

SIMONS FOUNDATION

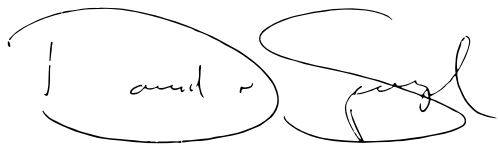
Annual Report

2021 Edition



The Simons Foundation is pleased to present you with this copy of our 2021 annual report. The year 2021 was filled with transitions for our scientists, grantees and staff that led to exciting developments and discoveries. We hope you enjoy reading about just a few of them.

You can view additional media related to these articles by visiting the report’s digital edition at **simonsfoundation.org/report2021** or by scanning the QR code below.



David N. Spergel
President

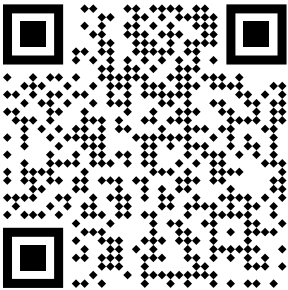


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LETTER FROM THE CO-CHAIRS

Significant changes in the Simons Foundation's leadership occurred in 2021, when David Spergel became its new president and we transitioned to co-chairs of the board of directors. We had left our mark after 27 years, and the time was right for us to step back from day-to-day operations and pass the reins to a new leader. To explain a little more about this decision, here's a bit of history describing the evolution of our vision.

Back in 1994, when we first filed papers to start the Simons Foundation, we never imagined the opportunities ahead of us. We soon decided to focus on advancing mathematics and the basic sciences. Jim provided funds and direction to keep the organization growing and thriving, and Marilyn led its administration, in addition to overseeing the foundation's outreach efforts. Along the way, we built a talented team to seek out new areas to explore and outstanding researchers to support.

As the foundation's programs evolved, so, too, did our long-term view. We came to see ourselves as the foundation's guardians for just a time. After all, math and science research is an enduring investment that transcends lifetimes, and we wanted the foundation to be there to support future mathematicians and scientists and continue our mission of advancing the frontiers of knowledge. And, as we contemplated the future, we happily recognized that we had an outstanding leader in David Spergel, an astrophysicist and founding director of the Flatiron Institute's Center for Computational Astrophysics.

David is creative, innovative and collaborative. He infuses every room with camaraderie and a sense of shared purpose. He brings a new and different energy to the culture of the Simons Foundation. Importantly, David shares our belief that math and science are critical investments and shares our vision of a vast and ever-changing frontier of discovery. We are confident in David's leadership as we step into our new roles as co-chairs of the board.



Working together with the foundation's board members is inspiring and beneficial. They are stellar; some are old friends of the foundation, some are new, but all the scientists who have joined are accomplished researchers experienced in matters such as pedagogy, administration or government. The board's composition, dictated by our bylaws, assures the foundation's continued commitment to fundamental research: The majority of board members must be scientists or mathematicians themselves. They are a visionary board of directors guiding us and now David as well.

Transitions are a time for looking ahead and imagining possibilities. We anticipate continued growth and expansion with David at the helm and under the board's guidance. With fresh ideas, new energy and a global landscape of outstanding researchers in mathematics and the basic sciences, the Simons Foundation renews its commitment to supporting excellence in science.

With curiosity and wisdom, we hope to pursue our noblest goals.

A handwritten signature in black ink, reading "Marilyn Simons".

Marilyn Hawrys Simons, Ph.D.
Co-Chair

A handwritten signature in black ink, reading "Jim Simons".

Jim Simons, Ph.D.
Co-Chair

LETTER FROM THE PRESIDENT

2021 has been a year of transitions for the world, for the Simons Foundation — and for me, personally.

For the world, in 2021, we saw effective COVID-19 vaccines come online in record time to combat a global pandemic. These vaccines have significantly reduced (though not eliminated) the dangers of SARS-CoV-2. The mRNA vaccines, which saved millions of lives worldwide in 2021, represent a remarkable triumph of science. But this success story began decades ago with basic curiosity-driven science — the same type of science that is the pillar of the Simons Foundation's research programs. Back in 1961, while working to understand the fundamental processes that are the basis of life, François Jacob, Sydney Brenner and Matthew Meselson discovered mRNA. Building on this basic discovery, in the 1990s, Katalin Karikó had the vision that mRNA could help fight disease. Today, mRNA vaccines are protecting us against COVID-19 and enabling the Simons Foundation and society to begin transitioning to a new normal.

For the Simons Foundation, this has been a year of transitions as well. From the foundation's inception until 2021, Marilyn Simons was president, and Jim Simons led the scientific mission and served as board chair. Together, they created one of the most original and innovative American philanthropies of our day. The Simonses' vision, strategy, creativity and generosity have yielded an organization with a unique character and an impressive track record. Under Jim and Marilyn's leadership, the Simons Foundation set up the Flatiron Institute, improved our understanding of the genetics of autism, and helped establish and strengthen research institutes throughout the world. The foundation has supported teachers through Math for America, and boosted public engagement with science through *Quanta Magazine*, *Spectrum*, Science Sandbox and Sandbox Films.

For me, personally, 2021 marked a significant intellectual and personal transition. While



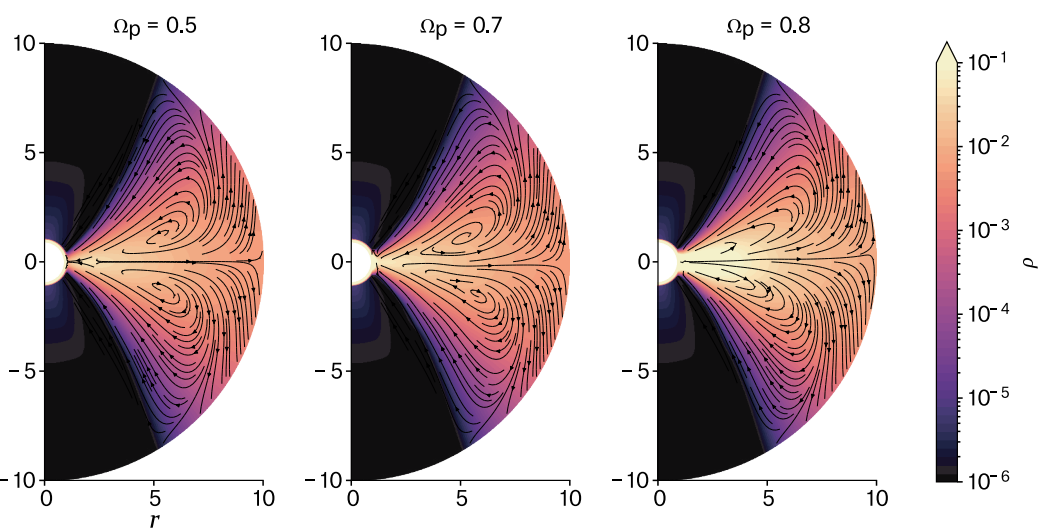
supporting and mentoring young scientists and promoting the development of my field have always been important to me, my past intellectual life chiefly focused on astrophysics. This year, I had the chance to understand more deeply the wide range of science impacted by the Simons Foundation — and to reflect on the responsibility that comes with that impact. I had a lot of fun learning about the exciting work that the Simons Foundation is supporting across the scientific frontier!

When I think about our past successes and future goals, I keep coming back to the idea of conversation. By enabling novel conversations through the interactions at the Flatiron Institute and our many collaborations and research programs, we are changing the dialogue in areas ranging from microbial ecosystems to number theory to autism science. Further, through our commitment to diversity, equity and inclusion, we're working to significantly increase the number of students from underrepresented groups who can participate in those conversations, earn basic science doctorates, and enhance the diversity and culture of our workplace. This report provides a glimpse into some of this inspiring work over the past year and points toward an exciting future filled with possibilities.

A handwritten signature in black ink, reading "David N. Spergel".

David N. Spergel, Ph.D.
President

WORLDS AWAY



Cross sections of simulated gas disks around a Jupiter-like planet spinning at either 0.5, 0.7 or 0.8 times the angular velocity required to tear the world apart. Lighter coloring denotes higher gas density, while arrows show flow direction. Only in the 0.8 scenario does material flow outward at all elevations at the equator. With such a speedy spin, the planet sheds mass and loses angular momentum.
Credit: J. Dong et al./The Astrophysical Journal 2021

Thirty years ago, we knew of just one planetary family — our own. Today, astronomers have cataloged nearly 5,000 planets orbiting other stars, many of which are unlike anything in our solar system.

“We’re in a new era where hypothetical questions about other worlds have become concrete areas of scientific research,” says Julianne Dalcanton, the just-minted director of the Flatiron Institute’s Center for Computational Astrophysics (CCA). “There’s an incredible amount of work to be done.”

The CCA is helping write the next chapter of exoplanet discovery. Computer simulations are revealing the forces that shape individual planets and entire planetary systems. New computing tools are helping astronomers interpret the incoming torrent of telescope data. Work is even afoot on an upcoming planet-finding instrument capable of finding a nearby Earth twin.

The CCA’s planet formation group, led by Phil Armitage, develops sophisticated computer simulations to explore how planets form. Early last year, group members zeroed in on one aspect

of how giant planets like Jupiter and Saturn bulk up. When these planets are young — less than a million or so years old — they are encircled by rings of gas and dust. These circumplanetary disks supply material to nascent worlds as they transition into full-fledged planets. But there are many questions about how those disks supply their budding planets and speed up or slow down the planets’ rotations.

As material moves from disk to planet, intuition suggests that the planet should spin ever faster, much as figure skaters twirl faster when they draw in their arms. A strong magnetic field emanating from a planet could apply the brakes, but it’s unclear whether all young planets have magnetic fields strong enough to arrest their spins before they fly apart.

So Armitage, CCA associate research scientist Yan-Fei Jiang and Pennsylvania State University graduate student Jiayin Dong simulated how fluid flows in a circumplanetary disk feeding an unmagnetized mostly-gas planet. The simulations show that the planet’s spin self-stabilizes at some maximum rate, shedding excess material and momentum back into the disk.

“That’s a unique state that wasn’t well recognized before our study,” says Dong, who was a CCA predoctoral student in 2020. Although this simulation captures just one snippet of the planet formation saga, it could help explain why known giant planets don’t spin faster than they do.

Once a planet forms, that’s not the end. Planetary systems keep evolving. Another piece of the puzzle comes from a cohort of planets that seems to be ... missing.

Among planets that orbit close to their stars, there is a dearth of those roughly 1.5–2 times Earth’s width. On one side of this ‘radius valley’ are ‘mini-Neptunes,’ gassy planets smaller in diameter than their namesake. On the other side are rocky worlds bigger than our own — the ‘super-Earths.’

To tackle this mystery, a team led by the CCA’s Trevor David took a subset of the planets discovered by NASA’s Kepler Space Telescope and sorted them by the age of their host star. The team found that the properties of the missing planets depend heavily on the star’s age. “The radius valley appeared emptier for younger stars,” David says. “And a lot of that emptiness was due to a lack of the very largest super-Earths.”

For stars younger than about 2–3 billion years old, there were few planets about 1.5–1.8 times as wide as Earth. For older stars, the absence wasn’t as noticeable, and it had shifted: There were more super-Earths and fewer mini-Neptunes.

The reason, the team thinks, is that over billions of years the mini-Neptunes lose their atmospheres, which are cooked off by a hot planetary core or spirited away by energetic starlight. What was once a gassy mini-Neptune transitions into a rocky super-Earth.

The radius valley’s discovery required rigorous observations of thousands of planets and their stars. And that work required computer algorithms working behind the scenes, letting astronomers interpret gobs of data.

That’s where folks like the CCA’s Dan Foreman-Mackey come in. “A lot of the work I do doesn’t directly produce splashy results,” says Foreman-Mackey. “I provide a lot of the plumbing that then goes to enable some of those results.”

Foreman-Mackey is part of a CCA group developing computing tools for analyzing telescope data. Historically, such work has been largely ad hoc, with individual astronomers writing code themselves. “We’re trying to remove some of that burden,” he says.

One project led by Foreman-Mackey provides efficient tools for inferring an exoplanet’s properties — its orbit, mass, atmosphere thickness — from observations of its star. Another venture, led by the CCA’s Rodrigo Luger, calculates how continents, oceans and clouds alter how sunlight reflects off a spinning planet as it orbits its star. Someday, astronomers might use this tool to map a planet from hundreds of light-years away, based on the trickle of light that reaches Earth’s telescopes.

This sort of computing expertise has also helped the CCA partner with international collaborators in forging a precision planet-finding project.

The Terra Hunting Experiment will use a spectrograph, which slices starlight into its component wavelengths. When installed on the Isaac Newton Telescope on La Palma in the Canary Islands, it will take meticulous measurements of the subtle motions of stars that are pulled to and fro by the gravitational tug of unseen planets.

Scheduled to start observations in 2023, this spectrograph will join an elite handful of instruments so precise that they can detect the signature of an Earth-mass planet on an Earth-like orbit around a sunlike star. What’s more, the project will get a whopping 50 percent of the available time on the telescope for 10 years — an allocation that will let the project find worlds that others can’t.

