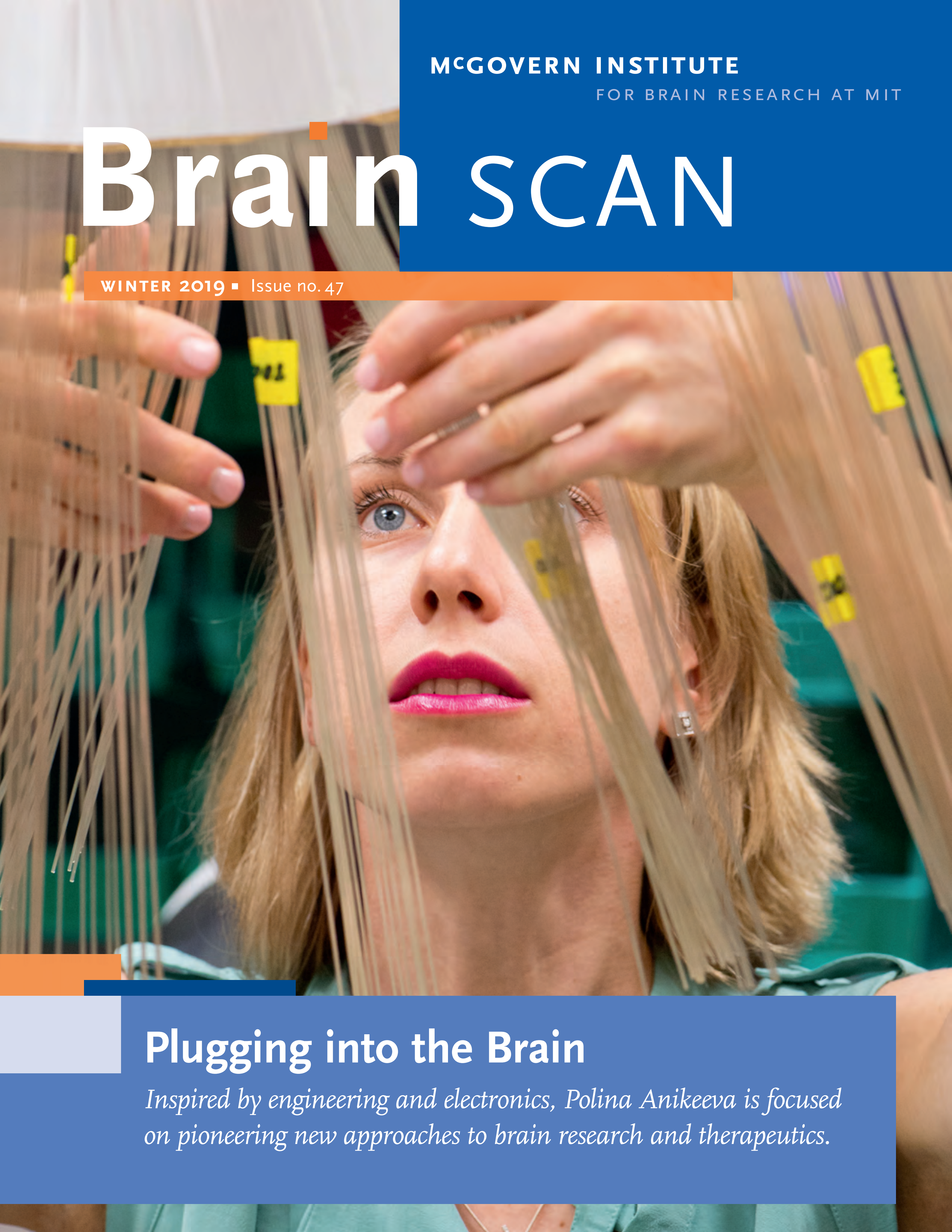
McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

Brain SCAN

WINTER 2019 ▪ Issue no. 47



Plugging into the Brain

Inspired by engineering and electronics, Polina Anikeeva is focused on pioneering new approaches to brain research and therapeutics.

FROM THE **DIRECTOR**

In 2018, we expanded our team, adding associate investigators Polina Anikeeva and Josh McDermott. Polina has appointments in the Department of Materials Science and Engineering and Brain and Cognitive Sciences. She develops revolutionary brain research technologies with magnetic devices so large that an electrical upgrade was required during installation. Our building engineer worried that a malfunction could take down the Cambridge power grid. This is an exaggeration (hopefully, as her lab is beneath my office!), but it is no stretch to say that Polina's lab uses powerful equipment for beneficial ends. Josh McDermott is an associate professor in the Department of Brain and Cognitive Sciences. Using sophisticated models and neuroimaging, he studies auditory processing, even in noisy environments. This is important for addressing hearing impairments.

