A Hybrid Method Combining Improved StochSim with SSA for Solving Systems with Multistate species

Zhen Liu[1] and Yang Cao[2]

***Short Abstract* — Morton-Firth and Bray's stochastic simulator (StochSim) is one important method for stochastic modeling and simulation. Following our detailed comparison [4] between StochSim and Gillespie's stochastic simulation algorithm (SSA) [1], we proposed improvements on StochSim, by eliminating the *pseudo-molecules* and deriving adaptive step size formula. Based on the improvements, a hybrid method is proposed to combine the advantages of the two methods. Analysis and numerical experiment results demonstrate that, for systems with both multistate species and a large total population, the hybrid method exhibits extraordinary performance. We believe this hybrid method provides an efficient simulation algorithm to bridge the rule-based model and reaction-based model.**

***Keywords* — StochSim, SSA, hybrid method**

I. Background

StochSim is an object-oriented algorithm applied in many biological systems. In this method, molecules are all represented by objects which carry their own properties. The simulation procedure is straightforward and easy to implement [3,4]. By first selecting objects for possible reactants, its efficiency is hardly affected by the number of reactions involved. This essentially makes it a favorable method to handle systems containing multi-state species.

Nevertheless, StochSim suffers from a small but fixed time step, which is proportional to the inverse of *N*, the maximal total number of molecules in the system. Therefore, the performance of the StochSim is low when dealing with systems with large total populations [4,5].

II. An Improved Version of StochSim

We have improved StochSim in two aspects.

A. *Eliminating pseudo-molecules*

The original StochSim uses pseudo-molecule objects to differentiate uni-molecular reactions from bi-molecular reactions. Although this definition simplifies the whole procedure, it adds redundant information into the system, and makes the method less efficient. We have derived an improved algorithm that does not need the pseudo-molecules.

B. *Taking adaptive step size*

In the original StochSim, the total number of molecules, denoted by *N*, is fixed. The step size Δt is also fixed and calculated before simulation as a function of *N* and reaction rates. For many realistic systems the actual total number of molecules in system may change dynamically. The fixed *N* and Δt will cause low efficiency. We have derived an adaptive step size formula to enable adaptive modification of Δt to achieve the balance of accuracy and efficiency. The derived formula also takes into consideration the improvement that eliminates the pseudo molecules.

III. A Hybrid Method

Since the SSA has higher efficiency in simulating systems with large populations, while confined by ones with multi-state species [4,5], we have proposed a hybrid algorithm, by partitioning a system into two subsystems, one for StochSim and the other for SSA.

Numerical experiment results demonstrate that the new method has much better performance than either of the original algorithms for systems with both multistate species and a large total population.

IV. Conclusion

Based our previous analysis on the advantages and disadvantages of StochSim and SSA, we have proposed improvement on the StochSim and further proposed a hybrid method that has the advantages from both StochSim and SSA. The hybrid method is tested with numerical examples.

[1] Department of Computer Science, Virginia Tech, Blacksburg, VA24061. E-mail: zhenliu@vt.edu

[2] Department of Computer Science, Virginia Tech, Blacksburg, VA24061. E-mail: ycao@vt.edu

References

[1] D. Gillespie. Exact stochastic simulation of coupled chemical reactions, J. Phys. Chem., 81:2340-61, 1977.

[2] C. Morton-Firth, D. Bray. Predicting temporal fluctuations in an intracellular signaling pathway. J. theor. Biol., 192:117-128, 1998.

[3] C. Morton-Firth, T. Shimizu, D. Bray. A free-energy-based stochastic simulation of the rat receptor complex. J. Mole. Bio., 287:1059-1074, 1999.

[4] Liu Z and Cao Y, Detailed comparison between the StochSim and SSA, submitted to IET Systems Biology, 2007.

[5] Pettigrew MF, H. Resat. Modeling signal transduction networks: A comparison of two stochastic kinetic simulation algorithms. J. Chem. Phys., 123:113707, 200