

Mutli-compartment model of synaptic plasticity

E. Paxon Frady 

We introduce a biophysical model of a neuron that can accurately replicate many classical plasticity experiments including work by Golding et al demonstrating the importance of dendritic spikes for the induction of LTP. The model uses Hodgkin and Huxley channel dynamics across multiple compartments. It includes the familiar sodium and potassium channels, as well as AMPA, NMDA, and VGCC channels which follow the kinetic equations presented in Destexhe et al (AMPA, NMDA) and Abarbanel et al (VGCC). Along with voltage, calcium concentration is a primary state variable and it is responsible for signaling plasticity changes following the simple calcium control hypothesis presented by Shouval et al, which describes two thresholds for plasticity: one that induces LTD and a higher one that induces LTP. Results from Markram et al, Bi & Poo and Sjostrom et al were also replicated using the model showing the different effects relative spike-timing, stimulation frequency, and cooperativity have on plasticity can be implemented using biophysically known mechanisms and a simple calcium-based learning rule.

Golding et al demonstrate that dendritic spiking is strongly correlated with the induction of LTP even when somatic action potentials were locally blocked using TTX. Like what was reported in the Golding experiments, only strong or cooperative stimulations were able to elicit LTP in our model when the somatic action potential was blocked. A low-density distribution of sodium and potassium channels in the dendrites most accurately explains the findings of Golding's experiment, and shows how the spatial distribution of proteins can be used to alter the properties of a neuron. Plasticity was only induced when excitation was strong enough to elicit a dendritic spike by these channels, showing the necessity for the existence of active channels in the dendrites. However, too high of a channel density (especially potassium channels) resulted in large, but skinny dendritic spikes – both factors reducing the magnitude of the plasticity signal. Shouval et al report a similar problem with action potentials being too fast to effectively induce plasticity using NMDA channel kinetics as the primary mechanism; this is reconciled by this model through the use of low-density channels to make the dendritic spike broader. These experiments demonstrate how the circuit can manipulate a neuron's properties using the spatial extension of the dendritic tree. Further, this model shows that the localization and density of active channels determines how activity in the circuit influences the properties of the neuron.

This model can easily be expanded to include more details of the molecular events underlying plasticity and action potential generation, which may lead to a more complete understanding of the affect of these details on the properties of the neuron. More usefully though, a detailed model such as this one can be used to help illuminate the abstract functional goal these processes are implementing. Finding the simplifying rules that can explain the characteristics of neurons is a first step towards understanding the how neurons are performing computation.

1. *Biophysical model of synaptic plasticity dynamics*. Abarbanel, H.D.I., Gibb, L., Huerta, R., Rabinovich, M. I. 2003, Biological Cynernetics, Vol. 89, pp. 214-226.

2. *Kinetic Models of Synaptic Transmission*. **Destexhe, A., Mainen, Z.F., Sejnowski, T.J.** 1998, *Methods in Neuronal Modeling*.
3. *Dendritic spikes as a mechanism for cooperative long-term potentiation*. **Golding, Nace L., Staff, Nathan P. and Spruston, Nelson.** July 18, 2002, *Nature*, Vol. 418, pp. 326-331.
4. *A quantitative description of membrane current and its application to conduction and excitation in nerve*. **Hodgkin, A., Huxley, A.** 1952, *Journal of Physiology*, Vol. 117, pp. 500-544.
5. *A unified model of NMDA receptor-dependent bidirectional synaptic plasticity*. **Shouval, H. Z., Bear, M. F., Cooper, L. N.** 16, 2002, *Proceedings of the National Academy of Sciences*, Vol. 99, pp. 10831-10836.
6. *Rate, Timing, and Cooperativity Jointly Determine Cortical Synaptic Plasticity*. **Sjostrom, Per Jesper, Turrigiano, Gina G. and Nelson, Sacha B.** December 20, 2001, *Neuron*, Vol. 32, pp. 1149-1164.
7. *Regulation of Synaptic Efficacy by Coincidence of Postsynaptic APs and EPSPs*. **Markram, Henry, et al.** 1997, *Science*, Vol. 275, pp. 213-215.