SIMONS FOUNDATION

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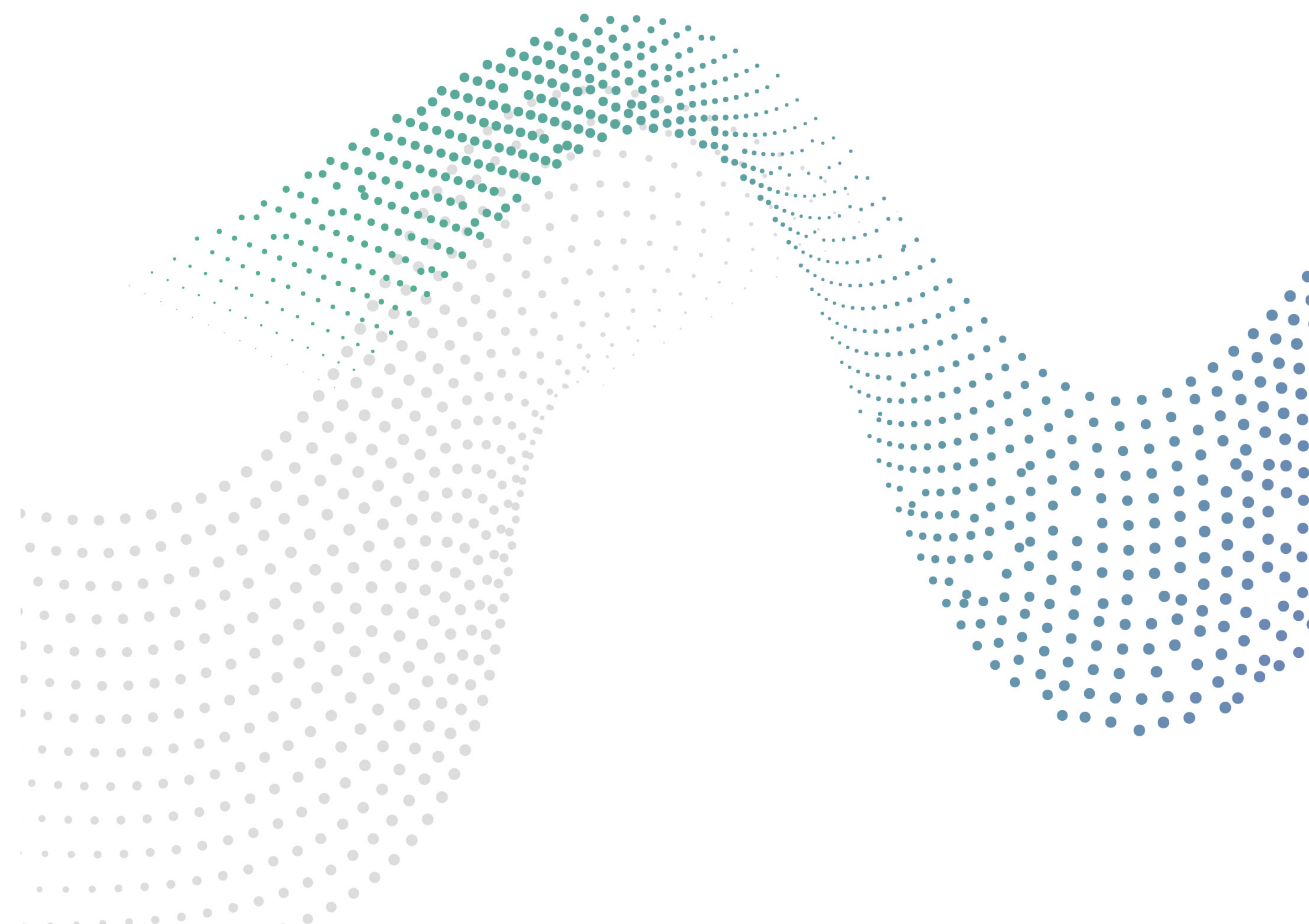
SIMONS FOUNDATION

Annual Report

2016 Edition



Cover

This illustration depicts the abstract concepts of gathering together and moving as a current. The graphic was inspired by models simulating the flocking behaviors of birds, and also by the theme of this report: meetings and interfaces, both real and virtual.

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LETTER FROM THE PRESIDENT

After delivering an eloquent and passionate speech on the thrill of scientific research and discovery, the Nobel Prize-winning physicist Saul Perlmutter took questions from the audience. The participants — administrators and researchers from multiple universities — were there to discuss the importance of increasing private philanthropic support for basic science research. There was a discussion of the challenges of communicating the importance of scientific research to the public, when the frontiers of science have moved so far beyond what most of us learned in school. Perlmutter's responses were uplifting and inspiring: He talked about the value of building relationships with everyone and having a sense of partnership in discovery. He spoke about the remarkable discoveries that are possible when scientists and funders work together toward a common goal, forming strong long-term relationships. With stirring words and dynamic gestures, he conveyed the message that we could be part of something bigger and greater than ourselves when we work as a group to push the boundaries of scientific knowledge and understanding.

What better example of what we can accomplish collectively than the detection of gravitational waves, which was announced in February 2016? This remarkable success was made possible through the hard work of more than a thousand researchers and the steadfast support of the National Science Foundation. Predicted by Albert Einstein in 1915, ripples in the fabric of space-time were observed for the first time as two black holes in a distant part of the universe merged, sending gravitational waves to Earth, where they were detected by the Laser Interferometer Gravitational-Wave Observatory (LIGO). While the LIGO experiment is paradigmatic of the tremendous possibilities to be realized through large-scale scientific collaboration, there are many other examples, large and small, of fruitful partnerships of scientists, mathematicians, and public and private donors.

At the Simons Foundation, we also support science through a host of cooperative, collaborative projects. In this year's annual report, you will read about our own new research center, the Flatiron Institute, which brings together in one building computational scientists from different fields, in the hope of developing mathematical research tools that can be applied to their own field as well as others. You will also read about the Simons Observatory in the Atacama Desert in Chile, where research teams representing four institutions are working together to detect information from our very early universe by studying the cosmic microwave background. In our SFARI program report, you will learn about our efforts to build a dataset for autism research, thanks to the help of thousands of families and individuals — and facilitated by the internet and social media.

Throughout this annual report, you will learn about group efforts in a myriad of forms: research institutes, multi-institutional efforts, interdisciplinary collaborations, teams, partnerships, conferences, workshops, lectures and even social media. We explore the different ways collaborations may be fruitfully organized in our article on Simons Collaborations. Even the illustrations we've chosen for this report reflect our theme of confluence and convergence. Like Saul Perlmutter, we share the view that, together, we can do amazing things.

As we ponder in awe our new understanding of the world around us, from fundamental particles to the cosmos, we can delight in all that we have learned and eagerly anticipate many more new discoveries.

We hope you enjoy reading about our work.

Marilyn Hawrys Simons, Ph.D.
President

LETTER FROM THE CHAIR

Over the course of 2016, we have been focused on building — both literally and figuratively — our new Flatiron Institute. This in-house unit is a generalization of the biology-focused Simons Center for Data Analysis (SCDA), which we started three years ago, to a series of centers focused on different areas of computational science. SCDA is now called the Center for Computational Biology. To house this effort, we acquired an 11-story building directly across the street from our present quarters on 21st Street. It is now undergoing extensive renovation and, when completed in June 2018, will house 250 scientific workers. It will also include a new 100-seat auditorium and a dining hall with capacity to serve all Simons Foundation personnel. Three of the floors are now occupied, with others gradually coming on stream.

The seed of this idea was planted in 2012. In June of that year, we hosted a roundtable of distinguished scientists at the Buttermilk Falls Inn in Milton, New York, to discuss the desirability of the foundation funding long-term, goal-driven collaborative research projects. As part of the discussion, attendees were invited to "propose interesting programs poised for progress that we might consider funding over a 10-year period." Suggestions came from various fields, and we have gone on to establish a number of them through our collaborations. But one participant, the mathematician Ingrid Daubechies, had a slightly different proposal — to establish a permanent center for computational science. Given that I had made the money to start the foundation through sophisticated statistical analyses of financial data, I loved the idea, and wanted to start such a center within the walls of the foundation itself so I could contribute to its development.

Our initial effort was focused on biology, and we were fortunate to recruit Leslie Greengard to head the effort. Greengard, an outstanding applied mathematician with deep knowledge of biology, came to us from New York University's Courant Institute of Mathematical Sciences. He recruited a marvelous team of computationally inclined biologists, and after two years, things were going so well we decided to generalize the program.

The next area we determined to establish was computational astrophysics, and again we were fortunate to recruit an outstanding leader, David Spergel from Princeton University. He came in September 2016 with nine people, and many more will be arriving in September 2017. In the seven months that Spergel has been with us, he has created a whirlwind of activity, turning what is now called the Center for Computational Astrophysics, or CCA, into the hub of computational astrophysics in the Northeast.

The third area of focus is quantum physics, condensed matter physics with a bent toward materials science, and depending heavily on extensive computation. Once again we found a great leader, this time in Antoine Georges of the Collège de France, and he will arrive this coming September with seven or eight recruits. Our own Andrew Millis, who has headed physics on the grant-making side, will move over to the Center for Computational Quantum Physics as Georges' co-director.

Each of these centers will grow to roughly 55 people, and there is room in the building for one more, the area of which has not yet been determined. Knitting the centers together is the Scientific Computing Core, servicing all of the discipline-oriented units and headed by two remarkable people, Nick Carriero and Ian Fisk, formerly of Yale University and CERN, respectively. This team is expected to grow to 15 people.

Somewhere along the line, we realized that this enterprise needed a name, and given that the foundation is located in the heart of Manhattan's Flatiron District, 'Flatiron Institute' seemed perfect.

Having learned of its origins, you may read of its activities and accomplishments in the pages that follow.

Jim Simons, Ph.D.
Chair

FLATIRON INSTITUTE

In 2013, the Simons Center for Data Analysis (SCDA) was launched at the Simons Foundation with a goal of creating new computational tools to analyze the vast amounts of data being generated and collected in biology. As SCDA thrived, the foundation decided to use the same model in other areas of science. SCDA, later re-named the Center for Computational Biology, or CCB, would eventually come to be the seed project for the much larger-scale Flatiron Institute, a new division of the Simons Foundation, which began operations in 2016 and employs 60 scientists — so far.

Unlike the Simons Foundation's grants programs that support researchers at academic institutions, Flatiron is an intramural research program, and its working scientists are full-time foundation employees. The institute is a place for researchers and programmers to work closely on computational problems in the basic sciences. "The idea was to create a research environment where we could take on long-term problems that were drawn from science and treat them with mathematical rigor," says Leslie Greengard, founding director of SCDA and now director of the CCB at the Flatiron Institute.

Currently, the Flatiron Institute comprises the CCB and the Center for Computational Astrophysics (CCA), directed by David Spergel, an astrophysicist at Princeton University. In addition to these centers, Flatiron will soon have a Center for Computational Quantum Mechanics, to be co-directed by Antoine Georges of the Collège de France and Andrew Millis of Columbia University (also currently associate director for physics at the Simons Foundation).

A fourth research center on a yet-to-be-decided subject will complete the institute, filling the last two of its eight research floors. The remaining two floors and roof will be home to a dining hall, a boardroom and a state-of-the-art lecture hall that seats 100 people. The institute also has a data center in the basement with the capacity to power and cool 250 kilowatts of equipment. Architects at New York City-based Perkins Eastman filled 162 Fifth Avenue with glass-walled conference rooms and offices, classrooms, and large, open spaces with comfortable couches. Blackboards encourage collaboration and virtual aquaria encourage meditative thought.

Research at the Flatiron Institute is supported by the Scientific Computing Core (SCC), co-directed by Nick Carriero, formerly of Yale University, and Ian Fisk, formerly of CERN. The SCC handles the significant computing infrastructure needs for the institute, as well as some of the computation and data-intensive activities of the foundation. The SCC maintains about 4,200 cores and 4 petabytes of storage (a petabyte is 1 million gigabytes) at the institute, with additional cores and storage at satellite facilities located on Long Island and in San Diego. Plans are under way to add more computing cores in the upcoming months.

"Academia has not found a way to provide a comfortable home for the computational sciences in house," Greengard says. The Flatiron Institute answers that unmet need for high-quality, well-supported software designed for the types of problems that arise in basic science research. The traditional 'publish-or-perish' academic model makes long-term computational projects untenable for scientists who are trying to write grants and get tenure. Furthermore, after a program is written, it needs updating and ongoing support. The standard academic model tends to prioritize new productions at the expense of the less glamorous but necessary work of maintaining and improving existing codes. The Flatiron Institute aims to provide a place where scientists and programmers are free to prioritize that computational work. All this is with an eye to advancing science everywhere, and the codes being written will be made available to the broader community as open-source software.

Flatiron is expected to employ 250 scientists and programmers by the time all four centers are established and staffed. Although the Flatiron scientists' work tends to be contained within the confines of 162 Fifth Avenue, the scientists have also, by design, been absorbed into foundation life across the street, attending lunch, lectures and staff meetings alongside their Simons Foundation colleagues.

Each Flatiron center supports various smaller research groups. The CCB tackles questions in biophysics, genomics, neuroscience, systems biology, signal processing and structural biology. Researchers from the CCB's genomics group, for example, have used machine learning to understand and predict noncoding variants in DNA, and their biophysics group looks at modeling fluid-structure interactions at a sub-cellular level. Another avenue of research for the CCB is image and signal processing, especially in microscopy, where the raw data tends to be quite noisy and automatic analysis is difficult and error-prone. "Converting experimental data into the kind of information biologists can usefully interpret is a complex problem, and it drives a significant part of our algorithmic work," says Greengard.

The CCA currently has two research groups. The statistical astronomy group, which Spergel co-leads with David Hogg of New York University, is developing new methods to extract information from large, complex and noisy datasets. The group applies these methods to astrophysical datasets ranging from exoplanets to stars in our own galaxy to cosmological measurements.

