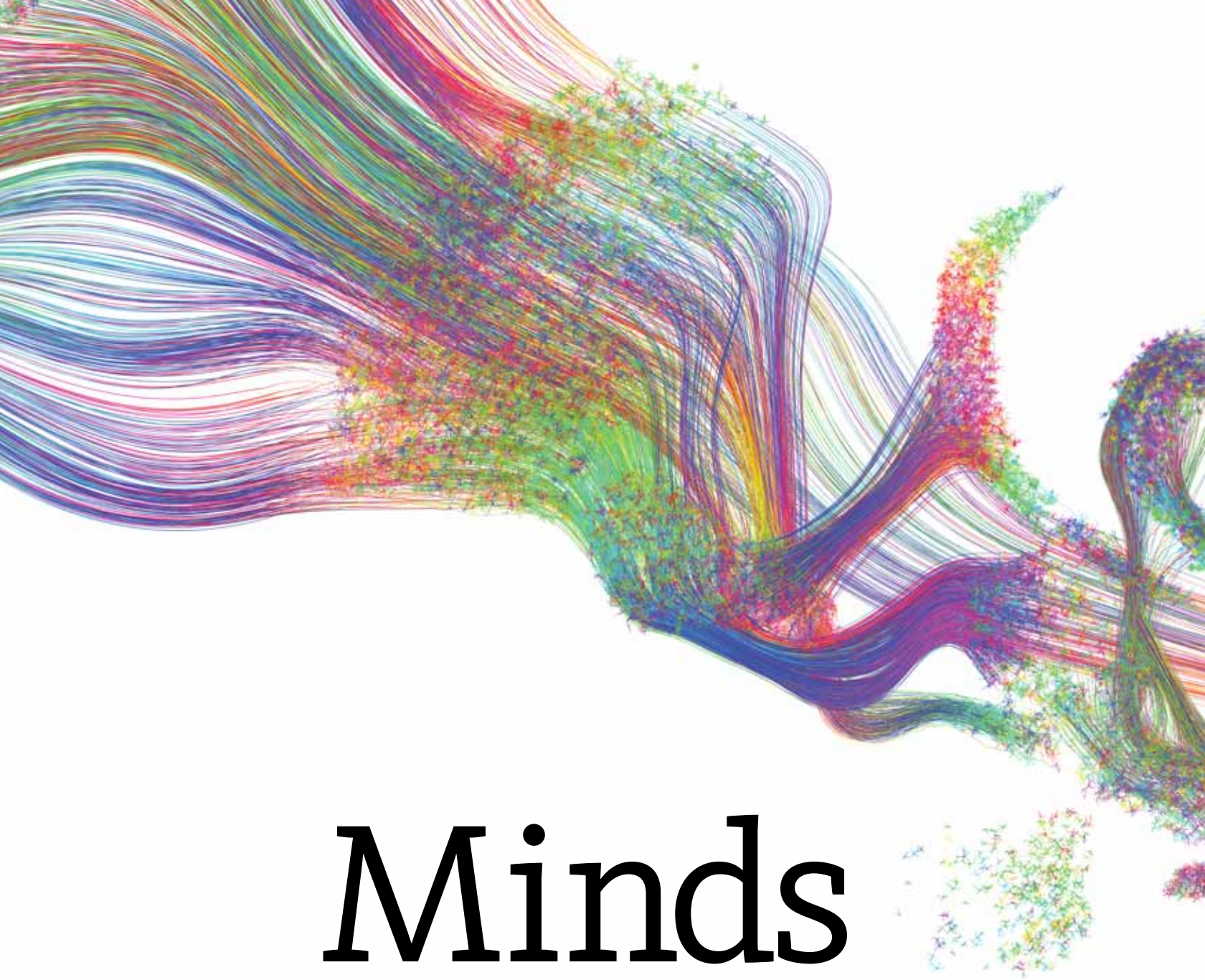


Minds ON THE Brain

by Lori Oliwenstein

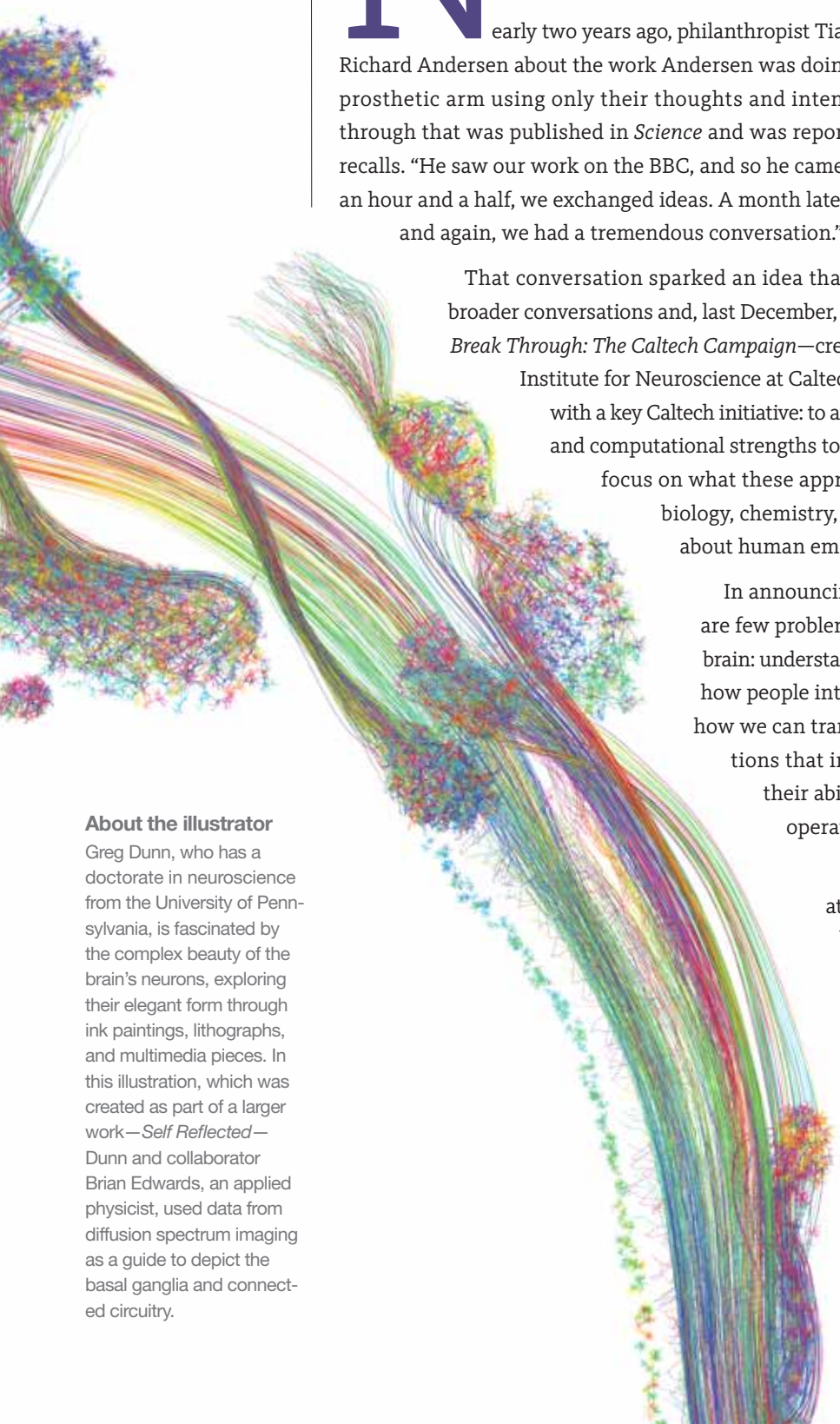
Nearly two years ago, philanthropist Tianqiao Chen emailed Caltech biologist Richard Andersen about the work Andersen was doing to help paralyzed patients operate a prosthetic arm using only their thoughts and intentions. "We had just had a big breakthrough that was published in *Science* and was reported throughout the world," Andersen recalls. "He saw our work on the BBC, and so he came here to meet with me. We talked for an hour and a half, we exchanged ideas. A month later, he came with his wife, Chrissy Luo, and again, we had a tremendous conversation."

That conversation sparked an idea that became a proposal that led to broader conversations and, last December, to a $115 million gift that—as part of *Break Through: The Caltech Campaign*—created the Tianqiao and Chrissy Chen Institute for Neuroscience at Caltech. The Chens' gift dovetailed perfectly with a key Caltech initiative: to apply Caltech's unique interdisciplinary and computational strengths to the study of the brain, with a particular focus on what these approaches can reveal about the brain's biology, chemistry, and even its engineering, as well as about human emotion and behavior.

In announcing the gift, Rosenbaum said, "There are few problems as important as understanding the brain: understanding how people think; understanding how people interact with the world; understanding how we can translate that knowledge into interventions that improve people's lives and improve their ability, both mentally and physically, to operate in society.

"The Chen Institute for Neuroscience at Caltech will let us do something special because we are now bringing individual talents together to transform the study of the brain.

