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MODEL OF THE QUANTAL ACTIVATION OF NMDA RECEPTORS AT A HIPPOCAMPAL SYNAPTIC SPINE. T.M. Bartol Jr., T.J. Sejnowski*. Computational Neurobiology Laboratory, Salk Institute, 10010 N. Torrey Pines Rd., La Jolla, CA 92037.

A Monte Carlo simulation of a hippocampal area CA1 synaptic spine was undertaken. The simulation included the three-dimensional geometry of a synaptic spine, the release and random-walk diffusion of each transmitter molecule in a quantal packet of glutamate, and the activation by glutamate of NMDA receptors present on the postsynaptic membrane. The kinetic rate constants used to model the NMDA receptor were held fixed at the values reported by Lester & Jahr (The Journal of Neuroscience, 1992, 12:635-643). Thus, the free parameters in the model were the number of transmitter molecules contained in a quantal packet (N), and the NMDA channel density on the postsynaptic membrane (σ_{nmda}). N and σ_{nmda} were adjusted so that ~10 NMDA channels would be in the open state at the peak of receptor activation (Bekkers & Stevens, Nature, 1989, 341:230-233). The time course of glutamate concentration in the cleft following quantal release had a rapid component decreasing from ~2 mM to 0.5 mM in <100 μs and a slower component which kept glutamate concentration at ~0.1 mM for over 1 ms. In agreement with experimental results (Lester & Jahr) the ensemble average time course of the modeled NMDA receptor activation was unaffected by the value of N or σ_{nmda}. It was also found that over a limited range of values for σ_{nmda}, a best fit to the peak activation criteria could be acheived by keeping the product of $N^*\sigma_{nmda}$ constant and that outside this range a fit could only be obtained by increasing N at a given value of σ_{nmda}. This result suggests that $N^*\sigma_{nmda}$ may be operating at a minimum value in vivo and that the actual value of N could be determined if one could measure σ_{nmda}.

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