Department of Brain and Cognitive Sciences

The Department of Brain and Cognitive Sciences (BCS) continues in its long-standing mission to understand the brain and, in doing so, to learn how it gives rise to the mind. Believing that such an understanding requires an approach that is simultaneously broad and deep, BCS seeks to create a diverse, multidisciplinary environment of interrelated areas and levels of investigation. BCS is a unique department—one of a very few that successfully balance the tension between the breadth needed to understand the brain in its totality and the focus required for field-leading research.

The department is complemented and strengthened by its association with the Picower Institute for Learning and Memory (PILM) and the McGovern Institute for Brain Research (MIBR); 22 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, eight of whom also hold appointments in the Picower Institute for Learning and Memory and 14 in the McGovern Institute for Brain Research. Two faculty members have joint appointments at the Broad Institute, two have dual appointments in the Harvard-MIT Division of Health Sciences and Technology, three are Howard Hughes Medical Institute (HHMI) investigators, and two hold the special title of Institute Professor.

The faculty are distinguished by their accomplishments and honors: eight are members of the National Academy of Sciences, three of the Institute of Medicine, and 11 of the American Academy of Arts and Sciences. Our faculty includes one National Medal of Science awardee, five winners of the Troland Award from the National Academy of Sciences, three recipients of the Society for Neuroscience Young Investigator award, and two recipients of the Society for Experimental Psychologists Young Investigator award.

The interdisciplinary nature of neuroscience and cognitive science is highlighted by the number of joint appointments held by BCS faculty members, as well as those granted to faculty of other departments. Secondary appointments in BCS are currently held by nine faculty members, with representation from Mechanical Engineering, the Media Lab, Biology, Biological Engineering, Electrical Engineering and Computer Science, and the MIT Sloan School of Management. BCS faculty members in turn hold secondary appointments in many of those departments, as well as in Physics and Linguistics.

In January 2011, Myriam Heiman and Feng Zhang joined the department as assistant professors. Both hold joint appointments at the Broad Institute, with Heiman based at the Picower Institute for Learning and Memory and Zhang based at the McGovern Institute for Brain Research.

In spring 2011, both Joshua Tenenbaum and Pawan Sinha were approved for promotion to professor, and Rebecca Saxe was approved for promotion to associate professor with tenure.

Graduate Program

Sixteen graduate students entered in fall 2010. Two of the incoming students were funded by Singleton Presidential Graduate Fellowships, four by Singleton Fellowships, and two by Norman B. Leventhal Fellowships. Six were supported by a departmental National Institutes of Health training grant, one was funded by a fellowship associated with the new Molecular and Cellular Neuroscience interdepartmental graduate program, and one was funded by an Ida M. Green Fellowship through the Office of the Dean for Graduate Education.

During this year, 18 students graduated with the doctorate. Ten of them took postdoctoral positions in universities or research institutions (at MIT, Brown, Princeton, Harvard Medical School, or HHMI). Of the remaining eight, one is an assistant professor at Stanford University, one is an assistant professor at University of California San Diego, one is a software usability engineer and human factors scientist at BALEX Corporation, one is education outreach coordinator at Max Planck Florida Institute, one is a research scientist and lecturer at Harvard and MIT, one is a machine learning specialist at Google, and one is a continuing medical student at Harvard.

Nine current students were honored for excellence in undergraduate teaching and one for excellence in graduate teaching; eight were commended for continuing dedication to teaching.

Undergraduate Program

BCS currently has 127 undergraduates, with 51 graduating seniors. Thirty-seven freshmen joined the department as new majors at the end of the spring 2011 term.

Nine students received outstanding research awards and 16 students were recognized for outstanding academic work in the department.

Five majors were Burchard Scholars and four were inducted into Phi Beta Kappa.

Development Activities

BCS continues to build momentum in its development activities. In June of 2010, Barbara Vejvoda joined the department as senior development officer—a new position for BCS. The department's first resource development plan for 2011–2015 was created and rolled out in FY2011.

