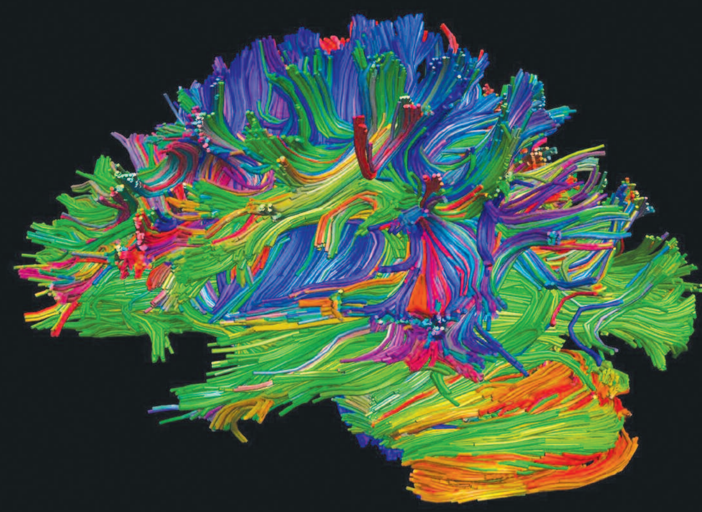
Brain SCAN

McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

Issue no. 15 *Winter 2010*



From the director

In this issue we celebrate the research accomplishments of Emilio Bizzi, who has charted new territory in understanding how the brain controls movement. I am also excited to announce two new communications initiatives: the launch of our redesigned website and the release of our new feature video, 'Welcome to the McGovern Institute.'

Over the past few months, Emmy-nominated producer John Rubin has been filming at the McGovern Institute and interviewing our faculty members. The result is a compelling 20-minute feature video that highlights our mission to understand the brain in health and disease. John and his team have also produced a short trailer for the feature video, along with profiles of individual faculty members. I am pleased to share these videos with you on our new website at http://mcgovern.mit.edu.

This issue of *Brain Scan* features the work of my colleague Emilio Bizzi, who has devoted his career to one of the greatest challenges in neuroscience: understanding how the brain controls voluntary movements. Although his main focus has been on the basic science of movement, Emilio's work is also shedding new light on the problem of stroke and the challenge of developing better rehabilitation methods for stroke patients.

In this issue we also celebrate the achievements of some of our youngest researchers. Undergraduates Ugwechi Amadi in Ki Goosens' lab and Caroline Huang in John Gabrieli's lab were named Rhodes Scholars, and Tanya Goldhaber in Nancy Kanwisher's lab was awarded a Marshall Scholarship. We congratulate these young scientists and wish them the best in their future careers.

I am thrilled to announce that we are awarding our annual Scolnick Prize in Neuroscience to Lily and Yuh-Nung Jan of University of California San Francisco, for their work on the development and function of the nervous system. We will host their award lecture on Friday May 28. Meanwhile, I hope you will visit our new website and join our mailing list to stay in touch with all the latest news from the institute.

Bob Desimone, Director

Cover art: An image from an animated brain sequence in our feature video.

Image courtesy Satrajit Ghosh / MIT

Emilio Bizzi, Institute Professor and a founding member of the McGovern Institute.

Photo courtesy Kent Dayton

LEARNING THE MOTIONS

Emilio Bizzi's discoveries about how the brain translates our plans for movement into action could, among other things, improve rehabilitation techniques for stroke and brain injury.

Watching a baby try to reach for a toy reminds us that the motions we take for granted are really quite complex. We have about 600 muscles in our body, and each one is supplied by hundreds or thousands of motor neurons. For even the simplest action, the brain must determine which combination of these neurons will activate the right set of muscles with the right forces at the proper time.

Moreover, every new movement is unique. For example, the toy is never in exactly the same position relative to the baby's body. But somehow the brain generalizes from experience to calculate the forces and trajectories needed to perform a new version of this apparently simple action.

