Department of Brain and Cognitive Sciences

The mission of the Department of Brain and Cognitive Sciences (BCS) is to understand how the brain gives rise to the mind. BCS is 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. The department's belief is that building links between these levels is the key to understanding how the brain gives rise to the mind. This understanding of the mechanisms of the mind is the key to solving disorders of the mind, building intelligent machines, and dramatic advances in education. It will also lead to other myriad and unpredictable world-changing consequences.

Because the path from mechanistic, basic science to translation is both critical and unpredictable, BCS strives 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 or translational connections are visible. BCS also upholds 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 the department is that all these levels of analysis are pursued in an integrated and synergistic way. There are very few other academic departments in the world organized as is BCS—in most universities, the study of the brain (neuroscience) and the study of the mind (cognitive science) are housed in separate buildings, 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, giving BCS the opportunity to continue to lead in its mission. 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. The overall strategy focuses on bolstering the subcommunities that naturally crosscut the units housed in 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 Professor Bob Desimone, PILM Director Professor Li-Huei Tsai, Simons Center for the Social Brain Director Professor Mriganka Sur, Center for Brains, Minds, and Machines 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 clearly

informed departmental decisions are made, and that all the 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 many functions without the support of the faculty, and BCS continues to espouse a culture of shared effort. The following faculty members have notably stepped up to continue in or take on key leadership roles over the past three years:

- Professor Michale Fee (associate department head for education and chair of the BCS Education Committee)
- Professor Laura Schulz (undergraduate officer)
- Professor Matt Wilson (graduate officer and chair of the BCS Graduate Student Admissions Committee and BCS Graduate Student Affairs Committee)
- Professor Nancy Kanwisher (BCS space oversight)
- Associate Professor Alan Jasanoff (chair of the BCS Seminar Committee)
- Professor Pawan Sinha (chair of the BCS Diversity Committee)
- Professor Mark Bear (postdoctoral officer for the BCS community)

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

Although the department is grateful to those who have assumed leadership roles, BCS has a huge hole to fill because of the recent passing of BCS Professor Suzanne Hammond Corkin, professor emerita of neuroscience. Not only did Suzanne make a large and lasting impact on the field of cognitive neuroscience, she also made a huge impact on the lives of the junior faculty members by serving as chair of the BCS Junior Faculty Mentorship Committee over the past three years. Suzanne will be dearly missed.

Faculty

BCS faculty members are widely recognized as being among the leaders in their respective fields. The faculty includes one Nobel Prize winner, nine members of the National Academy of Sciences (including two emeritus members), five members of the National Academy of Medicine, 14 members of the American Academy of Arts and Sciences (including two emeritus members), 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 three recipients of the Society for Neuroscience Young Investigator Award.

The McGovern Institute and the Picower Institute are critical components of the BCS community: 28 of the 36 BCS primary faculty members are also investigators in MIBR and PILM. The department itself is a critical, nearly fully encompassing umbrella that seeks to enable the success of those two great institutes. All 11 of the PILM investigators have either their primary or secondary appointments in BCS, and 17 of 18 MIBR investigators have their primary or secondary appointments in BCS.

Two BCS faculty members have core appointments at the Broad Institute and two have joint appointments at the Institute for Medical Engineering & Science. Two more hold the special title of Institute Professor.

The interdisciplinary nature of neuroscience and cognitive science is highlighted by the number of BCS faculty members with joint appointments. The faculty who held joint appointments this past year in BCS represented Chemical Engineering, Mechanical Engineering, the Media Lab, Biology, Biological Engineering, 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 the Department of Linguistics and Philosophy.

Development

Development efforts continue to be an important focus for BCS. In June, Rachel Donahue joined the department as director of strategic scientific development—a new position for BCS. Donahue holds a PhD in neurobiology from Harvard University and is well versed in the importance of philanthropic efforts, as she has been on the receiving end of such efforts as a graduate student and postdoctoral associate. These experiences have given her a unique perspective and have laid the groundwork for her role here in BCS.

The department's top fundraising priority continues to be increasing fellowship support for graduate students. This support is a vital component of BCS's ability to attract the very best young scientists and to ensuring that BCS remains a leader in education and research. The current goal is to build an endowment capable of fully supporting our graduate students for at least their first three years in the department. The Champions of the Brain Fellows community continues to be an important way for the department to secure both endowed and expendable fellowship funding.

In addition to fellowship support, BCS is deeply committed to increasing its unrestricted research funds. Such financial flexibility is critical in a climate where government funding has leveled off and competition among the department's peers has intensified. Internal research funding is an integral part of the ability to support talented faculty in pursuing bold ideas that lead to innovative, cutting-edge research, and to the high-risk, high-reward projects that can lead to groundbreaking discoveries. Discretionary support also helps attract and retain faculty, invest in technology and tools, and recoup under-recovery costs from foundation support.

To achieve these goals, the department's comprehensive fundraising efforts will focus on identifying new donors as well as engaging current donors who are excited to support the needs of the department. It is hoped that events such as the Champions of the Brain Fellows dinner and the upcoming Brains on Brains Symposium in May 2017 will help BCS continue to cultivate these relationships. To complement these efforts, we are creating new fundraising materials with the goal of providing updated and improved information to current and potential donors.

