Department of Brain and Cognitive Sciences

Mission

The mission of the Department of Brain and Cognitive Sciences (BCS) is to understand how the brain gives rise to the mind. We are a department with a unique vision, anchored in the idea that a deep understanding of the mind requires the synergy of multiple levels of analysis: characterization and investigation of human cognitive phenomena in both normal and disordered states; the neuronal circuits, algorithms, and representations in the brain that underlie those phenomena; and the cellular and molecular mechanisms that implement, maintain, and potentially repair those circuits. We believe that building links between these levels is the key to understanding how the brain gives rise to the mind. We know that this understanding of the mechanisms of the mind is the key to solving disorders of the mind, building intelligent machines, and realizing dramatic advances in education, and that it will also lead to myriad other unpredictable world-changing impacts.

Because the path from mechanistic, basic science to translation is both critical and unpredictable, BCS aims to offer an environment in which the world's most talented researchers can pursue new ideas about the underlying mechanisms of the brain and how they give rise to the mind, and then collaborate when larger groups are needed and/or translational connections are visible. We also uphold a core value of MIT — that sufficient explanations of these processes must ultimately be rooted in the language of mathematics and computational theory.

A unique and defining identity of our department is that we pursue all these levels of analysis in an integrated and synergistic way. There are very few other departments in the world organized as BCS is — in most universities, the study of the brain (neuroscience) and the study of the mind (cognitive science) are housed in separate buildings, and often on separate campuses. At MIT, the Brain and Cognitive Sciences Complex, also known as Building 46, houses the McGovern Institute for Brain Research (MIBR) and the Picower Institute for Learning and Memory (PILM) as well as the department. The mission of BCS thus spans research, teaching, and training in both neuroscience and cognitive science.

Leadership

The department plays an important "umbrella" role in building and strengthening the brain and cognitive science community at MIT. Our overall strategy, which focuses on bolstering the sub-communities that naturally crosscut the entirety of Building 46, has helped to lower the walls between the various units and created opportunities for the community to come together.

Building-wide leadership: The BCS Council includes BCS department head Jim DiCarlo (chair), MIBR director Bob Desimone, PILM director Li-Huei Tsai, Simons Center for the Social Brain (SCSB) director Mriganka Sur, Center for Brains, Minds, and Machines (CBMM) director Tomaso Poggio, and senior and junior faculty members spanning all

areas of the department. The BCS Council meets monthly and serves as an advisory committee to ensure that departmental decisions are strongly informed and that all leaders in the building are comfortable with and enthusiastic about those decisions.

BCS faculty leadership roles: The department would not be able to plan and execute its myriad needs without the support of the faculty, and we continue to espouse a culture of shared effort across the faculty. The following faculty have notably stepped up to continue and/or take on leadership roles over the last three years:

- Professor Michale Fee (associate department head for education and chair of the education committee)
- Professor Laura Schulz (undergraduate officer)
- Professor Matt Wilson (graduate officer and chair of the Graduate Admissions Committee and Graduate Affairs Committee)
- Professor Nancy Kanwisher (BCS space)
- Associate professor Alan Jasanoff (chair of the Seminar Committee)
- Professor Sue Corkin (chair of the Junior Faculty Mentorship Committee)
- Professor Pawan Sinha (chair of the Diversity Committee)

All primary BCS faculty actively serve on one or more of these committees.

Faculty

BCS faculty members are widely recognized as being among the leaders in their respective fields. Our faculty includes one Nobel Prize winner, 10 members of the National Academy of Sciences (including one emeritus), six members of the Institute of Medicine, 15 members of the American Academy of Arts and Sciences, one National Medal of Science awardee, one winner of the Kavli Prize, seven winners of the Troland Award from the National Academy of Sciences, and four recipients of the Society for Neuroscience Young Investigator Award. Twenty-six of the 38 BCS primary faculty are also investigators in the McGovern and Picower Institutes. All 12 of the PILM investigators have either their primary (nine) or secondary (three) appointments in BCS, and 18 of 19 MIBR investigators have their primary (17) or secondary (one) appointments in BCS. Two faculty members have joint appointments at the Broad Institute, two have joint appointments at the Institute for Medical Engineering and Science, and two hold the special title of Institute Professor.

The interdisciplinary nature of neuroscience and cognitive science is highlighted by the number of BCS faculty with joint appointments. The faculty members who held joint appointments this past year in BCS represent Chemical Engineering, Mechanical Engineering, the Media Lab, Biology, Biological Engineering, Electrical Engineering and Computer Science, and the Sloan School of Management. BCS faculty members in turn hold secondary appointments in many of those departments, as well as in the Linguistics section of Linguistics and Philosophy.

Community Building

Strengthening community at all levels within BCS and our affiliated institutes has been among our top priorities. Our strategy is to support the sub-communities that horizontally integrate across the institutes in Building 46 — faculty, postdocs, graduate students, undergraduate students, and staff. More specifically, we aim to create an environment where each sub-community is empowered and able to flourish in directions that stem from their constituencies. For example, at the faculty level, BCS department head Jim DiCarlo created standing committees and empowered each of them to take ownership over areas of importance to the various members of the BCS community. DiCarlo has invited all BCS faculty members to be part of at least one committee (but not more than two). These committees report progress to the full faculty on a semiannual basis. Several committees also include staff, postdoc, and student representatives.

We have also worked to identify and empower leaders among various sub-communities who can organize events and represent the concerns of those sub-communities to the department. Each group also receives support from staff who provide them with access to departmental resources and act as conduits for presenting the departmental leadership's ideas to each sub-community. We continue to make particular progress with the BCS Community Postdoctoral Association with the support of Dr. Sonal Jhaveri, BCS director of postdoctoral affairs, and that of other BCS staff. The postdoc association that began within the Picower Institute has expanded to serve postdocs from BCS and all of our affiliated institutes.

