Brain SCAN

MCGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

Issue no. 2 *Spring 2006*

From the Director

This second issue of our McGovern Institute quarterly newsletter introduces a series devoted to some of the latest research advances by our faculty. In this issue, we consider research on the brain mechanisms that allow us to recognize objects in the environment by sight.

Loss of vision is a major health problem around the world. In the United States alone, more than a million people are legally blind, and it is estimated that three times that number suffer from less severe visual impairments that nonetheless affect the quality of life. Blindness can strike from many causes, including both eye disease and trauma—we are sadly seeing more of our soldiers returning from the war in Iraq with head and eye injuries, for example. A better understanding of how the brain uses information from the eye will be critical as we try to develop either new treatments for retinal disease, or even a "neural prosthesis" that would bypass the biological retina and supply visual information directly to the brain. A better understanding of how the brain recognizes the objects would likely also result in secondary, technological spinoffs such as current computer-vision recognition programs. Today, even the best of these are woefully inadequate in complex visual environments.

Although recognizing, say, the face of your child may seem effortless, the brain mechanisms that allow for that recognition turn out to be fantastically complex. Indeed, it has been estimated that nearly half of the human brain has at least some visual function! Progress in understanding these brain mechanisms will require a multi-level effort, ranging from molecular biology through systems neurophysiology and brain imaging to computation and theoretical modeling.

In this issue of *Brain Scan*, you will read about how some of our McGovern Institute faculty are tackling these problems, including Professor Nancy Kanwisher's use of human brain imaging to uncover "special purpose" recognition circuits in the human brain, and the team approach of Professors Jim DiCarlo and Tommy Poggio, who are pooling their talents in neurophysiology and computational modeling to understand recognition at the level of neural networks. A picture of the brain's recognition systems is now beginning to emerge.

Bob Desimone, Director

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 one of the great challenges of modern science—the development of a deep understanding of thought and emotion in terms of their realization in the human brain.

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

ON PERCEPTION — OBJECT RECOGNITION

Recognizing objects in the visual world is among the most complex and important problems the brain must solve.

Professor Nancy Kanwisher

We humans are visual organisms, but visual perception does not come easily. Vision commands almost one half of our brain's cortex, and it requires more computational power than even MIT engineers can fathom. Much of that power is devoted to how we recognize objects in the world around us. Our ability to instantly, accurately sum up an object (is it a snake? a beloved face? a freight train?) enables us to respond to our environment in appropriate, often life-saving, ways.

Object recognition is no trivial task, because a visual image does not enter our brains as a developed photograph. Rather, it is like the grid of pixels on a digital camera: an array of millions of numbers indicating light and color on our eye's 10 million or so photoreceptors. As you walk down the street, billions of bits of visual information strike your field of view. That view refreshes itself continuously as objects move, lighting changes, or you shift your eyes. Still, the briefest glimpse is often enough to recognize even a never-before-seen object. In a fraction of a second, its visual input runs from the retina through increasingly higher levels of the visual stream until it reaches the cognitive regions of the brain.

In the course of that journey, the neurons sort through the visual input for meaningful shapes, sizes, and configurations. Somehow the brain creates representations of objects from those arrays that the cognitive areas of our brain can understand and act upon. Understanding that "somehow" is the work of three McGovern Institute investigators: Nancy Kanwisher, James DiCarlo, and Tomaso Poggio.

A Whole Brain Approach

In some ways, learning about how the brain works is like auto mechanics: you understand how parts function by seeing what happens when they break. Stroke patients with damage to a small brain region, for example, are unable to recognize faces, but have no trouble with other types of objects. To many scientists, that evidence indicates that at least some regions in the visual cortex are highly specialized, rather than multi-purpose.

