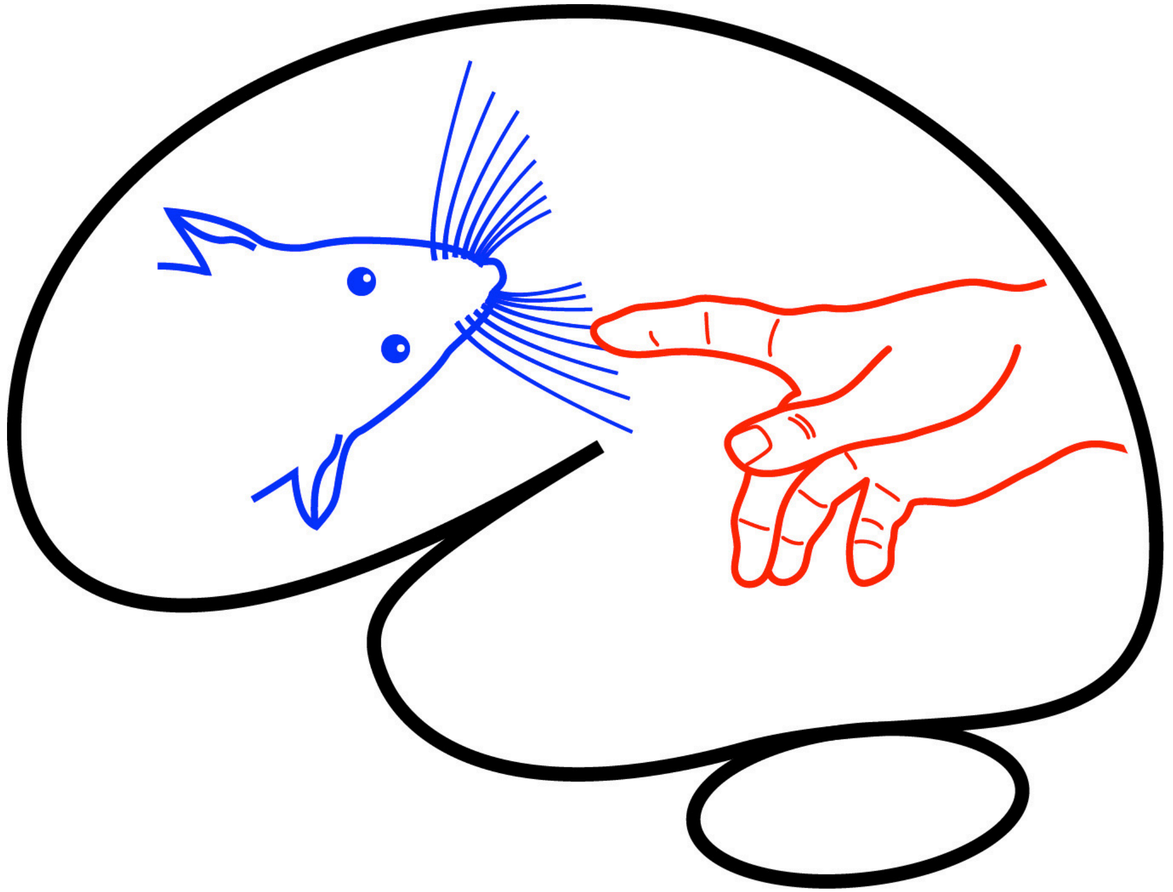


Scientific project design in integrative neurosciences

Carl Petersen

Today's presentation

1. Course overview
2. Introduction to neuronal circuits for sensory decision-making
3. Introduction to experimental methodology
4. Introduction to data formats and analysis methods

Summary

BIO493 - "Scientific project design in integrative neurosciences"

Prof. Carl Petersen, Myriam Hamon and Tâm Nguyen

In this course, students will investigate causal neuronal network mechanisms underlying sensory-guided decision-making in mice. Students will analyse published data to develop integrative neuroscience research projects including the design of new experiments to test specific falsifiable predictions.

Students will work together in small groups to write a joint ~20 page report to be handed in by the end of the semester, which will count for two-thirds of the final grade.

Each individual student will also give a ~15 minute oral presentation during the semester, which will count for one-third of the final grade.

Weeks 1 and 2

Week 1 – 10th September 2025 – 8:15-10:00 – CE 1100

08:15-09:00 - Carl Petersen will present :
i) Course overview
ii) An introduction to neuronal circuits and sensory-guided decision-making in mice.

09:15-10:00 - Carl Petersen will present :
iii) An introduction to experimental methodology including mouse behavior, optogenetics and extracellular recordings of action potential firing using *Neuropixels* multisite electrodes.
iv) An introduction to data formats and analysis methods.

Week 2 – 17th September 2025 – 8:15-10:00 – CE 1100

08:15-09:00 - Carl Petersen will present :
AIND-VBN dataset : A dataset from the Allen Institute for Neural Dynamics (Seattle) – "*Visual Behavior Neuropixels*"

09:15-10:00 - Carl Petersen will present :
EPFL-CDN dataset : A dataset from EPFL Laboratory of Sensory Processing – "*Context Delay Neuropixels*"

Weeks 3 and 4

Week 3 – 24th September 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Group formation and first discussions in groups - "*Ideas for your research project*"
6 groups of 4 students – 3 groups study AIND-VBN and 3 groups study EPFL-CDN

Week 4 – 1st October 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
First round of presentations by each group (6 x 15 minutes) – "*What is the high-level overview of your group's research project?*" - **Graded (1/3 of final grade)**

Weeks 5 and 6

Week 5 – 8th October 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Second discussions in groups - "*Define the specific focus of your research project*"

Week 6 – 15th October 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Second round of presentations by each group (6 x 15 minutes) – "*Final plan - What is the specific goal of your group's research project?*" - **Graded (1/3 of final grade)**

Holiday week

Weeks 7 to 10

Week 7 – 29th October 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Coding & discussion

Week 8 – 5th November 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Third round of presentations by each group (6 x 15 minutes) – "*Update on your group's research project*" - **Graded (1/3 of final grade)**

Week 9 – 12th November 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Coding & discussion

Week 10 – 19th November 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Fourth and final round of presentations by each group (6 x 15 minutes) – "*Final oral presentation of your group's research project*" - **Graded (1/3 of final grade)**

Summary

Week 11 – 26th November 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Coding & discussion

Week 12 – 3rd December 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Coding & discussion
Submit first draft report – Before Friday 5th December at 17:00, send draft to carl.petersen@epfl.ch, myriam.hamon@epfl.ch, and tam.nguyen@epfl.ch.

Week 13 – 10th December 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Feedback on draft report to each group

Week 14 – 17th December 2025 – 8:15-10:00 – CE 1100

08:15-10:00 - Carl Petersen, Myriam Hamon and Tâm Nguyen
Final discussion
Submit final report – Before Friday 19th December at 17:00, send final report and Python code to Carl Petersen (carl.petersen@epfl.ch) – **Graded (2/3 of final grade)**

Report

Report format *(20-pages max)*:

P. 1	**Cover page** – project title & authors *(1-page max)*
P. 2	**Summary** – summary of research proposal *(1-page max)*
P. 3-7	**Introduction** – background knowledge *(5-page max)*
P. 8-12	**Preliminary data** – your analyses of dataset *(5-page max)*
P. 13-17	**Research plan** – new experiments / analyses / models *(5-page max)*
P. 18	**Impact** *(1-page max) – how will your project advance the field?*
P. 19-20	**References** *(2-page max)*

Your report should include figures and references within the 20-page limit.

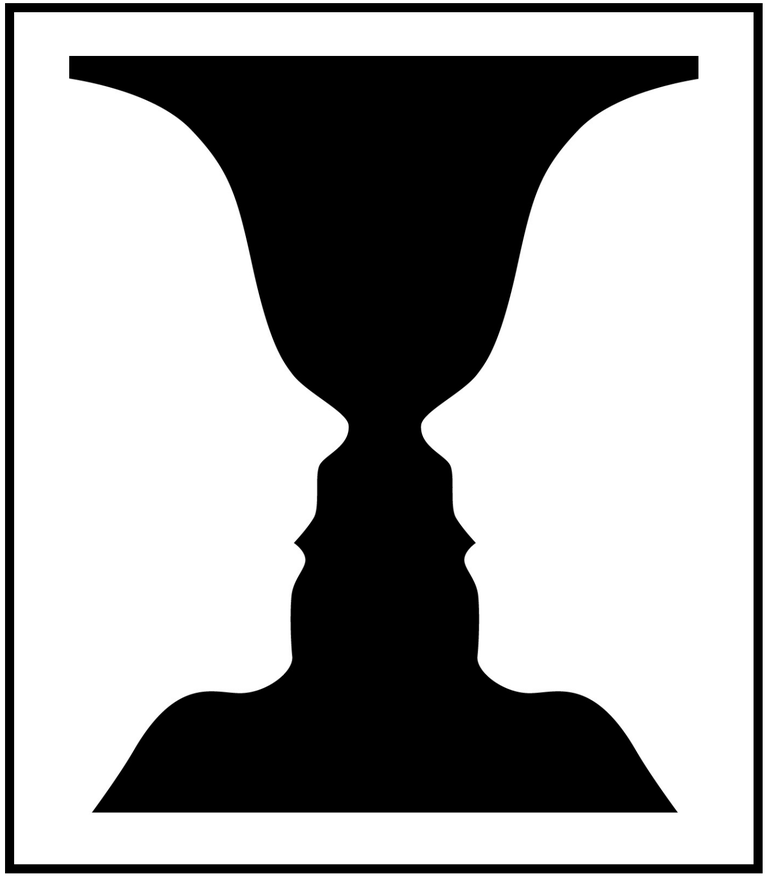
References should follow this format: FamilyName Initials, FamilyName Initials, … (Year) Title. Journal Volume: Pages. DOI with link.
e.g. Esmaeili V, Tamura K, Muscinelli SP, Modirshanechi A, Boscaglia M, Lee AB, Oryshchuk A, Foustoukos G, Liu Y, Crochet S, Gerstner W, Petersen CCH (2021) Rapid suppression and sustained activation of distinct cortical regions for a delayed sensory-triggered motor response. Neuron 109: 2183-2201. doi: 10.1016/j.neuron.2021.05.005

