

Electrophysiology Workshop

Misi Voroslakos

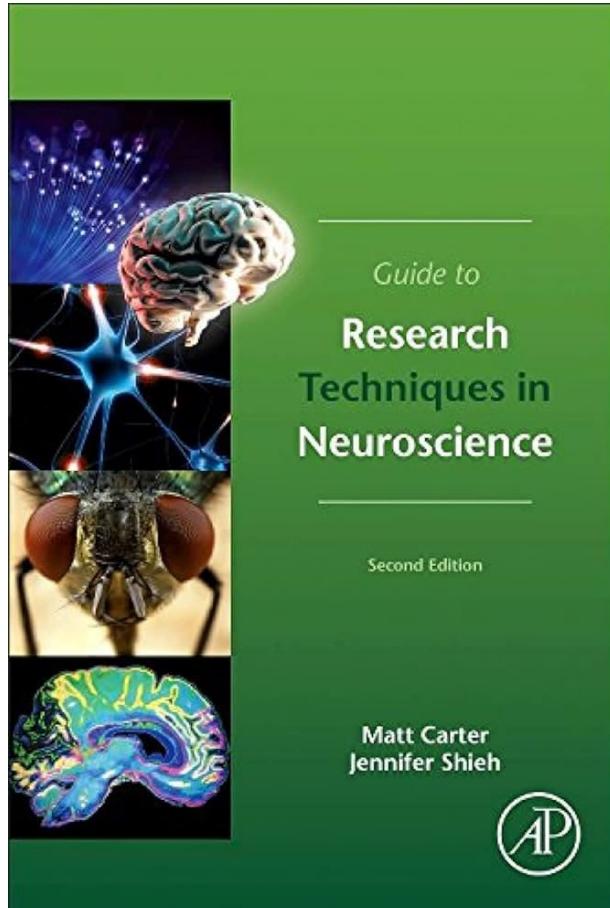
Postdoc

Buzsaki Lab

2025. 12. 11.

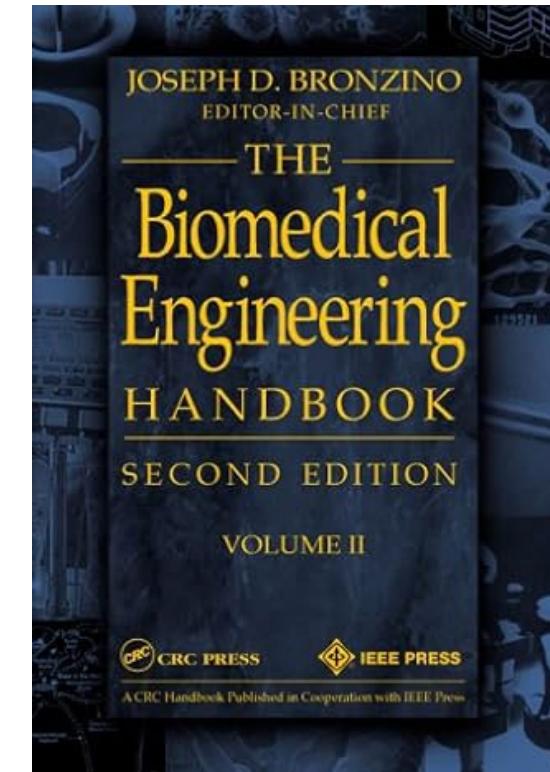
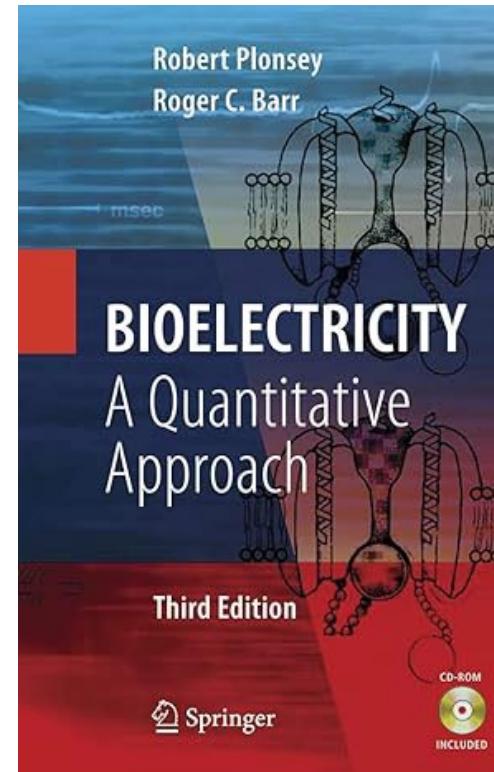
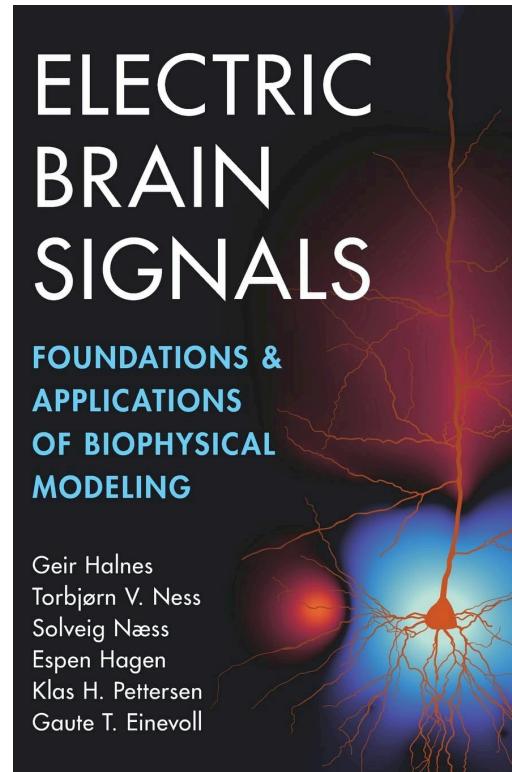
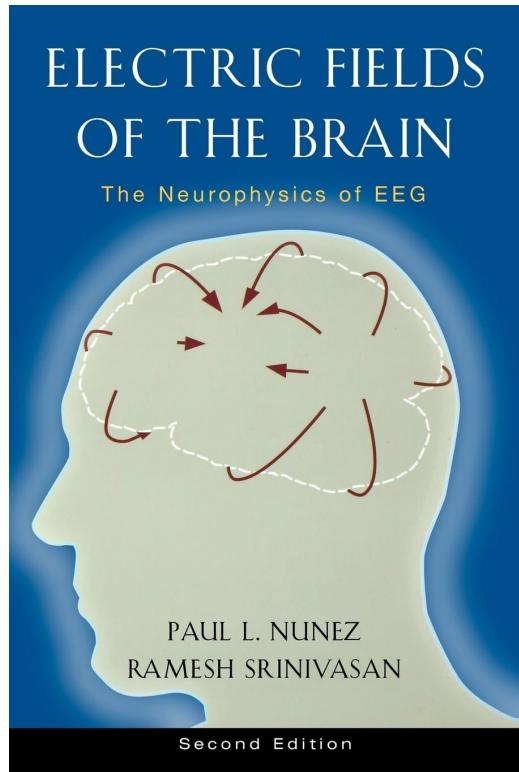
Postdoc Led- Electrophysiology Workshop

Background reading materials



- **Chapter 3 - Stereotaxic Surgeries and In Vivo Techniques**
- **Chapter 4 – Electrophysiology**
- **Chapter 8 - Manipulating Neural Activity**

Background reading materials



Section II
Section V
Chapter 70

Background reading materials

M01

Microelectrodes, Microelectronics, and Implantable Neural Microsystems

Progress in development of tiny electrodes, cables, circuitry, signal processors and wireless interfaces promises to advance understanding of the human nervous system and its disorders.

By KENSALL D. WISE, Life Fellow IEEE, AMIR M. SODAGAR, Member IEEE, YING YAO, Member IEEE, MAYURACHAT NING GULARI, GAYATRI E. PERLIN, AND KHALIL NAJAFI, Fellow IEEE

nature reviews methods primers

<https://doi.org/10.1038/s43586-025-00399-7>

Primer

 Check for updates

In vivo microelectrode arrays for neuroscience

Nathaniel P. Williams  ^{1,2}, Mihaly Voroslakos³, Delin Shi  ^{1,2}, May Yoon Pwint  ^{1,2}, Vittorino Lanzio⁴, Hongwei Mao  ^{2,5}, Pavlo Zolotavin⁶, Euisik Yoon  ^{4,7,8,9}, Thomas Stieglitz  ^{10,11}, Chong Xie  ^{6,12,13}, Timothy D. Harris  ^{14,15}, Andrew B. Schwartz  ^{1,2,5} & Xinyan Tracy Cui  ^{1,2}✉

The origin of extracellular fields and currents — EEG, ECoG, LFP and spikes

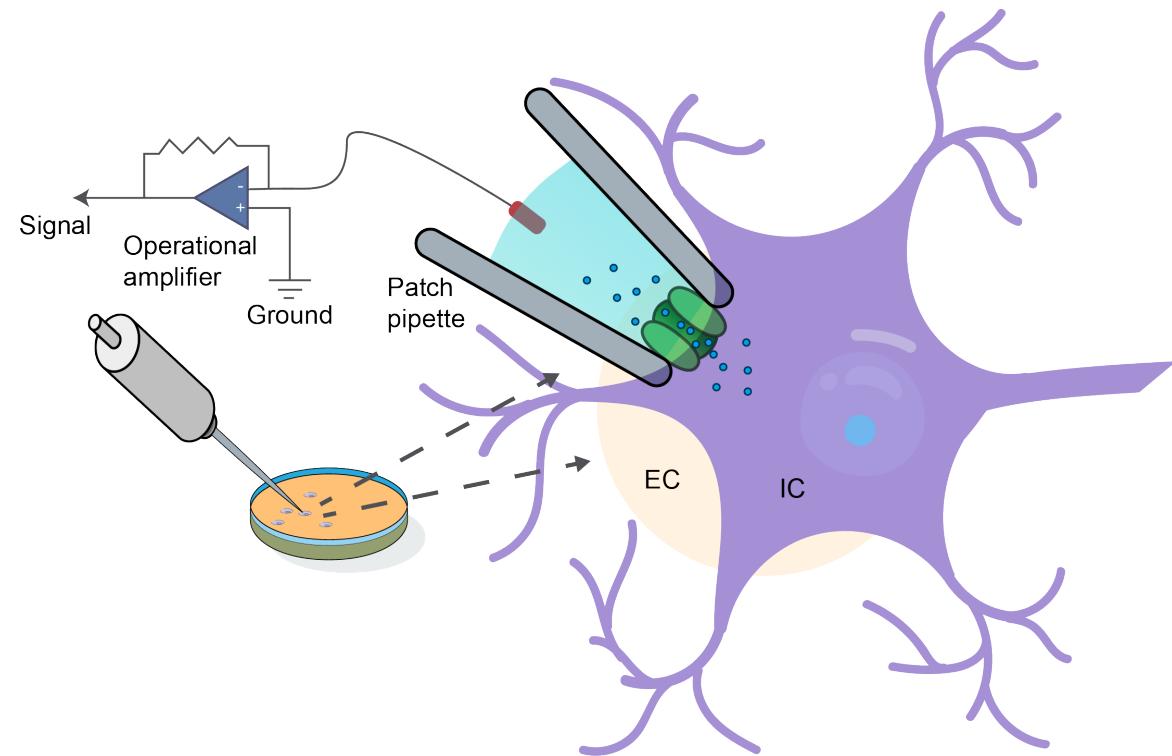
György Buzsáki^{1,2,3}, Costas A. Anastassiou⁴ and Christof Koch^{4,5}

REVIEW ARTICLE

State-of-the-art MEMS and microsystem tools for brain research

John P. Seymour¹, Fan Wu², Kensall D. Wise^{1,3} and Euisik Yoon^{1,3}

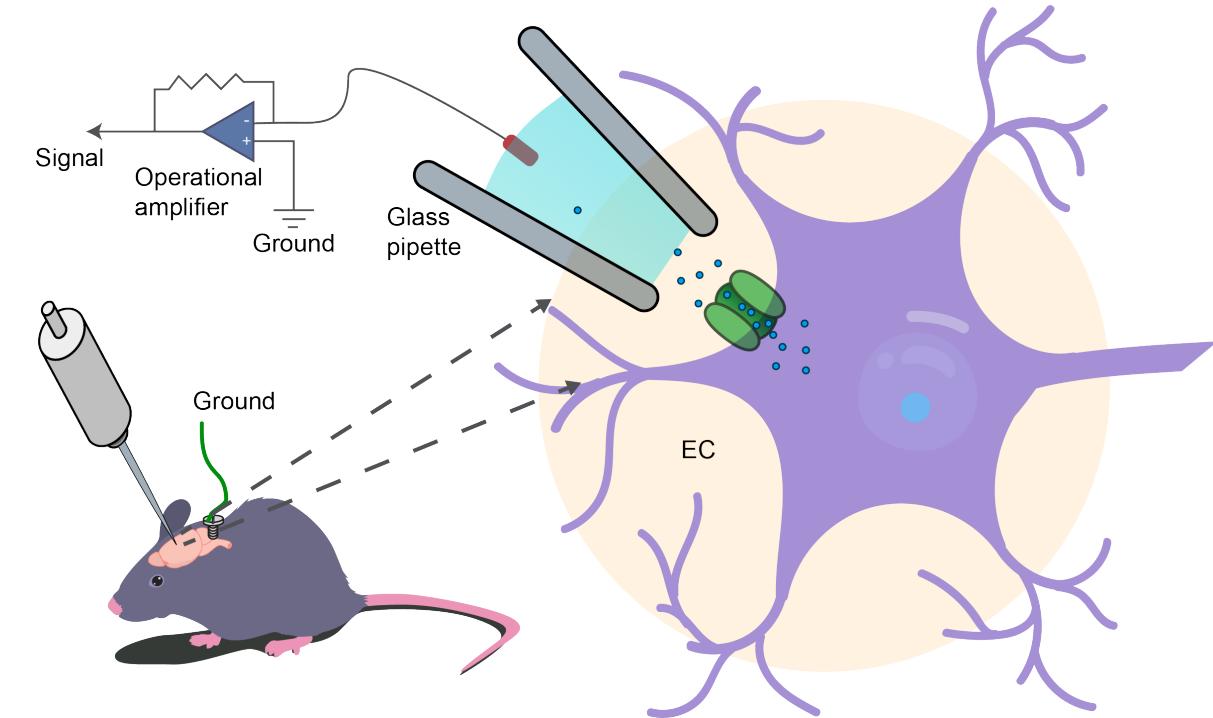
Intracellular recording



1930s–1950s: Glass micropipettes
“Intracellular revolution”

- Resting potential, AP shape, synaptic potentials
- Acute, mostly stationary preps

Extracellular recording



1953: Metal-filled glass micropipette

- Dowben & Rose, Science

1957: Tungsten microelectrode

- Hubel, Science
- reliable single units, chronic-ish in vivo

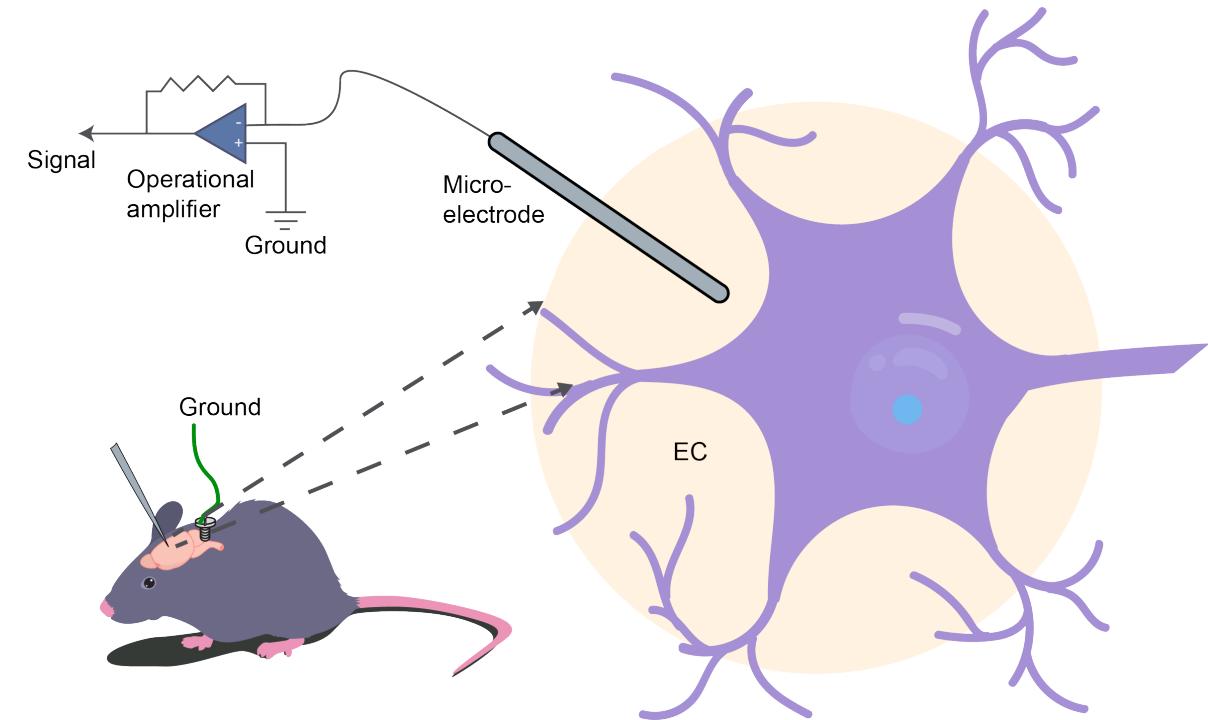
1958: Microwire bundles & chronic implants

- Strumwasser (steel), Olds (nickchrome)
- Long-term single units in unrestrained animals

Video worth watching



- Prof. Ken Wise
 - The Rocky Road to Neurotechnology
 - 1966 – 2016 overview of technology



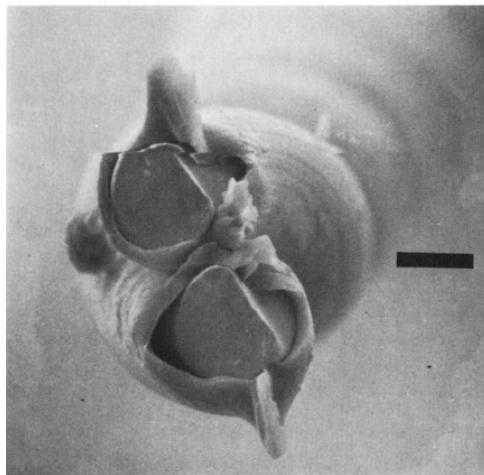
A brief history of electrode technology

Our history of microelectrode technology starts in the 1950s.

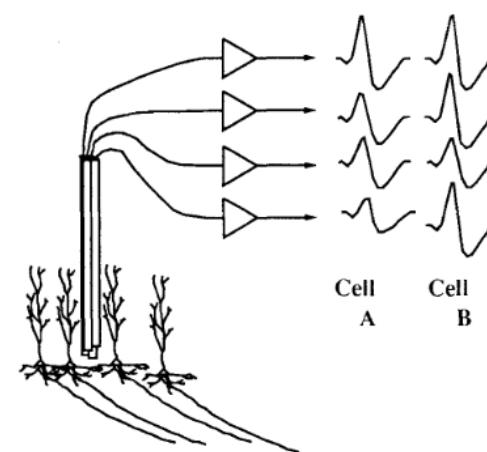
<https://www.neuronexus.com/a-brief-history-of-electrode-technology/>

The stereotrode: A new technique for simultaneous isolation of several single units in the central nervous system from multiple unit recordings

1983

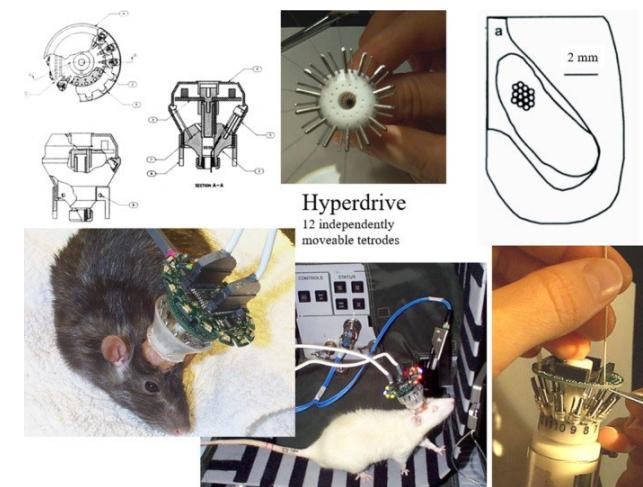


1993



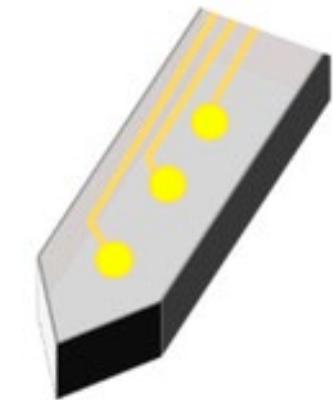
Tetrode
Phase relationship
between hippocampal
place units and the
EEG theta rhythm

1999

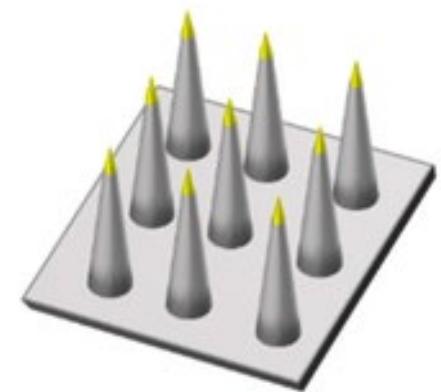


Hyperdrive (Bruce McNaughton)

1990-



(i) Michigan-type



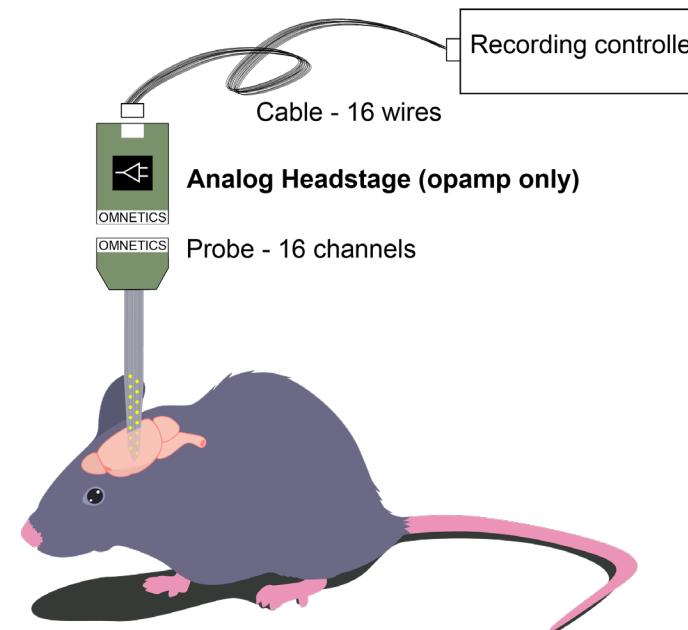
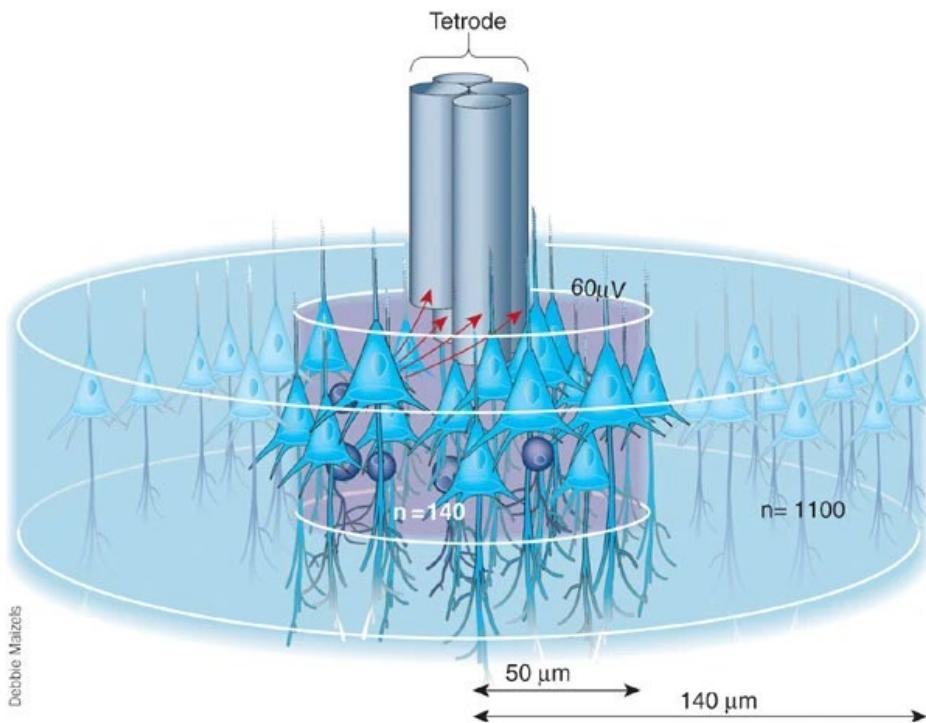
(ii) Utah-type

Goals and limitations (for engineers)

