Brain SCAN

McGOVERN INSTITUTE
FOR BRAIN RESEARCH AT MIT

Issue no. 18 Fall 2010

From the director

This year represents a double anniversary for us – it has been ten years since the founding of the McGovern Institute and five years since we moved into our new building – so it is a fitting time to celebrate our past accomplishments and future aspirations.

Jane Pauley, Pat McGovern, Lore Harp McGovern, Alan Alda and Bob Desimone at the institute's anniversary celebration.

Photo courtesy of Justin Knight

When I became director of the McGovern Institute in 2004, I was privileged to join a truly stellar group of founding faculty members that had been assembled by my predecessor Phil Sharp, the founding director of the institute. I am deeply gratified that all of them are still here at the institute continuing to contribute major advances to the field. They have been recognized with many honors over the past decade. To mention only a few of the highlights, Bob Horvitz shared the 2002 Nobel prize, Ann Graybiel was awarded the 2001 National Medal of Science, and in 2006 Emilio Bizzi was elected president of the American Academy of Arts and Sciences. In addition to their own accomplishments, the founding faculty has guided the growth of the institute, including the recruitment of 11 new full and associate members since its foundation.

On October 14, we held our 10th anniversary celebration with keynote talks from Gerald Fischbach, Jane Pauley and Alan Alda. This event was also an opportunity for me to acknowledge the generosity of our many donors, and to highlight some of our own research accomplishments, especially those of our newest colleagues. As we enter our second decade, I am confident that these outstanding colleagues will keep the McGovern Institute at the forefront of what I believe will be a new age of discovery about the human brain.

Bob Desimone, Director

Institute director Bob Desimone speaking at the 10th anniversary event.

Photo courtesy of Justin Knight

UNDERSTANDING THE CIRCUITS OF THE BRAIN

Research at the McGovern Institute spans many different questions and technologies. But one overarching theme, according to institute director Bob Desimone, is the need to understand the brain in terms of neural circuits.

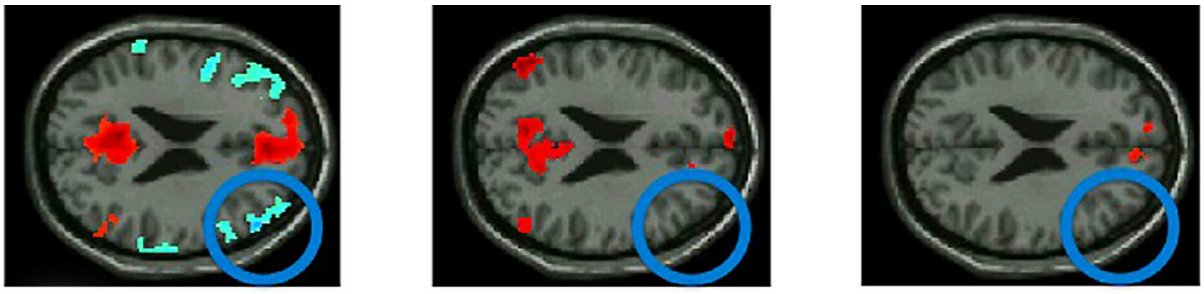
At the McGovern Institute's 10th anniversary celebration on October 14th, director Bob Desimone talked about the institute's accomplishments over the past decade and about his aspirations for the future. In particular he emphasized the importance of understanding neural circuits.

"Neuroscientists have traditionally studied the brain using many different approaches: genetics, electrophysiology, pharmacology, human neuroimaging and so on," he explains. "But we are now seeing a convergence of these approaches at the level of circuits. We can now start to see beyond the brain's enormous complexity, and to realize that it is built from circuits that share many underlying common principles. By understanding how these circuits work, we will gain new depth of insight into the biological basis of our own mental lives, while at the same time laying the foundations for a new understanding of brain disease."

In his keynote speech, Desimone illustrated his point by presenting some recent discoveries, in particular from the new faculty members who have joined the institute since it was founded in 2000. The following examples are drawn from his talk.

