

MCGOVERN INSTITUTE

FOR BRAIN RESEARCH AT MIT

# Brain SCAN

SUMMER 2013 ■ Issue no. 28

## Modern Thinking

*How technology is changing neuroscience*



## FROM THE DIRECTOR

When Pat and Lore McGovern founded the McGovern Institute, their vision was one of open collaboration, taking advantage of the incomparable range of technological expertise and opportunities that exist within and around MIT. One way that we have been building on that vision is through the McGovern Institute Neurotechnology (MINT) program, which is featured in this issue. The goal of the program is to support the development of new technologies for neuroscience research, and over the past 7 years, we have launched a wide range of innovative projects, in areas from nanotechnology to computer science to genomics. As I read these MINT project proposals, I am constantly amazed at the inventiveness of my MIT colleagues, and grateful for the opportunity to work with so many talented people.

Continuing on the theme of technology, I'm pleased to say that we are almost finished installing a new MRI scanner at our Martinos Imaging Center. The engineers are now fine-tuning the scanner's magnetic fields, and we expect to be up and running within a few weeks – effectively doubling our capacity for brain imaging and opening the door to a host of new studies on human brain function.

**Bob Desimone, Director**  
Doris and Don Berkey Professor  
of Neuroscience

*On the cover:  
White matter fiber tracts in the adult human brain, visualized using a diffusion-weighted MR imaging scan.*

*Image courtesy of Zeynep Saygin (MIT)*



## The McGovern Institute Neurotechnology Program exemplifies how technology is changing neuroscience.

On a brisk sunny day in early April, McGovern Institute Director Robert Desimone and his colleague Ed Boyden looked out across the White House lawn in Washington DC. They had been invited there, along with some 75 other leading researchers, to join President Obama as he announced a new initiative to invest in technologies for brain research. In the president's words, the new initiative will "[give] scientists the tools they need to get a dynamic picture of the brain in action and better understand how we think and how we learn and how we remember." The so-called BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative ultimately aims to help researchers find new ways to treat, cure, and even prevent brain disorders.

# Modern Thinking

## *The McGovern Neurotechnology Program at 7 Years*

While the details of the President's initiative are still being worked out, the McGovern Institute already has a longstanding interest in neurotechnology. When Desimone became director in 2005, co-founders Patrick and Lore Harp McGovern encouraged him to establish the McGovern Institute Neurotechnology (MINT) Program, to take full advantage of MIT's many collaborative opportunities.

"For me one of the attractions of coming to MIT was the opportunity to work with people who were developing new technologies that could be revolutionary if applied to the brain," says Desimone.

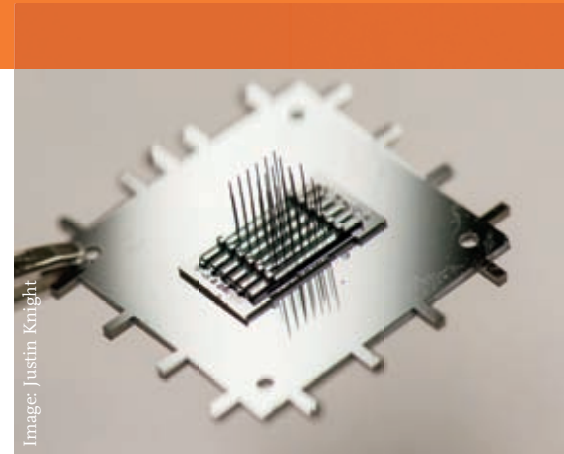
MIT, with its world-class engineering expertise, was ideally positioned for such an effort. "All that was needed was the catalyst, a way to break down barriers between engineers and neuroscientists and to speed up their interactions," says MINT director Charles Jennings, who was recruited by Desimone to run the program. "It's partly a matter of funding, but it's also about connecting people and maintaining strong channels of communication."

Today, the MINT program has supported over 25 projects, involving collaborations across at least 10 departments at MIT as well as several outside institutions. The list is eclectic, ranging from nanotechnology to neural prosthetics, from molecular genetics to management science. Among the latest projects, for example, one will explore nanodiamonds as sensors of neural activity; another will build a new super-resolution microscope; and another aims to develop an implantable device for blocking nerve conduction.

"Not every project is successful, but that's ok," says Jennings. "We're fortunate that we can afford to take chances on ideas that might be difficult to fund through more traditional sources. It's a bit like venture funding—if nothing ever fails we're probably not taking enough risks."

