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Presentation Abstract

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Presentation Title: The computational impact of local dendritic protein translation on synaptic plasticity and memory

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Abstract: The stabilization of long-term synaptic plasticity beyond a few hours requires the synthesis of new proteins. However, unlike most other proteins, these plasticity-related proteins (PRPs) are not synthesized in the neuron's cell body but are instead translated primarily in dendrites near the activated synapses. Recent experiments demonstrate that, after translation, PRPs are restricted to small spatial domains close to the site of synthesis (~100 um), roughly the size of a single dendritic branch (Govindarajan et al., 2011). Despite the crucial role of this process in long-term memory, its general function and consequences are not known. We used computational modeling to study this problem.
Our novel simplified model of synaptic plasticity in a dendritic neuron was based on data from the rodent hippocampal CA3-CA1 synapse. The model included AMPA receptor dynamics in dendrites, spines and synapses (via trafficking and exo/endocytosis), generic synaptic kinase and phosphotase dynamics and PRP dynamics. Early LTP/LTD occurred through elevation of spine exo/endocytosis rates and up/downregulation of PSD trapping of AMPARs. In contrast, late (PRP-dependent) LTP/LTD was mediated by up/down regulating the number of AMPAR 'slots' in the PSD (Redondo and Morris, 2011).
Next, we analytically calculated the expected effects of each biological parameter on synaptic plasticity rules, including inter-synapse distance, inter-stimulus time interval, PRP diffusivity, PRP synthesis/degradation rates, and kinase/phosphotase decay rates. We found that each protein synthesis event created a spatio-temporal window within which synaptic strength changes were consolidated. Synaptic changes that occurred outside this window were forgotten within hours.

We used the model to ask how local dendritic PRP translation affects synaptic dynamics and memory storage. The model's synaptic dynamics fell into one of three different regimes, depending on conditions: 1) competitive, 2) cooperative, and 3) independent. Competition occurred when PRPs were scarce (few 'strong' PRP-translation-inducing synaptic stimuli and many nearby 'weak' synaptic stimuli). Cooperation, in contrast, occurred when PRPs were abundant (when the number of strong synaptic stimuli outnumbered nearby weak synaptic stimuli). Synaptic stimuli separated in space and/or time were independent.
Dendritic translation also improved memory storage of important items, because unimportant items (synaptic changes from weak stimuli) were often not consolidated. This helped to reduce the detrimental effects of overwriting on important memory retention.

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TRANSLATION

DENDRITE

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