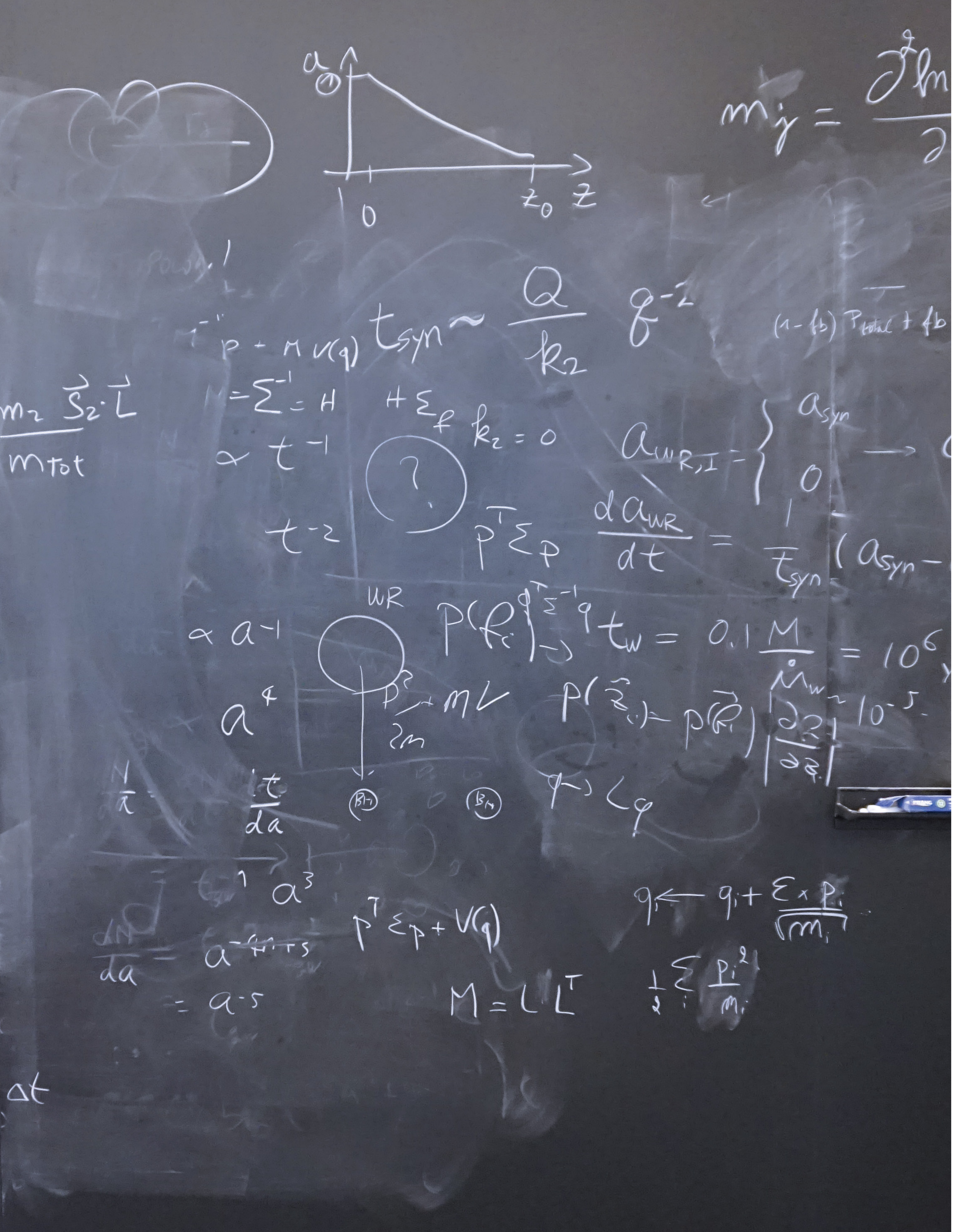
The other group focuses on galaxy formation and is co-led by Rachel Somerville, who holds a joint position at Rutgers University and Flatiron, and Greg Bryan, who holds a joint position at Columbia University and Flatiron. This group's focus is on developing sophisticated numerical simulations of the formation of galaxies and supermassive black holes. One of the challenges of modeling galaxy formation is that galaxy formation is the result of processes acting over a vast range of scales: from individual stars and black holes to cosmological scales of billions of light-years. The group plans to adopt a novel approach to this problem by carrying out numerical experiments to study the 'small-scale' processes (such as how dense gas is converted into stars within galaxies, or how energy emitted by accreting black holes affects their host galaxies) and implementing the insights they gain into larger-scale simulations. "This project is too big for any one researcher to be able to tackle. The breadth of expertise that we gather at the CCA enables us to realistically take on a project like this," says Somerville.

The galaxy formation group will also serve the research community by creating a publicly available database of the simulation outputs and mock observations created from them. "There's always more you can do with any simulation," Somerville says. Making this database freely available will allow others to benefit from the work done at Flatiron.

The SCC, in addition to providing all-important computing capacity, helps researchers' codes run faster and better by adapting them to make efficient use of the institute's computational resources. Flatiron scientists typically prototype programs on their own desktop or laptop computers, but the techniques that work on small computers often need to be modified in order to run well on a high-performance computing cluster. When scientists are ready to move from their laptops to an SCC cluster, "that transition often requires some collaborative effort," Carriero says. "We want to make sure the computing is not what's limiting their progress." The Flatiron Institute is forming close relationships with universities and other research institutes. "We want to make sure that the computational biology we do is tied to concrete problems," Greengard says. As a result, Flatiron researchers typically have outside collaborators whose experiments influence the modeling and data analysis questions taken on in the CCB. "Our ongoing collaborations have generated a lot of enthusiasm on both sides."

In the long run, researchers hope that the institute will support cross-disciplinary work as well. Although it is not always obvious, many of the same computational tasks come up in different scientific areas, from biology to astrophysics. "We do fluid dynamics, biologists do fluid dynamics," Spergel says. "Their equations are applied on the scale of cells, ours are applied on the scale of galaxies. Still, we use the same fundamental equations." By making it easy for researchers from the different centers to work together, Flatiron will make it possible for researchers in the different areas to learn from one another. "We are already becoming a place where people come to learn new algorithms and approaches. Because of the way we span fields, we have the potential to be a unique place in transferring information, approaches and techniques between areas," Spergel says.

In the hallways of the institute, the scientists and other staff have all the spirit and momentum you'd expect at an ambitious, one-of-a-kind startup. "The mix of people here is different from the mix anywhere else I know," Spergel says. "At most universities and industry labs, computational biologists don't run into computational physicists at lunch. Here, we do."



"The idea was to create a research environment where we could take on long-term problems that were drawn from science and treat them with mathematical rigor."

- Leslie Greengard

CENTER FOR COMPUTATIONAL BIOLOGY: BIOPHYSICAL MODELING

The DNA inside a cell's chromosomes contains a blueprint for assembling and regulating all the cell's proteins, but that blueprint is not simply lying open, waiting to be read. Instead, tiny 'machines' within the cell are constantly thumbing through the pages, moving the fibers of DNA to bring certain regions together into useful combinations. And when a cell divides, the chromosomes get moved about even more: A spindle structure pushes and pulls them into formation and escorts them into the newly born cells.

"All of this movement factors into how cells work and how they divide," says Michael Shelley, leader of the biophysical modeling group at the Center for Computational Biology in the Flatiron Institute, a division of the Simons Foundation. "It's not just a matter of molecules and chemical reactions — there's physics in there, and fluid dynamics too."

Shelley and his collaborators are developing mathematical models to describe how spindles form and chromosomes move. Their work is part of an emerging field called 'active matter' that studies, as Shelley puts it, "how biological systems put themselves together." Unifying soft condensed matter physics with the life sciences, active-matter problems "go right to the heart of fundamental aspects of biology," says Shelley, who is also an applied mathematician at New York University.

Active matter focuses on systems — spindles in a cell, swarms of bacteria, schools of fish or flocks of birds — made up of many individual components that collectively generate motion or mechanical stresses. Finding the equations governing these collective behaviors could bring researchers closer to a quantitative theory of some of life's central phenomena.

Doing so will require a deep understanding of the role fluids play in such systems, Shelley says. "The fluid is what lets individuals in a system 'talk' to each other remotely," he says. "Individuals may run into or push each other, but the fluid they move can organize them collectively."

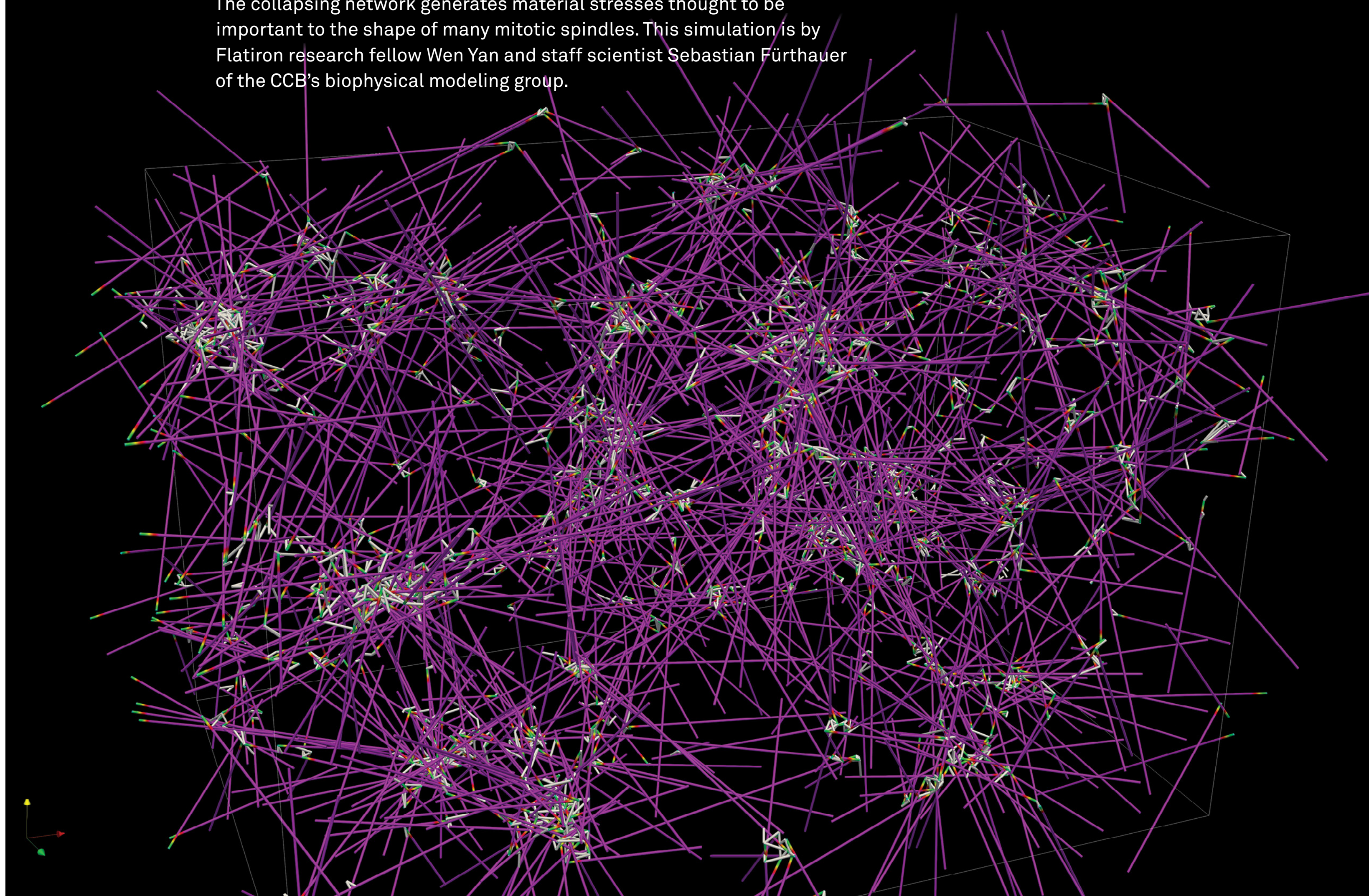
Fluid flow is a driving force in both microscopic systems, such as cellular spindles, and macroscopic systems, such as schools of fish. Yet fluid dynamics also poses a special challenge when it comes to establishing a unified theory of such systems. In microscopic systems, the fluid communicates the motion of one component across the system almost instantly. If the individual component stops moving, the fluid also stops moving and communication ceases. But in the water and air through which schools of fish and flocks of birds move, information can live on, like the vortex trails left by an airplane, even if the components stop moving. Reconciling the immediate loss of information in some systems with its lingering effects in others will be a challenge, Shelley says.

For now, Shelley's group is focusing on developing computer models and simulations of the interactions between a cell's fluid cytoplasm, its spindles and other cellular structures.

"In this cellular-mechanics world, we're doing a level of computational fluid dynamics that no one else does," Shelley says. He hopes his team's numerical and computational tools will allow researchers to work on other problems in active matter.

"It's going to be exciting figuring out how we can interface with the other groups in the center," Shelley says. "It's going to push all of us into thinking about problems we might not ever consider otherwise."

A computer simulation of a network of microtubules that has contracted due to the pulling action of dynein motor proteins traveling along them. The collapsing network generates material stresses thought to be important to the shape of many mitotic spindles. This simulation is by Flatiron research fellow Wen Yan and staff scientist Sebastian Fürthauer of the CCB's biophysical modeling group.



CENTER FOR COMPUTATIONAL ASTROPHYSICS: GAIA SPRINT

On a dark night in the Southern Hemisphere, the Milky Way arcs across the blue-black sky. Off to one side are two hazy splotches of stars, the Small and Large Magellanic Clouds, two of the Milky Way's nearest neighboring galaxies. When we gaze at these galaxies, it can be hard to imagine the intimate interactions they have had with each other, and with our own galaxy. But with data from the European Space Agency's Gaia spacecraft, the Magellanic Clouds' history with the Milky Way and the orbits of stars within our galaxy are becoming a bit clearer.

Launched into space in 2013, the Gaia probe was designed to measure the location and motion of stars within the Milky Way. By 2018, it will have collected data on about 1 billion stars, roughly 1 percent of stars in the galaxy. "This data will transform what we know about the physics of stars and the formation and evolution of the galaxy," says David Hogg, an astronomer at New York University and a consultant at the Flatiron Institute.

In September, Gaia mission scientists released data from the spacecraft to the astronomy community. Eager to dig into it, Hogg and others at Flatiron's Center for Computational Astrophysics (CCA) held the first Gaia Sprint in October. This was the CCA's first large meeting, but many more are expected to follow.

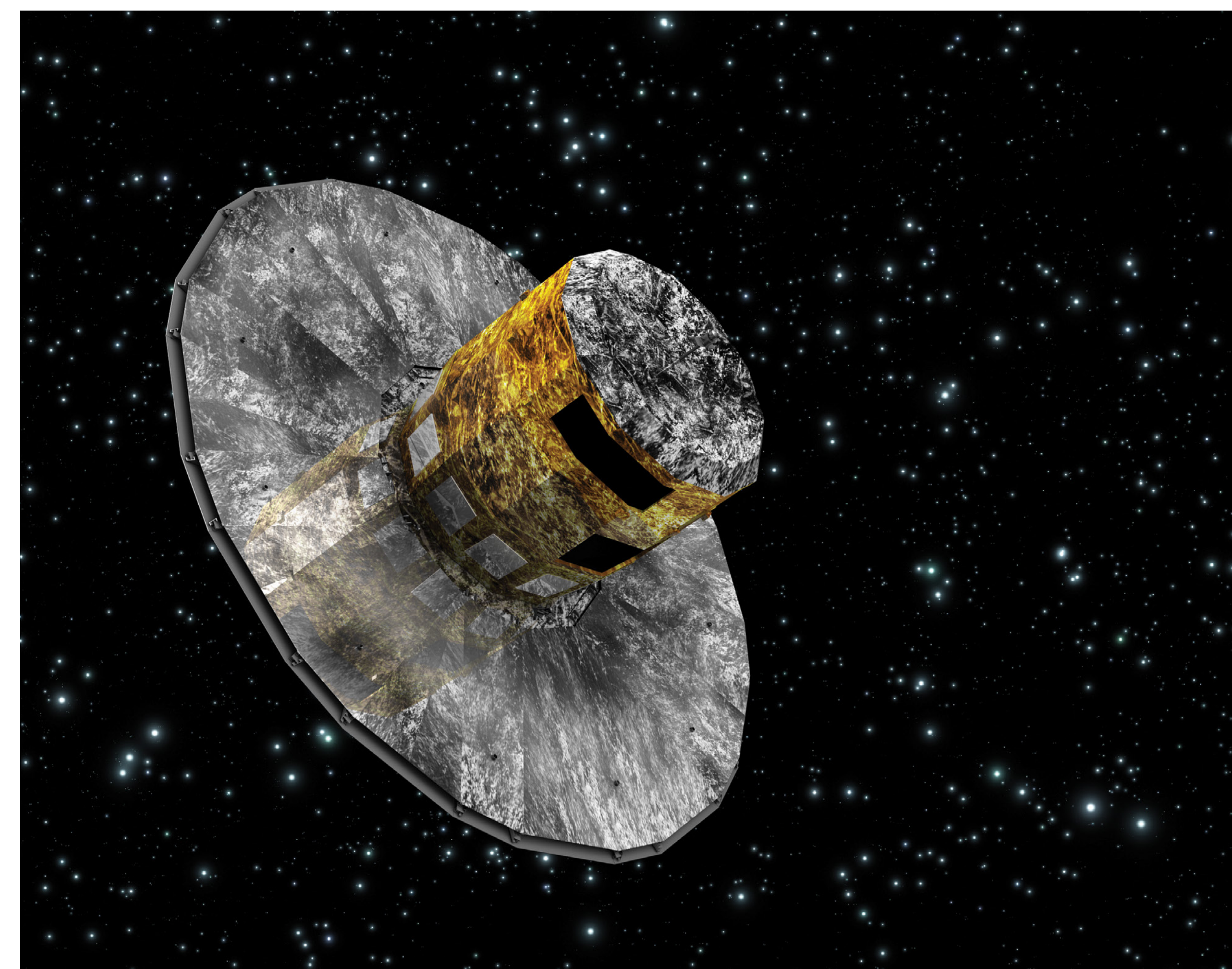
During the weeklong workshop, attendees gave rapid-fire talks on what types of questions they would use the Gaia data to answer, and then 'hacked' the data, looking for new insights into the structure and evolution of the galaxy and its stars.

