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Development of Model Neuron Encoding the Realistic Learning Rule

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Makoto Nishiyama
New York University School of Medicine

Kyonsoo Hong
New York University School of Medicine

Activity-dependent synaptic modifications, long-term potentiation (LTP) and depression (LTD) are essential in information processing and storage in neural networks. Thus, understanding mechanisms of synaptic modifications are crucial in understanding learning and memory functions. The long-term goal of our research is to understand how synaptic modifications are involved in information processing in hippocampal neural network. However, the complexity of central neural networks hinders addressing these issues through biological approaches alone. Therefore, we propose to combine electrophysiological and computational modeling approaches to develop a model neuron system encoding synaptic modifications induced by repetitive, correlated pre- and postsynaptic activity in rat hippocampal slices. These studies will enable us to predict how synaptic modifications modulate the multiple spatiotemporal-distinct inputs in neuronal networks that are beyond current electrophysiological techniques.

GABAergic activities are known to serve as a driving force for hippocampal oscillations that underlie spatial memory processing. How spatiotemporal regulation of GABAergic functions contribute during repetitive, correlated pre- and postsynaptic activity in the CA1 neural network, which likely occur during hippocampal θ/γ oscillations, is, however, largely unknown. By whole-cell recording and computational modeling from CA1 pyramidal cells, our recent studies reveal that postsynaptic $GABA_A$ inhibition directs timing- and magnitude-dependent spike-timing-dependent LTD (*t*LTD) at the θ frequency, while presynaptic $GABA_B$ inhibition directs frequency-dependent *t*LTD at α/β frequencies, which bounds the expression of spike-timing-dependent LTP (*t*LTP) at excitatory synapses at θ/γ frequencies. This *t*LTP at the θ frequency was accompanied in parallel by *t*LTP at inhibitory synapses onto the soma, which bear a resemblance to the spatiotemporal feature of the θ oscillation found in hippocampal neural networks *in vivo*. Postsynaptic $GABA_A$ excitation, on the other hand, augmented *t*LTP at the γ frequency, revealing bifunctional GABAergic activity. We, therefore, propose that spatiotemporally regulated GABAergic activities direct timing, magnitude and frequency-dependencies of spike-timing dependent synaptic plasticity (STDP) at excitatory synapses, and a similar mechanism may underlie hippocampal oscillation-governed information processing.