

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 3rd Annual Retreat September 12–14, 2004 at the Sea Crest Resort on Cape Cod, Falmouth, Massachusetts. There were approximately 100 participants from the labs of the McGovern investigators as well as a few visitors from other departments at MIT. Similar to the previous year, each lab put forth two members who each gave a 15-minute presentation on their current research. A lobster and clam bake and a well-attended poster session rounded out our activities.

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

Our Second Annual Scolnick Prize lecture and dinner was held April 14, 2005. The winner, Dr. Judith Rapoport, gave a late afternoon talk, followed by a well-attended dinner at the MIT Faculty Club. The Scolnick Prize recognizes an outstanding discovery or significant advance in the field of neuroscience.

Our annual symposium took place May 13, 2005 in the Wong Auditorium at MIT. The symposium title was Smart Molecules and featured six well-known speakers in the field.

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, Merck and Company Inc.; 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 Scientific Advisory Board met on April 14, 2005 and will meet again in Spring 2007. Members of the Board 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

James DiCarlo was awarded the 2005 MIT School of Science Prize for Excellence in Undergraduate Teaching

Ann Graybiel was awarded La Fondation IPSEN pour la Recherche Thérapeutique's Neuronal Plasticity Prize. The prize is awarded to a researcher in recognition of an outstanding contribution in the field of neuronal plasticity. Dr. Graybiel was also awarded an honorary doctorate of science from Tufts University, Medford, Massachusetts, 2005.

Alan Jasanoff, an associate member of the McGovern Institute, received funding through the Raymond and Beverly Sackler Foundation.

Nancy Kanwisher was elected to the National Academy of Sciences.

Tomaso Poggio was the keynote speaker (among other conferences) at the SigGraph workshop, 2005; at the Swiss Federal Institute of Technology Zurich (ETH) 150 year anniversary; at the International Conference on Mathematical Harmonic Analysis (Hangzhou, China). Dr. Poggio also was chairperson of the conference Future of Information and Communication, Venice, Italy, 2005; was co-organizer of the Workshop on Learning Theory at the Foundations of Computational Mathematics Conference in Santander, Spain, 2005; served as a member of the committee for a special issue of the Foundations of Computational Mathematics journal in honor of Steve Smale; was named member of the Scientific Advisory Board of the Institute for Scientific Interchange Foundation, Turin, Italy, and of the Comitato di Esperti dell'Istituto Superiore di Studi in Tecnologie dell'Informazione e della Comunicazione (ISICT), Genoa, Italy.

Research

Research in the Emilio Bizzi laboratory focused on the study of the physiological mechanisms of motor control. Over the past year they have investigated the role of sensory feedback in the activation and organization of synergies. Most muscle synergies were identified as shared synergies, suggesting that electromyographics (EMGs) of locomotor behaviors are generated primarily by centrally organized synergies. Both the amplitude and temporal patterns of the activation coefficients of most shared synergies, however, were altered by deafferentation, suggesting that sensory inflow modulates activation of those centrally organized synergies. Sensory feedback might adapt recruitment of muscle synergies to behavioral constraints, and the few synergies specific to the intact or deafferented states might represent afferent-specific modules or feedback reorganization of spinal neuronal networks.

They also investigated one of the most common NMDA-elicited outputs, the adduction-caudal extension-flexion rhythm, and examined the relationship between the different force phases in terms of synergies and topography. Two distinct EMG patterns produce caudal extensions and only one of the two patterns is used in most sites. These two patterns map at distinct locations in the lumbar cord. Within individual sites rhythms, linkages are found among the synergies used to produce adductions, the onsets of flexions after caudal extensions, and the synergy pattern producing the caudal extensions.

Finally, they examined the mechanical stability properties of hindlimb-hindlimb wiping movements of the spinalized frog. One hindlimb, the wiping limb, was implanted with 12 EMG electrodes and attached to a robot that both recorded its trajectory and applied brief force perturbations. In the perturbed behaviors, they found that the initially large displacement attributable to the perturbation was compensated such that the final position was statistically indistinguishable from the unperturbed final position in all of the frogs, thus indicating the dynamic stability of these movements. Deafferentation of the wiping limb did not significantly affect the stability of the wiping reflex. Thus they found that the intrinsic viscoelastic properties of the hindlimb conferred robust stability properties to the hindlimb-hindlimb wiping behavior. This stability mechanism may simplify the control required by the frog spinal motor systems to produce successful movements in an unpredictable and varying environment.

Robert Desimone's research focuses on disorders of perception, attention, and memory that frequently accompany the major mental diseases. To understand the neural mechanisms of these mental processes, his lab is recording the activity of neurons in the extrastriate and prefrontal cortex of nonhuman primates engaged in tasks requiring visual discrimination, attention, and memory. They then use the results from the neurophysiological studies to make predictions about the physiological organization of human cortex.

James DiCarlo's lab continues to focus their work on understanding the neuronal representations that support the brain's remarkable ability to recognize objects under a very wide range of viewing conditions. In one line of work they have been examining the role of visual experience in the real world in supporting this ability. This year, they discovered that specific, subtle alterations in the visual world that are invisible to the human subjects can alter a property of their visual recognition that was previously assumed to be rock solid—the ability to recognize objects in different positions. They are continuing ongoing physiology work in nonhuman primates to examine similar effects at the neuronal level. In collaboration with Professor Nancy Kanwisher's group, they are continuing their exploration of the effect of visual experience on the brain's representations of visual objects at the level of fMRI in both human and nonhuman primates.

