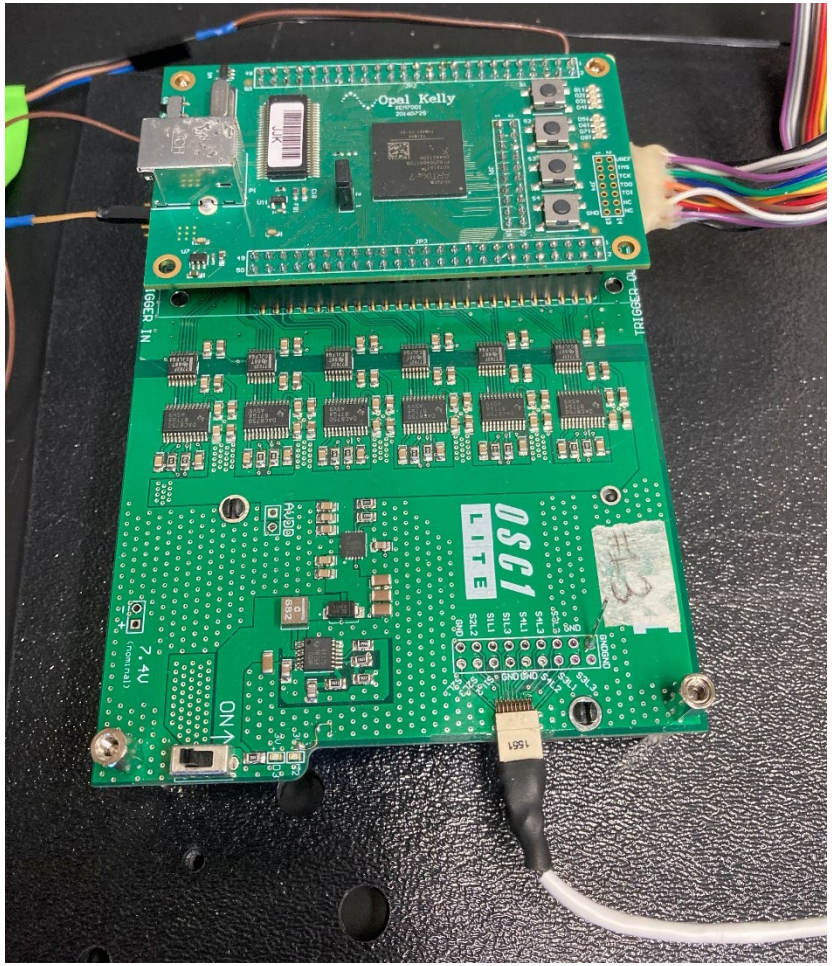
Voltage mode

- Function generator
+
Breakout board



Used by Sam McKenzie @ NYU BuzsakiLab

Controlling µLED Optoelectrodes - OSC1Lite

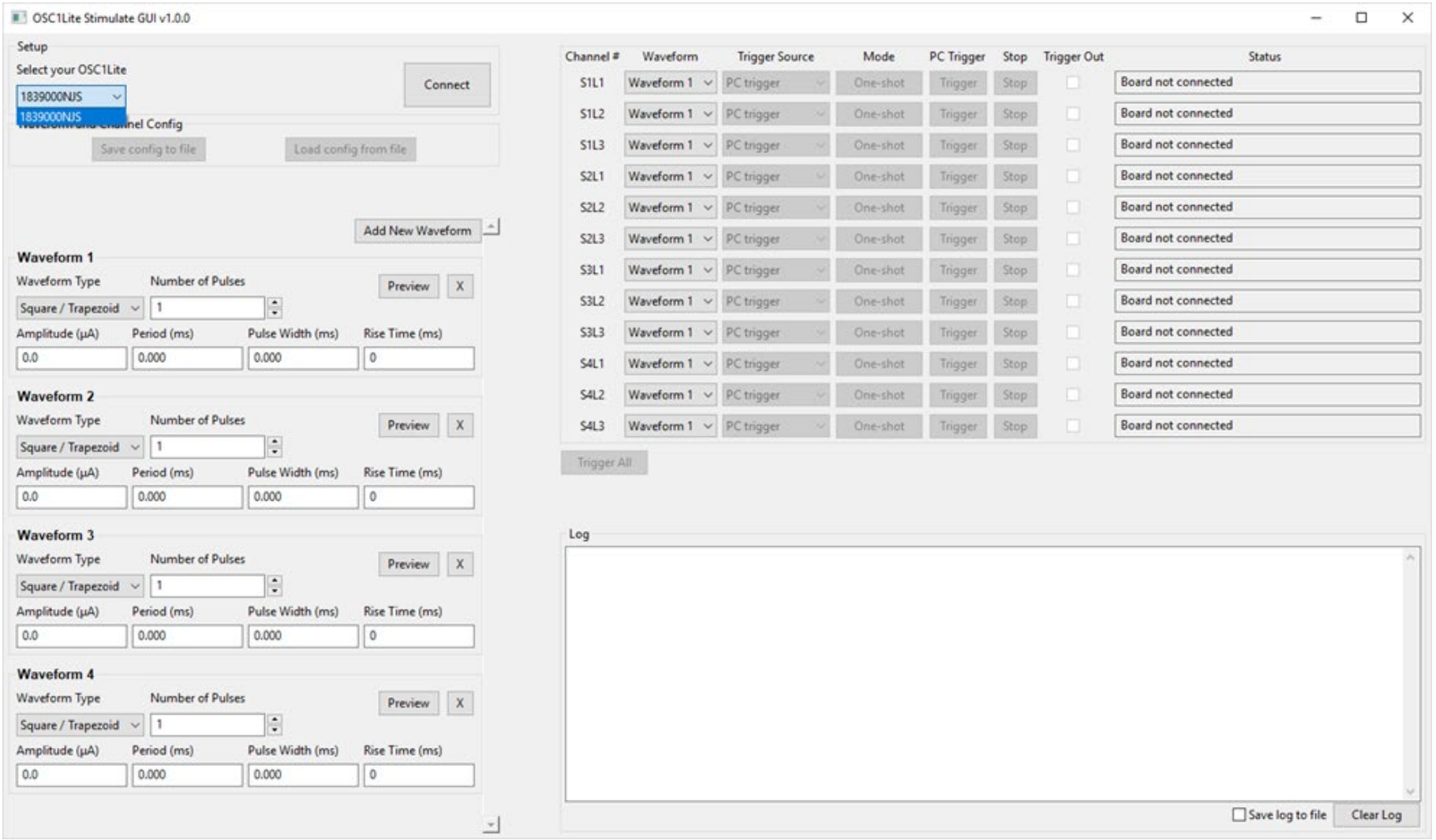


OSC1Lite features[1]

- 12-channel independent current drivers
- Current range 1 µA –100 µA (400 nA resolution)
- Custom waveforms
- Trigger in/out

[1]More details at https://github.com/YoonGroupUmich/osc1lite/blob/ref200/OSC1Lite_Manual_v2.docx

