

BRAINSCAN Fall 2020 — ISSUE 53

BREAKTHROUGHS, PEOPLE & IDEAS

Celebrating 20 years of progress, the researchers who propel us forward, and our predictions for the future.



n this special anniversary issue of BrainScan, we pause to reflect on some of our accomplishments and consider what lies ahead. Some of the amazing developments of the past 20 years, such as CRISPR, may seem entirely unexpected and "out of the blue." But they were all built on a foundation of basic research spanning many years. With the incredible foundation we are building right now, I feel we are poised for many more "unexpected" discoveries in the years ahead.

I predict that in 20 years, we will have quantitative models of brain function that will not only explain how the brain gives rise to at least some aspects of our mind, but will also give us a new mechanistic understanding of brain disorders. This, in turn, will lead to new types of therapies, in what I imagine to be a post-pharmaceutical era of the future. I have no doubt that these same brain models will inspire new educational approaches for our children, and will be incorporated into whatever replaces my automobile, and iPhone, in 2040. You can read some other predictions from our faculty at the end of this issue.

Our cutting-edge work depends not only on our stellar line up of faculty, but the more than 400 postdocs, graduate students, undergraduates, summer students, and staff who make up our community. For this reason, I am particularly delighted to share with you a supplementary section of the newsletter featuring McGovern's rising stars — 20 young scientists from each of our labs — who represent the next generation of neuroscience.

And finally, we remain deeply indebted to our supporters for funding our research, including ongoing support from the Patrick J. McGovern Foundation. In recent years, more than 40% of our annual research funding has come from private individuals and foundations. This support enables critical seed funding for new research projects, the development of new technologies, our new research into autism and psychiatric disorders, and fellowships for young scientists just starting their careers. Our annual fund supporters have made possible more than 42 graduate fellowships, and you will read about some of these fellows in this issue.

I hope that as you read these pages, you will feel as optimistic as I do about our future.

ROBERT DESIMONE

Director, McGovern Institute Doris and Don Berkey Professor of Neuroscience

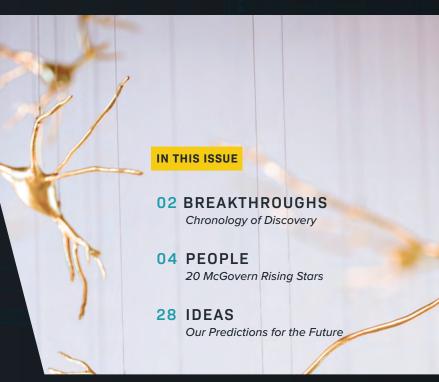


LETTER FROM OUR CO-FOUNDER

Twenty years ago, our dream to create a first-class institute for brain research became reality, and the McGovern Institute planted its flag at MIT. Pat and I founded the institute because we deeply believed that nothing is impossible and that solutions can be found for anything. Did we have high expectations? Yes. But we also knew that the right people, a can-do attitude, and brilliant scientific rigor coupled with sufficient resources would lay the foundation and pave the way.

The poet Theodore Roethke once said "what we need is more people who specialize in the impossible." Our inaugural director, Phil Sharp, and the six founding investigators—Emilio Bizzi, Nancy Kanwisher, Tomaso Poggio, Martha Constantine-Paton, H. Robert Horvitz, Ann Graybiel—represented just that.

Twenty years later, I am filled with pride about how far we have come under the great leadership of our second direc-Let's celebrate all that makes us human and stay together tor, Bob Desimone, who kept a keen eye on our initial vision on this journey of discovery. I extend my gratitude and conand expanded that vision as our research breakthroughs gratulations to our great McGovern family and a heartfelt invited new opportunities. The discoveries at the McGovern thank you to all of our supporters who create hope in the Institute are numerous, from finding signatures of the social face of despair. As Pat would say, "the best is yet to come!" brain in infants to seeing the brain in exquisite detail with expansion microscopy and, of course, pioneering the revo-LORE HARP MCGOVERN lutionary CRISPR gene editing technology in human cells. Co-Founder, McGovern Institute



We are proud to be home to five centers — the Poitras
Center for Psychiatric Disorders Research, the Hock E. Tan
and K. Lisa Yang Center for Autism Research, the Center for
Brains, Minds and Machines, the Martinos Imaging Center,
and the newly established K. Lisa Yang and Hock E. Tan
Center for Molecular Therapeutics in Neuroscience.
I am particularly excited about our addiction science
initiative, an ambitious undertaking which promises to
transform our understanding of addiction and create
new, scientifically-driven treatments for people suffering
from this complex disorder.

