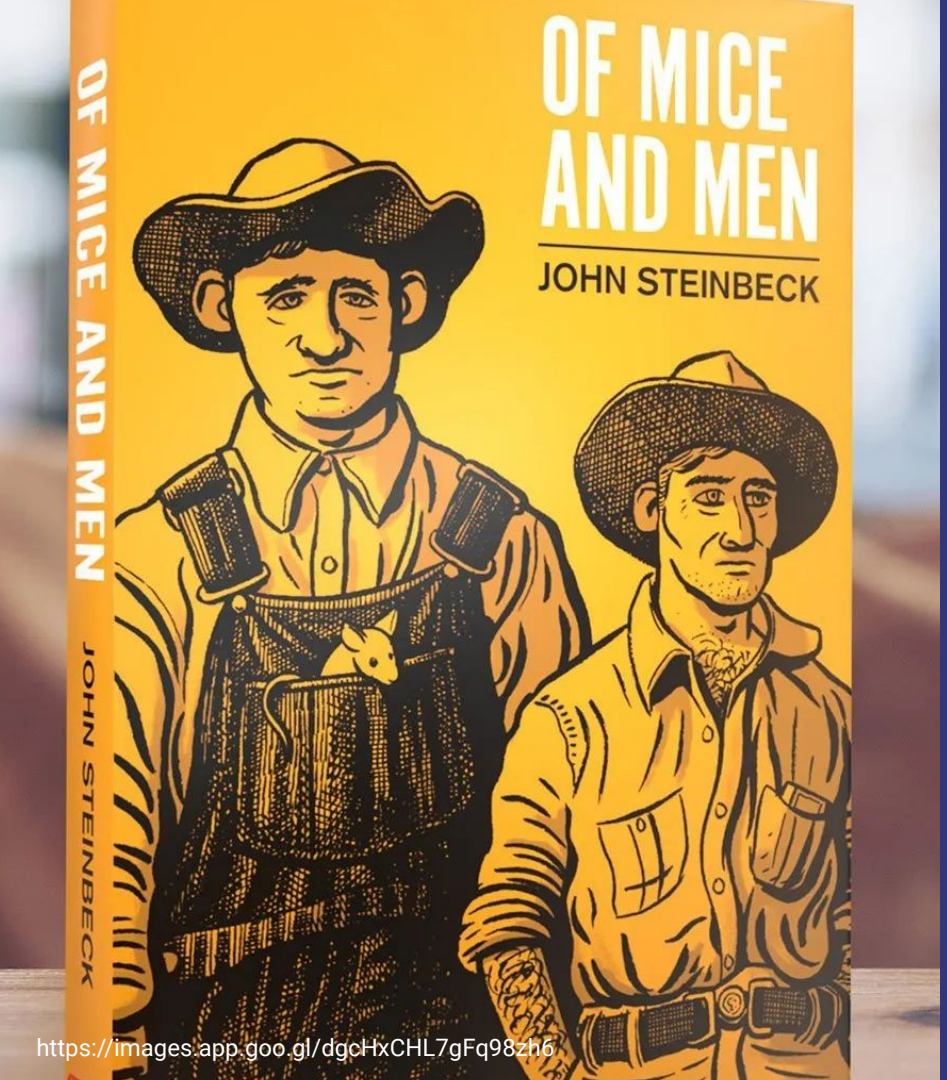
Of Mice and Men

A very personal intro to ephys alignments using the IBL GUI

Sonja Förster | January 2024

Pic by Robin Haak, Netherlands Institute for Neuroscience (NiN), Amsterdam, NL; 2023



https://images.app.goo.gl/dgcHxCHL7gFq98zh6

Did you think of this?

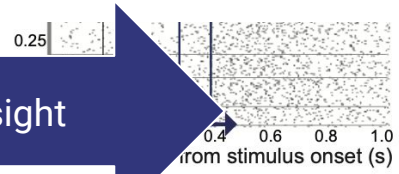
Well, really good book -
but not the content
of today's talk.

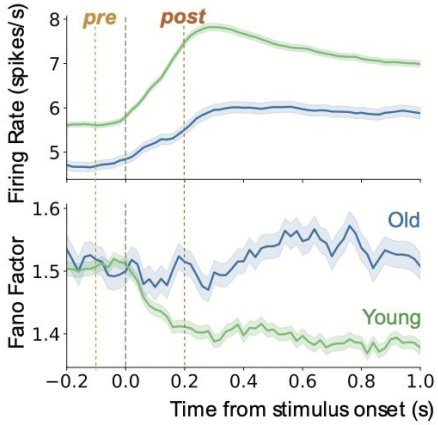
Pic by Robin Haak, Netherlands Institute for Neuroscience (NiN), Amsterdam, NL; 2023

From mouse to insight

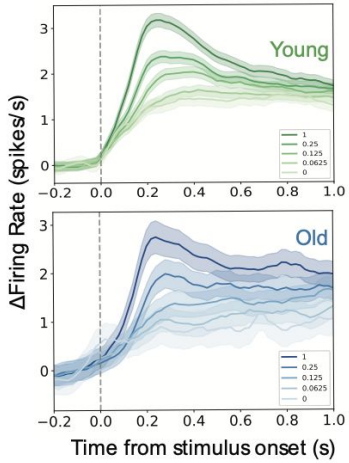
Age-related changes in neural variability in a decision-making task

Fenying Zang[1*], Anup Khanal[2], Sonja Förster[1], International Brain Laboratory, Anne K Churchland[2], Anne E Urai[1]
[1] Leiden University, The Netherlands [2] University of California Los Angeles, USA *f.zang@fsw.leidenuniv.nl

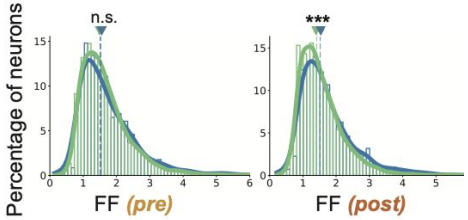




Neural responses are modulated by contrast levels of visual stimuli.



