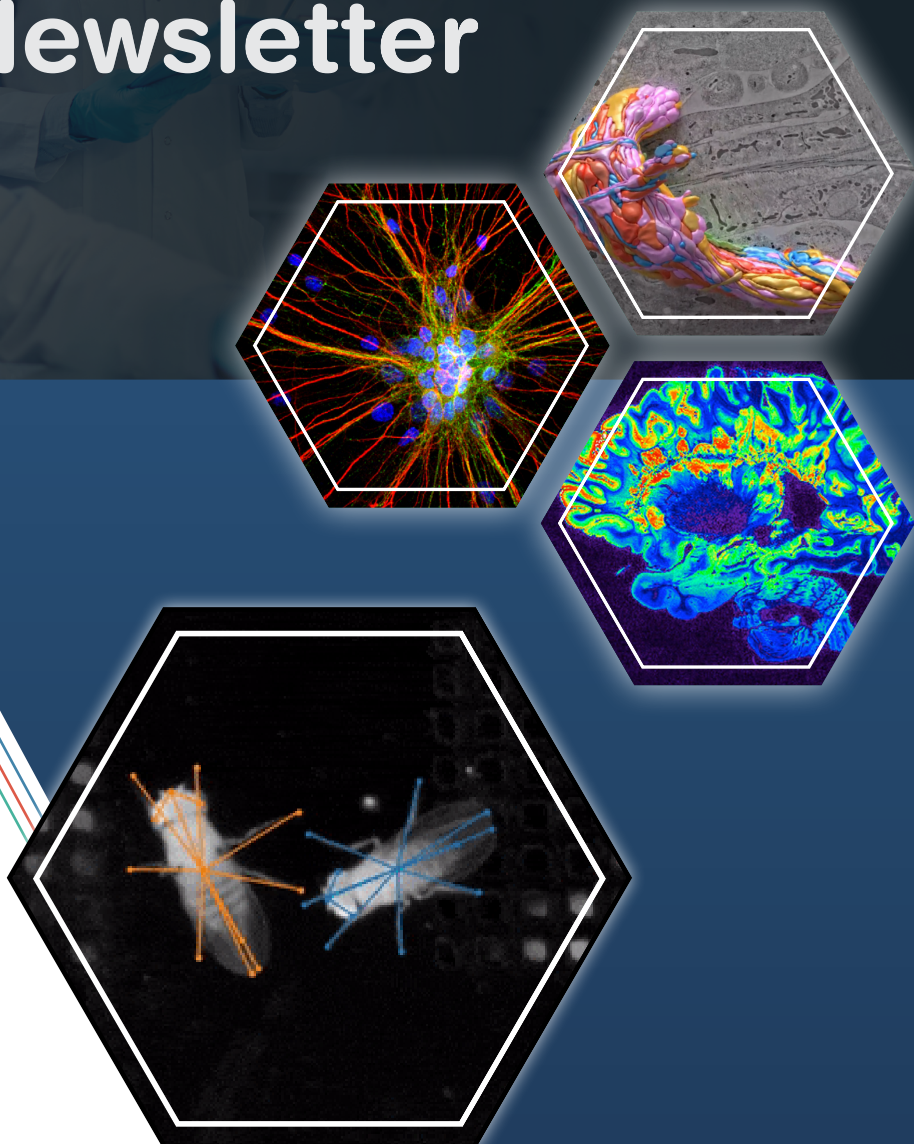
JANUARY 2021

Toolmakers Newsletter



ISSUE 01

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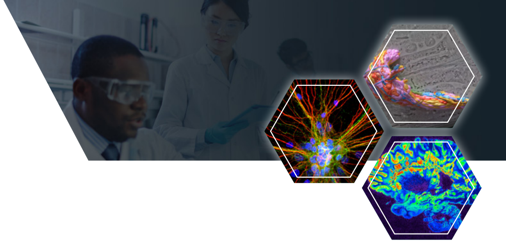
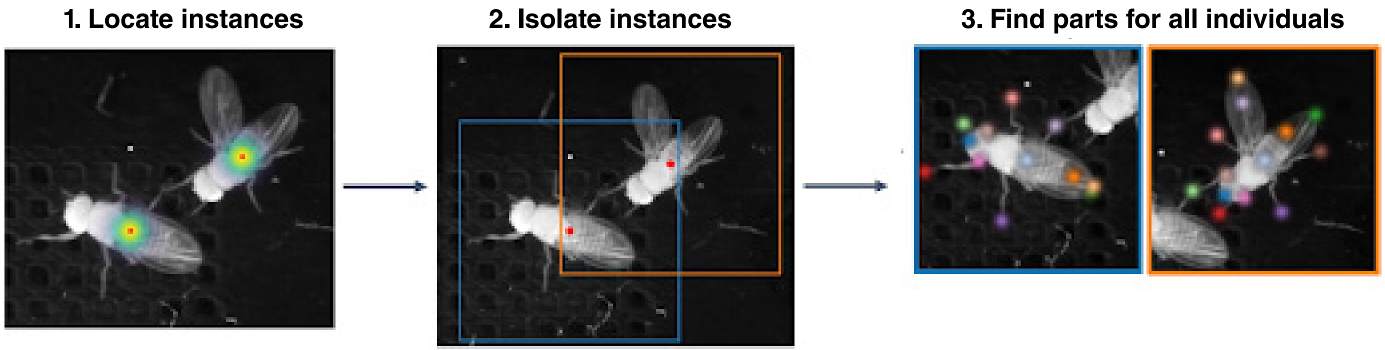
BRAIN INITIATIVE



Welcome to the Toolmakers Newsletter!

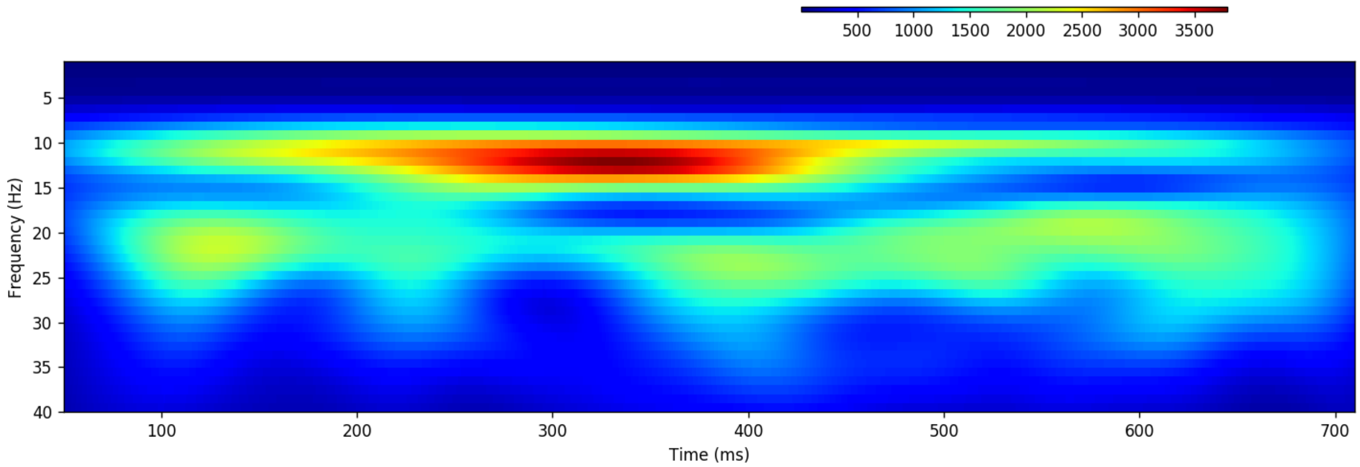
The *Brain Research Through Advancing Innovative Neurotechnologies®* (BRAIN) Initiative is a collaborative research endeavor that has been working for the better part of the last decade to understand the complexities of the human brain. Now, at the halfway point of this project, new tools and technologies are starting to emerge. However, advances in neurotechnology don't happen overnight; they take immense creative energy of investigators and their teams and years to develop, design, and distribute. However, as these new tools emerge, it is clear that the investment in the BRAIN Initiative has paid off. Here we highlight these pioneers and their breakthroughs in the field of neuroscience.