The fundraising effort—especially in terms of supporting scientific inquiry in brain diseases and disorders and the potential for translational medicine in these areas—requires external friends and partners who can open doors to potential philanthropic investors. Our primary objective is to continue to identify and deeply engage both current and new donors who will support the needs of the department, its faculty and

students, and more broadly, collaborative neuroscience research initiatives at MIT. Our strategic resource development plan focuses on evaluating and qualifying existing leadership donors with an emphasis on engaging them at a higher level of support. The development program includes individual giving, foundation support, donor communications, stewardship, and events. The development staff conducts specific stewardship activities to engage past donors and strengthen their attachment to BCS, while evaluating their interest and inclination to continue their support. Additionally, approaches ranging from engaging faculty and alumni to prospect research and events and networking are helping to identify a much-needed, expanded pipeline of prospective supporters. More than 35 new prospective donors for BCS and PILM have been screened, researched, and identified since September 2010. The outstanding gift proposal pipeline as of June 30, 2011, totaled $27 million.

Boosting the BCS alumni and parent annual fund giving is also a priority. A multiyear development tactical plan rooted in broad-based fundraising strategies is being developed. This year, the Class of 1985—under the fundraising leadership of 25th reunion class president Inge Gedde and fellow alumni Tim Aune and Prisca Marvin—spearheaded a special effort to raise class funds for the Autism Research Fund and BCS.

We remain committed to pursuing funding for high-risk/high-reward projects that can lead to breakthrough discoveries. We believe that the Department of Brain and Cognitive Sciences and the neurosciences at MIT are poised to make discoveries of historic proportion. There is a serious need for flexible, internal research funding that will allow our talented BCS faculty to pursue bold new ideas and invite cross-Institute collaborations that will have maximal impact. Flexible research funding catalyzes the projects that can lead to major advances, which is vital for neuroscience research to achieve its full potential at MIT.

We are creating new fundraising materials, case statements, and a variety of other communications with the goal of providing improved and additional communications to current and potential donors. Our website and social media efforts must also serve as tools for attracting philanthropic interest. Components of our existing website and social media pages may also be redesigned not only to appeal to our faculty, alumni, and students, but also to invite donors into our BCS community. Accessible, interesting, and current information will allow our donors to delve into the work and mission of BCS and its affiliates.

Some Research Highlights

Several discoveries from Suzanne Corkin's lab will advance the diagnosis and treatment of Parkinson's disease (PD). Lab members created new multispectral MRI tools to visualize clearly, for the first time, key structures that are damaged in the disease—the substantia nigra (SN) and the basal forebrain (BF). Consistent with neuropathological studies suggesting that degeneration begins in the brainstem and spreads upward, Corkin and colleagues found that degeneration, in living patients, affected the SN before the BF. Early-stage PD patients had significantly decreased SN volumes, and more advanced patients showed little additional volume loss. In contrast, BF volume loss occurred later in the disease, with a marked decrease in the more advanced patients but

not in the early cases. The new multispectral tools provide improved MRI biomarkers for tracking the degeneration of the SN and BF and allow researchers to examine the relative contributions of these areas to cognitive impairments.

Ann Graybiel and her colleagues carry out research that is directly related to the range of clinical disorders associated with the basal ganglia, including motor disorders such as Parkinson's disease and neuropsychiatric disorders such as obsessive-compulsive disorder, anxiety disorders, and autism. They have found that two genes that they originally discovered are strongly dysregulated in relation to the motor problems that Parkinson's disease patients encounter when taking levodopa. These genes also are dysregulated in the striatum of Huntington's disease (HD) patients and in the striatum of mouse models of HD. This gene could be a target for new therapeutic approaches to HD. Graybiel and her colleagues have discovered a cortical site that controls anxiety-like behavior, a promising new lead for therapeutic work. They are also working intensively on the basic science underlying how we make habits and why it is so hard to break them. They found that the "habit circuit" imprints a habit pattern of neuronal activity even more strongly than normally if a sensory cue for which habitual behavior should be performed is given up front—a phenomenon familiar to anyone trying to make or kick a habit. They discovered that habits, under natural conditions and without instruction, develop to optimally efficient patterns—perhaps the good side of habit formation that makes habits so prevalent in our behavior.