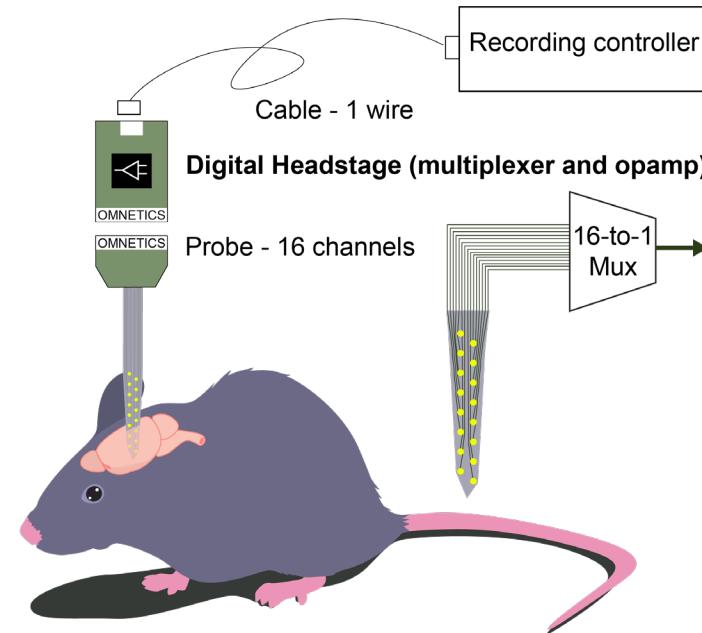
M03

Channel count

As many channels as possible



Until 2010



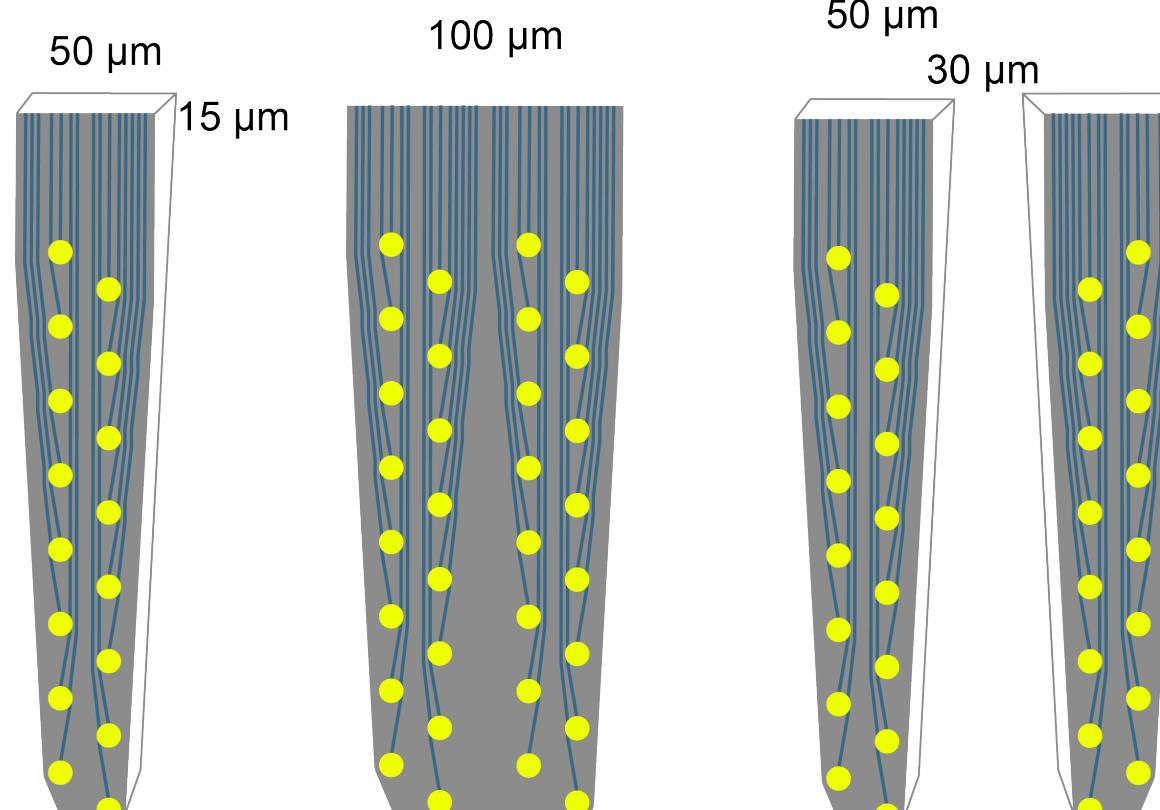
Since 2010
Intan Technologies

Goals and limitations (for engineers)

M03

Channel count

As many channels as possible



Same time

Minimize tissue damage

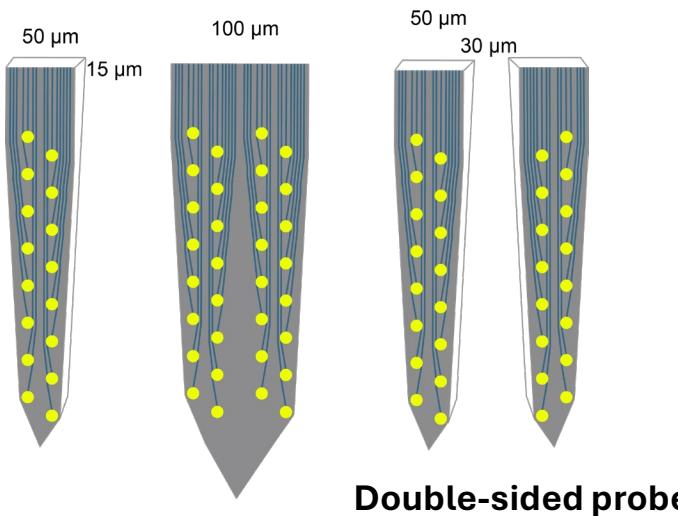
Double-sided probe

Goals and limitations (for engineers)

M03

Channel count

As many channels as possible



Number of metal lines (green) limit the number of channels

Same time

Minimize tissue damage

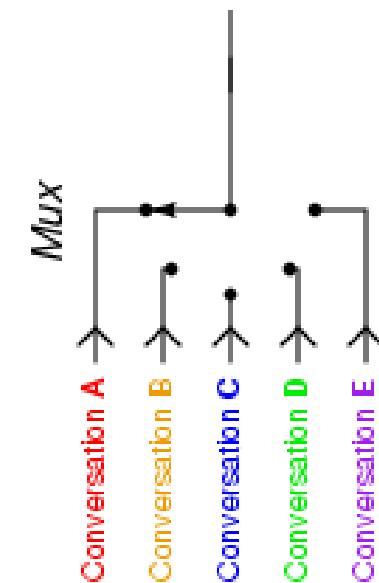
CMOS probes

Neuropixels: 384 channels

SiNAPS: 1024 channels

Active electronics on the probe shanks.

Multiplexing on the shank



My electrophysiology journey

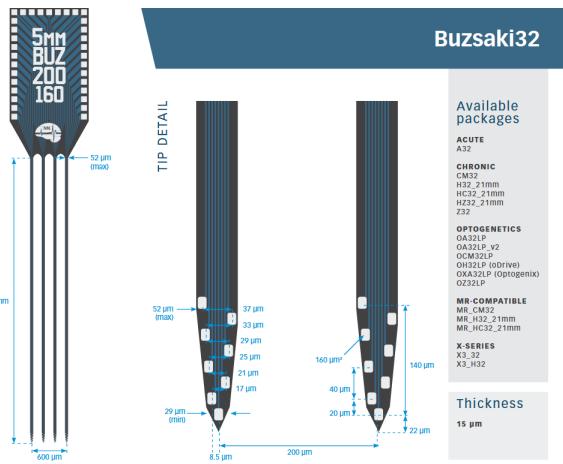
Martfű, Hungary (6000 people)



Szeged, Hungary → MD/PhD



2 x 32-channel probes (2013)
(anesthetized rats)

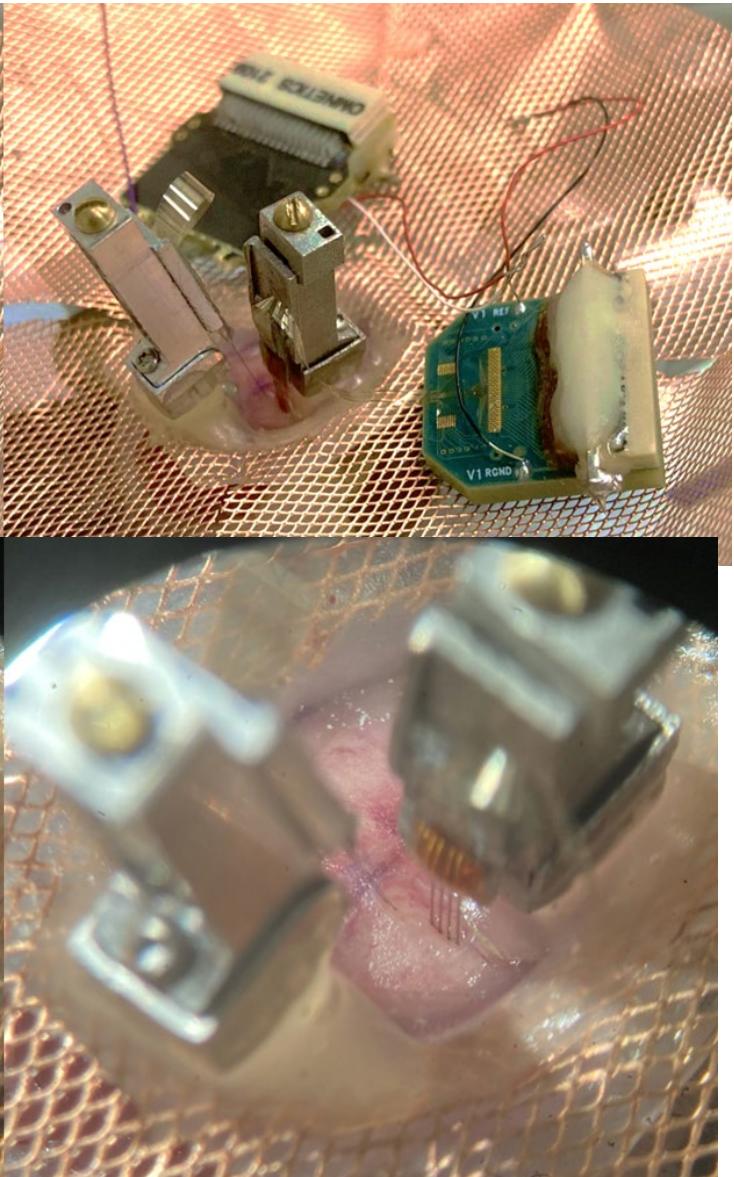


U of M, Ann Arbor

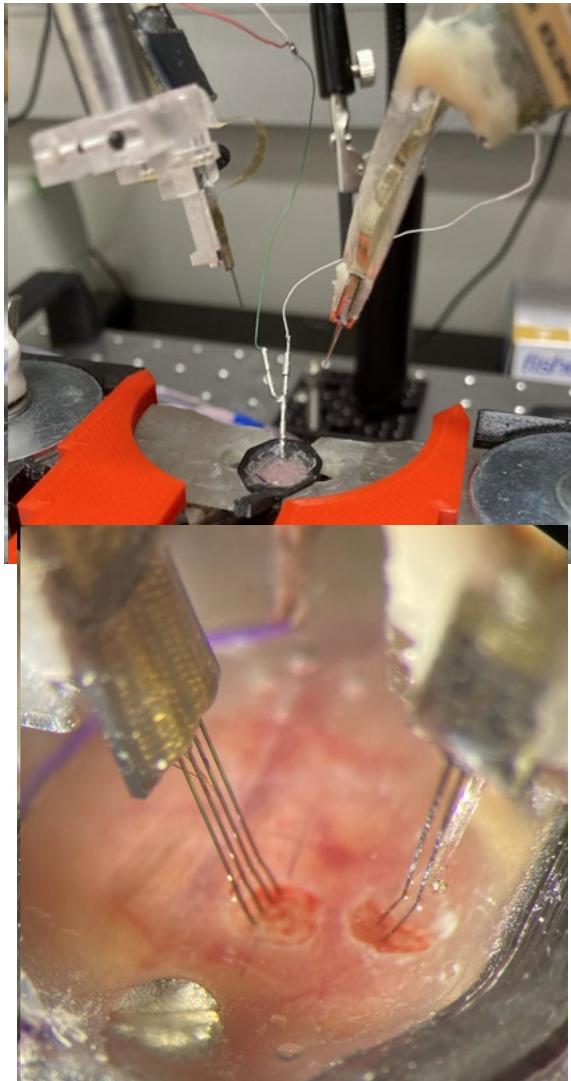


- Optogenetics
 - Optrode
 - Micro-LED probe
 - Waveguide probe
- Freely moving mice
- Head-fixed mice
- Freely moving rats
- Flexible probes
- Opto flexible probes
- Large-scale ephys
 - Neuropixels
 - SiNAPS
 - Hecto-STAR

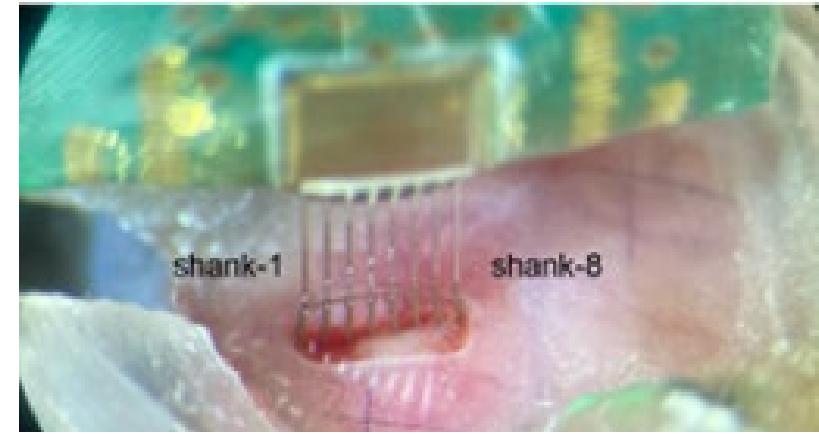
DBC-128 + micro-LED
(freely moving mouse)



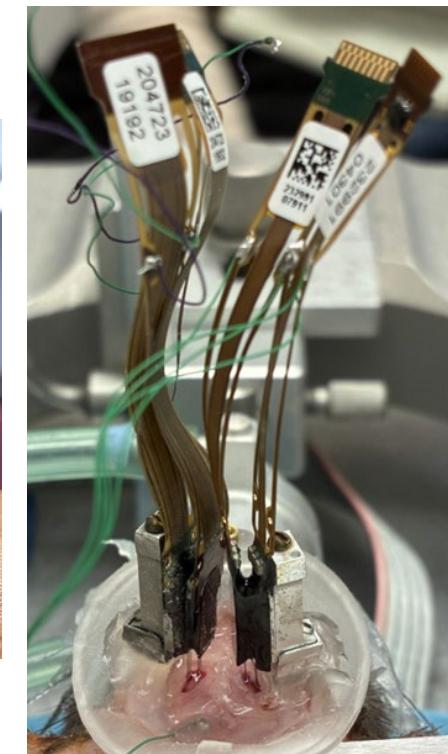
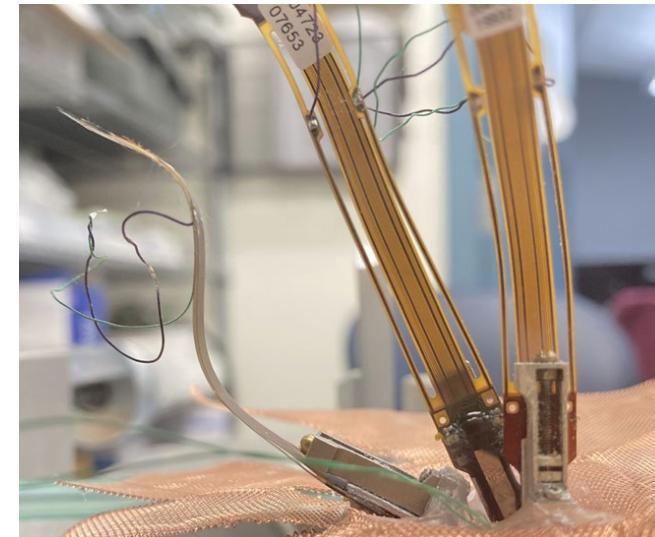
DBC-128 +
Cambridge optrode
(head-fixed mouse)



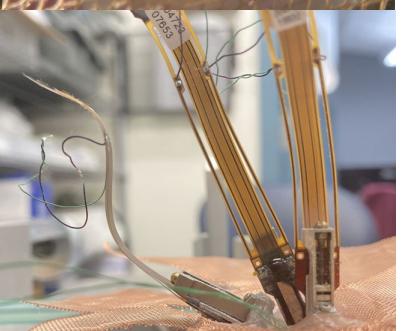
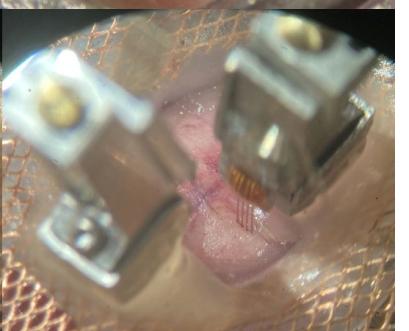
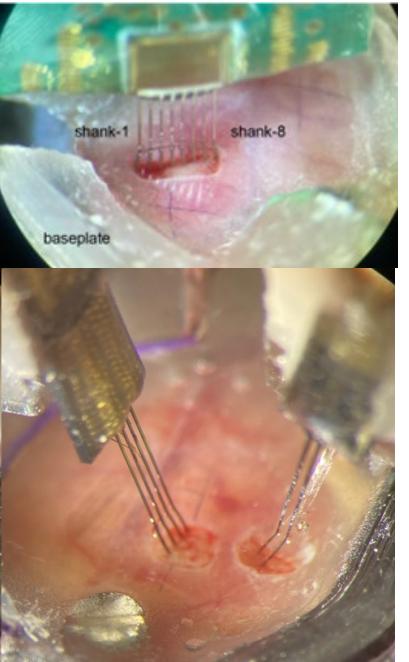
1024-channel SINAPS (freely moving mouse)



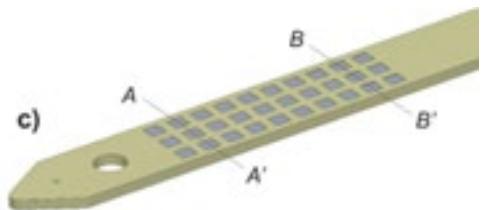
Multi-NP2.0 in rats



Experience with flexible probes



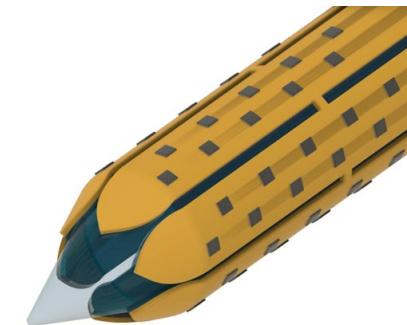
MANTA probe



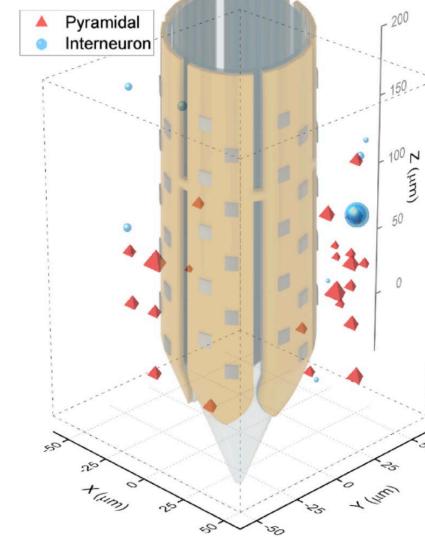
**Polyimide probe
(4 μm thickness)**



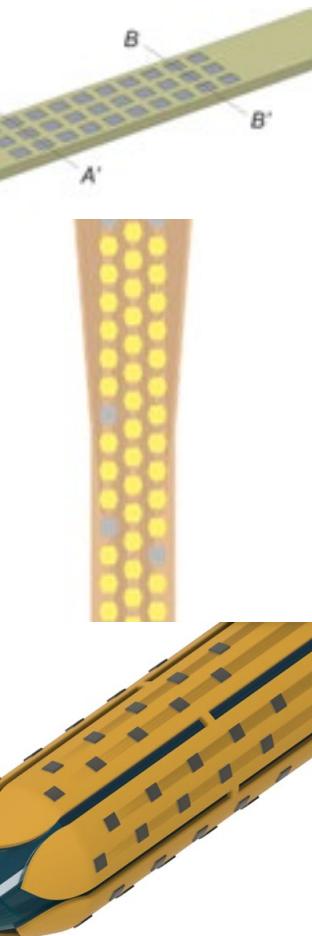
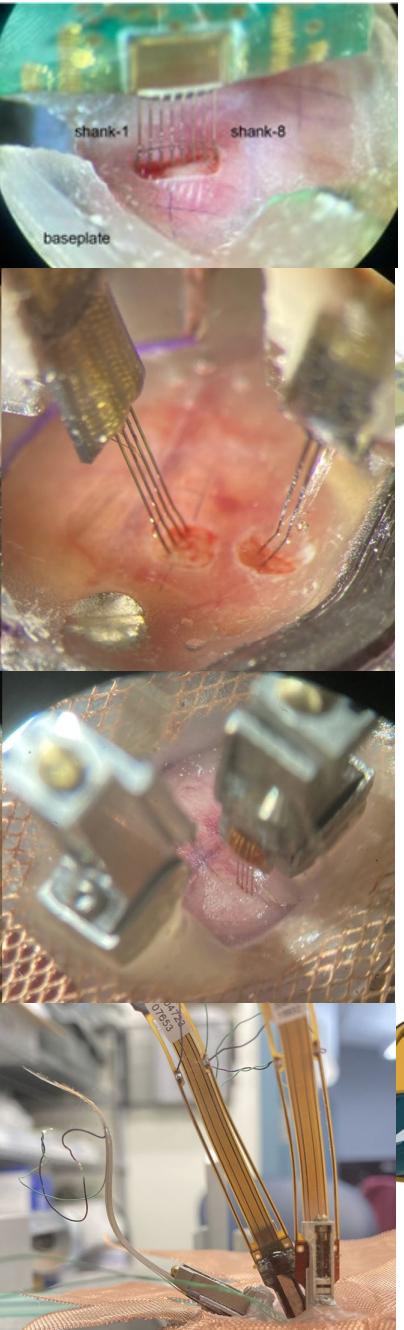
3D origami



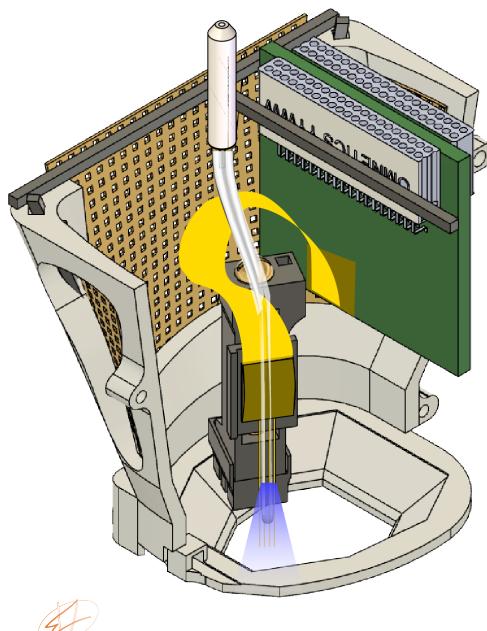
a



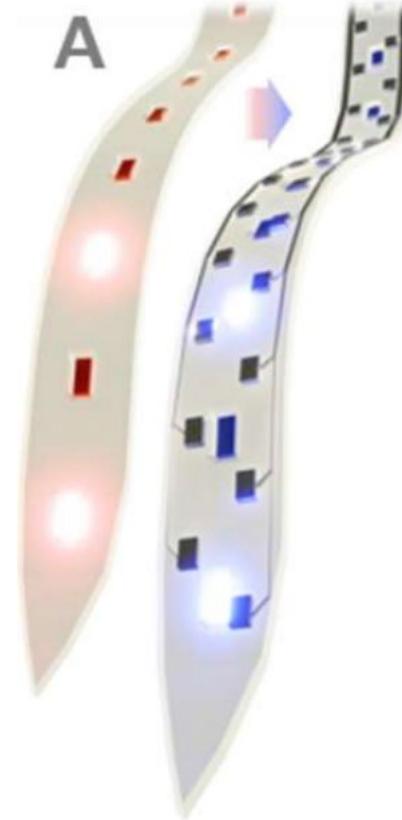
Experience with optogenetic probes



Optrode



Flexible
Micro-LED

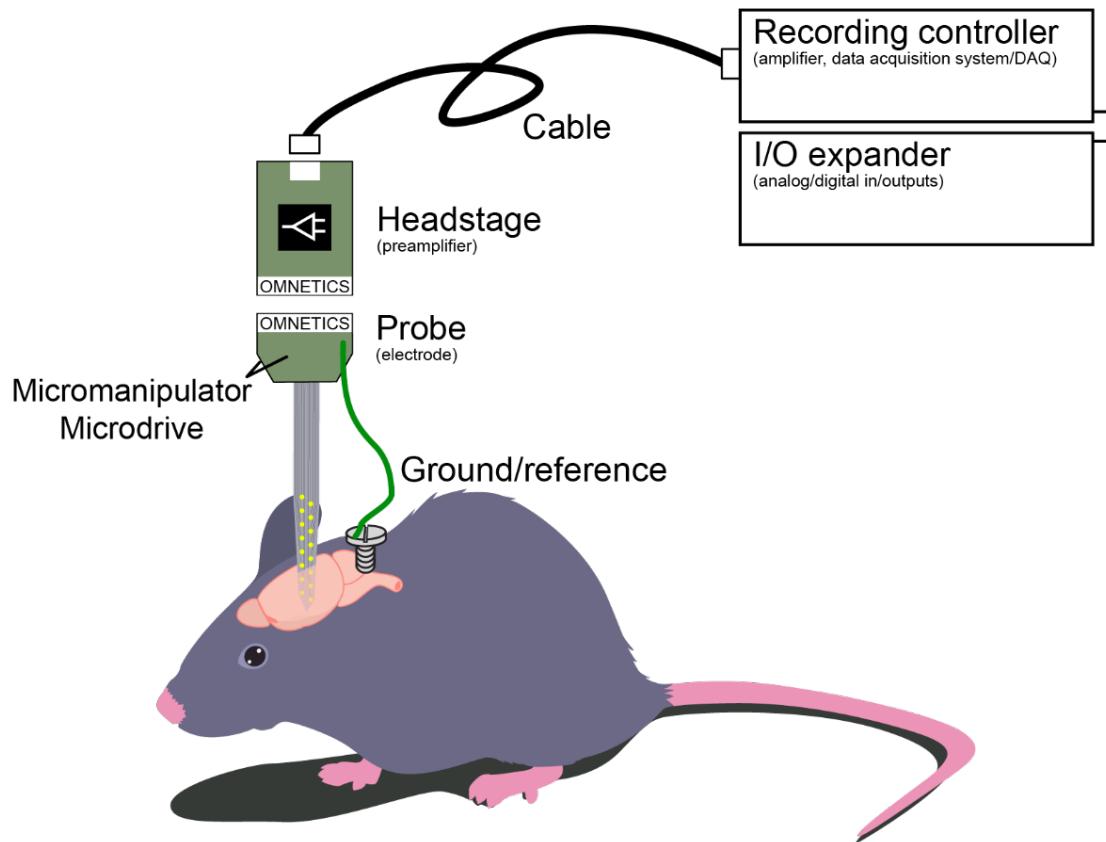


Micro-LED



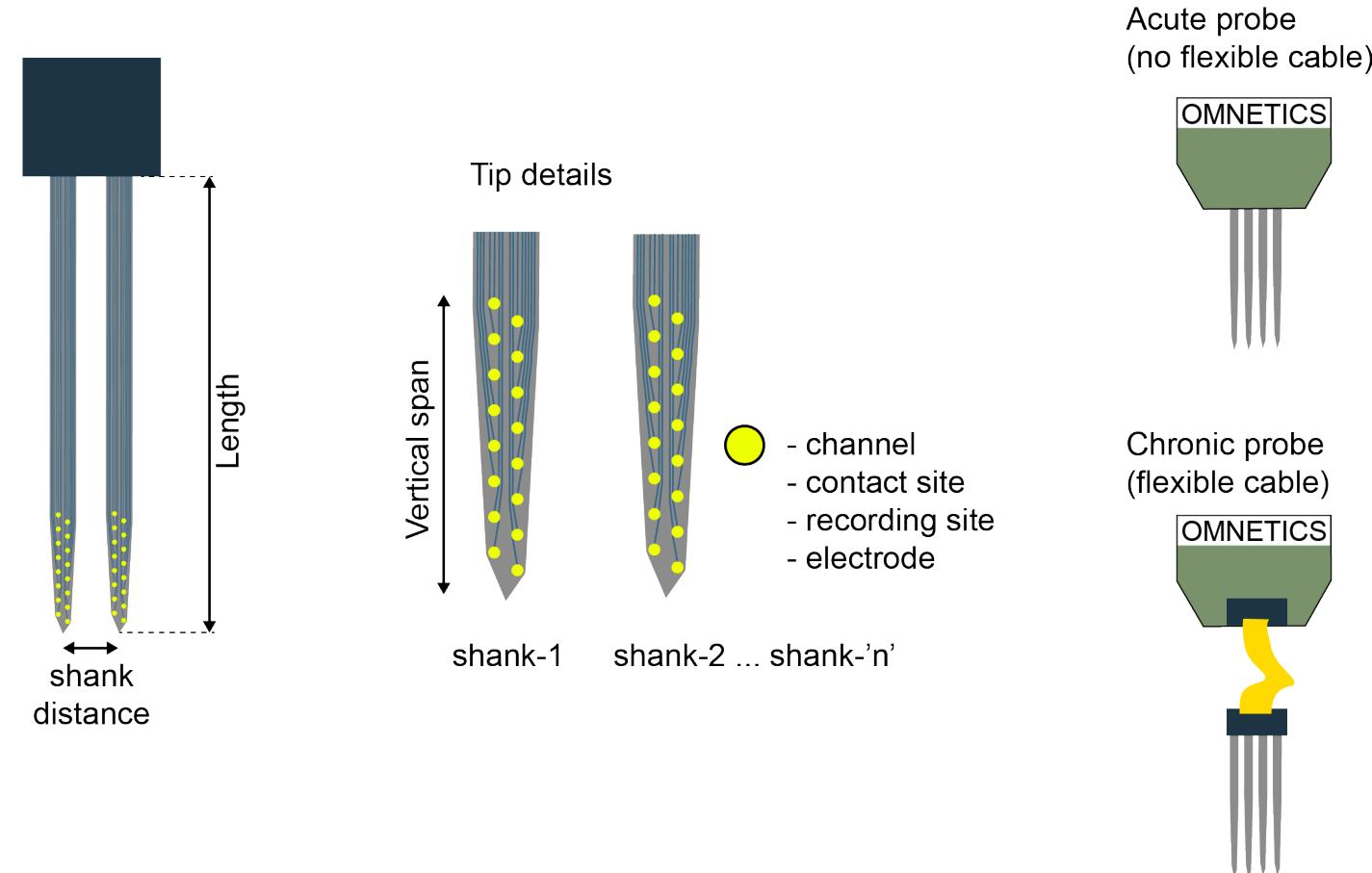
<https://www.youtube.com/watch?v=xhNoUiityVk>

