

spring 2010

bcS news



Massachusetts
Institute of
Technology



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brain+cognitive sciences



A Message from the Department Head Mriganka Sur

**This has been one
of the strongest
years for faculty
and student
recruiting in quite
some time**

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As spring arrives in Cambridge, the urge to think of things in terms of seasons and cycles becomes difficult to resist. In that spirit, and with your kind indulgence, I offer these words about the season of renewal that I see taking place within BCS.

The timeline associated with graduate admissions is one of the most influential in the Department's yearly calendar and, with the most recent cycle just concluded, I am pleased to report that this year's applicant pool was one of the strongest in recent memory. In particular, the Molecular and Cellular Neuroscience program, a joint effort between BCS and Biology, attracted a large number of applicants—a direct result, I am convinced, of the collaborative training and research that the faculty associated with the program have been promoting.

The incoming class is rich in quality as usual, and in a significant change from last year, in quantity as well. You may recall that we took steps to limit the size of last year's class in the face of an uncertain fiscal environment. While we continue to be cautious about staying within our means, successful funding outcomes coupled with the generosity of notable Department benefactors will allow us to enroll 16 students in the next academic year, an increase of 45%. For this we thank, in particular, Barrie and Al Zesiger, Jeff and Nancy Halis, Paul and Anne Marcus, and Barbara and D. Reid Weedon, each of whom has donated one or more graduate fellowships to BCS in the last year. We are truly grateful for their support.

The BCS faculty is also experiencing a renewal. Following one of the strongest recruiting years that any of us can remember, the Department has made a number of offers to outstanding junior faculty candidates and expects to make still more over the next few months. The strength of the candidate pool is especially remarkable in that it extends to all areas of investigation within BCS. Given the trajectory of the Department's growth over the last decade, the relative dearth of hiring over the last two years due to budget restrictions has seemed rather dramatic; this year will more than make up for this.

Finally, funding for research in BCS is enjoying something of a renewal as well. At the same time that we are experiencing a short-term burst of funding due to the Federal stimulus package, a more sustained investment in resources that will benefit the entire Department is also underway. Among the facilities that will come on-line in the next year are a new MEG scanner, a 2-photon microscopy suite, and a stem cell facility. All of these represent significant enhancements to the core infrastructure of BCS.

On the Cover

Neural wiring of the rabbit retina reconstructed using tools and techniques developed specifically for the emerging field of connectomics.

This picture is assembled from images created using serial block-face scanning electron microscopy. The resulting stack of images is then analyzed to create a detailed reconstruction of the original tissue.

Connectomics seeks to develop the tools to create connectomes – structural summaries of neural networks – and to analyze these connectomes to better understand the brain. Using convolutional network machine learning approaches, Professor Sebastian Seung's lab has developed a number of the high-throughput processing tools that are increasingly needed to handle the very large data sets that this research can produce.

This image was created by Viren Jain, Srinivas Turaga and Sebastian Seung from BCS in collaboration with Kevin Briggman, Moritz Helmstaedter, and Winfried Denk from the Max Planck Institute for Medical Research, Heidelberg.

A Center for Moral Judgement in the Brain

In a recent paper published in the **Proceedings of the National Academy of Sciences**, post-doc Liane Young and BCS Professor Rebecca Saxe report that it is possible to affect a person's ability to make moral judgements by interfering with activity in a specific region of the brain.

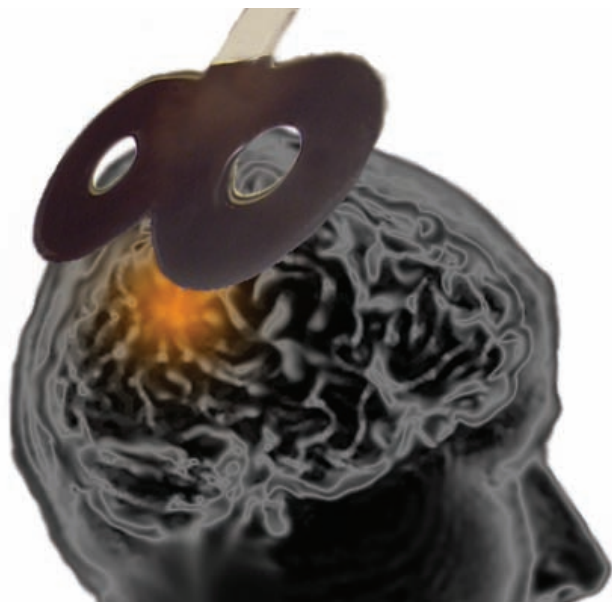
Rebecca has focused much of her research on the right temporo-parietal junction (RTPJ), which she has shown to be highly active when we think about other people's intentions, thoughts and beliefs. The ability to infer the intentions of others – frequently referred to as 'theory of mind' – is necessary to constructing moral judgements, and Rebecca and Liane wanted to see what would happen were the RTPJ not functioning correctly.