In a review published in *New England Journal of Medicine,* Emery Brown provided a detailed systems neuroscience analysis of the differences and similarities among general anesthesia, sleep, and coma. His analysis of the neurophysiology and neuroanatomy underlying the clinical signs, behavioral responses, and EEG signatures associated with certain intravenous anesthetic drugs showed that general anesthesia is more accurately described as a reversible coma rather than sleep. This work has been widely reported in the lay press including interviews with Dr. Brown that have appeared in the *New York Times*, *Science News,* and *Scientific American* and on the National Public Radio program *Fresh Air.* In a second review (Brown et al., *Annual Review of Neuroscience*, 2011), Dr. Brown again uses the systems neuroscience paradigm to analyze five different states of altered arousal created by anesthetic drugs. This analysis shows that each altered arousal state can be characterized in terms of its specific behavioral and physiological features, as well as the molecular targets and neural circuits in which the drugs are purported to act. These two publications make clear as never before to the anesthesiology, neuroscience, and lay communities that general anesthesia is a neuroscience phenomenon and that the way the drugs create this state is not a mystery.

Mriganka Sur's laboratory uses cutting-edge technologies for imaging cells and molecules in the intact brain to reveal their roles in synaptic plasticity and cortical function. Combined with novel probes, these methods have revealed unexpected mechanisms of cortical plasticity, the role of specific cell classes in cortical circuits, and mechanisms of brain disorders. In the past year, his laboratory identified a subset of microRNAs (miRNA) whose expression is differentially regulated by visual experience, and showed that inhibition of one of the miRNAs, miR-132, impaired visual cortex plasticity. His laboratory demonstrated that specific inhibitory interneuron classes

have specific response features and particular roles in the cortical processing of visual signals. By analyzing mice that are deficient in specific genes of autism and examining the effects on signaling molecules at synapses, his laboratory has proposed a therapeutic for Rett syndrome that has entered clinical trials. This discovery points to an exciting breakthrough in autism research.

Gerald Schneider has been investigating methods for reconnecting parts of the brain that have become disconnected by brain damage. They have demonstrated two different techniques that have accomplished this for subcortical pathways of the visual system in adult animals. Recently, using segments of peripheral nerve as bridges to support and direct regenerating axons, they found that they can direct regrowing axons to an anomalous target. Even when the reconnection causes maladaptive function, the brain may adapt over time so the behavior becomes adaptive. How this occurs is still under investigation.

In a recent paper, Martha Constantine-Paton's laboratory (with Marnie Phillips a postdoctoral fellow and a previous BSC graduate student as first author) has shown that eye closure in young mice and rats during the normal period of eye opening causes cortical collicular axons to retract their connections to maturing superior colliculus neurons. Interestingly, the predominance of beta gamma wave activity in the visual cortex in pups during the period eye opening appears to slow the latency of cortical output neurons in layer V relative to activity driven by the retina—a situation opposite from that seen when eyelids are open. This difference is postulated to disrupt normal spike-timing plasticity in superior colliculus neurons receiving input from both sources, which would normally allow later developing cortical axons to co-innervate collicular neurons already driven by the retina. The finding suggests that deprivation of early pattern vision can have potentially deleterious effects on many efferents from primary visual cortex, an issue that has not previously attracted much attention from visual and developmental neuroscientists but could have important implications for recovery of normal pattern vision after early childhood disruption.

