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Mathematical modeling of the *Drosophila* neuromuscular junction

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An important challenge in neuroscience is understanding how networks of neurons go about processing information. Synapses are thought to play an essential role in cellular information processing however quantitative and mathematical models of the underlying physiologic processes that occur at synaptic active zones are lacking. We are generating mathematical models of synaptic vesicle dynamics at a well-characterized model synapse, the *Drosophila* larval neuromuscular junction. This synapse's simplicity, accessibility to various electrophysiological recording and imaging techniques, and the genetic malleability intrinsic to *Drosophila* system make it ideal for computational and mathematical studies.

We have employed a reductionist approach and started by modeling single presynaptic boutons. Synaptic vesicles can be divided into different pools; however, a quantitative understanding of their dynamics at the *Drosophila* neuromuscular junction is lacking [4]. We performed biologically realistic simulations of high and low release probability boutons [3] using partial differential equations (PDE) taking into account not only the evolution in time but also the spatial structure in two dimensions (the extension to three dimensions will be implemented soon). PDEs are solved using UG, a program library for the calculation of multi-dimensional PDEs solved using a finite volume approach and implicit time stepping methods leading to extended linear equation systems be solvedwith multi-grid methods [3,4]. Numerical calculations are done on multi-processor computers for fast calculations using different parameters in order to asses the biological feasibility of different models. In preliminary simulations, we modeled vesicle dynamics as a diffusion process describing exocytosis as Neumann streams at synaptic active zones. The initial results obtained with these models are consistent with experimental data. However, this should be regarded as a work in progress. Further refinements will be implemented, including simulations using morphologically realistic geometries which were generated from confocal scans of the neuromuscular junction using NeuRA (a Neuron Reconstruction Algorithm). Other parameters such as glutamate diffusion and reuptake dynamics, as well as postsynaptic receptor kinetics will be incorporated as well.

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