

Neurons with the Arch gene are sensitive to light.  
Credit: courtesy of Brian Chow, Xue Han, and Edward Boyden/MIT

A research team led by neuroengineer Edward Boyden has identified a class of proteins that can be used to modify neurons in such a way that exposing them to yellow-green light makes them stop sending signals. This kind of selective brain silencing, reported in *Nature* in January, could not only help treat brain disorders but also allow researchers to investigate the roles that different types of neurons play in normal brain circuits and the ways those circuits can go wrong.

Boyden, an assistant professor in the Media Lab and an associate member of the McGovern Institute for Brain Research at MIT, first demonstrated the use of light to reduce neuron activity in 2007. However, the feat was performed in cells, not living animals, and the silencing was not as precise. In the new study, the researchers used a different protein--one that inhibits neurons more strongly, silences more brain tissue, and returns to its original state within milliseconds after the light is shut off, at which point it can be activated again.

With the newly identified protein, called Arch, brain silencing is "extremely clean and digital," says Boyden. "The other one was more like a volume knob turning up and down."

The researchers' "optogenetic" technique for controlling neuron activity combines genetic and optical technologies. First, they used a virus to deliver the gene that codes for the Arch protein into the brain cells of living mice. The protein functions as a proton pump, moving protons through the cell membrane to alter the cell's voltage. They also implanted an externally controllable light source inside the mice's brains. When yellow-green light shines on the proton pumps, they force protons out of cells, lowering the voltage inside the cells and preventing them from firing.

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The researchers, who screened light-sensitive proteins from bacteria, plants, and fungi, discovered the Arch proton pump in *Halorubrum sodomense*, a strain of archaeobacteria that lives in the Dead Sea. "This is the result of mining the wealth of the natural world--genomic diversity and ecological variation--to discover new tools that can empower scientists to study complex systems like the brain," Boyden says.

His lab is working with dozens of groups at different institutions to assess neuron silencing as a potential therapy for epilepsy, chronic pain, and post-traumatic stress disorder. In collaboration with Robert Desimone's lab at the McGovern Institute at MIT, his group is conducting preclinical studies that will assess the technology's safety and efficacy in nonhuman primates. In future studies, the researchers plan to use their neuron-silencing tools to examine the neural circuits of cognition and emotion.

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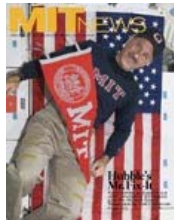
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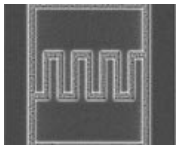
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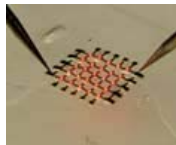
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