We are also striving to improve communications and deepen collegiality across the BCS community. The department hosts regular BCS-wide faculty meetings (once a month) and regular BCS-wide faculty lunches (one a month). DiCarlo sends a department-wide email at least once a month, highlighting community members' recent awards, honors, and achievements. BCS headquarters staff members also send a weekly e-mail summarizing community-relevant information.

In addition to the various research initiatives and coordinated faculty searches that involve all corners of Building 46, the leaders of MIBR, PILM, and BCS continue to work together on many events, including a building-wide seminar series and a building-wide holiday party. In 2014, we worked together to achieve our first building-wide overnight retreat, featuring talks, posters, and socializing. That event was very successful, attended by approximately 300 members of the BCS community (MIBR, PILM, and the rest of BCS). We plan to host a similar building-wide retreat every other year, with the next taking place in 2016.

Development

The department's development efforts are led by Elizabeth Chadis, assistant dean for development for the School of Science, and BCS senior communications and development assistant Rachel Traughber. Top fundraising priorities continue to include endowed and expendable fellowships for graduate students and postdocs, endowed career development chairs and professorships, and unrestricted research funds. The department's efforts to increase graduate student support through the nascent

Champions of the Brain Fellows Society has been successful, securing both endowed and expendable fellowship funding in its first year. In May 2015, the department hosted the fourth biennial Brains on Brains symposium, which also emphasized graduate students' scientific contributions to the department's research through student-led tours of laboratories in Building 46.Our hope is that events such as Brains on Brains and Champions will help us continue to cultivate relationships with supporters that have demonstrated their willingness to support the Institute, and encourage these newly identified fans of neuro and cognitive science research to support the department.

Education and Training

The study of mind, brain, and behavior has grown with unprecedented speed in recent years. New approaches, opened by developments in biology, engineering, and computer science, raise the hope that human beings, who have achieved considerable mastery over the world around them, may also come closer to an understanding of themselves. BCS provides its students with an interdisciplinary curriculum designed to educate them in these topics and prepare them for leadership. The undergraduate program provides tiered and broad instruction on topics drawn from molecular, cellular, and systems neuroscience; cognitive and perceptual psychology; applied mathematics; computer science and artificial intelligence; linguistics; and philosophy of mind. Multiple tiered pathways through the undergraduate program are possible to prepare students for a range of career paths, including research, healthcare, and industry. The graduate program provides advanced instruction on topics and research methods in one (or more) of four themes: molecular and cellular neuroscience, systems neuroscience, cognitive science, and computation. Our faculty teach 45 to 50 undergraduate and graduate courses each year.

Undergraduate Program

Now in the second year of undergraduate curriculum redesign, BCS continues to make progress toward providing students with opportunities to build a strong quantitative skill set and be rigorously exposed to an engineering-level description of neurons and neural circuits and the computations they carry out. Our goal is to give our students the skills and knowledge they need to appreciate and lead future advances in brain and cognitive sciences. The department's faculty has enthusiastically endorsed this vision, and has supported two major curricular changes to enable it: all BCS students are required to take both elementary computer programming and statistics; and all are required to take a new introductory-level course (9.40) covering quantitative and computational approaches to understanding the brain and behavior. This 12-unit course is designed to provide students with specific skills and rigorous habits of thought early in their education. To support our curriculum growth, the department hired technical instructor Daniel Zysman, who has training in systems and computational neuroscience and previous experience in the support, development, and instruction of quantitative courses.

Students majoring in BCS are often quite accomplished, and recognized as such. In 2014–2015, 21 seniors qualified for Sigma Xi. Forty-seven of our students received departmental awards for research and/or academic excellence from 2013 to 2015. Six BCS students were Burchard Scholars in 2014, three were named Amgen Scholars, one received MIT's 2014–2015 Emerson Fellowship award for music, and one was named a Rhodes Scholarship finalist in 2014.

Graduate Program

The department has also undertaken an effort to increase the quantitative rigor of the graduate program. During fall 2014, assistant professor Mehrdad Jazayeri developed and taught a set of quantitative materials for 9.011 BCS Core I, the systems graduate core course taken by all first-year graduate students. In January 2015, BCS technical instructor Daniel Zysman organized a Matlab training seminar that was open to the entire BCS community. Given the success of these initial efforts, we now plan to introduce a new graduate core course specifically focused on quantitative methods. In the long run, our plan is to teach general mathematical and computational tools and programming techniques relevant to students with a broad range of interests spanning cognitive, systems, and molecular neuroscience.

Over the past five years, the size of our graduate program has remained steady at around 100 students. Fourteen graduate students entered in fall 2014. Approximately one-third of these students were female, 15% to 20% were international students, and 15% were underrepresented minority students. Two of the new incoming students were funded by Singleton Presidential Graduate Fellowships, two by the ASTAR fellowship, and four by National Institutes of Health (NIH) training grant programs.

During this year, 11 students graduated with doctorates: Andrew Bolton, Gregory Hale, Melissa Kline, Jorie Koster-Hale, Brenden Lake, Joshua Manning, Joshua Siegle, Ethan Kowronski-Lutz, Andreas Stuhlmuller, Todd Thompson, and Tomer Ullman.