### **MINTing New Brain Tools**

Several years ago McGovern Investigator Ann Graybiel wanted to study deep brain structures using drugs that would target

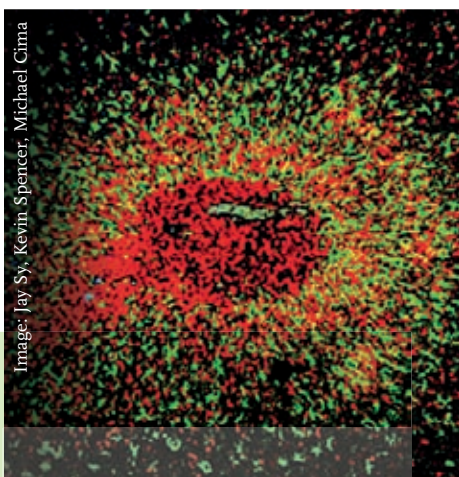


*An electrode array, developed in the Boyden lab, that can record neurons in multiple circuits throughout the brain.*

some cells but not others. But she had no way to inject tiny quantities of drugs deeply and precisely into the brain. Nor did she have the engineering expertise to devise such a tool in her own lab.

So Jennings connected her to MIT engineer Michael Cima, an expert on the design of medical devices. With the help of a seed grant from the MINT program they were able to design and build a working prototype for an “injectrode” that could inject tiny quantities of drugs with great precision, while simultaneously measuring their electrical effects at the injection site. They were later joined on the project by MIT Institute Professor Robert Langer, a renowned inventor and a longtime colleague of Cima. The three collaborators now have a multimillion dollar award from NIH to develop the technology further. They plan to test it in primate models of anxiety and depression, as a step toward eventual clinical applications.

“This is exactly what the MINT program is meant to do,” says Jennings. “We aim to support high-risk high-payoff projects, and to help researchers try new ideas quickly. We’ll give them just enough to do a pilot experiment, and if it works they are in a much stronger position to raise follow-on funding elsewhere.”



Probes made in the laboratory of Michael Cima are coated with biocompatible materials to reduce inflammation (red) and scarring (green) of brain tissue.



Photo: Justin Knight

Assistant Professor Polina Anikeeva examines a batch of fiber templates that will be extruded to form tiny opto-electronic neural probes.

## Striking a Cord

Threadlike and transparent, Polina Anikeeva’s implantable opto-electronic fibers must conform to the intricate shape of the backbone in order to reach the spinal cord. “The technology we’re developing is uniquely suited for hard-to-access structures that are constantly moving, flexing and bending,” says Anikeeva, who is applying her expertise in materials science to create these implants in collaboration with McGovern Investigator Emilio Bizzi.

The probes, which are extruded like pasta from soft metal and transparent polymers, are capable of sending and receiving both electrical and optical signals. Though the technology is still at an early stage, in tests with mice, Anikeeva has already been able to record neural signals and stimulate nerves with light using optogenetics. “When we stimulate we can even see the leg move,” she says, excited at the progress made since she received a MINT award last year.

Once the device is mature, Anikeeva and Bizzi hope to use it to map the connections between the spinal cord and motor cortex, something that is impossible with today’s technologies. “As we are gaining more understanding, we realize we need more and more advanced tools to continue exploring,” says Anikeeva, who is also working with McGovern Investigator Guoping Feng to develop a similar probe to study mouse models of autism.

In the longer term, Anikeeva hopes the spinal probe will evolve into a neuroprosthetic device that could, someday, restore motion to individuals with severed spinal cords. “This is one of the places where optogenetics could really make a difference in people’s lives,” she says.

## Engineering the Brain

Optogenetics has not yet been tested or approved for use in humans. But in one of the very first MINT projects, Boyden and Desimone took an important step toward that goal by applying optogenetics for the first time in non-human primates. Boyden, who subsequently joined the McGovern Institute, continues to pursue this work, and along with researchers at Massachusetts General Hospital recently published the first demonstration that optogenetics can induce behavioral effects in monkeys.

Now widely used in neuroscience research, optogenetics allows researchers to use light to control specific neurons in the living brain. In animal models of neuropsychiatric disorders such as Feng’s autistic mice, optogenetics can be used to perturb the neurons suspected to be involved, and to test ideas about how the disease might be treated.

