NATIONAL TAIWAN UNIVERSITY,
GRADUATE INSTITUTE OF BIOMEDICAL ENGINEERING AND BIOINFORMATICS

BEBI5009:
Mathematical Modeling of System Biology
Homework 4

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December 1, 2016

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Consider the reaction network

$$A \xrightarrow{k_1} B + C$$
$$B + C \xrightarrow{k_{-1}} A$$

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:

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

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

At steady state,

$$0 = -2k_1P^{ss}((2,1,0),t) + 2k_{-1}P^{ss}((1,2,1),t)$$
$$0 = -k_1P^{ss}((1,2,1),t) - 2k_{-1}P^{ss}((1,2,1),t) + 2k_1P^{ss}((2,1,0),t) + 6k_{-1}P^{ss}((0,3,2),t)$$
$$0 = -6k_{-1}P^{ss}((0,3,2),t) + k_1P^{ss}((1,2,1),t)$$
$$Also, \quad P^{ss}((2,1,0),t) + P^{ss}((1,2,1),t) + P^{ss}((0,3,2),t) = 1$$
$$\Rightarrow 0 = -2P^{ss}((2,1,0),t) + 2P^{ss}((1,2,1),t)$$
$$0 = -P^{ss}((1,2,1),t) - 2P^{ss}((1,2,1),t) + 2P^{ss}((2,1,0),t) + 6P^{ss}((0,3,2),t)$$
$$0 = -6P^{ss}((0,3,2),t) + P^{ss}((1,2,1),t)$$
$$P^{ss}((2,1,0),t) + P^{ss}((1,2,1),t) + P^{ss}((0,3,2),t) = 1$$
$$\Rightarrow P^{ss}((2,1,0),t) = \frac{6}{13}, \quad P^{ss}((1,2,1),t) = \frac{6}{13}, \quad P^{ss}((0,3,2),t) = \frac{1}{13}$$

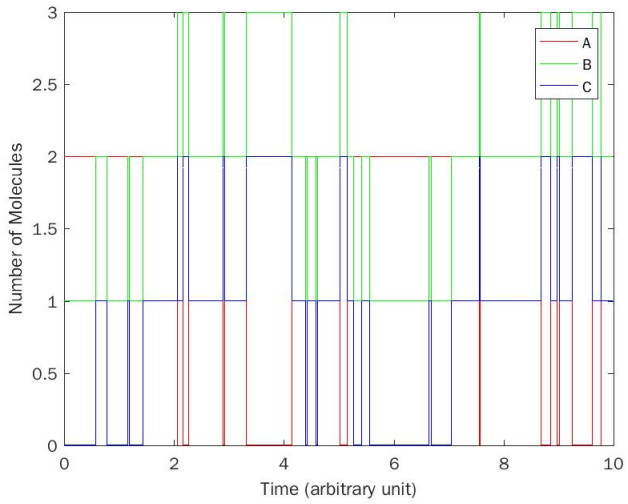
c) Simulate sample paths of N_A, N_B, and N_C using stochastic simulation algorithm (SSA). Set the initial condition of N_A, N_B, and N_C=(2,1,0) or (10, 5, 0) or (100, 50, 0)

$$R1 : A \rightarrow B + C \quad propensity : k_1N_A$$
$$R2 : B + C \rightarrow A \quad propensity : k_{-1}N_BN_C$$

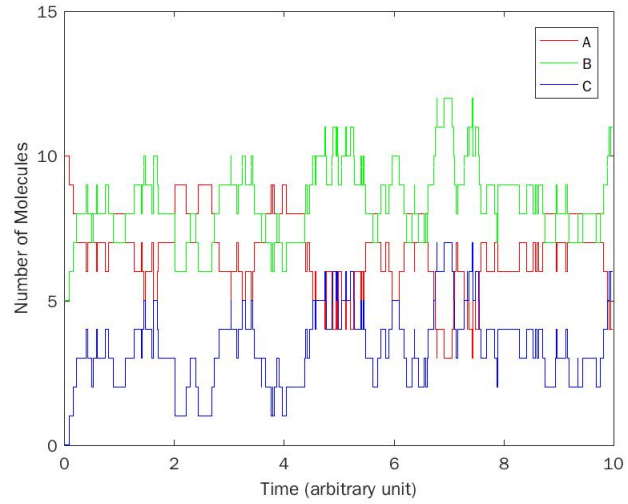
Note1: To calculate the waiting time, you will need to generate values of a random variable distributed according to an exponential distribution. You could simply generate a random

variable U drawn from the uniform distribution on the unit interval (0, 1), and T=-ln(U)/λ 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 exprnd(μ), where μ is the mean of the exponential distribution μ=1/λ.
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).

