# McGovern Institute for Brain Research

The McGovern Institute for Brain Research at MIT is committed to meeting two great challenges of modern science: understanding how the brain works and discovering new ways to prevent or treat brain disorders. The McGovern Institute was established in 2000 based on a gift from Lore Harp McGovern and the late Patrick J. McGovern.

## Faculty

For the period July 1, 2019, to June 30, 2020, we had 14 faculty and six associate members. Evelina Fedorenko was appointed as a McGovern Investigator in 2020, and Fan Wang, a tenured professor from Duke University, was recruited as an investigator, to start in January 2021. Guoping Feng was named associate director of the McGovern Institute.

## COVID-19 and the McGovern Institute

Our researchers rose to the coronavirus challenge. We conducted a large amount of research relevant to the coronavirus crisis. Feng Zhang has been collaborating with our McGovern Fellows, Omar Abudayyeh and Jonathan Gootenberg, to develop a rapid COVID-19 diagnostic that could be used by private individuals, small businesses, and schools. Feng has also released the How We Feel app with Ben Silbermann, chief executive officer of Pinterest, and a global team of researchers. This app allows tracking of symptoms and enables researchers to ask pressing questions about the progression of the virus.

Other researchers mobilized to bring their knowledge and skills to bear on mitigating some of the unexpected shortages. Jill Crittenden, a research scientist in the Graybiel lab, worked with a consortium to gather and curate information about the three main approaches for decontaminating N95 face masks. Shortages of these masks were causing health workers to resort to reusing masks. The consortium put together a website and a document that helped hospitals and other frontline organizations to quickly and easily examine the use and effectiveness of different decontamination protocols. Michael Wells, a former graduate student in Guoping Feng's lab, collaborated to set up a database where researchers who wanted to volunteer could offer up their skills. Crittenden also started a project to identify potential gene expression differences in the nasal epithelium of older adults versus children, to better understand why older adults are more vulnerable to infection.

Ed Boyden worked with Emery Brown to develop a low-cost ventilator for coronavirus patients. They believe their design is superior to some of the other low-cost ventilators in development elsewhere.

Ian Wickersham, head of our viral research core, worked to develop the basic viral elements for new vaccines as a backup to the worldwide efforts to develop a coronavirus vaccine. Ian is concerned that many of the vaccines in current development may not elicit a strong enough immune response to be effective and his new constructs could potentially help in that case.

McGovern laboratories also looked at the effects of the response to COVID-19. Rebecca Saxe worked to understand some of the effects of social isolation. Her lab posted their

findings indicating that loneliness in social isolation leads to neural craving responses similar to hunger.

Finally, we created a new page on our website that features stories from members of the McGovern community who rose to the challenge during the pandemic.

## Resource Development

Fundraising from individuals and private foundations remains a priority at the McGovern Institute. Staff hosted multiple donor cultivation events during the fiscal year, and faculty and staff met with more than 75 donors and prospects in Cambridge, London, New York, Florida, and California.

## New Addiction Initiative

With the recruitment of Fan Wang and the fundraising commitment of Lore Harp McGovern, we have developed a new addiction science program at the McGovern Institute. This collaborative initiative is launching with nine major research projects (some existing and some new) that examine critical questions of addiction across six McGovern laboratories: Wang, Graybiel, Anikeeva, Gabrieli, Jasanoff, and Boyden. Key research questions include: Why do some people become addicted while others do not? Can science help predict who will benefit from rehab programs? Can we develop a non-addictive alternative to opiates? If we raise resources, we may expand the program to include other laboratories within and outside of MIT in the next phase. We have spent the last several months developing our story, prospect list, and an overview brochure.

## McGovern Institute Centers

Our centers leverage the latest technologies in fast-moving fields like intelligence and intractable brain disorders.