Beyond excitement over these additions, we are searching for a new faculty member. It is so stimulating to hear our current faculty debate what each candidate from the incredible talent pool might bring to the McGovern Institute, making our whole more than the sum of our parts, and promising a bright future.

Bob Desimone, Director
Doris and Don Berkey Professor
of Neuroscience

On the cover: McGovern Associate Investigator Polina Anikeeva develops optoelectronic and magnetic devices to probe and manipulate the nervous system.
Photo: Justin Knight

Photo: Justin Knight

Driven by curiosity and therapeutic goals, Anikeeva leaves no scientific stone unturned in her drive to invent neurotechnology.

The audience sits utterly riveted as Polina Anikeeva highlights the gaps she sees in the landscape of neural tools. With a background in optoelectronics, she has a decidedly unique take on the brain.

"In neuroscience," says Anikeeva, "we are currently applying silicon-based neural probes with the elastic properties of a knife to a delicate material with the consistency of chocolate pudding—the brain."

A key problem, summarized by Anikeeva, is that these sharp probes damage tissue, making such interfaces unreliable and thwarting long term brain studies of processes including development and

Plugging into the Brain

Inspired by engineering and electronics, Polina Anikeeva is focused on pioneering new approaches to brain research and therapeutics.

aging. The state of the art is even grimmer in the clinic. An avid climber, Anikeeva recalls a friend sustaining a spinal cord injury. "She made a remarkable recovery," explains Anikeeva, "but seeing the technology being used to help her was shocking. Not even the simplest electronic tools were used, it was basically lots of screws and physical therapy." This crude approach, compared to the elegant optoelectronic tools familiar to Anikeeva, sparked a drive to bring advanced materials technology to biological systems.

Outside the Box

As the group breaks up after the seminar, the chatter includes boxes, more precisely, thinking outside of them. An associate professor in material sciences and engineering at MIT, Anikeeva's interest in neuroscience recently led to a McGovern Institute appointment. She sees her journey to neurobiology as serendipitous, having earned her doctorate designing light-emitting devices at MIT.

"I wanted to work on tools that don't exist, and neuroscience seemed like an obvious choice. Neurons communicate in part through membrane voltage changes and as an electronics designer, I felt that I should be able to use voltage."

Comfort at the intersection of sciences requires, according to Anikeeva, clarity and focus, also important in her chief athletic pursuits, running and climbing. Through long distant running, Anikeeva finds solitary time ("assuming that no one can chase me") and the clarity to consider complicated technical questions. Climbing hones something different, absolute focus in the face of the often-tangled information that comes with working at scientific intersections.

"When climbing, you can only think about one thing, your next move. Only the most important thoughts float up."

This became particularly important when, in Yosemite National Park, she made the decision to go up, instead of down, during an impending thunderstorm. Getting out depended on clear focus, despite imminent hypothermia and being exposed "on one of the tallest features in the area, holding large quantities of metal." Polina and her climbing partner made it out, but her summary of events echoes her research philosophy: "What you learn and develop

Photo: Justin Knight

"Preforms" can be drawn into fibers that are more compatible with delicate brain tissue.

is a strong mindset where you don't do the comfortable thing, the easy thing. Instead you always find, and execute, the most logical strategy."

In this vein, Anikeeva's research pursues two very novel, but exceptionally logical, paths to brain research and therapeutics: fiber development and magnetic nanomaterials.

Drawing New Fibers

Walking into Anikeeva's lab, the eye is immediately drawn to a robust metal frame containing, upon closer scrutiny, recognizable parts: a large drill bit, a motor, a heating element. This custom-built machine applies principles from telecommunications to draw multifunctional fibers using more "brain-friendly" materials.

"We start out with a macroscopic model, a preform, of the device that we ultimately want," explains Anikeeva. This "preform" is a transparent block of polymers, composites, and soft low-melting temperature metals with optical and electrical properties needed in the final fiber. "So, this could include electrodes for recording, optical channels for optogenetics, microfluidics for drug delivery, and one day even components that allow chemical or mechanical sensing." After sitting in a vacuum to remove gases and impurities, the two-inch by one-inch preform arrives at the fiber-drawing tower.

