Modeling Synaptic Plasticity: From Physiology to Cell Biology

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Synaptic plasticity is assumed to be the main substrate for learning. In modeling, plasticity is often described by rather abstract learning rules, but there is also interest in modeling its mechanisms. This implies modeling how the number of postsynaptic glutamatergic AMPA receptors (AMPARs) is controlled.

Initially, such models focused mainly on simulating aspects of the physiology, in particular to predict the calcium concentrations required to evoke plasticity. However, as brief calcium pulses trigger a plasticity change that requires at least ten minutes or more to reach steady state, it became clear that understanding of the signaling pathways involved was required. This led to the birth of molecular modeling of synaptic plasticity, which also required new software development.

After a brief historical overview I will present our recent work on a unified molecular model of cerebellar LTP and LTD, as this presents the current state of the art in molecular modeling. An important component of recent molecular models of synaptic plasticity has been exocytosis and endocytosis of AMPARs. But these trafficking processes have been simulated only at the plasma membrane, with the crucial subcellular trafficking pathways and their regulation being neglected.

To enable mechanistic modeling of trafficking we have developed Vesicle objects within the stochastic reaction-diffusion simulator STEPS (http://steps.sourceforge.net). I will discuss two unpublished models using the Vesicle objects: Rab-mediated recycling or degradation of AMPARs in LTD and the role of diverse vesicle pools in controlling the probability of transmitter release at hippocampal presynaptic terminals.

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