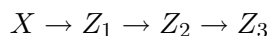


Exercise 2: Biological Circuits

A single regulator X regulates the three genes Z_1, Z_2, Z_3 . In the lecture we saw a system that responds to an input in a first-in, last-out manner, which means that the first gene turned on is the last one to be turned off.

Now the aim is to construct a system that behaves in a first-in, first-out manner, i.e. the gene that is turned on first should also be the first one to be turned off again, and the last gene to be turned on is supposed to be the last one to be turned off again.

One easy way to achieve this behaviour is to look at the following path of activation:



This means that gene Z_1 is only turned on if X is present above a certain threshold K_{XZ_1} . Gene Z_2 in turn is only switched on if gene Z_1 is present above a certain threshold $K_{Z_1Z_2}$ and Z_3 is only switched on if Z_2 is present above the threshold $K_{Z_2Z_3}$.

On the other hand, if X falls below the threshold K_{XZ_1} it will cause gene Z_1 to be switched off, which in turn leads to a subsequent switch-off of Z_2 and afterwards of Z_3 .

Thus we have that the genes Z_1, Z_2 and Z_3 behave in a first-in, first-out temporal order as response to the regulator X .

The corresponding ODE systems then reads as

$$\begin{aligned} X'(t) &= \beta_X(1 - \Theta(t - 5))\Theta(t - 1) - \alpha_X X(t) \\ Z_1'(t) &= \beta_{Z_1}\Theta(X(t) - K_{XZ_1}) - \alpha_{Z_1}Z_1(t) \\ Z_2'(t) &= \beta_{Z_2}\Theta(Z_1(t) - K_{Z_1Z_2}) - \alpha_{Z_2}Z_2(t) \\ Z_3'(t) &= \beta_{Z_3}\Theta(Z_2(t) - K_{Z_2Z_3}) - \alpha_{Z_3}Z_3(t) \end{aligned}$$

with β_i and $\alpha_i, i \in \{X, Z_1, Z_2, Z_3\}$, denoting the transcription and degradation rates and Θ denoting the unit step function. Initial conditions are given by $X(0) = 0, Z_1(0) = 0, Z_2(0) = 0$ and $Z_3(0) = 0$.

For the numerical simulations the transcription and degradation rates have been set to one.

In fig. 1 results for all thresholds set to 0.5 can be seen. Increasing the timespan for the transcription of the regulator X from 4 to 9 leads to the results in fig. 2.

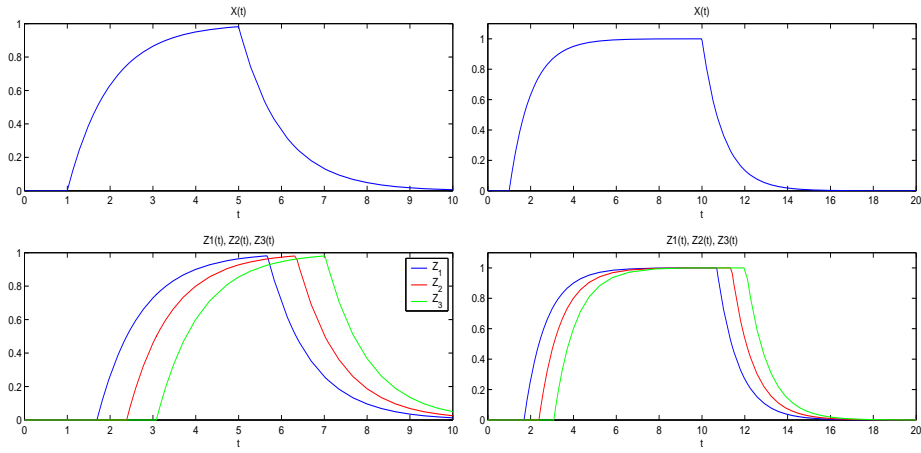


Figure 1: All thresholds K_{XZ_1} , Figure 2: All thresholds K_{XZ_1} , $K_{Z_1Z_2}$, K_{XZ_1} set to 0.5

Changing of the thresholds changes the timespan between the switch-on, switch-off of the individual genes (fig. 3).

Repeated input for X leads to a repeated FIFO-behaviour in genes Z_1 , Z_2 , Z_3 (fig. 4).

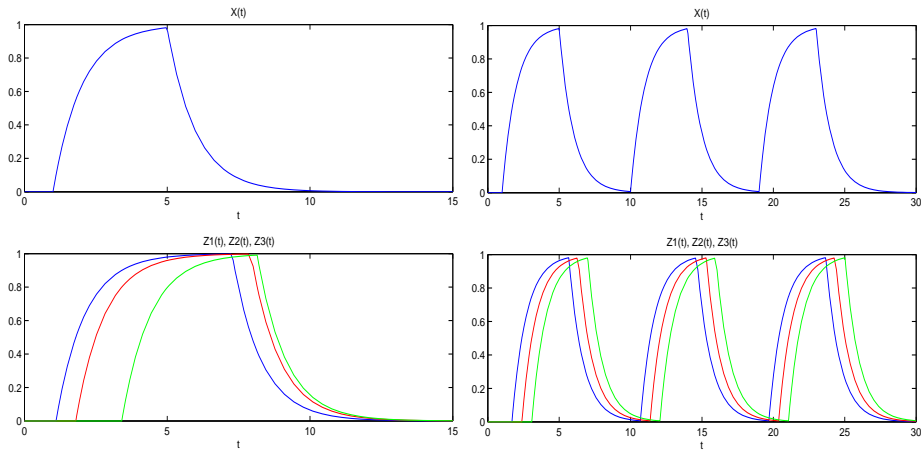


Figure 3: $K_{XZ_1} = 0.1$, $K_{Z_1Z_2} = 0.5$, Figure 4: Repeated input for X , $K_{XZ_1} = 0.8$, equal thresholds.