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Galerkin Spectral Method Applied to the Chemical Master Equation

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Abstract. Stochastic well-stirred chemically reacting systems can be accurately modeled by a continuous-time Markov-chain. The corresponding master equation evolves the system's probability density function in time but can only rarely be explicitly solved. We investigate a numerical solution strategy in the form of a spectral method with an inherent natural adaptivity and a very favorable choice of basis functions. Theoretical results related to convergence have been developed previously and are briefly summarized while implementation issues, including how to adapt the basis functions to follow the solution they represent, are covered in more detail here.

The method is first applied to a model problem where the convergence can easily be studied. Then we take on two more realistic systems from molecular biology where stochastic descriptions are often necessary to explain experimental data. The conclusion is that, for sufficient accuracy demands and not too high dimensionality, the method indeed provides an alternative to other methods.

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Key words: Master equation, spectral-Galerkin method, high dimensional problem, moving basis, chemical reactions.

1 Introduction

Stochastic descriptions of chemical reactions are necessary tools for understanding and explaining the mechanisms inside living cells. Models of intra-cellular systems frequently consist of fewer than 10^2 molecules of some of the species [26] implying that molecule discreteness makes the impact of stochasticity very pronounced. For instance, randomness has been shown to drive and improve the regularity of oscillations [46], create new steady-states [45] and cause separation in bistable systems [13].

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The *chemical master equation* (CME) is a popular and accurate stochastic model for chemically reacting systems. It is a consequence of the *Markov property*: if the system is measured at discrete times $t_1 < t_2 < \cdots t_n$, then the probability for the measurement (y_n, t_n) given the present state (y_{n-1}, t_{n-1}) does not involve earlier states. Typically, because of the existence of activation energies, reactive collisions between molecules are rare events as compared to nonreactive ones giving rise to a randomization and a loss of memory [24]. This loss of memory is then accurately captured by the Markov property and remains a valid approximation so long as the measurement scale is slower than the often extremely short auto-correlation time of the system.

The master equation is a differential-difference equation in D dimensions, where D is the number of reacting agents, and is therefore a very computationally intensive problem. Effective numerical methods are of both practical and theoretical interest.

Recent progress at *directly* representing the state-space and solving the CME include the *Finite state projection algorithm* [38], later improved using Krylov-subspace methods [5,36]. See also [18] where techniques from adaptive PDE-solvers are used in the context of the CME. For larger state-spaces, numerical solution of the *Fokker-Planck equation* [19] and adaption of the *Sparse grids technique* [29] have been suggested. As a master equation for *continuous* stochastic processes, numerical solution of the Fokker-Planck equation is an interesting subject in itself. There are, however, important cases for which the CME cannot be approximated by the Fokker-Planck equation [22]. The sparse grids technique aims to reduce the computational complexity of high dimensional smooth problems. Its application to the CME is quite recent and appear promising.

In the present paper we implement and apply a spectral method developed previously in the report [17] to the master equation. The method employs basis functions that are orthogonal with respect to a discrete measure in line with the discreteness of the solution and avoids the need for continuous approximations to the master operator. An interesting feature of our implementation is a built-in adaptivity of the basis which allows the basis functions to follow the dynamical behavior of the solution. Our proposed scheme is reminiscent of an approach for polyreaction kinetics considered earlier in [9], and we will further comment on this point in Section 5.

The "curse of dimension", the phenomenon that the complexity of traditional discretization methods applied to high-dimensional problems grows exponentially with the problem size is thus not removed, but it is mitigated. With a spectral method that converges exponentially, the resolution per dimension can be much smaller than any direct representation provided that the solution is smooth enough. As we shall see, another point in directly attacking the CME is the way stiff equations can be handled through suitable implicit time integration.

The paper is organized as follows. In Section 2 the master equation as a governing equation for stochastic chemical systems is discussed along with theoretical properties of importance to the numerical analysis. The spectral method is proposed in Section 3 where approximation and stability results developed in the report [17] are summarized. This section also discusses a plausible implementation in some detail, including the "moving