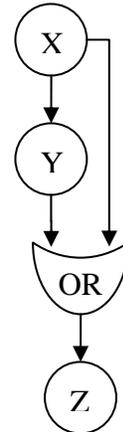1. Analyze the biomolecular feed-forward loop pictured. This motif
   contains an "OR gate," which means that Z is transcribed when
   either the concentration of X is above some threshold K_{xz} *or* the
   concentration of Y is above some threshold K_{yz} (or both).

   a. Make a sketch of the system showing the biomolecular
      components and the control interactions.
   b. Write model equations to represent the amount of proteins
      X, Y, and Z in the system. Explain any assumptions.
   c. Assuming that the activating signal S_y is always present,
      show plots of the protein concentrations over time as S_x is
      turned on and later turned off.
   d. Find an expression for the amount of time between the step
      change in X (on or off) and the beginning or ending of transcription of Z in
      response.
   e. What could be the biological function of this motif?

2. Let's test the accuracy of the logic function assumption.

   a. Create a numerical simulation using Matlab functions or
      Simulink of the biomolecular feed-forward loop motif
      (coherent type 1) with AND logic, depicted at the right. Use
      initial concentrations $Y = Z = 0$ and $X = 1$. Turn S_x on at $t = 0$
      and off at $t = 10$, and assume S_y is always present
      (activation/deactivation of X and Y via the signals S_x and S_y
      is practically instantaneous). For simplicity, use $\beta_z = \beta_y = 1$,
      $\alpha_y = \alpha_z = 1$, and $K_{xy} = K_{xz} = K_{yz} = 0.5$.
   b. Plot the concentrations of Y and Z over time. Compare
      results using the logic function assumption for transcription
      activation versus a Hill function activity model of order 2,
      i.e.,

      $$\text{transcription rate of Y} = \frac{\beta_y (X / K_{xy})^2}{1 + (X / K_{xy})^2} \quad \text{and}$$

      $$\text{transcription rate of Z} = \frac{\beta_z (XY / K_{xz} K_{yz})^2}{1 + (X / K_{xz})^2 + (Y / K_{yz})^2}.$$

   c. What is the delay in the response of Z to S_x (t_{ON} and t_{OFF}) in each case? Note that
      the logic function case should match the analytical solution.
   d. Is the logic function assumption valid?
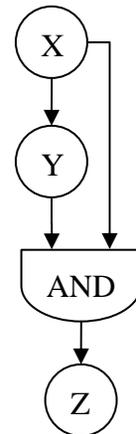
3. [Adapted from Alon 4.4] *The diamond motif.* The four-node diamond pattern occurs when X regulates Y and Z and both Y and Z regulate gene W.

   a. How does the mean number of diamonds scale with network size in random networks?

   b. What are the distinct types of sign combinations of the diamond (where each edge is either activation + or repression -)? How many of these are coherent?

4. [Adapted from Alon 5.4] What are the topological generalizations of the diamond pattern based on duplication of a single node and all of its edges? How are these different from DORs? Interestingly, most of the five-node generalizations of the diamond are network motifs observed in the neuronal network of *C. elegans*.

5. [Alon 6.3] Design a multi-layer perceptron with two input nodes, one output node, and as many intermediate layers as needed, whose output has a region of activation in the shape of a triangle in the middle of the X_1-X_2 plane.

6. [*Optional* for additional frequency response and Matlab practice] Work through Bequette's Module 6. Complete Problem 3, showing how you obtain your results including the required plots to obtain your answers and check your work.