Abstract View

HIGH SPATIAL AND TEMPORAL RESOLUTION ESTIMATES OF CALCIUM DYNAMICS IN DENDRITIC SPINES USING MCELL SIMULATIONS.

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Calcium plays a critical signaling role in many biological systems. For example, in the postsynaptic neuron, increases in Ca^{2+} concentration are believed to be essential for the induction of long-term potentiation and long-term depression, changes in synaptic efficacy thought to be the cellular mechanisms underlying learning and memory. Measurements of intracellular Ca^{2+} have typically relied on the use of fluorescent imaging where the sensors used buffer the Ca^{2+}, obscuring concentration measurements, and have limited spatial and temporal resolution. In postsynaptic spines, the spatial localization of Ca^{2+}-dependent effectors such as calmodulin, CaMKII and calcineurin make the measurement of Ca^{2+} concentration in the entire spine less than ideal. Using MCell, a Monte Carlo simulator, to monitor both the influx of Ca^{2+} into a spine and dendrite and its reactions with intracellular molecules, we have reproduced fluorescent transients measured in neocortical and hippocampal neurons. This has allowed determination of the unperturbed Ca^{2+} dynamics and suggests kinetics and concentrations of endogenous Ca^{2+} binding proteins. We have measured Ca^{2+} concentrations in microdomains throughout the spine showing highly heterogenous concentrations of free intracellular Ca^{2+}. Furthermore, we show the spatial and temporal activation of different Ca^{2+}-dependent effectors resulting from asynchronous pairing of pre- and postsynaptic action potentials. To complement experimental studies, we show how computer simulations can offer an alternate and complementary method of assaying intracellular Ca^{2+} dynamics and reactions.

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