Science at MIT

Summer 2023 **Published twice yearly**

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Sarah Costello and Phie Jacobs

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Sarah Costello

Contributing Writers:
Elizabeth Chadis, Jennifer Chu, Sarah Costello, Phie Jacobs, and Anne Trafton

Proofreader + Copyeditor:
Matthew Christensen and Phie Jacobs

Design:
Ink Design, inc.

Cover image:
Ellen Weinstein

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TABLE OF CONTENTS

Letter from the Dean

My fellow alumni and friends,

The summer 2023 issue of *Science@MIT* brings us back to basic, fundamental research. As scientists, this is what we do: We ask questions about the fundamental nature of the world around us. And each question leads to another question. This inquisitiveness is the hallmark of the scientific enterprise.

Our feature story exemplifies where that curiosity can lead. Professor Mriganka Sur in the Department of Brain and Cognitive Sciences is interested in how our brain develops and changes. How does our brain respond to inputs from other parts of our body and vice versa? When someone loses their sight, how do circuits rewire to compensate for that loss of information coming into the brain through the eyes? What changes at a molecular level? Is there a difference early on in development? Can this plasticity of neuronal circuits last through later stages of brain development?

These are long-standing questions that underpin our ability to learn and make decisions. The answers have impact ranging from understanding brain disorders to developing architectures for next-generation artificial intelligence. And we often don't know the impact that answering one of these questions will have in the future.

In this case, Mriganka's fundamental discovery — what he calls "ocular dominance plasticity" — became the rationale for others outside of MIT to develop clinical trials to test a potential therapeutic for the devastating disease known as Rett syndrome. Less than 15 years after his research was published in a 2009 *Proceedings of the National Academy of Sciences (PNAS)* paper, a drug called Trofinetide is now available to treat Rett syndrome.

Read an interview with Mriganka on page 4. "It is the dream of every neuroscientist to have an impact on the world in some way," he says — truly an amazing outcome of the sometimes long and unpredictable arc of scientific inquiry.

These types of questions — as well as the desire to impact the world — also drive scientists in other fields; and this issue of *Science@MIT* presents profiles of the faculty and graduate students who ask them. In the realm of cosmology, which encompasses my own field of astrophysics, Martin Luther King Jr. Visiting Scholar Brian Nord models galaxy clusters and their effect on distorting light traveling through the cosmos. His statistical models allow him to understand both dark matter that pulls the universe together, as well as dark energy, the mysterious force driving the universe's expansion. Learn more on page 7.

Physics faculty member Phiala Shanahan is attempting to ask new questions about the Standard Model of Physics and dark matter from the other end of the scale. How do the interactions between elementary particles in one proton relate to the behavior of interactions between multiple protons? Turns out, this question isn't answered yet but will form the bridge to help us get from quarks and gluons within one proton to the protons within atoms that make up the visible matter of our world — as well as their interactions with the universe's invisible dark matter. Read more about Phiala's work on page 11.

In between the universe-scale and the elementary-particle scale, Gabriela Schlau-Cohen in the Department of Chemistry began with questions about plants and their ability to photosynthesize. How do these photosynthetic light-harvesting proteins work both individually and as part of the larger protein complexes and networks? How do they change in response to different amounts of sunlight? In her current work, Gabriela uses answers from those previous questions to engineer nanostructures that can be even more efficient than plants at harvesting light. Read about her other questions on page 9.

Energy and climate science underpin the questions asked by Timur Cinay, our current holder of the E. Alan Phillips Fellowship for Environmental Sustainability supported by a generous gift from alumna Audrey Buyrn. Timur will help to set up an experimental device in the ocean off of the Galápagos Islands to study the dynamics of marine microbes and their emissions of the greenhouse gas nitrous oxide.

In the rest of the issue, we offer the stories of other great questions and answers from some of the top minds within the MIT School of Science. Applied mathematician Peter Shor gives his account of the development of his eponymous algorithm. Biologist and emerita professor Nancy Hopkins tells of the gender-based roadblocks on the way to her discoveries in a presentation for International Women's History Day about the book *The Exceptions*.

Like Nancy and Peter, Brian and Phiala, Gabriela and Timur, I hope you, too, will stay curious and support our scientists in our quest for answers — and more questions — here at MIT Science.

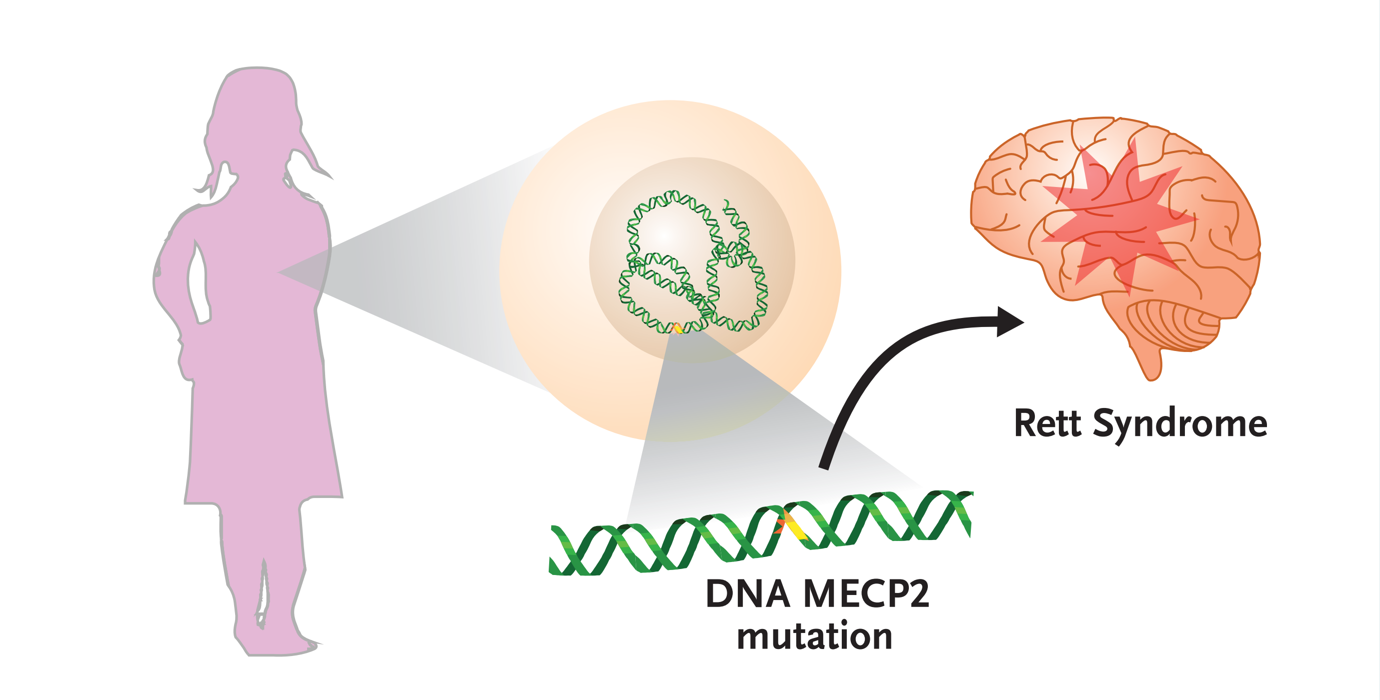
With my very best wishes,

Dean Nergis Mavalvala PhD '97

3 Questions: Mriganka Sur on the research origins treating Rett syndrome

On March 10 the FDA approved Trofinetide, a drug based on the protein IGF-1; the MIT professor's original research showing that IGF-1 could treat Rett was published in 2009

David Orenstein | Picower Institute for Learning and Memory



Mutation of the MECP2 gene on the X chromosome causes Rett syndrome, a severe neurodevelopmental disorder. *Illustration: Tom DiCesare*

Rett syndrome is a devastating developmental disorder, principally occurring in girls, caused by mutations in the gene MECP2 that leads to severe cognitive, motor, and other symptoms. As such, the March 10 approval by the U.S. Food and Drug Administration of the first-ever treatment for the disorder, a drug called Trofinetide based on the natural protein IGF-1, brings new hope to patients and their families.

The approval is also a dream come true for Mriganka Sur, Paul E. and Lilah Newton Professor of Neuroscience in The Picower Institute for Learning and Memory and the Department of Brain and Cognitive Sciences at MIT. His lab's preclinical discoveries in mice, particularly a highly influential paper published in 2009, provided the first demonstration that injecting IGF-1 or its peptide fragment could reverse the effects of reduced or altered MECP2. This provided a mechanism-based rationale for IGF-1 as a potential therapeutic intervention. And Sur's lab has never stopped studying Rett syndrome since.

The research began nearly 20 years ago when his lab was studying a famous phenomenon in neuroscience: When an animal's eye is blocked during a critical period of development, the brain shifts neural connections called synapses to devote more brainpower to the unblocked eye. Sur's lab investigated the molecules involved in this flexibility, or "ocular dominance plasticity," and discovered IGF-1's role. Here, Sur discusses his Rett syndrome research.

Q: How did your lab discover that IGF-1 might be a potential Rett syndrome therapeutic?