Education and Training

The educational mission of BCS is to train students in the knowledge and methods needed to "reverse engineer" the mind. The BCS vision is anchored in the idea that a deep understanding of the mind requires study across multiple levels of analysis: characterization and investigation of human cognitive phenomena in both normal and disordered states, the algorithms and representations in the brain that underlie those phenomena, the neuronal circuits that execute those algorithms and convey those representations, and the cellular and molecular mechanisms that implement, maintain, and potentially repair those neural circuits.

Understanding these mechanisms of the mind is the key to solving disorders of the mind, building intelligent machines, and making dramatic advances in education, which will foster a scientific environment that can achieve world-changing impacts. The department provides its students with an interdisciplinary curriculum designed to educate them in these areas and prepare them to be future ambassadors of science. The intensive undergraduate program in BCS is a tiered system that builds on the expertise gained at each preceding level. Beginning with broad courses, students gain foundational knowledge of topics drawn from molecular, cellular, and systems neuroscience, cognitive and perceptual psychology, applied mathematics, computer science and artificial intelligence, linguistics, and the philosophy of mind. These multiple tiered pathways through the undergraduate program are designed to prepare students for a range of possible career paths, including research, health care, 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. As part of the undergraduate and graduate curriculums, BCS faculty taught a total of 48 subjects this past year.

Undergraduate Program

Now in the third year of the redesign of its undergraduate curriculum redesign, BCS has provided its students with opportunities to build a strong quantitative skill set and be exposed to a rigorous, engineering-level description of neurons and neural circuits and the computations they carry out. All undergraduates in BCS learn elementary computer programming and statistics, and take the foundational course (9.40 Introduction to Neural Computation) that covers quantitative and computational approaches to understanding the brain and behavior.

Students majoring in BCS are often quite accomplished and are recognized as such. In AY2016, nine undergraduates were invited into the Xi Chapter of Phi Beta Kappa and two were inducted into Tau Beta Pi and Eta Kappa Nu.

Institute awards for undergraduates include the Walle J. H. Nauta Award for Outstanding Research in Brain and Cognitive Sciences (14) and the BCS Hans Lukas Teuber Award for Outstanding Academics (nine). Students also received awards such as the Priscilla King Gray Award and the Ronald E. McNair Scholarship Award, the Emerson Fellowship, and the Palitz Fellowship. A BCS student was the MIT Symphony Orchestra competition winner during the MIT Awards Convocation.

Graduate Program

The department has continued efforts to increase the quantitative rigor of the graduate program. During fall 2015, Assistant Professor Mehrdad Jazayeri successfully developed and taught a quantitative course for first-year graduate students, 9.014 Quantitative Methods and Computational Models in Neurosciences. The course taught mathematical and computational tools and programming techniques relevant to students with a broad range of interests, spanning cognitive systems and molecular neuroscience. It received a perfect evaluation by all student attendees and Dr. Jazayeri received the departmental award for excellence in graduate teaching.

Over the past five years, the size of the BCS graduate program has remained steady at around 100 students (approximately 2.5 graduate students per faculty member). Eighteen graduate students entered in fall 2015. Forty percent of the department's students are female, 40% are international students, and there is a growing proportion of underrepresented minority students (currently 11%). Eight of the incoming students were funded by Singleton Presidential Graduate Fellowships, one by a Hilibrand Fellowship, three by the ASTAR fellowships, and six by National Institutes of Health (NIH) training grant programs.

During this year, 12 students graduated with doctorates: Benjamin Deen, Eitan Kaplan, Silvana Konermann, Megan Krench, Stephen Allsop, Wilma Bainbridge, Leon Bergen, Matthew Greene, Julian Jara-Ettinger, Joseph Keller, Kyle Mahowald, and Nune Martiros.

BCS graduate students are highly accomplished; their excellence has been recognized regularly over the past year. Institute awards over the past year include the Angus MacDonald Award for Excellence in Undergraduate Teaching (nine), the Walle Nauta Award for Continuing Dedication to Teaching (two), and the Walle Nauta Award for Excellence in Graduate Teaching (two).

Postdoctoral Program

The directors of BCS, MIBR, and PILM deeply believe in creating and maintaining an environment where people can learn by doing unfettered science to achieve their career goals. Over the past year, BCS has worked on developing and executing a plan to enlarge the annual stipends that postdoctoral researchers receive here as scientists in training. Strong support for this effort has been found in discussions across MIT and with BCS faculty.

As of July 1, 2016, BCS had raised the postdoctoral minimum annual stipend rate for the BCS community (BCS, MIBR, PILM) to a level that is significantly above the current NIH Kirschstein National Research Service Award (NRSA) minimum. It is also above the level recommended by a recent National Academy of Sciences study of postdoctoral salaries ($50,000). Each postdoctoral associate will receive at least this level of annual stipend support, regardless of years of experience. In the future, the stipend will be indexed to the NIH NRSA award for a researcher with four years of experience. That is, as the NIH raises this award to account for the cost of living, the BCS community rate will rise in tandem. The NRSA annual rate is currently $51,120. This new annual stipend policy applies to both postdoctoral fellows and postdoctoral associates.

The department recognizes that members of the postdoctoral community have been eager to see annual stipends that are in line with competing institutions (e.g., Stanford University). BCS believes that this new policy accomplishes this, and that this effort will further free postdoctoral associates to focus on building their careers by doing unfettered science during the postdoctoral training period.

