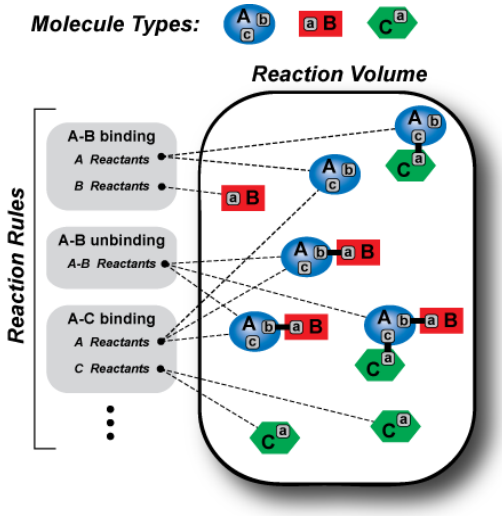
NFsim: The Network-Free Stochastic Simulator

http://emonet.biology.yale.edu/nfsim

Overview

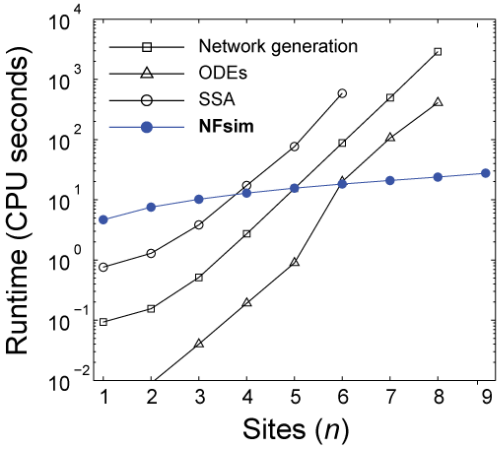
Managing the overwhelming numbers of molecular states and interactions is a fundamental obstacle in building predictive models of biological systems. NFsim is a practical, versatile and efficient biochemical reaction simulator that overcomes the complexities of combinatorial molecular interactions. By adopting a rule and agent-based approach, NFsim provides orders of magnitude speedup over traditional ODE and stochastic methods for many complex biological systems. Additionally, reaction rates can be defined as arbitrary functions of molecular microenvironments to provide powerful coarse-graining capabilities, for example to merge Boolean and kinetic representations of biological networks. Together, the new features and high performance of NFsim open the door to modeling new classes of systems that were previously inaccessible to general-purpose simulators.



Key Features

- Efficient simulation of large, complex, biochemical reaction networks (see *Performance* section below)
- Advanced coarse-graining capabilities to simplify complicated or unknown reaction mechanisms
- Operates seamlessly with BioNetGen and uses BNGL, a formal rule-based model specification language
- An easy-to-use scripting language for changing parameters and reaction rates mid-simulation
- Interactive model debugger for assessing and validating reaction events as they occur
- Comprehensive output options, allowing sophisticated model analysis such as single molecule tracking
- Includes Matlab-based post-run analysis functions and scripts for rapid visualization of results
- Fully object-oriented and reusable software for facilitating 3rd party extensions and modifications
- In-depth instruction manual with a documented suite of example models
- 100% free and open source (under the GNU Public License), tested on Windows, Mac, and Linux

Performance Characteristics



The runtime performance of NFsim scales with the number of biochemical rules in a model, not with the total number of reactions or molecular configurations. To illustrate, consider a protein that can be phosphorylated at multiple independent sites, a common component of signal transduction networks. As the modeler adds details of more sites, the number of molecular configurations and reactions grows as 2^n where n is the number of sites. Performance and memory requirements of optimized ODE solvers and the stochastic simulation algorithm (SSA) lag proportionally, making simulation impossible with these methods when modeling more than about 8 sites. With NFsim, there are no such limits on the state space of a system, so modeling as many sites as needed is not only possible, but tremendously efficient.