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Researchers Find New Mode of Information Storage in the Brain

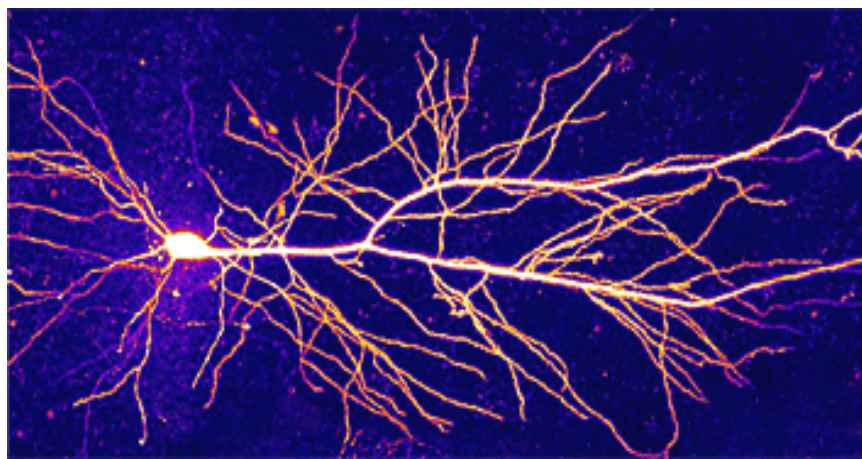


Image Title: Two-photon image of a hippocampal CA1 pyramidal neuron showing the extensively branched dendritic arborization. Each individual branch is a potential substrate for higher-order information storage. - Judit Makara

Howard Hughes Medical Institute researchers have discovered a new way that neurons can store information--and their studies are providing a fresh view of the computational power of neurons.

The outstretched surface of a neuron meets and communicates with neighboring cells at junctures called synapses. At a given time, a single neuron may receive input at hundreds of these. Researchers have long known that information is stored when the strength of these connections change, a process called synaptic plasticity.

The new research by Jeffrey C. Magee and his colleagues at HHMI's Janelia Farm Research Campus shows that neurons can fine tune their information processing through a mechanism that the researchers call “dendritic plasticity.”

"This form of plasticity is distinct from--and complementary to--the more traditional synaptic plasticity."

- Jeffrey C. Magee

Synapses are supported on tiny mushroom-shaped spines, a multitude of which sprout from dendrites that branch out from neurons. Each spine acts as a receiving station for chemical signals—neurotransmitters—from neighboring neurons. Neurons use dendritic plasticity to adjust how they respond to incoming signals that target the neuron's dendritic branches. This feature changes the ability of the synapses on those branches to communicate information to the next neuron.

The researchers published their findings in the March 27, 2008, issue of the journal *Nature*. Attila Losonczy and Judit Makara, both members of Magee's laboratory, were coauthors of the study.

Dendrites, the large branches that extend from the main body of a neuron, are covered with receptors that collect signals from other neurons. When bursts of neurotransmitter from a nearby neuron land on a dendrite's receptors, they trigger an electrical wave called a local dendritic spike. If the local dendritic spike is powerful enough it can propagate to the main body of the neuron, generating an action potential output or nerve impulse.

According to Magee, researchers knew that intermittent input from nearby neurons can trigger weak dendritic spikes that typically remain in the dendrites, as they are not strong enough to travel all the way to the main body of the cell. However, if these local spikes showed plasticity—adjusting themselves to become stronger after repeated input—they could eventually generate a nerve impulse, providing a means of information storage different from that produced by synaptic plasticity.

To search for these types of changes, Magee and his colleagues devised new techniques that permitted them to observe how a single neuron responds to specific patterns of input at precise locations in the neuron. To do so, they stimulated individual synapses in slices of rat hippocampus—an area deep within the brain that is known as the seat of memory.

They knew that adding neurotransmitter to the cells would have activated all their synapses indiscriminately, so they used a modified form of the neurotransmitter in which each molecule was sequestered in its own molecular “cage.” The cages could be unlocked and the neurotransmitter released with a laser pulse - which Magee and his colleagues targeted to the exact spot on the dendrite that they wished to stimulate. Using a laser that could be repositioned rapidly, they stimulated clusters of synapses at nearly

the same time.

In the brain, a single neuron may receive input at hundreds of synapses, each firing up to hundreds of times per second. The neuron processes these incoming signals differently depending on when and where they arrive. As they released their caged neurotransmitter onto the brain slices in the laboratory, Magee and his colleagues aimed to mimic the complexity of the patterns of input that functional neurons receive.

When they did so, Magee said, they saw a spike of localized activity within the dendritic branch they had targeted. “When we gave this input pattern repeatedly,” he said, “the electrical excitability of just the one branch that was receiving the input went way up.” Importantly, the activity spikes the researchers observed in the dendritic trees could adjust to become strong enough to propagate to the cell's axon, triggering a nerve impulse, said Magee.

The researchers also analyzed the effects of stimulating multiple dendritic branches. These studies revealed significant details of how the branches interacted with one another to allow the propagation of local spikes of activity that ultimately contributed to triggering a nerve impulse in the whole neuron.

Magee said that his group's experiments have demonstrated a new form of plasticity in neuronal circuitry that is important for information storage. “This form of plasticity is distinct from--and complementary to--the more traditional synaptic plasticity,” he said. He explained that as repeated signaling increases the strength of a synaptic connection--a process called long term potentiation (LTP)--this would increase the input onto a particular dendritic branch.

“So you have this interesting positive feedback, which is not often found in biological systems, that could perhaps increase the persistence of LTP synaptic plasticity,” he said.

In terms of information storage, said Magee, the localized dendritic plasticity they discovered could enable neurons to store the repeated occurrence of particular patterns of neuronal activity that could represent a complicated stimulus.

“For example, when an animal is in a particular location in a maze, it produces a specific pattern of firing in the hippocampus called a `place field,” he explained. “That place field is a pretty complicated function of many of the stimulus features of the environment. And those complicated features could be stored in the excitability profile of these dendritic branches.”

The next step will be behavioral studies in living animals, Magee said. The researchers will explore whether changing the environment of an animal—adding toys, other animals, and other stimulating objects that promote learning—induces plasticity in dendritic branches.