We will continue to search and probe the brain until there are no more questions left to be answered. We will get closer to understanding its complexities, revealing the meaning of intelligence in the healthy brain, while also respecting and understanding those that are different. As Roethke penned, "What is madness but nobility of soul at odds with circumstance!"

BREAKTHROUGHS

A chronology of discoveries by McGovern faculty

LOCALIZING LANGUAGE

Kanwisher discover a network

for language, a seminal finding

that upends dominant theories

STROKE SYNERGY

AUGUST 20, 2012

Emilio Bizzi identifies

distinctive "muscle synergy"

patterns in stroke patients

that are now being used to

rehabilitation programs in

the clinic.

develop more individualized

of brain regions specialized

Ev Fedorenko and Nancy

AUGUST 30, 2011

of the time.

ARTIFICIAL VISION

FEBRUARY 23, 2007

Tomaso Poggio creates a computer model that mimics human vision — technology that is now used in "smart" vehicles to recognize pedestrians, cyclists, and other vehicles.

OLD HABITS DIE HARD

OCT 19, 2005

Ann Graybiel identifies patterns of neural activity in the basal ganglia that change when habits are formed and broken—which may explain why bad habits like addiction are so hard to shake.

2000

PAYING ATTENTION

MAY 28, 2009

Bob Desimone finds that neurons in two brain regions fire in synchrony when we pay attention, and that disruptions in these brain waves may be linked to attention disorders such as ADHD.

DEVELOPING CONNECTIONS

JANUARY 14, 2006

By studying the formation and modification of synapses, Martha Constantine-Paton

discovers how the visual system in the developing brain is wired in response to activity and experience.

CRISPR REVOLUTION

JANUARY 3, 2013

Feng Zhang reports the first use of CRISPR for genome editing in human cells, setting off a revolution in neuroscience and biomedical research around the world.

EXPANDING BRAINS

JANUARY 15, 2015

Ed Boyden invents expansion microscopy, a method that physically enlarges brain tissue up to 100-fold, providing stunning high-resolution images of the nanoscale structure of the brain.

MRI SENSOR

MAY 1, 2014

Using magnetic resonance imaging (MRI) and a specialized molecular sensor, Alan Jasanoff maps neural signals with high precision over large areas of the living brain for the very first time.

TIME KEEPER

OCTOBER 8, 2015

Mehrdad Jazayeri discovers

networks of neurons that stretch or compress their activity to control timing, providing evidence that timing is a distributed process and that there is no single master clock in the brain.

SINGING IN THE BRAIN

NOVEMBER 30, 2015

Michale Fee identifies neural patterns birds use to learn their songs, unlocking a clue to how the human brain may generate complex sequential behaviors like speaking a sentence or delivering a tennis serve.

MIND READING

MARCH 12, 2018

Using a miniature MRI coil custom-tailored for smaller heads, **Rebecca Saxe** discovers that children as young as three have a brain network dedicated to interpreting the thoughts of other people.

SCANNING FOR DISEASE

JANUARY 21, 2016

John Gabrieli finds brain differences in children who

are vulnerable to depression before symptoms appear, suggesting that brain scans may identify children at high risk for developing mental illness later in life.

ALS GENE

MAY 4, 2018

H. Robert Horvitz discovers that C9orf72, a gene linked to familial amyotrophic lateral sclerosis (ALS), helps eliminate waste products in cells — a key contribution to our understanding of this important gene.

UNIQUELY HUMAN

OCTOBER 18, 2018

Mark Harnett discovers that human dendrites have different electrical properties from those of other species — a finding that may explain the enhanced computing power of the human brain.

AUTISM MODEL

JUNE 12, 2019

Using CRISPR, Robert Desimone and Guoping Feng engineer monkeys to express a gene mutation linked to autism—the new model could help scientists develop better treatments for neurodevelopmental disorders. н

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VISION QUEST

MAY 2, 2019

Jim DiCarlo performs the most rigorous testing to date of computational models that mimic the brain's visual cortex and shows that artificial neural networks can be used to control brain activity.