Parts of an extracellular ephys system



- Recording probe/electrode/device
- Microdrive/shuttle/drive/manipulator
- Headstage/preamp/amplifier
- Recording cable
- Recording device/DAQ
- I/O expander/analog_digital inputs
- Ground, reference

'Anatomy' of a probe



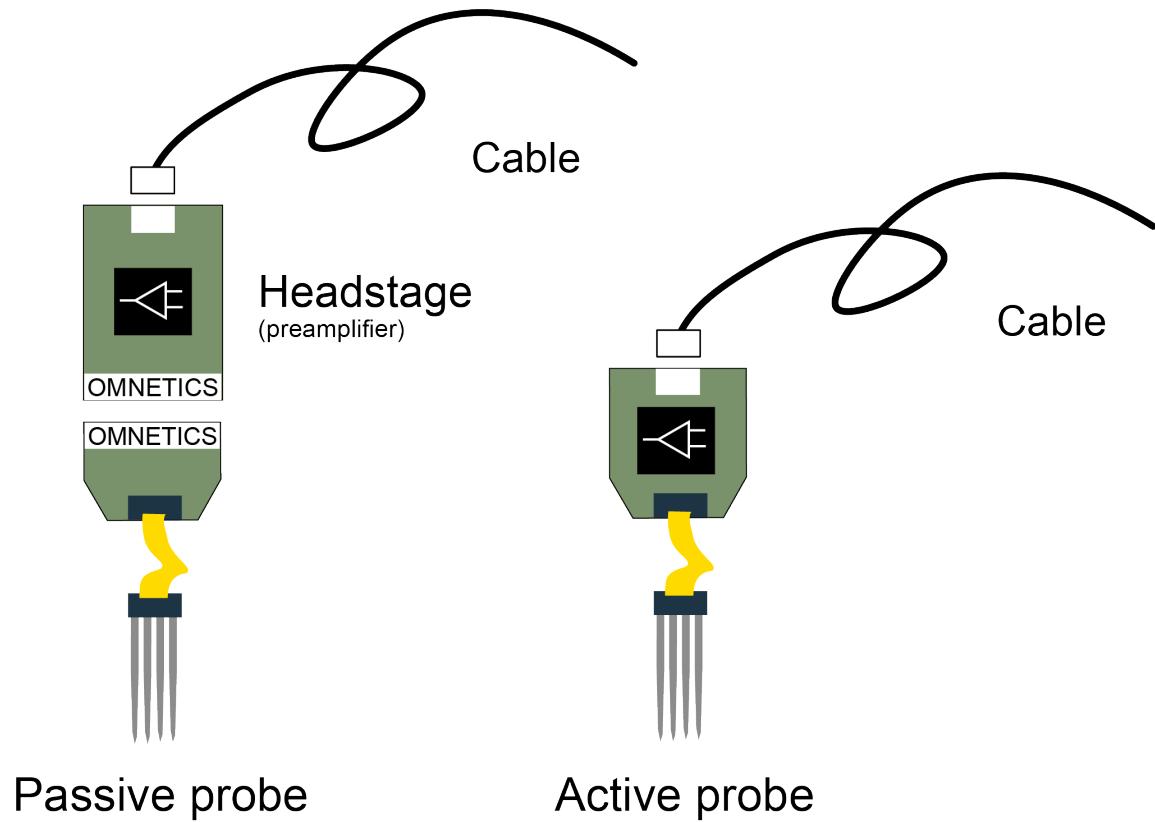
Acute probe

- No flex cable, very low noise
 - Parallel lines pick up EMI
- Head-fixed preparation
 - Awake, anesthesia

Chronic probe

- Flexible cable (yellow part) allows mechanical decoupling
- Attached to a Microdrive/shuttle
- Freely moving preparation
 - Can be used in head-fixed

'Anatomy' of a probe



Mouse weighs ~ 20-30 g

- We can place up to 20% of body weight

Passive probe

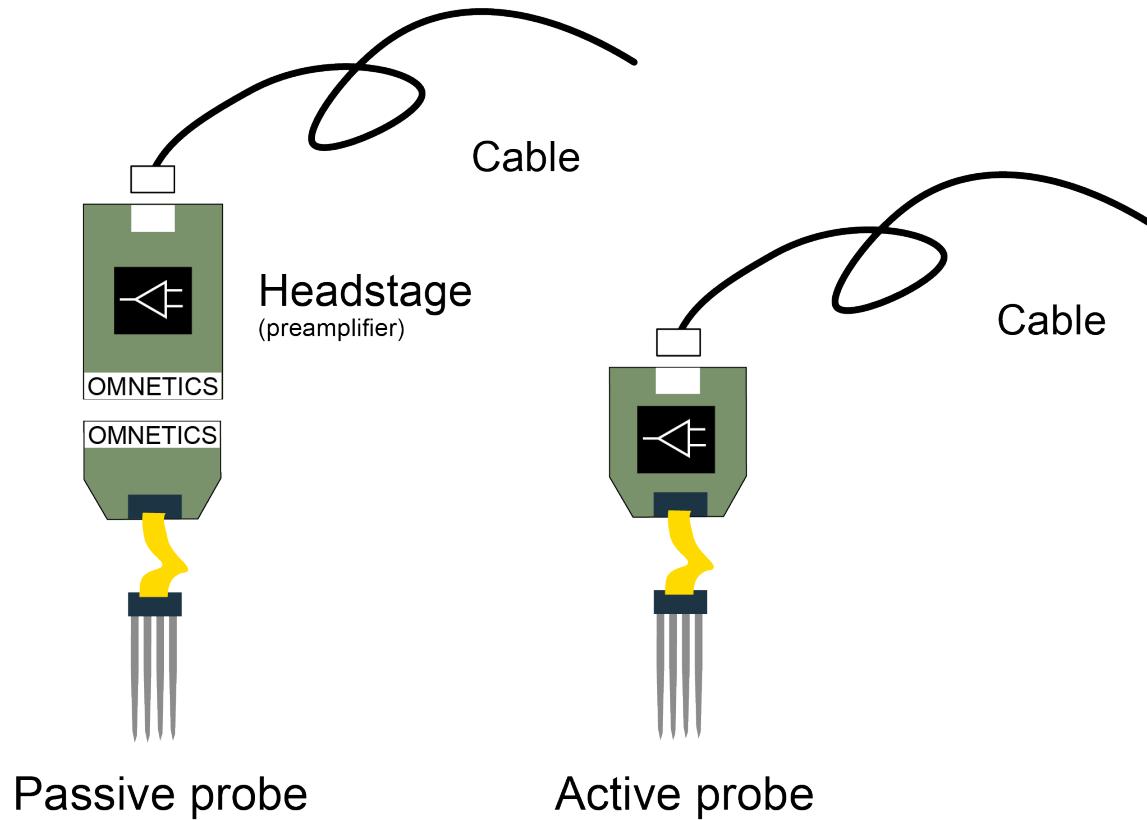
- Probe itself is **0.6 – 0.8 g**
- Headstage is **1.2 g**
 - **Animal must carry it during behavior!**

Active probe

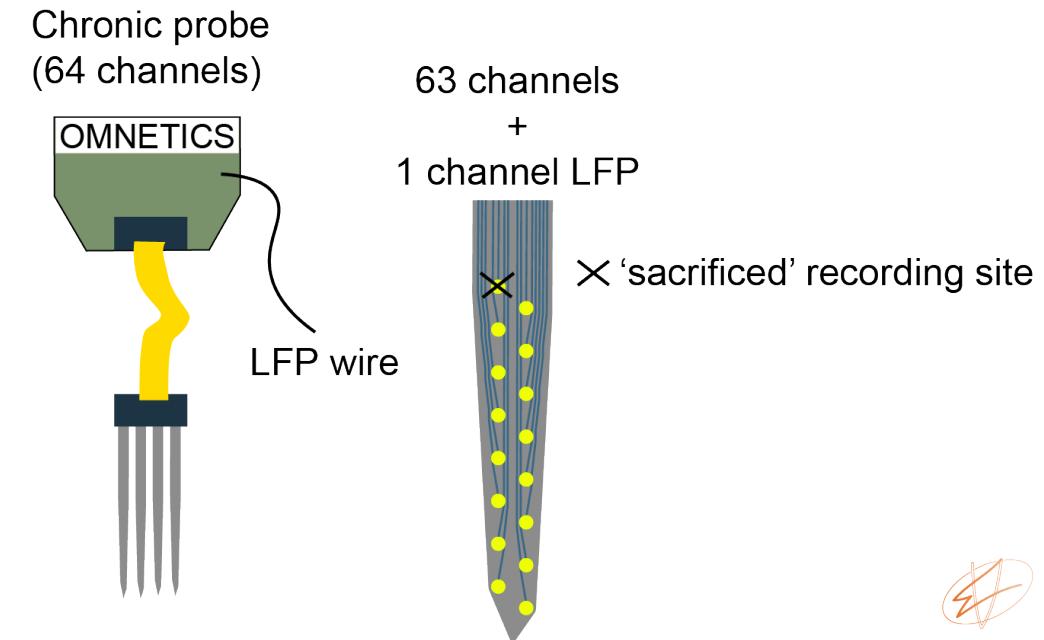
- Probe itself is **0.6 – 1.2 g**

MiniAmp (Cambridge)

'Anatomy' of a probe



Multi-regional recordings with wires



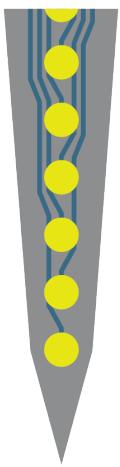
Silicon probes

16 / 32 / 64 / 128 / 256 channels

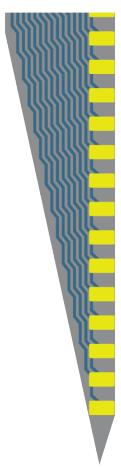
5 or 10 mm

M04

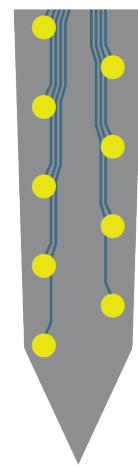
Linear



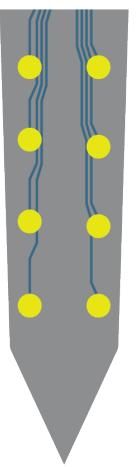
Edge



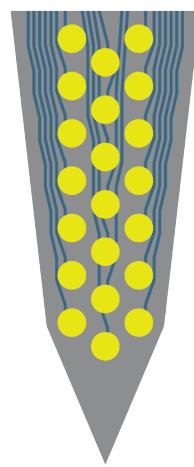
Staggered



Poly2



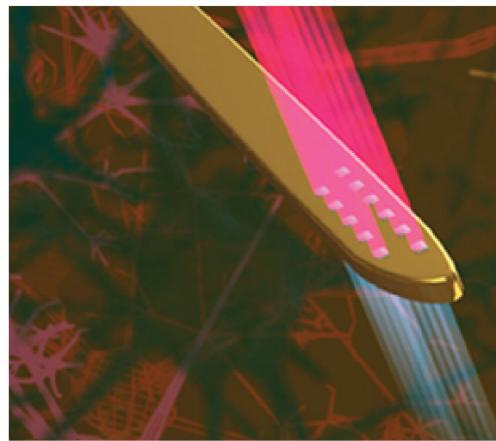
Poly3



Buzsaki

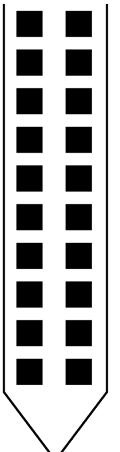


Double-sided



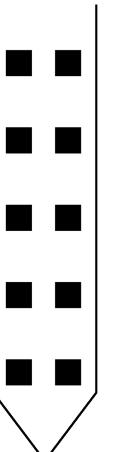
CMOS probes

Neuropixels



384 out of 5120
10 mm

SiNAPS



1024 channels
5 mm

Cambridge Neurotech
IMEC
NeuroNexus
Plexon

(Alphabetical order)

'Anatomy' of a probe

Group-1

Freely moving mouse, targeting dorsal CA1. Your primary goal is to maximize the number of simultaneously recorded single units from the pyramidal cell layer.

Group-2

Mouse somatosensory cortex and study laminar information processing: how inputs and outputs differ across layers (L2/3, L4, L5, L6).

Group-3

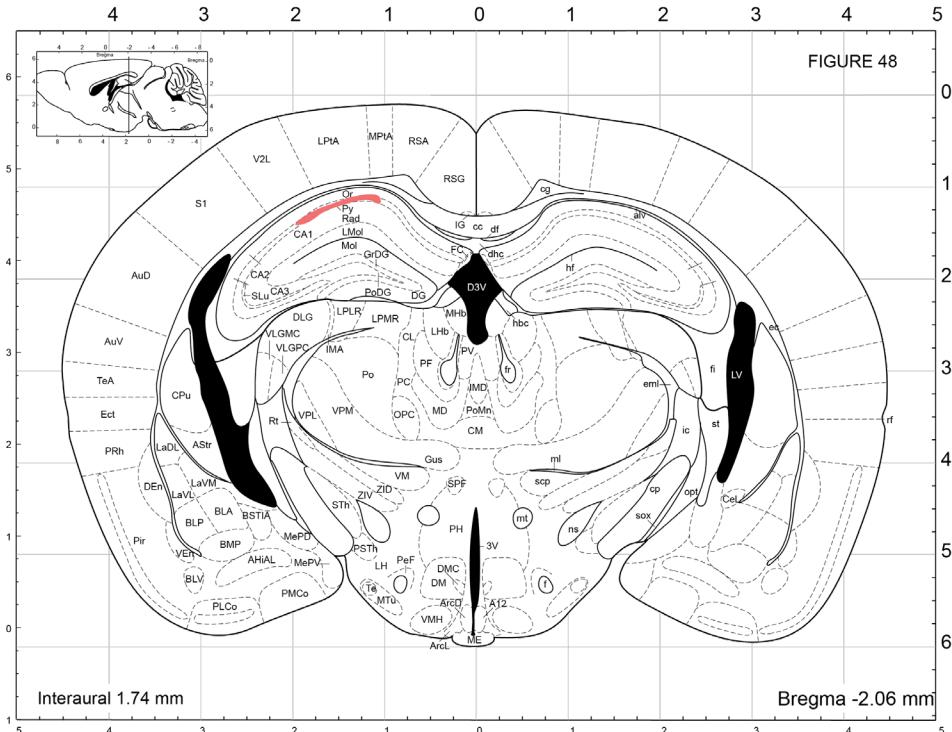
Freely moving mouse, targeting CM nucleus of thalamus. Maximize single unit yield.

Group-4

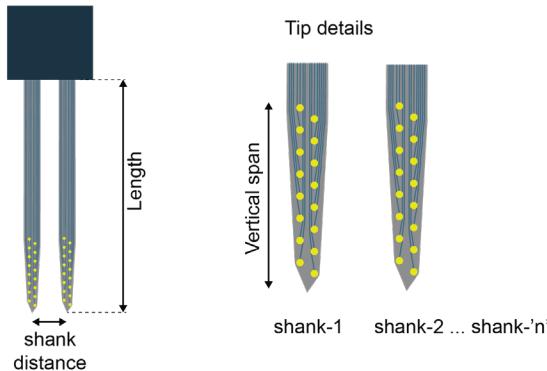
Freely moving rat, targeting putamen and motor cortex. Maximize single unit yield in both regions.

Group-1

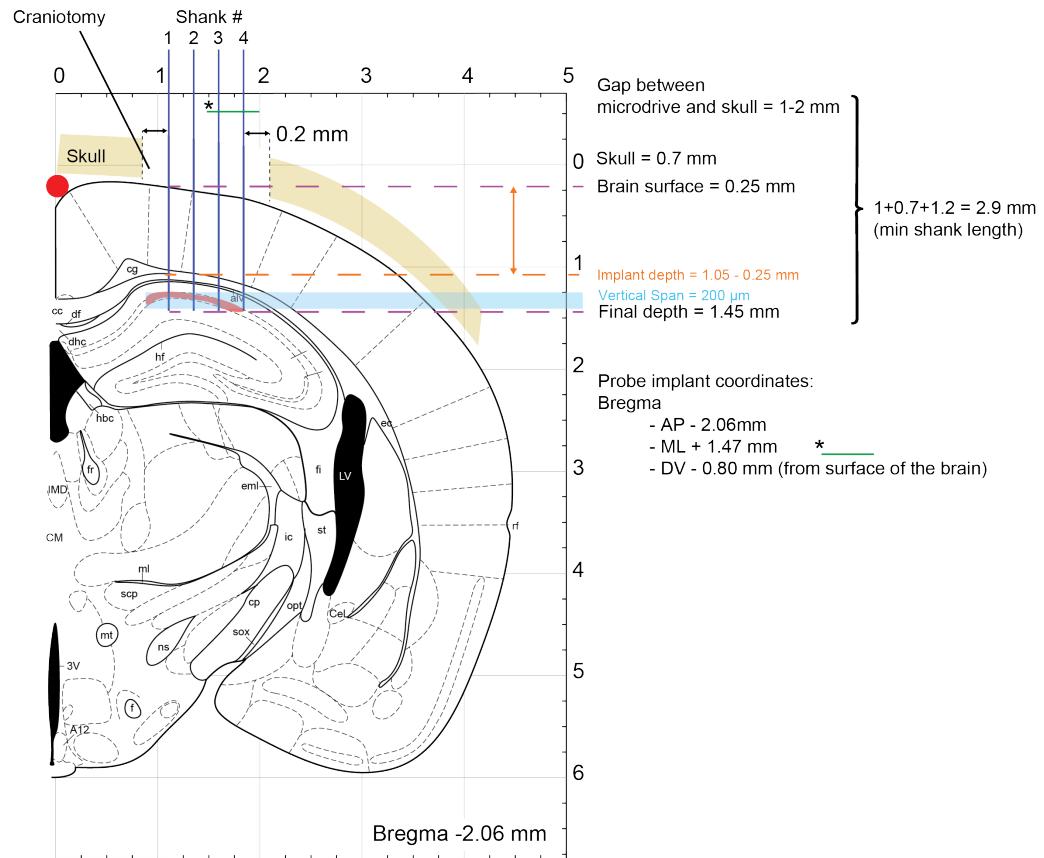
M04



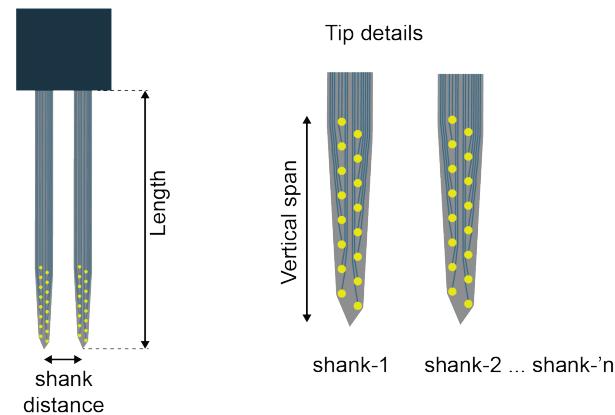
Select a probe that maximize the number of simultaneously recorded single units from the pyramidal cell layer.



Length of shank:
Number of shank:
Number of channels:
Vertical span:
Channel layout:



Select a probe that maximize the number of simultaneously recorded single units from the pyramidal cell layer



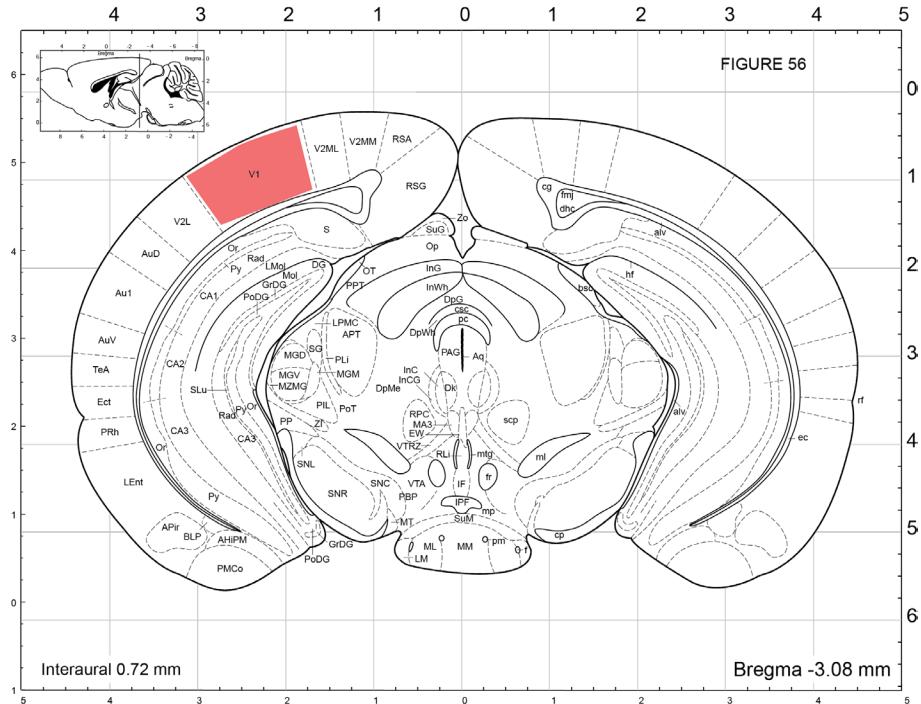
- Length of shank: 5 mm
- Number of shank: 2-4
- Number of channels: as many as possible
- Vertical span: 2-300 μm
- Channel layout: poly2 to higher density

My choice:

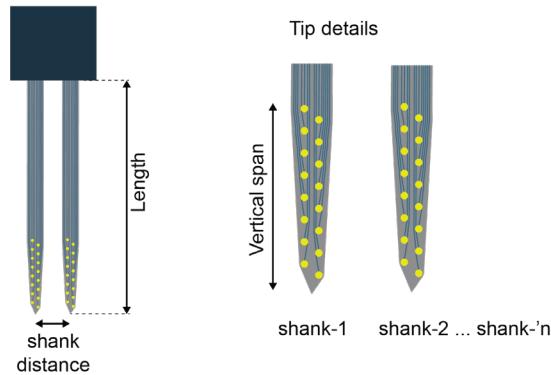
- double sided 128-channel
- poly3
- 128-5 Cambridge Neurotech

Group-2

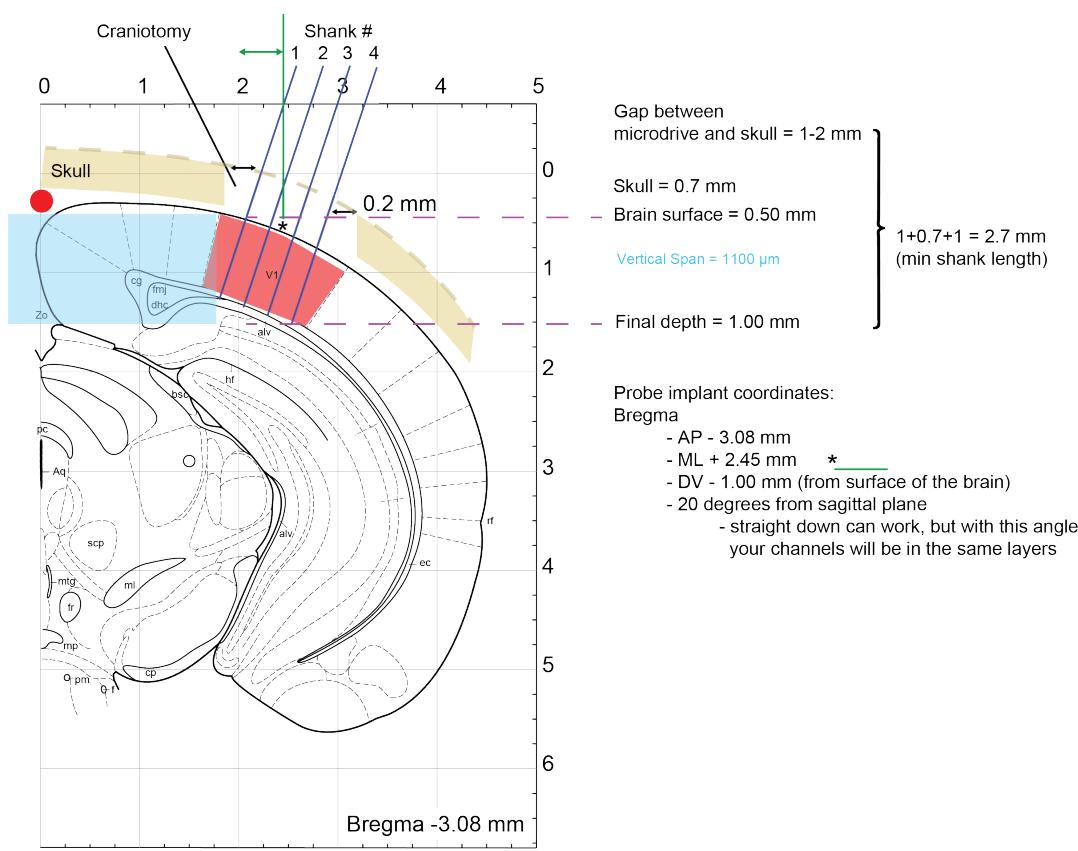
M04



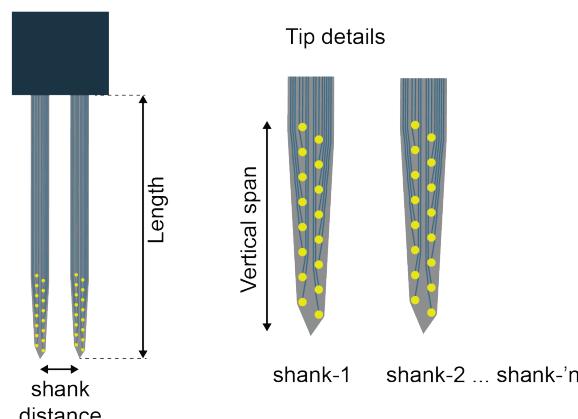
You want to record from mouse primary visual cortex and study laminar information processing: how inputs and outputs differ across layers (L2/3, L4, L5, L6).



