

Caltech

CHEN TIANQIAO
& CHRISSEY
INSTITUTE



YEARS

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A Letter from the Chens

Five years ago, we were inspired to found the Tianqiao and Chrissy Chen Institute for Neuroscience after hearing about a tetraplegic man who could control a robot arm with his thoughts. We flew to Pasadena to see for ourselves, and were blown away by the brave, innovative, and ultimately life-changing research we saw.

We continue to be inspired every day by the incredible work being done at Caltech. From pioneering brain-machine interface technologies to extraordinary explorations in optogenetics, imaging, systems neuroscience, neuroeconomics, and more, the Chen Institute for Neuroscience team is producing cutting-edge research with real-world impact. We couldn't be prouder of their achievements, and we're honored to have supported their efforts.

At the ribbon-cutting for the new Chen Institute building this year, a faculty member told us that good science requires a leap of faith. You need to jump forward boldly, she explained, even if you don't know exactly where you'll land. Through the Chen Institute, we've aimed to give Caltech's neuroscience community a launchpad from which to leap further, as well as a safety net to enable young researchers to take bigger risks, forge new connections, and unleash their creativity.

We've also sought to create a focal point for Caltech's entire scientific community, and for a broader community of researchers. Collaboration across both interdisciplinary and geographical boundaries has never been more important, and the Chen Institute at Caltech is leading the way by bringing together researchers from diverse backgrounds to drive brain research in new and unexpected directions.

Neuroscience has never been more important. In studying the brain, we're exploring the mysteries of human existence; finding new ways to understand the world around us; and developing new ideas and technologies with which to forge a brighter future for ourselves and our children.

It's been an honor to join the Institute for Neuroscience team on this vital journey, and we're deeply grateful to Caltech for welcoming us in. We're here for you, and we're looking forward to the next five years.

Tianqiao Chen

Chrissy Luo

An Extraordinary Partnership

From the beginning, Tianqiao Chen and Chrissy Luo had a vision. A vision to translate profound understanding of how the brain works into treatments that will improve people's lives; to elucidate human perception of the world; to enhance healthy brain function and mitigate the consequences of damaged brain function.

The Chens' vision dovetailed with Caltech's aspirations. We are an Institute that discovers knowledge for the ages and seeks to invent technologies that improve people's lives today. Tianqiao and Chrissy's vision and Caltech's aspirations came together with the founding of the Tianqiao and Chrissy Chen Institute for Neuroscience at Caltech.

We are delighted to celebrate five years of collaboration, innovation, and progress. The Chen Institute for Neuroscience has galvanized the university's neuroscience community, raised its profile in the world, and propelled discovery that illuminates the mysteries of the brain and defines what it means to be human.

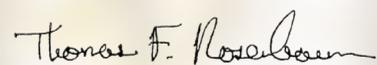
The extraordinary partnership and friendship of Tianqiao Chen and Chrissy Luo are critical to the Chen Institute's success. Their shared vision and philanthropy has made possible this transformative initiative.

From their earliest interactions with Caltech investigators, Tianqiao and Chrissy's empathy and commitment to benefit others was obvious. Today, they continue to advance our work in service of society. Moreover, their personal connections speak to the dedication to our scholars that underlies their generosity and for which we are grateful.

The Chen Institute at Caltech brings together a diverse group of scientists and engineers to catalyze our capacious approach to neuroscience, incorporating interdisciplinary and computational methods to address fundamental issues and technological interventions. The Chen Neuroscience Research Building provides a state-of-the-art facility and an ideal environment for research groups to exchange ideas. This enterprise is bolstered by grants for interdisciplinary research and graduate fellowships that cultivate the next generation of intellectual leaders.

The rewards of this remarkable effort can be seen by the many impactful findings that already have emerged. The development of robotic limbs to assist paralyzed people, insights into how we make decisions, and strategies to deliver therapeutic genes across the blood-brain barrier represent a small sample of these exciting advances.

It is a privilege to be on this journey of discovery with Tianqiao and Chrissy. They enable our scholars to be fearless in revealing the complexities and beauty of the brain. Together we look forward to celebrating the breakthroughs that lift the human condition.



Thomas Rosenbaum
President, California Institute of Technology



INTERDISCIPLINARY RESEARCH



Research Without Borders

Interdisciplinary collaboration is in the Chen Institute's DNA

Over the past five years, the Chen Institute for Neuroscience at Caltech has emerged as a focal point for interdisciplinary and collaborative research — a process that has taken place organically, but not

From grant programs that enable students to try out new ideas, to retreats and symposia that bring people together, everything that happens at the Chen Institute is designed to foster the free exchange of ideas. "Even when

Our mission is to build community and bring people together.

by accident. "Our mission is to build community and bring people together," explains executive director Mary Sikora. "We want to get economists and chemists and physicists and biologists in the same room, talking about neuroscience and sparking ideas off one another."

students are hanging out socially, they're never far from a whiteboard, so they end up writing equations and talking over their ideas," Sikora says. "Everything we do is about breaking down barriers and getting people talking."

A Home for Neuroscience

That's especially visible in the Chen Neuroscience Research Building, a 150,000 square foot facility that embodies the Institute's commitment to collaboration. With hubs for interdisciplinary collaboration, plug-and-play suites to support a range of research needs, and other design features to draw researchers together, the copper-clad building is both a local landmark and a physical hub for brain science at Caltech.

Collaboration has both an intellectual dimension and a physical dimension," says Chen Institute director David Anderson. "The new building

brings us all together, and gives us a physical place to meet and share ideas."

When Anderson himself moved into the new building, he found his office was located between those of computer scientist Pietro Perona and psychologist Ralph Adolphs. Since then, Anderson has tapped Perona's expertise in machine vision to turbocharge his animal behavior experiments, and co-authored a book on emotional states with Adolphs.

"When you bring people into close proximity — physically, intellectually, and socially — their interactions ignite and lead

to new science," Anderson says. "Not every meeting leads to breakthroughs but if we can strike enough of these sparks, some of them will explode into something really transformative."

It helps that Caltech itself is a magnet for top researchers and students from around the world. "Last year was the biggest class in the history of neuroscience at Caltech, and it's thanks to the way the Chen Institute has drawn together the neuroscience community," says Chen Scholar Yuki Oka, who earned his PhD in Japan before coming to Caltech. "People want to be part of what we're doing."

Supporting The Next Generation

The Chen Institute's interdisciplinarity encourages students to learn not just about a single narrow area of study, but about all the different technologies and philosophies that shape modern neuroscience. Incoming graduate students rotate through multiple labs before deciding their research focus. "We don't see a distinction between research and education," says Carlos Lois, director of the Chen Center for Neuroscience Education. "If you're doing good research, then you're always learning — from the other people in your lab, from your advisers, from your peers."

The Chen Graduate Fellowships give students supplementary funding to rotate through additional research labs or dive deeper into specific problems. "The

Chens have really given us a tremendous opportunity," Anderson says. "They're committed to training the next generation of brain scientists, and giving them the broad intellectual and technical toolkit needed to

Neuroscience. "The Chen Fellows are an amazing resource for us as researchers," Gradinaru says. "Because of the way they're funded, they have more flexibility and freedom, and that naturally leads to

If you're doing good research, then you're always learning. They're committed to training the next generation of brain scientists, and giving them the broad intellectual and technical toolkit needed to work across disciplines. That's incredibly valuable.

work across disciplines. That's incredibly valuable."

Moving between labs, students become a kind of connective tissue that helps faculty to draw on technologies, methods, and insights from across Caltech, says Viviana Gradinaru, director of the Center for Molecular and Cellular

new collaborations." Student researchers helped Gradinaru introduce new technologies such as AI and computational neuroscience into her work on adenovirus-enabled optogenetics, opening new research possibilities that could one day lead to new therapies for Parkinson's Disease.

Opening Up New Possibilities

Creative interdisciplinary research isn't just about bringing people together — it's also about giving them the resources they need. In addition to graduate fellowships, students benefit from Chen Graduate Innovator grants, which provide \$10,000 to fund projects unrelated to students' core research. "That seed funding is a significant chunk of change for a student project — and we fund about five of them each year," says Doris Tsao, director and leadership chair of the T&C Chen Center for Systems Neuroscience. "It's a way of supporting crazy ideas, and it has a really big impact."

The Innovator grants are already generating extraordinary research: Guruprasad Raghavan grew neurons in a dish then

coaxed them to grow into a "cortical computer," while Annie Erickson used machine vision to explore the neural processes underpinning a praying mantis's predatory strikes. "It's been super-refreshing to work on something different," says Erickson, who typically works on flight behavior in fruit flies. "It lets you flip the script and do something completely unrelated to what you'd usually be studying."

The Chen Institute also gives faculty opportunities to take their research in new directions. Traditional funding sources don't leave much room for blue-sky thinking, explains Chen Scholar Dean Mobbs, who studies the neural processes underlying fear and panic. "Most grant-based funding is extremely

conservative," he says. "But the Chen Institute really values creativity and encourages us to think differently."

That's especially important when you're working on the cutting edge of modern neuroscience, agrees Brain-Machine Interface Center director Richard Andersen. "It's hard to get funding when you just want to explore," he says. Having the Chen Institute's support has enabled Andersen's team to build long-lasting relationships with tetraplegic patients, and to develop new robotic prosthetics, without worrying about whether funding will dry up. "Outside funding comes and goes, but the Chen Institute has given us real stability," Andersen says. "I don't know where we'd be without it."



Interdisciplinary Research



Feeling Frisky?