During this past year, a long-time member of BCS, Dr. Sonal Jhaveri, has officially retired from the Institute. Dr. Jhaveri began her career at MIT as an undergraduate student and has made a lasting mark on the department in her latest role as director of postdoctoral affairs for the Building 46 community. Although Dr. Jhaveri will be missed, the postdoctoral community remains in good hands with Professor Marc Bear as postdoctoral officer and the support of the human resources representatives across the building.

Selected Research Highlights

Edward Adelson

The Adelson laboratory's main effort is directed at artificial touch sensing with GelSight, which is an optical tactile sensing technology based on an elastomeric sensor. Superhuman sensitivity to touch, texture, and microscale topography can be achieved. Of particular interest now are tangential measurements, such as friction, shear, and slip. The Adelson laboratory is collaborating with Mandayam Srinivasan (haptics, Department of Mechanical Engineering) and Alberto Rodriguez (manipulation, Mechanical Engineering). The laboratory continues to work on material perception and material appearance, developing a technique using band-sifting operators to manipulate image statistics so as to change the appearance of surfaces in photographs—for example, making skin look wetter or making metal look more worn. Researchers are also studying the appearance of translucency, and are making synthetic materials, both in the laboratory and on the computer, to test the perception of these qualities. The laboratory is applying image statistics and machine learning to novel problems in vision, including the unsupervised learning of states and transformations in image collections.

Marc Bear

The Bear laboratory made good progress last year on the three research fronts it is pursuing: the synaptic basis for amblyopia, the pathophysiology and treatment of genetic disorders causing intellectual disability and autism, and the synaptic and circuit mechanisms for visual recognition memory. Perhaps the most important single discovery was the basis for visual recognition memory, expressed behaviorally as longterm habituation to a familiar visual stimulus. Researchers found that synaptic plasticity within the primary visual cortex was necessary for learning, and that a circuit involving a specific class of inhibitory interneuron was necessary for expression of the memory. Other highlights were the receipt of the IPSEN Foundation prize for neuronal plasticity based on the laboratory's work on autism, and being the runner-up for the Beckman-Argyros Award in vision.

Emilio Bizzi

Researchers in the Bizzi laboratory continue to pursue their primary research interest—the understanding of how the brain controls voluntary movements. To this end, they have 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 question, Bizzi laboratory collaborators and researchers 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). Modular organization might help to simplify the production of movements by reducing the degrees of freedom that have to be specified. The laboratory's work 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 various vertebrates (humans, monkeys, mice, and frogs), researchers in the Bizzi laboratory have shown that the control of limb movements is facilitated by the presence of muscle synergies. The results indicated that a small number of synergies account for a large fraction of variation in muscle activity during movement.

Emery Brown

The Brown laboratory demonstrated that children from 0 to 6 months old have distinctly different EEG patterns under general anesthesia compared with adults. In fact, children 0 to 3 months of age have distinctly different EEG patterns from children 4 to 6 months of age in the same circumstances. Researchers explained why these differences mostly likely reflect differences in brain development. Work in the Brown laboratory also demonstrated in rodents that optogenetic stimulation of the thalamic reticular nucleus, a major control center for information coming out of the thalamus, can produce slow oscillations in the cortex and thalamus. These slow oscillations are associated with a decreased state of arousal, suggesting that it may be possible to produce the altered states of arousal associated with general anesthesia by control of specific brain targets.

Martha Constantine-Paton

In the past year, the Constantine-Patton laboratory completed production of a CRISPR-Cas9 tool that removes the dominant negative MYOVa gene from dissociated Flailer mouse cortical neuron cultures and eliminates the abnormal high-frequency firing of these cells. Researchers also successfully used microfluidics chambers in an experiment where single dissociated motoneurons on one side of the chamber sent single axons through one of a row of very thin channels to innervate dissociated muscle fibers in a second chamber on the opposite side of the channels. This setup allows high-magnification imaging of anterograde and retrograde organelle movement through the channels. These will be used in studies where motoneurons from amyotrophic lateral sclerosis (ALS)–mutant mice innervate either muscle fibers from the same ALS mutant or wild-type (WT) muscle fibers, or where WT motoneurons innervate muscle fibers from an ALS mutant. Survival of motoneuron and muscle fibers will also be quantified in each set of chambers. If these experiments prove successful in demonstrating defective

axon transport or survival, or both, researchers in the Constantine-Paton laboratory plan to collaborate with ALS physician and researcher Dr. Robert Brown, professor and chair of neurology at the University of Massachusetts Medical School. The collaboration would allow the Constantine-Patton laboratory to obtain induced pluripotent stem cells derived from the cells of ALS patients and transformed into neurons and muscle fibers to determine if the same defects are observed in human cells carrying the same mutations. If these experiments succeed, the laboratory staff plans to use cell biological techniques to track the mechanisms underlying the changes in organelles transported by microtubules or f-actin fibers to determine the immediate causes of ALS.

