Stochastic chemical kinetics and the total quasi-steady-state assumption: application to the stochastic simulation algorithm and chemical master equation

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Abstract

Recently the application of the quasi-steady-state approximation (QSSA) to the Gillespie algorithm was suggested for the purpose of speeding up stochastic simulations of chemical systems that involve both relatively fast and slow chemical reactions [Rao and Arkin, J. Chem. Phys. 118, 4999 (2003)]. Improved numerical efficiency is obtained by respecting the vastly different time scales characterizing the system and then by advancing only the slow reactions exactly, based on a suitable approximation to the fast reactions. We considerably extend the work of Rao and Arkin by applying it to numerical methods for the direct solution of the Chemical Master Equation (CME) and in particular to the Krylov Finite State Projection algorithm. In addition we extend the mathematical framework of the approximation scheme and point

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out some important connections to the literature on the (deterministic) total QSSA (tQSSA) and place the stochastic analogue of the QSSA (in all forms) within the more general framework of aggregation of Markov processes, which naturally suggests a family of related numerical methods. We apply the new methods to Michaelis-Menten enzyme kinetics, competitive inhibition, and a component of the λ-phage genetic switch and two further models of enzyme kinetics arising in the mitogen-activated-protein kinase cascade: a model of the dual phosphorylation scheme and the Goldbeter-Koshland switch. Overall we report dramatic improvements by applying the tQSSA to the CME-solver.