Length of shank:
Number of shank:
Number of channels:
Vertical span:
Channel layout:



You want to record from mouse primary visual cortex and study laminar information processing: how inputs and outputs differ across layers (L2/3, L4, L5, L6).



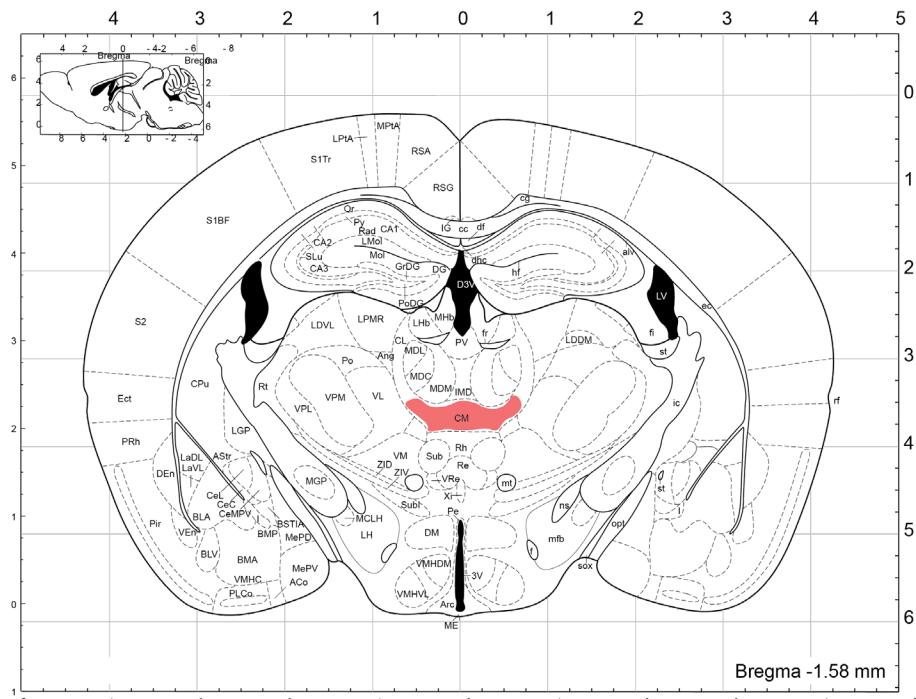
- Length of shank: 5 mm
- Number of shank: 4 or more
- Number of channels: 128 or NP or SiNAPS
- Vertical span: 900 μ m
- Channel layout: poly2

My choice:

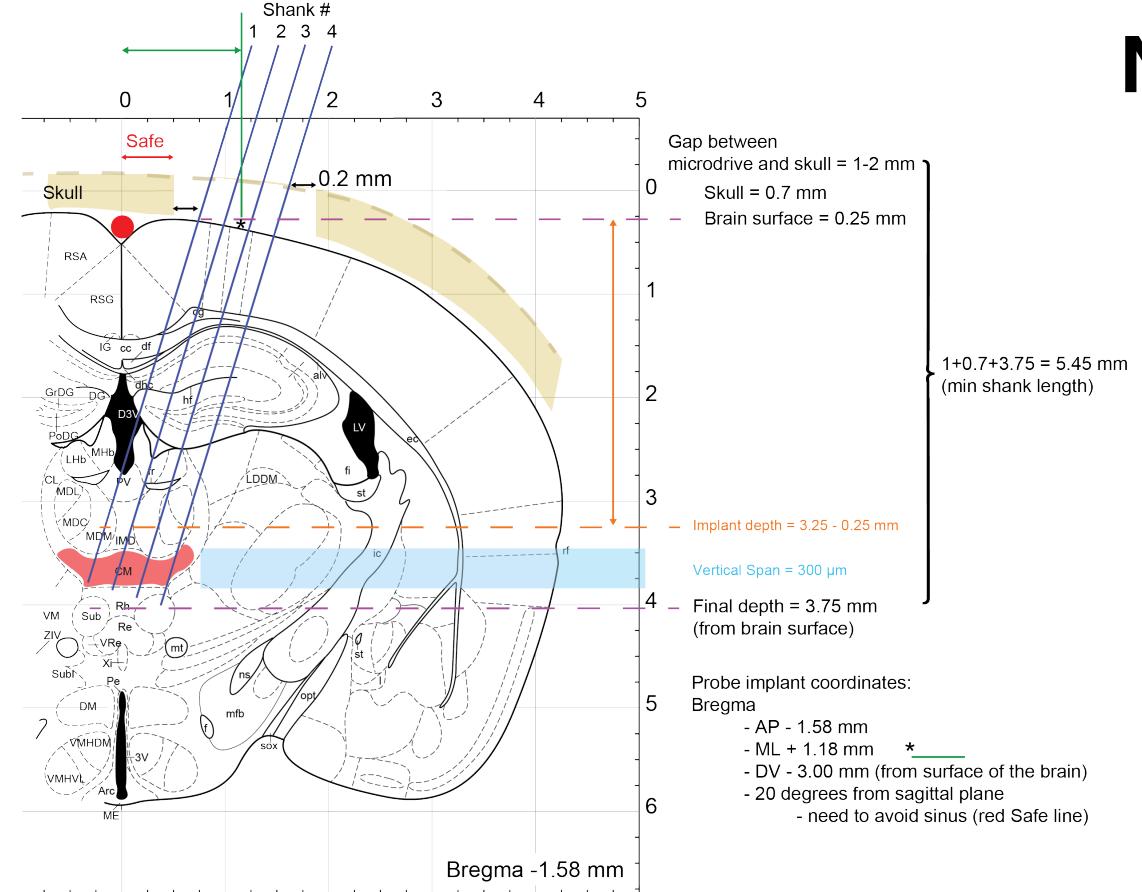
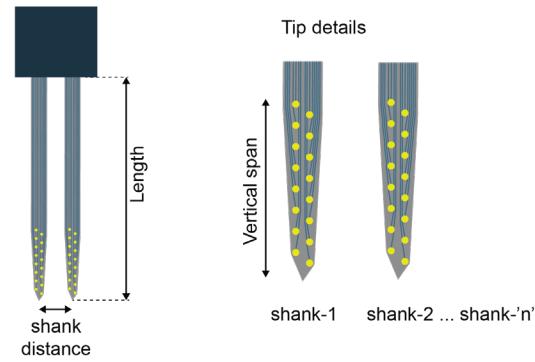
- NP 2.0
- $384 / 4 = 96$ channels / shank
- good spatial and unit yield

Group-3

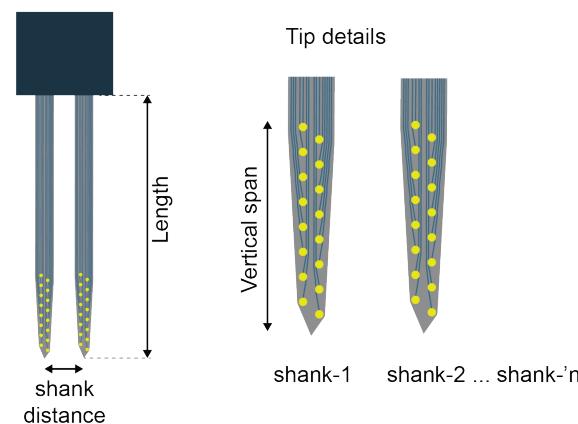
M04



Select a probe that reaches thalamus and gives high density in the thalamic segment.
Explain how you would align the probe (angle, depth) to cover CM thalamus.



Select a probe that reaches thalamus and gives high density in the thalamic segment.
Explain how you would align the probe (angle, depth) to cover CM thalamus.

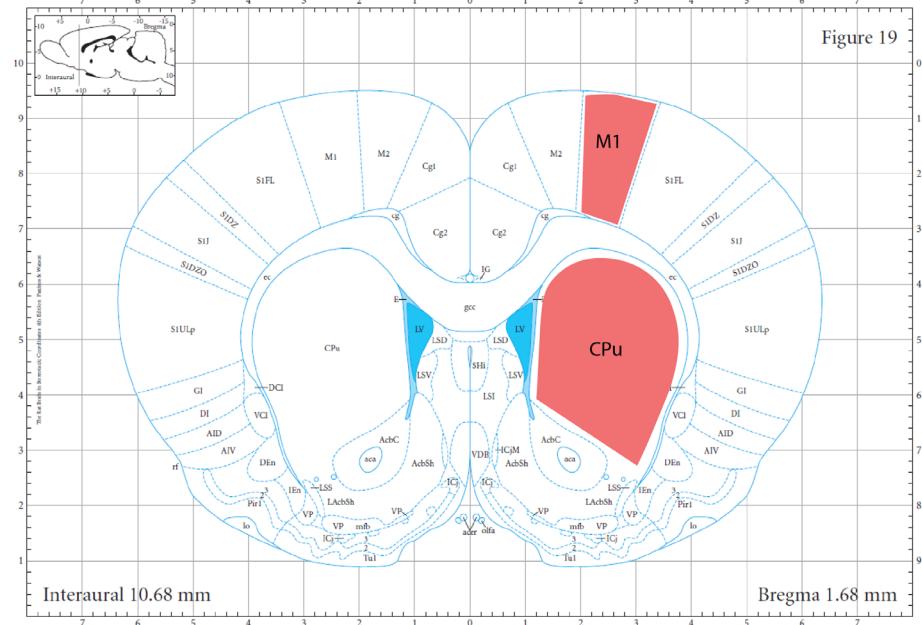


Length of shank: 10 mm
Number of shank: 4
Number of channels: 128
Vertical span: 400 μ m
Channel layout: poly2

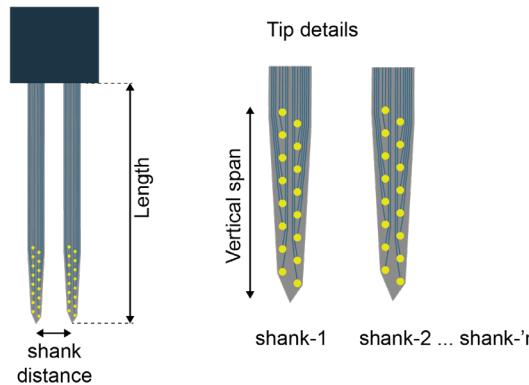
My choice:
- 128 channel poly 2

Group-4 (RAT)

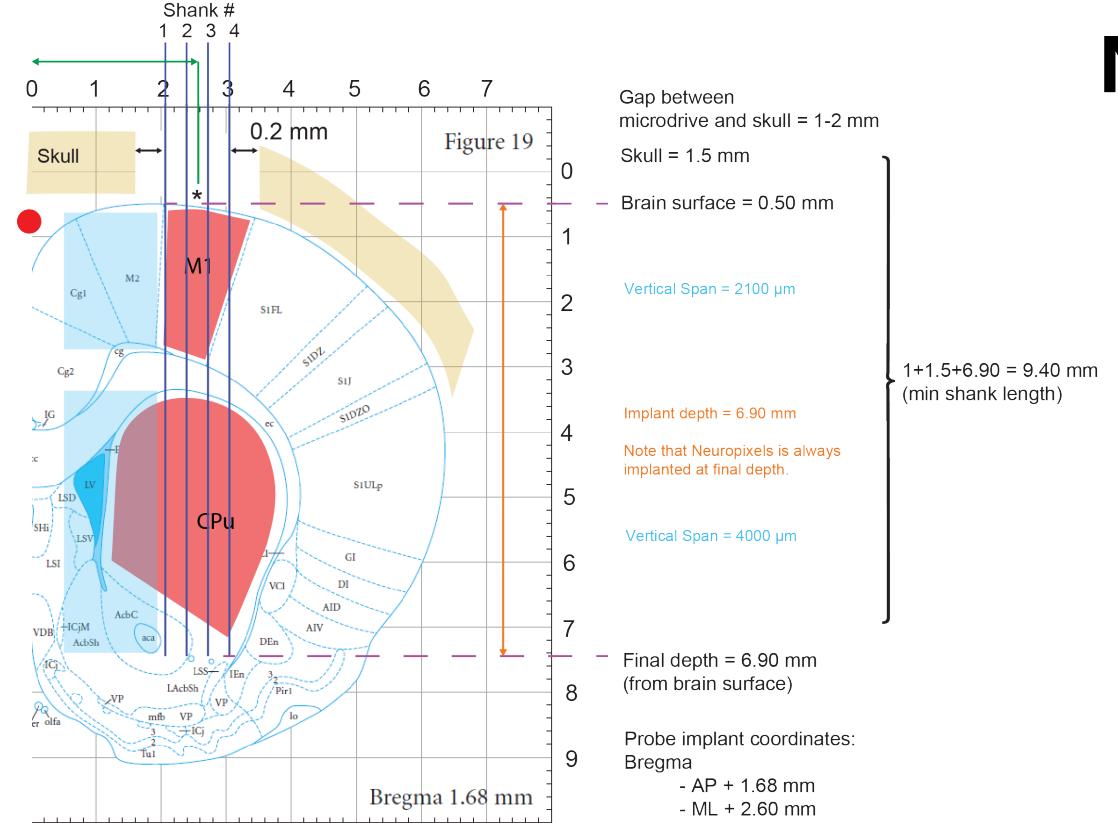
M04



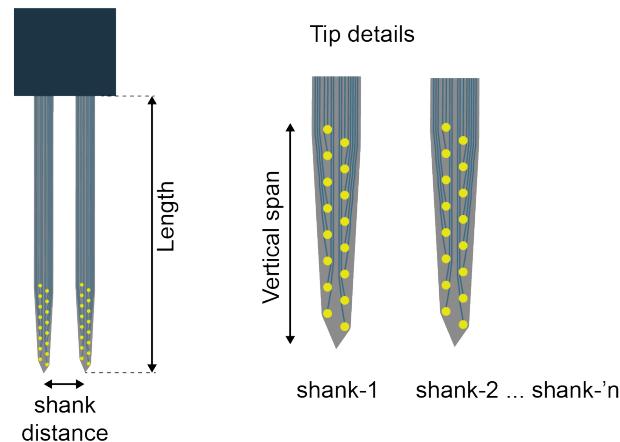
Select a probe that records from CPu and M1.



Length of shank:
Number of shank:
Number of channels:
Vertical span:
Channel layout:



Select a probe that records from CPu and M1.

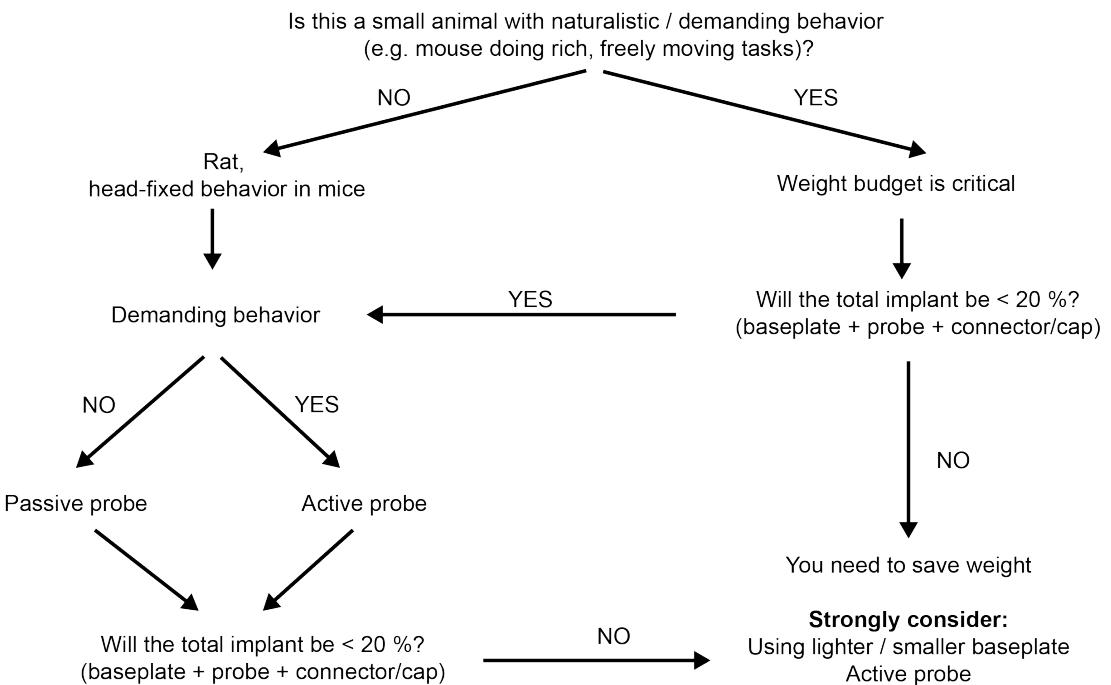


Length of shank: 10
Number of shank: 4
Number of channels: 384
Vertical span: 2100 and 4000
Channel layout: poly2 or linear

My choice:
- Neuropixels 2.0

Choosing a silicon probe for surgery

M04



Passive probe setup

The headstage sits higher, center of mass is a bit further from the skull.
Cheaper and modular – probe failures don't destroy the entire active system
Easier to swap probes / reuse headstages

Works well when:

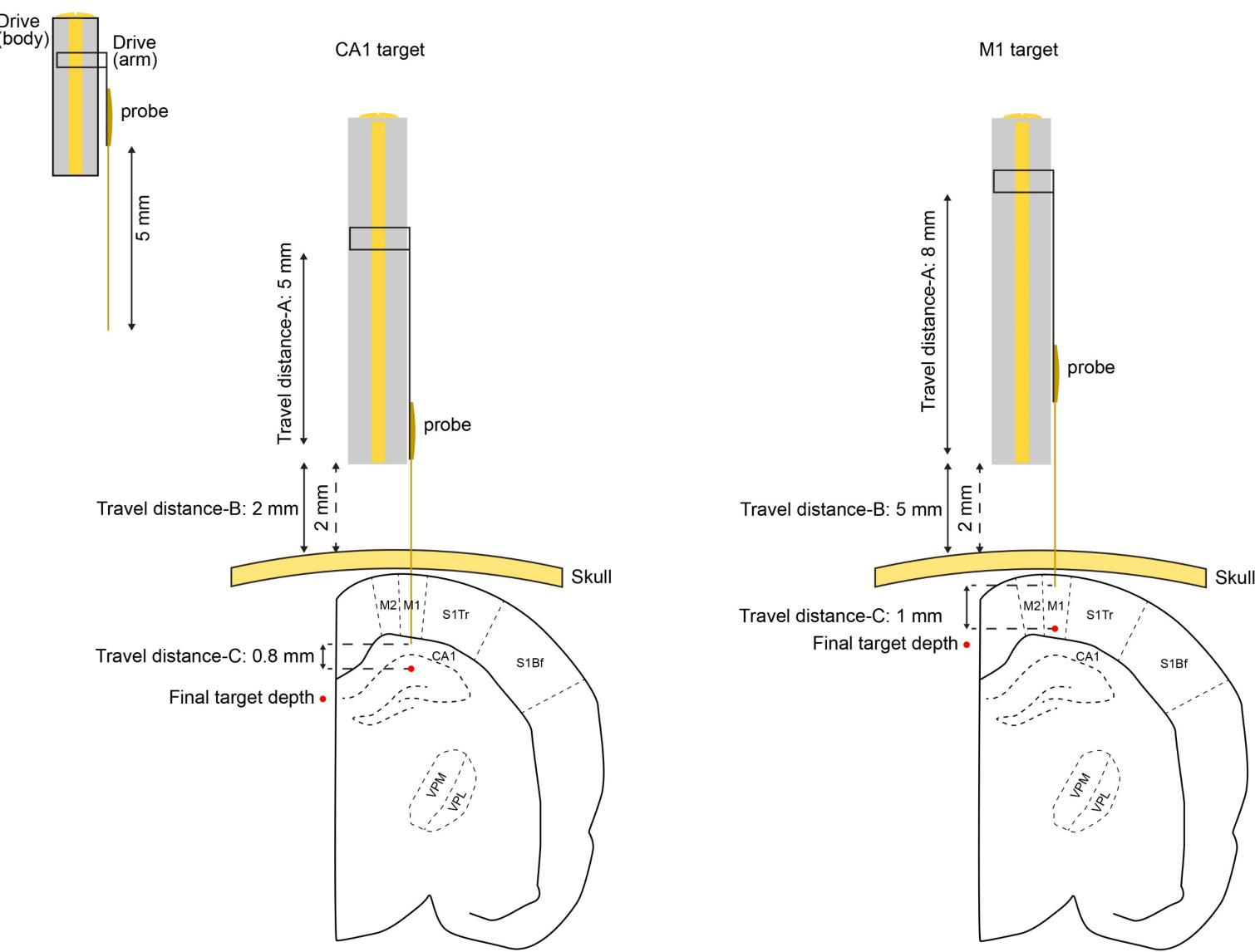
Animal is larger or behaves fine with a bit more weight / torque
You're less constrained by ultra-naturalistic behavior.

Active Probe

The headstage is shorter and the center of mass is closer to the skull.
This reduces torque on the neck and makes behavior more natural.

BUT

If the probe fails, you effectively lose the whole active assembly (probe + ASIC + PCB) – more expensive to sacrifice.
Good when you absolutely don't want implant weight to be the limiting factor for behavior.



Travel distance-A: total travel distance that the arm can move downwards inside the drive before hitting the bottom of the drive.

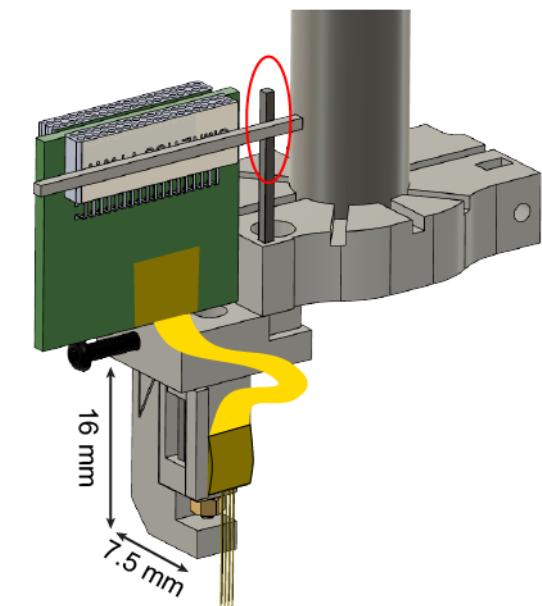
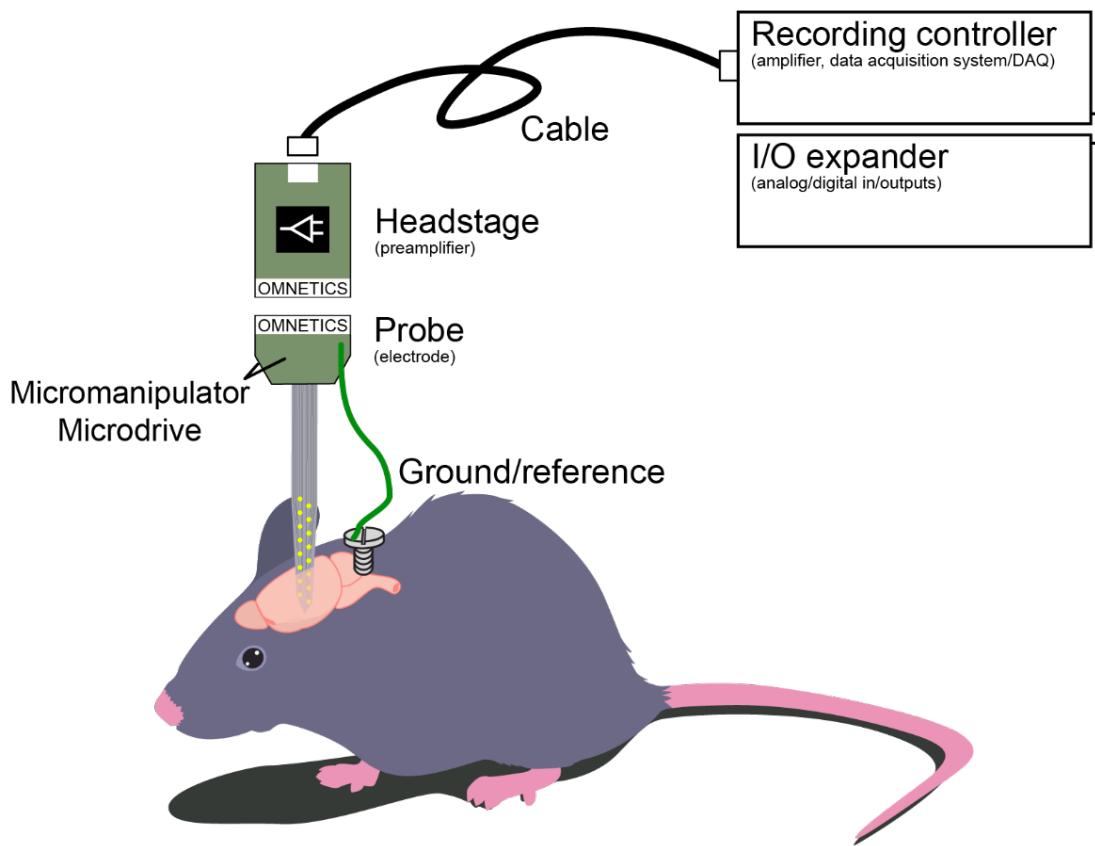
Travel distance-B: total travel distance that the arm can move downwards before hitting the skull.