It takes a team to tell when a mouse is in the mood for love. Led by David Anderson, Chen Institute experts from fields including biology, machine vision, AI data-processing, mathematical modeling, and medicine studied the brains of male mice engaged in same-sex mounting behavior. Their findings: most of the time, neurons associated with aggression rather than lust lit up when mice engaged in same-sex mounting, suggesting a dominance display rather than sexual attraction.

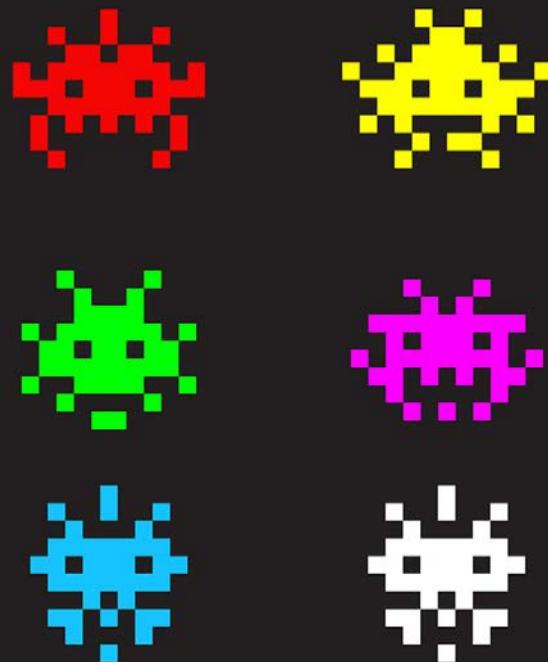


Sneaky Bugs

Entomologist Joe Parker studies rove beetles — tiny bugs whose furry abdomens secrete mind-controlling chemicals that allow them to sneak into ant colonies. The beetles have trained ants not only to stop attacking them, but to groom them, regurgitate food for them, and even carry them to their nurseries so they can devour the ants' eggs. Fusing genomics, molecular biology, chemical ecology, and neuroscience, Parker's work offers insights into the evolution of social behaviors, and the way we relate to other species.

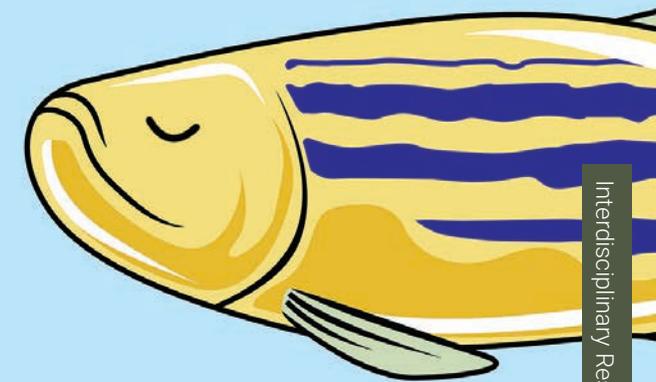
Game On

In John O'Doherty's lab, researchers are teaching an AI to play classic video games including Pong and Space Invaders. While humans can learn the rules of a new game in moments, it takes days of nonstop playing for a neural network to figure out what it's supposed to do. Teaching 'bots to blast the baddies more effectively could lead to AI tools that can identify salient details and interpret novel scenarios more effectively, making them more useful in real-world settings.



Sleep With the Fishes

The genetics of sleep are poorly understood — but that's changing thanks to biologist David Prober's aquarium full of zebrafish. Prober's team identified chemical messengers that regulate sleep in zebrafish, then worked with Harvard researchers to explore the chemicals' role in human sleep. Using data from 500,000 people, the team showed that genes relating to the chemical pathways are associated with sleep quality — a breakthrough that could lead to new treatments for sleep disorders that affect tens of millions of Americans.



Interdisciplinary Research



7 INTERDISCIPLINARY CENTERS

Welcome to the Watering Hole

Neuroscientists must come together to drive research forward, says Chen Institute director



“The Institute’s inclusivity is very important. We don’t restrict it to people who are professional neuroscientists — we try to attract people into neuroscience.”

David J. Anderson
Seymour Benzer Professor of Biology
Investigator, Howard Hughes Medical Institute
Tianqiao and Chrissy Chen Institute for Neuroscience Leadership Chair
Director, Tianqiao and Chrissy Chen Institute for Neuroscience

To do science that really matters, you need to build a community — and that’s why the Chen Institute is so important, says director David Anderson.

“If Caltech is like a savannah, then we’re the watering hole that draws all the different animals together,” Anderson explains. Biologists, computer scientists, and psychologists are all very welcome, Anderson says — but so too are philosophers, astronomers, applied physicists, and even geologists. (Take a bow, Joe Kirschvink, who studies the way brainwaves respond to the Earth’s magnetic fields.) “Caltech is the ideal place to recruit people from different disciplines to work on different problems in brain science,” Anderson says. “The Institute’s inclusivity is very important. We don’t restrict it to people who are professional neuroscientists — we try to attract people into neuroscience.”

Anderson was himself a late arrival to brain research: a successful stem cell researcher, he pivoted into neuroscience in search of new ways to leverage his expertise in molecular biology. “I do my best work when I get into a field in its early stages,” he explains. Along the way, he has forged collaborations with psychologist Ralph Adolphs and machine vision researcher Pietro Perona, sparking creative new approaches that Anderson says has made his research far more rewarding.

Today, Anderson explores the emotional lives of animals in a bid to shed light on the neural circuitry that underpins the inner workings of the human mind. In one recent study, Anderson developed a machine to annoy fruit flies by using a puff of air to repeatedly knock them off their feet. That allowed him to study the insect’s agitated response — and, eventually, to identify the specific neurons that mediated the bug’s irate state.

“Many people think of emotions as uniquely human,” Anderson says. “But animals

most excited about as I look to the future,” he says. “The interactions between basic neuroscience and medicine and new technologies will lead to transformative changes in how many brain diseases are treated.”

Getting to that point requires exactly the kind of teamwork the Chen Institute was created to foster, Anderson says. “I’ve worked in many different areas of biology, and neuroscience is the most interdisciplinary field I’ve come across,” he says. “A single paper could include everything from optogenetics, to electrophysiology, to

If Caltech is like a Savannah, then we’re the watering hole that draws all the different animals together

and insects also have enduring internal states that influence their behavior, much as our own actions are shaped by our emotions.”

Exploring those states — by studying peeved flies or terrified mice, say — offers insights into human emotion, and could ultimately yield more effective treatments for emotional disorders such as depression or anxiety. “Right now, taking an antidepressant is like dumping oil all over your car engine and hoping some winds up in the right place,” Anderson says. At the Chen Institute, researchers are creating better kinds of oil, figuring out where it needs to get to, and finding more targeted ways to get it there, he explains. “That’s what I’m

microendoscopic imaging, to computational analysis of neural activity, to quantitative and computational analysis of animal behavior. No one lab can be expert in all of those areas, so collaboration is absolutely essential.”

As the Institute’s director, Anderson’s job is to help individual researchers to pursue their visions — but also to encourage them to break down barriers and push scientific understanding forward. “We’re creating a sense of community and fostering collaboration across interdisciplinary boundaries, because we know that’s what will lead to breakthroughs on the cutting edge of our field,” he says.

From Thought to Action

The **Brain-Machine Interface Center** is building life-changing robot prosthetics

Richard Andersen is on a mission to help people to drink beer and play videogames.

Okay, so there's a bit more to it than that: the people Andersen wants to help are quadriplegics, with spinal injuries that have left them unable to move their limbs. To help his paralyzed subjects to raise a Bud or blast the bad guys, Andersen's team at the Chen Brain-Machine Interface Center surgically implants electrodes into their brain, then takes simultaneous readings from hundreds of neurons to allow subjects to control an on-screen cursor or a robotic prosthetic simply by thinking about it.

A handful of other labs have attempted similar feats, but most have implanted electrodes into patients' motor cortex, which controls physical movement. While that makes intuitive sense, it leads to jerky, hard-to-control motions since subjects have to consciously think about how to move a robot arm — left a bit, right a bit — in order to achieve their goal.

Andersen's key breakthrough came when he implanted electrodes further upstream, in the posterior parietal cortex (PPC) — the part of the brain where goal-oriented movements are originally planned. By deciphering the way gestures are encoded in the PPC, Andersen's team can allow subjects to trigger smooth, fluid actions with a single thought,

rather than having to consciously coordinate all the component movements that comprise a single gesture.

The results are impressive: besides lifting a beer or playing shoot-'em-ups, Andersen's subjects can now use a brain-controlled robot arm to almost effortlessly grasp objects, shake hands, play rock-paper-scissors, paint pictures, and even operate a blender to make a smoothie. "It's remarkable how much you can decode from a small number of neurons," Andersen says.

It's hard to get funding for truly exploratory research, and the Chen Institute provided the stability we needed. We wouldn't be where we are today without them.

