2018

Berkeley Neuroscience
HELEN WILLS NEUROSCIENCE INSTITUTE

Pulse

A Message from our Directors

Ehud Isacoff

Director, Helen Wills Neuroscience Institute and Berkeley Brain Initiative (2013-present)
Professor of Neurobiology, Molecular and Cell Biology Department

The heart of Berkeley Neuroscience is always our outstanding faculty members, their students and postdocs, and their individual research pursuits. So it is always a great pleasure to welcome new members to the family. Welcome to David Foster (Psychology), Na Ji (Physics and MCB), Markita Landry (Chemical and Biomolecular Engineering), Teresa Puthussery (Optometry), Rowland Taylor (Optometry), and Kevin Weiner (Psychology). We look forward to Eric Betzig (Physics and MCB) joining us this summer. I also want to congratulate our faculty members who have won prestigious awards as well as federal BRAIN Initiative funding to generate paradigm-shifting neurotechnologies.

Berkeley Neuroscience was founded on the principle that bringing faculty from diverse disciplines together in a common quest to understand the brain will move the field of neuroscience forward. The launch of the Berkeley Brain Initiative has amplified our multidisciplinary efforts, by defining new ambitious aims and generating productive collaborations between disciplines and with neighboring universities and industry partners. We made significant progress toward several of our major research initiatives this year, as described in the following pages.

A major aim in neuroscience is to use the knowledge gained from invasive animal studies of the brain to inform our understanding of human cognition. This has been difficult because animal and human studies have been performed at disparate scales. That is changing, thanks to technological advancements our faculty are working hard to achieve. Our Ultra-high resolution MRI will enable researchers to zoom in on the human brain, while our all-optical Million Neuron Cortical Modem will enable researchers to zoom out on the animal brain.

Our focus for the coming year is to enable the next wave of progress with a major fundraising campaign, to create new research capabilities and facilities, to hire additional top-notch faculty, and to expand support for students and postdoctoral fellows.

Michael Silver

Director, Neuroscience PhD Program (2017-present)
Associate Professor of Optometry and Vision Science and Neuroscience

It is an honor for me to assume the position of Director of the Neuroscience PhD Program, following Dan Feldman's five years of outstanding leadership and service to our neuroscience community.

Over the past year, our students have made critical contributions to many discoveries across all of neuroscience. After earning their PhD, our program alumni continue to make significant impact in careers in academia and industry. Since we awarded our first PhD in 2006, the vast majority of our 88 graduates have taken a postdoctoral research position. There are currently 25 alumni with academic faculty positions, 23 who are postdocs, and 29 who hold industry positions in a wide variety of companies.

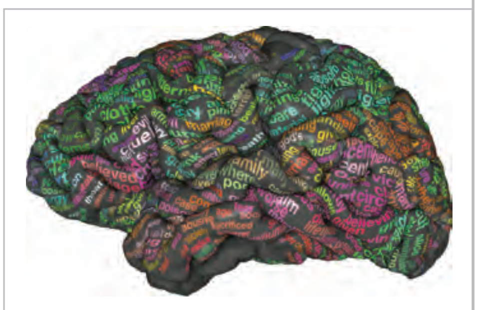
In the coming year, I look forward to many more research discoveries and technological breakthroughs by our neuroscience community and the continuing scientific development of our graduate students. With this group as part of the next generation of leaders in our field, the future of neuroscience is very bright indeed!

Major Research Initiatives

One third of Berkeley Neuroscience faculty are dedicated to the study of human cognition, asking questions about how we perceive the world, learn, age, process emotion, and make decisions to act. Another half study the neural correlates of perception and behavior using animal models. The technological advancements below will enable these parallel research efforts to come together and inform one another.

Unprecedented resolution for brain circuitry mapping

New MRI scanner design can image microcircuitry of the human cortex



Functional MRI recordings recently yielded insights into language perception. Ultra-high resolution MRI will produce more detailed functional maps of the cortex and reveal how they relate to the underlying circuitry.
Image courtesy of Jack Gallant.