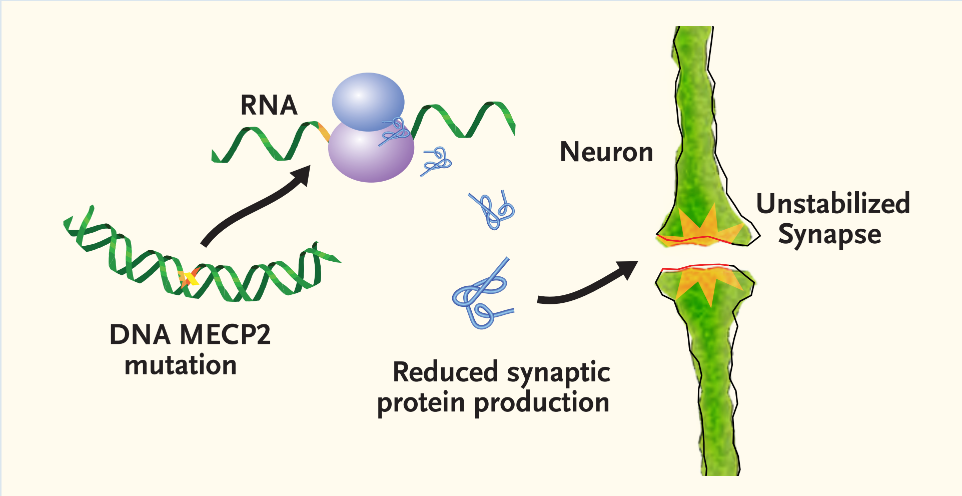
A: We decided to study the molecular basis of ocular dominance plasticity using a large-scale, unbiased screen. An interesting gene set that changed when an eye was closed was the IGF-1 gene set named for the growth factor IGF-1. When we checked one week after closing the eye, a binding protein for IGF-1 had gone up. It soaked up a lot of IGF-1. That suggested that to make connections change you must decrease molecules like IGF-1.

This was published in a paper in 2006 in *Nature Neuroscience*, where Daniela Tropea, who was a postdoc in the lab, led the experiments. The icing on the cake was when Daniela delivered a peptide form of IGF-1 to the brain. When she did that and closed the eye, thereby overcoming the reduction of IGF-1, then this shift of synapses did not happen. The addition of IGF-1 into the brain stabilized synapses and made them resistant to change, essentially making them adult-like.

In 2007 the lab of Adrian Bird in Edinburgh made a mouse line in which they could keep MECP2 in check for the first five or six weeks of life, so that the mice began to develop Rett syndrome-like symptoms. But then Adrian's lab turned the gene back on and the mice largely recovered. I was immediately struck by this discovery. It showed that Rett syndrome is not a disorder of degeneration, it is a disorder of aberrant and even abnormally prolonged development: loss of MECP2 likely reduces molecules that the brain requires for normal development, but adding back these molecules could enable the brain to develop normally, at least to some extent.

The developing brain shows pronounced plasticity, as demonstrated by ocular dominance plasticity in the visual cortex. This plasticity occurs only during early life, and not later. If mice missing MECP2 had aberrantly prolonged development, they should show this plasticity later in life as well. Daniela and I decided to do an experiment to test this idea. We asked whether we could use our visual cortex paradigm to ask, is there prolonged plasticity into adulthood in Rett model mice and can we reverse it by adding IGF-1? We did this using Rett model mice from the lab of Rudolf Jaenisch at the Whitehead Institute for Biomedical Research.

Mriganka Sur's fundamental research into molecular mechanisms of synaptic plasticity in the brain enabled his lab to discover the role that a protein called IGF-1 could play in treating Rett syndrome. *Photo: Faith Ninivaggi*



Mutated MECP2 DNA, upon transcription into RNA, results in reduced production of proteins needed to stabilize the circuit connections between neurons, called "synapses." *Illustration: Tom DiCesare*

Unlike in normal mice, where there is only a critical time window of plasticity in the visual cortex, Rett model mice showed an effect of closing one eye even in adulthood. We immediately then asked, is there reduced IGF-1 in the brain? And there was, and there was increased IGF-1 binding protein. These mice were in a state of perpetual plasticity.

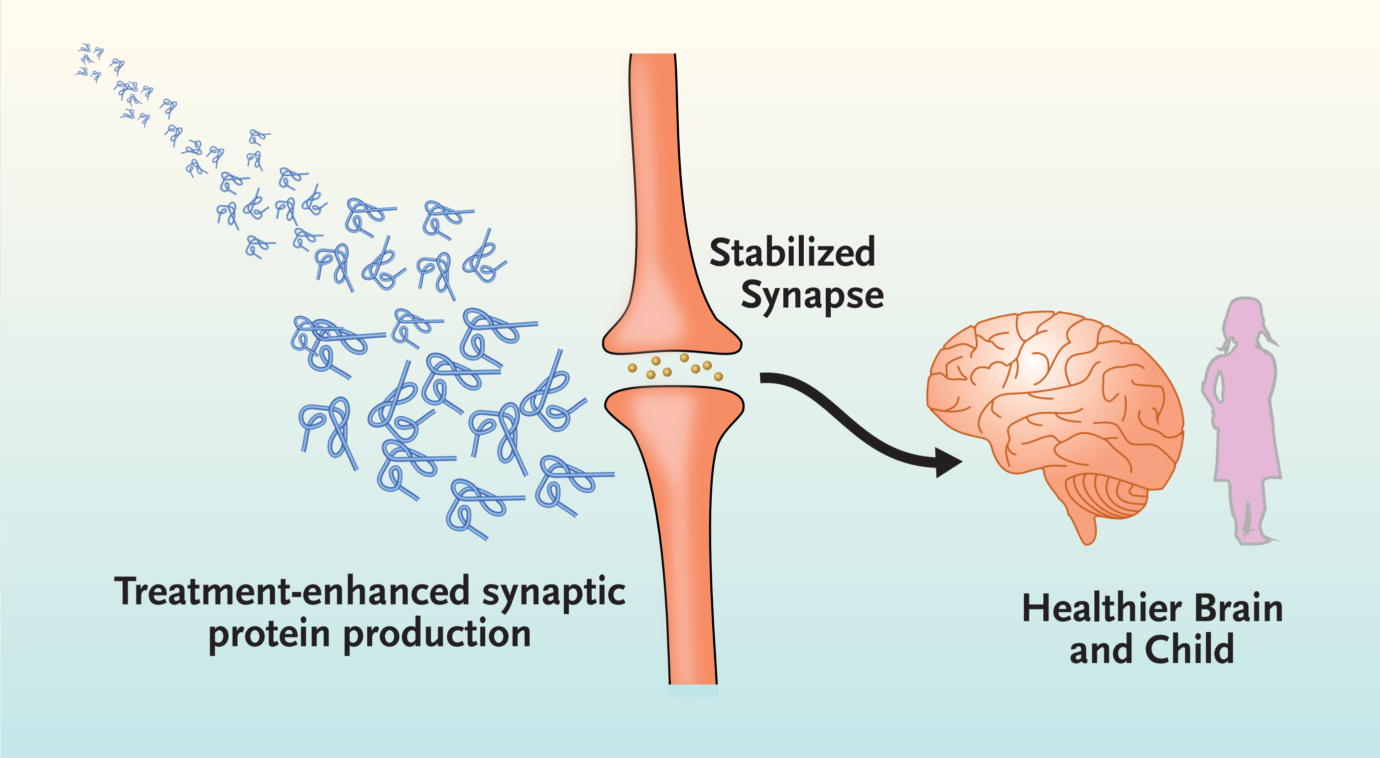
We reasoned if we could give adult Rett model mice a peptide form of IGF-1 via injection the effect of this perpetual plasticity should go away, meaning that the animals should not show an effect of the eye being closed — as occurs when mice normally mature. And that's what happened. We showed that IGF-1 peptide increased expression of a number of synaptic molecules and made excitatory synapses stronger. This provided a powerful mechanism for explaining the effects of the drug. Finally, we asked, do the mice do better in other ways? We found that the mice lived longer, that they moved better, and other symptoms improved.

We published that discovery in 2009 in *PNAS*: In a mouse model we showed that by understanding the molecules underlying Rett syndrome's prolonged development and plasticity we could intervene to potentially offset the molecular and synaptic deficits and treat the disorder. This is the foundational discovery behind Trofinetide and its mechanism of action in Rett syndrome.

Q: Tell us about your lab's continued work on fundamental mechanisms of Rett syndrome?

A: We've never stopped working on Rett syndrome. It's a devastating disorder, and there is certainly still much left to learn.

In 2014 we published another paper in *PNAS* showing that doses of recombinant human IGF-1 were effective in mice.



Treatment with an IGF-1 peptide supplies proteins needed to enhance stabilization of synapses, leading to more mature, stable synapses and healthier circuits supporting brain functions such as behavior and cognition. *Illustration: Tom DiCesare*

And I was also the co-author in that same journal later that year showing encouraging results in a small human clinical trial.

We've also done more research, right up to the present day, to understand the fundamental mechanisms of how the genetic mutations perturb brain development. In 2017 using induced stem cell cultures derived from patients and normal subjects, we found that when MECP2 is lacking, microRNAs critical to proper brain development become misregulated. Overexpression of the microRNAs prevented new neurons from being born, whereas inhibiting the microRNAs enabled healthy neural birth. This was a surprisingly early effect of Rett syndrome that we demonstrated directly in human neurons and their progenitors.

Last year we used an innovative combination of advanced imaging methods and human stem cell-derived organoids to show that in Rett syndrome, the migration of neurons to the cerebral cortex becomes much slower and highly erratic. These discoveries led to the sobering realization that there can be very early changes in brain development due to the genetic mutations of Rett syndrome.

Q: What is the significance of seeing this basic research achieve clinical utility and impact?

A: By studying plasticity in normal mice and the fundamental mechanisms by which synapses change, and hence change brain function and behavior, we moved into analyzing the effect of a gene that underlies a devastating brain disorder. IGF-1 peptide has become the very first molecule to reach this stage for any developmental brain disorder in that it is a mechanism-based therapeutic. Based on an animal model and doing the mechanistic analysis of why does the gene affect the brain and how might we offset it, we set the course for the first drug to treat Rett syndrome.