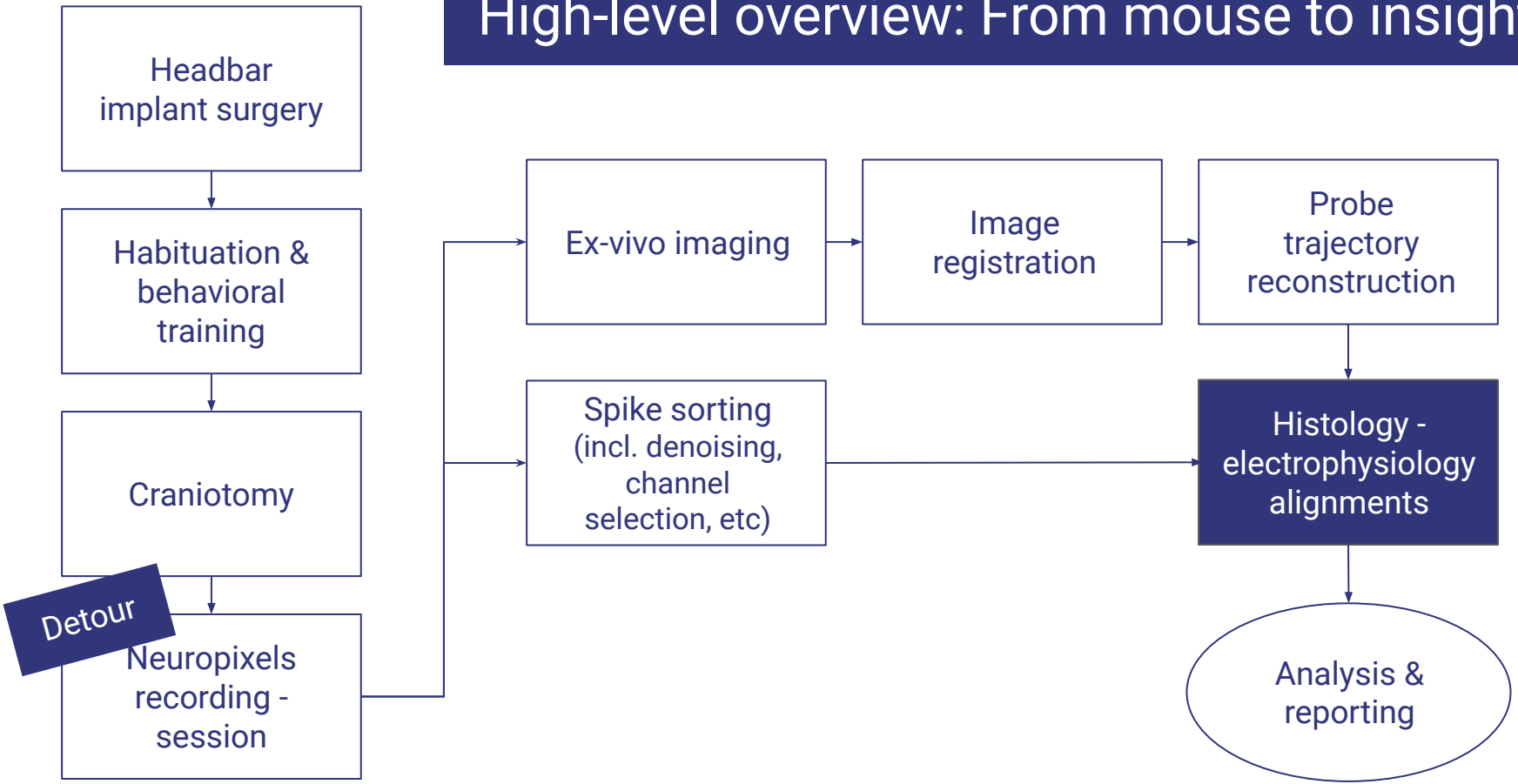
3. Aging effect: Comparison between gro



- Older mice have larger post-stimulus neural variability than young mice in LP

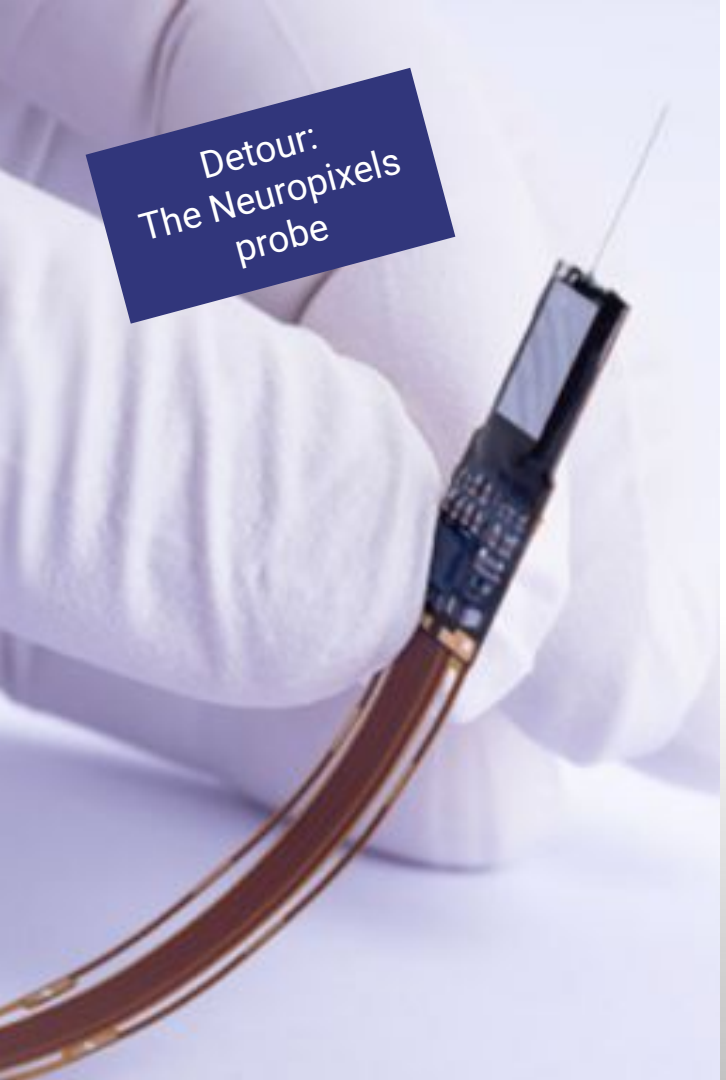
How to get from mouse to insight

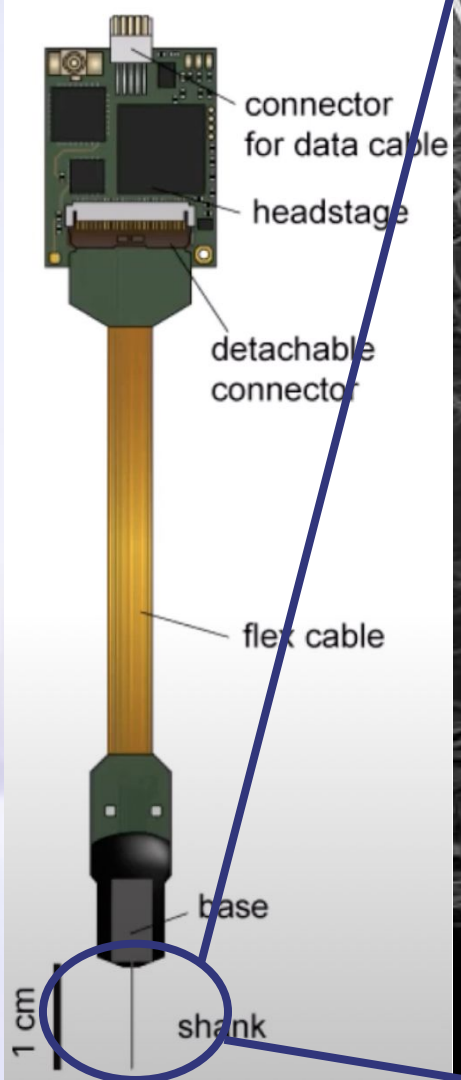
High-level overview: From mouse to insight

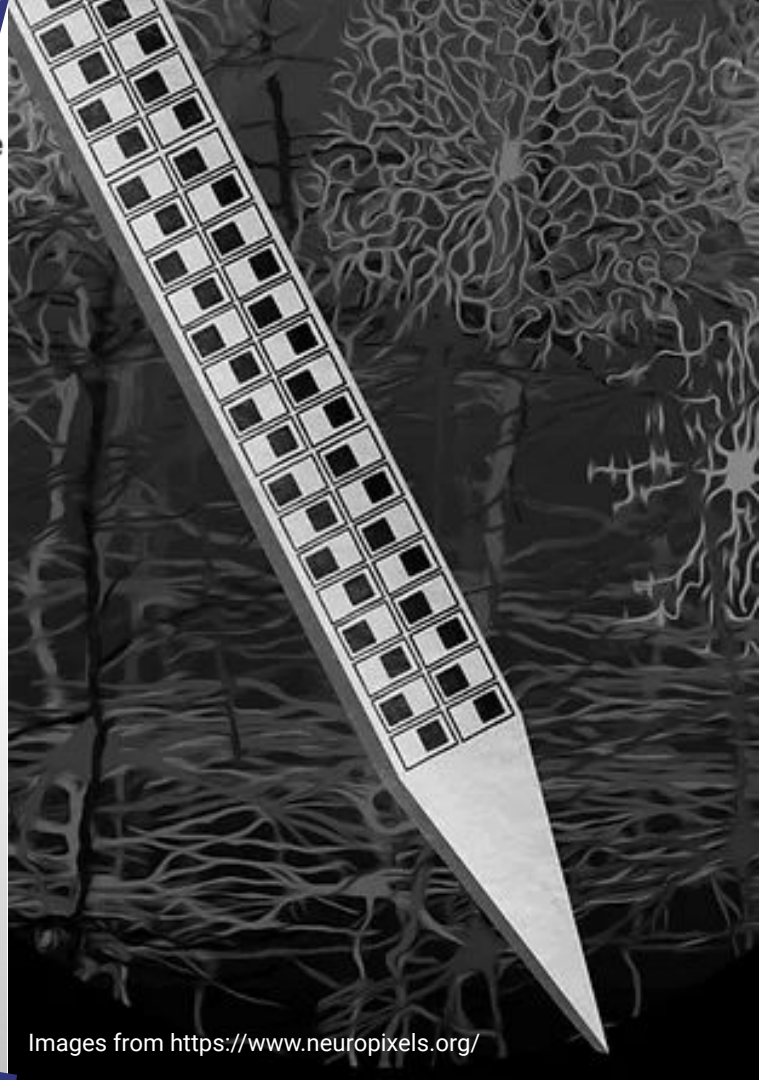


Adapted from IBL et al. 2022b; IBL et al. 2022c

Detour: The Neuropixels probe



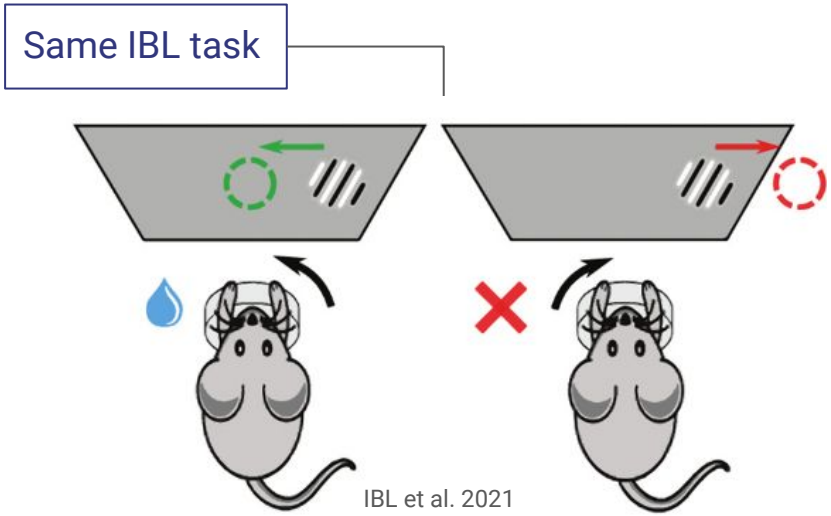


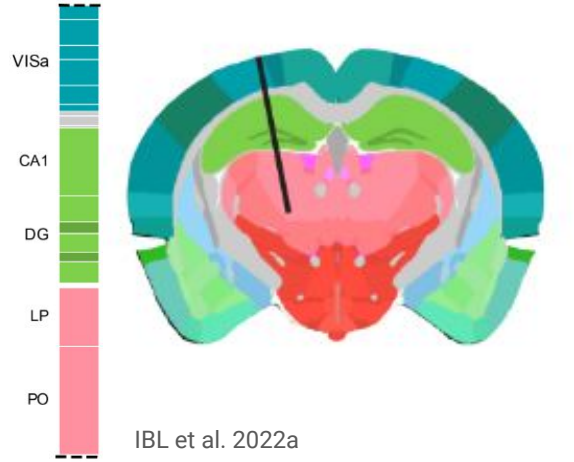


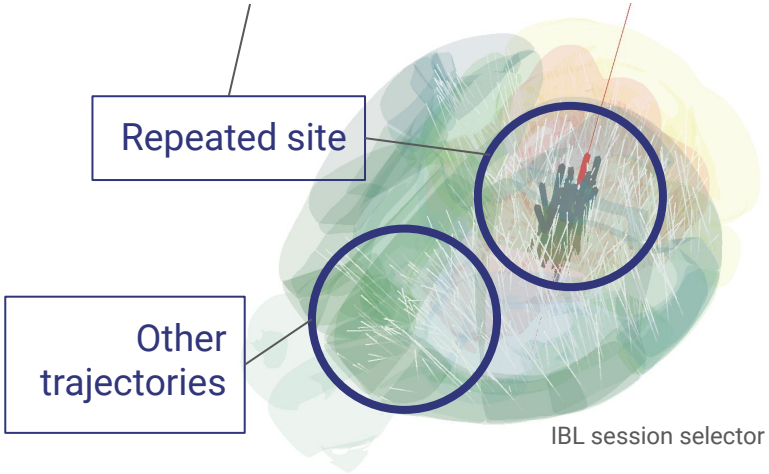
Images from https://www.neuropixels.org/

Our context:

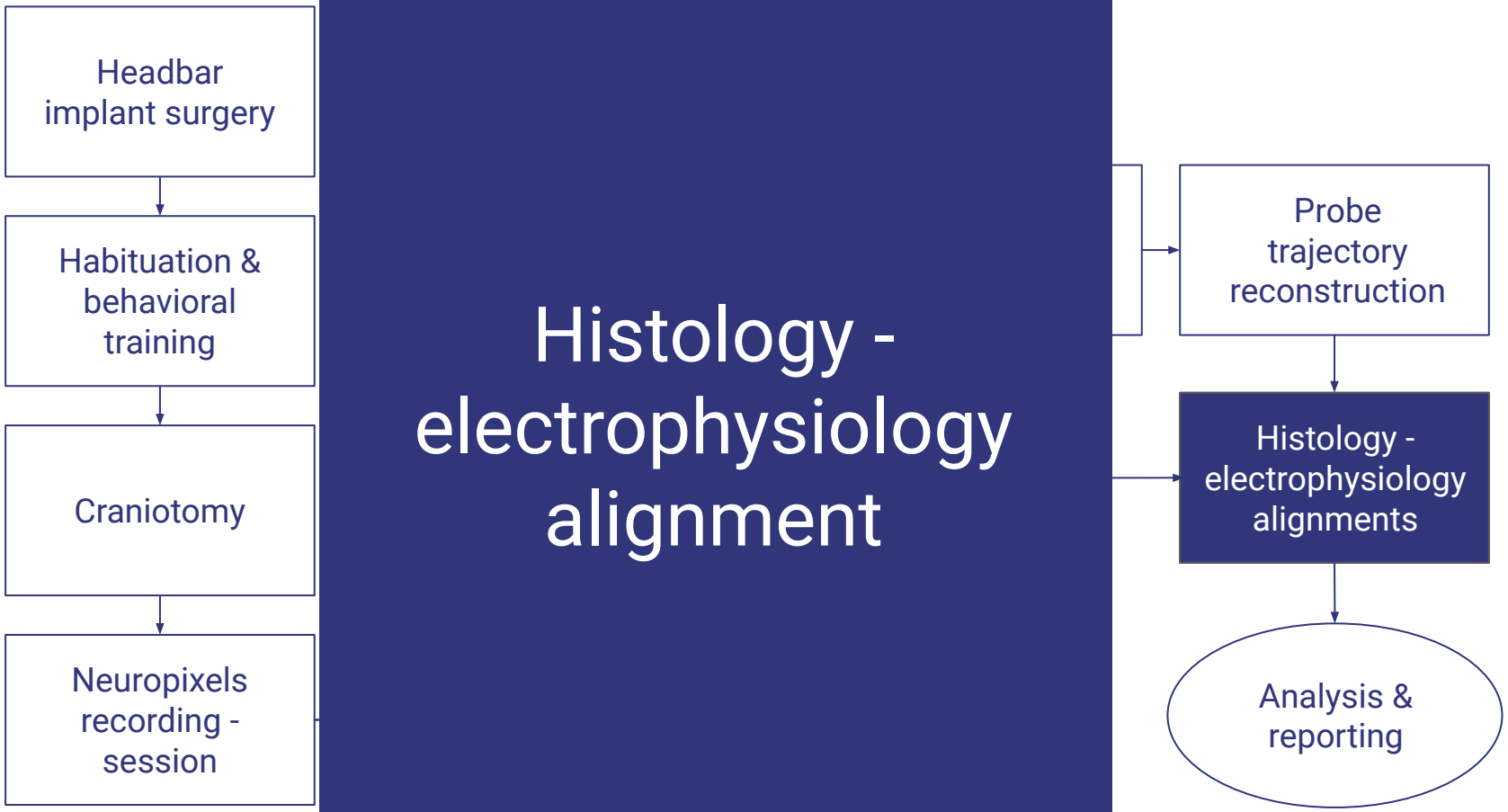
Dr Anne Urai's lifespan project
→ old mice: 10 - 19 months







