

# Bioengineering 424: Systems and Synthetic Biology

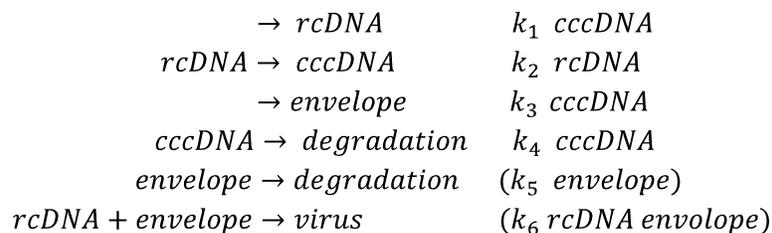
Feb 28, 2011

Homework Assignment

## [50] Question 1

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:  $k_1 = 1$ ,  $k_2 = 0.025$ ;  $k_3 = 1000$ ;  $k_4 = 0.45$ ;  $k_5 = 2$ ;  $k_6 = 7.5E^{-6}$ .

The rate law for the first reaction is assumed to be  $k_1 cccDNA$

The rate law for the third reaction is assumed to be  $k_3 cccDNA$

The rate law for the sixth reaction is assumed to be  $k_6 rcDNA envelope$

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:

Using the model, answer the following two questions:

### A) Deterministic Simulation

[10] Derive and write out the differential equations for the virus model.

[10] Using Jarnac or some other suitable tool, set up a deterministic simulation, simulate up to 200 time units and plot the evolution of the three species.

### B) Stochastic Simulation

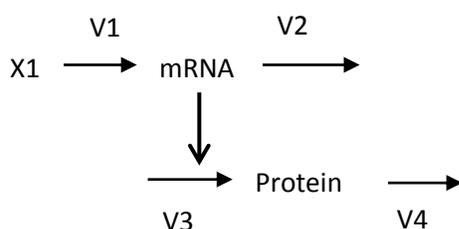
[30] Using Jarnac or some other suitable tool, simulate the model stochastically. Carry out 100 simulations using the same initial conditions. Record the rate of virus production at time = 200 (ie at the end of the run) for each of the 100 points, plot a frequency plot of the virus production rate. These runs may take a while (10 to 15 mins).

Compare the simulation results with the deterministic simulation. Explain the difference.

**Hint:** Carry out a number of single runs of the stochastic simulation and observe the concentration of cccDNA over 10 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 and explain the difference.

**[50] Question 2.** In this question you will investigate a model that mimics protein synthesis.



The rate laws for this model are:

$$v_1 = k_1 x_1$$

$$v_2 = k_2 mRNA$$

$$v_3 = \frac{100 mRNA}{K_{m_1} + mRNA}$$

$$v_4 = k_4 Protein$$

Carry out two types of simulation on this model, deterministic and stochastic. Protein and mRNA levels can be set to zero at the start of the simulation. Run a simulation for about 200 time units (or whatever is convenient) and plot the graphs for mRNA and Protein.

Investigate the model under two sets of parameters:

1.  $k_1 = 80$ ;  $k_2 = 200$ ;  $K_{m_1} = 10$ ;  $k_4 = 1$ ;

2.  $k_1 = 0.1$ ;  $k_2 = 0.25$ ;  $K_{m_1} = 10$ ;  $k_4 = 1$ ;

[15] **a)** What difference do you observe when you carry out stochastic simulations using the two parameter sets?

[35] **b)** Explain in mechanistic terms why the two behaviors are different. To help you answer his question, observe closely the difference in the two parameter sets.