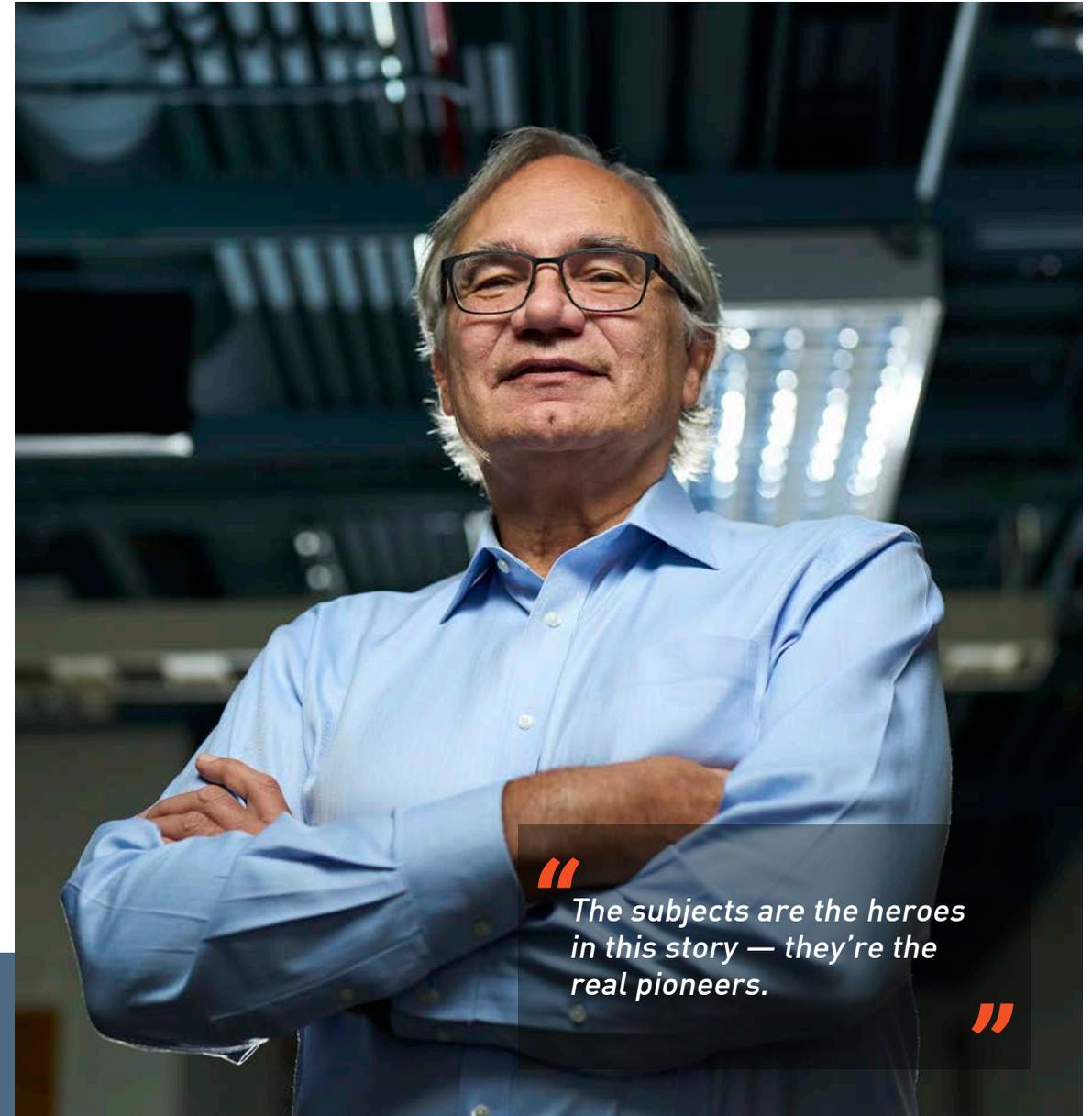
Andersen is modest about his achievements. "The subjects are the heroes in this story — they're the real pioneers," he says. But he acknowledges that he and his graduate students find it thrilling to help a paralyzed person interact with the world in a new way. "It's absolutely inspiring, because you can see the results of your work instantly, and it's clear how much it means to the subjects," he says.

The Chen Institute itself grew out of Andersen's extraordinary work: the Chens traveled to Caltech from Singapore after

seeing a news report on his work, and were captivated by its potential to change lives. The conversations that grew out of that first visit ultimately led to the founding of the Chen Institute. "Their support has made an enormous difference," Andersen says. "It's hard to get funding for truly exploratory research, and the Chen Institute provided the stability we needed. We wouldn't be where we are today without them."

There's still plenty left to explore. Andersen's team is now working to use implanted electrodes to print information back to the brain, enabling subjects to get the sensory feedback required for truly dextrous control of a prosthetic limb. Researchers are also exploring the PPC's dense connections to other parts of the brain, including areas connected to language. "This approach gives us an unprecedented window onto how the brain works," Andersen says. "Reading directly from people's brains gives us a huge opportunity to learn things that simply weren't possible before."

With only a handful of labs capable of taking detailed readings directly from the human brain, Andersen's team is at the bleeding edge of BMI research. That's both a daunting responsibility and a thrilling opportunity, Andersen says. "We're going places where nobody has been before," he adds. "Pretty much everything we do is a first."



“The subjects are the heroes in this story — they’re the real pioneers.”

Richard Andersen

*James G. Boswell Professor of Neuroscience
T&C Chen Brain-Machine Interface Center Leadership Chair
Director, T&C Chen Brain-Machine Interface Center*

Meet The Toolmaker

At the **Center for Molecular and Cellular Neuroscience**, researchers are turbo-charging nature's Trojan horses



“Why wait around for someone else to fix things for you when you can do it for yourself?”

Viviana Gradinaru
Professor of Neuroscience and Biological Engineering
Investigator, Heritage Medical Research Institute
Director, Center for Molecular and Cellular Neuroscience

For her first trick, Viviana Gradinaru made a rat's brain disappear.

Frustrated by the difficulty of untangling the axonal bunches affected by deep-brain stimulation used to treat Parkinson's disease, Gradinaru figured out how to replace the brain's opaque lipids with transparent gel without disturbing the cellular architecture. The result: milky tissue became as clear as water, enabling Gradinaru to trace axonal pathways across the brain — and creating a powerful new research paradigm now widely used by neuroscientists.

“I'm a toolmaker,” Gradinaru explains. “Why wait around for someone else to fix things for you when you can do it for yourself?”

Gradinaru's can-do approach to brain research dates back to her childhood in rural Romania, then under Communist rule. Growing up amidst frequent blackouts and chronic shortages, her family often had to improvise solutions to the problems they faced.

Gradinaru brings that same spirit to her role as director of the Center for Molecular and Cellular Neuroscience. These days, though, Gradinaru's preferred tools aren't hammers, wrenches, or even transparent rat brains — they're viruses.

Drawing on Frances Arnold's Nobel-winning research on forced evolution, Gradinaru's

team uses machine learning to rapidly create viruses capable of selectively targeting specific kinds of cells, and even of sneaking beyond the blood-brain barrier to deliver their genetic payloads to brain cells. They've already taught viruses to sidestep the blood-brain barrier in rats, and forthcoming research will repeat the trick in both New and Old World primates. “Viruses are nature's Trojan horse,” Gradinaru explains. “We're using them to deliver genes anywhere in the brain, using a single IV injection.”

That's a game-changer because it enables the use of optogenetics — genetic

We're incredibly lucky — we've been given a mission and the resources we need to accomplish it

material that causes neurons to fire when exposed to light — as both a research tool and, potentially, a therapeutic intervention. Gradinaru's lab has been at the forefront of optogenetics research for years, pioneering the creation of optogenetic payloads that are non-toxic to mammals, and also creating highly sensitive optogenetics that can be triggered by light filtering through the skull rather than by implanted light sources.

Breaking past the blood-brain barrier is a key additional step because it allows viruses to deliver optogenetics without the need for them to be injected

directly into the brain. That makes research simpler, and also makes human optogenetics more feasible.

That will one day make it possible to easily trigger precisely selected brain circuits, opening the door to non-invasive brain stimulation to treat illnesses such as Parkinson's Disease. “Increasingly, we're shifting from creating tools and methods, to finding ways to actually treat people,” Gradinaru says. “It feels kind of scary — it's not just about writing papers now, it's about helping real humans.”

Gradinaru's methods for creating less toxic, more

targeted optogenetics are already being used by hundreds of labs worldwide, opening new frontiers in gene therapy. Gradinaru says she tries to ensure the Center's PhD researchers don't feel burdened or intimidated by that responsibility, but also wants them to remember the real-world value of the work they're doing. “The best science happens when you're having fun and following your passions,” Gradinaru says. “But at the same time, we're incredibly lucky — we've been given a mission and the resources we need to accomplish it. We have to take that seriously, because anything else would be a wasted opportunity.”

Looking Inside the Brain

Caltech's **Brain Imaging Center** fuses neuroimaging and machine analytics

Your IQ is printed on your brain — if you know where to look.

As director of Caltech's Brain Imaging Center, Ralph Adolphs has found that with sophisticated brain imaging and complex computational models, it's possible to predict someone's score on an IQ test with remarkable accuracy based on images of their activity. "This shows why Caltech is such a great place to do neuroimaging," Adolphs says. "We've got amazing equipment, but we can add one key ingredient — Caltech's strength in mathematics and computer science — to bring our data to life."

When Adolphs began his career studying patients with brain lesions, it was impossible to extract such rich insights from neuroimaging. In fact, he says, researchers really only used imaging to diagnose lesions, and relied on observational assessments to study the way lesions impacted cognition. "The kind of high-quality functional imaging we do at the Brain Imaging Center really only became possible in the last 10 years or so," he says. "It's a very new technology."