MAGNETIC DRUG DELIVERY

AUGUST 19, 2019

Using magnetic nanoparticles, Polina Anikeeva invents a technology to deliver drugs at precise times and in specific areas of the brain.

PITCH PERFECT

SEPTEMBER 19, 2019

In a cross-cultural study with

members of a remote Bolivian

that perception of musical pitch

tribe, Josh McDermott finds

varies across cultures and is

not a universal phenomenon.

BRAIN'S COMPASS

AUGUST 12, 2019

Ila Fiete identifies a brain circuit that distills complex information about the environment into a simple abstract compass in the brain—without which, "we would be lost in the world."

SENSORY GATEKEEPER

JULY 22, 2020

Guoping Feng and Mike

Halassa map the thalamic reticular nucleus, the brain's gatekeeper for sensory information, in unprecedented detail — providing potential drug targets for sensory symptoms of autism.

ALIM LADHA

Graduate Student, Zhang Lab

2019–20 HOCK E. TAN AND K. LISA YANG CENTER FOR AUTISM RESEARCH FELLOW

Long before he knew he wanted to become an engineer, Alim Ladha spent hours taking apart Xbox controllers to figure out how they work. Today, as a graduate student in Feng Zhang's lab, Alim tinkers with genetic code rather than computer circuits and motherboards. And his efforts may very well lead to a breakthrough in testing for COVID-19.

Together with Feng Zhang and McGovern Fellows Omar Abudayyeh and Jonathan Gootenberg, Alim has adapted the CRISPR gene editing technology to detect trace amounts of the COVID-19 virus. The new CRISPR-based research tool delivers results in an hour in a one-step reaction, advancing the technology closer to an at-home testing tool.

"Our dream is to see someone who has never used a pipette before perform a COVID test in the comfort of their own kitchen," Alim says. "Thanks to all of the amazing support we have received, this dream has the very real opportunity to become a reality." GGGCC

Photo: Michael D. Spencer

PEOPLE

20 McGovern Rising Stars

They are brilliant, innovative, and driven. Their passion for neuroscience is contagious.

These 20 McGovern "rising stars" — each from one of our 20 labs — represent the future of neuroscience.

We invite you to read their stories and be inspired.

NICOLAS MEIRHAEGHI

Imagine tossing a ping pong ball into the air with one hand and catching it with the other. After practicing it a few times, imagine doing it again with your eyes closed. There's a good chance you'll catch the ball, even without looking at it. This is the type of oddity Nicolas Meirhaeghe studies as a graduate student in Mehrdad Jazayeri's lab.

His work explores how we plan and perform movements in the face of uncertainty. In particular, he tries to understand how information coming from the outside world through our senses gets combined with our internal expectations when we practice the same movement over and over again. He also studies how complex patterns of neural activity change when inexperienced individuals progressively turn into experts, and learn to rely less on what they see, and more on what they expect.

Photo: Michael D. Spencer

Shannon Johnson wants to build tools that help people. Perhaps this is why she was drawn to the lab of Ed Boyden, who is best known for developing revolutionary neuroscience tools like optogenetics and expansion microscopy.

From volunteering at community science events to rethinking the American education system, Shannon believes science should be accessible to all. And as a graduate student in Ed Boyden's lab, she builds tools that help scientists access the inner workings of living neurons.

"The current tools used to image neural activity are analogous to black and white silent films," Shannon explains. "We want to build technologies that provide more of an HD movie experience."

In just two years, Shannon has done just that. Together with her colleagues, she created a molecular tool that provides unprecedented access to living cells. By engineering proteinbased sensors to cluster in living neurons, her tool creates a glittering map of activity within the cell.

SHANNON JOHNSON

Graduate Student, Boyden Lab

2020-21 K. LISA YANG AND HOCK E. TAN CENTER FOR MOLECULAR THERAPEUTICS FELLOW

ANNA IVANOVA

Graduate Student, Fedorenko Lab

Ever since she was a child growing up in Moscow, Anna Ivanova has been intrigued by language. In high school, she could speak four languages including her native Russian, but it was in college that she began to wonder how language is represented in the brain.

