Class 424 Advanced Systems and Synthetic Biology

Due date: 5 Feb, 2010, 11.45pm

Gene Expression Kinetics Assignment

The following table shows free energy changes for the binding of an activator, A, to two operator sites, OR1 and OR2. The promoter is only active when both operator sites are occupied. The symbol '-' in the table indicates 'not bound'.

State	OR1	OR2	ΔG (kcal)
0	-	-	0
1	A	-	-12
2	-	A	-12.5
3	A	A	-26.5

It is known that the maximal activity of the activator is 50 nmoles sec^{-1} $cell^{-1}$.

1. From the table above, determine whether there is a cooperative interaction between the two operator sites. Explain your reasoning. If so, is the cooperativity positive or negative?

2. Write out the gene expression rate law and generate a plot of the expression rate as a function of activator concentration.

3. If A is actually a dimer formed from monomers made by an upstream gene, build a computer model that includes the dimerization of A and the rate law from 2. Plot the rate of expression as a function of **monomer units**.

4. Estimate in any way you wish the cooperativity index for the data you generated in 2 and 3. What effect has the dimerization had on the response?

Input Number 1 — A1, A2 → [box] → C1, C2, C3 — Output Number; Input Number 2 — B1, B2
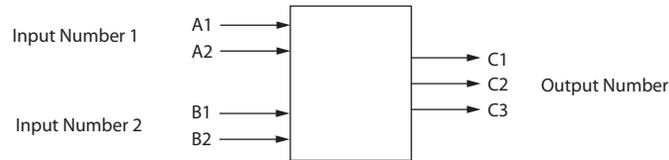
Modeling Assignment using TinkerCell

Design a genetic circuit that can be used to add two, two bit numbers. The figure below shows the inputs and outputs of the system. Two numbers are presented to the module in the form of two bit binary numbers. Each input number will therefore range from 0 to 3. The output will comprise of three proteins that will represent the sum of the two numbers. The three bits on the output include two bits for the sum and one bit for the carry. If you are not familiar with binary addition, a starting point will be to investigate half adders and full adders.

1. Provide a schematic of your design and include details on the rate equations you used for each gate in the model. When building the model, include your own rate laws, do not use the rate laws that Tinkercell automatically generates

2. Provide a small selection of simulation results that validate the design (Hint: Focus in the steady state outputs of the network)

3. Given an assessment of TinkerCell in the construction of the network. Comment on:

a) The ease of using TinkerCell to construction networks

b) The ease of using TinkerCell to simulate and study networks

4. Give a summary of your design's main features in a table by including the following: State the number of transcription factors involved in your design; state the number of operator and promoter sites used; if the average length of a coding sequence of 1000 bases with an additional 150 bases for the control sequence give an estimate of how long the DNA will be to construct your device; at a cost of 40 cents per base, estimate the cost of synthesizing your device.

Hint: Build the model in stages, make sure each stage works as you expect before proceeding to the next stage.