McGovern Institute for Brain Research

The McGovern Institute for Brain Research at MIT is a research and teaching institute committed to advancing human understanding and communications. The goal of the McGovern Institute is to investigate and ultimately understand the biological basis of higher brain function in humans. The Institute is conducting interdisciplinary research that combines and extends the results of recent breakthroughs in three major, interrelated areas: systems and computational neuroscience, imaging and cognitive neuroscience, and genetic and cellular neuroscience.

Activities

The McGovern Institute held its 4th Annual Retreat on June 4–6, 2006, at the Hotel Viking in Newport, Rhode Island. The format was similar to that of past years with postdocs and students giving talks, a keynote address, and a poster session. We also had Ki Goosens, our newest addition to the McGovern Institute faculty, and John Gabrieli, an associate member of the McGovern Institute, speak. The keynote speaker, Andy Schwartz, gave a well-received talk on the development of a neural prosthesis. A special activity for the group was a sunset sail on a schooner.

We embarked on an extensive faculty search during fall 2005 and spring 2006. We reviewed over 150 applications and interviewed 10 candidates, and anticipate hiring one candidate from this search.

The Institute's Third Annual Scolnick Prize lecture and dinner was held April 25, 2006. The winner, Dr. Michael Greenberg, gave a late afternoon talk, followed by a well-attended dinner at the McGovern Institute. The Scolnick Prize recognizes an outstanding discovery or significant advance in the field of neuroscience.

We held a symposium on imaging to celebrate the opening of the Martinos Imaging Center at the McGovern Institute. The daylong symposium featured seven speakers on the subject of imaging the human brain in health and in disease. Held in the new brain and cognitive sciences complex on May 31st, it was an oversubscribed event that was incredibly well received.

The McGovern board of directors meets quarterly, in July, October, January, and April. The membership of the board has not changed since its inception and consists of Patrick McGovern; Lore McGovern; Elizabeth McGovern; Gerald Fischbach, Columbia University; Robert Langer, MIT; Edward Scolnick, Broad Institute; Robert Silbey, MIT; Sheila Widnall, MIT; and Torsten Wiesel, Rockefeller University.

The Institute is also guided by a distinguished scientific advisory board composed of some of the world's most prominent neurobiologists. The board last met on April 14, 2005 and will meet again in spring 2007. Members are John Duncan, Medical Research Council, England; Eric Kandel, Columbia University; Nikos Logothetis, Max-Planck Institute for Biological Cybernetics; Carla Schatz, Harvard Medical School; Charles Stevens, Salk Institute; and Robert Wurtz, National Eye Institute.

Awards and Honors

Emilio Bizzi was awarded the Empedocles Prize for 2005. He was elected to the Institute of Medicine of the National Academies (2005) and is president-elect of the American Academy of Arts and Sciences (2006). Dr. Bizzi was also awarded the President of Italy Gold Medal for achievements in science.

James DiCarlo was awarded the 2005 Surdna Research Foundation Award through MIT and the 2006–2009 McKnight Scholar Award in Neuroscience through the McKnight Foundation.

Ann Graybiel was named to the Harold S. Diamond professorship, National Parkinson Foundation. Dr. Graybiel was the invited speaker for the following lectures:

- Distinguished Lecture and Rodolfo Rivas Memorial Lecture, University of Maryland;
- Plenary Lecture, Gordon Conference on Catecholamines, Andover, NH;
- Plenary Lecture, Spanish Society on Neuroscience, Madrid, Spain;
- Heller Lecture in Computational Neuroscience, Hebrew University, Jerusalem, Israel;
- Millward Memorial Lecture, Brown University, Providence, Rhode Island.

H. Robert Horvitz received the James R. Killian, Jr. Faculty Achievement Award (MIT), 2006, an honorary DSc from Pennsylvania State University, 2006 and the Centennial Medal, Harvard University, 2005.

Alan Jasanoff, an associate member of the McGovern Institute, became a joint faculty member in MIT's Biological Engineering Division in the spring of 2006. He was also recently named to the Norman Rasmussen Career Development Chair in Nuclear Science and Engineering. Jasanoff received a 2006 Technological Innovations in Neuroscience Award from the McKnight Foundation, which will support in vivo testing of the new family of MRI calcium sensors his laboratory has developed.

