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Model of inter-spine dynamics of PSD-95 molecules and its application to synaptic plasticity

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We present a model of stochastic molecular transport in spiny dendrites. In this model the molecules perform a random walk between the spines that trap the walkers. If the molecules interact with each other inside the spines the trapping time in each spine depends on the number of molecules in the respective trap. The corresponding mathematical problem has non-trivial solutions even in the absence of external disorder due to self-organization phenomenon. We obtain the stationary distributions of the number of walkers in the traps for different kinds of on-site interactions between the walkers. We analyze how birth and death processes of the random walkers affect these distributions.

We apply this model to describe the dynamics of the PSD-95 proteins in spiny dendrites. PSD-95 is the most abundant molecule in the post-synaptic density (PSD) located in the spines. It is observed that these molecules have high turnover rates and that neighboring spines are constantly exchanging individual molecules. We propose that the geometry of individual PSD-95 clusters determines the dependence of trapping times on the number of molecules inside the trap and thus can vary from spine to spine. Furthermore, we suggest that activity-dependent reorganization of the PSD-95 cluster can lead to synaptic plasticity in a form of long-term potentiation (LTP). In the model this is achieved by spine specific activity-dependent ubiquitinization of PSD-95 molecules, which transiently reduces the amount of PSD-95 in the spine but change the geometry of the PSD-95 cluster in such a way that self-organization process results in the overall increase of the number of PSD-95 molecules associated with LTP. We also show that such a dynamics of the PSD-95 molecules can set up the conditions for anomalous diffusive transport inside spiny dendrites and predict the distribution of the PSD sizes which has features of both exponential and Poisson distributions.

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