"Together, the Chens and Caltech have identified this as a major area of investment, and together we will establish a partnership that will change the world."



About the illustrator

Greg Dunn, who has a doctorate in neuroscience from the University of Pennsylvania, is fascinated by the complex beauty of the brain's neurons, exploring their elegant form through ink paintings, lithographs, and multimedia pieces. In this illustration, which was created as part of a larger work—*Self Reflected*—Dunn and collaborator Brian Edwards, an applied physicist, used data from diffusion spectrum imaging as a guide to depict the basal ganglia and connected circuitry.

What Their Charge Is

David Anderson, the Seymour Benzer Professor of Biology and a Howard Hughes Medical Institute Investigator, has been named the inaugural holder of the Tianqiao and Chrissy Chen Leadership Chair and director of the institute. In an interview, Anderson talks about how the new institute will shape neuroscience at Caltech.

The motivation for inquiry into the brain is twofold. One is to satisfy our innate curiosity about how this complex machine works. The other is to try to gain understanding that will help improve human health and welfare in general.

Advances in our understanding of the brain circuits of emotion, for example, will help us to understand and treat psychiatric disorders. Advances in understanding how we learn and remember will help us to treat learning disabilities and perhaps to improve memory and retention. On the other side of it, understanding how the brain functions as a computing device will help inform our engineering of computers that are inspired by the biology of brain-circuit architecture.

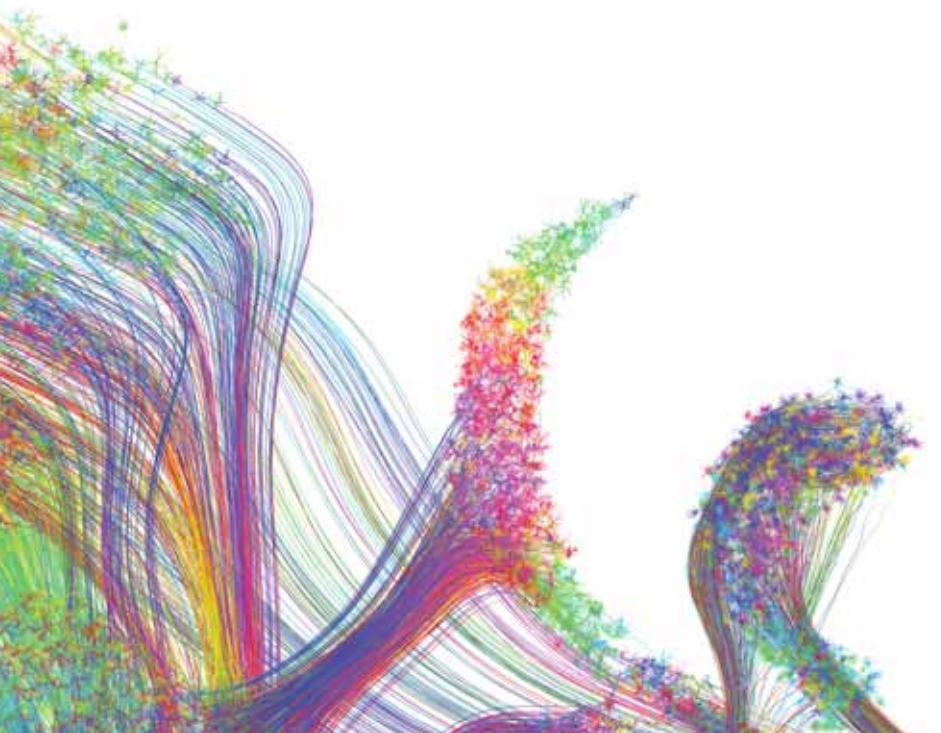
The Chen gift will allow us to encourage exploration into areas that are not yet ready for government funding and, most importantly, that are at the interface between different scientific disciplines, particularly biological sciences and physical and computational sciences.

Neuroscience, arguably more than any other aspect of biology, is a science that requires intense computation, because understanding the brain is about understanding how billions and billions of neurons function in orchestras to regulate our thoughts and behavior. To do that we need new engineering-based technologies to make measurements, which in turn generates big data. This data requires computational approaches to make sense of it and theory to model it. What Caltech has to offer to a greater extent than most other institutions is the marriage between the biology of the brain and the mathematics of the brain.

I see my role as institute director as maximizing the engagement of the Caltech community in neuroscience research, particularly in recruiting people who have not previously participated in research into this area. The opportunity that the Chens have provided us with is the chance to change not only the type of problems that we can solve here but the way we approach those problems.

