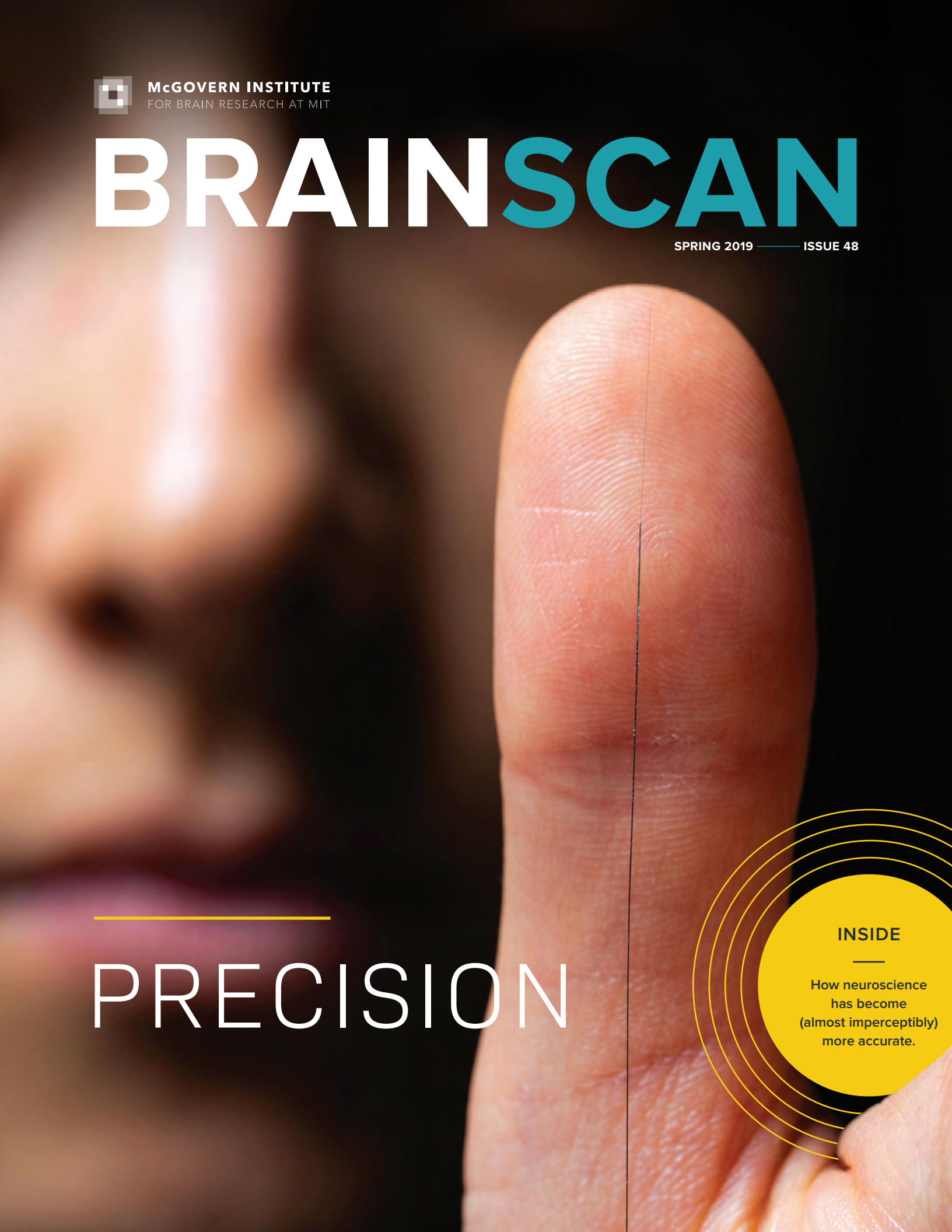


McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

BRAINSCAN

SPRING 2019 — ISSUE 48

PRECISION

INSIDE

How neuroscience has become (almost imperceptibly) more accurate.

