

Poster presentation

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Modeling stochastic calcium dynamics in the dendritic spines: a hybrid algorithm

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Stochastic fluctuation plays an important role in biology. In a small subcellular compartment like dendritic spines of pyramidal hippocampal cells, the basal level of Ca²⁺ concentration (~100 nM) entails six Ca²⁺ ions. In such a small volume, the stochastic nature of chemical reactions considerably influences intracellular signal transductions [1]. In fact, Ca²⁺ is an important intracellular second messenger regulating many postsynaptic enzymes which in turn trigger modifications of synaptic strength or structure. Most of these interactions are highly nonlinear. For these reasons, we need an efficient and accurate stochastic simulation method to study synaptic functions.

One solution to this problem is a stochastic simulation algorithm (SSA) developed by Gillespie for simulating spatially homogeneous chemical systems [2]. For spatially inhomogeneous system such as intracellular environments, a major modification of the Gillespie algorithm is required. For example, Bernstein [3] subdivides the simulated volume into small cells and models the diffusion of molecules between neighboring elements as a Markov transitions process treated as a special kind of "reaction". This method was shown to accurately reproduce the macroscopic limit of reaction diffusion system with cubic autocatalytic reactions. However, a much higher simulation speed is desired for practical applications. Hybrid algorithms were proposed to solve this problem [4,5]. In these algorithms, the reactions are partitioned into fast and slow based on the propensities and the population of

the different species: the former (fast component) is simulated deterministically and the latter stochastically.

However, such a hybrid scheme becomes problematic and produces inaccurate results especially in a stiff system. For example, dendritic spines contain NMDA receptors whose kinetic transitions are relatively slow but inject fast diffusing Ca²⁺ ions into the spines which control the subsequent biochemical signaling cascades. Because of this stiffness of our system, the propensities of the "slow" subset of reactions do not change smoothly in time and consequently the fast-slow partitioning failed to describe the calcium dynamics. In this paper, we describe a novel hybrid stochastic algorithm to overcome this problem. In short, we developed a different partitioning strategy to avoid the conflicts between fast and slow systems in the simulation. We compare our results with the fully stochastic algorithm and the fully deterministic methods. Using this hybrid algorithm, we show how the stochastic fluctuations of Ca²⁺ dynamics influence the induction of synaptic plasticity.

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