

Nested stochastic simulation algorithms for chemical kinetic systems with multiple time scales

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Abstract

We present an efficient numerical algorithm for simulating chemical kinetic systems with multiple time scales. This algorithm is an improvement of the traditional stochastic simulation algorithm (SSA), also known as Gillespie's algorithm. It is in the form of a nested SSA and uses an outer SSA to simulate the slow reactions with rates computed from realizations of inner SSAs that simulate the fast reactions. The algorithm itself is quite general and seamless, and it amounts to a small modification of the original SSA. Our analysis of such multi-scale chemical kinetic systems allows us to identify the slow variables in the system, derive effective dynamics on the slow time scale, and provide error estimates for the nested SSA. Efficiency of the nested SSA is discussed using these error estimates, and illustrated through several numerical examples. © 2006 Elsevier Inc. All rights reserved.

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1. Introduction

The stochastic simulation algorithm (SSA in short), also known as the Gillespie algorithm and originally introduced in the context of chemical kinetic systems, has found a wide range of applications in many different fields, including computational biology, chemistry, combustion, and communication networks [20,10,11]. Besides being an effective numerical algorithm, SSA is also a model for chemical kinetic systems that takes into account the discreteness and finiteness of the molecular numbers as well as stochastic effects. This feature makes it an attractive alternative to the approach of using systems of deterministic ODEs, particularly in situations when the stochastic effects are important [9]. In addition, since SSA uses less modeling assumptions and is therefore closer to the first principle models, it is often easier to determine the parameters in the model. In fact, the main modeling parameters are the rate functions which can in principle be computed using the rate theories [21].

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The disadvantage of SSA is that it is computationally more expensive to handle than the systems of ODEs. Besides being stochastic in nature, the system often involves many disparate time scales. This is easy to appreciate, since chemical reaction rates often depend exponentially on the activation energy. For a deterministic system of ODEs, this results in the stiffness of the ODEs, for which many efficient numerical methods have been developed [12]. However, the situation for SSA is much less satisfactory.

In recent years, this issue has received a great deal of attention and some important progress has been made. The main idea, pursued in different forms by many people, is to model the effective dynamics on the slow time scale, by assuming that the fast processes are in quasi-equilibrium [13,25,22,3,4]. In [13], a multi-scale simulation method was proposed in which the slow and fast reactions are simulated differently. The slow reactions are simulated using Gillespie algorithm and the fast reactions are simulated using Langevin dynamics. In [25], a similar multi-scale scheme is proposed in which the fast dynamics is simulated using deterministic ODEs. Both the approaches in [13,25] require that the volume of the system be sufficiently large in addition to having well-separated rates. [22] proposes a scheme based on the quasi-equilibrium assumption by assuming that the probability densities of the fast species conditioned on the slow species is known exactly or can be approximated, e.g. by normal distributions. The same quasi-equilibrium assumption is used in [3,4], except that the probability density of the fast species conditioned on the slow species is computed via a modified process called the virtual fast process.

The method proposed in [3,4] is more general than previous methods, but it still has limitations. It assumes the equilibrium distributions of the fast processes can be approximated by simple functions and the fast species are independent of each other at equilibrium. Moreover, the rate functions of the slow processes are also assumed to be of special forms and are approximated empirically by solving a system of algebraic equations. These limitations are removed in the recent work, [7], in which a nested SSA is proposed to deal with the time scale issue. This work relies only on the disparity of the rates, and makes no a priori assumption on what the slow and fast variables are, or the analytic form of the rate functions. The recent work in [23] is much closer to our work in spirit. It also adopted a nested structure with inner loop on the fast reactions and the outer loop on the slow reactions. However, the outer loop algorithm is significantly different from ours, without faithfully capturing the effective dynamics on the slow time scale. In particular, they also resort to a partition into slow and fast species, a partition that is avoided in our work.

It is worthwhile to emphasize that, as we will see in Section 3, the algorithm proposed in [7] is quite general and seamless. In particular, it makes no explicit mentioning of the fast and slow variables. At a first sight, this might seem surprising, since there are counterexamples showing that algorithms of the same spirit do not work for deterministic ODEs with separated time scales [8] if the slow variables are not explicitly identified and made use of. But in the present context, the slow variables are linear functions of the original variables, as a consequence of the fact that the state change vectors $\{v_j\}$ s are constant vectors, and this is the reason why the seamless algorithm works.

However, unlike the original SSA which is exact, the nested SSA is approximate and to understand the errors in the nested SSA, it is important to understand what the slow and fast variables are and what the effective process is on the slow time scale. These issues were dealt with briefly in [7], and one main purpose of the present paper is to study them in more detail. This will allow us to estimate the optimal numerical parameters and the overall cost of the algorithm. In addition, we will discuss various extensions of the nested SSA, as well as important implementation issues such as adaptively determining slow and fast processes.

The paper is organized as follows. In Section 2, we define the slow variables and derive the effective dynamics on the slow time scale for chemical kinetic systems with two disparate time scales. Section 3 introduces the nested SSA for the special case when the system has two disparate time scales. Error estimates for the nested SSA are proved and illustrated through numerical examples. We also elaborate on why the nested SSA algorithm is seamless, and when a similar seamless algorithm can be developed in the context of ordinary differential equation such as, for instance, the ones that arises from the chemical kinetic system in the large volume limit. Then in Section 4, we show how to adaptively determine the partition of the system into slow and fast reactions during the simulation. Finally, in Section 5, we discuss the effective dynamics and nested SSA for system with multiple (more than two) well-separated time scales. In this case, both the averaging principle and the nested SSA can be applied iteratively, similar to the case in iterated homogenization [1]. We also study the system over the diffusive time scale.

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