Department of Brain and Cognitive Sciences

Mission

The Department of Brain and Cognitive Sciences (BCS) has been driven for the 43 years of its existence by the mission of understanding how the brain works and how it gives rise to the mind. In the pursuit of this objective, BCS has created a diverse, multidisciplinary environment of interrelated areas and levels of investigation providing the greatest opportunities for significant insight into key questions. Today, BCS is the only department of its kind, balancing an extraordinary breadth of inquiry with the focus and exactitude required for field-leading research. BCS remains a unique department with a unique vision.

The department is complemented and strengthened by its association with the Picower Institute for Learning and Memory and the McGovern Institute for Brain Research; 20 of 38 BCS primary faculty are also investigators in these centers. With the brain and cognitive sciences complex bringing researchers from all three entities together in the same building, BCS holds a special role, acting as an umbrella and providing the academic home for all teaching and research into the brain and mind at MIT.

Faculty

BCS faculty are widely recognized as being among the leaders in their respective fields. Of 47 total faculty, 38 hold primary appointments in BCS, 9 of whom also hold appointments in the Picower Institute for Learning and Memory and 11 in the McGovern Institute for Brain Research. Two faculty have dual appointments in the Health Sciences and Technology Program of MIT and Harvard; four are Howard Hughes Medical Institute investigators. The faculty is distinguished by its accomplishments and honors: eight are members of the National Academy of Sciences, three of the Institute of Medicine, and 10 of the American Academy of Arts and Sciences.

Effective July 1, 2009, associate professor James DiCarlo was granted tenure. In January 2009, Yingxi Lin and Weifeng Xu joined the department with additional appointments in the McGovern Institute and the Picower Institute, respectively. In addition, Mriganka Sur agreed to a third term as department head and Matthew Wilson was named to the new position of associate department head for education.

The interdisciplinary nature of neuroscience and cognitive science is highlighted by the number of the joint appointments held by BCS faculty members as well as those granted to faculty of other departments. Joint appointments in BCS currently number nine with representation from Linguistics, Mechanical Engineering, the Media Lab, Nuclear Science and Engineering, Biology, Biological Engineering, Electrical Engineering and Computer Science, and the Sloan School of Management. BCS faculty members in turn hold joint appointments in many of these units as well as Physics, Computer Science and Artificial Intelligence Laboratory, and the Clinical Research Center.

Graduate Program

Seventeen graduate students entered in fall 2008. Two of the new incoming students were funded by Singleton Presidential graduate fellowships, and three were funded by the Singleton fellowships. Six were supported by departmental National Institutes of Health training grants, and one was funded by the Ida Green fellowship administered by the Office of the Dean for Graduate Students.

During this year, one student graduated with a master's of science and 13 students graduated with doctorates. Four of them took postdoctoral positions in universities or research institutions (two in BCS at MIT, one in the Psychiatry Department at Stanford School of Medicine, one in the Department of Anesthesia and Critical Care at Massachusetts General Hospital). Of the remaining nine, one is chief executive officer and one is chief technical officer of Navia Systems; one is a lecturer (assistant professor) at the University of Adelaide; one is a scientist at Exponent Failure Analysis Associates; one is a math and science teacher at Dorchester Collegiate Academy charter school; one is a performance solutions designer for Carney Inc.; one is a research associate at Windham Capital Management, LLC; and one is a consultant at the Boston Consulting Group.

Seven students were honored for excellence in undergraduate teaching and four were commended for continuing dedication to teaching.

The Course 9 Major

For AY2009, Course 9 featured an undergraduate population of 154 with 56 graduating seniors. Forty-two freshmen joined the department as new majors at the end of the 2009 spring term.

Ten seniors received outstanding research and 11 seniors received perfect grade point average (GPA) awards. An additional 23 juniors and sophomores were recognized for outstanding research and/or academic work in the department.

Also, 34 students had perfect GPAs this past semester and were acknowledged by the department.