LAB NOTES

Viewpoints from McGovern experts

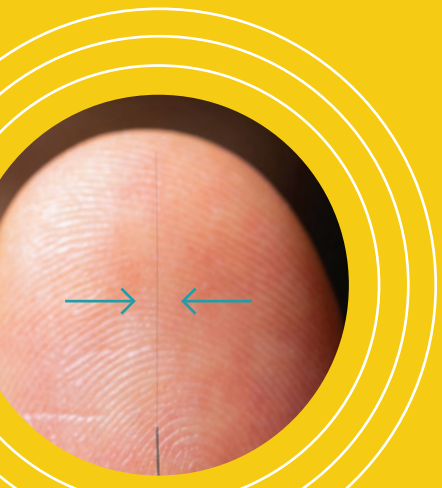
The word precision is increasingly relevant to the diverse approaches McGovern investigators employ to understand the brain.

More accurate tools are being developed to probe the brain, including the miniscule probe on the cover, created by Graybiel lab postdoc Helen Schwerdt, to track neurotransmitters in tiny brain structures.

Neural and cognitive assessments are beginning to address individual learning needs, and, as you'll read in this issue, artificial neural networks have reached an unprecedented level of precision. Where neuroscience once shed light on the brain, these applications have the potential to split that ray of light like a prism – revealing a more precise picture of the brain in health and disease.

ROBERT DESIMONE

Director, McGovern Institute
Doris and Don Berkey Professor of Neuroscience



DID YOU MISS IT?

Nearly imperceptible to the human eye, this ultrathin probe developed in the Graybiel lab targets brain microstructures with pinpoint accuracy.

Algorithms of Intelligence

How the DiCarlo lab fine-tuned its machine vision system to precisely control neural activity.

Machine vision systems are more and more common in everyday life, from social media to self-driving cars, but training artificial neural networks to "see" the world as we do — distinguishing cyclists from signposts — remains challenging. Will artificial neural networks ever decode the world as exquisitely as humans? Can we refine these models and influence perception in a person's brain just by activating individual, selected neurons?

The DiCarlo lab, including CBMM postdocs Kohitij Kar and Pouya Bashivan, are finding that we are surprisingly close to answering "yes" to such questions, all in the context of accelerated insights into artificial intelligence at the McGovern Institute for Brain Research, CBMM, and the Quest for Intelligence at MIT.

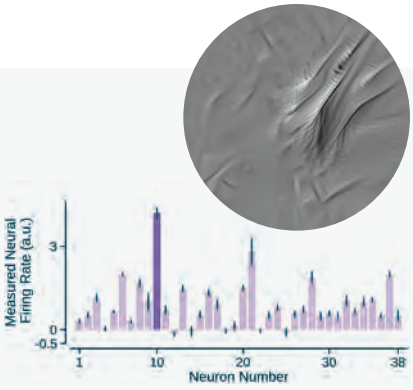
PRECISION MODELING

Beyond light hitting the retina, the recognition process that unfolds in the visual cortex is key to truly "seeing" the surrounding world. Information is decoded through the ventral visual stream, cortical brain regions that progressively build a more accurate, fine-grained, and accessible representation of the objects around us.

McGovern Investigator James DiCarlo (left) and postdocs Kohitij Kar and Pouya Bashivan overlaid by a projection of images synthesized by their deep neural network.

One Hot Neuron

This image (top), synthesized by DiCarlo's deep neural network, activates a single targeted neuron (dark purple) in the primate visual cortex, a level of precision unmatched by previous models.



"One next step is to couple this new precision tool with our emerging understanding of how neural patterns underlie object perception. This might allow us to create arrangements of pixels that look nothing like, for example, a cat, but that can fool the brain into thinking it's seeing a cat."

— JAMES DICARLO

Artificial neural networks have been modeled on these elegant cortical systems, and the most successful models, deep convolutional neural networks (DCNNs), can now decode objects at levels comparable to the primate brain. However, even leading DCNNs have problems with certain challenging images, presumably due to shadows, clutter, and other visual noise. While there's no simple feature that unites all challenging images, the quest is on to tackle such images to attain precise recognition at a level commensurate with human object recognition.