Given these complexities, it is not surprising that we need time and practice to master a new motor skill. Yet once we do master a skill, we rarely forget it and can often perform it "on autopilot." Motor memories are much more stable than other memories such as facts and figures because they are encoded differently in the brain. As a result, we can often retrieve motor memories almost effortlessly. This may be a matter of survival, suggests Bizzi: "It's the law of the jungle. You can't forget how to run when you need to escape from a tiger."

But motor memories can be lost, through stroke, brain injury and other disorders, often with devastating personal and social consequences. In these patients the spinal cord and muscle connections are usually intact, but the brain can no longer generate the right commands to produce normal movement. Yet because some patients do recover from stroke, we know that the chain of command can sometimes be restored and normal movements regained.

Bizzi hopes that by better understanding how those motor commands are generated, researchers can develop faster and more effective rehabilitation strategies. In the longer term, this may also lead to new prosthetic devices. "We need better neuroprosthetics for amputees and people with motor disabilities," he says. "After an era of basic discoveries, the field has reached a stage where we can make real progress in these areas."

The road from Rome to MIT

Bizzi became interested in neuroscience after receiving a medical degree from the University of Rome. “It seemed that neuroscience was on the verge of important breakthroughs and I wanted to be part of that,” he recalls. He earned the Italian equivalent of the Ph.D. in 1968 from the University of Pisa while conducting research on motor learning at the National Institutes of Health in Maryland.

MIT invited him to join the Department of Psychology in 1969 as its first neurophysiologist—a turning point for a discipline that had traditionally seen the mind as separate from the brain. At MIT, he studied the control of eye and limb movements, work that led to his election to the National Academy of Sciences in 1986. Other honors followed, including membership in the Institute of Medicine, the American Academy of Arts and Sciences (he was elected secretary in 1999 and president in 2006) and the Italian National Academy.

In 1986, he became the first chair of the newly formed Department of Brain and Cognitive Sciences, laying the groundwork for the growth of neuroscience research at MIT. In 2000 he became a founding member of the McGovern Institute. MIT bestowed its highest honor for faculty on him in 2002, naming him Institute Professor. The admiration is mutual. “Over the years I have been occasionally enticed to consider returning to Italy,” Bizzi notes, “but MIT is where I love to be.”

Emilio Bizzi with postdoctoral associate Robert Ajemian and technical assistant Adam Ellsworth.

Modules of motion

In recent years, Bizzi has focused on two related questions. How does the brain handle the enormous complexity involved in making even the simplest movement? And how does the brain learn a new motor task and then generalize that learning to each new variation of the task?

As the baby example suggests, the central nervous system solves a gigantic problem every time we execute a movement. No existing computer can analyze the myriad variables involved in contracting, flexing, or rotating a multi-jointed limb.

For many years, scientists wondered how the nervous system tackles this problem. Must the brain search through every possible combination of muscle activation to find one that will produce a desired motion? Or does the central nervous system establish mini-command centers, or modules, in the spinal cord that relieve the brain of this onerous oversight?

Bizzi is a prominent advocate of the module proposal. “It’s the same logic we use when tackling any big problem,” he says. “Break it down into smaller components you can analyze.” Specifically, he thinks that the central nervous system handles the daunting variables involved in executing a movement by grouping sets of muscles and their innervating neurons into integrated, synergistic units.

In earlier work with frogs, Bizzi serendipitously discovered that electrically stimulating certain places in the spinal cord caused the limb to move to a defined position. He realized that he was stimulating neural circuits that simultaneously activated of a group of muscles as a functional unit, or module. Different stimulation sites produced different patterns of muscle activity, suggesting that the spinal cord’s circuitry encoded a number of different modules. It has been difficult to prove that such

A subject uses a robotic arm to steer a cursor towards the center of the screen. The movement is disrupted by an external force, which the subject eventually learns to counteract.

modules exist in higher organisms because of the complexity of modeling how they would work. But by collaborating with a new generation of computational experts who are developing novel methods, such as iterative algorithms, Bizzi has gathered evidence for the existence of modules in the limbs of rodents, monkeys and people.