### Hock E. Tan and K. Lisa Yang Center for Autism Research

This center, founded by Hock E. Tan and K. Lisa Yang, was created to support and catalyze new research approaches and potential treatments for individuals affected by autism spectrum disorder (ASD). The center emphasizes novel projects that are difficult to fund through traditional grants. By concentrating research efforts on new models, therapeutic approaches, and a push toward understanding changes in the human brain, the center aims to better detect, treat, and potentially prevent the most severe forms of ASD. The center is focusing on the following research goals:

- New Models, led by Guoping Feng, is a team that seeks to create new models of autism using CRISPR gene-editing tools. Using these models, the team is examining the cellular, molecular, and behavioral outcome of monogenic mutations linked to autism and aims to identify promising therapeutic avenues.
- Human Studies will encompass research such as the Tan-Yang Center's effort, led by Rebecca Saxe, to characterize the brain regions and networks that are impacted by ASD and to robustly test the clinical relevance of observed brain differences.

- John Gabrieli is embracing the strengths of individuals diagnosed with ASD by researching their "affinities," or strong passions for a specific topic, to examine the reward circuitry and language networks in the brain. His team is studying whether affinities can elicit "typical" activation in regions of the brain that are sometimes assumed to not be engaged in autism.
- Polina Anikeeva is working on the gut-brain connection, developing new tools to rigorously examine how gastrointestinal dysfunction can arise in ASD and to better understand the links between the enteric (gut) nervous system and central nervous system.
- The Tan-Yang Center is pioneering gene-therapy approaches to ASD using CRISPR editing systems. This effort is led by Feng Zhang, who pioneered CRISPR gene editing in mammalian cells. The center is developing new methods for delivery and novel forms of gene therapy that could potentially provide treatment options for those living with autism.

## Poitras Center for Psychiatric Disorders Research

In the years since the Poitras Center for Psychiatric Disorders Research was established at the McGovern Institute in 2007, research into psychiatric illness has surged. The invention of optogenetics, first reported in 2005, allowed our scientists to control and study the activity of neural circuits with a precision previously unimaginable. New imaging methods provide us with ever more detailed pictures of brain activity both in humans and in animal models. Advances in microscopy are revolutionizing our view of the brain's fine structure. The Poitras Center has enabled numerous discoveries and technical advances, many of which have been published in top scientific journals such as *Nature*, *Science*, and *Cell*. As a result of these advances, the center has leveraged millions of dollars in federal grants and private funding. Poitras Center support has made possible national and international collaborations with renowned researchers and clinicians and provided a vital source of support for the next generation of neuroscientists and biological engineers.

The Poitras Center has enabled us to appoint two of our faculty into endowed positions. The James W. (1963) and Patricia T. Poitras Professor of Neuroscience, established in 2003, is currently held by Guoping Feng. The James and Patricia Poitras Professorship in Neuroscience, created in 2017, is an endowed professorship currently held by CRISPR pioneer Feng Zhang.

## The Center for Brains, Minds and Machines

The Center for Brains, Minds and Machines continues as a multi-institutional National Science Foundation Science and Technology Center dedicated to the study of intelligence—how the brain produces intelligent behavior and how we may be able to replicate intelligence in machines. This effort is a multi-institutional collaboration headquartered at the McGovern Institute with managing partners at Harvard University.

### McGovern Institutes in China

The McGovern Institute continues to collaborate and interact with the three International Data Group (IDG)–McGovern Institutes in China at Tsinghua University, Beijing Normal University, and Peking University. We also have a continuing collaboration with Shenzhen Institutes of Advanced Technology.

## Board of Directors

The McGovern Institute Board of Directors meets quarterly, in July, October, January, and April. The membership of the board for FY2020 consisted of Lore McGovern, Elizabeth McGovern, Michelle Bethel, Michael Sipser (MIT), Robert Langer (MIT), James Poitras, and Lisa Yang.

## The McGovern Institute Leadership Board

The McGovern Institute Leadership Board meets once per year. The Leadership Board participates in programming at the McGovern Institute and interacts with the director and faculty members throughout the year, providing critical funding and strategic advice to the McGovern Institute.

## Major Events

### The Edward M. Scolnick Prize in Neuroscience

The Scolnick Prize committee selected Joshua Sanes, the Jeff C. Tarr Professor of Molecular and Cellular Biology, as the winner of the 2020 prize. The prize was scheduled to be awarded in person but then postponed due to a ramp-down of on-site operations because of COVID-19. Professor Sanes will present his prize lecture in the spring of 2021. Sanes, who focused the power of molecular genetics toward understanding how synapses are built, is being recognized for his numerous contributions to our understanding of synapse development. He becomes the 16th researcher to win the prestigious prize, established in 2004 by Merck to honor Edward M. Scolnick, who spent 17 years holding the top research post at Merck Research Laboratories.

