

NATIONAL TAIWAN UNIVERSITY,
GRADUATE INSTITUTE OF BIOMEDICAL ENGINEERING AND BIOINFORMATICS

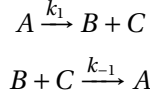
BEBI5009:
Mathematical Modeling of System Biology
Homework 4

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Consider the reaction network



- a) Suppose that the system starts with two molecules of A, one molecule of B, and no molecules of C, that is $(N_A, N_B, N_C) = (2, 1, 0)$. Determine the set of possible states the system can adopt and write the chemical master equation that describes the corresponding probability distribution.

All possible states of (N_A, N_B, N_C) are $(2, 1, 0)$, $(1, 2, 1)$, $(0, 3, 1)$. Corresponding chemical master equation is:

$$\begin{aligned} \frac{d}{dt}P((2, 1, 0), t) &= -2k_1P((2, 1, 0), t) + 2k_{-1}P((1, 2, 1), t) \\ \frac{d}{dt}P((1, 2, 1), t) &= -k_1P((1, 2, 1), t) - 2k_{-1}P((1, 2, 1), t) + 2k_1P((2, 1, 0), t) + 6k_{-1}P((0, 3, 2), t) \\ \frac{d}{dt}P((0, 3, 2), t) &= -6k_{-1}P((0, 3, 2), t) + k_1P((1, 2, 1), t) \end{aligned}$$

- b) Take $k_1 = 1 \text{ (time}^{-1}\text{)}$ and $k_{-1} = 1 \text{ (time}^{-1}\text{)}$, and solve for the steady-state probability distribution.

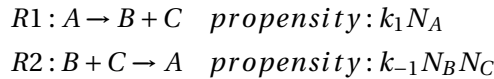
At steady state,

$$\begin{aligned} 0 &= -2k_1P^{ss}((2, 1, 0), t) + 2k_{-1}P^{ss}((1, 2, 1), t) \\ 0 &= -k_1P^{ss}((1, 2, 1), t) - 2k_{-1}P^{ss}((1, 2, 1), t) + 2k_1P^{ss}((2, 1, 0), t) + 6k_{-1}P^{ss}((0, 3, 2), t) \\ 0 &= -6k_{-1}P^{ss}((0, 3, 2), t) + k_1P^{ss}((1, 2, 1), t) \end{aligned}$$

$$\text{Also, } P^{ss}((2, 1, 0), t) + P^{ss}((1, 2, 1), t) + P^{ss}((0, 3, 2), t) = 1$$

$$\begin{aligned} \Rightarrow 0 &= -2P^{ss}((2, 1, 0), t) + 2P^{ss}((1, 2, 1), t) \\ 0 &= -P^{ss}((1, 2, 1), t) - 2P^{ss}((1, 2, 1), t) + 2P^{ss}((2, 1, 0), t) + 6P^{ss}((0, 3, 2), t) \\ 0 &= -6P^{ss}((0, 3, 2), t) + P^{ss}((1, 2, 1), t) \\ P^{ss}((2, 1, 0), t) + P^{ss}((1, 2, 1), t) + P^{ss}((0, 3, 2), t) &= 1 \\ \Rightarrow P^{ss}((2, 1, 0), t) &= \frac{6}{13}, \quad P^{ss}((1, 2, 1), t) = \frac{6}{13}, \quad P^{ss}((0, 3, 2), t) = \frac{1}{13} \end{aligned}$$

- c) Simulate sample paths of N_A , N_B , and N_C using stochastic simulation algorithm (SSA). Set the initial condition of N_A , N_B , and $N_C = (2, 1, 0)$ or $(10, 5, 0)$ or $(100, 50, 0)$



Note1: To calculate the waiting time, you will need to generate values of a random variable distributed according to an exponential distribution. You could simply generate a random

variable U drawn from the uniform distribution on the unit interval $(0, 1)$, and $T = -\ln(U)/\lambda$ will be an exponential random variable, where λ is the rate parameter of the exponential distribution. In this example, λ would be the sum of the reaction propensities.

Another way to generate exponential random number is to use Matlab function `expnrnd(μ)`, where μ is the mean of the exponential distribution $\mu = 1/\lambda$.

Note2: You might need to change the value of k_1 and k_{-1} for different initial conditions due to the volume changes. Use $(k_1, k_{-1}) = (1, 1)$, $(1, 1/5)$ and $(1, 1/50)$ ($time^{-1}$) for I.C. = $(2, 1, 0)$, $(10, 5, 0)$, and $(100, 50, 0)$.

- d) Set the initial condition of N_A , N_B , and $N_C = (2, 1, 0)$. Analyzed the statistics of your ensemble, and compare to the steady state probability distribution in (b)
- e) Write down a deterministic model for the chemical reaction following the mass action law. Simulate the concentration changes of A, B, C with the parameter $k_1 = 1(s^{-1})$ and $k_{-1} = 1(mM^{-1}s^{-1})$. Set initial concentrations $[A], [B], [C]$ as 2, 1, and 0mM. Compare simulation results in (c)

According to the question,

$$\begin{aligned}\frac{d[A]}{dt} &= -k_1[A] + k_{-1}[B][C] \\ \frac{d[B]}{dt} &= k_1[A] - k_{-1}[B][C] \\ \frac{d[C]}{dt} &= k_1[A] - k_{-1}[B][C]\end{aligned}$$

The simulation result is shown in following figure: