Molecular and Neural Computation (CSE P 590)
Homework 4

1. Gene Activation

Suppose you have an activatible gene that is nominally in an "off" state. The gene can be in two states:

- g_{ON} represents the gene in an "on" state with the gene bound to an activator *A*. An "on" gene produces a gene product *m.*
- g_{OFF} represents the gene in an "off" state where there is no activator bound to the gene

This system can be described with the following chemical reaction network:

$$g_{OFF} + nA \underset{k_-}{\overset{k_+}{\rightleftharpoons}} g_{ON}$$

$$g_{ON} \xrightarrow{\alpha} m$$

$$m \xrightarrow{\gamma} \emptyset$$

a. Suppose that the ratio of g_{ON} and g_{OFF} quickly comes to steady state. Write down a differential equation that describes the rate at which *m* changes as a function of the concentration of activator *A*.

b. Given the following parameters,

$$k_+ = 100$$
$$k_- = 10$$
$$n = 2$$
$$\alpha = 1$$
$$\gamma = 1$$

Solve for the following:

- The maximum steady-state concentration of *m* with infinite activator.
- The minimum steady-state concentration of *m* with no activator.
- The amount of activator necessary for ¼ maximum steady-state concentration.
- The amount of activator necessary for ¾ maximum steady-state concentration.

2. **Multistate Gene Activation and Repression**
Suppose you now have a gene that can be activated or repressed. There is one binding site for an activator *A*, and one binding site for a repressor *R*.

   a. What are the states of the gene? Suppose that for any gene state, the expression level of the gene is binary—either "on" or "off". Come up with a table describing the expression level for each gene state. If you think there is more than one option for a table entry, choose one and describe why you chose that option.

   b. Write down a chemical reaction network that describes how the gene moves between states.

   c. Assume that "on" genes produce a gene product, and that gene product is degraded at a rate γ (like in problem 1). Using Hill functions, write down an expression for the rate of at which *m* changes as a function of the concentration of activator *A* and repressor *R*.

   d. ***Extra credit:*** Make up values for the rates in your chemical reaction network. Plot a heat map for the dose response curve for this system (i.e. the x-axis is the concentration of *A*, the y-axis is the concentration of *R*, and the color at (x,y) corresponds to the steady-state level of *m*.

3. **Finite State Machines**
Mealy machines are a type of finite state machine where the machine emits an *output symbol* on every state transition.
http://en.wikipedia.org/wiki/Mealy_machine

   a. Suppose you have two streams of binary data, and you would like to compute the sum of these two streams. Design a Mealy machine where the output of the machine is the summation of the two input streams.

      Hint: You might consider your machine to take three input symbols corresponding to the sum of the two current digits. For example, if your two streams are,

      1001
      0011

      then the input to your machine might be the string,

      1012

   b. Using the method discussed in class, write down a gene regulatory network that implements your Mealy machine.

4. **Summarize a Research Article**
   Search google scholar for an article involving CRISPR that interests you. Summarize the results of the research, why you find it interesting, and suggest some ways you might use the technology.

   You might find the UW Proxy Bookmarklet useful for this problem: http://www.lib.washington.edu/help/proxyTools.html