Brain SCAN

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for brain research at mit

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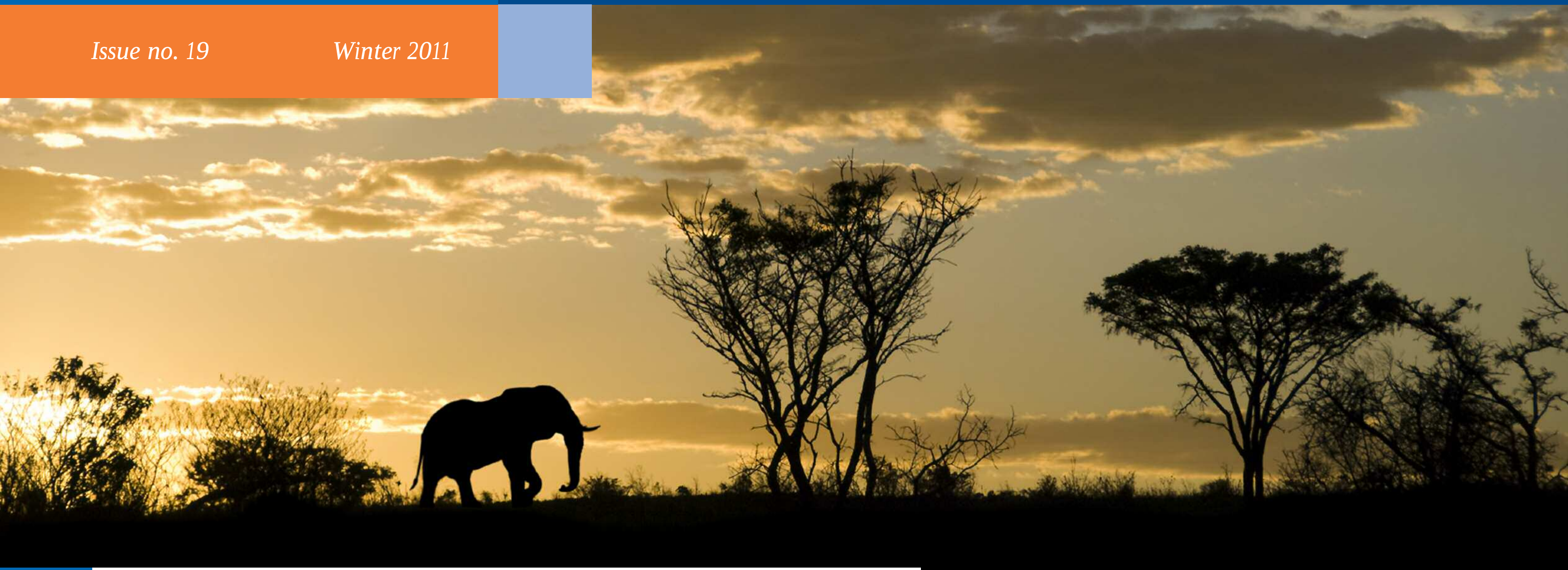


From the director

In this issue we highlight the eclectic career of Tomaso Poggio, one of the world's leading computational neuroscientists and a founding member of the McGovern Institute.

Tomaso Poggio has developed a computer program that can detect, with similar accuracy to human observers, whether a scene contains an animal.