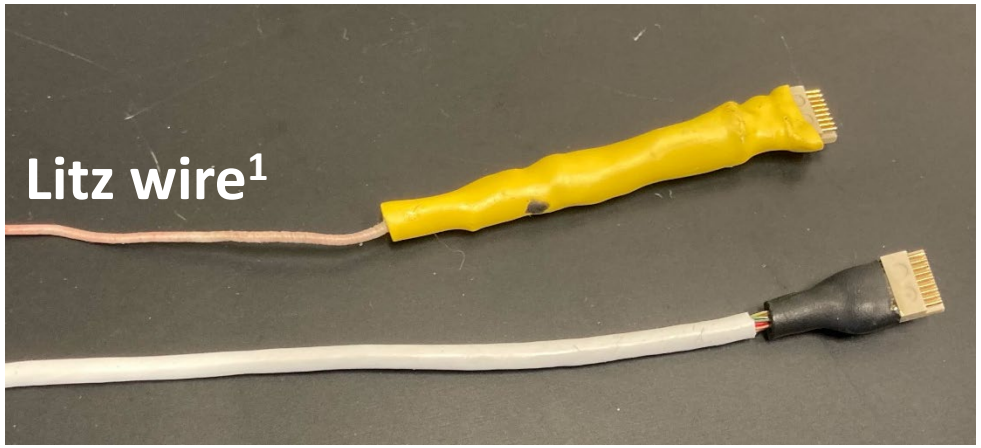
Controlling µLED Optoelectrodes - OSC1Lite GUI



[1]More details at https://github.com/YoonGroupUmich/osc1lite/blob/ref200/OSC1Lite_Manual_v2.docx

