A Runge-Kutta Framework for Tau Leaping

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***Short Abstract* — Tau leaping is an approach for accelerating stochastic simulations of chemically reactive systems. Despite its recent popularity, the method has yet to find widespread use in systems biology. A possible explanation is that, in its simplest form, tau leaping is analogous to a forward-Euler ODE integrator, which is usually insufficient for practical problems. To address this issue, we have developed a general framework for implementing higher-order versions of tau leaping. The approach extends on previous work in this area by considering aspects of the tau-leaping algorithm beyond just the generation of reaction firings, such as tau selection and post-leap checking.**

***Keywords* — Tau leaping, stochastic simulation, Runge-Kutta methods.**

I. Background

TAU leaping [1-3] is a promising approach for accelerating the stochastic simulation of biochemical reaction networks. In its simplest form, the tau-leaping algorithm is analogous to the simple forward-Euler method for numerically integrating ordinary differential equations (ODEs) [1]. Since many higher-order ODE integration methods exist with properties far superior to forward Euler, it is natural to investigate whether analogous tau-leaping methods are possible. Some higher-order tau-leaping methods have already been proposed. In his seminal paper on tau leaping [1], Gillespie proposed a simple higher-order extension, termed the "estimated-midpoint" method, which is analogous to an explicit second-order Runge-Kutta method. Burrage and Tian [4] proposed the Poisson Runge-Kutta (PRK) methods as a generalization of this idea. Rathinam et al. [5] and Cao et al. [6] have proposed implicit tau-leaping methods that are analogous to the backwards-Euler and trapezoidal ODE integration methods.

II. Approach

We present a general framework for implementing higher-order Runge-Kutta variants of tau leaping. We deconstruct the basic tau-leaping algorithm into four steps: (i) tau selection, (ii) reaction classification, (iii) firing generation, and (iv) post-leap checking. Tau-selection procedures come in two varieties: pre-leap [1-3] and post-leap [7]. Reaction classification can be as simple as segregating "critical" reactions with small reactant populations [3] or can be more sophisticated, e.g., partitioning reactions into groups, ranging from discrete-stochastic to continuous-deterministic, based on the current values of the reaction rates [8]. Firing generation usually involves generating Poisson random numbers and is the aspect of the tau-leaping algorithm that has been investigated most within the context of higher-order approaches [1,4-6]. Finally, post-leap checking can involve simply ensuring that species populations do not become negative [3] or can require that the "leap condition," on which the method is based, is strictly adhered to [7]. We show how to generalize these four steps within a Runge-Kutta context while retaining previous approaches [1-8] as special cases.

III. Conclusions

The approach has been applied to the "partitioned-leaping algorithm" [8-10], a tau-leaping variant, and implemented within the open-source modeling and simulation platform BioNetGen [11]. The current implementation is limited to explicit methods but will be extended to implicit methods in the near future. Forward-Euler, estimated-midpoint and 4th-order Runge-Kutta are supported as standard methods. However, any explicit Runge-Kutta method can be used by defining a Butcher tableau [4] in a standard format input file. Results will be presented that illustrate the advantages of higher-order implementations of tau leaping in terms of improved simulation accuracy and efficiency [12].

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