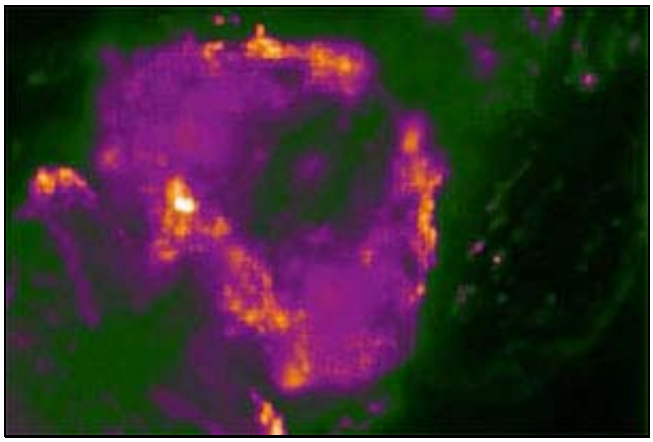
Neuronal Imaging System Shows Bigger 3-D Picture

CAMBRIDGE, Mass., and VIENNA, May 19, 2014 — A new technique could lead to a better understanding of how neuronal networks process sensory information and even how behavior is created in the brain.

A team from MIT, the University of Vienna and the Research Institute of Molecular Pathology has developed an imaging system that can show neural activity and generate 3-D movies of a living animal's entire brain at the millisecond timescale.

“Looking at the activity of just one neuron in the brain doesn't tell you how that information is being computed,” said Ed Boyden, associate professor of biological engineering and brain and cognitive sciences at MIT. “If you want to understand how information is being integrated from sensation all the way to action, you have to see the entire brain.”



Researchers can now image the entire neuronal system of a living animal thanks to a new light-field imaging microscopy technique. Courtesy of MIT.

In a recent study, researchers simultaneously imaged the activity of an entire brain of a zebrafish larva, as well as every neuron in a 1-mm Caenorhabditis elegans worm, using a new brain mapping system.

The latter was used because it is the only organism for which the entire neural wiring diagram is known. The worm has 302 neurons, each of which was imaged as it performed natural behaviors such as crawling. The researchers also observed its neuronal response to sensory stimuli, including smells.

Using an optimized microscope based on light-field imaging, the new method created 3-D images by measuring the angles of incoming rays of light.

While such imaging is not new, this was the first time the technique was used to image neural activity, the researchers said. Until now, doing so over a large volume, in 3-D and at high speed had not been possible. The new technique also produces 3-D images more quickly than with a traditional laser beam, as it demonstrates millisecond neuronal firing as it occurs.

This type of microscope emits light from the sample, which is sent through an array of lenses and refracted in different directions. Each point of the sample generates about 400 points of light that can then be recombined using a computer algorithm to recreate a 3-D structure.

“If you have one light-emitting molecule in your sample, rather than just refocusing it into a single point on the camera the way regular microscopes do, these tiny lenses will project its light onto many points,” Boyden said. “From that, you can infer the three-dimensional position of where the molecule was.”

Neuroscientists could benefit from the new technique, as it could offer more information about the biological basis of brain disorders.

“We don't really know, for any brain disorder, the exact set of cells involved,” Boyden said. “The ability to survey activity throughout a nervous system may help pinpoint the cells or networks that are involved with a brain disorder, leading to new ideas for therapies.”

As detailed as the faster light-field microscopy process is, the researchers noted that there is a shortcoming: It produces lower-resolution scans than techniques that slowly scan samples individually. The team is now working to improve this so it can be used to image parts of neurons, such as their long, branching dendrites.

The researchers plan to combine the new technique with optogenetics, too, which would enable neuronal firing to be controlled by shining light on cells that are engineered to express light-sensitive proteins. By stimulating a neuron with light and observing the results elsewhere in the brain, they could determine which neurons are participating in particular tasks.

The work was funded by the Allen Institute for Brain Science; the National Institutes of Health; the MIT Synthetic Intelligence Project; the IET Harvey Prize; the National Science Foundation; the New York Stem Cell Foundation Robertson Award; Google; the Center for Brains, Minds and Machines at MIT; and Jeremy and Joyce Wertheimer. The research is published in *Nature Methods* (doi: 10.1038/nmeth.2964).

For more information, visit www.mit.edu.