BIGGER THAN A BUILDING

Hundreds of people have blazed their career trails after doing research at the Picower Institute, creating an 'alumni' community that spans the globe and a wide variety of roles

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Neuroscience News

SPRING 2021

THE PICOWER INSTITUTE
FOR LEARNING AND MEMORY

DIRECTOR'S **MESSAGE**

Dear Friends,

At a research institute, our most obvious "deliverable" is discovery, readily measured in papers published. But we also take tremendous pride in something else: That hundreds of Picower people who have made these discoveries possible then go out into the world with the training, knowledge and inspiration they gained here to change the world even more. In this issue we feature our first-ever foray into counting and celebrating this community.

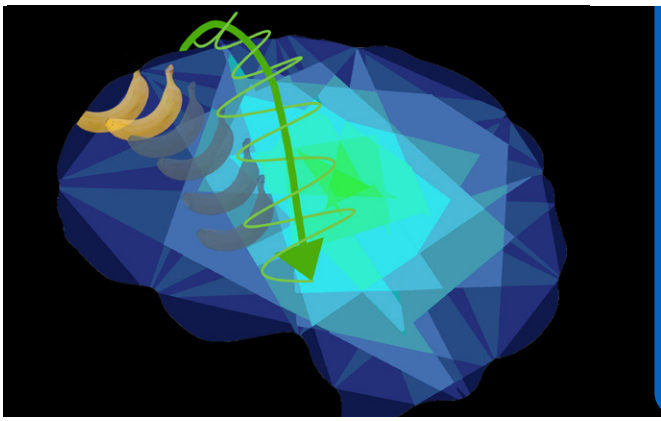
By any accounting, our alumni and former research staff compose an influential cohort that is making an impact in many different ways all over the world. You can read about what they are doing now, and what their time here meant to some of them, on page 8.

This community is one that will continue to grow. The new research advances and papers you can read about in this issue reflect the hard work of young scientists and scholars whose future largely lies ahead. As you can read on the immediately following pages, they have revealed how the brain keeps track of what we see, how it infuses a sense of timing in memory, how we override reflexes, and how we highlight what's surprising. Other studies showcase innovations such a way to watch neurons in the act of fine tuning their response to experience, and a system for advanced analysis of 3D 'minibrain' tissue cultures.

Some of you reading this may be among those who've stood at our lab benches and walked our halls, but whether you have or not, we are grateful for your engagement with us through this newsletter and in other ways. Our events have gone online in the Covid era, for instance, and as we think more about the impact of travel on climate, we foresee continuing to produce events online even after physical gatherings are safe again. Please join us as often as you can. You are welcome in our global, growing community.

LI-HUEI TSAI, DIRECTOR
The Picower Institute for Learning and Memory

As you look around, mental images bounce between right and left brain



When an object shifts in our field of view, the memory trace is transferred from one hemisphere to the other. Image by Jessica Bell.

Ask anyone from a quarterback scanning the field for open receivers to a mom watching her kids at the park: We depend on our brain to hold what we see in mind, even as we shift our gaze around. This capability of "visual working memory" feels effortless, but a new study shows that the brain works hard to keep up. Whenever a key object shifts across our field of view—either because it moved or our eyes did—the brain immediately transfers a memory of it by re-encoding it among neurons in the opposite brain hemisphere.

The finding, published in *Neuron*, explains how we can keep continuous track of what's important, even though our visual system's basic wiring requires mapping what we see on our left in the right side of our brain and vice versa.

"You need to know where things are in the real world, regardless of where you happen to be looking or how you are oriented at a given moment," said study lead author Scott Brincat, a postdoctoral researcher in the lab of Picower Professor Earl Miller, the senior author. "But the representation that your brain gets from the outside world changes every time you move your eyes around."

The memory transfer, which occurs in mere milliseconds, recruits a new group of neurons in the prefrontal cortex of the opposite brain hemisphere to store the memory. This new ensemble of neurons encodes the object based on its new position, but the brain continues to recognize it as the object that used to be in the other hemisphere's field of view.

That ability—to remember that something is the same thing no matter how it's moving around relative to our eyes—is what gives us the freedom to control where we look, Miller said.

"If you didn't have that, we would just be simple creatures who could only react to whatever is coming right at us in the environment, that's all," Miller said. "But because we can hold things in mind, we can have volitional control over what we do. We don't have to react to something now, we can save it for later."

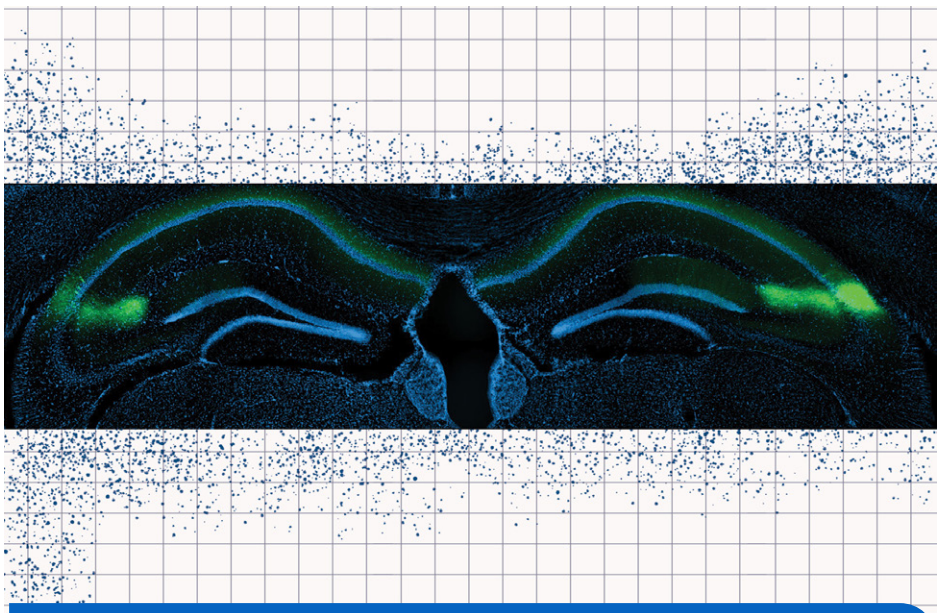
In the lab, the researchers measured the activity of hundreds of neurons in the prefrontal cortex of both brain hemispheres as animals played a game where they had to remember what they saw. On some rounds they had to change their gaze so that the object they had to remember shifted in their mind's field of view. The team trained a computer program to identify patterns in neural activity that indicated the memory of the object image. The analysis showed that when the animals shifted their gaze across the screen, neural activity encoding the memory information shifted from one brain hemisphere to the other.

