OpenScope 2022-2023 Annual Report

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U24 NS113646

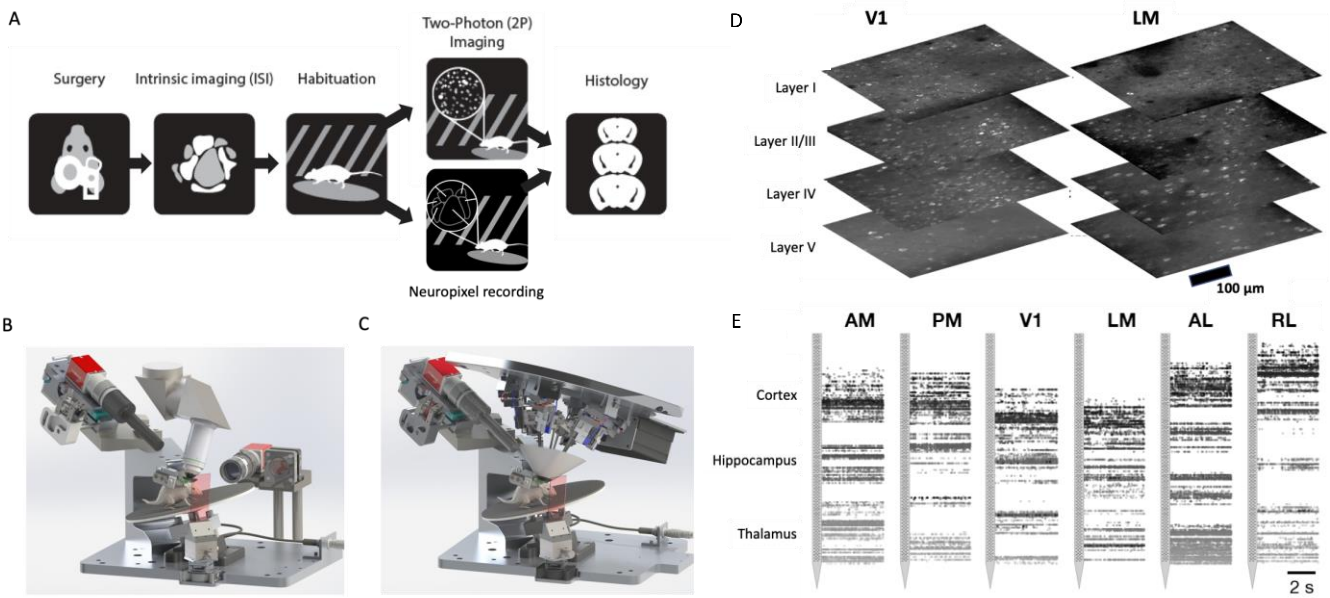
About OpenScope

OpenScope

OpenScope opens the Allen Brain Observatory pipeline to the community—enabling theoretical, computational, and experimental scientists to test sophisticated hypotheses on brain function in a program analogous to astronomical observatories that survey the night sky.

Once a year, OpenScope invites external scientists to propose experiments to be run on the Allen Institute pipeline. These proposals are competitively reviewed for scientific merit and feasibility by a panel of leading experts from the international community. If selected, the proposed experiments are performed with the Allen Institute's verified, reproducible, and open protocols for *in vivo* Neuropixels electrophysiology or two-photon calcium imaging. Any resulting data is made freely available to the selected applicants and to the broader community. The goal is to lower barriers to testing new hypotheses about brain function, bring new computational and theoretical talents to the field, and enhance the reproducibility of results in brain research—thereby accelerating progress toward an integrated understanding of neural activity in health and disease.

The OpenScope Program is supported by the National Institute Of Neurological Disorders And Stroke of the National Institutes of Health under Award Number U24NS113646. (This content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health)



Two End-to-End data pipelines

The OpenScope platform tests novel hypotheses on brain function using an established data collection pipeline. The platform utilizes cutting-edge behavioral training, Neuropixels recordings, and two-photon calcium imaging. The resulting data is curated, standardized, and disseminated with open standards and is eventually released to the public after a one-year embargo.

The OpenScope program provides the community access to:

- End-to-end standardized experimental platform including brain surgery, animal training, neuronal recordings (*in vivo* Neuropixels electrophysiology or two-photon calcium imaging), and brain reconstruction.
- Animal behavior training to test novel hypotheses of brain function.
- Data standardization and sharing via NWB files in the cloud.
- Datasets that are cross-referenced through shared standards and data access, allowing further meta-analysis by the community.
- Dissemination of results as selected teams analyze and submit their outcomes to bioRxiv and peer-reviewed journals.

