

1096-VL-2168

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Intracellular chemical reactions are best modeled by a Markov process in continuous time with the non-negative integer lattice as state space. The jump rates typically depend on certain system parameters. Computing the parametric sensitivity of system's behavior is essential in determining robustness of systems as well as in estimating parameters from observed data.

Monte Carlo methods for numerical computation of parametric sensitivities fall into three categories: finite difference (FD) methods, pathwise derivative (PD) method and the Girsanov transform (GT) method. It has been numerically observed in chemical kinetics applications as well as in other fields such as Operations Research that the PD method when applicable is more efficient (has lower variance) than the GT method. We provide a theoretical explanation as to why this is the case.

We provide both analysis and numerical results showing that for a class of Markov processes known as density dependent processes, the efficiency of the GT method scales as  $\mathcal{O}(N^{1/2})$  while that of a regularized PD method and most FD methods scale as  $\mathcal{O}(N^{-1/2})$ , where  $N$  is the system size parameter. In many practical systems  $N$  is modestly large and as such one expects the GT method to be not very efficient. (Received September 17, 2013)