How They'll Get It Done

The Chen Institute at Caltech involves faculty from across Caltech's six academic divisions, creating a campuswide interdisciplinary community of neuroscientists, biologists, chemists, physicists, engineers, computer scientists, and social scientists, all with the shared goal of understanding the fundamental principles that underlie brain function. It comprises five centers, each with a unique charge and each led by a researcher whose work is already shaping the future of neuroscience at Caltech.



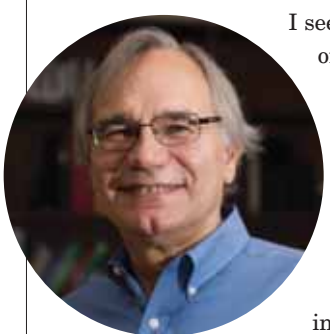
For more information about the Chen Institute at Caltech, go to neuroscience.caltech.edu.

The T&C Chen Brain-Machine Interface Center

Led by Richard Andersen, T&C Chen Brain-Machine Interface Center Leadership Chair; James G. Boswell Professor of Neuroscience

A brain-machine interface is a method of recording or stimulating the brain and connecting it bidirectionally to a machine. An example of this in our research would be decoding the intent of paralyzed subjects, then using that information to control a robotic limb or computer.

The advance we have made at Caltech is to record from a more cognitive part of the brain so we can, in a fraction of a second, decode the intent of the subject and execute the movement. When the subject thinks, "I want to pick up a glass of water," we can decode that and then with smart robotics achieve very smooth movements. It is both an intuitive and a very smooth operation, so it's been a real advance in the field.



It takes my breath away every time I see the subject sitting there in his or her wheelchair being able to, just through their thoughts, control robotic limbs or play a virtual piano or type on a virtual keyboard. It is just an amazing thing, and it thrills the patients as well. It is the first time since their injury that they can actually interact physically with the world around them in tasks that previously required limb movements.

Through the T&C Chen Brain-Machine Interface Center, we hope to achieve three major goals. One is scientific, discovering how populations of neurons work together to produce these sensations, perceptions, and intentions. The second is clinical, helping paralyzed patients and patients more generally with neurological diseases that affect both perception and movement. The third is advancing neurotechnologies to allow for less invasive or noninvasive recordings of high detail from the human brain. This will be, to my knowledge, the first brain-machine interface center more broadly examining perception, intent, and the capabilities of the human.

This gift from the Chens will be so central to what we can do. In patient trials, continuity is critical. We need funding stability over a period of years for a complex, large interdisciplinary group that is centered on the patients and also the environment around them. Now, we can be sure that we will have no disruption in the research or in the clinical trials as they progress.

The T&C Chen Center for Social and Decision Neuroscience

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

We are interested in what's going on in the brain when people are making decisions that mostly affect themselves, and when they are interacting with other people.

We will attack problems such as limited willpower and self-control, particularly in decisions about food, drug addiction, and procrastination. Early evidence indicates that an area called the dorsolateral prefrontal cortex, underneath your temple, keeps in mind the distant, bad outcomes from tempting choices in order to exert self-control.

One of the hallmarks of the T&C Chen Center for Social and Decision Neuroscience is that we use many different tools. Working closely with the technicians in the Caltech Brain Imaging Center (the CBIC), we use functional magnetic resonance imaging, or fMRI, to enable us to see bloodflow throughout the brain. We also use EEG, which measures activity near the cortical surface at a rapid time scale (every one millisecond) to see fast and slow thinking. We also study people with damage in certain areas: If a person has a broken amygdala, for example, and they cannot tell whether another person is afraid, we can be sure that the amygdala is a necessary part of a circuit for detecting fear.

Fact:

Caltech helped create the field of neuroeconomics, in which researchers use experimental approaches to understand how the human brain makes complicated decisions.

The establishment of this center is an acknowledgment that the study of the neural activity that creates human decisions, based in the Division of the Humanities and Social Sciences, is an important part of neuroscience at Caltech. It also will help us plan long-run studies, five or 10 years, in which we can build up a solid understanding of the brain brick by brick. We can try a dozen new approaches, some of which will be dead ends, knowing that when one approach does work, we have the capacity to pour time and energy into it to see where it takes us. We can turn money into science, knowing we can afford to follow the science wherever it leads us.