Jo Bovy, a CCA consultant and an astrophysicist at the University of Toronto, used the data to make the most precise calculations to date of the Oort constants. Named for their discoverer, astronomer Jan Oort, the constants were first measured in 1927. They describe how stars orbit the center of the galaxy. Bovy's calculations showed that stars near the sun orbit the galactic center with a speed of 220 kilometers per second. His analysis also confirmed that these orbits aren't simple circles. "They're so much more complex, probably as a result of the Milky Way's spiral structure," Bovy says.

Cambridge astrophysicist Vasily Belokurov used the Gaia data to identify a specific type of variable star in the Milky Way and in the neighboring Magellanic Clouds. His analysis showed that some of those variable stars actually aren't in either Magellanic Cloud, but rather are flowing between them. Also, a stream of hot young stars flows from the Small Magellanic Cloud to the Large Magellanic Cloud, as if they were torn from the small cloud and pulled toward the larger one, something astronomers haven't observed before. According to Belokurov's analysis, the variable stars sit a little bit closer to the Milky Way than the hot young stars. "This suggests that the Milky Way has been bullying the clouds, pushing their gases around," Belokurov says. If confirmed, the discovery could help astronomers describe the hot, gassy halo that envelops the Milky Way.

Since October, more than a dozen papers that began with the Gaia Sprint have been posted online. The CCA plans to hold more meetings and conferences in the future to establish itself as a new global nexus for computational astronomy. Bovy and Belokurov say that had they not attended the Gaia Sprint, they might not have been able to perform these analyses. Their success and others', Hogg says, got him thinking about the role the CCA might play in the scientific community. "We want CCA to be a place of doers," he says. "The first Gaia Sprint shows that we are."

An artist's rendering of the Gaia spacecraft. Launched in 2013, Gaia is sending back to Earth extremely precise measurements of more than 1 billion stars in the Milky Way, enabling myriad new inquiries into the physics and evolution of the galaxy. Copyright European Space Agency.



SIMONS COLLABORATIONS

It was the collaboration that begat more collaborations: Nearly two dozen eminent scientists gathered together at the Buttermilk Falls Inn in Milton, New York, in 2012 for two days of intensive discussion. The Simons Foundation had invited the researchers — all groundbreakers in disciplines such as physics, biology, mathematics and computer science — to swap ideas about how to take the foundation's support for path-finding basic science research to the next level. They were charged with identifying ambitious, cross-disciplinary projects that might unfurl over the course of decades, rather than months or years. "I thought large-scale, goal-driven collaboration in such projects might be a useful way to advance certain areas of science," Jim Simons recalls. "We were getting advice from some really thoughtful people — that's the power to convene."

Because of this "power to convene," the discussions at Buttermilk Falls served as the genesis of a host of ambitious programs called Simons Collaborations — 10 to date — in mathematics, physical sciences, life sciences and brain research. The first collaborations to launch are now coming into their own and serve to shed light on the unique ways that scientists and discovery-driven investigators collaborate.

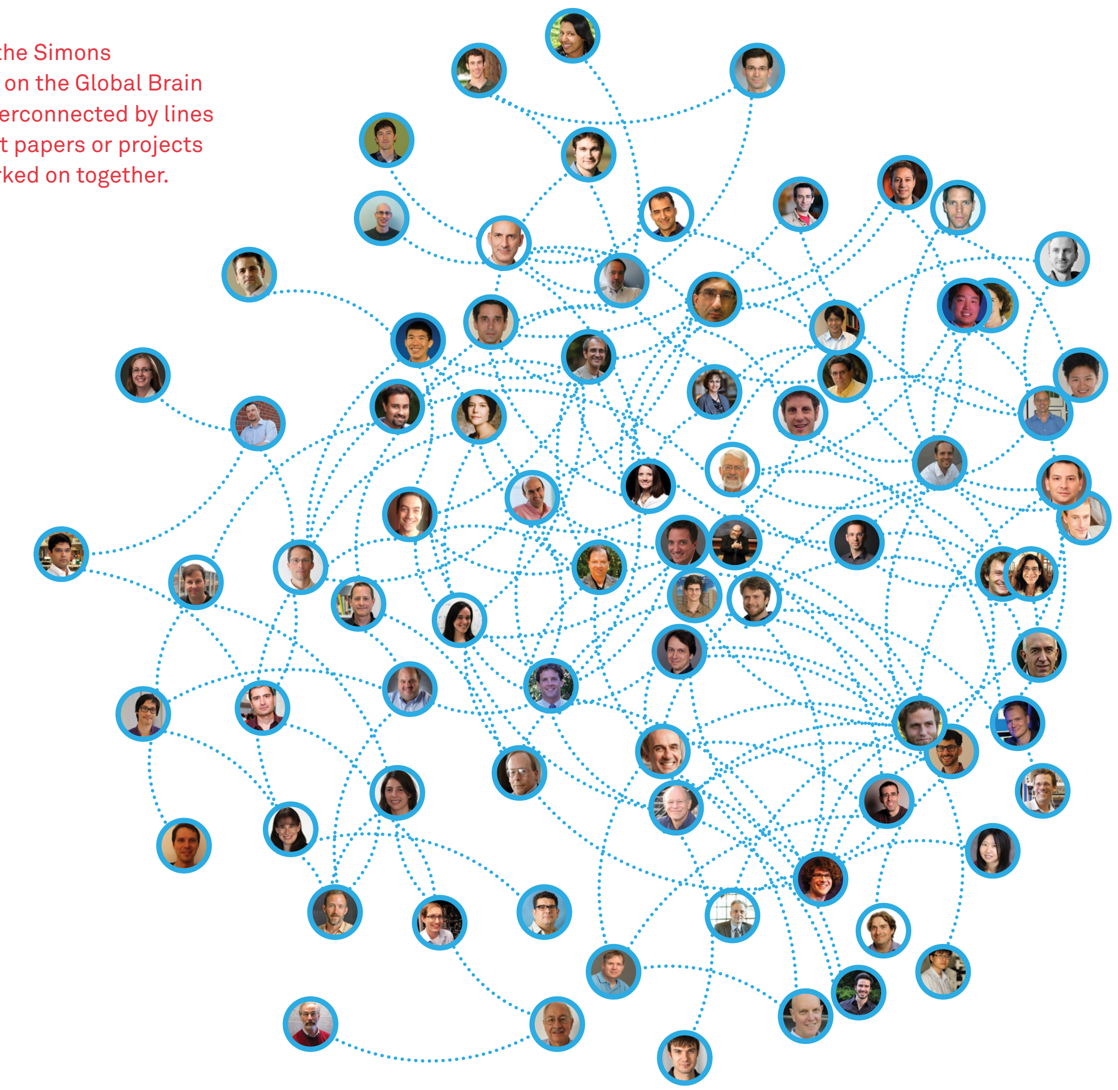
One of the first initiatives to emerge from the convention in Buttermilk Falls was the Simons Collaboration on the Global Brain (SCGB). The term 'global brain' refers to the neuronal processes that cascade across different regions of the brain in coordinated patterns to produce not just externally observable processes such as sensory reception and physical action, but also "decisions, perceptions, memories — things that don't depend on necessary external stimuli," says Gerald Fischbach, the foundation's distinguished scientist. "The goal is to understand the coding and dynamics of neurons during such internal mental states. What happens when you're just thinking?"

This investigation into cognition's 'black box' is made possible by new technologies that allow researchers to observe brain behavior at the so-called 'mesoscopic scale' — effectively measuring the activity of hundreds or thousands of individual neurons simultaneously. But beneath SCGB's advanced methods lies a brand of collaboration that is equally revolutionary. Each SCGB grant is awarded jointly to a pair of investigators: one theorist and one experimentalist. "In the rest of the world, the experimentalists stick to their experiment and don't think much about the mathematics involved," Fischbach says. "But that's not the case here." Building in this unusual collaboration at the foundational level is essential to SCGB's success. "If you want to record certain neural systems at this scale, you've got to describe how you're going to analyze the data beyond simple number crunching," Fischbach says. "You have to have your theory of what's going on."

Theory also takes center stage in the seven collaborations hosted by the Mathematics & Physical Sciences division. Unlike experimental physicists, who can coalesce by the hundreds around a single, immensely expensive instrument (think CERN's Large Hadron Collider), theoreticians "can do most of their day-to-day work without direct help from other people," says Andrew Millis, the foundation's associate director for physics. But in new and colorfully named Simons Collaborations such as "The Non-Perturbative Bootstrap," "Special Holonomy in Geometry, Analysis and Physics" and "Cracking the Glass Problem," theoreticians now cultivate fruitful connections with one another by sharing their work and their ideas at regular collaboration meetings.

"We could just take the same amount of money and simply give it as direct grants to each of the individuals, and not require them to talk to each other on a regular basis," says Millis. "But what we're doing in these domains is an experiment: a different mode of working that we hope will produce new and better science. Although these collaborations have not been running for long, the indications look good: We have lots of examples of creative work done jointly by people who would not otherwise be working together."

Scientists in the Simons Collaboration on the Global Brain are shown interconnected by lines that represent papers or projects they have worked on together.



Meanwhile, in the Life Sciences division, experimentalists cross disciplines freely in the Simons Collaboration on the Origins of Life (SCOL), which synthesizes multiple scientific specialties in an attempt to solve one of Earth's most stubborn mysteries. "We create interactions among people who wouldn't normally even talk to each other — who might have trouble even understanding the science that's being done in each other's lab," says Marian Carlson, geneticist and director of life sciences at the foundation. "Chemists who are trying to understand chemical reactions that could have occurred on early Earth talk to astronomers who think about what molecules might have been brought here from space. It's just a whole different level of broadening one's scientific perspective."

Yet even in 2017, sometimes a dose of 19th-century-style expeditionary fieldwork is necessary to move the needle on other questions in the life sciences. That's what the Simons Collaboration on Ocean Processes and Ecology (SCOPE) provides, in the form of repeated research cruises to Station ALOHA, a 4-kilometer-deep water column in the Pacific Ocean, north of Hawai'i. SCOPE aims to comprehensively model ocean microbiology at multiple scales of time and space. And although computer simulation and remote sensing from satellites and seaborne drones play an important role in taking measurements, "you still have to actually go out there and look," Carlson says. "And these are incredibly hard conditions, doing experiments on a moving ship. You have to bolt your microscope to the lab bench. These people are amazing adventurers in addition to being good scientists."

But for all of their varied formats, all of these ambitious forms of scientific collaboration function in essentially the same way: by getting advice from fellow discoverers. "We're good at getting experts to convene," Simons says. "I doubt that we'll know all the answers to these questions in 10 years — but we'll probably have advanced the subjects a fair amount in the process."

FUNDING EARLY-CAREER SCIENTISTS

As Yunji Wu Davenport was finishing up her Ph.D. at the California Institute of Technology in 2015, she decided it was time to face up to several years' worth of soul searching. Davenport had been studying HIV antibodies and antigens — a topic she enjoyed, but one she couldn't see herself pursuing long term. She had recently taken an intensive two-month course on microbial diversity at the Marine Biological Laboratory in Woods Hole, Massachusetts — a program supported by the Simons Foundation to encourage more people to move into that field of research — and the subject had captured her imagination. Davenport wanted to change her research focus, but the prospect was intimidating. "I would be entirely outside my comfort zone, and would have to learn everything from scratch," she says.

Davenport decided to apply for a postdoctoral fellowship offered by the Jane Coffin Childs Memorial Fund for Medical Research. Daringly, she "simply wrote down the project and ideas that most excited me, without much regard for what would be fundable or popular," she says. "I decided that trying to do the research I really wanted to do was worth the risk of failure." Davenport's passion for her subject came across: She was awarded a three-year fellowship sponsored by the Simons Foundation and is now at Harvard University, where she is studying the discovery and characterization of microbial small molecules.

Davenport's three-year fellowship is one of several types of awards the Simons Foundation offers to support scientists in the early stages of their careers, from their first postdoctoral position through, in some cases, the first eight years of a tenure-track faculty appointment. These years — in which a scientist must define a research program and then gradually take on the responsibilities of a faculty member — are among the most vulnerable in a scientist's career, but they can also be among the most exciting.

"Young people often have the most innovative ideas," says Marian Carlson, the Simons Foundation's director of life sciences, noting also that early-career grants require less money to leverage much greater future payoff.

While some of these programs are solo efforts by the foundation — for example, the SFARI Bridge to Independence Award and the Simons Investigators in the Mathematical Modeling of Living Systems fellowships — some are in collaboration with other philanthropies, including the Howard Hughes Medical Institute (HHMI), the Bill & Melinda Gates Foundation, the Life Sciences Research Foundation and the Esther A. & Joseph Klingenstein Fund. Combining resources allows these organizations' awards programs to reach even more outstanding researchers, Carlson says.

Through its early-career awards, as with its other programs, the foundation tries to fill gaps in federal funding — by supporting international scholars, research projects that are too risky to secure government support, and important but underfunded areas of science, for example. The Simons Early Career Investigator in Marine Microbial Ecology and Evolution Awards cover a scientific field that, despite its importance for understanding the environment, receives little funding from the federal government or other philanthropies, and so is particularly difficult for early-career researchers to break into.

"Early-career scientists represent the future of science in this country and the world," Carlson says. "If we don't enable them to launch their careers successfully, we'll just miss out on a generation of scientists."

Bridging the Gulf

The primary goal of many of these awards is to give early-career scientists the time and space to do whatever it is they do best. So, unlike research grants that make specific demands of grantees, many Simons programs impose few restrictions. For instance, Faculty Scholars — who are funded by a program launched in 2016 by the Simons Foundation along with HHMI and the Bill & Melinda Gates Foundation — are simply required to spend at least half of their professional time doing research.

The Faculty Scholars program "will provide these scientists with much-needed flexible resources, so they can follow their best research ideas," says David Clapham, HHMI's vice president and chief scientific officer.

Other awards focus on helping early-career scientists navigate the perilous waters between a mentored postdoctoral position and a tenure-track faculty appointment. "It takes a lot of effort to launch your own program: to learn to take on students and train postdocs and begin to teach," Carlson says. Early-career scientists are less proficient than established scientists at competing for large research awards, she says, and they must often write many applications to receive a grant. "That's a lot of time for a young investigator struggling to get everything going."

In autism research, where the number of tenure-track positions has been decreasing even as interest in the field grows, the SFARI Bridge to Independence (BTI) Award is designed to help senior postdoctoral fellows advance to faculty positions. "SFARI is known for bringing new blood into the autism field by funding outstanding senior investigators from other disciplines," says Alice Luo Clayton, SFARI senior scientist. "And the BTI award was developed to help sustain the next generation of these scientists in the autism field, by providing support at a critical juncture in their career."

Understanding the competitive faculty-hiring landscape, SFARI added a unique feature to its award program: Awardees who are hired as faculty are promised generous support over the first three years of their appointment, sweetening the deal considerably for an institution considering a hire. Holly Stessman credits the award with helping her to win an assistant professorship at Creighton University in Omaha, Nebraska, where she is now studying genetic drivers that are common to two completely different diseases: autism and cancer. "The Bridge to Independence Award made me a more competitive candidate when I was interviewing for positions," she says.

The award allowed her to immediately set up her lab, where she soon enlisted two technicians and an undergraduate student. This support will enable her, she says, "to pursue more complex experiments during the first few years of my career, instead of having to wait for my first award to land after starting my new position."

