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Toolmakers Newsletter

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In this issue

BRAIN INITIATIVE

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Welcome Back to the Toolmakers Newsletter!

Welcome to the second *Brain Research Through Advancing Innovative Neurotechnologies®* (BRAIN) Initiative Alliance Toolmakers Newsletter of 2022!

In this issue, we share with you four more exciting tool advancements in neuroscience: OpenScope by Dr. Jérôme Lecoq; the Polymer Implantable Electrode (PIE) Foundry by Dr. Ellis Meng and Dr. Dong Song; Neurodata Without Borders (NWB) by Dr. Oliver Rübel; and the CMU Array by Dr. Eric Yttri and Dr. Rahul Panat. Let's explore the latest breakthroughs from these BRAIN investigators!

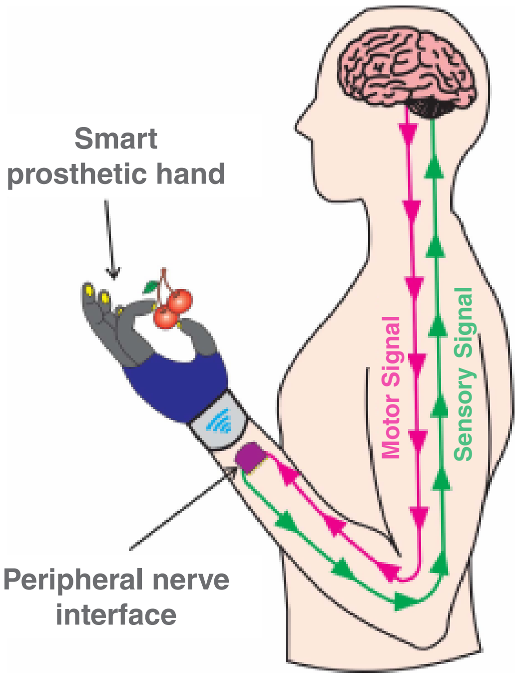


Image: Peripheral nerve interfaces necessary for brain-controlled prostheses. Credit: *Cobo et al., 2018, Journal of Microelectromechanical Systems.*

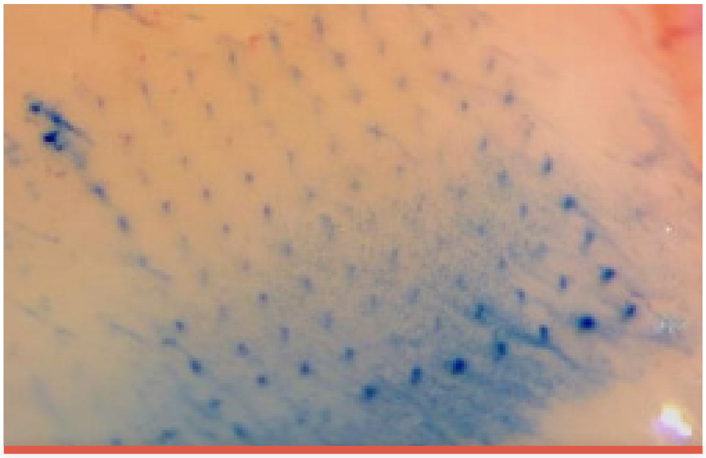


Image: Evans blue dye left behind from the successful insertion of a dense (6400 shanks/cm^2), 10×10 array of 20 µm diameter array with zoomed image (right). Credit: *Saleh et al., 2019, bioRxiv*.

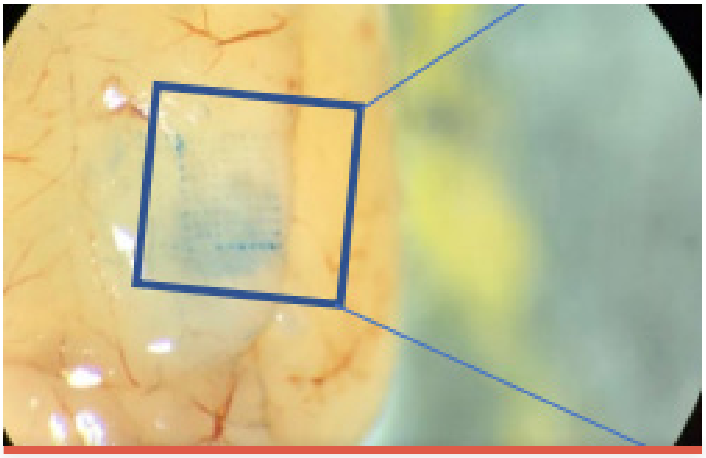


Image: Evans blue dye left behind from the successful insertion of a dense (6400 shanks/cm^2), 10×10 array of 20 µm diameter array with zoomed image (right). Credit: *Saleh et al., 2019, bioRxiv.*