Tomaso Poggio was the keynote speaker (among other conferences) at the SIGGRAPH workshop, 2005; at the ETH 150 year anniversary; at the International Conference on Mathematical Harmonic Analysis in Hangzhou, China; and at the Institute for Pure and Applied Mathematics conference held in Mexico. He was the chair of the Future of Information and Communication conference held in Venice in 2005. Dr. Poggio was the coorganizer of the Workshop on Learning Theory of Foundations of Computational Mathematics in Spain in July 2005. He is a member of the committee for a special issue of *Foundations of Computational Mathematics* in honor of Steve Smale and was named to the scientific advisory board of both the Institute for Scientific Interchange Foundation and of the Comitato di Esperti dell'ISICT.

Research

Bizzi Lab

In the last year the Bizzi Lab has investigated motor learning and motor consolidation in humans and monkeys. In one set of experiments the Bizzi Lab used repetitive transcranial magnetic stimulation (TMS) (15 minutes of 1Hz) delivered to the area M1 prior to learning a novel dynamic task. They then tested the subjects' ability to recall these dynamics 24 hours later and found that repetitive TMS stimulation prior to learning did not affect initial adaptation, but did hinder next-day performance relative to controls. These results suggest that M1 may be critical to the early stages of memory consolidation.

The Bizzi Lab also investigated the role of intermittent practice in the consolidation of recently acquired memories. The current view of memory consolidation states that a memory is transformed from a labile to a stable state in a gradual, time-dependent fashion. Their results indicated that the subjects who had practiced intermittently, due to the presence of catch trials, appeared able to retain their initial learning despite interference. Not so when subjects were exposed to constant practice conditions. Catch trials may be beneficial to memory consolidation by providing distinct error cues that disambiguate novel and null-field environments.

Another set of experiments showed that adaptation to novel dynamics and implicit learning of a sequence of movements can be acquired simultaneously and without significant interference or facilitation.

Using monkeys, members of the Bizzi Lab are exploring whether neural cortical oscillation (local field potentials) convey information about the direction of arm movements and motor learning of a new dynamics. This work is relevant to the generation of stable neural signals for prosthetic devices. Finally, using intact frogs, the Lab is investigating the changes of muscle synergies induced by external perturbation to which the animals adapt.

DiCarlo Lab

Professor James DiCarlo's lab continues to focus on understanding the neuronal representations supporting the brain's remarkable ability to recognize objects under a very wide range of viewing conditions. In one line of work they are examining the role of visual experience in the real world in supporting this ability. Last year, they discovered that specific, subtle alterations in the visual world, which are invisible to the human subjects, can alter a property of their visual recognition previously assumed to be rock solid—the ability to recognize objects in different positions. This year the DiCarlo lab completed a neurophysiology study that revealed that related effects of visual experience are found in high-level neuronal patterns of activity in nonhuman primates. The Lab is continuing our exploration of this line of work, using both neurophysiology and computational modeling. The Lab has several ongoing collaborations with other groups in the McGovern Institute. Along with Professor Tomaso Poggio's group, the group is working to better understand how object information is represented along the ventral visual stream, and they have made important progress on the relationship between selectivity for visual objects and tolerance for viewing those objects in cluttered scenes. In collaboration with Professor Nancy Kanwisher's group, the DiCarlo lab has recently completed studies using fMRI in both human and nonhuman primates to gain new understanding of the spatial organization of shape information in high-level visual cortex.

Graybiel Lab

The Graybiel Lab continues to focus its research on functional studies of the basal ganglia and cortico-basal ganglia loops. In the last year they have made significant progress in recording awake behaving animals as they learn and perform complex sequential tasks, and in examining the genetic basis of key aspects of basal ganglia function. First they completed a study, published in *Nature,* in which they tracked the remarkable changes that occur in the activity patterns of neurons in the striatum of the basal ganglia as rats learn a maze task requiring them to decide which way to run on the basis of instruction cues. The Graybiel Lab found a wholesale change in the striatal activity patterns as the animals learned. Remarkably, when the animals were then exposed to extinction training, the acquired patterns gradually unraveled. But then when the animals were put back in the original training situation, the acquired patterns popped up as though they had never disappeared. These findings not only help to delineate what goes on at a neural systems level as animals learn procedures or "habits," but also show a truly remarkable switching from an acquired pattern of neural function to an earlier one and then back again.