A lot of the early work was Daniela's insight in terms of how to think about basic mechanisms of developmental plasticity and apply them to brain disorders. This was completely uncharted territory as to whether plasticity would be a phenomenon underlying developmental disorders, and whether the visual cortex in the mouse could then model the disorder. And finally, we had the idea that a molecule that has a role in regulating this plasticity can be applied to the disorder. Many ideas in science don't work out, but this one did. Several people from my lab participated in the discovery. We also could not have tested these ideas without our collaboration with Rudolf Jaenisch and his lab. He was very generous with his lab's resources — we had no grant funds for this work at that time — and our labs have now collaborated on several studies since then.

It is the dream of every neuroscientist to have an impact on the world in some way. And this is my dream come true!

Understanding our place in the universe

Martin Luther King Jr. Scholar Brian Nord trains machines to explore the cosmos and fights for equity in research

Phie Jacobs | School of Science

Brian Nord first fell in love with physics when he was a teenager growing up in Wisconsin. His high school physics program wasn't exceptional, and he sometimes struggled to keep up with class material, but those difficulties did nothing to dampen his interest in the subject. In addition to the main curriculum, students were encouraged to independently study topics they found interesting, and Nord quickly developed a fascination with the cosmos. "A touchstone that I often come back to is space," he says. "The mystery of traveling in it and seeing what's at the edge."

Nord was an avid reader of comic books, and astrophysics appealed to his desire to become a part of something bigger. "There always seemed to be something special about having this kinship with the universe around you," he recalls. "I always thought it would be cool if I could have that deep connection to physics."

Nord began to cultivate that connection as an undergraduate at Johns Hopkins University. After graduating with a BA in physics, he went on to study at the University of Michigan, where he earned an MS and PhD in the same field. By this point, he was already thinking big, but he wanted to think even bigger. This desire for a more comprehensive understanding of the universe led him away from astrophysics and toward the more expansive field of cosmology. "Cosmology deals with the whole kit and caboodle, the whole shebang," he explains. "Our biggest questions are about the origin and the fate of the universe."

Dark mysteries

Nord was particularly interested in parts of the universe that can't be observed through traditional means. Evidence suggests that dark matter makes up the majority of mass in the universe and provides most of its gravity, its nature largely remains in the realm of hypothesis and speculation. It doesn't absorb, reflect, or emit any type of electromagnetic radiation, which makes it nearly impossible for scientists to detect. But while dark matter provides gravity to pull the universe together, an equally mysterious force — dark energy — is pulling it apart. "We know even less about dark energy than we do about dark matter," Nord explains.

For the past 15 years, Nord has been attempting to close that gap in our knowledge. Part of his work focuses on the statistical modeling of galaxy clusters and their ability to distort and magnify light as it travels through the cosmos. This effect, which is known as strong gravitational lensing, is a useful tool for detecting the influence of dark matter on gravity and for measuring how dark energy affects the expansion rate of the universe.

After earning his PhD, Nord remained at the University of Michigan to continue his research as part of a postdoctoral fellowship. He currently holds a position at the Fermi National Accelerator Laboratory and is a senior member of the Kavli Institute for Cosmological Physics at the University of Chicago. He continues to investigate questions about the

MLK Visiting Scholar Brian Nord's work focuses on how to improve the ways in which we make scientific discoveries — developing algorithms, designing experiments, and re-envisioning research communities. *Photo: Courtesy of the researcher* origin and destiny of the universe, but his more recent work has also focused on improving the ways in which we make scientific discoveries.

AI powerup

When it comes to addressing big questions about the nature of the cosmos, Nord has consistently run into one major problem: although his mastery of physics can sometimes make him feel like a superhero, he's only human, and humans aren't perfect. They make mistakes, adapt slowly to new information, and take a long time to get things done.

The solution, Nord argues, is to go beyond the human, into the realm of algorithms and models. As part of Fermilab's Artificial Intelligence Project, he spends his days teaching machines how to analyze cosmological data, a task for which they are better suited than most human scientists. "Artificial intelligence can give us models that are more flexible than what we can create ourselves with pen and paper," Nord explains. "In a lot of cases, it does better than humans do."

Nord is continuing this research at MIT as part of the Martin Luther King Jr. (MLK) Visiting Scholars and Professors Program. Earlier this year, he joined the Laboratory for Nuclear Science, with Jesse Thaler in the Department of Physics and Center for Theoretical Physics (CTP) as his faculty host. Thaler is the director of the National Science Foundation's Institute for Artificial Intelligence and Fundamental Interactions. Since arriving on campus, Nord has focused his efforts on exploring the potential of AI to design new scientific experiments and instruments. These processes ordinarily take an enormous amount of time, he explains, but AI could rapidly accelerate them. "Could we design the next particle collider or the next telescope in less than five years instead of 30?" he wonders.

But if Nord has learned anything from the comics of his youth, it is that with great power comes great responsibility. AI is an incredible scientific asset, but it can also be used for more nefarious purposes. The same computer algorithms that could build the next particle collider also underlie things like facial recognition software and the risk assessment tools that inform sentencing decisions in criminal court. Many of these algorithms are deeply biased against people of color. "It's a double-edged sword," Nord explains. "Because if [AI] works better for science, it works better for facial recognition. So, I'm working against myself."

Culture change superpowers

In recent years, Nord has attempted to develop methods to make the application of AI more ethical, and his work has focused on the broad intersections between ethics, justice, and scientific discovery. His efforts to combat racism in

> "Our biggest questions are about the origin and the fate of the universe."

STEM have established him as a leader in the movement to address inequities and oppression in academic and research environments. In June of 2020, he collaborated with members of Particles for Justice — a group that boasts MIT professors Daniel Harlow and Tracy Slatyer, as well as former MLK Visiting Scholar and CTP researcher Chanda Prescod-Weinstein — to create the academic Strike for Black Lives. The strike, which emerged as a response to the police killings of George Floyd, Breonna Taylor, and many others, called on the academic community to take a stand against anti-Black racism.

Nord is also the co-author of Black Light, a curriculum for learning about Black experiences, and the co-founder of the Change Now, which produced a list of calls for action to make a more just laboratory environment at Fermilab. As the co-founder of Deep Skies, he also strives to foster justice-oriented research communities free of traditional hierarchies and oppressive power structures. "The basic idea is just humanity over productivity," he explains.

This work has led Nord to reconsider what motivated him to pursue a career in physics in the first place. When he first discovered his passion for the subject as a teenager, he knew he wanted to use physics to help people, but he wasn't sure how. "I was thinking I'd make some technology that will save lives, and I still hope to do that," he says. "But I think maybe more of my direct impact, at least in this stage of my career, is in trying to change the culture."

Physics may not have granted Nord flight or X-ray vision — not yet, at least. But over the course of his long career, he has discovered a more substantial power. "If I can understand the universe," he says, "maybe that will help me understand myself and my place in the world and our place as humanity."

Gabriela Schlau-Cohen: illuminating photosynthesis

Using ultrafast spectroscopy, the chemistry professor studies the energy transfer that occurs at femtosecond timescales inside plant leaves

Anne Trafton | MIT News Office

During photosynthesis, chlorophyll in plants absorbs packets of energy called photons from the sun's rays. This energy is then transferred to a series of other chlorophyll molecules organized by protein scaffolds, funneling the energy into the next stage of photosynthesis.

Those early light-harvesting stages of photosynthesis involve repeated excitation of pigments, as photons are passed between them. To capture these highly dynamic processes, MIT Associate Professor Gabriela Schlau-Cohen employs ultrafast spectroscopy, a technique that uses extremely short laser pulses to study events that happen on timescales of femtoseconds to nanoseconds.

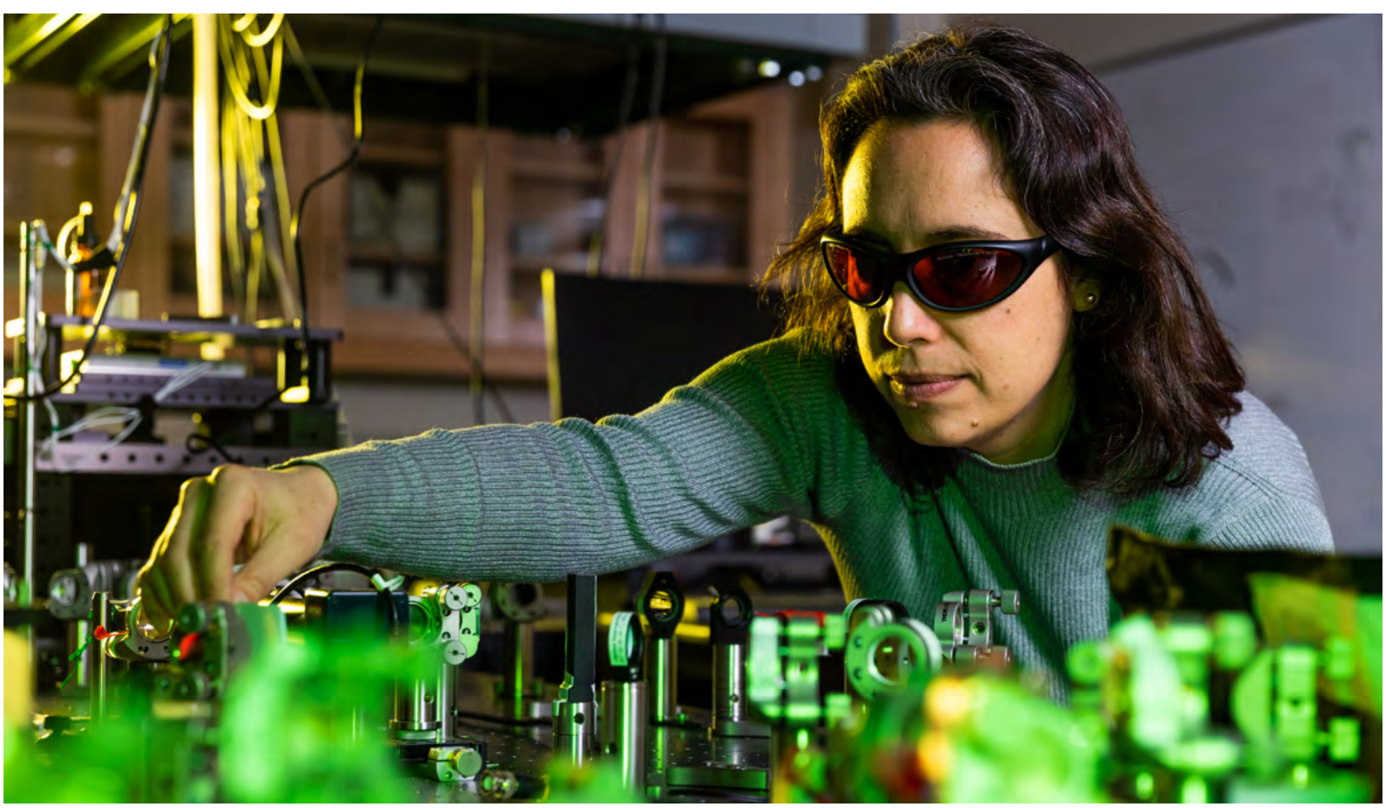
With this approach, Schlau-Cohen has made discoveries that reveal how photosynthesis is regulated under different light conditions, as well as how plants protect themselves from damage by dissipating excess sunlight.

