

Abstract

Verifying causal effects of neural circuits is essential for proving direct a circuit-behavior relationship. However, techniques for tagging only active neurons with high spatiotemporal precision remain at the beginning stages. Here we developed the soma-targeted Cal-Light (ST-Cal-Light) which selectively converts somatic calcium rise triggered by action potentials into gene expression. Such modification simultaneously increases the signal-to-noise ratio (SNR) of reporter gene expression and reduces the light requirement for successful labeling. Because of the enhanced efficacy, the ST-Cal-Light enables the tagging of functionally engaged neurons in various forms of behaviors, including context-dependent fear conditioning, lever-pressing choice behavior, and social interaction behaviors. We also targeted kainic acid-sensitive neuronal populations in the hippocampus which subsequently suppressed seizure symptoms, suggesting ST-Cal-Light's applicability in controlling disease-related neurons. Thus, the versatile ST-Cal-Light system links somatic action potentials to behaviors with high temporal precision, and ultimately allows functional circuit dissection at a single cell resolution.