As for Davenport, who summoned up the courage to switch research paths after her Ph.D., receiving the Jane Coffin Childs fellowship provided one other key benefit: validation of her leap into the unknown. "Moving into a new field lends itself to a lot of second-guessing," she says. "Receiving the JCC fellowship has allowed me to put more trust in my instincts, and it has given me the confidence to continue taking risks as an increasingly independent scientist."

Bridge to Independence Award finalists Tomasz Nowakowski (second from left) and Rui Peixoto (second from right) at the April 2016 SFARI Science meeting. SFARI customarily invites finalists to its semi-annual gatherings of SFARI Investigators.

SIMONS SOCIETY OF FELLOWS

When Keith Hawkins finishes his three-year stint as a junior fellow in the Simons Society of Fellows, he wants to walk into the Hayden Planetarium at the American Museum of Natural History in New York City and project onto the dome a picture of the Milky Way that no one has seen before: one in which each point of starlight would be color-coded by its chemistry.

"Imagine color-coding the stars by the amount of magnesium present in their atmospheres. If there are globs of stars with tons of magnesium, they will just pop out immediately. That's what we call chemical cartography," says Hawkins, a postdoctoral researcher in astronomy at Columbia University. "My entire research program here as a Simons fellow is designed around being able to do galactic chemical cartography for the first time."

Previously, data to do this type of mapping has been limited to a few thousand stars. However, the European Space Agency's Gaia spacecraft is starting to provide spectroscopic data on many, many more stars, Hawkins says. He adds that the Simons fellowship gives him the freedom in his research to pursue such an ambitious project as making a large-scale chemical map of the Milky Way. It also has forced him to think about communicating his work to other scientists and potentially even the general public, which is why he is considering the Hayden Planetarium as a place to share his work.

Gerald D. Fischbach, the foundation's first Simons Society of Fellows senior fellow, says the program was founded in 2014 to foster young scientists' ability to pursue innovative research ideas. "This is a time that is very critical for a young investigator," he says. "The fellowship gives these scientists three uninterrupted years to pursue their ideas without having to worry about funding or a job search at the same time." The fellowship is also designed to encourage intellectual interactions across disciplines and across research centers in New York City.

"One benefit of this fellowship program is that the junior and senior fellows are in the city, so you can envision New York, with its outstanding academic institutions, as a campus of its own," says senior fellow Carol Mason, professor of pathology and cell biology, neuroscience and ophthalmic science at Columbia University. "With this 'city campus,' the fellowship program brings together beginning and more seasoned individuals from different areas of science: physics and mathematics, neuroscience and life science, and astronomy. 'Never the three shall meet,' usually," Mason says.

Bringing together this diverse group of young and veteran scientists inspires everyone to work on communicating their research to others. "You're forced to interact with people who don't know the technicalities of your science. This shapes how you speak about your work and encourages you to be able to talk about your science with other scientists, and also maybe frame your work in a way that those who aren't formally trained in science can understand," Hawkins says. "Something I am interested in is improving science literacy in the U.S., and this fellowship helps you to think about your work in a way that makes it more accessible."

To continue to improve their ability to speak to each other about their work, the junior fellows established a symposium series, in which five or six of the young scientists and one of the senior fellows give 10-minute talks on their research and take questions. During these talks, the fellows can discuss their research in a relaxed setting but go deeper into their work than they do at their weekly dinners. "While we get a reasonably good idea about what people are researching from our conversations at the weekly dinners, I have personally found the short talks to be a great way to gain a more in-depth understanding," says junior fellow Benjamin Harrop-Griffiths, a postdoctoral researcher at New York University's Courant Institute of Mathematical Sciences.

The junior fellows are chosen for articulating their research in an accessible manner, and for pushing the envelope of knowledge in their respective fields. "The senior scientists who recommend these young researchers call the junior fellows pioneering, and it's true," Mason says. "They propose, and execute, innovative research that has the potential to change their respective fields." Such ability to pursue cutting-edge research projects comes from the structure of the fellowship, she explains. It is a three-year program, and exceptionally selective, with only about 10 fellows chosen each year. With fellowships given by the National Institutes of Health, it's harder to obtain funding for a proposal that is high-risk, especially as the pool of money shrinks. "Here, young researchers can do this," Mason says.

The opportunity to take such risks is essential for making themselves competitive on the job market, says junior fellow Boris Leistedt, a postdoctoral researcher in cosmology at New York University. "In astronomy, these days the job market is very difficult. If you want to build a reputation and a career, you have to take risks and solve difficult problems with ambitious projects. That can be hard to do when you are applying for fellowships and jobs every year," he says. "What's nice about this fellowship is that it is for three years and you have the independence to do your own project, not necessarily take on a supervisor's idea. When you look at the track record of who discovered what and what academic positions they were in at the time, you see they made major advances because they took risks and they tried something crazy, maybe something too crazy to put on a job application."

Leistedt and Hawkins also say that they enjoy meeting the senior fellows because they offer insight into what hiring committees are searching for in new tenure-track recruits. "We can ask, 'If you were hiring now, what would you be looking for now?'" Hawkins says. "We also get insight into what these different fields were like in the 1970s and 1980s. Being able to interact with the senior fellows is unique. You get very different ideas about the different fields because each is distinct in its history and culture."

Hawkins says he also appreciates the community aspect of the fellowship. "You wouldn't have this kind of community in a prestigious astronomy fellowship. It would be significantly more about the science and highly technical, so it's nice to hear about what the other fellows are doing and learn about the physics of bird feathers or biogenetics," he says. "Many are doing work that may have a more direct impact on the world than astronomy. It's nice to be reminded of that and also be able to share with others the excitement of astronomy and its ability to advance human knowledge."

A total of 27 fellows attended the four-day Simons Society of Fellows retreat in Bal Harbour, Florida, in April 2016.

SIMONS OBSERVATORY

The Simons Array will integrate more than 22,000 detectors operating in four frequency bands at one of the world's premier cosmological observing locations: the Atacama Desert of northern Chile, which lies at 5,200 meters elevation.

For more than 50 years, scientists have probed the cosmic microwave background — the afterglow of the Big Bang — for hints about what the universe looked like in its infancy. The existence of this cosmic radiation, which comes at us from all directions, is what first convinced cosmologists that the Big Bang theory was correct, and it has since allowed them to capture what has been called a 'baby picture' of the universe.

Yet in this snapshot, the 'baby' is already about 380,000 years old, because before that time the universe was a hot, opaque plasma that did not allow any photons to escape. A lot happened in the universe in those first 380,000 years, and cosmologists would like to know precisely what.

No light reaches us from before that time, but a theory called 'cosmic inflation' suggests that events from the earliest moments of the universe have left a distinctive signature on the cosmic microwave background. And now, two teams of cosmologists are joining forces to try to read this signature, by means of the Simons Observatory, a new astronomy facility under way in Chile's Atacama Desert. The initiative will merge and expand two previous projects, known as POLARBEAR and the Atacama Cosmology Telescope (ACT) project, with the aim of bringing cosmic microwave background experiments to the next level.

"With this collaboration, we are proposing to do something grand," says Suzanne Staggs of Princeton University, who has led the ACT project along with Mark Devlin of the University of Pennsylvania, Lyman Page of Princeton University, and David Spergel of the Simons Foundation's Flatiron Institute and of Princeton University. "We are taking the search for signals of cosmic inflation to an entirely new scale."

The theory of cosmic inflation proposes that approximately a trillionth of a trillionth of a trillionth of a second after the Big Bang, the universe underwent an exponentially fast expansion. If that did indeed occur, tiny gravitational waves that arose out of quantum fluctuations in the early universe should have gotten stretched into waves with macroscopic wavelengths. These primordial gravitational waves would in turn have stretched and condensed space, creating swirling patterns in the cosmic microwave background known as B-modes — patterns big enough to potentially be detected, by an instrument sensitive enough to pick up their extremely faint signals.

The Simons Observatory aims to create just such an instrument. The initiative is funded by the Simons Foundation and the Heising-Simons Foundation, with a five-year grant to the University of California, San Diego; the University of Pennsylvania; the University of California, Berkeley; Princeton University; and the Lawrence Berkeley National Laboratory. It aims to construct several new telescopes that will be equipped with as many as 50,000 light-collecting detectors, about 10 times as many as any other project operating today.

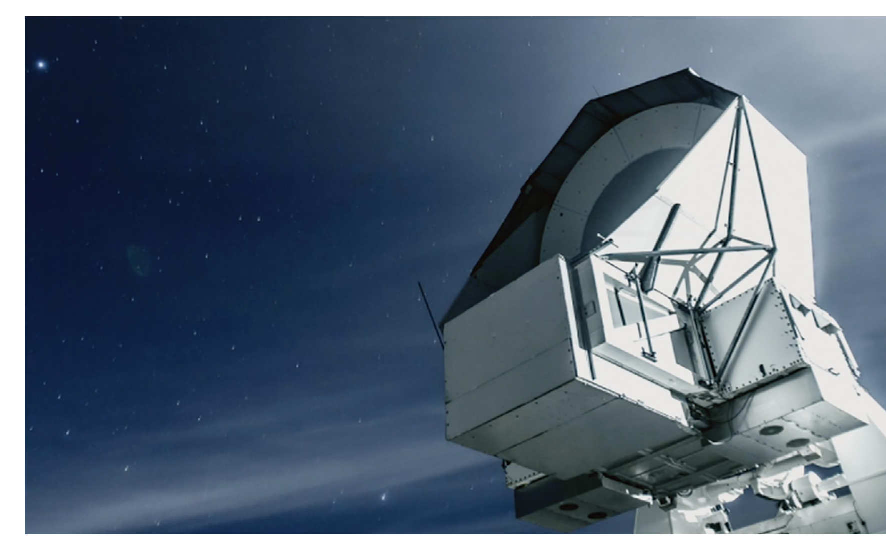
The effort will help set the stage for an even larger research initiative, still in its conceptual stage, that may be sponsored by the U.S. Department of Energy and the National Science Foundation. That project could eventually have as many as 500,000 detectors operating on multiple telescopes at ground-based observatories around the world.

Detecting B-modes would provide strong support for the theory of cosmic inflation. Their detection "might even be the first, and only, experimental evidence for quantum gravity — a sort of holy grail for physicists," says Brian Keating, a cosmologist at the University of California, San Diego, and director of the Simons Observatory. Keating has also led the POLARBEAR project, together with Adrian Lee of the University of California, Berkeley. Alternatively, if B-modes are not observed, the Simons Observatory would put a stringent limit on the amplitude of primordial gravitational waves, perhaps weakening the case for cosmic inflation. The goal of the project is to collect the best data possible to support or overturn the current conception of cosmic inflation, Spergel says. Either way, he says, the data could lead to a much deeper understanding of the earliest moments of the universe.

Data from the Simons Observatory may also help resolve many other open problems in cosmology. For instance, they could help cosmologists determine the masses of ghostly elementary particles called neutrinos, and provide new insights into the formation of structure in the universe and the nature of dark matter and energy. "What excites me personally about this work is what we will discover beyond primordial gravitational waves," Staggs says.

The POLARBEAR and ACT teams are currently working together to design a set of state-of-the-art telescopes and detectors. The two teams have previously used different detector technologies and data analysis techniques, Staggs says, and they are now sharing wisdom. "There's a coming together of fairly big personalities, which are really melding well," she says.

The collaboration is changing the culture of cosmic microwave background research in other ways, too. "We're involving a ton of young people," Staggs says. "Graduate students, post-docs and young faculty are taking on significant roles in this project, which is great, especially for the newly minted or not-yet-tenured researchers. They now have an opportunity to show how good they are at leading."



The first of three Simons Array telescopes, in operation since 2012. In 2018, it will be equipped with advanced 'sinuous' antenna-coupled bolometer arrays to measure the cosmic microwave background's large-scale B-mode polarization, constrain the properties of ghostly cosmic neutrinos and remove foreground contamination from images.

SIMONS INVESTIGATOR: ALEXEI KITAEV

Simons Investigator Alexei Kitaev's work has decisively influenced many areas of quantum and condensed-matter physics. Kitaev is Ronald and Maxine Linde Professor of Theoretical Physics and Mathematics at the California Institute of Technology and has been a Simons Investigator since 2015. He was awarded a MacArthur 'genius' fellowship in 2008, a Fundamental Physics Prize in 2012, the Dirac Medal in 2015 and the 2017 Oliver E. Buckley Condensed Matter Prize, which he shares with Massachusetts Institute of Technology physicist Xiao-Gang Wen.

Kitaev's most widely known work — for which he was awarded the Buckley Prize — is credited with kick-starting the field of topological quantum computation. A topological property is a global feature of a surface or space that is not changed by smooth deformations. For example, if you have a sheet of dough with holes in it, the number of holes does not change if you bend or twist the dough without tearing or breaking it.

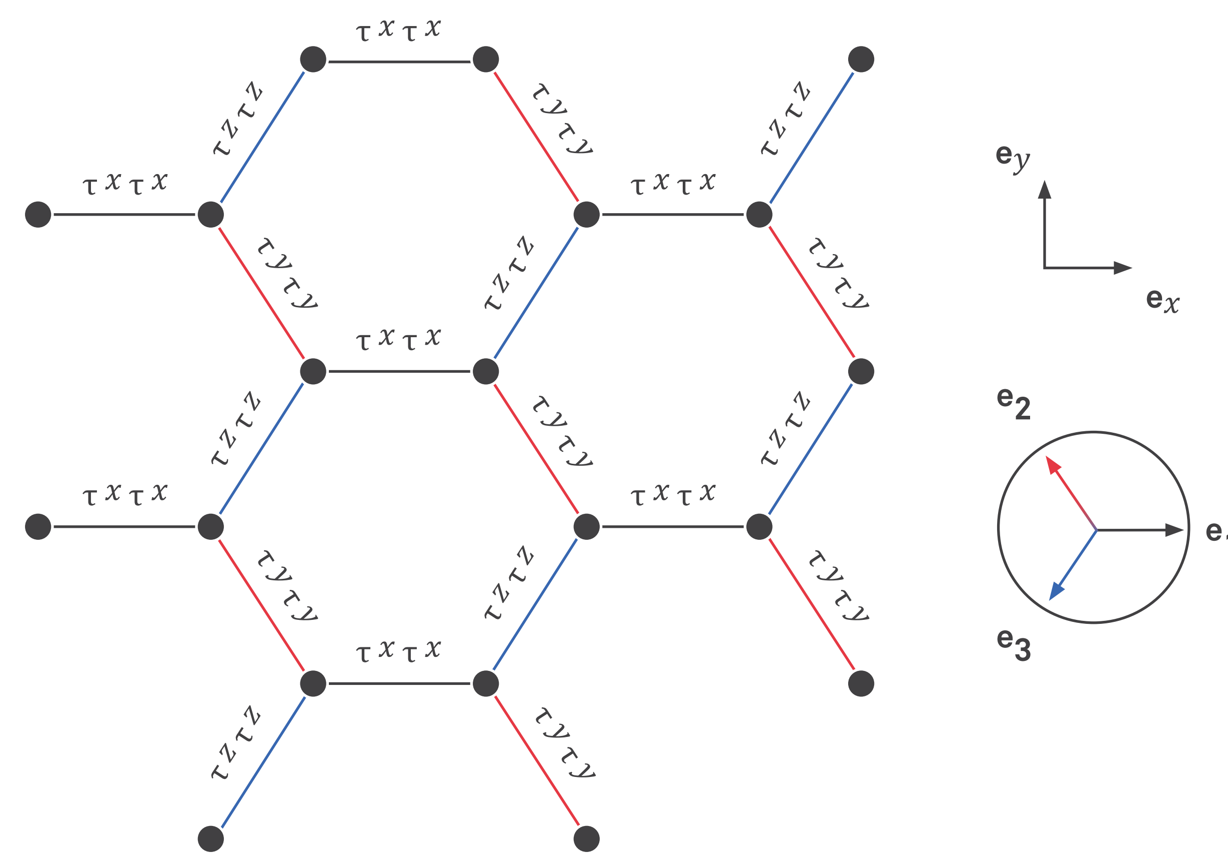
It has been known for decades that topological properties are important in physics; last November's Nobel Prize was awarded for work along these lines. Kitaev's contribution was to extend those properties to quantum systems: specifically, he found that topological invariants of quantum mechanical wave functions can be used to encode information ('qubits') in a quantum computer, and that the topological nature of the properties means that the qubits cannot be disrupted by environmental changes. Kitaev introduced theoretical models with topologically protected degrees of freedom and showed that these models can be organized into a universal quantum computer capable, in principle, of performing all needed operations. His models also provide key suggestions for creating physically realizable systems. Although current technology does not yet enable a quantum laptop, Kitaev's ideas are a key part of the basis for a worldwide effort to realize quantum computation and topological data storage.