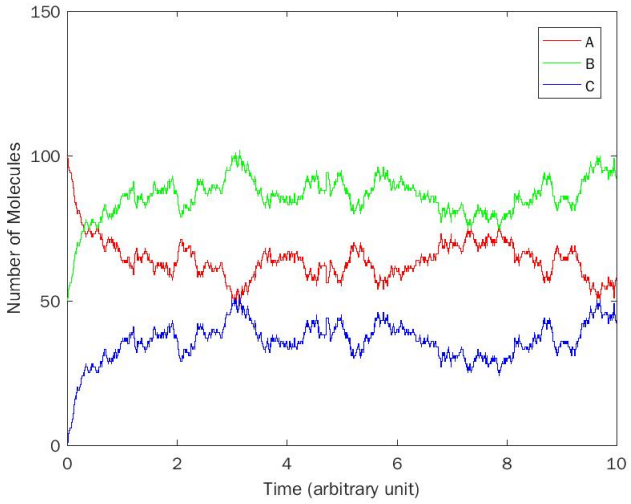
The simulation result of N_A, N_B, and N_C=(2,1,0)



The simulation result of N_A, N_B, and N_C=(10, 5, 0)

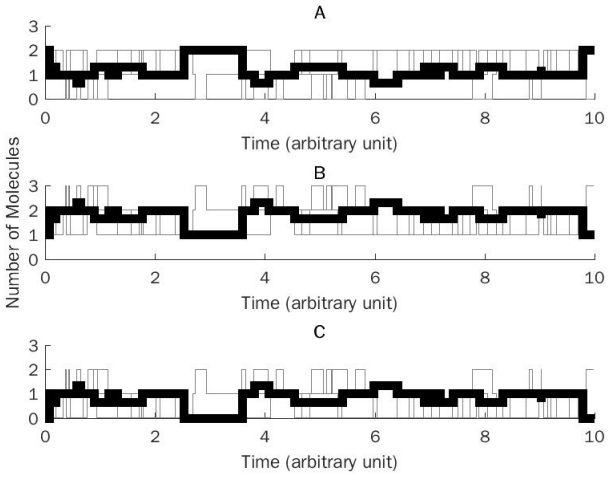


The simulation result of N_A, N_B, and N_C=(100, 50, 0)

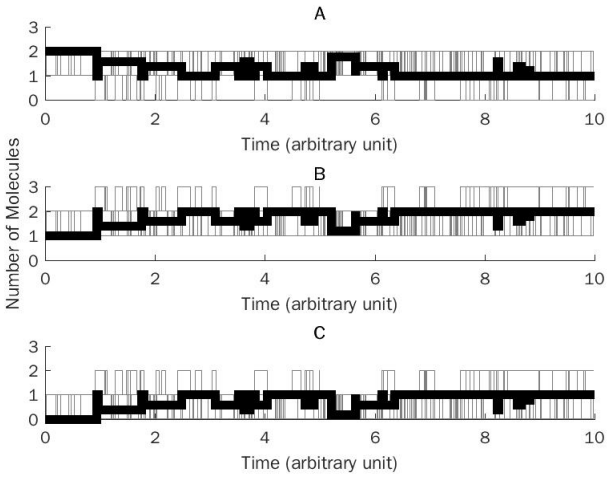


d) Set the initial condition of N_A, N_B, and N_C=(2, 1, 0). Analyzed the statistics of your ensemble, and compare to the steady state probability distribution in (b)

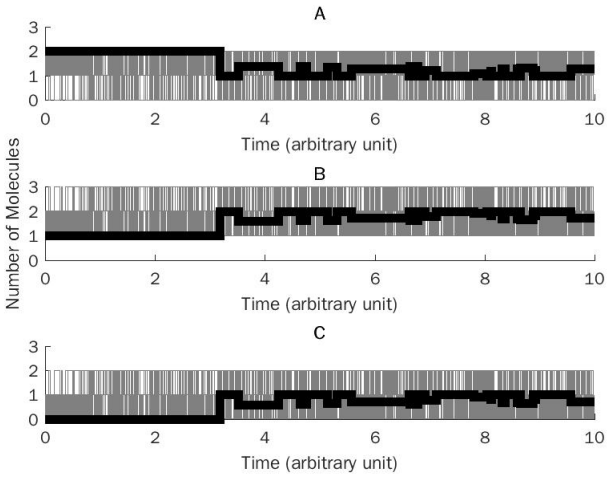
The simulation result of an ensemble of 3 sample paths (the bold line represents the average behaviour):



The simulation result of an ensemble of 10 sample paths:



The simulation result of an ensemble of 100 sample paths:



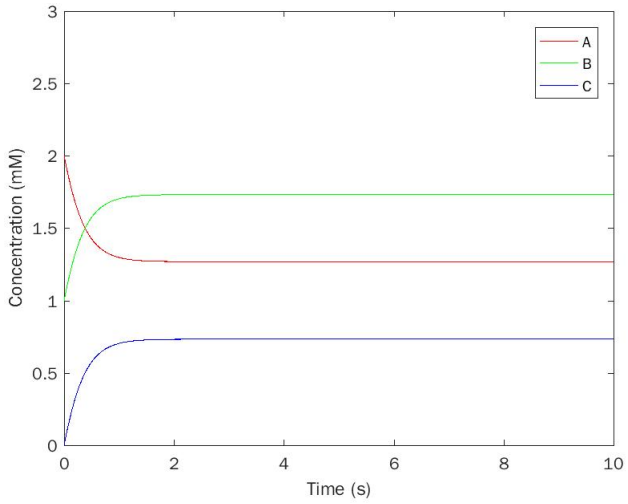
As the ensemble size increases, the averaged behavior approaches the deterministic prediction. I sampled the distribution of states at 10, which is already at steady-state, but the probability distribution of N_A, N_B, and N_C=(2,1,0), (1,2,1), (0,3,2) are 0.01, 0.01, 0.98. It is quite different from the result we derived in (b). It may due to the simulation conducted in a discrete manner, and the boundary conditions that should be followed further constrained and modified the original behaviour of the system.

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, we can easily list following equations:

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

The simulation result is shown in following figure:



Compared to the results obtained in (c), random behavior is not well-described by the deterministic simulation for small population size. Whereas it's a good description for large population size.