He believes this modular organization is key to understanding how the brain controls movement. “Grouping muscles into a small set of modules simplifies the problem,” he explains. “It allows the brain to control

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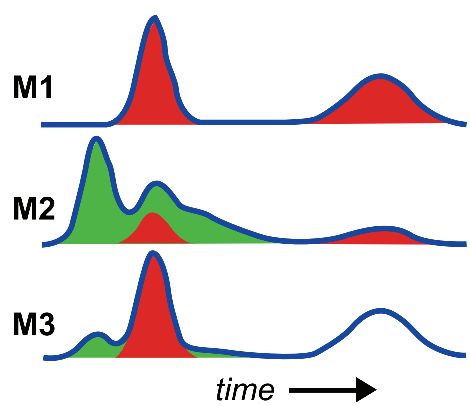


*Graphic illustrating how two modules (*shown in green and red*) can control complex patterns of activity in three muscles (*M1, M2, and M3*).*

Adapted from Cheung VCK et al. PNAS 2009 a large number of muscles with just a few signals from the regions involved in programming voluntary movements."

To make different movements, the brain combines those signals in different ways. Bizzi compares this combinatorial modularity to written language: "With just a limited set of letters, we can construct an infinite number of words and sentences."

Rehabilitating rehab

In addition to helping to explain a fundamental scientific mystery, Bizzi hopes his work will lead to better rehabilitation methods for victims of stroke and brain injury.

There are about 700,000 strokes per year in the United States, and many more brain injuries. Most of these will affect the motor system, often leading to lifelong disabilities. "Motor disability is one of the most common and devastating problems in neurology," says Bizzi. "But rehabilitation therapy is slow and primitive because it is not based on any good theory. It's very important to speed up this process and make it more effective by approaching it in a more principled way."

Bizzi recently collaborated with clinical neurologists in Venice, Italy and at Spaulding Rehabilitation Hospital in Boston in examining muscle activity in stroke patients as they performed different reaching movements. The patients had stroke damage in only one cortical hemisphere, so one arm was impaired while the other was unaffected. Along with his postdoc Vincent Cheung, Bizzi compared the activity patterns in the two arms, and showed that the same modules were present in both arms but their activation and combination was disrupted specifically on the affected side.

Now, with a new grant from the National Institutes of Health, Bizzi and collaborators at Spaulding hope to track a group of stroke patients and find out how the activation of modules changes throughout the rehabilitation process. "We also want to know if some modules are more affected than others, and if so, can we speed up a patient's recovery by focusing on the most affected modules? This could give us a degree of specificity that has been missing in rehabilitation therapy."

In his own words:
Bizzi describes his research in a video profile on the McGovern Institute website.

The best is yet to come

Bizzi relates how he learned neuroscience "from scratch" after medical school, and then taught himself physics and math so he could study movement. But he thinks progress in understanding motor control and learning has lagged behind other fields of neuroscience because it is harder to study.

"There's a divide between those who study motor behavior and learning at the level of skills versus at the level of neurons, and it's a challenge to relate neurophysiology, psychophysics, neural network theory, differential geometry, and behavior," he explains. In the course of his career, Bizzi has formed many collaborations within the fields of biomechanical and electrical engineering, materials science, robotics, and computer science—areas that traditionally do not overlap.

Within the McGovern Institute, Bizzi also collaborates with Tomaso Poggio on computational methods, and with Ki Goosens on the genetics and molecular biology of motor learning—and of recovery of function following brain injury—in rodents. He also has a longstanding collaboration with Neville Hogan in the MIT department of mechanical engineering, and he is now collaborating with neurosurgeons to develop new methods to study brain plasticity in monkeys as they learn new skills.

"I think the field is just now on the brink of being able to investigate motor problems, and the most important discoveries will come in the following decades," Bizzi says. As much as he loves art, classical music, ancient history, and tennis, he would also love to be reborn and start again now in neuroscience, like today's young scientists whose future achievements will rest on the foundation of knowledge that his generation has helped lay down. ■

Poitras Center Supports Psychiatric Research

The Poitras Center for Affective Disorders Research was established in 2007 through a generous gift by Patricia and James Poitras '63 to support research into the causes of depression, bipolar disorder, and other major psychiatric disorders.