A series of experiments was run using transcranial magnetic stimulation (TMS) to selectively interfere with brain activity in the RTPJ. TMS uses a magnetic field applied to a small area of the skull to create weak electric currents that temporarily impede brain cells' ability to fire normally. A series of protocols had TMS applied either before or during questioning that asked participants to make moral judgments that require an understanding of other people's intentions – for example, a failed murder attempt.

After reviewing the results of experiments, the researchers found that when the RTPJ was disrupted, subjects were more likely to judge failed attempts to harm as morally permissible. The conclusion, therefore, was that TMS interfered with subjects' ability to interpret others' intentions, forcing them to rely more on outcome information to make their judgments.

Rebecca believes that while understanding other people's intentions is critical to judging them, it is just one piece of the puzzle and the Saxe lab is continuing its work to understand the processes and structures of the brain that are involved in moral judgement.

This research was supported by The National Center for Research Resources, the MIND Institute, the Athinoula A. Martinos Center for Biomedical Imaging, the Simons Foundation and the David and Lucille Packard Foundation.



Researchers in Rebecca Saxe's lab have found that disrupting the RTPJ can affect the ability to make moral judgements.
Image: Alvaro Pascual-Leone

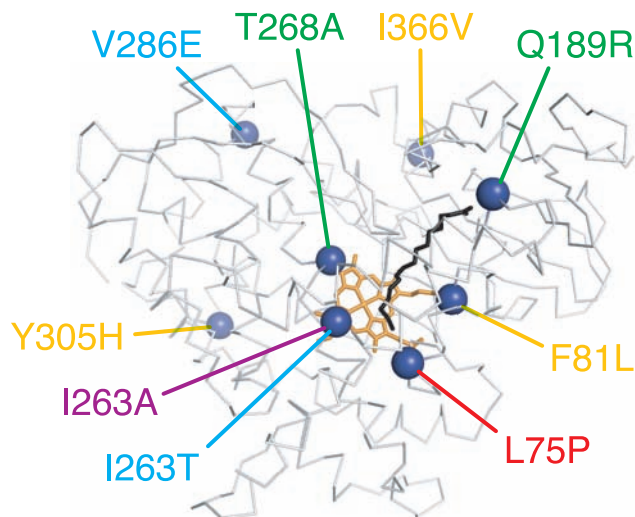
Beyond BOLD: New MRI Sensor Targets Dopamine

Professor Alan Jasanoff and a team of chemical engineers from Caltech have jointly developed the first magnetic resonance imaging (MRI) contrast agent that is sensitive to a specific neurotransmitter. The new sensor was developed using directed evolution techniques to modify the heme domain of the naturally-occurring bacterial cytochrome P450-BM3. The result is a molecule that shows a high affinity for the neurotransmitter dopamine and that can also be detected using MRI.

Traditionally, functional MRI brain imaging has relied on indirect measures of neural activity such as blood flow – the BOLD response. As useful as it is, BOLD only gives information about general activity, and it does so at a relatively low level of precision. Jasanoff and others in the field have recognized this problem and have directed their research efforts toward developing new contrast agents that can allow fMRI to measure brain activity directly and with a higher level of precision.

To build the new sensor, Jasanoff and his colleagues used the technique error-prone PCR to produce a number of mutations of the gene for P450-BM3. Each mutated gene was introduced into *e. coli* bacteria, which then produced variations on the wild-type protein. Following testing, two BM3-based sensors were found to bind well with dopamine and not with other neurotransmitters.

Although challenges remain, Jasanoff is excited by the results and will continue to look for improved dopamine sensors as well as contrast agents that target other processes in the brain.



