Stochastic Simulations of Reaction-Diffusion Models

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ABSTRACT

Reaction-Diffusion models are key components of models in developmental biology. These reaction diffusion processes can be mathematically modeled using either deterministic partial differential equations or stochastic simulation algorithms. Here we discuss the stochastic simulations on both linear and non-linear Reaction-diffusion models using the Tau leaping Algorithms.

1 Introduction

Reaction-diffusion systems are mathematical models that describe how the concentration of one or more substances distributed in space changes under the influence of two processes: local chemical reactions in which the substances are converted into each other, and diffusion which causes the substances to spread out in space.

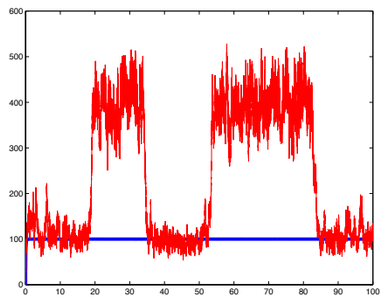
To motivate the use of stochastic modeling in cells, we demonstrate that stochastic modeling can explain qualitative behavior in cells that deterministic models can not.
Let us consider the system of chemical reactions for chemical A introduced by Schlogl [1]

$$2A \underset{\kappa_2}{\overset{\kappa_1}{\rightleftarrows}} 3A, \quad \phi \underset{\kappa_4}{\overset{\kappa_3}{\rightleftarrows}} A$$

, the corresponding ODE of the above reactions:

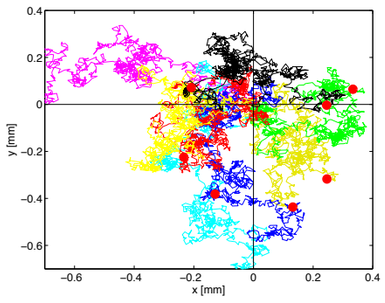
$$\frac{da}{dt} = -\kappa_2 a^3 + \kappa_1 a^2 - \kappa_4 a + \kappa_3$$

We take $\kappa_1 = 0.18 min^{-1}, \kappa_2 = 2.5 \times 10^{-4}\ min^{-1}, \kappa_3 = 200\ min^{-1}$ and $\kappa_4 = 37.5\ min^{-1}$. The above ODE has two stable steady states. i.e, at 100 and 400. The ODE solution is converging to a one stable point depend on the initial condition, where as stochastic simulation the number of molecules switching to both the steady states for large time.



Diffusion

Diffusion is the random migration of molecules arising from motion due to thermal energy

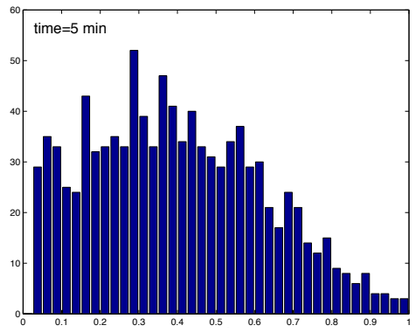


2 Compartmental Based Approach

We divide the computational domain $[0, L]$ into K compartments of length $h = L/K$. We denote the number of molecules of chemical species A in the i-th compartment $[(i-1)h, ih]$ by $A_i, i = 1, ..., K$. Then our diffusion process is described by the system of chemical reactions

$$A_1 \underset{d}{\overset{d}{\rightleftarrows}} A_2 \underset{d}{\overset{d}{\rightleftarrows}} A_3 \underset{d}{\overset{d}{\rightleftarrows}} ..... \underset{d}{\overset{d}{\rightleftarrows}} A_K \tag{1}$$

where d is given by $d = \frac{D}{h^2}$, D is diffusion constant and h is the compartmental length.



$A_{16}(0) = 500 = A_{17}(0)$ and $A_i(0) = 0\ for i \neq 16, i \neq 17$. $d = 0.16 sec^{-1}$

3 Reaction-Diffusion Model

3.1 Linear Model

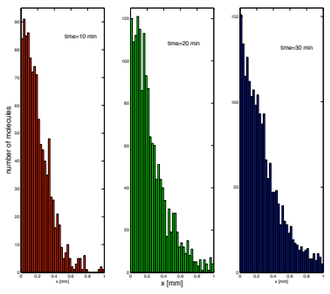
In this section we add chemical reactions to the the molecular diffusion which were presented in the previous section

$$A_1 \underset{d}{\overset{d}{\rightleftarrows}} A_2 \underset{d}{\overset{d}{\rightleftarrows}} A_3 \underset{d}{\overset{d}{\rightleftarrows}} ..... \underset{d}{\overset{d}{\rightleftarrows}} A_K \tag{2}$$

$$A_i \xrightarrow{k_1} \phi, \text{ for i} = 1, 2, ..., \text{K}. \tag{3}$$

$$\phi \xrightarrow{k_2} A_i, \text{ for i} = 1, 2, ..., \text{K}/5. \tag{4}$$

Equation(2) describes diffusion. In particular, the rate constant d is given by $d = \frac{D}{h^2}$. Equation (3) describes the degradation of A and is, in fact, equation applied to every compartment. Equation(4) describes the production of A in the first $K/5$ compartments. (e.g. in part [0,L/5] of the computational domain).