Insatiably curious, Kitaev has now shifted his research from quantum computing to questions about black holes and quantum gravity. One of the questions he is tackling is related to the black hole information paradox: Is information permanently destroyed when matter falls into a black hole? The standard theory of black holes suggests that the answer is yes, but the standard theory of quantum mechanics predicts otherwise. Several years ago, Ahmed Almheiri, Donald Marolf, Joseph Polchinski and James Sully sharpened the question to one having to do with the fate of an observer who crosses the event horizon of a black hole. Do they sail through as though nothing has happened, or do they abruptly encounter a so-called firewall?

"I'm not sure if the question has a solution," Kitaev says. "There may be no consistent picture." Even understanding whether there is a solution would require wrangling with entanglement between entities inside and outside the black hole. To tackle the problem, Kitaev is studying a 'toy model,' a simplified system of assumptions and equations that makes the question more tractable by paring down the number of dimensions studied. "I started from scratch and looked for the simplest model possible," he says.

Kitaev is also pursuing one of the holy grails of physics: how to quantize gravity. Many researchers have looked to string theory as a potential solution to the problem, but once again, Kitaev is hoping that by studying simpler models he may be able to obtain insights that can be leveraged toward a more complete understanding of how gravity works at a quantum scale. "I just hope that studying models of black holes where both quantum mechanics and gravity play important roles will eventually help to construct a more general theory," he says.

One of Kitaev's models: spins with a particular designed set of interactions may form a topologically non-trivial state.



$$\mathbf{e}_\gamma = \mathbf{e}_x \cos\theta_\gamma + \mathbf{e}_y \sin\theta_\gamma$$

$$\{\theta_\gamma\} = \{0, 2\pi/3, 4\pi/3\}$$

GRADIENTS CRUISE

Merge models with field observations, warm water with cold, low-nutrient waters with high, the North Pacific Subtropical Gyre with the subpolar gyre, and the marine picocyanobacteria *Prochlorococcus* with *Synechococcus* — and the result is the 2016 Gradients Cruise.

From late April to early May, oceanographers onboard the research vessel Ka`imikai-O-Kanaloa, led by Ginger Armbrust and Angelicque White, worked to test the latest ocean ecosystems model from Mick Follows. All three are Simons Collaboration on Ocean Processes and Ecology (SCOPE) Investigators. Follows is a professor in the marine biogeochemical modeling group called the Darwin Project at the Massachusetts Institute of Technology. The Darwin Project — funded by the Simons Foundation, the Gordon and Betty Moore Foundation, the National Science Foundation and NASA — works to develop a large-scale global model for marine microbial communities based on models of ocean circulation, biogeochemistry and the associated communities of plankton.

Steaming north from its operational base in Honolulu, the ship, with its mixed team of experimentalists and mathematical modelers, traveled out of the warmer, nutrient-sparse subtropical gyre and into the cooler, productive waters of the subpolar gyre. The most interesting location for the scientists, however, was the transition zone, where the two gyres come together.

"We were on the edge of the gyres," says Armbrust, principal investigator of the Gradients program. "We set up to explicitly test some of the assumptions and predictions that come out of the Darwin Project ecosystem model along the transition between the two gyres."

The physical and geochemical components of the ocean simulations for the model have been around since the mid-1990s. Over the last 10 years, Follows' group has been developing, extending and advancing the ecological component. "[The model] is continually evolving, so the predictions used for Gradients were based on our most recent iteration just prior to the cruise," he says.

The data collected on the cruise have provided Follows and his team with much information to modify and improve the model. The team expected to see enhanced productivity — measured by an increase in microbial cells — across the transition between gyres where iron, nitrogen compounds and other nutrients are delivered and mixed in a ratio compatible with the demands of the organisms. The subtropical gyre lacks nitrogen, whereas the subpolar is short of iron: Each, therefore, has a distinct ecosystem. (Water masses are often characterized by their most limiting nutrient, as it usually determines which microorganisms can survive there and how large that population can grow.) A mixed system reduces the limitations on the microbial populations and potentially allows a more diverse and productive system.

"When you bring those waters together, you have the optimum nutrient ratio that will allow for enhanced productivity," Armbrust explains.

Yet in fact, although the model accurately predicted many of the big-picture ecosystem changes seen during the expedition, several surprises arose. Most unexpected was a resurgence of the subtropical cyanobacteria *Prochlorococcus* after the ship crossed into the transition zone.

"We anticipated a decline of *Prochlorococcus* and an increase of *Synechococcus* as we approached the transition zone from the south, which we see," says Follows. "However, as the cruise continued northwards, the *Synechococcus* population declined and *Prochlorococcus* rallied, becoming abundant again." The results were the same when the ship sailed back through the transition zone, indicating that the data are "really reproducible, not just transient features — these are real features," Armbrust says.

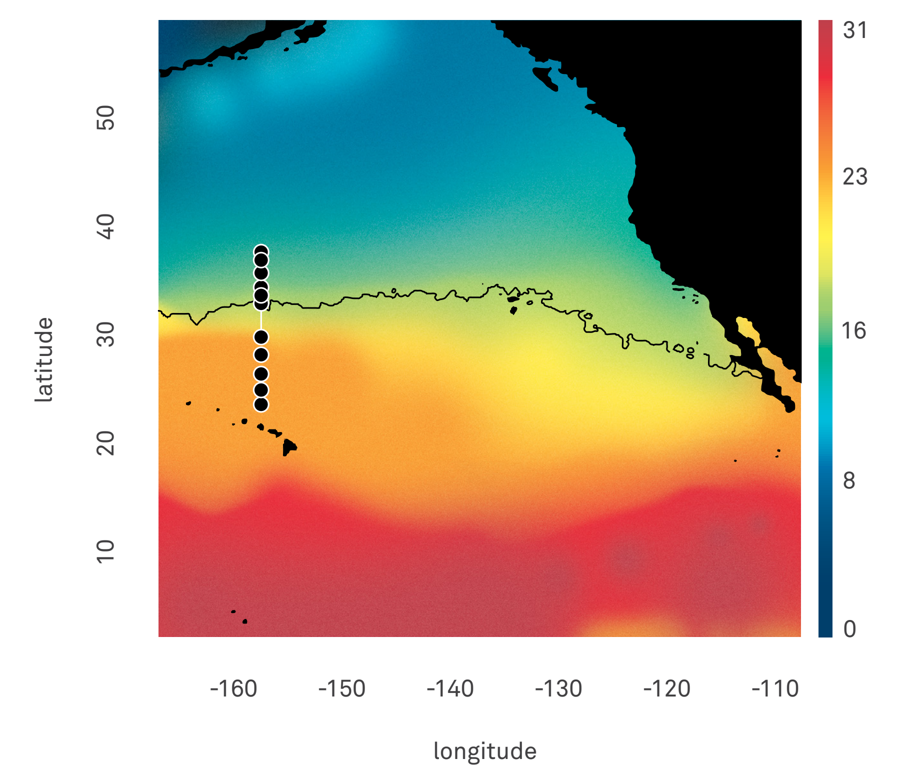
The most likely explanation for the resurgence of *Pro* and a decline in *Syn* is that the ship encountered a remnant or an eddy of subtropical water that had maintained structure within the transition zone. This water mass may also be a long-standing or recurring feature of the recent ocean circulation in the region. "This specific detail was not predicted by the model simulations, nor could we expect it to predict all of the fine-scale details of the circulation," Follows says.

But although the model cannot simulate the specific details of the fine-scale ocean circulation that led to the resurgence in *Prochlorococcus* within the transition zone, it might be able to capture the statistical likelihood of such events occurring, Follows says. "This resurgence is an event that might be expected to occur from time to time, but predicting a specific individual case is not possible."

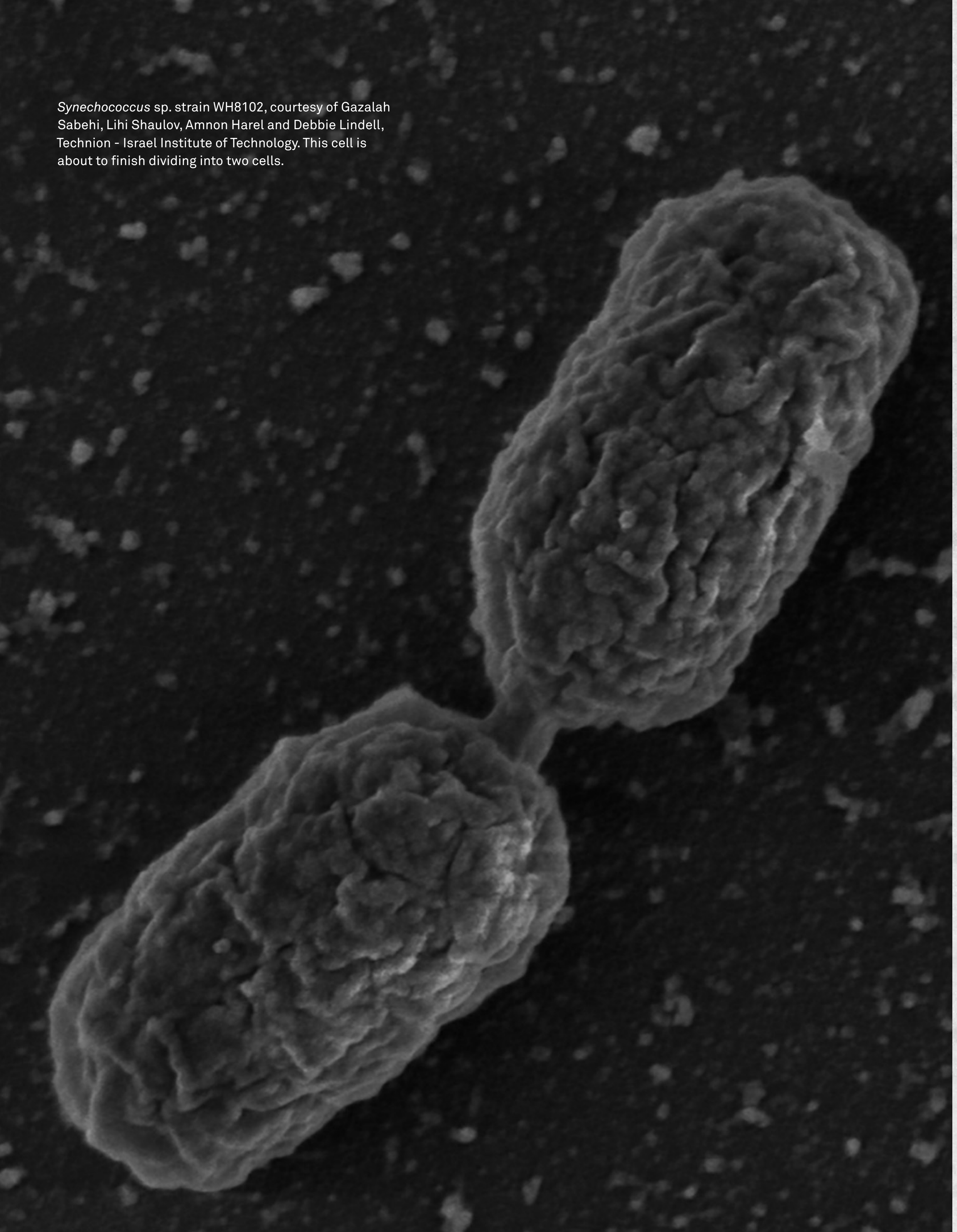
Refining the model means rethinking some base assumptions, too. "I suspect death rates are too high," Follows says. "The low abundance of modeled phytoplankton and the lack of dramatic changes in the modeled community composition along the transect both suggest to me that predation by grazers in the model is, in some sense, too strong." Such a change to the model, along with other tweaks such as reclassifying the relationships between observed and modeled organisms, may help better predict the abundances of picoplankton and, specifically, picoeukaryotes observed. It could also help predict the pronounced shift between *Prochlorococcus*- and *Synechococcus*-dominated waters.

Overall, the model predicted large-scale ecosystem changes well; it also gave a qualitatively accurate view of what to expect as to the size structure of particles and the elemental composition of particulate matter. "I was pleasantly surprised," Follows says. "These are relatively new aspects of our modeling framework and significant in our efforts to model and understand the ocean carbon cycle."

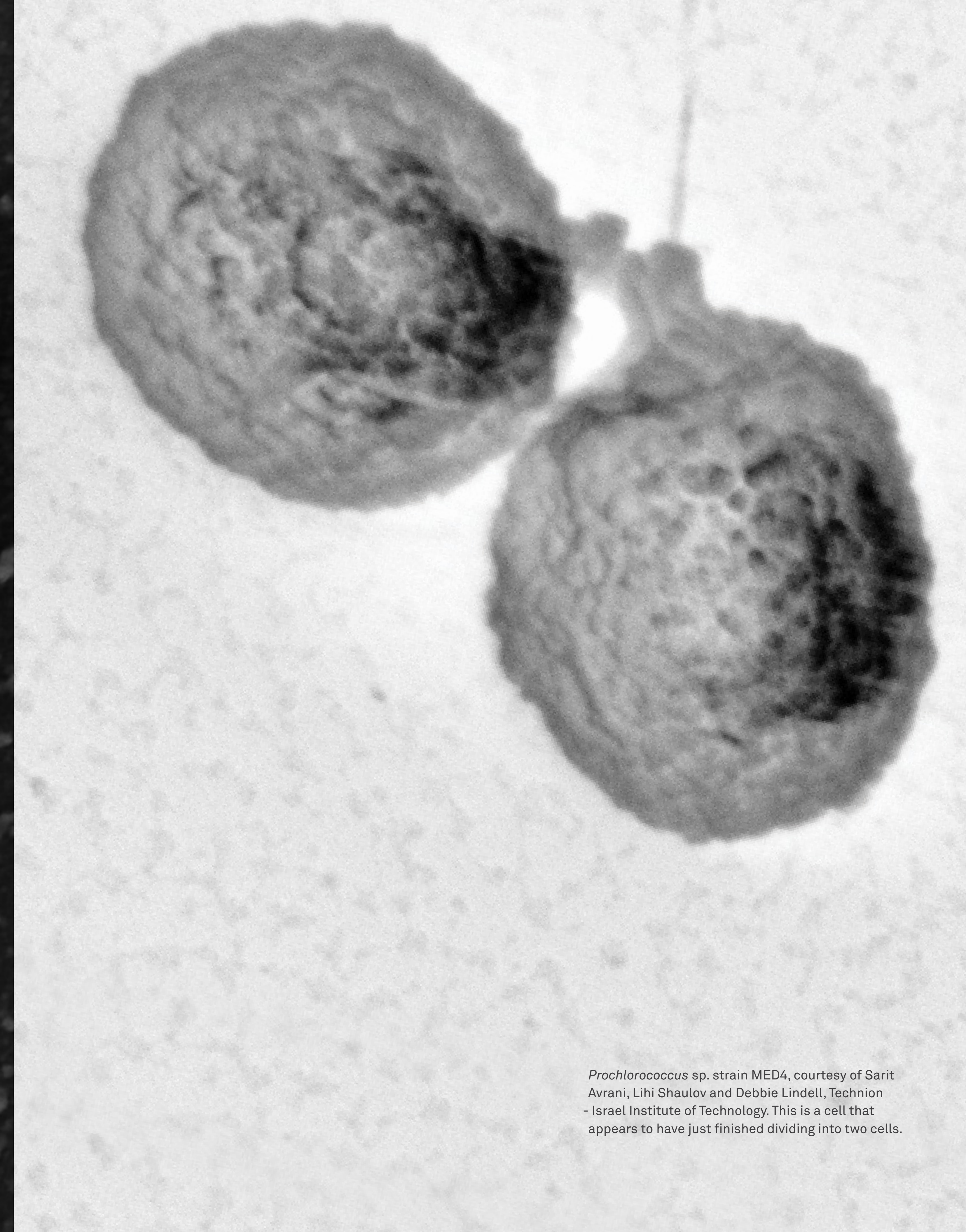
For Follows, the success of the Gradients Cruise comes from determining how to improve the models. "It has been really fun and unusual to work closely with the empiricists — it has developed a closer relationship between modelers and empiricists which, I believe, is very fruitful. I feel that it is stimulating more rapid progress on the modeling side."



