Commun. Comput. Phys.
doi: 10.4208/cicp.290313.051213s

Vol. **15**, No. 4, pp. 1207-1236
April 2014

Strong Convergence and Speed up of Nested Stochastic Simulation Algorithm

Can Huang and Di Liu*

Department of Mathematics, Michigan State University, East Lansing, MI 48824, USA.

Received 29 March 2013; Accepted (in revised version) 5 December 2013

Available online 21 January 2014

Abstract. In this paper, we revisit the Nested Stochastic Simulation Algorithm (NSSA) for stochastic chemical reacting networks by first proving its strong convergence. We then study a speed up of the algorithm by using the explicit Tau-Leaping method as the Inner solver to approximate invariant measures of fast processes, for which strong error estimates can also be obtained. Numerical experiments are presented to demonstrate the validity of our analysis.

AMS subject classifications: 65C30, 60H35

Key words: Stochastic simulation algorithm, biochemical reacting network, strong convergence.

1 Introduction

The stochastic simulation algorithm (SSA) by Gillespie [12, 13], which can be formulated as an equation of jump diffusion processes [23], provides the world a benchmark for the numerical simulation of intra-cellular biochemical networks, such as gene expression and regulation. The algorithm is exact in the sense that the probability distribution of particular realizations being simulated is the same as the solution of the chemical master equation (CME) describing the process. The CME is a set of ordinary differential equations with enormously high dimension if the number of the states of the corresponding network is large. Although SSA gives us a Monte Carlo approach to compute the CME, it becomes less efficient when applied to the so called stiff systems, in which reaction channels and reacting species with two or more different time and concentration scales coexist. There have been many approaches overcoming this difficulty, such as the celebrated Tau-Leaping method [6, 14] and Nested Stochastic Simulation Algorithm (NSSA) [7, 8].

NSSA relies only on the disparity of the rates, and makes no a priori assumption on the form of the slow and fast variables, nor upon the analytic form of the rate functions.

*Corresponding author. *Email addresses:* canhuang@math.msu.edu (C. Huang), richardl@math.msu.edu (D. Liu)

The main idea is to capture the effective dynamics on the slow time scale by assuming the fast processes to reach a quasi-equilibrium in a sufficiently short time. Weak convergence of NSSA can be found in [8]. Strong convergence of NSSA is still open and this paper tries to fill in the gap.

In this paper, we will further investigate the speed up of NSSA. One key component of implementation is the approximation of the invariant measure of the fast process. Several authors studied the ergodic approximation of a stationary distribution in the case of Brownian diffusions, see [26,29,30] among others. Computation of the invariant measure of stochastic differential equation driven by a Lévy process is investigated in [32], where the intensity of the Lévy process, different from SSA, is independent of the state. In this paper, we will adopt the Tau-Leaping method to sample the quasi-equilibrium of the fast processes in NSSA, which will enable us to use larger time steps when concentrations of reacting species in the fast reactions are high. Note that strong convergence analysis of multiscale schemes for standard SDE is performed in [9,24]. However, the extension in this work is not trivial due to the necessity of establishment of invariant measure for fast processes described by the τ-leaping method and the analysis of the associated generator in the form of a difference operator.

In the following sections, we will first provide the notations for SSA, NSSA and Tau-Leaping method. Then we will prove the strong convergence of NSSA, when either direct SSA or Tau-Leaping method is used as the Inner solver for the fast processes. Finally, numerical examples will be provided to test the error estimates.

2 Stochastic simulation algorithms

As a model taking into account of stochastic effects at the molecular level, SSA considers an isothermal, spatially homogeneous mixture of chemically reacting network in a fixed volume V. Suppose there are N_S species of molecules, with M_R reactions. Let $x_i \in N$ denote the number of molecules of species S_i. Then, each reaction R_j can be characterized by a propensity function $a_j(x)$ where $x=(x_1,x_2,\cdots,x_{N_S})$ and a state change vector $\nu_j \in N^{N_S}$. We write $R_j=(a_j,\nu_j)$. Given state x, the probability that reaction R_j fires on an infinitesimal time interval dt is independent from other reactions and is given by $a_j(x)dt$. The state of the network after the jth reaction is $x+\nu_j$. $a_j(x)$ usually takes the form of polynomials or rational functions in terms of x. From [23], SSA can be formulated as a stochastic differential equation in the following form:

$$dX_t=\sum_j \int_0^\infty \nu_j \mathbf{A}_j(q,X_t)\mathcal{P}(dt,dq), \tag{2.1}$$

where

$$\mathbf{A}_j(q,X_t)=\begin{cases} 1, & q\in\Big(\sum\limits_{i=1}^{j-1}a_i(X_t),\sum\limits_{i=1}^{j}a_i(X_t)\Big), \\ 0, & \text{otherwise}, \end{cases} \tag{2.2}$$