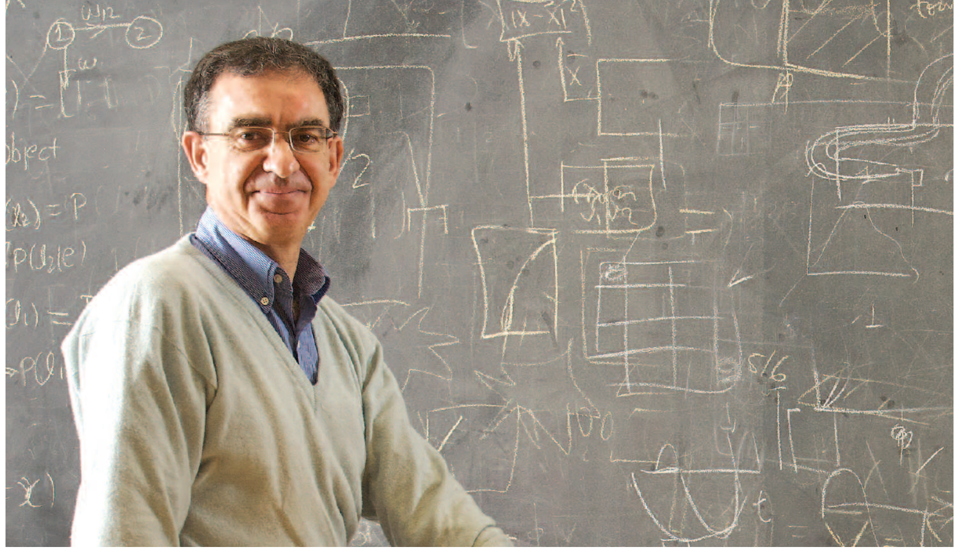
Photo courtesy of istockphoto

Some philosophers have questioned whether the brain can ever understand the brain, and although I do not share this pessimistic view, there is no doubt that the complexity of the brain poses a unique challenge to human understanding. We cannot hope to understand a system of 100 billion neurons without the help of computers, and nobody has contributed more to the study of computational neuroscience than my colleague Tomaso Poggio. His rigorous mathematical approach, along with his insistence that theoretical models must be closely tied to experimental research, has helped to transform our understanding of human vision. His work has also led to many practical applications, in fields ranging from cancer genetics to digital cameras and smart cars. Tommy continues to break new ground, most recently as co-director of the MIT Intelligence Initiative, an ambitious new program to understand how intelligence arises in the brain and how it can be replicated in machines.

In other news, I am delighted to announce a new annual lecture in honor of my predecessor Phillip Sharp, the founding director of the McGovern Institute. The Sharp Lecture, which will be held at the McGovern Institute each fall, is sponsored by a generous gift from Biogen-Idec, a leading biotechnology company that Phil helped to create. We are grateful to the company for this opportunity to honor Phil's extraordinary accomplishments as a Nobel Prize-winning researcher, an administrative leader and a pioneer in the biotechnology industry.

Elsewhere in this issue, you can read about our new two-photon microscope facility, and about some of our recent work on autism, habit formation, and the development of new technologies to address these and other challenges of understanding brain function.

Bob Desimone, Director



Tomaso Poggio, a founding member of the McGovern Institute.

Photo courtesy of Kent Dayton

COMPUTING INTELLIGENCE

By developing theories of how the brain learns from experience, Tomaso Poggio is also helping to engineer smarter machines.

Growing up in Italy in the 1950s, Tomaso Poggio was fascinated by the now-classic science fiction book "Flowers for Algernon," in which a mouse named Algernon and a man named Charlie undergo an experimental operation to raise their intelligence. Algernon aces increasingly difficult maze problems, and Charlie's IQ soars from 68 to 185. But soon, both degenerate again. "I was drawn to scientific questions about intelligence," Poggio recalls. "What is it? How can we improve it? Could we make intelligent machines that could solve scientific problems like time travel?"

Although he has not tried to build a time machine, his work on "thinking machines" does have a science fiction feel to it. He is one of the most cited scientists in his field, working at the cusp of computer science and brain research, and through his work, such futuristic concepts as artificial vision and machine learning have become a reality, with many practical applications.

He has also transformed the way computer scientists study complex problems such as visual object recognition. Traditionally, programmers tried to design machine vision systems from scratch, using the logic of engineering. But Poggio has taken a different approach, trying instead to understand how the brain solves the problem and then building models that mimic the brain's own solution. These brain-inspired models are proving more powerful than traditional engineering programs, and are driving new research directions in both computer science and brain research.

Too Young for Paradise

At the beginning of Poggio's career, neuroscience and computer science were not mature enough to tackle the question of intelligence, so he looked for more tractable problems. For his doctoral dissertation in physics at the University of Genoa, he proposed using holography (which reconstructs objects from scattered light) to increase memory storage in computers. He came up with an idea that motion detection might work in a similar way to holography. His advisor recommended spending a month testing his idea with Werner Reichardt, a pioneer in the emerging field of computational neuroscience and director of the newly founded Max-Planck Institute for Biological Cybernetics in Tuebingen, Germany. Although the holography idea went

As a child in Italy, Poggio became interested in the problem of understanding human intelligence.