This image depicts the course of the 2016 Gradients Cruise. The research vessel Ka`imikai-O-Kanaloa traveled from Hawai'i, in the North Pacific Subtropical Gyre, north to the subpolar gyre and back again. The colors shown correspond to sea surface temperature as measured by satellite. Courtesy of Francois Ribalet of the University of Washington.



Synechococcus sp. strain WH8102, courtesy of Gazalah Sabehi, Lihi Shaulov, Amnon Harel and Debbie Lindell, Technion - Israel Institute of Technology. This cell is about to finish dividing into two cells.



Prochlorococcus sp. strain MED4, courtesy of Sarit Avrani, Lihi Shaulov and Debbie Lindell, Technion - Israel Institute of Technology. This is a cell that appears to have just finished dividing into two cells.

SIMONS COLLABORATION ON THE GLOBAL BRAIN

What motivates us to train for a marathon? How do we decide between chocolate cake and apple pie? And what role do our memories play in such choices? These inner workings of the brain have traditionally been difficult to study. The Simons Collaboration on the Global Brain (SCGB), launched in 2014, explores these questions by pairing new technologies for monitoring the brain with powerful computational and modeling techniques. The collaboration, led by David Tank of Princeton University and an executive committee, supports an interactive community of 73 scientists.

The SCGB was made possible by a recent technological revolution in neuroscience: For the first time in the field's history, researchers can monitor the activity of thousands of neurons at single-cell resolution using various innovative sensors. These include high-density electrode arrays to track electrical changes and molecular tools to assay calcium concentration, an indirect measure of neuron activity. Scientists can also manipulate neuronal activity with optogenetics — a method by which neurons are genetically engineered so that they may be turned off and on with light — and then test the role those neurons play in cognition.

SCGB investigators are employing these tools to decipher the electrical and chemical activity of neural circuits and to examine how such neural codes — the language that neurons use to communicate — change over time to produce our thoughts and actions. They will explore how dynamic patterns of activity recall a memory, imagine the future or perform mental arithmetic. With the answers to these questions, neuroscientists can begin to build a mechanistic understanding of brain function.

Because the scientists also need new mathematical approaches to make sense of the huge volume of neural data being generated, the SCGB funds collaborations between experimentalists and theorists that combine the latest innovative technologies for recording and stimulating neural populations with the most powerful forms of analysis and modeling. "Investigators meet frequently to discuss experimental approaches, theory, models and computations that impact their individual projects. And they share data as it emerges," a level of interaction that makes the SCGB distinct from other collaborations, says Gerald D. Fischbach, distinguished scientist and fellow at the foundation.

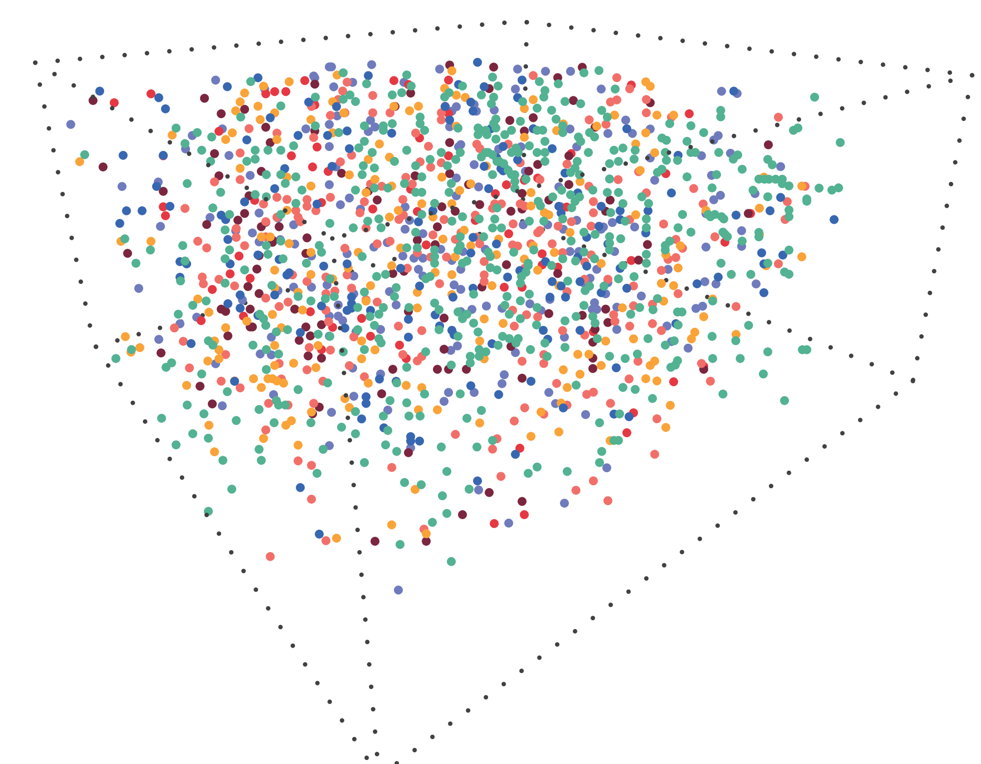
Today, the great majority of SCGB awards include two or more investigators, but a number of informal collaborations have emerged as well. SCGB investigators reported more than 50 newly formed collaborations last year, both within the SCGB and beyond. "The SCGB is a great catalyst for bringing together mathematicians and neuroscientists in a serious way — not just to hear each other talk," says Markus Meister, a neuroscientist at the California Institute of Technology and SCGB investigator. "The individual projects are diverse, dealing with memory, decisions, judgments and other internal mental states, but they all share a common goal — to define algorithms by which populations of active nerve cells correspond to internal mental states," says Fischbach.

For example, computational neuroscientist Shaul Druckmann and experimentalist Karel Svoboda, both from the Howard Hughes Medical Institute's Janelia Research Campus in Ashburn, Virginia, are working to understand how the brain holds information, such as a phone number, in short-term memory. They discovered that the memory system is designed with redundancy in mind: Just as computers have backup memory systems, the brain appears to have a backup system for short-term memory.

Druckmann and Svoboda drew this conclusion by watching rodents trained to remember the location of an object for a short period. During the task, the scientists recorded neural activity in a brain region known as the premotor cortex, which spans both the left and right hemispheres of the brain. They found that if they briefly silenced the neural activity on just one side, the activity pattern tied to that memory quickly bounced back, undoing the temporary freeze and restoring activity to a pattern similar to that which occurs under normal conditions. However, if the scientists silenced both sides of the premotor cortex, or silenced only one side when the connection between hemispheres was severed, the memory was lost. The findings, published in *Nature*, suggest that neural activity in one hemisphere can act as a backup copy for short-term memory.

Even more significant was the discovery that the brain seems to select which neural activity to protect. The rodents' brains restored only the activity pattern that was most tightly tied to the object's location. Just as engineers build backup systems for the critical parts of a machine but not for the dispensable parts, the brain seems to ensure that the essential components of neural activity are resilient or resistant to damage. Druckmann says this is the most important outcome of the study. "It means that the concept of taking activity and decomposing it into important and non-important parts is not just something we as theoreticians like to do," he says. "The brain also respects this principle — it doesn't bother to correct the parts that aren't important."

The Druckmann and Svoboda labs are now extending the cutting-edge technology to silence neurons even more precisely. In future experiments, they hope to identify neural activity patterns relevant to short-term memory more specifically, and to determine whether changing those patterns alters behavior. "We want to push the patterns around a bit and see how they rearrange themselves," Druckmann says.



These dots correspond to functioning neurons in the premotor cortex; the varying colors indicate that some neurons are highly active (brighter colors) during a memory task, whereas others are less active (darker colors).

SPARKING AUTISM RESEARCH

The past decade has witnessed the confirmation of the idea that autism is frequently caused by spontaneous gene mutations — and that the genes responsible may be discovered by sequencing large numbers of families affected by the condition. Sequencing studies of cohorts such as the Simons Simplex Collection — a repository of genetic, biological and behavioral data from more than 2,600 families consisting of one child with autism and unaffected parents and siblings — have already established more than 70 high-confidence autism risk genes and several hundred more candidate genes.

But between 500 and 1,000 genes are believed to underlie the condition, and researchers have long known that uncovering them all will require a much larger number of families. To tackle this challenge, in April 2016 SFARI announced the launch of SPARK (Simons Foundation Powering Autism Research for Knowledge), an initiative that will collect behavioral profiles and DNA samples from 50,000 families affected by autism over the next four years. Already, the initiative has enrolled more than 20,000 individuals with autism.

Having genetic data from 50,000 families should bring the autism research community closer to 'saturation' in terms of cataloging the genetic causes of autism, says Wendy Chung, the initiative's principal investigator and SFARI's director of clinical research. "At SFARI, one of our basic beliefs is that a true understanding of the genetic causes of autism will anchor us in terms of understanding the biological mechanisms," Chung says. "So 50,000 families became the goal for SPARK."

SPARK's mission is much broader than creating a catalog of autism genes. The initiative also aspires to foster a mutually beneficial community of researchers and families. All families who join SPARK agree to be notified of opportunities to participate in future studies, so SPARK could help overcome one of the biggest hurdles individual autism researchers face: recruiting enough participants who are eligible for their studies. The initiative's leaders hope that this relationship will lay the foundation for autism research for years to come.

"A researcher contacted me recently, for example, asking me how many verbal children between 6 and 10 are enrolled in SPARK," says Pamela Feliciano, SPARK's scientific director. "SPARK will make this data available and searchable online so researchers can see how many people meet the criteria for their studies."

As researchers carry out studies on the SPARK cohort, the data they add to the collection will make SPARK increasingly valuable, Chung says. "This is a long-term investment to create an infrastructure for the autism research community for a very long time."

Building Partnerships

Because of its heterogeneity — both genetic and phenotypic — autism has come to be seen not as a single condition, but as many related conditions. "The challenges are not the same for everyone on the spectrum, and the supports and treatments won't be the same either," Chung says.

Families who enroll in SPARK have the option of being informed if the initiative discovers a mutation that accounts for the individual's autism. "We believe that we will be able to return results to 5 to 10 percent of families in the beginning," Feliciano says. "As our knowledge grows, that number will increase."

As SPARK enrolls more and more families and discovers new autism genes, it will identify individuals with any one of the known autism risk genes who can be asked to participate in further research. Doing so will allow researchers to study particular genetic subtypes of autism and, down the road, potentially create customized treatments for autism. It will also allow families with shared genetic causes to form communities, potentially through the Simons Variation in Individuals Project, which currently provides a forum in which families with any 1 of about 50 different genetic variants can come together.

SPARK's creators want the initiative to be rewarding for the families who participate, so in addition to returning genetic results to some families, the initiative also offers webinars on topics related to autism, and provides individualized findings from the behavioral questionnaires for each child, which families can bring to their health care providers to help inform the child's care. "As we're learning, we want to make sure that we're not just keeping all these data for researchers, but that the families are learning about themselves at the same time," Chung says. SPARK's webinars in its first nine months of operations have attracted about 1,800 attendees.

The families will also tell researchers, Chung hopes, about the issues that are most important to individuals and families with autism. "We view SPARK not just as a research cohort, but as a partnership with families," she says.

To enable the initiative to scale to 50,000 families, SPARK's creators have tried to make it easy to join. Individuals can register online and then fill out a questionnaire and collect family members' saliva samples at home, which are returned to SPARK by mail. To recruit families, the initiative has given grants to 24 clinical sites across the country that host major autism centers. SPARK's leaders have also reached out to autism community and advocacy groups, which are helping to get the word out. SPARK's investigators plan to do genomic analyses on participants' saliva samples. These analyses will include both sequencing, which will help identify rare genes that cause autism, and genotyping, which will highlight more common genetic variants that don't necessarily cause autism individually, but that might be responsible for the condition when combined with the right mix of other genetic variants or environmental triggers. "We hope that this approach will cover all genetic angles," Chung says.

So far, the initiative has sequenced about 500 families. It plans to release these genetic data for scientists' use in 2017, Feliciano says. "SPARK will make data available to eligible scientists as soon as it is ready."

The initiative is generating an enthusiastic response from families affected by autism, many of whom have shared their stories on SPARK's website and on social media, posting pictures and commentary under the hashtag #WeAreSpark. "That has been incredibly gratifying," Chung says. "We're all starting to come together."

Sawyer, age 7, and Owen, age 9, are SPARK participants from Lake Tapps, Washington.

SIMONS VARIATION IN INDIVIDUALS PROJECT

In 2010, as genetic analyses of families in the Simons Simplex Collection (SSC) were pinpointing specific genetic variants associated with autism, SFARI scientists recognized the opportunity to invert the experiment. The SSC starts with families that have a child with an autism diagnosis, and looks for genetic risk factors underlying the condition. What could be learned, then, by going in the other direction: starting with individuals that have one of these risk factors, and studying their features?

From this 'gene first' concept was born the Simons Variation in Individuals Project (Simons VIP), which began by collecting genotypic and phenotypic data from more than 200 individuals, along with their family members, with variations in a genomic region called 16p11.2. Those data have given rise to more than 25 research papers.

In the years since the Simons VIP's start, whole-exome sequencing of the SSC and other collections has led to the discovery of dozens of genes implicated in autism. These studies provide compelling evidence that autism is not a single condition, but a collection of many related conditions.