James DiCarlo

The goal of DiCarlo's research group is a computational and mechanistic understanding of the brain mechanisms that underlie visual object and face recognition. The group is 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 to take incoming visual images and untangle object and face identity from confounding variables such as object position, scale, and pose. To build that understanding, the group collects data using large-scale neurophysiology, brain imaging, neural perturbation methods (e.g., optogenetics), and behavioral testing in human and nonhuman subjects, and they construct and compare computational models that aim to emulate and predict those key empirical data. In the past year, they have made three new advances: that the ventral stream conveys, at its top level, explicit neural population representations of other object latent variables, such as position, size, and pose; that a simple computational model can explain how those neural population patterns explain and predict perceptual reports of object identity, category, and other object variables; and that deep convolutional neural network models inspired by the neuroanatomy of the ventral stream are natural explanatory models for all of these key empirical phenomena. The group is currently using optogenetic tools to test these computational models more deeply by asking if specific perturbations of neural activity lead to specific, predicted perturbations in a perceptual report. As the research group builds deeper understanding of the models, they intend 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

In a paper published in *Nature*, the Feng laboratory demonstrated for the first time that the neurobiological defects and autistic-like behaviors found in the Shank3 mutant mouse model of autism are reversible in adult mice, giving rise to hopes for developing an effective treatment for autism. Second, recent genetic studies revealed significant overlaps of genes that indicate risk of major psychiatric disorders. However, how different mutations of the same gene cause or contribute to different disorders is not clear. Using unique mouse models, researchers in the Feng laboratory revealed the molecular and circuit mechanisms of how two different mutations of the Shank3 gene, one linked to autism and one linked to schizophrenia, could contribute to or cause these two disorders; this work appeared in *Neuron*. Mutations of the PTCHD1 gene

accounts for about 1% of autism patients with intellectual disability. Using PTCHD1 mutant mice, researchers in the Feng laboratory discovered that thalamic reticular nucleus dysfunction plays a critical role in attention deficits, hyperactivity, and sleep disturbance. They also discovered cellular mechanisms of PTCHD1 mutations that may provide a potential pathway for developing treatment; this work was scheduled to appear in *Nature*.

Steven Flavell

In the past year, Steven Flavell completed postdoctoral training at Rockefeller University and began setting up his laboratory at MIT; it opened on January 16, 2016. The goal of the laboratory is to understand how neural circuits generate long-lasting behavioral states. By monitoring and manipulating the simple, well-defined nervous system of *C. elegans*, researchers aim to identify cellular and circuit mechanisms that organize animal behaviors over seconds, minutes, and hours. The work was focused on developing several projects to the point where they can be handed off to individual postdoctoral associates and graduate students. These projects include identifying novel ion channels that allow neurons to detect satiety signals generated while feeding, generating new *C. elegans* strains that will be used to identify gene expression changes that underlie long-lasting forms of memory, and conducting pilot studies to perform simultaneous calcium imaging of every neuron in the *C. elegans* nervous system. There are clear, promising directions for these projects; reagents have already been generated and, in the case of the ion-channel project, real progress has been made. To execute these projects, the Flavell laboratory hired one laboratory technician and two talented postdoctoral associates, one of whom graduated from the BCS PhD program and the other from Harvard University's Program in Neuroscience.

John Gabrieli

In the US, the difference in academic achievement between higher- and lower-income students is substantial and growing. The Gabrieli laboratory investigated neuroanatomical correlates of this gap in adolescents in whom academic achievement was measured by statewide standardized testing. Cortical thickness in all lobes of the brain was greater in students from higher-income backgrounds than those from lower-income backgrounds. Greater cortical thickness was associated with better test performance. These results represent the first evidence that cortical thickness in higher- and lower-income students differs across the brain and that cortical thickness is related to scores on academic achievement tests. Next, researchers asked whether brain connectomics can predict response to treatment for a neuropsychiatric disorder better than conventional clinical measures can. Pretreatment resting-state brain functional connectivity and diffusion-weighted structural connectivity were measured in patients with social anxiety disorder to predict subsequent treatment response to cognitive behavioral therapy. Multimodal connectomics yielded a fivefold improvement in predicting treatment response, relative to conventional clinical measures. Connectomics of the human brain, measured by widely available imaging methods, may provide brain-based biomarkers supporting precision medicine that can guide patients with neuropsychiatric diseases to optimal available treatments, and thus translate basic neuroimaging into medical practice.

Edward Gibson

The Gibson laboratory has focused on how information processing, such as communicative pressures and working memory, shapes language knowledge structures and language use, and on how cognition (including aspects of language) is related to culture. One recent project shows that all human languages minimize dependency lengths between words, to some degree. That is, when producing a sentence, speakers of all languages prefer to put words that go together to form larger meanings close together in the sentence, given an option to put them further away. For example, the sentence "John put out the trash that was in the kitchen" (where "out" is beside "put") sounds more natural than the sentence "John put the trash that was in the kitchen out" (where "out" is far from its head verb "put"). Researchers in the Gibson laboratory showed this effect in parsed texts from 37 languages in a 2015 *Proceedings of the National Academy of Sciences* article (Richard Futrell was first author).More recently, the laboratory has been investigating cognition in a remote language and culture, that of the Tsimané in the Bolivian Amazon. For example, in the domain of number, children in industrialized nations progress through a stereotypical series of subset-knower levels, successively learning the meaning of "one," then "two," then "three." Then, typically at around ages three to six, children undergo an apparent conceptual shift and rapidly acquire the meanings of many higher-number words all at once. A similar developmental trajectory is present in the Tsimané, but it is delayed by approximately four years, so that children become full counters at around eight years old. In the past year, researchers in the Gibson laboratory published work in *Developmental Science* that showed that the notion of what is "fair" depends on a person's understanding of number. Children who understand numbers divide resources according to the output of a worker; children who do not understand numbers divide resources in half, independent of the output of a worker. This effect is independent of age. The Tsimané provided a resource to be able to distinguish such hypotheses, where children learn numbers at highly variable times in their lives.