To target the light more accurately within the brain, Boyden and MIT electrical engineer Cliff Fonstad have used MINT funding to develop a 3-D array of wave-

guides, tiny light-conducting channels with mirrored ends that can deliver light pulses in complex patterns within a targeted brain region. In future they plan to incorporate recording electrodes into their devices and to use different colors that will allow multiple types of neurons to be controlled simultaneously. “We’re trying to speak the language of the brain with light,” says Boyden.

## The Big Picture

Boyden’s words echo one of the stated goals of President Obama’s Initiative, which is to create an activity map of the brain. Ultimately researchers would like to do this at the level of individual nerve impulses, but with trillions of impulses happening every second this is still a remote goal. “We need to map the forest before we try to count every tree,” says Desimone.

For a 50,000-foot view of human brain activity, researchers can turn to neuroimaging. The method known as functional MRI (fMRI), for example, works by detecting local changes in cerebral blood flow, which are visible because blood contains iron. By using fMRI to scan subjects as they perform different mental tasks, researchers have been able to attribute specific functions to many different brain areas.



Photo: Justin Knight

*Charles Jennings, director of the MINT Program, helps to develop collaborations between neuroscientists and other researchers within and beyond MIT.*

“But fMRI is still a very indirect way to measure brain activity,” says bioengineer Alan Jasanoff, an associate member of the McGovern Institute. “Ideally, we’d like to use MRI to look at other changes that are more directly linked to the brain’s electrical activity.”

So Jasanoff is developing new magnetic agents that will make this possible. One of his early projects was a MINT-supported collaboration with MIT chemist Stephen Lippard to develop an agent to detect calcium ions, which regulate the release of neurotransmitters. “It turned out to be harder than we hoped, but we haven’t given up yet,” says Jasanoff.

**“We need to map the forest before we try to count every tree.”**

— Robert Desimone

Meanwhile, his lab has developed other agents that can detect neurotransmitters such as dopamine, revealing their 3-D distribution as they are released in the living rat brain. “We’re trying to learn how the spatial and temporal patterns of specific signaling molecules relate to the functioning of the brain as a whole,” he explains.



Official White House Photo by Chuck Kennedy

*President Barack Obama with NIH Director Francis Collins, announcing the President’s BRAIN Initiative on April 2, 2013.*

## Engineering the Future

Now that MINT has been underway for several years, it has become part of the fabric of McGovern. “Rather than simply focusing on new discoveries, we also have goals to develop the next generation of technologies for neuroscience research,” says Desimone. “And when something works, we want to make it as widely available as possible. Many of these tools will have applications that we can’t even anticipate at the outset. The more people use them, the greater the impact will be.” ■

## New Scanner Delivered to Martinos Imaging Center



Photo: Doreen Reuchsel

The 13-ton MRI scanner is hoisted by a crane outside the Martinos Imaging Center.

The McGovern Institute for Brain Research is installing a new 3-tesla MRI scanner for human neuroimaging. After months of planning and construction, the \$2M scanner, a Siemens Magnetom Trio, was delivered to the Martinos Imaging Center on July 25.

The core of the scanner is a large electromagnet, weighing around 13 tons and containing superconducting coils that are chilled in liquid helium to within a few degrees of absolute zero. It is housed in a custom-built room, with a specially reinforced floor to support the scanner's weight, and with some 5000 steel panels to shield the system from RF interference.

The acquisition of the new scanner was made possible by Bruce Dayton, Jeffrey and Nancy Halis, the Simons Foundation, and an anonymous donor. The scanner is expected to be fully operational by the fall, and will be used for a wide range of studies on brain function, in both children and adults. ■

## McGovern Makes Room for Big Data

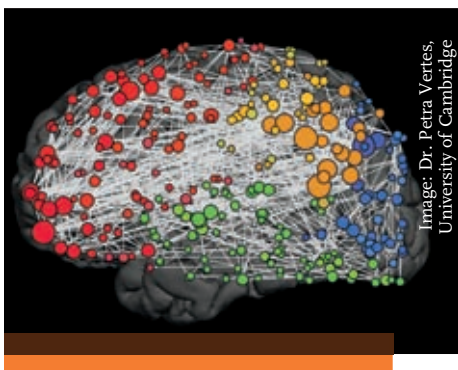


Image: Dr. Petra Vertes, University of Cambridge

Graphical representation of human brain activity.

