Computational reconstitution of spine calcium transients from individual proteins

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Abstract

A stochastic model which simulates Ca^{2+} transients in spines from principal molecular components was built using MCell. Kinetic models were taken from *in vitro* studies for nine different proteins. Voltage changes were modelled in NEURON. The simulation worked, demonstrating that the *in vitro* data can be used for *in vivo* modelling.

Methods

MCell was used for the simulation. It allows for spatial modelling of the molecules as well as binding/unbinding and molecule pumps.

Geometry

A section of neuropil was modelled as a $6 \times 6 \times \times 5 \mu m$ cuboid. This was based on images of actual hippocampal neuropil taken by electron micrographs.

Stimuli

Two types of stimulus were used. One simulating an EPSP caused by glutamate release. One a backpropagating action potential, caused by an injection of current into the axon hillock.

Source of Ca^{2+} Influx

The following sources of Ca^{2+} influx were simulated:

Glutamate receptors AMPA receptors and NMDA receptors were placed on the post-synaptic membranes overlying the post-synaptic dendrites. Certain densities per micro metre were used to decide how many receptors to place.

Voltage Dependent Calcium Channels The biggest source of Ca^{2+} influx in the simulation. Things considered here were the density of VDCC, which is not well known, the different types of channel, L, R, and T, and the activation and deactivaton dynamics of each type of channel.

Glutamate transporters

Cytosolic Ca^{2+} Binding Proteins

The following binding proteins were simulated within the cell cytoplasm:

Immobile cytosolic Ca^{2+}-binding proteins The molar concentration used was $78.8\mu M$ with a K_D of $2.0\mu M$. The concentration of this type of buffer has estimates from $10\mu M$ to $100\mu M$.