Kanwisher explores such specialized areas by having human volunteers lie in a functional magnetic resonance (fMRI) machine while looking at images, such as faces, leg, cityscapes, farms, cars, or cups. The brain scans show discrete regions of the brain becoming more active (they appear brighter on the scans) at the sight of specific types of images. In studying which highlighted areas correspond to which objects, Kanwisher identified several new, functionally distinct structures in the brain. One of them, the fusiform face area (FFA), selectively lights up for faces, whether human, animal, or abstract. It even lights up when the subject merely thinks about a face, and Kanwisher showed that you can tell whether the subject is imagining a face by looking at their brain scans! People with damage to this brain region cannot recognize faces, even those of their family and closest friends.

However, some brain scan studies showed that this area also responds to objects, particularly bodies. A graduate student in the Kanwisher lab, Rebecca Schwarzlose, suspected that there were actually two brain regions in such close proximity that traditional fMRI images blurred them together. A new, high-resolution generation of fMRI gave Schwarzlose sharper images that clearly showed the FFA only responding to faces and never bodies, while an abutting region responded only to bodies, not faces. Those results were published in the *Journal of Neuroscience* in late November, 2005.

In research still underway, Kanwisher is exploring how these brain areas get organized in the first place. We might be "hardwired" to recognize a face, for reasons of biological survival, but what about a pen? We must learn to recognize pens, cars, and iPods by experience, yet very little is known about how we learn new objects and how ongoing experience changes object recognition.

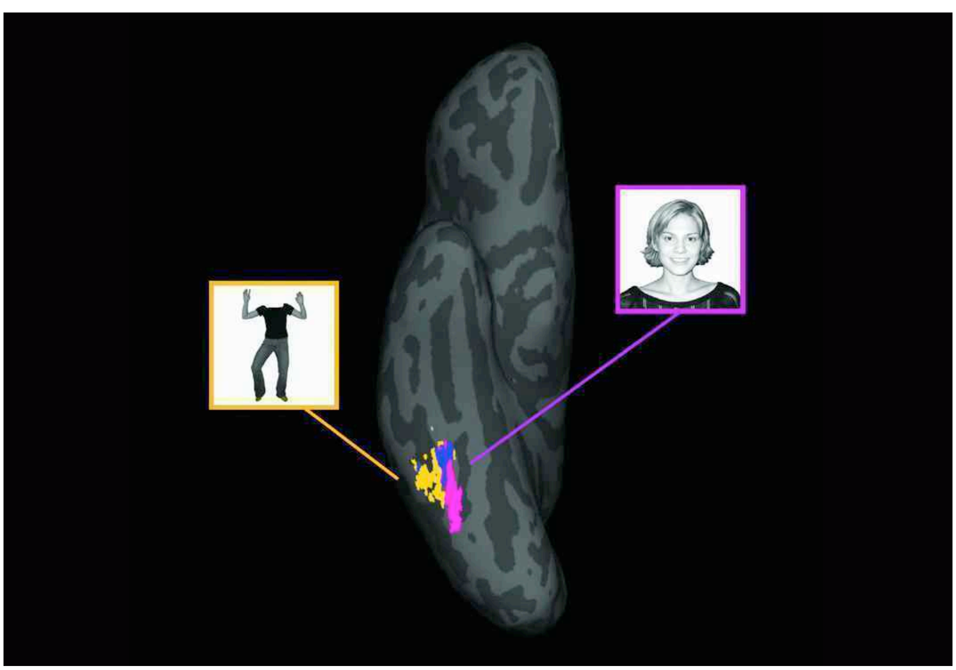
To find out, she is looking to see if there are other very specialized regions of the brain for functions that are too modern in nature to have become hardwired in the brain, such as recognizing the written word. In addition, she is collaborating with the DiCarlo lab, using even higher-powered fMRI images, to study an analogous region in monkeys as they learn to recognize objects. DiCarlo can then probe those regions with electrodes to study what fMRI scans are revealing at the level of individual neurons.