On the front cover: Top Right Hexagon: An image still from a video of the *C. elegans* brain, including every nerve and muscle fiber, being reconstructed by serial-section electron microscopy. Credit: Daniel Witvliet, University of Toronto and Harvard University, 2020. **Top Central Hexagon**: Four-week-old rat cortical neurons labeled for dendrites (red), axons (green), and nuclei (blue). Credit: Karthik Krishnamurthy, Davide Trotti, Piera Pasinelli, Thomas Jefferson University, 2020. **Bottom Right Hexagon:** A pseudo-colored image of high-resolution gradient-echo MRI scan of a fixed cerebral hemisphere from a person with multiple sclerosis. Credit: Govind Bhagavatheeshwaran, Daniel Reich, National Institute of Neurological Disorders and Stroke, National Institutes of Health, 2016. **Bottom Central Hexagon:** Brain waves. Credit: The Allen Institute, 2022.

OpenScope – Dr. Jérôme Lecoq

At the Allen Institute in Seattle, WA, Dr. Jérôme Lecoq is an expert in neurophysiology and part of the OpenScope team, a community-driven platform that tests novel hypotheses to measure neural activity using the established Allen Brain Observatory data collection pipeline. OpenScope was created to be analogous to the kind of scientific collaboration that astronomical observatories foster—a place for scientists to work together to incentivize a marketplace of ideas.

OpenScope gives scientists access to the Allen Brain Observatory, a pipeline and data archive of *in vivo* recordings from the mouse visual cortex that allows scientists to test sophisticated hypotheses about brain function.

Once a year, Dr. Lecoq and others encourage theoretical, computational, and experimental scientists to submit a proposal to use OpenScope's two-photon or Neuropixels capabilities. A blinded expert panel reviews applications and selects proposals based off feasibility and scientific merit. If selected, scientists provide external inputs like visual stimuli, and then the Allen Institute carries out the full experiment. Scientists receive their data through an online repository so they can analyze data and write a report outlining their results for publication.

In the summer of 2022, three projects will be selected to participate in OpenScope. "We plan to further expand in the coming years with a more extensive set of brain areas and the addition of behavioral training," says Dr. Lecoq. The next round of applications will be open in summer of 2022.

Data sharing and scientific collaboration are at the heart of OpenScope. The project encourages and supports open source, open data, and standardized protocols and practices. All datasets collected through OpenScope are cross-referenced through shared standards and data access, which allows further meta-analyses and comparisons by the neuroscience community.

Image: OpenScope concept. Credit: Benedicte Rossi, Allen Institute, 2021.

OpenScope uses Neurodata Without Borders (NWB) to help standardize new physiological data for cloud data deployment and analysis. Learn more about NWB below on page 5.

OpenScope

If you're eager to learn more about OpenScope, you can visit the OpenScope website and consider attending the Neuropixels and OpenScope workshop from September 21-23, 2022. This workshop will take place at the Allen Institute and the University of Washington and will give participants the opportunity to tour and learn about the *in vivo* physiology tools and techniques. Workshop applications are due June 1, 2022.

> "We initially started with two-photon only experiments. Last year, thanks to NIH funds, we incorporated Neuropixels…giving access to the two leading techniques to record individual neurons. — *Dr. Jérôme Lecoq*

Polymer Implantable Electrode Foundry – Dr. Ellis Meng and Dr. Dong Song

Dr. Ellis Meng, Dr. Dong Song, and their team at the University of Southern California recently created the Polymer Implantable Electrode (PIE) Foundry, a resource that provides neuroscientists with free training, testing, and custom-made devices related to implantable, microfabricated, and polymer-based microelectrode arrays. It overcomes the challenge of sourcing reliable, long-term, and stable recording for single-unit neural activity by offering a catalog of products and services to guide neuroscience research.

