Print this Page

Presentation Abstract

Program#/Poster#:	432.3/E9
Title:	Presynaptic Calcium dynamics and geometrical constraints on plasticity in a hippocampal synapse
Location:	Hall A-C
Presentation Time:	Monday, Nov 17, 2008, 3:00 PM - 4:00 PM
Authors:	***S. NADKARNI**[1], T. M. BARTOL, Jr[2,1], T. J. SEJNOWSKI[2,1,3], H. LEVINE[1]; [1]Ctr. Theoretical Biol Physics, UC San Diego, La Jolla, CA; [2]Computat. Neurobio. Lab., The Salk Inst. for Biol. Studies, La Jolla, CA; [3]Howard Hughes Med. Inst., Bethesda, MD
Abstract:	The probability of vesicular neurotransmitter release is governed by calcium dynamics acting in microdomains in presynaptic boutons. In CA3-CA1 hippocampal synapses the release probability can vary over a broad range and can be modulated leading to facilitation or depression of synaptic transmission that can last from milliseconds to minutes in a stimulus dependent manner - a manifestation of synaptic plasticity. The molecular machinery involved in plasticity is highly organized and interacts nonlinearly to give rise to the complex patterns of neurotransmission observed experimentally. We use MCell to perform realistic 3D Monte Carlo simulations of the molecular interactions that regulate vesicular release in a model CA3-CA1 hippocampal synapse. Our computational experiments allow us to simultaneously investigate the structural and activity dependent constraints that underlie neurotransmitter release by tracking the behavior of individual molecules as they diffuse and interact with one another in 3D. Our simulations suggest that a physiological stimulus train is sufficient to trigger calcium induced calcium release (CICR) from stores in the endoplasmic reticulum (ER), via Inositol triphosphate receptors (IP3Rs) channels in the ER of the presynaptic terminal. This leads to a sustained increase in base level calcium and a consequential augmented probability of neurotransmitter release that lasts several seconds, a novel form of short term potentiation. However, this effect can go from facilitation to depression depending on the exact arrangement of the CICR machinery as well as the timing of the stimulus train. Our simulations also allow us

to make an experimentally testable prediction on the channel cluster distance and channel number in the presynaptic terminal of a hippocampal CA3-CA1 synapse that is based on the variance of the release probability. Furthermore, we explore the effect of buffer mobility and changes in effective diffusion of calcium on neurotransmitter release probability.

Disclosures: **S. Nadkarni** , None; **T.M. Bartol**, None; **T.J. Sejnowski**, None; **H. Levine**, None.

Support: NSF-PHY0216576

NSF-PHY0225630

NIH-R01GM069630

NIH-P01NS044306

Howard Hughes Medical Institute

[Authors]. [Abstract Title]. Program No. XXX.XX. 2008 Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, 2008. Online.