Selection process

A double-blinded selection process

We established a two-stage selection process under the guidance of the OpenScope Scientific Steering Group. Applicants first submit a 2-page Letter Of Intent (LOI) that is screened for feasibility by internal Allen Institute reviewers. If there are more than 15 feasible proposed proposals, the LOIs are scored and ranked for scientific merit by external reviewers. The top-scored (up to 18) feasible LOIs are then invited to submit 6-page full proposals, which are again scored by blinded internal and external scientific reviewers.

The top 6-7 projects are discussed by the Scientific Steering Group, where the committee considers overarching programmatic goals and portfolio balance to make the final selection. The external reviewers include neuroscientists from across the community, and the entire process is blinded.

In July 2022, we posted our Request for Proposals (RFP) detailing the types of projects allowed, the application format, and upcoming due dates. For this application cycle, we received 11 LOIs in early September 2022. The entire selection process (submission, reviews, and private communications) was managed online via a secured platform (https://www.submittable.com).

Nine teams were invited to submit full proposals, and one did not move forward as they were not feasible for the listed capabilities in the RFP. On Nov 22nd, we received 8 full proposals that were distributed across 6 external reviewers who kindly volunteered to help this community effort. All reviewers signed Confidentiality Agreements and were blinded to the applicants' identity. The top-scored 7 proposals were sent forward to the OpenScope Scientific Steering Group along with the reviewer ranking and notes. The selected 3 projects for 2023 were approved and selected on January 31st by the Scientific Steering Committee.

Projects Recommended for Award in 2022-2023

Neuropixels project 1:

Vision2Hippocampus

Chinmay Purandare, Postdoctoral Scholar UCSF, Krishna Choudhary Postdoctoral Scholar (former) UCLA, Siddharth Jhamale PhD Student UCLA US, Mayank Mehta Full Professor UCLA US

Neuropixels project 2:

TemporalBarcode

Pamela Reinagel: Associate Professor UCSD

Two-photon project 1:

SequenceLearning

Michael Berry Associate Professor Princeton University

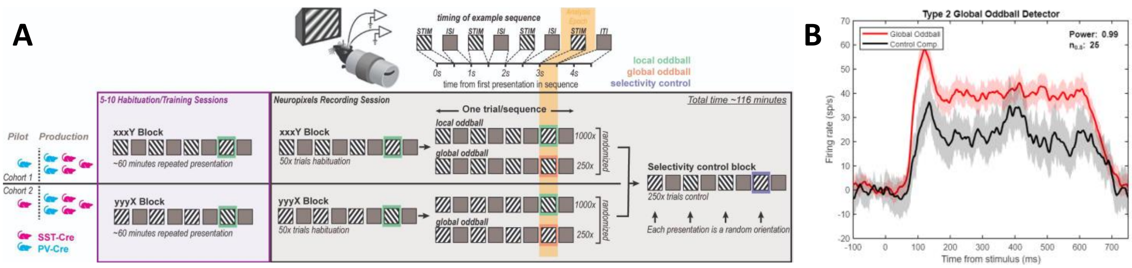
Non-selected teams' identities and projects remain blinded and confidential. Applications included teams from North America (7) and Europe (4) and included applicants from both the theoretical and experimental neuroscience community.

