Abstract View

INFLUENCE OF GLUTAMATE TRANSPORTERS ON SPILLOVER IN A MONTE CARLO MODEL OF HIPPOCAMPAL NEUROPIL

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The goal of this study was to explore the effect of glutamate transporter density on spillover activation of AMPA and NMDA receptors at neighboring synapses by diffusion of glutamate in extracellular space following fast excitatory synaptic release at an active synapse. We used MCell, a Monte Carlo simulator of molecular signaling, to study the release of glutamate and diffusion in 3-D geometrical reconstructions of the hippocampal neuropil. Our 3-D neuropil model contained repeating motifs with the appropriate shape and spacing to match experimentally measured values for hippocampal tortuosity, extracellular volume fraction, and glutamate transporter concentration. The model simulates, on the microsecond time scale, the random walk of every glutamate molecule in a synapse after vesicular release. Here we compare the spillover activation of AMPA and NMDA receptors following 100Hz burst release at an active synapse for two different astrocyte conditions: (1) uniform surface density of glutamate transporters and (2) concentrated glutamate transporters on membrane facing the active synapse. Transporter saturation was analyzed and the average radial diffusion distance of the quanta was calculated for each release in the burst. Preliminary results in a model with uniform glial transporter surface density show that transporter saturation near the active synapse enhanced radial glutamate spillover, and transporter saturation increased with each subsequent vesicular release in a burst. This will be compared with the results from a second model with glutamate transporters concentrated in glial membrane facing the active synapse.
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