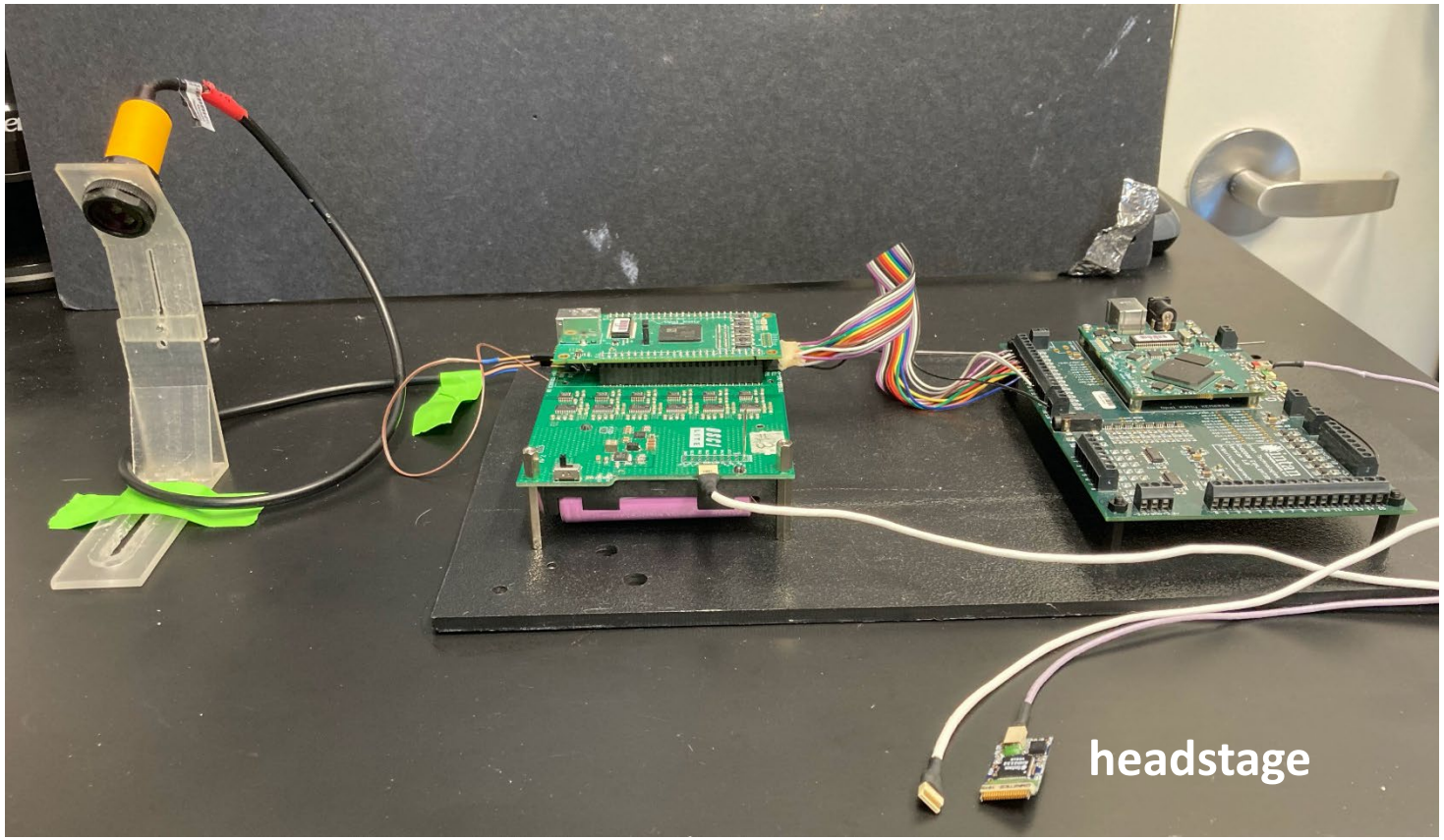
Controlling µLED Optoelectrodes

Stimulation cable



