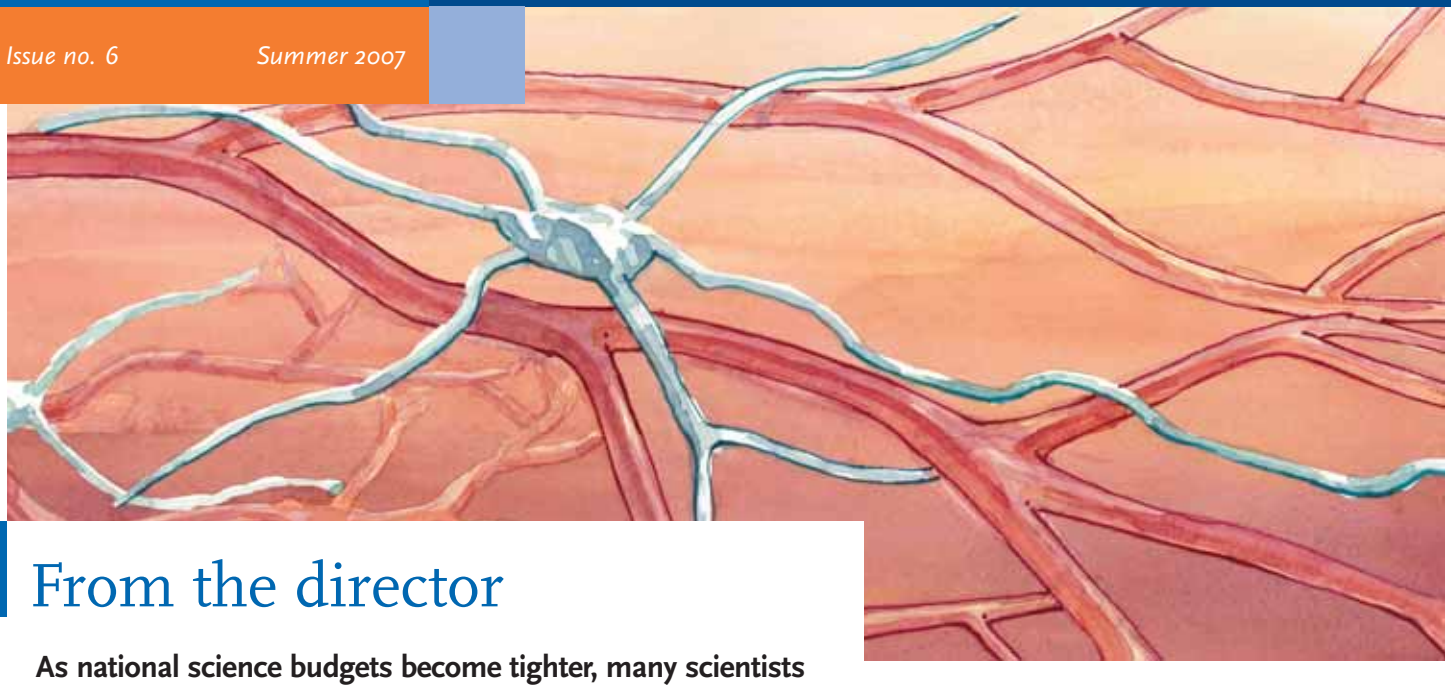
Brain SCAN

McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

Issue no. 6 Summer 2007



From the director

As national science budgets become tighter, many scientists become more conservative in their research, because risk-taking can lead to a loss of funding. Yet, great discoveries in science typically require taking new paths into uncharted territory.

An artist's conception of the interaction of blood vessels and neurons, described in Chris Moore's hemo-neural hypothesis on pages 2–4.

Image courtesy Julian Wong

A wonderful example of someone taking creative risks in neuroscience is Chris Moore, a faculty member in the McGovern Institute and The Department of Brain and Cognitive Sciences at MIT. Chris has developed a novel hypothesis about an important brain system—the vast web of blood vessels that interact with neurons in ways we are only beginning to understand. Chris is taking a fresh look at that interaction, with implications for understanding the relationship between the body and the mind. Practically speaking, his research might help us understand, diagnose, and treat some brain diseases, and better utilize one of our most powerful neuroscience tools, functional magnetic resonance imaging (fMRI). Because of the tremendous potential benefits to basic and translational neuroscience, we thought this risk was worth taking and we initially provided some McGovern discretionary funds and a Schoemaker Fellowship to support Chris's work. Now, we are joined by someone who also understands the importance of innovation in basic science, Thomas F. Peterson, Jr. '57, who has stepped forward with a major donation to Chris's efforts. This gift will help facilitate an exciting collaboration with the Cleveland Clinic Heart Brain Institute. You may read about Chris's research and Tom's wonderful new commitment to it in this current issue.

The timeliness of Chris's research was evident in our 2nd annual Brain Imaging Symposium, "Plumbing the Mind," in which researchers from around the world described their newest findings regarding the interaction between the vasculature and neurons. The symposium also coincided with the arrival of our second magnetic resonance machine, a very powerful 9.4 Tesla magnet for animal studies. Both of these events are also described inside.

We're also pleased to describe in this issue new collaborations—one international and one within MIT—that are also forays into uncharted territory for the McGovern Institute.

