

Bioengineering 499C: Systems and Synthetic Biology

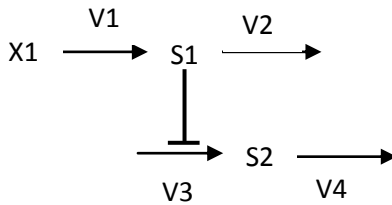
April 25, 2007

Homework Assignment #3B

Due: 2nd May 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.** Consider the following simple gene network. Transcription factor S1 is made at a rate V1 and degraded at a rate V2. S1 can inhibit the expression of protein S2. S2 degrades at a rate V4.



The rate laws for this network are (Note the simple inhibition law on v3):

$$v_1 = k_1 x_1$$

$$v_2 = k_2 S_1$$

$$v_3 = \frac{k_3}{K m_1 + S_1}$$

$$v_4 = k_4 S_2$$

Build this network using Jarnac or some other suitable software application. Initialize the parameters to:

$k_1 = 100$; $k_2 = 25$; $k_3 = 10$; $K m_1 = 0.1$; $k_4 = 1$; $X_1 = 1$;

Initialize $S_1 = 4$ and $S_2 = 5$. These values are roughly at the steady state point.

Run a deterministic simulation of this pathway, record the steady state concentration of S2 here:

a) Steady State Deterministic Concentration of S2 =

Now run a stochastic simulation of this pathway. Because S2 will fluctuate you will need to compute the mean steady state concentration. You will need to compute the mean concentration of S2 using the following formula:

$$\text{Mean } S_2 = \sum_{i=1}^{n-1} S_{2i} \frac{(t_{i+1} - t_i)}{t_n}$$

Where t_n = the time at the end of the simulation (as recorded in the result matrix!) and $t_1 = 0$. S_{2i} is the concentration of S2 at time point i

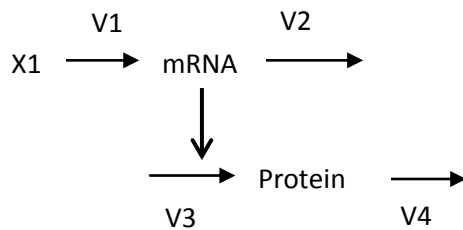
b) Compute the mean concentration of S2 using the above formula and record it here:

Mean S2 =

c) Explain why it is necessary to use the above formula to compute the mean S2 rather than simply summing up all the S2 concentrations and computing the average.

d) Explain why the deterministic and stochastic steady state levels are different?

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



The rate laws for this model are:

$$v_1 = k_1 x_1$$

$$v_2 = k_2 mRNA$$

$$v_3 = \frac{100 mRNA}{Km_1 + mRNA}$$

$$v_4 = k_4 Protein$$

Protein and mRNA levels can be set to zero at the start of the simulation. Run a simulation for about 200 time units and plot the graphs for mRNA and Protein.

Investigate the model under two sets of parameters:

1. $k_1 = 80$; $k_2 = 200$; $Km_1 = 10$; $k_4 = 1$;

2. $k_1 = 0.1$; $k_2 = 0.25$; $Km_1 = 10$; $k_4 = 1$;

a) What difference do you observe in the two simulations?

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.