X-ray crystal structure of wild-type BM3h protein showing the locations of amino acid substitutions resulting from the directed evolution process.
Image: Alan Jasanoff

BCS Makes Good Use of Stimulus Funding



Photos: Kent Dayton

Emilio Bizzi, Bob Desimone, and Ed Boyden all received NIH Challenge Grants

BCS researchers have enjoyed significant success in sourcing funding originated through the American Reinvestment and Recovery Act (ARRA) passed by Congress in 2009. Among the awards were two NIH Challenge Grants – high-priority projects providing up to \$1 million in funding for two years – given to University Professor Emilio Bizzi and to a joint project between Professors Bob Desimone and Ed Boyden.

Emilio Bizzi will be using the funding from his Challenge Grant to identify and track the processes of motor synergy development during stroke rehabilitation using a two-pronged approach of genetic studies in animal models combined with clinical work being conducted at Spaulding Rehabilitation Hospital in Boston. Although the scientific merits of a project that is among the 1% of 20,000 applications funded would seem obvious, Emilio notes that the process of applying for the Challenge Grant was, at least in part, a matter of good timing. He and his collaborators had just finished publishing a paper and were considering next steps when the request for applications was announced. With a solid ‘bench-ready’ project that would take about two years to complete, a Challenge Grant was a natural fit.

Bob Desimone and Ed Boyden were similarly successful with their application ‘Optogenetic Control of Attention Through Prefrontal Synchrony.’ Funded through the National Institute of Mental Health, the research will make use of new optogenetic technology, which can be used to stimulate cortical neurons with millisecond precision. By stimulating one portion of the prefrontal cortex (FEF) while recording from another (V4), Bob and Ed hope to shed light on fundamental mechanisms of attention – mechanisms that may be important to disorders such as schizophrenia, depression, and ADHD.

In addition to the Challenge Grants, BCS investigators received funding for more than 10 of the 68 stimulus research projects awarded to MIT by the NIH. Among these, Ted Adelson was awarded a significant grant to study visual material perception, Martha Constantine-Paton received supplemental funding for a two-photon microscope and Mriganka Sur will be studying the molecular and functional mechanisms that underlie binocular vision.

ARRA projects are awarded with the understanding that the monies provided will be used rapidly to provide as much economic benefit as possible in terms of employment and spending. Although there are obvious challenges to trying to pace science to meet economic objectives, the BCS investigators take their stewardship role seriously and are working to produce the best science they can while also meeting the larger objective of fiscal stimulus.

Noteworthy

FACULTY

Bob Desimone has won the Helmholtz Award of the International Neural Network Society.

Earl Miller gave the 2009 A.J. Carlson Memorial Lecture at the University of Chicago, and was the 2009 Engineering Distinguished Lecturer for the National Science Foundation.

Tomaso Poggio was awarded the 2009 Okawa Prize, named an AAAS Fellow, and was the 2010 Distinguished speaker, Heller Lecture Series in Computational Neuroscience at The Hebrew University of Jerusalem, Israel in January.

POST-DOCS

Aaron Andalman won the Capranica Prize in Neuroethology as well as the 2010 Harold M. Weintraub Award from the Fred Hutchinson Cancer Research Center.

Neville Sanjana received an Honorable Mention in the 2009 Olympus Bioscapes International Digital Imaging Competition at the American Society for Cell Biology (ASCB) conference in San Diego. The award was given for his movies of growing axons.

STAFF

Graduate Administrator **Brandy Baker** won the Infinite Kilometer award last Fall.

STUDENTS

Graduate student **Retsina Meyer** was awarded the Hugh Hampton Young Memorial Premium Fellowship for 2009/2010. The fellowship was created to foster the development of outstanding individuals with a great breadth of vision and interests, and the capacity for technical leadership.

Second year graduate student **Laura Lewis** was named the recipient of a Canadian Institute of Health Research Doctoral Research Award. Of the 739 applications that were considered, only two awards were given in Laura's category. The award will provide three years of support for her graduate studies.

Faculty Profile: Yingxi Lin

Born and raised in Southern China by two academics, Yingxi was imbued with the importance of education. Like most children in China growing up on university campuses, Yingxi's initial instruction was in a university-affiliated school, where she could have stayed until college. Instead, for her middle and high school years, she opted to attend a top selective school for Guangxi Province. "I was drawn to the boarding school because I wanted to meet kids from diverse backgrounds," Yingxi says, "and I made so many life-long friends. They were like my siblings."