Photo courtesy of Tomaso Poggio

"You can't model the brain unless you are closely connected with physiological and behavioral experiments."

nowhere, the one-month visit to Tuebingen turned into a faculty appointment and a stay of ten years. Poggio was informally promised the position of institute director himself – with tenure for his entire lab, freedom from grant writing or obligatory teaching, and a chauffeured Mercedes. "But my wife and I thought we were too young to be in heaven and that we needed a little purgatory first," he jokes, explaining his decision to join the MIT faculty in 1981. "A tough environment is good. And I welcomed the challenges and opportunities posed by brilliant MIT students."

Poggio has remained at MIT ever since. In 2000, he was the first founding member of the McGovern Institute, helping director Phil Sharp to choose the other founding members and to hire new junior faculty members. He currently directs MIT's Center for Biological & Computational Learning.

Parallel Tracks

During his first decade at MIT, Poggio worked mostly on low-level vision, modeling how the brain recognizes motion, shapes, textures, and so on. But around 1990, he decided the time was right to tackle the problem of intelligence that had fascinated him for so long. "I came to believe that learning is the key to intelligence," he explains, "and the essence of learning is the ability to generalize from individual examples." A prime example is visual object recognition. Each new view of an object represents a unique pattern of pixels on the retina, yet somehow the brain learns from past experience to interpret these new patterns, which it has never encountered before, as examples of familiar objects.

Poggio began to study the problem of learning on two parallel tracks. He developed machine learning theory and incorporated the resulting algorithms into computer vision systems. In particular, he applied learning techniques to detect faces and to find people in street scenes – work that has led to pedestrian-detector systems in cars. His research has touched on many other areas, including health informatics, biomedical imaging, cancer genetics, and even financial market predictions. The range and impact of his publications recently earned him the title of "most eclectic scientist" from the Virtual Italian Academy – one of the many honors he has accumulated.

In parallel with his machine learning work, Poggio also collaborated with experimental neuroscientists to understand how real brains accomplish object recognition. Since the 1960s, neuroscientists had seen the visual system as being organized as a hierarchy of brain areas. "This theory seemed too simplistic to me, so I started object recognition as a short project to disprove it. But when we developed a mathematical model to mimic this hierarchy, it worked better than expected…so I got stuck on modeling how the brain recognizes objects."

Learning to See

Poggio's model replicated what neuroscientists knew about how information from the eyes flows through the visual stream. The lower levels processed simple features such as edges and lines. Higher levels compiled that information into shapes, and still higher levels assigned an identity, such as cat or car, and a category, such as animal or vehicle.

Modeling how the brain recognizes three-dimensional objects, like a face, was a more difficult challenge. The working theory was that the brain must somehow contain a 3-D graphical model of the face. Poggio, who was skeptical of this theory convinced a neuroscientist colleague, Nikos Logothetis, to train monkeys to recognize visual objects on a computer screen and then record from neurons in higher areas of the visual cortex. The results suggested that rather than using a single 3-D representation, the brain stores different views of parts of the object in sets of dedicated neurons that are tuned to each view. The combined activity of those neurons responds to the identity of an object regardless of its size, shape or orientation. In 1999, he published this model in a widely cited *Nature Neuroscience* paper.

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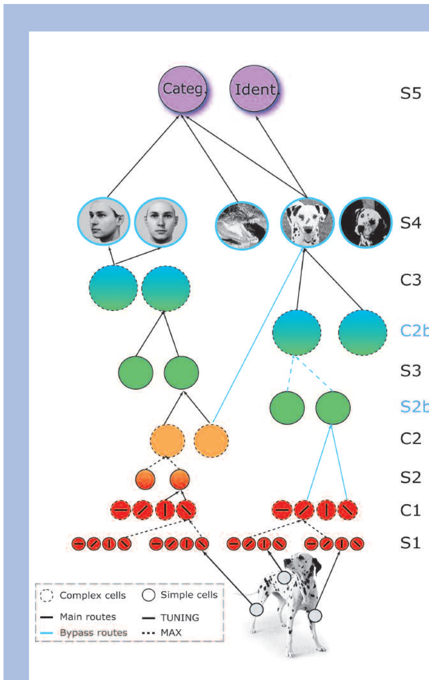