Mark Harnett

The Harnett laboratory studies how the biophysical features of neurons, including ion channels, receptors, and membrane electrical properties, endow neural circuits with powerful processing capabilities, ultimately allowing them to perform the complex computations required to drive adaptive behavior. The laboratory officially opened on July 1, 2015, successfully hiring two senior postdoctoral associates with training in slice electrophysiology, along with a junior postdoctoral researcher experienced in experimental engineering and in vivo physiology, and a laboratory technician. Researchers in the laboratory then purchased equipment and reagents, set up a two-photon in vitro microscope with patch clamp electrophysiology to perform cellular analyses of dendritic function, and began performing experiments. The laboratory continued to build and optimize its equipment for in vivo calcium imaging and electrophysiology during navigation and sensorimotor behavior. Researchers also established a collaboration with a neurosurgical team at Massachusetts General Hospital; the surgeons have agreed to supply fresh tissue from human brain resections. This will allow the Harnett laboratory to perform in vitro experiments comparing the computational power of human neural circuits with those of rodents.

Myriam Heiman

In the past year, the Heiman laboratory developed a workflow to conduct genetic screening in the mouse brain. Using this approach in a pilot screen, researchers identified the gene Gpx6 as a protective factor against mutant Huntingtin's effects in mouse models of Huntington's disease. In a separate study, researchers used the cell type–specific translating ribosome affinity purification methodology to profile the gene expression changes that occur in specific cell types in mouse models of Huntington's disease. The work revealed that the polycomb repressive complex 2 (PRC2) is responsible for most of this deregulation.

Mehrdad Jazayeri

The Jazayeri laboratory is on its way toward a comprehensive characterization of neural signals in several cortical and subcortical areas involved in Bayesian integration and timing. Researchers have developed an animal model and have begun to elucidate the mechanisms of belief propagation (i.e., thinking ahead) in cortical circuits. They have also discovered that several neural systems in the brain measure elapsed time relative to the expected time of future goals, actions, and events, and made an exciting discovery about the geometry of neural activation patterns that allow the brain to harbor multiple learned representations without interference. The laboratory's work includes development of a detailed biophysical model for Bayesian integration that has led to specific hypotheses about neural signals; these are currently being tested by experiments in animal models.

Yingxi Lin

The main interest of the Lin laboratory 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. In the past few years, researchers in the laboratory have been developing a versatile neuronal activity mapping system to map the neuronal ensembles involved in encoding experiences. Last year, they finished the development and optimization of the system and submitted the first paper describing the system for publication, which received very positive reviews from *eLife*. Building on the mapping system, it is now possible to investigate distinct neuronal ensembles that are defined by different molecular and cellular events following experiences. Researchers have also discovered a genetic pathway that's important for the homeostatic regulation of the neural circuit; a manuscript describing these findings is being prepared for publication. The Lin laboratory is also building a neuronal activity atlas of the developing mouse brain, which is believed to be the first of its kind. We have succeeded in securing funding for the purchase of a light sheet microscope.

J. Troy Littleton

With the long-term goal of understanding how synapses communicate and undergo plasticity, the Littleton laboratory is using *Drosophila* as a model system to characterize the molecular mechanisms for neurotransmitter release, and how release can be regulated at individual release sites known as active zones. Neurotransmitters can be released during evoked fusion following an action potential, or through spontaneous fusion of vesicles in the absence of nerve stimulation. Researchers took advantage of

the spatial arrangement of release sites and clustered receptors at *Drosophila* synapses to analyze evoked release probability at individual release sites by measuring the Ca^{2+} influx that occurs through postsynaptic glutamate receptors following vesicle fusion. They generated a myristoylated variant of a genetically encoded green fluorescent protein that was sensitive to Ca^{2+} (GCaMP6s) and that robustly detects postsynaptic responses to both evoked and spontaneous synaptic vesicle fusion events; this allowed researchers to determine how release probability and release mode are regulated at individual release sites. The ability to map out single active zone release probability and correlate it with presynaptic properties such as active zone protein content, presynaptic Ca^{2+} entry, or synaptic vesicle state will provide new insights into how glutamatergic synapses can transmit information to postsynaptic partners.

Joshua McDermott

As part of an ongoing effort to understand the auditory cortex, the McDermott laboratory developed a signal processing method to manipulate the extent of temporal structure in speech and used it to reveal a speech-selective region of the auditory cortex. Because this region responds equally to foreign-language and English speech, it appears to be involved in analyzing the acoustic structure of speech and may be a precursor to linguistic processing. In a separate project, researchers developed a decomposition method for analyzing functional magnetic resonance imaging responses, and used it to discover a distinct brain region containing neurons that are highly selective to music. Together, these findings suggest two distinct pathways in the auditory system underlying the recognition of sound. Researchers also began to investigate the perception of reverberation: the echoes that are introduced by the environment, distorting sound but also providing information about the world around us. They were able to show that human listeners can partially decompose reverberant sound into the sound source and the reverberation produced by the environment, and that the ability to do so depends on statistical regularities of naturally occurring reverberation. This work helps to explain the robustness of auditory recognition to reverberation and introduces a new scene analysis problem in audition.