Learning to sing

Michale Fee, who joined the McGovern Institute in 2003, studies bird song, an ideal model system for understanding how neural circuits control a complex learned behavior. Fee, who trained as an engineer, has developed many new technologies to make precise recordings from the brains of birds as they learn to sing. With the help of these tools he has identified a brain region that drives babbling in young birds and he has shown where in the brain trial-and-error learning occurs. He has also shown profound parallels between these circuits and the corresponding human structures that are disrupted in Parkinson's disease. One of his most remarkable findings is the discovery of a brain area that controls the song's tempo: warming this area causes song to speed up, and cooling it slows the song down. In work published in October he showed how this brain area keeps track of time, through a mechanism that resembles a cascade of falling dominos. It seems very likely that similar circuits exist in other species including humans, and Fee's work has pointed the way to finding these "neuronal timers" elsewhere.



John Gabrieli has found altered patterns of connectivity in patients with schizophrenia or bipolar disorder, including similarities that suggest shared biological mechanisms.

Controlling brain circuits with light

In order to probe, and eventually control, the behavior of neural circuits, researchers need new and more precise technologies to manipulate the activity of specific cells within the living brain. The technique known as optogenetics, pioneered by McGovern Institute associate member Ed Boyden, has made it possible to achieve this using light. Starting with light-sensitive microorganisms, Boyden and colleagues (including Feng Zhang, who will join the institute in 2011) have been able to isolate the light-detecting molecules from these organisms and express them in the living brain. This allows researchers to control brain activity with extraordinary precision, targeting specific cell types and switching them on and off at will.

Optogenetics is now used by hundreds of research labs, including many at MIT, and it is also being explored as a new form of therapy. One early application is likely to be retinal blindness; Boyden and his collaborators have already shown in mice that optogenetics can restore light sensitivity to the surviving circuitry of the retina after the natural light-sensitive cells have been lost.

Modeling disease in mice

Many psychiatric disorders have a strong genetic component, and one important goal for the McGovern Institute is to understand how these genetic alterations lead to brain dysfunction. Guoping Feng, who joined the institute from Duke University earlier this year, is using the tools of mouse genetics to trace the link from genes to pathological behaviors. For example, he has developed strains of mice that show repetitive grooming behavior reminiscent of human obsessive-compulsive disorder (OCD). In collaboration with clinical geneticists he has found that similar genetic variants are associated with human OCD. Most recently, he has developed another strain of mice that show both repetitive behaviors and deficits in social interaction, two defining characteristics of autism. Feng is now working to identify the specific circuits affected in these mutant mice. The answers will reveal important clues to human disease, and will provide a platform for testing new therapies.

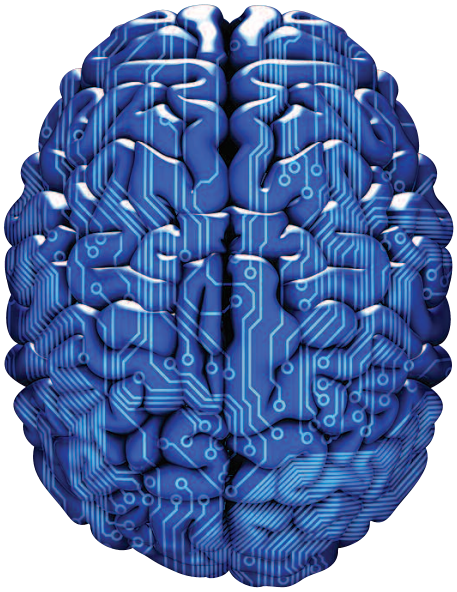
Brain markers of human disease

Research at the McGovern Institute spans many species, but ultimately the brain of greatest interest is our own. John Gabrieli, who directs the Martinos Imaging Center within the McGovern Institute, is collaborating with clinical psychiatrists to study schizophrenia and bipolar disorder, and to understand how the genetic risk factors for these diseases affect human brain function. One of his current goals is to examine how these conditions affect the so-called default network, an interconnected set of brain structures that are especially active during self-reflection.

Identifying patterns of brain activity that are associated with disease is valuable because it will help us understand what brain circuits are affected by different diseases, leading to new and more biologically based disease classifications. It can also help predict who is at risk for these diseases and who will respond best to a given therapy. And finally, understanding these patterns of brain activity can help us measure whether a therapy is actually working, perhaps before any behavioral effects are apparent.