### The Phillip A. Sharp Lecture in Neural Circuits

The annual Phillip A. Sharp Lecture in Neural Circuits (endowed by Biogen Idec in honor of the McGovern Institute's founding director, Phillip Sharp) was to be given in spring 2020 by Eve Marder, the Victor and Gwendolyn Beinfield Professor of Biology at Brandeis University. Postponed until Spring 2021, the title of her talk will be: "Differential Resilience of Neurons and Networks to Perturbation."

### Building 46 Colloquium Series

The McGovern Institute, the Picower Institute for Learning and Memory, and the Department of Brain and Cognitive Sciences continued to support a weekly colloquium series in Building 46 on Thursdays at 4 pm. The talks are followed by a public reception. In fall 2019, the McGovern Institute hosted Benjamin Hayden (September 19) and Gwyneth Card (November 7).

## Core Facilities

The McGovern Institute operates several core laboratories that serve the local neuroscience community as well as members of the McGovern Institute. These include:

- **The Martinos Imaging Center at MIT**. The Martinos Center provides access to neuroimaging technologies, including two 3T MRI (magnetic resonance imaging) scanners for human brain imaging, a 9.4T MRI scanner for small animal imaging, a magnetoencephalography scanner, and an electroencephalography system. There is also a coil fabrication lab and a mock MRI scanner to help subjects (especially children) adapt to the scanning environment.
- **The two-photon microscopy core**. This core features a sophisticated two-photon system with four lasers to support two-color imaging and uncaging. The system includes two workstations configured for slice physiology and whole animal work. It was upgraded to include an electrophysiology system. The core is managed by McGovern Institute faculty member Mark Harnett and is provided free of charge to those in Building 46.
- **The OpenMind computing cluster**. This cluster was established in 2014 to provide the MIT brain research community with access to state-of-art computing resources. The cluster is housed at the Massachusetts Green High Performance Computing Center (MGHPCC) in Holyoke, MA, with a 10G link to the MIT campus.

## McGovern Institute Neurotechnology Program

The McGovern Institute Neurotechnology Program (MINT) continues to provide seed funding for collaborations between McGovern laboratories and researchers from other disciplines within MIT, with a focus on developing new technologies for brain research. Since its establishment in 2006, the MINT program has supported over 40 projects. Collaborating principal investigators are from multiple departments and schools at MIT.

## Awards and Honors

Ed Boyden was one of four scientists to win the 2019 Warren Alpert Foundation Prize for pioneering work that launched the field of optogenetics, a technique that uses light-sensitive channels and pumps to control the activity of neurons in the brain with a flick of a switch. Boyden also won the 2019 Croonian Medal and Lecture by the Royal Society, which honors "exceptional researchers who are making outstanding contributions to science."

Nominated by peers and students, Mehrdad Jazayeri was chosen to receive a 2019 School of Science teaching prize to acknowledge his "exemplary efforts in teaching graduate and undergraduate students."

Nancy Kanwisher has been named this year's winner of the George A. Miller Prize in Cognitive Neuroscience. The award, given annually by the Cognitive Neuroscience Society, recognizes individuals "whose distinguished research is at the cutting edge of their discipline with realized or future potential to revolutionize cognitive neuroscience." Kanwisher will deliver her prize lecture, "Functional Brain Imaging," at the 2020 Cognitive Neuroscience Society annual meeting in Boston in March 2020.

The School of Science announced that Michael Halassa is one of 14 faculty members who were appointed to named professorships for junior faculty. The faculty members selected for these positions receive additional support to pursue their research and develop their careers. Halassa will hold the three-year Class of 1958 Career Development Professorship.

Two McGovern scientists were been named STAT Wunderkinds. Sam Rodriques (Boyden lab) and Jonathan Strecker (Zhang lab) were recognized as "trail-blazing scientists that are on the cusp of launching their careers."