"Then we heat it and pull it, and the macroscopic model becomes a kilometer-long fiber with a lateral dimension of microns, even nanometers," explains Anikeeva. "Take one of your hairs, and imagine that inside there are electrodes for recording, there are microfluidic channels to infuse drugs, optical channels for stimulation. All of this is combined in a single miniature form factor, and it can be quite flexible and even stretchable."


Photo: Justin Knight

Anikeeva holds "preforms" containing elements that can be customized as specific neural probes or delivery devices.


Photo: Polina Anikeeva

An avid rock climber, Anikeeva appreciates the degree of focus and logic that is necessary to succeed in the sport.

Construction Crew

Anikeeva's lab comprises an eclectic mix of 21 researchers from over 13 different countries, and a range of expertizes, including materials science, chemistry, electrical and mechanical engineering, and neuroscience. In 2011, Andres Canales, a materials scientist from Mexico, was the second person to join Anikeeva's lab.

"There was only an idea, a diagram," explains Canales. "I didn't want to work on biology when I arrived at MIT, but talking to Polina, seeing the pictures, thinking about what it would entail, I became very excited by the methods and the potential applications she was thinking of."

Despite the lack of preliminary models, Anikeeva's ideas were compelling. Elegant as the fibers are, the road involved pain-staking, iterative refinement. From a materials perspective, drawing a fiber containing a continuous conductive element was challenging, as was validation of its properties. But the resulting fiber can deliver optogenetics vectors, monitor expression, and then stimulate neuronal activity in a single surgery, removing the spatial and temporal guesswork usually involved in such an experiment.

Seongjun Park, an electrical engineering graduate student in the lab, explains one biological challenge. "For long term recording in the spinal cord, there was even an additional challenge as the fiber needed to be stretchable to respond to the spine's movement. For this we developed a drawing process compatible with an elastomer."

The resulting fibers can be deployed chronically without the scar tissue accumulation that usually prevents long-term optical manipulation and drug delivery, making them good candidates for the treatment of brain disorders. The lab's current papers find that these implanted fibers are useful for three months, and material innovations make them confident that longer time periods are possible.

Magnetic Moments

Another wing of Anikeeva's research aims to develop entirely non-invasive modalities, and use magnetic nanoparticles to stimulate the brain and deliver therapeutics.

"Magnetic fields are probably the best modality for getting any kind of stimulus to deep tissues," explains Anikeeva, "because biological systems, except for very specialized systems, do not perceive magnetic fields. They go through us unattenuated, and they don't couple to our physiology."

In other words, magnetic fields can safely reach deep tissues, including the brain. Upon reaching their tissue targets these fields can be used to stimulate magnetic nanoparticles, which might one day, for example, be used to deliver dopamine to the brains of Parkinson's disease patients. The alternating magnetic fields being used in these experiments are tiny, 100-1000 times smaller than fields clinically approved for MRI-based brain imaging.

Tiny fields, but they can be used to powerful effect. By manipulating magnetic moments in these nanoparticles, the magnetic field can cause heat dissipation by the particle that can stimulate thermal receptors in the nervous system. These receptors naturally detect heat, chili peppers and vanilla, but Anikeeva's magnetic nanoparticles act as tiny heaters that activate these receptors, and, in turn, local neurons. This principle has already been used to activate the brain's reward center in freely moving mice. Siyuan Rao, a postdoc who works on the magnetic nanoparticles in collaboration with McGovern Investigator Guoping Feng, is unhesitating when asked what most inspires her.

"As a materials scientist, it is really rewarding to see my materials at work. We can remotely modulate mouse behavior, even turn hopeless behavior into motivation."

Pushing the Boundaries

Such collaborations are valued by Anikeeva. Early on she worked with McGovern Investigator Emilio Bizzi to use the above fiber technology in the spinal cord. "It is important to us to not just make these devices," explains Anikeeva, "but to use them and show ourselves, and our colleagues, the types of experiments that they can enable."

Far from an assembly line, the researchers in Anikeeva's lab follow projects from ideation to deployment. "The student that designs a fiber, performs their own behavioral experiments, and data analysis," says Anikeeva. "Biology is unforgiving.

Anikeeva examines fibers in the lab with graduate student Alice Lu.

You can trivially design the most brilliant electrophysiological recording probe, but unless you are directly working in the system, it is easy to miss important design considerations."

Inspired by this, Anikeeva's students even started a project with Gloria Choi's group on their own initiative. This collaborative, can-do ethos spreads beyond the walls of the lab, inspiring people around MIT.