Bob Desimone, Director

A SEAT FOR BLOOD AT THE NEUROSCIENCE TABLE: THE HEMO-NEURAL HYPOTHESIS

According to Christopher Moore's new theory, blood flow is more than just meal delivery for neurons that become hungry when they're active. Blood itself plays a key role in the brain's information processing.

Christopher Moore

What if computation in the brain wasn't only about neurons? What if blood flow were also an important actor in brain computation? Chris Moore thinks that's the case, and he has developed a bold new theory to describe what he thinks actually happens in the brain.

It's well established that blood flow increases as neurons become more active, so blood flow serves as an after-the-fact marker of regional brain activity. But in Moore's theory, the increased blood itself modulates neural activity by changing the responses of neurons in that local region, such as how excited the neurons become in response to a sensory stimulus. These changes in a given neuron's properties will affect its contribution to information processing.

If his theory is correct, analyzing blood flow can teach us a lot about how the brain's information processing works in both health and disease. It provides a new insight into how damage to the vascular system might impact brain function in diseases ranging from migraine to epilepsy, and that insight could lead to new therapeutic approaches to brain disease and injuries. Moreover, this new perspective will make functional magnetic resonance imaging (fMRI) a more powerful tool than ever imagined.

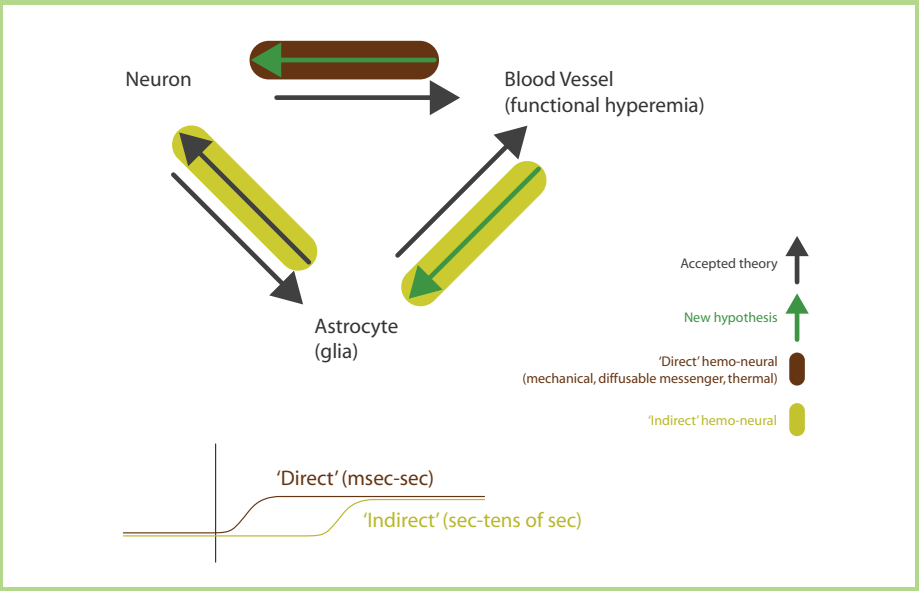
Translating Blood Flow into Information Processing

Functional magnetic resonance imaging (fMRI) already stands as one of the most powerful tools available to neuroscientists, referenced in over 15,000 articles in the last 15 years. It's a non-invasive way of peering inside the brain to learn how different brain regions process information as we try to memorize a math function, reflect on our happy childhood, or consider whether to bet on a dark horse. This imaging tool works because blood flows to the local brain regions that are processing that information.

It happens that MRI machines detect increases and decreases in blood flow as certain brain regions become more or less active. Although the exact relationship between the MRI signal and neural activity is not fully understood, fMRI technology essentially uses blood flow as a convenient marker for monitoring the otherwise inaccessible neural activity, letting us see, via the magnet used in the MRI machine, the hotspots of activity created by such brain processes.

The Hemo-Neural Hypothesis:
Black arrows indicate the accepted theory: 1) neurons can drive blood vessels to expand, creating increased blood flow (functional hyperemia); and 2) neurons can drive astrocytes (a type of glia) which can also induce increased blood flow. White/Green arrows indicate the new hypothesis: Increased blood flow can influence neural activity, either directly and quickly (brown) or indirectly and slowly (yellow) by modulating astrocytes, which are already known to influence neurons.

Diagram courtesy Julian Wong (artist) and Christopher Moore (McGovern Institute)



The classic theory suggests that blood flow increases because the neurons that become more active increase their metabolic activity and need more oxygen and glucose, and also use blood to remove the waste products generated by this activity. For the past 10 years, though, Moore has wondered whether blood has a role in the brain beyond metabolism. He recently published the fruits of that pondering—a thought-provoking theory called the Hemo-Neural Hypothesis—as an invited review in the *Journal of Neurophysiology*.

Moore agrees that when neurons become more active, they recruit more blood flow, but says that's not where the story ends. The increase in blood flow—and volume—next acts back on the local neural circuit that called for the blood, transforming the neurons' properties and changing the excitability of that circuit in a way similar to many neurotransmitters. Just as neurotransmitters like serotonin and dopamine play essential functions in modulating neural networks in an activity-dependent way, so might blood flow.

