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Poster presentation

Modeling the effects of GABA-A inhibition on the spike timing-dependent plasticity of a CA1 pyramidal cell

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A detailed CA1 microcircuit (MC) model of the hippocampus has been recently advanced to investigate the biophysical mechanisms by which hetero-association of spatio-temporal input patterns is achieved in the hippocampus [1,2]. The network model consisted of pyramidal (P) cells, basket (B) cells, axo-axonic (AA) cells, bistratified (BS) cells and oriens lacunosum-molecurale (OLM) cells. Inputs to the network came from the entorhinal cortex (EC), the CA3 Schaffer collaterals and medial septum (MS). The EC input provided the sensory information, whereas all other inputs provided context and timing information. The MS input paced the network theta rhythm activity. Storage and recall of memories were separated into different functional theta half-cycles. Storage was accomplished via a local spike timing-dependent plasticity (STDP) rule mediating hetero-association of the postsynaptic PC response due to the incoming EC input and the CA3 input spike pattern on the pyramidal cell stratum radiatum (SR) AMPA synapses. The model simulated the timing of firing of different hippocampal cell types relative to the theta rhythm and proposed functional roles for the different classes of inhibitory interneurons in the storage and recall cycles of input patterns. Memory capacity and recall performance of the MC model were quantitatively studied. Particular emphasis was given as to how the temporal patterning of the inputs interacted with the STDP learning to either promote or inhibit pattern storage and hence ultimately pattern recall. In this work, we extend the STDP rule applied to the PC-SR AMPA synapses of the CA1 MC model with a Ca^{2+} dynamics STDP model applied to the PC-SR NMDA synapses in order to study how GABA inhibition affects the detailed CA^{2+} dynamics underlying synaptic plasticity on the NMDA synapses of the CA1 pyramidal cells. Experimental studies has shown that GABAergic inhibition in the proximal stratum radiatum (SR) dendrite of the hippocampal CA1 pyramidal neuron is probably responsible for the observed symmetry-to-asymmetry transition of the STDP curve [5]. Recent computational works from our group [3,4] predicted that symmetry-to-asymmetry transition is strongly dependent on the frequency band (theta vs. gamma), the conductance value of $GABA_A$ inhibition and the relative timing between the GABAergic spike train and the pre- and post-synaptic excitation. Two distinct long-term depression (LTD) tails of the symmetrical STDP curve were shown to be centered at +10 ms, +40 ms and -10 ms, respectively. The largest LTP value and the two distinct LTD tails were inversely proportional to the increase of GABA conductance. With this work we continue to investigate the effects of the GABA inhibition on the STDP learning curve in the presence of more complex excitatory inputs such as triplets, quadruplets and bursts. We explore in more detail the effects on the STDP curve of various gamma frequency sub-bands (40 Hz, 75 Hz and 100 Hz), the $GABA_A$ conductance value and the relative timing of the GABA inhibition with the complex excitatory inputs. An important implication of these results is that they raise the possibility that GABAergic interneurons can be "trained" to fire at specific times and frequencies, and con-

sequently facilitate or depress the encoding and retrieval of information in the hippocampus.

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