Stochastic Modeling and Simulation of Chemotaxis Signaling Network

Yang Cao[1] and Zhen Liu[2]

***Abstract* — Stochastic modeling and simulation is critical for the quantitative study of the randomness in biochemical network. In this paper two important stochastic simulation algorithms, StochSim and SSA, are compared based on a quantitative complex model of the signal network in E. Coli chemotaxis. A multiscale model of chemotaxis is constructed using slow-scale SSA framework, and improvements to Gillespie's original SSA are proposed for multistate variables and spatial dynamics simulation.**

***Keywords* — Chemotaxis, SSA, slow-scale SSA, StochSim**

I. Introduction

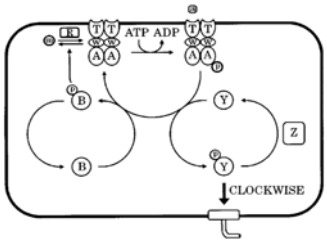
In complex biochemical networks that make up living systems, the small number of reactant molecules often result in dynamical behavior that is discrete and stochastic rather than continuous and deterministic. Stochastic modeling and simulation provide quantitative tools for investigating such behavior and numerically determining if a proposed mechanism is consistent with experimental observations. Two fundamental stochastic simulation algorithms designed for biochemical systems have appeared in literature. One is the well-known Gillespie's algorithm, also known as SSA[2,3]; The other is the StochSim[4], an object-oriented stochastic simulation algorithm. Many successful stories based on biological complex systems have been told using one of the two algorithms. However, some fundamental questions remain open, for example, will the two algorithms generate same simulation results? What are the advantages and disadvantages for the two algorithms? Here we present theoretical analysis and numerical comparison based on the stochastic model of the *Escherichia coli* chemotaxis signaling network, which has provided insights into biological robustness and bacterial individuality. From this comparison, further improvement to the Gillespie algorithm is proposed to deal more efficiently with multistate variables that appear in some particular biological systems.

II. StochSim and SSA

SSA is considered as an exact stochastic simulation algorithm as it follows the same distribution that rules the chemical master equation (CME). In each step SSA generates two random numbers, based on rigorously derived distribution, for the time and index of the next reaction. StochSim is a object-based algorithm. In each step StochSim randomly selects two molecules and generates another random number and compare it with a reaction probability table to see if these two molecules will react. If they are, implement the reaction; otherwise skip this step and proceed to the next one. From a first glance these two algorithms are quite different. But with a detailed analysis we have proved that when the stepsize chosen in StochSim is small enough, both of them will generate the same distribution. Thus in the accuracy perspective both of them are the same. However, with a detailed computational cost analysis, we have shown that SSA is much more efficient than StochSim.

[1]Department of Computer Science, Virginia Tech. ycao@cs.vt.edu
[2]Department of Computer Science, Virginia Tech. zhenliu@vt.edu

III. Chemotaxis Model



The bacteria chemotaxis exhibits non-genetic variation that may be explained by the inherent randomness in biochemical systems. A stochastic model of E. coli chemotaxis signal network[5, 6] has been proposed and simulated using StochSim. We have constructed a similar stochastic model using our algorithm slow-scale SSA[1] that is based on SSA but focused only on slow-scale reaction channels. Numerical experiments confirmed our analysis by showing that both the two algorithms generate the same distribution but SSA is tens of times faster than StochSim.

IV. Conclusion and Further Improvement to SSA

W have demonstrated the same accuracy and much higher efficiency of SSA compared with StochSim. However, there is a special advantage of StochSim over SSA: the flexibility for multistate variables and spatial information analysis. Further improvements for SSA are then proposed to handle these situations.

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