OpenScope 2021-2022 Annual Report

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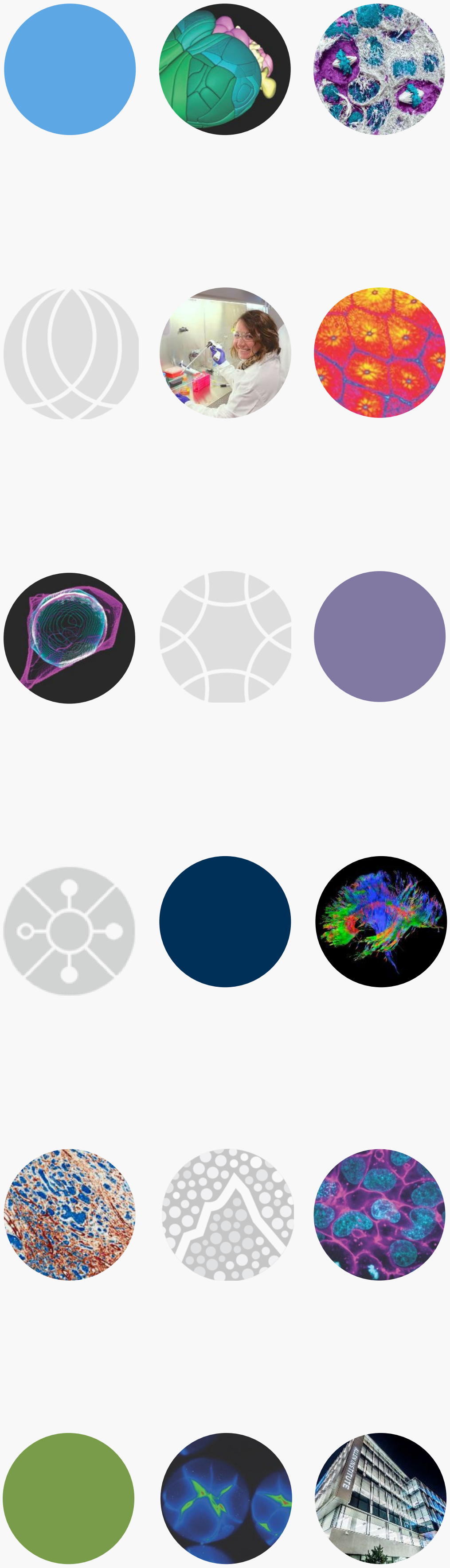
U24 NS113646



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.

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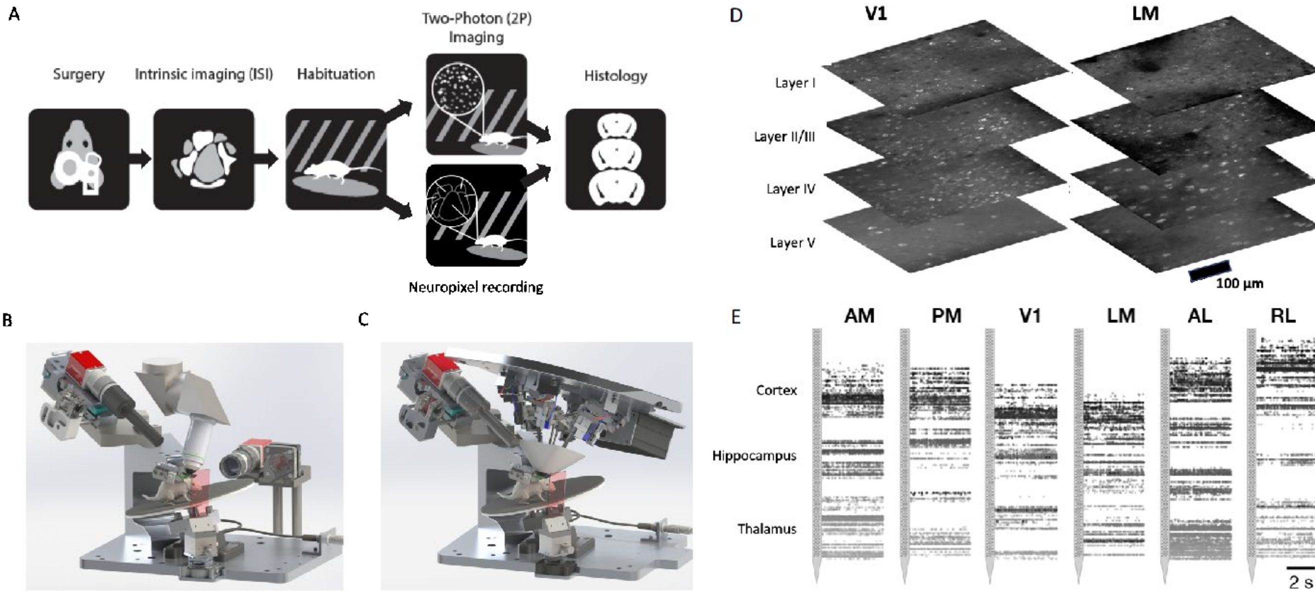