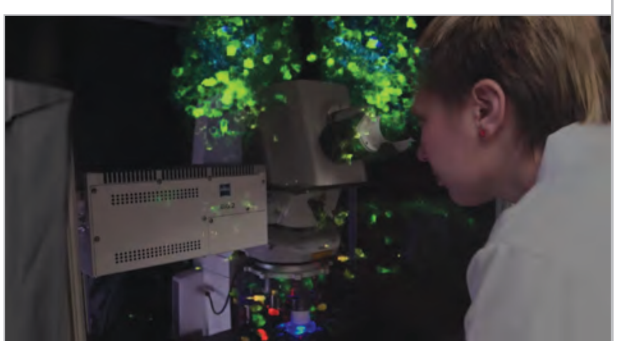
The human cerebral cortex contains about 20 billion neurons. These neurons are arranged into thousands of microcircuits, called cortical columns, which are networked together to form hundreds of anatomically and functionally distinct cortex areas. To understand human cognition, we need to visualize the coordinated activity of cortical columns across the cortex, and map the connections between them.

The best tool to non-invasively scan the structure and function of the human brain is magnetic resonance imaging (MRI). However, the best MR scanners at present cannot separate out signals from individual cortical columns. A multi-institutional team of scientists led by Adjunct Professor of Berkeley Neuroscience **David Feinberg,** PhD, MD, has completely redesigned critical 7T MRI components to boost resolution by a factor of 20. This is enough to visualize individual cortical columns and layers, and to identify thousands of brain circuits never before seen in humans.

Feinberg's team was awarded two grants totaling $18.53M from NIH plus $7M in campus funds to build the ultra-high resolution MR scanner at Berkeley. Once complete, this instrument will be a boon to basic research on human brain function, and will be used to study and diagnose neurodegenerative and neuropsychiatric disorders. It will provide "the most advanced view yet of how properties of the mind, such as perception, memory and consciousness, emerge from brain operations," said Feinberg.

Million neuron cortical modem

Testing theories of brain function in animals and humans



PhD Program student Irene Grossrubatscher measures and manipulates the coordinated activity of thousands of neurons in live zebrafish embryos as they engage in behaviors. The cortical modem will allow similar experiments in other animal models and humans.
Image from the video, "DARPA at Berkeley."

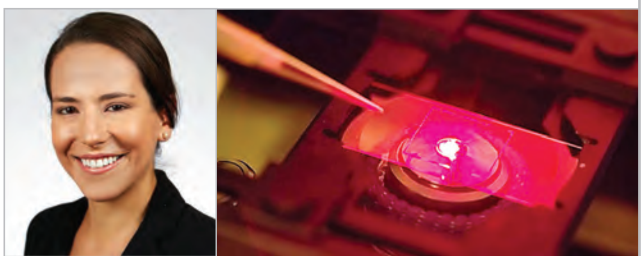
Chemical and genetic optical tools have revolutionized the field of neuroscience by enabling researchers to simultaneously measure and manipulate neural activity of hundreds of neurons at single cell resolution. To uncover the neural dynamics that give rise to perception and behavior, we need a window into larger populations of neurons, and we need to be able to compare animal and human studies.

This year, Berkeley researchers were awarded a contract for up to $21.6M from DARPA to create an all-optical cortical modem that can both record from a million neurons (read) and deliver patterned neuronal stimulation to hundreds of neurons (write) in the cortex. This window into the brain will enable neuroscientists to systematically test theories of brain function in animals and, eventually, in humans. DARPA envisions a future where a cortical modem may be used to stimulate visual perceptions for those who have lost their sight.

The cortical modem team includes engineers **Laura Waller, Ren Ng, Rikky Muller** and **Jose Carmena,** biologists **Hillel Adesnik** and **Ehud Isacoff,** and psychologists and computational neuroscientists **Jack Gallant, Fritz Sommer** and **Bruno Olshausen.**

Faculty Accomplishments

The Radical Ideas in Brain Science Challenge

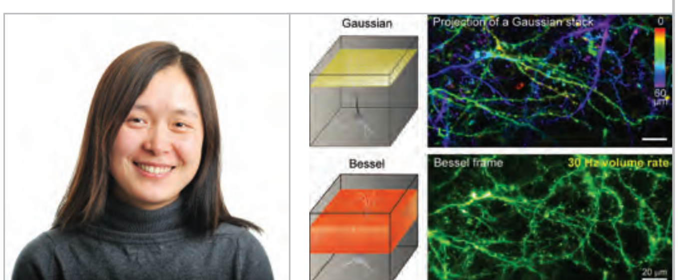


Markita Landry is developing nanosensors and infrared fluorescence microscopy to image brain chemistry.