BCS graduate students are also highly accomplished. Institute awards over the past year include the Angus MacDonald Award for Excellence in Undergraduate Teaching (eight), MIT Graduate Women of Excellence (three), the Walle Nauta Award for Continuing Dedication to Teaching (one), and the Walle Nauta Award for Excellence in Graduate Teaching (one). Recognitions received outside of MIT include the Glushko Dissertation Award (an annual award given to the four to five best PhD theses in all of cognitive science) and an Emerging Explorer Award from National Geographic, which seeks to identify and support “young trailblazers whose ideas are helping change the world.”

Selected Research Highlights

Edward Adelson

The Adelson lab is continuing to develop artificial touch sensors based on GelSight, in which an elastomeric fingertip with an embedded optical system extracts highly detailed information about texture, shape, and force. The lab showed that the sensors greatly improved performance on robotic manipulation. In addition, the sensor now captures tangential forces as well as normal forces, so that it can detect friction and slip during manipulation. The lab has made progress on material perception, especially in the area of translucency, studying the similarity spaces and features of both real and synthetic translucent objects and showing that lighting direction can greatly alter the appearance of translucent materials (as opposed to opaque materials, where lighting direction has little effect). In the area of image statistics, the lab showed that it is possible to do state-of-the-art contour detection using pointwise mutual information (PMI). Unlike other methods that use labeled data and supervised learning over large databases, the Adelson

lab works with single images and unsupervised learning, showing that a remarkable amount of structural information is available in simple local measurements.

Marc Bear

The Bear laboratory studies visual cortical plasticity and the pathophysiology of diseases associated with autism and intellectual disability. A recent highlight was the lab's discovery that repeated presentations of a visual sequence over a course of days resulted in evoked response potentiation in mouse V1 that was highly specific for stimulus order and timing. Notably, after V1 was trained to recognize a sequence, cortical activity regenerated the full sequence even when individual stimulus elements were omitted. These results advance the understanding of how the brain makes "intelligent guesses" on the basis of limited information to form visual percepts and suggest that it is possible to study the mechanistic basis of this high-level cognitive ability by studying low-level sensory systems. The lab also described a novel behavioral extinction assay to model impaired cognition in mouse models of neurodevelopmental disorders; provided evidence that extinction is exaggerated in the fragile X mouse model; and uncovered possible limitations of metabotropic glutamate receptor–based pharmacotherapy.

Emilio Bizzi

The Bizzi lab continues to pursue the understanding of how the brain controls voluntary movements. To this end, the lab has focused on two related questions: how the brain handles the enormous complexity involved in making even the simplest movement, and how the brain learns a new motor task and then generalizes that learning to each new variation of the task. With respect to the first theme, Bizzi and collaborators have provided evidence for a modular organization of the spinal cord in lower and higher vertebrates (rats, frogs, and monkeys). A "module" is a functional unit in the spinal cord that generates a specific motor output by expressing a specific pattern of muscle activation (muscle synergy). Such an organization might help to simplify the production of movements by reducing the degrees of freedom that need to be specified. The Bizzi lab has also shown that the muscle synergies used for generating locomotor behaviors are centrally organized, but their activation is modulated by sensory feedback so that the final motor output can be adapted to the external environment. In monkeys, the lab has shown that the control of grasping is facilitated by the presence of arm and forearm muscle synergies. These results indicate that a small number of synergies account for a large fraction of variation in muscle activity during grasping of objects of different size.

Emery Brown

The Brown lab developed a new Bayesian spectral decomposition framework — spectrotemporal pursuit — to compute spectral estimates that are smooth in time and sparse in frequency. Using a statistical interpretation of sparse recovery, the lab derives efficient algorithms for computing spectrotemporal pursuit spectral estimates. The Brown lab applies spectrotemporal pursuit to achieve a more precise delineation of the oscillatory structure of human electroencephalogram and neural spiking data under propofol general anesthesia. Spectrotemporal pursuit offers a principled alternative to existing methods for decomposing a signal into a small number of oscillatory components. By selectively activating brainstem cholinergic neurons to determine

their role in REM sleep regulation, the lab found that activation of cholinergic neurons during non-REM sleep increased the number of REM sleep episodes but not REM sleep duration. The Brown lab's data demonstrates that brainstem cholinergic neurons are important modulators of REM sleep, and clarifies their role in REM sleep initiation.

Martha Constantine-Patton

In the past year, the Constantine-Patton laboratory completed two whole-cell patch studies toward which it had been working for more than five years. 1) The lab made and used siRNA against the MAGUKs that hold NMDARs at glutamate synapses, and showed that siRNA KD of SAP102 eliminated NMDAR-LTD but left NMDAR-LTP intact. 2) The lab made and used (again in work over the past five years) chimeric NMDAR subunits; one replaced the cytoplasmic domain (cd) of GluN2A with that of GluN2B, and the other replaced the cd of GluN2B on GluN2A. The lab then injected one of these constructs into the VC layer 2/3 of the GluN2A KO mouse or the floxed GluN2B mouse and tested LTP and LTD from layer 4 to 2/3 with whole cell patch clamp on the altered neurons. The lab found three of these constructs that produced LTP but eliminated LTD. If its currently submitted grant is funded, the lab will test whether the developmental refinement of synapses during visual development is dependent on NMDAR LTDa; this belief, although currently widely accepted, has not been testable, since antagonists that block NMDARs block both LTP and LTD. Several publications now detail how glial cells remove synapses during refinement and how the immediate early gene ARC is involved in this same process, and although this does not preclude NMDAR action, the assumption that NMDAR low-frequency stimulation weakens these synapses in the first place must be tested in vivo.