Two End-to-End data pipelines

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 the proposed projects are feasible for the Allen Institute pipeline, the LOIs are scored for scientific merit by external reviewers. The top-scored 15 feasible LOIs are then invited to submit 6-page full proposals, which are again scored by blinded internal and external scientific reviewers.

The top 5-6 projects are brought before the Scientific Steering Group, where they consider overarching programmatic goals and portfolio balance to make the final selection. The external reviewers include 11 neuroscientists from across the community, and the entire process is blinded.

In July 2021, 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 17 LOIs in early September 2021. The entire selection process (submission, reviews, and private communications) was managed online via a secured platform (https://www.submittable.com).

Thirteen teams were invited to submit full proposals, and four did not move forward as they were not feasible for the listed capabilities in the RFP. On Nov 22nd, we received 12 full proposals that were distributed across 11 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 5-6 proposals were sent forward to the OpenScope Scientific Steering Group. The selected 3 projects for 2022 were approved and selected on January 14th by the Scientific Steering Committee (excluding one member removed to prevent a conflict of interest).

Projects Recommended for Award in 2021-2022

Neuropixels project 1:

Neural Circuitry Underlying Detection of Local and Global Prediction Errors

Vanderbilt University: Alex Maier, Andre Bastos, Jacob Westerberg

Neuropixels project 2:

Utilizing Illusory Contours to Elucidate the Neural Mechanism of Binding

UC Berkeley: Hyeyoung Shin, Hillel Adesnik

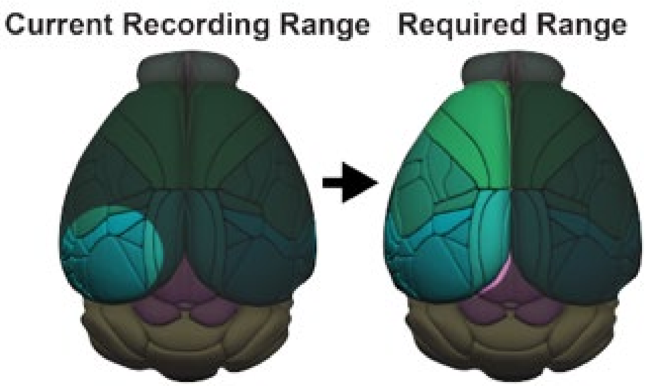
Two-photon project 1:

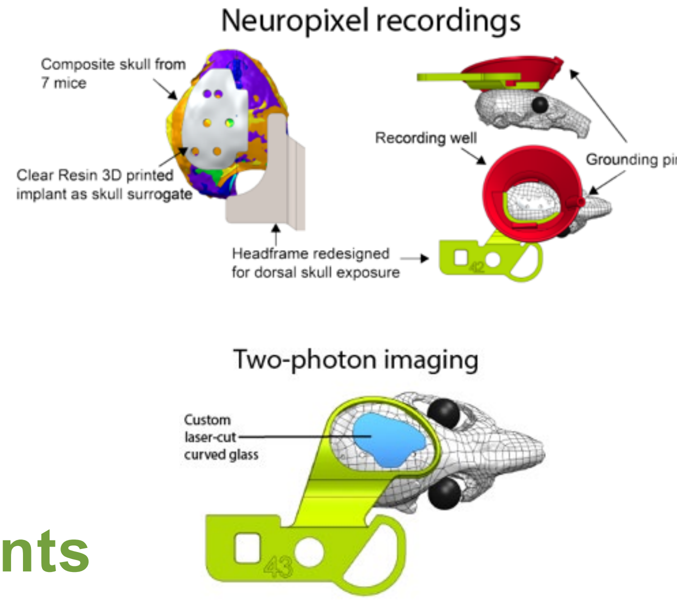
Predictive Learning and Somato-dendritic Coupling

McGill University: Blake Richards & York University: Joel Zylberberg

Non-selected teams' identities and projects remain blinded and confidential. Nevertheless, it is worth mentioning that projects were coming from all other the world. Applications included teams from the Middle-East (2), North America (7), South America (1) and Europe (2) and included applicants from both the theoretical and experimental neuroscience community.