"We are really interested in understanding the dynamics of electronically excited states, in photosynthesis and other systems," she says. "We're studying how energy can migrate through molecular systems and what controls the nature of that migration and its efficiency, particularly in the large protein networks that you find in photosynthesis."

She also uses other spectroscopic techniques to study how proteins rapidly change their conformation when they bind to specific targets — for example, when receptors found on cell surfaces bind to stimuli such as growth factors or other signaling molecules.

Molecular interactions

As a high school student in the suburbs of Philadelphia, Schlau-Cohen enjoyed chemistry and was particularly intrigued by the phenomenon known as wave-particle



MIT associate professor of chemistry Gabriela Schlau-Cohen uses ultrafast spectroscopy to capture dynamic processes such as the transfer of energy between photosynthetic proteins and pigments. *Photo: Jake Belcher* duality: the concept that physical matter can have both wavelike and particle-like properties.

“I remember learning about wave-particle duality in my high school chemistry class, which is when I really became interested in chemistry. I had a really talented chemistry teacher who made all of the molecular interactions come alive,” she says.

At Brown University, she majored in chemical physics, which allowed her to explore the physical properties of molecules and molecular systems. There, she used ultrafast microscopy to study rapid processes such as energy moving between the electronic states of molecules.

After graduating from college, she spent three years in New York as a community organizer for the Working Families Party, where she worked on campaigns such as helping to raise the minimum wage for New York State.

“Social and economic justice causes were always something that was really important to me and that I was involved in throughout high school and college, so that was an interest that was present along with chemistry,” she says. “But as I was doing that work, I started to miss the intellectual challenge of science, and that led me to think about returning to science, so then I applied for grad school.”

She decided to go to the University of California at Berkeley, where she worked in a lab that used a type of ultrafast spectroscopy called multidimensional spectroscopy. Using this technique, she studied the energy transfer that occurs in photosynthetic light-harvesting complexes, down to the level of individual proteins within the complex.

“As we were studying these photosynthetic proteins, the simulations that I was doing in conjunction with the experimental work were showing that if you just looked at just one protein, the behavior of that protein was not just quantitatively but qualitatively different than what we could see in the ensemble,” she says.

As a postdoc at Stanford University, she went on to analyze the behavior of those individual photosynthetic proteins more closely, using single-molecule spectroscopy. She found that different copies of the same proteins could change shape, which changes how long they store energy from the sun.

Protein dynamics

When applying for faculty positions, Schlau-Cohen says she was drawn to MIT by the students’ talent and enthusiasm for science.

“When I visited MIT, one of the things that really stood out was the caliber of the students and the intellectual environment they were creating where we could have these really stimulating and exciting conversations about science,” she says. “Throughout MIT, there’s this real excitement about science and an interest in understanding how things work and how we can control how things work.”

Since starting her MIT lab in 2015, Schlau-Cohen has continued studying light-harvesting systems. She uses ultrafast spectroscopy to study how these systems transfer energy over long distances and how their efficiency is regulated in response to changes in sunlight. To help achieve that, she also works on improving the spectral bandwidth (which allows them to observe a wider range of energy levels) of ultrafast spectroscopy and the temporal resolution of single-molecule spectroscopy.

Her lab has published several papers in which they elucidated the mechanisms that allow plants to adjust the amount of energy captured from the sun when exposed to different weather conditions, and how they prevent sun damage. Single-molecule measurements of a protein called light-harvesting complex stress-related revealed that it plays a key role in controlling these responses in green algae and moss.

Working with other MIT faculty members, including Mark Bathe, a professor of biological engineering, and Adam Willard, an associate professor of chemistry, she is also working on designing synthetic light-harvesting materials, using DNA origami structures as scaffolds.

“Our goal is to develop nanostructures with similar or even better emergent properties than photosynthetic light-harvesting systems, so that we can really achieve control over the evolution of light energy in a way that mimics or even exceeds the performance of nature,” she says.

In another area of research, Schlau-Cohen studies how proteins can respond to their environment by changing their structure. This shape shifting is a key element of cellular signal transduction systems, which control the flow of information within and between cells.

In one recent paper, she and Bin Zhang, an MIT associate professor of chemistry, analyzed how the epidermal growth factor receptor changes its conformation when it binds to its target. They discovered a large-scale structural shift that helps the receptor activate growth pathways inside the cell when activated by the epidermal growth factor.

“We’re interested in the structures of these proteins, and in how biological systems respond to changing environments by changing the structure and thus the function of their protein building blocks,” Schlau-Cohen says.

Phiala Shanahan is seeking fundamental answers about our physical world

With supercomputers and machine learning, the physicist aims to illuminate the structure of everyday particles and uncover signs of dark matter

Jennifer Chu | MIT News Office

In 2010, Phiala Shanahan was an undergraduate at the University of Adelaide, wrapping up a degree in computational physics, when she heard of an unexpected discovery in particle physics. The news had nothing to do with any of the rare, exotic particles that physicists were searching for at the time. Rather, the revelation revolved around the mundane, ubiquitous proton.

That year, scientists had measured the proton's radius and discovered that the particle was ever so slightly smaller than what previous experiments had reported. This new measurement threw into question what physicists had assumed was well-understood: What exactly was the size of the proton?

What would then be coined the "proton radius puzzle" immediately drew Shanahan's interest, prompting a more fundamental question: What else don't we know about this seemingly straightforward particle?

"Protons and neutrons make up 99 percent of visible matter in the universe," she says. "I assumed that, just like the mass of the proton is known very precisely, the size would be too. That was one moment fairly early on when I realized, there really are fundamental questions that we still have no answers to."

The proton puzzle was one impetus that propelled Shanahan to pursue theoretical particle and nuclear physics. Today, she is the Class of 1957 Career Development Associate Professor of Physics at MIT, having recently received tenure at the Institute.

In her research, she seeks a fundamental understanding of our physical world. Using the equations of the Standard Model of Physics as her guide, she is looking for fundamental bridges — concrete, mathematical connections between the behavior of elementary particles, such as the quarks and gluons within a single proton, and the interactions between multiple protons, which coalesce into the visible matter we see around us.

Associate Professor Phiala Shanahan's research focuses on particle and nuclear theory and applying machine learning to understand the fundamental interactions of nature. *Photo: Gretchen Ertl*

Tracing these fundamental connections will ultimately help physicists recognize breaks in our understanding, such as instances when a proton interacts with dark matter, which is thought to make up 85 percent of the total mass in the universe and for which the Standard Model — our best representation of our physical understanding — has no explanation.

"We are trying to understand how you can bridge understanding from our most fundamental theory — this beautiful predictive theory of fundamental particles — all the way up to nuclear physics," Shanahan says.

Up for a challenge

Shanahan was born in Sydney, Australia, and spent most of her childhood and early education in the suburbs of Adelaide, where she earned a scholarship to attend an all-girls school. She quickly took to studying math and science, learning new languages, and playing a variety of instruments.

"At the time, I don't think you could've picked me for a scientist rather than a musician or a linguist," she says.

After high school, Shanahan stayed local, attending the University of Adelaide, where she took classes in Latin and ancient Greek, and played in a cover band on the weekends. She also pursued a bachelor's degree in high-performance computational physics, which she chose almost as a personal challenge.

"It was the hardest degree to get into at the time, and I thought, 'I want something challenging,'" she recalls.

Her interest in physics began to crystallize after hearing of the proton radius puzzle one day in a research seminar. She also discovered that she enjoyed research, after accepting an offer to work as a summer assistant in the lab of her undergraduate advisor, Anthony Thomas, who specialized in nuclear physics. She continued working with Thomas through graduate school, also at the University of Adelaide, where she earned a PhD in theoretical nuclear physics.

"I'd already been caught by this idea that we didn't know nearly as much about the proton as I thought, so my PhD was about understanding in great detail the structure of the proton and what we could add to that understanding," Shanahan says.

