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Poster presentation

Molecules for memory: modelling CaMKII

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Introduction

Long-term modifications of synaptic strength, such as long-term potentiation (LTP) or long-term depression (LTD) are thought to underlie some forms of learning and memory. At the excitatory glutamate synapse, LTP is dependent on calcium influx through the N-methyl-D-aspartate (NMDA) receptor and subsequent activation of calcium/calmodulin-dependent protein kinase II (CaMKII). The NMDA receptor, CaMKII, and its activator calmodulin are all embedded in a complex hyperstructure consisting of more than 180 molecules [1] that acts as as a "synaptic plasticity nanomachine". Our current work aims at exploring CaMKII function in the context of the NMDA receptor complex

Materials and methods

We used StochSim [2] to carry out stochastic single-particle simulations. Molecules react with each other according to probabilities computed from kinetic constants. An important feature of StochSim is that different states (e.g. open/closed, phosphorylated/unphosphorylated at a specific site) or combinations of different states can be represented. Reactions can modify the state of a molecule, and likewise, the state of a molecule can have an influence on its propensity to participate in a given reaction.

Results

A series of models of CaMKII has been created to explore the interplay between phosphorylation, interaction with other proteins, conformational change and kinase activity. Simulations have been carried out using the stochastic simulator StochSim [2]. So far, the model was successful in explaining the effect of calmodulin binding and Thr286 autophosphorylation on CaMKII conformation. Furthermore, it suggests functional implications for CaMKII binding to the NR2B subunit of the NMDA receptor.

Conclusion

A series of models have been created to explore CaMKII function in the context of the NMDA receptor complex. First simulations using StochSim confirm mechanisms described in the experimental literature and suggest further predictions about the system. Future work includes the extension of the model to include a larger number of processes and interaction partners.

References

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