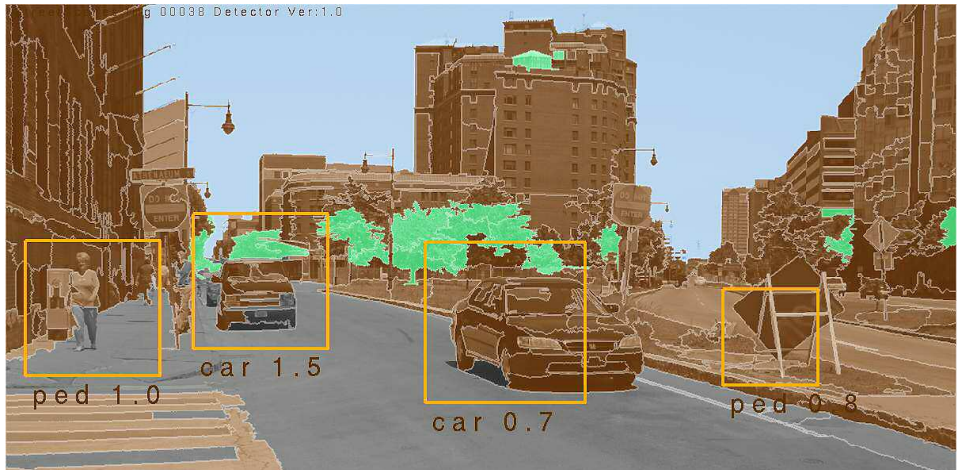
In Poggio's model, simple visual elements such as lines are compiled into more complex shapes and eventually into recognizable object categories.

Image courtesy of Tomaso Poggio

Converging Efforts

Poggio's two lines of research, machine learning and neuroscience, began to converge around five years ago, when he and his collaborators decided to test the brain-based model on a series of complex scenes. In one study, they used street scenes to see if the model could recognize cars, pedestrians, signposts, and the like. In another, they asked the model whether photos of real-world scenes contained an animal.

The model performed as well as human subjects, and even made the same kinds of errors as people on ambiguous images. Significantly, the model outperformed a variety of other state-of-art machine vision systems.



Poggio has developed an algorithm for detecting pedestrians and other objects in street scenes – an important goal for building intelligent vehicles.

Image courtesy of Tomaso Poggio

"We didn't develop our model to actually predict human behavior or to be used for computer vision. But our results told us that a biologically-inspired model really does reflect how the human brain processes visual information, and that nature's solution is more powerful than engineering solutions," explains Poggio. "So I no longer keep my computer science and neuroscience research separate."

Recognizing Actions

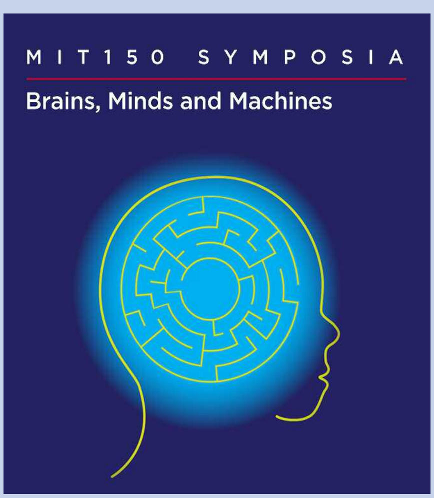
Poggio continues to develop his model, for example incorporating the influence of attention when scanning a cluttered scene. He has also extended the model to recognize actions in video sequences, harnessing the computing power of newly developed graphics processing units to handle the massive quantities of data involved. The model can learn to categorize behaviors in laboratory mice as accurately as human observers – a valuable skill considering that it can take a day or more for a human expert to annotate just one hour of video.

"Researchers who study neurological and psychological disorders need accurate and unbiased classifications, so having automated tools would be enormously helpful," he says. "We have such tools for analyzing the genes that contribute to disease, but no corresponding techniques for quantifying their behavioral effects." Poggio hopes to change that, and to help uncover the complex relationship between genes and behavior, initially in animals but ultimately also in human patients.