The decade of the neural circuit

Desimone cited these examples to illustrate his central point: to understand the brain, we must study its circuits, using a wide range of experimental systems and technologies. As the McGovern Institute enters its second decade, Desimone is optimistic. "Over the next ten years, with the help of these new technologies and others yet to be invented, I believe we will lay the foundations for a new understanding of brain function. This in turn will lead to a new generation of treatments for brain disorders, beyond anything that we can currently imagine." ■



In addition to the presentation by Bob Desimone, the anniversary celebration featured keynote talks from Gerald Fischbach, Jane Pauley and Alan Alda. Videos of their talks can be seen on our website.

"I want to be helpful in getting scientists to communicate their science with more vividness and more clarity." **– Alan Alda**

The future of autism research

As scientific director of the Simons Foundation, **Gerald Fischbach** is a leader in the search to understand the biological causes of autism.

Autism has a strong genetic component, and identifying the risk genes is a central goal for the field. Several of these genes are known to be involved in synaptic function, pointing to a possible synaptic deficit in autism. Three of these synaptic genes were originally identified through a project to understand the effects of black widow spider venom. Fischbach cites this as a prime example of curiosity-driven research leading to unforeseeable practical implications, underlining the importance of pursuing basic and translational goals in parallel.

To understand the actions of these genes, mouse models are essential, says Fischbach. But to identify the specific circuits that are affected and to understand how this causes deficits in social cognition, he emphasizes that we must also study humans, "the prime species for autism research in the coming decade."

Normalizing mental illness

Leadership Board member and broadcast journalist **Jane Pauley** spoke candidly about being diagnosed with bipolar depression at the age of 50 and about the need to "normalize" mental illness. Just as cancer has moved from the shadows to pink ribbons and races for the cure, she noted, mental illness must shed its public aura of fear and shame.

It was a long struggle to crawl back from "the dark precipice of mental illness," which included a period of hospitalization. In spite of such anguish and anxiety, Pauley says she had hope even from the beginning. Medicine helped, but Pauley also credits the capacity to open up about her situation in public forums, including her first public acknowledgement of her illness at the McGovern Institute opening in 2005. Today Pauley sees a shift in how people regard mental illness. Her personal goal, she concluded, is to "banish ugly, out-of-date attitudes" and replace them with "new neural connections, positive associations."

The art of science communication

When he is not on stage or in a film, **Alan Alda** has worked to advance the public understanding of science. Drawing on his own experiences as the long-time host of the PBS series *Scientific American Frontiers*, Alda encourages scientists to use their own voices when communicating their research to the general public. By posing a series of unscripted questions to scientists around the world, Alda discovered that "an amazing thing happened on their end: the real 'them' came out. They weren't lecturing me, but connecting with me and trying to get me to understand. These conversation modes brought out not only their own personalities, but the science through their personalities."

Alda speculates that this kind of communication must somehow involve the brain's social communication systems. He challenged researchers to unravel the neurological basis for the kind of communication "that makes us human, and that someday may help scientists all over the world to speak in their own voices." ■

Gerald Fischbach (left), Jane Pauley, and Alan Alda.

Photos courtesy of Justin Knight

New Gifts Support China Collaborations and Disease Research

We are delighted to report on three new contributions to the McGovern Institute this fall.

Hugo Shong, General Partner of IDG Capital Partners, has made a $1 million pledge to support new collaborations between the McGovern Institute and China.

"This pledge is my gift to Pat McGovern in honor of the tenth anniversary of the McGovern Institute," said Shong, who joined IDG in 1991. The contribution, which builds upon a gift by Shong to the institute in 2008, is to be used for the development of McGovern programs in China over the next ten years.

"Global collaborations are critical to the advancement of our understanding of the brain," says institute director Bob Desimone. "We are enormously grateful for Hugo's gift, which will allow us to keep up our end of the new Chinese collaborations that his original contribution helped us to establish."