“That’s an unprecedented amount of observing time,” says the CCA’s Megan Bedell, who works on novel ways to analyze current exoplanet data as well as the torrent expected from the Terra Hunting Experiment. “We’re trying to find tiny signals that are swamped by complicated noise. So we need to get creative in the approaches that we use to model that noise if we’re going to pick out the signals of Earth-like planets.”

The exploration of worlds beyond the solar system is still in its infancy. “It takes a diversity of approaches and people, all looking at different aspects of these problems, to move our understanding along,” Dalcanton says.

SONYA HANSON: HER WORK IS HEATING UP

Once hooked, Sonya Hanson doesn’t give up. She still plays the French horn her father gave her when she was 9 years old (most recently with the L Train Brass Band in Manhattan). And three years into her graduate research, when Hanson realized her project wasn’t working, she did not despair. Instead, she changed tack.

“Her incredible resilience got her through it, even when her experiments didn’t work,” says Simon Newstead, a professor at the University of Oxford and one of Hanson’s Ph.D. advisers.

In a biochemistry Ph.D. program sponsored by the National Institutes of Health (NIH) and the University of Oxford, Hanson had set out to understand how a heat-sensing protein in mammals works. The protein TRPV1 binds to capsaicin, the main ‘hot’ chemical found in chili peppers, and is a member of a family of proteins activated by temperature. She first attempted to determine its structure.

At the time, a technique called X-ray crystallography was the standard method for determining protein structure. Before they can be investigated using X-ray crystallography, molecules must be isolated and ordered into a precise, yet fragile, crystal structure — something hard to do with a large, complex protein. In the case of TRPV1, it proved impossible.

“So I pivoted to computational simulations to look at how capsaicin interacted with the lipid bilayer surrounding TRPV1,” says Hanson.

The ability to attack a problem from both the experimental and computational fronts defines Hanson as a scientist. “Such expertise is quite rare,” says Kenton Swartz, a senior investigator at the NIH and another of Hanson’s Ph.D. advisers. “It’s hard to find someone with the skills and patience at the lab bench and also the mathematical and computational sophistication.”

“Sonya belongs to a completely new generation of scientists,” says Nobel Prize winner Joachim Frank, a professor at Columbia University, and one of Hanson’s postdoctoral advisers and a current collaborator.

A member of the Flatiron Institute’s Center for Computational Biology (CCB) since January 2021, Hanson adds a new layer to the center’s investigations. “We have scientists looking at genomes, cells and embryos, and now Hanson is looking at individual molecules,” says Stas Shvartsman, head of the CCB’s Developmental Dynamics group. As a member of the new Structural and Molecular Biophysics collaboration within the Flatiron Institute between the CCB and the Center for Computational Mathematics (CCM), Hanson will bring both her experimental and computational prowess to bear on some of the most pressing scientific questions around how proteins do their jobs — and even on the very methods scientists use to make those inquiries.

Thirteen years since starting her Ph.D., Hanson remains fascinated by heat-sensing proteins. In marine bacteria and plants, these ‘biological thermometers’ are key to understanding the global carbon cycle and crop yields, and in humans the proteins are targets for pain therapies. The 2021 Nobel Prize in physiology or medicine was awarded to the scientist who discovered TRPV1’s role in heat sensing. “That was validation that it’s not just me who’s interested in heat sensing,” Hanson says. Many of these heat sensing proteins are membrane channels that open and close in response to temperature and, in doing so, control the flow of charged particles across a cell membrane, sending important signals to other parts of an organism. But the details of this process, including those for TRPV1, remain unknown. To really understand how these proteins work, scientists need a detailed understanding of their structures and how those change with temperature.



Sonya Hanson studies the molecular mechanisms behind key biological processes.

Enter technology: In a boon for structural biology, a technique called cryogenic electron microscopy (cryo-EM) emerged as a viable alternative to X-ray crystallography and, in fact, was used to determine the structure of TRPV1 in 2013. As the name suggests, cryo-EM involves rapidly cooling a collection of molecules to very low temperatures (minus 170 degrees Celsius or lower) before imaging them with an electron beam. Cryo-EM eliminates the protein crystallization step of X-ray crystallography — the same step that thwarted Hanson’s first graduate school efforts. (Cryo-EM has been so impactful in deciphering the structure of biological molecules that its inventors, Joachim Frank among them, were awarded the Nobel Prize in chemistry in 2017.)

Hanson says the very nature of biological temperature sensors makes them difficult to study. As heat is added, the molecules in a sample will assume a variety of disparate shapes, like dancers whirling to fast music. Cryo-EM cools a sample so quickly that different molecules within it retain all of those multiple structures. Controlling for this heterogeneity with imaging algorithms is far from straightforward and is a key part of Hanson’s current efforts. She, along with CCM teammate Pilar Cossio (with whom she co-leads the Structural and Molecular Biophysics collaboration), will work to resolve the heterogeneity in cryo-EM data, again from both experimental and computational angles.

Now, in collaboration with Frank and other scientists at the Flatiron Institute, Hanson is exploring how to better resolve the heterogeneity of three-dimensional structures in cryo-EM. “We need to take the many degrees of freedom in a three-dimensional biological system and simplify it into a two-dimensional system” in a machine-learning algorithm, Hanson explains. The effort also includes a surprising collaborator: Hanson’s father, Andrew Hanson, an emeritus professor of computer science at Indiana University with extensive research experience in machine vision. “It turned out my dad is an expert in the problem of representing the orientation parameters of 3D objects like molecules,” Hanson says.

And in collaboration with Shvartsman, Hanson is innovating around understanding protein conformational heterogeneity. Using models of the physical movements of atoms and molecules, called molecular dynamics simulations, Hanson is exploring how mutations in the amino acid sequence of a protein affect its structure and, ultimately, its biological function. “The simulations will probe the functional ramifications of mutations, and in doing so will marry the molecular scale with the scales of the cells and tissues,” says Shvartsman.

At Flatiron, Hanson is grateful for the ability to follow her interests from her Ph.D. days. “I have an intellectual freedom here,” she says. “I couldn’t imagine a better environment for interdisciplinary work like mine.”

BOB CARPENTER: ALWAYS LEARNING, ALWAYS INNOVATING

Bob Carpenter created Stan, a probabilistic programming language that has revolutionized statistics research and is used in industries from pharmacology and finance to sports analytics and marketing. As one might expect, Carpenter is up for tackling new problems in any field and has transitioned fluidly between jobs in academia and industry during his career.

“I like working on high-performance algorithms that push the state of the art of what can be done,” says Carpenter, a senior research scientist who joined the Flatiron Institute’s Center for Computational Mathematics (CCM) in spring 2020. “It doesn’t really matter to me what I’m working on: I’m happy to work in bioinformatics, computational biology or quantum physics.”

Carpenter revels in the fact that “cross-fertilization is one of the real joys of being at CCM,” whose mission is to create new mathematical approaches, algorithms and software to advance scientific research in multiple disciplines. For instance, after hearing an introductory talk by CCM biophysicist Pilar Cossio, Carpenter and other Flatiron researchers leapt at the chance to collaborate. They published a paper in *Scientific Reports* in July 2021, showing a new way to model how molecules structure themselves under different energy conditions. Carpenter has also worked on algorithms to deal with genomics data with Center for Computational Biology associate research scientist Jamie Morton, now a principal investigator at the National Institutes of Health researching links between the gut biome and autism. And Carpenter’s arrival at the CCM two weeks before lockdown permitted him to help the U.K. Health Security Agency with COVID-19 models.

All of Carpenter’s collaborations arise from his expertise and urge to innovate, but they continue because working with Carpenter is, it turns out,



Bob Carpenter’s work on projects such as the Stan probabilistic programming language has benefited a wide assortment of fields, in the sciences and beyond.

terribly refreshing. He happily criticizes his own work and ideas. “He’s really unusual in being so forthright,” says one colleague, Columbia University statistics professor Andrew Gelman. “We all criticize our own stuff in private, but he just doesn’t play by the same rules that most people play by.”

Making Up His Own Rules

As a child in working-class Detroit, Carpenter was fascinated by computers and probabilities. In the 1960s, he was gifted an early Digi-Comp — an early mechanical computer constructed from a kit

— and precociously tried to map out a game tree for tic-tac-toe. Role-playing games such as Dungeons & Dragons made him “really get into probability by calculating odds, making up my own games and figuring out how they work.” After he read *Gödel, Escher, Bach: An Eternal Golden Braid*, the Pulitzer Prize-winning book on cognition by Douglas Hofstadter, the teenaged Carpenter decided to focus his career on artificial intelligence and logic.

“I tailored my own undergrad program knowing I wanted to do AI,” Carpenter recalls. “There weren’t really programs for that. Michigan State let me put together a course around what I thought AI was, so I could take philosophy of mind, psycholinguistics and cognitive anthropology.”

Carpenter’s academic career saw him hopping between departments: math for his bachelor’s degree, cognitive science and computer science for his Ph.D. at the University of Edinburgh, and finally computational linguistics at his tenured position at Carnegie Mellon University. The thread of AI ran through it all, as his academic research focused on how computers process the natural language of humans.

However, dissatisfied with the management aspects of academia after eight years as a professor, Carpenter joined Bell Labs just as natural language processing was transitioning from theoretical to concrete thanks to leaps in computing power: “All of a sudden, the stuff I was doing on the black-board became real.”

Back to Academia on His Own Terms

A challenge encountered while in the industry catalyzed Carpenter’s return to academia after a decade as a programmer. His machine-learning startup required ginning up new and unique training databases for each client, as the computers needed to train on different sets of data. That data wrangling made him curious about the dependability of the training sets — which led him to Bayesian statistics.

Bayesian statistics applies probability theory to real-life problems. Carpenter starting hanging out with Gelman, who co-wrote the seminal textbook *Bayesian Data Analysis*. He loved learning about the field so much that he became a postdoc with

Gelman, alongside a freshly minted Ph.D. named Matt Hoffman. Gelman threw his new hires a challenge: Create a programming language to express the models in one of his books.

The approach Carpenter and Hoffman wanted to try, called Hamiltonian Monte Carlo, required calculating derivatives of a computer program. Because computer programs are, at their core, a series of functions, you can differentiate them in the same way that you take derivatives in calculus. But such calculations are time consuming and prone to error when done by hand.

In a huge breakthrough, Hoffman, now at Google, developed the No-U-Turn Sampler algorithm, or NUTS, to solve the problem. Carpenter then implemented it in a user-friendly language based on BUGS, the first probabilistic programming language. The team named the new language Stan, after mathematician Stanisław Ulam, who invented Monte Carlo methods. Of NUTS, Carpenter says, “it has seriously changed statistics such that we’re able to sample models a couple orders of magnitude bigger than before. We take problems that BUGS would solve in 24 hours and solve them in 10 minutes.”

Nowadays, Carpenter is excited about the Pathfinder algorithm he’s developing for a project led by Gelman postdoc Lu Zhang. Originally created to speed up one part of Stan, the algorithm ended up with broader implications: They’ll be able to run computations “a couple orders of magnitude faster.”

“I haven’t been excited about something like this since NUTS came out; I’ve never been this excited about an algorithm that I’ve co-developed,” Carpenter says, glowing.

Between Pathfinder, COVID work, supporting Stan and its 40 independent developers, a book with Gelman, and chatting generally with physicists at Flatiron, Carpenter has leapt at the chance to learn new things while at the CCM and humbly tries to innovate wherever he can.

“I get a lot of joy out of talking to people and learning stuff, so I’ve always taken the job where I can go to learn the most.”

INSECT BRAIN CONNECTOMES, COURTESY OF AI



Neuroscientists are mapping the tiny brains of mini-wasps. Credit: Alexey Polilov

The developers of neural networks, a powerful methodology in artificial intelligence, drew inspiration from the human brain, with its webs of connected neurons. Now, neural networks are returning the favor, helping us to understand our own brains. Researchers around the world are working to reconstruct connectomes: wiring diagrams of brains. Until very recently, that required tracing neurons by hand through thousands of thin slices of tissue, a painstaking task. But now teams, including those at the Simons Foundation’s Flatiron Institute, are leveraging AI to automate the process and help them build computer models of this most mysterious organ.

Mitya Chklovskii, Jingpeng Wu and Kazunori Shinomiya from the Flatiron Institute’s Center for Computational Neuroscience (CCN) and Pat Gunn from its Scientific Computing Core are hard at work mapping the brain of the mini-wasp (*Megaphragma amalphantum*), a tiny insect only a

fifth of a millimeter long. “It’s a really cool creature,” Chklovskii says. “It’s really small. It has only 4,000 neurons in its head. But it has sensory organs, just like bigger insects. It can see, smell, hear and fly and mate and all that. And it somehow does it with a smaller nervous system, one that’s easier to understand.”