Beyond Perception

Over the years, Poggio has collaborated with many of the world's leading scientists, including Francis Crick, co-discoverer of DNA's double helix structure; David Marr, a founding figure in vision research; and now the distinguished mathematician Steve Smale, winner of the Fields Medal, the mathematical equivalent of a Nobel Prize. Many of Poggio's former students have become distinguished scientists themselves, contributing to industry, engineering, finance, business, computer science, robotics, web search engines and more. His work has also attracted more mathematicians to learning theory, which has accelerated the research – as has his commitment to making computer processing freely available and more user-friendly to researchers.

Poggio's next big goal is to go beyond modeling the "what and where" of visual object recognition to the general problem of intelligence. He believes that to understand intelligence in a deeper way we need a new cycle of basic research with a tight integration of neuroscience, computer science and cognitive science. "I believe that only the collective intelligence of an interdisciplinary group of scientists will be able to begin solving the greatest problem in science—how the brain works." ■



Intelligence Initiative

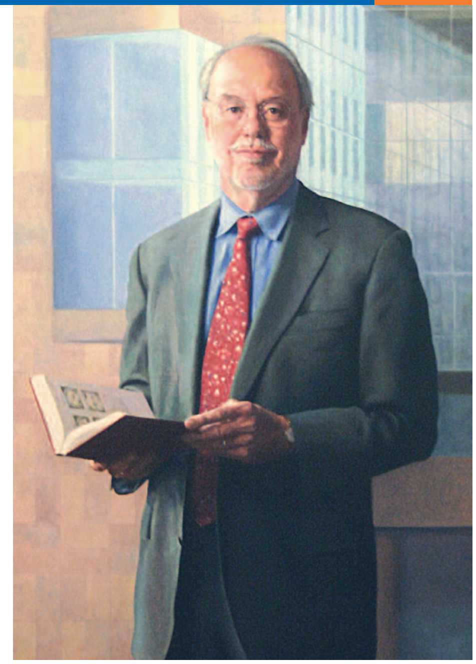
Poggio is one of the leaders of the newly formed MIT Intelligence Initiative (I2), which will be highlighted in the symposium "Brains, Minds and Machines" to be held in May 2011 as part of MIT's 150th anniversary celebrations. ■

Biogen-Idec to Endow Lecture Honoring Phillip Sharp

The McGovern Institute is pleased to announce the establishment of an annual lecture in honor of Phillip Sharp, who served as founding director of McGovern Institute from 2000-2004. Sharp, who shared the 1993 Nobel Prize for his discovery of split genes, has also served as chair of the MIT Biology Department and head of MIT's Center for Cancer Research (now the Koch Institute). He now holds the title of Institute Professor, the highest academic honor at MIT. As founding director of the McGovern Institute, he oversaw the planning for the institute's home in Building 46 and the appointment of the founding faculty.

In addition to his academic career, Sharp has also been a pioneer in the biotech industry, helping to found three companies. One of these is Biogen-Idec, whose generous support has made the new lecture possible. Biogen, as it was known prior to its 2003 merger with IDEC Pharmaceuticals, was one of the first biotechnology companies, and Sharp served on its board of directors for almost 30 years following its founding in 1978. During that time Biogen-Idec has been at the forefront of the biotech revolution, growing into a Fortune 500 company with over $4 billion in annual revenues. Its major focus is now diseases of the nervous system, and we are delighted to highlight the company's achievements and Phil's contribution to its success through this lecture.

The Sharp Lecture will be on the theme of neural circuits. It will take place annually in the fall, and will be followed by a reception. The inaugural speaker and date will be announced in the next few weeks. ■



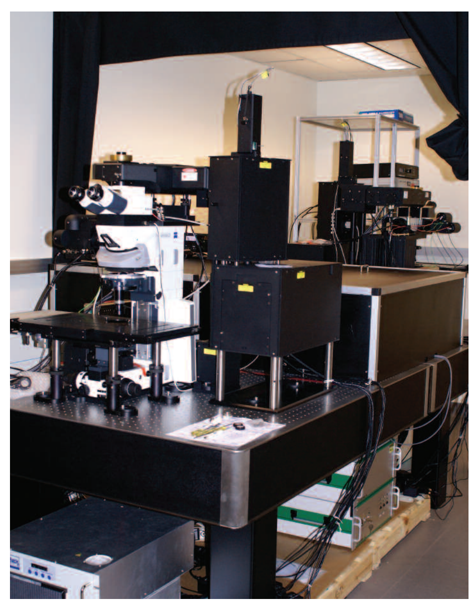
This portrait of Phil Sharp, by artist Richard Whitney, hangs in the McGovern Institute headquarters.