Jim DiCarlo

The DiCarlo research group seeks a computational understanding of the brain mechanisms that underlie visual object and face recognition. The group is currently focused on understanding how neuronal population transformations carried out by a series of brain processing stages — called the primate ventral visual stream — are effortlessly able, with incoming visual images, to untangle object and face identity from other latent image variables such as object position, scale, and pose. The group has demonstrated that populations of neurons at the highest cortical visual processing stage (IT) rapidly convey explicit representations of object identity and category, even in the face of naturally occurring image variability that makes this problem extremely challenging for current computer systems. Using a combination of large-scale neurophysiology, brain imaging, neural perturbation methods (e.g. optogenetics), and behavioral testing, the group is investigating the neuronal mechanisms and fundamental cortical computations that underlie the construction of these powerful, high-level neural representations and their linkage to perceptual report. To build that understanding, the group constructs and compares computational models that aim both to emulate and predict the responses of neurons and neuronal populations at each stage along the ventral visual processing stream, and to emulate and predict the perceptual reports of both human and nonhuman subjects. The group has made two recent discoveries: 1) that the precise patterns of measured neural activity can be accurately predicted by specific models from a class of bioconstrained, computational models, and 2) that direct optogenetic perturbation of the IT neural activity produces changes in perceptual report

that are predicted by such models. As the research group continues to seek even deeper understanding, it aims to use this understanding to inspire and develop new computer vision systems, to provide a basis for new neural prosthetics (brain-machine interfaces) to restore or augment lost senses, and to discover how high-level visual representation is altered in human conditions such as agnosia, dyslexia, and autism.

Guoping Feng

The Feng lab demonstrated for the first time that neurobiological defects and autistic-like behaviors in Shank3 mutant mouse model of autism are reversible in adult mice, giving rise to hope for developing effective treatment (manuscript under revision). Additionally, recent genetic studies revealed significant overlaps of risk genes in major psychiatric disorders. However, how different mutations of the same gene cause or contribute to different disorders is not clear. Using unique mouse models, the lab revealed molecular and circuit mechanisms of how two different mutations of the Shank3 gene, linked to autism and schizophrenia respectively, could cause or contribute to these two disorders (manuscript submitted). Last, the lab discovered cellular and circuit mechanisms by which PTCHD1 mutations cause intellectual disability and autism, illuminating a potential pathway for developing treatment. Mutations of the PTCHD1 gene account for about 1% of autism patients with intellectual disability (manuscript under revision).

John Gabrieli

The Gabrieli lab's new finding about the brain basis of attention deficit hyperactivity disorder (ADHD) (Mattfeld et al., Brain, 2014) was noted in a New York Times article in October 2014. About half of patients with childhood ADHD (which occurs in 11% of US children) persist in their diagnosis as adults, but the other half of patients remit from the diagnosis. Nothing had been known about the functional brain difference between those who persist versus those who remit. To characterize the neurobiological differences and similarities of persistence and remittance, the lab performed resting-state functional magnetic resonance imaging in individuals who had been longitudinally and uniformly characterized as having or not having ADHD in childhood and again in adulthood. Intrinsic functional brain organization was measured in patients who had a persistent diagnosis in childhood and adulthood, in patients who met diagnosis in childhood but not in adulthood, and in control participants who never had ADHD. A positive functional correlation between posterior cingulate and medial prefrontal cortices, major components of the default-mode network, was reduced only in patients whose diagnosis persisted into adulthood. This is the first evidence for a neurobiological distinction between persistent and remitted ADHD.

Edward Gibson

The Gibson lab has focused on two questions: (1) How do communicative pressures shape language knowledge structures and language use? In recent years, the lab has shown that sentence processing can be usefully shown to involve rational inference, correcting noise in the communication channel. One recent project suggests that the ERP component known as the P600 — a positive-going waveform, peaking at about 600 msec, which has been proposed to be due to syntactic error detection — is plausibly a response

to rational error correction more generally: the P600 may occur when encountering a part of a sentence that is easily correctible, such as in "Every Tuesday, John mow / mows the lawn," where "mow" can be corrected to "mows." Not only does the P600 occur for correctible syntactic errors (like the example above), but it also occurs for other correctible errors, like "The storyteller told an amusing antidote / anecdote." (2) How does cognition (including aspects of language) relate to culture? Here, the lab has been investigating cognition in a remote language/culture, the Tsimane', in the Bolivian Amazon. In the domain of number, in industrialized nations, children progress through a stereotypical series of subset-knower levels, successively learning the meaning of "one," then "two," then "three." Then, typically at around age 3-6, children undergo an apparent conceptual shift and rapidly acquire the meanings of many higher-number words all at once. We have demonstrated the presence of a similar developmental trajectory in the Tsimane', but delayed by approximately four years, so that children become full-counters at around eight years old. This likely indicates that the incremental stages of numerical knowledge — but not their timing — reflect a fundamental property of number concept acquisition, which is relatively independent of language, culture, age, and early education.

Ki Goosens

One of the Goosens lab's most important accomplishments this year was to link a specific problem in serotonin-based neural processing to excessive fear. While dysfunction of serotonergic tone has long been believed to contribute to disorders involving excessive negative emotion such as post-traumatic stress disorder (PTSD), it is often believed that impaired serotonin activity at the synapse is the underlying cause of such pathologies. The lab demonstrated that increases in serotonin release can also lead to psychopathological features. Using a rodent model of PTSD in which a prior history of stress exposure renders the animal more susceptible to excessive fear learning during trauma, the lab showed that repeated stress enhances fear memory by recruiting a serotonergic memory consolidation process that is not present in unstressed animals. The Goosens lab also showed that this is because stress enhances the sensitivity of the amygdala, one part of the brain that processes fear, to aversive cues by enhancing the levels of a specific subtype of serotonin receptor. This is important because it suggests that a serotonergic receptor antagonist, rather than a selective serotonin reuptake inhibitor (SSRI, the most commonly used pharmacological treatment for PTSD), would be more appropriate for the treatment of PTSD.

