

# Bioengineering 499C: Systems and Synthetic Biology

April 22, 2007

Homework Assignment #3

Due: 29<sup>th</sup> April 2008

Points awarded for each question are indicated in square brackets. Return assignment with your name clearly indicated at the top of your answer sheet. [Total points: 100]

## [50] Question 1.

Implement the Gillespie method and use it to simulate the equilibration reaction,  $A \rightleftharpoons B$ . Try simulating the system with different starting concentrations of A and B. For example:

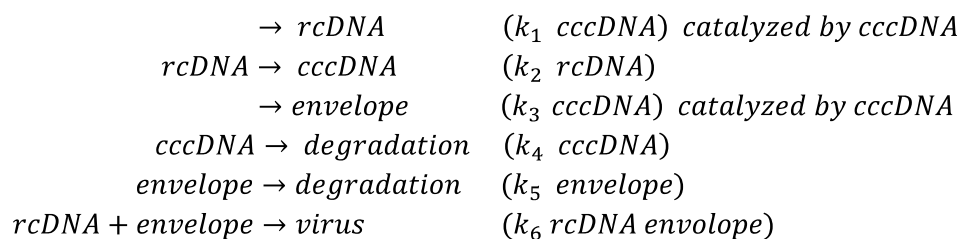
A	B
10	0
100	0
500	0

Hand in the plots you obtain and a listing of the software you used to implement the Gillespie method.

## [50] Question 2.

The following model is a highly simplified scheme for Hepatitis B viral infection.

Relaxed circular DNA (rcDNA) infects a live cell. rcDNA is converted to closed circular DNA which forms the template for mRNA synthesis. cccDNA codes for the envelope protein which when combined with newly synthesized rcDNA forms new virus. The model can be represented in reaction form as:



In this model there are three state variables, cccDNA, rcDNA and envelope protein. The values for the rate constants are:  $k_1 = 1$ ,  $k_2 = 0.025$ ;  $k_3 = 1000$ ;  $k_4 = 0.25$ ;  $k_5 = 2$ ;  $k_6 = 7.5E^{-6}$ .

The rate law for the first reaction is assumed to be  $k_1 \text{ cccDNA}$

The rate law for the third reaction is assumed to be  $k_3 \text{ cccDNA}$

The rate law for the sixth reaction is assumed to be  $k_6 \text{ rcDNA envelope}$

All other reactions are modeled using simple mass-action kinetics. The initial conditions for every simulation should be:

cccDNA = 1; rcDNA = 0 and envelope = 0,

The presence of one molecule of cccDNA in the initial conditions represents a cell infected by one virus. Carry out two sets of simulations:

### **A) Deterministic Simulation**

Derive and write out the differential equations for the virus model.

Using Jarnac, set up a deterministic simulation, simulate up to 200 time units and plot the evolution of the three species.

### **B) Stochastic Simulation**

Using Jarnac, simulate the model stochastically using the same initial conditions. Carry out 500 simulations using the same initial conditions and average all 500 runs to plot to average change in molecules numbers of cccDNA, rcDNA and envelope protein.

Compare the average simulation results with the deterministic simulation. You should observe that the average concentrations are significantly lower than the single deterministic run. Your task is to explain why this is so.

In order to provide a clue, carry out a number of single runs of the stochastic simulation and observe the concentration of cccDNA over 200 time units.

In summary, show plots for the deterministic and average stochastic simulations. Show two single run stochastic plots that illustrate the particular effect that makes the stochastic simulation different from the deterministic one. Explain the difference.