Earl K. Miller

The Miller laboratory has gained new insights into the role of brain oscillations (brain waves) in brain function. For example, researchers have found that, during learning, the prefrontal cortex and hippocampus synchronize at different frequencies following correct versus incorrect guesses. One frequency seems to support strengthening of neural connections (remembering); the other weakens them (forgetting). Researchers have also found that unique patterns of brain wave synchrony develop between the prefrontal cortex and striatum during category learning, as if the wave patterns are forming the networks that learn the new categories. Another line of work is providing insight into how brain waves may be the limiting factor that explains why we can only think one thought at a time (i.e., cognitive capacity).

Elly Nedivi

Bipolar disorder (BD) is a prevalent and severe mood disorder that is characterized by recurrent episodes of mania and depression. Both genetic and environmental factors

have been implicated in BD etiology, but the biological underpinnings remain elusive. Recent genome-wide association studies for identifying genes that confer risk for schizophrenia, BD, and major depression identified an association between single-nucleotide polymorphisms (SNPs) in the SYNE1 gene and increased risk of BD. The BD-associated SNPs map within the gene region that is homologous to the part of rat Syne1 encompassing the brain-specific transcripts that encode CPG2, a postsynaptic neuronal protein localized to excitatory synapses and an important regulator of glutamate receptor internalization. The Nedivi laboratory mapped the human SYNE1 transcriptome, focusing on the CPG2 locus, validating several CPG2 transcripts (including ones not previously annotated in public databases), and identified and cloned a full-length CPG2 cDNA that is expressed in the human neocortex, hippocampus, and striatum. Using a gene knock down/replacement strategy, researchers demonstrated that human CPG2 protein is functionally equivalent to rat CPG2 in regulating glutamate receptor internalization. This study provides a valuable gene-mapping framework for relating multiple genetic disease loci in SYNE1 with their transcripts, and, in particular, for evaluating effects of missense SNPs identified by patient genome sequencing on neuronal function.

Tomaso Poggio

Research in the Poggio laboratory concerns the problem of learning in both biological organisms and computers, because learning is at the heart of the problem of building intelligent machines and of understanding how the brain works. The laboratory's work spans mathematics, engineering, and the neuroscience of learning. The main focus of Poggio's own work is to complete a theory of learning in shallow and deep hierarchies, extending i-theory. The framework of i-theory derives the properties and theorems of a cortical architecture that learns to compute representations invariant to unknown transformations experienced during the life of the organism. Invariant representations allow supervised learning with very few labeled examples—a trademark of biological organisms and a significant difference with respect to existing artificial intelligence approaches.

Gerald Schneider

The Schneider laboratory continues to make and record observations of experienced central visual persistence phenomena, focusing on specific changes that occur when blood glucose is lower than normal. The images, seen for a very short time after the eyes are closed, are predictive in nature, indicating an awareness of a central model. The blood glucose changes have allowed the separation of three distinct mechanisms. Researchers in the Schneider laboratory have begun to interact with researchers in the Sinha laboratory because of their interest in failures of prediction in autism. The Schneider laboratory continues to compile and transcribe records of blood-glucose tests made over the past 20 years, with descriptions of effects of hypoglycemia that include phenomena that have been observed over a period of 50 years. Detailed cataloging of records from 2007 to 2014 shows results for 24,908 tests, done five to 14 times per day (average 8.52 per day). The variability of the effects—neurological and psychological in nature—is fascinating, but many effects have recurred in a consistent fashion. Researchers have also found clear changes that have occurred over the years, indicating

that the brain adapts to hypoglycemia sufficiently to enable more normal functioning of some brain processes. while others show less adaptation.

Laura Schulz

The Schulz laboratory's most important accomplishment this year was the completion of its laboratory online developmental research platform, Lookit. In 2015, researchers completed replication studies of three laboratory-based studies that confirmed the viability of Lookit as a method for remote data collection for studies of children aged from 11 months to five years that used methods including violation of expectation, preferential looking, and verbal responses. In striking contrast to laboratory-based studies, the demographics of participants on Lookit nearly mirrored US census data with respect to race, scioeconomic status, and linguistic diversity. Pending development by the Center for Open Science, all code will be released under an open-source license. This platform is likely to expand access to both more representative populations and rare populations, make it easier to conduct large-scale longitudinal studies, detect small and graded effects, generate data sufficient for testing computational models, and better assess individual differences and developmental change. This tool will also increase reproducibility and transparency in developmental research. More, in connecting families and scientists, Lookit offers exciting new opportunities for education and outreach. As a venue for "citizen science" as well as scientific research, Lookit stands to expand the scope of both the questions scientists ask and the people they reach.