In 2017 we launched The Radical Ideas in Brain Science Challenge, made possible through the generosity of Berkeley Brain Initiative donors Andrea and Peter Roth. This campus-wide competition for $300K in seed funding incentivizes collaborations across disciplines to make progress on the focus areas of the Berkeley Brain Initiative.

Our first award went to a team led by **Markita Landry,** Assistant Professor of Chemical and Biomolecular Engineering, Sloan Research Fellow in Neuroscience, and Chan Zuckerberg Biohub Investigator. Landry aims to advance the frontiers of neuroscience and psychiatry by creating new tools to study brain chemistry. For the Radical Ideas in Brain Science Challenge, Landry is developing dopamine nanosensors, and is teaming up with **Linda Wilbrecht, Marla Feller,** and **Jose Carmena,** who are using these sensors to study motivation, learning, social interactions, control of movement, and retinal circuits.

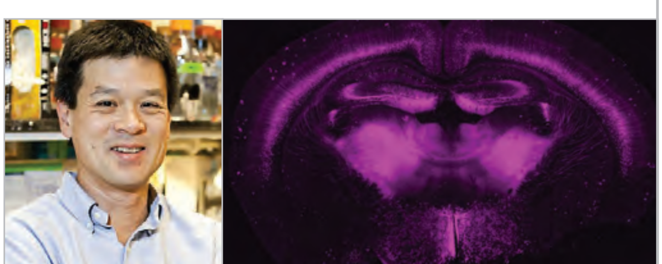
Na Ji awarded $2.7M from NIH BRAIN Initiative



Na Ji integrated Bessel focus scanning technology into a two-photon microscope to obtain 3D images of dendrites and dendritic spines at high speed, 30 Hz.

To understand information processing in neurons and neural circuits, we need to monitor neural activity in 3D at high speed throughout the living brain. Na Ji, Associate Professor of Physics and MCB, was awarded funds to accomplish just that. Having demonstrated 30 Hz volumetric imaging of neurons with Bessel focus scanning technology (BEST), Ji is now working to further optimize BEST performance. Her goal is to monitor whole-brain activity in the fly at >10 Hz and neuronal activity throughout the depth of the mouse cortex at ~2 Hz.

John Ngai leads Berkeley team in $65.5M NIH BRAIN Initiative consortium



John Ngai is systematically profiling gene expression of individual brain cells to classify them into cell types, then using a CRISPR-based approach to fluorescently tag each cell type in the mouse brain.
From Berkeley News, Photo by David Stafford and Rebecca Chance.

A major, multi-institutional effort is being made to build a comprehensive atlas of cell types and connections in the mouse brain. John Ngai's Berkeley team will use single-cell transcriptomics to generate a complete census of cell types in the brain, and use CRISPR gene editing technology to produce mice with each cell type tagged, both incredibly valuable resources for the neuroscience community. "Knowing how many different types of neurons there are in the brain has been an enormous, unsolved problem since Ramon y Cajal's initial description of neurons more than 100 years ago," Ngai said in a statement. "It is exciting that we can now develop and integrate tools from multiple disciplines to reveal the diversity of cell types in the brain, the most complex organ in the body."

Publications

RESEARCH DISCOVERIES

Lights on learning

Cortico-striatal feedback required to learn brain control of an external device

Areas of the brain that get input from the eyes can be hijacked to control something outside the brain, such as a computer that generates a tone. Yellow arrows represent feedback between the rat's visual cortex and striatum, which is key to learning new tasks.
From Berkeley News, image by Ryan Neely.

How does the brain learn to control an external device? In a study published in *Neuron*, researchers from the Costa lab at Columbia and the **Carmena lab** at UC Berkeley trained neurons that normally process visual input to control a computer-generated tone, and uncovered general circuit mechanisms for learning.

The co-first authors of the study, **Ryan Neely** and **Aaron Koralek,** are both recent graduates of the Neuroscience PhD Program. In a Q&A with Ryan Neely, he wrote, "I hope that this work will provoke discussion about commonalities in cortical function and how cortical circuits are tuned. My adviser, Dr. Carmena, often conceptualizes that the whole brain is wired for action. You might imagine that the cortex is capable of many different 'actions,' whether they be physical actions, cognitive actions, or perceptual actions. I think our work teases the notion that the learning process involved in a broad spectrum of mental or physical actions might be supported by a common sub-cortical circuit involving the basal ganglia – at least in an operant learning context."

