

Hacking Fluorescent Proteins to Image Brain Electrical Activity

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The ability to image brain activity is critical to understand how we learn, think, sense, plan movements, and behave. It can also help understand how neurological disorders impact brain function, paving the way for cures or treatments. Major challenges to imaging the brain in animal models of neurological diseases are that brain activity is rapid (millisecond-timescale) and operates at spatial scales down to less than a micron. There are existing tools to image neural activity, but they have important limitations, such as being too slow to follow fast brain activity, having poor spatial resolution, being unable to record from many brain cells, or only allowing imaging at the very surface of the brain.

We seek to address these unmet needs in brain imaging by developing genetically encoded voltage indicators (GEVIs), which are proteins who emit flashes of light when neurons are active. Because GEVIs are biological (proteins), they can be produced by the animals themselves, eliminating the need for invasive placement of sensors such as electrodes. An additional benefit is that simple genetic methods can be used to restrict GEVI expression to specific cell types (e.g. neurons producing a specific kind of neurotransmitter), enabling neuroscientists to study the respective functions of genetically distinct groups of neurons.

In this talk, I will discuss our efforts to engineer GEVIs with sufficient performance for routine optical imaging of brain activity in animal models, highlighting both successes and challenges. We also present recent applications of this technology and discuss what is feasible now and what we anticipate will become possible with future indicator development. As GEVIs are further engineered, we anticipate that they will become broadly used by the neuroscience community to eavesdrop on brain activity with unprecedented spatiotemporal resolution.