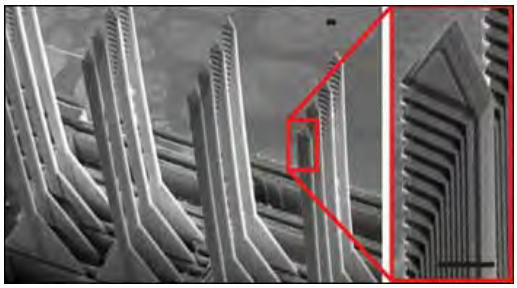
A 3-D Light Switch for the Brain

CAMBRIDGE, Mass., Nov. 19, 2012 — A new tool that delivers precise points of light to living brain tissue in three dimensions could one day help treat Parkinson's disease and epilepsy; it could even aid in the understanding of consciousness and how memories form.

Biologists and engineers at MIT developed the three-dimensional "light switch" using a technique that manipulates neurons with light, known as optogenetics. The method, only a few years old, sensitizes select brain cells to a particular color of light. By illuminating precise areas of the brain, scientists can selectively activate or deactivate the individual neurons that have been sensitized.

Optogenetics allows scientists to play a more active role in probing the brain's connections, to fire up one type of cell or deactivate another and then observe the effect on a behavior, such as quieting a seizure. "You can see neural activity in the brain that is associated with specific behaviors, but is it important?" said Ed Boyden, a synthetic biologist at MIT and a pioneer in the field of optogenetics. "Or is it a passive copy of important activity located elsewhere in the brain? There's no way to know for sure if you just watch."



A scanning electron microscope image of the 3-D array with close-up of a single light-emitting probe. The close-up reveals several light ports along the probe's edge. Images courtesy of A.N. Zorzos, J. Scholvin, E.S. Boyden and C.G. Fonstad/*Optics Letters*.

Entire circuits within the brain can now be explored with the new 3-D tool, which so far has been tested on mice. The 3-D array is precise enough to activate a single kind of neuron, at a precise location, with a single beam of light; previous techniques did not have the same precision. Probes delivering electricity to the brain could manipulate neurons, but they cannot target individual kinds of cells, Boyden said. Drugs can turn neurons on or off, but not on such a quick time scale, nor with such a high degree of control.

A previous version of Boyden's device looked like a needle-thin probe with light-emitting ports along its length; these ports allowed scientists to manipulate neurons along a single line. The new tool contains up to 100 of these probes — each just 150 µm across — in a square grid, so the device looks like a series of fine-toothed combs laid next to each other with their teeth pointing in the same direction.

By adding a third dimension to the light-delivery capabilities, researchers can make any pattern of light they want within the volume of a cubic centimeter of brain tissue, using a few hundred independently controllable illumination points. The implants do not cause any discomfort because the brain lacks pain receptors.

An optical image of the 3-D array with individual light ports illuminated. The array looks like a series of fine-toothed combs laid next to each other with their teeth pointing in the same direction.

Neurons in the brain are not naturally responsive to light, so scientists sensitize these cells with molecules called opsins, light-detecting proteins naturally found in bacteria and algae. Different colors of light turn on different flavors of opsin.

type of opsin it was sensitized with and the color of light used to illuminate it. This gives neuroscientists an unprecedented level of control over individual neurons in the brain, and could be used to study the memory process, the difference between being awake and asleep, and the connections between memory and emotion.

A better understanding of the brain may lead to another benefit: therapy. If particular types of cells malfunction in a particular disease, scientists may be able to use a modified 3-D array as a neural prosthesis that could help treat the neurological condition. For example, light could be used to stop overactive cells from firing, alleviating the uncontrollable muscle action of Parkinson's disease. Implants that correct hearing deficiencies also are being explored with this method.

While the new device is effective in bringing light to the brain, challenges must be overcome before optogenetics can be used for medical therapy, Boyden said. Scientists are still investigating whether the body will detect the opsin proteins as foreign molecules and reject them; gene therapy also will have to prove itself if neurons are to be effectively sensitized with opsin.

The findings appeared in *Optics Letters*.

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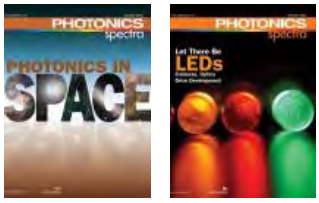

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