



THE ULTIMATE OPTICAL

# Voltage Sensor

*Off to the Races . . .*

**A** longstanding dream in neuroscience has been finding a way to monitor neural activity across the entire brain. In the 1960s, the only way to record a neuron's voltage was to stick an electrode in it, an approach limited to a few cells at a time. The person who changed all that is Larry Cohen of Yale University, who has been a near-constant summer presence at the MBL since 1962. "Larry is the original 'Mr. Light,'" says David Gadsby of Rockefeller University. "He pioneered the study of brain activity using electro-optical measures."

Cohen started his journey after co-discovering that when neurons fire, they undergo changes in light scattering and other optical properties. Perhaps a camera could record such changes, and use them as a proxy for electrical activity? The idea was "pretty far out," says Cohen's MBL colleague George Augustine. But it was evidently fertile, as functional neuroimaging is now a huge endeavor, at the MBL and around the world.

In 1973, Cohen, Vicencio Davila, and Brian Salzberg at the MBL successfully made the first optical recording of a leech neuron firing. They did this by bathing the neuron in a fluorescent dye. When the neuron fired, the fluorescence changed, and a detector captured the change. Since then, with many contributions from MBL researchers, various optical sensors have been introduced, the latest being genetically engineered ones that, in principle, can target specific neurons. Today, the race is on to design better sensors, ones that give fast, big signals and—crucially—show which individual neurons in a brain region fire, and when. Two promising sensors are Cohen's latest, called ArcLight, and one from Adam Cohen of Harvard (MBL Physiology alumnus, 2007), called Arch.

"Once we get that ultimate sensor, it's off to the races, in terms of mapping the connectome," says Augustine, who recruited Larry Cohen to the Center for Functional Connectomics (see p. 10). "When that happens, everybody is going to jump into the game. Things are poised right now, ready to blow." • — DK

*A neuron expressing the ArcLight Q239 probe visualized with confocal microscopy. Image courtesy of Larry Cohen*