Good intro to the task: https://www.youtube.com/watch?v=RUSJAJw1B6U


Headbar implant surgery
Habituation & behavioral training
Craniotomy
Neuropixels recording - session
Histology - electrophysiology alignment
Probe trajectory reconstruction
Histology - electrophysiology alignments
Analysis & reporting

Histology - electrophysiology alignment

Histology image (slice of brain tissue)

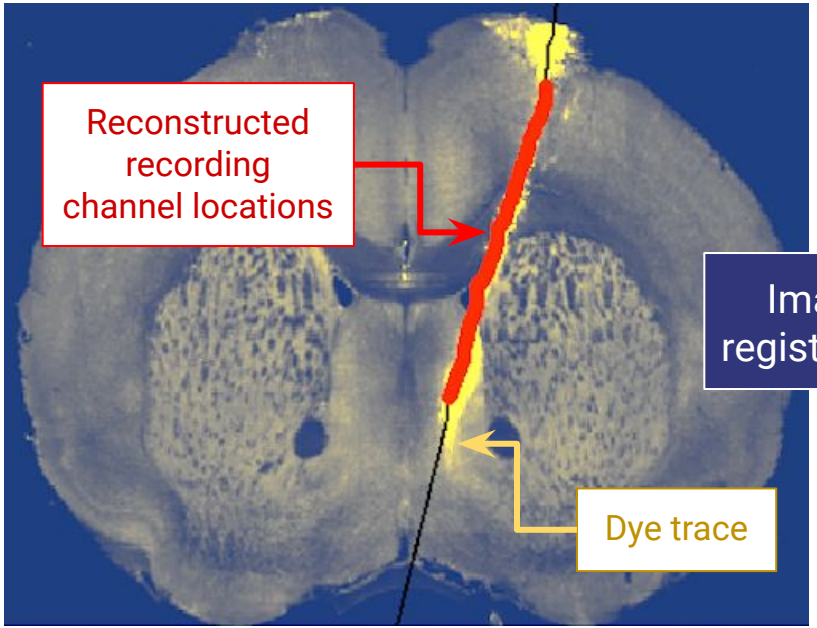
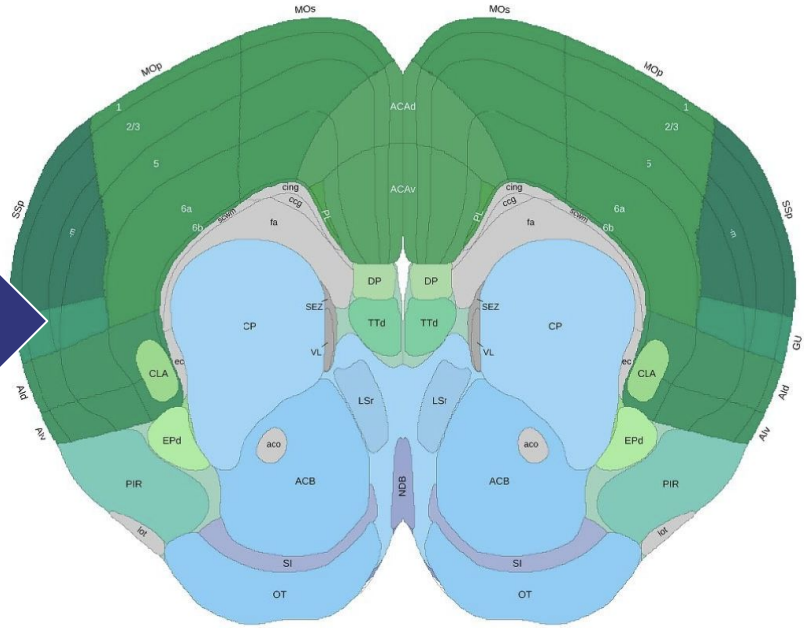


Image registration

Allen atlas template (roughly same slice)



Allen atlas: Mouse, adult, 3D coronal

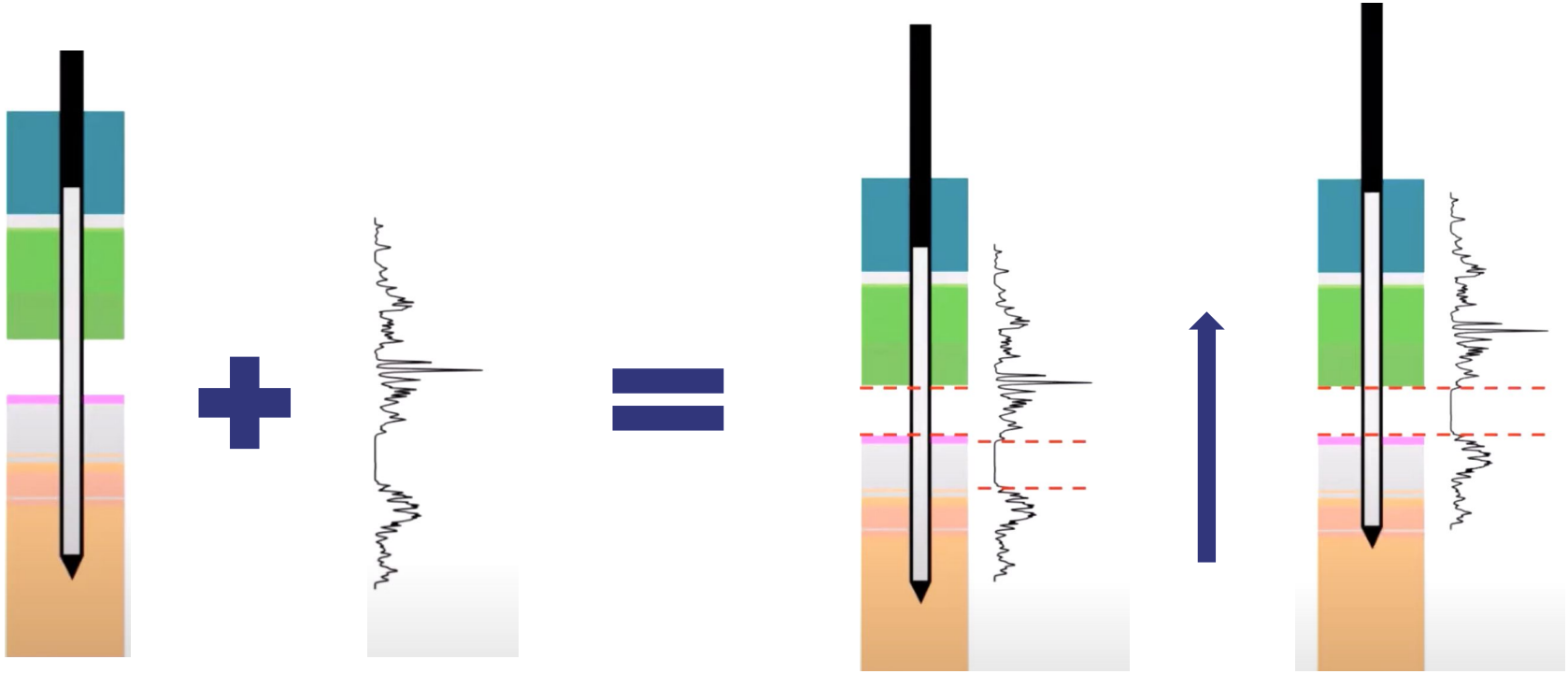
Challenges to image registration

- Brain sizes (and structures therein) vary between animals → scaling / warping leads to mapping differences.
- Tracing / probe reconstruction is inaccurate.
- Dye diffuses into surrounding tissue.

https://images.app.goo.gl/1Rye5MUHsZmB6SsA6

https://www.youtube.com/watch?v=JWzj_vZYr-g

Histology - **electrophysiology** alignment



Goal: get a proper scaling factor!

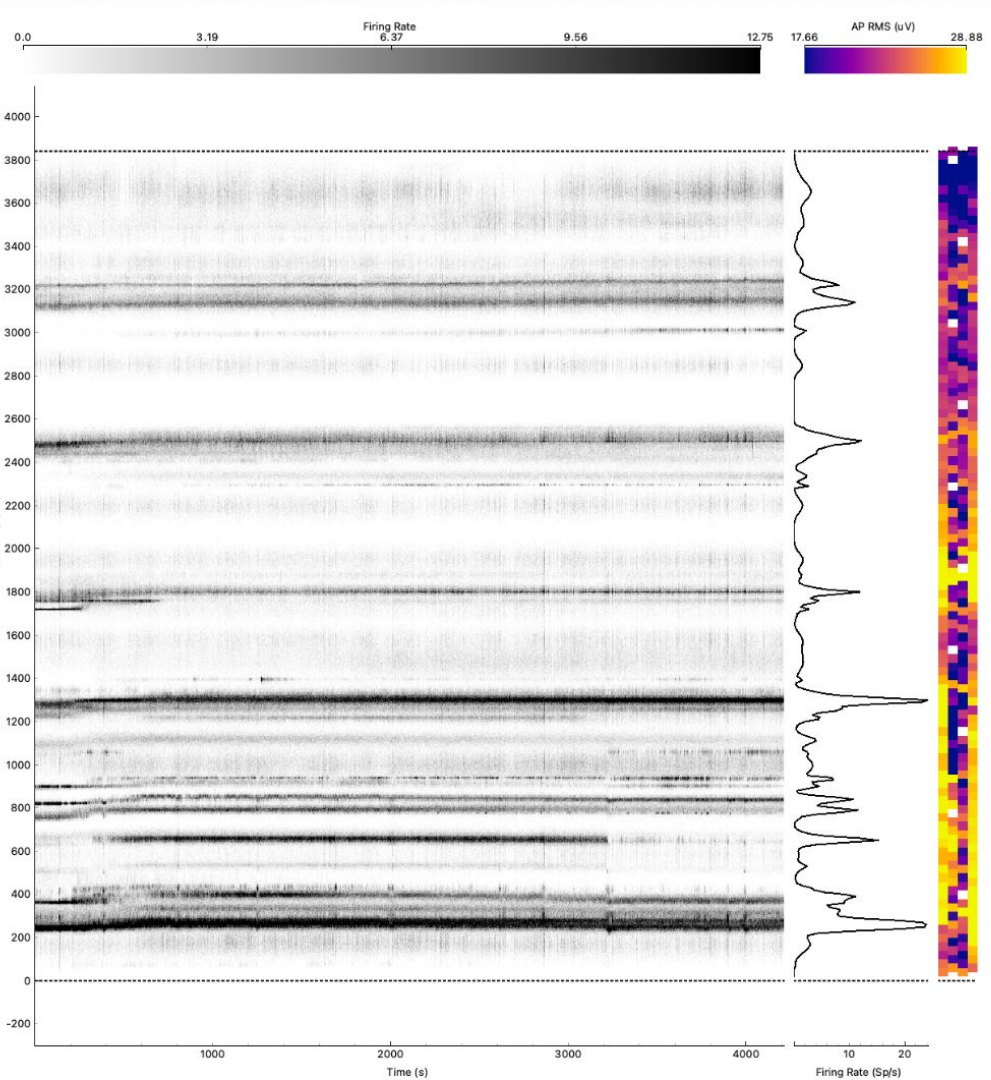
https://www.youtube.com/watch?v=JWzj_vZYr-g

Let’s try:

Find landmarks, identify ephys features, align.