To explore this question, she joined the lab of Ev Fedorenko, known for having discovered a brain network specialized for language. Anna wondered, is this same network involved in other cognitive functions? Do words in a book evoke the same brain response as images with similar meaning? Using neuroimaging techniques, Anna has found that the language system in the brain is recruited, but not required, to process the meaning of an image or a scene. These results suggest that we can think—or find meaning in the world—without language. But how these meaningful concepts are represented in the brain, is a mystery that Anna hopes to solve in her next chapter.

HELEN SCHWERDT

Research Scientist, Graybiel Lab

When she's not wandering deep in the Blue Ridge Mountains, you will find Helen Schwerdt tinkering with microscopic fibers in Ann Graybiel's lab. A research scientist with a background in electrical engineering, Helen builds ultrathin probes that target brain microstructures with pinpoint accuracy.

Neurons communicate with both electrical and chemical signals, yet brain activity is often studied with tools that measure only electrical signals. Helen's probes detect both, in multiple brain locations—at the very same time.

"We know that chemical signals precede and regulate electrical activity," she says, "so understanding the relationship between the two is important if we want to understand the healthy and diseased brain."

Helen has zeroed in on Parkinson's disease, a brain disorder marked by a massive loss of dopamine and abnormal increases in electrical signaling. By tracking these aberrant signals over time, Helen's probes may help finally crack the code of this debilitating disease.

Photo: Michael D. Spencer





YASAMAN BAGHERZADEH Postdoctoral Fellow, Desimone Lab

After working with children with neurological disorders, Yasaman Bagherzadeh became determined to pursue a career in neuroscience. This pursuit would ultimately lead Yasaman 6000 miles from her hometown of Tehran, Iran to the lab of Bob Desimone at MIT.

With Desimone, she studies how the brain pays attention and hopes what she learns will help people with ADHD and related disorders.

"I want to know how we can sustain our attention in a world filled with distractions," she says.

Using magnetoencephalography, a neuroimaging technique that measures tiny magnetic fluctuations at the surface of the head, she has found that people can actually improve their attention by observing real-time displays of their own brain waves and attempting to control them.

A nationally ranked badminton player, Yasaman splits her time between the lab and the gym, but she remains focused on developing therapies to help people with a range of brain disorders. \bigcirc

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Why do people cheat? And how should they be punished? These are the questions that Setayesh Radkani explored in an ethics class in college, and the results took her by surprise.

"It turns out that there are many different reasons people cheat," she says, adding that some cheat to be perceived as the best in the

class while others cheat to avoid the potentially dire consequences of failing a class. "This makes the path to punishment quite complicated."

Setayesh joined Rebecca Saxe's lab to further explore the question of punishment through a cognitive neuroscience lens. Whom do we punish? And why? What processes operate inside the mind and brain when we make moral decisions? Setayesh is also using the tools of computational neuroscience in Mehrdad Jazayeri's lab to learn how the social and moral mind is structured.

In the end, she hopes these experiments will enrich our understanding of human nature.

ANDREW BAHLE

Graduate Student, Fee Lab

As a former musician who spent hours practicing and fine-tuning his craft, Andrew Bahle is intrigued by how baby birds learn to imitate the song of their father.

"It is magical to witness a young bird's imitation of his father's song crystallize out of hours of mistakes, babbling and trial and error," he says.

As a graduate student in Michale Fee's lab, Andrew uses tiny, silicon probes and birdsized microscopes to record brain activity while young zebra finches learn to sing their tutor's song. He hopes to learn how and where in the brain the memory of this song is stored because it may shed light on the brain circuits involved in imitation.

Understanding these circuits may also help us understand how humans work towards long-term goals—like learning to play Flight of the Bumblebee on a piano or pursuing a PhD at MIT.

ARGHYA Mukherjee,

Postdoctoral Associate, Halassa Lab

As a child growing up in an Indian coal mining city with significant socioeconomic disparities, Arghya Mukherjee became very interested in how our environment shapes the decisions we make in life. This interest led him directly to Mike Halassa's lab, where he studies the brain circuits involved in decision-making and how these circuits go awry in people with schizophrenia. "Once we identify these circuits," Arghya explains, "we can fix them." An approach, he says, that is much more precise than bathing the brain in drugs that were developed more than fifty years ago.

