Optogenetics: controlling brain cells with lasers

17:37 07 January 2010 by **Ewen Callaway**
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Brain cells can be switched on and off like light bulbs using newly identified microbial proteins that are sensitive to the colour of laser light.

The discovery is the latest in the fast-moving field of optogenetics, which has already given researchers unparalleled control over brain circuits in laboratory animals. The technology may lead to treatments for conditions such as epilepsy, Parkinson's disease and blindness. *New Scientist* explains the science and its promise.

How do scientists control brain cells with lasers?

Neurons fire when electrically charged atoms – ions – flood in and out of them, creating a tiny electric potential across their membranes. In 2005, a team at Stanford University in California reported that light-sensitive microbial proteins that also move ions can cause the same changes when they are genetically engineered into neurons.

One algal protein, channelrhodopsin-2, turns neurons on when bathed in blue light, while its foil, halorhodopsin, silences neurons under yellow light.

If these proteins are already around, what's new?

Channelrhodopsin-2 works swimmingly: it recently helped identify a brain circuit that, when activated, may ease symptoms of Parkinson's.

However, halorhodopsin has fallen short of hopes. The protein fails to fully silence neurons and grows sluggish after repeated cycles of light, says Ed Boyden, a neuroscientist who worked on both proteins at Stanford with his colleague Karl Deisseroth: "It didn't work very well and it hasn't found much of an application."

Now, Boyden's team at the Massachusetts Institute of Technology has discovered two new light-sensitive proteins that are up to the task, at last offering an on/off switch for brain cells. "We can do digital shutdown of neurons," he says.

Why is that useful?

For one, the new proteins give researchers the power to tease out how specific brain circuits underlie behaviour, Boyden says. They can be genetically engineered into specific kinds of neuron, such those involved in forming certain kinds of memories. These cells could then be turned off in laboratory animals to see how their behaviour changes.

Furthermore, one of the newly discovered proteins, called Mac, shuts off neurons under blue light instead of yellow. By expressing Mac in one cell type and a yellow-sensitive "off switch" protein in another, it would be possible to independently silence two sets of neurons that originate in a single area, such as the prefrontal cortex, but dart off to different parts of the brain.

Will optogenetics ever be used to treat diseases in humans?

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It's hard to say. However, clinical trials may begin in the next decade, says Boyden, who is involved in a company, Eos, that aims to use optogenetics to treat blindness. Another fledgling firm is hoping to apply the technology to spinal cord injuries.

The success of these efforts will depend on the ability to safely and effectively send genes and light to neurons – no easy feat.

Even if human brains never come under the control of lasers – as those of flies, mice and even monkeys now have – optogenetics will almost certainly lead to medical breakthroughs, Boyden contends.

If optogenetic research can establish the brain circuits disturbed in neurological and psychiatric illnesses, these cells could be targeted with drugs or more established technologies such as deep brain stimulation. "We can use these tools for real principles of treatment," he says.

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