Checking out the Inner Works

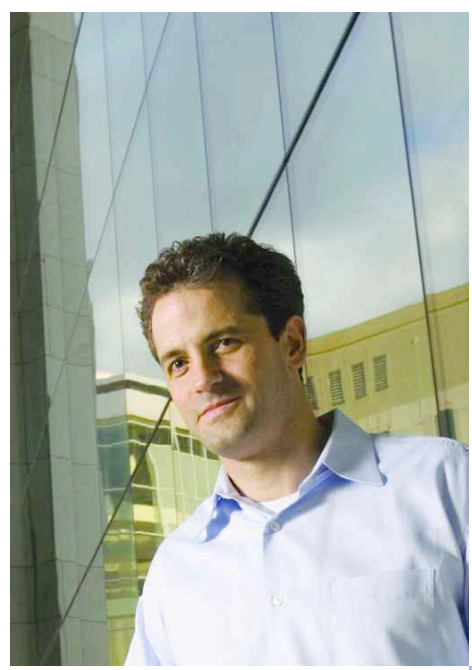
While Kanwisher looks at the whole brain in humans, James DiCarlo inspects it on the micro-scale in monkeys, to see how the neurons fire in response to objects. In his lab, researchers train monkeys on object recognition tasks and use electrodes to record the activity of hundreds of individual neurons, focusing on the monkey's inferior temporal cortex, or IT, where neurons are known to respond selectively to different classes of objects. For example, at some sites neurons respond more to fruits than vehicles, while others show the opposite pattern. Importantly, these preferences remain consistent even when the objects appear in different positions or sizes (as they do in the real world)—an essential property for a good object recognition system.

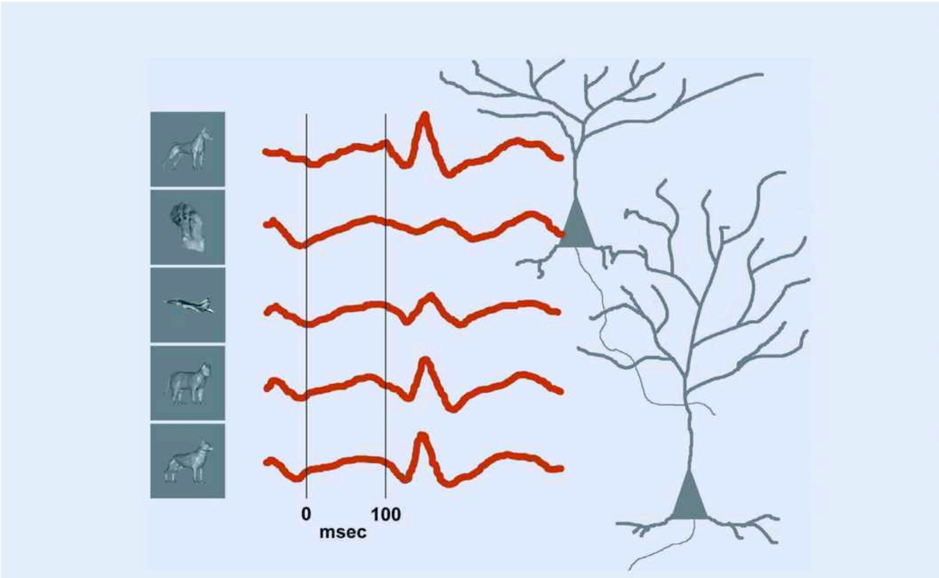
In essence, electrode recordings by DiCarlo and others reveal a similar preference for specific objects at the cellular level that Kanwisher finds on the macro level in human fMRI studies. But do a burst of spikes and a bright spot on an fMRI scan mean the same thing? Previously, scientists generally assumed—or hoped—that electrode studies in monkeys might relate to fMRI studies in humans. Now, in a collaboration with Tomaso Poggio's lab, DiCarlo has found new evidence that should help clarify that relationship.

In this image, the bottom surface of the brain is schematically inflated to show the two spatially close but functionally distinct regions with face selectivity (pink) and body selectivity (yellow). Purple indicates where these selectivities overlap. Image by Rebecca Schwarzlose, MIT



Professor James DiCarlo





In this graphic, neural signals in the monkey's inferotemporal (IT) cortex appear 100 msec after images of a dog, hand, airplane, cat, and a different dog are shown. Local field potential signals (LFPs, in red) are emitted by the web of input activity, mostly from the neurons' dendrites (the gray, tree-like branches). Graphics on this page by Chou Hung and Gabriel Kreiman, McGovern Institute for Brain Research at MIT.