Scientific outcomes

Preliminary scientific highlights from 2022-3 selected projects

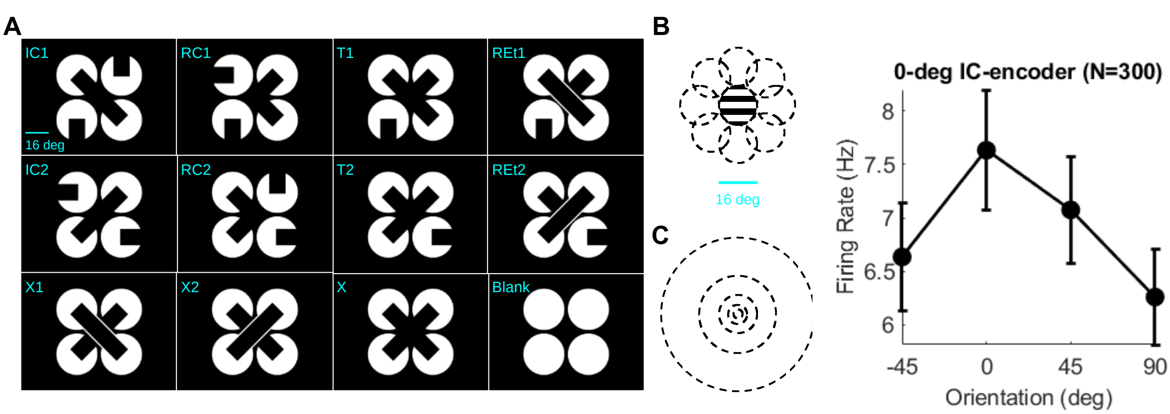
The following are single figure snapshots from all 3 previous projects. It is to be noted that data collection for these projects started and completed in 2022 so some of these results could very much mature and change over the year. These figure are meant to illustrate the start of an extensive data analysis effort by the analysis teams.

Neuropixels project 1:
Neural Circuitry Underlying Detection of Local and Global Prediction Errors



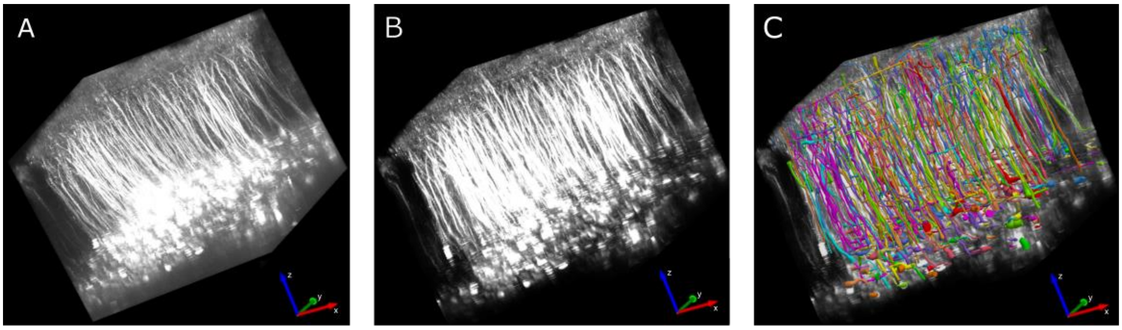
The GlobalLocalOddball project is interested in comparing two types of error responses in the thalamo-cortical network. They hypothesize that a local oddball (involving a stimulus with a short scale spatio-temporal structure) will recruit local cortical circuits, contrary to a global oddball (involving longer distance spatio-temporal structures) will recruit the cortical hierarchy more broadly. **A.** Experimental design of the visual stimuli for the OpenScope GlobalLocal Oddball project (Neuropixel 1). **B**. Analysis of stimuli-evoked responses in OpenScope datasets collected in 2022. A marked response to Global Oddballs can be noted on this analysis compared to the control group.

Neuropixels project 2:
Utilizing Illusory Contours to Elucidate the Neural Mechanism of Binding



The Illusion project aim to test how distant visual stimuli form connected neuronal representations. They use optical illusion as a proxy to trigger on or off these representations. **A**. Experimental design for the visual stimuli for the OpenScope Illusion project (Neuropixel 2). The stimulus set is composed of Illusory contours (ICs) created by two opposing complementary cut circles. In addition, it contains control stimuli to measure the response to complementary combinations of circles and non illusory contours (Ret and X) as well as blank stimuli. **B**. In part of the session, we present windowed gratings of different sizes (**C**) to measure the response of cells to different orientations. **D.** Based on this experimental design, and using datasets that we collected in 2022, the project team was able to confirm the presence of illusory contour responses in our recordings in mice. A subset of the cells (N=300) significantly responded to horizontal ICs. Interestingly, the orientation selectivity of these cells on average matched the illusory contour direction.

Two-photon project 1:
Predictive Learning and Somato-dendritic Coupling



The DendriticCoupling project aims to test whether somatic and dendritic compartments of the same pyramidal cell could play different roles in computing sensory error signals. To that end, we collect high-definition cortical stacks that enable the morphological reconstruction of pyramidal processes. **A.** Raw high-resolution in vivo 2-photon calcium imaging z-stack from mouse Visp. **B.** Combined z-stack after denoising with DeepInterpolation and processing. **C.** Preliminary tracing of pyramidal neurons in z-stack using Neurolucida 360. These reconstruction will be used to match the activity of somatic and dendritic compartments across the layer I and the somatic layer.