Development Activities

BCS enjoyed a significant boost to its resource development efforts from a new agreement that has the department sharing a development officer and staff with the Picower Institute. Among the noteworthy results of the last year are a $7.5 million grant to establish the Simons Initiative on Autism and the Brain, new endowed graduate fellowships from BCS visiting committee members Jeffrey Hallis and Al and Barrie Zesiger, and a significant seed gift from Prisca and Kim Marvin to establish the Autism Research Fund. BCS also increased its development outreach with a number of events, including breakfast seminars featuring department faculty as well as the well-attended "Brains on Brains"—an afternoon-long program of talks and panel discussions highlighting MIT's research efforts into diseases and disorders of the brain.

Some Research Highlights

Mark F. Bear's laboratory seeks to understand how experience modifies the brain. It has long been assumed that experience-dependent synaptic plasticity in the visual cortex is confined to a critical early postnatal period. Research by Bear's laboratory has forced a revision of this view. Using behavioral and electrophysiological approaches, his laboratory found remarkable plasticity in the visual cortex of adult rodents. In related work, the laboratory has provided the first demonstration that learning induces long-term synaptic potentiation in the hippocampus. Bear's laboratory also continues to aggressively study fragile X syndrome (FXS), the most common form of mental retardation and a known genetic cause of autism. Work in Bear's laboratory has established that many aspects of FXS can be corrected by reducing signaling through metabotropic glutamate receptors, a finding with significant therapeutic implications.

Emery Brown's experimental research uses systems neuroscience approaches to study the mechanisms of general anesthesia in human and in animal models. This year they completed two human studies that allowed them to develop detailed characterizations of the behavioral and neurophysiological features of loss and return of consciousness induced by general anesthesia. Their neural signal processing research has developed several new techniques this year, including a way to measure the signal-to-noise ratio of individual neurons, new harmonic regression methods to analyze calcium imaging data, a new tomographic reconstruction algorithm to measure visual receptive fields in moving bar visual neurophysiological experiments, a new multivariate point process model for neural spike trains, and a semi-Markov model of cortical up-down states.

Martha Constantine-Paton's lab is focused on developing glutamate neurotransmission and its modulation during development. Their basic research emphasis is on development of the rodent visual pathway during the second to the fourth postnatal week when the eyes open, synaptogenesis is at its peak, and visual acuity and interactions between the visual cortex and visual colliculus are at their peak. They have shown that the eye-opening event is necessary for the normal refinement of the corticocollicular projection. In addition, they have begun to explore the involvement of the glutamate system in neurological disease. For example, they set up an international collaboration in her laboratory to study early development of brain and spinal cord circuitry in a mouse model of amyotrophic lateral sclerosis in which motor neurons die, usually within four years of diagnosis, which usually occurs in mid-adulthood.

Yingxi Lin's laboratory focuses on understanding how neuronal activity regulates the development and function of GABAergic synapses. Despite being key elements of neural circuit plasticity and stability, the mechanisms governing GABAergic synapse development are relatively poorly understood, because the molecules involved are largely unknown. They recently discovered a novel activity-regulated transcription factor, Npas4, as a crucial molecular link between neural excitation and GABAergic synapse development. They are currently using forward genetics to characterize the transcription program downstream of Npas4 that is important for the development of inhibitory circuits. Their research will address fundamental questions in neuroscience and identify potential therapies for neurological disorders.

Research continues in Richard Wurtman's lab on the implications of their discovery that administering a triad of phosphatide precursors, orally, can increase the production of synaptic membrane, dendritic spines, and, very likely, new synapses themselves and can also thereby enhance cognitive functions in experimental animals. An initial large-scale clinical trial on 212 patients with mild Alzheimer's disease, half of whom received a placebo (double-blind) and half the phosphatide precursors, satisfied a predetermined primary endpoint, with cognitive function (as assessed by using a modified-for-Alzheimer's-testing Wechsler test) improving significantly after 12 weeks of treatment. A second, larger clinical trial, to involve 500 American patients, was initiated several months ago; approximately 100 have been enrolled to date.