In a second series of experiments the Lab found that one of the genes cloned in their laboratory, CalDAG-GEFI, is necessary for the form of learning called sensitization. An example of sensitization is a scenario in which an animal is given a drug such as amphetamine day after day, and as time goes by the animal reacts more and more strongly to the drug, engaging in repetitive, stereotypic behaviors that increase as the daily dosages are repeated. The Graybiel Lab generated a CalDAG-GEFI knockout mouse, and this mouse fails to show sensitization when repeatedly exposured to amphetamine. They have also found that the CalDAG-GEFI knockouts fail to exhibit striatal LTP (long term potentiation), thought to be a biomarker for the learning process. Remarkably, the knockouts passed many other tests with flying colors, despite their lack of striatal LTP and their failure to show sensitization. They conclude that CalDAG-GEFI is a molecule essential for critical behavioral responses to drugs of abuse and that this molecule is also critical for highly selective striatal mechanisms of plasticity. This study so far has been reported in abstract form.

In their third series of experiments the Lab collaborated with investigators in New Zealand who have for many years collected brain material of patients who suffered from Huntington's disease (HD), a disorder that produces extensive degeneration of the striatum and profound symptoms that affect both motor behavior and mood. They performed an extensive analysis of these brains along with a parallel analysis of the symptomatology suffered by the patients. The results of this study strongly suggest that the striosomal compartment of the striatum is differentially affected in HD patients with predominant mood disorder symptoms. This result is remarkable in view of the fact that HD results from a single gene mutation. Graybiel Lab research results suggest that the Huntington's disease gene can differentially affect the striosome and matrix compartments of the striatum, and, as a result of this differential impact, can produce different symptoms in different patients. This study is under review at *Brain*.

Professor Alan Jasanoff

Alan Jasanoff is an associate member of the McGovern Institute. His major research accomplishments in the last year include completion of two studies demonstrating properties of and refinements to the MRI calcium sensors, and another study characterizing the evolution of brain responses to sensory stimulation in rodents during the first weeks of postnatal development. The developmental experiments were performed in part as collaborations with Martha Constantine-Paton's laboratory.

Kanwisher Lab

The Kanwisher Lab continues its exciting and fruitful collaboration with Jim DiCarlo. They will soon submit their second joint paper, this one on fMRI scanning in monkeys. In the last year the Kanwisher Lab has developed new behavioral methods of studying the reorganization of visual cortex in adulthood, and they continue their fMRI work on this topic. The Lab has also developed a new method for asking which pattern data in visual cortex participate in perceptual discrimination tasks. Finally, they think they may have discovered a new kind of evidence for precise feedback to primary visual cortex. All of these studies are ongoing, along with many other projects.

Poggio Lab

The Poggio Lab (25 researchers, including students, postdocs, visitors, and staff) focuses on research on the problem of learning, which they believe is at the core of understanding how the brain works and how intelligence is synthesized in machines. Their research effort is at three different levels: theory (foundations of learning theory and development of learning algorithms), engineering applications (bioinformatics with the Department of Biology, computer vision, trainable man–machines interfaces), and computational neuroscience (models of visual cortex underlying object recognition in collaboration with Miller's, Ferster's, Koch's and DiCarlo's labs in using the models as a tool to analyze, interpret, and plan experiments).

Over the last several years, the three levels of research have been relatively independent, though fruitful interactions often took place. In the last year, however, a surprising synergy between the different directions of research has emerged. A theory of the feed forward path in the ventral stream of visual cortex turned out to perform as well or better than state-of-the-art computer vision systems on difficult recognition problems of natural images. It also performs at human level in rapid categorization tasks of natural images. The model is consistent with known (or predicted and then experimentally verified) physiological properties of cells in several cortical areas. Furthermore, the architecture assumed in their model has strong relations with key aspects of learning algorithms as suggested by learning theory. The theory of the visual ventral stream is the main tool in their collaboration with several experimental labs at MIT (Desimone, DiCarlo, Oliva, and Miller), Harvard, Georgetown, CalTech, and Northwestern.

The Poggio lab funding is diversified among the National Science Foundation, the National Institutes of Health (Conte Center for Neuroscience), Defense Advanced Research Projects Agency, the Office of Naval Research, and private companies.

Personnel

Tom Byrne, a clinical professor of neurology and health sciences and technology at Harvard Medical School, has been appointed an associate member of the McGovern Institute.

Robert Desimone
Director
Professor of Brain and Cognitive Sciences

More information about the McGovern Institute for Brain Research can be found at http://web.mit.edu/mcgovern/.