These modulations can occur on a fast timescale, through direct interaction between blood and neurons, Moore predicts. But they can also take a slower, indirect route, when blood interacts with the helper cells in the brain, glia, which in turn then modulate neurons. (Accumulating evidence suggests that neurons and glia, and glia and blood vessels, mutually influence each other.) He also proposes several mechanisms of action along both routes, described later in this article.

If experiments from Moore's lab and others bear out this theory, neuroscientists will have to revise their understanding of how information processing in the brain is conducted, Moore says. They will have to add an entirely new biological system to the process.

A New Look at fMRI

This theory casts a whole new light on fMRI and what it tells us. Traditionally, this signal has been regarded as a one-directional "readout" or marker for changes in neural activity. That readout will still be valid under the new theory, but it will represent a two-way street that will allow researchers to predict how neural activity might respond after being influenced by the recent increase in blood flow.

In other words, if blood flow impacts neural activity, fMRI brain scans don't just reveal an indicator signal. They also show part of the causative process within the system itself. This additional layer of meaning increases the complexity in interpreting the fMRI signal, but that interpretation will have much more significance. Instead of observing that blood is flowing to a region in response to past neural activity, researchers will also have to ask: How is blood flow going to change neural activity in this region in the near future?

New Clinical Insights and Avenues

Moore believes his hypothesis could have substantial clinical implications. It could change the way we diagnose and treat Alzheimer's disease, which recent studies suggest starts with vascular decline before neurons themselves die. Alzheimer's symptoms, especially at onset, could partially result from the loss of a major neuromodulatory system, blood flow.

In stroke, a major factor in cognitive and functional decline is loss of blood flow to a region. Perhaps it's not just cell death that may be leading to post-stroke impairment, but also the loss of a major modulatory agent because of damage to the vascular system itself.

Similarly, in epilepsy, people often have unusual vasculature in the areas where seizures arise. If blood flow modulates neural activity, epilepsy may result from a loss in blood-dependent regulation, which Moore's theory suggests may normally keep neural activity in check. If this control knob is lost, abnormal, or damaged, the brain may show runaway excitation.

continued, page 4

Mechanisms of Action

How could blood flow actually translate into neural activity? Moore points to a wealth of data that have never been interpreted in this light before but that he believes provide a route for communication between the vascular and neural systems.

First, the mechanical mechanism. Certain neurons have ion channels that open in response to mechanical pressure. Opening the ion channels changes the membrane potential of the neuron, and that changes how it fires in response to stimulation. It turns out that some brain regions, including the neocortex, have high concentrations of several such ion channels. Thus, when-blood volume increases, the dilating blood vessels and increased flow and volume could influence neurons locally.

Second, blood contains numerous diffusible factors, such as nitric oxide, that are known to influence neural activity. Increasing blood volume will also increase the local concentration of these factors, modulating local neurons as they diffuse out of blood vessels.

Third, blood flow largely determines brain temperature, and changes in temperature affect the excitability of neurons. An increase in blood flow to a region will change the brain's temperature in that region, possibly modulating neural activity at that time.

All of these mechanisms probably modulate neural activity on a dual time course. Blood's direct impact on neurons would change the functionality of a local brain area in rather rapid fashion (milliseconds to seconds). But the mechanisms may also work slowly, through the glia that connect to both neurons and blood vessels. Glia, for example, respond to very minute mechanical changes and diffusible factors. This second proposed 'indirect' pathway probably operates at a slower pace (seconds to tens of seconds).

With the help of graduate student Rosa Cao, Moore has been gathering intriguing evidence to support this hypothesis for the past 2 years. Cao attributes her ability to work intensively on this innovative project to the McGovern Institute's Shoemaker Fellowship, because the research is too 'risky' to receive traditional grant funding. Two other graduate students, Ulf Knoblich and Bryan Higashikubo, have recently made major contributions to ongoing studies.

Beyond the Neuron Doctrine

In proposing this theory, Moore joins a small but growing contingency of neuroscientists who chafe at the 'neurocentric' textbook view of brain activity. Neurons are not the sole proprietor of brain activity. Since blood vessels and glia may be playing a role in information processing, Moore teasingly suggests that we might have to rename the field of 'neurobiology' to better capture the reality of biological information processing.

To his knowledge, the hemo-neural hypothesis is an entirely different view from any previously proposed in the modern era. "Blood flow isn't included as part of anyone's operative model of information processing in the brain," he asserts. "It's time blood had a seat at the table."

Actually, one person did previously propose a similar theory, Moore notes. Aristotle, the ancient Greek philosopher, believed that the heart was the seat of the mind, and so blood circulation carried out information processing. Perhaps the Greeks were onto something all those years ago. ■

Tom Peterson funds Hemo-Neural Hypothesis

Tom Peterson in his Cleveland Ohio Lab.

Thomas F. Peterson, Jr. '57 has once again shown his consummate understanding of the value of scientific inquiry in choosing to support Chris Moore's novel hypothesis. As a successful engineer, inventor, and businessman, Tom appreciates the fact that success in any field requires creative risk-taking, and in making his new commitment to Chris notes that, "Results in successful research are often serendipitous, and by definition, serendipity is unpredictable. We must encourage it if it is to bloom and welcome it when it does."