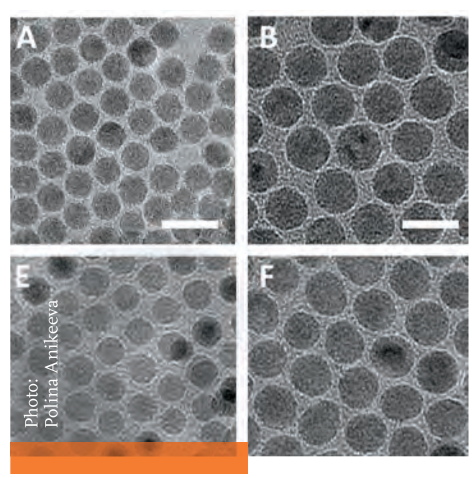
"We often work with a teaching instructor, David Bono, who is an expert on electronics and magnetic instruments," explains Alex Senko, a senior graduate student in the lab. "In his spare time, he helps those of us who work on electrical engineering flavored projects to hunt down components needed to build our devices."

These components extend to whatever is needed. When a low frequency source was needed, the Anikeeva lab drafted a guitar amplifier.

Queried about difficulties that she faces having chosen to navigate such a broad swath of fields, Anikeeva is focused, as ever, on the unknown, the boundaries of knowledge.

"Honestly, I really, really enjoy it. It keeps me engaged and not bored. Even when thinking about complicated physics and chemistry, I always have eyes on the prize, that this will allow us to address really interesting neuroscience questions."

With such thinking, and by relentlessly seeking the tools needed to accomplish scientific goals, Anikeeva and her lab continue to avoid the comfortable route, instead using logical routes toward new technologies. ■



Nanoparticles being used in Anikeeva's research on magnetic modalities for interfacing with the nervous system.

Josh McDermott Named McGovern Associate Investigator

We are delighted to announce that perceptual scientist Josh McDermott has joined the McGovern Institute as an associate investigator. McDermott, an associate professor in MIT's Department of Brain and Cognitive Sciences, studies how people hear and interpret sound.

Operating at the intersection of psychology, neuroscience, and engineering, McDermott has made groundbreaking discoveries about how people derive information from sound in order to make sense of the world around them. His long-term goals are to improve treatments for those whose hearing is impaired, and to make possible the design of future machine systems that mirror human abilities to interpret sound.

In addition to these pursuits, McDermott has a parallel interest in music; specifically, how we perceive it, why we appreciate it, and how these abilities vary across cultures. This passion is evident in his office, where thousands of records line the shelves from his graduate years working as a club and radio DJ.

"Music is a playground for the auditory system," he explains, "and the right experiments have the potential to provide insight." ■

Photo: Kris Brewer

McDermott's interest in music is reflected in the record collection in his office.

Photo: Eduardo Undurraga

McDermott conducts a sound experiment in a village in the Bolivian rainforest.

Appel Family Gift Supports Neurodevelopmental Research

A generous gift to the McGovern Institute from Polly and Peter Appel is accelerating research into the neurobiological mechanisms impacted by mutations in the *Shank2* gene. Scientists have established that Shank2 is a critical scaffolding protein that helps regulate communication between neurons in the brain, yet little is known about the downstream effects that can occur when mutations in *Shank2* arise. Thanks to the Appel family's support, researchers in the lab of Guoping Feng are undertaking several investigations into the significant changes that mutations in *Shank2* can cause at the synaptic, cellular, circuitry and behavioral levels.

The Appel family is investing in basic research at McGovern to better understand their son Jarret's rare condition, dubbed "Jarret Syndrome," which manifests in extraordinary memory and musical abilities and difficulties with cognition and learning. Their goal, and that of researchers in the Feng Lab, is to identify molecular pathways and targets that could provide new, effective treatment strategies for neurodevelopmental disorders such as Jarret Syndrome. ■

Photo: Appel family

Jarret Appel, son of McGovern supporters Polly and Peter Appel.

RESEARCH NEWS

Cognitive flexibility—the brain's ability to switch between different rules or action plans depending on the context—is key to many of our everyday activities. These neural representations of task rules are maintained in the prefrontal cortex, the part of the brain responsible for planning action. A new study from **Michael Halassa's** lab has found that a region of the thalamus is key to the process of switching between the rules required for different contexts. In a separate study, **Halassa** has managed to develop tasks that dissociate lower from high level brain functions so that the processes disrupted in ADHD subjects can be pinpointed. His findings illustrate how brain function is disrupted in ADHD, and highlights a role for perceptual deficits in this condition.