She then attended Tsinghua University in Beijing, which appealed to her because of its interdisciplinary options. "The engineering program there helped me build instruments to be used in physics experiments," she says, "and Tsinghua allowed students to add research to their curriculum." After hours, she would build computer interface boards and write assembly codes to collect signals from nuclear physics experiments.

Because Chinese government policy precluded graduates from going abroad unless they had relatives there, Yingxi

"Overcoming obstacles is a required part of training in science."

stayed at Tsinghua to pursue a combined MS and PhD. The level of research there was 10 to 20 years behind that of other countries, so an eventual change in Chinese policy brought her to the Physics Department at Harvard. While pursuing research in medical physics, Yingxi took an HST class on MRI here at MIT, where she learned about Nuclear Magnetic Resonance (NMR) used to look at the atomic structures of molecules. Even though her high school biology classes hadn't interested her much, Yingxi became fascinated by the hypothesis-driven approaches used in modern biology. She did a rotation in Gerhard Wagner's NMR lab at Harvard Medical School, which developed NMR techniques and studied protein structures. "I went from knowing almost nothing about it to being truly wowed."

Neuroscience seemed to her the most challenging and exciting field in biology, and so Yingxi began research in Dr. Michael Greenberg's lab at Children's Hospital. "I was worse than a UROP," she says, remembering how challenging the work was for her, not having had any formal biology or neuroscience training. Her PhD thesis project was to study structural function of transcription factors. In

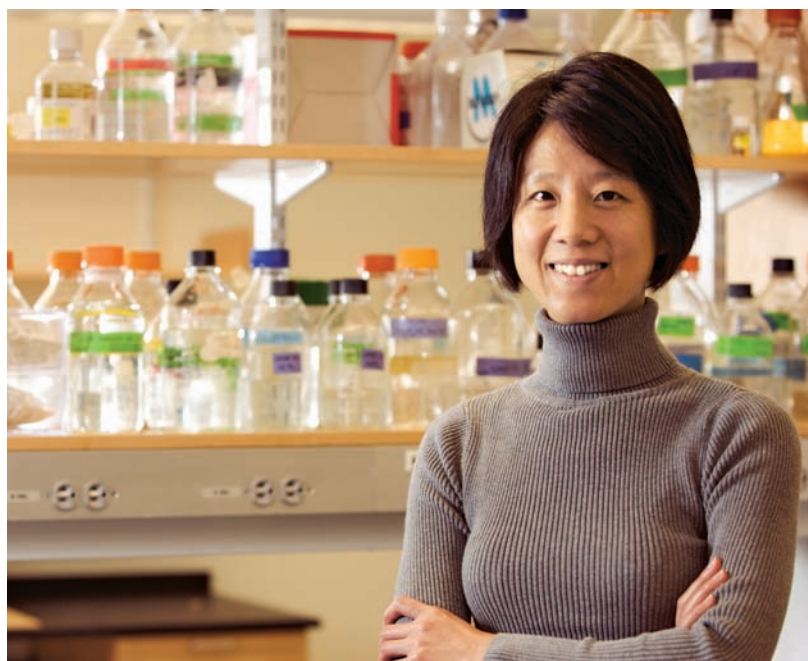


Photo: Kent Dayton

1996, Dr. David Allis and colleagues identified the first histone acetyltransferase (HAT) and showed that it is a homolog of the yeast transcriptional activator GCN5 (tGCN5). This groundbreaking work directly linked histone modification to transcription regulation for the first time. Yingxi collaborated with Dr. Allis and solved the structure of the HAT domain of tGCN5 with its cofactor, which was the first structure of a nuclear HAT. It was essential to produce large quantities of protein from limited amounts of bacteria for NMR structural studies. Purifying GCN5 meant many months of painstaking labor. The protein then turned out to be unstable at NMR experimental temperature, which Yingxi eventually solved by stabilizing it with its cofactor. The size of the protein made it difficult to solve its structure via conventional spectroscopic methods, so she had to develop new methodology along the way. In the end, it was very gratifying to meet the challenges and to be first to make the discovery. Yingxi believes that "overcoming obstacles is a required part of training in science."