Ongoing developments





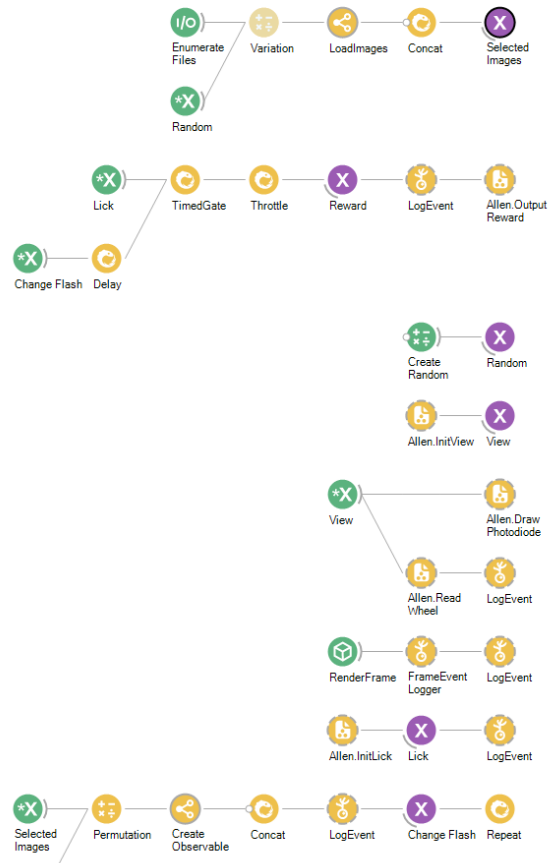
Surgical developments

While the current observatory hardware is limited to recordings from the visual circuit, we aim to progressively expand our capabilities to the largest number of brain areas possible. In 2021, we initiated new surgical and hardware developments on both the Neuropixels and two-photon platforms. Our goal is to deploy new recording capabilities first on the Neuropixels platform (2022 RFP), followed by the two-photon imaging platform (2023 RFP). On both platforms, we aim to provide access to the entire dorsal surface of a cortical hemisphere (see above **Figure**). For Neuropixels recordings, this will allow us to target both cortical and subcortical areas.

To achieve this ambitious goal, we adapted a surgical procedure initially developed at Stanford University (the “crystal skull,” Kim et al., 2016). For Neuropixels, we developed a 3D printed plastic implant that replaces the entire section of the mouse skull over the left hemisphere (see above **Figure**). Pre-determined holes can be placed in the plastic to allow the targeting of specific brain areas. This procedure was surgically validated and pilot Neuropixels recordings demonstrated that we could successfully target new brain areas.

For two-photon imaging, the process requires a glass instead of a plastic implant. We first contacted glass manufacturers to determine their glass manufacturing capabilities at scale. Our partnership with these manufacturers allowed us to design a laser-cut, curved glass coverslip covering half of the mouse dorsal brain. The precise shape and curvature of the glass implant was iterated on using a 3D printed plastic replica with real mouse surgeries. A glass manufacturer is currently manufacturing this iterated design.

On both platforms, we redesigned our head plate to be compatible with our recording hardware (see green part in **Figure**).



Bonsai integration

All behavioral components at the Allen Institute are currently running through a python internal codebase that was not designed for community-wide adoption. To open up the observatory to the broader community, we need an OpenSource codebase and software ecosystem that can be replicated across laboratories. Due to its current community adoption, we chose a 10-year-old programming language developed at the Champalimaud Center for the Unknown and UCL (https://bonsai-rx.org). In the first half of 2021, we piloted the use of Bonsai to control Behavioral experiments and measured its performance. This effort was tracked on a dedicated public repository. A public report is available here.

