Model Neuron Encoding the Realistic Learning Rule
Makoto Nishiyama
New York University School of Medicine

Activity-dependent synaptic modifications, long-term potentiation (LTP) and depression (LTD) are essential for information processing and storage in neural networks. Thus, understanding mechanisms of synaptic modifications are crucial for 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 networks. In this project, we used combined approaches of whole-cell recording and computational analysis to demonstrate the sophisticated mechanism of gating of spike timing-dependent LTD by differential GABAergic inhibitory activities at excitatory synapses in CA1 pyramidal cells. Our main findings are 1) postsynaptic GABAA-mediated inhibition gates the timing- and EPSC amplitude-dependent LTD induced by the spike-timing protocol at the frequency. This gating mechanism limits the induction of LTP to a 15-msec time window, and imposes a cooperative requirement for LTP induction. 2) Presynaptic GABAB-mediated inhibition gates the frequency-dependent LTD at and frequencies, thereby reinforcing the appearance of LTP at and frequencies.

The broader impact of this work, in addition to the discovery of the GABA-mediated gating function of the spike timing-dependent LTD, is that it suggests the possibility that intrinsic neuronal activities of and oscillations in the hippocampus can dictate each individual synaptic gain. This work also provides insight into the molecular dynamics by which the interaction of slow-kinetic IPSPs and NMDA channels (decay time constants of > 40 msec and >25 msec, respectively) creates 10 msec-temporal resolution for bidirectional synaptic plasticity. To accomplish this project, two Japanese students, one with an engineering background and neither biological training nor English speaking, and the other with a broad knowledge of both biology and computer science and educated in the US, were collaborated closely with the PI.

PI Website

http://www.med.nyu.edu/people/nishim01.html

Publications

Nishiyama, M., Togashi, K., Yoshida, N., Aihara, T., Kitajima, T. and Hong, K. Gating of spike timing-dependent long-term depression by GABAergic activity in the hippocampus. (Submitted)