In this issue, we are proud to report on: the new, user-friendly neural modeling software called Human Neocortical Neurosolver (HNN) developed by Dr. Stephanie Jones; the design and fabrication of a multi-channel Wireless Floating Microelectrode Array (WFMA) device that can stimulate the brain's visual center by Dr. Philip Troyk; a deep learning software framework that tracks animals' limbs from video — SLEAP (Social LEAP Estimates Animal Poses) by Talmo Pereira; and the development of miniaturized open source microscopes by NeuroNex's Drs. Daniel Aharoni and Peyman Golshani. Come with us as we explore some of the latest and greatest from BRAIN Initiative investigators.



Above: In SLEAP's top-down mode, a network first finds each animal and then a separate network estimates the pose of each animal. Image obtained from https://sleap.ai/.

Below: A spectrogram of brain activity modeled using the HNN software.



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:** SLEAP software being used with flies. Credit: Talmo Pereira, Princeton University, 2020.

Building a Bridge Between Experimental and Computational Neuroscience — Dr. Stephanie Jones

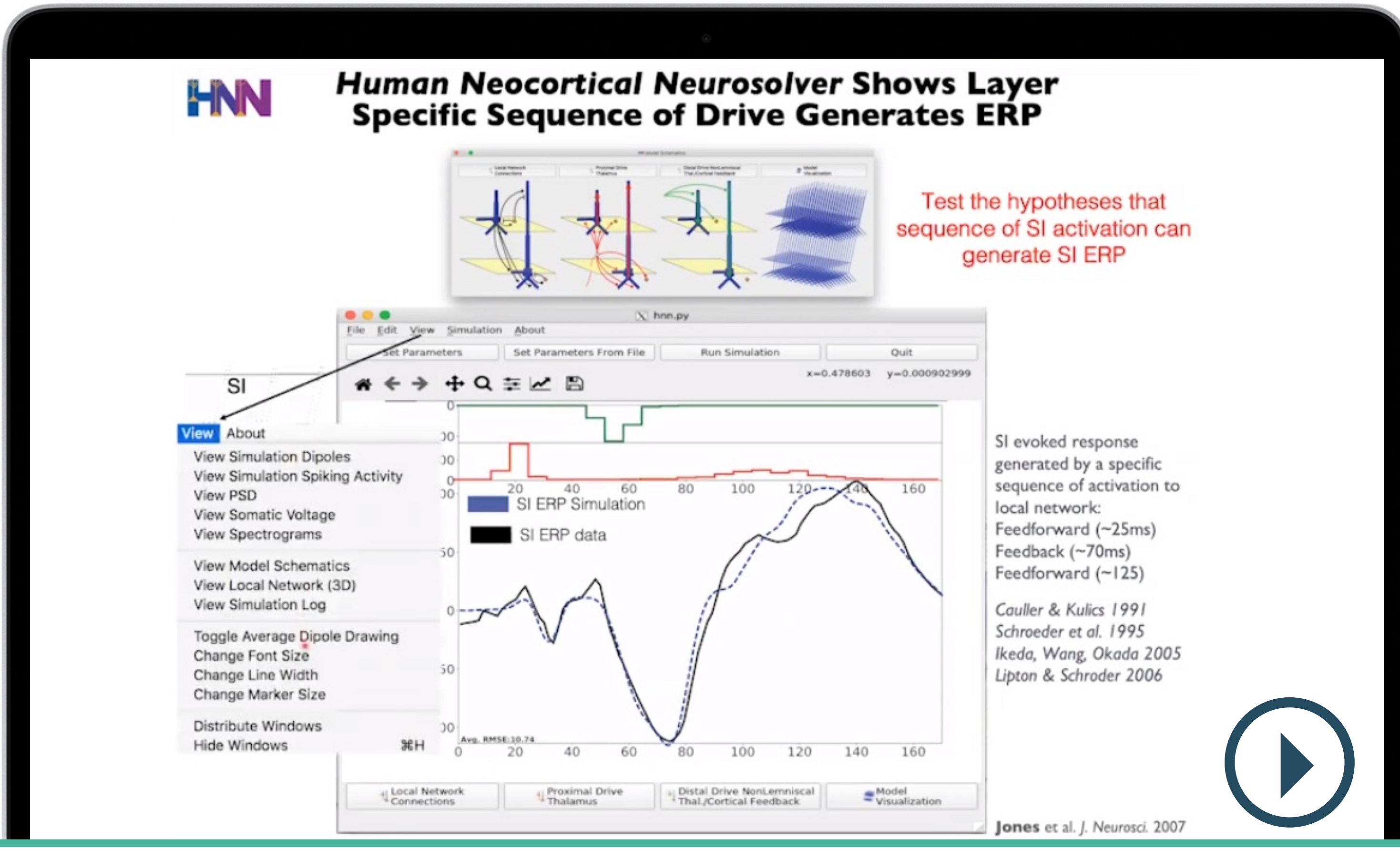


Image: Dr. Stephanie Jones' recent talk at the 2020 Allen Institute Modeling Workshop. Watch the full presentation here.

Dr. Stephanie Jones, an Associate Professor at Brown University, is working at the intersection of experimental and computational neuroscience to further the mission of the BRAIN Initiative. She and her team recently published their landmark study introducing the Human Neocortical Neurosolver software tool. While both electro- and magneto-encephalography (EEG/MEG) provide reliable markers of brain function, there are difficulties relating these macroscopic signals to any underlying cellular- and circuit-level neural generators. This fundamental limitation constrains the use of EEG and MEG data to translate the findings into new therapies for neural pathologies, such as autism spectrum disorder. Thus, Dr. Jones and her team built the Human Neocortical Neurosolver (HNN). The HNN is a user-friendly software tool to test and develop hypotheses on the circuit mechanism underlying EEG/MEG data. HNN provides an interface that allows researchers to work interactively between model and data without needing to alter the underlying mathematical model or the open-source code. The HNN runs on high performance computers through the Neuroscience Gateway Portal and Amazon Web Services. The Jones Lab even provides tutorials on how to simulate the most commonly measured neural signals. Further, researchers can compare simulated signals to recorded data and easily manipulate the model parameters to develop and test alternative hypotheses for the