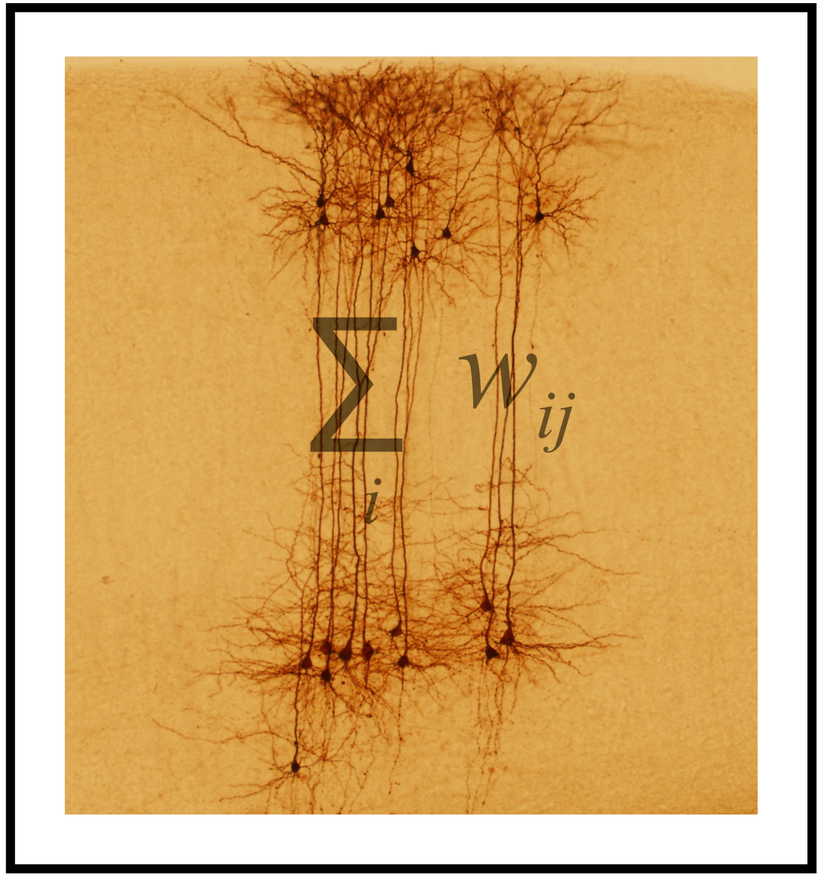
Your report should be accompanied by the Python code you used – include in your email.

Today's presentation

1. Course overview
2. Introduction to neuronal circuits for sensory decision-making
3. Introduction to experimental methodology
4. Introduction to data formats and analysis methods

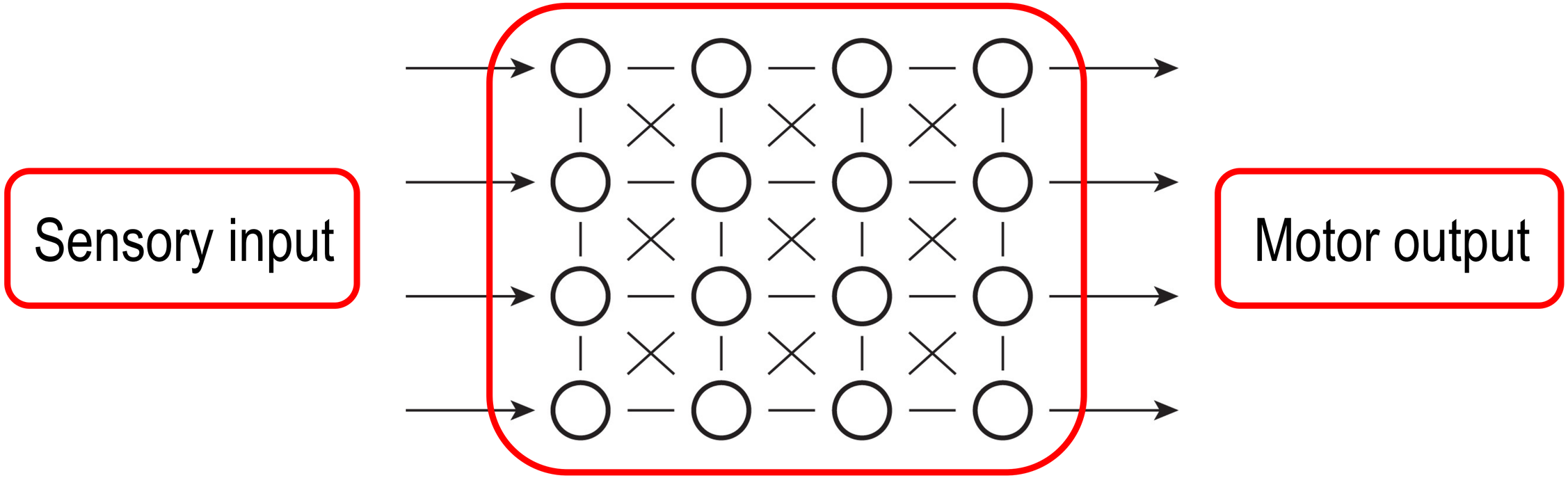
Neuronal mechanisms of sensory perception





Lefort et al., 2009

Sensory perception is subjective



Causal mechanisms

1. Sensory-guided decision-making task
2. **Measure** neuronal activity and correlate with task performance
3. **Manipulate** neuronal activity and correlate with task performance
4. **Model** neuronal activity and correlate with task performance

Today's presentation

1. Course overview
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The mammalian brain

Mouse

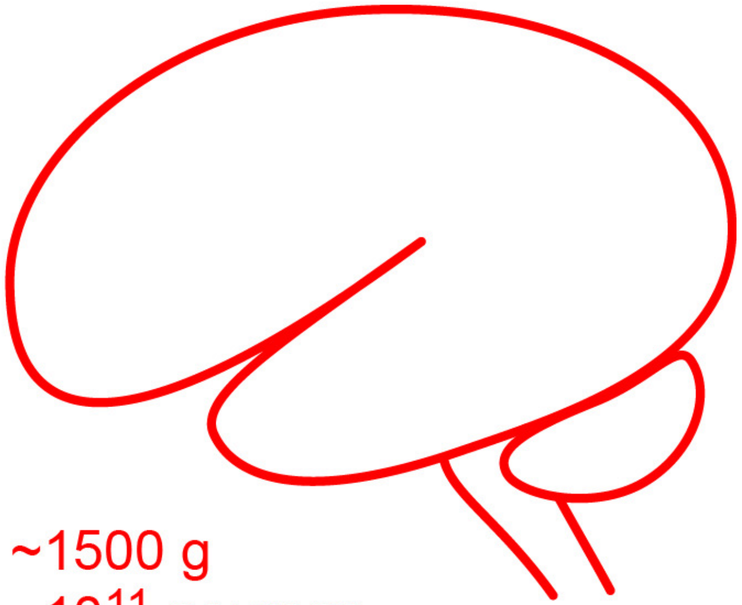
~1 g
~10^8 neurons

5 cm

Macaque

~100 g
~5 x 10^9 neurons

Human



~1500 g
~10^{11} neurons

Mouse genetics

www.ncbi.nlm.nih.gov

www.ncbi.nlm.nih.gov/gene

NCBI Resources How To

Gene: mus musculus gria2

Save search Advanced

Display Settings: Tabular, 20 per page, Sorted by Relevance Send to:

Results: 10

Filters activated: Current only. Clear all to show 10 items.