Chris in turn responds: "I couldn't be more excited about interacting with Tom. As a scientist and engineer, he believes in and studies scientific discovery. We've had wonderful conversations. Tom's gift is essential to this line of research and could not be timelier. I'm also thrilled to be collaborating with Ed Boyden of MIT and the Cleveland Clinic Heart-Brain Institute. The Clinic is a world leader and a perfect partner in trying to see if these ideas, and the techniques to test them, have relevance in a clinical context. It's a great win-win situation."

Tom's previous gifts to MIT include the creation of the Thomas F. Peterson, Jr. conservator position in the Libraries, as well as support for the digitization of the Vail Balloon Prints within MIT's renowned Vail Collection. Also, under Professor Markus Zahn, Tom has sponsored a course VI Master's Degree replicating results of his charge measurement apparatus patent, and support for two graduate students to study the feasibility of using ferro fluids as a cancer treatment by affecting their location and temperature within an MRI environment using mathematically derived fields.

High Resolution MRI Machine Arrives

Last May, the Martinos Imaging Center at the McGovern Institute received MIT's first scanner for noninvasive imaging of the human brain, a 3 Tesla Siemens magnetic resonance imaging (MRI) machine. This spring, thanks to an anonymous donor, a new, more powerful scanner moved in next to it. This scanner, a 9.4 Tesla Bruker magnet with a small (20 cm) bore, will be used for rodents and small primates, live cell cultures and chemical preparations, and the development of new imaging technologies.

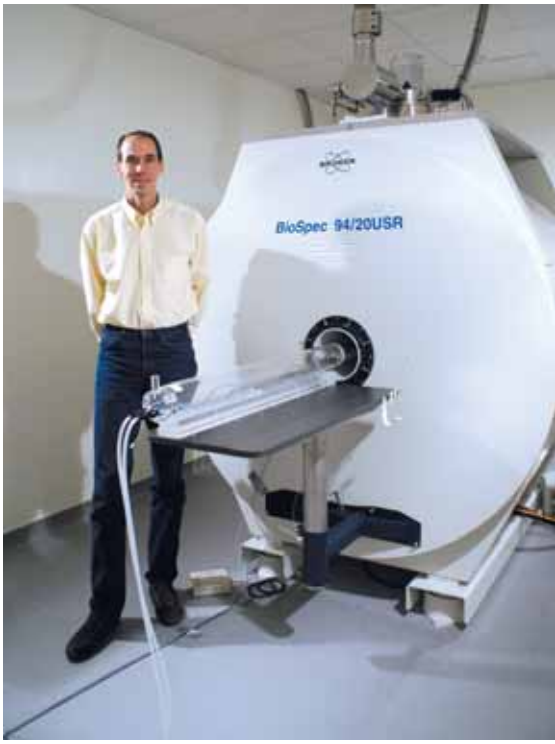
Having the two scanners just steps apart will facilitate moving between human and animal studies and also studying the effects of newly identified genes and molecules on brain function in live animals.

Tesla refers to the strength of the magnet, and the 9.4T can resolve MRI signals down to 50 microns, smaller than the dot on this 'i' and small enough to resolve small clusters of neurons. Christopher Moore and Alan Jasanoff will jointly oversee the scanner.

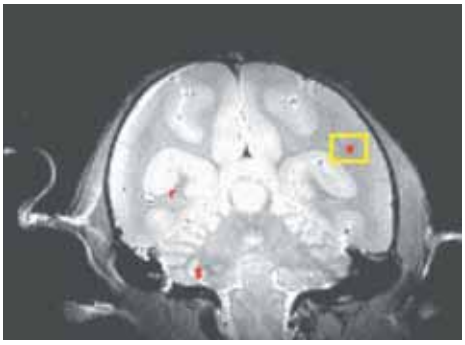
Moore recently demonstrated how imaging animals at such fine resolution can reveal new insights about the human brain. Using the 9.4T, he pinpointed brain regions in New World monkeys never known to be involved in tactile sensation. Then, using the 3T machine he looked for—and found—that unsuspected function in the analogous human brain region. Moore will also use the 9.4T to track blood in the brain, to test his new hypothesis that vascular signals play a role in information processing. (See pages 2–4.)

Jasanoff plans to use a classic paradigm of reward behavior in awake and behaving rats to examine neural activity patterns across the entire brain. He is also collaborating with Susan Lindquist at the Whitehead Institute to do live imaging on mouse models for neurodegenerative diseases. He will also use the scanner for cellular, molecular, and chemical studies to test the properties of the new MRI contrast agents to apply to next-generation functional imaging (see the Summer 2006 *Brain Scan*), and other imaging technologies.

The new scanner will be available to researchers in the community in hopes that it will facilitate interdisciplinary work in neurodegenerative diseases, systems neuroscience, developmental biology, cancer research, and new imaging technologies. ■



Steven Shannon, MR Research Technologist, with the 9.4 Tesla MRI scanner.



Top: New World squirrel monkey is small enough to fit in the 9.4T scanner; Bottom: Activation of visual area by tactile stimulation of monkey's forepaw.