The hidden link

Identifying cognitive processes that transform perception into action

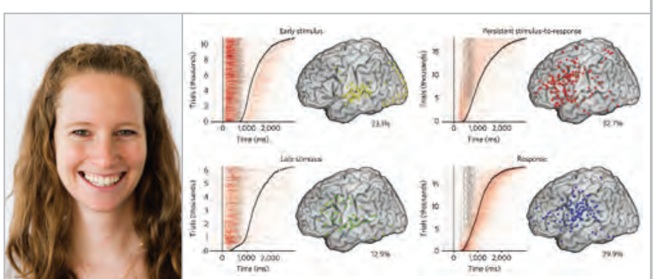


Figure from "Persistent neuronal activity in human prefrontal cortex links perception and action," Nature Human Behaviour, by Matar Haller (pictured) et al.

Berkeley researchers want to know how the brain uses incoming sensory information to generate actions. In a study published in *Nature Human Behaviour*, the **Knight lab** found that the prefrontal cortex is the central hub of a distributed cortical network that becomes active during the time between stimulus presentation and behavioral response.

First author and recent PhD Program graduate **Matar Haller** writes, "In this paper we defined a new analysis technique that enabled us to group neuronal populations across cortex in an objective, data-driven manner. We found robust functional heterogeneity across cortex that was more strongly correlated with behavior than activity derived from classical regions of interest. This finding can inform standard analysis techniques that test hypotheses based primarily on predefined regions of interest."

The path to happiness is complicated

Dopamine circuitry in the brain

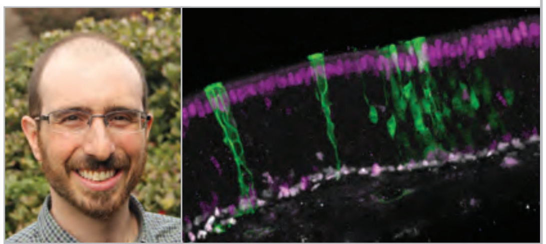
Cookies, a rewarding stimulus, are used to depict a simplified dopamine circuit.
Design by Christine Liu using cookie cutters by Crystal L. Lantz.

Through in-depth studies of dopamine circuitry, the **Lammel lab** discovered that there are different dopamine sub-circuits that produce opposing behaviors. In a study published in *Neuron*, they demonstrated that stimulation of one sub-circuit resulted in reward seeking, while stimulation of the other sub-circuit caused general behavioral inhibition.

First author and postdoctoral fellow **Hongbin Yang** writes, "In order for a species to survive in a changing environment the brain needs to constantly coordinate between positive and negative environmental stimuli (e.g., stimuli that promote pleasure or pain). If we understand the underlying circuitry and the neural code that mediates this decision process, we can ultimately develop better treatment strategies for addiction and other neuropsychiatric disorders where dysfunction of the neural systems underlying motivated behaviors have been strongly implicated."

The promise of stem cells

Regeneration in the adult nervous system



Example of lineage-traced cells in the regenerating olfactory epithelium, including sustentacular (support) cells, neurons, and stem cells.
Photo by Levi Gadye (pictured).

Some neural tissues in the periphery can completely recover following injury by regenerating sensory neurons and other cell types that have been damaged. In a study published in *Cell Stem Cell*, researchers in the **Ngai lab** tracked stem cells that were generated following injury. The authors utilized sophisticated single-cell techniques to monitor changes in gene expression as the stem cells differentiated into neurons and other cell types. They discovered mechanisms used by stem cells in response to injury, which may provide insight into neurogenesis and repair in other neural tissues.

Co-first author and recent PhD Program graduate **Levi Gadye** expands on this idea, saying, "The stem cells of the olfactory epithelium do remarkable things in the nose, but they would be more valuable as a potential therapy if we knew how to grow them in Petri dishes. If the right conditions were worked out for propagating these stem cells *in vitro*, scientists could grow millions of them from just a few thousand harvested from a patient's nose, and then conceivably transplant them into the brain to replace damaged brain tissue. In other words, it would be great to see a research group finally tame adult olfactory stem cells for medical purposes."