Name/Gene ID	Description	Location	Aliases
Gria2 ID: 14800	glutamate receptor, ionotropic, AMPA2 (alpha 2) [*Mus musculus* (house mouse)]	Chromosome 3, NC_000069.6 (80682904..80803204, complement)	GluA2, GluR-B, Glur-2, Glur2
Grid2 ID: 14804	glutamate receptor, ionotropic, delta 2 [*Mus musculus* (house mouse)]	Chromosome 6, NC_000072.6 (63256832..64701910)	B230104L07Rik, GluD2, GluRdelta2, Lc, Lc<J>, MMS10-AC, Ms10ac, cpr, ho, nmf408, tpr
Gria1 ID: 14799	glutamate receptor, ionotropic, AMPA1 (alpha 1) [*Mus musculus* (house mouse)]	Chromosome 11, NC_000077.6 (57011571..57330244)	RP23-102H8.1, 2900051M01Rik, Glr-1, Glr1, GluA1, GluR-A, GluRA, Glur-1, Glur1, HIPA1, gluR-K1

NCBI - National Center for Biotechnology Information

www.jax.org

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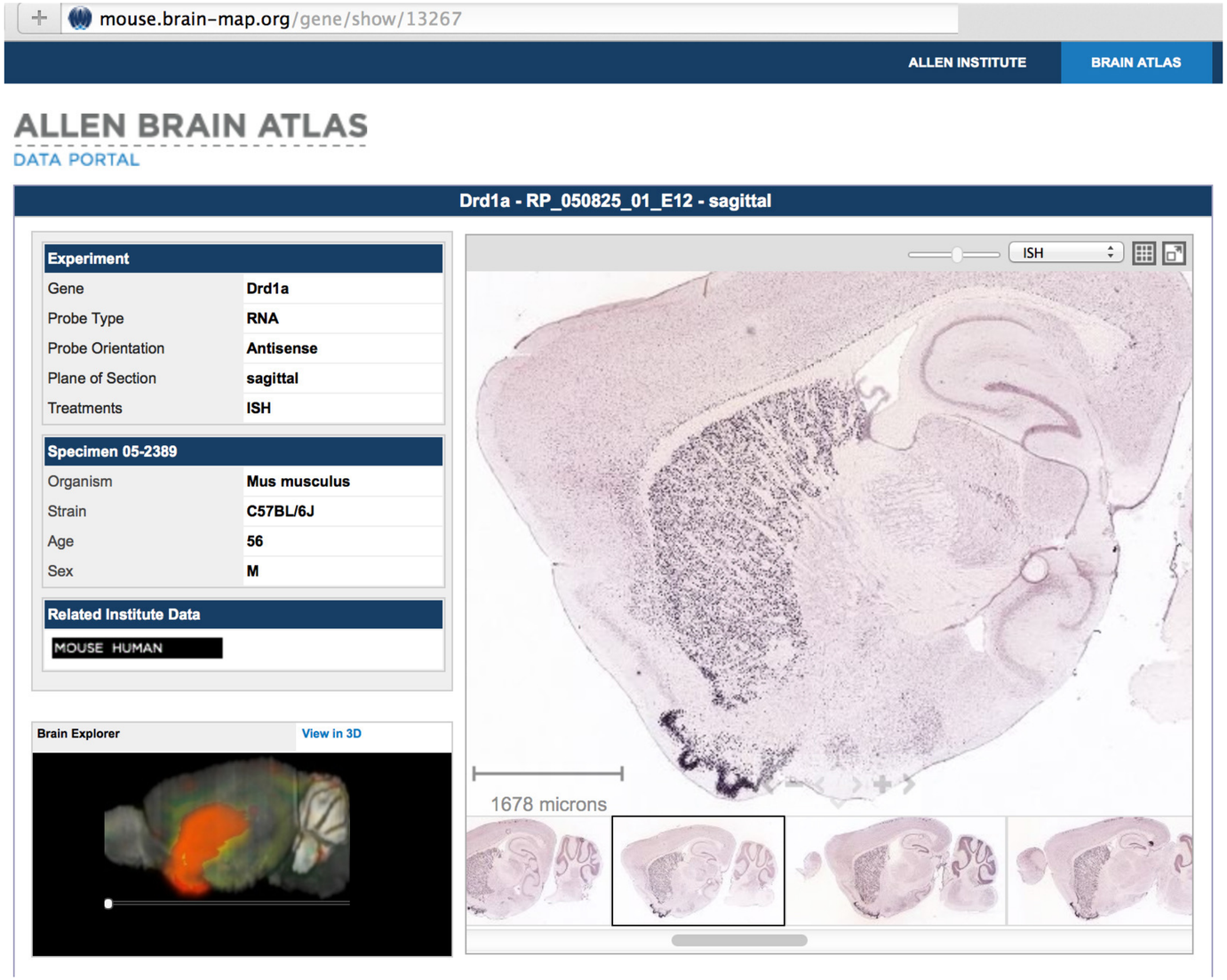
Gene-expression maps of the mouse brain



www.brain-map.org

Allen Brain Atlas

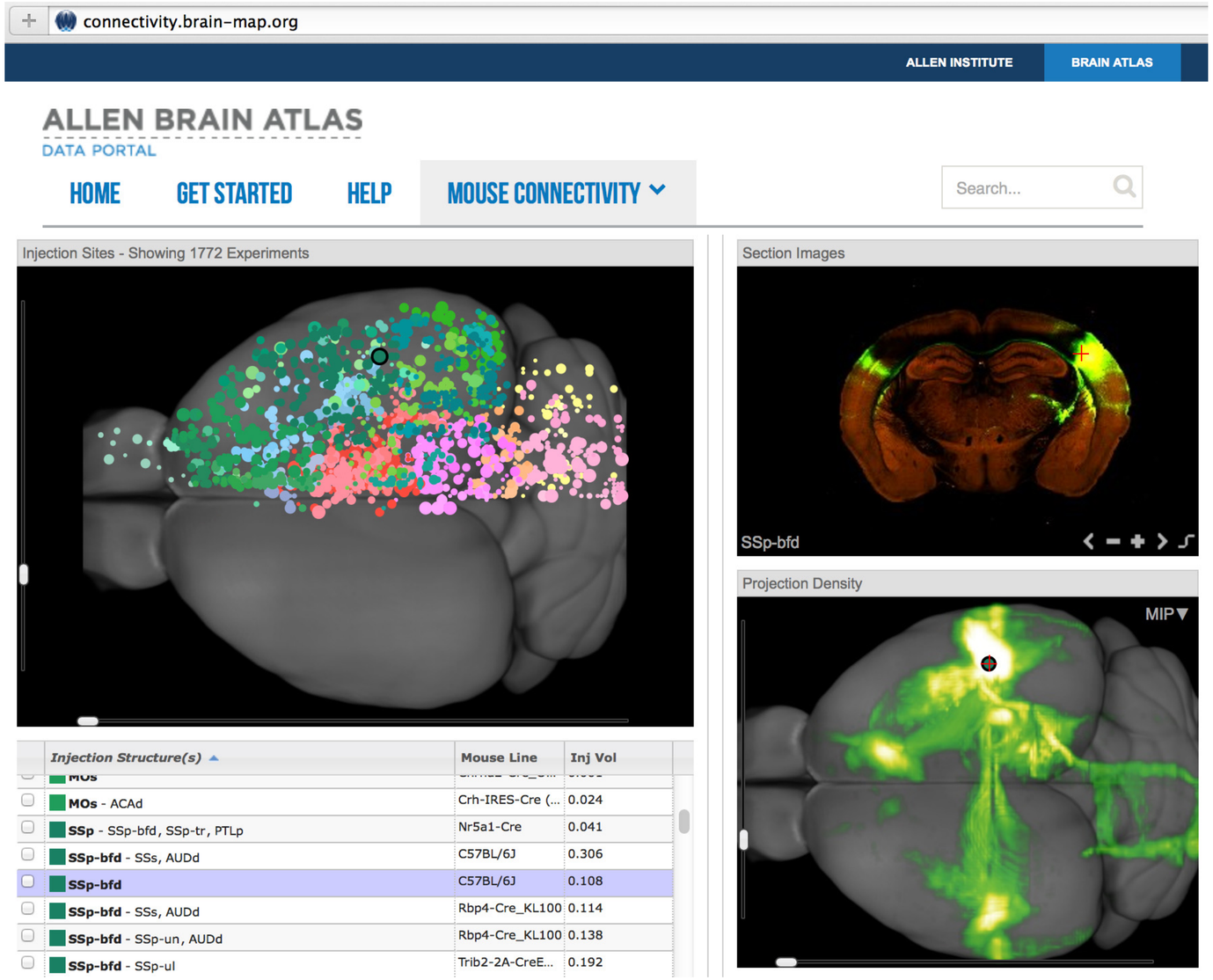
Complete gene expression atlas of the mouse brain.