In a recent push, Kar and DiCarlo demonstrated that adding feedback connections, currently missing in most DCNNs, allows the system to better recognize objects in challenging situations, even those where a human can't articulate why recognition is an issue for feedforward DCNNs. They also found that this recurrent circuit seems critical to primate success rates in performing this task.

This is incredibly important for systems like self-driving cars, where the stakes for artificial visual systems are high, and faithful recognition is a must.

NOW YOU SEE IT

As artificial object recognition systems have become more precise in predicting neural activity, the DiCarlo lab wondered what such precision might allow: could they use their system to not only *predict*, but to *control* specific neuronal activity?

To demonstrate the power of their models, Bashivan, Kar, and colleagues zeroed in on targeted neurons in the brain. In a paper recently published in *Science*, they used an artificial neural network to generate a random-looking group of pixels that, when shown to an animal, activated the team's target, a target they called "one hot neuron." In other words, they showed the brain a synthetic pattern, and the pixels in the pattern precisely activated targeted neurons while other neurons remained relatively silent.

These findings show how the knowledge in today's artificial neural network models might one day be used to noninvasively influence brain states with neural resolution. Such precise systems would be useful as we look to the future, toward visual prosthetics for the blind.

Such a precise model of the ventral visual stream would have been inconceivable not so long ago, and all eyes are on where McGovern researchers will take these technologies in the coming years.

IN FOCUS

Expansion microscopy provides unprecedented resolution of individual neurons and their connections.

STRETCHING THE LIMITS

Expansion microscopy is a technique developed in the Boyden lab that uses a hydrogel to swell brain tissue, revealing nanostructures in unprecedented detail.

A new adaptation of this technology, called expansion lattice light sheet microscopy (ExLLSM), is even more precise. ExLLSM provides super-resolution images of nanoscale structures across large volumes of brain tissue—a feat that would be impossible with conventional microscopes.

This image shows a subset of excitatory neurons in the mouse cortex labeled with a fluorescent protein and imaged with ExLLSM. (Not shown are the neurons in this same volume that weren't labeled). Even with such sparse labeling, the result is a stunning portrait of the neural complexity in this tiny volume.

Width of a Single Hair

Sharper Image

ExLLSM images are 4x sharper than conventional microscopy images (comparison shown here) and can distinguish microstructures as little as 60 nm apart.

MASTERMINDS

Postdoc Ruixuan Gao (right) and former postdoc Shoh Asano (left) collected and processed one petabyte of data to create this and other super-resolution ExLLSM images for their 2019 *Science* paper with Ed Boyden.

“With ExLLSM, we can image at large scale without losing sight of nanoscale biomolecules.”

— ED BOYDEN

37 minutes required to create this image

Investment targets gene therapy for Rett syndrome

Mutations in a single gene underlie almost all cases of Rett syndrome, a rare and debilitating neurodevelopmental disorder that occurs almost exclusively in girls. A generous commitment from the Rett Syndrome Research Trust (RSRT) will give McGovern researchers the opportunity to zero in on these mutations with gene editing technologies and potentially treat this debilitating disease.

Rett syndrome is caused by mutations in *MECP2*, an X-linked gene essential for the normal development of brain cells. Symptoms typically appear during the toddler years, and children with this disorder progressively lose their ability to walk, speak, and use their hands. Many children exhibit features similar to autism spectrum disorders.

A $2.3 million commitment from the RSRT will fuel a new research initiative at the McGovern Institute to explore how CRISPR-Cas13 tools may be used to correct *MECP2* mutations in RNA. The research will be led by McGovern Investigators Guoping Feng, Feng Zhang, and Robert Desimone.

Ila Fiete Becomes Associate Investigator

Ila Fiete, an associate professor in MIT's Department of Brain and Cognitive Sciences, recently joined the McGovern Institute as an associate investigator. Fiete is working to understand the circuits that underlie short-term memory, integration, and inference in the brain. To do this, Fiete uses multiple tools including pure theoretical approaches to examine neural codes, building numerical dynamical models of circuit operation, and techniques to extract information about the underlying circuit dynamics from neural data.