Adolphs still spends much of his time studying people with atypical brains — including people with autism, patients with lesions to the amygdala or corpus callosum, and even people who've had half of

their brain surgically removed. But these days, he uses advanced imaging, tools such as eye trackers, and computational tools to extract far richer insights into how brain structures and cognition interact. "We're looking at atypical brains in order to try and understand how the healthy brain produces cognition and emotions," he says. "For me, the big question is how it can be that an organ like the brain manages to produce our

For me, the big question is how it can be that an organ like the brain manages to produce our experience of the world.

experience of the world." The Brain Imaging Center is the perfect place to ask such questions, Adolphs says, because it's a dedicated research facility where students and faculty from across Caltech can access powerful equipment for studying the brains of both humans and animals. "At most universities, you'd be sharing these machines with a medical school, and having to ration out time on the machines," he says. "At Caltech, everyone has access, and we have time to explore."

That's crucial because it enables researchers to go



“Running a lab like mine requires physicists, experts in AI and machine learning, clinical psychologists, and people with expertise from all kinds of different domains.”

Ralph Adolphs

*Bren Professor of Psychology, Neuroscience, and Biology
Director, Caltech Brain Imaging Center*

Allen V. C. Davis and Lenabelle Davis Leadership Chair

deeper, and spend far longer imaging individual subjects than would be possible at many other imaging labs. "Most neuroimaging datasets are based on one-hour scans, but at Caltech we're able to scan subjects over tens or even hundreds of hours in order to get really dense, fine-grained data about their brains," he explains.

For one ongoing project, Adolphs scans subjects while they binge-watch movies or sitcoms. "It keeps them awake and interested," he explains. He then uses machine learning to automatically extract features from the shows they watched, and compare it to their brain activity. "We can check what's happening on screen — if it's a face, or an object, or something exciting or funny or sad — and get really rich, naturalistic insights into how that affects brain activity," Adolphs says. "And it's all automated, which makes a huge difference."

Researchers will always need access to the latest imaging tools, Adolphs adds, but Caltech's interdisciplinary culture is the BIC's real secret weapon. "Today, running a lab like mine requires physicists, experts in AI and machine learning, clinical psychologists, and people with expertise from all kinds of different domains," he says. "It's incredible to have all these powerful tools available. But we need to work together in order to understand how the brain works."

Looking For the Turtle's Underbelly

At the **Center for Systems Neuroscience**, researchers are decoding the brain's cognitive functions.

Where's the best place to look for a turtle's underbelly? For Doris Tsao, the answer is obvious: deep inside a monkey's brain.

As director of the Center for Systems Neuroscience, Tsao has spent her career searching for what scientists call the "turtle's underbelly" — the soft, penetrable spot that allows you to dig in and solve a hard, apparently intractable problem. For Tsao, the hard problem is the way that the brain makes sense of the three-dimensional world, based only on information from the senses — and the entrypoint is the way that monkeys make sense of human faces.

By sinking electrodes into the brains of macaque monkeys, Tsao can record the way neurons flare in response to signals from the retina. Early in her career, Tsao made a name for herself — and netted a MacArthur grant — by identifying clusters of cells, dubbed "face patches," that react only when the monkey is looking at a face. After years of painstaking analysis and mathematical modeling, Tsao has now decoded that neural activity, allowing her to reconstruct a photorealistic image of the face a monkey sees based only on the activity of its neurons.

By figuring out how the brain processes vision relating to one special class of objects — faces

— Tsao hopes to one day solve deeper mysteries including the way we visualize and model the world around us, and the way that cascades of sparking neurons give rise to conscious experiences. "Systems neuroscience involves looking at the way groups of neurons work together in order to answer big questions," Tsao says. "We're the ones who want to understand how the brain works."

This is an incredibly exciting time to be a neuroscientist — but it's also a daunting time, because you have to learn so much.

That ambitious goal leads researchers in many different directions, including Mikhail Shapiro's groundbreaking work using ultrasound to decode neural activity; David Prober's efforts to untangle the mysteries of sleep by studying zebrafish; and Mark Meister's illumination of the "lightbulb moments" that mice experience as they learn to navigate mazes. "We're all following our own curiosity — it's not like physics where everyone's pushing forward together using unified theories," Tsao says.

The fragmented nature of brain research makes it all the more important for organizations like the Center for Systems Neuroscience to join the dots,

and help researchers develop a common language, Tsao says. "I believe there are fundamental principles that govern how the brain works — but to find them, there needs to be synthesis across labs, and across our whole field," Tsao explains. Achieving that synthesis demands a uniquely broad perspective on the workings of the brain, encompassing biology, psychology, mathematics, and even engineering. "I can't think of a more interdisciplinary field," Tsao says. "This is an incredibly exciting time to be a neuroscientist — but it's also a daunting time, because you have to learn so much."

That's where the Chen Institute comes in, Tsao adds, by giving researchers the freedom to follow their interests, but also creating a meeting-place where they can share their ideas and learn from researchers in other fields and disciplines. Students, too, benefit from learning in such a vibrant environment, because keeping an open mind and tracing connections between disciplines is the best way to find the next turtle's underbelly, and prepare to solve the hard problems of tomorrow. "The students are our future, and we want to encourage them to be as creative and fearless as possible," Tsao says. "They're going to carry that forward, and make the next big discoveries."



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Doris Tsao
*Professor of Biology
T&C Chen Center for Systems Neuroscience
Leadership Chair
Howard Hughes Medical Institute Investigator
Director of the T&C Chen Center for Systems Neuroscience*

Punk Rock, Stocks, and Electric Shocks

At the [Center for Social and Decision Neuroscience](#), economics has never been weirder

Colin Camerer likes to take a walk on the weird side.

In the 1980s, as a grad student at the University of Chicago's buttoned-down Booth School of Business, he raised eyebrows by launching a successful punk record label, signing bands including the Dead Milkmen and Big Black. "It started as an economics experiment," he says. "But it also taught me to work with people who had huge egos that didn't always line up with their talent — not an unhelpful preparation for work in academia."

While researching financial decision-making at the Wharton, Booth, and Kellogg business schools, Camerer found himself increasingly drawn to brain science. "I'd started in experimental economics, back when that was a weird thing to do — then it became more popular, so I needed to find something even weirder," he says. Today, Camerer leads the Chen Center for Social and Decision Neuroscience, and is one of the founders of the field of neuroeconomics, using brain imaging and computational neuroscience to probe beyond the limits of traditional economics.

"Economists ignore the fact that decisions happen in the brain," he explains. "But that means they're leaving unexplored some very interesting and puzzling areas."



“We always start with the presumption that our basic research will eventually translate into helping other fields — from medicine, to business, to government regulators.”

Colin Camerer
Robert Kirby Professor of Behavioral Economics
T&C Chen Center for Social and Decision Neuroscience Leadership Chair
Director, T&C Chen Center for Social and Decision Neuroscience

Many of Camerer's experiments involve monitoring brain activity while subjects complete decision-making tasks, often by competing against one another for cash prizes, and using mathematical modeling to explore the reasons why people make certain decisions. That approach has given Camerer's team new insights into how the brain operates as a market bubble swells and bursts; how cognitive biases lead traders to incorrectly hold or sell stocks; and how poker players decide whether to bluff or fold.

Neuroscience has given us the tools to go out into the field and start asking really cool questions.

"We're still laying the groundwork, but one day we'll be able to spot a rogue trader by looking at their brain activity, or create an app that will help people overcome biases to make smarter financial decisions," he says. "We always start with the presumption that our basic research will eventually translate into helping other fields — from medicine, to business, to government regulators."

Because Camerer's team describes decisions in mathematical terms, they can also quantify deviations from normal or optimal behavior,

making it possible to define and quantify psychiatric symptoms with far more specificity and precision than is ordinarily possible. Patients with borderline personality disorder, for instance, typically fail to take opportunities to rebuild trust during collaborative games. "That's something you can express in numbers, instead of just hazy, subjective descriptions of symptoms," Camerer says. "Combined with brain evidence about where those decisions happen, it could one day lead to new treatments too."

Increasingly, Camerer is looking to explore more naturalistic forms of decision-making, from the way that people decide whether to hit the gym or stay home, to the ways that police officers perceive and make decisions about civilians of different ethnicities. In one recent study, he used wearable devices to measure physiological markers in real time as subjects navigated a haunted house, and monitored their social decision-making as they stumbled through rooms full of live cockroaches, received powerful electric shocks, and underwent mock executions. "You'd never be able to get ethical approval to do this kind of study in the lab," he laughs. "Neuroscience has given us the tools to go out into the field and start asking really cool questions."

Don't Be Afraid to Go a Little Crazy

The **Center for Neuroscience Education** aims to foster students' independence

Young zebra finches learn their song within a few months of hatching, then sing the same sequence of notes, over and over, for the rest of their lives — unless Carlos Lois gets his hands on them first.

In Lois's lab, researchers trace the connections of neurons that make birdsong possible, then selectively perturb individual cells or broader neural pathways in a bid to disrupt the birds' chirruping. "We're introducing noise into the system," Lois explains. "What we're finding is that the finch's brain is able to resist that noise, and constantly update itself to prevent degradation."

That's a big deal, Lois adds, because the area of the finch's brain involved in learning and producing birdsong is structurally similar to human vocal control centers — and like finches, humans preserve information in their brains over a period of years or decades. Figuring out how information is stored safely, even in a noisy and failure-prone system, could help unlock new ways to tackle aging and neurodegenerative disorders. "Neurons are relatively faulty, and if you have a stroke you can lose millions of neurons in a matter of minutes," Lois says. "But one way or another, in many cases, we're able to regain much of the information that was lost."