Images courtesy Mitul Desai, McGovern Institute

Plumbing the Mind: Brain Imaging Symposium

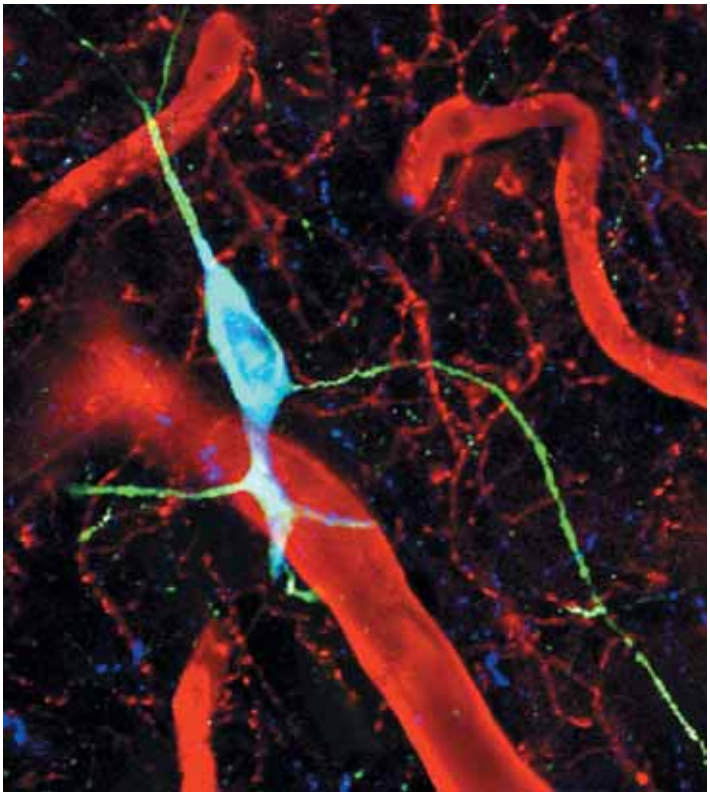
The Martinos Imaging Center hosted its second annual Symposium, entitled "Plumbing the Mind: Brain Activation and the Regulation of Cerebral Blood Flow," on May 15, 2007. The McGovern Institute and the Harvard-MIT Health Sciences and Technology Department (HST) co-sponsored the event.

Christopher Moore opened the morning session, which focused on the mechanisms of neurovascular coupling. Neurovascular coupling lies at the heart of functional magnetic resonance imaging (fMRI) and refers to the fact that as neurons in a particular region become more active, they recruit more blood flow to that region. This increase in blood flow, called functional hyperemia, is seen as a correlate of neural activity. The four morning speakers addressed many unresolved questions about how neurovascular coupling works: How do neurons and their helper cells, glia, actually generate the local increase in blood flow? Which imaging technology can optimally show this increase in blood flow? Can we go beyond functional hyperemia to acquire three-dimensional maps of all the neural activity in the brain? Speaker Martin Lauritzen articulated the current limitations in brain imaging. "You think you know what you're looking at," Lauritzen said, "but you don't."

In introducing the afternoon session, Alan Jasanoff described the limitations of our current 'magnifying glass' for reading out neural activity in the brain. Briefly, functional hyperemia is an indirect measure—it probably actually measures metabolic activity, rather than neural activity of interest to neuroscientists.

The four afternoon speakers shared their technological approaches for studying activity at the level of neurons. A combination of ultra-low-field MRI, magnetoencephalography, PET imaging, and direct neural imaging may enable precise measurement of the direct consequences of neural activity in specific brain regions. Two-photon microscopy of blood vessels is revealing the sequence of responses from neural activity to vascular dilation, and blood flow from arterioles to capillaries to veins. Optical imaging may resolve images at the level of cortical columns in the millisecond time domain on which the 'mind' itself presumably works. Also, a new vascular space occupancy (VASO) fMRI technique provides a clearer view of cerebral blood flow.

Throughout the day, the audience also learned about the potential clinical implications of better imaging blood flow in the brain for neurodegenerative diseases, epilepsy, and stroke. For example, early Alzheimer's disease shows a characteristic pattern of blood loss in the hypothalamus that could lead to a non-invasive means for early detection. ■



A neuron wraps its dendrite around a microvessel in the cortex. Because neurons receive signals through their dendrites, this image supports Christopher Moore's theory that the vascular system influences neural processing. Edith Hamel (McGill University) presented this image at the Plumbing the Mind Symposium held here in May 2007.

Summer Seminars on Neurotechnology

The McGovern Institute Neurotechnology (MINT) Program and the Center for Integration of Medicine & Innovative Technology (CIMIT) held a series of four July seminars on the clinical applications of neurotechnology. Each seminar featured a pair of speakers, who approached the theme from both basic and clinical perspectives.

4th Annual Scolnick Lecture: Burning Questions About Pain

David Julius, professor and vice chair of the Department of Cellular and Molecular Pharmacology at University of California at San Francisco, received the 4th annual Edward M. Scolnick Prize in Neuroscience on May 21, 2007. In his award lecture, "From Peppers to Peppermints: Natural Products as Probes of the Pain Pathway," he discussed his groundbreaking research on the perception of heat (whether from peppers or fire) and cold (from menthol or ice).