NIH Stimulus Funds Support Shared Microscope Facility

Two-photon microscopy has revolutionized cellular neuroscience since its invention 21 years ago, by providing high-resolution fluorescence images of cells within the living brain. The McGovern Institute was able to acquire a 2-photon microscope several years ago through a gift from Leadership Board member Tom Peterson '57 (see Spring 2009 issue of *Brain Scan*). Demand for this technology continues to grow, and the institute is now acquiring another 2-photon system, with support from a NIH stimulus grant.

The new system was custom-built for the institute by Wisconsin-based Prairie Technologies Inc., and includes two workstations. One is used to examine neurons in culture, where the environment can be very precisely controlled. The other will be used to visualize individual neurons in the intact living brain, revealing both their 3-D shape and their electrical activity—something that was impossible prior to the invention of 2-photon microscopy.

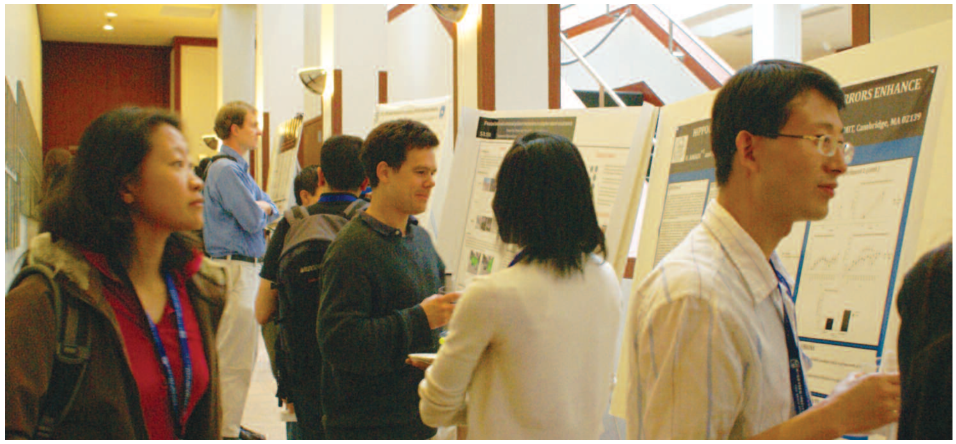
The machine has been installed and is undergoing testing. It is expected to be operational in March 2011, and will be operated as a core facility, available to all MIT neuroscience researchers on a fee-for-service basis. ■



The new 2-photon microscope facility will be available to all MIT neuroscience researchers.

How to Get Ahead in Science: Advice from the Director

Bob Desimone, director of the McGovern Institute, was recently invited to speak to an audience of MIT postdocs as part of a series on scientific career development. His talk, "The four M's of career success," is summarized below:



Students and postdocs at the 2010 McGovern Institute retreat.

Merit: Of the four M's, this is the most important: to get ahead in science, you must tackle and solve significant problems, and discover answers that other scientists care about. No other skill can substitute for scientific merit, so this must be the first goal of every young scientist.

Mentors: Every successful scientist has benefited from mentors – friends and colleagues who have been through similar experiences themselves and can help point the way. Mentoring takes many forms; providing day-to-day advice, being a sounding board for new ideas, making introductions, writing letters of recommendation, and providing advice on key career decisions. To be a successful young scientist you must seek out and cultivate mentors who are respected and well-connected – and don't hesitate to ask their advice when you need it.

Marketing: Some scientists may feel that "marketing" has negative connotations, but there is nothing false or manipulative about trying to present yourself and your work in the best possible way. Giving well-prepared talks is important, but you must also learn to give fluent "elevator pitches" and informal explanations, delivered with spontaneity at the right level for the audience and the occasion. Young scientists must also develop networking skills; look for opportunities to present your work, and to talk about it with your fellow scientists. This comes easier to some people than others, but it's not necessary to be a 'social butterfly' to master this skill – scientists are always interested in each other's work.