For this study, which was reported in the February 2, 2006 *Neuron*, Gabriel Kreiman in the Poggio lab and Chou Hung in the DiCarlo lab analyzed two distinct types of IT signals. The first was the "spiking" activity of neurons in response to a view of an image, which is the traditional way to study object preference. But the same electrode picks up another signal not usually analyzed. That signal measures the local field potential (LFP), a more diffuse but very rich signal that contains a different type of information. Instead of telling how strongly an individual neuron fires in response to an image, the LFP provides a measure of what's stimulating the neuron: the steady buzz from the surrounding neighborhood, including the combined input from other neurons.

Unexpectedly, that surrounding buzz suggested that the neurons that prefer very similar objects cluster into mini-neighborhoods—on a scale similar to the fine-grain regions seen in high resolution fMRI studies. If so, using this new method to study object preferences could elucidate what fMRI is measuring in humans—and bridge the gap between fMRI studies in humans and electrode studies in animals. Closing that gap in understanding could add a new dimension to Kanwisher's studies.

In addition, analyzing the recordings showed that the incoming LFPs already contain significant information about the object's identity—and might aid the Poggio lab in deciphering the brain's computational processes.

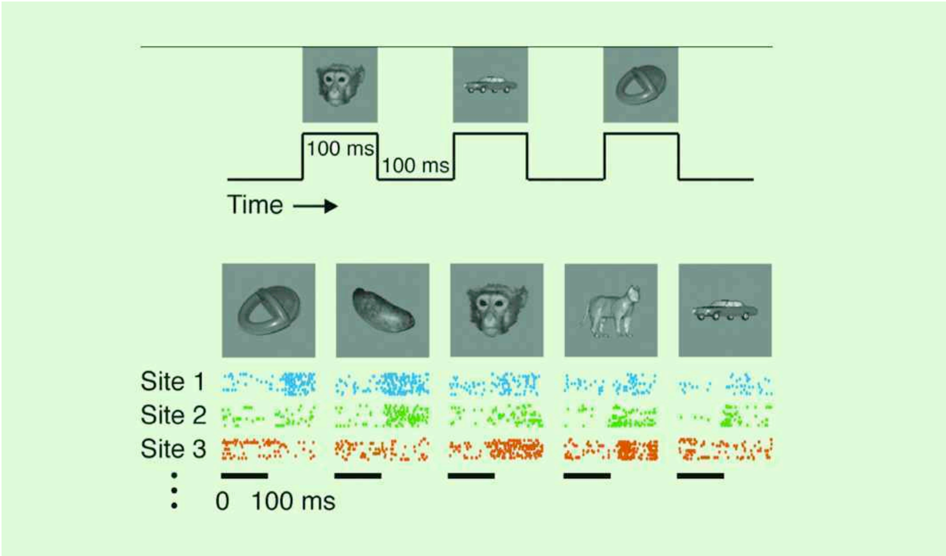
How the Visual Cortex Recognizes Objects

To Tomaso Poggio, studying object recognition is a good proxy for understanding intelligence itself. Object recognition exemplifies the basis of intelligence: the ability to learn by generalizing from individual examples to identify and categorize new objects.

The Poggio lab has modeled some of the core computations the brain uses to recognize new objects, based on numerous physiological studies about how different neurons in the cortex's visual stream respond to images. Over the past 5 years, they developed a theory that explains and predicts how neurons in the various regions of the visual cortex will identify and classify visual objects. The team described the full theory in a 2005 technical report by Poggio and lab members Thomas Serre, Minjoon Kouh, Ulf Knoblich, Charles Cadieu, and Gabriel Kreiman.