Even with only 4,000 neurons to deal with, constructing the mini-wasp connectome by hand would take decades. Shinomiya recalls that as a postdoctoral fellow, about 10 years ago, “I did manual tracing by painting the neurons one by one, and it’s a really slow and painful process. I spent maybe two years and painted only 60, 70 neurons” in a fruit fly. Two years ago, Flatiron started automating the process, building on methods developed at Princeton University, where Wu was a postdoc.

The CCN’s plan is to map an entire mini-wasp brain over the next three years, but before they could map anything, they needed raw data. Alexey Polilov’s lab at Moscow State University catches a mini-wasp, fixes it and stains the dead specimen to increase visual contrast and then embeds it in epoxy to hold its shape. From there, Harald Hess’s team at the Janelia Research Campus, where Chklovskii previously led a connectome project, uses a scanning electron microscope to ablate one surface layer at a time using an ion beam, capturing images along the way. They send this stack of digital images to the CCN for their connectome work.

The group is starting with the insect’s vision, automating the mapping of the part of the brain called the optic lobe. To do this, they must first create ground-truth data — human-generated labels of neurons in part of the optic lobe that teach the computer how the neurons in the rest of the lobe should be labeled. “People actually sit there and they color in the neurons, exactly like kids and their coloring books,” Chklovskii says. Those annotators also label the synapses, the junctures through

which neurons communicate with each other. Using those ground-truth data, Wu trains artificial neural networks to accurately label the whole lobe.

Still, networks make errors, so the annotators (also called proofreaders) are currently correcting the automated annotations. Wu will then add the updated labels to the networks’ training data to help them improve before they are applied to the rest of the brain.

Wu says training the system “sounds simple, but its implementation has a lot of details.” The full computational pipeline involves at least 10 algorithmic steps, he says, including training neural nets for segmenting neurons and detecting synapses, as well as other algorithms. The segmentation network makes only fuzzy suggestions, and another homemade software tool converts those suggestions into discrete three-dimensional outlines of neurons. Another step combines the neural outlines and the synapses. Wu also had to figure out how to distribute image chunks and computation tasks across many computer nodes and then stitch the predictions together smoothly. Many of these tools existed previously but didn’t interact well with his distributed computation framework. Wu is rewriting much of the pipeline algorithms from scratch into one coherent system with some adjustments, which he will make open source. Meanwhile, Gunn is figuring out how to store and access the data on the servers — “gluing it into our way of doing things.”

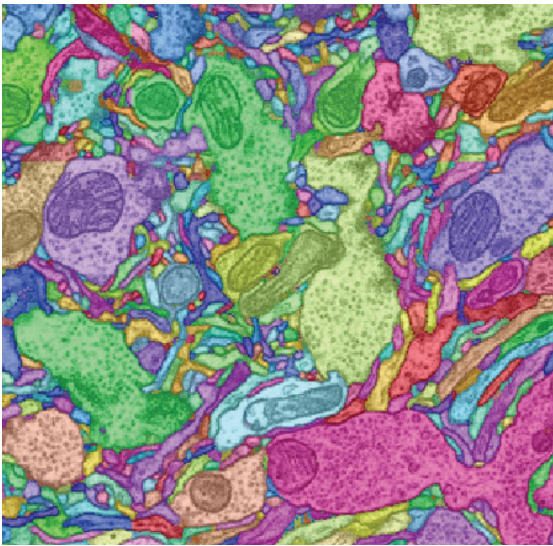
The end result will be not just a three-dimensional painting but a schematic map of which neurons are connected to which others through their many branches and synapses. In one rendering, it might look like a subway map. Scientists can then use the map to ask all sorts of questions. Shinomiya, for example, would like to “identify the minimal subset of neurons necessary for survival.” The mini-wasp’s small size and short life span can help narrow the scope: Anything in its brain is likely to be important for tasks like seeing and flying, whereas neurons that exist only in larger systems — the fruit fly (*Drosophila melanogaster*), for example — might be redundant. He also wants to catalog homologous neurons, those that serve similar purposes in the circuitry of several species, which could shed light on evolution.

The scientists also hope to run simulations of insect cognition using a connectome-based model. “By

deleting this neuron or inhibiting this neuron, what will be the output?” Shinomiya says. Such simulations are harder to interpret in models with many more neurons. The fruit fly brain, for instance, contains more than 100,000 (and the human brain about 86 billion). According to Gunn, “If we’re successful with this species, this may become a new model organism for neuroscience.”

“One of the unique features of the mini-wasp is that we can image the whole head,” Chklovskii says. In the fruit fly, whose connectome other labs are constructing, “they scoop the brain out, and the eyes are actually not attached.” But insect eyes have many facets — about 30 in the mini-wasp — and the facets are not identical. “So the optics are slightly different, the receptors are different. And that difference is reflected in how the neural circuits process the information. And so having both the optics and the neural circuit in one specimen is a unique advantage of our preparation,” Chklovskii says.

The project continues to evolve as the team progresses. Wu just published a paper on a technique that represents neurons not as voxels (volumetric pixels) but as clouds of points, a solution that will help fix segmentation errors. He hopes to develop the approach further. And in January the team received high-quality scans of a new mini-wasp specimen. “This new dataset is very promising for the reconstruction of most neurons in the mini-wasp brain,” Shinomiya says. “So I’m pretty excited to work on this.”



A cross section of the optic lobe of an insect’s brain. Artificial neural networks trained using human-produced data can quickly and accurately label neurons (denoted here by different colors) and synapses. Credit: Chklovskii group

'STRANGE' CONNECTIONS

Physicists have a strange problem. In some metals — dubbed ‘strange metals’ — electrical current does not respond to temperature changes in the same way it does in more conventional metals, such as copper.

This seemingly minor curiosity points to a fundamental problem: The reigning theory of how electrons move through solids — a conceptual tour de force that has held sway for more than 60 years — has its limits.

At the Flatiron Institute’s Center for Computational Quantum Physics (CCQ), researchers are tackling this quandary head on. By developing techniques to solve complex quantum problems on computers, CCQ scientists have shown that one theoretical model long suspected to be key to exploring strange metals does, in fact, predict strange metal behavior.

What’s more, this same model has deep mathematical connections to black holes and theories of quantum gravity, raising the prospect that the computational techniques developed at the CCQ can help bridge two seemingly disparate fields of inquiry.

“The fact that there is this remarkable connection ... shows how concrete problems in quantum condensed matter physics can connect to deep theoretical physics questions,” says CCQ director Antoine Georges.

All metals resist the flow of electrical current, and as metals get hotter, this resistance increases. Electrical resistance has many causes, but one that is of fundamental importance is the scattering of electrons off of other electrons. In normal metals, this contribution to the resistance changes with the square of the temperature — double the temperature, and the resistance quadruples. But in strange metals, the electron-electron contribution is linear — double the temperature, double the resistance.

“This cannot be explained in a typical framework of metals,” says Flatiron research fellow Alexander Wietek. “That’s why it’s called strange.”

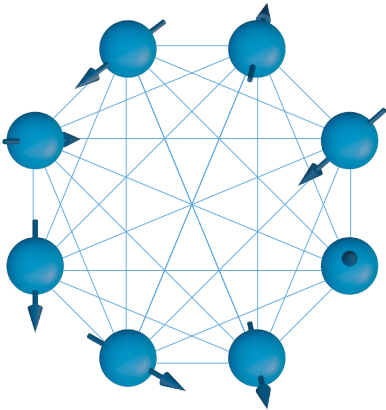
In the standard theoretical framework, current is carried by electrons — or, more precisely, electron-like ‘quasiparticles.’ Interactions among these quasiparticles lead to the normal dependence of resistance on temperature. Strange metals require a new way of thinking, in which there are no quasiparticles: Electrons are no longer individuals but rather a fully interconnected quantum soup. “We’ve been working on models that can actually predict such a behavior,” Wietek says.

Enter the Sachdev–Ye–Kitaev, or SYK, model: equations that describe how electrons interact with one another via their spins, or intrinsic angular momentum. “It’s perhaps the simplest model in which the complete absence of quasiparticles can be demonstrated,” Georges says.

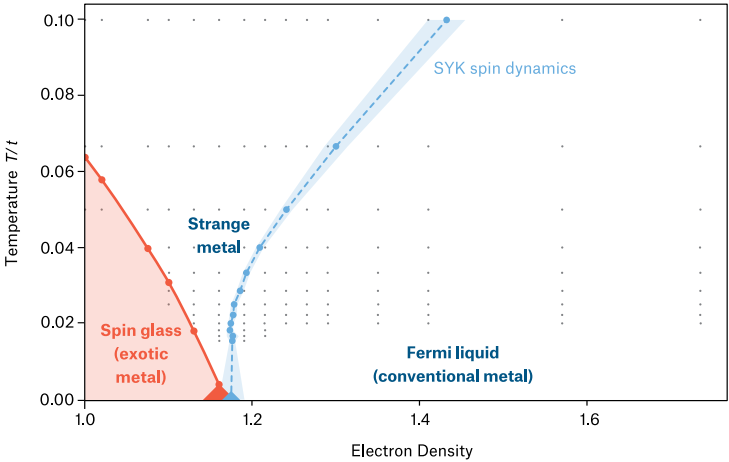
In the original formulation of the SYK model, every electron ‘senses’ every other electron, and any two electrons may randomly adjust their spins to point in the same direction or in opposite directions. However, when the equations are tweaked to permit the electrons to move, the energy levels allowed by the model match what one expects if quasiparticles aren’t present, a hallmark of strange metals discovered by CCQ senior research scientist Olivier Parcollet in the late 1990s as part of his Ph.D. thesis at the École Normale Supérieure in Paris.

“So it’s a natural thing to use this as a model of strange metals and see what happens,” Georges says.

However, even simple models of interacting quantum particles can be difficult to work with, challenging computers to store and manipulate the humongous number of particles and variables at play.



In the SYK model, every electron tries to align or anti-align its spin with every other electron with random strength. Credit: Lucy Reading-Ikkanda/ Simons Foundation



A phase diagram based on numerical computations (gray dots) at varying temperatures and electron densities. At high density, the system acts like a conventional metal. At low density, there is a phase transition (red line) to an exotic spin-glass metal. Along the blue dashed line, electron spins have a special ‘SYK spin dynamics’ behavior. At temperatures near absolute zero, the extrapolated locations (triangles) of the spin-glass transition and SYK dynamics join, indicating a common origin. Above the meeting point, the system exhibits ‘strange metal’ properties. Source: P. Dumitrescu, N. Wentzell, A. Georges and O. Parcollet; Credit: Lucy Reading-Ikkanda/ Simons Foundation

But this is where the CCQ excels. The center’s mission is to develop and refine computational techniques for calculating how ensembles of quantum particles interact with one another. Getting a computer to manipulate the SYK model with realistic electron properties — a longtime challenge in this field — fits the CCQ’s mandate.

One well-trodden approach to computing the properties of many interacting particles is to focus on just one ‘embedded’ particle and calculate how it interacts with everything else. This ‘quantum embedding’ strategy often requires additional approximations, but in the case of the SYK model, it provides an exact solution if the system is infinitely large. An alternative approach is to randomly sample how particles interact within a finite system. A project at the CCQ led by Flatiron research fellow Philipp Dumitrescu followed the first path, while a collaboration led by Alexander Wietek and Harvard graduate student Henry Shackleton followed the second one.

The work is paying off. Both teams were able to calculate what happens in the SYK model as the number of electrons changes. At high electron densities, the model behaves as a conventional metal, but when the population of electrons is

sparse, it transitions into a quantum spin glass, an exotic state of matter. Notably, the 2021 Nobel Prize in physics was awarded to Simons Investigator Giorgio Parisi for elucidating such states of matter, in which electrons’ spins never quite settle into their preferred alignment.

Still, right at the transition, near absolute zero, the model acts like a strange metal. This confirms that CCQ researchers now have a way to further explore the physics of strange metals. The phase transitions also mirror those seen in copper-oxide superconductors, which suggests that the SYK model may be a playground for better understanding why these materials put up zero resistance to electric current below a certain relatively high temperature.

What’s more, the SYK model may have something to teach physicists about black holes. “When I proposed the model, this wasn’t on my mind at all,” says Harvard physicist Subir Sachdev, the ‘S’ in SYK and a CCQ consultant.

Black holes and strange metals might seem to have nothing to do with one another, but there are deep similarities. For one, both are ultrafast ‘scramblers’ — that is, if you disturb either of them in any way, they settle back down as fast as nature allows (a fact recently verified for black holes by the LIGO/ Virgo collaboration). It also turns out that the SYK model can be reformulated to describe the energy fluctuations near certain types of black holes.

Put in mathematical terms, the equations that describe both strange metals and black holes share a ‘duality’ — they are two representations of the same information. That duality arises from the fact that in both black holes and strange metals, particles are strongly entangled with one another.

Tackling one question could help with the other. “There’s a whole community of people who are now using numerical solutions of the SYK model to address deep questions on how black holes evaporate, what’s inside of a black hole and how information leaks out of a black hole as it evaporates,” Sachdev says. “These are questions that you couldn’t address before.”