Arghya has identified two brain circuits — one that stabilizes activity in the prefrontal cortex (the part of the brain responsible for planning action) and the other that allows us to be flexible with our decisions and action plans. Arghya won't rest until he's found a way to manipulate these circuits and help people suffering from this debilitating psychiatric disorder. Most self-driving cars are stumped by harsh weather. A stop sign partially obscured by snow may cause an autonomous vehicle to misbehave in unexpected ways, but humans somehow effortlessly slow their own vehicles to a stop.

As a postdoc in the DiCarlo lab, Tiago Marques is developing computational models that, like our brains, can adapt to a wide range of challenging scenarios—such as obeying traffic rules regardless of the weather.

He combines engineering and neuroscience approaches to tweak existing AI models of vision to behave more like we do. Tiago engineers artificial neurons to "see" objects in the same way actual neurons do (as shown in the right column), making his models less likely to be fooled under challenging circumstances.

"We are our brains," he says. "By developing models that better resemble human vision, we are advancing our understanding of what makes us unique." TIAGOMARQU

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QUIQUE TOLOZA

Graduate Student, Harnett Lab

Quique Toloza studied physics, biology and Spanish literature in college, but it was a series of neuroscience classes that really ignited his imagination.

"Using tools developed to solve problems in physics," Quique explains, "is a beautiful way to study the rich behaviors and emergent dynamics of the brain. I think that's the coolest natural phenomenon you could possibly study."

Quique has since found his niche as a graduate student in Mark Harnett's lab studying the powerful processing capabilities of individual neurons — specifically dendrites, the elaborate tree-like branching structures that receive signals from other neurons.

His computational models, combined with experiments performed in the lab, are revealing how the complex calculations made by individual dendrites contribute to the unique computational power of the human brain. While he draws heavily from his background in physics, two secret ingredients also power his work: black metal (the music, not the material) and lightsaber battles with his lab mates.



YENA HAN

Graduate Student, Poggio Lab 2020–21 LORE HARP MCGOVERN FELLOW

DIPON GHOSH

Postdoctoral Fellow, Horvitz Lab

It was the mystery of the unknown that originally attracted Dipon Ghosh to biology in college, and it is a mysterious behavior of the microscopic roundworm *C. elegans* that now drives his postdoctoral studies in H. Robert Horvitz's lab.

C. elegans do not possess eyes or the light-sensitive photoreceptors that humans use to see colors, yet Dipon discovered that these worms can somehow decide whether to eat or avoid bacteria based on color. He identified two genes that worms use to "sense" colors and found that

How is it that we recognize an apple whether it's green or red, on a tree, or in a bowl with other fruit? Seems obvious to us, but machine vision systems struggle to recognize objects under varying conditions.

Yena Han wants to understand why humans are so good at this, even after seeing an object only once.

Photo: Michael D. Spencer

In the Poggio lab, she is applying her electrical engineering and computer science background toward developing more humanlike computer vision systems.

"Consider how children learn," she explains. "They're presented with a stream of unfamiliar objects and yet they learn to recognize them quickly, under all kinds of conditions. My goal is to engineer computer models that mimic this kind of human behavior."

Yena is well on her way, having already engineered a model that outperforms other machine vision systems in seeing the world the way humans do.

Photo: Michael D. Spencer

corresponding genes exist in other species, including humans, and are involved in how cells respond to stresses, including light. Dipon believes the worm might tap into this ancient stress response to detect — and avoid — pigments associated with toxic bacteria.

Dipon's curiosity might reveal new roles for retinal cells—including how they protect themselves against damage caused by light—and perhaps also a more vivid picture of how we experience color.

JIMIN PARK

Graduate Student, Anikeeva Lab

When Jimin Park first joined Polina Anikeeva's lab, he didn't know the difference between a mouse and a rat. He was a materials scientist who used electrochemical techniques to build energy devices and metal implants for broken bones—but the brain was new territory.

"Fixing bones is very different than fixing the brain," he says. "I had to learn everything new, from mouse surgeries to choosing materials that work in the brain. I also had to learn patience."

Fortunately, Jimin is a remarkably quick study. Tapping into his electrochemical expertise, he created fibers that are compatible with delicate brain tissue and can generate nitric oxide on demand in the brain. Nitric oxide is an important signaling molecule in the body, but its precise role has been difficult to pin down, until now.