neural origin of their signals. The ability of HNN to associate signals across multiple scales makes it a unique tool for translational neuroscience research. How might this technology be used? One example might be found in the interpretation of circuit-level differences in children with autism compared to typically-developing children. For her critical work bridging the gap between computational and experimental research with the HNN software, Dr. Jones recently won the BIOMAG2020 Mid-Career Award. Without a doubt, this BRAIN investigator and her team are making great strides in computational neuroscience and democratizing their tool along the way.

Working to Restore Vision by Stimulating the Brain — Dr. Philip Troyk

At the Illinois Institute of Technology, Dr. Philip Troyk is working to further our understanding of neural interfaces and prosthetic devices, some of which may soon help visually impaired people see. He has pioneered the design and fabrication of a multi-channel Wireless Floating Microelectrode Array (WFMA) device for the purpose of stimulating the brain's visual centers with the ultimate goal of restoring vision in visually impaired people. The WFMA device allows stimulation and recording from both the central nervous system and the periphery through a wireless link. The WFMA device is a mere 5 mm in diameter and can interface to 16 electrodes without the use of any wires or tethers. Wireless control is key; the device's power and communication are achieved through a magnetic wireless link, meaning that no tethering is needed, which allows for natural freedom of movement. Currently, it is being deployed for neuroscience research through a joint effort by MicroProbes for Life Science and Sigenics, Inc. Dr. Troyk, as CEO of Sigenics, Inc., is leading this effort with the help of the BRAIN Initiative. The WFMA is ideal for the implantation of a large number of arrays simultaneously in the same animal, allowing a multitude of cortical locations to be targeted at the same time. Furthermore, the cutting edge WFMA device is currently in testing for the human Intracortical Visual Prosthesis (ICVP) project, and it will be adapted in the near future to support a variety of cortical, peripheral, and spinal implants. In fact, preliminary testing of the WFMA in acute and chronic rat models supports the feasibility of using this platform technology for numerous peripheral and central nervous system applications. This means that Dr. Troyk's research may be able to one day not only restore vision but lead to brain interfaces that can restore movement following spinal cord injury. Altogether, Dr. Troyk's project represents an economically valuable breakthrough in neuroscience that will soon improve the lives of people around the world.