Guoping Feng won the Frank E. Perkins Award for Excellence in Graduate Advising at MIT.

Omar Abudayyeh was named one of MIT Technology Review's 35 Innovators Under 35.

Rebecca Saxe was awarded a prestigious Guggenheim Fellowship.

## Summary of Research Advances

- How expectation influences perception, July 15, 2019, *Neuron:* The Jazayeri lab has found brain activity patterns that encode our beliefs and affect how we interpret the world around us.
- Brain region linked to altered social interactions in autism model, July 26, 2019, *Nature Neuroscience:* In a SHANK3 mouse model, Guoping Feng has found that restoring activity of a specific forebrain region called the anterior cingulate cortex reverses social traits associated with autism.
- Finding the brain's compass, August 12, 2019, *Nature Neuroscience:* The Fiete lab has identified a brain circuit in mice that distills "high-dimensional" complex information about the environment into a simple abstract object in the brain. This abstract compass, according to the researchers, is a one-dimensional ring that represents the current direction of the head relative to the external world.
- A new way to deliver drugs with pinpoint targeting, August 19, 2019, *Nature Nanotechnology:* The Anikeeva lab has developed a system to deliver medical treatments that can be released at precise times, are minimally invasively, and that ultimately could deliver those drugs to specifically targeted areas such as a specific group of neurons in the brain.
- Benefits of mindfulness for middle schoolers, August 26, 2019, *Behavioral Neuroscience* and *Mind, Brain, and Education:* Two new studies from the Gabrieli lab suggest that mindfulness—the practice of focusing one's awareness on the present moment—can enhance academic performance and mental health in middle schoolers. The researchers found that more mindfulness correlates with better academic performance, fewer suspensions from school, and less stress.
- Hearing through the clutter, September 2, 2019, *Nature Communications:* A new study by Josh McDermott sheds light on how the brain accomplishes the task of extracting meaningful sounds from background noise, findings that could one day help to build artificial hearing systems and aid development of targeted hearing prosthetics.

- Perception of musical pitch varies across cultures, September 19, 2019, *Current Biology:* A McDermott lab study has found that, unlike residents of the United States, people living in a remote area of the Bolivian rainforest usually do not perceive the similarities between two versions of the same note played at different registers (high or low). The researchers suggest that our ability to interpret musical notes depends on the types of music we have been exposed to over the course of our lives.

- Better sleep habits lead to better college grades, October 1, 2019, *Science of Learning:* Researchers in John Gabrieli's lab, in collaboration with Jeffrey Grossman (Department of Materials Science and Engineering), used Fitbit technology to follow the sleep patterns of 100 students in an MIT engineering class. They found a strong relationship between the amount of sleep students get and their grades. In addition, the consistency of sleep habits was important. When students went to sleep also mattered: students who went to bed after 2 am performed less well in tests, no matter how much actual sleep they got.

- Controlling our internal world, October 7, 2019, *Nature Neuroscience:* As we move through the world, the brain must have an internal model of the body to control, predict, and make almost instantaneous adjustments to motor commands. So-called "internal models" are a fundamental concept in engineering and have long been suggested to underlie control of movement by the brain, but what about processes that occur in the absence of movement, such as contemplation, anticipation, planning? Using a novel combination of task design, data analysis, and modeling, Mehrdad Jazayeri and colleagues now provide compelling evidence that the core elements of an internal model also control purely mental processes.

- New method visualizes neurons as they compute, October 9, 2019, *Nature:* Using a fluorescent probe that lights up when brain cells are electrically active, Ed Boyden and colleagues have shown that they can image the activity of many neurons at once in the brains of mice. They developed a technology that allows neuroscientists to visualize the activity of circuits within the brain and link them to specific behaviors. This technique, which can be performed using a simple light microscope, could allow neuroscientists to visualize the activity of circuits within the brain and link them to specific behaviors.

- Drug combination reverses hypersensitivity to noise, October 21, 2019, *Neuron:* People with autism often experience hypersensitivity to noise and other sensory input. Michael Halassa and Guoping Feng have now identified two brain circuits that help tune out distracting sensory information, and they have found a way to reverse noise hypersensitivity in mice by boosting the activity of those circuits.

- Controlling attention with brain waves, December 4, 2019, *Neuron:* The Desimone lab has found that people can enhance their attention by controlling their own alpha brain waves based on neurofeedback they receive as they perform a particular task. This is the first time that this cause-and-effect relationship has been seen and it suggests that it may be possible for people to learn to improve their attention through neurofeedback.

- Single neurons can decode distinct landmarks, December 9, 2019, *Neuron:* The organization of many neurons wired together in a complex circuit gives the brain its ability to perform powerful calculations. Work from the Harnett lab recently showed that even single neurons can process more information than previously thought, representing distinct variables at the subcellular level during behavior.

- Brain biomarkers predict mood and attention symptoms, January 3, 2020, *JAMA Psychiatry:* Mood and attentional disorders among teens are an increasing concern for parents, society, and peers. Susan Whitfield-Gabrieli and colleagues found that signatures predicting future development of depression and attentional symptoms can be detected in children as young as seven years old.

- How dopamine drives brain activity, April 1, 2020, *Nature:* Using a specialized MRI sensor, the Jasanoff lab has discovered how dopamine released deep within the brain influences both nearby and distant brain regions. Dopamine plays many roles in the brain, most notably related to movement, motivation, and reinforcement of behavior. However, until now it has been difficult to study precisely how a flood of dopamine affects neural activity throughout the brain. Using their new technique, the MIT team found that dopamine appears to exert significant effects in two regions of the brain's cortex, including the motor cortex.

- New COVID-19 resource to address shortage of face masks, April 2, 2020: McGovern research scientist Jill Crittenden is a member of a new consortium that provides guidance for healthcare workers on decontamination and reuse of N95 face masks. Crittenden joined a team of 60 scientists and engineers, students, and clinicians drawn from universities and the private sector to synthesize the scientific literature about mask decontamination and create a set of best practices for bad times.

- How We Feel app to track spread of COVID19 symptoms, April 3, 2020: A major challenge for containing the spread of COVID-19 in many countries has been the inability to quickly detect infection. Feng Zhang, Ben Silberman, and collaborators across scientific and medical disciplines are coming together to launch an app called How We Feel that will allow citizen-scientists to self-report symptoms.

- 3 Questions: Omar Abudayyeh and Jonathan Gootenberg on COVID19 tests, April 6, 2020: Two CRISPR scientists explain how COVID-19 tests work, why they're in short supply, and how a CRISPR tool may help solve the problem.

- Researchers achieve remote control hormone release, April 10, 2020, *Science Advances*: Abnormal levels of stress hormones such as adrenaline and cortisol are linked to a variety of mental health disorders, including depression and posttraumatic stress disorder. The Anikeeva lab has devised a way to remotely control the release of these hormones from the adrenal gland using magnetic nanoparticles. This approach could help scientists learn more about how hormone release influences mental health and eventually offer a new way to treat hormone-linked disorders.

- Optogenetics with SOUL, April 29, 2020, *Neuron:* Optogenetics has revolutionized neurobiology, allowing researchers to use light to activate or

deactivate neurons that are genetically modified to express a light-sensitive channel. However, activating neurons deep within a given brain, especially a large primate brain (but even a small mouse brain), is challenging and currently requires implanting fibers that could cause damage or inflammation. Guoping Feng and colleagues have overcome this challenge, developing optogenetic tools that allow non-invasive stimulation of neurons in the deep brain.

- SHERLOCK-based one-step test provides rapid and sensitive COVID-19 detection, May 5, 2020: Feng Zhang, Omar Abudayyeh, and Jonathan Gootenberg have developed a new diagnostics platform called STOP (SHERLOCK Testing in One Pot) COVID. The test can be run in an hour as a single-step reaction with minimal handling, advancing the CRISPR-based SHERLOCK diagnostic technology closer to a point-of-care or at-home testing tool.

- Universal musical harmony, June 16, 2020, *Nature Communications*: Many forms of Western music make use of harmony, or the sound created by certain pairs of notes. A longstanding question is why some combinations of notes are perceived as pleasant while others sound jarring. Are the combinations we favor a universal phenomenon? Or are they specific to Western culture? Through research trips to the Bolivian rainforest, the McDermott lab has found that aspects of the perception of note combinations may be universal even though the aesthetic evaluation of note combination as pleasant or unpleasant is culture-specific.