The team also found that the interhemispheric transfer of a memory consistently occurred with a signature change in brain rhythms. As the transfer occurred, the synchrony across hemispheres of very low frequency "theta" waves and high frequency "beta" waves rose and the synchrony of "alpha/beta" waves in a middle frequency range declined. This push-and-pull pattern of rhythms closely resembles one that Miller's lab has found in many studies of how the cortex employs rhythms to transmit information.

Brain circuit encodes timing in **memory**

When we experience a new event, our brain records a memory of not only what happened, but also its context, including the time and location. A new study sheds light on how the timing is encoded in the hippocampus, and suggests that time and space are encoded separately.

The researchers identified the circuit that mice used to store information about the timing of when they should turn left or right in a maze. When this circuit was blocked, the mice were unable to remember which way they were supposed to turn next. However, disrupting the circuit did not appear to impair their memory of where they were.



Pyramidal cells (green) in the CA2 region of the hippocampus help store critical timing information. Image by Tonegawa Lab, edited by MIT News

The findings in the *Proceedings of the National Academy of Sciences* add evidence for the idea that when we form new memories, different populations of neurons in the brain encode time and place information, the researchers say.

"There is an emerging view that 'place cells' and 'time cells' organize memories by mapping information onto the hippocampus. This spatial and temporal context serves as a scaffold that allows us to build our own personal timeline of memories," says lead author Chris MacDonald, a research scientist in the lab of senior author Susumu Tonegawa, Picower Professor of Biology and Neuroscience at the RIKEN-MIT Laboratory of Neural Circuit Genetics at the Picower Institute.

In 2011, MacDonald and the late Howard Eichenbaum, a professor at Boston University, discovered cells that keep track of time in a part of the hippocampus called CA1.

In that study, MacDonald, who was then a postdoc, found that these cells showed specific timing-related firing patterns when mice were trained to associate two stimuli — an object and an odor — that were presented with a 10-second delay between them. When the delay was extended to 20 seconds, the cells reorganized their firing patterns to last 20 seconds instead of 10.

In the new study, the researchers wanted to investigate which other parts of the brain might be feeding CA1 timing information. Some previous studies had suggested that a nearby part of the hippocampus called CA2 might be involved in keeping track of time. CA2 is a very small region of the hippocampus that has not been extensively studied, but it has been shown to have strong connections to CA1.

To study the links between CA2 and CA1, the researchers used an engineered mouse model in which they could use light to control the activity of neurons in the CA2 region. They trained the mice to run a figure-eight maze in which they would earn a reward if they alternated turning left and right each time they ran the maze. Between each trial, they ran on a treadmill for 10 seconds, and during this time, they had to remember which direction they had turned on the previous trial, so they could do the opposite on the upcoming trial.

When the researchers turned off CA2 activity while the mice were on the treadmill, they found that the mice performed very poorly at the task, suggesting that they could no longer remember which direction they had turned in the previous trial.

"When the animals are performing normally, there is a sequence of cells in CA1 that ticks off during this temporal coding phase," MacDonald says. "When you inhibit the CA2, what you see is the temporal coding in CA1 becomes less precise and more smeared out in time. It becomes destabilized, and that seems to correlate with them also performing poorly on that task."

When the researchers used light to inhibit CA2 neurons while the mice were running the maze, they found little effect on the CA1 "place cells" that allow the mice to remember where they are. The findings suggest that spatial and timing information are encoded preferentially by different parts of the hippocampus, MacDonald says.

"One thing that's exciting about this work is this idea that spatial and temporal information can operate in parallel and might merge or separate at different points in the circuit, depending on what you need to accomplish from a memory standpoint," he says.

MacDonald is now planning additional studies of time perception, including how we perceive time under different circumstances, and how our perception of time influences our behavior. Another question he hopes to pursue is whether the brain has different mechanisms for keeping track of events that are separated by seconds and events that are separated by much longer periods of time.

The circuits where executive control **overcomes instinct**

Sometimes you swerve by reflex. Sometimes you choose to steer. Circuits in the brain help you do both.

When riding your bike through the city you might have two very different reasons to steer: plain old reflex when a car cuts you off or executive control when you see street signs that indicate your next turn. A new study by MIT neuroscientists shows how the brain is wired for both by tracking the specific circuits involved and their effect on visually cued actions.

The research, published in *Nature Communications*, demonstrates in mice that neurons in the anterior cingulate cortex (ACC) area of the prefrontal cortex, a region known for exerting executive control, projects connections into an evolutionarily older region called the superior colliculus (SC). The SC carries out basic commands for reactive, reflexive movement. A key finding of the study is that the purpose of the ACC's connections to the SC is to override the SC when executive control is necessary.

"The ACC provides inhibitory control of this ancient structure," said senior author Mriganka Sur, Newton Professor of Neuroscience in The Picower Institute. "This inhibitory control is a dynamic entity depending on the task and its rules. This is how a reflex is modulated by cortical control."

Lead author Rafiq Huda, an assistant professor at Rutgers University and a former postdoc in Sur's lab, added that by looking at specific circuits between the ACC and both the SC and the visual cortex (VC), the researchers could resolve uncertainty about how the cortex regulates more basic brain regions during decision-making.