Image: Overview of the Vision Prosthesis project (top).

Video: Dr. Philip Troyk explains how the BRAIN Initiative is helping the WFMA project.

Developing Deep Learning Software Frameworks to Track Animals — Talmo Pereira

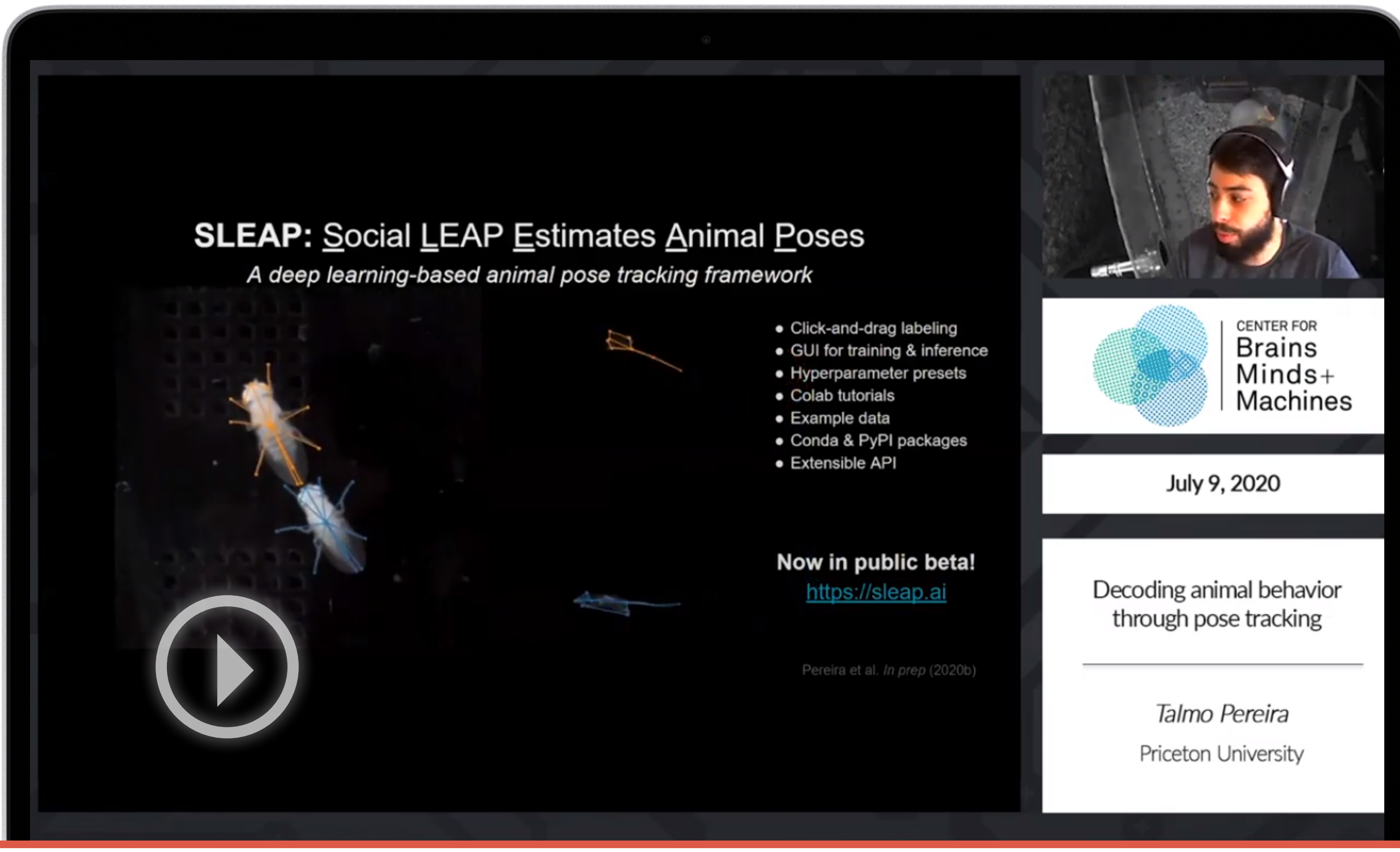
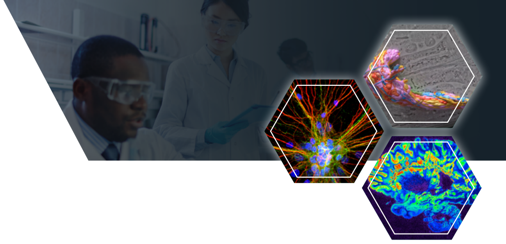