We have also received an anonymous gift of $150,000 in support of Ann Graybiel's Parkinson's disease research. This contribution follows on a similar $100,000 anonymous gift to the Graybiel lab last year. "This gift is extraordinary for us," Graybiel says. "It allows us to push to the very edge of what is technically possible in our lab. It will help us to advance our understanding of the basal ganglia and, ultimately, to improve therapies to treat or prevent neuropsychiatric conditions like Parkinson's disease. I am profoundly inspired by this gift and will transmit my inspiration as much as I can to the young people working in my lab."

Robert Buxton, a member of the McGovern Institute Leadership Board and Executive Vice President of Peter Kimmelman Asset Management LLC, has once again chosen to support disease-based research at the institute. For Buxton, whose son suffers from serious mental illness, the motivation for his gift is crystal-clear. "Autism and bipolar disorder have been devastating for our family," Buxton explains. "Research at the McGovern Institute will be the salvation for kids and adults affected by these disorders."

Hugo Shong, General Partner of IDG Capital Partners, pledges support for new collaborations between the McGovern Institute and China.

In renewing his financial commitment, Buxton cites the significance of the interdisciplinary approach at the McGovern Institute. Such an approach, he feels, gives McGovern an edge over other institutions. "There is a clear mission at the McGovern Institute," he says. "They have top-notch scientists using a systems engineering approach to understand the brain. It will be these pathfinders who eventually find the answers to the devastating disorders of the brain." ■

Leadership Board member Robert Buxton talks with Ann Graybiel.

Photo courtesy of Justin Knight

Fellowships Awarded to Four Young Neuroscientists

Four graduate students at the McGovern Institute are the newly announced recipients of fellowships that are made possible through the generosity of our donors. The students presented their research to the Leadership Board and Friends of the McGovern Institute at a private event preceding the 10th anniversary celebration in October.

Newly appointed fellows Mark Howe (top left); Vivian Hsieh (top center); Zeynep Saygin (top right); and Retsina Meyer (left, speaking with Leadership Board member Pat Poitras)

Photos courtesy of Justin Knight

Mark Howe, a graduate student in Ann Graybiel's lab, is the first recipient of the Gorenberg Fellowship, which was newly established by Leadership Board member Mark Gorenberg. Howe studies dopamine activity in the basal ganglia, deep brain structures that are involved in both directing and motivating behavior. By studying the mechanisms in basal ganglia circuits that allow animals to learn and execute a new set of behaviors, he hopes to pinpoint elements of the circuit that are affected in disorders like Parkinson's disease and drug addiction.

Vivian Hsieh received the graduate student fellowship of the Friends of the McGovern Institute for her work in Alan Jasanoff's lab. Hsieh is developing new molecular sensors that she hopes will expand our ability to image the living brain in all its biochemical complexity.

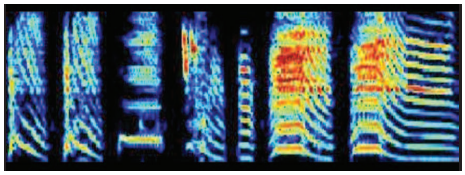
The Sheldon and Janet Razin Fellowship was awarded to Zeynep Saygin, a graduate student in John Gabrieli's lab, for her research on the development of new methods for visualizing long-distance connections in the human brain. Saygin is using a method called diffusion tensor imaging, or DTI, to examine the connections to and from brain regions that are implicated in fear, anxiety, and potentially in conditions such as depression, anxiety disorders and autism.

Retsina Meyer was awarded the Shoemaker Fellowship for her research in Ki Goosens' lab. Meyer is studying how stress contributes to the formation of fearful memories. By understanding these mechanisms, it may be possible to develop more effective treatments for anxiety disorders, depression, and other psychiatric disorders. ■

Institute Researchers Make Strong Showing at San Diego Meeting

The McGovern Institute was strongly represented at the Society for Neuroscience annual meeting in San Diego, California. Members of the institute presented 76 posters and talks at the November meeting, almost twice as many as last year. ■

RESEARCH NEWS



The song of the zebra finch lasts about one second, and is almost identical from one performance to the next.

Image courtesy of Dan Rubin and Michale Fee

As anyone who as ever picked up a guitar or a tennis racket knows, precise timing is often an essential part of performing complex tasks. By studying the brain circuits that control bird song, **Michale Fee** has identified a "chain reaction" of brain activity that appears to control the timing of the song. His findings are published in the Oct 24 issue of *Nature*.

