BMC Neuroscience

Poster presentation

Open Access

Temporal sensitivity of protein kinase A activation in a stochastic reaction-diffusion model of late phase long term potentiation

Myungsook Kim, Rodrigo Oliveira, Wonryull Koh and Kim Blackwell*

Address: Molecular Neuroscience Department, George Mason University, Fairfax, 22030, USA

Email: Kim Blackwell* - kblackw1@gmu.edu

* Corresponding author

from Eighteenth Annual Computational Neuroscience Meeting: CNS*2009
Berlin, Germany. 18–23 July 2009

Published: 13 July 2009

BMC Neuroscience 2009, **10**(Suppl 1):P202 doi:10.1186/1471-2202-10-S1-P202

This abstract is available from: http://www.biomedcentral.com/1471-2202/10/S1/P202

Introduction

The ability of neurons within the hippocampus to differentially respond to specific temporal and spatial patterns of stimulation underlies the storage of memory and information in neural circuits. Signal transduction pathways are critical for information storage and alterations in key signaling molecules, such as the cAMP-dependent protein kinase (PKA) signaling pathway, modify both hippocampus-dependent learning and a form of synaptic plasticity known as late-phase long-term potentiation (L-LTP). The induction of late phase LTP (L-LTP) in the CA1 region of the hippocampus requires several kinases, including CaMKII and PKA, which are activated by calcium-dependent signaling processes and other intracellular signaling pathways. Many of the biochemical reactions leading to activation of these critical kinases are localized to dendritic spines. The small size of theses spines implies that small numbers of molecules are involved; the presence of anchoring proteins and the morphology of neurons implies that molecules are inhomogeneously distributed. Therefore, to accurately model these cellular signaling events requires software for stochastic reaction-diffusion systems.

Methods

We developed a spatial, stochastic, computational model of CA1 signaling pathways to investigate the sensitivity of PKA to spatial and temporal patterns of stimulation. The model is implemented using NeuroRD, novel software for efficient computational modeling of stochastic reaction-diffusion systems. The model describes the interactions of calcium and cAMP signaling pathways and is based on published biochemical measurements of two key synaptic signaling molecules, PKA and CaMKII. The model is stimulated using four 100 Hz tetani separated by 3 sec (massed) or 5 min (spaced), identical to experimental L-LTP induction protocols.

Results

The cAMP concentration is larger in response to massed, as compared to spaced stimulation, similar to the results observed for a deterministic model. Though cAMP directly activates PKA, the ability to differentiate the effect of temporal stimulation pattern on PKA activation depends on morphological factors such as the size of the spine head, and whether PKA is anchored in the spine. In very small spines without anchoring, only a few molecules of PKA are activated; thus the effect of stimulation, much less temporal pattern, is not apparent. In contrast, in large spines temporal stimulation pattern influences PKA activation, and spaced stimulation produces a larger cumulative activity than massed stimulation. This leads to enhanced phosphorylation of Inhibitor-1, and inhibition of protein phosphotase 1. Additional simulations further explore the effect of anchoring and protein co-localization on PKA activation in response to LTP stimulation.

Acknowledgements

The support of HFSP (program grant RGP0001/2005) and NIH (RO1 AA180660) is gratefully acknowledged.