Some known features and landmarks

- Silent bands in corpus callosum and other fibre tracts.
- High firing rate activity in upper third of CA1 (Hippocampus).
- Dentate gyrus (DG): high power in low frequency band (LFP) → spiking in 30-80 Hz band.
- Silent bands in DG-mo layers sandwich around DG-sg layer with higher firing rate.
- Pyramidal cell layers (eg, Layer V in cortex, hippocampal areas CA1, CA3): high firing rate & high amplitude (peaks).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9.56
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28.88
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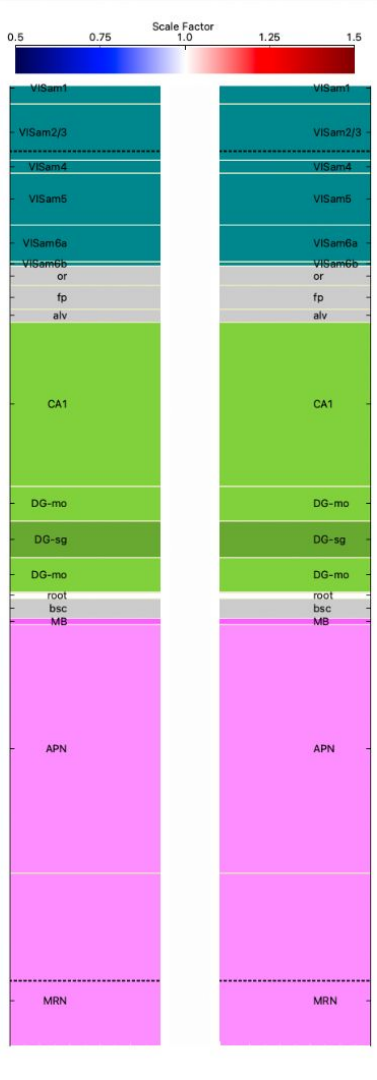
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
1000
2000
3000
4000
Time (s)
10
20
Firing Rate (Sp/s)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1.0
1.25
1.5
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VISam2/3
VISam4
VISam5
VISam6a
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or
fp
alv
CA1
DG-mo
DG-sg
DG-mo
root
bsc
MB
APN
MRN
VISam1
VISam2/3
VISam4
VISam5
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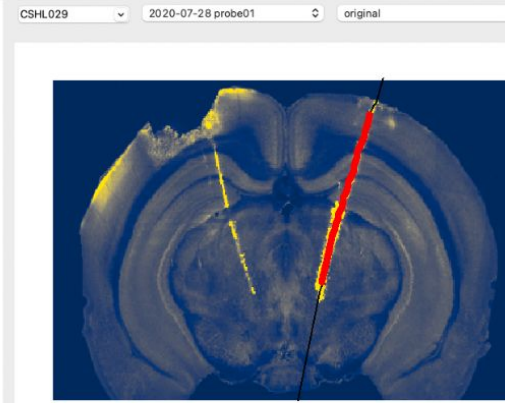
APN
MRN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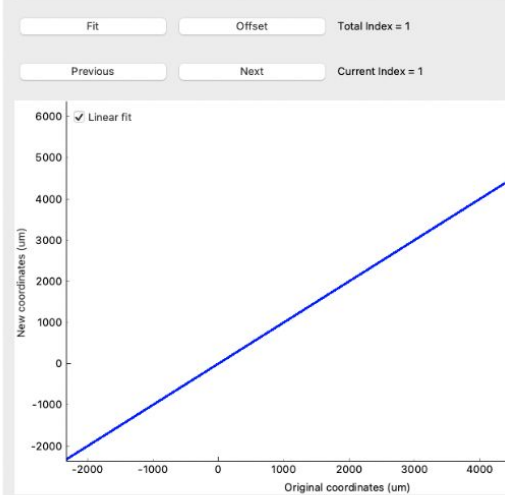
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1000
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-1000
-2000
New coordinates (um)
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-1000
0
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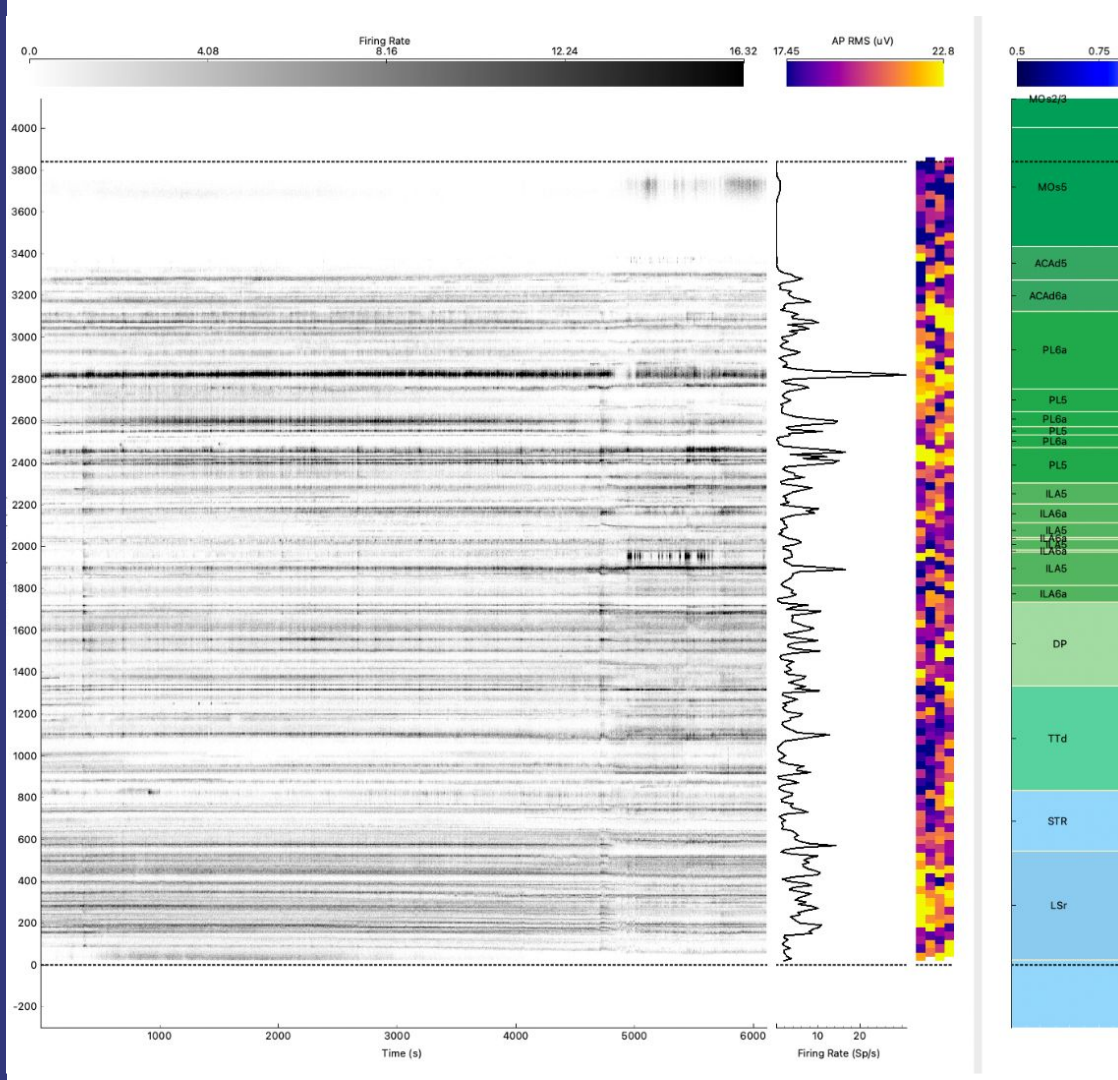
2000
3000
4000
Original coordinates (um)
Reset
Upload

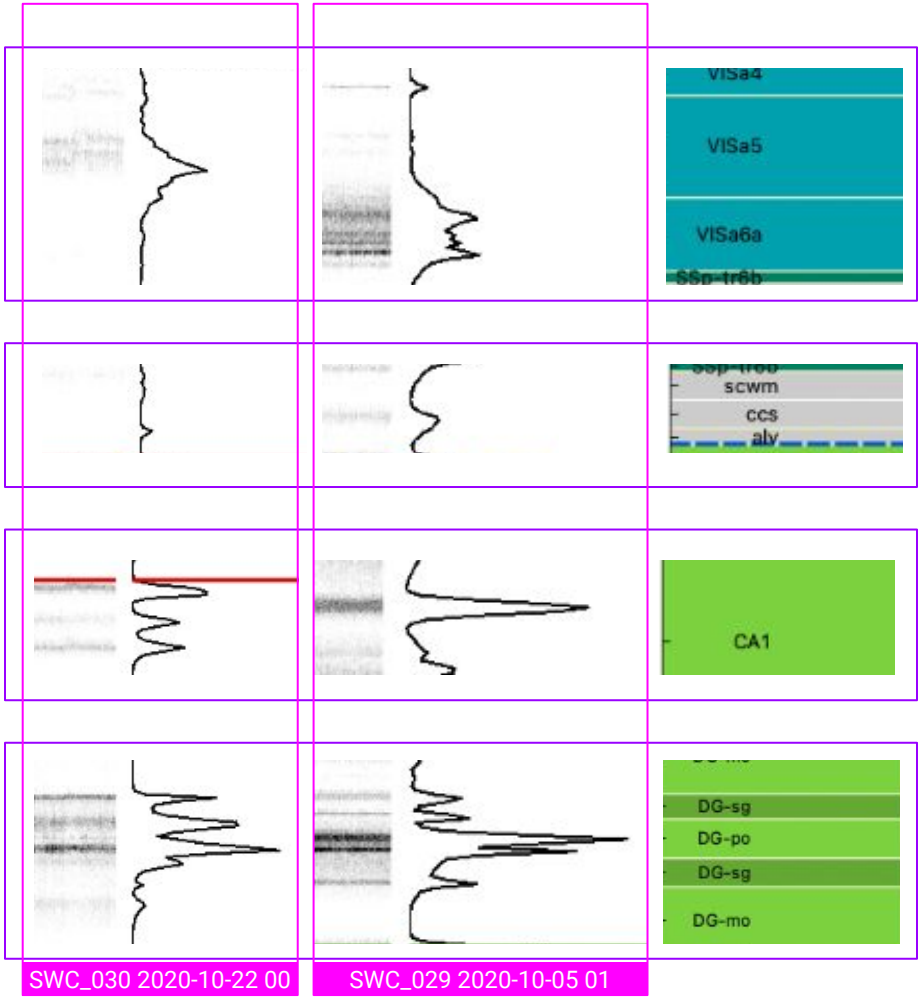
Life demo

https://github.com/int-brain-lab/iblapps/blob/master/atlaselectrophysiology/ephys_atlas_gui.py

Just look for specific landmarks!