Ann Graybiel

Habits and decision-making are important part of our daily lives, but they can become abnormal in such disorders as autism, obsessive-compulsive disorder, and depression. The Graybiel lab uses a variety of experimental techniques, including high-density chronic recording, optogenetics, voltammetry, and molecular biology, to discover neural pathways that underlie these processes. The lab discovered that the human form of the "language gene" FoxP2 strongly influences the transition from deliberative to habitual behavior. These results, published in *PNAS,* were widely reported by various media sources, including *Science, Discover,* Reuters, NBC, and BBC. The lab found, in rats, that a class of interneuron in the striatum that releases acetylcholine encodes the positive and negative outcomes of behavior and controls activity of striatal output neurons. These

findings were published in *Neuron.* In nonhuman primates making a decision to accept or reject an offer based on positive and negative outcomes expected to follow, the lab has identified neural signals related to the actual value of the offer and those related to motivation induced by the option, and found that two different frontal decision networks are differentially involved in these two key factors underlying decision-making. These findings were published in *Journal of Neuroscience*.

Myriam Heiman

In the past year, the Heiman research group has described the development of a new genetic screening methodology that allows synthetic lethal screens to be conducted in the mammalian central nervous system. The principle of synthetic lethality is that factors that are dispensable in a healthy cell are rendered essential in a diseased cell; these factors thus define the pathways responsible for increased cellular vulnerability in that disease. Our synthetic lethality screening in mouse models of Huntington's disease (HD) reveals that a glutathione peroxidase, Gpx6, can regulate the emergence of HD model symptoms in mice. This year the group has also completed the first study to describe cell type-specific changes to gene expression in mouse models of Huntington's disease. This study has revealed that the polycomb repressive complex 2 (PRC2) likely has a major role in regulating the alterations to gene expression seen during HD progression in the mammalian striatum. Both of these accomplishments highlight molecular mechanisms linked to HD progression and reveal new therapeutic targets.

Mehrdad Jazayeri

The Jazayeri lab studies how brain circuits integrate internal and external cues to predict future events in the face of uncertainty, using an interdisciplinary approach to investigate underlying computational algorithms, neural circuits, and biophysical mechanisms. For example, using a range of behavioral experiments in humans, the lab has developed a detailed quantitative model of how the brain uses a probabilistic scheme, known as Bayesian integration, to combine prior knowledge with sensory cues. In a set of complementary neurophysiology experiments in nonhuman primates (NHPs), the lab has begun to understand how such probabilistic computations are mediated through interactions between populations of neurons at different nodes of the circuit. More recently, the lab has been working to develop a protocol for recording signals from the inside of individual neurons in NHPs performing complex tasks, which may be among the most difficult experiments performed in animal models. If successful in adapting this recording technique to the study of behavior in NHPs, the lab will be able to examine the neural basis of such cognitive functions as probabilistic reasoning at the level of biophysical properties and synaptic mechanisms of individual neurons.

Nancy Kanwisher

The Kanwisher lab, with Josh McDermott and joint grad student Sam Norman-Haignere, is cracking wide open the functional organization of high-level auditory cortex. The lab found a region selectively engaged in the processing of pitch (reported last year), in addition to distinct functional components for speech sounds and for music. These results are robust and emerge from hypothesis-neutral discovery methods in which people are scanned listening to a wide array of natural sounds. The lab is now also

seeing the same organization in ECOG recordings. Second, the lab has found a striking similarity in the functional organization of lateral IT cortex in monkeys, and ventral regions in humans: in each case, three parallel bands are preferentially engaged in perception of faces, then color, then places. This similar organization suggests that lateral cortex rotated onto the bottom of the brain over primate evolution, perhaps pushed ventrally to make room for language and speech cortex. Third, the lab found, using eye trackers, that adults with autism have normal attentional disengagement and normal preferential attention to faces, two findings that are at odds with most of the literature. Further, in an ongoing collaboration, the lab is asking the same question of toddlers just diagnosed with autism — an important group, because they are less affected by remediation and are, in a sense, closer to the "native" form of autism. So far, the just-diagnosed toddlers look very much like adults with austism spectrum disorder (ASD), in having normal attentional disengagement and normal social preferences.

Yingxi Lin

The main interest of the Lin lab is to explore the cellular and molecular mechanisms by which neuronal activity is coupled to modifications of neural circuits that lead to long-term behavioral changes. The lab has developed a versatile tool to map the neuronal ensembles involved in encoding experiences. In the last year, the lab has optimized the tool, and the first paper is ready to be submitted for publication. The lab has also developed several versions of the tool, which will allow investigation of neuronal ensembles defined by different molecular and cellular events following experiences. In addition, the lab has also discovered a genetic pathway important to the homeostatic regulation of the neural circuit.

Joshua McDermott

The McDermott lab developed a method to localize candidate computations in the auditory cortex using fMRI, involving a comparison between the brain responses to synthetic and natural sounds matched according to a candidate set of neural response functions. The lab's experiments with this method reveal that existing models of auditory computation explain the responses in primary auditory cortex nearly perfectly, but explain almost nothing about the responses of the furthest reaches of non-primary cortex, providing a benchmark for the lab's ongoing efforts to develop models of mid- and high-level auditory computation. As part of these efforts, the lab trained deep neural networks on speech recognition tasks, and found that their responses explain much more of non-primary auditory cortical responses than do other existing models. The lab also continued its explorations of sound texture perception, with two key discoveries: first, that texture statistics are averaged over a time scale of several seconds, much longer than known auditory mechanisms, and second, that the averaging process seems to be blind to outliers, indicating a "quick and dirty" bottom-up mechanism. In addition, the lab's work on sound segregation has produced evidence that segregation cues are much richer than traditionally appreciated, suggesting novel methods for sound enhancement in hearing aids.