[1]Used by Sam McKenzie @ NYU BuzsakiLab

‚Typical' setup



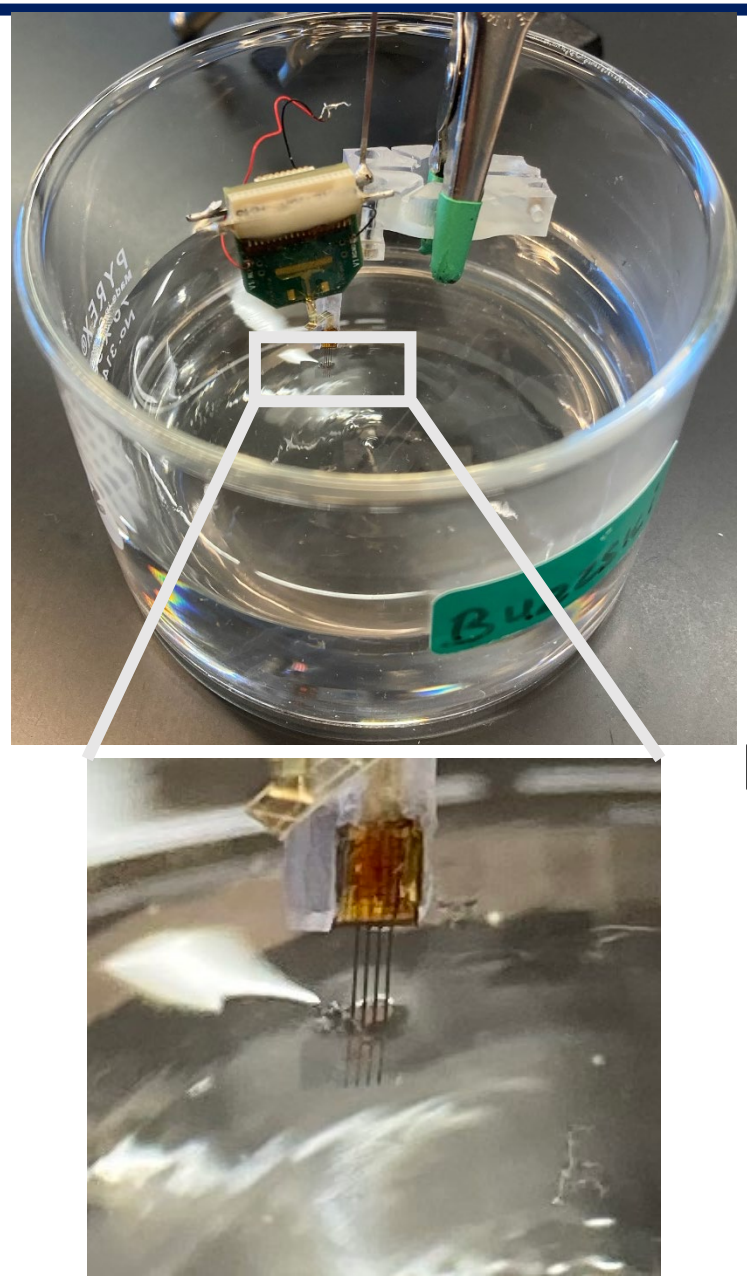
Analog sensor (IR gate)

