

TOOLBOX

Technique follows calcium trail to track changes in signaling

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Researchers have genetically engineered neurons to fluoresce in response to the calcium signals they emit when they fire, according to a study published 18 October in *Neuron*¹.

The fluorescence allows researchers to see changes among subtypes of neurons in unsedated mice. It may also offer insights into the brain activity of people with autism.

The labeling offers a broader view of how different neurons interact than has previously been possible in an animal model.

The researchers engineered neurons in two strains of mice to express a molecule called GCaMP3 that senses calcium levels. This molecule fluoresces only when calcium concentration increases in a neuron after it fires.

Both mouse strains have strong expression of the molecule across multiple brain regions, including the olfactory bulb, the cortex, the hippocampus and the cerebellum. However, each strain shows stronger expression in different layers of neurons within these regions. Comparing these differences may reveal how neurons work together to form circuits.

Other groups have delivered calcium sensors to cells via a virus or *in utero*, but were unable to achieve uniform expression across cells or animals. The calcium dyes delivered via virus are also toxic, limiting the time researchers can observe neurons. Stable expression in the mice in the new study allows the researchers to follow the animals throughout their lifetime.

Confirming findings from previous research, the scientists found that different smells activate different areas of the olfactory bulb. Mice habituate to the odor, meaning that their response lessens over time. The fluorescence emitted by the engineered mice is stronger than with other calcium sensors, the study found.

The researchers looked at the signals in both anesthetized and awake (but restrained) mice. They detected spikes of calcium in single **dendritic spines**, the signal-receiving branches of neurons, on the millisecond scale.

The researchers are working to track mice that are fully mobile, allowing them to watch neurons light up as the mice go through their daily lives. They are also engineering neurons in mouse models of autism and obsessive-compulsive disorder.

REFERENCES:

1. Chen Q. *et al. Neuron* **76**, 297-308 (2012) **Abstract**