Earl K. Miller

The Miller lab discovered a mechanism that supports trial and error learning (Brincat and Miller, Nature Neuroscience, in press). Two brain areas, the prefrontal cortex (the executive) and hippocampus (the memorizer), "hummed" together at different frequencies following correct vs wrong guesses. If correct, they hummed at 16 Hz (beta); if wrong, they hummed lower (at theta 3-4 Hz). Previous work has suggested that beta humming strengthens neural connections, and theta humming weakens them. Thus, a correct guess is remembered because the brain hummed at the "remember note" (beta), and a wrong guess is forgotten because the brain hummed at the "forget note" (theta). The lab discovered that synchronized brain humming plays a role in learning visual categories (e.g., "cats" versus "dogs") (Antozoulatos and Miller, 2014, Neuron). As animals learned new categories, there was an increase in synchrony of beta frequencies (16 Hz) between two areas critical for category learning, the prefrontal cortex and basal ganglia. There were different patterns of humming for each of the two categories. Thus, the synchronized humming may help form the neural circuits that learn new categories.

Elly Nedivi

Older concepts of a hard-wired adult brain have been overturned in the last decade by imaging studies visualizing synaptic remodeling in vivo. Such remodeling events are commonly thought to mediate rearrangements in microcircuit connectivity. Using three-color labeling and spectrally resolved two-photon microscopy, the lab simultaneously tracked in vivo the structural dynamics of excitatory and inhibitory postsynaptic sites on individual neurons in mouse neocortex. The lab found that, on a daily basis, inhibitory synapses on dendritic spines are exceptionally dynamic, largely because many of them disappear and reappear in the same location. This is in contrast to the stability of excitatory synapses on the same spines. When the postsynaptic element of recurrent synapses disappears, the presynaptic inhibitory axon remains in place, potentially serving as a placeholder for its return. This reversible type of synapse structural dynamics indicates a fundamentally new role for inhibitory synaptic remodeling — flexible, input-specific gating of stable excitatory connections.

Tomaso Poggio

The Poggio group is researching the problem of learning in both biological organisms and computers, since learning is at the heart of the problem of both building intelligent machines and of understanding how the brain works. Thus, the group's work spans three research directions: mathematics, engineering, and neuroscience of learning. This fits perfectly with the mission of the thrust "Theories of Intelligence" that Poggio is leading within the Center for Brains, Minds, and Machines. Within that thrust, Poggio is developing the math and the computer simulations of a theoretical framework to understand, in biologically plausible terms, evolution, learning, circuits, and, above all, computational function of the ventral stream. The starting point of the theory is that the main function of the forward hierarchical architecture of the ventral stream is to compute representation of images that are invariant to transformations experienced during the life of the organism. Invariant representations allow supervised learning with very few labeled examples — a trademark of biological organisms.

Mary C. Potter

The Potter laboratory followed up its research on perception and memory for rapidly presented pictures, which were published early in the year and spotlighted on the MIT website in January. The lab completed replications that varied the method to test the generality of its initial findings. These experiments included randomization of nontarget pictures in sequences, randomly mixing durations with blocks, and varying the proportion of nontarget trials. In all cases, results were consistent with the lab's initial claims that viewers can gain some conceptual understanding of some pictures with presentations as brief as 13 ms, sufficient to perform above chance when attempting to detect a target on the basis of a name. In new experiments, the lab is tracking the effects of providing a spoken name just before, during, or after the presentation of the picture sequence.

Gerald Schneider

The Schneider lab conducted a case study of the psychological and neurological effects of hypoglycemia by organizing and analyzing more than 50,000 records of blood glucose (BG) recordings made over the course of the last 20 years, plus additional records and descriptions of abnormally low BG levels from the previous 30 years. Analysis demonstrates changes over the years that indicate improvements in the brain's ability to function in low-BG states. The records also indicate distinct categories of brain alterations in these states. Many behavioral effects are not predictable from BG levels alone, although some regular patterns are indicated.

Laura Schulz

One important line of work in the Schulz lab this past year has focused on understanding the principles that underlie children's intuitive theory of rational action. The Schulz lab has proposed that children have a "naïve utility calculus," supporting representations of both agent-invariant and agent-dependent aspects of costs and rewards. This sensitivity enables children to draw inferences about unobservable properties of agents, including differences in their competence, values, and motivations. It also supports a richer model of theory of mind, suggesting that children understand not only that beliefs and desires jointly determine action, but also that beliefs and desires are not independent: agents have beliefs about their desires, and agents may learn their own utility function by acting.