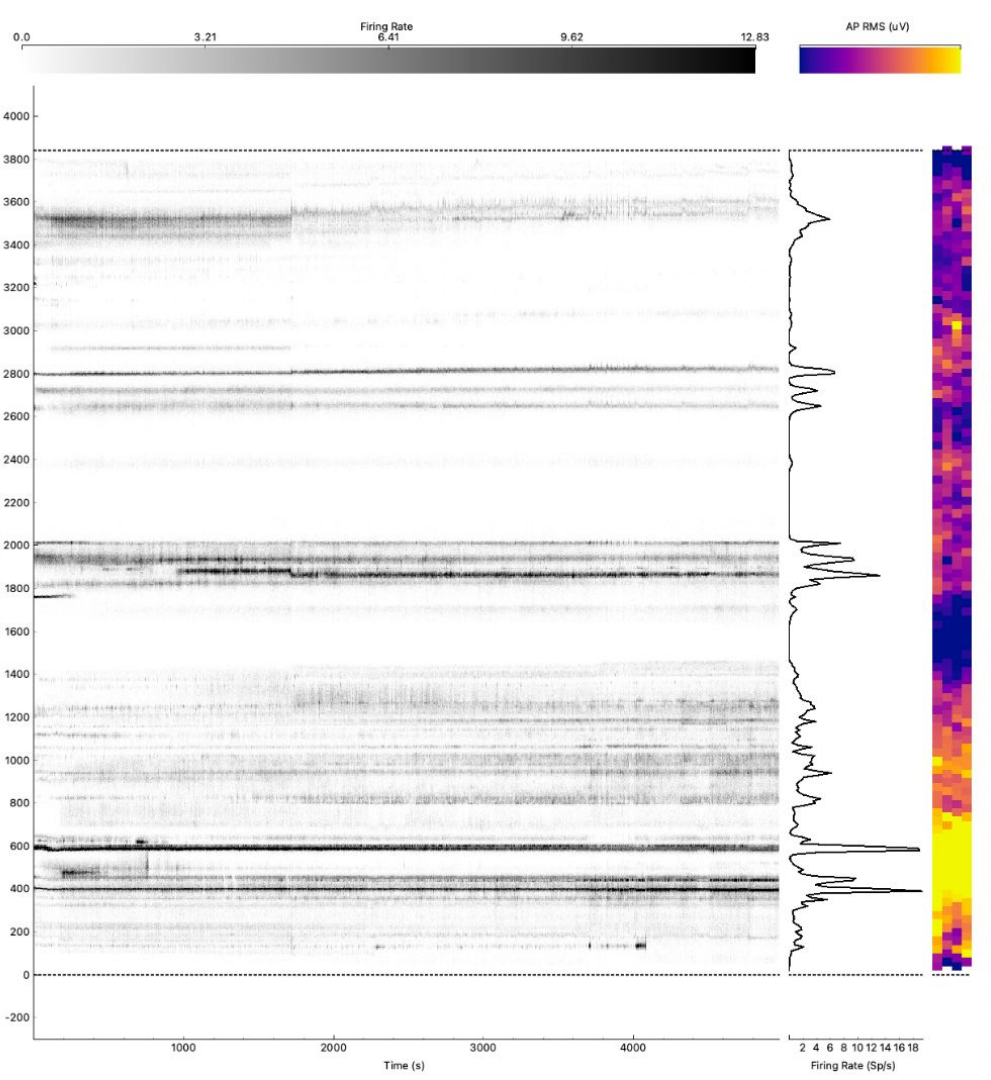
Landmarks??

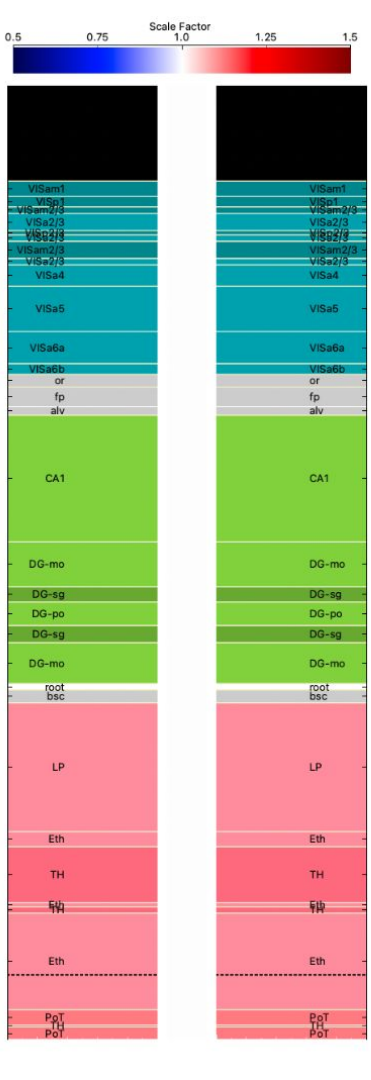


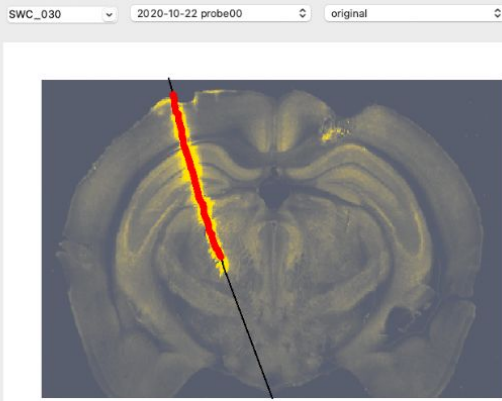


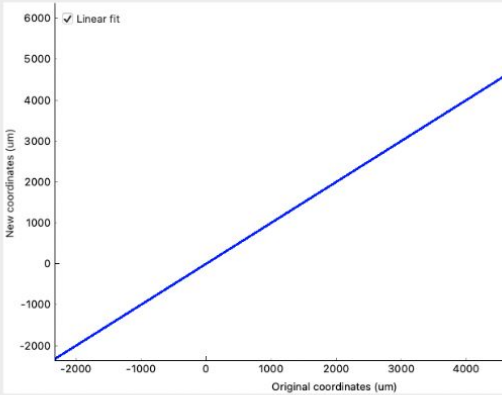
Just look for the same ephys features!

Same ephys features??









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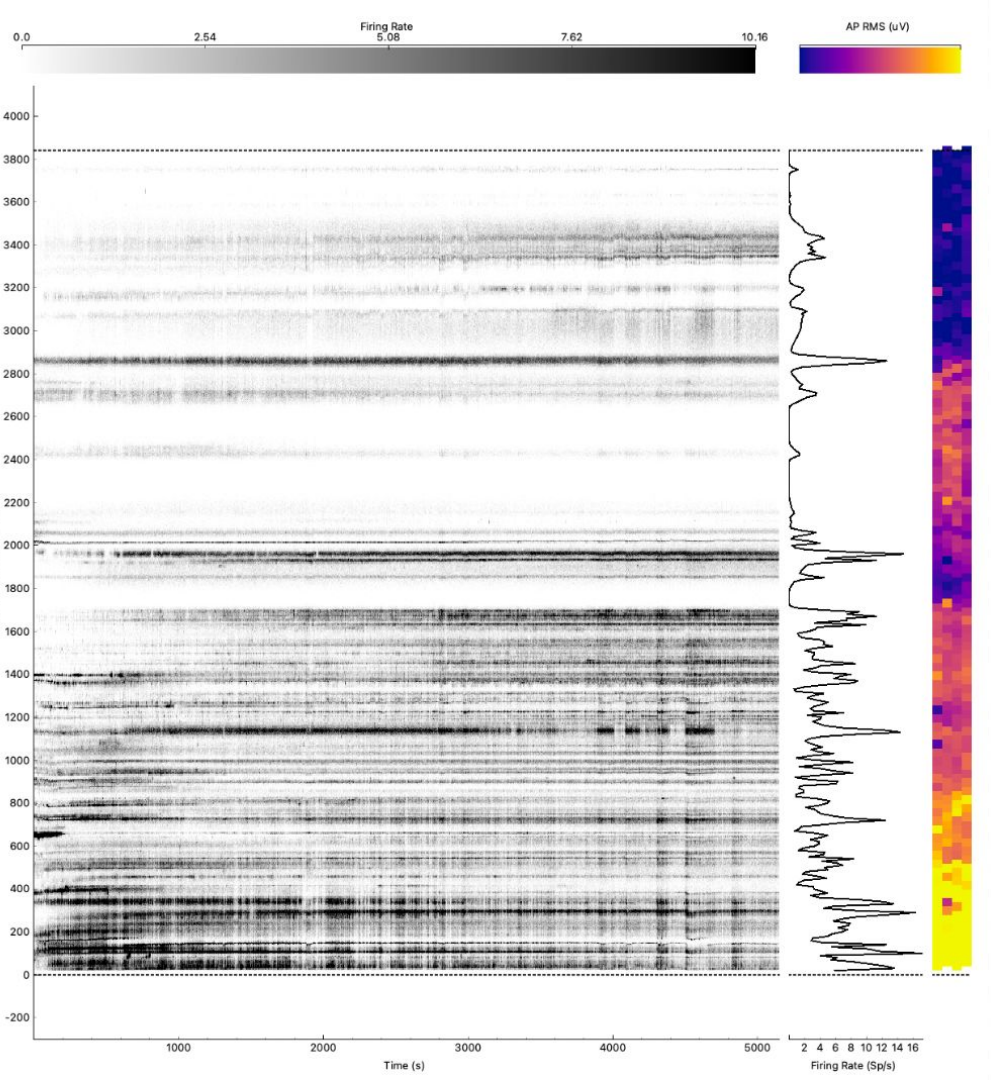
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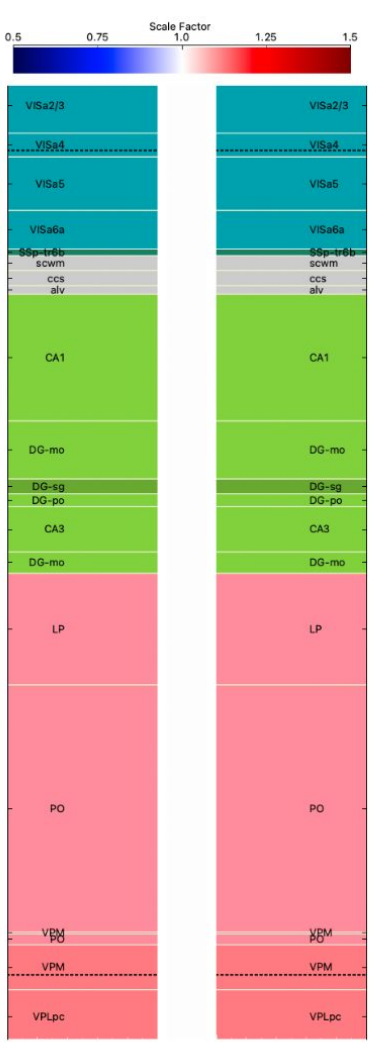
AP RMS (uV)
Time (s)
Firing Rate (Sp/s)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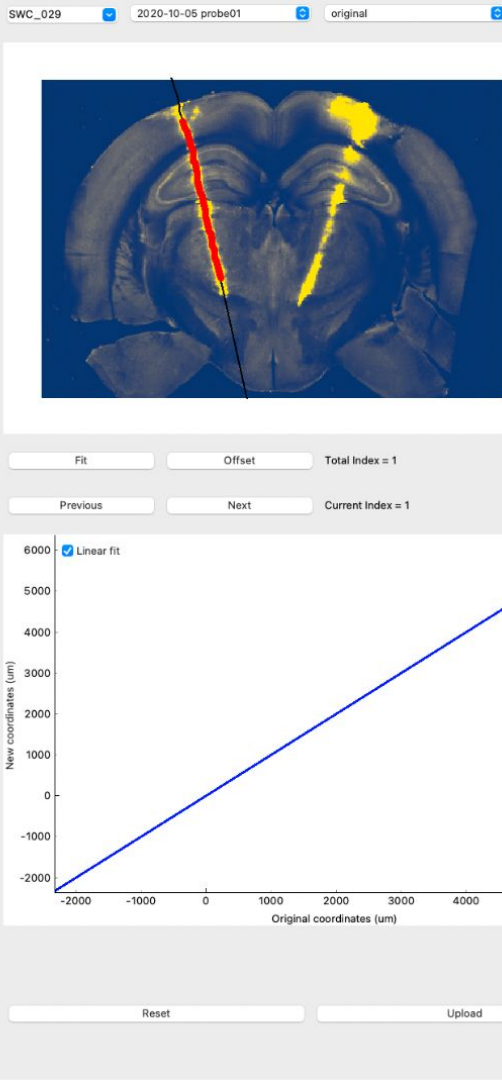
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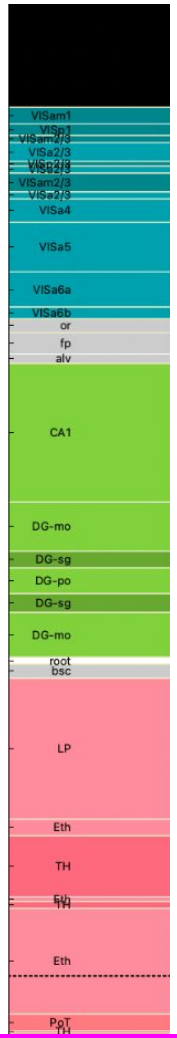
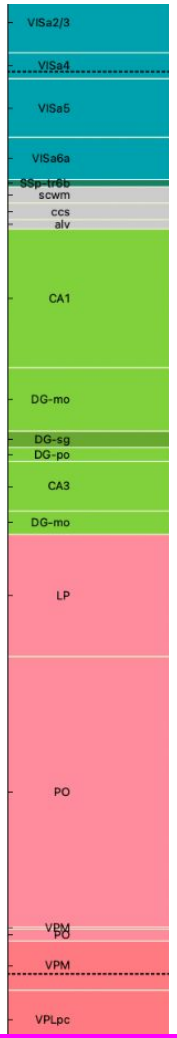
Original coordinates (um)
Reset
Upload