Read full Q&As about these research discoveries on our website: neuroscience.berkeley.edu/tag/phd-student-publications/

PERSPECTIVES

The emperor's new wardrobe

Rebalancing diversity of animal models in neuroscience research

In a *Science* review, **Michael Yartsev** reports that neuroscience has been converging on a handful of standardized animal models, limiting our understanding of the brain, and suggests that we change tack. Comparative studies are needed to determine whether or not scientific findings generalize across species. Yartsev convincingly argues that comparative studies are especially important for translational research, where animal studies are used to identify therapies that may work in humans.

Why We Sleep

Matthew Walker's *New York Times* bestseller, "Why We Sleep: Unlocking the Power of Sleep and Dreams," guides readers through decades of research and clinical practice to answer many important questions about sleep. Walker's book aims to bring awareness to what he calls a "silent sleep loss epidemic." Insufficient sleep is a risk factor for, or cause of, every major disease killing individuals in first world countries.

Four ethical priorities for neurotechnologies and AI

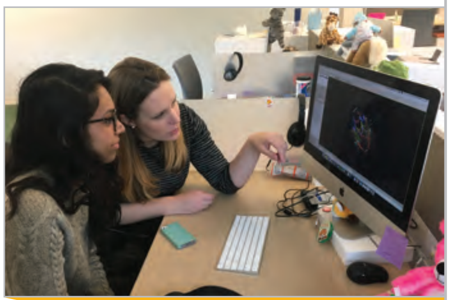
A man with a spinal-cord injury (right) prepares for a virtual cycle race in which competitors steer avatars using brain signals.
Photo BSIP/UIG/GETTY.

A working group comprised of neuroscientists, engineers, clinicians, and ethicists say that new ethical guidelines are needed for rapidly advancing brain-computer interface technologies. In a *Nature* commentary, the group (including our own **Jose Carmena** and **Jack Gallant**) highlights four areas of concern. Neural devices that connect to the internet are a **privacy** risk for the user. Neural devices that stimulate the brain must allow individuals to maintain their **agency and identity.** Technological **augmentation** of human abilities raises issues of equitable access and discrimination. Technologies are subject to the **bias** of their creators, and as such can privilege certain groups and harm others. The authors recommend regulations and best practices to keep these concerns in check.

Alumni Profiles

The changing brain

Allyson Mackey studies the human brain during development and learning



Allyson Mackey (right) working in her lab at UPenn.

"People are the most important part of science. For science to be fun, you have to be working with people that you like and respect."
Allyson P. Mackey, PhD Program alum (entering class of 2007)

Allyson Mackey is currently Assistant Professor of Psychology at the University of Pennsylvania, where her research group uses neuroimaging to study human brain plasticity during learning. In particular, Mackey is interested in the influence of socioeconomic status on the developing brain, and academic interventions that may reduce the income achievement gap.

Mackey's PhD studies in **Silvia Bunge's lab** showed how intensive training can improve reasoning ability and change brain structure and connectivity. As a postdoc in John Gabrieli's Lab at MIT, she identified neuroanatomical differences in adolescents from higher income versus lower income groups.

In her own lab, Mackey's group collects their own neuroimaging data and takes advantage of the rich set of developmental neuroimaging data now openly available. With these big data sets her lab is able to ask better questions about how specific environmental influences shape the developing brain.

Berkeley Neuroscience: Why did you choose the Berkeley Neuroscience PhD Program?

APM: I was looking for labs that did developmental neuroimaging and there weren't many at the time. I was drawn to Silvia's research and made her this pitch that I was interested in socioeconomic status and she was open to the idea. When I visited I felt like faculty respected students and treated them as their intellectual equals in a way that I found very inspiring..

Working side by side

Ariel Rokem is a data scientist for academia

Ariel Rokem talking with attendees of Neurohackademy, an annual summer course he co-organizes at the University of Washington eScience Institute.
Photo by Chris Gorgolewski.

"Once we figure out how to collaborate, there are a lot of things we can do that we couldn't do otherwise."
Ariel Rokem, PhD Program alum (entering class of 2005)

Ariel Rokem is a Data Scientist at the University of Washington eScience Institute, where he collaborates with researchers from diverse fields to develop and maintain software for the analysis of large data sets. Rokem describes his path from experimental scientist to data scientist as a gradual shift. By the time Rokem joined the Berkeley Neuroscience PhD Program he had taken extra classes in math and programming, spent a year doing electrophysiological and computational studies of the grasshopper auditory system, and completed a master's degree studying the differences in hearing and memory between blind and sighted people. During both his PhD studies with **Michael Silver** at Berkeley and postdoc with Brian Wandell at Stanford, Rokem continued doing experimental studies while taking on side projects developing software to analyze human neuroimaging data.