Pawan Sinha

The Sinha laboratory's main research theme of visual learning has seeded several projects in domains as diverse as blindness, autism, and machine learning. *A theory of autism:* The famously multifaceted phenotype of autism has engendered the view that the search for core causes may be futile; the condition may be the outcome of a constellation of unrelated neural insults. As a counterpoint to this view, the lab has proposed a theory of autism according to which many seemingly disparate aspects of the disorder may be manifestations of a common cause. A paper on this research published late last fall in *PNAS* is in the top 1% of over 90,000 articles tracked by the journal. *Visual development after recovery from blindness:* Being able to bring the gift of sight to congenitally blind children as part of Project Prakash is a continuing source

of joy for the Sinha lab. Last year, the lab characterized three fundamental aspects of vision and cognition in newly sighted children. The data, which revealed dramatic developmental changes, are helping define the landscape of neural plasticity late in life — its extent as well as its limitations — with implications for basic science and clinical practice. *Tactile figure perception and education for the blind:* A scientific puzzle with great practical relevance is the difficulty of conveying graphical information via touch. Embossed pictures are hard for the blind to interpret by touch, reducing access to crucial educational material, especially in the sciences. The lab has developed a hypothesis to account for these difficulties and proposed an alternative strategy. Experimental tests of the approach have shown that it provides significant gains in comprehensibility of graphical material, and that it can play a role in improving educational access for the blind. *Neural markers of face identification:* As a precursor to studying the development of face identification in the newly sighted, we need to know what the corresponding neural signatures are in the typically developing brain. Surprisingly, this fundamental question has been largely unanswered thus far. Using techniques from machine learning to mine high-density neural recordings, the lab has revealed early activity in the brain that signals face familiarity — an exciting result, since it sets the stage for probing normal development, as well as disruption, of the neural correlates of face identification.

Mriganka Sur

In the past year, the Sur laboratory made three important contributions. First, the lab developed novel methods for very large scale recording, from thousands of single neurons simultaneously across multiple areas and depths of the cerebral cortex in mice performing behavioral tasks, using two-photon imaging of genetically encoded calcium indicators. Second, the lab proposed a new mechanism of synaptic plasticity in the developing visual cortex, and revealed the role of astrocytes in modulating excitatory-inhibitory circuits that shape visual responses. Third, the lab demonstrated that a crucial mechanism underlying Rett Syndrome, a devastating neurodevelopmental disorder, is the failure of synapses to mature due to deficits in a growth-promoting molecular signaling pathway; the lab demonstrated the validity of a mechanism-based therapeutic molecule for Rett Syndrome and further proposed a next-generation therapeutic involving combinations of molecules.

Joshua Tenenbaum

The Tenenbaum lab studies the basis of common-sense knowledge, and how it is learned. In 2014, the lab made several important advances focused on common-sense knowledge in the context of visual scene understanding. (1) The lab developed a general computational architecture based on probabilistic programming for modeling human vision as "inverse graphics": an observed image can be cast as the output of a graphics program that takes as input the three-dimensional scene, and the goal of vision is to "run the graphics program" backwards to guess the scene most likely to have generated the image. The lab's architecture can be applied to many problems including face recognition, human body pose identification, and generic object recognition. It also yields insights into the neural circuits that the brain uses to solve these problems. (2) Scene understanding is not just about inferring what is where, but also about predicting what will happen. The lab has proposed to model predictions in visual scenes with an "intuitive physics engine." Previously the lab showed that this model could explain

how people predict the motions of rigid solid objects, but in 2014 the lab extended this model to handle non-rigid objects and fluids, based on particle system simulations, and the lab showed that it provided a good quantitative account of people's predictions for how liquids with different viscosity and stickiness will flow. The lab also showed that by computing probabilistic counterfactual simulations in a physics engine model, comparing what would have happened to object X if object Y had not been present in a scene to what actually happened to X, it could explain people's sense of causality: the extent to which Y was responsible causally for some event involving X. (3) Common-sense scene understanding is not only about physics, but also about psychology: understanding the mental states of agents acting in a scene, in order to predict what they will do in the future and interact with them more effectively. The lab has developed several new models of intuitive psychology based on assuming that people treat others as if they are planning actions under a rational utility calculus trading off costs and rewards, and shown that these models can describe how children and adults infer and evaluate the intentions of other actors, including the moral permissibility of someone's actions.

Susumu Tonegawa

The Tonegawa lab published four papers in high-profile journals during the 2014 calendar year, in *Nature Neuroscience* (February), *Science* (February), *Cell* (May), and *Nature* (August). Respectively, these findings focused on hippocampal CA2 circuits; the function of temporal association memory; neuronal oscillations' relationship to working memory; and the neural circuits controlling the valence of memory. The *Nature* paper represents the latest in a string of research on the identification, characterization, and manipulation of memory engram cells and their circuits. These efforts will continue in 2015.

Kay Tye

In the past year, the Tye lab has made great progress on several fronts, all associated with understanding the neural basis of emotional/motivational valence. 1) The lab expanded its exploration of basolateral amygdala projections to different regions, as shown by a publication showing a causal role for the amygdala-ventral hippocampal projection in social behavior (Felix-Ortiz and Tye, J Neurosci 2014). 2) The lab made major strides in several collaborative projects, including the use of calcium imaging in social behavior and the development of novel opsins (Gunaydin et al., Cell, 2014, and Chuong et al., Nat. Neurosci, 2014). 3) The lab identified a neural circuit that selectively controls compulsive overeating but does not alter hunger-driven feeding, and the lab recorded from projection-identified neurons in the LH-VTA loop for the first time (Nieh et al., Cell, 2015, featured as cover story). Media outlets covering this story included Forbes, The Scientist, and SciShow, which created a video about the study that was viewed more than 200,000 times in the first week.

Kenneth Wexler

The Wexler lab received a MISTI seed grant (20K) (in collaboration with professor Martin Hackl of Linguistics) for research on acquisition of Japanese. In cooperation with professor Koji Sugisaki (Japan), the lab is conducting experiments on Japanese

that relate to its experimental work in English on the properties of focus particles in the development of language, in preparation for the submission of a larger external grant. The lab also obtained experimental results on the acquisition of "only" that will strongly clarify an outstanding open problem in semantic development. Last, the lab discovered that Japanese children do not compute inverse scope even under prosodically highlighted conditions, but they do achieve inverse scope under scrambling conditions, which is very important for the theory of development. The lab is following up with English experiments on prosodically marked quantifiers.

