

STODE - automatic stochastic simulation of systems described by differential equations

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ABSTRACT

One of the foremost challenges facing biologists is an understanding of complex biochemical systems such as those found in cells. Although we are still far from achieving this goal, experimental data is accumulating rapidly and theoretical models are becoming increasingly sophisticated. The computer simulation of these models provides an important way in which theoretical understanding can be verified against existing experimental knowledge.

In generating such models, it is often more convenient to characterise biochemical systems in terms of sets of ordinary differential equations (ODEs) describing their dynamics, rather than as the more fundamental chemical reactions of the system (e.g. [1]). While for high particle numbers a time-course of the system may be obtained without problem by numerically integrating the set of ODEs, at low particle numbers the continuity assumption implicit in the differential equation approach breaks down and it may be more appropriate to consider other methods. One such approach is to perform a stochastic simulation of the system, which although somewhat slower, has the advantage that it is valid even for very low particle numbers [2].

In this paper we describe STODE, a program we have developed to enable the automatic parsing and stochastic simulation of biochemical systems initially described by a set of ODEs. In this it differs from existing packages [3, 4, 5] which perform stochastic simulations but are not able to handle ODEs as input. We give an overview of the algorithm used and discuss the implementation, capabilities and user interface of STODE.

Some of the problems which may be encountered in performing stochastic simulations at low reactant populations are discussed. To investigate these, we apply the program to a simulation which normally involves Michaelis-Menten kinetics. It is seen that even for low particle numbers, the Michaelis-Menten terms can be applied as long as the general assumptions for these terms hold.

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