Publications and peer-reviewed posters linked to OpenScope projects

- **Next-generation brain observatories**. Koch, Christof; Svoboda, Karel; Bernard, Amy; Basso, Michele A; Churchland, Anne K; Fairhall, Adrienne L; Groblewski, Peter A; Lecoq, Jérôme A; Mainen, Zachary F; Mathis, Mackenzie W, Neuron, 110, 22, 3661-3666, 2022
- **L2/3 and L5 pyramidal neuron somata and apical dendrites exhibit distinct responses to unexpected violations of visual flow**. Gillon et al., COSYNE 2020
- **Learning from unexpected events in the neocortical microcircuit**, Pina, Gillon et al., COSYNE 2021
- **Differential encoding of temporal context and expectation across the visual hierarchy**, Wyrick et al., COSYNE 2022
- **Learning from unexpected events in the neocortical microcircuit**, Gillon et al. bioRxiv 2021
- **Parallel inference of hierarchical latent dynamics in two-photon calcium imaging of neuronal populations**, Prince et al., bioRxiv 2021
- **Measuring Stimulus-Evoked Neurophysiological Differentiation in Distinct Populations of Neurons in Mouse Visual Cortex**, Mayner et al., eNeuro 2021

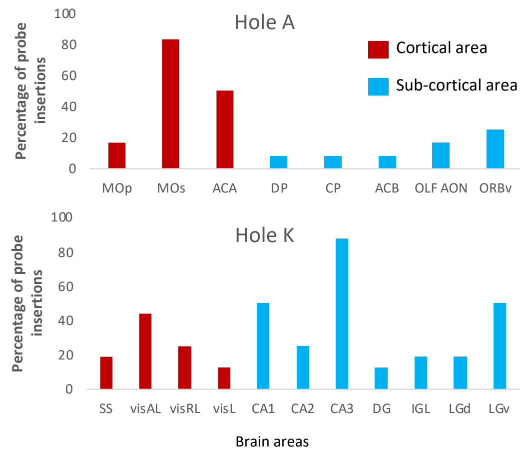
Ongoing developments

A

B

Hole	# insertions
A	12
B	8
C	14
D	11
E	16
F	14
G	13
H	15
I	3
J	4
K	16
L	8
M	15
N	13
O	12
P	7

C



Quantification of Neuropixels targeting using the newer full dorsal implant. **A.** Top view of the new 3D printed dorsal implant design with pre-drilled holes. Each hole was assigned a unique letter. **B.** We performed a number of experiments across all holes in A. Each number represent the number of times a probe was inserted. **C.** For holes A and K, we plotted the percentage of insertions that reached a given brain areas under the hole. Both cortical (red) and sub-cortical areas (blue) were identified for each hole. It is to be noted that a given insertion will go across multiple areas at the same time.