The Poggio lab has now used several methods to verify that the theory can account for the physiological responses of neurons at different stages in the visual cortex. In one such test, they collaborated with the DiCarlo lab to see if the theory agreed with the actual recordings of neurons in monkeys as they learned to recog-

This graphic shows how neurons in a purely visual brain region (IT) respond selectively to different images. As pictures were randomly presented to the monkey during specific intervals (top), neurons at different sites in IT produce distinct patterns of activity to each picture (bottom). For example, neurons at site 1 favor the toy and the yam, while neurons at site 3 prefer the monkey face and the cat.



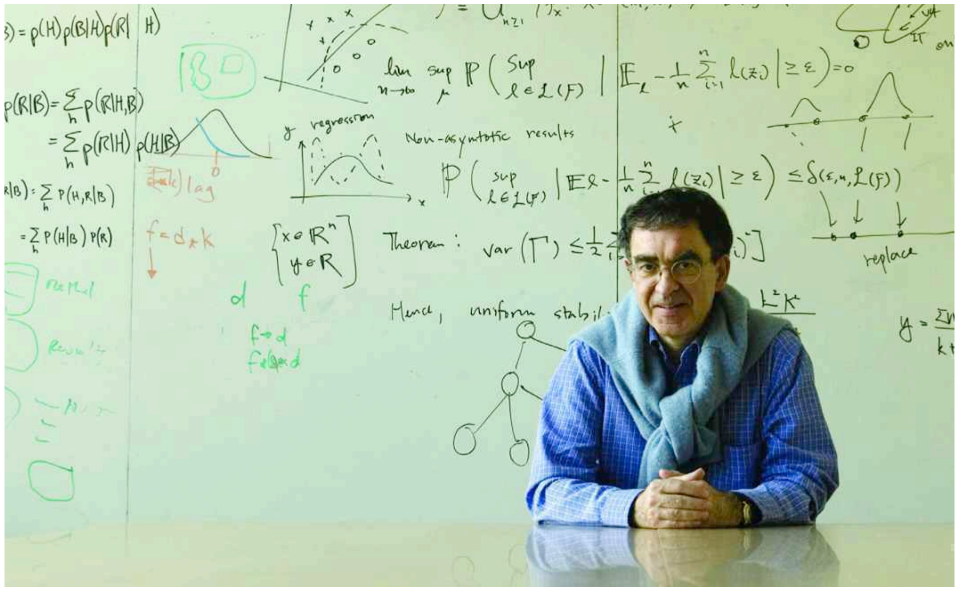
nize objects. In the experiments, two monkeys viewed different objects grouped into categories, such as faces, toys, and vehicles, which appeared in different sizes and positions in the visual field. Using electrodes, Chou Hung recorded the activity of hundreds of neurons from the critical object recognition region (IT). Then, Kreiman used a learning algorithm or classifier, which simulates the brain's computations, to decipher the neural code and associate each object with a particular pattern of neural signals.

The results, which were reported in a November 2005 issue of *Science*, contained some remarkable insights. First, just a split second's worth of recorded signals from just several hundred neurons (out of millions) was enough for the algorithm to recognize an object. Moreover, Poggio's computational model produced the same results as the monkeys themselves—meaning the model was quite realistic and accurate.

But the most interesting result is that the new model outperforms the best computer vision systems on several difficult recognition tasks on real-world natural images. Even more surprisingly, under certain test conditions the model does as well as humans—a first for any computational model based on the biology of the visual system. Still, there is a long way to go before such models can match our easy agility in negotiating the nuanced appearances of the myriad objects in the everyday world.

Clearer Vision

Understanding how the visual cortex—and by extension the whole cortex—works would be a major breakthrough towards designing intelligent systems for such applications as surveillance systems, devices that could warn drivers about a wayward pedestrian or an out-of-control approaching car, or even brain-machine interfaces for visual prosthetics that may imprint the correct pattern in the brain and allow a blind person to see. Ultimately, understanding how the brain represents the external world has ramifications for treating neural disorders that involve recognition deficits, such as agnosias, autism, dyslexia, or schizophrenia.