To make their findings, the team first traced circuits going into and out of the ACC from both the VC and the SC, confirming that the ACC was in a prime position to integrate and process information about what the mice saw and what to do about it.

After tracing these ACC-SC and ACC-VC circuits, the team then trained mice to play a video game that required both sensation (seeing a cue on one side of the screen or the other) and action (spinning a trackball to move the cue). One group of mice had to move the cue inward toward screen's center. The other group had to move the cue outward toward the screen's edge. In this way, cues could be on either side visually and different groups of mice had to move them according to different rules.

Under natural conditions the SC would reflexively direct movement of the mouse's head, for instance swiveling toward a stimulus to center it in view. But the scientists needed to keep the head still to make their observations, so they devised a way for mice to steer the stimulus on the screen with their paws on a trackball.

Over a series of experimental manipulations, the mice essentially experienced two basic situations: One in which the correct movement would be consistent with moving the object into the center of their field of view—a natural reflex—and one in which the correct movement would be to move it further toward the edge of their field of view—a counterintuitive action done only when rules require.

As the mice played, the scientists observed the activity of neurons in the various regions to learn how they responded during each task. Then the researchers manipulated the neurons' activity using optogenetics, a technique in which cells are genetically engineered to become controllable by flashes of light. These manipulations allowed the scientists to see how inhibiting neural activity within and between the regions would change behavior.

When the scientists inactivated neurons in the SC, they found that mice struggled to make the natural reflexive movement. When the scientists instead inactivated input from the ACC to the SC, mice did the reflexive movement correctly *more* often but performed worse in making the counterintuitive movement required by task rules. The job of ACC inputs, it seemed, was to override the SC's reflexive inclination. When that override was disabled, the SC's preference for moving a cue into the middle of the field of view was unchecked. But the ability of the mouse to move stimulus further out of the field of view was compromised.

"Those results suggest that the SC and the ACC-SC pathway facilitate opposite actions," the authors wrote. "Importantly these findings also suggest that the ACC-SC pathway does so by modulating the innate response bias of the SC."

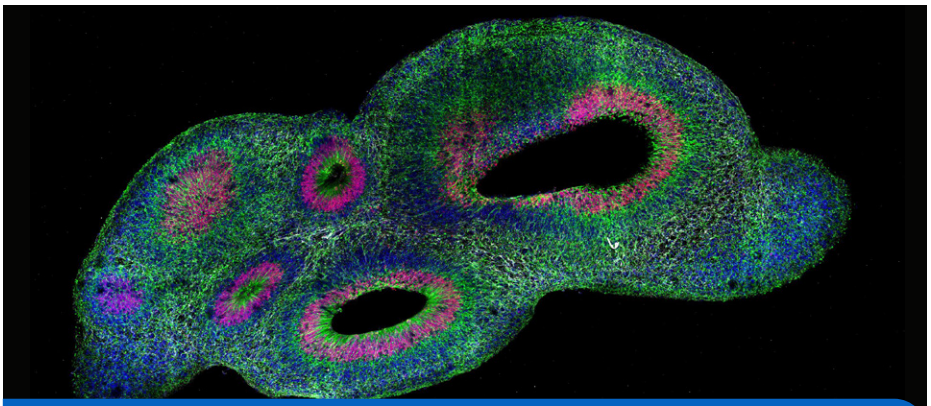
Sur said the findings accentuate the importance of the prefrontal cortex (in this case, specifically the ACC) in endowing mammals with the intelligence to follow rules rather than reflexes, when needed. It also suggests that developmental deficits or injury in the ACC could contribute to psychiatric disorders.

'SCOUT' helps researchers analyze **'minibrains'**

The ability to culture cerebral organoids or "minibrains" from stem cells has given scientists experimentally manipulable models of human neurological development and disease, but not without confounding challenges. No two organoids are alike and none of them resemble actual brains. This "snowflake" problem makes scientifically meaningful comparisons difficult. To overcome that limitation, MIT neuroscientists and engineers have developed a new pipeline for clearing, labeling, 3D imaging and rigorously analyzing organoids.

Called "SCOUT" for "Single-Cell and Cytoarchitecture analysis of Organoids using Unbiased Techniques," the process can extract comparable features among whole organoids despite their uniqueness – a capability the researchers demonstrated via three case studies in their new paper in *Scientific Reports*. In one of the case studies, for example, the team reported new patterns of disruption in organoid development from Zika virus infection, providing new insights into why babies born to infected mothers can exhibit severe neurological deficits.

"When every organoid is a snowflake and has its own unique combination of features, how do you know when the variability you observe is because of model itself rather than the biological question you are trying to answer?" asked study co-lead author Alexandre Albanese, a research scientist in the lab of the paper's senior author, Associate Professor Kwanghun Chung. "We were interested in cutting through the noise of the system to make quantitative comparisons."



This cross-section of an organoid processed with SCOUT shows cells labeled with various antibodies to highlight different cell types

Albanese co-led the research with former MIT chemical engineering graduate student Justin Swaney. The team has taken the added step of sharing their software and protocols on GitHub so that it can be freely adopted. Chung said that by sharing many of his lab's tissue processing, labeling and analysis innovations, he hopes to speed up biomedical progress.

"We are developing all these technologies to enable more holistic understanding of complex biological systems, which is essential to accelerate the pace of discovery and the development of therapeutic strategies," said Chung, an investigator in The Picower Institute and the Institute for Medical Engineering and Science. "Disseminating these technologies is as important as developing them to make a real-world impact."

Brain **waves** guide us in spotlighting surprises

A new study finds that "predictive coding"—a dynamic interplay of different brain wave frequencies, rather than dedicated circuitry—appears to govern the brain's knack for highlighting what's surprising and downplaying what's predictable.