Being a Mensch: Reputations travel fast in the scientific world, and if you develop a reputation as a helpful and supportive colleague, others will reciprocate. Science these days is a very collaborative enterprise, and you need the goodwill of your colleagues in order to be successful at it. ■

Meet our Donors: Pat and Jim Poitras

In a new three-minute video available on our website, Patricia and James Poitras '63 describe their motivation to establish the Poitras Center for Affective Disorders Research at the McGovern Institute. "I look at it as an investor," says Jim. "I'd love to see another two, three, four people step forward and make an equal commitment." ■

Save the Date: Annual McGovern Symposium

The McGovern Institute will hold its annual symposium on Tuesday May 10, 2011. The theme this year is the development and function of inhibitory circuits within the brain. The organizer is Yingxi Lin of the McGovern Institute. The event is free and open to the public but registration is required. Symposium information and registration will be available on our website this spring. ■

Feng Zhang, who joined the McGovern faculty in January, described a new method for manipulating gene expression, developed during a fellowship at Harvard in the laboratory of genomics pioneer George Church. By modifying natural bacterial proteins, the authors were able to create "designer" transcription factors that can be used to alter the expression of any gene of interest. The new technology, reported in *Nature Biotechnology*, is likely to have widespread applications in biomedical research.

Ann Graybiel published a paper suggesting that one function of basal ganglia is to segregate habitual behaviors into defined time chunks. The authors recorded brain activity in rats as they learned to navigate a maze with the help of an instructional cue (a tone indicating which way to turn). As the animals mastered the task, neurons in the striatum began to show large bursts of activity at the start and end of each run, as if bracketing the now-familiar behavioral sequence.

Ed Boyden, **Chris Moore** and colleagues from MIT, Harvard, Boston University and Tufts University, have developed a way to selectively activate neurons in the awake mouse brain with light and then track the resulting activity in other brain regions, using functional magnetic resonance imaging (fMRI). By comparing their results with human brain scans, researchers could learn a great deal about the brain circuits involved in disorders such as epilepsy, schizophrenia, autism and post-traumatic stress disorder. "Being able to link the human neuroimaging data to the actual circuit elements that generate those patterns could be very powerful," says Boyden.

In a new study published in *Proceedings of the National Academy of Sciences (PNAS)*, **John Gabrieli** has found that autistic adults were more likely than non-autistic adults to blame someone for accidentally causing harm to another person. The results support the theory that autism involves an inability to infer the thoughts of other people, a skill known as "theory of mind." Gabrieli's findings were reported by the *Los Angeles Times* and *U.S. News & World Report*.

In different study, also published in *PNAS*, Gabrieli and colleagues reported that brain scans may be able to predict which children with dyslexia are likely to improve their reading skills over time. If the findings are confirmed in larger studies, brain scans could be used as a prognostic tool to guide therapeutic interventions. They could also help scientists develop new teaching methods that take advantage of the brain pathways that dyslexic children use to compensate for their disability. ■

fMRI scan of the awake mouse brain showing regions of activity driven by optical stimulation.

Image courtesy of Ed Boyden, Mitul Desai, Itamar Kahn, and Chris Moore

Brain scans may predict reading improvement in children with dyslexia.

Image courtesy of istockphoto

AWARDS AND HONORS

Ed Boyden has been invited to share his optogenetics research this March at the prestigious annual TED conference, at which "the world's most fascinating thinkers and doers...are challenged to give the talk of their lives." Boyden has also received a CAREER Award from the National Science Foundation, designed to "support junior faculty who exemplify the role of teacher-scholars through outstanding research, excellent education and the integration of education and research." The optogenetics technique that he coinvented was recently named 2010 "Method of the year" by the journal *Nature Methods*.

TED Ideas worth spreading

Postdoctoral associates Wenting Wan, of Guoping Feng's lab, and Gabriel Belfort, of Yingxi Lin's lab, were among four postdocs to receive fellowships from the Simons Initiative on Autism and the Brain. These grants were established by the Simons Foundation to "promote innovative, collaborative, and interdisciplinary research that is targeted toward a deeper understanding of autism." ■

Annual Holiday Party

On December 8, members of the McGovern Institute and their families joined colleagues from the Picower Institute and the Department of Brain and Cognitive Sciences for a holiday party. The event, which was held in the atrium of Building 46, was hosted jointly by all three groups, and featured live music from MIT's a cappella group, *The Chorallaries*, and a magic show and gingerbread station for the youngest guests.

Photos courtesy of Najat Kessler

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

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