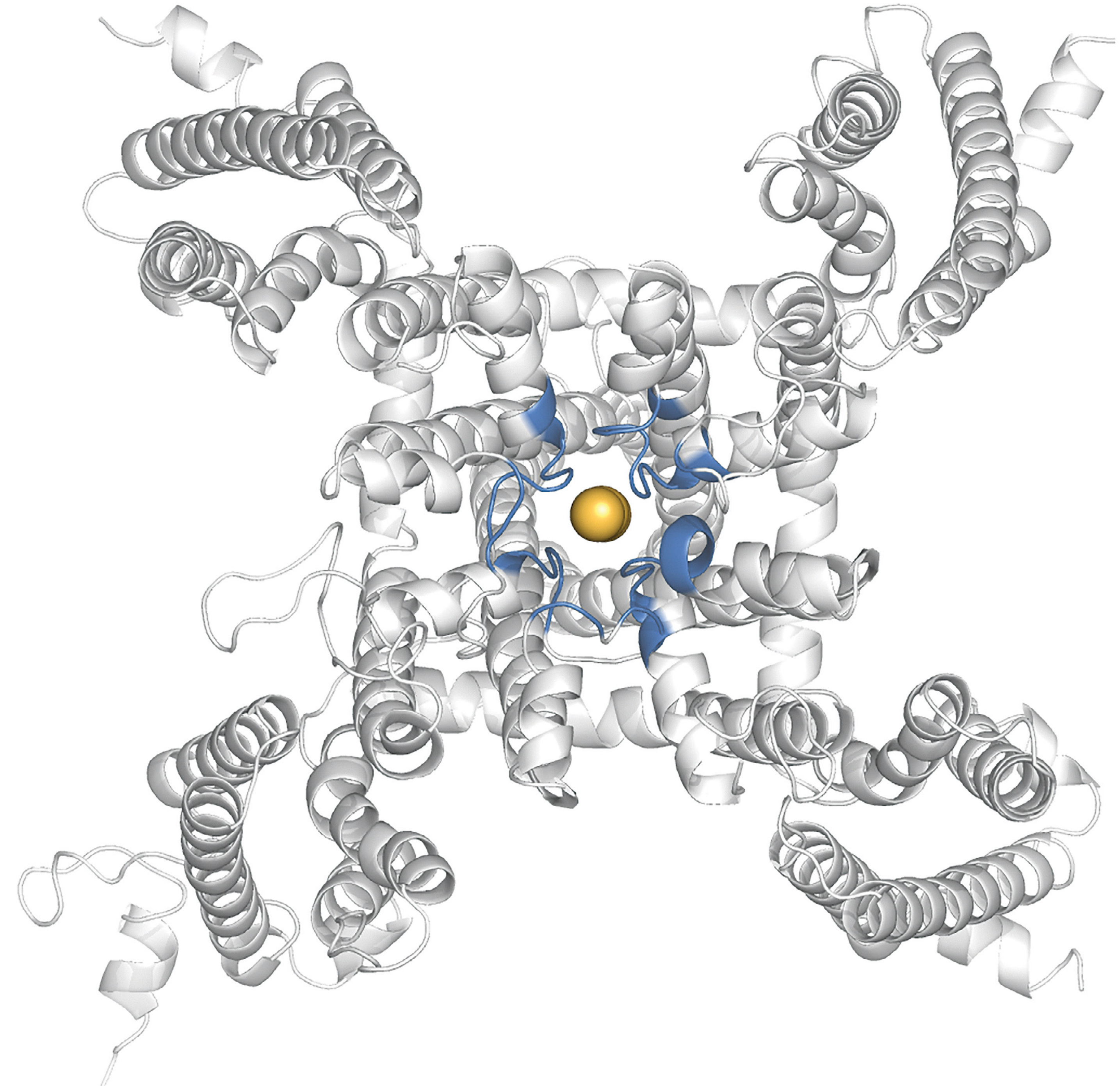
To try to understand the different genetic versions of autism — with the hope of eventually coming up with tailored therapies for them — the Simons VIP has greatly expanded its scope over the past two years. The project has reinvented itself as a virtual meeting place for researchers and individuals with mutations in 1 of more than 50 autism-linked genes.

The project, in its new form, has enrolled more than 569 individuals with genetic variants. For some of the genetic variants, dozens of families have been recruited; less common variants have turned up fewer families. "These are not just rare conditions, they're ultra-rare conditions," says Wendy Chung, the project's principal investigator and director of clinical research at SFARI.

Whereas the first incarnation of the Simons VIP did a 'deep dive' study of individuals with 16p11.2 variations, bringing families into clinics for behavioral testing, collection of biospecimens, brain imaging and neurological exams, the expanded project instead collects phenotypic information online, to make it easier for families to join the study. It also focuses on bringing researchers and families together. Already, for instance, the pharmaceutical company Roche has partnered with the Simons VIP to carry out clinical evaluations and electroencephalography studies of 10 individuals with mutations in the autism risk gene SCN2A. The data arising from that study — like all data associated with the Simons VIP — have been made freely available through SFARI Base.

The project enables families to connect with each other to share wisdom, and also to communicate questions to researchers. The project ran its first virtual family meeting on December 1, 2016. The largest single-gene family group — SCN2A, which includes more than 73 registered families — held an in-person meeting during the summer of 2016, which several Simons VIP and SFARI researchers attended. "We had families from around the world," Chung says. "They were in the scientific meeting, contributing and learning."

Finding others with a shared diagnosis can be a profound experience for families, says John Spiro, SFARI's deputy scientific director. "It's been deeply moving for everyone to see the families support each other," he says. "There's nobody with dry eyes at these meetings."



Mutations in the SCN2A gene, which codes for the sodium channel Nav1.2, are now recognized as among the most recurrent risk factors for autism. Interestingly, mutations in some parts of the channel seem to confer risk for autism, whereas mutations in other parts of the channel confer risk for epilepsy. A deeper understanding of the structure of the channel should aid in the development of molecules that interact with it to modify its function, potentially offering therapeutic benefit. The Simons VIP has been working with families that carry mutations in SCN2A to gain a deeper understanding of the relationship between genotype and channel function/behavioral phenotype. Pictured here is a sodium ion passing through the (blue) channel pore.

Image courtesy of Arthur J. Campbell and Florence Wagner, Stanley Center for Psychiatric Research at the Broad Institute, Cambridge, Massachusetts

SFARI RESEARCH ROUNDUP

The Simons Foundation Autism Research Initiative (SFARI) currently funds more than 350 researchers, known as SFARI Investigators, who carry out groundbreaking autism research across the globe. Their work spans a wide range of subjects — from building brain cells from scratch in the lab to understanding how hypersensitivity to touch may relate to social difficulties. Below are some highlights of SFARI Investigators' research in 2016.

Reversing Autism Symptoms

A new study suggests that it may be possible to reverse some behavioral traits linked to a particular form of autism as late as adulthood, at least in mice. SFARI Investigator Guoping Feng of the Massachusetts Institute of Technology and his collaborators looked at mice with nonfunctioning copies of SHANK3, an autism risk gene believed to contribute to about 1 percent of all autism cases. They found that these mice can recover from traits such as obsessive grooming and social deficits if the gene gets turned on, even in adulthood.

SHANK3 is one of many genes involved in the formation of synapses, the junctions between neurons that allow them to send signals to each other. In mice lacking SHANK3, neurons in a brain region called the striatum communicate at synapses less effectively than do those of control mice. But turning the gene on in adulthood reverses this deficit and also rescues the mice's obsessive grooming and social deficits, the researchers reported February 25, 2016, in *Nature*.

Activating SHANK3 in the adult mice does not reverse all the traits related to the mutation: The mice continue to show signs of anxiety and motor difficulties, such as having trouble balancing on a rotating rod. But when the researchers activated SHANK3 in three-week-old mice — an age corresponding to childhood in people — the mice's motor deficits eased and, to some extent, so did their anxiety. The findings highlight the importance of identifying developmental windows in which autism therapies may be administered with the greatest efficacy. Yet they also offer hope that some symptoms may be reversible even late in life.

Touching Anxiety

Hypersensitivity to touch may be largely responsible for the anxiety and social difficulties that are hallmarks of autism, a new mouse study suggests. Mice engineered to lack one of two autism-linked genes (MECP2 or GABRB3) in neurons that relay touch signals to the brain and spinal cord develop anxiety and social problems later in life. SFARI Investigator David Ginty of Harvard Medical School and his colleagues reported the findings July 14, 2016, in *Cell*. By contrast, mice that lack MECP2 in some cortical neurons but not in the touch neurons outside the brain show no differences in anxiety or social behavior compared with healthy mice.

Ginty's team found that mice lacking two other autism-related genes, SHANK3 and FMR1, are also hypersensitive to touch stimuli. And in mice lacking MECP2 or GABRB3, touch signals run to the spinal cord without the dampening that usually happens in healthy mice. Many people with autism report heightened sensitivity to touch, and the new results support the idea that this sensitivity may underlie these individuals' social difficulties.

Although autism researchers tend to focus on the brain, the new study suggests that treatments that target the peripheral nervous system — which connects limbs and organs to the brain or spinal cord — may play an important role in easing the social problems associated with autism. Unlike drugs that act on brain cells, drugs that act on peripheral neurons do not have to cross the blood-brain barrier, which greatly expands the range of potential therapies. Such treatments may need to be administered early in development, however: Ginty and his colleagues found that turning off the genes in peripheral neurons affects social behavior only if done before adulthood.

Unpacking the Mechanisms of an Autism Disorder

A mouse study published October 19, 2016, in *Neuron* pinpoints some of the biological underpinnings of Smith-Magenis syndrome, a rare condition linked to autism. The syndrome, caused by a deficiency of a gene called RAI1, is characterized by motor problems, obesity, intellectual disability and social difficulties. Similarly, mice that lack RAI1 are obese and struggle with learning, memory and balance.

Researchers had previously established that RAI1 controls the expression of other genes, but they didn't know which genes. The new study, led by SFARI Investigator Liqun Luo of Stanford University, has identified a subgroup of these genes that are involved in the assembly of neuronal circuits. By examining mice that lack RAI1 in particular types of brain cells, the research team has provided insight into how the gene's absence produces the symptoms of Smith-Magenis syndrome.

The researchers found that the loss of RAI1 in excitatory neurons (ones that promote brain activity) has no apparent effect when the gene is deleted in the cerebral cortex. But if the gene is absent in other parts of the brain, the mice develop motor problems, intellectual deficiencies and obesity. In particular, deleting RAI1 from excitatory neurons in the hypothalamus dampens expression of HTR2C and BDNF, two genes involved in reducing appetite. The study suggests that a drug that activates HTR2C, already approved by the U.S. Food and Drug Administration to treat obesity, may help individuals with Smith-Magenis syndrome control their weight.

Pinning Down Microglia's Role

Two recent studies by SFARI researchers have offered both a toolbox for studying microglia — the brain's resident immune cells — and new insights into their role in Rett syndrome. This autism-related syndrome is marked by cognitive and physical regression, breathing and movement difficulties, and intellectual disability.

Microglia, which are involved not only in destroying pathogens but also in pruning synapses, are thought to play a role in a variety of neurological disorders, such as Parkinson's disease, Alzheimer's disease and schizophrenia. It has been difficult for researchers to assess these cells' roles in detail, however. Until recently, the only way to study human microglia in the lab was to use microglia from postmortem brains, which are in short supply.

Now, a team led by SFARI Investigator Rudolf Jaenisch of the Massachusetts Institute of Technology has developed a method for making microglia out of stem cells reprogrammed from skin cells. The microglia the researchers created express many of the behaviors of microglia in living people — for example, they are capable of engulfing small objects, move through a culture of neurons and other brain cells, and travel quickly toward injured brain cells.

The team also grew microglia from a stem-cell line that carries a mutation in MECP2, the gene responsible for Rett syndrome. These microglia were exceptionally small, offering researchers a hint about the cells' role in the condition.

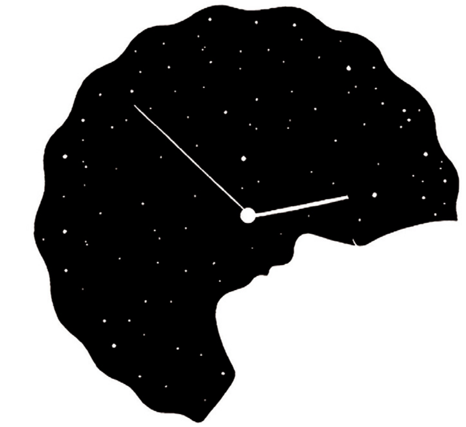
Meanwhile, however, a second study suggests that MECP2 mutations in microglia are not the primary driver of Rett syndrome. Instead, microglia's role may come into play largely in the final stages of the syndrome.

The research team behind the study, led by SFARI Investigator Beth Stevens of Boston Children's Hospital, had previously shown that microglia prune weaker synapses in the brains of healthy mice as part of normal development. In the new work, published July 26, 2016 in *eLife*, Stevens' group found that microglia in mice with Rett syndrome prune too many connections — but only near the end of the mouse's life. This suggests that microglia do not play a causative role in the disorder, but instead exacerbate it.

Knocking out MECP2 only in microglia does not produce Rett-like symptoms in mice, the team found, and these microglia behave normally. The study suggests that microglia contribute to the end stage of the condition by dismantling circuits weakened by the loss of MECP2 in other types of cells in the central nervous system.

DIGITAL GATHERINGS: *SPECTRUM* AND *QUANTA* MAGAZINES

Pep Boatella's lead illustration from "Living Between Genders," a *Spectrum* feature story by Deborah Rudacille, depicts the precariousness of living both as a person with autism and as a transgender person.



An illustration by Mrzyk & Moriceau, from *Quanta*'s "Why Sleeping Beauty Is Lost in Time," by Pradeep Mutalik. The famous Sleeping Beauty problem has divided probability theorists, decision theorists and philosophers for more than 15 years.

Spectrum and *Quanta*, the two editorially independent magazines funded by the Simons Foundation, cover completely different topics: *Spectrum* covers autism research, and *Quanta* focuses on math, physics and computer science, as well as basic research in biology. But they have a lot in common as well. Both cover topics that mainstream media has neither the resources nor the dedicated science writers to cover in-depth, and both strive to foster community and lively conversation among their readers.

Spectrum aims to make current advances in autism research as accessible as possible. "Scientists who work on autism research are really diverse," says Apoorva Mandavilli, editor-in-chief of *Spectrum*. They are neuroscientists, geneticists, psychologists and behavioral scientists. Some are clinicians and others work in labs remote from people with the condition. "They don't all have the same background or use the same jargon, so our approach is to avoid jargon and write at a level that is clear and accessible," Mandavilli says. As a result, *Spectrum*'s work is valuable for both scientists and interested lay readers, who tend to be people with autism and their families and friends.

Autism can be a heated topic of discussion, but *Spectrum* keeps its comments section constructive by posting clear guidelines and moderating comments that do not conform to them. In addition to respecting rules of common decency, commenters must refrain from posting medical advice or promoting any products. Claire Cameron, the site's engagement editor, follows discussions in the comments section and on social media sites and syndication partners' sites. When people ask questions, she often relays those questions to the researchers themselves. "We don't want people to think they're just shouting into a void," she says. "We really do want it to be a discussion."

Lay readers can ask questions of the researchers, but they can also give feedback about how the research aligns (or doesn't) with their own experiences of autism. "Often when we cover a paper, they'll say, 'This is exactly my experience; this is how I've dealt with things,' but we've also seen the reverse: people saying, 'This is the exact opposite of what I've seen,'" Mandavilli says. "It's an interesting perspective for us and for scientists."

Spectrum also creates community through its free monthly webinar series, in which scientists give talks on their research, followed by a question-and-answer session. Through articles, comments sections, and webinars, *Spectrum* not only serves the scientific community, but has also become a unique meeting place for the autism community. People with autism and their families can gain access to researchers whose work might affect their lives — and researchers get feedback about their work from people they might not normally encounter. "Over time, our site has become a middle ground for these often-separated communities to talk to each other," Mandavilli says.

Whereas *Spectrum* engages the autism research community, *Quanta Magazine* sparks lively discussions about mathematics, physics, theoretical computer science and basic biology — areas often neglected by traditional science media. "What is gravity? Does dark matter exist? How do prime numbers behave?" editor-in-chief Thomas Lin says. "We've carved out a niche for scientifically curious people who love to debate fundamental ideas."

Like *Spectrum*, *Quanta* moderates comments to cultivate an informed, civil conversation, taking pains to keep the level of discourse high. Editors relay particularly interesting or insightful questions to authors of articles and to researchers, who often chime in to answer. Some researchers use the comments section to offer thoughtful critiques; others occasionally offer to collaborate.

And readers are taking note. As a reader named Josh commented on a popular *Quanta* article, for which 261 comments were approved, "I was expecting the usual Creationism vs. Darwin/Science/Physics/Chemistry debate, but these [comments] are great. Looks like chemists and scientists debating and what not. … Actual sources being cited. What if the whole internet was like this?"

Quanta delivers to its readership a variety of content types: long, detailed feature stories, shorter blog posts, interviews with scientists and also a regular puzzle series that has developed a passionate following. "We're not afraid to ask our readers to think a little bit," Lin says. The puzzles can be quite challenging and involved — some readers even write computer programs to solve them.

"There's a whole subcommunity centered around this puzzle column," he says.