Pawan Sinha

The past year has been a productive one for the Sinha laboratory, whose overarching research themes—understanding object representations, their acquisition, and their disorders—have seen fruition in several specific results. Researchers completed a study probing a key question regarding facial representation in the human brain: what are the neural correlates of familiar face perception? A combination of the latest electrophysiological and computational techniques led to a partial answer to this question. The laboratory's results not only resolve some puzzling discrepancies between macaque and human data, they also serve as a launch pad for probing what aspects of facial structure contribute to identification. Researchers' work on visual function acquisition after late sight onset also yielded compelling evidence regarding the genesis of classic perceptual phenomena that have been studied for more than a century. (These results were highlighted as a cover story in *Science*.) In addition, a paper published by laboratory researchers about a year ago contained a new theoretical account of autism; that paper has had a significant effect on the field and is in the 98th percentile of all papers followed by Altmetric. Over the past several months, guided by this theory, researchers in the Sinha laboratory have obtained experimental results that offer new insights into diverse, and seemingly distinct, aspects of autism symptomology, including sensory hypersensitivities and motor difficulties. The theory has also led other laboratories to explore the functional consequences of specific genetic mutations, thus building a bridge between molecules on the one extreme and high-level behavior on the other.

Mriganka Sur

The Sur laboratory discovered the neural circuit underlying a powerful form of temporal coding in the visual cortex. Cholinergic modulation of the cortex causes robust desynchronization and strong decorrelation of responses between neurons. Using novel technologies, the researchers discovered that intracortical cholinergic inputs to the mouse visual cortex specifically and differentially drive a defined cortical microcircuit. These inputs facilitate somatostatin-expressing inhibitory neurons that in turn inhibit parvalbumin-expressing inhibitory neurons and pyramidal neurons. These findings demonstrate a mechanistic basis for temporal structure in cortical populations and the crucial role of neuromodulatory drive to specific inhibitory-excitatory circuits in actively shaping the dynamics of neuronal activity. In a review article, Sur and Sahin described how the genetic heterogeneity of brain disorders can be leveraged into mechanistic analyses and precision medicine.

Joshua Tenenbaum

The Tenenbaum laboratory studies both the basis of commonsense knowledge and how it is learned. In 2015, researchers made several important advances focused on commonsense knowledge in the context of visual scene understanding, social cognition, and concept learning. One of these advances was the development of a general computational architecture based on probabilistic programming for modeling human vision as "inverse graphics"—that is, an observed image can be cast as the output of a graphics program that takes the three-dimensional scene as input, and the goal of vision is to "run the graphics program" backward to guess the scene that is most likely to have generated the image. This 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. The laboratory's paper on this work received a Best Paper (honorable mention) award at the IEEE Computer Vision and Pattern Recognition conference. Another advance made by the Tenenbaum laboratory is related to its work in social cognition, which has examined the cognitive basis of human collective intelligence. The research is built on a well-developed literature on the mechanisms of collective intelligence in nonhuman animal species. A recent experiment designed to study collective sensing in groups of fish was adapted in order to better understand the mechanisms that may underlie the emergence of collective intelligence in human groups. Humans in the adapted experiments act at a high level (like fish) but with two additional behaviors: independent exploration and targeted copying. These distinctively human activities may partly explain the emergence of collective sensing in the task environment at group sizes and on time scales that are orders of magnitudes smaller than were observed in fish. A first paper on this work was presented at the 2015 Cognitive Science Conference and received an award for Best Paper in Computational Modeling of Applied Cognition. Another advance came from the observation that people who are learning new concepts can often generalize successfully from just a single example, yet machine learning algorithms typically require tens or hundreds of examples to perform with similar accuracy. People can also use learned concepts in richer ways than conventional algorithms for action, imagination, and explanation. In December, researchers in the Tenenbaum laboratory published a paper describing a computational model that captures these human learning abilities for a large class of simple visual concepts: handwritten characters from the world's

alphabets. The model represents concepts as simple programs that best explain observed examples under a Bayesian criterion. On a challenging one-shot classification task, the model achieves human-level performance while outperforming recent deep learning approaches. Researchers in the Tenenbaum laboratory also present several "visual Turing tests" probing the model's creative generalization abilities, which, in many cases, are indistinguishable from human behavior. This paper was featured on the cover of *Science* and was covered by dozens of press outlets, including the *New York Times*, the *Washington Post*, the *Toronto Star*, *Popular Science*, *Technology Review*, and CBS News.

Kay Tye

The Tye laboratory published six publications in 2015. In one study, published in *Cell*, researchers found that lateral hypothalamus neurons projecting to the ventral tegmental area (VTA) specifically encoded the learned action of seeking rewards. On the theory that actions repeated many times become habits that can lead to compulsion, researchers activated these neurons and demonstrated that they could drive eating in animals that were full and increase the punishment mice would tolerate to obtain sugar. Inhibiting this circuit reduced compulsive overeating but did not alter feeding driven by hunger, suggesting that compulsive overeating and hunger are driven by separate circuits. In a second study, the amygdala, a region important for both positive and negative emotional processing, was shown to operate as a divergence point. Specifically, researchers found that amygdala neurons projecting to two different targets were intermingled but served opposing purposes in fear and reward conditioning. This study, published in *Nature*, looked at the synaptic changes, anatomical targets, causal relationships, and genetic identity of the neurons that drive reward-seeking and punishment avoidance in the amygdala. Together, these two studies provided compelling evidence that the function of neurons is dictated more by the target to which they are projecting rather than where they are located.

Matthew Wilson

Spatial learning requires the hippocampus, and the replay of spatial memory sequences during hippocampal sharp wave-ripple events of quiet wakefulness and sleep is believed to play a crucial role in that learning. To test whether the coordination of VTA reward prediction error signals with these replayed spatial sequences could contribute to this process, researchers in the Wilson laboratory took recordings from neuronal ensembles of the hippocampus and VTA as rats performed appetitive spatial tasks and subsequently slept. The work demonstrated for the first time that reward signals were reactivated along with hippocampal memories during quiet wakefulness, but not during sleep, suggesting a fundamental difference in memory processing in these two states.