For her postdoctoral training, Yingxi studied neuronal activity-dependent gene regulation in neurons. Her goal was to identify genes important for the development of synapses and neural circuits. She realized that a missing link in the field is that no one knows how our experiences change the inhibitory connections in the brain. From an engineering point of view, they function as negative feedback mechanism to keep the stability of neural circuits. When they are disrupted, it can lead to devastating neurological disorders such as epilepsy, mental retardation and autism. However, how inhibition is regulated remained an under-

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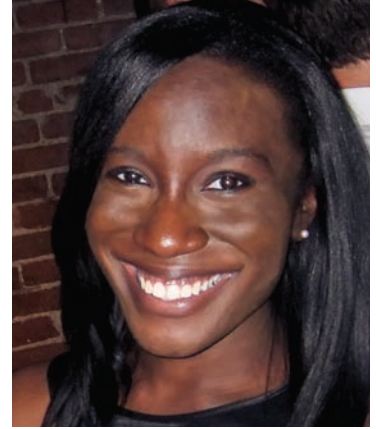
BCS Students Net Impressive Haul of Scholarships

The Class of 2010 has had a very good year with Course 9 undergrads winning three of the five Rhodes and Marshall Scholarships awarded to MIT students. BCS majors Ugwechi Amadi and Caroline Huang, who will be studying at Oxford University as Rhodes Scholars, are part of a record year for the Institute – this being the first year that 3 students have received this prestigious honor. Joining them for studies in the UK is Tanya Goldhaber, who will be a Marshall Scholar at Cambridge University.

Ugwechi Amadi, who served as President of the Brain and Cognitive Sciences Society, is a double major in BCS and Literature. An aspiring neurologist, she has availed herself of the many opportunities for research as an undergraduate at MIT. In addition to her UROP with Professor Ki Goosens, she has found time to work in a lab at Massachusetts General Hospital. And Ugwechi is equally serious about her literature studies, having been selected as an MIT Burchard Scholar in 2008 – a recognition of her excellence in the humanities.

Caroline Huang's extensive list of achievements features a frequent recurrence of the word 'public' - which makes perfect sense as she plans to pursue a doctorate in public health from the Ethox Centre at Oxford, where she will study the ethics of healthcare practice. From the first, Caroline has dedicated much of her considerable energy to outreach and public advocacy activities. As a freshman, she was a founder of MIT's chapter of Camp Kesem, a nonprofit student-run summer camp for children of cancer patients. As a BCS major with a minor in psychology, Caroline has been a UROP with Professors John Gabrieli and Laura Schulz.

Tanya Goldhaber may consider herself an engineer first, but her minor in brain and cognitive sciences has convinced her that there is much about human behavior that engineers could afford to understand. Her research in Professor Nancy Kanwisher's lab has focused on the neural and cognitive mechanisms underlying visual perception and cognition. Tanya plans to pursue a doctorate in design at the Engineering Design Centre at Cambridge.



Ugwechi Amadi (top) and Caroline Huang

BCS Debuts New Outreach and Diversity Programs



BCS Senior Research Scientist Sonal Jhaveri (center) leads a sheep brain dissection lab during the July HHMI workshop for biology teachers as participants Mary Dulko (left) from Brookline High School and Lydia Breen (right) from Stoneham High School look on.

BCS has launched two new programs with the goals of improving the depth of brain science education at the high school level and of enhancing the diversity of student populations in the fields of cognitive science and neuroscience. Held over the summer, a new internship program and a teacher's workshop on the brain provide rich opportunities for the Department to share its enthusiasm for science in general, and, particularly, the sciences of the brain and mind.

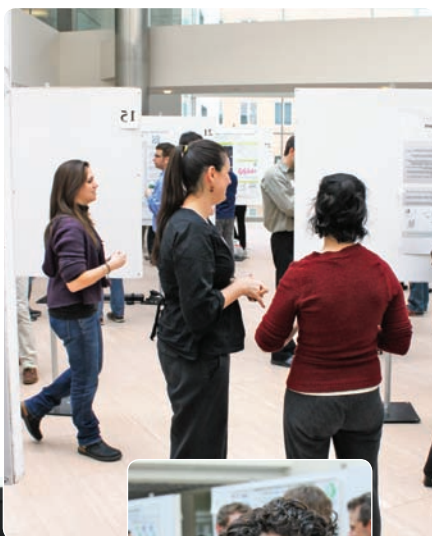
The new undergraduate summer research internship program seeks to identify and recruit talented students from small institutions and minority groups, and encourages them to pursue graduate degrees at top schools. It is hoped that the program will be an effective and powerful tool to enhance the diversity of students in the BCS graduate program. The first cohort of six BCS summer interns will start this coming June, and will be hosted by the Gabrieli, Litteton, Moore, Poggio, Saxe, and Tsai labs. The summer program is funded jointly by the MIT School

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Scenes from the BCS Holiday Party



Graduate Interview Day



New Beginnings

Postdoc **Emile Bruneau** became engaged to Stephanie Elson. They will be getting married in the Fall of 2010.