LED driver (OSC1Lite)

Ephys recording (Intan USB Eval Board)

Cleaning the probe

- Chemical cleaning
  - Overnight DI water
  - Overnight contact lens solution[1]
  - Overnight DI water
- Mechanical cleaning
  - Removing tissue particles with needle
  - Insert probe into phantom brain



DI water

24h

Enzymatic solution

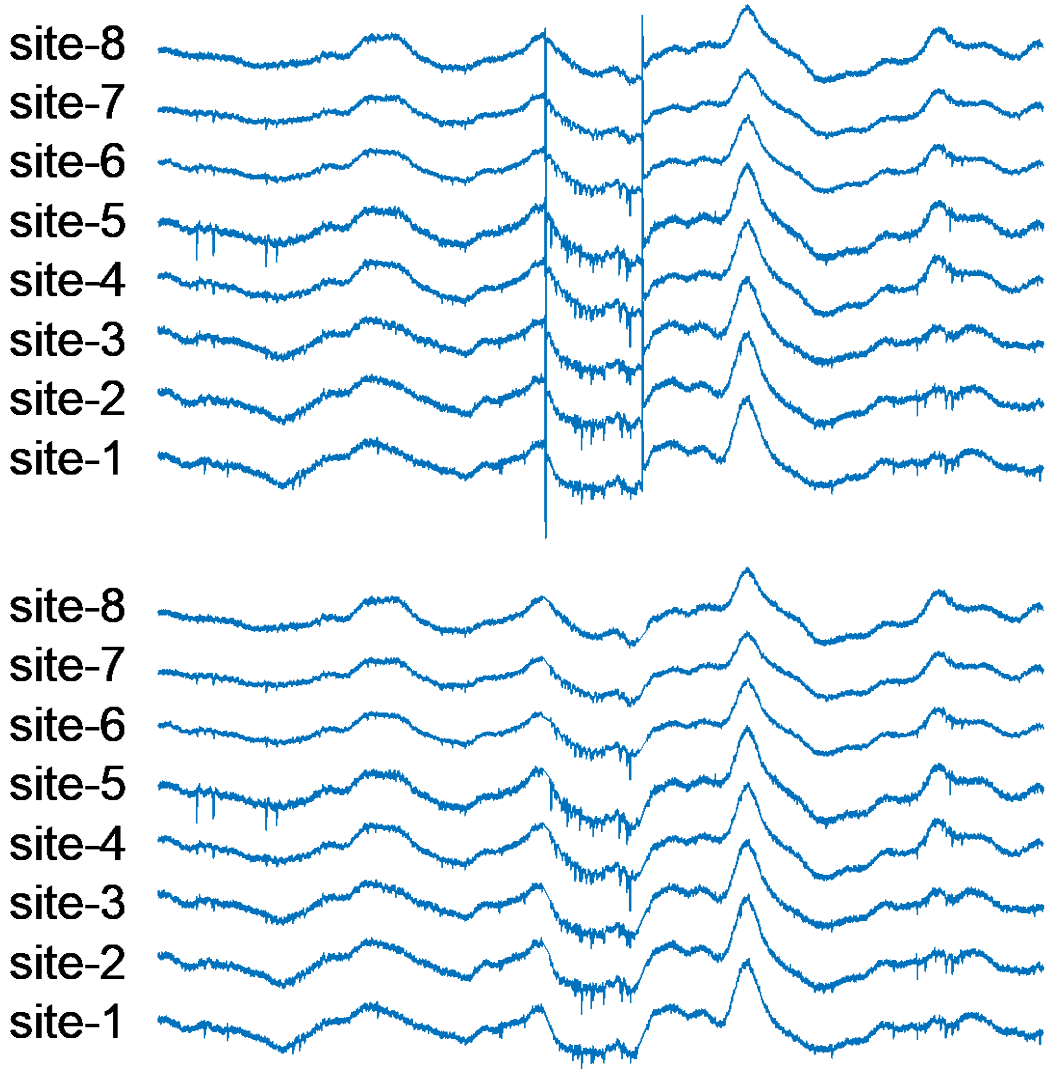
24h

DI water

[1]Ultrazyme® Enzymatic Cleaner

Data processing

- Record neuronal activity
- Detect artifacts if any
  - Interpolate over artifacts
    - **Data is lost**
  - Reduce artifacts
    - Use ‚new' artifact-free uLED probes
    - Pulse-shaping
- Run spike sorting
  - Acute recordings with drift
    - KiloSort2 can perform better
  - Chronic recordings
    - Any spikesorting software can be used



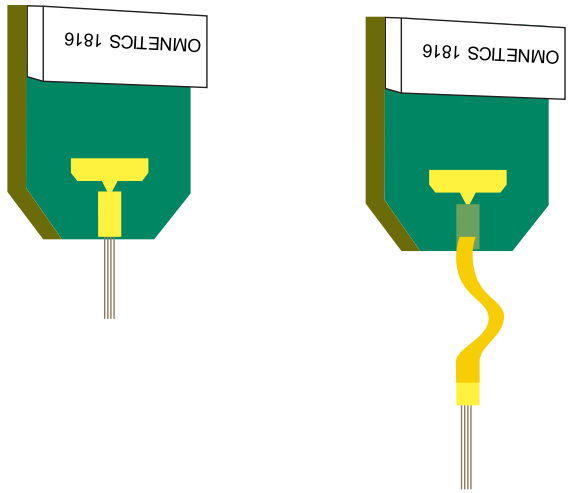
Q&A from last week's webinar:

- Is internal body heat a factor in the accuracy of the data obtained by the probe?
  - Internal body heat will always affect neuronal activity.[1]
    - The effect is independent of recording device.