Jimin's fibers—and his patience—have provided researchers with a tool to study how this gas influences the nervous, circulatory, and immune systems.

NAN LI

Research Scientist, Jasanoff Lab

make this happen.

Photo: Michael D. Spencer

Nan has developed molecular functional magnetic resonance imaging (fMRI)

Nan Li wants to see the neurons, circuits and whole brain regions that make us who we are. As a research scientist in Alan Jasanoff's lab, she's building the tools to

"The world isn't one-dimensional," she says. "Shouldn't the images of our brains also be dynamic and three-dimensional?"

strategies with a specialized sensor that tracks how dopamine influences nearby and distant brain regions. Where traditional fMRI reveals general brain activity based on blood flow, Nan's sensor tells us which type of cells in the brain become active and where the neurotransmitter travels throughout the brain—providing a more comprehensive and detailed picture of the brain's activity.



VICTORIA BEJA-GLASSER

2020-21 FRIENDS OF THE MCGOVERN INSTITUTE FELLOW

Alzheimer's disease (AD) while others escape this irreversible and progressive

Based on large-scale genetic studies, Victoria Beja-Glasser believes a clue may lie in a little-known gene called ABCA7. When mutated, it increases the risk for AD, especially in non-Caucasian populations.

After graduating from Mount Holyoke with a degree in neuroscience and four years as a forward on their NCAA field hockey

team, Victoria joined Guoping Feng's lab to pursue her interest in age-related brain disorders. She honed in on ABCA7 because few people have studied the gene and because she can study its effects in multiple species.

- "This gene is highly conserved," she explains, which means it has remained essentially unchanged throughout evolution.
- "So if we find something in a mouse model, there's a good chance we can shed light on its role in humans."

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HEATHER Kosakowski

Graduate Student, Kanwisher and Saxe Labs

Why do people do bad things?

This is the question that gnawed at Heather Kosakowski, who endured a difficult childhood, including years in the foster care system followed by a stint with the Marines. But it was the moment her daughter Hannah was born that inspired Heather to really explore this question, using the tools of cognitive neuroscience.

"The only way to understand what happens when things go wrong in the brain," she says, "is to understand what happens when they go right."

In the Saxe lab, Heather scans babies as young as two weeks, looking for signatures of the social brain. Using a miniature MRI coil custom-tailored for smaller heads, Heather is the first scientist to discover that infants have brain regions that selectively respond to faces, bodies, and scenes. Her work provides an unprecedented glimpse into the newborn mind and the functional organization of the human brain.

Photo: Michael D. Spencer

LIRON ROZENKRANT Postdoctoral Fellow, Gabrieli Lab

Photo: Michael D. Spence

Liron Rozenkrantz is fascinated by the placebo effect—so fascinated, in fact, that she moved her family from Israel to Cambridge to explore this phenomenon with cognitive neuroscientist John Gabrieli.

"The moment I learned that the brain is not a passive organ, that it actively generates how we view the world," she says, "was a complete game changer for me. This means that expectations we hold can actually shape the reality we perceive!"

In the Gabrieli lab, Liron is exploring how our beliefs and expectations influence our perception of the world. Using brain imaging technologies together with sophisticated behavioral investigations, she hopes to learn whether we can actually harness these beliefs to improve our lives.

Liron is particularly enthusiastic about the relevance of her research to the world today. In the so-called post-truth era, how we view reality may be more important than ever.

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As a graduate student in Ila Fiete's lab, Sugandha (Su) Sharma uses mathematical tools to study how the brain helps us navigate the world.

"It's fascinating that the same brain regions that help us navigate through a city, can also help us infer relationships in family trees and social hierarchies," says Su. The brain continuously computes the body's position in space and makes adjustments to that estimate as we move about. Su is particularly interested in how the brain extrapolates information from one spatial environment to navigate new and different environments.

Our ability to navigate a labyrinth, for example, depends on a so-called "cognitive map," or a mental representation of our physical environment. Su studies how this map is learned and organized in the brain so that we can quickly and efficiently find our way in the physical—and social—world.