As animals reacted to predictable and surprising images, neural activity measurements showed that low frequency alpha and beta brain waves, or rhythms, originating in the brain's frontal cognitive regions tamped down neural activity associated with predictable stimuli. That paved the way for neurons in sensory regions in the back of the brain to push forward information associated with unexpected stimuli via higher-frequency gamma waves. The backflow of alpha/beta carrying inhibitory predictions typically channeled through deeper layers of the cortex, while the forward flow of excitatory gamma carrying novel stimuli propagated across superficial layers.

"These interactions between beta and gamma are happening all over the cortex," said Earl Miller, Picower Professor and co-senior author of the study in *Proceedings of the National Academy of Sciences.* "And it's not generic – it targets the processing of specific stimuli."

The findings extend much of Miller's recent work, which has shown that in the prefrontal cortex, working memory depends on bursts of beta rhythms from deep layers regulating gamma frequency activity in more superficial layers. Those findings built on research published in 2012 by postdoc André Bastos, who is lead author of the new paper. The lab's recent studies suggest that this push and pull between the frequency bands is a common regulatory system of information flow in the cortex. Moreover, the new paper demonstrates experimentally that it has a key role in predictive coding (as Bastos began to theorize in 2012), not just working memory.

Predictive coding appears to become disrupted in autism spectrum disorders. Some people with autism struggle to regard familiar stimuli as such, treating everything as new and equally salient. That can interfere with learning to recognize predictable situations and the ability to generalize about experience.

"Because you are not able to tamp down and actively regulate predicted information, the brain is in a constant state of surging information forward which can be overwhelming," Bastos said.

'Playing chess, not checkers,' neurons dynamically control myelination

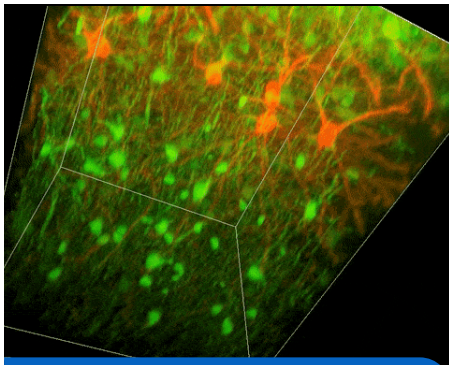
Harvard and MIT researchers have discovered a new way that the brain responds to stimuli, with different types of neurons using myelin in different ways. By dynamically controlling myelin, the insulating coating around their long axon projections that helps with signal conduction, neurons have more ways to adapt to changes. Published in *Science*, the study in mice advances scientists' understanding of how the brain works and opens avenues for exploring new disease mechanisms.

The prototypical image of a neuron depicts the axon with a series of equally sized, evenly spaced pieces of myelin. However, the lab of co-senior author Paola Arlotta, the Golub Family Professor of Stem Cell and Regenerative Biology at Harvard University, showed in 2014 that the picture is more complicated: different types of neurons show different patterns of myelination, with varying lengths of myelin or no myelination on some segments. In the new study, her lab teamed up with co-senior author Elly Nedivi, William R. (1964) & Linda R. Young Professor of Neuroscience in the The Picower Institute, to delve deeper into how myelination patterns might change over time.

The researchers used mouse models where specific neuron types were fluorescently labeled. They changed the animals' sensory input by closing one eye, then tracked how the brain responded using a custom-built *in vivo* imaging system in Nedivi's lab.

"Our multicolor method enables the simultaneous visualization of both the myelin and the axons it was wrapping," Nedivi said. "This allowed us to closely track how myelin was changing over time as mice reconfigured the visual cortex as sight became deprived in one eye."

The researchers found that even though they tracked neurons that were next to each other and part of the same network, different cell types had different responses — specifically, inhibitory neurons remodeled their myelin much more than excitatory neurons. The unique capacity to change their myelin opens up possibilities for the neurons, said Sung Min Yang, lead author and postdoctoral fellow in the Arlotta lab.



Researchers used a live imaging system to capture both neurons (red) and their surrounding myelin (green) at the same time. Credit: Arlotta Laboratory, Harvard University.

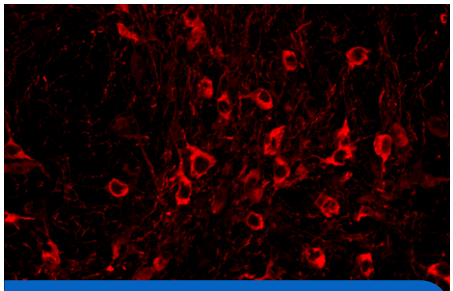
"It turns out that neurons do not move myelin around in a consistent way, as in a game of checkers where every game piece has the same move," Yang said. "Instead, the brain is playing chess, where different neurons — or pieces — can move in different ways."

Scientist seeks **Parkinson's** insights in gene expression

Picower Institute Associate Professor Myriam Heiman has earned a new grant from the G. Harold and Leila Y. Mathers Foundation to screen for genes that could help brain cells withstand Parkinson's disease. The three-year project began Jan. 1, 2021.

Dopamine-producing neurons in a brain region called the substantia nigra are known to be especially vulnerable to dying in Parkinson's disease, leading to the severe motor difficulties experienced during the progression of the incurable, chronic neurodegenerative disorder. The field knows little about what puts specific cells at such dire risk, or what molecular mechanisms might help them resist the disease.

In her research on Huntington's disease, another incurable neurodegenerative disorder in which a specific neuron population in the striatum is especially vulnerable, Heiman has used an innovative method her lab pioneered to discover genes whose expression promotes neuron survival, yielding potential new drug targets. The technique involves conducting an unbiased screen in which her lab knocks out each of the 22,000 genes expressed in the mouse brain one by one in neurons in disease model mice and healthy controls. The technique allows her to determine which genes, when missing, contribute to neuron death amid disease and therefore which genes are particularly needed for survival. The products of those genes can then be evaluated as drug targets. With the new award, Heiman's lab plans to apply the method to study Parkinson's disease.