Now, some 2 ½ years later, the center has supported more than seven projects, enabled the recruitment of a new McGovern faculty member with expertise in psychiatric disease, and established strong collaborations with local clinical research institutions and with colleagues at MIT and the Broad Institute.

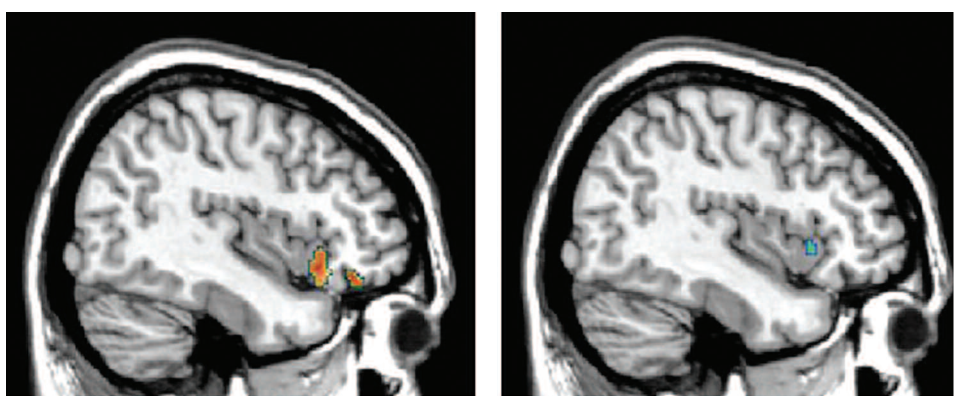
The Center recently recruited a new faculty member, Guoping Feng, who will hold the Poitras Professorship of neuroscience when he joins the McGovern Institute in the spring of 2010. Feng studies synaptic connections and their disruption in mouse models of human brain disorders. He has developed a variety of genetic technologies to study the mechanisms underlying psychiatric diseases, including obsessive-compulsive disorder and bipolar disorder.

In addition to animal work, the Poitras Center supports many studies on human patients. In collaboration with psychiatrists at Massachusetts General Hospital, McGovern scientists have found patterns of abnormal activity in schizophrenic patients that could reveal the underlying causes of this disorder and may also aid diagnosis and treatment choices. Specifically, the researchers found that patients with schizophrenia exhibited an overactive 'default' network in the brain—a network typically involved in self-reflection—both during a restful state and during the performance of a difficult task. The scientists suggest that this may reflect an inability of people with schizophrenia to direct mental resources away from internal thoughts and feelings and toward the external world in order to perform complex tasks.

Now, building on the schizophrenia results, McGovern scientists are collaborating with researchers at McLean Hospital to determine whether this 'default' brain network is similarly overactive in patients with bipolar disorder.

In two other studies, researchers are scanning patients undergoing treatment for depression and social anxiety disorder to look for markers of the psychiatric diseases as well as possible brain changes in response to treatment. Early results suggest that differences in brain structures may predict how well a person with anxiety disorder responds to a combination of drug treatment and cognitive behavioral therapy. ■

In 2007, Patricia and James Poitras '63 committed $20 million to the McGovern Institute to establish the James W. and Patricia T. Poitras Center for Affective Disorders Research. The center is now bearing fruit in the form of strong scientific collaborations both within and beyond MIT as well as advances in our understanding of schizophrenia, bipolar disorder, depression, anxiety disorder, and ADHD. ■



Bipolar patients (L) and healthy control subjects (R) show opposite patterns of brain function in the frontal lobe, shown here as orange (positive) or blue (negative) patches superimposed onto a standard anatomical brain template.

Image courtesy Susan Whitfield-Gabrieli / MIT and Dost Ongur / McLean Hospital

Three McGovern Students Awarded Marshall and Rhodes Scholarships

Tanya Goldhaber

Ugwechi Amadi

Caroline Huang

Images courtesy MIT News Office

Three McGovern students are among the 40 Marshall Scholars and 47 Rhodes Scholars who will study at Oxford and Cambridge universities next year. Both scholarship programs select candidates from an intensely competitive field on similar criteria—outstanding scholarship, noteworthy service, and potential for future contribution to national or international welfare.