PIE Foundry offers ready-to-use standard probes, quick replication of user-submitted designs, design and fabrication, material and device testing, and quality control services. It also provides virtual and on-site training for multielectrode array design, implantation, and implementation in neuroscience studies. According to Dr. Meng, training and custom design and fabrication have been the most popular PIE Foundry services.

Scientists using PIE Foundry can incorporate its polymer-based probes and electrodes into their own research. For example, they can experiment with cuffing and paddling electrodes to stimulate peripheral or spinal nerves, transparent, non-magnetic probes for MRI or optical imaging, and penetrating probe arrays for chronic recording.

All of PIE Foundry's resources are free to use, requiring a proposal submission to gain access. All projects are selected based on scientific merit. If you're a researcher interested in becoming a PIE Foundry user, Dr. Meng recommends signing up for a workshop. You can also reach out to PIE Foundry staff at PIEFoundry@usc.edu or visit the PIE Foundry website.

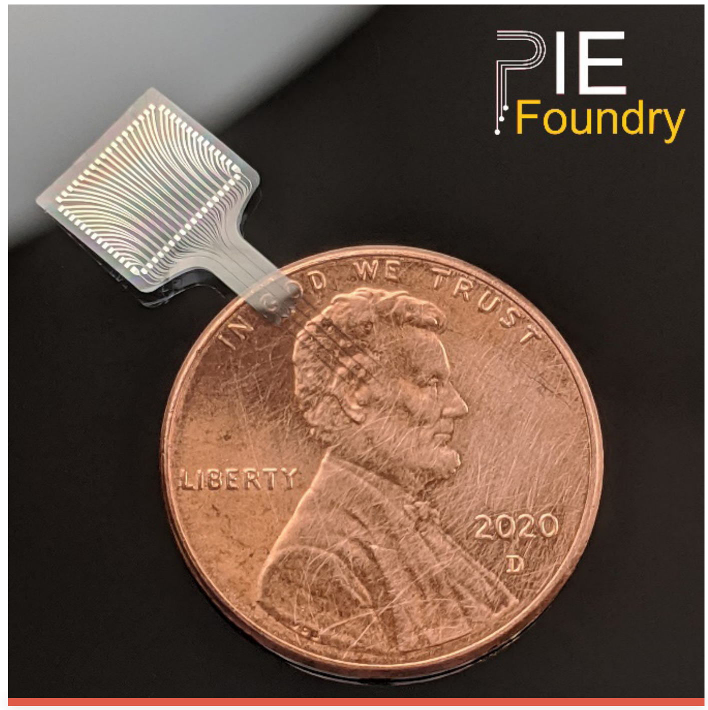


Image: Standard template polymer penetrating probes shown with a penny. Credit: PIE Foundry, 2022.

> "A key mission is to standardize and democratize access to polymer-based microfabricated multi-electrode arrays."
>
> *— Dr. Ellis Meng*

Neurodata Without Borders – Dr. Oliver Rübel

Neurophysiology datasets can be expensive to collect, tedious to share, and hard to reuse, but Neurodata Without Borders (NWB) is here to help make data open and accessible. Dr. Oliver Rübel used these challenges as motivation to create NWB, an ecosystem for neuroscience data standardization.

NWB is software that provides neuroscientists with a common standard to share, build, archive, and use common analysis tools for neurophysiology data. It helps standardize data to make it packageable, sharable, interchangeable, and reusable.

The tools and standards that make up NWB can handle large amounts of complex neurophysiology data. They work with a few main components: specification language, data application programming interfaces (APIs), data standard schema, and data storage. Combining these elements ensures that NWB data can be understood by anyone familiar with NWB, and that it can be read by both humans and machines. NWB also provides software and APIs for reading and writing data, and standardizes what metadata is required to make collections of data easily findable.

NWB works with existing and emerging data technologies on the web, MATLAB, Python, and other platforms to support needs across the data lifecycle. A growing number of neurophysiology analysis and visualization tools support NWB, driving collaboration and allowing NWB to truly realize its vision of enabling reproducible neuroscience.

