COLUMBIA | Zuckerman Institute
MORTIMER B. ZUCKERMAN MIND BRAIN BEHAVIOR INSTITUTE

The Collective Mind: Mathematical Model Reveals Key to Brain's Unrivaled Computing Power

~ A Q&A with Stefano Fusi, René Hen, Mazen Kheirbek and Fabio Stefanini ~

Your brain is not a computer. Your childhood memories, your ability to master tennis or ride a bike, your feelings of guilt, love and morality, are not governed by any sort of centralized information processor.

Instead, recent evidence has pointed to a far more wondrous mechanism: a highly distributed network of brain-cell activity. To investigate this mechanism, scientists have long studied the behavior of individual brain cells. But in a mouse study published today in Neuron*, a Columbia University team offers a new way forward. By using a powerful method to track large groups of brain cells in real time, combined with advanced mathematical modeling tools, the researchers reveal striking new details about the brain's inner 'collective mind.'*

We spoke with the paper's authors, Stefano Fusi, PhD, Fabio Stefanini, PhD, Mazen Kheirbek, PhD and René Hen, PhD, about what their discovery means for efforts to decode the brain, as well as implications for the burgeoning field of neuromorphic engineering, which is focused on building technology inspired by the brain.

The brain is often compared to a computer. Is that comparison accurate?
Stefano Fusi: Not quite. For one thing, traditional computers are organized differently. They are controlled by a complex central processing unit, a CPU, with only a few connections to other parts of the computer, like its memory. The CPU can execute billions of mathematical operations per second, but only one at a time. By comparison, the brain has no such centralized hub. In addition, its individual elements — brain cells — are a million times slower. Yet somehow the brain is vastly more powerful than any computer at performing some tasks.

Fabio Stefanini: The building blocks of the brain, including neurons, a type of brain cell, encode information in a very distributed way. Neurons all work together to process information, like individual birds flying together as a single, coordinated flock.

Fusi: In fact, a single neuron is, on its own, not especially powerful. Basically, all it does is count how many electrical impulses it received from other neurons, sending out an impulse of its own when this count reaches a certain threshold. We wanted to understand how these simple units, by forming a distributed network, produce the complexity that underlies everything our brain can do.

How have neuroscientists traditionally studied brain activity, and how is your study different?
Mazen Kheirbek: Until recently, we could only record the activity of small groups of neurons at a time. If you wanted to understand how a mouse builds a mental map of its environment as it moves through a maze, for instance, you would monitor a few neurons. If they switched on, you assume those neurons are involved in navigation.

René Hen: This is how scientists discovered a type of neuron called place cells. Place cells act like an internal GPS; they switch on when the animal is in a particular position in a maze. A lot of attention has been paid to these cells, which are easy to monitor because they emit strong electrical signals.

But the vast majority of cells are not easy to record and interpret — especially in brain areas involved in memory, like the hippocampus and one of its most important subregions called the dentate gyrus. The activity of these neurons has often been discounted as noise.

Kheirbek: We and others began to hypothesize that this noisiness is actually important. And now, thanks to recent advances in microscopy and mathematical modeling, we can now monitor hundreds of neurons at once — and look for patterns in the noise.

For this research, how did you begin your investigations?
Hen: We focused on the dentate gyrus, which helps the brain distinguish between two similar but distinct locations. Because the dentate gyrus is located deep in the brain and its neural activity is sparse compared to neighboring regions, it has traditionally been difficult to study.

Kheirbek: We used a tiny, powerful microscope developed by Mark Schnitzer and his team at Stanford University School of Medicine. With this device, we recorded hundreds of neurons simultaneously in the dentate gyrus in mice as the animals freely explored their habitats.

Hen: Studying this kind of behavior is difficult. The mouse runs around, turns this way and that and experiences a multitude of sensory inputs. It is therefore not easy to connect the animal's exploratory behavior to its neural activity. But we hoped to overcome that challenge: first, by recording from hundreds of neurons at once, and second, by teaming up with Drs. Fusi and Stefanini, both computational neuroscientists, to make sense of the massive amounts of data we had collected.