Most people have habits that guide them through daily life. The brain patterns that drive these habitual behaviors are not well-understood, but a new study out of **Ann Graybiel**'s lab shows that habit formation appears to be an innate tendency that is fine-tuned by experience — specifically, by the costs and rewards of certain choices. Her study is published in the Oct 25 issue of the *Proceedings of the National Academy of Sciences*, with an accompanying commentary by Terrence Sejnowski of the Salk Institute. The story was also picked up by WBUR, Boston's NPR station.

In a paper published in the journal *Nature Communications*, **Tomaso Poggio** describes a new computer system that can classify mouse behaviors from video recordings. The new system is as accurate as human observers, and will be a valuable tool for measuring the behavioral effects of drugs and gene mutations that target the nervous system.

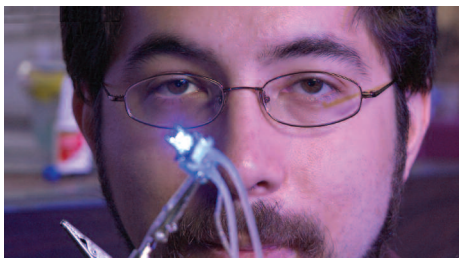
Understanding how the brain recognizes objects is a central challenge for understanding biological vision, and for designing artificial vision systems. In a study published in the Sept 23 issue of the journal *Neuron*, **Jim DiCarlo** provides new evidence that the brain learns to solve the problem of object recognition through its vast experience in the natural world. ■

Tomaso Poggio has developed a computer method that can automatically classify mouse behaviors.

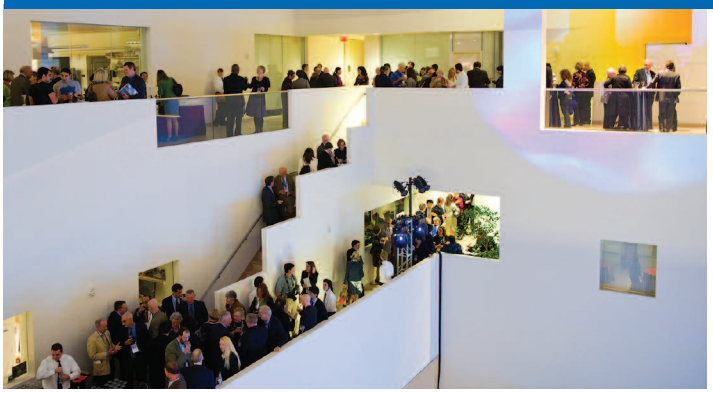
AWARDS AND HONORS

With an h-index value of 92, **Tomaso Poggio** is now considered among the most highly cited Italian scientists, according to the Virtual Italian Academy (VIA). The h-index, which is used to measure a scientist's productivity and apparent scientific impact, is based on how many highly cited papers a scientist has published, and how many times each of these papers is cited in other publications. Poggio's publication profile extends beyond computational neuroscience into other disciplines, earning him the VIA title of "most eclectic scientist."

The Paul G. Allen Family Foundation has named **Ed Boyden** among the first scientists to receive their Distinguished Investigator Award. The seven inaugural investigators were selected based on their "potential for major breakthroughs" and for research that complements work being done at the Allen Institute for Brain Science. Boyden's $1.3 million award will fund his efforts to invent new electronics and software for creating real-time electrical maps of the brain in three dimensions. ■



Ed Boyden develops tools to control the activity of individual neurons in the brain.



McGovern Institute 10th Anniversary Photo Gallery

On October 14, Pat and Lore McGovern were joined by over 200 friends and supporters of the McGovern Institute to celebrate the 10th anniversary of the institute's founding. More photos from the event, along with videos of the keynote talks, can be found on our website.

The entire photo album from this event can also be viewed on our facebook page: http://www.facebook.com/mcgoverninstitute

Guests at the 10th anniversary celebration mingle during a cocktail reception (left); Pat and Lore McGovern give dinner remarks (top right); Guests watch a soundsuit presentation choreographed by Nick Cave of the Art Institute of Chicago (bottom right).

Photos courtesy of Justin Knight

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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