Genetically-defined cell-types

Transgenic or knock-in of GFP, Cre-recombinase, …
Cre-LoxP system for precise genetic manipulation
LoxP = **ATAACTTCGTATA**GCA**TA**CAT**TATACGAAGTTAT**

Highly-specific genetic manipulation in well-defined cell-types.
Essential for causal and mechanistic understanding of brain function.
Cre-LoxP system is part of a family of recombinases e.g. Flp-FRT

Projection maps of the mouse brain

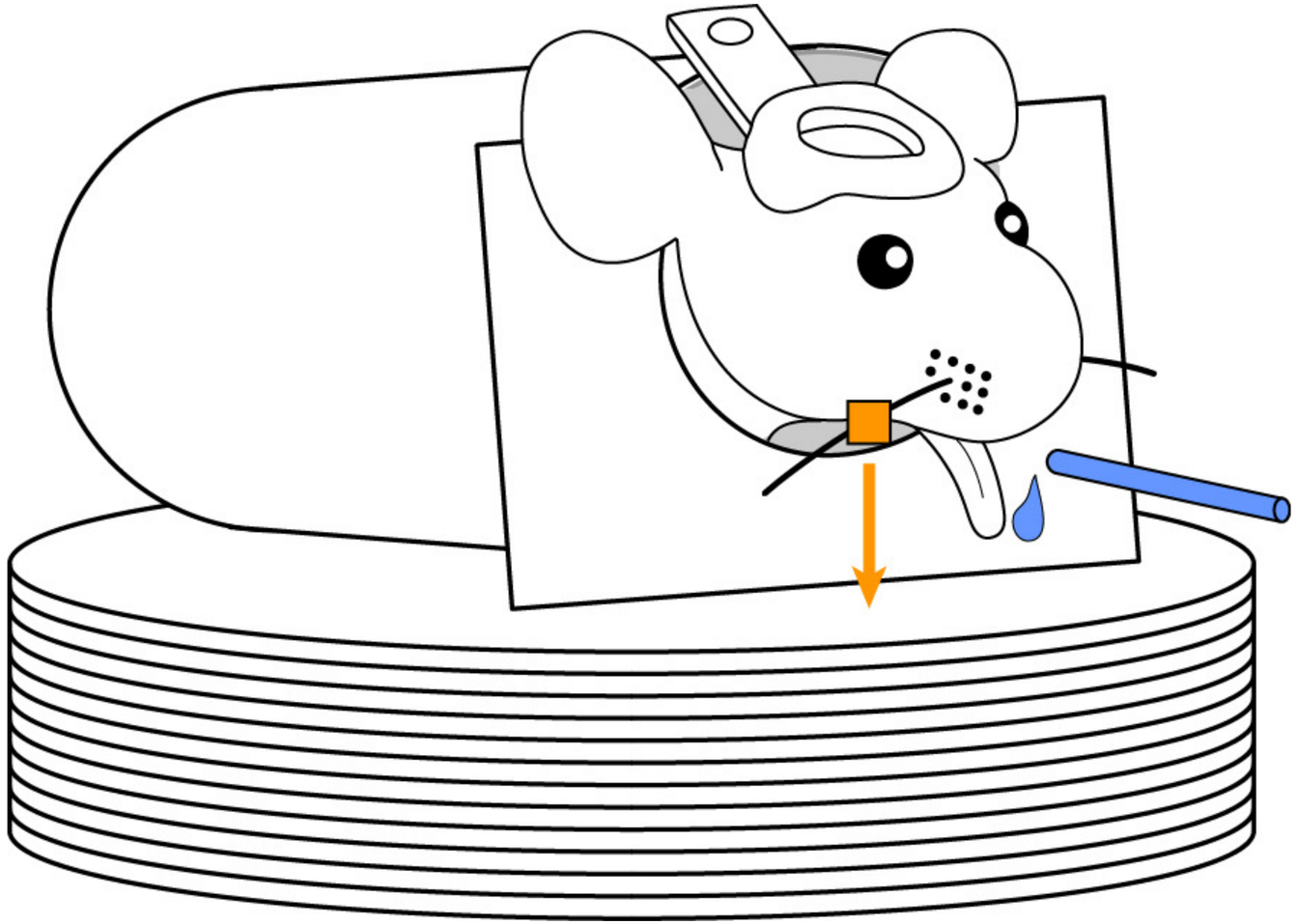


www.brain-map.org

Allen Brain Atlas

Long-range connectivity map of the mouse brain.

Head-restrained mouse behavior



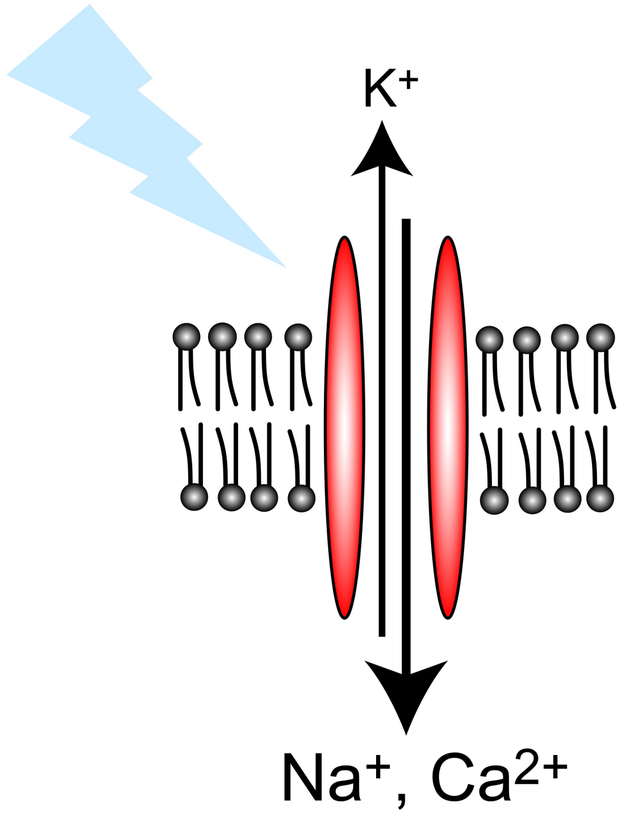
Sachidhanandam, Sreenivasan, Kyriakatos, Kremer & Petersen, 2013

High-speed video

A light-activated cation channel

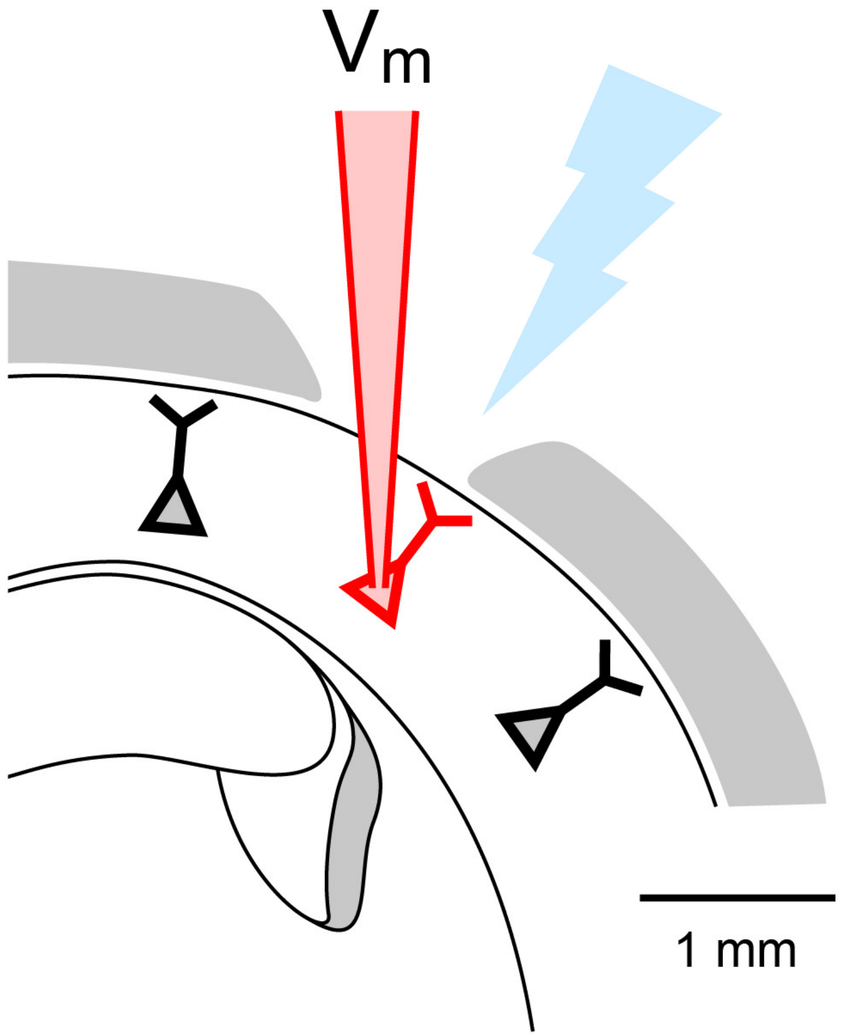
Channelrhodopsin-2 (ChR2) is a light-activated cation channel, cloned from the green algae *Chlamydomonas reinhardtii*.