Like many other fields of technology, brain research is increasingly driven by "big data," requiring massive computing power to analyze and store the results. The ever-growing demand for computing resources is an important bottleneck for many research projects. Now, thanks to the generous support of an anonymous donor, the McGovern Institute is establishing a new computing cluster as a shared resource for the MIT neuroscience community, one that will greatly expand researchers' access to high-performance computing. ■

## Motor Symposium Videos Now Online



Photo: Justin Knight

Sandro Mussa-Ivaldi of Northwestern University delivers a lecture at the annual symposium.

The annual McGovern Institute symposium, which took place on May 8, featured nine talks on the subject of motor control and the motor cortex. Photos and video of the symposium are available on our website. ■

## RESEARCH NEWS

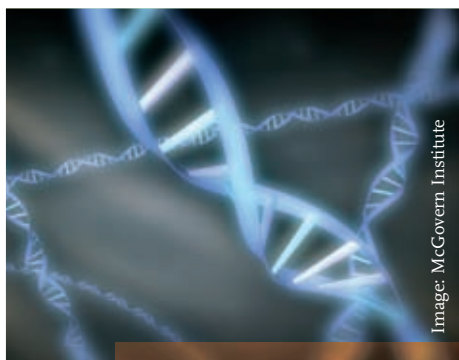


Image: McGovern Institute

**Feng Zhang's** lab has developed a new way to control gene expression with light. The method exploits a light-sensing mechanism from plants, which can be targeted to any gene of interest using customized DNA-binding proteins. This versatile method is likely to have many applications in basic and disease research.

By activating a brain circuit that controls compulsive behavior, researchers in **Ann Graybiel's** lab have shown that they can block compulsive behavior in mice—a result that could help researchers develop new treatments for diseases such as obsessive-compulsive disorder (OCD) and Tourette's syndrome. In a separate study, Graybiel's lab used a technique known as optogenetics to prevent habits from forming in the brain.

**Watch Ann Graybiel and her researchers describe their findings in video interviews on our website.**

A new study from **John Gabrieli** and colleagues casts doubt on a previous and widely publicized claim that memory training can raise human intelligence. In an attempt to replicate the finding, the MIT researchers confirmed that practice improves performance on the specific task, known as dual n-back; unfortunately, however, the effect did not generalize to other standardized measures of intelligence.

**Martha Constantine-Paton** and colleagues have studied a mutant mouse strain known as Flailer, showing that it has a defect in a cellular motor that is needed to transport synaptic proteins to their proper sites. Flailer mice also show many behavioral abnormalities, and may be a useful model for studying the neural circuits affected by psychiatric disorders.

**Bob Horvitz** and colleagues have identified a genetic pathway in nematode worms that controls the response to re-oxygenation following oxygen deprivation. A similar mechanism in humans may contribute to reperfusion injury, which can follow strokes or heart attacks when blood flow is restored.

**Ki Goosens** and colleagues are studying how the brain responds to stress. Using a method similar to human gene therapy, Goosens and colleagues found that raising the level of growth hormone could reverse some of the behavioral effects of stress. ■

## AWARDS AND HONORS

**Feng Zhang** is one of three recipients of the inaugural Vallee Foundation Young Investigator Award. The award recognizes “outstanding young scientists at a critical juncture in their careers” and provides discretionary funds for biomedical research. Zhang will share the \$750,000 prize with Kirsty Spalding of the Karolinska Institute and David Tobin at Duke University.

Zhang was also appointed the W.M. Keck Career Development Professor in Biomedical Engineering at MIT. ■



*Feng Zhang, who received a Young Investigator award from the Vallee Foundation.*

# EVENTS



## McGovern Institute Annual Retreat

This year, the McGovern Institute held its annual retreat at the beautiful Sea Crest Resort in Falmouth, Massachusetts. More than 150 McGovern faculty, staff, researchers, and students attended the 2-day event, which featured 16 talks, a poster session, and a clam bake by the beach. Pictures from the retreat are posted on our website. ■



■ *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 Patrick J. McGovern and Lore Harp McGovern, who are committed to 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:** Charles Jennings, Julie Pryor  
**Writer:** Elizabeth Dougherty  
**Director of Development:** Kara Flyg  
**Design:** Sametz Blackstone Associates, Boston

■ © Copyright 2013, McGovern Institute for Brain Research at MIT



## MCGOVERN INSTITUTE

FOR BRAIN RESEARCH AT MIT

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