> Jenelle Feather is so enchanted by the cochlea—a bony labyrinth in the inner ear that transforms sound vibrations into nerve impulses—that she wears a handcrafted silver cochlea pendant around her neck.

"I've always been curious about how humans perceive the world," she says. Her particular interest

Photo: Michael D. Spencer

JENELLE FEATHER

Graduate Student, McDermott Lab

2020-21 FRIENDS OF THE MCGOVERN INSTITUTE FELLOW

lies in what happens after the cochlea transforms sound waves into nerve signals. "I want to understand how the brain interprets this transformed representation of incoming sound."

Jenelle is specifically interested in auditory textures — sounds that are composed of many similar elements, but are perceived as single noise — like rain, wind, and fire. As a graduate student in Josh McDermott's lab, Jenelle discovered that computational models of auditory systems capture human texture perception fairly well, but stumble on other domains like speech perception. She is now building artificial neural networks that more accurately mimic how humans perceive sound.

WHAT DOES THE FUTURE HOLD?

Some of our faculty share their predictions for the next twenty years of neuroscience.

"By leveraging materials chemistry and physics, we envisage devices that will monitor and modulate specific recentors in neurons and non-neuronal cells during behavior. These tool "By leveraging materials chemistry and physics, we envisage devices that will monitor and modulate specific receptors in neurons and non-neuronal cells during behavior. These tools will onerate at scales of individual proteins and will eliminate the need for hardware." modulate specific receptors in neurons and non-neuronal cells during behavior. These will operate at scales of individual proteins and will eliminate the need for hardware." "I predict we will be able to watch genes and cells in real time as they compute and change in disease states, precisely man how they are organized, and even control their functions with Jos I "I predict we will be able to watch genes and cells in real time as they compute and change in disease states, precisely map how they are organized, and even control their functions with molecular precision. This will allow us to design ultra-targeted therapies for complex disease." disease states, precisely map how they are organized, and even control their functions with molecular precision. This will allow us to design ultra-targeted therapies for complex diseases."

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"I hope that our understanding of the brain—how it functions and how it goes awry in neurologic and neuro-"I hope that our understanding of the brain—how it functions and how it goes awry in neurologic and neuro-psychiatric diseases—will be at the stage that cancer biology is at today, with a fundamental understanding of the biology and with novel notent therapeutics based on that understanding. It is the investment over the nas psychiatric diseases—will be at the stage that cancer biology is at today, with a fundamental understanding of the biology and with novel potent therapeutics based on that understanding. It is the investment over the past decades in basic aspects of biology that has led to the revolutionary advancements in cancer treatments and the biology and with novel potent therapeutics based on that understanding. It is the investment over the past decades in basic aspects of biology that has led to the revolutionary advancements in cancer treatments, and it is only with a similar investment in the study of basic aspects of nervous system biology—how the nervous decades in basic aspects of biology that has led to the revolutionary advancements in cancer treatments, and it is only with a similar investment in the study of basic aspects of nervous system biology—how the nervous system develops and works—that such advances will occur in the field of neuroscience." it is only with a similar investment in the study of basic aspects of nervous system biology. system develops and works—that such advances will occur in the field of neuroscience." H. ROBERT HORVITZ

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"In the last 20 years, we've made great strides in modeling cognition and basic circuit interactions

in the brain. In the next 20 years, we will connect the two: how circuit interactions give rise to sophisticated cognition — the brain/neural basis of cognition."

"We will see great expansion of gene therapy in clinics and we will have cures for many severe neurodevelopmental and neurological disorders that are caused by simple genetic mutations.

neurodevelopmental and neurological disorders that are caused by simple genetic mutatio single cell technologies will empower us to develop drugs that precisely tream modulating brait disorders with minimal side effects. Lalso envision non-invasive devices for modulating brait

"We will see great expansion of gene therapy in clinics and we will have cures for many severe neurodevelopmental and neurological disorders that are caused by simple genetic mutations. Single cell technologies will empower us to develop drugs that precisely treat psychiatric

Single cell technologies will empower us to develop drugs that precisely treat psychiatric disorders with minimal side effects. I also envision non-invasive devices for modulating brain functions such as attention, sleep, and emotion."

"Brain imaging and cognitive neuroscience will offer new views of how variation in brain structure and function makes each of us unique, and this will fuel a revolution in personalized mental health

JOHN GABRIELI

disorders with minimal side effects. I also envision functions such as attention, sleep, and emotion.