MAPPING THE GENOME OF THE UNIVERSE

One would be forgiven for thinking that the Simons Collaboration on Learning the Universe sounds as absurdly ambitious as a ‘Theory of Everything.’ But, it turns out, nothing is off the table. “We’d like to understand the big questions,” says collaboration director Greg Bryan, an astronomy professor at Columbia University. “Where did we come from? What is the fate of the universe? Why does it look the way it does?” These questions are huge, to say the least, but scientists in the collaboration believe that they will be able to shed new light on these age-old mysteries in the next few years.

In the early days of the expansion of the universe, matter was nearly uniformly distributed. The tiny deviations from true uniformity would evolve under forces such as gravity to create areas that were more and less dense, eventually coalescing into the galaxies, planets and stars we see today. “If we knew exactly what those initial fluctuations were at that very early time, then we could predict the current universe,” Bryan says. Unfortunately, the beginning of the universe was a long time ago, and no one was there to look around.

So Learning the Universe researchers must instead deduce the past by observing the current universe and working backward. “We have good observations of the universe now, and going back in time quite a ways,” says collaboration principal investigator Shirley Ho, an astrophysicist at Princeton University and group leader of Cosmology X Data Science at the Flatiron Institute. “It’s like if we have a good video of a person’s life from high school to 30 years old — but we want to use it to figure out their genome.”

A great deal of the collaboration’s work involves trying out different initial conditions of the matter and energy in the universe, the equivalent of individual genes in a person’s genome, and

determining whether our current observations are consistent with a universe that grew up with those ‘genes.’ One of the biggest challenges is the sheer size of the genome they are working with: There are on the order of a million parameters that must be determined. “No one has tried to do such a high-dimensional inference problem before,” Ho says.

In addition to addressing the distribution of matter in the early universe, the researchers must confront questions about the physical laws governing the early universe in order to understand why it progressed the way it did. The rate of expansion of the universe is one of the core mysteries the collaboration seeks to grasp. Nearly 25 years ago, cosmologists and astrophysicists discovered that not only was the universe expanding, but its expansion was accelerating. Until that time, standard models had predicted that the gravitational attraction between all matter in the universe should be causing expansion to slow overall. Physicists developed the idea of ‘dark energy’ to explain the acceleration, but what exactly dark energy is and how it functions are still unknown.

An undertaking this complex and vast in scope requires input from multiple disciplines. Experts in simulating the evolution of galaxies take initial conditions and create computer models that show how those conditions change over time. But the collaboration needs millions, if not billions, of these simulations, and at the present time, the simulations run much too slowly. That’s where a second group comes in. The machine-learning group is working to speed up the simulations, eventually by many orders of magnitude, so that they can perform more simulations with the same amount of computing power. “If we can run a million simulations in the time it used to take one, it means we can try a million different recipes of the genome,” Ho says. Before the Learning

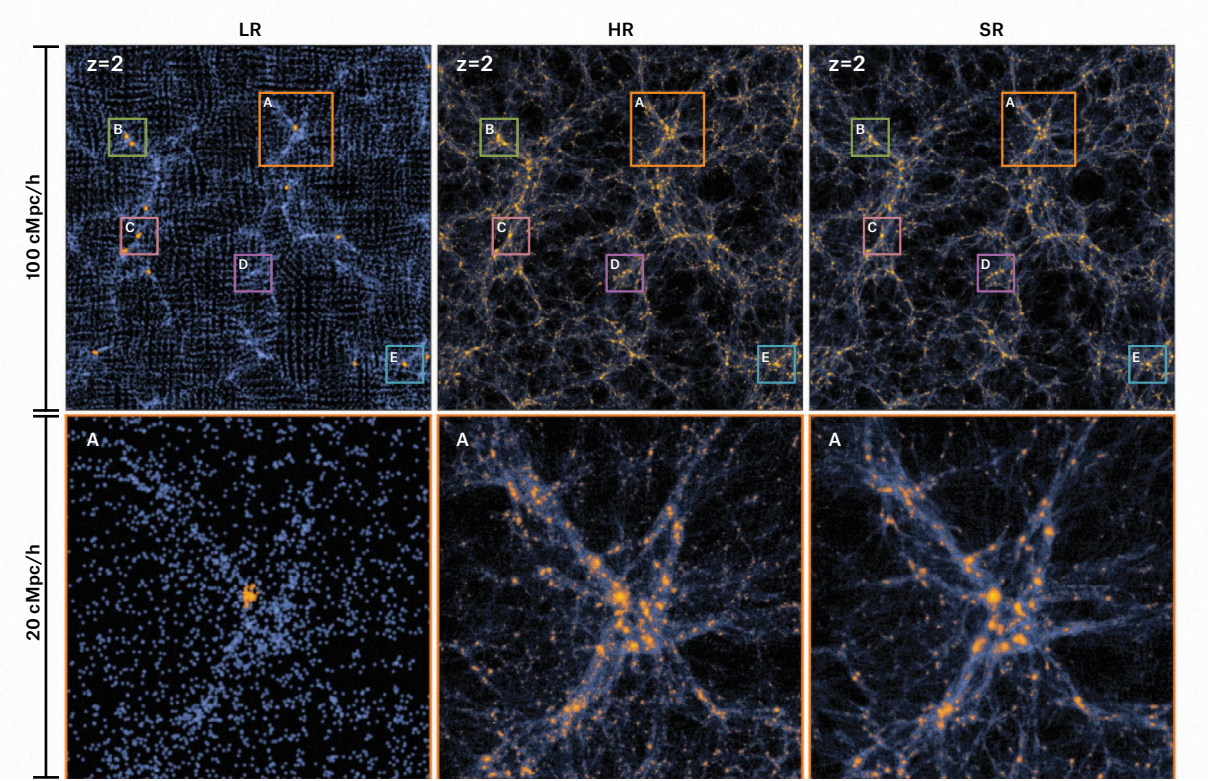
the Universe collaboration began, she and her colleagues used convolutional neural networks, the same kind of machine-learning technique used in image recognition software, to speed up simulations of dark matter particles, generating the ‘skeletons’ of the simulated universe. “That step usually took a day or so; now, it takes milliseconds because of what we developed,” she says.

A third group made up of cosmologists, both theoretical and observational, oversees the comparison of models to real data and helps the collaboration determine which aspects of the observable universe should be compared to aspects of the simulated universes to determine how similar the universes are. The final group in the collaboration consists of statisticians, who develop new techniques to define how probable it is that a simulated model is consistent with our present-day universe. Because of the size of the problem they are working on, traditional techniques that compute a quantity known as the likelihood are intractable; instead, the statisticians are working on developing implicit likelihood inference methods that allow them to get at the relevant probabilities in a different way.

As the collaboration develops, improvements by each group will circle around to the other groups, improving all models in terms of both accuracy and speed. Although there are challenges inherent in working across fields with different jargon and training, each area of expertise is needed to tackle the collaboration’s ambitious goals. “We all have to bring in our point of view and knowledge and try to figure out how to get this working,” Ho says.

Collaboration members are realistic: They know that they will not solve all of cosmology in a few years. If they can show that the new tools they are developing are successful for a few data sources and a few specific problems, they and other groups of researchers will be able to apply the same techniques to information coming in from new telescopes, expanding the problems they work on.

“We want to demonstrate that we can do what we want to do for this subset of cosmological problems,” Bryan says. “Our goal is to show that this is a viable path.”



Three simulations of a region of space 480 million light-years across (top row), with zooms of the box marked “A” shown in the bottom row. The first simulation (left column) was run at low resolution; the second (middle column) was carried out at high resolution; the third (right column) used machine learning to augment the low-resolution simulation as if it had been run at high resolution, but at a fraction of the computational cost. Credit: Y. Li et al./*Proceedings of the National Academy of Sciences* 2021

MANY ELECTRON COLLABORATION'S LEGACY OF COOPERATION

The behavior of electrons determines almost all a material's properties, from magnetism and conductivity to texture and color. Since launching in 2014, the Simons Collaboration on the Many Electron Problem has investigated how the quantum mechanics of interacting electrons within materials — particularly semiconductors, metals and superconductors — creates their macroscopic properties. The researchers' ultimate hope is that one day scientists will be able to design and develop materials with sought-after properties such as high-temperature superconductivity.

After years of fruitful research, dozens of research papers, and the development of new methods and tools, the collaboration is now in its final year. Though the Many Electron collaboration is ending, its contributions will live on, most importantly through the partnerships it has fostered within the field, says collaboration director Andy Millis. Collaboration members have backgrounds in quantum chemistry, physics, materials science and computer science. As with many Simons collaborations, one of the collaboration's strengths is that it spurred partnerships across a broader range of disciplines than traditional grants tend to do.

"It created, to a much greater extent than we previously had, a cadre of computationally inclined physicists with a culture of collaboration and cooperation," says Millis, who is also co-director of the Flatiron Institute's Center for Computational Quantum Physics (CCQ). "It took a lot of great people who were out there in the community and helped link them and their students and post-docs together."

Such teamwork is essential given the daunting nature of the problem at hand. Keeping track of the quantum interactions between the billions or trillions of electrons in the tiniest piece of solid matter is vastly more difficult even than it sounds, because the peculiar 'entanglement' properties of quantum mechanics create highly unusual and nonintuitive correlations. Chemists have traditionally approached the problem by devising techniques that are effective for gaining a precise understanding of the behavior of small collections of atoms or molecules, but these techniques cannot easily scale up to solid systems. "It is absolutely not trivial to go from a molecular problem to a solid problem," says Dominika Zgid, a collaboration principal investigator at the University of Michigan.



Physicist Michel Ferrero of the French National Centre for Scientific Research (CNRS) presents during the kickoff meeting for the Simons Collaboration on the Many Electron Problem in 2014.

"You have to deal not only with the larger scale of the many electron problem, but also with entirely new phenomena."

Some of the collaboration's researchers are therefore devising methods that can bring the quantum chemistry of collections of interacting electrons from the molecular level up to the solid level. They are taking multiple approaches, including cluster embedding (which considers manageably small fragments of material at the full quantum interaction level coupled with a background that's treated more approximately), tensor networks (which represent quantum states in ways that efficiently capture the quantum entanglement) and Monte Carlo simulations (which use random sampling to compute solutions).

Because the collaboration brings together researchers who use different techniques to study the same questions, it is no surprise that some of its most significant achievements have involved comparing the results of multiple methods on the same problems, a process called benchmarking. "The problems we deal with are so hard that every approach has some severe limitations," says Millis. "If you look at something obtained by one method in isolation, you don't quite know what to make of it." By comparing the results of simulations with different sources of uncertainty, benchmarking allows researchers to determine the situations in which various methods are most reliable and what strengths and weaknesses the methods have. Since 2015, collaboration researchers have published a series of benchmarking papers addressing progressively more complex and realistic situations.

The Hubbard model, a simple model of interacting particles in a lattice that often serves as a useful 'toy' model, has played a central role in a number of the collaboration's projects. Since the 1980s, scientists have assumed that the Hubbard model is the simplest one that could describe high-temperature superconductivity. The benchmarking effort started by the collaboration has now yielded a clear understanding of many properties of the model. Still, it is not known for certain that the model could actually support superconductivity at temperatures high enough to be relevant to materials science. Collaboration researchers' investigation showed that the simplest version of the model with certain commonly used parameters does not actually support superconductivity. "Honestly, this particular result was kind of a bummer," says Shiwei Zhang,

a former collaboration principal investigator who is now at the CCQ, "but it's important to know, if you're chasing superconductivity." Yet although this result was disappointing and perplexing, it does not rule out superconductivity in other parameter regimes. Researchers are currently exploring those possibilities and investigating related models with slightly different physics that may enhance superconductivity.

In the past year, another line of research has focused on incorporating relativistic corrections into quantum chemistry models. These are important for compounds that include heavy elements, such as uranium, plutonium and iron. The plentiful protons in these atoms provide a stronger electromagnetic pull, accelerating nearby electrons to high enough velocities for special relativity to play a large role. By including these effects, researchers can use the same computer code whether their materials are molecular lightweights or heavyweights.

As they wind down their projects, the researchers are working to ensure that the programs they have written during the collaboration will find applications outside it. "We are right at the edge where we can start transferring some of our technology to materials science," says Nikolay Prokof'ev, a principal investigator from the University of Massachusetts Amherst.

Looking beyond its scientific successes, the collaboration has also shaped the way the Simons Foundation supports other projects. For example, the collaboration was a catalyst for the creation of the CCQ, and many of the first scientists hired by the CCQ came from the collaboration. "The early success of the Many Electron collaboration helped to identify this area as scientifically and intellectually valuable to the foundation," says Zhang. It was also one of the first large, multidisciplinary projects funded by the Simons Foundation, and it became tangible proof of the potential of these ambitious groups of researchers. "It's now become much more common to take multi-probe approaches to theoretical problems in this field," says Garnet Chan, a collaboration principal investigator from the California Institute of Technology. "That was a fashion that was set within this collaboration, so I think it has had some impact on the practice of science."