Professor Tomaso Poggio

The Burnett's Gift Encourages Collaborative Research

Leadership Board member Dr. Gerald Burnett and his wife Marge have made a multi-year commitment in support of the ongoing collaboration between the Poggio and DiCarlo laboratories. Having received his B.S. and M.S from MIT in Electrical Engineering and Computer Science, and his Ph. D from Princeton in Computer Science and Communications, Jerry Burnett has long been aware of the complex challenges researchers face in understanding perception. Today, as one of the founders and CEO of Avistar, a leading provider of networked video communications, he is equally aware of the profound practical applications such an understanding could produce.

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At the opening of the McGovern Institute in November, Bob Desimone pointed out that it has been over thirty years since an MIT researcher thought he could solve the problem of perception in a summer if he just put his mind to it. That was before neuroscientists realized just how complex the brain itself is and how intricate, and important, a function perception is. Today, as tools become more sophisticated and promising, we need to support collaborative research efforts, particularly regarding object recognition. Marge and I believe Tommy and Jim's work promises to take this field to a new level, which will serve as a platform for many useful and much needed applications for artificial vision systems of all kinds." —Jerry Burnett

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Understanding the brain's computations requires very close collaborations between theoretical and experimental labs. Jerry and Marge Burnett's vision and generosity will help the McGovern Institute become a leader in this interdisciplinary research direction." —Tommy Poggio

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Our ability to easily perceive and recognize people, places, and things is so powerful and deeply embedded in our brain's wiring and computations that most of us take it for granted. We thank Jerry and Marge Burnett both for their appreciation of the benefits that will come from understanding the brain's remarkable ability to solve this problem, and for their support for the McGovern Institute's interactive approach to achieve that goal."—Jim DiCarlo

National Alliance on Mental Illness of Massachusetts featured the McGovern Institute at its 2005 Annual Convention

McGovern Institute Director, Robert Desimone spoke to over 350 family members, consumers, providers, friends, and supporters of NAMI-MA at the invitation of its president, Phil Hadley and its Executive Director, Toby Fisher. NAMI-MA is the state chapter of the nation's largest grassroots mental health organization dedicated to improving the lives of persons living with serious mental illness and their families. Founded in 1979, NAMI has become the nation's voice on mental illness, a national organization including NAMI organizations in every state and in over 1100 local communities across the country that join together to meet the NAMI mission through advocacy, research, support, and education.

MIT's Speakers Series Features McGovern Institute

Director Robert Desimone spoke to over 100 guests in New York for the MIT Speakers Series on Thursday, February 9, 2006. Dr. Desimone's presentation, entitled "How the Brain Pays Attention," included an overview of the McGovern Institute as a whole, and also a description of his own recent work, which suggests that the ability to focus attention on the task at hand depends on brain mechanisms that synchronize the timing of activity in distributed neural circuits. Richard Raysman '68 and Kenneth Wang '71 hosted the event, which took place at the offices of Brown Raysman. After a long, enthusiastic question and answer period, Ken Wang hosted a dinner party in his home in honor of Dr. Desimone and the Institute.

BAMM: Boston Area Mouse Meeting

The McGovern Institute and the Broad Institute have formed the "Boston Area Mouse Meeting" or BAMM, a forum for discussing the experimental models and techniques for studying psychiatric diseases and neurological disorders using mice. Mouse models enable researchers to study many different strains of mice and investigate how genes influence the development of the nervous system, the progression of diseases like Alzheimer's, and behavioral characteristics associated with anxiety disorders, schizophrenia, and other mental illnesses.

For the January 19 meeting, David Sabatini (Department of Biology, MIT) and Stephen Elledge (Department of Genetics, HMS) led a lively discussion about the "applicability of RNAi libraries to the dissection of neurodegenerative and neuropsychiatric disease etiologies in mouse models."

For more information, please contact Shannon Landerer (Shannonl@mit.edu) or Laura Clarage (lclarage@broad.edu).