To reach and engage new audiences, *Quanta* and *Spectrum* syndicate articles to *Scientific American*, *The Atlantic*, *Wired* and other publications. And conversations inspired by *Quanta* and *Spectrum* articles often spill over to heavily trafficked social media platforms such as Reddit, Hacker News and Facebook. Lin says: "Though it can feel like the Wild West at times, I'm fascinated by where, how and why people share our stories across social media. It's an opportunity to see how different audiences engage with the big, new ideas we write about."

SCIENCE SANDBOX: UNLOCKING SCIENTIFIC THINKING

Philanthropic efforts to introduce lay audiences to science tend to fall into two categories: The first, more traditional, approach is familiar to anyone who has ever visited a museum exhibit, tuned in to a documentary on public television or browsed an educational website. These efforts are like lighthouses: They beckon people brightly and illuminate, but they tend to summon those who are already comfortable sailing over. That's where the complementary approach comes in, which could be described as 'meeting people where they already are.' These projects are not lighthouses but instead are like brightly colored buoys — they may not beckon like a lighthouse, but you can place more of them strategically in the water.

The Simons Foundation's new education and outreach initiative, Science Sandbox, was designed with the latter approach in mind — to meet people where they are and expose them to the thrills of the scientific process and scientific thinking. The initiative provides grants and support to projects that seek to inspire scientific thinking in people who may not live in a city with a world-class museum, may not watch public television regularly, or may not even be aware that science is something they can relate to.

Developed in 2016 and publicly launched in early 2017, Science Sandbox takes its name from the place where children often get their first taste of self-directed curiosity and collaborative experimentation — the same values that underpin discovery-driven science research. The initiative's manifesto — 'unlock scientific thinking' — makes clear the notion that instead of treating people as passive participants in learning, we should treat them as what they already are: naturally active explorers of their own worlds. Science Sandbox's diverse board of advisers, which includes accomplished scientists, educators, entrepreneurs and artists, reflects this expansive view.

To act as a catalyst for 'unlocking scientific thinking,' Science Sandbox functions as more than a grant-maker. Its charter includes language about "amplify[ing] our awardees' impact" in extra-monetary ways, which often happens in the form of informal introductions that the foundation facilitates. A distribution partnership between Vice's science and technology vertical — Motherboard — and filmmaker Elliot Kirschner, whose documentary film "A Brief History of Fat" was supported by Science Sandbox, proved especially fruitful. "Typically, Motherboard and Vice don't show any film that isn't produced and developed in-house," says Boyana Konforti, director of Education & Outreach at the Simons Foundation.

"We did not do anything more than bringing the two entities together, but Motherboard was very intrigued by Elliot's ability to bring together very sophisticated science and storytelling, and they found a very natural way to work together."

Another place where science education happens naturally — and at massive scale — is Wikipedia. The Science Sandbox-supported Wikipedia Year Of Science 2016 encouraged science educators to charge their students with writing Wikipedia entries instead of term papers. This project expanded the concept of 'education and outreach' by recruiting researchers to participate in the 'edit-a-thons' hosted at existing scientific conferences, such as the 2016 meeting of the American Association for the Advancement of Science (AAAS) in Washington, D.C. These events not only reach scientists where they already are, but draw them into discourse already happening on Wikipedia by teaching them the basics of editing content and encouraging them to write and edit articles themselves, in their areas of expertise.

"This was when the Zika virus and the discovery of gravitational waves were really hitting the newspapers," Konforti recalls of that first AAAS edit-a-thon. "Scientists edited Wikipedia pages for almost six hours, and the pages were viewed many tens of millions of times since the conference. That's a very, very big reach, and the impact that you get on Wikipedia users is just incredible."

Another Science Sandbox-supported event in 2016, produced by U.K.- and U.S.-based Guerilla Science, also gathered people together in a peer-to-peer way. Sensory Speed Dating invited singles and couples in New York to the House of Yes, an edgy performance-art venue in Brooklyn's industrial district of Bushwick, to experience "a greater understanding of the subconscious processes that drive our behavior and desires." Participants experimented with such unorthodox dating rituals as donning pulse monitors to identify fluttering hearts, inhaling other participants' odors to detect 'pheromonal communications,' and staring into each other's eyes for a full minute without speaking.

For Madeline Kaye, a self-described "total science illiterate" who attended Sensory Speed Dating with her boyfriend, it was Guerilla Science's choice of venue that first piqued her interest. "I'm a big fan of House of Yes," she says. "You could go there on any ordinary Tuesday, and it's glitter and go-go dancers. Not exactly a square crowd." She left the event feeling not only that the scientific content had lent "an additional energy to the room," but also that it had broadened her understanding of what she had previously considered "amorphous" sexual attraction. "It really comes down to the fact that we're still animals," she says, "and we'll perceive certain signals in certain ways no matter what."

Mark Rosin, Guerilla Science's U.S. director, describes the organization's mission as building up a sense of "science identity" in members of the public just like Kaye — which isn't the same thing as teaching facts. "The point of something like Sensory Speed Dating isn't remembering the exact Latin name of a particular microbe," he says. "It's about building a cultural connection between people's interests as they are, and what science has to offer those interests."

"The foundation is keen to see what new projects Science Sandbox will undertake next year," says Marilyn Simons, president of the foundation. "We hope our grantees and partners will relay the joy of experimentation — and revive the sense of play we felt as children in the playground sandbox."

Guerilla Science speed daters explore touch as a means to increase chances of a 'match.'

MATH FOR AMERICA: MT^2

Front row, from left to right: M*f*A Master Teachers Marvin Antebi-Gruszka, Dee Dee Dyer, Andrew Wille, Alexander Dvorak and Shannon Guglielmo.

"Math isn't fundamentally about numbers — it's a way of thinking about the world," says John Ewing, president of Math for America (M*f*A).

In its own words, M*f*A works to "make teaching a viable, rewarding, and respected career choice for the best minds in science and mathematics." To that end, M*f*A identifies outstanding K-12 mathematics and science teachers and awards renewable four-year fellowships, which provide stipends and connect teachers with one another to foster collaboration and ongoing learning. The goal is to inspire outstanding teachers to stay in the classroom, as well as to amplify their impact while they are there. There are currently more than 1,000 M*f*A teachers in New York City.

M*f*A prides itself on what it calls a "teacher-to-teacher" approach to professional development: M*f*A teachers lead a variety of courses each semester for and with their peers. As part of this community-building activity, M*f*A holds an annual event called MT^2 — Master Teachers on Teaching — in which M*f*A Master Teachers give TED-style talks and share their expertise with the M*f*A community.

The title of this year's MT^2 was "The State of STEM-ocracy," with talks from 11 Master Teachers focusing on democratic fairness and due process in science, technology, engineering and math (STEM) education and society. The event — scheduled to coincide with Election Day on November 8 — drew almost 200 teachers to Manhattan's Flatiron District, where they were joined by more than 100 more teachers online (the event was streamed). "Every year, we try to hook into something that's going on in the rest of the country, and this year the hook seemed pretty obvious," says Ewing. "The teachers were fielding a lot of questions in their classes, and we wanted to bring those conversations to the whole community."

Among the Master Teachers speaking to the theme of "STEM-ocracy" were Adam Zaid, who gave a talk about how the mathematics of voting can produce unexpected majorities and pluralities in elections, and Shannon Guglielmo, who demonstrated how students can design their own graph-theory lessons about the layout of access points to New York City's public transit system. And Andrew Wille delivered a surprising presentation inspired by Lewis Carroll, about how even the rules of mathematical logic may not have 'fairness' built into them.

The theme of democratic equity as it impacts STEM education came out in ways unrelated to national politics as well. M*f*A Master Teacher Michelle Sims, a high school algebra teacher at Morris Academy for Collaborative Studies in the Bronx, was inspired by a talk given by an elementary school math teacher who bridged the skills gap for her incoming students by having them work together in small groups, with lessons targeted to their particular level of proficiency. After hearing the talk, Sims decided to implement a variation on the same idea in her own high school classroom.

Marvin Antebi-Gruszka, a fourth-year M*f*A Master Teacher, approached the evening's theme from an unusual angle with his talk, "Cleaning Up Our Ideas on Confusion and Ignorance: Why Not to Just Sweep Them Under the Rug." As most STEM educators necessarily focus on helping their students master the curricula, Antebi-Gruszka drew attention to an equally necessary part of the learning process: confusion and failure. He asked: Could teacher focus on producing 'right answers,' without encouraging the mistake-driven processes that underlie the understanding of those answers, be subtly corrupting the process of learning STEM subjects?

"It's really important as teachers for us to recognize that students don't come to us as prodigies," Antebi-Gruszka says. "Most people who become teachers tend to have done well in school, so we don't necessarily come with that experience of what it was like to struggle or fail." To fill in this intellectual empathy gap, Antebi-Gruszka offered up a painful experience from his own childhood: the "week-in, week-out process of disappointing my mother," who always found fault in the way Antebi-Gruszka cleaned up the house. "I just didn't understand what I had done wrong, and I didn't understand how I could get better," he recalls. "And it's often very difficult to bring that level of empathy to our own students."

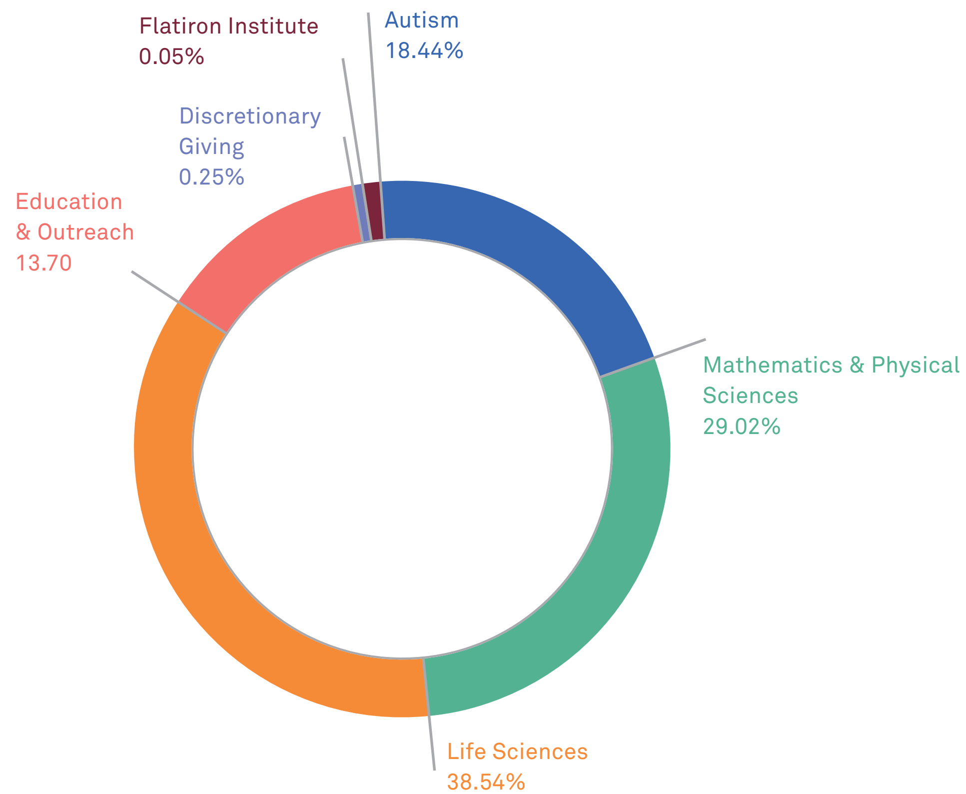
Events such as MT^2 not only foster M*f*A's mission directly but also highlight the centrality of mathematics in society. "Math is everywhere in elections and in civic life," Ewing says. "It's in the way states redistrict themselves. It's the way they ensure valid election results. And in cases where there are not just two but three or four candidates in an election, it's the way candidates strategize about building their campaigns: using mathematics.

And math can help us see inequities and unfairness," he says. "It can shine light onto the places in society where we are dividing things up, and help people determine whether the process is fair. The truth is, math is not quite so abstract these days."

Marcelle Good, M*f*A Master Teacher

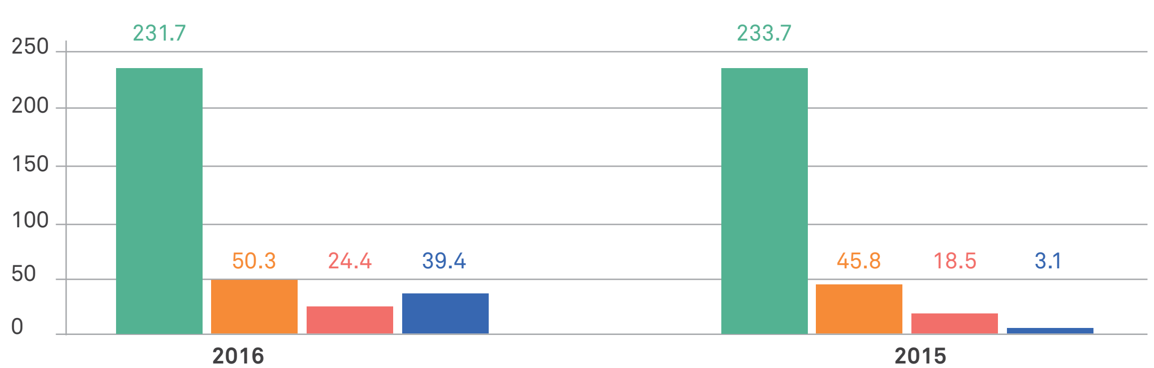
FINANCIALS

2016 Grant Payment by Category



Proportions of Expenses
(Cash Basis) $'s in Millions

- Grants Paid
- Program
- General and Administrative
- Capital Expenditures



BALANCE SHEET

Assets	**12/31/16**	**12/31/15**
Cash and Cash Equivalents	160,564,010	169,844,932
Investment Portfolio	2,653,820,929	2,440,414,626
Property and Equipment, Net	206,583,733	20,931,788
Other	3,214,330	3,479,954
Total	**3,024,183,002**	**2,634,671,300**

Liabilities	**12/31/16**	**12/31/15**
Accounts Payable	9,615,952	8,524,426
Deferred Lease Liability	151,455,946	4,159,666
Grants Payable	524,286,998	526,432,734
Deferred Excise Tax Liability	20,410,979	17,842,402
Total	**705,769,875**	**556,959,228**
Net Assets	**2,318,413,127**	**2,077,712,072**

INCOME STATEMENT

Revenue	**For 12 Months Ended 12/31/16**	**For 12 Months Ended 12/31/15**
Contributions	80,250,000	53,625,959
Investment Income	467,433,950	510,250,269
Total	**547,683,950**	**563,876,228**

Expenses	**For 12 Months Ended 12/31/16**	**For 12 Months Ended 12/31/15**
Grants Paid	231,726,910	233,732,496
Change in Grants Payable	(2,954,477)	137,769,224
Program	54,272,854	43,836,811
General and Administrative	15,563,652	12,670,144
Depreciation and Amortization	3,618,989	2,952,560
Taxes	4,754,967	6,031,389
Total	**306,982,895**	**436,992,624**
Net Income	**240,701,055**	**126,883,604**

MATHEMATICS & PHYSICAL SCIENCES INVESTIGATORS

Simons Investigators

Mina Aganagic
Ian Agol
Igor Aleiner
Andrea Alu
Rajeev Alur
Sanjeev Arora
François Baccelli
Ngô Bảo Châu
Andrei Beloborodov
Andrei Bernevig
Manjul Bhargava
Dan Boneh
Michael Brenner
Garnet Chan
Moses Charikar
Ingrid Daubechies
Maarten V. de Hoop
Michael Desai
Daniel Eisenstein
Alex Eskin
Jonathan Feng
Paul François
Victor Galitski
Surya Ganguli
Sharon Glotzer
Shafi Goldwasser
Ben Green
Alice Guionnet
Larry Guth
Christopher Hacon
Oskar Hallatschek
Patrick Hayden
Chris Hirata
Russell Impagliazzo
Piotr Indyk
Randall Kamien
Marc Kamionkowski
Charles Kane
Anton Kapustin
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