A direct trace

After finishing her education in Australia, Shanahan looked to take her next step, outside the country. With funds from a traveling fellowship, she planned out a two-month tour of physics departments and facilities across Europe and the United States, including at MIT. The experience was a whirlwind, as Shanahan was introduced at every stop to new ideas and avenues of research.

"The mind expansion was really exciting," she says.

When she came home to Australia, she found she was keen to keep on the research track, and to live abroad. Soon, she packed her bags for a postdoc position in MIT's Department of Physics. She arrived at the Institute in 2015 and spent the next two years researching the interactions of gluons, the elementary, force-carrying particles that bind to quarks to form a proton.

"It's very difficult to measure experimentally certain aspects of the gluon structure of a proton," Shanahan says. "I wanted to see what we could calculate, which at the time was quite a new thing."

Until then, Shanahan considered herself a mostly "pen-and-paper" theorist. But she wanted to see how far the behavior of gluons — interactions known as quantum chromodynamics — could be directly traced using the equations of the Standard Model. To do so would require large-scale numerical calculations, and she found herself learning a new set of computational tools and exploring ways to search for fundamental interactions among gluons using machine learning — a novel approach that Shanahan was one of the first to adopt, and which she continues to pursue today.

A creative space

After finishing her postdoc, she spent a year as a faculty member at the College of William and Mary and as a senior staff scientist at the Thomas Jefferson National Accelerator Facility before returning to MIT in 2018 as an assistant professor in the Center for Theoretical Physics. Before she put down campus roots, Shanahan spent the fall semester at the Perimeter Institute for Theoretical Physics in Ontario, Canada, as part of a fellowship that supports female physicists. The program provided food and board for fellows, and also delivered meals to their offices — all with the goal of freeing the physicists to focus on their work.

"That program really gave me the launchpad for what became my research agenda as a new faculty member," she says. "It all started from that quiet time where I could actually think for hours at a time. That was incredibly valuable, and it gave me the space to be creative."

At MIT, she continues to study the equations of the Standard Model to understand the quantum dynamics of gluons and quarks, and the structure of the proton, as well as the interactions that underpin nuclear physics, and what the fundamental behavior of certain nuclei can tell us about the conditions of the early universe.

She is also focusing on nuclei that are used in dark matter experiments, and is looking to map out the space of nuclear interactions that can be explained concretely through the Standard Model. Any interactions outside of this fundamentally derived space could then be a sign of dark matter or other phenomena beyond what the Standard Model can explain.

"Now my research group is going in all sorts of directions," she says. "We are using every tool at our disposal, from pen-and-paper calculations, to designing and running new algorithms on supercomputers, to really understand new aspects of the structure and interactions of the matter that makes up our universe."

Seeing the world in high definition

Graduate student Timur Cinay charts the path of wind over ocean dead zones

Phie Jacobs | School of Science

A typical morning in the Galápagos starts with a swim.

Timur Cinay, a PhD student in the MIT Department of Earth, Atmospheric and Planetary Science (EAPS), rises with the sun and marvels at the beautiful views of San Cristóbal Island. Before breakfast, he takes a dip in the Pacific Ocean, where, on most days, he's able to count a squad of sea lions among his swimming companions.

Now, though, it's time to get to work. After breakfast, Cinay heads to the Galápagos Science Center (GSC), an academic research facility located near the western tip of the island, just a stone's throw from the beach. The GSC, which was created by the University of North Carolina at Chapel Hill and the Universidad San Francisco de Quito, hosts researchers from around the world as they conduct interdisciplinary research in a variety of different fields.

Cinay is here on behalf of Andrew Babbin, the Cecil and Ida Green Career Development Professor in the MIT EAPS department. Babbin's lab — the BabLab, as it's colloquially known — has partnered with the GSC to establish a monitoring site for marine nitrous oxide emissions. Cinay, who has played a commanding role in the project since arriving at MIT two years ago, hopes the data the lab collects will provide insight into the present and future of our planet's climate.

Cinay spent his youth in a small town in western Turkey, where he bore firsthand witness to the devastating impact of climate change. As a result of rising global temperatures, droughts and wildfires in Turkey have become increasingly frequent and severe, with 2021 marking the nation's driest year in two decades. Agricultural workers, including many members of Cinay's family, have been impacted by drought.

In 2017, Cinay traveled to the United States, where he majored in chemistry and environmental science at the University of Rochester. After taking a class on marine biogeochemistry modeling, he became interested in the forces of water, wind, and climate, as well as the intersections of chemistry and computer modeling. As an undergraduate researcher, he specialized in physical chemistry and chemical oceanography, with a particular focus on greenhouse gases such as methane.

Graduate student Timur Cinay conducts research at the Galápagos Science Center where he has established a monitoring site for marine nitrous oxide emissions. *Photo: Courtesy of the researcher*

After earning his bachelor's degree, Cinay decided to pursue a PhD in climate science at MIT, where he is this year funded through the E. Alan Phillips Fellowship for Environmental Sustainability created by Audrey Buyrn '58, SM '63, PhD '66 wife of the late Alan Phillips. "Everyone was very keen to try to attract him to their institution," Babbin recalls. "My pitch was science with trips to the Galápagos," he adds with a laugh.

The BabLab is dedicated to all things biogeochemistry: an expansive field overlapping with chemical oceanography, which explores the chemical components of our oceans, and marine microbiology, which looks at the tiny organisms that inhabit them. Most of their research projects focus on the cycling of marine nitrogen, its control on life in the ocean, and its effects on climate.

Finding the shadow zone

Nitrous oxide has a major impact on climate change. It is a greenhouse gas that traps atmospheric heat with nearly 300 times the potency of carbon dioxide. Once it reaches the stratosphere, it also reacts with high-energy oxygen atoms to form nitric oxide, a compound that destroys ozone. Over the past few decades, concentrations of this gas have been rising. The increase has been mostly attributed to the use of artificial fertilizer, but the BabLab is concerned with the undetermined secondary effects of global climate change — warming oceans could add insult to injury by pouring even more nitrous oxide into the atmosphere. Unfortunately, our current understanding of the ocean's role in nitrous oxide emission is limited by a lack of direct data.

Nitrous oxide is mainly produced by marine microbes that have adapted to survive in areas with low oxygen levels, which are known as oxygen minimum zones or shadow zones. These dead zones are rare and are usually localized to remote areas, which hinders the taking of direct measurements. The BabLab's past investigations into nitrous oxide emissions have been conducted on the open ocean as part of research cruises, a method Babbin describes as "both exciting and harrowing." He and his team have weathered hurricanes and faced the frustration of the Covid-19 pandemic.

Then, a few years ago, a brilliant undergraduate researcher in Babbin's lab — Elisabeth Boles, Class of 2018 — showed that atmospheric chemistry measurements could be used to monitor a previously described emission hot spot in the eastern tropical Pacific Ocean, a region that includes the Galápagos Islands.

This discovery laid the groundwork for the BabLab's current project, which aims to continuously monitor nitrous oxide production from their GSC monitoring site. They plan to use a highly sensitive instrument — a cavity-ring spectrometer — to provide by-the-second feedback about interactions between ocean and atmosphere over the entirety of next year. Computer modeling performed back on MIT's campus can chart the path these gases are taking across the ocean and reveal more about the ocean's role in rising nitrous oxide levels.

Small scale, high resolution

"One of the things I'm really excited about is the scale," Cinay says of the nitrous oxide monitoring project. While previous measurements covered small time frames, the GSC continuous monitoring site will be able chart the movement of nitrous oxide over the course of seasons as well as seconds. This new method, Cinay explains, will take our image of marine emissions from pixelated to high-definition. "That increase in resolution is quite exciting," he says.

But the image will have to wait until a few practical problems are resolved. The cavity-ring spectrometer isn't terribly large — "the size of a few desktop computers," Babbin says — but it's taken a huge amount of work to program and now faces the mundane but frustrating task of traveling from MIT's campus to San Cristóbal Island. Once there, Cinay and other members of the BabLab will spend quite a lot of time climbing ladders and running plumbing lines through the GSC in order to get the instrument running.

"It'll certainly be an endeavor," says Babbin, who notes that Cinay will still probably be waking up early and swimming with sea lions. "He's able to make the most out of any individual situation," Babbin says. "His personal connection to the world around him really is amazing."

Ever since coming to MIT, Cinay has appreciated how the BabLab brings together many different types of science, from computer modeling to chemistry, and he's embraced the interdisciplinary nature of his surroundings. Although his background is in chemistry and environmental science, he's spent the past two years developing new skill sets, including the engineering and software required for setting up the spectrometer. In the lab, he's known for his ability to think up creative approaches and solutions to research questions, which he backs up with hard work and expertise.

"It's really special to just see how his brain works," Babbin says. "That's been the best."

The BabLab hopes to keep the GSC station running for years to come, providing increasingly higher-resolution information about the ocean's role in nitrous oxide emissions. This research will be key to predicting future changes in climate and finding ways to mitigate them.

Babbin has similarly high hopes for his lab members. "Timur has a great career ahead of him," he says. "It's going to be spectacular."

Nature's allies

Audrey Buyrn '58, SM'63, PhD'66 recently created a fellowship to honor her late husband E. Alan Phillips, '57, PhD'61 and to continue to fund environmental science research. *Photo: Sam Kittner*

Audrey Buyrn met her husband Alan Phillips when they were both graduate students in the lab of nuclear physicist Professor Emeritus Lee Grodzins. These newly minted professors held academic teaching positions in the East until 1969 when they left for California to work at the Lawrence Berkeley National Laboratory (LBNL). It was there they began to hike and backpack in the Sierras many weekends.