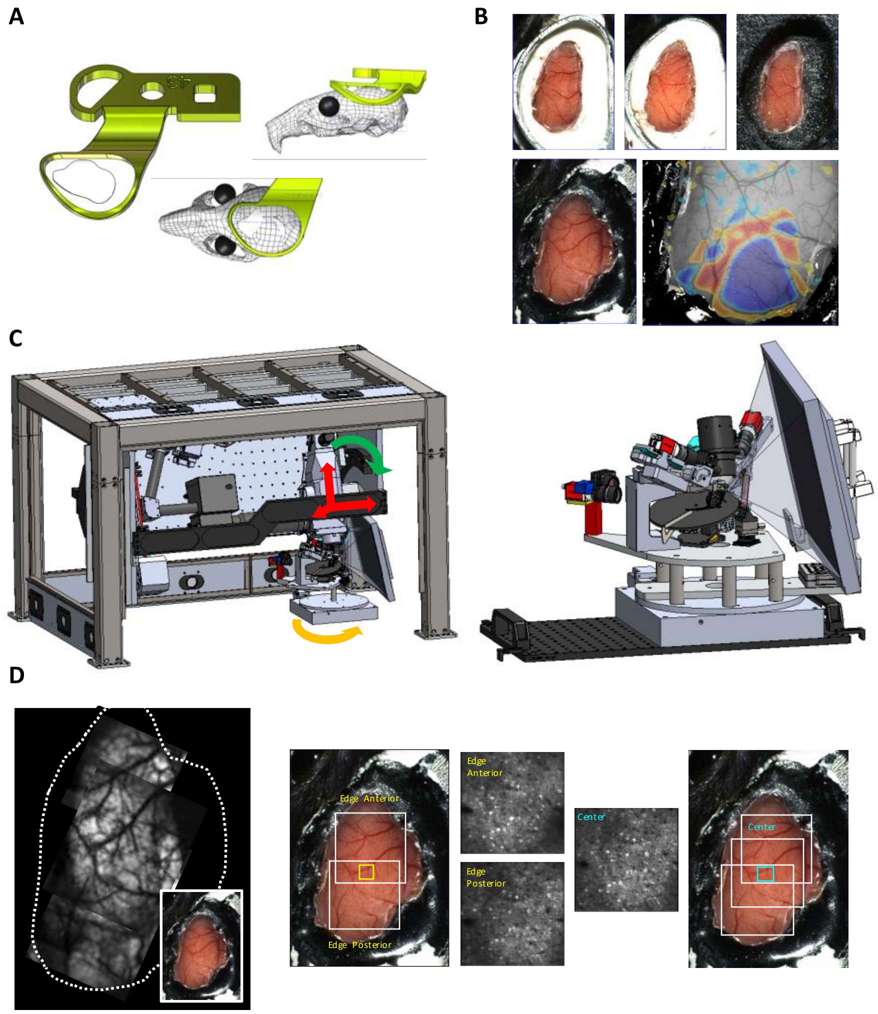
Ephys Surgical developments

For electrophysiological recordings, we aimed to offer a more extensive set of neuronal targets (beyond the existing visual brain area targets) for the second application cycle (opened in 2022-2023). In 2021, we developed a 3D printed plastic implant that replaces the entire section of the mouse skull over the left hemisphere. Pre-determined holes can be placed in the plastic to allow the targeting of specific brain-areas. This procedure was surgically validated in 2021 and pilot Neuropixels recordings demonstrated that we could target new brain areas with success. In 2022, we scaled implementation of this preparation (see Figure 2 A, B) and are now performing this surgical preparation routinely. This allowed us to offer the expanded targeting capabilities to the second OpenScope RFP.

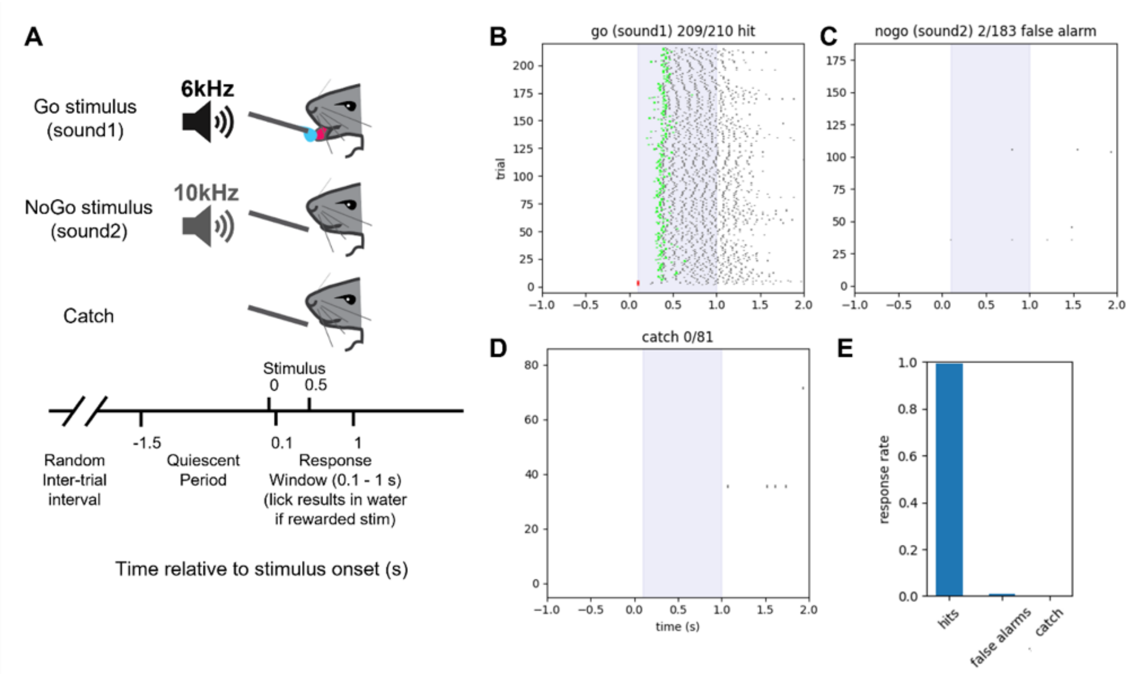
Per our goals, we quantified the targeting efficiency for positioning individual probes in a subset of holes, both for cortical and sub-cortical targets (see Figure). Cortical areas are more reliably targeted compared to sub-cortical areas, depending on the overall size of the brain area of interest. The figure illustrates that we can readily starts recording from larger brain areas both cortical and sub-corticals. We expect our targeting precision to improve over the years.