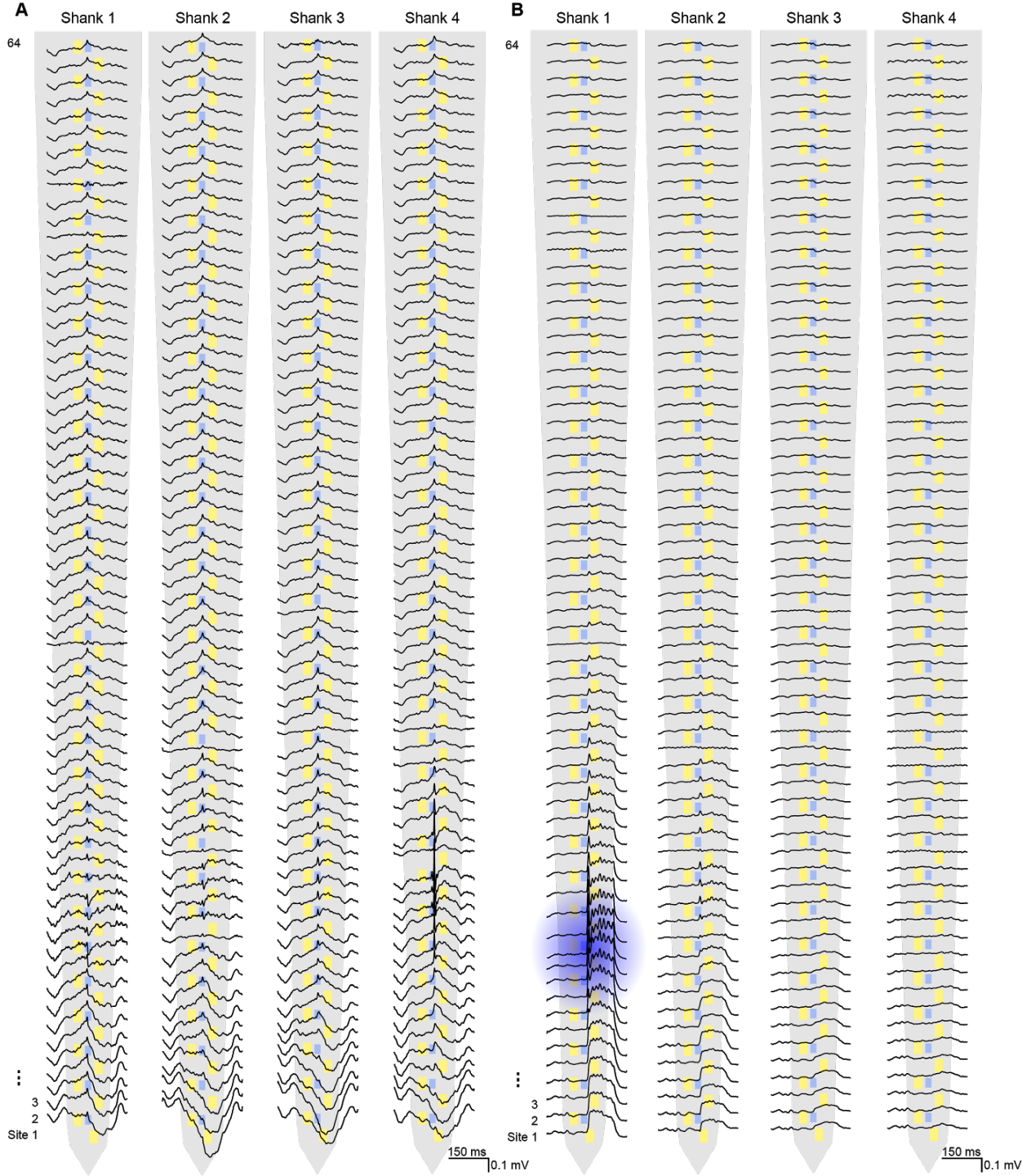
- Can µLED optoelectrode heat brain tissue?
  - Not really
    - The amount of light we are using is very low.
    - Silicon is a very good heat conductor.
  - But keep in mind that long (> 10 s), continuous light stimulation can heat brain tissue.[2]

[1]Csernai et. al., 2019; [2]Kim et. al., 2016 (IEEE)