One key insight from Lois's research: copies of information

stored elsewhere in the brain can be used as a kind of backup, allowing degraded information to be reconstructed. To understand that process, Lois is gradually building a roadmap of the brain's connections in multiple animals of the same species, testing for similarities and variations in the ways neurons connect to other regions of the brain. It's a slow process, but a vital one. "To a large extent, the brain remains a black box," he says. "To understand how the brain stores and preserves information,

The goal is to produce graduate researchers who are independent in their thinking, and who know that right now is the perfect time to be idealistic and optimistic about the work they're doing.

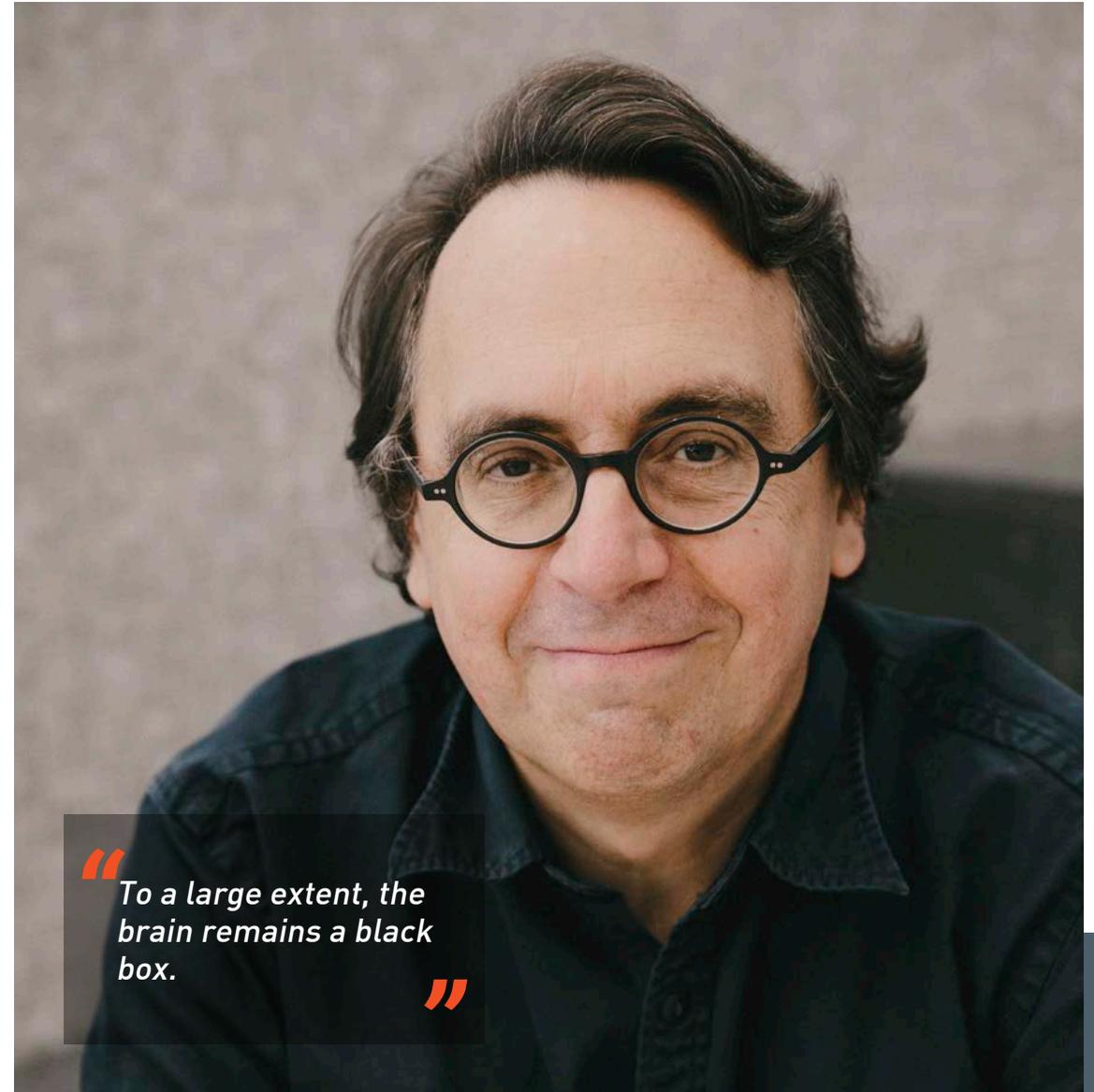
we need to know how that wiring diagram is created, and how it is reorganized over time."

Executing on that vision requires a commitment to interdisciplinary collaboration. "I'm first and foremost an experimentalist," Lois says. "But some of the techniques we have now are so powerful that there's a disconnect between the data we can gather, and our ability to process and interpret it. As we look to the future, we'll need more collaborations

between experimentalists and data scientists — and we'll need to make sure those two groups can understand each other and work together."

As director of the Center for Neuroscience Education, Lois says he does what he can to give students hands-on experience in his own laboratory, but also experience working with data and computational experts who can turn raw data into powerful new insights. "In the Renaissance, the great masters of art — Michelangelo and Leonardo and so on — all had their workshops where people learned by working together," he says. "That's really how science education should be too — not formal education, but students learning by doing science alongside people with more experience or different points of view."

The Chen Institute makes that possible both by fostering interdisciplinary collaboration, and by providing grants and other resources that encourage students to try research projects of their own, even in areas that aren't directly related to their PhD theses. "That empowers the students to think a bit outside the box, and try something that's a little unconventional — or totally crazy," he says. "The goal is to produce graduate researchers who are independent in their thinking, and who know that right now is the perfect time to be idealistic and optimistic about the work they're doing."



“To a large extent, the brain remains a black box.”

Carlos Lois
Research Professor of Biology
Director, T&C Chen Center for Neuroscience Education



The Next Frontier

For the newest Center, big data brings big opportunities

Breakthrough neurotechnologies are generating enormous datasets, including recordings of neural activity, machine vision-enabled studies of animal behavior, sophisticated brain imaging, and continuous data from wearable or implanted sensors. That represents an enormous opportunity — but only if researchers can find the signals amidst the noise, and turn a tidal wave of data into meaningful insights.

To address that challenge, the Chens are marking the fifth anniversary of the Tianqiao and Chrissy Chen Institute for Neuroscience at Caltech by launching the Center for Data Science and Artificial Intelligence (DataSAI) — a new research hub dedicated to the analysis and interpretation of big datasets.

“By helping students at Caltech to sharpen their data science skills, DataSAI will enable incredible research,” explains Tianqiao Chen. “Chrissy and I strongly believe these skills are the key to the future of neuroscience.”

Chrissy and I strongly believe these skills are the key to the future of neuroscience.

Co-directed by Professors Lior Pachter and Pietro Perona, DataSAI will develop new tools for data generation and analysis, and offer workshops, a Visiting Scholar’s program, student internship opportunities, and stipend support for second-year graduate students.

“As brain researchers, we all know that data is an incredible resource, but also a challenge,” says Perona. “DataSAI will give the next generation of scientists the tools and training they need to succeed, and put cutting edge analytics at the center of brain research across Caltech.”



CHEN SCHOLARS

Beyond the Amygdala

Dean Mobbs left school aged 15 to become a house painter and a boxer — but in his 20s, he fell in love with psychology after reading about the Milgram experiment. “I think every researcher is really trying to find their own Milgram experiment — the one that defines their career,” he says. Mobbs returned to school, gained a PhD, and went on to work at Stanford, University College London, Cambridge, and Columbia before coming to Caltech in 2016 to found the Fear Lab.

A longtime fan of zombie movies, Mobbs had always been intrigued by the way his feelings of fear heightened as the undead lumbered gradually closer to their victims. Based on that insight, Mobbs has spent his career studying fear in naturalistic contexts — in one case, even using faked video feeds to convince subjects there was a live tarantula crawling toward them as they lay in an MRI machine. “It’s a step forward from simple Pavlovian fear conditioning, toward more dynamic measures of defensive behaviors,” he explains.

As a Chen Scholar, Mobbs uses brain imaging and creative experimental methods — often using

sophisticated virtual environments to simulate the experience of being hunted or chased — to study the way fear operates in real-world settings. In so doing, Mobbs has described the way the brain switches between higher-level circuitry when planning responses to distant threats, and more evolutionarily ancient midbrain circuitry when responding to nearby or fast-approaching threats. “We used to think that fear was just about the amygdala,”

he says. “But we’ve shown for the first time that the context of any given threat elicits different

neurocircuits — in the hypothalamus, the prefrontal cortex, the list goes on.”

That’s important because it suggests that anxiety disorders, panic disorders, and PTSD are mediated by distinct neural circuitry, significantly impacting the efficacy of both pharmaceutical and therapeutic interventions. “Right now, we’re still using grenades instead of fly-swatters to treat these disorders,” Mobbs says. “By functionally dissecting this circuitry, we hope to develop more targeted, personalized, and individualized approaches to helping patients.”



Dean Mobbs

Chen Scholar
Professor of Cognitive Neuroscience
Allen V. C. Davis and Lenabelle Davis Leadership Chair
Director, Caltech Brain Imaging Center

Right now, we’re still using grenades instead of fly swatters to treat these disorders.

A Thirst for Knowledge

As a graduate student in Japan, Yuki Oka was fascinated by the way that a few hundred olfactory receptors could capture a seemingly limitless variety of fragrances and stench. The more Oka learned, though, the more he felt something was missing. “We knew a lot about the way senses like smell worked at the periphery, but I wanted to know how that sensory information was translated and interpreted by the brain,” he explains.