Travel distance-C: total travel distance that we want to move inside the brain (region dependent).

We always want to keep 1-2 mm gap between the skull and drive body. This is the space that we fill up with dental cement to secure the drive. If it is too close, it's difficult to fill it up. If it's too far, then we need to put a lot of cement, making the whole structure less resistant to mechanical stress (the center of mass is moving upwards).

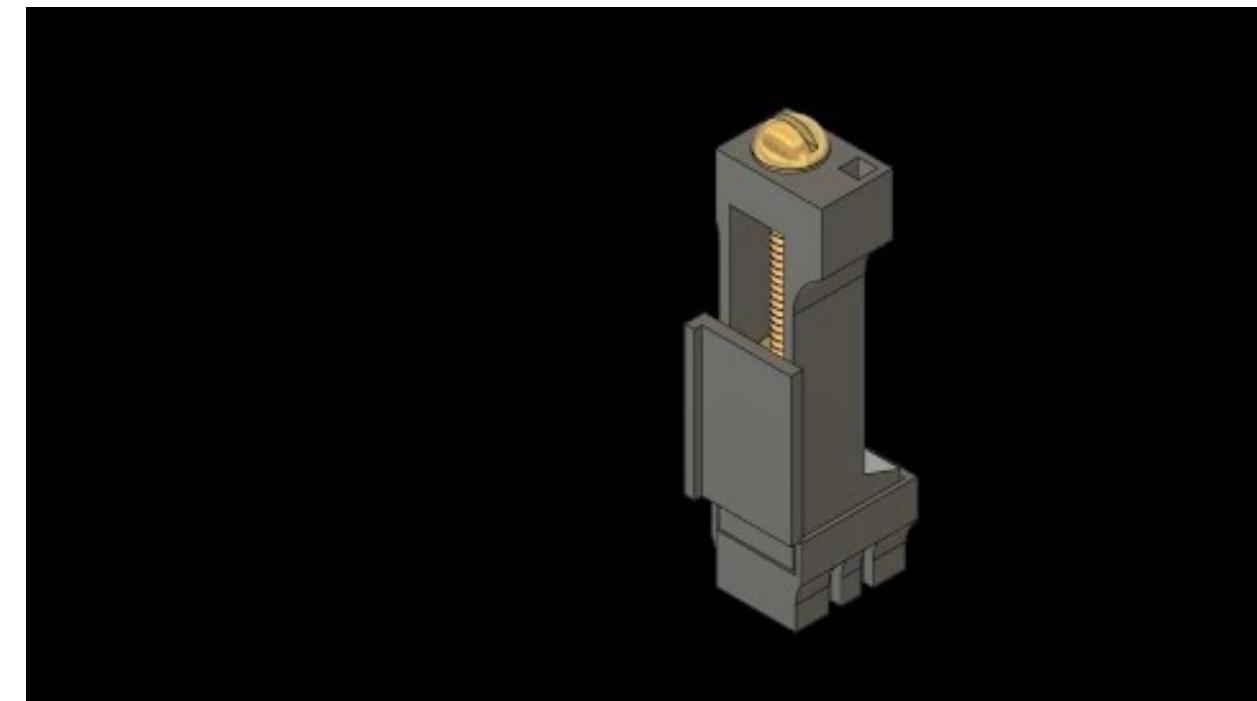
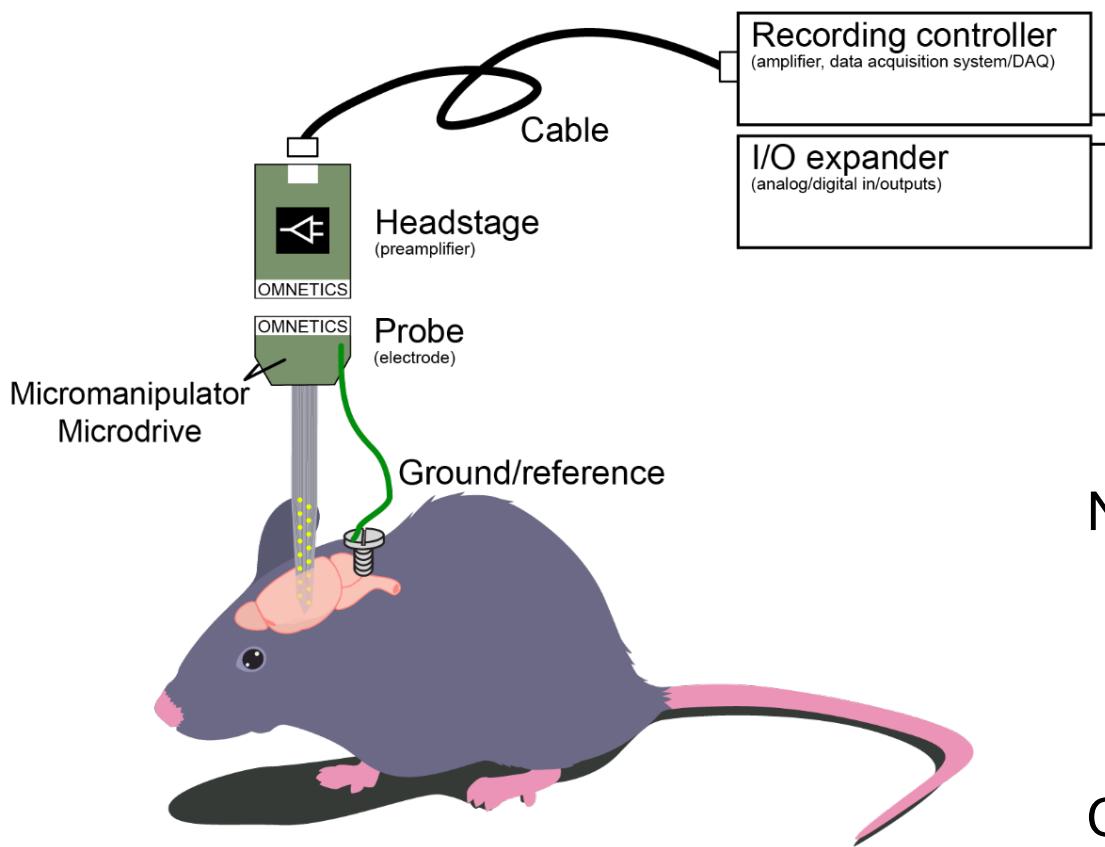
If we want to keep this distance constant we need to move the arm before surgery if we target different brain regions.

Microdrive, shuttle (just choose one:D)



<https://www.cambridgenurotech.com/nanodrives>

Microdrive, shuttle



[Play from](#) 1:09 (it takes 1 hour to do what you see here for 7 seconds. Conclusion: try to understand and then adapt new methods.

None of the open-source will work

- Printer tolerance, not updated github, ‘secrets’ are not shown, etc.
- Contact first author if you have issues, try to visit the lab

Commercial ones are 10x more expensive

- There is quality control, they work as intended

Microdrive vs Neuropixels: unit yield vs spatial coverage (more details)

Microdrive (move probe physically)

- Implant ~2-300 μm above target; advance slowly (e.g., $\frac{1}{4}$ – $\frac{1}{8}$ turns of $\sim 280 \mu\text{m}/\text{turn}$)
- Advance \rightarrow **wait hours** \rightarrow check signals (avoid tissue dimpling/buckling)
- **Pro:** entering into fresh tissue \rightarrow **highest unit yield**, new cells every few days
- **Con:** slow, mechanical complexity, limited simultaneous spatial coverage

Neuropixels (move channels)

- Implant to span target; after recovery **map anatomy**, then pick channels along shank
- **Pro:** huge spatial coverage, multi-region simultaneity, great for circuit timing
- **Con:** **unit loss from day 1** is common; chronic yield usually < microdrive

Take-home: *unit yield vs spatial coverage — pick your poison.*

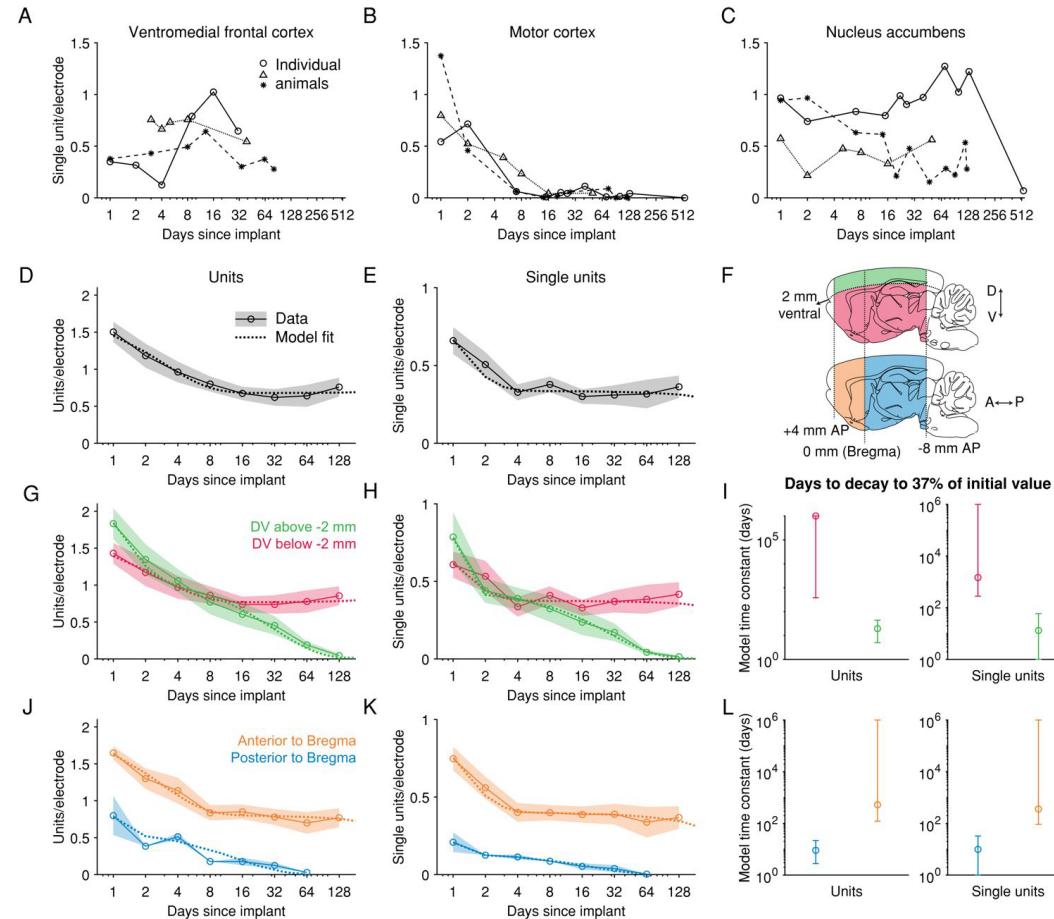
Microdrives

- <https://elifesciences.org/articles/65859> (videos are available)
- <https://bio-protocol.org/en/bpdetail?id=4137&type=0>
- <https://www.jove.com/v/3568/large-scale-recording-neurons-movable-silicon-probes-behaving>
- <https://www.nature.com/articles/s41598-017-03340-5>
- <https://www.sciencedirect.com/science/article/pii/S0165027006002883>
- <https://www.cambridgenurotech.com/nanodrives>
- <https://www.3dneuro.com/products/r2drive/>
- https://www.neuronexus.com/product_documentation/microdrive/

Neuropixels holders

- <https://www.biorxiv.org/content/10.1101/2023.12.22.572441v2>
- <https://elifesciences.org/articles/98522>
- <https://www.nature.com/articles/s41596-021-00539-9>
- <https://www.protocols.io/view/chronic-recoverable-neuropixels-in-mice-e6nvwjo87lmk/v2>
- <https://elifesciences.org/articles/47188>
- <https://elifesciences.org/articles/59716>

Losing cells over time with Neuropixels

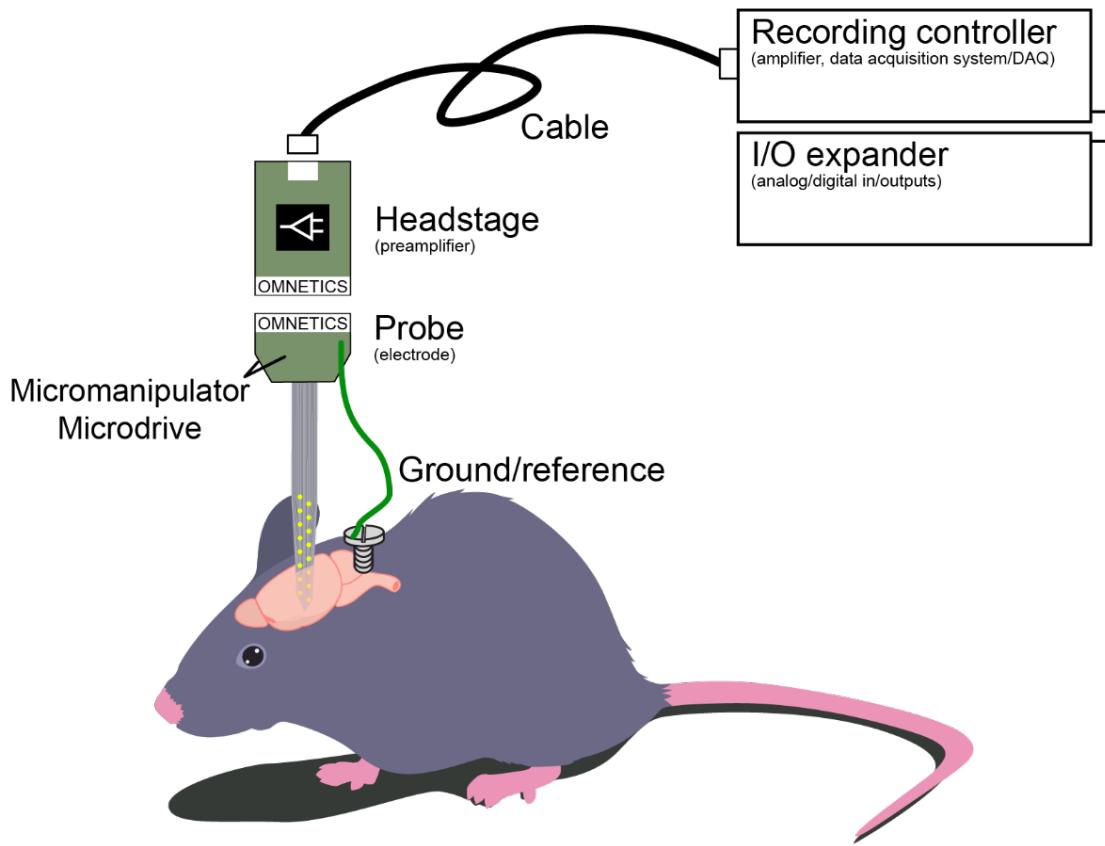


- <https://elifesciences.org/articles/59716>
- Note that single-unit yield is getting worse over days.
- This happens with all silicon probes if you don't move them, hence the Microdrive solution.

Ground and reference

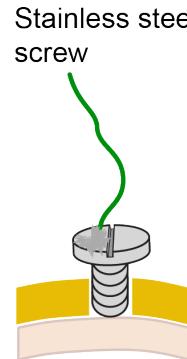
Ask ten people and you'll get ten different answers.

https://www.youtube.com/watch?v=_XFqGOXRdm4

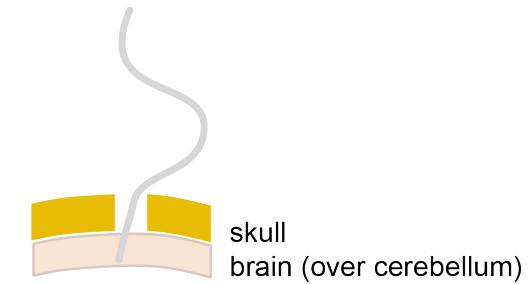


Ground and reference choice

Stainless steel screw

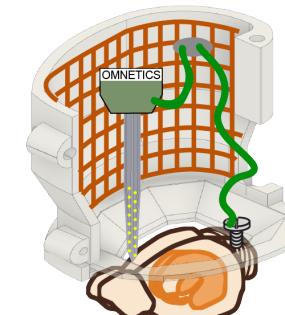


Stainless steel wire
Platinum wire

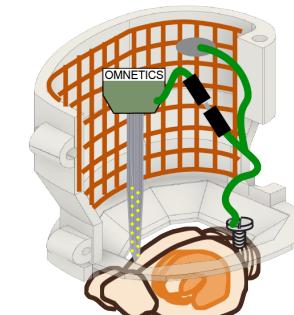


Ground and reference connection

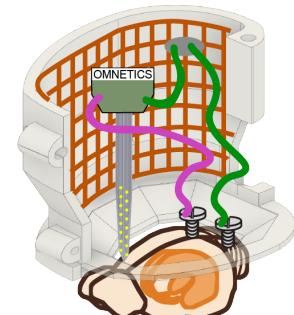
All ground/reference are soldered to copper mesh



All ground/reference are attached using pin header



All ground are soldered to copper mesh
Reference is soldered to probe REF



Ground and reference

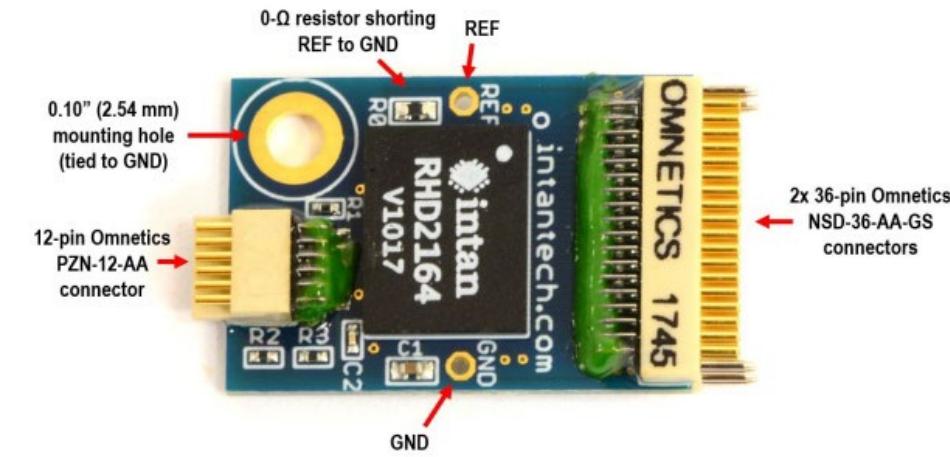
"A ground connection is needed to establish a common DC voltage between the tissue and the amplifiers. In the old days where the amplifiers were across the room from the electrodes with long wires in between, a separate reference wire was useful because it would pick up (roughly) the same interference as the signal electrode wires on the long cable going to the amps, and then the differential amps would cancel this interference.

But now that we have tiny headstages with amp mounted a few mm away from the electrodes, interference isn't a big problem, so it works well just to tie the reference to ground."

Reid Harrison, Ph.D.
Intan Technologies

[Read MORE on ground and reference](#)

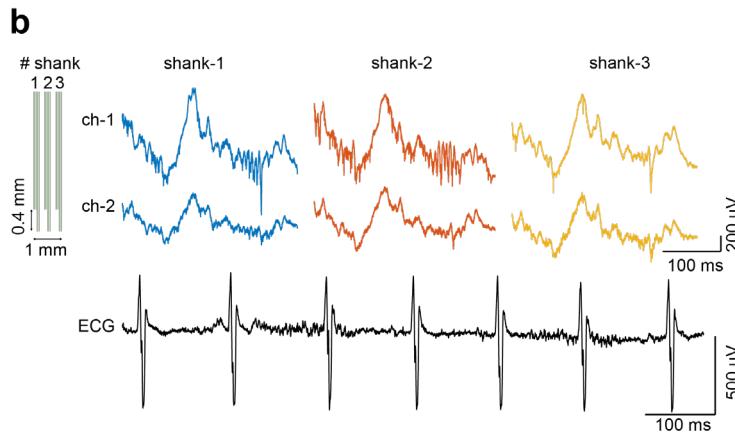
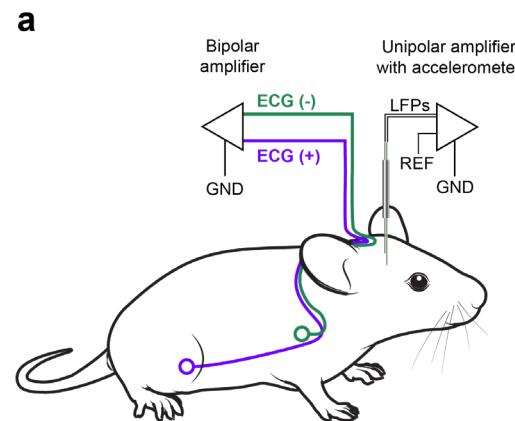
[Grounding and Referencing for
Electrophysiology Recording Systems](#)



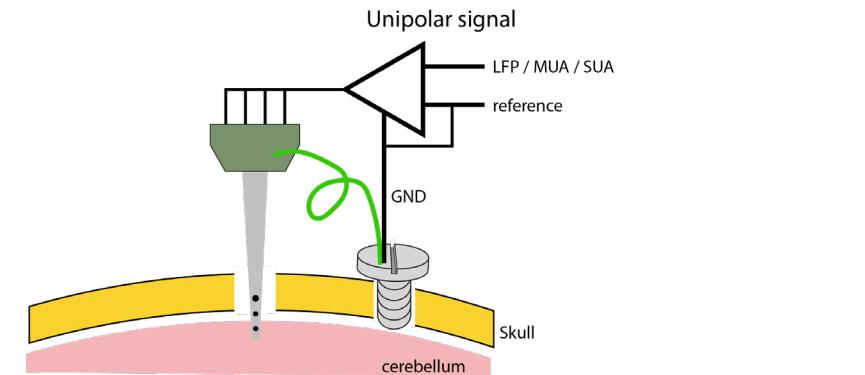
Ground and reference: Keep it separate if

If you record other biopotentials

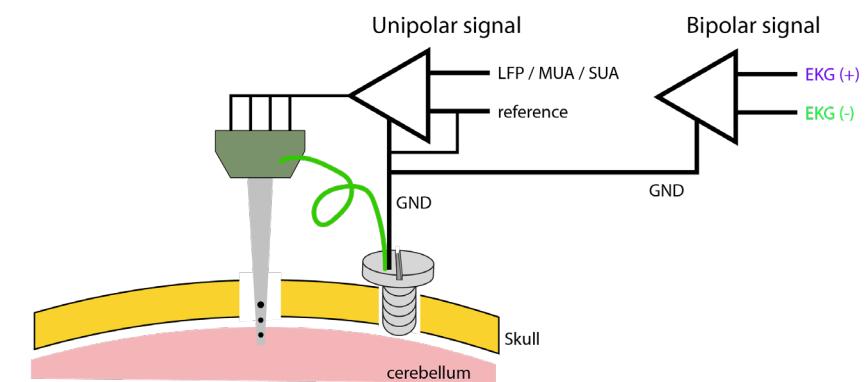
- EMG
- ECG



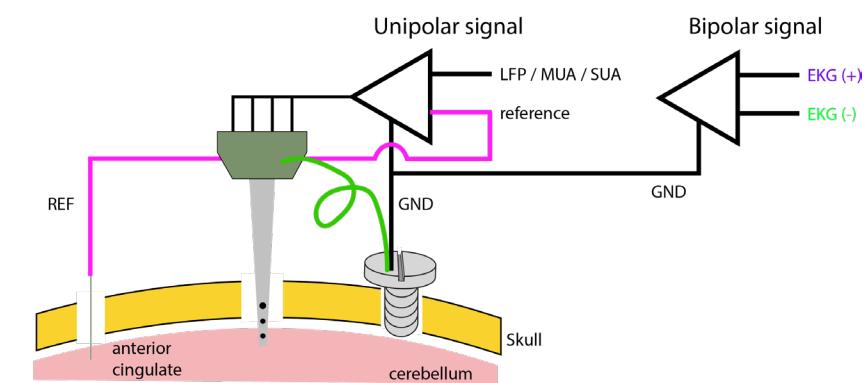
Recommended
Ephys only config



Shared Gnd/Ref will
introduce noise



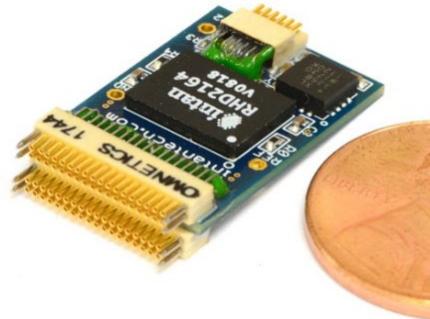
Separate Gnd/Ref



Headstage, cable, recording controller



OpenEphys



Intan Tech

Headstage, cable, recording controller

OpenEphys 20k

IMEC for Neuropixels only 10k

Plexon ~50k

Tucker Davis ~50k

Spike Gadgets ~20k

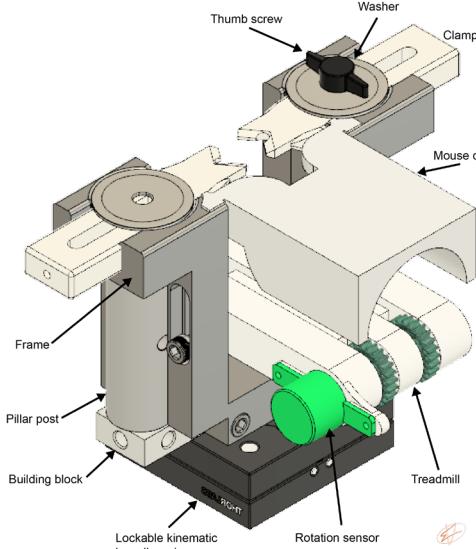
Intan Tech 20k

And some more, again just choose one

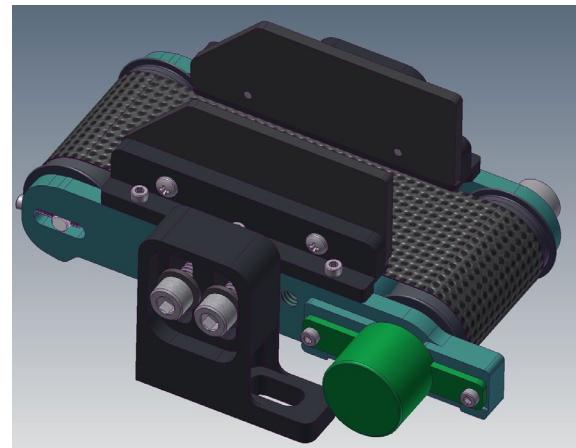
Head-fixed setup

M07

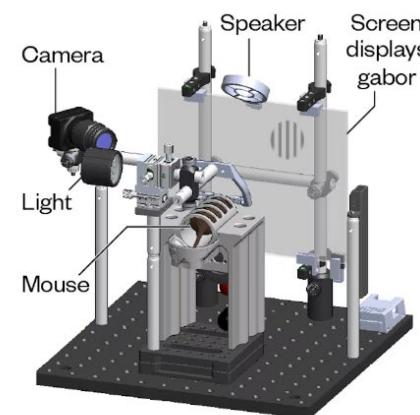
Rinberg's lab (NYU)



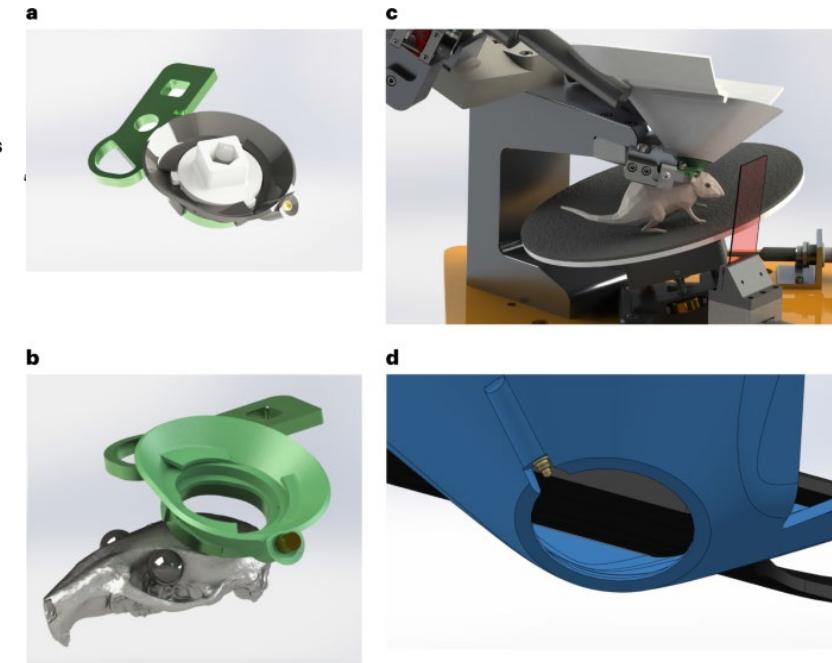
Janelia low-friction



IBL



Allen Institute



Many more...