A. MURAT EREN: A COMPUTER SCIENTIST PIVOTS TO MARINE MICROBES

Last August, A. Murat Eren, who goes by “Meren,” leaned over the edge of a boat off the coast of Hawai‘i. Then, holding a 20-liter plastic jug, he submerged his arm into the Pacific Ocean and filled the container with water teeming with microscopic life. Recalling the moment in his blog, he wrote, “This was the first time in my life I was physically contributing to the generation of samples that we were going to use to understand things later.” By “things,” Meren was referring to how ocean microbes respond to changes in their environment. And what tickled Meren most was that despite being a trained computer scientist, he was now firmly entrenched in the world of marine microbiology. Meren feels there is no question more fascinating than how marine microbial communities adapt to the planet’s changing environment. “It’s a problem that influences all life on Earth,” he says.

After studying computer engineering in Turkey, Meren moved to the United States and began doctoral research on machine learning and signal processing at the University of New Orleans. Later, in a different lab, Meren saw how powerful computation could be for addressing biological problems. He developed a computational method to quantify microbe diversity. “The biology grew on me,” he says, “and I realized I didn’t want to do anything else.” So after graduating in 2011, Meren headed to Woods Hole, Massachusetts, for a postdoctoral position in Mitch Sogin’s lab at the Marine Biological Laboratory. There, he formed a small team to develop a computational platform for comparing the genomes of a collection of microorganisms, such as the microbes found in a seawater sample. The software, called *anvi’o* (ANalysis and VISualization platform for ‘Omics data), enables robust biological analysis through a graphical interface that Sogin says reflects not only Meren’s prowess in computation and biology but also his creative talent and photography background. “He’s a world-class intellect,” says Sogin.

Last year, Meren was named a Simons Early Career Investigator in Marine Microbial Ecology and Evolution. The award helps launch the careers of investigators in the field, including scientists making the jump to marine microbiology from another discipline. In this role, Meren wants to identify the subtlest microbial responses to environmental change. “We know almost all microbes respond to a change of a few degrees in temperature. But what is the smallest fraction of temperature that will register a change, and what kind of change?” he asks. The impact of this work spreads beyond the ocean surface, as microbial communities in places ranging from deep-sea hydrothermal vents to the human digestive system all adapt to changes in their environment. In fact, Sogin says that because of the difficulties in doing experiments on the human microbiome, researchers look to insights from marine environments that are amenable to experiments. Although he is intensely passionate about marine environments and what they can tell us about the planet, Meren also keeps a foot in human microbiome research. “I learned everything about the human microbiome from Meren,” says Tao Pan, a professor of biochemistry at the University of Chicago who collaborates with Meren. The two met at a party six years ago, when Meren was a new professor in the University of Chicago’s department of medicine. That encounter led to their collaboration, ongoing even as Meren transitions to a new, marine-focused position as a professor at the Helmholtz Institute for Functional Marine Biodiversity in Germany.

On a Zoom call from Germany, Meren describes the project that led him to hang over the edge of that boat scooping up ocean water last summer. To detect the tiniest of microbial changes, Meren, in collaboration with Pan, studies a certain kind of RNA, called transfer RNA, or tRNA. In the cell, tRNAs carry the building blocks of proteins, amino



A. Murat Eren, wearing white dishwashing gloves, hangs over the side of a boat to collect his first seawater sample in Hawai‘i’s Kāne‘ohe Bay in August 2021. Credit: Evan Barba

acids, to the ribosome where proteins get assembled. However, tRNAs have a lot of wiggle room to make changes in the protein recipe when needed, such as during environmental stress. Signatures of these changes can be found in expressed versions of tRNAs called tRNA transcripts. By sequencing tRNA transcripts, Meren hopes to detect signals of microbial adaptation to the environment. “If we are going to see changes in microbial responses to an environmental perturbation, whether it is rapidly changing UV exposure, or temperature, or pH, it is reasonable to expect that these changes will first manifest in alterations in the tRNA pool,” he says.

Over 48 hours in August, Meren, in collaboration with Michael Rappé of the Hawai‘i Institute of Marine Biology, led a team of scientists to collect ocean water samples at sites off the coast of Oahu. In his blog, Meren described setting up a lab in a building next to the dock. He wrote, “In just a few hours, we had a fully operational lab with every essential equipment for the completion of this project,” including 48 Ferrero Rocher chocolates. (Snacks are vital, he says.)

In another collaboration, Meren is working with Mary Ann Moran, a Simons Collaboration on Principles of Microbial Ecosystems investigator and a professor of marine sciences at the University of Georgia. Together, they’re looking at how ocean

microbes influence the carbon cycle. Meren hopes the tRNA sequencing results from Hawai‘i with Pan and Rappé will yield new insights here, as well. “We’re at the point now where we have lots of data, and the bottleneck now is how to make sense of it in a meaningful way. That’s where Meren’s strengths lie,” says Moran.

Meren’s collaborators remark on how he supports the broader scientific community. “Meren has a deep and unwavering social and educational commitment,” says Bana Jabri, a professor of medicine at the University of Chicago who collaborates with Meren on human microbiome studies. For example, *anvi’o* is an open-access platform. And at the start of the pandemic, Meren saw shuttered labs halt the research of many graduate students and postdocs. So he offered online courses on data-enabled microbiology. The first course attracted 2,000 signups within 24 hours. Meren had to pivot to YouTube because his Zoom account only allowed 500 participants.

Meren’s path from computer science to marine biology satisfies his intellectual curiosity and desire to help the planet but, he says, comes with funding challenges. “True cutting-edge research is high risk and difficult to fund, but also high reward. Without the Simons Foundation, this kind of time-critical work wouldn’t be possible.”

NEUROSCIENCE FELLOWS FLOURISH

The right support at just the right time can help people navigate from one phase of life to another — say, from being a student to running a lab. That’s precisely the aim of the postdoctoral fellowship grants awarded by the Simons Collaboration on the Global Brain (SCGB). The SCGB currently supports 96 collaborating principal investigators who seek to illuminate the neural processes between perception and action using new experimental and modeling tools.

But also to that end, in 2014, 2015 and 2016, the SCGB funded several three-year postdoctoral fellowships, supporting a total of 21 promising neuroscientists as they found their way from graduate school to faculty positions. The fellows have flourished, and most now run their own labs.

Matthew Kaufman is a former SCGB fellow, now with his own lab. After earning a doctorate at Stanford University, he spent five postdoctoral years at Cold Spring Harbor Laboratory on Long Island before becoming a professor at the University of Chicago in 2018. At Cold Spring Harbor, he worked with neuroscientist Anne Churchland, studying the way mice integrate sensory information and make movement decisions.

Kaufman wanted to better identify the locations of active neurons, which required use of a two-photon microscope. Two-photon microscopy allows researchers to image living tissue and label different cell types. Kaufman combined this with a method called calcium imaging, in which neurons glow when active. “If you look at a bunch of these genetically modified neurons, they literally blink every time they fire,” Kaufman says. The tools allow him to combine computational brain models with biological data, like cell type identity. “These are really the right experiments to answer the question I’m most interested in,” he says.

The SCGB not only provides funding to its fellows but also includes them in meetings of the full collaboration, fostering new working relationships. Kaufman appreciates the connections he made during his fellowship, several of them through annual SCGB meetings. He’s even filed for a patent with two other SCGB grantees on an application of Artificial Intelligence to medical imaging.

Another former postdoctoral fellow now running his own lab is Scott Linderman, a statistician at Stanford. Linderman earned a doctorate in computer science at Harvard and then completed a fellowship at Columbia, helping experimental neuroscientists analyze their data. Before starting graduate school, he was a software engineer at Microsoft. “Developing robust, accessible software tools is something that I get a lot of joy out of,” Linderman says. While at Microsoft, he also started reading books about the brain — the beginning of his migration toward neuroscience.

At Columbia, he worked with Liam Paninski, a leading neuroscientist, and David Blei, an expert in machine learning. “The fellowship made it very easy for me to sit between these two worlds,” he says. “I could make contributions to core machine learning at the same time as I was developing a toolkit that would be unique and valuable in neuroscience. I think in many ways, my postdoc goals were perfectly aligned with the SCGB mission.”

Now, at Stanford, “our bread and butter is modeling large-scale neural recordings,” he says. “They might be electrophysiological or optical recordings, for instance, from calcium imaging.” Increasingly, Linderman is combining brain data with videos of animals’ actions. “If we can better model behavior,” he says, “we can then tie it to neural signals in new and interesting ways.”

In addition to designated SCGB fellows are the postdoctoral fellows who work in the SCGB labs. One of those fellows was Sue Ann Koay, who now leads her own research group at the Howard Hughes Medical Institute’s Janelia Research Campus in Virginia. Her transition was stark: Trained in high-energy physics, she’d worked on the search for dark matter at the Large Hadron Collider before deciding she wanted to work on experiments on a smaller scale. “Biology seemed to be so very different, much messier,” she says.

As a Dicke fellow in Princeton University’s physics department, she walked into the office of David Tank, a neuroscientist and director of the SCGB, and said she wanted to learn about the brain — having no background knowledge and no lab skills, but with data analysis chops. He took her on. Together they placed mice on spherical treadmills in front of virtual-reality screens and had them navigate virtual mazes. Meanwhile, they recorded brain activity. Today, she aims to extend these methods to free-form exploration in virtual reality. “The ability to explore space is fundamental to all animals,” she says. “And it generalizes to comprehension of abstract spaces” — such as paths to solving a Rubik’s Cube. Looking back, she says, “David has a long history of helping people transition. And I’m incredibly grateful.”

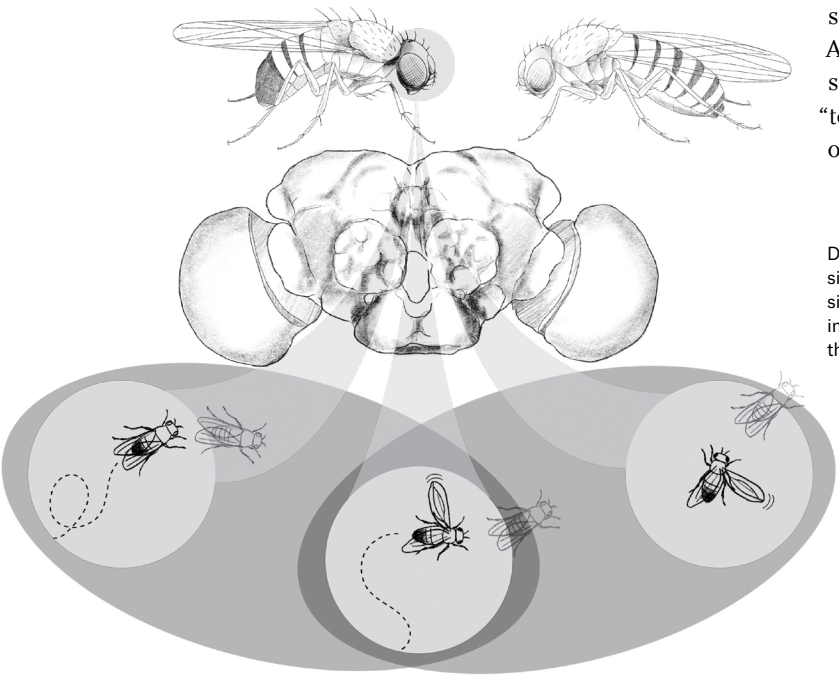
The SCGB has also recently instituted two new grant programs to support up-and-coming scientists from underrepresented backgrounds working in neuroscience. The SCGB Undergraduate Research Fellowship (SURF) Program funds college research assistants to work in SCGB-funded labs, and the Transition to Independence (TTI) fellows program supports postdoctoral fellows transitioning to faculty roles.

Osama Ahmed, a neuroscientist at Princeton, was in the first class of independence fellows and will launch his own lab at the University of Washington this fall. He studies multitasking. “Why is it that we can easily perform some things at the same time — like I’m talking and gesturing right now,” he says, “but texting and driving is much harder? I think it’s a deep observation that might tell us something about the constraints of the nervous system.”

Ahmed studies fruit flies, placing them on spherical treadmills as he records from their brains with calcium imaging and monitors their behavior with high-resolution cameras. He can also tweak their neural signals using optogenetics. “It’s a fantastic system to work in,” he says. “All of that in combination to address this very old question.” The funding will allow him to buy a microscope for brainwide imaging, and potentially to recruit others to study new multitasking paradigms in the fruit fly. “The grant will help me focus on some high-risk, high-reward projects,” he says.

Ahmed recalls working at a thrift store in high school before earning a place in the Monell Science Apprenticeship Program and later joining a neuroscience lab. “It’s actually kind of bonkers,” he says, “to think that I’m here today about to launch my own lab.”

