PROFILE

Ed Boyden
The Synthetic Neurobiologist

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Explaining what a "neuroengineer" is might be challenging, but Ed Boyden, the leader of the Synthetic Neurobiology Group at MIT, is up to the challenge. "Over the years," Boyden says, "we've found a good vocabulary for talking about the issues." The brain is a computer, he explains, a complex electrical and chemical piece of circuitry that entirely mediates our relationship to the outside world. Boyden, and the people he works with, seek to use the methods of engineering to understand this complex system—and understand how to debug and repair the system when it breaks.

These metaphors are apt considering that Boyden studied physics and electrical engineering as an undergraduate. He was motivated to get a Ph.D. in neuroscience, he says, because the brain is one of the most complex physical and electrical systems around. The basic components of this system, neurons, come in thousands of different varieties, and many diseases can be attributed to the dysfunction of particular varieties of neurons.

Early on, Boyden says he was fascinated by the problem of "dialing in information" to particular varieties of neurons in particular parts of the brain. Many different approaches to this problem have been explored, including the use of electrical and magnetic signals. The method of optogenetics that Boyden developed in collaboration with Karl Deisseroth, Georg Nagel, and others uses a counterintuitive signaling mechanism: light, delivered into the brain on a fiber-optic cable.

The "-genetics" in optogenetics refers to the genetic modification of neurons. The brain is not naturally responsive to light. To make the technique work, Boyden needed to coax blind neurons to react—quickly—to a

light source. A pivotal moment occurred in early 2004 when Boyden (in true graduate student form) was in the lab at 1 a.m. With him were some neurons that had been genetically modified to produce channelrhodopsin-2, a protein that helps green algae move toward light. When he flashed a blue laser at the neurons, they produced precise and predictable electrical signals in response. Boyden had the beginnings of a high-bandwidth input channel straight into the brain.

This success, however, preceded several setbacks. Boyden's work was rejected by *Science* on the grounds that "we hadn't made any discoveries beyond finding that channelrhodopsin-2 functioned well in neurons." As Boyden tells it, it got worse from there. In 2005 he was applying for academic positions, and the people he spoke with seemed split between the view of the *Science* reviewers and the view that "all this is science fiction." (He recalls thinking "You can't both be right!" with some frequency.)

Initial setbacks were certainly matched by later successes. Optogenetics has been used to observe and manipulate the neural basis of learning, addiction, and fear in mice, and even to restore sight to blind mice by making other neurons in the retina photosensitive. Beyond mice, the technique has been applied successfully in studies involving everything from zebrafish to (nonhuman) primates. These successes won optogenetics the title of 2010 Method of the Year by *Nature Methods*. "I would say that it's very important—if you're correct—to be persistent," Boyden observes dryly about the experience, though he emphasizes the "if you're correct" bit.

The MIT Media Lab turned out to be a good academic match for Boyden, where he started a group called Neuroengineering and Neuromedia. Since then he's worked hard at presenting his ideas through a blog, a series of hands-on courses for MIT undergraduates, and the multi-month preparation for his talk at the TED conference. The term "synthetic neurobiology" itself is a good example of Boyden's eye for useful terminology. It was first serendipitously suggested by Doug Lauffenburger, the head of MIT's Department of Biological Engineering. The field of synthetic biology is concerned with developing good abstractions layers that can enable the engineering of living organisms. Boyden thought the term captured his group's goals well enough that he renamed the group!

Boyden is clearly excited about the work his group is doing, which goes far beyond his existing work on optogenetics. About a third of his colleagues are working on molecular engineering problems, he says, and another third are working on neural devices to read signals out of the the 3-D structure of the brain.

When asked about how narrow or broad he wants his future research focus to be, Boyden's response is simple: "We are engineers." He and his colleagues will go where there are important problems to be solved.

If you're interested in learning more, Ed Boyden's TED talk "A Light Switch for Neurons," as well as the very approachable article "A History of Optogenetics: The development of tools for controlling brain circuits with light," can be found at syntheticneurobiology.org.