Advantages

High throughput
'Single setup' → can be months
Virtual reality
Every day a 'success'

Great for

Preliminary data collection
Circuit mapping
Pupil measurement
Controlled stimuli delivery
(odor, tactile, visual)

Disadvantages

No sleep (animals can be trained to 'sleep')
Limited time to record

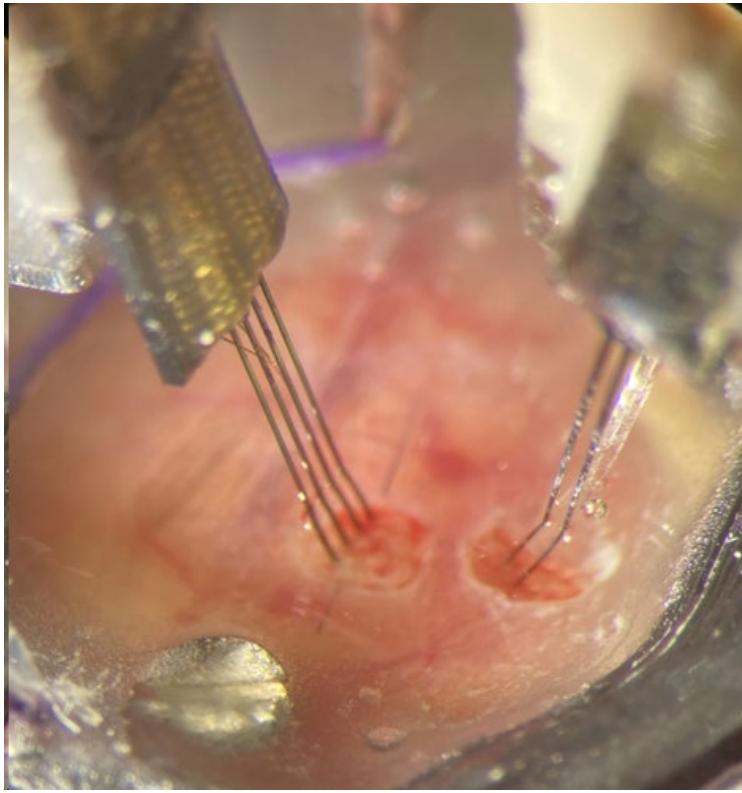
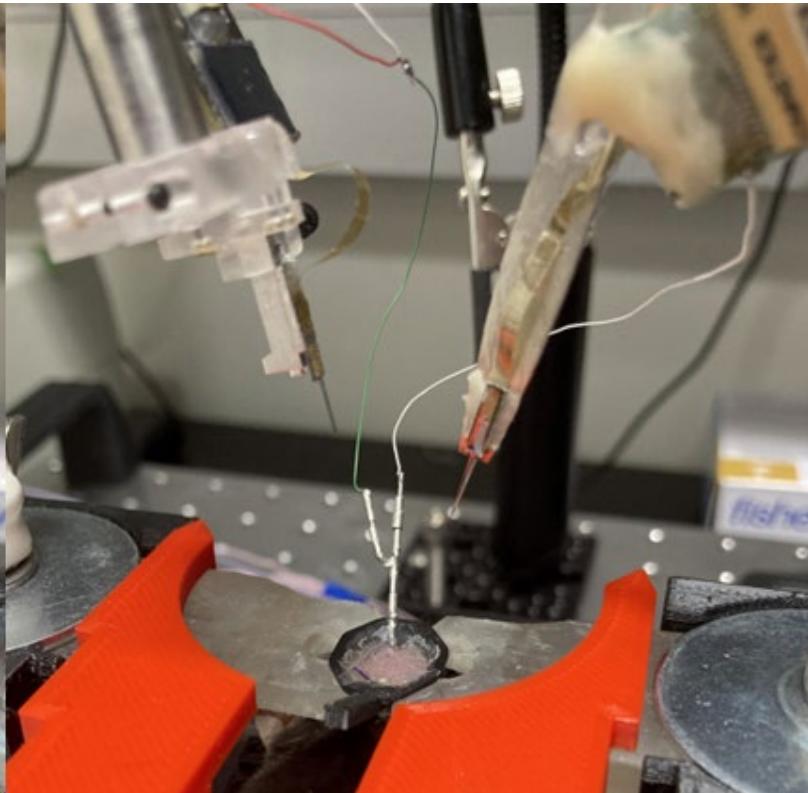
Head-fixed setups (most popular ones)

- <https://www.janelia.org/open-science/low-friction-rodent-driven-belt-treadmill>
- <https://elifesciences.org/articles/63711>
- https://github.com/misiVoroslakos/3D_printed_designs/tree/main/Treadmill_Rinberg
- <https://www.sciencedirect.com/science/article/pii/S0165027020303459>
- <https://PMC7617528/>

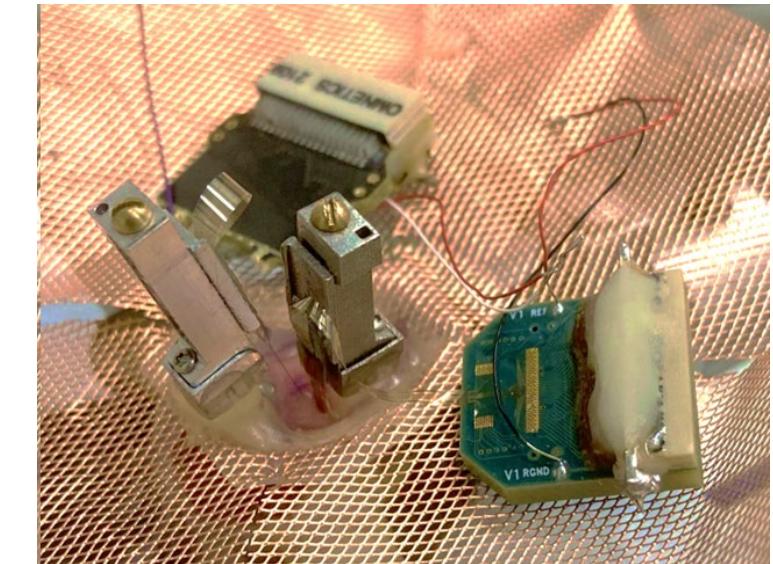
Head-fixed setup

M07

Preliminary data
Setting up surgery coordinates



Chronic surgery based on
head-fixed results

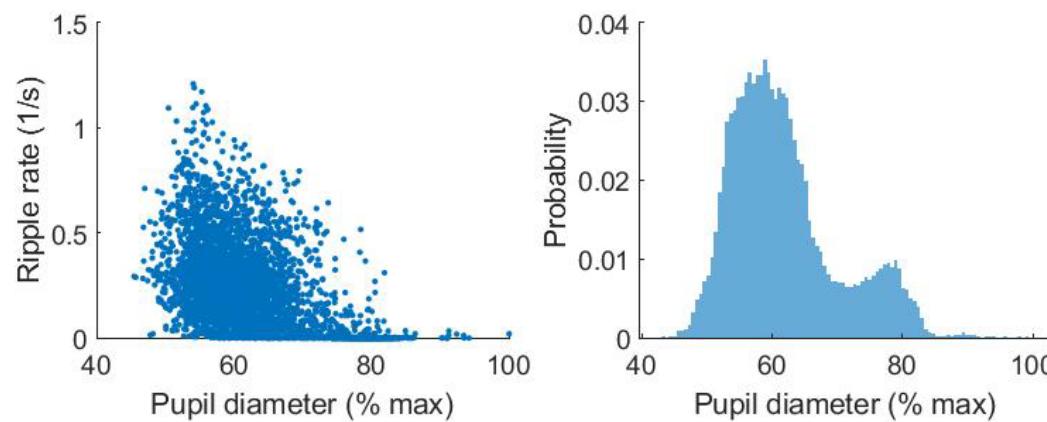
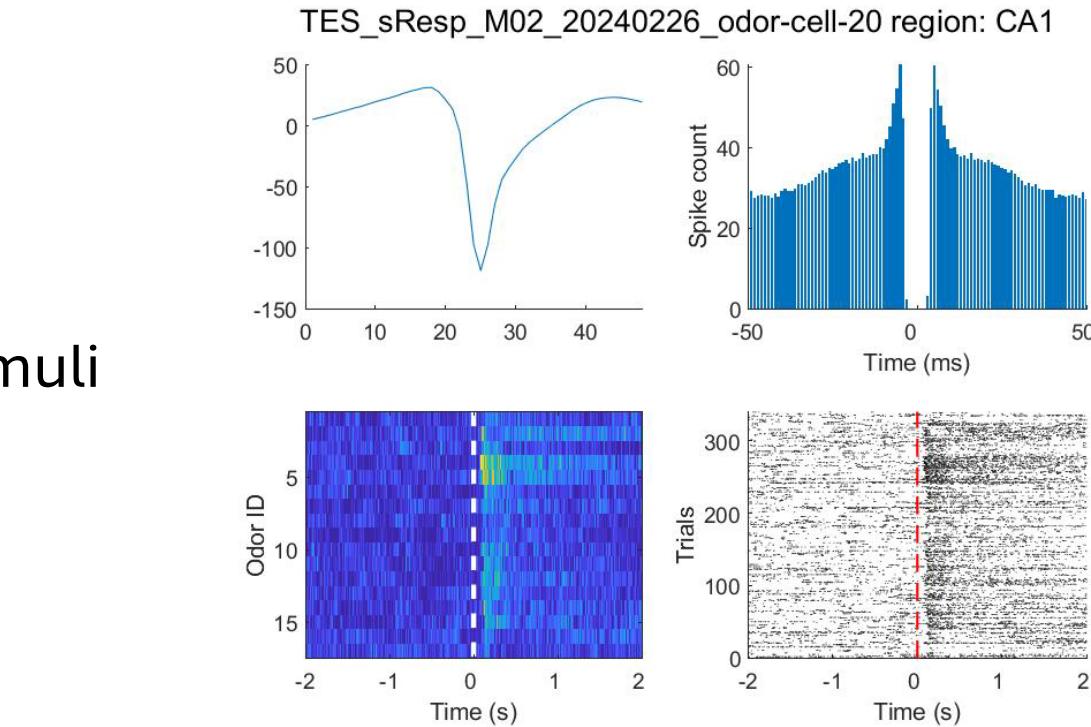
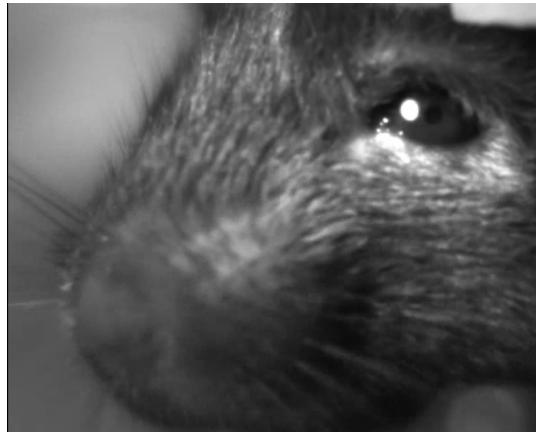


Head-fixed setup

M07

Allows

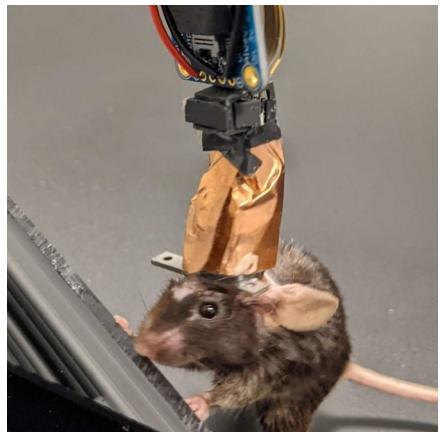
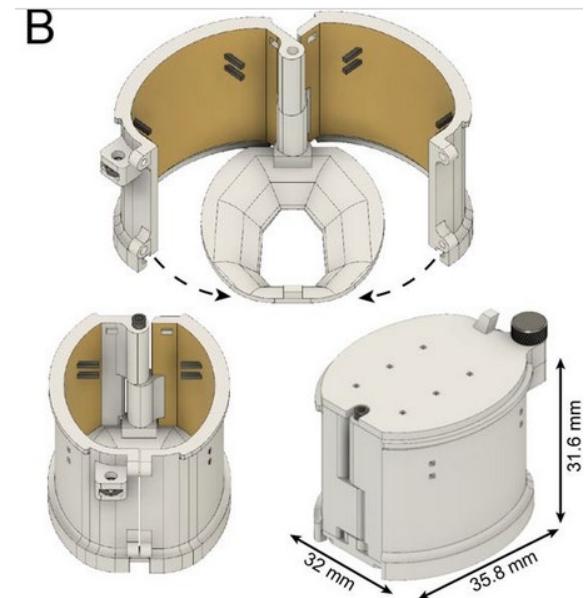
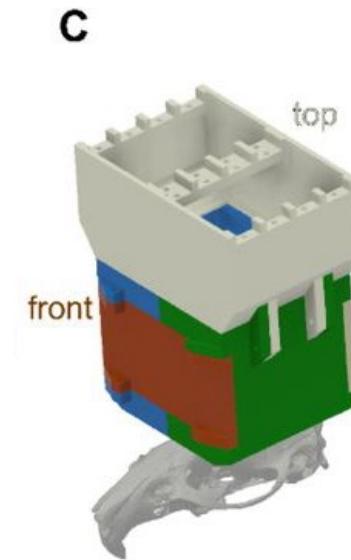
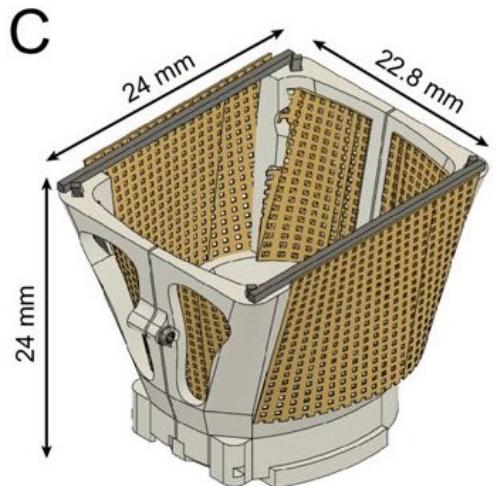
- Controlled delivery of stimuli
 - Whisker, odor, tactile
- Pupil measurement



Freely moving experiments

M07

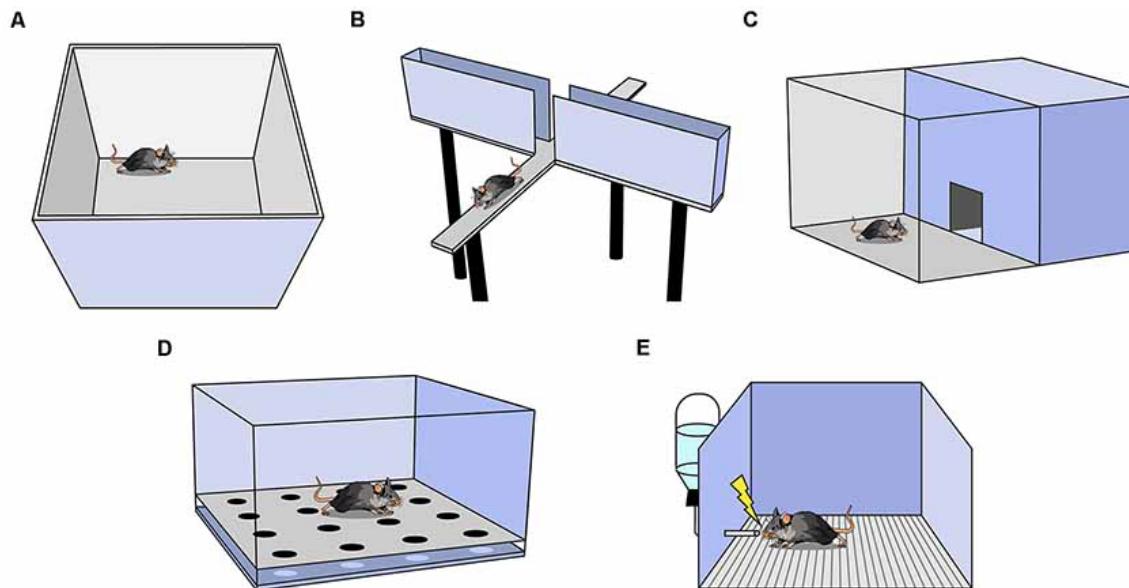
Protection of implant



https://www.youtube.com/watch?v=SgM9TPbf_Y
https://www.youtube.com/watch?v=_MYBLJf-178
<https://www.youtube.com/watch?v=14ev8umGzIg>

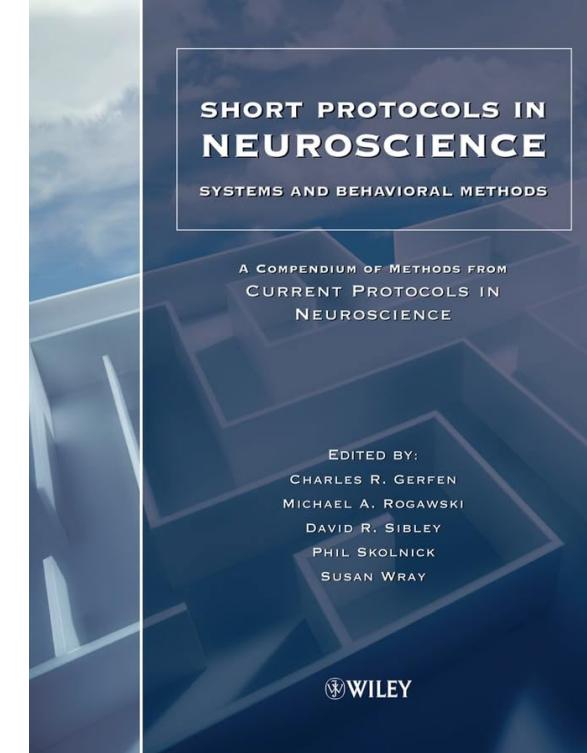
Freely moving experiments

M07



<https://neuroscience.stanford.edu/shared-resources/behavioral-functional-lab/services-and-rates/behavioral-models>

<https://www.frontiersin.org/journals/behavioral-neuroscience/articles/10.3389/fnbeh.2020.00145/full>



Freely moving experiments

M07

Again, ‘just’ choose one and adapt it...

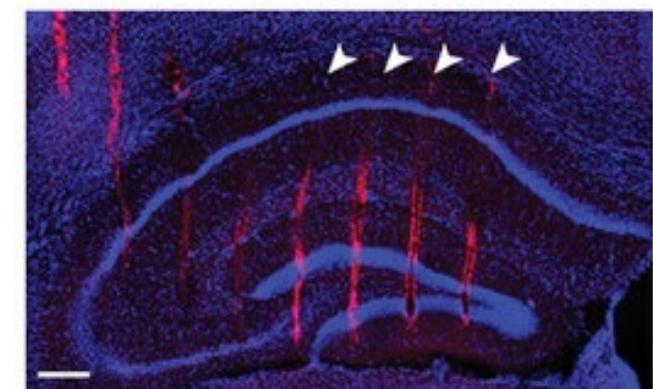
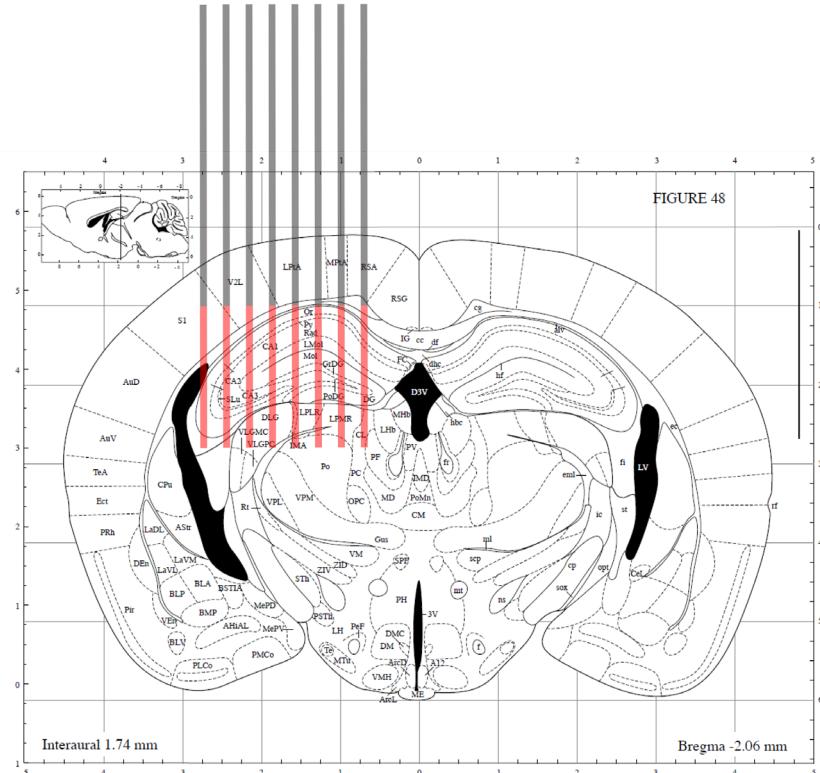
Practice on plastic skull

Practice surgery

https://github.com/buzsakilab/3d_print_designs/tree/master/Rodent_models

Plan surgery
Apply Dil on probe
Adjust if necessary

Bregma - 2 mm
first shank is ML+0.75 mm, center is 1.75mm
2.75 mm from brain surface



An adaptable, reusable, and light implant for chronic Neuropixels probes

Célian Bimbard , Flóra Takács, Joana A Catarino, Julie MJ Fabre, Sukriti Gupta, Stephen C Lenzi, Maxwell D Melin, Nathanael O'Neill, Ivana Orsolic, Magdalena Robacha, James S Street, José Teixeira, Simon Townsend, Enny H van Beest, Arthur M Zhang, Anne K Churchland, Chunyu A Duan, Kenneth D Harris, Dimitri M Kullmann, Gabriele Lignani, Zachary F Mainen, Troy W Margrie, Nathalie L Rochefort, Andrew M Wikenheiser, Matteo Carandini, Philip Coen  ... [show less](#)