After arriving at Caltech in 2014, Oka set out to answer this question by exploring fluid homeostasis — the way the brain keeps the body’s water and salt levels in balance. To precisely drive salt and water ingestion, the brain needs to combine a variety of sensory data from the mouth and elsewhere in the body in order to maintain a healthy equilibrium. In fact, Oka found, structures in the forebrain and hindbrain peek out from behind the blood-brain barrier to gauge hydration by “tasting” blood directly — “like a tongue in the brain,” he says.

Building on this work, Oka’s team has now identified specific neurons and circuitry that monitor internal water balance and trigger cravings for salt or water. Using neural manipulation techniques including optogenetics to trigger those cells causes lab mice to scurry for water or munch frantically on rock salt. Oka is also studying the way that sensory signals such as

gulping reflexes or salty tastes inhibit the thirst brain appetite neurons, even before water or sodium reaches the bloodstream, and how the neurons interact with dopamine-based reward systems to make it pleasurable to swig a cold drink or munch on salty chips when your body’s fluids are out of balance.

Federal funding agencies are typically wary of exploratory research, Oka says, so the Chen Institute’s support has been vital as he continues to map the brain’s thirst circuitry. In coming years, that could lead to new treatments for metabolic disorders related to abnormal water and salt ingestion. And because thirst neurons protrude beyond the blood-brain barrier, they make especially attractive targets for pharmaceutical interventions for these populations, Oka explains.

Oka is currently collaborating with multiple labs at Caltech. This work includes developing implantable osmolality sensors that will capture real-time information about fluctuating salt and fluid levels in the bloodstream. The aim, he explains, is to keep deepening our understanding of the way the brain integrates inputs from across the body. “We know a lot about how the brain senses the external world,” he says. “But this gives us a platform to learn how the brain detects the internal world.”



Yuki Oka

Chen Scholar
Professor of Biology
Investigator, Heritage Medical Research Institute

CHEN GRADUATE FELLOWS

Art Appreciation for AIs

Sanghyun Yi wants to make computers think more like people. In one of his first research projects at Caltech, Sanghyun created an algorithm capable of successfully judging the aesthetic merit of artworks based on visual features such as color and contrast. “That’s only a starting point – we didn’t consider the emotional impact or social context of a piece of art,” he says. “But it’s the foundation for more complex models that mirror the way people approach these kinds of complex judgments.”

Now, Sanghyun is using the same approach to study the way people make intuitive decisions about how to complete a task. By studying people’s interactions with

objects in a virtual environment, he’s created an algorithm that describes their decision-making processes; now, he’s comparing that algorithm with their brain activity to ensure it accurately reflects the neural processes underlying their decisions.

The end-goal, Sanghyun explains, is to create AI algorithms that function more like the human brain, using heuristics and intuitions instead of solving problems by applying rigid rules or using brute force. “People are still much better than AIs at many tasks,” he says. “If we have a better understanding of the brain’s processes, we may be able to create better AIs too.”



Sanghyun Yi,
PhD candidate,
Social and Decision Neuroscience

Science is For Everyone



Daniel Pollak,
PhD candidate,
Neurobiology

Daniel Pollak fell in love with brain research after seeing a drawing of an action potential in a research paper. “I thought it was really beautiful,” he says. “That’s pretty much why I’m studying neuroscience.” Now, he’s hoping to bring that same feeling of joyful discovery to schoolchildren in Pasadena and across the country by creating and promoting citizen science projects that will help kids to fall in love with STEM. “I want to bring laypeople into the scientific process,” he explains.

Using a Chen Graduate Innovator grant, Daniel created ERGo!, a citizen science kit that gives school children everything they need to conduct sophisticated electrophysiology experiments using bugs they can find in their backyard. The first kit, which Daniel plans to distribute with a DIY educational neuroscience company called Backyard Brains, enables kids to learn

more about how insects’ retinas respond to changes in ambient light. “It’s a fairly simple preparation, and there’s a lot you can learn,” Daniel says. “And you can do it on any insect you want, so it opens up the field for wild cross-species comparisons.”

As a volunteer with Pasadena Community College’s Upward Bound program, Daniel, along with his collaborators, Jahel Guardado (alumnus of PCC and current graduate student in neuroscience at NYU), Dr. Zeynep Turan, and Dr. Etienne Serbe, spent part of his summer running science workshops for local high-schoolers, introducing them to the ERGo! kit and encouraging them to play around with STEM concepts and experiments. “My goal is to make these kids into real scientists,” he says. “I want them to get interested, and choose their own projects, and develop a question, and follow it through.”

Fly, My Beauties

How does a fruit fly fly? There’s more to it than just flapping their wings, says Annie Erickson: to stay aloft, a fly must think fast to avoid obstacles and other fast-moving insects. To study that phenomenon, Annie built a miniature flight simulator: a cylindrical panel of LEDs that creates an

arena, we can study exactly what’s happening when they speed up or slow down, or carry out other aerial maneuvers.”

Studying the way flies’ brains respond to incoming information and send out quickfire motor signals could provide new insights into

By putting the fly in this virtual reality arena, we can study exactly what’s happening when they speed up or slow down

immersive environment for a fly, complete with puffs of air to simulate gusts of wind.

Held immobile on a rod, the fly can zip through the virtual environment and respond to stimuli; meanwhile, Annie and her colleagues can peer through the top of the fly’s head to see which neurons are firing as the insect whizzes along. “Fruit flies have relatively small brains, but they’re expert fliers,” Annie says. “By putting the fly in this virtual reality

how brains process sensory and motor information, Annie says.”

It’s helpful to start by asking these questions in simple organisms — it lets us identify neurons of interest, and manipulate them in ways you couldn’t with a human,” she explains.



Annie Erickson,
PhD candidate,
Neurobiology

Neuroengineering Custom Treatments



Sabera Talukder,
PhD candidate,
Neurobiology

Sabera Talukder has a confession to make: she doesn't really care how the brain works. "The work I'm doing kind of sits on top of all that foundational research," she explains. "I'm not a scientist who's trying to understand everything that's going on — I'm an engineer who's trying to build cool tools."

Sabera's research focuses on building machine learning models to extract neural information and synthesize custom treatments. Using computer science and artificial intelligence, Sabera is finding new ways to make data from implanted neural electrodes more useful to patients, clinicians, and researchers. Her current research focuses on spotting patterns in data from Parkinson's and epilepsy patients' electrodes. She then uses these patient-specific insights not only to build generalizable models that benefit the entire patient population but also deliver individualistic treatments. This could make it possible to fine-tune brain stimulation treatments or to identify the brain structures involved in epileptic episodes without the need for trial and error or lengthy observation

periods. The hope is that "instead of sitting for hours in the clinic with electrodes in your brain, we could recommend a treatment plan that is customized to you automatically," she explains.

Achieving this requires complex mathematical modeling and deep learning techniques since there is no common language with which to understand what the neural data represents. Challenges include the limited amounts of high-quality electrode data available for study, the inconsistency of electrode distribution among patients, and the difficulty of reconciling the data analysis with wide-ranging clinical diagnoses observed among those afflicted with Parkinson's or epilepsy. "It's a hard set of problems," she says. However, Sabera believes there is much to be optimistic about. Within the past decade, classically difficult problems in machine learning such as image classification, language generation, and predictive modeling have all seen huge advances. "We're hoping that it will be ready for use in other labs by the end of 2022."

Once More With Feeling

Most researchers at the Brain-Machine Interface lab listen in on brain activity to help paralyzed patients control robotic prosthetics with their minds — but Isabelle Rosenthal is part of a team that's working to send small currents back to the brain to generate tactile sensations.

That could one day enable the development of prosthetics that give tactile feedback as they're used, enabling patients to

being touched — and then see what happens when we change what their virtual body looks like, or alter the visual context," she explains.

Learning how the brain encodes perceptions, and manipulating that process to evoke conscious sensations, requires teamwork: some BMI researchers focus on direct stimulation, and others, like Isabelle, seek to understand the brain's processes. "The thing I really like about Caltech is that you

We're all kind of working on our own different pieces of the puzzle

use them with far greater dexterity. "It's potentially the difference between the claw you use to grab a gift in those strip-mall machines, and a prosthetic that feels like it's really part of you," Isabelle says. "But before we can achieve that, we need to understand how touch is encoded in the brain."

To answer that question, Isabelle uses virtual reality to explore how visual and tactile awareness interact to create conscious sensory experience. "I can monitor what happens in the brain as a subject sees themselves being touched, or imagines

get such a variety of different perspectives," Isabelle says. "We're all kind of working on our own different pieces of the puzzle."

Above all, it's thrilling to ask tough questions while simultaneously working on potentially life-changing technologies. "It lets me bridge between philosophical questions about the nature of experience, and work that genuinely has a real-world impact," Isabelle says.



Isabelle Rosenthal,
PhD candidate,
Computation and Neural Systems

Fostering Collaboration, Community, and Diversity



The vibrant interdisciplinary research being done by both students and faculty at Caltech is a testament to the Chen Institute's commitment to fostering collaboration, community and inclusivity, says director David Anderson. Still, there's always more that can be done. One key priority for the next five years will be to work to make both the neuroscience faculty and the student body more diverse — something with which STEM programs across the country have historically struggled.

Chen Institute programs such as the Diversity & Inclusion Awards, honoring students who drive diversity initiatives, and the BrainWAVE program for undergraduate research, are helping to push things forward, Anderson says. "One of the most exciting things about the future are our efforts to increase diversity in our pool of neuroscience students and faculty," Anderson says. "The Chen Institute is working hard to increase diversity across the board."