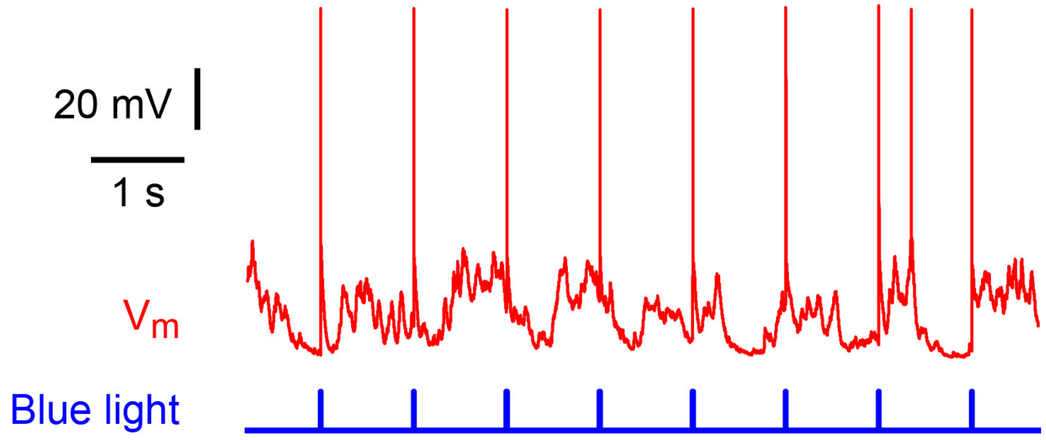
Retinal is bound to ChR2 and changes conformation from all-*trans* to 13-*cis* upon photon absorption.

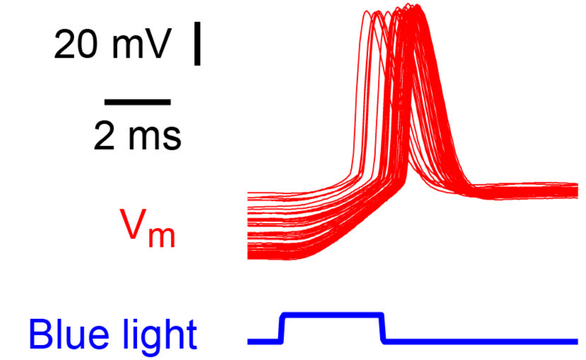


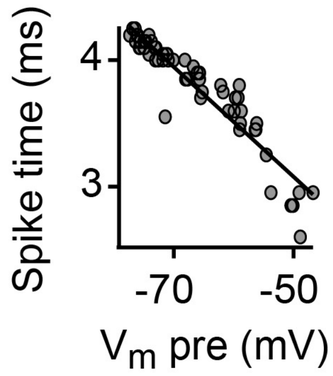
Nagel, Szellas, Huhn, Kateriya, Adeishvili, Berthold, Ollig, Hegemann, Bamberg (2003) *Channelrhodopsin-2, a directly light-gated cation-selective membrane channel.* Proc Natl Acad Sci USA 100: 13940-13945.