Dopamine producing neurons in the brain's substantia nigra. Image by Preston Ge.

"There is currently no molecular explanation for the brain cell loss seen in Parkinson's disease or a cure for this devastating disease," Heiman said. "This award will allow us to perform unbiased, genome-wide genetic screens in the brains of mouse models of Parkinson's disease, probing for genes that allow brain cells to survive the effects of cellular perturbations associated with Parkinson's disease. I'm extremely grateful for this generous support and recognition of our work from the Mathers Foundation, and hope that our study will elucidate new therapeutic targets for the treatment and even prevention of Parkinson's disease."

Picower Institute joins international declaration on equity and inclusion

At the Society for Neuroscience's online Global Connectome meeting Jan. 12, an international group of brain scientists launched the ALBA Declaration on Equity and Inclusion with the endorsement of more than 100 major international scientific institutions including The Picower Institute. The declaration aims to raise awareness and provide a concrete set of actions that individuals and scientific institutions can commit to in order to make their organizations more equitable and inclusive.

"Members of underrepresented groups face persistent barriers to equitable representation in science, technology, engineering and mathematics, particularly at advanced stages," the declaration states. "The cost of this loss of talent is high—for individuals, for research, and for society as a whole."

Neuroscientist Megan Carey, chair of the ALBA Declaration Working Group, said the declaration provides specific ways institutions and individuals in brain science can effect positive change, specifically by combatting implicit bias and improving workplace culture.

"The declaration outlines concrete, evidence-based actions that individuals and organizations at any level can take in order to make their environments more equitable and inclusive," Carey said. "We believe that adopting these principles will benefit all members of the research community."

Actions outlined in the declaration include steps to recognize and counteract bias; increase allyship and advocacy for brain scientists from underrepresented groups; improve recruiting, hiring and retention practices; and promote an equitable workplace culture by creating a more positive environment, establishing transparent career structures and ensuring healthy work-life balance.

"As the declaration notes, members of underrepresented groups have faced many persistent barriers," said Li-Huei Tsai, director of The Picower Institute and Picower Professor of Neuroscience at MIT. "The Picower Institute recognizes that it can help to end that persistence and break those barriers down. By joining this declaration we are affirming our dedication to embodying the values and engaging in the actions that will overcome bias and racism and promote allyship, equal opportunity and a welcoming, inclusive and diverse neuroscience research environment."

Steven Flavell earns Sloan Research Fellowship

Award supports fundamental research on how the brain generates internal states that guide animal behavior

With a competitive new research fellowship from the Alfred P. Sloan Foundation, Associate Professor Steven Flavell will have a new source of support over the next two years to study how the nervous system generates long-lasting behavioral states that last minutes and hours.

"The Sloan Research Fellowship Program recognizes and rewards outstanding early-career faculty who have the potential to revolutionize their fields of study," according to the foundation, which provides $75,000 of funding with the prestigious fellowship.

Flavell said the award will help him conduct experiments that uncover the basis of how organisms neurally represent needs and desires, such as hunger, and then act upon them in their environments, such as by roaming around in search of food.

"Over the course of each day, an animal's nervous system may transition between a wide range of internal states that influence how sensory information is processed and how behaviors are generated," he said. "These states of arousal, motivation, and mood can persist for hours, play a central role in organizing human behavior, and are commonly disrupted in psychiatric disease. However, the fundamental neural mechanisms that generate these states remain poorly understood."

Flavell's lab plans to use a multidisciplinary experimental approach in their studies, which employ the simple model of the *C. elegans* worm whose nervous system contains only 302 neurons. Though simple, the model has proven to produce important insights across many areas of biology.

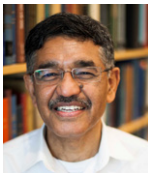
"We envision that these studies will ultimately reveal fundamental principles of neural circuit function that may generalize across animals," Flavell said.

Flavell joins six other Picower Institute faculty members (Bear, Choi, Littleton, Miller, Nedivi and Wilson) in earning a Sloan Research Fellowship.

"I'm honored to be included among so many talented current and previous Sloan Fellows, and I'm deeply appreciative of the Alfred P. Sloan Foundation for supporting our work," he said.

School of Science recognizes researchers





Congratulations to Picower Institute researchers (left to right) Quentin Ferry of the Tonegawa Lab, Hiruy Meharena of the Tsai Lab, and Jitendra Sharma of the Sur Lab on earning Infinite Expansion (Kilometer) Awards from MIT's School of Science. The school created the awards in 2012 to highlight the contributions of postdoctoral scholars and research scientists (or equivalents). Award recipients are not only exceptional scientists, but also show deep commitment to junior colleagues, participating in our educational programs, working with the MIT Postdoctoral Association, or contributing some other way to the Institute.

BIGGER THAN A BUILDING:
THE GLOBAL PICOWER COMMUNITY

Our first ever census of alumni and former research staff shows a thriving community that spans the globe and many different roles.

When our vision statement (for instance on the back of this issue) begins with the words "The Picower Institute is a community of scientists…" we aren't just referring to people currently at MIT. We are also thinking of hundreds of Picower alumni and former research staff who, our first-ever census shows, can be found across the country and around the globe. After all, virtually every Picower discovery or innovation arises from the essential contributions of people who after gaining training in Picower labs then continue to shape the future in myriad ways in their diverse careers. The impact of the institute, therefore, lives in its people, not just its published papers.

"It's a pleasure and a privilege to be at the Picower Institute for many reasons," said Picower Professor and Institute Director Li-Huei Tsai. "At the top of the list is the chance to know and work with brilliant and dedicated researchers who after making an impact here go on to keep advancing the field and changing the world. We cherish these relationships and celebrate their progress and achievements."

We sought to include not just formal MIT alumni, but all manner of people who have worked in our labs—research scientists, postdocs, graduate and undergraduate students and technicians—to advance the study of the brain in health and disease. Each person in that large and growing group numbering at least 440 men and women has advanced neuroscience knowledge and, in turn, has been shaped as a scientist by being here.

