

Bioengineering 499C: Systems and Synthetic Biology

May 06, 2008

Homework Assignment 4

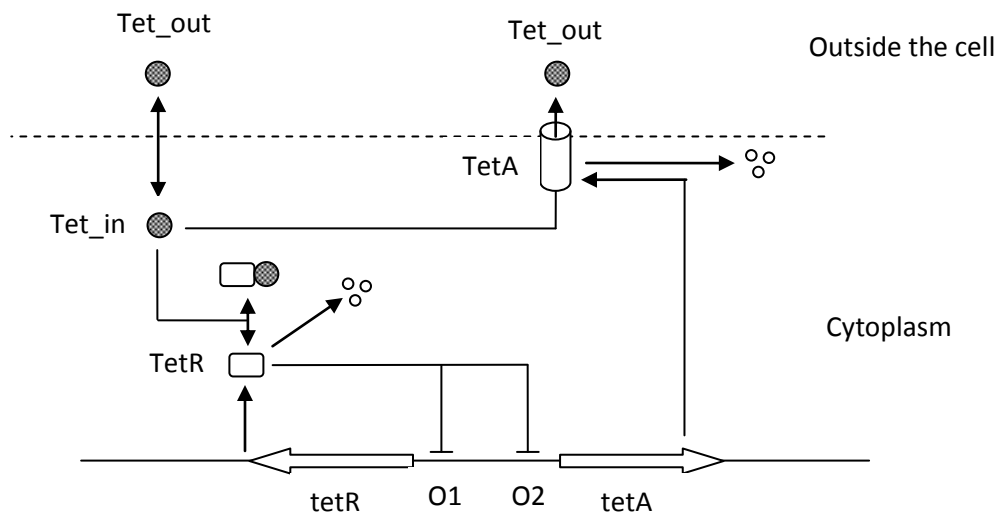
Due: 13th May 2008

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]

Question 1. Build a dynamic differential equation model of the Tetracycline operon. A basic model of the network is shown below. The operon comprises of two genes, *tetR* and *tetA*. *tetA* codes for a membrane pump, TetA, which can pump tetracycline out of the cell. Tetracycline can also freely diffuse in and out of the cell. You can assume simple mass-kinetics for the diffusion of tetracycline and simple irreversible Michaelis-Menten kinetics for the pump. You should assume that the pump has much higher activity relative to the free diffusion of tetracycline into and out of the cell.

Note that the model should include simple degradation steps for both TetR and TetA. The remainder of the model includes gene repression and a binding equilibrium between tetracycline and TetR. You can assume tight binding between tetracycline and TetR, for example, the binding rate constant can be 10,000 greater than the unbinding constant.

tetR codes for a repressor gene, TetR which can repress both *tetR* and *tetA* via **two separate** operator sites, O1 and O2 so that the relative repression can be adjusted. TetR can bind tetracycline forming an inactive complex which is unable to repress *tetR* and *tetA* expression. It is known that the Hill coefficient for repression is approximately 1.8.



[20] a) Write out the reaction model that you will use in the investigation.

[10] b) Write out your suggested gene expression rate laws for the repression of TetR on the operator sites.

[35] c) Investigate how the steady state concentration of tetracycline inside the cell is influenced by the relative strength of repression (eg by changes in the Hill coefficient, Michaelis constant and catalytic constant) on the two operator sites, O1 and O2. You should investigate this as a function of fixed external tetracycline.

[35] d) Investigate whether the rise time in the concentration of the pump protein upon addition of external tetracycline is influenced by the relative strength of repression on the two operator sites, O1 and O2.