In the last year, Carlos Lois and his lab have studied two main areas: the integration of new neurons in the postnatal brain and the generation of cellular diversity in the embryonic brain. Using in vivo two-photon microscopy, they have discovered a new mechanism of neuronal migration by which new neurons move through the postnatal brain in the absence of scaffolds to guide their migration. This finding has important implications for the potential use of stem cells to treat neurological disorders. They have devised a new genetic system to regulate the electrical activity of neurons and have found that the survival of new neurons in the adult brain depends on their reaching a minimal threshold of electrical activity, regardless of the precision of that activity. This observation could explain the high prevalence of neurological diseases caused by hyperexcitability, such as epilepsy.

Research in Laura Schulz's early childhood cognition lab focuses on curiosity, exploration, and causal learning. Causal knowledge is both critical and mysterious: critical, because it allows us to change the outcome of events, mysterious because causal relations must be inferred rather than observed. In her work, she looks specifically at how children learn from sparse data and integrate domain-specific knowledge with novel patterns of evidence. This work bridges her interest in a variety of areas, including philosophy of science, conceptual development, and theory of mind.

The work of Mary Potter's lab focuses on the first moments of processing meaningful material such as letters, words, and pictured scenes. They present sequences of such stimuli by rapid serial visual presentation, either asking the viewer to detect a target (e.g., any letter among digits or a picture of a picnic among other pictures) or testing later memory for what was seen. They have found that such stimuli can be detected and reported with a presentation rate as high as 10 or even 20 per second, but a second target occurring within 200–500 milliseconds is apt to be missed. With the collaboration of Brad Wyble, they have developed a computational model of this phenomenon, the attentional blink. In current work, they are testing and extending this model.

Ann Graybiel's lab focuses on the habit system of the brain, which, remarkably, turns out to be the same brain complex that is disordered in neurologic disorders such as Parkinson's disease, Huntington's disease, and dystonia; "motor-plus" disorders; and neuropsychiatric disorders such as obsessive-compulsive disorder and Tourette syndrome and likely also in attention deficit disorder/attention deficit hyperactivity disorder and aspects of schizophrenia. The lab has made several important discoveries

during the past year. They found that two genes they previously identified were differentially dysregulated in the brains of rats exhibiting dyskinesias induced by prolonged L-DOPA therapy, suggesting new therapeutic methods to prevent or minimize the unwanted side effects of this widely used treatment. In mice, they discovered ensemble activity of neurons in the sensorimotor region of the striatum that relates to both stability of the global framework of a preestablished behavioral procedure and flexibility of detailed representation of individual sensory and motor events.

Weifeng Xu studies information processing in the nervous system, which depends on electrical signal propagation along the neuron and the chemical and electrical signal relay across neurons, referred to as synaptic transmission. Neurons constantly modify their molecular content to change their excitability and synaptic efficacy in order to process and store information in the network. Deregulation of neuron excitability and synaptic efficacy is often manifested in neurological and psychiatric disorders and is thought to underlie some of the cognitive impairments and dysfunctions often seen in these diseases. Proteins are the key mediators of these processes and the prime targets for pharmacological interventions. Although the molecular components of these physiological phenomena were worked out in pioneering work, the precise function and molecular interplay in most cases remain elusive. Using a combination of molecular manipulations in single neurons and a deep analysis of their electrophysiological properties, they can dissect the molecular machinery for neural plasticity with unprecedented precision.

The focus of Troy Littleton's laboratory is to understand the mechanisms by which neurons form synaptic connections, how synapses transmit information, and how synapses change during learning and memory. To complement this basic research in neuroscience, they also study how alterations in neuronal signaling underlie several neurological diseases, including epilepsy and Huntington's disease. They combine molecular biology, protein biochemistry, electrophysiology, and imaging approaches with *Drosophila* genetics to address these questions. Despite the dramatic differences in complexity between *Drosophila* and humans, genomic analysis has confirmed that key neuronal proteins and the functional mechanisms they govern are remarkably similar. As such, they are attempting to elucidate the mechanisms underlying synapse formation, function, and plasticity using *Drosophila* as a model system. By characterizing how neurons integrate synaptic signals and modulate synaptic growth and strength, they hope to bridge the gap between molecular components of the synapse and the physiological responses they mediate.