"What really is unique about the Picower, and MIT in general, is the collection of talent and excellence, from the students to the postdocs up to the faculty," said **Thomas McHugh**, a team leader at the RIKEN Center for Brain Science in Wako Japan. "The quality of advice, collaboration and motivation that provides is very special and hard to duplicate."

[Thomas McHugh]

In 1994 McHugh became one of the very first graduate students and then postdocs at MIT's Center for Learning and Memory, which then became the Picower Center in 2002. Working in the labs of Picower Professor and institute founder Susumu Tonegawa and Sherman Fairchild Professor Matthew Wilson, McHugh helped pioneer MIT's genetic and electrophysiological studies of memory, and continues groundbreaking investigations of that most essential of brain functions in his own lab today.

"Throughout my career the questions, techniques and approaches to science I have pursued all have their roots in my training with Susumu and Matt," he said.

Though **Jingxuan Fan** is a much more recent Picower alumna at a much earlier stage of her career, the first year graduate student at Harvard University says she, too, takes inspiration from her time at MIT. Studying the circuit mechanisms controlling innate social behaviors as an undergraduate researcher in the lab of Associate Professor Gloria Choi helped to kindle her love of neuroscience.

[Jingxuan Fan]

"The time at BCS/Picower really helped me in figuring out my career passion and developing my scientific skills," she said. "I came to the Choi lab with zero experience in neuroscience. I am grateful for the huge amount of mentorship I got from my direct mentor Jeong Tae [Kwon] and also Gloria."

Many roles by many routes

The Picower Institute alumni community grows every time a Picower person throws a mortarboard into the late spring air or finds an exciting next job, be it in Cambridge or Copenhagen. The roles they've taken on span a diversity of endeavors.

According to our analysis, the majority of 315 former Picower doctoral students and postdocs have continued in academic and medical research. At least 108 now work as professors at universities and medical schools, training a next generation.

Among them is **Ania Majewska**, a professor of neuroscience at the University

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Ania Majewska

of Rochester Medical Center. As a postdoc in the Picower Institute lab of Newton Professor Mriganka Sur, Majewska studied how certain neural connections in the visual cortex, or synapses, remodeled their structure, a key mechanism of how the brain adapts and learns, a phenomenon called "plasticity." In her Rochester lab she studies the interactions of neurons and other brain cell types called glia in development, plasticity and disease.

Demba Ba

Demba Ba, now an associate professor of electrical and bioengineering at Harvard, was a graduate student at MIT and a postdoc in the lab of Edward Hood Taplin Professor Emery Brown. His postdoctoral research involved creating new time frequency representations of measurements of neural activity such as EEGs and electrical spiking. With Brown, an anesthesiologist, he applied these advances to understanding how these measures change in people under general anesthesia, which can improve patient care. At Harvard his research and teaching focus on statistical analysis, signal processing and optimization with continued applications to neuroscience and other fields.

Ba said that the ability to readily pair his theoretical work with experimental applications was a valuable feature of his work at MIT.

"My time at Picower helped me to learn how to work with experimentalists, and to work on theory/computational problems that can have an impact," he said.

And at the Ecole Polytechnique Fédérale de Lausanne in Switzerland, former Tsai lab postdoc **Johannes Gräff** is now an associate professor studying how "epigenetics," or factors affecting the physical process of gene expression, may contribute to susceptibility to post-traumatic stress disorder and how psychological interventions might help patients overcome persistent traumatic memories. At MIT he studied epigenetics in the context of Alzheimer's disease, finding in 2012 that specific epigenetic changes amid the disease created a "blockade" of gene expression that hindered memory recall.

Johannes Gräff

Many former postdocs and doctoral students—at least 98 by our count—are making contributions to biomedical innovation by working in industry, for instance at biotech, medical device and pharmaceutical companies.

Nate Cermak

Nate Cermak, a former postdoc in the lab of MIT Associate Professor Steven Flavell, is a neuroengineer at the Silicon Valley company Neuralink, which is developing a high-bandwidth, implanted brain-computer interface. BCI devices can help people with disabilities such as paralysis control computers and robots directly with their brain, improving ability and restoring independence.

Lea Hachigian

Meanwhile, **Lea Hachigian,** a former doctoral student in the lab of Associate Professor Myriam Heiman who studied how specific neurons become vulnerable amid Huntington's disease, has helped to found four companies as a biotech investor at the Boston-based Longwood Fund. She also serves as the CEO of one of them, ImmuneID, a firm focused on precision immunology approaches to allergy, oncology and autoimmunity.

"We invest in startup therapeutics companies working on cutting-edge biology," she said. "We also work directly with academics to start companies around their research to translate interesting findings into potential drugs for patients with severe disease."

Though the most popular destination among former Picower doctoral students and postdocs is the metro Boston area—approximately 88 have stayed in Massachusetts—the Picower alumni community in total spans at least 26 U.S. states and 23 countries on six continents.

Picower perspectives

Everyone's experience at Picower is unique and as their careers advance, alumni and former research staff attain an additionally unique perspective for reflection on what made their time here special. Among the sampling we interviewed, however, some clear themes emerged. They paint a picture of a place—both Picower specifically and MIT at large— where a strong sense of optimism, meaningful mentoring, and the eager collaboration of a close-knit community all combine to create a culture that encourages research and personal growth.

"There was a tremendous feeling of possibility at MIT," Majewska said. "Anything was possible and it made me think big and not be afraid of trying new things. My mentor, Mriganka Sur, really embodies the idea of going wherever the science takes you and I will be forever grateful to him for teaching me to embrace new directions and dive into the unknown."