Dr. Julius discovered the molecular pathways by which capsaicin, the substance that makes chilies taste hot, and other substances that taste hot or cold, as well as noxious chemicals like tarantula venom and inflammatory molecules interact with a family of receptors (the TRP ion channels) on pain sensitive neurons. He is now exploring other 'burning' questions. How do these channels detect noxious stimulants and communicate with the brain? How are sensitivity thresholds set—and also reset following tissue injury, such as when a touch that one normally barely notices becomes acutely painful when sunburned? He is also investigating targets within these pathways for pharmaceutical agents that can treat the major clinical problem of chronic, debilitating pain.

The McGovern Institute awards the yearly Scolnick Prize of $50,000 to recognize an individual who has made outstanding advances in the field of neuroscience. The prize was endowed by Merck & Co., Inc. and named in honor of Dr. Edward M. Scolnick, who served as President of Merck Research Laboratories until 2002 and is now an associate member at the Broad Institute of MIT and Harvard and a member of the McGovern Institute's governing board. ■

Boston Area Mouse Meeting (BAMM)

The McGovern Institute and Broad Institute are organizing a regular Boston Area Mouse Meeting (BAMM) series for researchers who work with mouse models and those who are developing behavioral models of psychiatric diseases, explains Ki Ann Goosens, one of the organizers. The June 20, 2007 meeting focused on mouse behavioral models for schizophrenia, depression, aggression, social stress, and social memory. To join the email list for announcements of future meetings, email Shannon Landerer at shannonl@mit.edu.

Dr. David Julius uses mouse models to study how chemicals in chili peppers, spider venom, and radishes activate pain receptors.

Photos courtesy Henry Hall, McGovern Institute (top) and David Julius, UCSF (middle and bottom).

From left to right, top to bottom: MIBR team aboard Heritage, one of two racing boats in a friendly competition during an afternoon break; Lore Harp McGovern and Patrick McGovern; Bai Lu at helm in Newport Harbor*; Dominique Pritchet; Jill Crittenden; Simone Overduin and Sue Corkin; Michale Fee; Bob Metcalfe, Tomaso Poggio, Bob Desimone, and Rahul Sarpeshkar.*

Photos courtesy Henry Hall and Bob Desimone, both of McGovern Institute*

5th Annual McGovern Institute Retreat

Pat and Lore McGovern joined research labs, faculty, staff, and guests at the 5th Annual retreat in Newport, RI on June 3–5, 2007. Young scientists from McGovern Institute labs described their research in poster sessions on Sunday evening and in presentations on Monday and Tuesday. The keynote speaker Bai Lu, a Senior Investigator at the NIH, described how his research on fear memory suggests a possible new therapeutic target for treating Post Traumatic Stress Syndrome. Charles Jennings explained the goals and projects of the McGovern Institute Neurotechnology Program, which he directs. Rahul Sarpeshkar, MIT Associate Professor in the Department of Electrical Engineering and Computer Science, gave an example of neurotechnology's promise: implanted wireless brain-machine interfaces using the brain's own glucose as an energy source. New Associate Member Ed Boyden (see page 9) awed the audience with the diverse potential therapeutic applications of his new technologies for controlling neural circuits. A researcher from each lab presented an ongoing research project. ■

New Associate Member: Ed Boyden

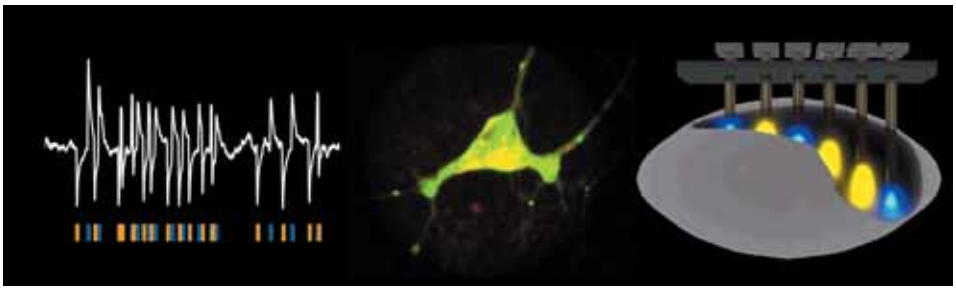
Edward Boyden, Ph.D., an Assistant Professor in the MIT Media Lab and the Department of Biological Engineering, joined the McGovern Institute as an Associate Member this July. Boyden develops and applies new technologies for analyzing and controlling neuronal activity in targeted ways. His research integrates genetic, molecular, optical, and other technologies.

He is already well known for his role in creating a genetically targeted way to activate and de-activate neurons with millisecond pulses of light. This technology may one day replace the electrodes currently used in brain stimulation devices for Parkinson's disease and depression. Boyden hopes to apply it in neural prosthetics for people with sensory nerve damage, and also for controlling epilepsy seizures and augmenting cognition in people with Alzheimer's disease and brain damage. For this innovation, which is now being widely adapted in neuroscience and neuroengineering, Technology Review TR35 named him one of the "35 outstanding innovators under age 35" in 2006. "We are extremely pleased to have Ed as part of our team, not least because he develops new technologies that could dramatically enhance our ability to precisely manipulate neural circuits and ultimately provide better treatments for human brain disorders," says Bob Desimone, Director. "Our faculty are looking forward to collaborating with this enthusiastic young scientist and, we hope, with other MIT Media Lab faculty members who are increasingly interested in neuroscience applications of their research."