When you delved into the data, what did you discover?
Stefanini: Rather than analyzing the activity of individual cells, we employed an algorithm that analyzed the *collective* activity of many cells. In so doing, we discovered that these

activity patterns were reflective of a much larger portion of the animal's experience than just the mouse's internal GPS..

Fusi: The key to this discovery was the population-level analysis, because it showed that the most obvious neurons — in this case, place cells — are not necessarily the most important units for representing an animal's location.

Individually, most neurons do not seem to represent the animals' location in a consistent way. But when we look at all of the them *together*, we realize that they actually cooperate; they encode several variables all at once, including the location of the animal, its direction of movement and speed.

What do these results mean for our understanding of the brain?
Kheirbek: With this study, we are now beginning to understand, on a moment-by-moment basis, how the dentate gyrus encodes information. And what we are discovering is making us rethink a lot about what we thought we knew about the brain.

Stefanini: The information encoded in the brain — whether it be remembering a location on a map or remembering the feeling of falling in love — is likely not be carried by one group of highly specialized neurons. Here, we've shown how information is encoded in a highly distributed, almost egalitarian way, with each neuron contributing in its own unique way.

And importantly, we find that this information should not be interpreted neuron by neuron, but at the population level. It's the difference between hearing individual notes versus hearing a symphony.

How could these findings be applied to technological efforts, such as neuromorphic hardware?
Fusi: Even the most powerful computers cannot perform some brain functions, which is why many researchers are looking at designing computers inspired by the brain. Today's attempts at such neuromorphic hardware tend to be limited in their ability to learn continually from experiences and adapt. Our findings represent a first step to understanding how populations of neurons in the hippocampus encode and memorize the myriad of variables experienced during navigation. If we work to replicate how memories are stored in the brain, we could create systems that are vastly more powerful, more compact and more energy-efficient.

###

Stefano Fusi, PhD, is the co-senior author of this paper, a principal investigator at Columbia's Zuckerman Institute and a professor of neuroscience at Columbia's Vagelos College of Physicians and Surgeons. He is also a member of Columbia's Center for Theoretical Neuroscience.

Fabio Stefanini, PhD, is the first author of this paper and an associate research scientist in the Fusi lab at Columbia's Zuckerman Institute. He is also a member of Columbia's Center for Theoretical Neuroscience.

Mazen Kheirbek, PhD, is the co-senior author of this paper and an assistant professor of psychiatry at the University of California, San Francisco. He completed this work as an assistant professor of clinical neurobiology (in psychiatry) at Columbia's Vagelos College of Physicians and Surgeons.

René Hen, PhD, is the co-senior author of this paper and a professor of pharmacology (in psychiatry) and of neuroscience at Columbia's Vagelos College of Physicians and Surgeons.

This paper is titled "A distributed neural code in the dentate gyrus and in CA1." Additional contributors include Lyudmila Kushnir, Jessica Jimenez, Nicholas Woods, Joshua Jennings and Garret Stuber.

This research was supported by the National Institute of Mental Health (R01 MH108623, R01 MH111754), IMHRO/One Mind Rising Star Award), the Swiss National Science Foundation's Early Postdoc Mobility grant (P2EZP2 15556), the National Science Foundation (NeuroNex program award DBI-1707398), the Kavli Foundation, the Gatsby Charitable Foundation, the Simons Foundation, the Schwartz Foundation, and the Helen Hay Whitney Foundation.

The authors declare no competing or financial interests.

Columbia University's Mortimer B. Zuckerman Mind Brain Behavior Institute *brings together a group of world-class scientists and scholars to pursue the most urgent and exciting challenge of our time: understanding the brain and mind. A deeper understanding of the brain promises to transform human health and society. From effective treatments for disorders like Alzheimer's, Parkinson's, depression and autism to advances in fields as fundamental as computer science, economics, law, the arts and social policy, the potential for humanity is staggering. To learn more, visit: zuckermaninstitute.columbia.edu.*