"The greatest thing about hiking in the Sierra Nevada is the complete isolation," Buyrn said in a 2010 interview in MIT's *Spectrum* magazine. "You get up into the high country and the number of people drop off. Then you leave the road, and more people drop off. When you leave the trails, you can go literally for a week or two without ever seeing anybody. There is a profound silence broken only by wind, streams, and birds; complete beauty: the world as it was when it was young."

After the end of their two years at California, they moved back East and settled in Great Falls, Virginia, where for 20 years Buyrn worked at the Office of Technology Assessment, and Phillips worked for 35 years at Science Applications International Corporation. The couple continued to travel out West a few times a year to enjoy the beauty and magnificence of the wilderness. As the years progressed, the avid hikers witnessed firsthand the deleterious effects of climate change and decided to act.

In 2007, Buyrn and Phillips established the Ally of Nature Fund used to fund exploratory projects in the School of Science "to prevent, reduce, and repair the adverse impacts of humanity on the natural environment." Over the years, this fund has supported numerous students and faculty working in the School of Science.

"When Alan and I established the Ally of Nature Fund in 2007, it was still possible to be an intelligent skeptic of climate change and to think that catastrophic environmental degradation was far off in space and time. This is no longer possible," says Buyrn. "The evidence is in front of our eyes, over and over again from every part of the world."

After Phillips died, Buyrn chose to honor him by establishing the E. Alan Phillips Fellowship in Environmental Sustainability. This newly endowed fellowship sits in the School of Science and is awarded to a graduate student working to understand, repair, or compensate for environmental degradation. Timur Cinay, the inaugural E. Alan Phillips Fellow, met with Buyrn last fall to thank her for her kind generosity that enabled him to attend MIT and work with Professor Andrew Babbin.

Cinay was an ideal choice to hold this fellowship, having seen firsthand the devastating impact of climate change in his native Turkey. (See page 13). "I think Alan would have enjoyed meeting Timur as much as I have. He is a young scientist passionate about his work, with big hopes for the future. I cannot think of a better way to support basic science than by supporting the young people who are dedicating their lives to making our world a better place for future generations."

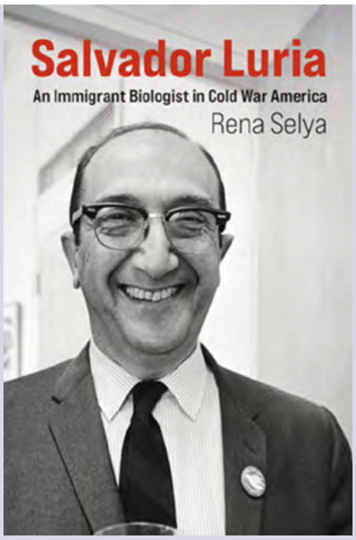
MIT School of Science is grateful to both Phillips and Buyrn for their philanthropic support, as well as Buyrn's advice in her service to the Dean of Science Advisory council.

If you have questions or would like to make a gift to the School of Science, please contact Elizabeth Chadis, Assistant Dean of Development at echadis@mit.edu or 617-253-8903.

Books from Science

The life of Luria

The first full-length biography of Salvador Luria profiles his life as a scientist and activist



Salvador Luria (1912–1991) led a storied career at MIT as a professor in the Department of Biology and the founding director of the MIT Center for Cancer Research, now the Koch Institute. From MIT Press, *Salvador Luria: An Immigrant Biologist in Cold War America* is a compelling portrait of the Nobel-winning scientist.

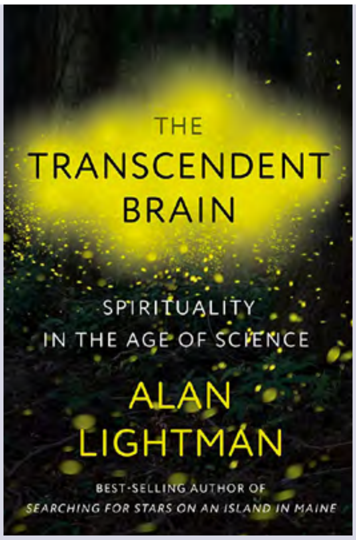
Perhaps best known for his research on bacteriophages, Luria conducted work with viruses and bacteria in the 1940s. He joined MIT in 1960, and continued on to break ground in molecular biology and cancer research through the 1980s. What's more, Luria helped build MIT Biology into the department it is today by fostering a culture of excellence and recruiting cutting-edge scholars.

Luria was as much an activist as a scientist. Born in Italy, Luria was a refugee of Nazi Europe. Once an American citizen, Luria became a grassroots activist on behalf of civil rights, labor representation, nuclear disarmament, and American military disengagement from the Vietnam and Gulf Wars — for a time even blacklisted from federal funding review panels.

Author Rena Selya draws on extensive archival research; interviews with Luria's family, colleagues, and students; and FBI documents obtained through the Freedom of Information Act to create a compelling portrait of a man committed to both science and society.

A scientist on spiritualism

Alan Lightman, professor of the practice of the humanities, connects the world of particles with the world of human experience



Staring at the stars, falling in love, or listening to music, humans sometimes feel a connection with things larger than ourselves. But these awe-inspiring experiences are not easily understood by science, which holds that all things can be explained in terms of atoms and molecules.

"I'm a materialist. Not in the sense of seeking happiness in cars and nice clothes, but in the literal sense of the word: the belief that everything is made out of atoms and molecules, and nothing more," Alan Lightman writes. "Yet, I have transcendent experiences."

In his latest book from Pantheon, *The Transcendent Brain: Spirituality in the Age of Science*, the novelist and physicist draws on intellectual history and conversations with contemporary scientists, philosophers, and psychologists to interrogate our place between these worlds. Can materialism explain our appreciation of beauty? Or our feelings of connection to nature and to other people? Is there a physical basis for consciousness, the most slippery of all scientific problems?

Lightman weaves his investigations together to propose what he calls "spiritual materialism" — the belief that we can embrace spiritual experiences without letting go of our scientific worldview.

The measuring tape heard round the world

Professor Emerita Nancy Hopkins and journalist Kate Zernike discuss the past, present, and future of women at MIT

Phie Jacobs | School of Science

Nancy Hopkins. *Photo: Barbara Lewin*

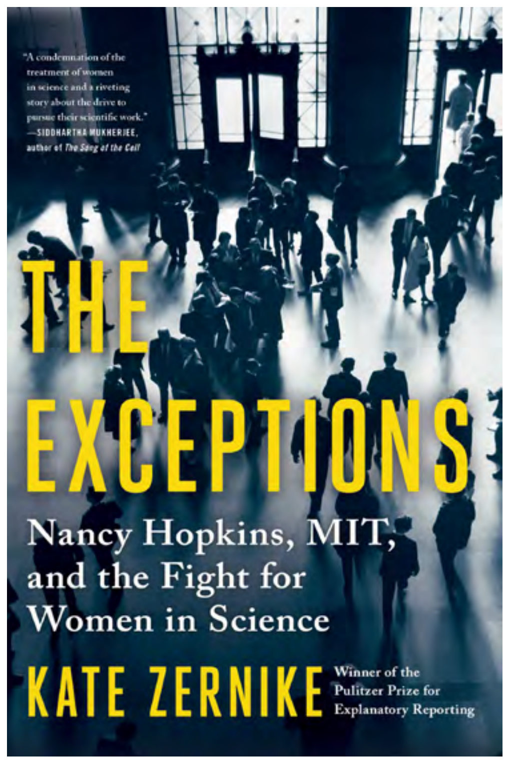
Kate Zernike. *Photo: Harry Zernike*

On a cloudy evening this past March, more than a hundred people gathered outside Boynton Hall for a conversation with journalist Kate Zernike and Amgen Professor of Biology Emerita Nancy Hopkins. The topic of discussion was Zernike's book, *The Exceptions: Nancy Hopkins, MIT, and the Fight for Women in Science*, which made its official debut at the end of February.

The Exceptions centers on the remarkable life and career of Nancy Hopkins and tells the story of 16 exceptional female scientists on the MIT faculty, who, with Hopkins as their unlikely leader, became heroes in the fight for gender equality. As a result of their work, in 1999 MIT publicly admitted to discriminating against its female faculty, a move that forced academic institutions across the country to reckon with pervasive sexism in science. Kate Zernike, now a correspondent at the *New York Times*, was a reporter at the *Boston Globe* at the time and was the first to break the story of MIT's historic admission.

The discussion, which fittingly took place on International Women's Day, began with an introduction from Nergis Mavalvala, Curtis (1963) and Kathleen Marble Professor of Astrophysics and dean of the School of Science, who sponsored the event with the Department of Biology. After welcoming attendees, both in-person and virtual, she shared an anecdote about the tools that scientists use to measure things. "I'm an experimental physicist," she explained. "My entire research career has been spent measuring very, very precise distances." As a result, Mavalvala was fascinated with a particular incident from Hopkins' career, which is chronicled in chapter 16 of *The Exceptions*.

In 1973, Hopkins became an assistant professor at MIT's Center for Cancer Research, which would later become the Koch Institute for Integrative Cancer Research. She spent more than a decade mapping RNA tumor virus genes before switching research fields to develop molecular technologies for working with zebra fish. The work required funding, equipment, and — most importantly — more space in which to house her fish tanks. But Hopkins' male colleagues routinely took up more than their fair share of all of those resources. After more than 10 years at MIT, Hopkins still had less laboratory space than any other senior faculty member in the building. The head of the cancer center refused to believe that things were so unequal, so one night in 1993, Hopkins got down on her hands and knees with a measuring tape and proved it.



Mavalvala, whose research depends on precise measurement, found herself particularly affected by the story. "I have this newfound regard for the lowly measuring tape," she declared.

