Reaction-Diffusion Modeling in the NEURON Simulator

Robert A McDougal[1], Michael L Hines[1], William W Lytton[23]
[1] Department of Neurobiology, Yale University, New Haven, CT 06520, USA
[2] Department of Physiology & Pharmacology, SUNY Downstate Medical Center, Brooklyn, NY 11203, USA
[3] Kings County Hospital, Brooklyn, NY 11203, USA
E-mail: robert.mcdougal@yale.edu

The NEURON simulator is a widely used tool for studying multiscale models from the level of ion channels up to the level of large multicolumnar neuronal network models. Although it has been possible to simulate intracellular chemical processes, this has been limited. We have now expanded the tool in order to fully support intracellular chemical dynamics including stochastic reaction-diffusion models and three-dimensional simulations. Arbitrary reaction schemes may be specified at run-time via a Python interpreter, with no separate compilation step required. Models can be imported from Systems Biology Markup Language (SBML) and other resources, facilitating collaboration between the neuroscience and cell biology communities.

A dendritic spine head has a volume of about half a femtoliter, so that only a few particles of a given chemical species, for example calcium ions, are present. By contrast, once these chemicals enter a dendrite, they encounter more uniformity. As calcium ions move randomly around the spine, there is the potential for large percentage deviations from the mean concentration. To study these effects, stochastic simulation is required. We utilize the Gillespie, and tau-leaping algorithms for these simulations, but our methods can easily be extended to other compartment-based approaches. This stochastic simulation must then be coupled to deterministic diffusion to handle the interface with the quasi-continuous environment of the dendrite.

Different chemical reaction-diffusion problems and different geometries require different approximations to solve adequately. For example, previous modelers have implemented radial diffusion as well as longitudinal diffusion, but this missed many biologically important phenomena. Full 3-dimensional spatial simulations has presented a number of challenges. Geometric details are critical; a spatial simulator must define the shape of the joins between dendritic sections. Numerical solvers like the alternating direction implicit method allow for quick, stable multi-dimensional calculations. Preliminary modeling shows the value of these techniques to understand how chemical and electrical dynamics interact in neuronal information processing.