There are now 91 publicly available datasets that use the NWB format, spanning from extracellular electrophysiology, intracellular electrophysiology, optical physiology, and behavior. These datasets also use a variety of species and research domains. In the future, Dr. Rübel and his team hope to shift their focus from the core schema and APIs to the large and growing ecosystem of NWB-related tools. They are also training users to both convert their data into NWB and analyze existing NWB data. “We are in the process of organizing a new type of event called NeuroDataReHack in collaboration with the Allen Institute’s OpenScope, DANDI, and the Kavli Foundation,” says Dr. Ben Dichter, NWB Community Liaison. The team hopes this event will generate new insights through secondary analyses of existing neurophysiology data.

> “NWB users benefit greatly from easy access to state-of-the-art tools, so continuing to support tool builders will be key for our growth.
>
> *— Dr. Oliver Rübel*

If you’re interested in learning more about the NWB ecosystem, be sure to read the new preprint article in bioRxiv. Dr. Rübel and his team also encourage those interested to attend the NWB User Days training workshop from July 25-28, 2022, focused around helping users convert their data to NWB. Here, you can receive lessons and one-on-one help to learn how NWB can read and interact with your data. The event is most suitable for graduate students and postdocs interested in learning how to use NWB. You can also contact the NWB team with questions on their website.

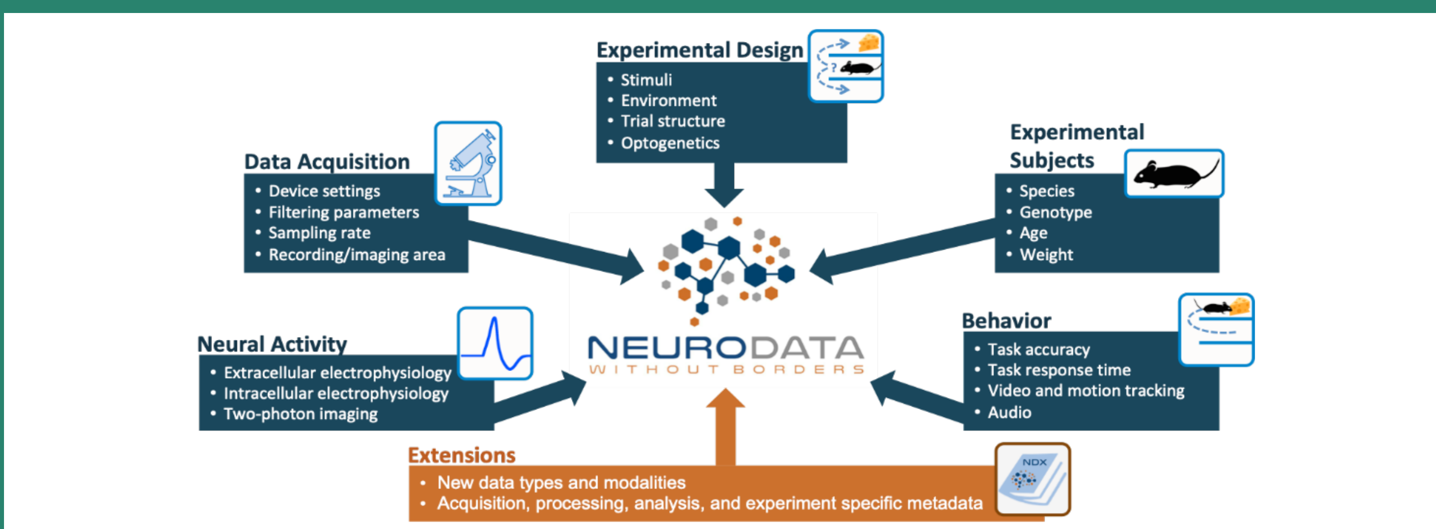


Image: Neurodata Without Borders (NWB) is a data standard that provides neuroscientists with a common approach to share, build, archive, and use analysis tools for neurophysiology data. Credit: Neurodata Without Borders, 2022.

Carnegie Mellon University ‘CMU’ Array – Dr. Eric Yttri and Dr. Rahul Panat

At Carnegie Mellon University, Dr. Eric Yttri and Dr. Rahul Panat led the creation of the CMU array, a customized, ultra-high-density microelectrode array constructed using 3D nanoparticle printing and computer-aided design. It can record from thousands of neurons across multiple targeted brain regions in mice, and may help create things like customizable brain-computer interfaces to aid neural prosthetics or to guide procedures that stimulate neurons in humans.

