Stochastic Reaction Network

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1 Introduction

The objective of this practical project is to program and study the variability of simple stochastic reactions, using the Gillespie algorithm. This practical work is based on [1]

function GILLESPIE($\mathbf{x}_0$, $\mathbf{k}$, T, V)
  $\mathbf{x} \leftarrow \mathbf{x_0}$
  $t \leftarrow 0$
  repeat
    //Compute the reaction rates
    $\{\lambda_{r_1}, \ldots, \lambda_{r_J}\} \leftarrow \lambda(\mathbf{x}(t), \mathbf{k})$
    $R_{tot} \leftarrow \sum_{r_i} \lambda_{r_i}$
    //Draw next reaction time
    $\delta_t \sim Exponential(\lambda = R_{tot})$
    Draw a reaction r_j with Prob. prop. to λ_j.
    $\mathbf{x} \leftarrow \mathbf{x} + V_{.,r_j}$
    $t \leftarrow t + \delta t$
  until $t \geq T$
end function

Fig. 1. Gillespie pseudocode

You are free to program these simple examples in your favourite language, but I'll only debug code written in my favourite language :)

2 Simple bio-chemical reactions

Write the programs to simulate the following bio-chemical reactions:

- $\emptyset \rightarrow_{k_1} A \rightarrow_{k_2} \emptyset$
- $A + B \rightarrow_k C$
- $A \rightarrow_k A + B$
- $A + B \leftrightarrow_{k_1} C \rightarrow_{k_2} D + E$

Execute your programs many times, and for each reaction compute the mean number of molecules and their standard deviations. Compare to the ODE results (you can write a simple Euler solver and/or solve the ODE analytically). Change the rate constants and analyze what happens.

3 Gene expression

Let us study a simple stochastic gene expression system. DNA randomly alternate between two states: open and closed. Open DNA is transcribed into RNA, RNA is translated into a protein. Finally RNA and proteins are degraded. The system of reactions is detailed hereafter:

$$dna^* \leftrightarrow_{k_1} dna$$

$$dna \rightarrow_k rna + dna$$

$$rna \rightarrow_k protein + rna$$

$$rna \rightarrow_k \emptyset$$

$$protein \rightarrow_k \emptyset$$

Keep k constant and record the amount of proteins along time for different rates k_1. Repeat the experiment many times, just as if you were measuring the amount of molecules in different clonal cells. Compute the means and standard deviations. What do you see?

4 Lotka-Volterra

Simulate the Prey-Predator Lotka Volterra system:

$$\emptyset \rightarrow prey$$

$$prey + predator \rightarrow 2predator$$

$$predator \rightarrow \emptyset$$

Did you notice any difference with respect to the ODE solutions?

5 Bifurcation

Consider the following system:

$$\emptyset \rightarrow_k A$$

$$\emptyset \rightarrow_k B$$

$$A + X \rightarrow_{k_1} 2X$$

$$2X \rightarrow_{k_{-1}} A + X$$

$$B+ > X \rightarrow_{k_2} C$$

Calculate the steady states of the system. Depending on the sign of $k_1 A^* - k_2 B^*$, the system has two stable steady states. Simulate different with different values for k_1 and k_2. What do you see?

6 SIR system

Write the equations of the SIR system and simulate it using the Gillespie algorithm and the tau-leaping algorithm

References

1. Soula, H.: Stochastic chemical reactions. BioComp-5BIM-TD (2013)