- COMMANDing drug delivery, June 23, 2020, *Cell Reports*: While we are starting to get a handle on drugs and therapeutics that might to help alleviate brain disorders, efficient delivery remains a roadblock to tackling these devastating diseases. Research from the Graybiel, Cima, and Langer labs now uses a computational approach—one that accounts for the irregular shape of the target brain region—to deliver drugs effectively and specifically.

- A focused approach to imaging neural activity in the brain, June 26, 2020, *Neuron*: When neurons fire an electrical impulse, they also experience a surge of calcium ions. By measuring those surges, researchers can indirectly monitor neuron activity, helping them to study the role of individual neurons in many different brain functions. One drawback to this technique is the crosstalk generated by the axons and dendrites that extend from neighboring neurons. Ed Boyden has developed a way to overcome that issue by creating calcium indicators that accumulate only in the body of a neuron.

- Producing a gaseous messenger molecule inside the body, on demand, June 29, 2020, *Nature Nanotechnology*: Nitric oxide is an important signaling molecule in the body, with a role in building nervous system connections that contribute to learning and memory, but it has been difficult for researchers to study exactly what its role is. Because it is a gas, there has been no practical way to direct it to specific individual cells. Now, Polina Anikeeva and colleagues have found a way of generating the gas at precisely targeted locations inside the body, potentially opening new lines of research on this essential molecule's effects.

## Press Mentions

- *Scientific American*, "A new twist on artificial muscles," July 11, 2019
- *Southern Living*, "Study suggests doing one simple thing is "almost magical" for your child's brain development," August 2, 2019
- *Washington Post*, "Using symbols, she calmed a nonverbal autistic boy on a plane. His dad was awestruck," August 30, 2019
- *Forbes*, "This remote Bolivian tribe does not hear pitch the same way most people do," September 21, 2019
- *Christian Science Monitor*, "Pitch perfect? How culture shapes the way you hear music," September 27, 2019
- *The Atlantic*, "What a new theory of attention says about consciousness," September 29, 2019
- *Scientific American*, "A new theory of obesity," October 2019
- The advent of genome editing by CRISPR was listed as a key scientific "discovery of the decade" by multiple media outlets, including *National Geographic*, National Public Radio, *The Hill*, *Popular Mechanics*, *Smithsonian* magazine, *Nature*, *Mental Floss*, and CNBC
- *Spectrum*, "Drug combination mutes sensitivity to noise in autism mice," November 25, 2019
- *ScienceNews*, "A conversation with Feng Zhang," December 2019
- *Washington Post*, "Why more kids are learning—and enjoying—yoga," January 4, 2020
- *New York Times*, "How are you feeling? Surveys aim to detect Covid-19 hot spots early," April 1, 2020
- CNBC, "Pinterest CEO launches self-reporting app to help track coronavirus spread," April 8, 2020
- *The Scientist*, "Deep brain optogenetic control without implants," April 30, 2020
- STAT, "Researchers develop a non-invasive way to manipulate neurons to study behavior," April 30, 2020
- STAT, "New CRISPR-based test for Covid-19 could be a simple, cheap at-home diagnostic," May 5, 2020
- Boston25 News, "Boston area researchers hope to create at-home COVID-19 test," May 5, 2020
- NPR, "Researchers hope new CRISPR technique could speed up coronavirus testing," May 5, 2020

- *New York Times*, "With CRISPR, a possible quick test for the coronavirus," May 5, 2020
- *Washington Post*, "FDA gives emergency authorization for CRISPR-based diagnostic tool for coronavirus," May 7, 2020
- *Times of Israel*, "A Jewish and a Palestinian scientist team up for MIT at-home coronavirus test," May 29, 2020
- *Forbes*, "The 30 Under 30 alums racing to develop at-home coronavirus test with CRISPR," June 10, 2020
- *MIT Technology Review,* "Innovators Under 35: Omar Abudayyeh," June 17, 2020
- Netflix, "Babies," June 19, 2020

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