Gräff recalls a similar "can do" optimism: "The overall atmosphere at the Picower was that of an enabling one. A 'Yes, we can' mood. The facilities, resources and people there are all excellent, and very inspirational. In my own lab, I try to convey this culture as well, by having enough resources and by encouraging people to not shy away from difficult questions and projects.

"I remember having an idea that I proposed to Li-Huei when I ran into her in the hallway," he said. "It was an important question, but it was also clear to me that it wouldn't be trivial to answer it. In other words, it would require a lot of energy and time to answer this question."

Without reservation, Tsai readily offered encouragement to "Just do it," Gräff said. "One year later, we had the answer to the question, and this ended up being an entire figure in our 2012 *Nature* paper."

McHugh, too, said he carries his inspiration from working with Tonegawa and Wilson through to his own lab: "The atmosphere at the Picower was one of excellence and established a standard that I aspire to."

Encouragement from their faculty mentors left important impressions on Cermak and Hachigian as well.

"Steve's lab, I think, was exceptional, both for his engagement in the research itself and his investment in supporting those in the lab," Cermak said. "The latter trait is all too rare in academia."

Hachigian said Heiman helped her to gain crucial skills for her career as a scientific investor and entrepreneur—specifically a

CONTINUES ON PAGE 10

A map represents how more than 200 former postdocs and graduate students have gone on from MIT to new jobs around the U.S. and the world. About 88 remain in Massachusetts.

BIGGER THAN A BUILDING

CONTINUED FROM PAGE 9

knack for rigorously and critically assessing biological data and an ability to clearly communicate science to broad audiences.

"One of my fondest memories of Picower was when I presented at my first 'Plastic Lunch' (a departmental seminar series)," she said. "I was terrified beforehand and had never presented my full research story before to a large audience. Myriam graciously worked with me to refine my messaging and slides, so when I ultimately presented I got incredible questions from the audience and even some requests for collaboration around my work. It felt so good to be able to share my science and for years after the fact I would run into people in the halls who would ask me how things were going with my Huntington's mice!"

Ba said it felt easy to interact with fellow researchers, even when—and especially—when they had a different approach to their work.

"As a theorist and computational person, I enjoyed the fact that one could 'bump into' experimentalists in the hall at will," he said. "Something about the distribution of theory/experimentalist labs at Picower somehow makes this possible. This helped me to keep my theory/computational questions grounded in data collected in actual experiments."

A particular delight, Ba said, was encountering Emilio Bizzi, an Institute Professor in the Department of Brain and Cognitive Sciences, who offered frequent encouragement.

Fan agreed: "I think it's very special that the department feels very close and compact. Being physically in the same building really facilitates the communications between different labs of distinct areas. I like all the seminar events and the receptions that happen afterwards where I could meet people of diverse backgrounds and stages of training. I ended up becoming friends with many graduate students and postdocs who provided me valuable career advice."

> "There was a tremendous feeling of possibility at MIT. Anything was possible and made me think big and not be afraid of trying new things"
>
> *Ania Majewska*

Hachigian adds that while collaboration comes readily at Picower where "everyone knows each other," it's also a huge benefit to be part of the larger MIT environment.

"While feeling like a tight-knit community, Picower is positioned at the epicenter of an incredible neuroscience ecosystem that contains hundreds of research labs across MIT, Harvard and the Broad Institute," she said. "Students and fellows get the best of both worlds with this setup- a close department but no scientific limits!"

Picower faculty, too, recall their lab alumni fondly. Tonegawa, for instance, noted McHugh's work as especially pioneering both for its methods of electrophysiological measurement and for its use of genetic techniques to focus on specific cell types. He also recalls how former postdoc Xiu Liu led a landmark effort of the lab, published in *Nature* in 2012, that for the first time mapped out the physical trace of a specific memory called an engram.

Learning and Memory memories

While such advanced research is emblematic of Picower's purpose, many alumni happily recall the personal alongside the professional. Fan recalls deep conversations in the break room with labmates. Cermak remembers retreats and outings featuring escape rooms and karaoke.