Mehrdad Jazayeri has discovered how the brain compensates for its own limitations during complicated mental computations. As in other situations where it has little confidence in its own judgements the brain attempts to overcome the problem at hand by relying on previous experiences.

Researchers commonly study brain function by monitoring two types of electromagnetism—electric fields and light. However, most methods for measuring these phenomena in the brain are very invasive. **Alan Jasanoff** has devised a new type of MRI sensor that can detect tiny electrical currents, as well as light produced by luminescent proteins.

Schizophrenia, a brain disorder that produces hallucinations, delusions, and cognitive impairments, usually strikes during adolescence or young adulthood. While some signs can suggest that a person is at high risk for developing the disorder, there is no way to definitively diagnose it until the first psychotic episode occurs. **Susan Whitfield-Gabrieli** and colleagues have identified a pattern of brain activity correlated with development of schizophrenia, which they say could be used as a marker to diagnose the disease earlier.

Neurons in the human brain receive electrical signals from thousands of other cells, and long neural extensions called dendrites play a critical role in incorporating all of that information so the cells can respond appropriately. Human dendrites have unique electrical properties, according to a new study by **Mark Harnett**, which may contribute to the enhanced computing power of the human brain.

Dopamine, a signaling molecule used throughout the brain, plays a major role in regulating our mood, as well as controlling movement. Many disorders, including Parkinson's disease, depression, and schizophrenia, are linked to dopamine deficiencies. **Ann Graybiel** and colleagues have developed a way to measure dopamine in the brain for more than a year, which they believe will help them to learn much more about its role in both healthy and diseased brains. ■

Photo: Lou Beaulieu-Laroche and Mark Harnett

Human neurons (right) have distinct biophysical properties compared to smaller rat neurons (left).

AWARDS & HONORS

Emilio Bizzi has received a Lifetime Achievement Award from the Italian Scientists and Scholars of North America Foundation.

At a ceremony in Toronto, **Ed Boyden** received the 2018 Canada Gairdner International Award for his role in the discovery of light-gated ion channel mechanisms and for the discovery of optogenetics.

Mark Harnett has been named a 2018 Vallee Foundation Scholar for his "original, innovative, and pioneering" work exploring the biophysical features of neurons.

Feng Zhang has been named winner of the 2018 Keio Medical Science Prize for "outstanding and creative achievements made in the life and medical sciences." ■

EVENTS

Pat McGovern (left) speaks with researchers from the IDG/McGovern Institutes in China at the 2013 McGovern Institute symposium.

Patrick J. McGovern Memorial Symposium

This spring, in collaboration with our sister institutes in China, the McGovern Institute is hosting a symposium in memory of our founder, Patrick J. McGovern, who passed away on March 19, 2014. The symposium will feature eight speakers from the IDG/McGovern Institutes at Beijing Normal University, Tsinghua University, and Peking University, as well as SIAT and MIT. The full-day symposium will take place on Monday, March 18, 2019 in 46-3002 (Singleton Auditorium). The event is free and open to the public, but registration is required. ■

The atrium of Building 46 sparkles with white lights during the holiday season.

Building 46 Holiday Party

Researchers and staff from the McGovern Institute, Picower Institute, and Department of Brain and Cognitive Sciences gathered in the atrium of Building 46 for a holiday meal and festivities. This is the twelfth year in a row that MIT's neuroscience community has celebrated the holidays with a party in the atrium. ■

The McGovern Institute for Brain Research at MIT is led by a team of world-renowned neuroscientists committed to meeting two great challenges of modern science: understanding how the brain works and discovering new ways to prevent or treat brain disorders. The McGovern Institute was established in 2000 by Lore Harp McGovern and the late Patrick J. McGovern, with the goal of improving human welfare, communication and understanding through their support for neuroscience research. The director is Robert Desimone, who is the Doris and Don Berkey Professor of Neuroscience at MIT and former head of intramural research at the National Institute of Mental Health.

Further information is available at: http://mcgovern.mit.edu

Brain SCAN
Quarterly Newsletter of the McGovern Institute

Editors: Sabbi Lall, Julie Pryor
Writer: Sabbi Lall
Director of Development: Kara Flyg
Design: Sametz Blackstone Associates, Boston

McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

Massachusetts Institute of Technology
77 Massachusetts Avenue 46-3160
Cambridge, MA 02139