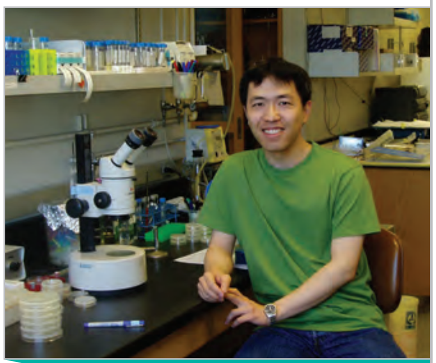
Rokem describes several key motivations for his current work: to create software that can take biomedical imaging data and make inferences that inform clinical decision making, to make research more reproducible and robust, and to put forth new collaborative models for practicing science.

Berkeley Neuroscience: What made this position at the eScience Institute a good fit for you?

AR: By the time I finished my postdoc, I realized I was not going to be a traditional researcher following the traditional faculty path. At the time the eScience Institute was getting off the ground and their focus was specifically on software, reproducibility, and collaborative models of working together between disciplines. It is an interesting model, and one that I really thrive within. All of the things that made me ill-suited to be a focused researcher in the traditional faculty model made me really good for what I am doing now. A lot of what I need to do is this lateral thinking of connecting between ideas in different disciplines.

To die will be an awfully big adventure

Peter Pan studies neuron aging



Pan as a PhD student in the Garriga lab.

"Science is science, and scientists should stick to science for its own good."

Peter Pan, PhD Program alum (entering class of 2003)

Chun-Liang (Peter) Pan is currently Associate Professor at National Taiwan University where he investigates the genetic program of neuronal aging and how neurons interact with other cell types to coordinate responses to stress. He studies these questions by taking advantage of the powerful genetic tools and relatively short life span of our favorite worm, *C. elegans*.

Pan has had a unique career path, from medical school to military service to studying fundamental neuroscience in *C. elegans*. He described his time as a PhD student in **Gian Garriga's lab** as "one of the most rewarding phases in my entire life." In addition to his thesis work on nervous system development and neurite pathfinding, it was here that he took courses in genetics and received a solid foundation in the basic biosciences. He also described his appreciation for the multidisciplinary nature of the Berkeley Neuroscience PhD Program and resulting exposure to the cognitive, systems, and engineering aspects of neuroscience.

Berkeley Neuroscience: Is there anything you would like to share with prospective Berkeley Neuroscience PhD Program students?

PP: I had a very stupid idea because I was a medical student by training, I thought I would be better off in a program that was associated with a medical school. And Berkeley was not like that. In the end I found the experience at Berkeley really dragged me out of my comfort zone and showed me a completely different aspect of scientific experience. I would encourage people to join Berkeley because it offers you a completely different perspective about science.

The stuff of friendship

Annaliese Beery studies the neuroendocrinology of peer affiliation

Annaliese Beery studies social behavior in voles.

"I guess I kind of like to do my own thing."

Annaliese Beery, PhD Program alum (entering class of 2003)

Annaliese Beery is currently Associate Professor of Psychology at Smith College. Beery has an infectious enthusiasm for her research, which is broadly concerned with how environment and experience affect the brain to influence behavior. A major focus of her lab is a continuation of the work she started during her PhD studies with **Irv Zucker** at UC Berkeley – the neuroendocrinology underlying variation in social behavior.

Neuroendocrinology refers to the bi-directional influence between hormones and the brain. Some hormones, such as oxytocin, play a big role in social behaviors. To see how oxytocin signaling varies with sociality, Beery traveled to multiple South American countries to collect samples from different species of rodents with varying social behavior. Back in the lab, she looks at how oxytocin receptor distribution varies across the brain samples from different species, and how that relates to behavior and phylogeny. "That's how we gain understanding of what generalizes across many different species and potentially to humans, and what is really specific," says Beery. "Comparative studies can inform our understanding of the evolution of social behavior and the mechanisms that support it."

Berkeley Neuroscience: What made Smith College a good fit for you?