Scolnick Prize Lecture

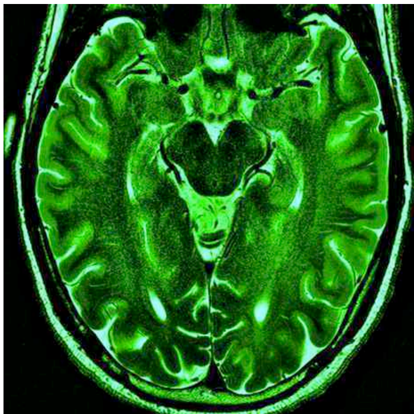
The McGovern Institute will present the third annual Edward M. Scolnick Prize in Neuroscience on Tuesday, April 25, 2006 to Dr. Michael Greenberg, FM Kirby Director of the Program in Neurobiology within the Children's Hospital/Harvard Medical School Department of Neurology. Dr. Greenberg will give a public lecture entitled "Signaling Networks that Control Synapses Development and Cognitive Function" from 4:00 pm to 5:00 pm at the McGovern Institute in the Brain and Cognitive Sciences Complex, 43 Vassar Street (building 46) in Cambridge. The event is free and open to the public.

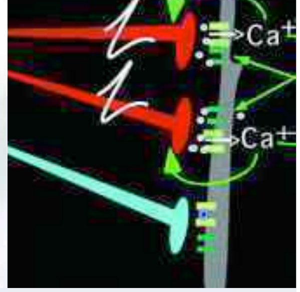
Dr. Greenberg researches how neurons respond to growth factors, neurotransmitters, and other extracellular and intracellular signaling pathways that regulate the development and function of the nervous system. He has elucidated the molecular bases for critical events in neural development, the neural responses to injury and disease, and potential therapies for neurological diseases and brain injuries.

The Scolnick Prize, which recognizes an outstanding discovery or significant advances in the field of neuroscience, consists of an award equal to $50,000 and is named in honor of Dr. Edward M. Scolnick, who stepped down as President of Merck Research Laboratories in December 2002 after holding Merck & Co., Inc.'s top research post for 17 years.

Brain Imaging Symposium

The McGovern Institute will host a Brain Imaging Symposium on May 30, 2006 in the auditorium of the Brain and Cognitive Sciences Complex. This event is free and open to the public. Details and registration will soon be available at: http://web.mit.edu/mcgovern.





Prizes and Awards

SHARP RECEIVES NATIONAL MEDAL OF SCIENCE

Phillip A. Sharp, the founding director of the McGovern Institute, MIT Institute Professor, and 1993 Nobel Laureate for physiology and medicine, now has another great honor to his name: the National Medal of Science. He received this nation's highest science award in a White House ceremony on February 13, 2006. The award recognizes Sharp's groundbreaking investigations of RNA interference (RNAi), a method of using short pieces of RNA to turn off genes. He is the second honoree from the McGovern Institute: Ann Graybiel received the award in 2001. Sharp was one of two MIT scientists to receive the award this year, and they join 43 other current and past MIT faculty honorees.

EMILIO BIZZI BRINGS HOME THE GOLD FROM ITALY

Dr. Bizzi received the President of Italy Gold Medal for Scientific Contributions on December 19, 2005 in Rome at the official residence of the president of the Italian republic, Mr. Azeglio Ciampi. He was nominated for the award by the secretary of research and education, Mrs. Letizia Moratti.

THOMAS BYRNE A FULL PROFESSOR AT HMS

Dr. Byrne has been named Clinical Professor of Neurology and Health Sciences and Technology at Harvard Medical School. He is also a member of the Pappas Center for Neuro-oncology at Massachusetts General Hospital and the Dana Farber/Harvard Cancer Center.

Become a Friend of the Institute!

The outpouring of support and interest generated by our November 4th opening has inspired the formation of a new organization—The Friends of the Institute. Members come from across the country and abroad, from diverse backgrounds and interests, to serve as ambassadors on behalf of the Institute. Friends of the Institute benefit from in-depth access to our scientists and their research initiatives, which will be the focus of organization's annual meeting. Members not only receive our quarterly newsletter and interactive online communication, but also regular invitations to lectures, seminars, symposia, and regional dinners.