Ophys Surgical developments

In 2022, we continued new surgical and hardware developments on the two-photon platform, with the goal of testing the performance of multiple variables under our two-photon imaging microscope (see Figure). We also redesigned our head plate to be compatible with our recording hardware and extensively modified our two-photon instrument to have sufficient degrees of freedoms to accommodate the large range of imaging positions now enabled under a full hemispheric imaging implant. We are still planning to deploy this capability in the next application call, per our initial timeline.

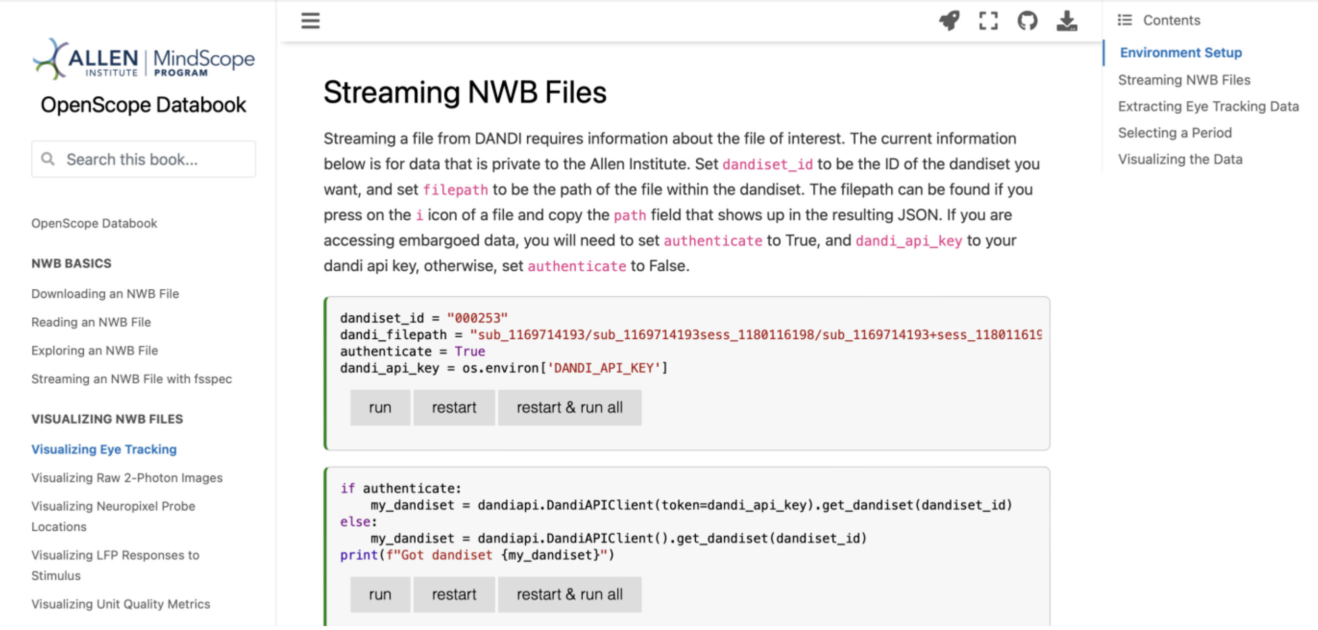


Development of full dorsal hemispheric imaging access for OpenScope. A. We first developed a custom 3D laser-cut, bended glass implant in partnership with outside suppliers. We then adapted our internal head-fixation holder (yellow) to this new implant shape. **B.** Surgical implantation of this glass implant was piloted and validated in 2022 and 2023, providing chronic access to half of the dorsal cortex in the mouse, from the visual cortex to the frontal cortex. We validated that we could still obtain complete Intrinsic Imaging map of the visual cortex using our standardized intrinsic imaging instruments (see bottom-right). **C.** Our mesoscope microscopes were adapted to provide sufficient degrees of freedom for imaging the entire range of imaging location (see colored arrows). We included a novel rotation platform under the mouse head-stage (yellow arrow). **D.** Left: We validated that we could image the entirety of the glass implant using tiled two-photon fields of view. Our tests confirmed that imaging quality was maintained across the dorsal surface provided we used separate imaging locations for the objective center (Edge anterior, edge posterior and center). Right: see a comparison of imaging quality when matching cells for all 3 imaging center locations.