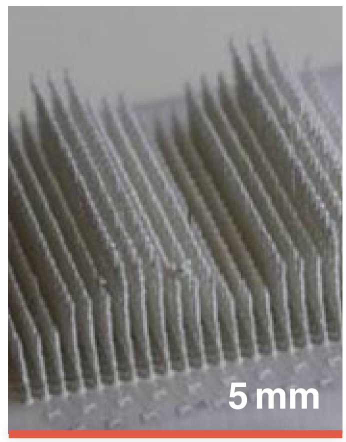
> “A high degree of customization is a distinguishing factor of this technology.”
>
> *— Dr. Rahul Panat*

The CMU array uses recent advances in micro- and nano-electronics manufacturing and applies them to neuroscience. It was developed using aerosol jet printing, a droplet-based 3D printing method that can create micro-scale needle-like projections. The 3D printer converts metal nanoparticles (e.g., silver or gold) into a mist of droplets and directs them at a point on a substrate. The droplets get stacked to create a 3D shank, or electrode, each of which can be customized to have their own length.

Customization is one of the largest benefits of the CMU array. The 3D printing process allows great structural control to easily customize or rapidly change things like probe height or layout to custom fit different structures. For example, the CMU array probes range from 20 μm to 10 μm in diameter, but the diameter can easily be increased. Additionally, because the shanks can be printed in arbitrary locations, they can be placed very close together to extract neural signals from the brain at higher magnitudes and densities than conventional materials. In fact, the CMU array can reach extremely high shank densities of up to 6,000 electrodes/cm².

The first publication outlining the CMU array’s capabilities appeared in 2019 in bioRxiv. Since then, Dr. Yttri and Dr. Panat have continued exploring uses for the CMU array and are currently in a validation phase to record from multiple areas of the brain—something not possible by any other method.

“We are highly excited about the prospect of recording from the 3D volume of the brain,” says Dr. Panat, “although this probe is still in development, we are in talks with several companies to commercialize this product.” For more information about the CMU array, contact CMU’s Panat Lab.



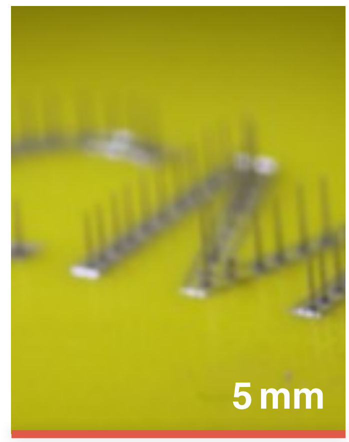
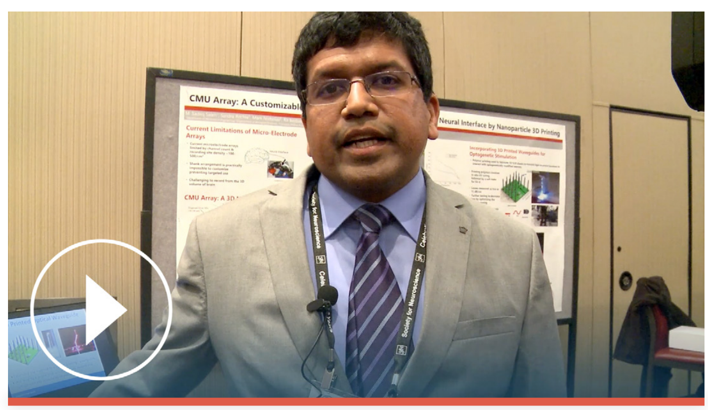


Image left: A 512-shank array with variable shank heights of 1.0, 1.5, and 2 mm, which demonstrates the possible customization of the probe. Credit: *Saleh et al., 2019, bioRxiv.*

Image right: A demonstration of the extent of flexibility in the design and fabrication of the shanks, with printed shanks bearing the CMU Array’s name. Credit: *Saleh et al., 2019, bioRxiv.*



Video: Dr. Panat describes how the BRAIN Initiative has catalyzed the development of their state-of-the-art CMU array.

Excited by the potential of the tools in this issue?! Stay tuned for our next issue and explore more products of BRAIN Initiative discoveries in our Toolmakers’ Resources page!