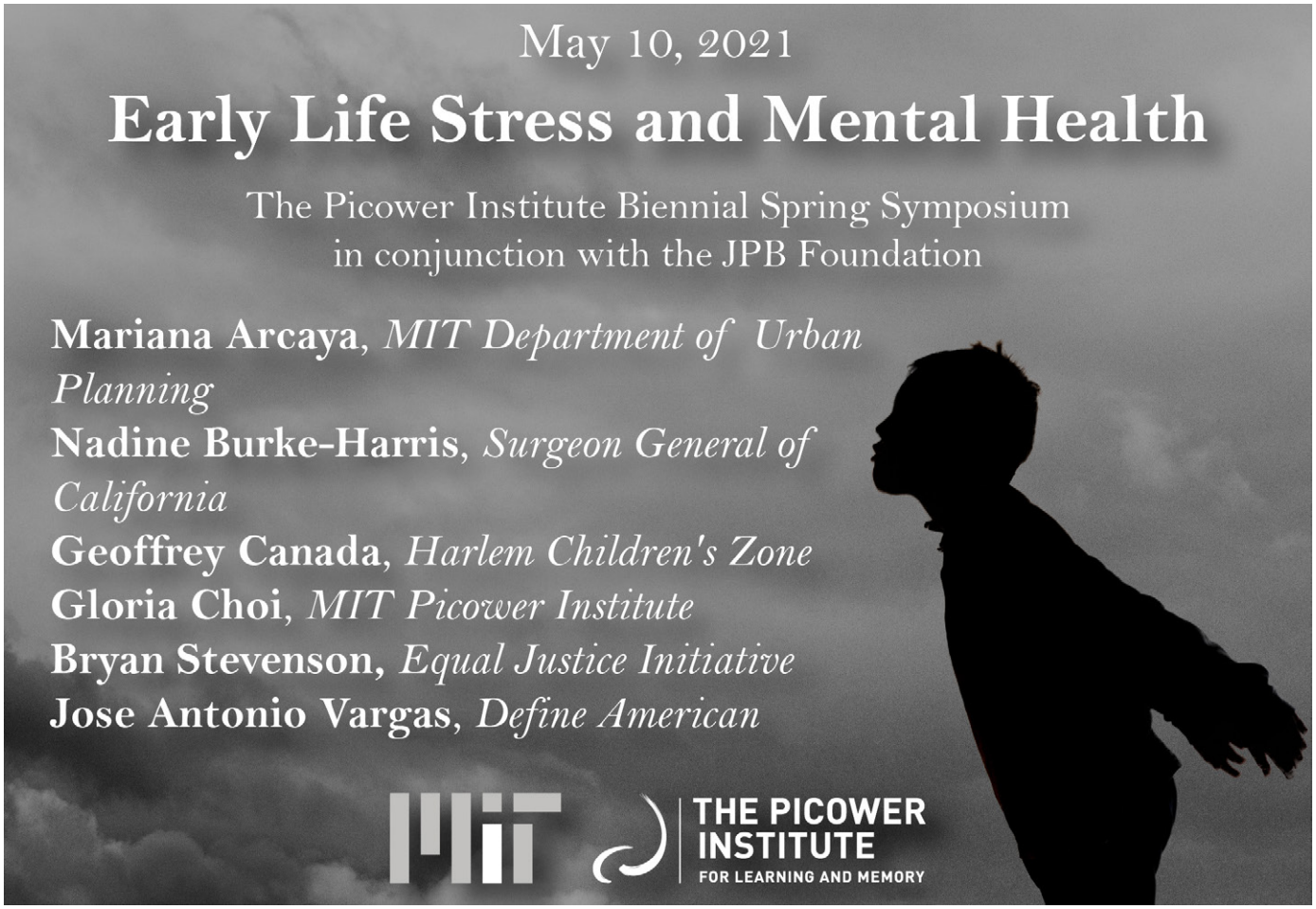
Majewska's memories range from little moments like lab lunches at Legal Seafood to major milestones, like getting married to her husband, a fellow postdoc, at the MIT chapel followed by a reception at the faculty club. McHugh, too, met his wife at Picower, though she is not the only lifelong friend he made here.

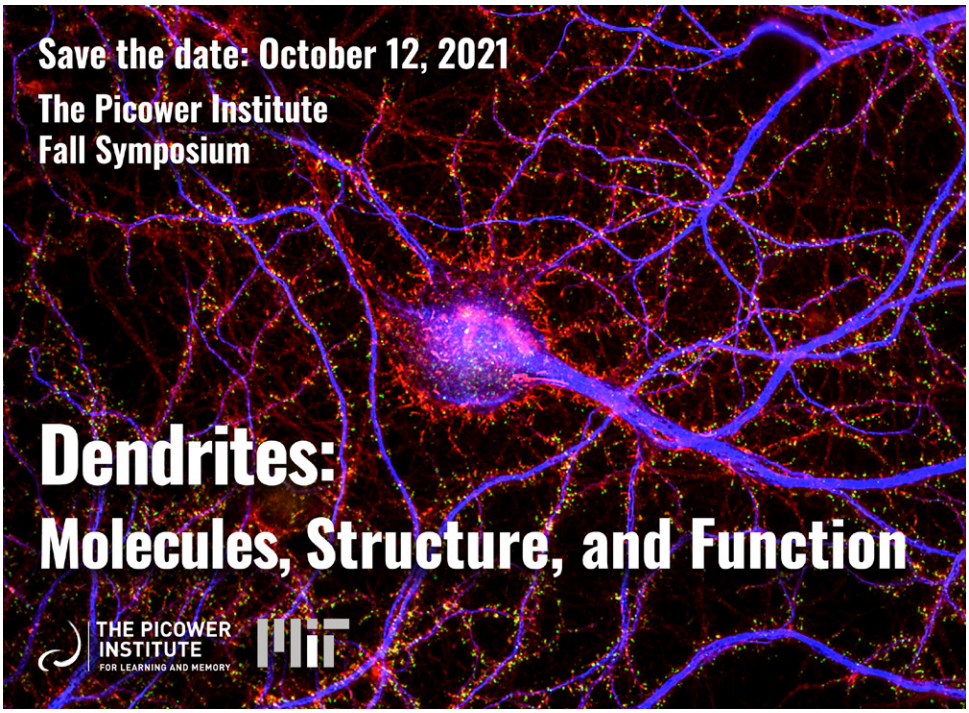
"At the end of the day the most enduring memories are of the more social aspects," he said. "The retreats, the Friday socials, the Tonegawa lab's annual beat down of the Wilson lab at the summer BBQ softball game."

The Picower Institute is a place of people with connections that remain no matter where they have gone or what they are doing now.

Upcoming **EVENTS**

For the *latest* information on all our lectures, symposia and other events, please visit: **picower.mit.edu/events**





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BOTTOM ROW: **Earl Miller**, Picower Professor of Neuroscience, Department of Brain and Cognitive Sciences; **Elly Nedivi**, William R. (1964) & Linda R. Young Professor of Neuroscience, The Picower Institute for Learning and Memory, Departments of Brain and Cognitive Sciences and Biology; **Mriganka Sur**, Paul E. Newton Professor of Neuroscience, Director of The Simons Center for the Social Brain; **Susumu Tonegawa**, Picower Professor of Biology and Neuroscience, Departments of Brain and Cognitive Sciences and Biology, Investigator, Howard Hughes Medical Institute, Investigator and Director of the RIKEN-MIT Center for Neural Circuit Genetics; **Li-Huei Tsai**, Picower Professor of Neuroscience, Department of Brain and Cognitive Sciences, Director, The Picower Institute for Learning and Memory; **Matthew Wilson**, Sherman Fairchild Professor in Neurobiology, Departments of Brain and Cognitive Sciences and Biology, Associate Director, The Picower Institute for Learning and Memory.

Choi photo by Justin Knight