"The story struck me, in a way that I think you more than any other audience can appreciate, as very MIT," Zernike recalled to the attendees. This sort of thing could only happen, she thought, at an institution whose Latin motto translates to "mind and hand."

When Zernike's editor tipped her off that something was happening at MIT regarding gender discrimination, she had initially been skeptical. It was 1999, and so many doors had already been opened for women — surely the fight for equality was pretty much over. If few women pursued careers in science, perhaps they just weren't interested. Science, after all, was a meritocracy.

Hopkins had spent much of her career assuming the same thing. For decades, she dealt with subtle and blatant instances of discrimination. She was told she could not teach genetics on the grounds that students wouldn't trust information coming from a female professor. Despite years of hard work and numerous ingenious discoveries, she struggled to obtain tenure. And she simply wasn't getting the same respect, money, or space that the men on the faculty did.

Hopkins eventually joined forces with 15 other women on the MIT faculty to bring the issue of gender discrimination to light. After four years of work, and with the unexpected endorsement of the university administration, they produced the 1999 "Study on the Status of Women Faculty in Science at MIT."

The results of the study suggested that science was not, in fact, a meritocracy. Women were interested in pursuing degrees and careers in science, but they encountered barriers every step of the way. Between blatant acts of discrimination and unconscious bias, it was just more difficult to make it as a woman in science.

Zernike adored that these women had addressed the problem the same way they would a science experiment — with rigorous data analysis and an MIT mind-set. But she was equally fascinated by MIT's response to the study's results — their willingness to admit shortcomings, and their dedication to making things better. "In my business," said Zernike, "that's known as a man bites dog story."

Though Zernike chose the title of her book to refer to the 16 exceptional female scientists who had the courage to openly acknowledge and fight back against discrimination, she also said it could apply as well to the Institute's administration. "I would say that MIT itself is the exception for having done this," Zernike said.

Following her talk, Zernike was joined on stage by Hopkins for a conversation about the writing of *The Exceptions*. Hopkins described knowing early on that her story and the stories of the 15 other female faculty members were exceptional and that they would need an "exceptional writer." "You have to have a rigorous *New York Times* reporter," she joked. "Somebody who gets the dirt."

The event ended with an audience Q&A session, during which audience members, including current MIT students, expressed frustration with the continued impact of sexism in science, and Zernike and Hopkins discussed the work that still remains to be done to achieve equality.

Don’t sleep on Hrvatin

Siniša Hrvatin explains his research in dormancy as part of the Dean’s breakfast lecture series

Sarah Costello | School of Science

On April 19, 2023, the MIT School of Science hosted a breakfast talk featuring Siniša Hrvatin, an assistant professor of biology and a core member of the Whitehead Institute for Biomedical Research. Nergis Mavalvala, the Curtis (1963) and Kathleen Marble Professor of Astrophysics and dean of the School of Science, introduced Hrvatin to a group of alumni and guests gathered on the sixth floor of the Samberg Conference Center.

Hrvatin studies how animals initiate, regulate, and survive states of stasis. While Hrvatin’s research focuses on dormancy, Mavalvala urged the early-morning crowd to stay alert — which turned out to be an easy ask thanks to his lively talk titled “Biology of Mammalian Torpor and Hibernation.”

To survive extreme environments, many mammals from squirrels to bears have evolved to decrease their metabolic rate and body temperature, entering a state called torpor. Hibernation is marked by several consecutive periods of torpor. Hrvatin’s initial breakthroughs, though, were in mice models.

Aiming to locate the neurons responsible for initiating torpor, he observed the mice’s brain activity before, during, and after fasting-induced torpor, then mapped the activity onto a 3-D model of the brain. Eventually, his search narrowed to a region of neurons in the hypothalamus, including those responsible for metabolism and skin temperature.

Assistant Professor Siniša Hrvatin studies states of stasis, such as mammalian torpor and hibernation, as a means to harness the potential of these biological adaptations to advance medicine. *Photo: Steph Stevens*

Friends, alumni, and donors such as Robert Crane '81 (*near*), Professor Craig Carter (*middle*), and Lee Selwyn '64, PhD '69 (*far left*) and Judy Selwyn SM '69, PhD '71 (*far right*) joined Dean Mavalvala for the second breakfast talk series this year. *Photo: Steph Stevens*

Next, Hrvatin had to figure out if these neurons were actually responsible for initiating torpor in the mice. To do so, the researchers added receptors to neurons that were active during torpor, effectively adding an on/off switch. Hrvatin reflected that the idea that they could induce torpor by reactivating the neurons, at first, "seemed far-fetched."

However, by screening more than 200 regions of the brain, the researchers were able to pinpoint a specific region of the hypothalamus, which they named avMLPA. When avMLPA neurons were stimulated in the mice, researchers observed a drop in their metabolic rate and core body temperature.

Using microfluidics, researchers proceeded to break down and sequence around 28,000 neurons in this region of the brain, identifying 36 different cell types. Only 342 neurons were active during torpor.

From there, the researchers leveraged neuroscience tools — installing fluorescent sensors of neuronal activity and optical fibers — to monitor the mice's brains in real time. These tools demonstrated a connection so clear that researchers could predict when the mice were in torpor just by looking at the computer screen. What's more, switching the same neurons off was shown to inhibit natural torpor in the mice.

"The results indicate that stimulating a population of neurons that are active during torpor, even in animals that aren't actively fasting, is sufficient to induce this state," confirmed Hrvatin.

Solving the many mysteries of torpor and hibernation, Hrvatin hopes, could lead to advancements in human medicine. Could these insights open the door for new treatments for metabolic disorders, or for muscle atrophy in bed-ridden patients? Might unlocking the mechanisms of how cells adapt to torpor improve organ transplants, during which organs are cooled down to minimize cell death, or even help to slow disease progression? What are the implications for slowing down epigenetic aging and potentially increasing the natural life span?

What if knowledge about states of suspended animation was applied to space travel?

"It is science fiction right now," Hrvatin concluded. "But I really do believe that by studying the biology behind this, we can learn how to harness the potential in several medical fields."

It’s a weird, weird quantum world

In MIT’s 2023 Killian Lecture, Peter Shor shares a brief history of quantum computing from a personal viewpoint

Jennifer Chu | MIT News Office

In 1994, as Professor Peter Shor, PhD ’85 tells it, internal seminars at AT&T Bell Labs were lively affairs. The audience of physicists was an active and inquisitive bunch, often pelting speakers with questions throughout their talks. Shor, who worked at Bell Labs at the time, remembers several occasions when a speaker couldn’t get past their third slide, as they attempted to address a rapid line of questioning before their time was up.

That year, when Shor took his turn to present an algorithm he had recently worked out, the physicists paid keen attention to Shor’s entire talk — and then some.

“Mine went pretty well,” he told an MIT audience yesterday.

In that 1994 seminar talk, Shor presented a proof that showed how a quantum system could be applied to solve a particular problem more quickly than a classical computer. That problem, known as the discrete logarithm problem, was known to be unsolvable by classical means. As such, discrete logarithms had been used as the basis for a handful of security systems at the time.

Shor’s work was the first to show that a quantum computer could solve a real, practical problem. His talk set the seminar abuzz, and the news spread, then became conflated. Four days after his initial talk, physicists across the country were assuming Shor had solved a related, though much thornier problem: prime factorization — the challenge of finding a very large number’s two prime factors. Though some security systems employ discrete logarithms, most encryption schemes today are based on prime factorization and the assumption that it is impossible to crack.

“It was like the children’s game of telephone, where the rumor spread that I had figured out factoring,” Shor says. “And in the four days since [the talk], I had!”

By tweaking his original problem, Shor happened to find a similar quantum solution for prime factorization. His solution, known today as Shor’s algorithm, showed how a quantum computer could factorize very large numbers. Quantum computing, once thought of as a thought experiment, suddenly had in Shor’s algorithm an instruction manual for a very real, and potentially disruptive application. His work simultaneously ignited multiple new lines of research in quantum computing, information science, and cryptography.

The rest is history, the highlights of which Shor recounted to a standing room-only audience in MIT’s Huntington Hall, Room 10-250. Shor, who is the Morss Professor of Applied Mathematics at MIT, spoke as this year’s recipient of the James R. Killian Jr. Faculty Achievement Award, which is the highest honor the Institute faculty can bestow upon one of its members each academic year.

In introducing Shor’s talk, Lily Tsai, chair of the faculty, quoted the award citation:

“Without exception, the faculty who nominated him all commented on his vision, genius, and technical mastery, and commended him for the brilliance of his work,” Tsai said. “Professor Shor’s work demonstrates that quantum computers have the potential to open up new avenues of human thought and endeavor.”

Peter Shor, the Morss Professor of Applied Mathematics, is this year’s recipient of the James R. Killian Jr. Faculty Achievement Award, which is the highest honor the Institute faculty can bestow upon one of its members each academic year. *Photo: Jake Belcher*

A quantum history

During the one-hour lecture, Shor took the audience through a brief history of quantum computing, peppering the talk with personal recollections of his own role. The story, he said, begins in the 1930s with the discovery of quantum mechanics — the physical behavior of matter at the smallest, subatomic scales — and the question that soon followed: Why was quantum so strange?

Physicists grappled with the new description of the physical world, which was so different from the classical Newtonian mechanics that had been understood for centuries. Shor says that the physicist Erwin Schrödinger attempted to "illustrate the absurdity" of the new theory with his now-famous thought experiment involving a cat in a box: How can it embody both states — dead and alive? The exercise challenged the idea of superposition, a key property of quantum mechanics that predicts a quantum bit such as an atom should hold more than one state simultaneously.

Spookier still was the prediction of entanglement, which posed that two atoms could be inextricably linked. Any change to one should then affect the other, no matter the distance separating them.