Postdoc **Aaron Andalman** is engaged to Wrenn Levenberg, an emergency room doctor at BMC. Prof. Ki Goosens and MGH Research Scientist Trey Hedden are the proud parents of Kalina Juliana Baylor, born February 7.

Thanks to son David, Technical Associate **Margo Cantor** is the happy grandmother of Eamon Charles Cantor, born March 10, 2010.

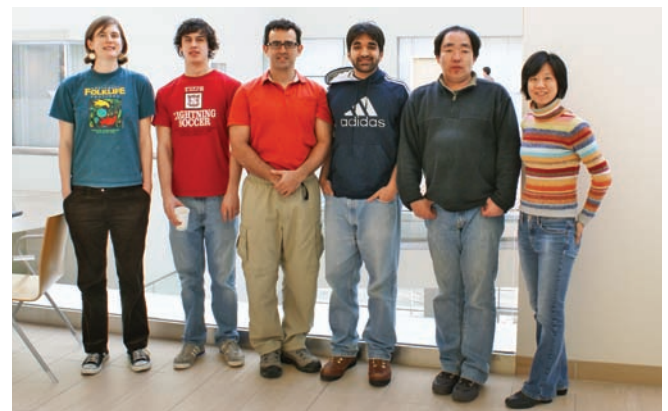
Research Scientist **Jill Crittenden**, husband Kyle and son Oliver were delighted to welcome a new addition to their family, Sylvia Crittenden, born Dec. 24, 2009.

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studied area in neurobiology due to the difficulties of the problem. Excited by the challenge and prospect of making a new discovery, Yingxi set out to identify key regulators of inhibitory synapses, a first step toward solving the problem. After years of hard work, she identified a novel molecular pathway that regulates the development of GABAergic synapses, the major type of inhibitory synapses in the brain.

She is continuing this line of work in her lab here, studying how GABAergic synapses are modulated in the brain by experience. Her lab is working to identify the molecular players needed for changing the inhibitory connections on neurons. She is also exploring how inhibition shapes the function of neural circuits and how GABAergic synapses are involved in information processing in the brain. In the future, Yingxi would like to fill the gap between molecular and systems neuroscience. “As a scientist, it is essential to reinvent yourself periodically,” she says, and believes she can do that here at MIT.

Outside of the lab, Yingxi enjoys art house movies, reading, exercising, and cooking. She often tries to recreate favorite restaurant dishes at home and finds the hobby scientific: “Cooking a new dish is like developing a new molecular biology protocol.” Yingxi most enjoys showing people how to do research—she very much favors a hands-on approach. She enjoys introducing newcomers to the excitement of scientific research. She had great mentors during her scientific career and would like to do the same in her own lab, opening doors for a new generation of scientists.



Yingxi Lin (right) and the members of her lab - (l to r): Robin French, Paul Jaffe, Gabriel Belfort, Kartik Ramamoorthi, Kenjiro Seki

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Lecturer Monica Linden leading a dissection for a rapt audience of seniors from Norfolk Agricultural High School.

of Science and by the Department. Dr. Mandana Sassanfar, who joined BCS last year to lead outreach and diversity efforts at the college and precollege level, will coordinate the program.

For a second year, BCS, in a joint program with the Department of Biology, will host a workshop on the brain for high school teachers. Last year's workshop had 16 participants from local schools, and featured lectures, demonstrations and lab exercises presented by members of the Gabrieli, Kanwisher, Moore, Saxe, and Tonegawa labs. This year's teacher workshop, “Vision and the Eye,” will again be supported by the Howard Hughes Medical Institute and the Eye Institute.

Also, this past March, BCS graduate and now Lecturer in the Department Monica Linden led several popular hands-on eye dissection activities for high school students during a science field trip to MIT. These high school and college outreach activities provide members of the BCS community with an opportunity to get involved in science education and mentoring at a time when neuroscience and cognitive science are emerging as the most exciting and challenging fields in science.