Same same … (hemisphere, trajectory)





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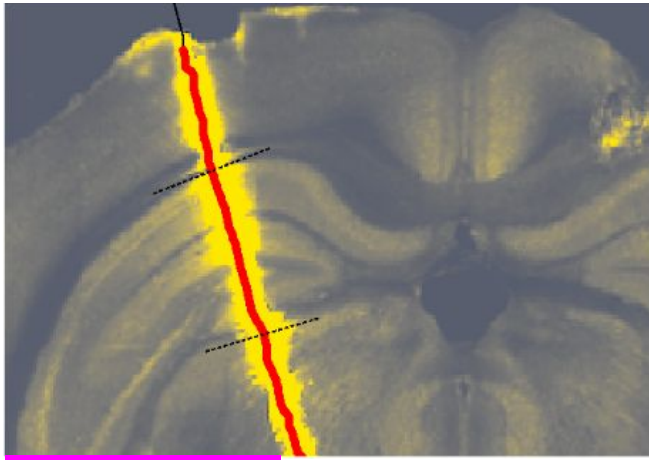

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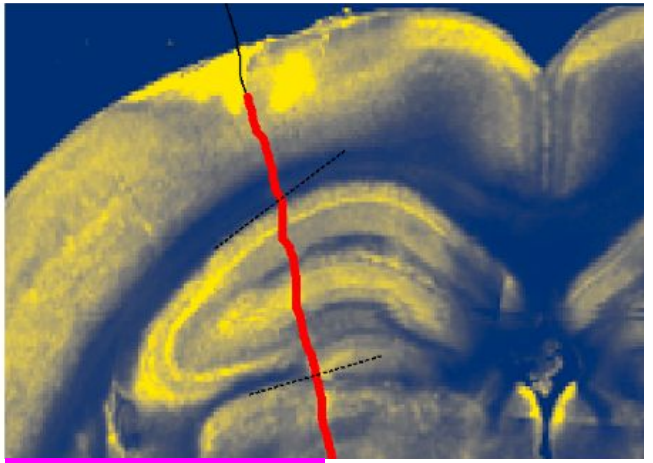

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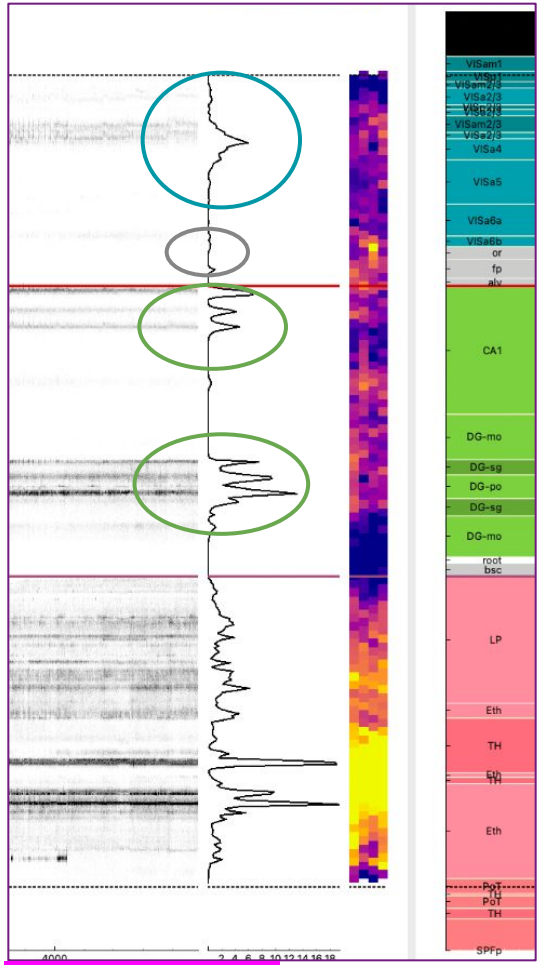
… but different



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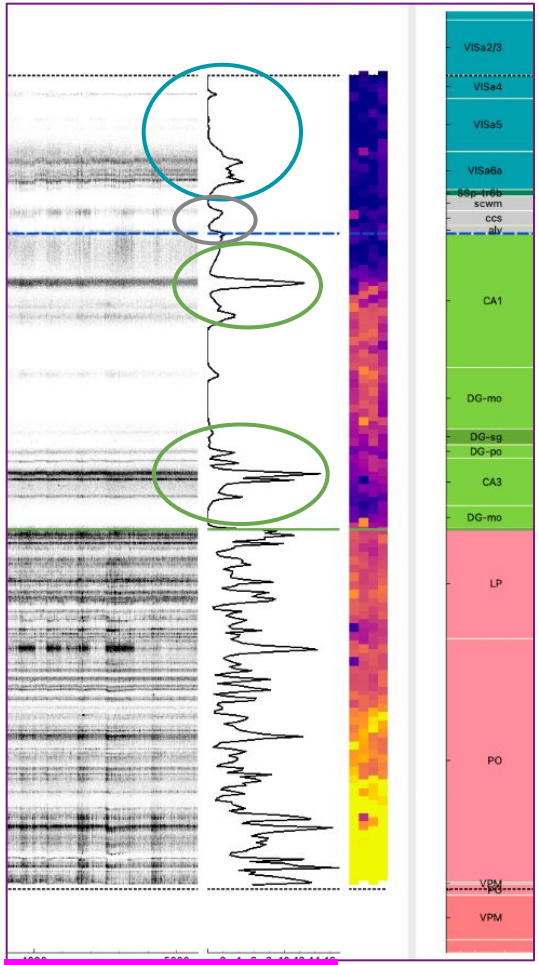


SWC_029 2020-10-05 01

For example

- neural yield
- Ephys features in same regions quite different

⇒ How much similar is the same?

Why these differences?

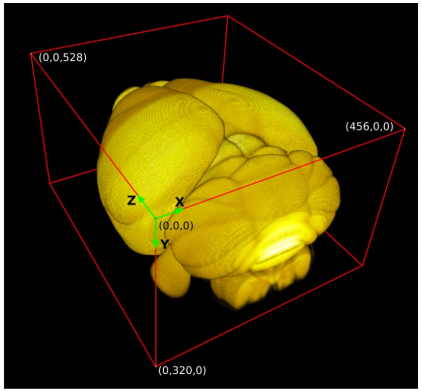
- Many manual and automated steps from mouse to insight → a lot can go wrong → **imperfections added up**.
- Each recording is from an **unique, alive animal**: engaged or not, in pain or fear, bad day or good, fast or slow, stimulus-targeted or not so much, impaired sight, itching eye…
- Each **session is error prone**: probe doesn't go in where planned, saline bath dries out (grounding issues), tissue damaged, broken channels…
- **Algorithms** can be wrong.

⇒ **Don't pretend precision** or un-ambiguity where it may just not be.

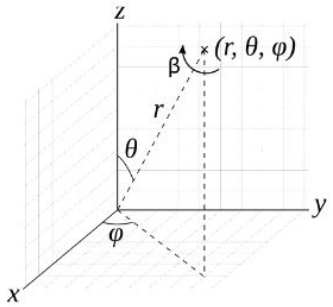
⇒ Ephys alignment means: **find what is shared** across insertions while **appreciating the uniqueness** of each animal and recording.

Luckily, a few things can help to guide decisions and support judgements.

