



THE ULTIMATE OPTICAL

# Voltage Sensor

A long-standing 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 best-in-class voltage sensors.