Piloting auditory behaviors

We expanded beyond visual stimuli to pilot auditory stimuli on the Allen Brain Observatory pipeline (see Figure). We piloted auditory cues and multi-sensory tasks with mice. Developing this task allowed us to select specific hardware requirements. Based on these pilots, we are modifying our pipeline hardware at scale across the pipeline. This includes adding speakers, computer hardware to control auditory equipment, as well as making our behavioral software pipeline more modular. This will allow us to potentially support auditory stimuli in future proposals.

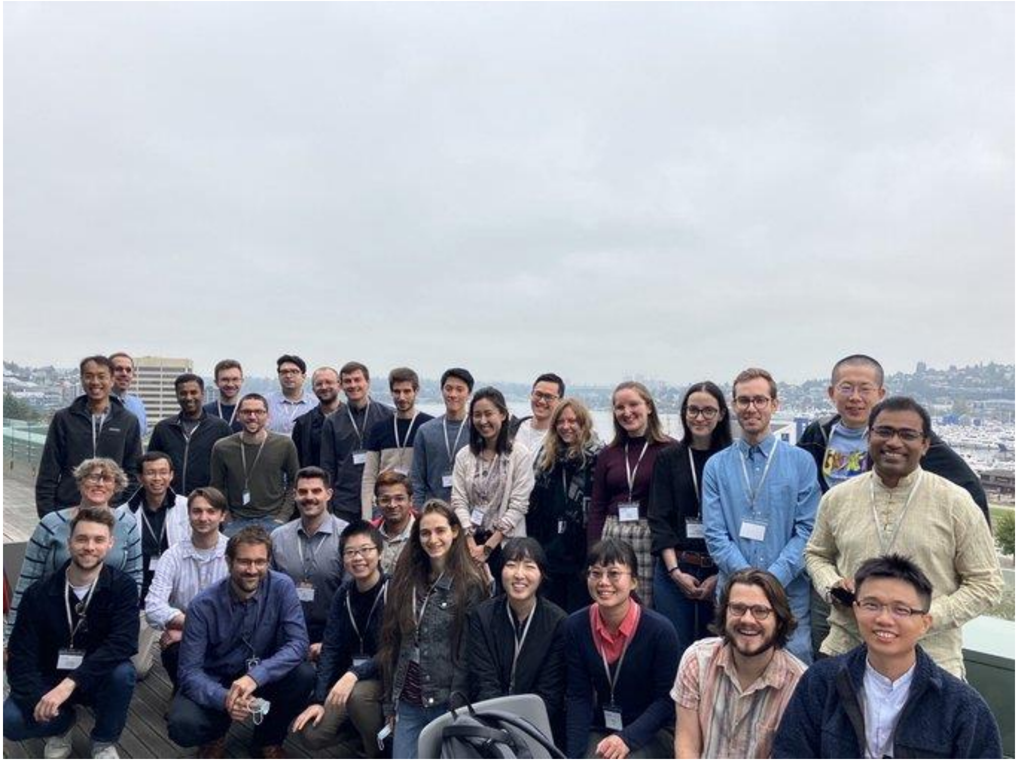


OpenScope DataBook

In 2022, we built the capability to convert and push NWB files to the Dandi archive, as stored on this public repository (https://github.com/AllenInstitute/OpenScopeNWB). This development proved to be instrumental in 2023 as we used this capability to push datasets to DANDI archive almost immediately following data collection. For OpenScope, it was the first year this pipeline went into action. We continually improved our approach throughout the year, generating NWB files both for two-photon imaging and Neuropixels recordings. This dataset includes some of the very first NWB files on DANDI with entirely raw data, sharing multiple TB of data. This capacity was key to our progress as we now can routinely share datasets in the cloud with external teams. We successfully used the embargoed capability developed by the DANDI team to manage sharing our datasets with credentials.

