

Scientists reveal how neuronal activity is timed in brain's memory-making circuits

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Theta oscillations are a type of prominent brain rhythm that orchestrates neuronal activity in the hippocampus, a brain area critical for the formation of new memories. For several decades these oscillations were believed to be "in sync" across the hippocampus, timing the firing of neurons like a sort of central pacemaker. A new study conducted by researchers at the California Institute of Technology (Caltech) argues that this long-held assumption needs to be revised. In a paper published in this week's issue of the journal *Nature*, the researchers showed that instead of being in sync, theta oscillations actually sweep along the length of the hippocampus as traveling waves.

"It was assumed that activity in the [hippocampus](#) is synchronized throughout," says Evgueniy Lubenov, a postdoctoral scholar at the Center for Biological Circuit Design at Caltech. "But when we looked simultaneously at many different anatomical locations across the hippocampus, we found instead a systematic delay in neuronal activity from site to site. Instead of the whole structure oscillating at once, we see traveling waves that propagate across the hippocampus in a consistent direction, along its long axis."

"In other words, the hippocampus has a series of local time zones, just like we have on Earth," adds Athanassios Siapas, associate professor of computation and neural systems and Bren Scholar at Caltech.

The hippocampus has long been known to be critical for the formation and maintenance of episodic memories—i.e., memories of experiences.

In the rat, hippocampal neurons also function as "place cells," only firing when the animal is in a particular spot in its environment. Lubenov and Siapas began to analyze the theta oscillations generated when [rats](#) move around and explore their environment. They watched how—and when—the rat's neurons fired relative to the rat's position and to the phase of the theta oscillations. They did these studies using multiple tetrodes—electrodes with four recording sites—that allowed them to simultaneously isolate the spiking of many individual neurons.

"Each of these neurons fires only in a restricted region of space," Lubenov says. "Furthermore, the spikes don't just happen any time—they pay attention to the phase of the ongoing theta oscillation. If you have access to the phase at which the neuron fired, you have additional information about where the rat was in space."

When the data about neuronal firing, oscillation phase, and rat location were combined, the researchers were able to show that neuronal activity indeed sweeps across the hippocampus in a wave, with its peak appearing in one region, then another, then another, rather than hitting the entire hippocampus in one synchronized pulse.

"This changes our notion of how spatial information is represented in the rat brain," notes Lubenov. "It was believed that the firing of hippocampal [neurons](#) encodes the physical location of the rat in its environment—in other words, a point of physical space. Our findings suggest that what is encoded is actually a portion of the rat's trajectory—that is, a segment of physical space."

"Such segments may be the elementary unit of hippocampal computation," adds Siapas. "Assume the path a rat takes in an environment is represented and stored as a sequence of point locations. If the rat visits the same location more than once, the representation becomes ambiguous. Representing the rat trajectory as a sequence of

segments oriented in space resolves such ambiguities."

This finding may also have significant implications for understanding how information is transmitted from the hippocampus to other areas of the brain. "Different portions of the hippocampus are connected to different areas in other parts of the brain. The fact that hippocampal activity forms a traveling wave means that these target areas receive inputs from the hippocampus in a specific sequence rather than all at once," explains Siapas.

In addition, Siapas notes, it's unlikely that this behavior is found only in rat brains; after all, theta oscillations are ubiquitous in mammalian brains. "I would expect the traveling-wave nature of theta oscillations to be a general finding, applicable to humans as well," he says.

And while it is not known whether human hippocampal cells function as place cells, as they do in rats, "it may turn out to be the case that the human hippocampus plays a role in providing spatial cues that are important to episodic memory," Lubenov speculates. "We don't know yet."

What we do know is that, by showing that theta oscillations travel across the hippocampus, the Caltech team will likely change the way neuroscientists think about how the hippocampus works.

More information: *Nature* paper -- "Hippocampal theta oscillations are travelling waves," [dx.doi.org/10.1038/nature08010](https://doi.org/10.1038/nature08010)

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