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MCELL: GENERALIZED MONTE CARLO COMPUTER SIMULATION OF SYNAPTIC TRANSMISSION AND CHEMICAL SIGNALING.

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We have developed MCELL, a software tool for 3D Monte Carlo simulation of ligand diffusion and chemical signaling, focusing on neurotransmitter release and quantal current generation at a peripheral (Bartol et al., 1991, Biophys. J. 59:1290; Anglister et al., 1994, Neuron 12:783; Stiles et al., 1996, PNAS, in press) and central synapse (Bartol et al., 1993, Soc. Neurosci. Abst. 19:1515). MCELL's generality has been expanded to allow simulation of multiple ligand and receptor classes, along with complex 3D arrangements of diffusion boundaries representing multiple cell or organelle membranes. Simulations are designed using a Model Description Language to define ligands and other molecular constituents (e.g. receptors, enzymes, uptake sites), the arrangement of boundaries, the timing of ligand release, and additional parameters. Thus, many processes in addition to synaptic transmission can now be modeled. We plan to make MCELL available to other investigators, and will present here its overall design, capabilities, system requirements, and planned future features. Tutorial simulations designed to highlight MCELL's use will be presented: (1) Random walk model of ligand diffusion, with net flux(es) in 1, 2, or 3 dimensions. (2) Subcellular structures defined by diffusion boundaries. (3) Ligand diffusion and chemical reaction (e.g. receptor binding and activation, enzymatic hydrolysis) within structures, for single or multiple classes of ligand and receptor. (4) Neurotransmitter release from a synaptic vesicle with changing fusion pore dimensions. (5) Quantal and multi-quantal synaptic current generation. Supported by NIH K08NS01776 (JRS), NS09315 (MMS), and The Howard Hughes Medical Institute (TJS).