Feng Zhang

The Zhang laboratory has played a leading role in the development of CRISPR-Cas9 and the related gene editing technologies that are now transforming biomedical research and applications. Over the past year, the Zhang laboratory has addressed three of the major challenges facing the CRISPR-Cas9 technology: the ability to deliver results in vivo, specificity, and the ability to use Cas9 for effective gene activation. For the first challenge, researchers scoured all of the known Cas9 sequences in the National Center

for Biotechnology Information databases, eventually finding a significantly smaller Cas9 that can be easily introduced into adeno-associated virus vectors. Zhang laboratory members then showed that this vector can mediate robust genome editing in vivo, in both the mouse liver and mouse brain. The same vector also produced therapeutic levels of physiological change. For the second challenge, researchers used protein engineering approaches to generate and enhanced version of Cas9 with undetectable levels of off-target activity. For the third challenge, researchers engineered the Cas9-RNA complex to enable the robust activation of any gene of interest. In addition, the laboratory's efforts have uncovered entirely new enzymes from the CRISPR systems—enzymes that open new directions for genome editing research beyond Cas9—and reported four new enzymes. Three of the new enzymes (Cpf1, C2c1, and C2c3) can be used for DNA targeting and one can be used for RNA targeting (C2c2).

Selected Awards and Honors

Associate Professor Ed Boyden was one of five scientists honored with the Breakthrough Prize in Life Sciences, given for "transformative advances toward understanding living systems and extending human life." He was also recently awarded a Banco Bilbao Vizcaya Argentaria (BBVA) Foundation Frontiers of Knowledge Award for his work on optogenetics. The BBVA awards are given annually for "outstanding contributions and radical advances in a broad range of scientific, technological, and artistic areas."

Professor Emery Brown has been selected a 2015 Guggenheim Fellow, became a full investigator in the Picower Institute for Learning and Memory, and was recently named a fellow of the National Academy of Inventors.

Assistant Professor Gloria Choi was named to the Samuel A. Goldblith Career Development Professorship.

Assistant Professor Kwanghun Chung was awarded a Packard Fellowship. The Packard Foundation invites 50 universities to nominate early-career professors from their institutions for the five-year $875,000 grants, which give emerging young scientists and engineers the freedom to take risks, pursue innovative ideas, and creatively explore new frontiers.

Professor James DiCarlo was named to the Peter de Florez chair of Neuroscience.

Professor John Gabrieli was elected to the American Academy of Arts and Sciences.

Professor and President Emerita Susan Hockfield has been chosen to serve as president-elect of the American Association for the Advancement of Science.

Assistant Professor Mehrdad Jazayeri was named to the Robert A. Swanson Career Development Professorship in the Life Sciences. He has also been selected for a Klingenstein-Simons Fellowship Award in the neurosciences.

Professor Nancy Kanwisher received the 2015 Outstanding Postdoc Mentor Award. The Brain and Cognitive Sciences Community's postdoctoral committee established this

award to recognize excellence in mentoring and to raise awareness of the essential role that mentors play in the career development of postdoctoral associates.

Assistant Professor Josh McDermott received a National Science Foundation Career Award. The award recognizes junior faculty members who exemplify the role of the teacher-scholar through outstanding research, excellent education, and the integration of education and research within the context of the mission of their organizations. He was also named to the Fred and Carole Middleton Chair in the department.

Professor Rebecca Saxe received the Arthur Smith Award for Distinguished Service to Student Life and Learning at this year's convocation.

Professor Jean-Jacques Slotine received the 2016 Rufus Oldenburger Medal. Given by the American Society of Mechanical Engineers, the medal recognizes significant contributions and outstanding achievements in the field of automatic control.

Professor Josh Tenenbaum was selected to receive the 2016 Howard Crosby Warren Medal from the Society of Experimental Psychologists. This is the oldest award in psychology, with a distinguished history dating to 1936.

Assistant Professor Kay Tye received a Presidential Early Career Award. Coordinated by the Office of Science and Technology Policy within the Executive Office of the President, awardees are selected for their pursuit of innovative research at the frontiers of science and technology and their commitment to community service, as demonstrated through scientific leadership, public education, or community outreach. She also received the Harold E. Edgerton Faculty Achievement Award. The award recognizes exceptional distinction in teaching, research, and scholarship, and is given annually to one individual from among the junior members of the MIT faculty.

Professor Shimon Ullman was elected to the American Academy of Arts and Sciences.

Associate Professor Feng Zhang received a Canada Gairdner International Award for his work on CRISPR. Created in 1959, the awards are given annually to recognize and reward the achievements of medical researchers whose work contributes significantly to the understanding of human biology and disease. He also was selected as a 2015 Blavatnik Award for Young Scientists in the Life Sciences national finalist. The award supports and honors outstanding scientists and engineers by encouraging and accelerating innovation through unrestricted funding and by recognizing their extraordinary achievements as vital contributions to science and society. He also received the 2015 Transformative Research Award from NIH. The award supports exceptionally innovative, unconventional, paradigm-shifting research projects that are inherently risky and untested.

James J. DiCarlo
Professor
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