Desimone's lab is working with Boyden to apply the light-activated control of neural circuits to higher order cognitive functions like attention and visual searching. Boyden is also using this technique to help Christopher Moore test his hemo-neural hypothesis (see pages 2–4), by shutting down the smooth muscle contractions that dilate and restrict blood vessels in the vein.

The McGovern Institute Neurotechnology (MINT) Program is sponsoring postdoctoral students in Boyden's lab for these collaborations. "Charles Jennings, MINT's director, connected the dots and was an incredibly important catalyst for getting these projects off the ground so quickly," says Boyden.

Boyden received a Ph.D. in Neuroscience from Stanford University in 2005. He holds a double B.S. in Physics and Electrical Engineering and Computer Science and a M.Eng. in Electrical Engineering and Computer Science from MIT. ■



Left: Electrically recorded neuronal inhibition or excitation driven by pulses of yellow and blue light, respectively, indicated by the bars beneath the trace. Center: A neuron expressing both channelrhodopsin-2 (for excitation driven by blue light) and halorhodopsin (for inhibition driven by yellow light), tagged with fluorescent proteins for visualization. Right: A schematic of optical fibers transmitting pulses of blue and yellow light for controlling subregions of the hippocampus, a brain region important for memory formation and compromised in disorders such as epilepsy.

Ed Boyden

Awards and Honors

Ann Graybiel received the "2007 NARSAD Distinguished Investigator Award" from the Mental Health Research Association (previously called National Alliance for Research on Schizophrenia and Depression) for May 1, 2007 to April 30, 2008. She will use the award to study a brain region implicated in obsessive-compulsive disorder and addiction. Graybiel also received honorary degrees from Hebrew University of Jerusalem and Queen's University, Belfast.

H. Robert Horvitz delivered the 2007 MIT Killian Award lecture, "Worms, Life, and Death: Cell Suicide in Development and Disease" on April 24, 2007. The Killian Award honors outstanding teaching and service to students.

Chinese Exchange Program

A new $500,000 gift from Hugo Shong, an International Data Group (IDG) executive, will establish a cooperative research program for postdoctoral fellows and neuroscientists at the McGovern Institute and Chinese universities. The exchange program will promote the application of advances in basic neuroscience research to the study of the human brain and devastating brain diseases and mental illnesses. Chinese and US researchers will conduct collaborative research at the McGovern Institute and the participating Chinese institutions, initially Tsinghua, Peking, and Hunan Universities. The program may also sponsor joint scientific meetings.

"The brain disorders we study at the McGovern Institute are global problems, and progress will surely depend on global collaborations," says Director Robert Desimone. "With its vibrant business climate and commitment to science, China can make great contributions to these research efforts, and we look forward to working with our Chinese counterparts as we begin this exciting partnership."

Mr. Shong is the Executive Vice President of IDG and founding General Partner of IDGVC Partners, one of the earliest venture capital funds in China with $800 million capital under management. He currently heads IDG's operations in publishing, market research, and events in the Asia Pacific region, and he is Chairman of the China Venture Capital Association (CVCA). Mr. Shong has a longstanding commitment to higher education and is currently a trustee of Boston University. He received a B.A. from Hunan University and studied journalism at the Graduate School of the Chinese Academy of Social Sciences. He then earned an M.S. degree from Boston University's College of Communication, did a research fellowship at the Fletcher School of Law and Diplomacy, and completed Harvard Business School's Advanced Management Program (AMP) program. ■

In Memoriam: Tom Pyle

The McGovern Institute mourns the passing of Thomas O. Pyle on July 18, 2007 after a 15-month battle with pancreatic cancer. Tom and his wife, Regina, were the founding chairs of the Friends of the Institute and hosted its inaugural meeting last November. Despite his illness, Tom participated in the life of the Institute, where he and Regina established a fellowship and a fund for research into the relationship between music and the brain.

Tom graduated from high school at 16 and attended MIT for a year, but left to work in television and advertising before entering Harvard's MBA Program as one of few students admitted there without a college degree. As noted by the *Boston Globe* and *New York Times*, Tom built Harvard Community Health Plan (now Harvard Pilgrim) into one of the nation's largest and most innovative health care providers during the 1980s, served on the Clinton health policy team in 1993, and later managed a health care subsidiary of MetLife. He also provided health policy advice for Boston Consulting and served on several corporate boards.

Everyone at the McGovern Institute is grateful for having known Tom. Together with Regina, we will host an event in his honor this fall.

Leadership Board Meeting

At the Leadership Board meeting on May 18, 2007, Bob Desimone described plans for focusing research efforts on psychiatric diseases and mental illness. He said that whole genome sequencing and new tools from molecular biology and brain imaging have for the first time made this translational research a practical goal. As examples, Ki Ann Goosens, Martha Constantine-Paton, and John Gabrieli discussed their basic research in the context of anxiety disorders and schizophrenia. Guest speaker Bruce Cohen, Director of the Shervert Frazier Research Institute and the Stanley Research Center at McLean Hospital, gave a talk entitled "A Psychiatrist's View of the Future."