The T&C Chen Center for Systems Neuroscience

Led by Doris Tsao, T&C Chen Center for Systems Neuroscience Leadership Chair; professor of biology; Howard Hughes Medical Institute Investigator

To think, remember, imagine, and see—all these amazing capacities of the brain come from billions of neurons with quadrillions of precise connections interacting to form the most remarkable dynamical system in the universe. Caltech has a strong emphasis on understanding things at a deep, fundamental level, exemplified by the founders Hale, Millikan, and Noyes. Will we ever be able to understand the brain completely, at the level that we now understand the basic laws of physics? That is what this new center seeks to find out. We are at an infant stage in this quest right now: mostly still describing how single neurons respond under different conditions. To move forward, we will need new experimental tools for observing large populations of neurons and new computational approaches for analyzing this data. The new center will help build this infrastructure.

Our lab's approach is unique in two ways. First, we want to understand the complete problem of vision—not just how an object is recognized or how it's localized but how the entire system works, including all the interfaces. Second, we are fearless about combining different techniques. We were one of the first labs in the world to combine fMRI with electrophysiology. That led to a whole new picture of how the part of the brain that's involved in object recognition is organized.

Fact:

In 1986, Caltech established the world's first graduate program in computation and neural systems, which continues to this day.

Systems neuroscience right now is a collection of silos, with researchers studying emotion, or vision, or decision making. This new center will inspire and enable us to work toward the larger goal of understanding how these different systems are talking to each other. How does a sensory percept trigger formation of a memory? How do internal states and sensory inputs interact to generate behavior? How does the brain decide when to route information from one area to another? Is there a general programming language that the software of the brain is written in? How do answers to these questions change across brain evolution?

The Center for Molecular and Cellular Neuroscience

Led by Viviana Gradinaru (BS '05), assistant professor of biology and biological engineering; Heritage Medical Research Institute Investigator

My group works on understanding neural correlates of behavior. The main problem we are currently working on is understanding how a very powerful therapy, deep-brain stimulation, works. There are difficulties around that, because the brain is a very complex organ. It is highly heterogeneous; it is difficult to map. These are our challenges.

The brain is not only difficult to study but also difficult to access since it is protected by the blood-brain barrier. This keeps pathogens at bay, but it also makes it difficult to deliver therapies to the brain. We are very excited about our latest work, where we've been able to engineer viral vectors to cross the blood-brain barrier and deliver products brain-wide. Those products can take the form of labels for anatomical mapping, but also therapies.

The Center for Molecular and Cellular Neuroscience will be instrumental in giving us a hub to exchange ideas

and amplify these technologies. We are excited about the potential of the teaching lab that's planned through the Chen Institute at Caltech, where students and teachers will work together on technology transfer and enhancement.

The Chen Institute at Caltech is instrumental in allowing us to understand the brain in all of its complexity, because there is an understanding that the brain is not about the molecules alone, or the cells alone, or behavior alone, but rather it is the interaction across the levels. The Chen Institute at Caltech has centers that address each of these levels and unifies them under one umbrella, with lead investigators working together for an integrated understanding of the brain.

The Caltech Brain Imaging Center

Led by John O'Doherty, professor of psychology

The Caltech Brain Imaging Center, or CBIC, was founded in 2003 through a gift from the Gordon and Betty Moore Foundation, and, over the last 13 years or so, we have been providing Caltech faculty, staff, researchers, and students with the research tools to obtain images of the living brain.

Here in our center, we can take structural pictures of the brain as well as use fMRI, which takes a second-by-second look at how activity in the brain changes in relation to the functions it is implementing. If a particular part of the brain is working more than another part, this causes a change in the amount of oxygenated blood flowing to that part of the brain. We can detect that signal, giving us insight into which portions of the brain are working at particular moments in time.

My main research question is trying to understand how the brain learns from experience to make good decisions for the future. Knowing this is fundamental to understanding ourselves as humans, and also impacts our comprehension of what happens when things go wrong in our capacity to make decisions.

The brain imaging center is a critical component of the overarching Chen Institute for Neuroscience at Caltech, providing facilities to faculty across not only humanities and social sciences but also biology and biological engineering as well as chemistry and chemical engineering. Through the facilities we offer here, we can provide a bridge between different types of research activities taking place across the Chen Institute at Caltech.

The philanthropists behind the Chen Institute at Caltech, Tianqiao Chen and Chrissy Luo, are committed to support brain research that promotes and improves the well-being of humanity. "We believe uncovering how the brain perceives, interprets, and interacts with the world is pivotal in so many aspects," says Chen. "This is the mission of our philanthropy."

"We chose Caltech as our first partner not just for their strong reputation as a leading research institution, but also for the admiration in their natural alignment with [our institute's] culture, which is focused on creating excellence and discovery," adds Luo.

To learn more about the Chen Institute at Caltech and to see a video about the institute's inception, visit **magazine.caltech.edu/post/minds-on-the-brain.**