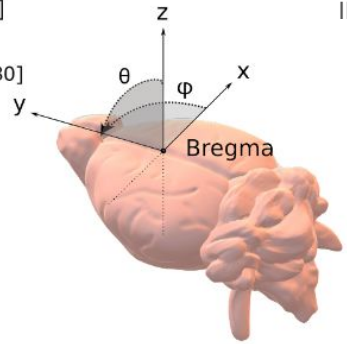
Don’t you forget: it’s 3D



IBL et al. 2022d

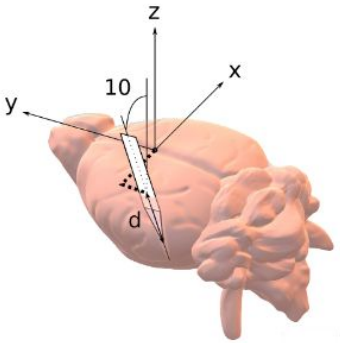


φ [0 ; 360]
θ [0 ; 180]
β [-180 ; 180]



IBL et al. 2022e

Concrete case example 2



x = -2000 um

y = -400 um

z = 0 um

θ = 10 deg

φ = 180 deg

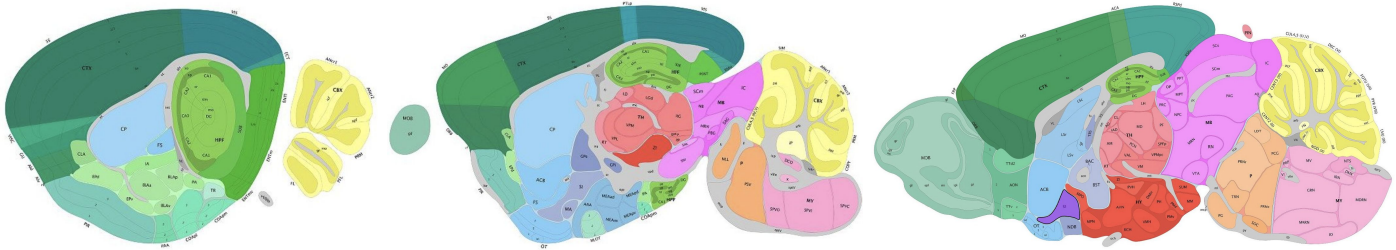
β = 0 deg

depth = 100 um

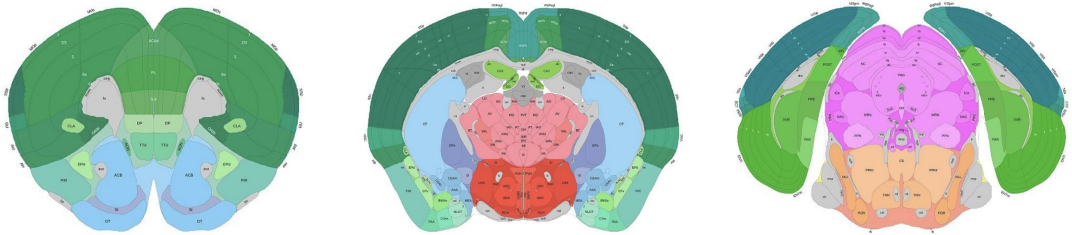
Axes @IBL:

- X = medial-lateral (ML)
- Y = anterior-posterior (AP)
- Z = dorsal-ventral (DV)

It can thus be helpful to mentally visualize the exact trajectory as much as possible through checking back and forth between different 2D atlasses, eg, sagittal and coronal views.

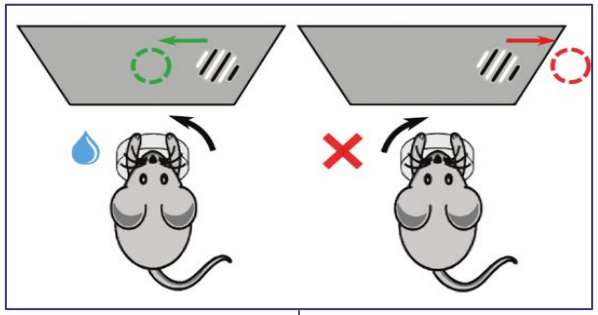


Allen atlas: Mouse, P56, sagittal



Allen atlas: Mouse, adult, 3D coronal

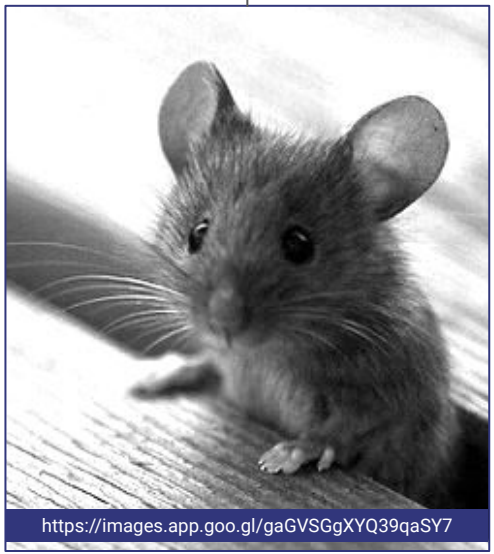
Don’t you forget: The probe is task-agnostic



IBL et al. 2021

Task-contingent activity

Task-agnostic activity



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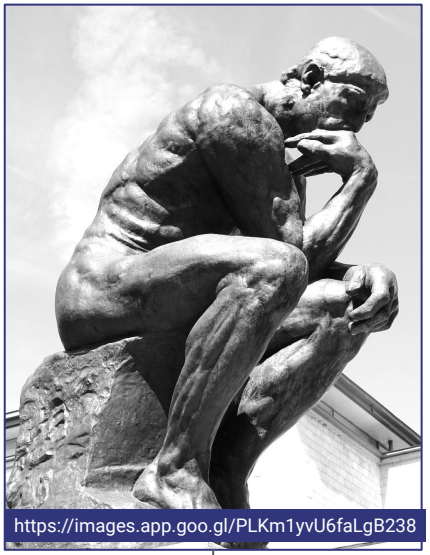

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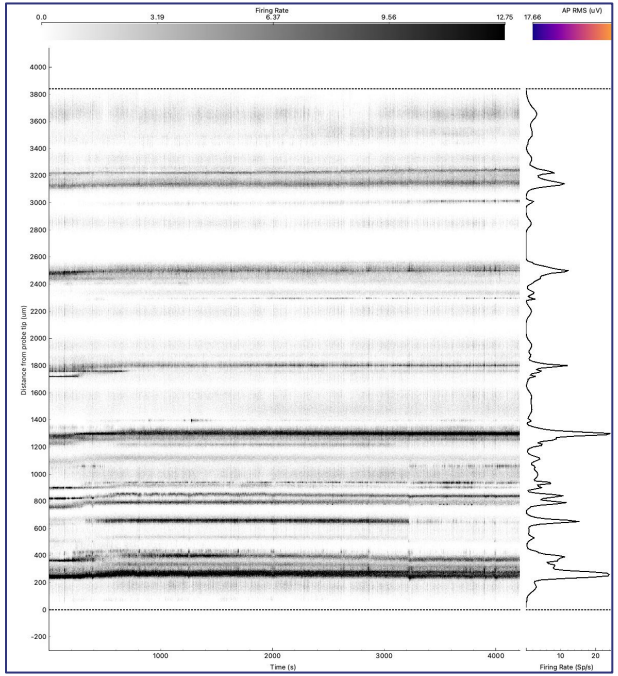
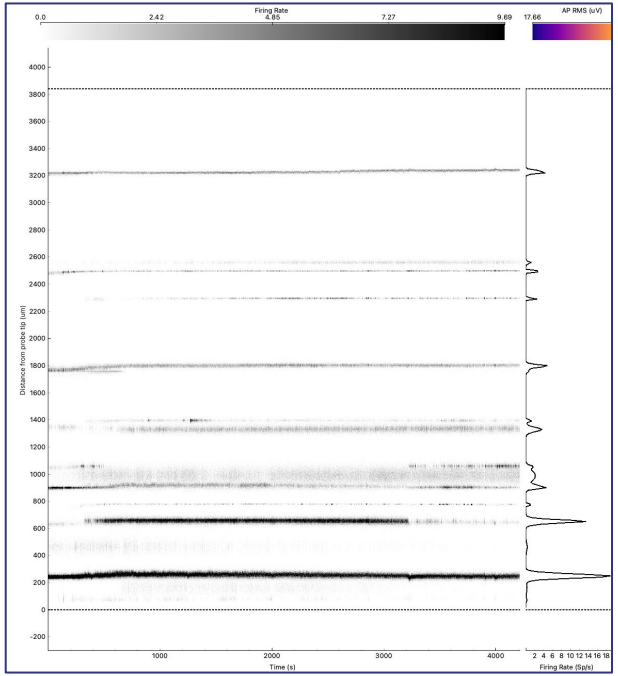
Human ignorance

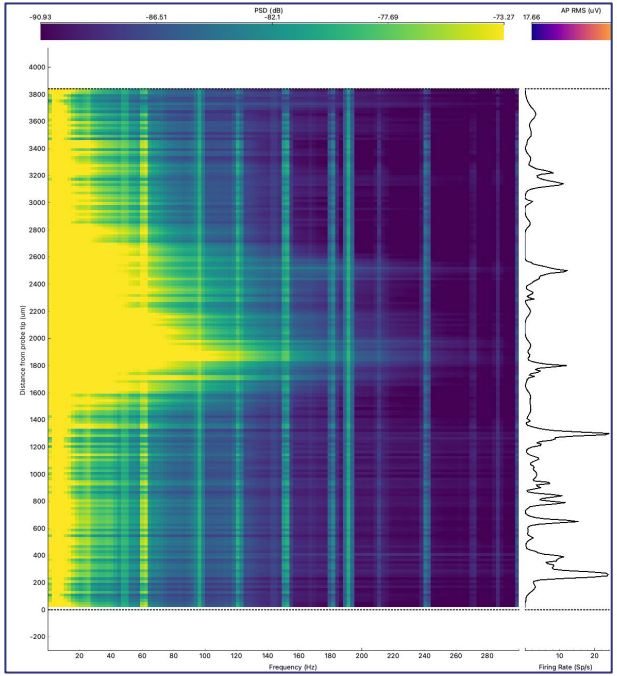
Check whether activity is actually activity



All units

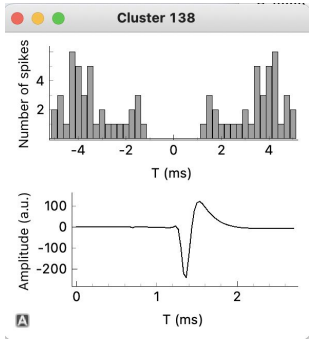


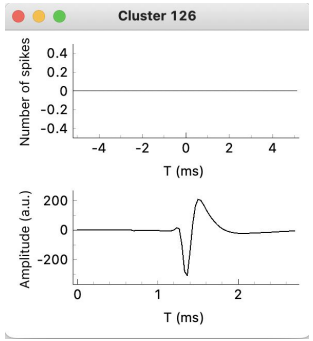
IBL good only

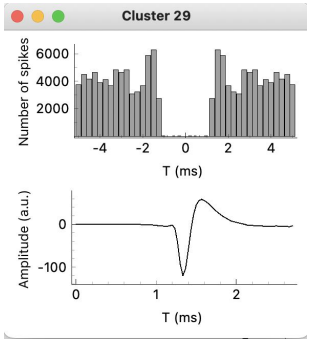


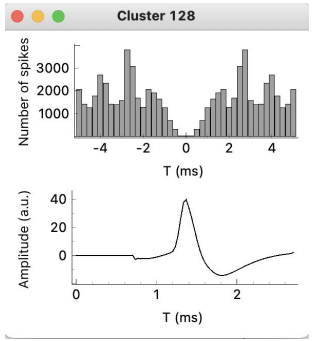
Vertical stripes - electrical noise

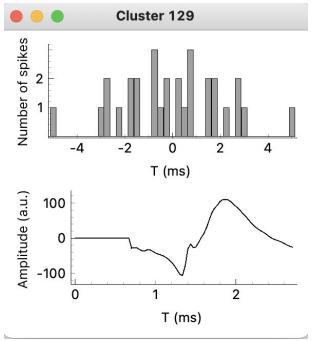
And whether clusters plausibly represent actual units