In collaboration with Professor Tomaso Poggio's group, they have completed a systematic characterization how object information can be "read-out" of inferior temporal (IT) cortex by downstream brain areas to support visual recognition. In a related line of work, the DiCarlo lab has continued their investigations of neuronal IT representations underlying visual recognition in real-world clutter. This year they discovered that IT neuronal responses to clutter (more than one object) can be remarkably well understood from their responses to single objects. This result greatly clarifies the existing literature and adds important constraints to computational models of visual recognition.

Ann Graybiel's lab continues to work on the "habit system" of the brain. They have new work that soon will appear in *Nature*, demonstrating by recording with many electrodes simultaneously what happens to brain activity in the basal ganglia as animals learn to perform a task that requires decision making, and what happens when they need to relearn. The brain cells reorganize their activity patterns, new cells are recruited, drop out, then come back. They imagine that these changes are fundamental fingerprints of learning in the brain's habit system. Graduate student Terra Barnes, and scientists Yasuo

Kubota, Hu Dan, and visiting scientist Dezhe Jin were active in this work. This work is of high relevance to understanding learning and memory mechanisms in the brain, and to understanding how it is that we make and break habits.

The Graybiel lab has discovered a gene that is critical for responses to addictive drugs such as amphetamines. This work, in which postdocs Jill Crittenden and Magdalena Sauvage and technical instructor Pat Harlan were active, was done by knocking out the gene. This discovery has relevance for the field of drug addiction and for the development of pharmaceutical reagents for this purpose, given that blocking the gene lowers a major effect of the repeated drug use.

The Graybiel lab has discovered that the frontal neocortex and the striatum in primates can develop highly stereotyped electrophysiological responses in repetitive visuo-motor tasks, and that these activities can come into synchrony and then fall out of synchrony, depending on the times during the task, as though they were in a push-pull collaboration with each other. This work was dependent on developing methods for long-term simultaneous recording from cortex and striatum in awake behaving primates (Fujii N, Graybiel AM. Time-varying covariance of neural activities recorded in striatum and frontal cortex as monkeys perform sequential-saccade tasks. *Proc Natl Acad Sci U S A* 2005 Jun 21;102(25):9032–7). This work is of high relevance to clinical studies related to Parkinson's disease, and also such disorders as obsessive-compulsive disorder, Tourette syndrome, and possibly schizophrenia.

Alan Jasanoff, an associate member of the McGovern Institute, joined the faculty in September 2004 and started up a new lab. His lab studies early development of somatosensory responses using fMRI and calcium-sensitive contrast agents for brain imaging.

Christopher Moore's laboratory is investigating the neural mechanisms of touch perception, and how rapid changes in neural organization ('dynamics') relate to rapid changes in perceptual function. To make the link between perception and neural activity, the lab takes a multilevel approach. In humans, in whom detailed perceptual studies can be more readily conducted, they employ techniques such as event-related fMRI during psychophysical performance to identify cortical areas relevant to tactile perception. In animal model systems, in which detailed neural activity can be more readily investigated, they employ imaging (fMRI and optical imaging) and electrophysiology to examine organization at the level of the cortical column and neuron.

The Moore lab has recently discovered that rat vibrissae are 'tuned,' so that they resonate when stimulated at specific frequencies. As a result, a spatial, somatotopic map of frequency-sensitivity is organized in the array of vibrissae across the rat face. This finding provides a novel mechanism for the transduction of tactile information and suggests that vibrotactile processing in the rodent parallels auditory processing (e.g., the spatial map of frequency coding established by resonance in the cochlea). The lab is currently studying the consequences of vibrissa resonance on neural encoding in the periphery and cortex.

The Poggio Lab (with some 30 to 40 researchers, including students, postdocs, visitors, and staff) focuses on research on the problem of learning, which they believe is at the core of the problem of understanding how the brain works and of synthesizing intelligence in machines. Their research effort is at three different levels: (a) theory—foundations of learning theory and development of learning algorithms, (b) engineering applications—bioinformatics with the Department of Biology, computer vision, trainable man-machine interfaces, and (c) computational neuroscience—models of visual cortex underlying object recognition in collaboration with the Miller, Ferster, Koch, and DiCarlo 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 feedforward path in the ventral stream of visual cortex turned out to perform as well as 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 our 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 our collaboration with several experimental labs at MIT, Harvard, Georgetown, Caltech, and Northwestern.

The Poggio lab's funding is diversified among the National Science Foundation, National Institutes of Health, Defense Advanced Research Projects Agency, Office of Naval Research and private companies.

Personnel

Robert Desimone was selected as director of the McGovern Institute at the July 2004 Board of Directors meeting and began his appointment at MIT in October 2004. Prior to coming to MIT, he was director of the Intramural Research Program at the National Institute of Mental Health for six years. Dr. Desimone is a member of the National Academy of Sciences and the American Academy of Arts of Sciences.

Laurie Ledeen was hired as the development and special projects officer for the McGovern Institute. Laurie was most recently at the Dana-Farber Cancer Institute where she was principal gifts officer.

Shannon Landerer was hired as an administrative assistant.

Robert Desimone

Director

Professor of Brain and Cognitive Sciences

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