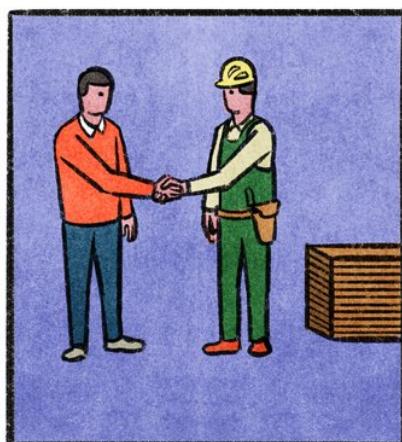
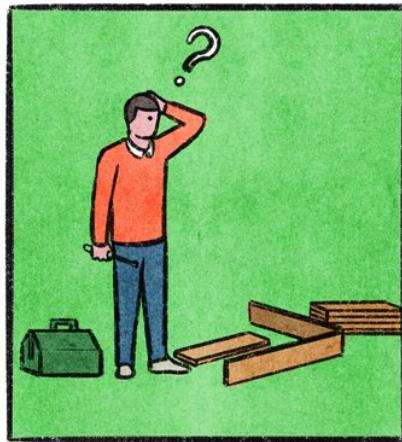
Lab	Probes (number & type)	Sharpening	Shank alignment	Grounding prep	Headstage
Carandini–Harris	1–2 × NP 2.0a, 4-shank	Yes (Narishige EG-45)	By eye	Ag wire shorting GND–REF, connected to headplate	Removable
Churchland	2 × NP 1.0	Yes (Narishige EG-45)	Checked in holder; Kapton on back; re-checked straightness	Ag wire shorting GND–REF, soldered to socket (bone-screw ground); separate screw socket for later detachment	Removable
Duan	1 × NP 1.0	Yes (Narishige EG-45)	By eye	Ag wire shorting GND–REF, soldered to grounding wire terminating in gold socket	“Permanent” epoxy block; recoverable via 3D-printed holder
Kullman/Lignani	1 × NP 1.0	Yes (Narishige EG-45)	By eye	Ag wire shorting GND–REF, soldered to additional Ag wire with male Mill-Max pin (to skull screw)	Removable
Mainen	1 × NP 1.0	Yes (Narishige EG-45)	Using graph paper	Ag wire shorting GND–REF	Removable
Margrie	1 × NP 2.0a or 2.0, 4-shank	Unsharpened	By eye	Ag wire shorting GND–REF	Removable
Rochefort	1 × NP 1.0	Unsharpened	By eye	Ag wire shorting GND–REF	Removable; docking surface cut at 44° for plate compatibility
Wikenheiser	1 × NP 1.0	Unsharpened	Using graph paper	Ag wire shorting GND–REF; additional Ag wire to male gold pin; matching skull-screw ground with female pin	Removable (SpikeGadgets); probe exit coated with silicone gel

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Lab	Species / strain	Prep surgery timing	Skull / headplate prep (very high level)	Craniotomy (method, size)	Insertion speed & manipulator	Implant fixation	Analgesia / other treatment (summary)
Carandini–Harris	Adult M/F C57BL/6J mice	Separate day (headplate)	Ti headplate; skull cleared; VetBond + multiple layers of NOA81, then removed at implant; Super-Bond plate Skull cleared; VetBond edges; headbar glued (Zap-a-gap); skull + headbar covered with Metabond	Biopsy punch or drill; Dural-Gel cover (1–1.5 mm)	3–5 µm/s (Sensapex)	RelyX Unicem 2, then Super-Bond; Kwik-Sil in one case	Isoflurane; carprofen + dexamethasone peri-op; meloxicam/carprofen ×3 d
Churchland	Adult male C57BL/6J mice	Same session	Skull exposed, aligned; dental-cement well around craniotomy; skull covered with Super-Bond; cerebellar ground pin Skull cleared; contralateral skull screw with silver-wire ground; MedBond cyanoacrylate on skull/suture/skin edges	Drill; Dural-Gel cover	5 µm/s (Neurostar)	Kwik-Sil + UV cement (Wave A1), then Metabond	Isoflurane; meloxicam + enrofloxacin peri-op and ×3 d
Duan	Adult female C57BL/6J mice	Same session	Skull cleared; contralateral skull screw with silver-wire ground; MedBond cyanoacrylate on skull/suture/skin edges	Drill; Dural-Gel in ~1 mm well	10–20 µm/s for first 100–200 µm, then 3–5 µm/s (Scientifica S-IVM Mini)	RelyX Unicem 2; ground socket plugged + cured; implant wrapped in Micropore	Isoflurane; meloxicam + cured; implant peri-op and ×3 d
Kullman/Lignani	Adult male C57BL/6J mice	Same session	Skull cleared; contralateral skull screw with silver-wire ground; MedBond cyanoacrylate on skull/suture/skin edges	Biopsy punch + diamond bur; Dural-Gel cover (1.5 mm)	3–5 µm/s (Sensapex)	RelyX Unicem 2, then Super-Bond; ZIF protected with parafilm	Isoflurane; buprenorphine peri-op; meloxicam + amoxicillin post-op

Why (and how) we need to professionalize neuroscience



Over the past few decades, neuroscience has become so broad and technically sophisticated that individual researchers can no longer fully understand the technical foundations of their experiments.

The average systems neuroscience project, for example, requires in-depth knowledge of

- **animal surgery**
- **mechanical engineering**
- **optical engineering**
- **electrical engineering**
- **statistics and computer science**



[Jakob Voigts](#)

Group leader

Howard Hughes Medical Institute

Surgery, open-source data resources

M07

Surgery planning software

PinPoint - https://virtualbrainlab.org/pinpoint/tutorials/tutorial_basics.html

Surgery video

Ask for a link from me at Voroslakos@gmail.com

Neuropixels training videos

<https://www.ucl.ac.uk/neuropixels/training/2025-neuropixels-course>

Neuropixels example dataset

<https://www.steinmetzlab.net/shared/>

Allen Institute Neuropixels dataset

https://allensdk.readthedocs.io/en/latest/visual_behavior_neuropixels.html

<https://www.3dneuro.com/resources/ephys-behavior-resources/>

Neuropixels is ‘just’ a fancy silicon probe.

80% of the knowledge can be applied to other silicon probes.

Synchronization, automation

M08

<https://open-ephys.github.io/gui-docs/Tutorials/Data-Synchronization.html>

Bonsai

<https://open-ephys.org/bonsai>

Arduino, raspberry PI

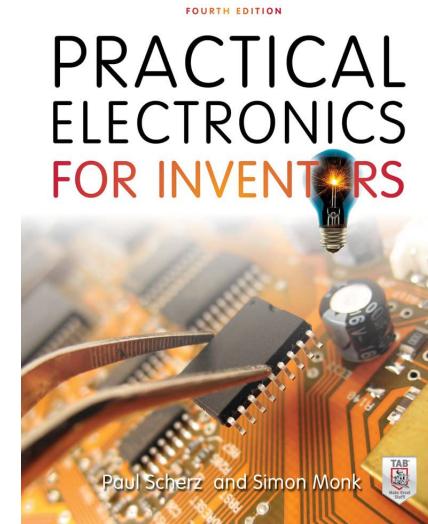
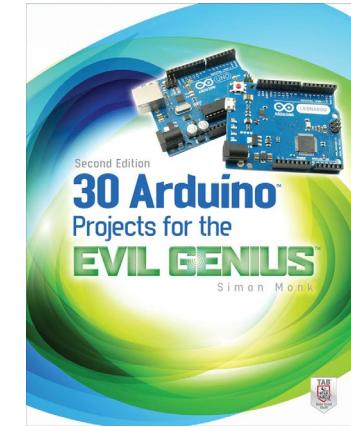
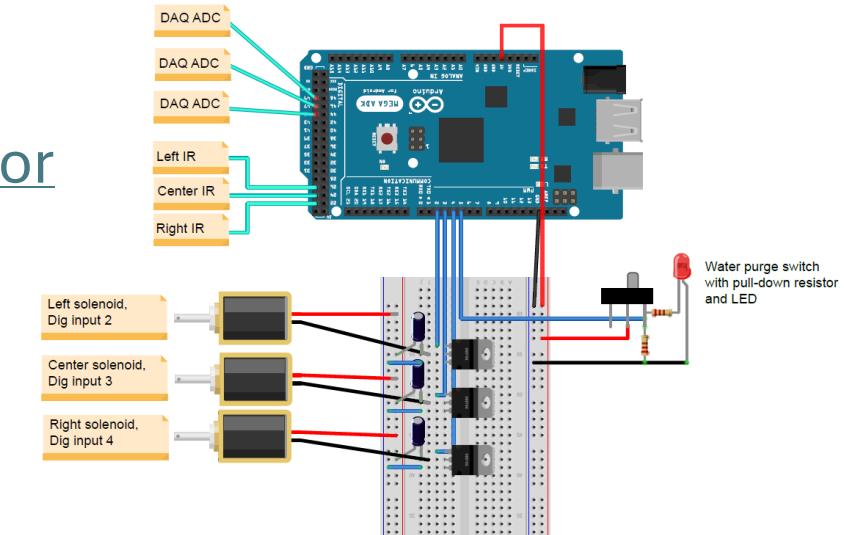
Infrared sensor, light sensor, vibration sensor

Sparkfun

<https://www.sparkfun.com/>

Adafruit

<https://www.adafruit.com/>

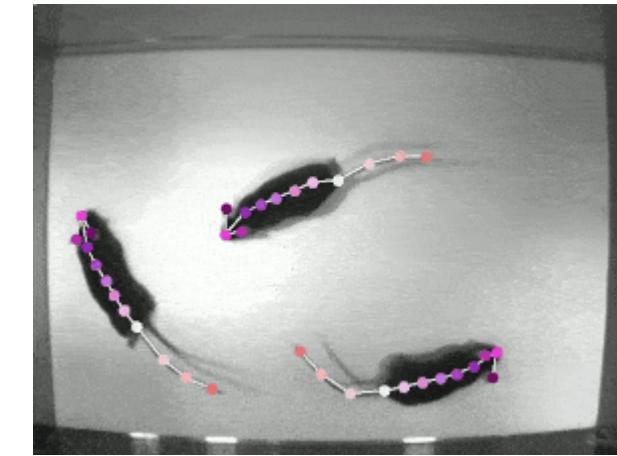


Behavior tracking

M08

DeepLabCut

<https://www.mackenziemathislab.org/deeplabcut>

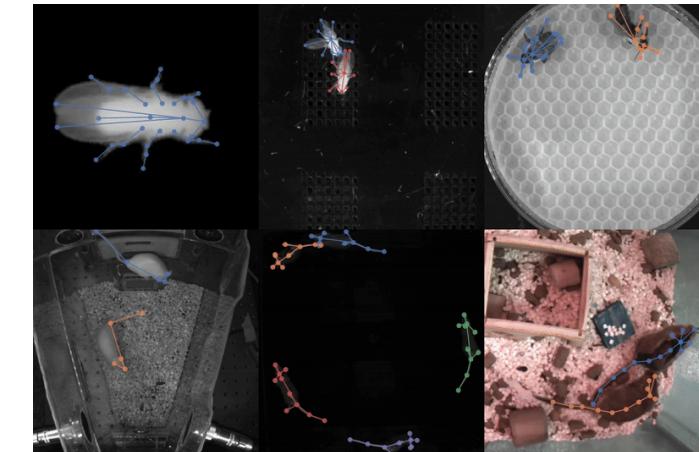


SLEAP

<https://sleap.ai/>

You need a good GPU (1-2 k price range, same one is needed for spike sorting).

Video analyzed in real time (30 min video takes 30 min to analyze).



Noldus

[Ethovision](https://www.noldus.com/en-us/ethovision) (10k, plus yearly subscription)

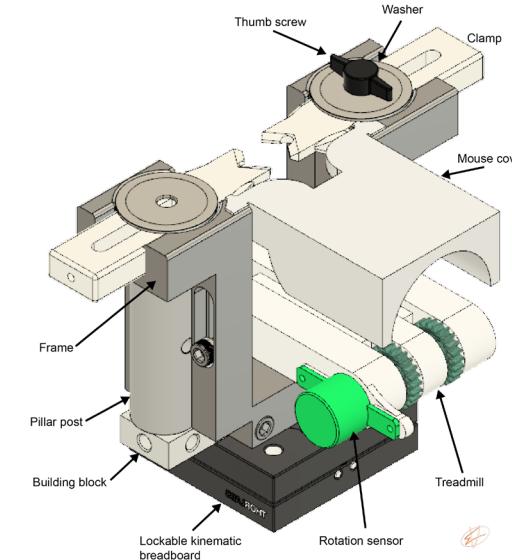
CAD design

M08

Autodesk Fusion

<https://www.youtube.com/watch?v=A5bc9c3S12g>

Autodesk Inventor, SolidWorks



If you have never used similar software before, it can take 1-2 months to get familiar with the concepts.

Is it worth your time to learn this?

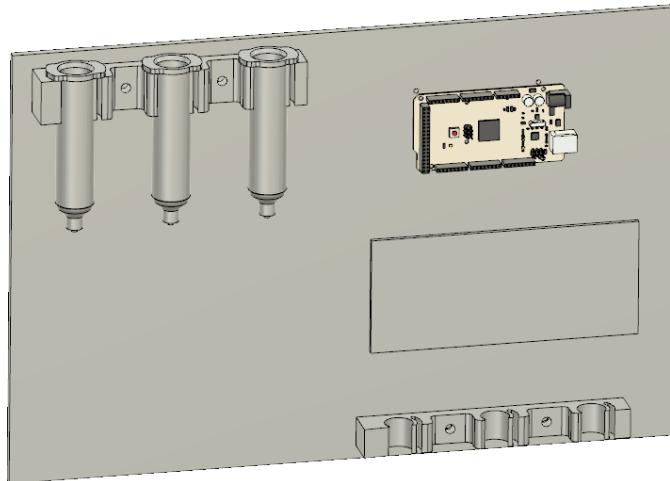
Our designs are very simple, so once you know how to use the software and where each buttons are, designing can be fast and easy (you can create nice figures for workshops, tutorials:D).

REMEMBER: most of the downloaded .stl files will not work. They are always adjusted to the printer's tolerance/specs. In my experience, nothing will work when you just download. SHOW our [GITHUB](#)

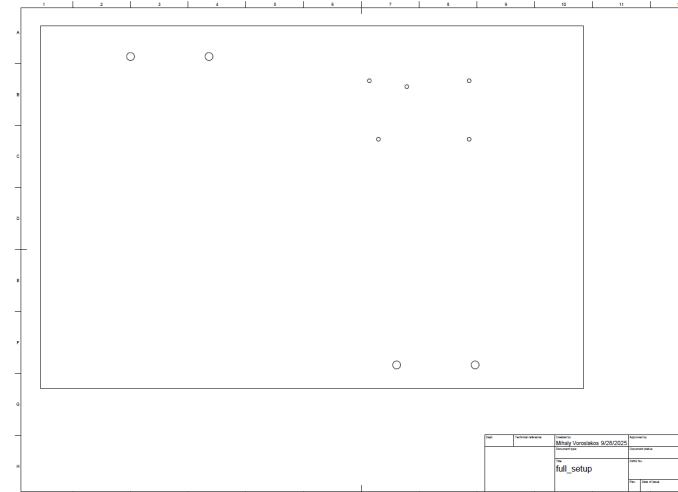
CAD design

M08

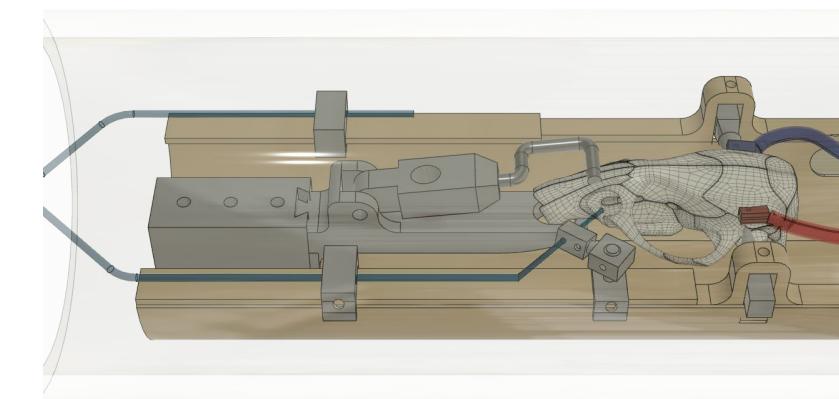
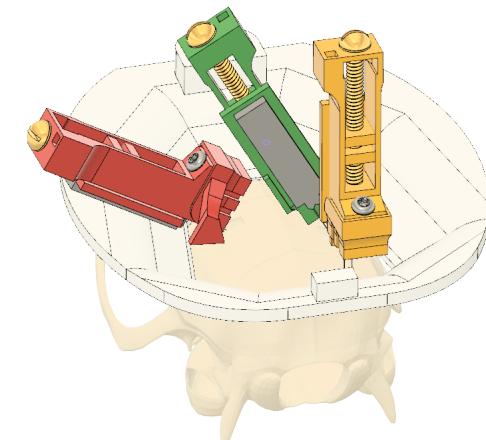
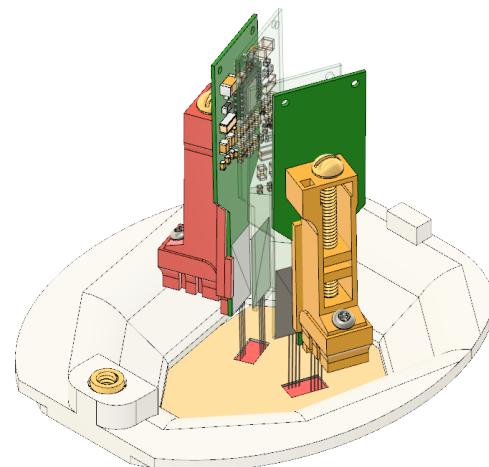
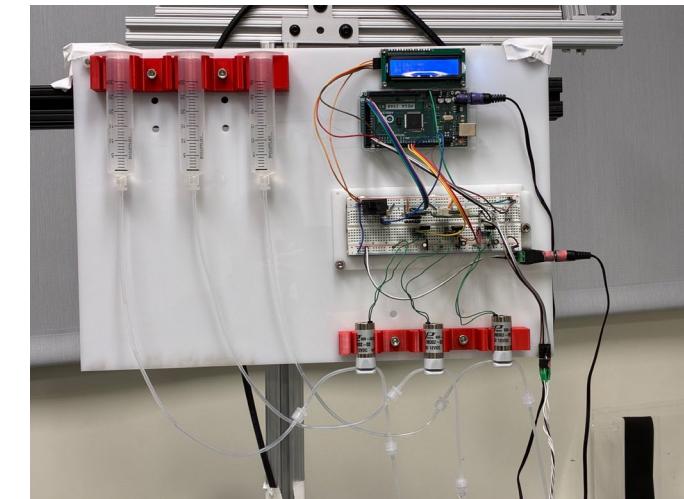
CAD design



CAD drawing for
laser cutter



Assembled
setup



Optogenetics

Optrode

- Optic fiber attached to a silicon probe
- Companies offer this service
 - Cambridge NeuroTech - <https://www.cambridgeneurotech.com/neural-probes/optogenetics>
 - NeuroNexus - https://www.neuronexus.com/training_videos/how-to-order-optrode/

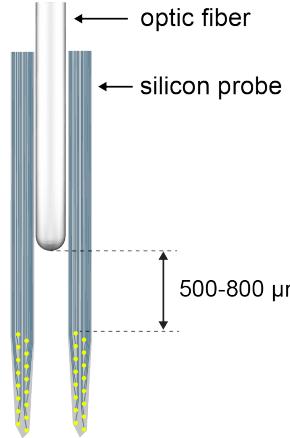
Light integrated on probe

- microLED probe - <https://plexon.com/products/neurolight-optoelectrode/>
- Neuropixel opto - <https://www.biorxiv.org/content/10.1101/2025.02.04.636286v1>

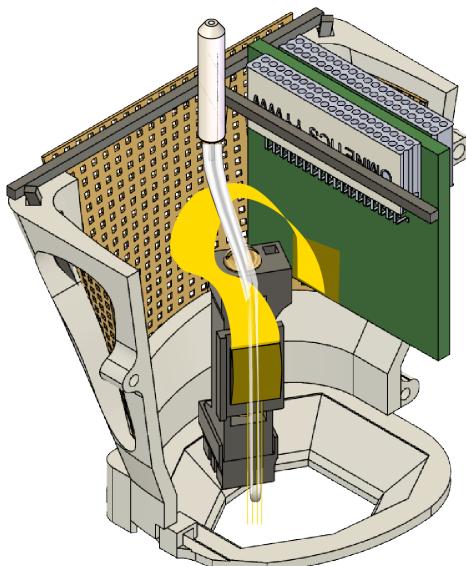
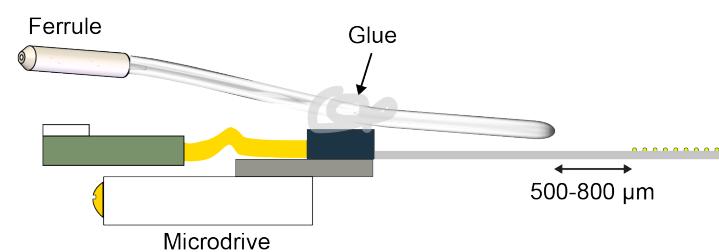
Optogenetics with optrode

M09

FRONT VIEW



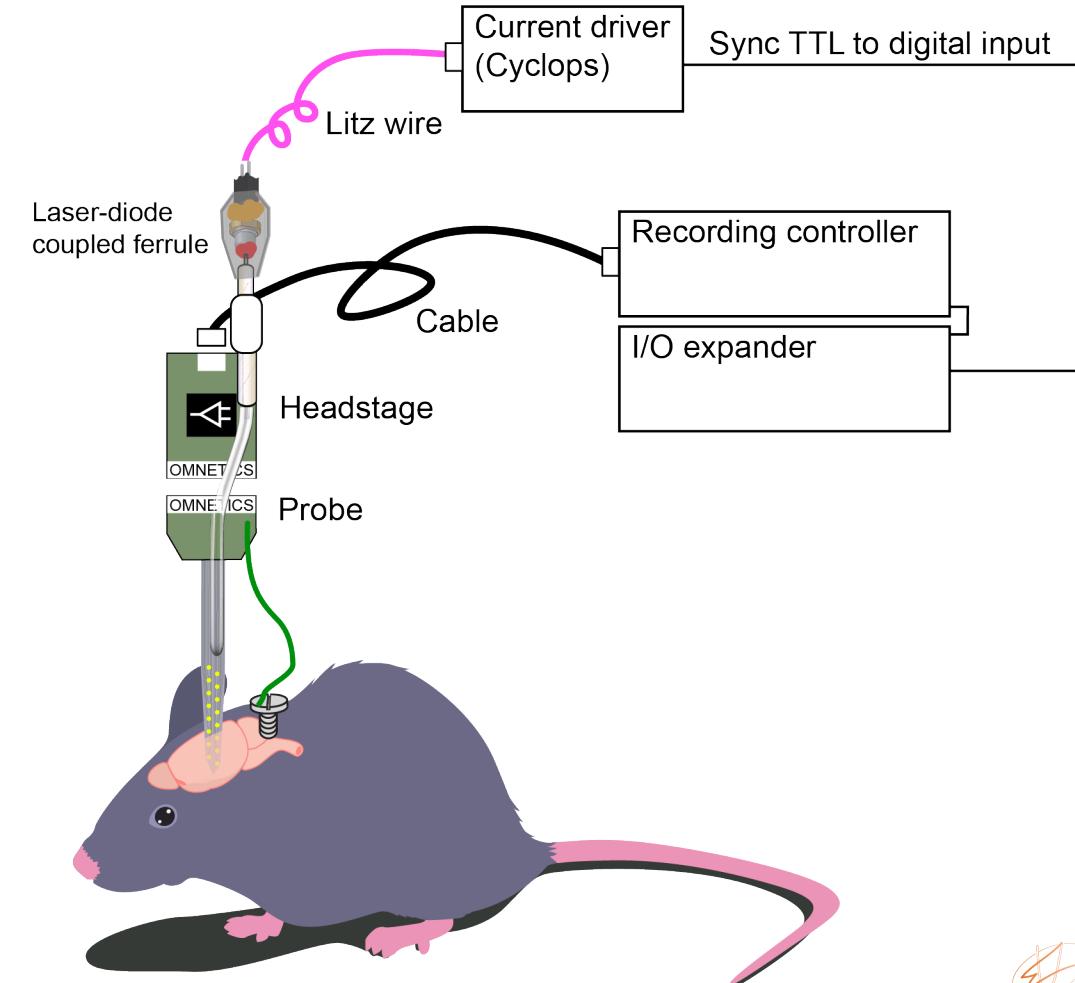
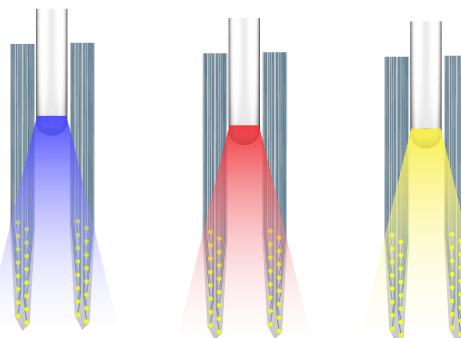
SIDE VIEW



Ferrule is attached to copper mesh during surgery.

Laser-diode coupled ferrule is attached to animal to deliver light into the brain.

Different colors can be applied depending on the color of laser diode.