µLED Optoelectrodes



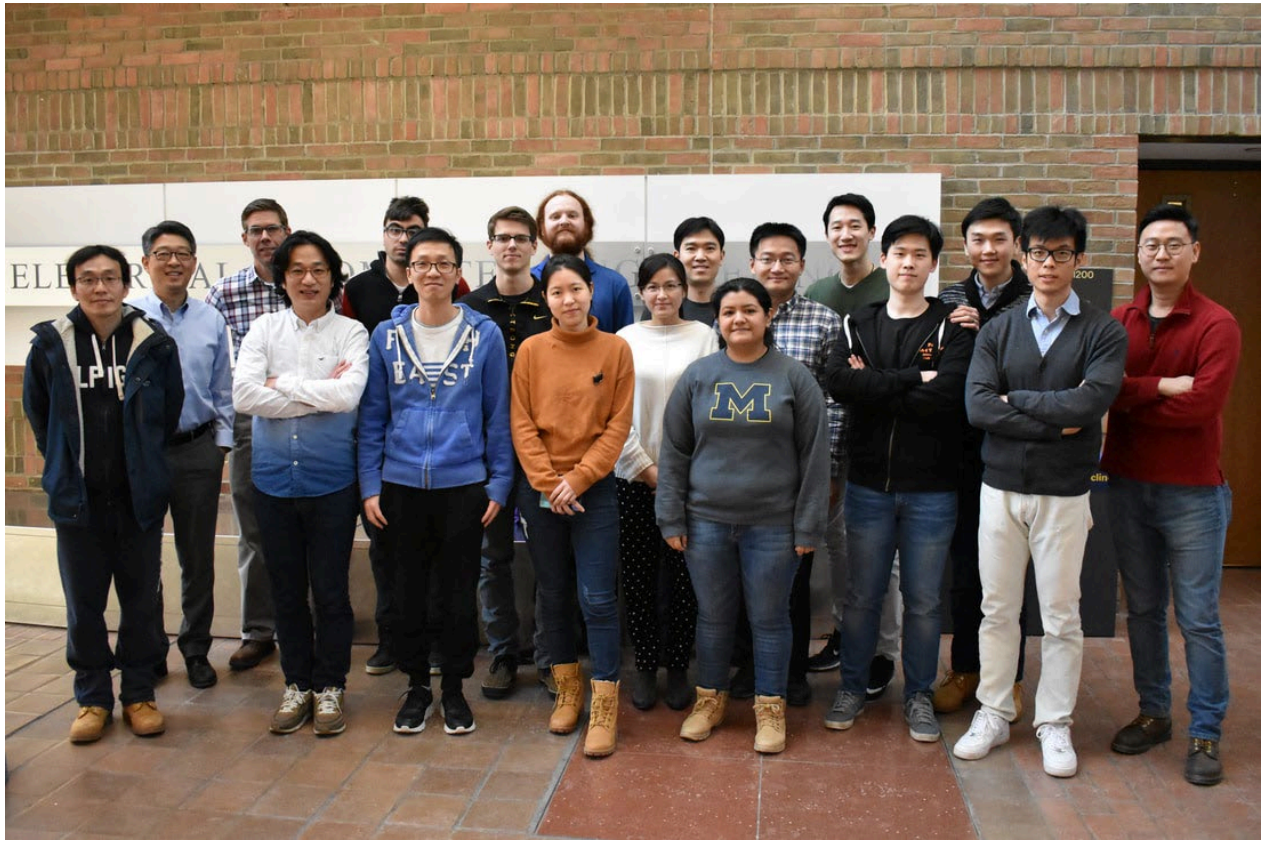
- Investigating local microcircuit effects
- High-density uLED probes can provide excellent spatio-temporal resolution



Acknowledgement

Buzsaki Lab

Yoon Lab



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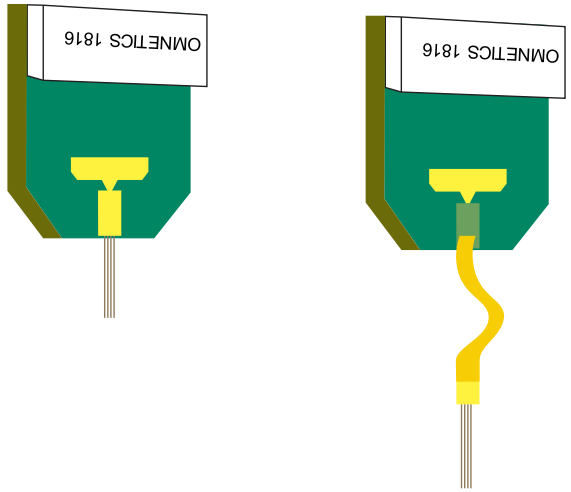
µLED Optoelectrodes



- Investigating local microcircuit effects
- High-density uLED probes can provide excellent spatio-temporal resolution

Useful links related to my talk

- MINT program
  - https://mint.engin.umich.edu/
- Yoon's lab github (micro-drive/OSC1Lite)
  - https://github.com/YoonGroupUmich
- Buzsaki's lab github (surgery base)
  - https://github.com/buzsakilab
- Spikesorting (there are many others)
  - https://github.com/MouseLand/Kilosort2

- **My contact:** voroslakos@gmail.com