Starting with no molecules of A in the above system, we plot the number of molecules in each compartment at different times. We consider molecules of A which are diffusing in the domain $[0, L]$, where $L = 1$mm, with diffusion constant $D = 10^{-4} mm^2\ sec^{-1}$

4 Non-linear Model

In the previous section, we studied an example of a reaction-diffusion model which did not include the second order chemical reactions. We considered only production and degradation. In this section, we will talk about the generalization of our approach to models which involves second-order chemical reactions too.

This is an example of patterning in developmental biology are the so-called Turing patterns [6] . They do not require any pre patterning. Molecules are subject to the same chemical reactions in the whole domain of interest. For example, let us consider a system of two chemical species A and B which react according to the Schnakenberg [7] system of chemical reactions.

$$2A + B \xrightarrow{k_1} 3A, \tag{5}$$

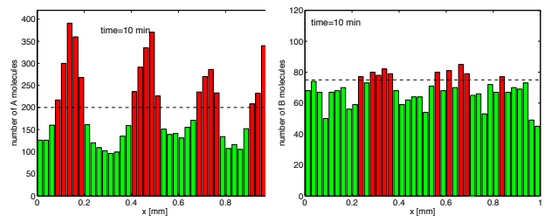
$$\phi \underset{k_3}{\overset{k_2}{\rightleftarrows}} A \tag{6}$$

$$\phi \xrightarrow{k_4} B, \tag{7}$$

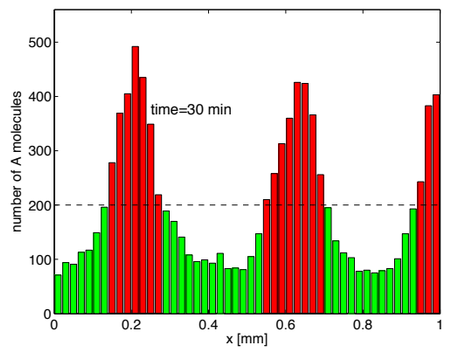
To simulate the reaction-diffusion problem with the Schnakenberg system of chemical reactions (5) - (7). We divide the computational domain $[0, L]$ into $K = 50$ compartments of length $h = \frac{L}{K} = 20\mu m$. We denote the number of molecules of chemical species A in the $i-$th compartment $[(i-1)h, ih]$ by A_i and Similarly for chemical species $B_i, i = 1, 2, ..., K$. Diffusion corresponds to two chains of "chemical reactions":

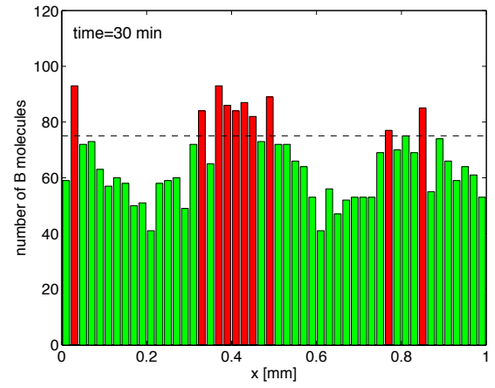
$$A_1 \underset{d_A}{\overset{d_A}{\rightleftarrows}} A_2 \underset{d_A}{\overset{d_A}{\rightleftarrows}} A_3 \underset{d_A}{\overset{d_A}{\rightleftarrows}} ..... \underset{d_A}{\overset{d_A}{\rightleftarrows}} A_K \tag{8}$$

$$B_1 \underset{d_B}{\overset{d_B}{\rightleftarrows}} B_2 \underset{d_B}{\overset{d_B}{\rightleftarrows}} B_3 \underset{d_B}{\overset{d_B}{\rightleftarrows}} ..... \underset{d_B}{\overset{d_B}{\rightleftarrows}} B_K \tag{9}$$



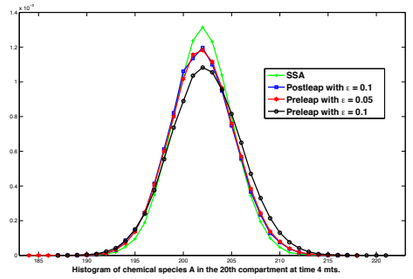
For the above reaction diffusion processes, values of rate constants as $k_1 = 10^{-6}$ sec^{-1},$k_2 = 1$ sec^{-1}, $k_3 = 0.02$ sec^{-1}and $k_4 = 3$ sec^{-1}. We denote the diffusion constants of A and B are $D_A$and D_B respectively and we choose $D_A = 10^{-5}\ mm^2$ sec^{-1} and $D_B = 10^{-3}\ mm^2$ sec^{-1}.





Conclusions

Turing Pattern model (5) -(9) is implemented with SSA[2] and Tau Leaping [4]-[5] algorithms in Fortran for 10^4 iterations.



Algorithm	ϵ	*CPUtime*
SSA[2]	-	331 mnts
Pre Tau[4]	0.1	11 mnts
	0.05	28mnts
Post Tau[5]	0.1	20mnts
	0.05	53mnts

Postleap algorithm with $\epsilon = 0.1$ gives the same accuracy as of Preleap $\epsilon = 0.05$, but preleap required 40% more CPU time than postleap.

References

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