Image: Talmo Pereira gives a tutorial for the Center for Brains, Minds and Machines on how to decode animal behavior through pose tracking with SLEAP. Watch the full video here.

In addition to lab principal investigators, trainees play a vital role in BRAIN Initiative tool development. At Princeton University, doctoral candidate Talmo Pereira, one such up-and-coming investigator, is a joint student in the labs of Drs. Mala Murthy and Joshua Shaevitz. Talmo Pereira is part of the team that developed Social LEAP Estimates Animal Poses (SLEAP). SLEAP is a deep learning software framework for general purpose multi-animal limb tracking from video. This software couples a graphical user interface for importing and annotating data with deep neural networks designed to locate and associate user-specified anatomical landmarks on unmarked animals – mostly flies. Use cases range from kinematic studies of animal movement, to quantification of social dynamics via multi-animal part tracking. SLEAP has since been used successfully in other animal models. In fact, this software was successfully used in this recently published study that utilized a machine-vision approach to measure pain in mice, as well as in this preprint that examined changes in behavior in fruit-flies, demonstrating its usability across species. This framework is open source, Python-based, and available to the public. Curious about how to use this software? The SLEAP website even has tutorials and guides on how to successfully implement this framework, from installation to exporting data for analysis. This framework is the successor to LEAP, another animal tracking framework published by Talmo Pereira a few years ago. With many accolades already (from the National Science Foundation's Graduate Research Fellow to Student Researcher at Google AI), Talmo Pereira is a scientist to keep your eye on.



Expanding Access to Transformative Microscope Tools — Drs. Daniel Aharoni and Peyman Golshani

At the University of California, Los Angeles (UCLA), Drs. Daniel Aharoni and Peyman Golshani lead the UCLA Miniscope project. Here, they are developing the most widely used, open source miniature microscope for neural recording in freely behaving animals. Through the support of the BRAIN Initiative, they are even developing Miniscopes specifically for use in larger animal models such as rhesus macaque monkeys and marmosets. Some of their Miniscopes are integrated with electrophysiology tools, enabling nearly simultaneous recording of both calcium-related fluorescence and neuronal spikes as animals behave. One of their most recent papers gives a breakdown of the spatial coding and interneuron synchronization in epileptic mice using a wire-free Miniscope. Their systems are currently in use in roughly 500 labs. They even have an open-access wiki page on building and using these scopes. However, Drs. Daniel Aharoni and Peyman Golshani aren't stopping there. They hope to continue expanding access to these transformative microscope tools across the world. In fact, this team already hosts national and international workshops where scientists can learn to build their very own Miniscopes. Microscopy in neuroscience will never be the same again with the advent of these small, versatile, and open source Miniscopes from these BRAIN investigators.