An annual membership fee of $1,500 is devoted to the Director's Discretionary Fund, which allows the Institute to respond to pressing needs and priorities based on our belief in entrepreneurial research. If you wish to learn more about becoming a Friend, please contact Laurie Ledeen, the Institute's Development and Special Projects Officer, Ledeen@mit.edu or (617) 324-0134, or visit us online at
http://web.mit.edu/mcgovern/html/Support_the_McGovern_Institute/impact.shtml

Leadership Board to Inflate the Brain Bubble

Bob Metcalfe, Chairman of the McGovern Institute Leadership Board, has proposed the "inflation" of the "Brain Bubble" as a way to promote the goals of the Institute, and he continued to spearhead that effort at the Board's second meeting on March 22, 2006.

The Board welcomed new members Mark Gorenberg and Jane Pauley, and spent the day with McGovern faculty members gaining an ever-increasing understanding of the Institute's research programs.

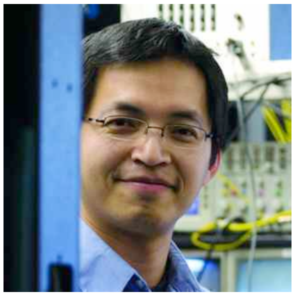
Just one example of ways in which individual members are inflating the Brain Bubble is the role they will play in "The Neurotech Industry Investing and Business Conference," which will take place on May 18, 2006 at the Westin San Francisco in Millbrae California. The Conference is organized by Zack Lynch, a Leadership Board member and Managing Director of NeuroInsights. Bob Metcalfe serves on the Conference's Advisory Board, and Lore McGovern, the Institute's co-founder, will be a guest speaker on the topic of Accelerating the "Decade of Translation."

New Funding for New Knowledge

The McGovern Institute is grateful to the following new donors.

Gerald and Marge Burnett
Kelly and Elizabeth Conlin
Eric Cosman
Robert G. and Patricia Y. Dettmer
Howard and Susan Finkelstein Foundation, Inc.
Ann Kaplan and Robert Fippinger
Michael and Judith Gaulke
Richard Hargreaves, on behalf of Imaging at Merck
Harvey Kaufman
Ann and Paul Marcus Foundation
Michael Norkus
Thomas and Regina Pyle
Raytheon Company
Carolyn Ring
Carina Ryan
Ira and Alice Steinman
Richard Vancil

MEET OUR TEAM MEMBERS



CHOU HUNG
Postdoctoral Associate, McGovern Institute, DiCarlo Lab

UNDERGRADUATE/GRADUATE SCHOOL
B.S. in Biology at California Institute of Technology; Ph.D. from Yale University

AREA OF INTEREST
Understanding the brain's object representation

"As I was finishing my undergraduate studies at Caltech, a paper by Manabu Tanifuji at RIKEN reported seeing the brain's mapping of object shapes. I've been interested in understanding the brain's object representation ever since."

GABRIEL KREIMAN
Postdoctoral Associate, McGovern Institute, Poggio Lab

UNDERGRADUATE/GRADUATE SCHOOL
B.S. in Physical Chemistry at University of Buenos Aires; Ph.D. from California Institute of Technology

AREA OF INTEREST
How neurons and circuits of neurons encode visual information

"The brain is the most complex system ever studied by science: there are more neurons in the brain than stars in the galaxy! Now in building 46 we're joining efforts at multiple scales and using different empirical techniques and theoretical approaches to try to decipher the biological codes in the brain."

REBECCA SCHWARZLOSE
Graduate Student, Brain And Cognitive Sciences, Kanwisher Lab

UNDERGRADUATE SCHOOL
Psychology at Northwestern University

AREA OF INTEREST
Visual processing of objects, faces, and bodies in humans

"Perhaps the biggest mystery about the brain is how it can distill such complicated phenomena as language and object recognition into abilities that feel so automatic that we don't even realize we're doing them. It is a joy to study a system that makes tasks as stunningly complex as recognizing a friend's face feel effortless and 'easy.'"

McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

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