"Nobody considered using this strangeness for information storage, until Wiesner," Shor said.

Wiesner was Stephen Wiesner, who in the late 1960s was a graduate student at Columbia University who was later credited with formulating some of the basic principles of quantum information theory. Wiesner's key contribution was a paper that was initially spurned. He had proposed a way to create "quantum money," or currency that was resistant to forgery, by harnessing a strange property in which quantum states cannot be perfectly duplicated — a prediction known as the no-cloning theorem.

As Shor remembers it, Wiesner wrote out his idea on a typewriter, sent it off for consideration by his peers, and was roundly rejected. It wasn't until another physicist, Charles Bennett, found the paper, "pulled it out of a drawer, and got it published," solidifying Wiesner's role in quantum computing's history. Bennett went further, realizing that the basic idea of quantum money could be applied to develop a scheme of quantum key distribution, in which the security of a piece of information, such as a private key passed between parties, is protected by another weird quantum property.

Bennett worked out the idea with Gilles Brassard in 1984. The BB84 algorithm was the first protocol for a crypto system that relied entirely on the weird phenomena of quantum physics. Sometime in the 1980s, Bennett came around to Bell Labs to present BB84. It was Shor's first time hearing of quantum computing, and he was hooked.

Shor initially tried to work out an answer to a question Bennett posed to the audience: How can the protocol be proven mathematically to indeed be secure? The problem, however, was too thorny, and Shor abandoned the question, though not the subject. He followed the efforts of his colleagues in the growing field of quantum information science, eventually landing on a paper by physicist Daniel

Lily Tsai, chair of the faculty, presents the award citation to Peter Shor.
Photo: Jake Belcher

Simon, who proposed something truly weird: that a system of quantum computing bits could solve a particular problem exponentially faster than a classical computer.

The problem itself, as Simon posed it, was an esoteric one, and his paper, like Wiesner's, was initially rejected. But Shor saw something in its structure — specifically, that the problem related to the much more concrete problems of discrete logarithms and factoring. He worked from Simon's starting point to see whether a quantum system could solve discrete logarithms more quickly than a classical system. His first attempts were a draw. The quantum algorithm solved a problem just as fast as its classical counterpart. But there were hints that it could do better.

"There's still hope in trying," Shor remembers thinking.

When he did work it out, he presented his algorithm for a quantum discrete log algorithm in the 1994 symposium at Bell Labs. In the four days since his talk, he managed to also work out his eponymous prime factorization algorithm.

The reception was overwhelming but also skeptical, as physicists assumed that a practical quantum computer would instantly crumble at the barest hint of noise, resulting in a cascade of errors in its factoring computation.

"I worried about this problem," Shor said.

So, he again went to work, looking for a way to correct errors in a quantum system without disturbing the state of the computing quantum bits. He found an answer through concatenation, which broadly refers to a series of interconnected events. In his case, Shor found a way to link qubits, and store the information of one logical, or computing qubit among nine highly entangled, physical qubits. In this way, any error in the logical qubit can be measured and fixed within the physical qubits, without having to measure (and therefore destroy) the qubit involved in the actual computation.

Shor's new algorithm was the first quantum error correcting code that proved a quantum computer could be tolerant to faults, and therefore a very real possibility.

"The world of quantum mechanics is not the world of your intuition," Shor said in closing his remarks. "Quantum mechanics is the way the world really is."

Quantum's future

Following his talk, Shor took several questions from the audience, including one that drives a huge effort in quantum information science today: When will we see a real, practical quantum computer?

To factor a large number, Shor estimates that a quantum system would require at least 1,000 qubits. To factor the very large numbers that underpin today's internet and security systems would require millions of qubits.

> "The world of quantum mechanics is not the world of your intuition."

"That's going to take a whole bunch of years," Shor said. "We may never make a quantum computer, ever ... but if someone has a great idea, maybe we could see one 10 years from now."

In the meantime, he noted that, as work in quantum computing has ballooned in recent years, so has work toward post-quantum cryptography and efforts to develop alternative crypto systems that are secure against quantum-based code cracking. Shor compares these efforts to the scramble leading up to Y2K, and the prospect of a digital catastrophe at the turn of the last century.

"You probably should have started years ago," Shor said. "If you wait until the last minute, when it's clear quantum computers will be built, you will probably be too late."

Shor received his PhD from MIT in 1985, and went on to complete a postdoc at the Mathematical Sciences Research Institute in Berkeley, California. He then spent several years at AT&T Bell Labs, and then at AT&T Shannon Labs, before returning to MIT as a tenured faculty member in 2003.

Shor's contributions have been recognized by numerous awards, most recently with the 2023 Breakthrough Prize in Fundamental Physics, which he shared with Bennett, Brassard, and physicist David Deutsch. His other accolades include the MacArthur Fellowship, the Nevanlinna Prize (now the IMU Abacus Medal), the Dirac Medal, the King Faisal International Prize in Science, and the BBVA Foundation Frontiers of Knowledge Award. Shor is a member of the National Academy of Sciences and the American Academy of Arts and Sciences. He is also a fellow of the American Mathematical Society and the Association for Computing Machinery.

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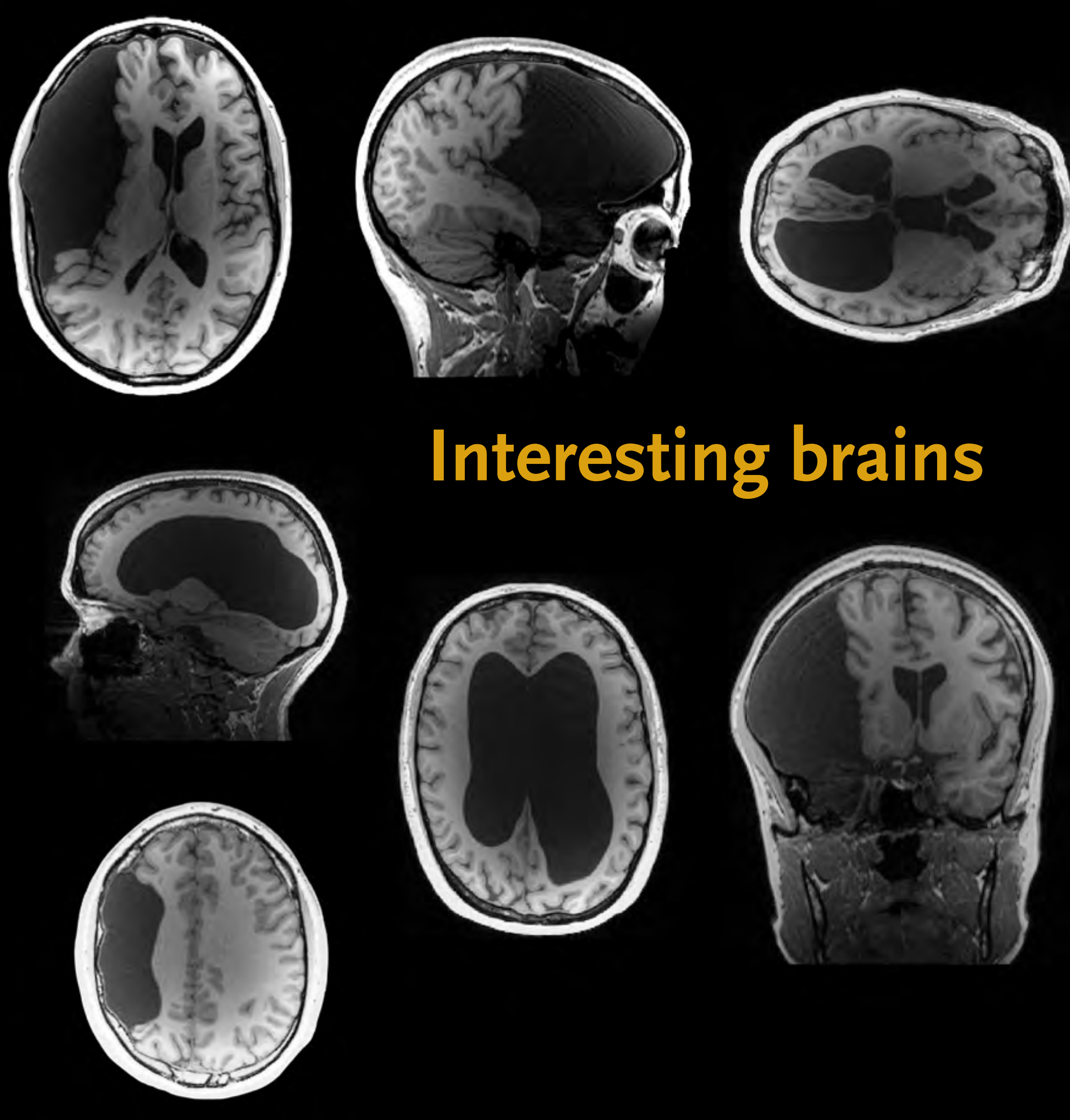
Interesting brains



"Unusual brains — and unusual individuals more broadly — can provide critical insights into brain organization and function that we simply cannot gain by looking at more typical brains," says Ev Fedorenko, the Frederick A. (1971) and Carole J. Middleton Career Development Associate Professor of Neuroscience at MIT and an investigator at the McGovern Institute for Brain Research. Developing individual-level fMRI paradigms for language research has been the focus of Fedorenko's early work. In one case, Fedorenko has studied the brain of E.G. — a woman with a stellar vocabulary who also has, likely since birth, been missing her left temporal lobe, a part of the brain known to be critical for language. Learn more about E.G.'s brain and other unusual brains at: interestingbrains.com.

A collection of anatomical fMRI from the Interesting Brains project. *Image: Hope Kean, Fedorenko lab*