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March 19, 2013

## A Laser Light Show in the Brain

Posted by *Gary Marcus*

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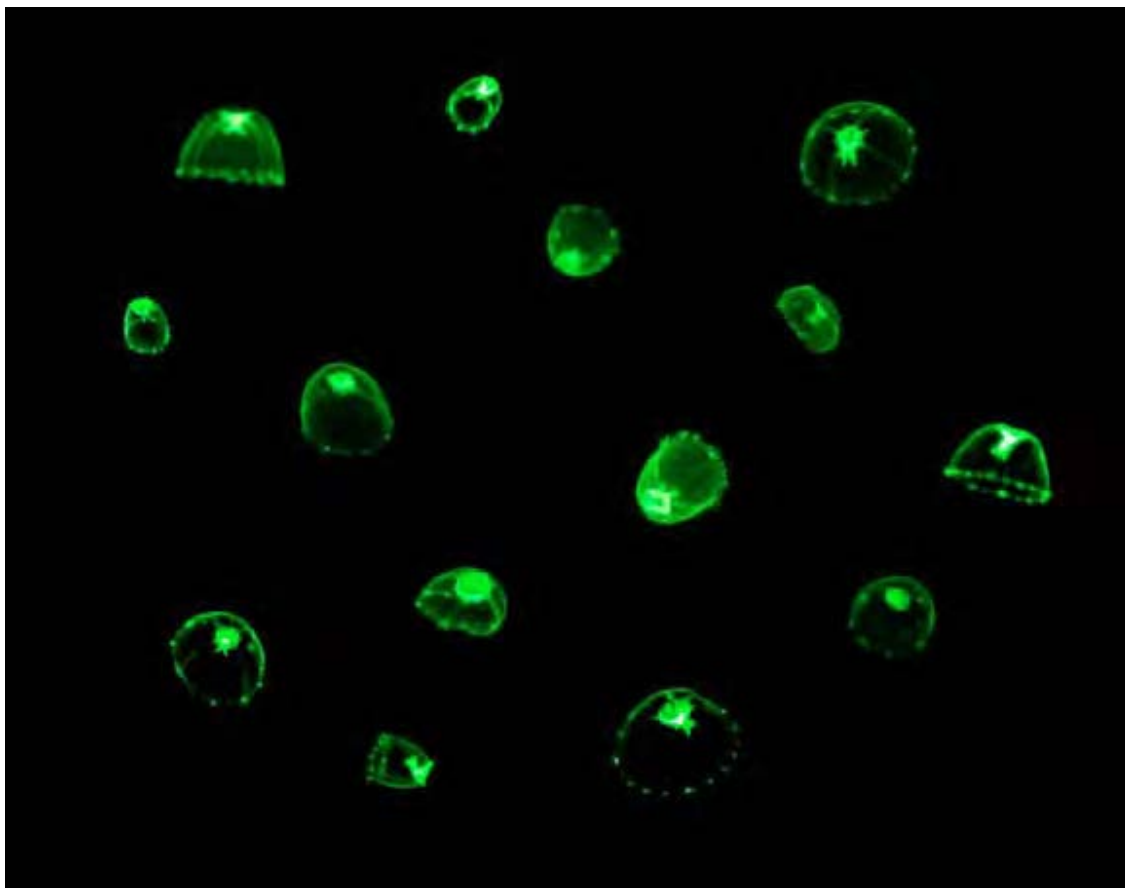
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In 1992, Martin Chalfie made a spectacularly useful discovery, which I like to think of as perhaps the greatest use of cut-and-paste. Chalfie began with the fact that every gene has two parts: an encoding sequence that, using RNA as an intermediate, specifies a set of amino acids from which a cell can synthesize a protein, and a regulatory sequence that specifies, indirectly, when and where that protein should be built. By attaching the protein-coding end of a gene called GFP—a protein borrowed from a jellyfish that glows under a black light—to the regulatory region of other genes, Chalfie invented a new way in which scientists could harness nature's toolkit to watch the actions of individual cells. It became possible to induce a particular class of neurons to shine under black light in order to ferret out what sort of circuit they might participate in.

In the summer of 2004, Ed Boyden and Karl Deisseroth, both working in the laboratory of Richard Tsien, took similar principles to an entirely new level, using the encoding sequence of a protein called ChR2, borrowed from unicellular green algae, which guides movement in response to light. In collaboration with Ernst Bamberg and Georg Nagel, Boyden and Deisseroth repurposed the gene into something new: a tool that could make individual neurons (or sets of neurons) fire on command. Boyden and Deisseroth then brought lasers, computers, and fibre optics into the mix, creating a way in which hundreds, or even thousands, of neurons could be manipulated in living, breathing animals with millisecond timing. (Previous techniques were less precise, and were largely limited to cells in a dish.) By shining lasers through optical fibres aimed at particular populations of neurons at specific times, a technique known as optogenetics, investigators can now effectively direct symphonies of light-induced neural activity inside the brain.

The impact of this on understanding neuroscience is immense. As Steven Pinker once put it (at the prompting of Stephen

Colbert), the secret to the brain is that “brain cells fire in patterns.” But the trick to understanding the brain is to understand which cells fire in which patterns—when and where. Before optogenetics, neuroscientists were faced with the intractable nightmare of separating causation from correlation, knowing (sometimes) which neurons were associated with a given process without knowing which ones actually performed a given computation. Neuroscientists were consigned largely to be spectators, with little insight into which neurons were truly doing the heavy lifting in any particular task. It was possible to watch brain cells in action, but not to perform controlled experiments at the micro level in a living organism. For anyone trying to understand the brain, this transition from onlooker to participant has been a godsend.

Optogenetics has already been adopted by roughly a thousand labs, in both in academia and industry, many directed by Nobel Prize winners. Earlier this week, Boyden and Deisseroth shared the 2013 Grete Lundbeck European Brain Research Prize, worth a million euros, with four others, for the discovery.

Boyden, now all of thirty-three years old, is currently hard at work on another collaboration, this one with the Georgia Tech mechanical engineer Craig Forest, developing a technique that involves using microrobots to automatically perform patch clamping, another procedure critical to understanding the brain. Patch clamping allows investigators to record the firing of individual neurons with great precision. It used to take talented graduate students months to master. Boyden’s hope, he explained to me, is to democratize the technique in way that will allow thousands of labs to use it, instead of a handful. Between optogenetics and automated patch clamping, scientists will be able to study the brain in ways we couldn’t have imagined two decades ago, automatically isolating circuits and determining their functions. Luckily, as a member of the younger generation, Boyden is a firm believer in open-sourcing; his techniques are available to all. You can even download the plans for building your own automated patch clammer on a Web site he helped set up.

Neuroscience needs theories as much as it needs techniques—but with techniques like Boyden’s, the field is finally on good footing.

*Gary Marcus, a scientist and the author of Guitar Zero, has written sixteen essays for The New Yorker, on topics ranging from to Noam Chomsky, Nate Silver, and Ray Kurzweil to challenges in neuroscience, robotics, and artificial intelligence.*

*Photograph by Charles Mazel/Corbis.*

## Keywords

- neuroscience;
- optogenetics;
- science

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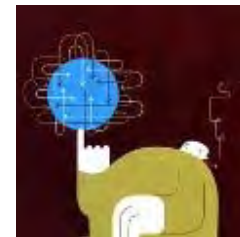
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