

mice. Once the calcium in FLiCRE-containing cells spiked—the cellular indication that the mouse is avoiding something—the cells glowed a permanent red that was visible through a microscope. The researchers also sequenced the RNA of the cells to see which ones contained the fluorescent protein, producing a cell-by-cell record of neural activity.

biochemical events, such as protein interactions or neurotransmitter release.

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"One goal was to map how [brain regions](#) are connected to each other in living animals, which is a really hard problem," said Christina Kim, a postdoctoral scholar in genetics at Stanford and co-lead author of the paper. "The beauty of FLiCRE is that we can pulse and activate neurons in one region and then record all of the connected downstream neurons. It is a really cool way to look at long-range brain activity connections."

Provided by Stanford University

In the next experiments, the researchers used the cellular activity map from the first experiments. They also adjusted FLiCRE so that the protein expressed the opsin protein, which can be controlled by orange light to alter neuronal activity. After activating FLiCRE in the cells, the researchers sent orange light through the fiber optic implant whenever the mice would enter a certain room. In response, the mice steered clear of that room, indicating that FLiCRE had indeed located cells in the brain that drive avoidant behavior.

A dream project

The development and testing of FLiCRE combined chemistry, genetics, biology and neuroscience, and many specialties within those disciplines. As a result, the tool has a wide range of possible applications, including in [cells](#) outside the brain, the researchers say.

"I moved to Stanford in 2016 with the hope of being able to carry out extremely interdisciplinary and collaborative projects such as this," said Ting. "This project has been one of the most rewarding aspects of my move to Stanford—seeing something this challenging and ambitious actually work out."

The researchers are now working on additional versions of FLiCRE, with a goal of streamlining the process. They are hoping to simplify its structure and also make it capable of working with other

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