During courtship, male flies run after their potential mates and sing by vibrating their wings. These two behaviors, running and singing, sometimes co-occur, making this a promising system in which to study how neural circuits drive multiple behaviors at the same time. Credit: Julie Johnson



FIVE YEARS OF SPARK

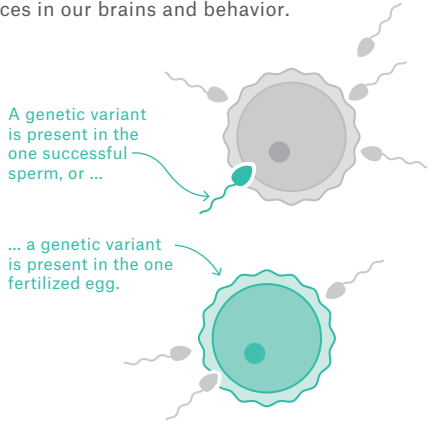
Hundreds of genes are thought to underlie autism, and identifying them could pave the way for a host of novel treatments. Yet each individual autism gene is mutated in only a tiny minority of people with autism, so small genetic studies miss most of these genes. To address this issue, in 2016 the Simons Foundation Autism Research Initiative created SPARK (Simons Foundation Powering Autism Research for Knowledge), with the goal of collecting behavioral profiles and DNA samples from 50,000 families affected by autism.

Five years later, the project has surpassed its original ambitions by a huge margin. More than 100,000 individuals with autism and their families have joined SPARK, making it the largest study of autism ever.

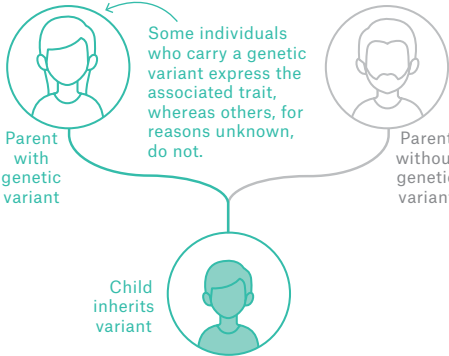
Genetic Discoveries in SPARK

SPARK has analyzed the exomes — the functional part of the genome — of more than 35,000 people with autism. These data have helped researchers identify new types of genetic changes associated with autism and better understand the biology behind individual differences in our brains and behavior.

SPARK research has helped identify **de novo variants** — rare genetic changes that arise in a person with autism but aren't present in either of their parents.



Additionally, SPARK data have identified **five inherited genes** not previously implicated in autism. The newly identified genes are inherited from parents who may or may not have autism.



Number of SPARK participants, cumulative by month

- Male adults with autism (18 years or older at registration)
- Male children with autism (under 18 years old at registration)
- Female adults with autism
- Female children with autism
- Biological parents of an individual with autism
- Biological siblings of an individual with autism

SPARK, a Timeline

December 22, 2015–December 2016

During the first phase, researchers collect and analyze data from the first 457 families to participate in the project. Families in the pilot group have changes in 26 different genes linked to autism. Most of these genes have already been strongly linked to autism. However, the SPARK analysis provides new support for several others.

April 21, 2016

National launch of SPARK and launch of the SPARK clinical site network, a network of the nation's leading medical schools and autism research centers that have joined SPARK to help recruit families affected by autism.

May 11, 2017

First release of genetic data to the broader research community.

July 12, 2017
First Research Match study launches.

September 20, 2017

The first meeting of the SPARK Community Advisory Council. Since SPARK's inception, the autism community has helped guide the project's work. The council comprises 62 members, including autistic adults, parents of children with autism and autism professionals.

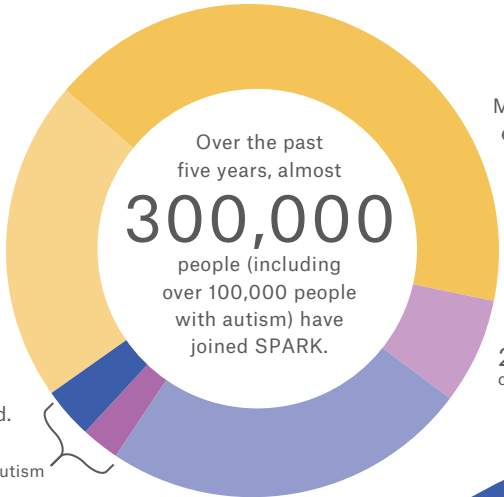
April 10, 2018

First individualized report delivered to SPARK families.

April 30, 2018
100,000th participant joins SPARK.

Our Participants

Most autism studies focus on children, but SPARK includes individuals from ages 2 to 92, allowing SPARK researchers to learn about and support people with autism as they pass through the different stages of childhood and adulthood.



Many autism studies have had trouble enrolling enough girls, as boys on the spectrum outnumber girls by about 4 to 1. SPARK researchers found that girls had different behavioral features from boys and that more specific diagnostic measures are needed with girls.

20,217 female children with autism

August 23, 2019
First SPARK genetic study published.

29
articles have been published from Research Match studies.

40,000
families have responded to at least one Research Match study invitation.

135
Research Match studies have been launched, and about 60 more have been approved.

75,000
participants (including 38,000 people with autism) have had their DNA sequenced.

70,000
participants have received personalized reports reflecting their individual behavior and development.

900
participants were notified of their autism-related genetic results within the past 12 months.

Research Match
SPARK's contributions go far beyond genetic studies. Through its Research Match program, the initiative has helped researchers connect with cohorts of families for more than 100 studies covering various topics, such as 'camouflaging' in teenagers, food selectivity, sleep and gender identity. SPARK has also given hundreds of participants a specific genetic explanation for their autism.

September 28, 2019
200,000th participant joins SPARK.

March 2020: Early in the COVID-19 pandemic
SPARK surveys participants to learn about:
• How the coronavirus 2019 (COVID-19) pandemic affected access to services and therapies.
• The availability and effectiveness of online and telehealth services.
• The overall emotional well-being of all participants.
• Attitudes toward COVID-19 vaccines.

Looking to the future
SPARK is committed to autism research for decades to come. By following people through their life span, SPARK will learn how autism changes with age. As the community grows, so does our understanding of autism.

Number of SPARK participants, cumulative by month

289,058

275,000

250,000

225,000

200,000

175,000

150,000

125,000

100,000

75,000

50,000

25,000

0

January 2016

January 2017

January 2018

January 2019

January 2020

January 2021

End 2021

UNDERSTANDING THE COGNITIVE AND BEHAVIORAL FOUNDATIONS OF AUTISM

“Autism spectrum disorder is ultimately defined as a condition of cognition and behavior,” says Alice Luo Clayton, a senior scientist at the Simons Foundation Autism Research Initiative (SFARI). Although SFARI is known historically for supporting and fast-tracking genetic and molecular work in ASD through grants and by developing resources for scientists, there have been recent booms in technology and in cognitive neuroscience, and SFARI is aiming to take advantage of them. In 2021 the program decided to expand its footprint by awarding \$7.9 million over three years to 11 research groups pursuant to its new Human Cognitive and Behavioral Science (HCBS) request for applications.

“We need to have multiple levels of analysis, from genes to molecules, to cells, to circuits, to cognition, to behavior — and integration across these levels — to really understand how all the different biological mechanisms are interacting with each other,” Luo Clayton emphasizes. “And in particular,” she adds, “we don’t have a really good quantitative, high-resolution understanding of the behavioral phenotypes in autistic individuals.”

Paul Wang, a deputy director for clinical research at the foundation and one of the program’s organizers, appreciates the funded projects’ diversity. “Some of the projects are designed to understand cognition and behavior in autism, and others go toward developing techniques to assess cognition, potentially on a really large scale,” he says. LeeAnne Green Snyder, a clinical research scientist at SFARI and another core organizer, notes that grants to study cognition and behavior in autistic people aren’t completely new to SFARI. “This program makes recognition of the value of these studies more official,” she says. “It’s creating a home for them.”

HCBS grantees will benefit from SFARI’s Simons Foundation Powering Autism Research for Knowledge (SPARK) database, with exome data

for 75,000 people with autism, and may use Research Match, SPARK’s program for matching participants to research studies. “Researchers are really excited and grateful for help in recruiting participants,” says Pamela Feliciano, SPARK’s scientific director. “To be able to just turn to us and get several hundred people to participate in their research is something that they would have spent months doing on their own.”

This year an HCBS grant went to a team led by Benjamin Scott, a neuroscientist at Boston University who studies perceptual decision-making: a way we accumulate evidence to build mental models of the external world. The primary goal of Scott’s project is to develop and use video games to evaluate different cognitive models of perception and decision-making across a range of individuals with autism. “One key aspect is to collect and analyze behavioral data from minimally verbal participants, a group that’s underrepresented in these types of behavioral studies,” Scott says.

Before his award, Scott gave rats tasks in which they responded to various scenarios involving noisy information, such as randomly flashing lights. A rat might earn a reward for, say, indicating which light flashed more. Scott’s colleagues suggested these tasks could also yield information on nonverbal humans’ cognition. When the pandemic hit, they started to prototype an online game, which they are now developing with their award. It is hypothesized that people with ASD will show unique types of errors, due to how they update their beliefs based on new information.

“Genetics is an important first step,” Scott says, “but what got me really excited about this request for proposals is that we can start to compare neurotypical and autistic individuals in a way that we can easily bridge with animal studies. We can ask how well these animal models reproduce the diversity in behavior we see across humans.”



A neurotypical infant engages with an at-home looking-time assessment. The assessment gauges how long participants gaze at different stimuli, which could provide insights into the factors that govern child development.

Researchers might then test various therapies on rats to develop a more accurate expectation of how the therapies might affect people.

A theme across HCBS projects, in some cases instigated by the pandemic but perennially useful, is to develop assessments that work remotely, in people’s homes. Elena Tenenbaum, a psychologist at Duke University, works with infants, often using looking-time paradigms: You deduce what interests or surprises young minds by how long babies look at things. She and collaborators will create at-home versions of looking-time tasks, using software to automate the detection of gaze direction in captured video.

The pilot study will validate the remote test’s ability to accurately capture foundational cognitive skills in infants known to be at high risk of autism at 6 and 12 months old. The study will also test whether the new automated eye-tracking software can capture gaze direction as accurately as human coders can. The final aim is to see if test performance predicts cognitive development, language outcomes and autistic behavior in toddlerhood, with a focus on differences in those who go on to develop signs of autism. Eventually, an even larger study might use the tasks to connect behavior to genetics, or to guide interventions. Tenenbaum calls SPARK Research Match a “phenomenal fit” for the project.

Also breaking new ground, HCBS grantee Dara Manoach, a neuropsychologist at Harvard University, studies sleep physiology. She says

that what brains do while asleep can be at least as revealing as what they do while awake.

“There’s been an explosion of research showing that sleep is not simply a passive, restorative state,” Manoach says. “It’s actually an active period of cognitive functioning that is important for memory consolidation.” But most studies of sleep and autism have had very small sample sizes, and they’ve been markedly inconsistent in both methods and results. To reconcile these inconsistencies, large study samples are needed: Her project will be a proof of concept for this.

Laboratory-based sleep studies are expensive and burdensome to both participants and researchers. Scaling up sleep research will require better solutions. In the first stage of Manoach’s project, neurotypical adolescents will nap in the lab while simultaneously wearing both traditional sleep-lab EEG equipment (the gold standard) and a comfortable headband with embedded EEG electrodes. Children with ASD will then test the best two devices at home for comfort and convenience. Finally, a larger group of children with and without ASD will use the better of the two to characterize their sleep physiology and how it relates to cognition and behavior. “The use of wearables to measure and manipulate sleep physiology at scale at home is a novel and very promising approach,” Manoach says. “I’m excited and hopeful.”

MATH FOR AMERICA: BUILDING COMMUNITY TO WEATHER TRANSITIONS

In March 2020, the COVID-19 pandemic caused the nation’s schools to abruptly shift to remote learning, creating new challenges for teacher communication and student learning.

“When students were fully remote, you really didn’t know who was having a hard time,” says seventh grade math teacher Morgan O’Brien. “We would say, ‘Take out your notebook and a pencil,’ but we couldn’t physically see if they did. We couldn’t manage the remote learning classroom the same way as the physical classroom. Now they’re back in school, and it’s a culture shock.”

Since returning to in-person teaching this year, O’Brien has found students struggling to take out materials when asked, to put away phones, to raise their hands in class — to “just be students.”

“I’ve never given a times table chart to a seventh grader, ever,” says O’Brien, now in her 11th year of teaching. “This year, I had to give out 10. They lack practice and exposure; they just don’t remember old material. It’s really hard to work with percentages and decimals if you don’t have 3 times 4 memorized.” Fortunately, O’Brien is working to address these issues in her classroom as a Math for America Master Teacher.

It’s no secret that teachers struggled in 2021 with the transition back to in-person teaching, even as the pandemic continued. Helping teachers with this latest transition has become a focus of the New York City nonprofit Math for America (MfA). Math for America has awarded four-year fellowships to outstanding teachers like O’Brien since 2004. The organization currently supports more than 1,000 teachers working in over 400 public schools across the city. Their highly competitive fellowships provide yearly stipends, grants and opportunities for professional development to cohorts of Master

Teachers to improve retention, teaching and professional development in schools, all of which ultimately leads to increased student learning.