Matthew Wilson

Using closed-loop optogenetic manipulation of activity in the hippocampus, the Wilson lab was able to enhance behavioral performance of mice solving a simple maze through selective gating of memory encoding and retrieval functions linked to the phase of intrinsic brain oscillations. The lab also identified a novel organization to the thalamic reticular nucleus — the network that regulates thalamic interactions with the cortex — that links sleep states and attention. Computationally, the lab developed new tools that advance the ability to decode brain activity in real time, which is critical for brain-machine interfacing.

Weifeng Xu

The Xu lab studies how experience induces changes in synaptic transmission (synaptic plasticity) important for information coding in the central nervous system. The lab uses a combination of molecular, electrophysiological, and behavioral analyses in the rodent model system to study critical players in synaptic plasticity and learning and memory. In one line of research, the lab discovered that different scaffold proteins influence synapses differently in aspects including dependency on neuronal activity, receptor trafficking, and the kinetics of synaptic responses. The lab is now starting to map out the landscape of synaptic diversity and signaling specificity controlled by scaffold proteins. Furthermore, the lab found that PSD-95, one prominent postsynaptic scaffold protein, is important for the durability of fear memory but not the initial acquisition of the memory, suggesting the involvement of PSD-95 in a specific phase of memory formation. In a second line of research, the lab found that experience-dependent translation of a small neuronal protein in the hippocampus gates contextual memory formation. The dynamic regulation of this neuronal protein is poised as a critical player in modulating calcium signaling, controlling the expression of synaptic plasticity and memory formation.

Feng Zhang

In the past year, the Zhang lab has accomplished a number of major research objectives aimed at development and application of genome editing technologies. *Technology development:* The lab published the first crystal structure of the Cas9 complex (Nishimasu et al., Cell 2014). This high-resolution structure has made it possible to do rational engineering of the Cas9 enzyme complex. Toward this end, the lab was able to use structure information to engineer a powerful transcription activator system for genome-scale gene activation (Konermann et al., Nature 2014) and to develop a split Cas9 system that is only active when a drug has been provided (Zetsche et al., Nature Biotechnology

in press). *Neuroscience applications:* The lab has been working hard to enable robust in vivo and/or high-throughput genome editing for studying gene function in the nervous system and disease processes. The lab developed both a transgenic mouse model (Platt et al., Cell 2014) and viral delivery systems (Swiech et al., Nature Biotechnology 2014) for achieving efficient genome editing in adult mouse brain. The lab has also made much progress toward using genome editing to model and study genetic contributions to neurological and psychiatric diseases (work in preparation for publication).

Selected Awards and Honors

Professor Guoping Feng received the 2014 Scientific Innovations Award, Brain Research Foundation, Chicago; the Simons Foundation Autism Research Initiative (SFARI) grant award; and the Massachusetts Life Science Center Capital Program grant award.

Professor John Gabrieli was named a Thomson Reuters Highly Cited Researcher.

Assistant professor Mehrdad Jazayeri received a Sloan Research Fellowship.

Professor Nancy Kanwisher received an Outstanding Mentor Award from the BCS Community Postdoc Association.

Assistant professor Yingxi Lin received the BCS Award for Excellence in Undergraduate Teaching.

Assistant professor Josh McDermott received the BCS Award for Excellence in Undergraduate Advising and an NSF CAREER award.

Professor Earl K. Miller was named an Amar G. Bose Research Fellow.

Professor Elly Nedivi received a UO1 grant in the first round of the BRAIN Initiative (co-PI Professor So, of Mechanical and Biological Engineering): Optimization of Transformative Technologies for Large Scale Recording and Modulation in the Nervous System. Proposal title: Next generation high-throughput random access imaging, in vivo.

Professor Tomaso Poggio was the recipient of the Society for Neuroscience Swartz Prize for Theoretical and Computational Neuroscience, recognizing an individual who has produced a significant cumulative contribution to theoretical models or computational methods in neuroscience.

Professor Molly Potter received the Vision Sciences Society's Davida Teller Mentorship Award.

Associate professor Laura Schulz received the American Psychological Association Distinguished Scientific Award for Early Career Contribution to Psychology.

Professor Pawan Sinha received the Pisart Vision Award conferred by Lighthouse Guild International, the inaugural Asia Game-Changer Award conferred by the Asia Society, and the Oberdorfer Award in Low Vision conferred by the ARVO Foundation for Eye Research.

Professor Mriganka Sur received an NIH BRAIN Initiative award and an NSF BRAIN Initiative EAGER award.

Assistant professor Kay Tye received the Committed to Caring (C2C) honor from the Office of the Dean for Graduate Education, recognizing outstanding mentorship; was named a NARSAD Young Investigator; received an Alfred P. Sloan Foundation Research Fellowship; was named one of *Technology Review's* Top Innovators Under 35 (TR35); and was named a Robertson Investigator by the New York Stem Cell Foundation.

Assistant professor Feng Zhang was named a Robertson Investigator by the New York Stem Cell Foundation; won a Society for Neuroscience Young Investigator Award (for CRISPR-Cas9 and optogenetics); received the Jacob Heskel Gabbay Award in Biotechnology and Medicine (for CRISPR-Cas9, shared with Charpentier and Doudna); was named in *Cell*'s "40 under 40," won a Young Investigator Award (for CRISPR-Cas9) from the International Society for Transgenic Technologies; won the National Science Foundation's Alan T. Waterman Award (for CRISPR-Cas9 and optogenetics); and was named in *Technology Review*'s 10 Breakthrough Technologies.

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