Having developed the ability to upload datasets to the cloud, we focused our attention on enabling reproducible analysis from DANDI cloud-storage. In collaboration with the DANDI team, we developed a Jupyter DataBook called “OpenScope DataBook” (https://github.com/AllenInstitute/openscope_databook) connected both to DandiHub cloud deployment (https://hub.dandiarchive.org/hub/) and linked to https://mybinder.org. This DataBook contains Jupyter notebooks describing how to access datasets on DANDI, both locally and in streaming mode. We also added exemplary notebooks on how to perform simple analysis like stim-aligned averages or eye tracking analysis. Critically, all our code is streaming the data within standardized environments so all analysis can be replicated directly in the cloud by pressing a single button. We intent for this Databook to grow over the years in collaboration with teams involved with the OpenScope projects. We also hope for the contributions from neuroscientists interested in sharing entirely replicable analysis, ran from DANDI archive data assets.

Outreach



Scientific workshops

To increase the impact of our scientific event in 2022, we co-organized both an online webinar and an onsite events called NeuroDataReHack. The online workshop happened on September 28, 2022 followed by the in-person hackhathon on October 3-5, 2022. Both events were extensively advertised on social medias and a dedicated web portal.

The webinar showcased on existing resources for Data ReUse, introduced the OpenScope project, as well as a roundtable discussion followed by an online poster session. Our goal for the event was to facilitate team formation across the field around Data ReUse. This event was opened to all scientists worldwide and is still available on YouTube. There were 244 registrants and 533 views on YouTube. An anonymized registrant list was sent to NIH as a deliverable and is attached to this report for reference.

The in-person hackathon was open to selected applicants. Each applicant described an existing data analysis project they intended to focus during the Hackathon. The event contained talks and presentation to facilitate the analysis of datasets uploaded to DANDI (both OpenScope datasets and coming from other laboratories). Eventually, each team could focus on the analysis they intended to do, leveraging the available expertise in neuroscience and software engineering. The event concluded with a presentation of all analysis that was achieved during the event.

Technical workshop

We held a 3-day technical workshop on September 21-23, 2022. This workshop was co-organized with the Allen Institute for Neural Dynamics, the Allen Institute MindScope Program, and the University of Washington.

In this workshop, participants from around the world had the opportunity to tour our *in vivo* electrophysiology and imaging facilities and learn the details of these methods from Allen Institute and UW scientists and staff. Lectures and demonstrations covered all aspects of generating high-quality physiology datasets, from surgery to behavior training to neural recordings. Participants also learned how to access data from the Allen Brain Observatory and about the OpenScope program. The workshop was advertised on social medias and a dedicated web portal.

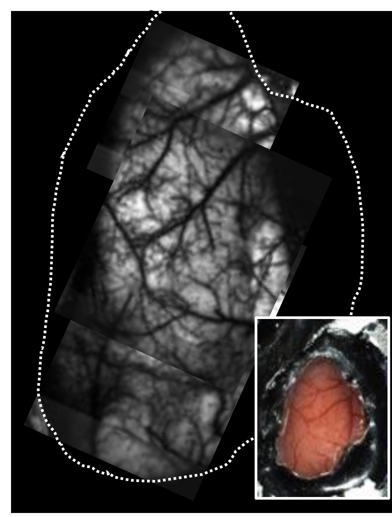
The workshop was geared towards graduate students, postdocs, staff scientists, and PIs with some experience with *in vivo* recordings. We received 137 applications and selected 40 final participants. The selection process prioritized wide distribution of attendees, aiming to avoid selecting applicants from the same institutions. In the end, attendees came from 40 different institutions. The workshop ended with a group discussion where attendees could give their feedback on the workshop and on the OpenScope program.

We are renewing this workshop in 2023 but moved the date earlier to June 2023. This is to allow workshop participants to apply to the OpenScope RFP 2023 call. Indeed, some participants left with the intent to apply in future years, based on what they learn during the workshop.

Request for Proposals in 2023-2024

We plan to release our yearly RFP in the early summer of 2023. It will be communicated on our web portal as well as through the Allen Institute social media accounts.

We plan to add new technical capabilities to this call. Thanks to the ongoing surgical development, we will expand the list of available imaging areas using the new recording and surgical protocol. The RFP will contain a list of candidate areas expanding beyond our initial vision-focused list.



OpenScope
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