AB: I went to a liberal arts college, and I love teaching, so I wanted a place where both research and teaching would be valued. Smith has a lot of support for science research with undergraduates, and sends more students to graduate school than almost any other liberal arts college. Did I mention the really great students? I appreciate being part of this excellent science education for women. I benefited from several awesome mentors during my early training (shout out to Julie Stokstad, Donna Rowley, and Liz Adler!), and it is a pleasure to mentor these incredible women in science.

Read full versions of alumni profiles on our website:
neuroscience.berkeley.edu/ph-d-program/alumni-profiles/

Honors and Awards

Yang Dan, Professor of Neurobiology and Howard Hughes Medical Institute Investigator, and **Ehud Isacoff,** Professor of Neurobiology, were elected to the National Academy of Sciences.

Marla Feller, Professor and Head of Neurobiology, **Mark D'Esposito,** Professor of Psychology and Director of the Henry H. Wheeler, Jr. Brain Imaging Center, and **Robert Knight,** Professor of Psychology, were elected to the American Association for the Advancement of Science.

Christopher Chang, Professor of Chemistry, Class of 1942 Chair, and Howard Hughes Medical Institute Investigator, and **Robert Knight,** Professor of Psychology, were elected to the American Academy of Arts and Sciences.

Stephen Brohawn, Assistant Professor of Neurobiology, was named one of three 2017 New York Stem Cell Foundation Robertson Neuroscience Investigators. His research aims to understand how the nervous system senses and responds to physical forces, such as touch or sound, and may provide a basis for the development of drugs that target these proteins to restore hearing loss.

Michael Yartsev, Assistant Professor of Bioengineering and Neuroscience, was awarded a 2017 Packard Fellowship for Science and Engineering to investigate the attributes of the mammalian brain that support the human ability to acquire language. To do this, Yartsev studies bats, one of the only known vocal-learning mammals on the planet.

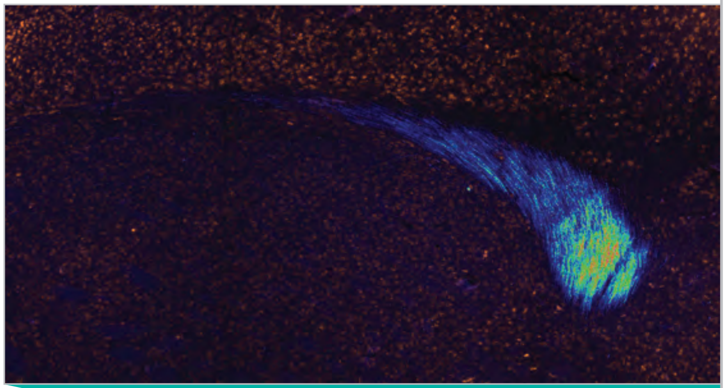
Kaoru Saijo, Assistant Professor of Immunology and Pathogenesis, was awarded a four-year Pew Scholar grant to investigate the role of the brain's immune cells, called microglia, in the development of depression.

Richard Kramer, Professor of Neurobiology, was named a Gund-Harrington Scholar to further develop a photoswitch drug candidate for retinitis pigmentosa.

Helen Bateup, Assistant Professor of Neurobiology, received the 2018 C.J. Herrick Award in Neuroanatomy and the 2017 Janett Rosenberg Trubatch Career Development Award for her contributions to understanding the molecular and cellular basis of neural circuit function, with direct implications for early childhood neurological diseases.

Stephan Lammel, Assistant Professor of Neurobiology, received a Hellman Fellowship for his research on midbrain dopamine circuits in reward-based behaviors and pathological changes in addiction and mood disorders.

Jose Carmena and **Michel Maharbiz,** Professors of Electrical Engineering and Computer Sciences, received a 2017 McKnight Technological Innovations in Neuroscience Award to further develop Neural Dust: an ultrasonic, miniature technology for wireless neural recordings in the brain.



Divided Night, by PhD Program student Tobias Schmid. The external capsule separates the striatum from the cortex in Rousettus aegyptiacus (Egyptian fruit bat). Different color layers are applied to the individual filters to create the appearance of a comet flashing across a divided night sky.

Ways to give

You can support the research efforts of our faculty, postdocs, and students by making an online donation at this link:

give.berkeley.edu/browse/index.cfm?u=136

To learn more about making a gift to neuroscience research at Berkeley, please contact:

Patrick Gutteridge
Senior Director of Development for the Berkeley Brain Initiative
gutteridge@berkeley.edu
510.664.4240

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