Channelrhodopsin-2 *in vivo*



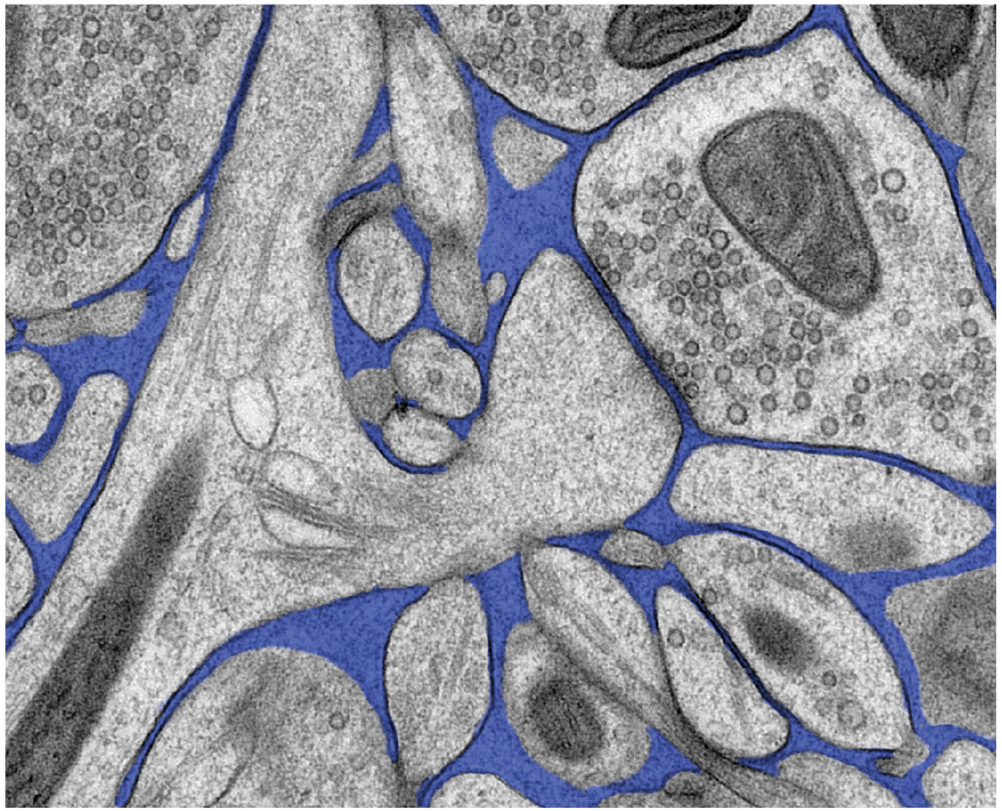




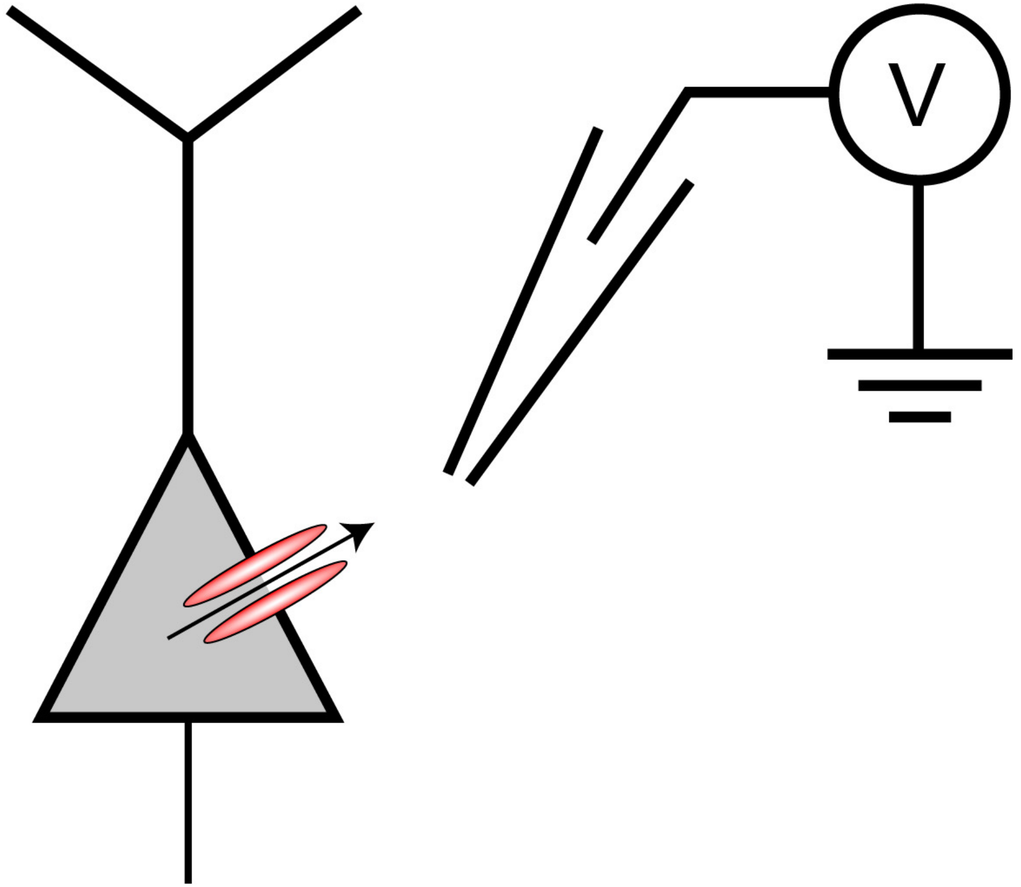


Mateo, Avermann, Gentet, Zhang, Deisseroth and Petersen, 2011

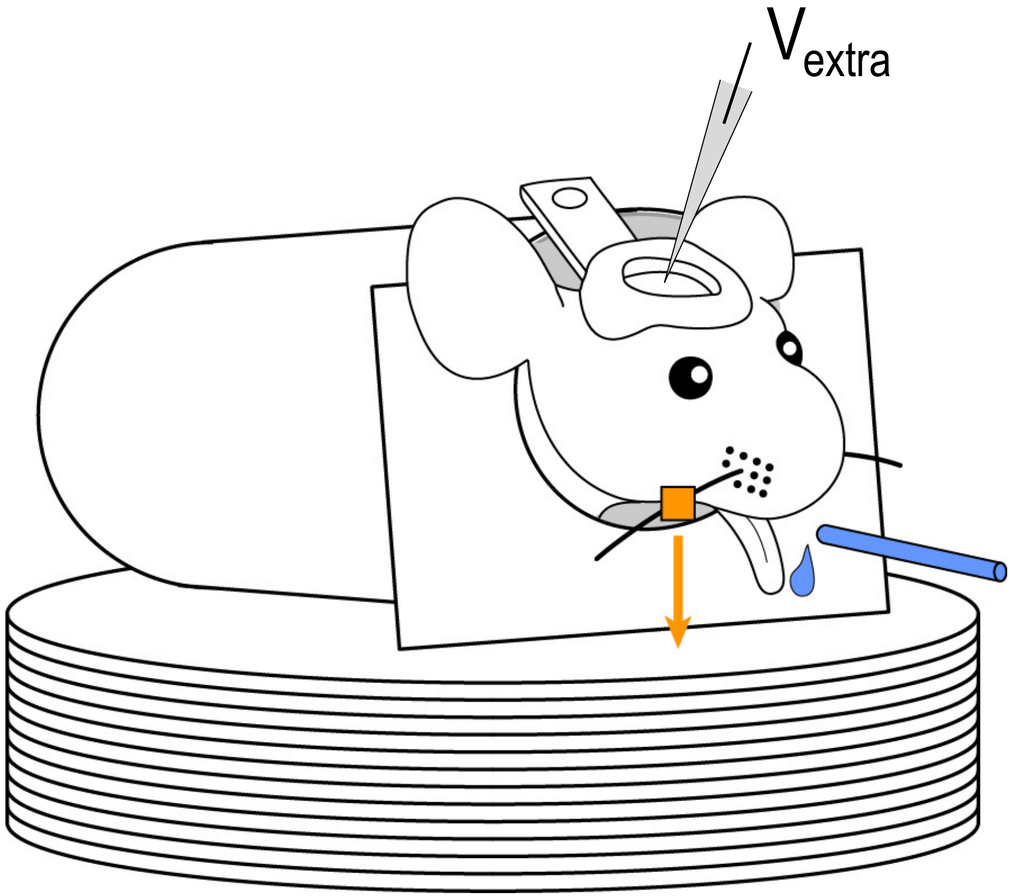
Extracellular potentials



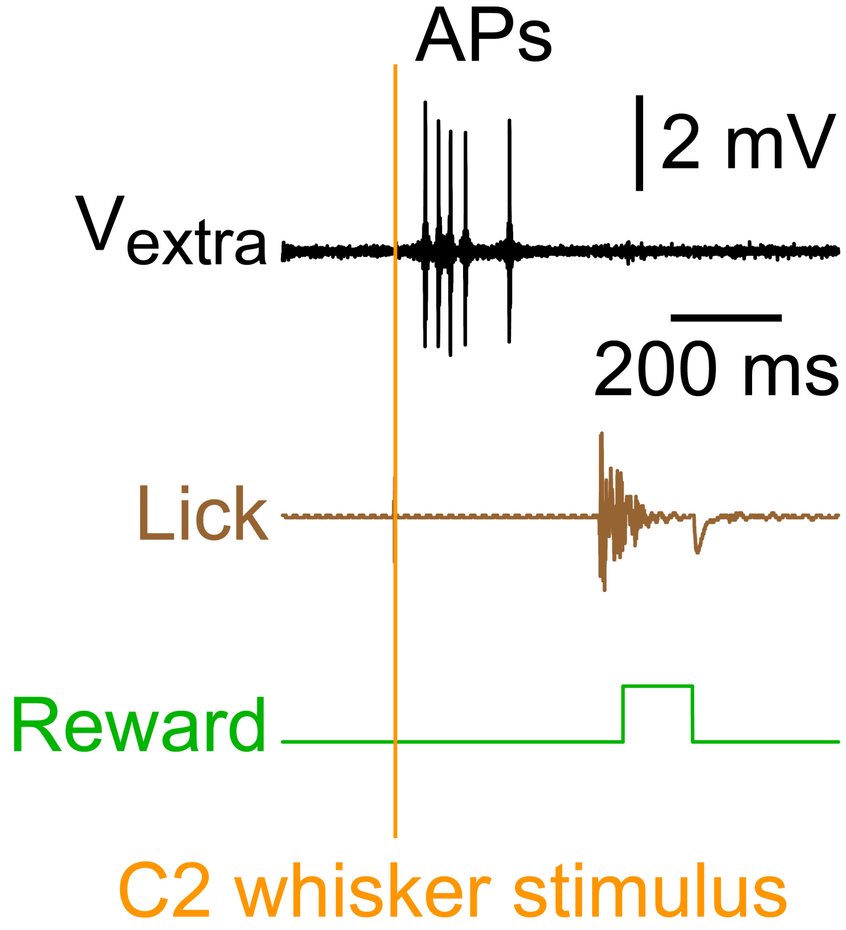
Korogod, Petersen and Knott



Extracellular recording of action potentials

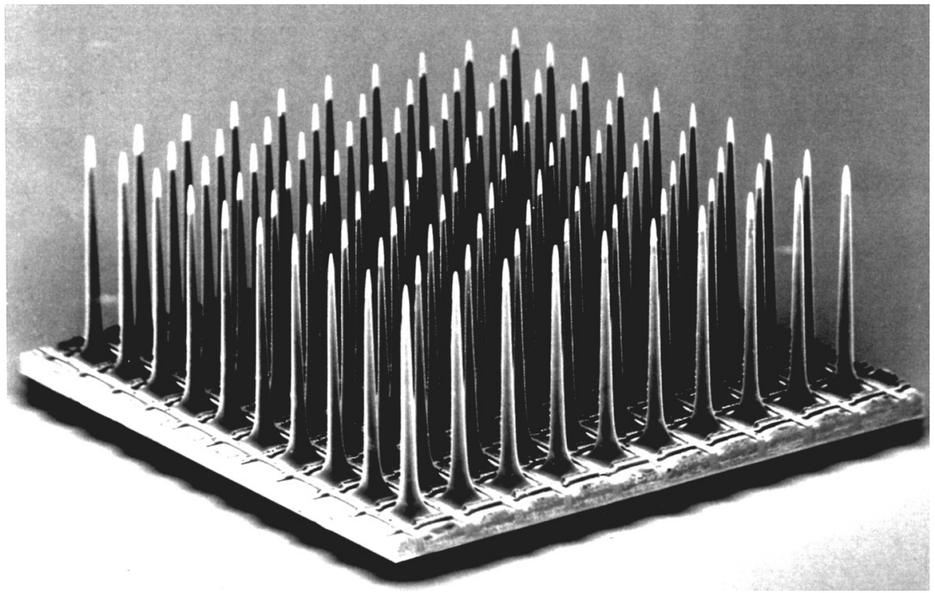


Sachidhanandam, Sreenivasan, Kyriakatos, Kremer & Petersen, 2013



Multichannel extracellular recordings

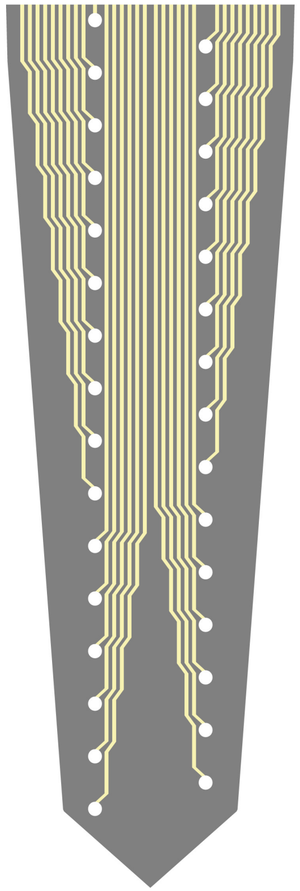
Electrode arrays



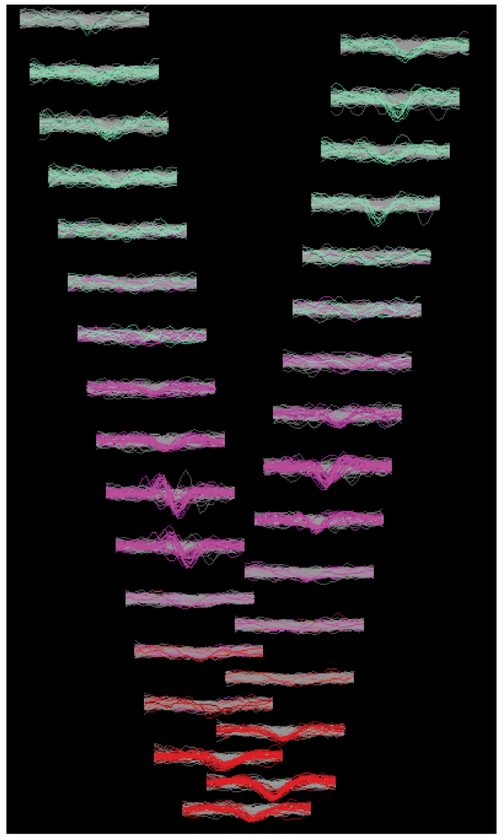
Utah array, Blackrock Microsystems

Hochberg et al., 2012
http://www.youtube.com/watch?v=ogBX18maUiM

Silicon probes



Neuronexus



Lapray and Petersen

Neuropixels probes

EPFL

LETTER

doi:10.1038/nature24636

Fully integrated silicon probes for high-density recording of neural activity

James J. Jun[1]*, Nicholas A. Steinmetz[2,3,4]*, Joshua H. Siegle[5]*, Daniel J. Denman[5]*, Marius Bauza[6,7]*, Brian Barbarits[1]*, Albert K. Lee[1]*, Costas A. Anastassiou[5,8], Alexandru Andrei[9], Çağatay Aydın[10,11], Mladen Barbic[1], Timothy J. Blanche[5,12], Vincent Bonin[9,10,11,13], João Couto[10,11], Barundeb Dutta[9], Sergey L. Gratiy[5], Diego A. Gutnisky[1], Michael Häusser[3,14], Bill Karsh[1], Peter Ledochowitsch[5], Carolina Mora Lopez[9], Catalin Mitelut[5,8], Silke Musa[9], Michael Okun[2,3,15], Marius Pachitariu[2,3], Jan Putzeys[9], P. Dylan Rich[1], Cyrille Rossant[2,3], Wei-lung Sun[1], Karel Svoboda[1], Matteo Carandini[4], Kenneth D. Harris[2,3], Christof Koch[5], John O'Keefe[6,7] & Timothy D. Harris[1]

[1]HHMI Janelia Research Campus, 19700 Helix Drive, Ashburn, Virginia 20147, USA. [2]UCL Institute of Neurology, University College London, London WC1N 3BG, UK. [3]Department of Neuroscience, Physiology and Pharmacology, University College London, London WC1E 6DE, UK. [4]UCL Institute of Ophthalmology, University College London, London EC1V 9EL, UK. [5]Allen