
A bimodal bioluminescent calcium indicator toward spatiotemporally-scalable imaging

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Abstract

For decades, fluorescence- and luminescence-based Genetically Encoded Calcium indicators (GECIs) have been developed to visualize intracellular calcium dynamics. However, each GECI is constrained in some ways. For example, high spatial and temporal resolution of fluorescence imaging requires external light illumination which can cause photobleaching, phototoxicity, and autofluorescence limiting applicability for studying light sensitive biological phenomena. Bioluminescence imaging overcame these restraints and enhanced compatibility with optogenetic tools. But the spatiotemporal resolution of bioluminescence imaging is worse than that of fluorescence. Here, we developed a novel bimodal fluorescence- and bioluminescence-based intensimetric calcium indicator (FB-GECI) using single fluorescent protein calcium indicator and a luciferase based binary complementation system. FB-GECI has a moderate calcium affinities for measurement of cytosolic calcium concentration. FB-GECI in bioluminescence mode possesses the highest dynamic range (2800%) of currently available bioluminescent GECI (ratiometric GECI CalfluxVTN (900%) and intensimetric GECI GeNL(Ca²⁺) (450%)). FB-GECI reveals cytosolic free calcium dynamics upon histamine stimulation in HeLa cell with high spatial and temporal resolution in both modes. The ability to be able to switch between fluorescent and bioluminescent mode with a single probe should benefit transgenic applications where micro and macro scale observation of cells or tissues, respectively, may be desirable. FB-GECI therefore extends the spatiotemporal window over which single calcium imaging probes operate.

Keywords: bimodal, calcium, scalable

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