Optogenetics during behavior: light delivery

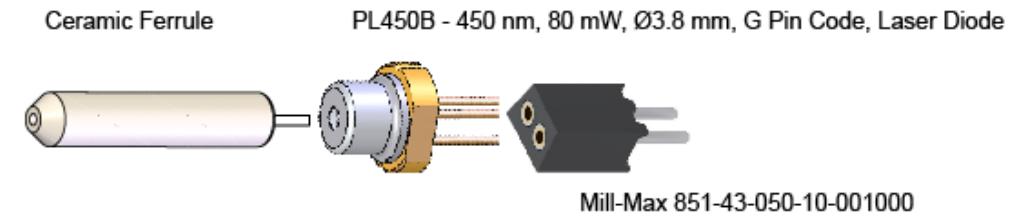
M09

Fiber patch cable → ferrule

- Simple, but cable drag/torque can affect behavior
- A good commutator helps reduce twisting forces for fiber-based setups

On-head diode + ferrule

- deliver *current* via thin flexible wires → better mobility

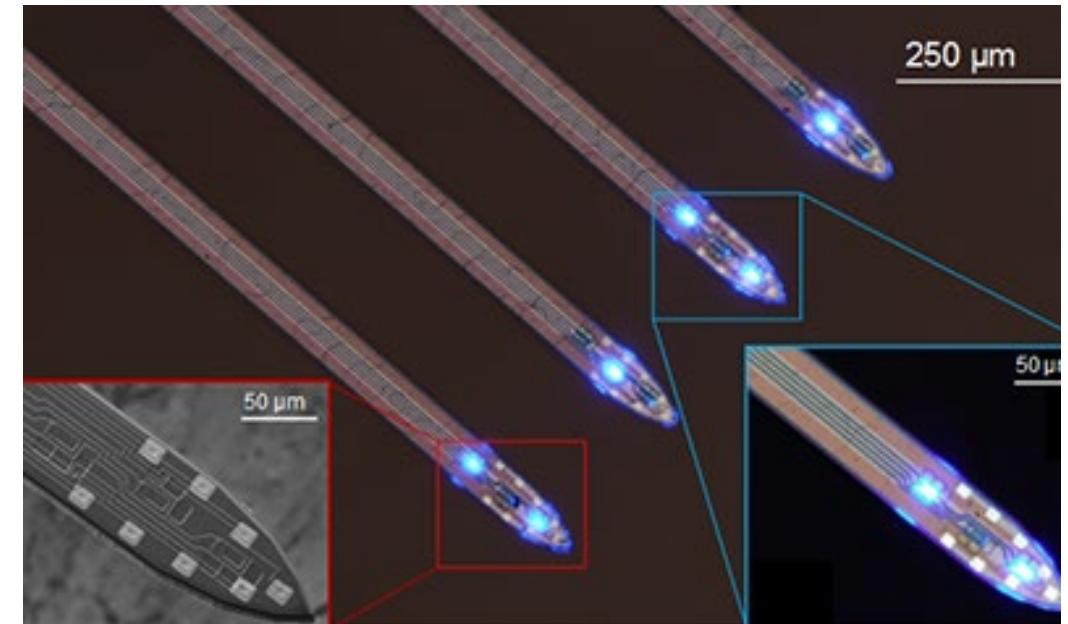


Fiber-to-silicon-probe attachment
example: [Stark et. al., 2012](#)

Optogenetics with microLED probe

Good for

- Local light delivery
 - Effect is restricted to one shank
- Local circuit interrogation
- Few 10-100s of neurons are affected



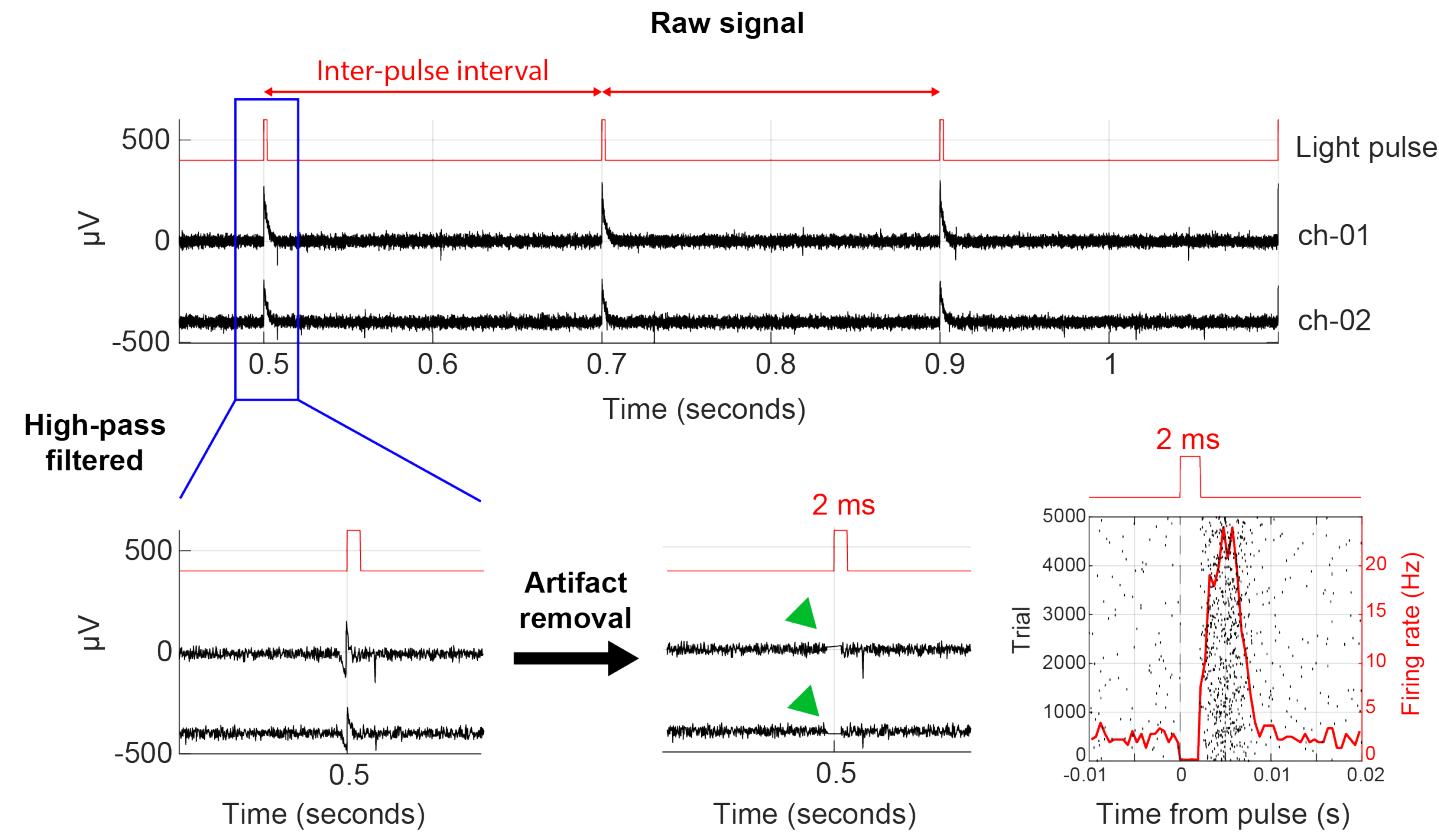
Source: <https://plexon.com/products/neurolight-optoelectrode/#1592930170634-2a8140fd-e25f>

Optotagging experiments

M09

Optotagging protocol

- Know opsin kinetics
- Pulse: <2 ms every 200 ms (5 Hz)
- Repetitions: ≥ 5000 (up to 10000)
- **Remove light artifacts before spike sorting**
- Expect increased spikes ≤ 8 ms
 - (longer may be polysynaptic)
- **Stats (SALT)**
 - $[P, I] = \text{SALT}(\text{SPT_BASELINE}, \text{SPT_TEST}, \text{DT}, \text{WN})$
 - Compares spike-latency histograms (modified Jensen–Shannon divergence)



Green arrows show the cut-out data segment.

Flexible probes

M10

Pros

- Potentially **less chronic inflammation / smaller long-term scar**, better for very long recordings (weeks→months).

Cons / reality check

- **Insertion is hard:** flexible shanks buckle, so you often need a temporary stiffener/shuttle (PEG-glued stiffener is common).
- The shuttle/stiffener can increase the acute footprint, so initial insertion damage may dominate if the delivery system is bulky.

Tech is improving (smaller-area shuttles exist), but it's still a "pick your poison" tradeoff for many labs.

Timeline intuition

Tissue encapsulation/scar around intracortical implants often becomes **dense around ~4–6 weeks** and then stabilizes—so early damage + early inflammation can set the ceiling for “forever” yield.

Flexible vs rigid

<https://www.nature.com/articles/s43586-025-00399-7>

Pick flexible if:

- You need *very long* duration interfaces and can invest in (or already have) a good insertion/shuttle solution.
- Your lab can reliably execute delicate implant procedures and protect the implant mechanically.

Pick rigid probes if:

- You need **coverage now** (large tissue volumes, multi-region simultaneity).
- You want maximal practicality/reproducibility across animals with less surgical “heroics.”

Flexible probes

- <https://www.science.org/doi/10.1126/sciadv.1601966>
- <https://app.jove.com/t/59957/chronic-implantation-of-multiple-flexible-polymer-electrode-arrays>
- <https://advanced.onlinelibrary.wiley.com/doi/full/10.1002/advs.202207576>
- <https://www.nature.com/articles/s41593-024-01692-6>
- <https://www.nature.com/articles/s41467-024-49226-9>

Flexible probes for human BCI

- <https://neuralink.com/>
- <https://axoft.us/>
- <https://precisionneuro.io/>

Flexible probe is preferred as it cannot break into the brain.

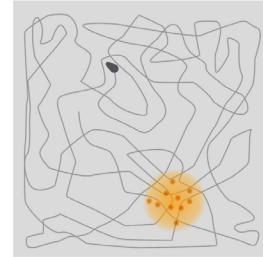
The field is moving toward:

- Recording more channels, more single units.
- Optogenetics in humans (Sahel et. al., 2021).
- Multi-color waveguide and uLED probes.
- Recording brain-body interactions.
 - Monitor heart-rate, temperature, blood sugar, blood pressure, etc.

BUT

- The Nobel Prize discovery was made by single wires and a lot of thinking...

The Nobel Prize in Physiology or Medicine 2014



John O'Keefe

John O'Keefe discovered, in 1971, that certain nerve cells in the brain were activated when a rat assumed a particular place in the environment. Other nerve cells were activated at other places. He proposed that these "place cells" build up an inner map of the environment. Place cells are located in a part of the brain called the hippocampus.

Fig. 1

May-Britt Moser and Edvard I. Moser

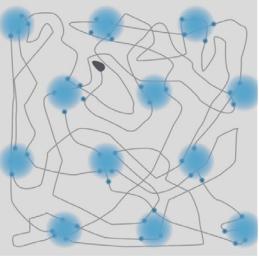
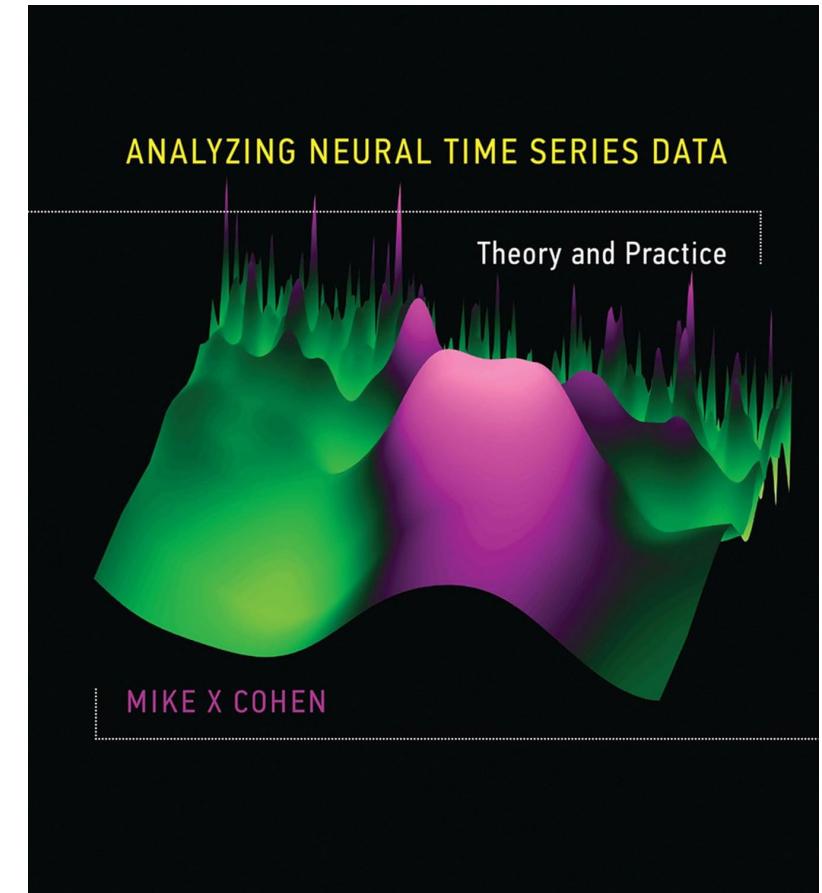
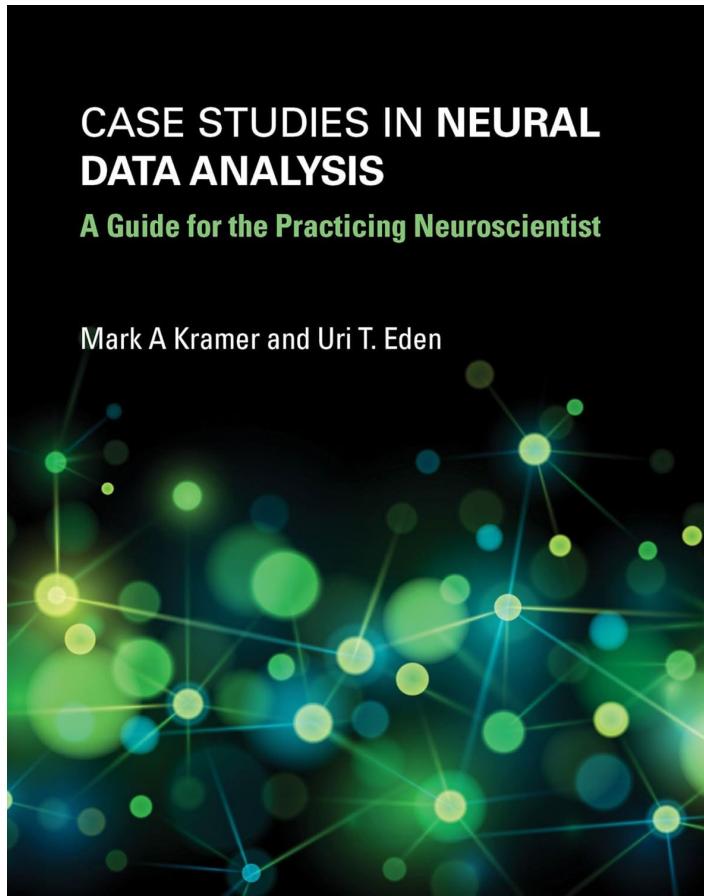


Fig. 2

May-Britt och Edvard I. Moser discovered in 2005 that other nerve cells in a nearby part of the brain, the entorhinal cortex, were activated when the rat passed certain locations. Together, these locations formed a hexagonal grid, each "grid cell" reacting in a unique spatial pattern. Collectively, these grid cells form a coordinate system that allows for spatial navigation.

Computational resources

- Python for the practicing neuroscientist: an online educational resource



Channel map creation (Headstage → Probe geometry)

Goal

- Translate **recording software channel ID** (headstage channel number)
- into the **physical recording site** on the probe (**shank, x/y location**).

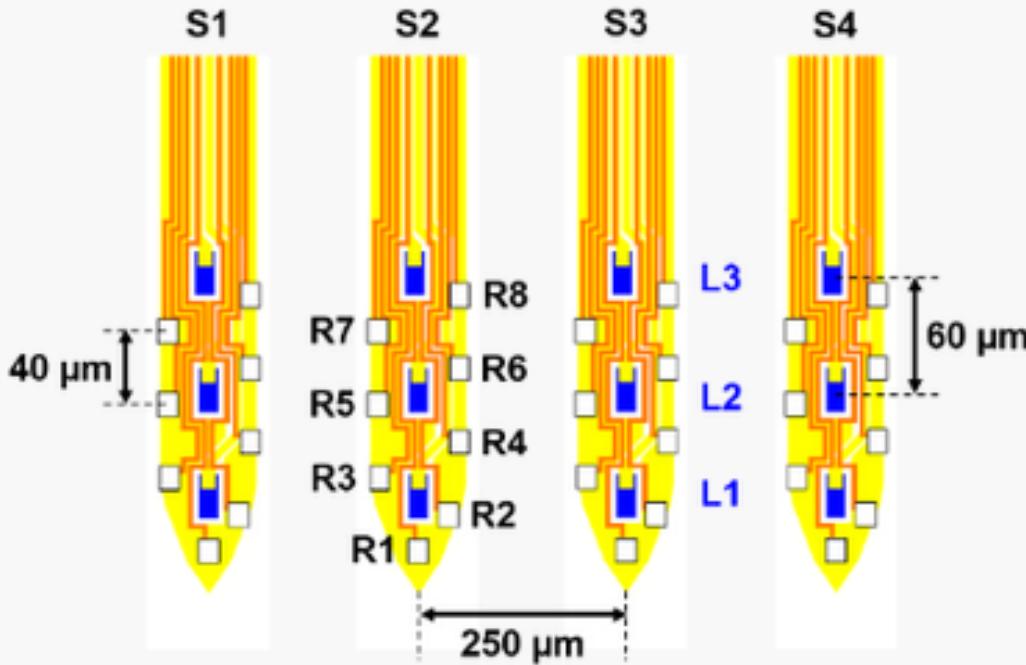
Inputs (3 different mappings)

- Probe recording channel layout (shank, x_um, y_um)
- Probe to connector pinout
- Connector to headstage pinout

Creating your channel map

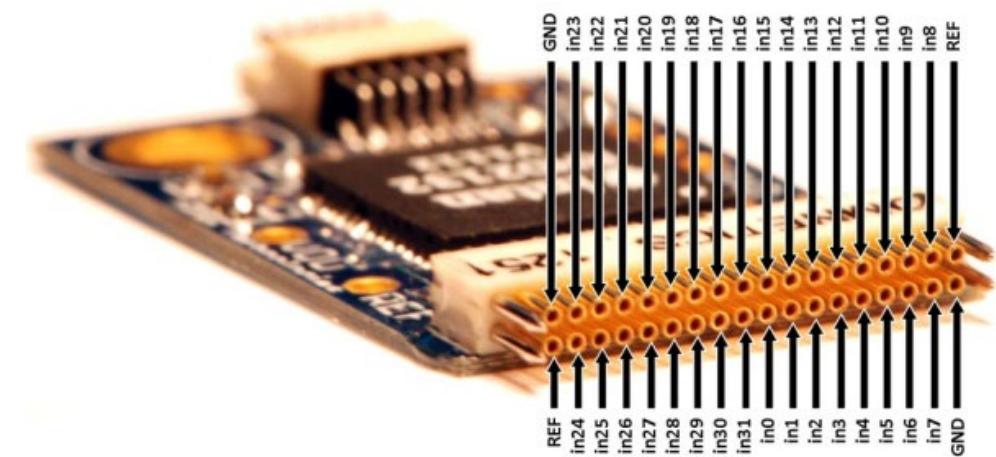
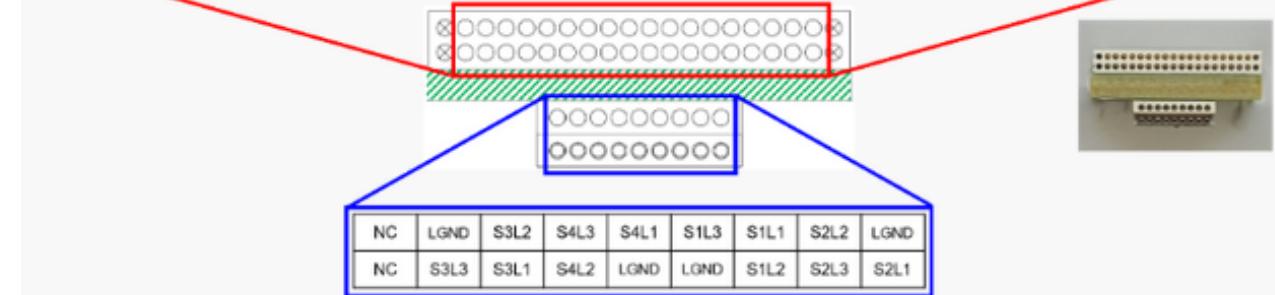
M11

Optoelectrode tip top view



PCB rear view

NC	S4R5	S4R1	S4R4	S4R8	S3R5	S3R1	S3R4	S3R8	S2R7	S2R3	S2R2	S2R6	S1R7	S1R3	S1R2	S1R6	GND
GND	S4R7	S4R3	S4R2	S4R6	S3R7	S3R3	S3R2	S3R6	S2R5	S2R1	S2R4	S2R8	S1R5	S1R1	S1R4	S1R8	REF



Creating your channel map

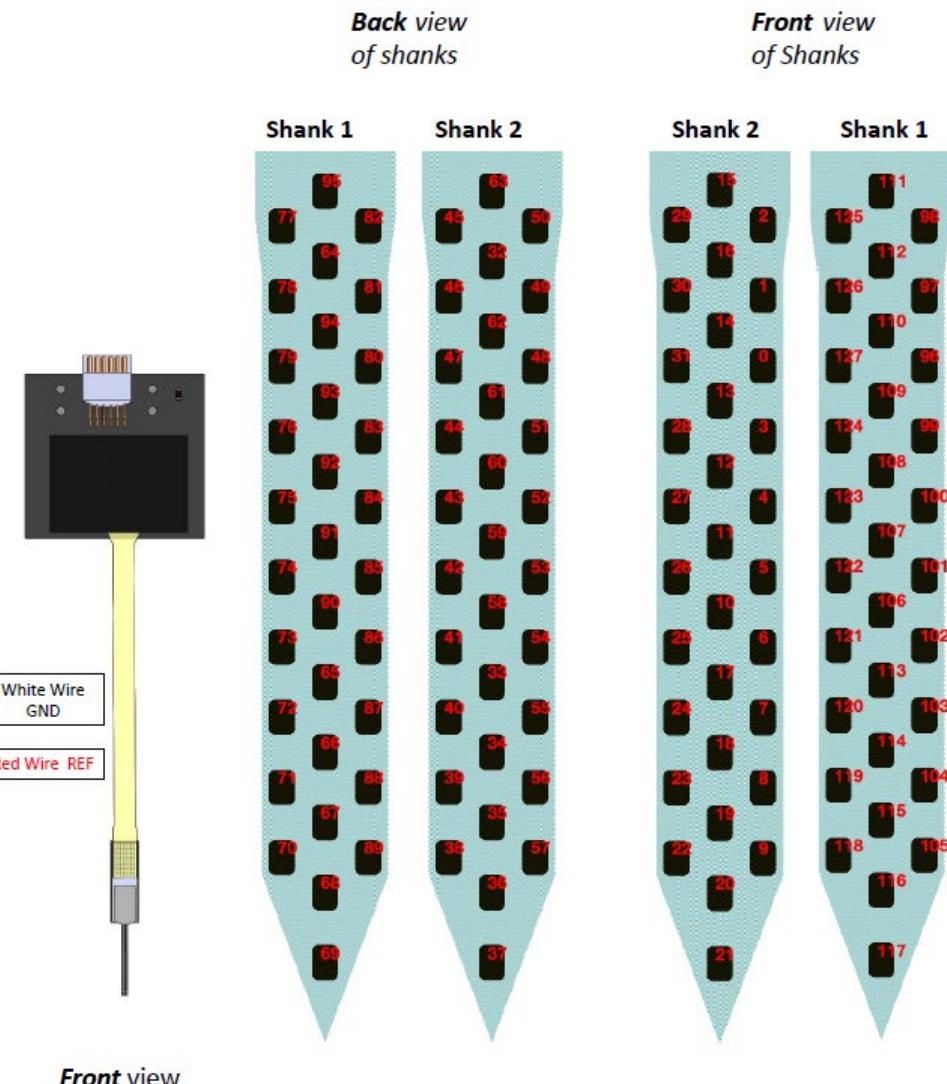
ASSY INT128

M11

Recording sites mapped to Intan system

Inputs for active probes

Probe recording channel layout (shank, x_um, y_um)



P64-13-D

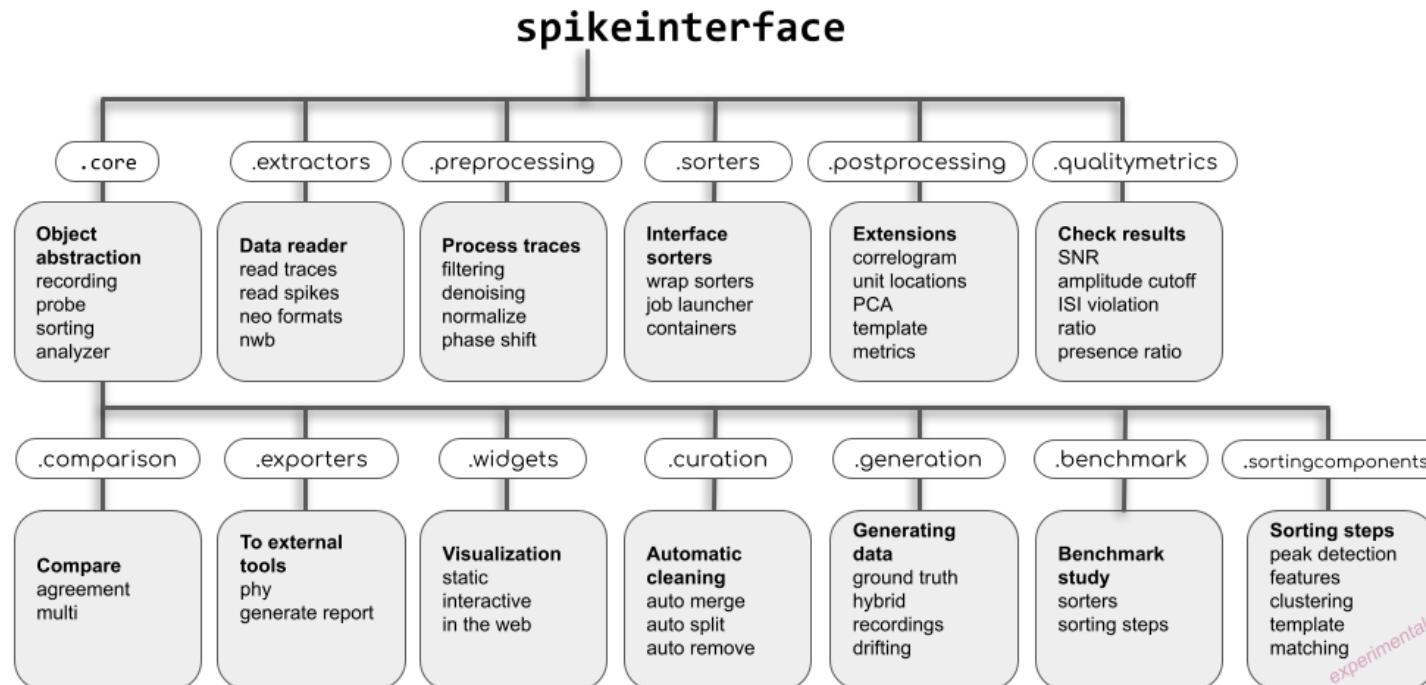
Preprocessing data

- Download Matlab functions [BuzsakiLab github](#).
- Data is available at [Zenodo](#).
- Matlab code is available at Github (Buzcode, CellExplorer, Local codes).

- bz_ConcatenateDats;
- bz_LFPfromDat(basepath);
- save([basepath filesep basename 'YOURmanipulation.manipulation.mat'], 'YOURmanipulation');
- RemoveArtefact_dat([basepath filesep basename '.dat'], artefact);
- removeNoiseFromDat(basepath, 'method', 'subtractMedian', 'ch', channels);
- [SleepScoreMaster](#)(basepath);
- TheStateEditor
- SpikeSort ([Kilosort](#) or similar)

Spikesorting

- Watch Neuropixels UCL training videos
- <https://spikeinterface.readthedocs.io/en/stable/>



If you have any questions:

Contact me at Voroslakos@gmail.com