Institute for Brain Science, 615 Westlake Avenue North, Seattle, Washington 98109, USA. [6]Department of Cell and Developmental Biology, University College London, London WC1E 6BT, UK. [7]Sainsbury Wellcome Centre, University College London, London W1T 4JG, UK. [8]Department of Neurology, University of British Columbia, Vancouver, British Columbia V6T 2B5, Canada. [9]imec, Kapeldreef 75, 3001 Heverlee, Leuven, Belgium. [10]Neuro-Electronics Research Flanders, Kapeldreef 75, 3001 Leuven, Belgium. [11]KU Leuven, Department of Biology, Naamsestraat 59, 3000 Leuven, Belgium. [12]White Matter LLC, 999 3rd Avenue 700, 98104 Seattle, USA. [13]VIB, 3001 Leuven, Belgium. [14]Wolfson Institute for Biomedical Research, University College London, Gower Street, London WC1E 6BT, UK. [15]Centre for Systems Neuroscience, University of Leicester, Leicester LE1 7QR, UK.
*These authors contributed equally to this work.

Jun *et al.* (2017) Nature 551: 232-236.

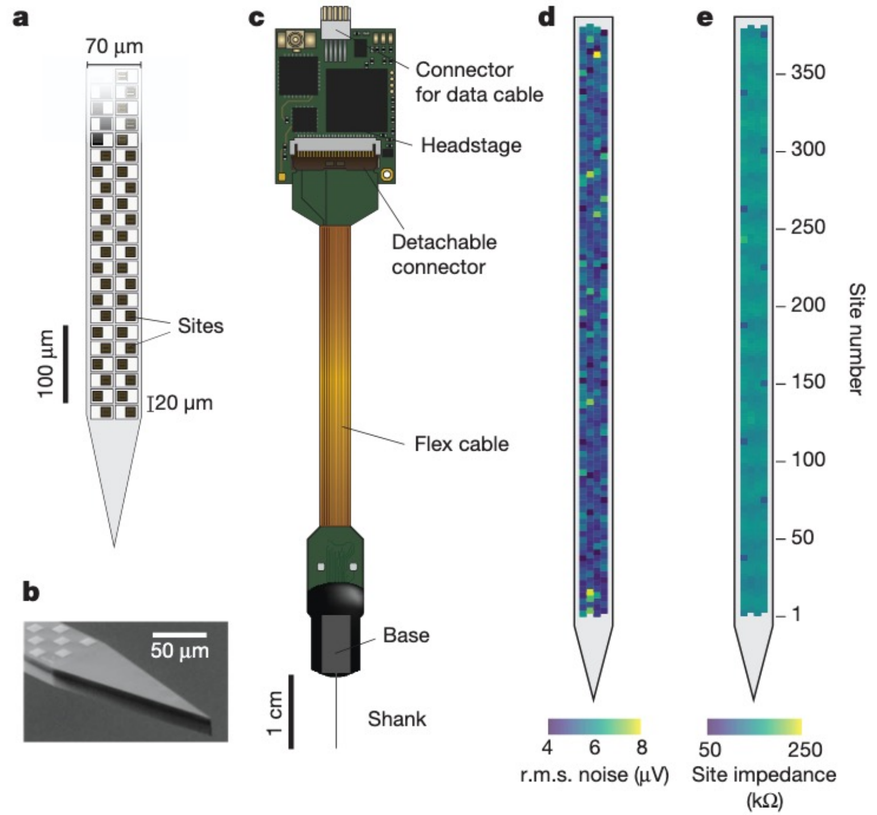


Figure 1 | The Neuropixels probe. a, Illustration of probe tip, showing checkerboard site layout (dark squares). **b**, Scanning electron microscope image of probe tip. **c**, Probe packaging, including flex cable and headstage for bidirectional data transmission. **d**, Example of r.m.s. noise levels of the AP band in saline, for 384 sites (switchable option). Mean ± s.d. = 5.1 ± 0.6 µV. **e**, Typical site impedance in saline, for 384 sites, measured for each site with sinusoidal 1 nA injected currents at 1 kHz (see Methods). Mean ± s.d. = 149 ± 6 kΩ.

Today's presentation

1. Course overview
2. Introduction to neuronal circuits for sensory decision-making
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Quantifying behavior - *DeepLabCut*

Mathis et al. (2018) Nature Neuroscience 21: 1281-1289.

nature neuroscience

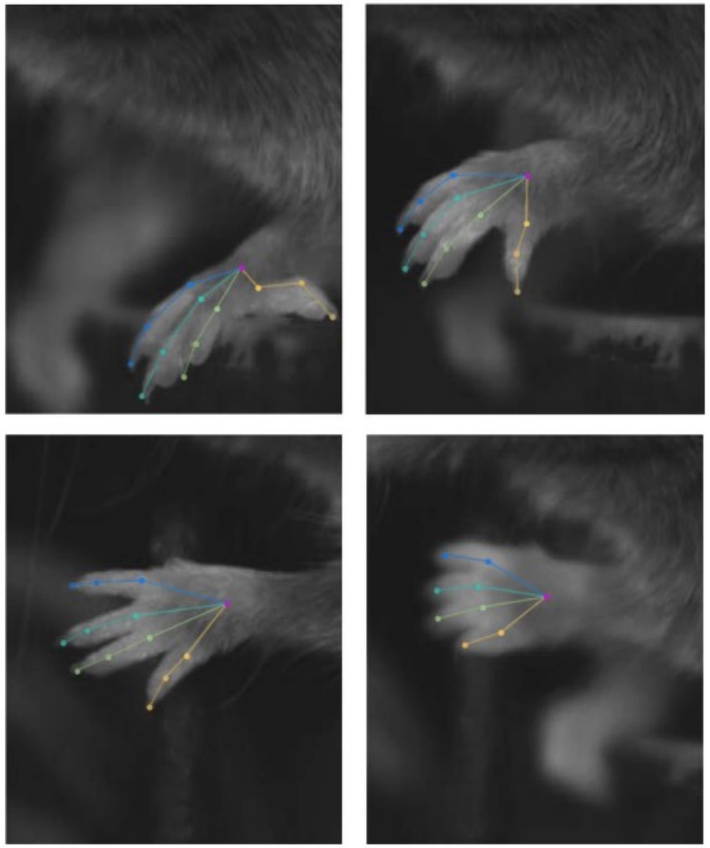
TECHNICAL REPORT

https://doi.org/10.1038/s41593-018-0209-y

DeepLabCut: markerless pose estimation of user-defined body parts with deep learning