BrainWAVE Fellowships

The Chen Institute for Neuroscience at Caltech established the BrainWAVE fellowship program in 2021 to offer opportunities for motivated undergraduate students interested in carrying out a summer research project in neuroscience at Caltech. BrainWAVE fellowships are awarded to non-Caltech undergraduates who plan to pursue a neuroscience-related PhD.

Successful candidates develop and conduct a research project and work alongside Caltech faculty, staff, graduate student researchers, and postdoctoral scholars throughout the 10-week period. During this time, BrainWAVE fellows also participate in activities within the Caltech neuroscience community.



Morgan Owens, a junior at the University of Texas at Austin, spent the summer working with Viviana Gradinaru on viruses — a level of hands-on research she hadn't previously been able to try out. Just as valuable, though, were the conversations over dinner or lunch with faculty and current Caltech grad students.

"It gave me a real experience of graduate student life," Owens says. "It's really helped me to figure out what I want to do next."

Isaias Ghezze, a rising senior at the University of California Santa Barbara, worked in Colin Camerer's lab, where he used JavaScript and PsychoPy to code online trust games.

"I learned a lot about using software for research, and also about the theory behind neuro-economics," he says.

Now Isaias is applying to PhD programs in social neuroscience — and using his newfound PsychoPy skills to code research projects of his own at UCSB. "There was a steep learning curve, but I'm definitely seeing the benefits," he says.

Case Western senior **Nathan Nadler** spent his summer in David Prober's laboratory, studying neuronal firing patterns in zebrafish with genes linked to autism-spectrum disorders. Learning to work with animal models, and to use techniques like staining, was eye-opening, Nadler says. So were the events and meet-and-greets that the Chen Institute staged for the BrainWAVE fellows. As Nathan says, "I got to meet so many people with so many different perspectives — it was truly a life-changing experience."

Duke junior **Sydney Hunt** spent her summer in Richard Andersen's lab creating a BMI that enabled a tetraplegic patient to control a robotic arm with their thoughts.

With no prior neuroscience experience, she used her skills as an Electrical and Computer Science major to show that incorporating augmented reality in BMIs improves the system's practicality.

"I am grateful for my growth this summer, especially when working directly with patients or lab members" she says. "WAVE helped me realize I want to study BMIs in graduate school!"

Emily Rainge, a Pomona College senior, worked with Tsui-Fen Chou to explore p97, a protein involved in autophagy, the process by which cells clean up damaged components. Rainge focused on PLAA, a little-understood protein that supports the clean-up process, and used sophisticated analytic methods to study its behavior in kidney cells.

Her research could one day help the Chou Lab devise new treatments for cancers and other serious ailments. "I will be forever grateful for the experience and lab skills I gained — and for the opportunity to network with Caltech professors and other young scientists," she says.



Connecting with NeuroTechers

Sometimes you want to do cutting-edge research, and sometimes you just want to carve a pumpkin. That's where NeuroTechers comes in: the student-led group hosts monthly events including parties, game nights, a book club — and, yes, a pumpkin carving get-together. "It's easy at Caltech to just focus on your work — but people also need to take a break sometimes," explains NeuroTechers treasurer and event organizer Sarah Wandelt.

That's been especially important during the pandemic, adds NeuroTechers president Isabelle Rosenthal, since until recently many students hadn't had the chance to

meet face-to-face. NeuroTechers stepped up by organizing digital get-togethers and social events to help everyone feel welcome. "We really felt for the students who were starting during the

We really felt for the students who were starting during the pandemic, so we wanted to help them make connections

pandemic, so we wanted to help them make connections," Isabelle explains.

NeuroTecher Kevin Mei organizes popular fireside chats — staged in front of a streaming video of a roaring

hearth — with Caltech professors, where students pepper them with questions about their research and their experience in academia. "The fireside chats have been a great way to get to know our professors," explains Kevin. "The discussions can range from personal anecdotes to scientific hypotheses, art or the role of science in society."

"It's about building community," Isabelle says. "Sometimes we just get together, and sit outside and talk — and those connections with people from other labs are really important, because they ultimately make us better scientists."

Supporting Women in Neuroscience

Globally, women make up half of neuroscience students, but only a third of faculty and less than 14% of tenured full professors. That's something Chen Institute Women in Neuroscience is determined to change by giving women a chance to connect and support one another. "We're trying to bring women from across campus together to share their experiences," says CWiN president Annie Erickson. "The female PIs, especially, have been very supportive — they're really good role models and mentors."

CWiN was founded by Chen Institute Diversity and Inclusion awardee Dawna Bagherian, who reached out to Viviana Gradinaru and Doris Tsao with the original

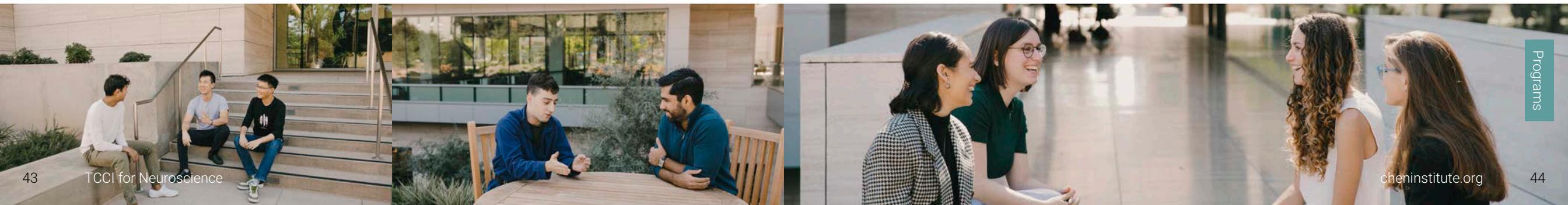
idea for the group. "They emailed back right away and said, absolutely — we're going to get you Chen Institute funding, and we'll support you 100%," Dawna recalls.

It's good to see that people in the field are recognizing that there's a problem, and working to create solutions

Key successes for CWiN include the installation of a sexual health vending machine, the introduction of a childcare program at institutional retreats, and the introduction of free menstrual products in restrooms across campus. "Researchers were having to take an hour out of their

workday to walk to Walgreens," Dawna says. "This was a concrete change that makes our campus a better place to be a person who menstruates."

The group also holds regular social events, Q&As with Caltech faculty, and lunches with female academics who visit campus. The hope, Erickson says, is that CWiN will help to create a critical mass that will ensure that more women enter neuroscience and go on to successful careers in years to come. "We're making improvements, although there's still a lot of work to be done," she says. "But it's good to see that people in the field are recognizing that there's a problem, and working to create solutions."





**WHERE
ARE
THEY
NOW ?**

From Neuroscience to VC

Anastasia Buyalskaya uses research to unlock investment opportunities

Anastasia Buyalskaya wants to build bridges between industry and academia. “We’re living in the golden age of social science,” she says, a point she made earlier this year in an article published in PNAS. “But an important piece of this is that we need to be able to speak the same language in order to collaborate.”

Buyalskaya came to Caltech from BlackRock Asset Management, where she founded the Behavioral Finance team. “I was already reading the behavioral science literature to inform my work improving investment decision making, but I wanted to see firsthand what it would be like to do my own academic research,” she says.

Working in Colin Camerer’s lab, Buyalskaya explored the

way that behaviors are shaped by habits, rather than by active consideration of pros and cons. “Economists usually think about decisions as being about maximizing utility, but it turns out that a lot of behavior is quite reflexive,” she explains.

Using machine learning to explore data on behaviors such as gym attendance and hand hygiene, she was able to explore the way that contextual cues like environment and time influence habit formation. “There is literature which claims that it takes 21 days to create a habit,” she says. “But we found that while some people do form habits after a month, for others it can take over a year. Habit formation is very context dependent.”

Understanding habit formation is critical for tech companies, which need users to interact

regularly with their products or content, Buyalskaya notes.

More broadly, behavioral science lets investors and founders make smarter, more structured decisions about how consumer behavior is changing, what kinds of problems they’re facing, and how likely any new solution is to succeed.

Today, Buyalskaya is trying to answer those questions as a behavioral scientist at Alpha Edison, the knowledge-driven VC firm. “We’re trying to understand how behavior is changing before it becomes obvious and what that means for the kinds of products and services that could be offered by startups,” she says.

Using proprietary datasets, search trends, surveys, and experiments, she works to provide more structured insights and testable hypotheses about the way that life is changing in the wake of the pandemic. “Research is addictive — once you start, it’s hard to stop,” she says. “I’ve been lucky to find a role in industry that lets me keep asking research questions and designing ways to test my hypotheses about human behavior.”



Data From a Few Drops of Blood

David Brown turned a side-project into a thriving life sciences startup

David Brown is a computer nerd at heart. “The brain is just, like, the coolest computer ever,” he says. “For me, computer science and neuroscience are two sides of the same coin.” Figuring out how that computer worked led Brown from AI projects, to brain-machine interface research, and finally to the messier world of neurobiology, using machine learning to understand engineered viruses capable of delivering genetic payloads to specific brain cells. “I wanted to go as deep as I could, and understand what was happening on a molecular level,” he explains.

Brown hoped to use viral gene therapy to create new Alzheimer’s treatments — a goal that also led him to start a side-project looking into blood markers of neurodegenerative diseases. That, in turn, led him to start playing around with a new technology that can extract tiny amounts of blood from the surface of the skin, with no need to poke a needle into someone’s vein. “This seemed like a way better way to get blood, but only if you can get meaningful information out of it,” he says. “So we created a protocol for getting data from RNA extracted from capillary blood cells.”