GUOPING FENG

treatments and educational practices that will empower flourishing in so many more of us."

"The next 20 years will be a golden age for AI systems that are not really intelligent but will enable us to are atly expand our effective intelligence. We will have self-driving cars that are safer than human-driven "The next 20 years will be a golden age for AI systems that are not really intelligent but will enable us to greatly expand our effective intelligence. We will have self-driving cars that are safer than human-driven cars on many specific roads and under some restrictions. They will be much better than they are today but they greatly expand our effective intelligence. We will have self-driving cars that are safer than human-driven cars on many specific roads and under some restrictions. They will be much better than they are today but the will be still far from human intelligence, especially in terms of breadth, flevibility and real understanding. on many specific roads and under some restrictions. They will be much better than they are today but they will be still far from human intelligence, especially in terms of breadth, flexibility and real understanding. I expect the same to be true for digital personal assistants like Aleva or Siri. They will be supprise however, it is a superior between the same to be true for digital personal assistants like Aleva or Siri. They will be supprise how one to be true for digital personal assistants like Aleva or Siri.

FENG ZHANG

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"Techniques for exploring how the brain works, across all levels, will escalate greatly in power. Huge improvements will be made in treatments targeted to the central and peripheral nervous systems – akin to the near-abolishment of polio, or to the treatment of type I diabetes. Organ systems will become recognized as interrelated parts of our biological makeup, so that information and treatment options can be shared. With parallel advances in other fields, such as engineering and physics, treatments will become less invasive or even fully non-invasive."

ANN GRAYBIEL

"Computing devices will integrate silicon and biological circuits to significantly expand the capability of computing devices with integrate sincon and biological directions to significantly expand the capability of computing. Continued advances in our ability to decode neural circuitry and development of synthetic computing. Continued advances in our ability to decode neural circuitry and development of synthetic complex neural tissues such as organoids will yield powerful biological devices. For example, a biological devices are presented as a biological device of the second device of the s device employing a synthetic smell circuitry will be able to detect years in advance that a person is developing Parkinson's disease based on that person's scent."

will be still far from human intelligence, especially in terms of breadth, flexibility and real understanding. I expect the same to be true for digital personal assistants like Alexa or Siri. They will be superior however, in terms of raw knowledge and connectivity. My personal bet is that real progress in AL over the next 50–100 expect the same to be true for digital personal assistants like Alexa or Siri. They will be superior however, in terms of raw knowledge and connectivity. My personal bet is that real progress in Al, over the next source of intelligence from neuroscience and computational neuroscience." terms or raw knowledge and connectivity. My personal bet is that real progress in AI, over the next 50–10 years, will come from the science of intelligence – from neuroscience and computational neuroscience."



Theoretical issues in deep networks PNAS

nstitute of Technology, Cambridge, MA 02139 Poggio^{s,1}, Andrzej Banburski^a, and Qianli Liao

Donoho, Stanford University Stanford, CA, and approved May 1, 2020 (received for re (4) Danish, Danoho, Stanford University, Stanford, CA, and approved May 1, 2020 terevised for.
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(7) Stanford Stanford University, Stanford, CA, and Stanford University, Stanford CA, and Stanford University, Stanford CA, and Stanford University, Stanford Universit roximation theory both snanow to approximate any continuous st. However, we proved that for functioned to the standard strategies function of the strategies of the host weight sharing) can avoid in characterizing minimization of type the weight directions rather user weight directions rather user is the relevant function underlying dassification correspond-to the relevant function underlying dassification constrained normalized networks. The dynamics of normalized problem is a being to those of the constrained problem is a being to a unit norm constraint. In parto a unit norm construct the same

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2. Approximation: We start with the first set of questions, summarizing-trefs, 3 and 6-9. The main result is that deep networks there are a guarantee, which shallow networks do not they can avoid the curse of dimensionality for an impor-ting on avoid the curse of dimensionality for a com-they can avoid the curse of dimensionality for a com-tage of the start of theoretical galation they can avoid the curse of problems, correspon functions, that is, function subset of compositions subset of compositions al-in the s app that can be deep are of the deep importantly, we ent functions

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