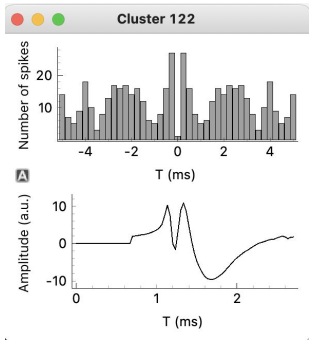


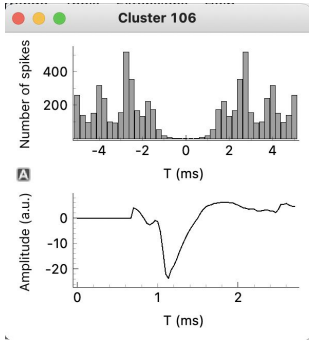


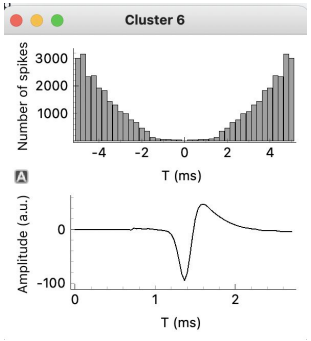


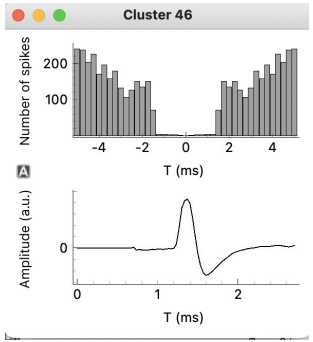


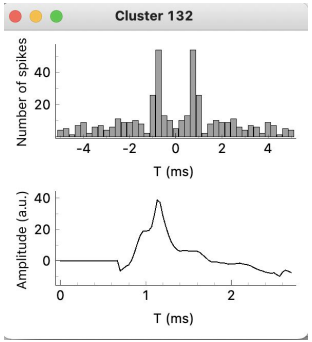




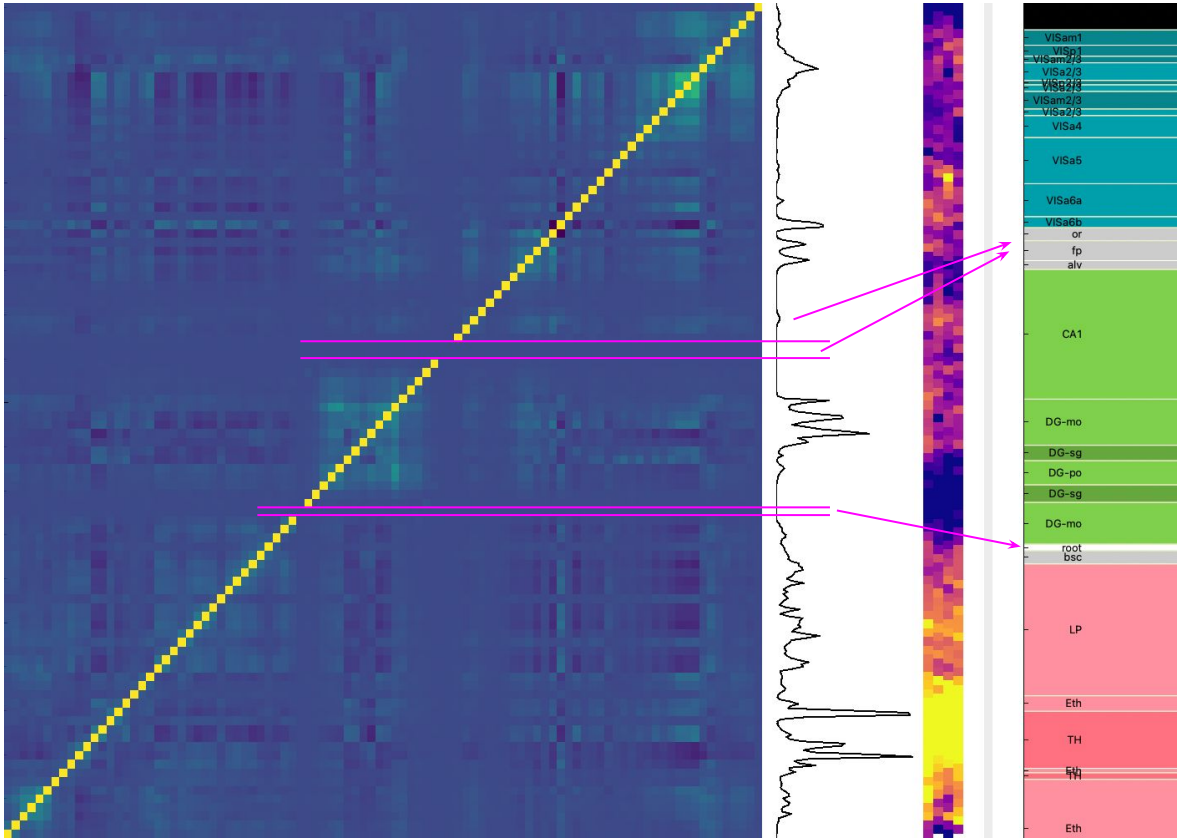






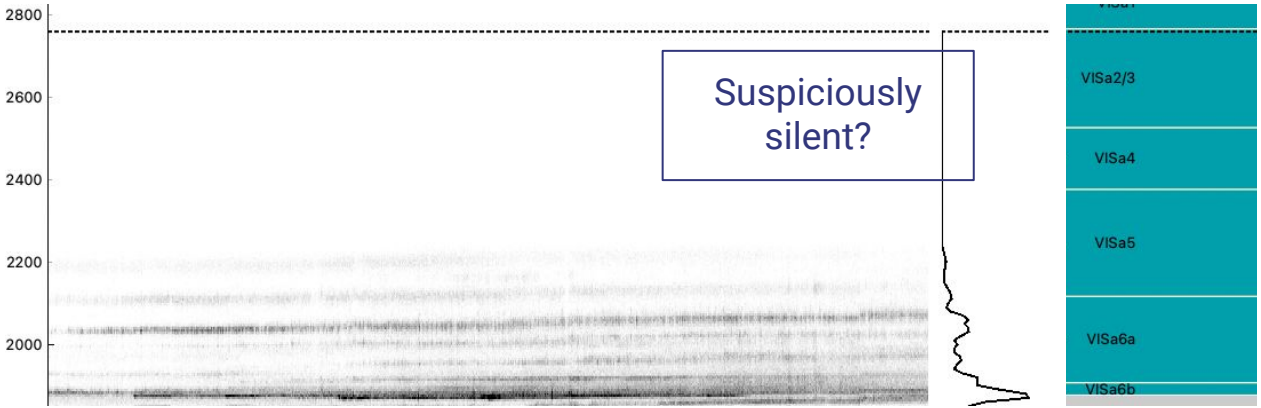


Are the silent bands silent? And how silent is silent?



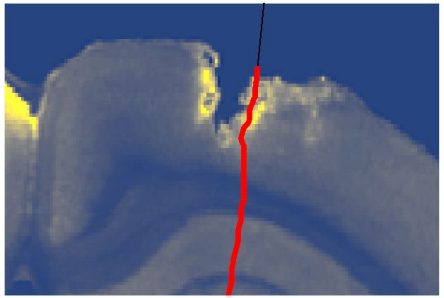
- White matter and other fibre tracts are supposed to be silent - overall → look out for axonal spikes.
- Hard to determine boundaries of silent ares? → check the correlation plot for *negative space*.

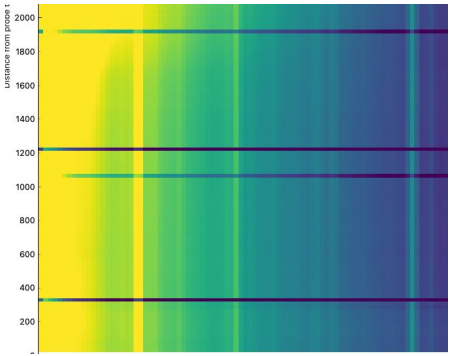
And why is no activity where there should be?



Suspiciously silent?

Tissue damage





Horizontal stripes - flat channels

- The most dorsal visual layers may die out → Tissue damage? Dried out?
- Horizontal stripes may indicate flat channels.

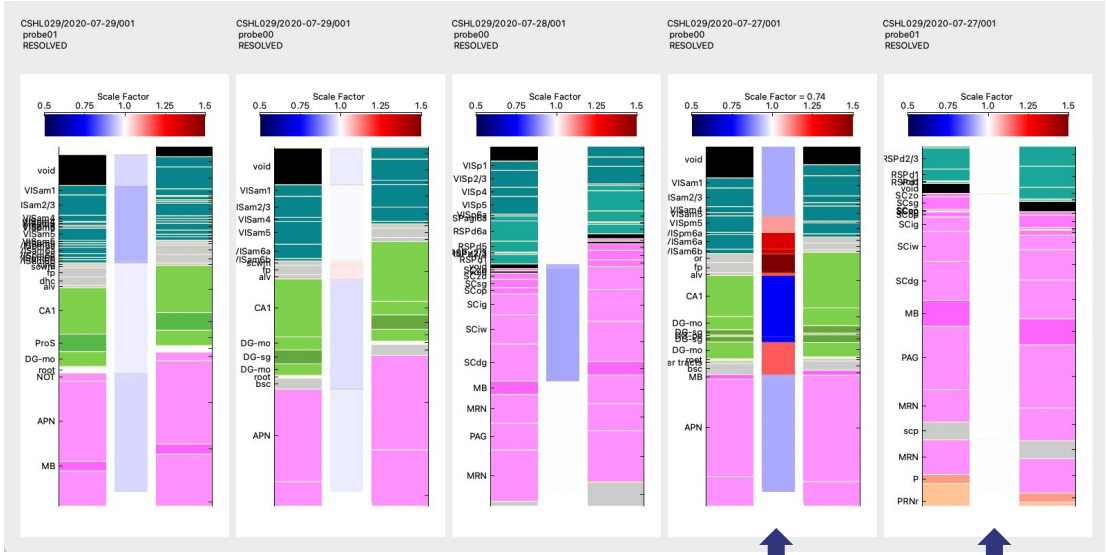
The likelihood of hitting the center

- Similar trajectories may still lead the probe to run through different subnuclei;
- or mingle along the edge.
- There’s more periphery as there is center.

⇒ Can reveal quite **different features** in the “same” region.

⇒ Be sensitive to the **periphery**: Don’t expect features to fall into the center of a nucleus or its boundary to neighbouring region.

A brain is a brain - the art of scaling



Ooops…

- Brain regions may be expressed differently across animals.
- Within one animal, however, size of brain regions is likely relative to physical size.

⇒ Unlikely to have compression & stretching in one animal.

⇒ Across sessions of this animal, scaling factor should be somewhat similar.

Thank you

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Pic by Robin Haak, Netherlands Institute for Neuroscience (NiN), Amsterdam, NL; 2023

References & Sources

IBL et al. (2021) Standardized and reproducible measurement of decision-making in mice. eLife 63711

IBL et al. (2022a) Reproducibility of in-vivo electrophysiological measurements in mice. bioRxiv 491042

International Brain Laboratory (2022b). Spike sorting pipeline for the International Brain Laboratory. figshare. Online resource. https://doi.org/10.6084/m9.figshare.19705522.v3

International Brain Laboratory (2022c). Data release - Brainwide map - Q4 2022. figshare. Preprint. https://doi.org/10.6084/m9.figshare.21400815.v6

International Brain Laboratory (2022d). Appendix 6: IBL protocol for registering the electrode location using LASAGNA. figshare. Online resource. https://doi.org/10.6084/m9.figshare.19698166.v2

International Brain Laboratory (2022e). Appendix 2: IBL protocol for electrophysiology recording using Neuropixels probe. figshare. Online resource. https://doi.org/10.6084/m9.figshare.19697896.v2

IBL session selector: https://viz.internationalbrainlab.org/app

IBL alignment software GUI: https://github.com/int-brain-lab/iblapps/blob/master/atlaselectrophysiology/ephys_atlas_gui.py

IBL alignment software GUI, user guide: https://github.com/int-brain-lab/iblapps/wiki