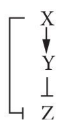
Exercise sheet 3
Systems Biology class 2014

April 9, 2014

Return by email to jean.hausser@weizmann.ac.il until April 13th 2014 at the latest with `[SB14] Exercise sheet 3` in the subject of the email.

1 Type three coherent feed-forward loop

Coherent type 3



Sketch the dynamics of the type-3 coherent FFL with AND logic at the Z promoter in response to upwards and downwards steps of Sx. Here, AND logic means that Z is produced if and only if both X^* and Y^* do not bind the promoter.

Are there delays in the production of Z? What regulation is carried out by this circuit: activation of Z by X or repression of Z by X? What is the regulatory benefit of X regulating Z through a type-3 coherent FFL compared to the simple regulation of Z by X?

2 Simulating a negative auto-regulation on the computer

Computer simulations are helpful in systems biology because they can help us gaining an intuitive understanding of how parameters affect circuit behavior even when the systems do not have analytical solutions. They can also help us appreciate how well analytical approximations of the circuit describe the actual circuit.

In this course, we will use Matlab to simulate different circuits.

1. Install Matlab on your computer or get access to a computer with Matlab. Room 101 in the Levine building has computers with Matlab installed. Alternatively, if you have some skills in programming, consider downloading and installing Scilab (`http://www.scilab.org/`), an open-source alternative to Matlab which uses a compatible syntax.

2. Get familiar with the basics of the language by going through the Matlab tutorial:
`http://www.mathworks.com/help/matlab/getting-started-with-matlab.html`

   For the course, it will be helpful to familiarize yourself with the material presented in the first seven tutorials of that web page:
   Desktop Basics, Matrices and Arrays, Array Indexing, Workspace Variables, Character Strings, Calling Functions, 2-D and 3-D Plots

   Depending on your previous experience with programming, it should take you between 30 min to 2 hours to work through these tutorials.

3. From the course website, download and run the script `NAR.m`. This script simulates the regulatory dynamics of a negative autoregulation circuit described by the following equation:

$$\frac{dX}{dt} = \beta \frac{1}{1 + (X/K)^n} - \alpha X \tag{1}$$

   Initially, the script is set up with the parameters $n = 1$, $K = 0.1$, $\alpha = 1$, $\beta = 1$.

4. Alter the script so that $\alpha = 0.1$, $\beta = 1000$, $n = 2$ and $K = 1$. In these simulations, what is the new value of the steady-state X_{st} for these parameters? Is the simulated value of X_{st} large compared to K? Compare the simulated X_{st} to the value given by the formula for the steady-state that you derived in exercise 2 of sheet 2:

$$X_{st} = K\left(\frac{\beta}{\alpha K}\right)^{\frac{1}{n+1}} \tag{2}$$

5. Alter the script so that $\alpha = 1$, $\beta = 1$, $n = 2$ and $K = 1$. What is the value of the new steady-state X_{st}? Is the simulated value of X_{st} large compared to K? Compare the simulated X_{st} to the value given by the formula for the steady-state given by Equation 2.

   Why are the steady-state X_{st} from the formula more different from the simulations than in the previous question? *Hint:* to obtain Equation 2, remember that we assumed that $\left(\frac{X}{K}\right)^n >> 1$.