“An important part of what we do right now is give people the opportunity to share their experiences,” says MfA president John Ewing. “Teachers who are creative and innovative about both online and in-person learning are able to share that with other teachers, including other MfA teachers and also with their colleagues and school.”

Pre-pandemic, there would be around 100 Master Teachers at the MfA Manhattan offices on any given weeknight, participating in and leading workshops or seminars. This year, two-thirds of programming is still virtual, but the Master Teachers are happy to be back in person, when possible, for informal conversations and connection before and after courses.

“We believe that if you cultivate the right kinds of communities for teachers, then good things are going to happen,” says MfA chief operating officer Michael Driskill.

The workshops themselves count as some of those “good things” — about 80 percent of the courses in the MfA professional development catalog are designed and run by teachers. The rest are talks or workshops facilitated by outside experts in education, research, math and science.

During their fellowships, MfA teachers participate in various courses, both at MfA and offsite. In these courses, they explore cutting-edge mathematical and scientific content, innovative teaching practices, and research-based professional development models such as professional learning teams (PLTs), in which Master Teachers explore a specific problem of practice in depth.

“The best parts of PLTs are all the discussions that come up that we hadn’t necessarily planned,” says Master Teacher Brandie Hayes, echoing the MfA ethos of community. “When someone asks, ‘Hey, how did you accomplish that?’ And then someone shares a little bit more.”

For instance, within one session focused on student agency and personalized learning, Hayes shared how she offered ‘hearties’ — personalized encouragement for students. Hayes’ collaborator, fourth grade teacher and MfA Master Teacher Sjene Kendrick, called them “a crowd pleaser” as she and other participants asked questions and then adapted the tool to use in their classrooms.

MfA offers its Master Teachers a rare professional community and the opportunity to work with teachers in other grades and at different schools. For instance, Kendrick invited some MfA middle and high school teachers to her class, and then visited their classes to see how older children learned the next progression in activities. “It’s cool to take PLTs with high school and middle school teachers, because that’s where my kids are going to be in a couple years,” Kendrick says. “There’s very limited opportunities for us to do that outside of MfA.”

In 2021, a year dominated by bad news, Kendrick and Hayes created a PLT called “Holding Onto the Silver Linings” that helped teachers focus on the positive aspects of the abrupt shift to remote learning in 2020. The team met monthly to share positivity, form professional goals and hold each other accountable, with the overarching intention of applying those silver linings in future years.

“Last year there was a push for social-emotional community time, time to get to know your kids and talk to them and let them talk to each other. That’s something that I’ve kept in 2021,” Hayes says. “That’s been an important part of the transition for me: making the time for not just academics, but also what’s happening with everybody.”

Similarly, O’Brien and Master Teacher Corey Levin led a PLT this year on “Middle School Mathematics: Strategies for Returning to the Classroom” as a follow-up to the PLT they organized last year on remote teaching and online tools like Jamboard and Google Classroom. This year the group discussed incorporating tools and best practices to support student growth in person. For example, O’Brien is

using Google Classroom and having her students make up their own math problems — for the first time in her career.

“There isn’t always a grand solution to the difficulties COVID has presented, but working together on all this is revitalizing,” Levin says. “As a result of many of the courses that we’ve led, I’ve been able to plan my lessons out in advance — something that wasn’t possible in the early stages of the pandemic.”

Informal conversations in PLT groups and with other Master Teachers push teacher learning and collaboration to new heights. Teachers bring back the new ideas they learn at MfA to their schools, where they improve their teaching and their colleagues’ teaching by sharing what they learn.

“Having an organization like MfA to support teachers in a situation like this is more important than ever,” Ewing says. “It shows why we need to build the teaching profession this way, to create a community to give teachers the ability to be trusted and enable them to do what they need to make things work in classes and school communities for their students.”



Math for America Master Teachers try out learning exercises about investigating global coral bleaching using real data during a fall 2021 workshop.

SHAPE-SHIFTING ENCOUNTERS WITH SCIENCE

In Flagstaff, Arizona, beneath the cracking American flags of a Fourth of July parade, a dusty white pickup totes a one-quarter-scale lunar rover behind it, escorted on foot by its creators, a proud high school robotics team. This celebration of science — believe it or not — has much in common with a rainbow-themed Pride Day float in Florida with dancers handing out diffraction glasses.

At both parades, held in 2019, grantees of the Science Festival Alliance successfully brought science to their communities by tailoring their approaches to different cultural contexts.

“What works in the Fourth of July parade at noon in Flagstaff isn’t the same thing that’s going to work in the nighttime Pride Parade on the Gulf Coast of Florida,” says Ben Wiehe, manager of the Science Festival Alliance, a collaborative network managed by the MIT Museum.

Science Sandbox, the grantmaking arm of the Outreach, Education and Engagement division at the Simons Foundation, supported grantees like the Science Festival Alliance, and through transitions from lockdowns to in-person events and sometimes back again. Since its launch in 2016, Science Sandbox has funded programs that target “people who might not identify as science enthusiasts, people who wouldn’t go to science museums,” says John Tracey, Science Sandbox program director.

“We feel that science has an intrinsic value and everyone should be able to access that and benefit from that in their own way,” says Ivvet Modinou, director of Outreach, Education and Engagement at the Simons Foundation. “We need to meet people where they are, as opposed to what traditionally happens where we expect them to come to us.”

The nonprofit organization Ciencia Puerto Rico, a Science Sandbox grantee since September 2020, uses community engagement to bring science to people. In response to the COVID-19 pandemic, after first creating its Aquí Nos Cuidamos (“Here we take care of each other”) toolkit of infographics, videos and other multimedia resources, the team hosted workshops for community stakeholders, including grassroots leaders, epidemiologists, educators and physicians.

Ciencia Puerto Rico then chose 10 community leaders to bolster the effort. Some of these leaders printed out Aquí Nos Cuidamos materials about mask wearing and social distancing and distributed them door to door. Another community leader assembled a group to clean up a playground and paint a mural.

“At first glance, you may think, ‘Painting a mural, what does that have to do with COVID?’” says Mónica Feliú-Mójer, director of communications for Ciencia Puerto Rico. “It turns out that it has everything to do with the pandemic — what that community needed was a low-risk space to come together and start healing from the effects of the pandemic.”

The relationships and community trust that Ciencia Puerto Rico built over the past year will serve as the bedrock for future community science projects. Feliú-Mójer envisions enabling community leaders to use science to address their needs and priorities, whether by cleaning up drinking water or by creating local science exhibits.

“It started as this science-engagement project and it became a community-engagement project,” Feliú-Mójer says. “It’s about building community with and around science. We’re making sure that the science is practical and useful in everyday life, but also that it resonates with the different realities of people.”

The idea of adapting to community needs was echoed by the Science Festival Alliance, which encouraged its 75 members to refrain from rashly transitioning cancelled in-person events to Zoom during COVID-19. “It was a really important time to listen,” says Wiehe. “If you are pushing out cheery, happy messaging and content online, you’re saying, ‘We’re doing great and we assume you are too!’ And if a quarter of your community is not doing great, then that messaging is almost oppressive.”

After a pause to take the pulse of their members’ communities early in the year, the Science Festival Alliance resumed support of its network of science festivals. Different areas of the U.S. have experienced the pandemic differently — so, while an El Paso festival created science murals, one in Jackson, Mississippi, followed school lunch buses to drop off science kits at children’s homes. And Huntsville, Alabama, held a large in-person science festival in the fall.

The ongoing Science Festival Alliance project Science in Vivo invites members to try atypical methods for science outreach, like the 2019 St. Petersburg and Flagstaff parades. “Most science outreach and education is about creating environments that we control,” Wiehe explains. “By asking practitioners to integrate science experiences into existing cultural gatherings, we’re asking them to create science experiences in settings that they don’t control.”

One team called Wiehe, discouraged by their lack of progress in creating big events or outreach experiences. To their surprise, Wiehe loved how the team embedded themselves in an existing culture. “Somebody in their backyard had a grill and they were inviting the kids from the block, and they wanted this group there,” Wiehe says. “It’s not some big event with huge crowds, but the trust of the neighborhood can be so much more important.”

In addition to scientists and science educators, artists can also effectively engage with science outreach. The incubator NEW INC, founded in 2014 within the New Museum in New York City, supports artists working at the intersection of art, technology and science. Last year, seven out of 39 teams and individuals were part of the Creative Science Track, funded by Science Sandbox.

“So many of our urgent, entire-system catastrophes relate to science and technology; we need to find ways to make sure that these great challenges of our time are made clear to people, and that they’re translated,” says Salome Asega, director of NEW INC. “Artists are primed to do exactly that kind of work.”

Creative Science Track grantees receive mentorship, professional development training and a workspace. They meet a few times a year to share their work with others. For instance, one group engages the public through silent ‘raves’ that include rituals involving nature and climate change.

“The thing the NEW INC program does so well is really pushing the boundaries of what’s possible,” Tracey says. “NEW INC provides a nurturing and catalytic structure around when scientists meet avant-garde artists.”

As Asega says, reflecting the goals of Science Sandbox, “A white paper can only get you so far, but an artist can make you feel.”

Ciencia Puerto Rico’s Aquí Nos Cuidamos project is an educational toolkit and community-engagement program promoting COVID-19 prevention, vaccination and mental health. Credit: Ciencia Puerto Rico



STRENGTHENING SCIENCE THROUGH DIVERSITY



Princeton neuroscientist Osama Ahmed is a Simons Collaboration on the Global Brain Bridge to Independence fellow.

The mission of the Simons Foundation is to advance the frontiers of basic science. Doing so necessitates drawing on all potential sources of talent. We therefore aim to significantly increase the number of students from underrepresented backgrounds who earn doctorates in basic science, and to enhance the diversity and culture of our own workplace.

In 2021, under the leadership of Co-Chairs Marilyn and Jim Simons and President David Spergel, a Diversity, Equity and Inclusion (DEI) framework and action plan was presented to our board of trustees. This framework focuses on increasing DEI in our workforce, in our workplace, in our grantmaking and in our outreach programs.

This work was informed by significant efforts, beginning in 2020, that led to the creation of a dedicated DEI office. The office is led by

Craig Wesley who, with DEI associate Dominique Harrison, coordinates diversity efforts across the organization. Our framework was also informed by extensive staff engagement including consultation with a steering committee and working groups, and by conversations with other science-focused organizations.

Throughout 2021, we began developing new foundation grant programs to improve diversity in science. The Simons Collaboration on the Global Brain launched two diversity initiatives, the Transition to Independence fellowships and the Undergraduate Research Fellowship (SURF) Program. The goal of SURF is to spark and sustain interest in systems and computational neuroscience among undergraduate students from diverse backgrounds underrepresented in neuroscience research. The program’s inaugural class included 29 fellows.

SFARI’s SPARK initiative launched its SPARK Research Match Diversity, Equity and Inclusivity request for applications to address historic disparities in research participation by Black or African American individuals. A DEI manager, Jibrielle Polite, was hired to help lead this work.

The Flatiron Institute hosted its first visiting Inclusion, Diversity, Equity & Advocacy (IDEA) scholar, Stephon Alexander, a theoretical physicist from Brown University, in 2020, and in 2021, Karín Menéndez-Delmestre, an astronomy professor at the Valongo Observatory of the Federal University of Rio de Janeiro in Brazil, came onboard. IDEA scholars are distinguished scientists who have strong scientific overlap with one or more Flatiron computational centers and a particular interest in increasing diversity and improving equity and inclusion within science. Menéndez-Delmestre leads a group of students and postdoctoral fellows in extragalactic astronomical research, and Alexander was instrumental in setting up the Simons-NSBP program (see the following story).

In the coming years, the foundation intends to expand grant programs and mentorship at all stages of the STEM pathway and increase our engagement with organizations that serve diverse communities. As an organization based in New York City, we have a tremendous opportunity to help create

an inclusive STEM ecosystem locally that will significantly increase the number of Black and Latine students who earn doctorates in fields where the Simons Foundation is active. The foundation is now invested in citywide programs that support an accessible STEM pathway from K-12 education through postdoctoral and early-career science, tracking diverse students’ success and assisting them in moving to the next stage. It is our hope that this model will work and, eventually, scale up to have even greater impact.

In regard to our own staff and workplace, we are striving to establish a culture of inclusion and belonging at the foundation. We have created employee resource groups for Black, Asian American and Pacific Islander, and Latine employees, and also for women, LGBTQ+ people and caregivers in our workforce. We will develop our leaders’ and managers’ DEI knowledge and capacities through professional development, training on inclusive hiring practices and support for open communication.

Diversifying science and our organization will require a long-term commitment, but one that will enhance our ability to advance our mission. We intend to hold ourselves accountable for achieving this, and will report progress on an annual basis to our board of trustees.

Shadé Eleazer, a Simons Collaboration on the Global Brain undergraduate research fellow, presents her findings on the mating behavior of small fruit flies.