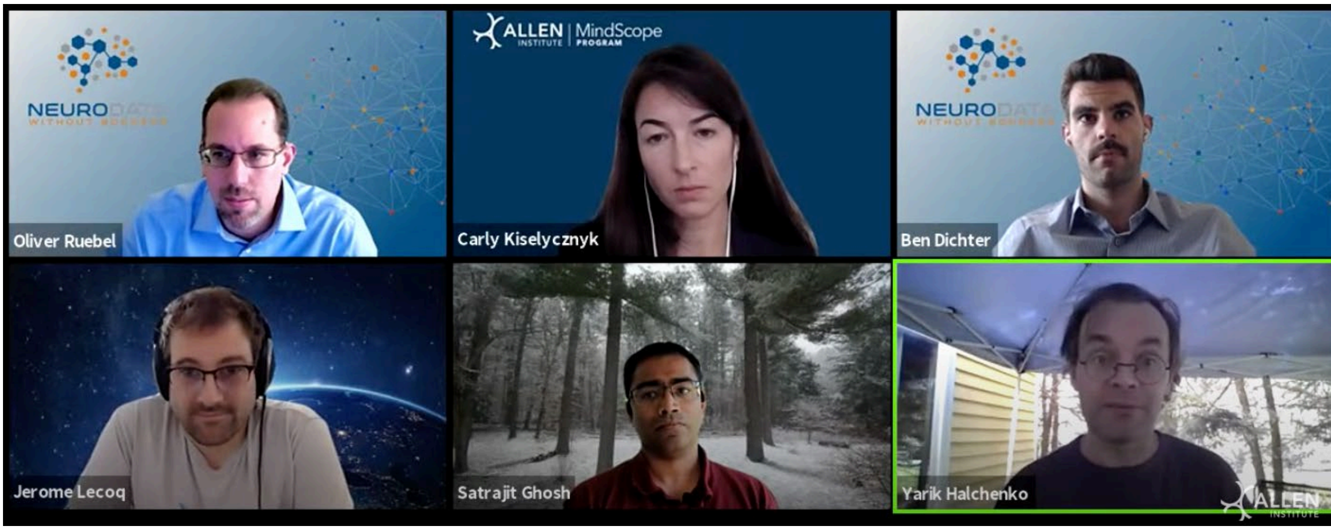
After validating Bonsai baseline performance, we implemented a standardized Bonsai behavioral template that will form the base for future deployment of "Experiment as software" on the Allen Institute pipeline. This template contains all standardized hardware logic (access to reward, access to licking responses, running hardware, etc.) and allows us to create new behavioral logics using those components. Using this template, we replicated all existing logic of the detection of change task in Bonsai (see here: and **Figure**). Separately, the detection of change task is already validated in our behavioral cluster using our existing python codebase (see Garrett et al., elife, 2020; Orlova et al., bioRxiv, 2021). This replication in Bonsai will support our transition to using Bonsai in future years.

Scientific outcomes

Publications and peer-reviewed posters from past OpenScope projects

- **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

Outreach



Scientific and technical workshops

On September 18th, 2021, we held an online workshop open to worldwide attendees. This workshop had 149 registered participants and is also available on YouTube. We used this workshop to describe the OpenScope program and the application process, as well as our plans for the upcoming years. Following the workshop, we had 60 requests for one-on-one consultations (20 scheduled) to answer and clarify questions that were not addressed by the workshop.

The one-on-one consultations also allowed us to assess what experimental capabilities were regularly requested and may have broad community interest for future RFPs. As we expected, we found that adding behavioral capabilities and new recording locations was a common request. In addition, several groups were interested in sending or receiving mice to/from our pipeline (either new transgenic mice or mice that underwent a specific procedure). Lastly, several groups asked about the possibility of drug injections in our protocol.

In 2022, we plan to renew our scientific workshop with the inclusion of more scientific content in collaboration with other resources within our ecosystem who have already partnered with NIH (NWB and DANDIarchive).

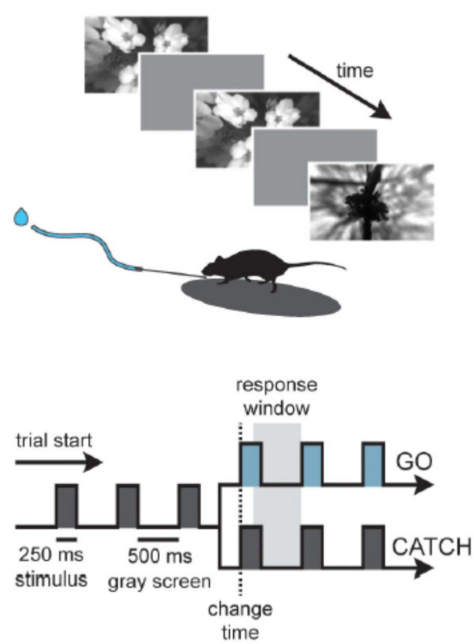
We will also hold an on-site technical workshop in the fall of 2022. Attendees will be able to learn about all our technical procedures to potentially leverage our standardized protocol in their own laboratory. This event will be communicated on our web portal and through Allen Institute social media platforms in the spring of 2022.

Request for Proposals in 2022-2023

We plan to release our yearly RFP in the early summer of 2022. 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 Neuropixels areas using the new recording and surgical protocol. The RFP will contain a list of candidate areas expanding beyond our initial vision-focused list.

Importantly, we will also add the ability to leverage behaving mice. Our first call with behavior will focus on leveraging our detection of change task (see Groblewski, Ollerenshaw et al., 2020 and **Figure**) and potential variations on this task.



OpenScope
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THANK YOU

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