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High-speed imaging method captures entire brain activity

22 May 2014

New technique to monitor complete nervous systems of living animals.

Researchers at the [Institute of Molecular Pathology](#) and the [Max F. Perutz Laboratories](#) in Vienna, Austria, have collaborated with scientists at MIT, Cambridge, MA, USA, to create an imaging system that reveals neural activity throughout the entire nervous system of living animals.

This technique, the first to generate 3D "movies" of entire brains in milliseconds, could help to discover how neuronal networks process sensory information and generate behavior. The work was first published earlier this month in *Nature Methods*.

The team have already used the new system to simultaneously image the activity of every neuron in the worm *Caenorhabditis elegans*, as well as the entire brain of a zebrafish larva, offering a more complete picture of nervous system activity than has been previously possible.

"The new method is an indispensable tool to understand how the brain represents and processes sensory information and how this leads to cognitive functions and behaviour," said physicist Alipasha Vaziri, a joint group leader at the IMP and MFPL and head of the Vienna University research platform Quantum Phenomena & Nanoscale Biological Systems, which led the project.

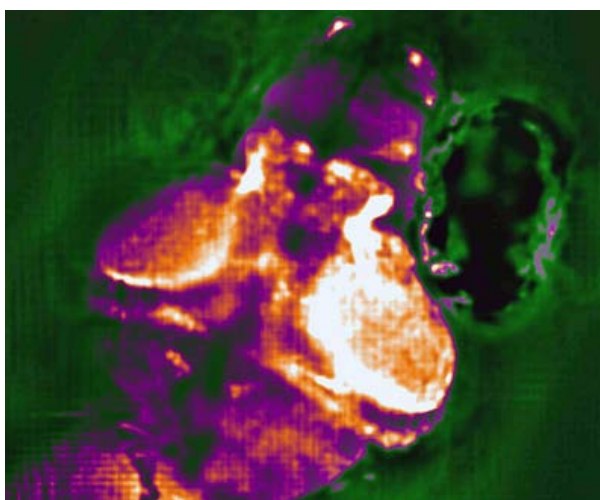
"Because of the enormous density of the interconnection of nerve cells in the brain, relevant information is often encoded in states of this densely interconnected network of neurons rather than in the activity of individual neurons." Vaziri's team developed the brain-mapping method together with researchers in the lab of Edward Boyden, an associate professor of biological engineering and brain and cognitive sciences at MIT.

High-speed functional 3-D imaging

Neurons encode information - sensory data, motor plans, emotional states, and thoughts - using electrical impulses called action potentials, which provoke calcium ions to stream into each cell as it fires. By engineering model organisms that carry fluorescent proteins that glow when they bind calcium, scientists can visualize this electrical firing of neurons in live animals.

Scanning the brain with a laser beam can produce 3D images of neural activity, but it takes a long time to capture an image because each point must be scanned individually. The research-team wanted to achieve similar 3D functional images but accelerate the process so they could see neuronal firing, which takes only milliseconds, as it occurs.

The new method is based on a technology known as light-field imaging, which creates 3-D images by capturing angular information of incoming rays of light. In the new paper, the researchers in Vienna and Cambridge built a light-field microscope which was optimized to have single neuron resolution and applied it, for the first time, to imaging of neural activity.



Brainwaves: Zebrafish larva brain showing pronounced neuronal activity.

With this kind of microscope, the light emitted by the sample is sent through an array of lenses that refracts the light in different directions. Each point of the sample generates about 400 different points of light, which can then

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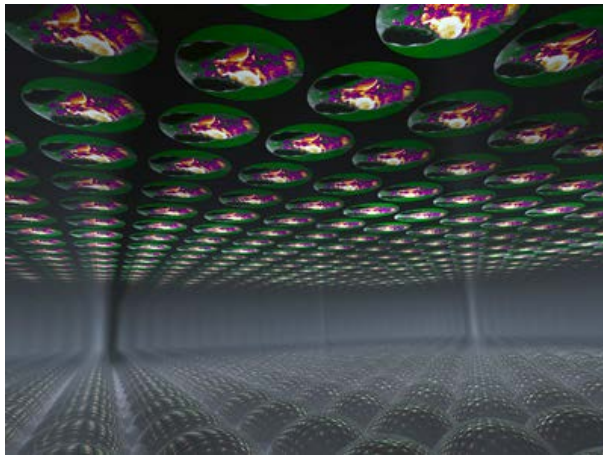
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Microlens array captures different perspectives of the sample.

be recombined using a computer algorithm to recreate 3-D structures.

“Compared to existing methods, our new technology allows us to capture neuronal activity in volumes up to a thousand times larger at ten times higher speed”, says Robert Prevedel, a postdoc in the Vaziri Lab and first author of the paper.

“We have eliminated the need to scan multiple layers, thus the temporal resolution is only limited by the camera sensor and the properties of the molecules themselves.” Prevedel built the microscope at the IMP in Vienna. Young-Gyu Yoon, a graduate student at MIT and co-first author, devised the computational strategies that reconstruct the 3D images.



Neurons in action

The researchers used the technique to image neural activity in the worm *C. elegans*, the only organism for which the entire neural wiring diagram is known. This 1mm-long worm has 302 neurons, each of which the researchers imaged as the worm performed natural behaviors, such as crawling.

To demonstrate the power of the new technology in higher organisms, they also studied larvae of zebrafish. Their nervous system consists of over 100,000 neurons that fire at a much faster rate, rather like humans. In the tiny larvae, the scientists were able to induce neuronal response to odor stimuli in around 500 neurons and track the nerve signals simultaneously in about 5000 activated neurons.

The scientists say that the findings could be ultimately useful in developing new types of algorithms that simulate functions of the brain and predict behaviour. Such models are in high demand in the area of machine learning and object recognition and classification.

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