



“Modeling the tripartite synapse at the nanoscale”

Speaker

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Location

via zoom

Abstract

Classic descriptions of the synapse include only the presynaptic terminal and postsynaptic density, often located on a spine. It is now generally accepted that astrocytic processes form an integral part of a structure called the tripartite synapse. Our long-term goal is to build detailed nanoscale models of tripartite synapses. At present, we have detailed separate models of each component and have combined simplified versions of these models into a preliminary tripartite synapse model.

This work builds on the STEPS software (<http://steps.sourceforge.net>) for stochastic reaction-diffusion simulations in irregular meshes. Recently we have expanded STEPS to model all key aspects of vesicle structure and function.

Using this technology, we were able to model all major phases of the synaptic vesicle cycle in a realistic hippocampal pyramidal cell synaptic bouton morphology at unprecedented levels of molecular and spatial detail, from docking and priming to fusion and recycling. Our model reveals highly dynamic and robust recycling of synaptic vesicles able to maintain stable and consistent synaptic release over time. We also reveal how synapsin and the cytosolic protein tomosyn-1 can cooperate to regulate the recruitment of vesicles from the reserve pool.

We are using the same vesicle technology to simulate AMPA receptor recycling and its regulation in hippocampal spines during the expression of synaptic plasticity. Finally, we have been building detailed models of how calcium release in astrocytic processes depends on nanoscale morphology of the astrocyte and of its organelles like ER and mitochondria.