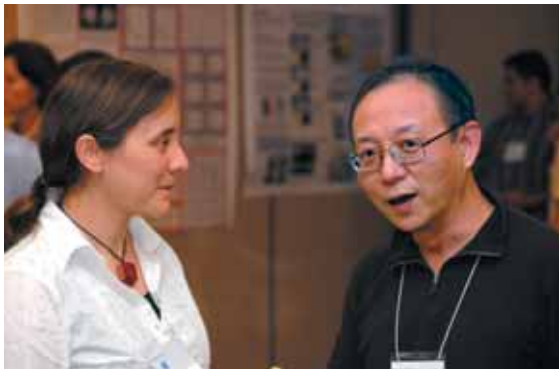
Funding Fear Memory Research

"I had an especially good month in May, so amidst MIBR's annual retreat in Newport, I asked Bob Desimone if he had any urgent opportunities I could back right then," recalls Bob Metcalfe, chairman of the Leadership Board. "Off the top of his head he explained how Ki Ann Goosens's work, which she had presented at the Leadership Board meeting in May, was blossoming and could benefit from bringing on several undergraduate researchers—this fall. So I went home and got my wife Robyn to write a $25,000 donation check, and Ki is off to the races."

Goosens investigates the interaction between chronic stress and fear and anxiety, which underlie many of the most prevalent mental illnesses. She focuses on how chronic stress changes the activity of the amygdala, the brain region that responds to fear, in ways that correspond to behavioral symptoms of stress. She has identified a suite of unknown genes that become more active in the amygdala of highly stressed animals that exhibit more fear and anxiety than normal. She uses sophisticated techniques to silence particularly interesting genes to determine whether these manipulations can either mimic or block the effects of chronic stress on amygdala function.

Bob's donation will fund two undergraduate researchers through MIT's Undergraduate Research Opportunity Program (UROP) through the summer of 2008. Depending on their interests, one student may help express the novel genes in vivo, and the other may help with the behavioral and physiological studies to see how the genes alter fear memory. "Having the undergraduate researchers in the lab will allow us to follow up some very exciting new leads in our work on stress and anxiety," Goosens says. "It's also great to get to know the undergraduates personally in the lab, instead of just in the classroom."

Bob Metcalfe '68 received the National Medal of Technology for leadership in the invention, standardization, and commercialization of Ethernet—'plumbing' for the Internet—on which he shares four expired patents, and of which a quarter billion new switch ports ship each year. Bob has been a venture capitalist with Polaris Venture Partners since January 2001 and is a Life trustee of MIT. ■



Ki Ann Goosens and Bob Metcalfe talk with Bai Lu of the National Institute of Mental Health (NIH), a keynote speaker at the McGovern Institute Retreat who researches brain mechanisms involved in building and extinguishing fear memories that contribute to Post Traumatic Stress Syndrome and depression.

Photos courtesy Henry Hall, McGovern Institute

IN THE NEWS

Tomaso Poggio's studies regarding a computational model for object recognition received world-wide attention, including articles in the April 4, 2007 *Economist* and the April 3, 2007 *New Scientist*.

The May 2007 *The Scientist* and the July 2, 2007 *New Yorker* featured the topic of the February 2, 2007 American Association of Arts and Sciences Symposium "Is There Science Underlying Truth Detection?" organized by Emilio Bizzi. Both articles highlighted Nancy Kanwisher's analysis of the inherent flaws in using current fMRI technology for lie detection.

Leadership Board Chairman Bob Metcalfe's article "It's all in your head" comparing neural and computer networks appeared in the May 7, 2007 *Forbes Magazine*.

Colloquia Honoring Research Careers

Colleagues honored Martha Constantine-Paton's research on synaptic plasticity during development at a colloquium held at the McGovern Institute on June 23, 2007.

"A Journey Through Computation" feted Tomaso Poggio's pioneering studies in computational neuroscience and computer vision systems. This event took place in the baroque San Filippo Neri Oratory in historic Genoa, Italy on June 14–16, 2007.

Left: H. Robert Horvitz, Joe Paton, Martha Constantine-Paton, Alex Horvitz, and Chris Paton

Right: Tomaso Poggio, lower center, surrounded by family and colleagues

Photos courtesy Sandor Manik and the Statistical Learning and Image Processing of the Genova University Research Unit.

The McGovern Institute at MIT is a neuroscience research institute committed to improving human welfare and advancing communications. Led by a team of world-renowned, multi-disciplinary neuroscientists, The McGovern Institute was established in February 2000 by Lore Harp McGovern and Patrick J. McGovern to meet two of the great challenges of modern science—understanding human thought and emotion and discovering how to prevent or treat brain diseases and mental illness.

Additional information is available at: http://web.mit.edu/mcgovern/

Brain SCAN
Quarterly Newsletter of the McGovern Institute

Editor: Laurie Ledeen
Writer: Cathryn M. Delude
Design: Sametz Blackstone Associates, Boston

McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

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