SIMONS-NSBP PROGRAM GIVES BLACK PHYSICS UNDERGRADUATES RESEARCH EXPERIENCE

At the end of May 2020, in the wake of George Floyd’s killing, Stephon Alexander, Brian Keating and David Spergel — the leaders, at that time, of the National Society of Black Physicists (NSBP), the Simons Observatory and the Center for Computational Astrophysics at the Simons Foundation’s Flatiron Institute, respectively — began discussing how to take concrete action to counter racial injustices pervasive in our country. At that time, COVID-19 had just upended many college students’ summer plans. “There were going to be a lot of students sitting unemployed this summer, with a lot of potential,” Alexander recalls.

Out of this discussion was born the Simons-NSBP Scholars Program, a summer research experience for Black physics undergraduates, who are vastly underrepresented within the physics community.

“Black physics students face constant messaging from society, classmates, teachers, institutions — that they’re not cut out to be scientists,” says Alexander, a physicist at Brown University and a visiting researcher at the Flatiron Institute. “It’s a headwind that you’re always going against.”

Most summer research programs take many months to plan, but the pandemic created a sense of urgency to start the program that same summer. “The idea was somewhat crazy,” says Kasey Wagoner, a physicist at Princeton University and the Simons Observatory who directs the program. “But we pulled together a huge number of scientists who created time out of nowhere to mentor students.”

That July, the program virtually welcomed 21 undergraduates, who worked with mentors from



Simons-NSBP fellow Aaron Kebede of Lehigh University (center) and his mentor, Flatiron Institute research fellow Sultan Hassan (left), chat with Simons Foundation president David Spergel (right).



Scholars and mentors from the Simons-NSBP Scholars Program pose for a photograph during a June 2021 reception on the Flatiron Institute roof.

the Simons Observatory and the Flatiron Institute. The following year, the program brought 16 students to New York for an in-person program.

Simons-NSBP participants get the opportunity to do physics research on topics ranging from binary black hole simulations to software engineering for computational chemistry. Beyond offering research experience, the program aims to help students form what an American Institute of Physics report has called a “physics identity”— the feeling, Wagoner says, “that you have something to contribute and you’re linked in.” To that end, the program offered nearly daily workshops consisting of science lectures, informal scientific chats, social programming and career advice on subjects from applying to graduate school to impostor syndrome.

LaToya Anderson, who is pursuing a second bachelor’s degree in physics part time at Brooklyn College while working multiple jobs, had never met another Black physics major before joining the Simons-NSBP program in 2021. “I didn’t

realize how much I needed community until I saw how much it buoyed me to continue on my career trajectory,” she says.

Lawrence Edmond IV, another 2021 participant who has just finished a physics undergraduate degree at the University of California, Berkeley, found interacting with his cohort “a shock,” he says. “I had never experienced being able to have serious conversations about things like quantum gravity and dark energy with people who look like me.”

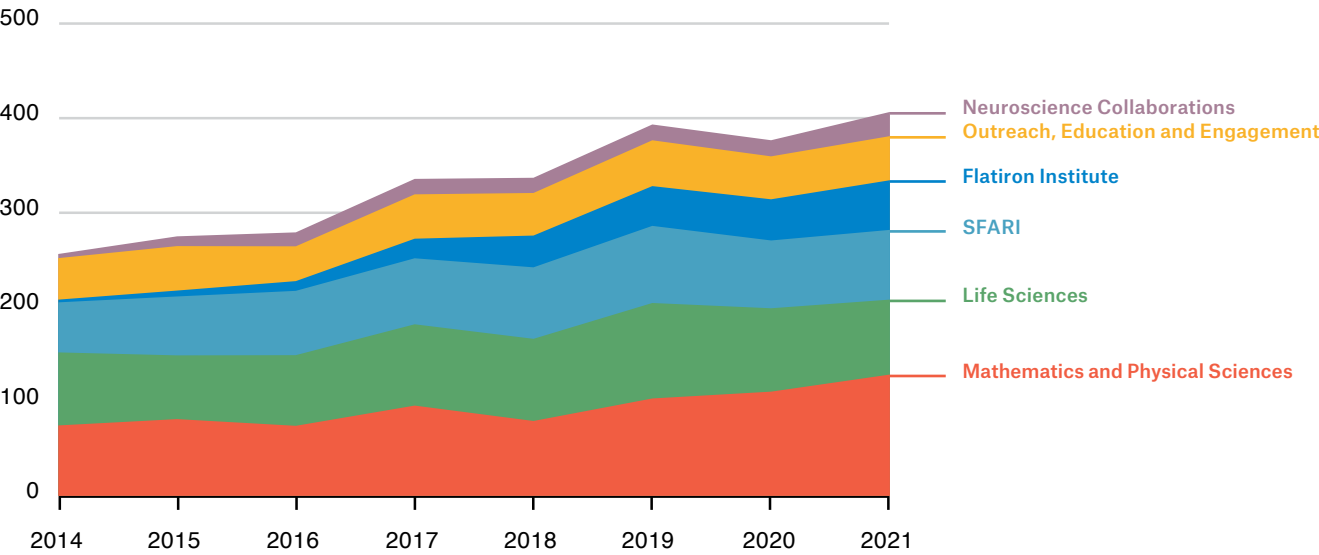
The program gives students the opportunity to hear from established physicists, many of them Black, about the process of becoming a scientist and obstacles they may encounter. We need to convince students, “You can do this, and you won’t be the first person to do this, and you won’t have to do it alone,” Wagoner says.

“It showed us that, even if it does matter what you look like, there’s space for you,” Edmond says. “That revolutionized how I carry myself in my career.”

FINANCIALS

TOTAL ANNUAL SPENDING

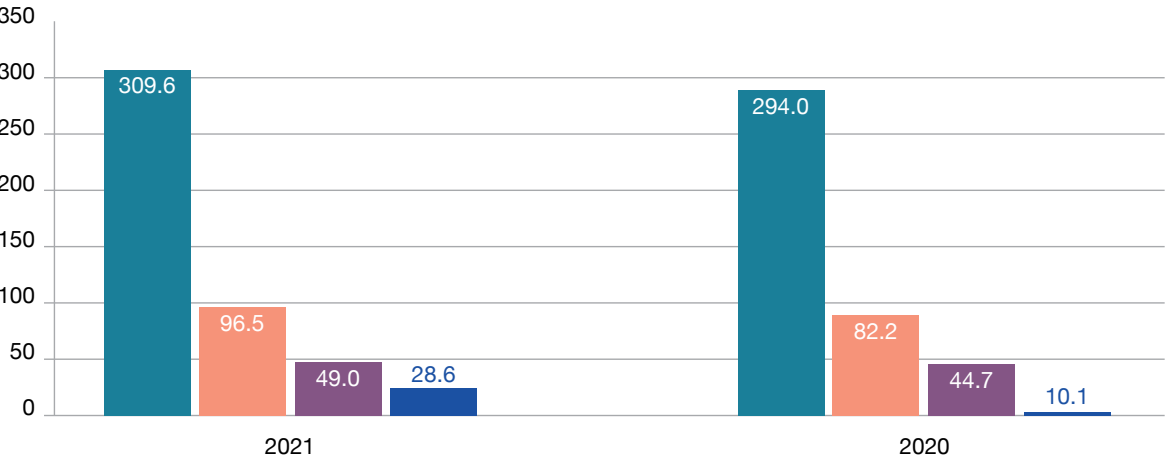
Grants and internal program expenses (by division by year, \$'s in millions)



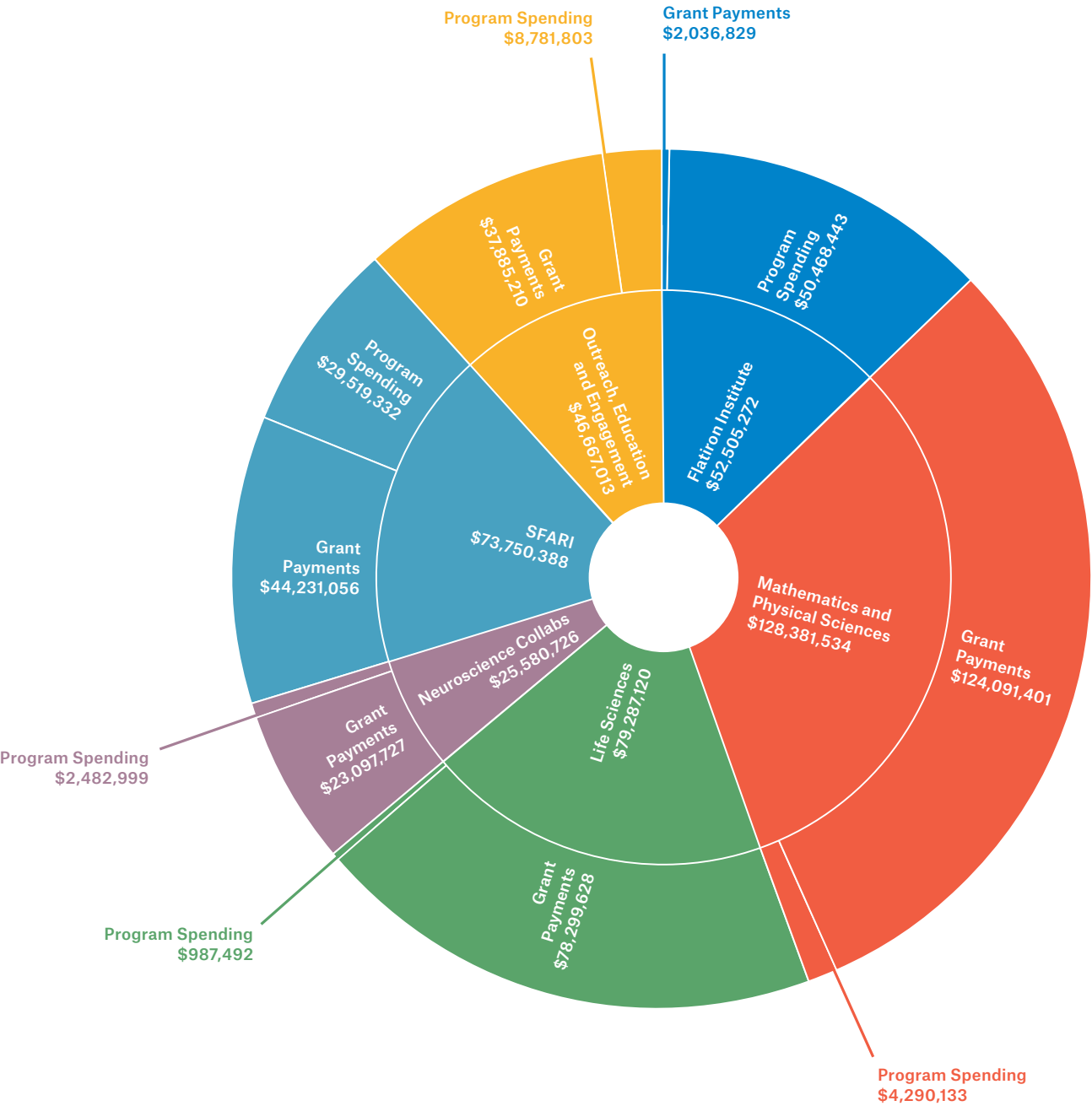
PROPORTIONS OF EXPENSES

(Cash basis, \$'s in millions)

- Grant Payments
- Flatiron Institute, SPARK and Other Internal Program Expenses
- Management and General
- Capital Expenditures



2021 GRANT AND PROGRAM SPENDING BY DIVISION



FINANCIALS

BALANCE SHEET

(Unaudited, in \$)

ASSETS	As of 12/31/21	As of 12/31/20
Cash and Cash Equivalents	297,469,205	111,410,392
Investments	4,366,534,331	3,882,216,743
Property and Equipment, Net	500,482,538	503,494,790
Prepaid Expenses and Other	18,601,317	17,407,186
Total Assets	5,183,087,391	4,514,529,111
LIABILITIES		
Accounts Payable	12,663,297	7,247,131
Grants Payable, Net	525,025,614	606,883,503
Mortgage and Lease Liabilities	345,603,216	344,676,903
Deferred Excise Tax Liability	14,567,785	14,567,785
Total	897,859,912	973,375,322
NET ASSETS		
Beginning Net Assets	3,541,153,789	3,170,013,026
Current Year Change in Net Assets	744,073,690	371,140,763
Total	4,285,227,479	3,541,153,789
Total Liabilities and Net Assets	5,183,087,391	4,514,529,111

INCOME STATEMENT

(Unaudited, in \$)

	For the Year Ended 12/31/21	For the Year Ended 12/31/20
REVENUE		
Investment Income	1,160,419,630	905,246,214
In-Kind Contributions	10,343,764	-
Rental Income	3,559,395	3,977,227
Other Program Income	1,361,746	396,662
Total	1,175,684,535	909,620,103
EXPENSES		
Program	371,659,136	479,945,804
Management and General	59,951,709	58,533,536
Total	431,610,845	538,479,340
Change in Net Assets	744,073,690	371,140,763

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