McGovern Welcomes Inaugural Fellows

Recent graduates Omar Abudayyeh and Jonathan Gootenberg have been named the inaugural fellows of the McGovern Institute. The fellows program supports highly talented and selected postdocs who are ready to initiate their own research program. As McGovern Fellows, the pair are planning to search broadly for new gene therapy tools and also to examine cellular changes linked to aging-related diseases.

Awards

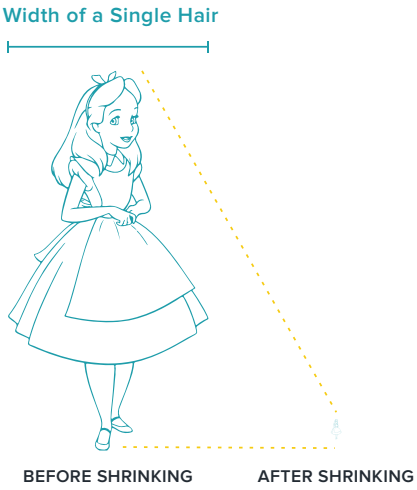
MICHAEL HALASSA | Max Planck Society Fellowship at the Max Planck Florida Institute for Neuroscience

REBECCA SAXE | "Committed to Caring" honor from MIT's Office of Graduate Education, awarded for excellent mentorship of graduate students

BRAIN IMAGING

Deep Brain Sensor

Calcium is a critical signaling molecule for most cells, and it is especially important in neurons. The **Jasanoff** lab has now devised a new way to image calcium activity that is based on magnetic resonance imaging (MRI) and allows them to peer much deeper into the brain. Using this technique, they can track signaling processes inside the neurons of living animals, enabling them to link neural activity with specific behaviors.



GENOME ENGINEERING

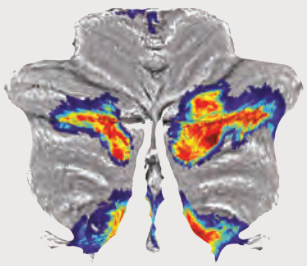
New CRISPR Platform

Feng Zhang, who first harnessed the revolutionary CRISPR-Cas9 and other systems for genome editing of eukaryotic organisms, has engineered another CRISPR system, called Cas12b. Cas12b has high target specificity and is small compared to Cas9 (SpCas9), making this new system more suited for *in vivo* delivery and applications.

NEUROTECHNOLOGY

Implosion Fabrication

The **Boyden** lab has invented a method to shrink objects to one thousandth the size of the originals. The technique, called "implosion fabrication," allows researchers to embed large-scale objects in expanded hydrogels and then shrink them to the nanoscale. These tiny structures could have applications in many fields, from optics to medicine to robotics.



"The cerebellum contains over half the neurons of the brain yet it's been largely ignored by cognitive neuroscientists. We're now discovering that it plays an integral role in language, emotion, memory, and even some neurodevelopmental disorders."

— ANILA D'MELLO | POSTDOC, GABRIELI LAB

COMPUTATIONAL NEUROSCIENCE

Connecting the Neural Dots

The **Fee** lab has developed an algorithm, seqNMF, that can recognize relevant sequences of neural activity, allowing researchers to extract structure from the internal life of the brain without being forced to make reference to inputs or output.

COGNITIVE NEUROSCIENCE

Decoding Faces

Using fMRI and MEG, the **Kanwisher** lab measured the brains' response to faces, and found that we register gender and age before we even recognize a face.

DID YOU KNOW

30%

of struggling readers don't benefit from standard interventions?

We want to know why.

John Gabrieli's lab is interested in finding out whether more targeted and precise interventions, early in reading development, might help a broader set of struggling readers.

The lab is currently looking for first and second graders to help researchers evaluate the impact of these more targeted interventions. The SUMMIT study will use cognitive, linguistic, and reading assessments to explore how children respond to an intensive summer reading and math program. The researchers, including postdoc Ola Ozernov-Palchik (pictured above), will also look at brain changes that may occur following the intervention, using non-invasive and child-friendly MEG and fMRI methods.

Interested in participating? Visit our website:
mcgovern.mit.edu/participate

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