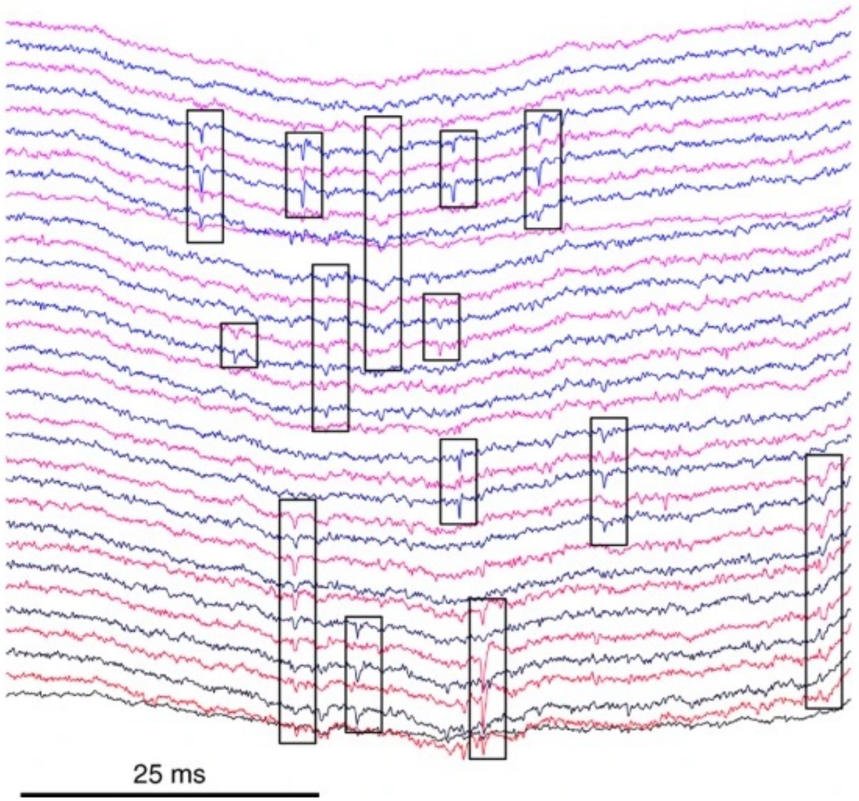
Alexander Mathis[1,2], Pranav Mamidanna[1], Kevin M. Cury[3], Taiga Abe[3], Venkatesh N. Murthy[2], Mackenzie Weygandt Mathis[1,4,8*] and Matthias Bethge[1,5,6,7,8]

Quantifying behavior is crucial for many applications in neuroscience. Videography provides easy methods for the observation and recording of animal behavior in diverse settings, yet extracting particular aspects of a behavior for further analysis can be highly time consuming. In motor control studies, humans or other animals are often marked with reflective markers to assist with computer-based tracking, but markers are intrusive, and the number and location of the markers must be determined a priori. Here we present an efficient method for markerless pose estimation based on transfer learning with deep neural networks that achieves excellent results with minimal training data. We demonstrate the versatility of this framework by tracking various body parts in multiple species across a broad collection of behaviors. Remarkably, even when only a small number of frames are labeled (~200), the algorithm achieves excellent tracking performance on test frames that is comparable to human accuracy.



Analysing high-density extracellular recordings

Raw voltage -> Action potentials



github.com/jamesjun/Kilosort2

README | Code of conduct | GPL-2.0 license

Kilosort2: automated spike sorting with drift tracking and template matching on GPUs

Welcome to Kilosort2, a MATLAB package for spike sorting electrophysiological data up to 1024 channels. In many cases, and especially for Neuropixels probes, the automated output of Kilosort2 requires minimal manual curation.

There is currently no preprint or paper for Kilosort2, so please read the wiki to find out how it works, and especially the drift correction section. Kilosort2 improves on Kilosort primarily by employing drift correction, which changes the templates continuously as a function of drift. Drift correction does not depend on a particular probe geometry, but denser spacing of sites generally helps to better track neurons, especially if the probe movement is large. Kilosort2 has been primarily developed on awake, head-fixed recordings from Neuropixels 1.0 data, but has also been tested in a few other configurations. To get a sense of how probe drift affects spike sorting, check out our "eMouse" simulation here and its wiki page.

To aid in setting up a Kilosort2 run on your own probe configuration, we have developed a graphical user interface where filepaths can be set and data loaded and visually inspected, to make sure Kilosort2 sees it correctly. The picture above is another GUI visualization: it shows the templates detected by Kilosort2 over a 60ms interval from a Neuropixels recording. The final output of Kilosort2 can be visualized and curated in the Phy GUI, which must be installed separately (we recommend the development version). Since Phy is in Python, you will also need the npy-matlab package.

NWB – Neurodata without borders

NWB v1 - Teeters et al. (2015) Neuron 88: 629-634
NWB v2 - Rübel et al. (2022) eLife 11: e78362

eLife TOOLS AND RESOURCES

The Neurodata Without Borders ecosystem for neurophysiological data science

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NWB – Neurodata without borders

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Abstract The neurophysiology of cells and tissues are monitored electrophysiologically and optically in diverse experiments and species, ranging from flies to humans. Understanding the brain requires integration of data across this diversity, and thus these data must be findable, accessible, interoperable, and reusable (FAIR). This requires a standard language for data and metadata that can coevolve with neuroscience. We describe design and implementation principles for a language for neurophysiology data. Our open-source software (Neurodata Without Borders, NWB) defines and modularizes the interdependent, yet separable, components of a data language. We demonstrate NWB's impact through unified description of neurophysiology data across diverse modalities and species. NWB exists in an ecosystem, which includes data management, analysis, visualization, and archive tools. Thus, the NWB data language enables reproduction, interchange, and reuse of diverse neurophysiology data. More broadly, the design principles of NWB are generally applicable to enhance discovery across biology through data FAIRness.

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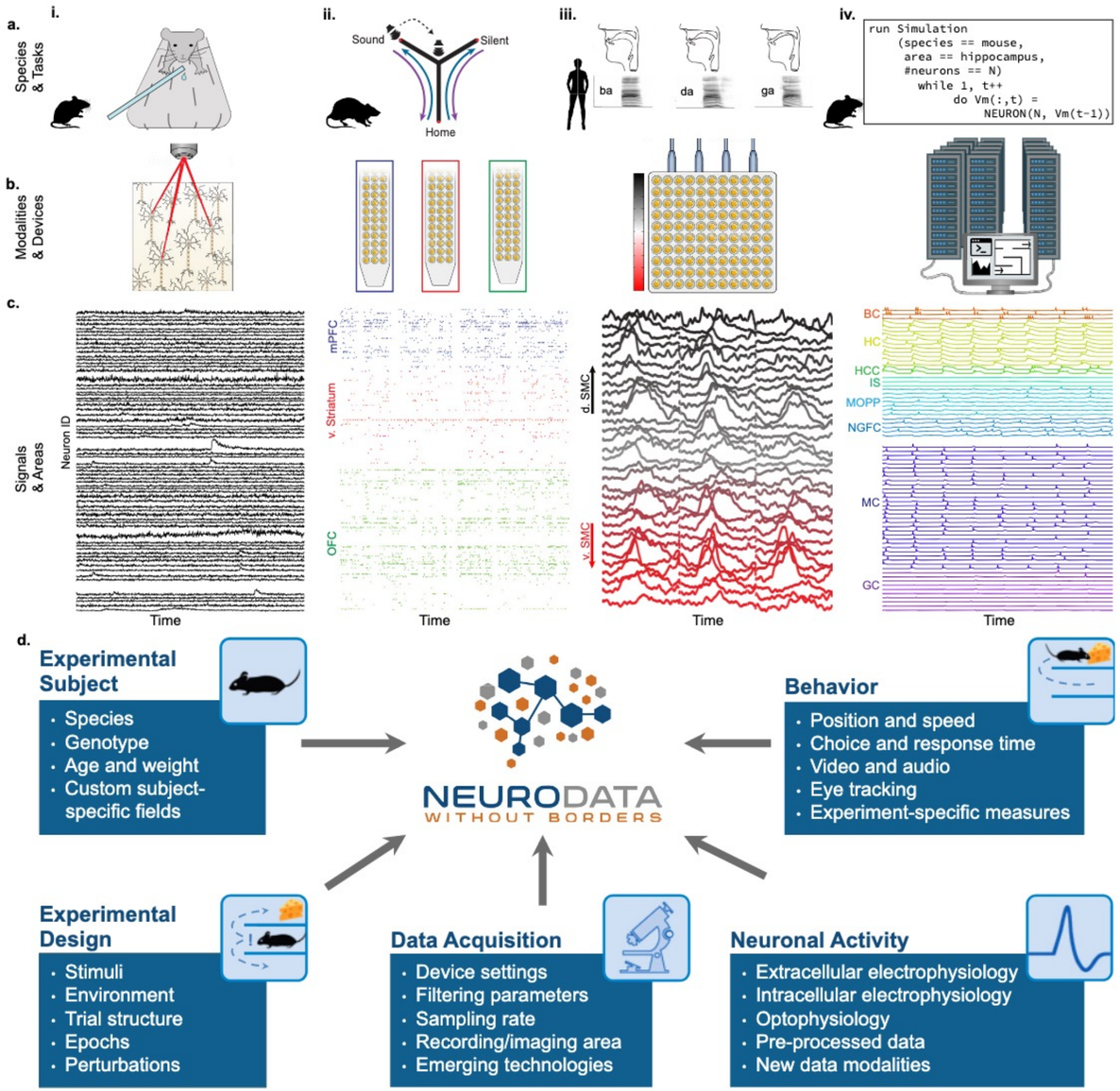

Data repositories

Zenodo

https://zenodo.org/

CERN

DANDI

https://dandiarchive.org/