Tanya Goldhaber, a research assistant in Nancy Kanwisher's lab, is the recipient of the Marshall Scholarship, one of only 62 students from MIT to win the prestigious scholarship since its establishment in 1953. In Kanwisher's lab, Goldhaber examined the brain mechanisms underlying human visual perception and cognition. "Tanya is beloved in my lab for her energy, enthusiasm, and amazing array of skills," says Kanwisher. "Tanya can do anything: she can build a roller coaster, play virtuoso violin, and run a brain stimulation experiment. We'll miss her, but we're thrilled for her and her exciting new opportunities." Starting in October Goldhaber will study for a PhD in engineering design at Cambridge University.

Ugwechi Amadi, a double major in brain and cognitive sciences and literature, is working in the laboratory of Ki Goosens, where she has been studying rodent models of post-traumatic stress disorder. Her work in Goosens' lab has been supported in part by Robert Metcalfe '68, founding chair of the McGovern Institute leadership board. Since coming to MIT in 2006, Amadi has held a number of student leadership roles, including president of the Brain and Cognitive Sciences Society.

"Ugwechi is a superstar—she is a true "self-starter" who has the confidence, maturity, and talent to perform experiments on her own," says Goosens. "I am incredibly proud of her. She is the kind of undergraduate that every professor wants in their lab. She will do great things at Oxford, and also at whatever school she eventually attends for her MD/PhD work." Ugwechi will begin her Rhodes scholarship at Oxford next year, where she plans to study for an M.Sc in psychological research.

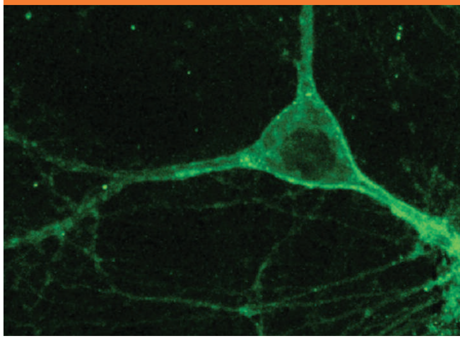
Another new Rhodes scholar is **Caroline Huang**, a brain and cognitive sciences major in John Gabrieli's lab, who is using MRI imaging to investigate brain areas associated with reading and dyslexia. She is also collecting data at the Boston Children's Museum for a study of causal learning in children. Huang, who plans to dedicate her life to healthcare advocacy, will pursue a doctorate in public health from the Ethox Centre at Oxford, where she will study the ethics of healthcare practice. ■

Labs of Their Own

The following McGovern researchers have obtained faculty positions within the past year:

- **Jess Cardin**, who was a postdoc in Chris Moore's lab, is now an assistant professor at Yale University School of Medicine.
- **Xue Han**, a postdoc with Robert Desimone, will become an assistant professor at Boston University this summer.
- **Michael Hurwitz**, a postdoc with Bob Horvitz, is now an assistant professor at Yale Cancer Center.
- **Itamar Kahn**, a visiting postdoctoral associate in Chris Moore's lab, will become a professor at the Technion in Haifa, Israel.
- **Ioulia Kovelman**, a former postdoc in John Gabrieli's lab, is now assistant professor at the University Michigan.
- **Michael Long**, a former postdoc in Michale Fee's lab, is now an assistant professor at New York University School of Medicine.
- **Long Ma**, who was a postdoc in Bob Horvitz's lab, is now an assistant professor at Central South University in China.
- **Niels Ringstad**, also a former postdoc with Bob Horvitz, is now an assistant professor at New York University.
- **Jason Ritt**, a former postdoc with Chris Moore, is now an assistant professor at Boston University.
- **Thomas Serre**, a former postdoc in Tomaso Poggio's lab, joined Brown University as an assistant professor this January.
- **Won Mok Shim**, who was a postdoc with Nancy Kanwisher, is now an assistant professor at Dartmouth College.
- **Ed Vul**, a postdoc with Nancy Kanwisher, will become an assistant professor at the University of California San Diego this fall.

IN THE NEWS



Mouse neuron expressing a protein called Arch that allows its activity to be controlled by light.