To understand how the human visual system accomplishes object recognition, we must understand how it determines that different images of the same object are equivalent. The ability to solve this "invariance problem" is what separates humans from machines and likely reflects deep cortical processing principles. James DiCarlo and colleagues have developed an animal model to study these principles by showing that neuronal populations in the high-level primate visual cortex have solved the invariance problem. In 2010–2011, they pursued three interrelated lines of work aimed at understanding the mechanisms that underlie this solution. First, they extended the discovery that the key neuronal response properties can be built from unsupervised, natural visual experience. Second, they found that these response properties are improved over earlier visual areas, and were provided with new quantitative constraints on the possible underlying mechanisms. Third, to explore those mechanisms, they implemented a large family of models that incorporate existing ideas and allow for testing real-world performance (competitive with state-of-the-art computer vision systems).

In a recent paper published in the *Proceedings of the National Academy of Sciences (PNAS)*, graduate student Steve Piantadosi, postdoc Hal Tily, and professor Edward Gibson demonstrated a substantial improvement on one of the most celebrated empirical laws in the study of language, Zipf's 75-year-old theory that word length is primarily determined by frequency of use. In accord with rational theories of communication, they showed across 10 languages that average information content is a much better predictor of word length than frequency. This indicates that human lexicons are efficiently structured for communication by taking into account interword statistical dependencies. This work provides evidence that lexical systems result from an optimization of communicative pressures, coding meanings efficiently given the complex statistics of natural language use. Researchers in the Gibson lab are currently pursuing several other predictions of the hypothesis that language has evolved for efficient communication.

When we try to do something and fail, we may not know whether we did something wrong or whether something is wrong in the outside world. In an article published in *Science*, BCS graduate student Hyowon Gweon and faculty member Laura Schulz showed that 16-month-old babies can use small samples of statistical evidence to solve this fundamental inference problem. Infants saw two different experimenters push a button to try to activate a green musical toy. In the Within-Agent condition, the toy activated once and failed to activate once for each experimenter; in the Between-Agents condition, the toy always activated for one experimenter and never for the other. The toy was given to the babies and never activated when the babies tried. The evidence in the Within-Agent condition (considering also the infant's failure) varies independently of the agent, suggesting the failure is due to the object; the evidence in the Between-Agents condition covaries with the agent, independent of the object, suggesting the failure is due to the agent. As predicted, infants who saw evidence consistent with some people being unable to work the toy tried to hand the toy to their parents for help; babies who saw evidence suggesting that the toy was broken were more likely to reach for a new toy (a red one that was always within reach). Consistent with formal models of induction, these results suggest that very young infants track the statistical distribution of events and can use minimal data to draw inferences that support rational action.

A study from Rebecca Saxe's lab, published this year in *PNAS*, found that in individuals born blind, parts of the visual cortex are recruited for language processing. The finding suggests that the visual cortex can dramatically change its function—from visual processing to language—illustrating the astonishing "plasticity" of human brain development. It also appears to overturn the idea that language processing can occur only in highly specialized brain regions that are genetically programmed for language tasks.

Mary Potter's lab, using rapid serial visual presentation (RSVP), found that observers can detect a target picture in a short stream of pictured scenes presented for 13 milliseconds each, even when all they know about the target is a name such as "couple smiling" or "cactus." Still more surprising, they can decide whether or not a name presented immediately after the sequence corresponded to one of the pictures in the sequence. The lab is testing a feed-forward model to account for these results.

In the last year, Ken Wexler's lab made a number of discoveries about linguistic capacity in developmental disorders. In a paper published in the *Journal of Speech, Hearing, and Language Research*, former postdoc Alexandra Perovic and Wexler showed that children with Williams syndrome show a disability in the structure of the "passive" operation, an important piece of basic linguistic ability. This disability exists even when compared to typically developing children of the same cognitive ability (IQ). Along with earlier published results from this lab, the findings count against an earlier view that children with Williams syndrome do not show a linguistic disability. Along with Perovic and Nadya Modyanova, a postdoctoral fellow, the lab also demonstrated that children with autism show a significant disability in the structure of "binding" operations, those that involve reference assignment (reflexives). Both these lines of work add to evidence for the growing view that genetic factors lead to particular grammatical disabilities in different syndromes, thus leading to the hope that genetic considerations can play a role in the explanation of the development of language.