The protocol proved a success, enabling Brown to extract rich data about a subject’s health. “It gives us a snapshot of what’s happening right now in a person’s body,” he explains. Now, Brown and fellow Caltech grad Tatyana Dobрева have launched a startup, ImYoo, to commercialize their technology

The Chen Institute brings together all the support and infrastructure and resources and expertise you need.

and create a social network allowing users to connect and share health-related information with people who have similar immunological profiles. “We want to give people really high-resolution data, and help them figure out

how to manage their health,” he explains.

With support from Caltech, ImYoo has secured a place in an accelerator, is in the process of raising \$500,000 in seed funding, and is working with several clinical and research partners for pilot studies, one of which involves understanding the role of neuroinflammation in migraines. It’s still early days, but Brown says his startup adventure shows the power of throwing together students from different disciplines and giving them the freedom to explore. “The Chen Institute brings together all the support and infrastructure and resources and expertise you need,” he says.

“So if you have an idea for a crazy project, go out and have fun.”



No More Mad Scientists

Xinhong Chen wants to make science more accessible for everyone



Xinhong Chen doesn't want people to think about mad scientists when they think about science.

"If you see science in a Hollywood movie, it's always some crazy scientists doing weird research that leads to disaster," he says. "We need to change that, and start communicating about science in ways that people can understand."

Xinhong's own research focuses on using viruses to deliver genetic material to carefully targeted cells — not just in the brain, but throughout the body - which could potentially provide better tools for gene therapy to treat neurological disorders.

A Chen Institute workshop helped Xinhong to create a three-minute video explaining his research project, then participate in a Caltech-wide three-minute thesis contest. "To clearly convey your years-long work to an audience in three minutes is extremely challenging and fun," he says. "It forces you to think about

the most important thing your research would bring to the world and what scientific information you'd want a stranger to take away after a short chat in a coffee shop."

To further promote scientific communication, Xinhong created a scientific blog together with fellow PhD students, aimed at introducing the story behind both exciting

We need to do great research, but we also need to be able to tell people about what we're doing.

basic research as well as innovation in the biotech industry to a broader audience. He also co-founded the U8 World Innovation Summit, a student-run, non-profit gathering that has drawn together numerous Nobel and Turing Award recipients, plus senior leaders from world organizations for conversations around science and technology.

"Communication has become really important to me," he says. "We need to do great research, but we also need to be able to tell people about what we're doing."

Pure Imagination

Varun Wadia uses implanted electrodes to decode people's thoughts



Varun Wadia knows what you're thinking — or at least, he knows whose face you're thinking about.

Early in his time at Caltech, Varun was captivated by Doris Tsao's work reconstructing photorealistic images of faces based on readings from small clusters of neurons in macaques' brains. He went to Tsao with a proposal to extend her work into human subjects — an extraordinary leap he realized might be possible if he worked with epilepsy patients fitted with deep-brain electrodes as part of their treatment. "She said — this sounds amazing, let's do it!" he recalls. Tsao set up meetings with several potential collaborators, eventually settling on Caltech's very own Dr. Ueli Rutishauser.

Today, Varun works with patients in Dr. Rutishauser's lab during the narrow windows in which they're undergoing treatment, and takes painstaking readings using electrodes whose placement is determined not by his research needs but by medical necessity. Despite

those constraints, Varun has been able to show that humans encode faces in much the same way as macaques, and to accurately reconstruct faces seen by human subjects based solely on electrode data. "I've verified that the same encoding model works in both species," he says. "That's probably my biggest finding so far."

Now, Varun is exploring whether visualizations are encoded differently if they are imagined rather than seen directly. That has the potential to unlock powerful new insights about the way people create internal models of the physical world, and use their imagination to interpret events and plan actions. "It's a fascinating basic science question, but it's also part of a bigger puzzle with huge implications," he says.

Where Are They Now?

Setting the Stage for Success

The Chen Neuroscience Research Building is a landmark addition to the Caltech campus



Since opening in January 2021, the Tianqiao and Chrissy Chen Neuroscience Research Building (CNRB) has become a landmark on the Caltech campus. Behind the copper-clad facade lie 150,000 square feet of research space designed from the ground up to

foster cross-disciplinary collaboration. The cutting-edge, \$210M facility makes it easy to move between open, sunlit laboratories and common spaces where faculty, postdocs, and students can mingle and discuss their ideas. "Research neighborhoods" encourage interdisciplinary

conversations, with customized laboratories nestling alongside lounge space where researchers and students can connect over coffee, map out ideas on nearby whiteboards, or use cutting-edge equipment to drive brain research forward.

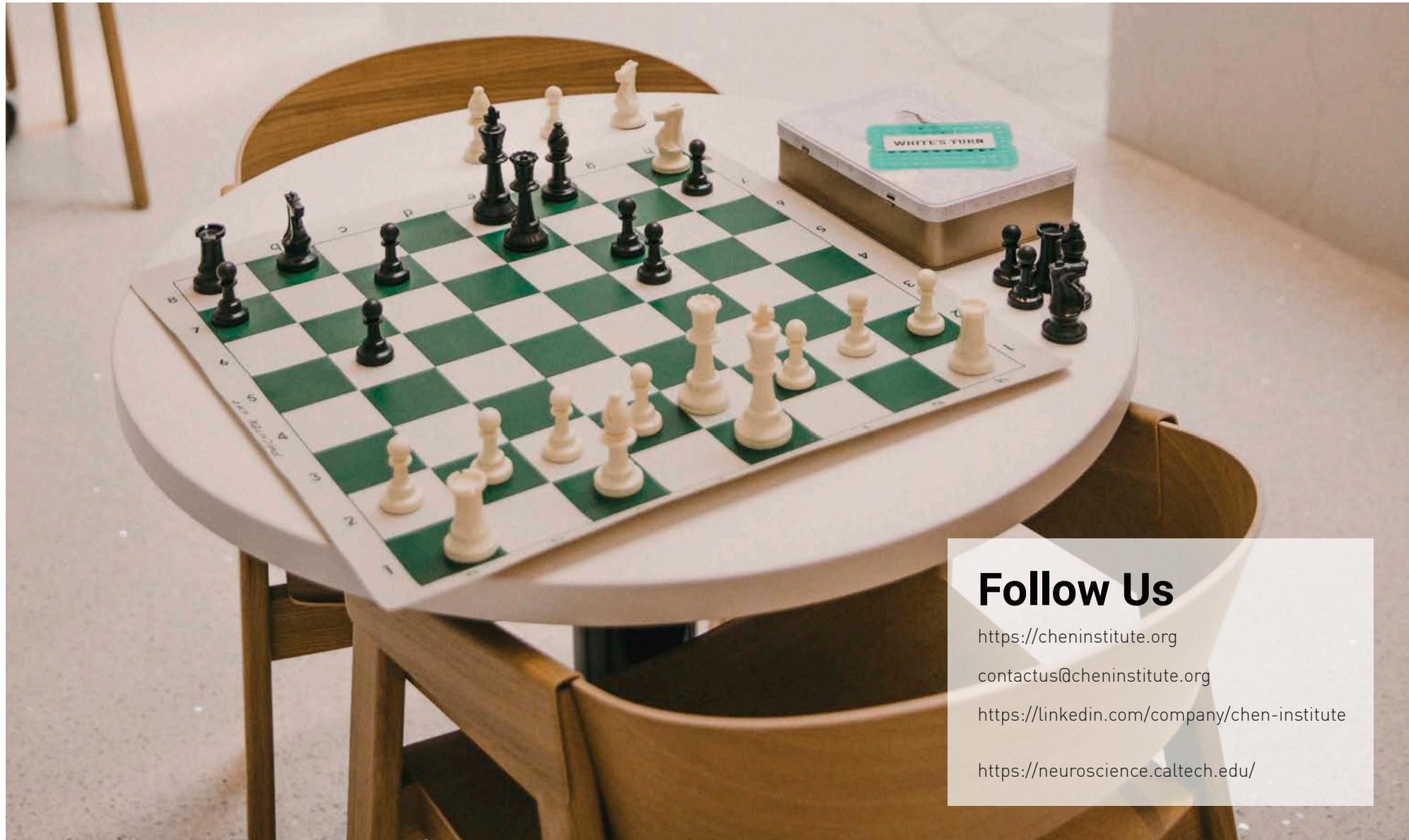
Chen Institute by the Numbers

<p>Chen Neuroscience Research Building</p>	<p>Meetings & Events</p>
<p>Jan 29, 2021 opening ceremony \$210M price tag 13 lab groups 150,000 sq. feet 5 stories</p>	<p>7 Chen Institute workshops 2 Chen Institute retreats 2 Chen Institute symposia 30 sponsored social events 41 visiting speakers</p>
<p>Constructing a Classic</p>	<p>Supporting Students & Science</p>
<p>545,326 mosaic tiles line the oculus 16,200 pounds of copper adorn the façade 67,200 cubic yards of dirt were excavated 2,100 steel beams support the building</p>	<p>5 BrainWAVE Fellowships worth \$45,000 \$1,604,650 awarded in support of research Graduate Fellowships worth over \$2.4M</p>
<p>The Stars of the Institute</p>	<p>An Award-Winning Building</p>
<p>2 Chen Scholars (so far!) 38 Chen Graduate Fellows 250 personnel in the building (and growing) 13 faculty members 57 affiliated faculty members 25,000 zebrafish residents</p>	<p>1 Gold LEED Certification Award 3 Design Build Institute of America Awards 1 Building Design + Construction Award 1 Associated General Contractors of California Award Nomination 1 Commercial Design Award, Pasadena Beautiful Foundation 1 North American Copper in Architecture Award</p>



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