Image courtesy Brian Chow, Xue Han and Ed Boyden / MIT

Ed Boyden developed a powerful new method to control brain activity using light. His findings were covered by the *BBC*, *Forbes*, the *Washington Post* and *U.S. News & World Report*.

BBC News, *ABC News*, *Financial Times*, *msnbc.com*, *Wired.com* and *BusinessWeek* reported on a study by **Ann Graybiel** and colleagues in Illinois, who found that the shape of a person's brain can predict how well they will perform on a video game.

John Gabrieli was interviewed by Alina Cho of CNN's *American Morning* for a segment on brains and intelligence.

Nancy Kanwisher was one of four key scientists interviewed by Charlie Rose for the PBS episode *Sight and Visual Perception*, which premiered on November 24. A recent study by Kanwisher and colleagues in Beijing on the heritability of face recognition was covered by *Scientific American* and *Wired.com*.

EVENTS

Lily Jan and Yuh-Nung Jan to Deliver Scolnick Prize Lecture

On May 28, the McGovern Institute will award the 7th annual Scolnick Prize in Neuroscience to Lily Jan and Yuh-Nung Jan of the University of California, San Francisco.

The Jans have been pioneers in the study of potassium channels, which are central to understanding the brain's electrical properties. Their genetic work on fruit flies has also provided many key insights into early brain development, including how the embryonic brain produces so many different types of neurons, and how these neurons form the distinctive shapes and connections that underlies the working of the brain.

Following the presentation of the award on May 28, the Jans will deliver a joint lecture at 4pm entitled "Dendrite morphogenesis and channel regulation: implications for mental health and neurological disorders." A reception will follow the lecture. The event is free and open to the public. Visit our website for more information: http://mcgovern.mit.edu

Lily Jan and Yuh-Nung Jan are the joint recipients of the 2010 Edward M. Scolnick Prize in Neuroscience.

Photo courtesy Noah Berger / UCSF

Join Our Mailing List

It is now easier than ever before to stay informed about what's happening at the McGovern Institute. Visit our new website and join our mailing list for print or email updates: http://mcgovern.mit.edu.

Facebook users can also become fans of the institute at http://www.facebook.com/mcgoverninstitute.

Awards and Honors

In December 2009, **Tomaso Poggio** was named a fellow of the American Association for the Advancement of Science (AAAS) which cited his "distinguished contributions to computational neuroscience, in particular, computational vision learning and regularization theory, biophysics of computation and models of recognition in the visual cortex."

Aaron Andalman, a postdoc in Michale Fee's lab, was awarded the 2009 Capranica Foundation Neuroethology Prize for his thesis work in birdsong trial-and-error learning. The prize recognizes "outstanding achievement or future promise in the field of neuroethology (neural basis of natural animal behavior) by young scientists early in their careers."

McGovern Institute Launches New Video

We are pleased to announce the launch of our new video, 'Welcome to the McGovern Institute.' This 20-minute video, produced by Emmy nominee John Rubin, shows how research at the Institute is pushing the frontiers of technology and providing new insights into brain disorders such as autism, Parkinson's disease, and mental illness.

The feature video, along with a short trailer can be found on our new website: http://mcgovern.mit.edu.

The McGovern website has been completely redesigned, with improved navigation and greatly expanded content, including a collection of video profiles of McGovern Investigators. As we approach our tenth anniversary, the new website reflects a decade of discoveries and our vision for the future. It includes detailed information about each of our 16 faculty members, and about the Institute's history and accomplishments. There are specific pages devoted to the ways in which the institute's research is advancing our understanding of the brain in health and disease. ■

McGovern researchers are featured in our video, which is freely available on our new website.

Save the Date: Annual Symposium

The McGovern Institute annual symposium will take place on Friday May 7, 2010. The main theme will be neural circuits, their relationship to behavior and implications for therapy. There will also be a keynote talk from Steven Paul, formerly Executive Vice President for Science and Technology at Eli Lilly, who will talk about the path from basic research to molecular medicine and new treatments for Alzheimer's disease. The symposium will be free and open to the public. Visit the McGovern Institute website to register for this event. ■

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, formerly the 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

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