Tomaso Poggio's lab is working on a theory of the ventral stream. At its core is the conjecture that the computational role of the ventral stream is to learn from visual experience (during development and continuously in life) visual invariances and to discount them for object recognition and for visual constancy. The theorems have led to simulations and to proposing new physiological experiments. The theory justifies and extends the model developed in the past, which accurately predicts human performance on certain visual perception tasks.

The Poggio lab, along with the Josh Tenenbaum lab, has also established an *Intelligence Initiative (I^2)* at MIT, with direct support from the dean of science. Central to this approach is a new integration of the three fields of cognitive science, neuroscience, and computer science/artificial Intelligence. The group has organized a workshop and several meetings with MIT faculty and has funded several seed research projects across departments and schools. Poggio was the main organizer of one of the MIT150 Symposia, titled "Brains, Minds, and Machines."

Three hundred years ago the Irish philosopher-scientist William Molyneux wrote to his friend, the philosopher John Locke, the following words: "Suppose a man born blind, and now adult, and taught by his touch to distinguish between a cube and a sphere of the same metal, ... Suppose then the cube and sphere placed on a table, and the blind man be made to see: query, whether by his sight, before he touched them he could now distinguish and tell which is the globe, which the cube...?" This question, which bears on important issues of shape representation and cross-modal communication, has so far remained unanswered. Addressing it entails finding appropriate subjects—congenitally blind from occlusive pathology such as cataract or other opacity. The visual system from the retina centrally must be functional so that clear optics and hence vision are potentially recoverable by state-of-the-art medical procedures. These must be followed as soon as possible, ideally immediately, by appropriate testing of transfer of object discrimination from vision to touch and vice versa. Patients must be mature enough to be capable of reliable discrimination testing. Project Prakash has provided professors Dick Held and Pawan Sinha with an opportunity to work with such patients. They report experiments with several individuals. Their results suggest a complete lack of

transfer from normal tactile discrimination to vision immediately after sight onset. Interestingly, however, they find evidence for touch-to-vision transfer and of cross-modal recognition about a week after surgery. The mechanisms of such rapid learning are currently unknown.

This year Edward Boyden's group continued to develop new molecules for optogenetic control of brain circuits using light; the group has distributed these tools to approximately 500 groups worldwide. The Boyden group, in collaboration with others at MIT and in other universities, also published the use of these tools to treat blindness in a mouse model, as well as several other papers including the ability to wirelessly control the brain using light and the ability to use fMRI to map brain circuits downstream of light. Boyden was recognized for his work on optical control of neurons by a number of awards this past year, including being invited to speak at the prestigious TED conference, being recognized for his inventive work in *Nature Methods*' 2010 "Method of the Year" feature, being named as one of the first Paul Allen Distinguished Investigators in Neuroscience, and receiving the NSF CAREER Award.

Selected Faculty Awards and Honors

Josh Tenenbaum was awarded the Troland Prize by the National Academy of Sciences.

Ann Graybiel received an honorary membership in the Movement Disorder Society and delivered a number of invited lectures in the United States and abroad, including the David Smith Lecture at Oxford University, England, and a Plenary Lecture at the Turkish Neuroscience Society, Istanbul, Turkey.

Susumu Tonegawa won the David M. Bonner Lifetime Achievement Award.

Rebecca Saxe received the MIT School of Science Award for Excellence in Undergraduate Teaching.

Laura Schulz received the BCS Award for Excellence in Undergraduate Teaching for 9.85 Infant and Early Childhood Cognition.

Suzanne Corkin received the BCS Award for Excellence in Undergraduate Advising.

Mriganka Sur
Department Head
Paul E. Newton Professor of Neuroscience