> A PRACTICAL GUIDE TO STOCHASTIC SIMULATIONS OF REACTION-DIFFUSION PROCESSES

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https://people.maths.ox.ac.uk/erban/Education/StochReacDiff.pdf

**stochastic vs deterministic**

modelling of biological systems where small molecular abundances of some chemical species make deterministic models inaccurate or even inapplicable. Stochastic models are also necessary when biologically observed phenomena depend on stochastic fluctuations (e.g. switching between two favourable states of the system)

BASICS

single chemical reaction (degradation) in Section 2.1, introducing a basic stochastic simulation algorithm (SSA) and a mathematical equation suitable for its analysis (the so-called chemical master equation).

A 🡪 B (not of interest) at rate = k

The rate constant k in (2.1) is defined so that k dt gives the probability that a randomly chosen molecule of chemical species A reacts (is degraded) during the time interval [t, t + dt) where t is time and dt an (infinitesimally) small time step.

P such that only 1 mol can be degraded at a time (or none, two+ is super unlikely)

Stochastic vs deterministic

We start with a simple example of stochastic switching between favourable states of the system, a phenomenon which cannot be fully understood without stochastic modelling. Then we illustrate the fact that the stochastic model might have qualitatively different properties than its deterministic limit, i.e. the stochastic model is not just “equal” to the “noisy solution” of the corresponding deterministic equations. We present a simple system of chemical reactions for which the deterministic description converges to a steady state. On the other hand, the stochastic model of the same system of chemical reactions has oscillatory solutions

make the Gillespie SSA more efficient 16,

(2,14) 23 SDES algorithmic introduction to stochastic differential equations

Theoretical or computational approaches for the analysis of suitable stochastic models are given in [25, 9].

nonlinear system of chemical equations for which the stochastic model has qualitatively different behaviour than its deterministic counterpart in some parameter regimes. The presented phenomenon is sometimes called **self-induced stochastic resonance** [27].

**> An Algorithmic Introduction to Numerical Simulation of Stochastic Differential Equations**

Desmond J. Higham†

For those inspired to learn more about SDEs and their numerical solution we recommend [6] as a comprehensive reference that includes the necessary material on probability and stochastic processes. The reviewarticle [11] contains an up-to-date bibliography on numerical methods. Three other accessible references on SDEs are [1], [8], and [9], with the first two giving some discussion of numerical methods. Chapters 2 and 3 of [10] give a self-contained treatment of SDEs and their numerical solution that leads into applications in polymeric fluids. Underlying theory on Brownian motion and stochastic calculus is covered in depth in [5]. The material on linear stability in section 7 is based on [2] and [12].

**> Discrete Stochastic Simulation Methods for Chemically Reacting Systems**

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However, if the system is small enough that the molecular populations of some of the reactant species are small, from one to thousands, discreteness and stochasticity may play important roles in the dynamics of the system. Such a case occurs often in cellular systems ([McAdams and Arkin, 1997](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3492891/#R24), [Arkin et al., 1998](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3492891/#R1), [Fedoroff and Fontana, 2002](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3492891/" \l "R12)), which typically involve copy numbers of one or two for the number of genes of a given protein, on the order of tens to hundreds for the corresponding RNAs and on the order of thousands for regulatory proteins and enzymes.

ASSUME Instead we consider the case where the dynamics of biochemical systems can be approximated by assuming that the reactant molecules are “well-stirred” such that their positions become randomized and need not be tracked in detail. When that is true, the state of the system can be defined simply by the instantaneous molecular populations of the various chemical species. The chemical reactions can be defined as events that change the state of the system following biochemical rules, changing the molecular populations by integer numbers.

ASSUME We assume that the system is confined to a constant volume and is well-stirred, or in other words is in thermal (but not chemical) equilibrium at a constant temperature. When this condition is broken, the spatial information of each species becomes important and the population information for the species will not be enough alone to determine the system dynamics.

VECTORS / METHODS For a well-stirred system, each reaction channel *Rj* can be characterized by a *propensity function aj* and a *state change vector* **ν** *j* ≡ (*ν* 1*j*,…, *ν Nj*). The propensity function is defined by the statement: <…>

ALTERNATIVE\_METHODS The Sorted Direct Method SDM is a little less efficient than the ODM but its adaptive feature makes it a very good strategy, particular in simulation of oscillation systems where a fast reaction in one time period may become slow in another time period. In that case, the dynamic indexing of this method is very useful. Logarithmic Direct Method the LDM has advantages for large biochemical system.

TAU\_LEAP\_PROBLEMS The Poisson random number (or its approximation) is unbounded. There is a small possibility that a large random number may exceed the number of some reactants and causes negative populations to occur. AND There are multiple reaction channels consuming the same reactant. When they fire at the same time, even though neither of them separately exhausts the number of that reactant, their overall effect may do so.

the NEGATIVE POPULATION PROBLEM systems in which some consumed reactant species are present in small number;

arises more often from multiple reaction channels consuming the same reactant, than from the unbounded Poisson random variable

negative populations typically arise from multiple firings of reactions that are only a few reaction events away from consuming all the molecules of one of their reactants

HYBRID SSA/TAU-LEAPING ALGORITHM 🡪 control parameter (no molecules) and critical reactions