Suzanne Corkin and her colleagues use behavioral, structural brain imaging (MRI), and functional brain imaging (fMRI) paradigms to address questions concerning the cognitive and neural basis of learning and memory in humans. The research participants include patients with global amnesia, Alzheimer's disease, and Parkinson's disease as well as young and older individuals without neurological disorders. The overarching goal of this research is to identify the cognitive processes that support different kinds of memory in humans and to relate those processes to specific brain circuits. Current research topics include further examination of emotional memory enhancement in healthy aging, and two new projects characterizing heterogeneity in Parkinson's disease and Alzheimer's disease.

Selected Faculty Awards and Honors

Discover magazine selected Ed Boyden as one of their 20 best scientists under age 40. Ed also received the MIT Alumni Class Funds award for excellence in educational innovation for his new series of courses on neuroengineering and neurotechnology.

John D.E. Gabrieli, Mriganka Sur, and Li-Huei Tsai were named fellows of the American Association for the Advancement of Science.

John Gabrieli and Rebecca Saxe received BCS awards for excellence in undergraduate teaching for 9.00 Introduction to Psychology and 9.61 Laboratory in Higher Level Cognition, respectively; professors Ki Ann Goosens, Carlos Lois, and Laura Schulz received BCS awards for excellence in undergraduate advising.

Ann M. Graybiel was named Institute Professor. She also received the Vanderbilt prize in biomedical science and was invited to give the Lord Adrian lecture at the University of Cambridge and the Mildred Trotter lecture at Washington University in St. Louis.

Work by Ted Gibson, graduate students Michael C. Frank and Daniel L. Everett, and postdoctoral associate Evelina Fedorenko involving the Pirahã people, a small group of hunter/gatherers living in the Amazon rain forest, was recently named number 39 in *Discover* magazine's list of the top 100 stories of 2008. The BCS researchers' findings are overturning some fundamental assumptions about the mind, as these Brazilians don't count and have no words for numbers.

Yasunori Hayashi received both the Japanese Society for the Promotion of Science prize and the Japan Academy Medal for his work on molecular mechanisms of hippocampal synaptic plasticity.

Neville Hogan was accorded the Henry M. Paynter outstanding investigator award by the American Society of Mechanical Engineers, Dynamic Systems and Control Division, in 2008

Earl Miller's paper, "An Integrative Theory of Prefrontal Cortex Function" (Miller and Cohen, 2001) was designated a current classic by Thomson Scientific as among the most cited papers in *Neuroscience and Behavior*.

The BCS fall 2007 award for excellence in undergraduate teaching (faculty) was given to Aude Oliva along with graduate students Tim Brady and Talia Konkle, and postdoctoral fellow George Alvarez was recently named number 86 in *Discover* magazine's list of the top 100 stories of 2008.

Tomaso Poggio was the tutorial speaker at Neural Information Processing Systems, December 2007.

Popular Science magazine has named MIT BCS faculty member Rebecca Saxe to its annual brilliant 10 list of the country's top young scientists to watch. She was also

recipient of the Fred and Carole Middleton career development chair and a Packard Foundation fellowship.

Li-Huei Tsai was named director of the Picower Institute for Learning and Memory.

Richard Wurtman was invited to be a guest lecturer by the Porcellati Foundation and the European Society for Neurochemistry at the 4th Biennial Conference on Advances on Molecular Aspects of Neurological Diseases that will be held in Leipzig on July 11–14, 2009. He was also named the 2009 William E.M. Landis lecturer in nutritional biochemistry at the University of Michigan.

Mriganka Sur
Department Head
Paul E. Newton Professor of Neuroscience

More information about the Department of Brain and Cognitive Sciences can be found at http://www.mit.edu/bcs/.