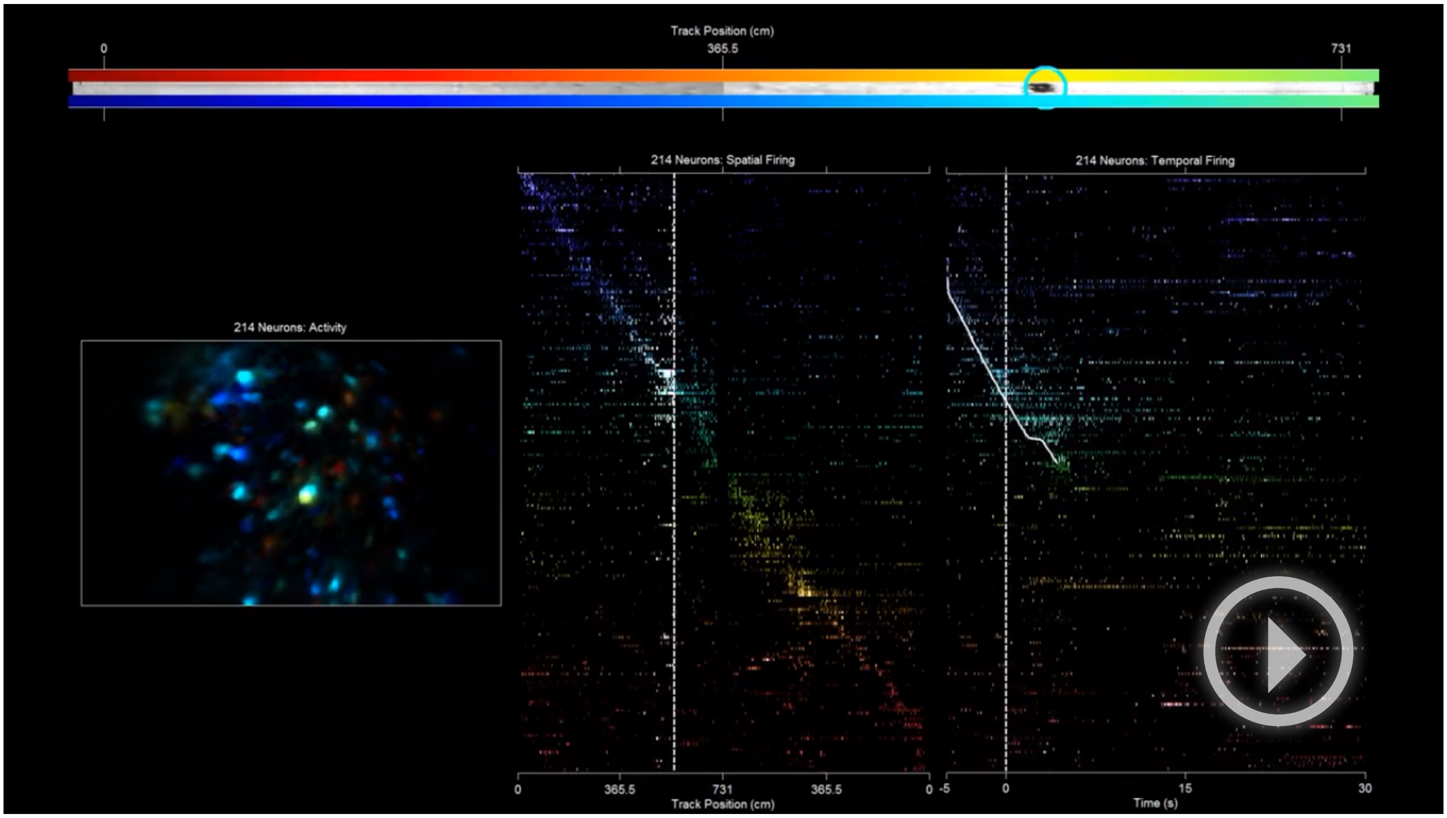


Image: Miniscope recording of place cells in a mouse on a 25-foot track. Watch this video and others of the Miniscopes in action on their YouTube channel.

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!