ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

ETHCSB computational systems biology

Pulse Generator, Exercise 3

Synthetic Biology SS 2012

To be submitted by Monday April 23rd to:

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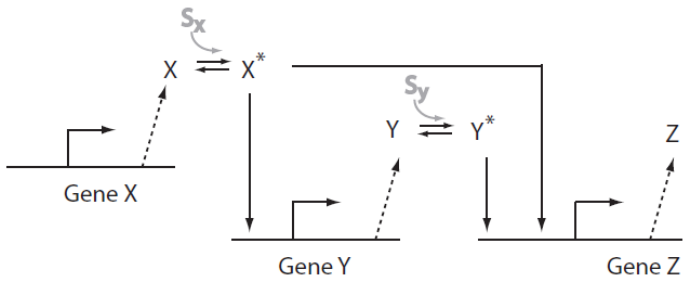
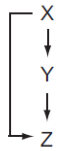
CAB 71.6 J

Feed-forward loop motif



- $X^* = X$ if $S_X = 1$, and $X^* = 0$ if $S_X = 0$,
- $Y^* = Y$ if $S_Y = 1$, and $Y^* = 0$ if $S_Y = 0$.



a) C1FFL

Assume S_Y=1 and X=1

Model formulation

$$\frac{dY}{dt} = \alpha_Y + k_Y \cdot \frac{(X/K_{XY})^n}{1+(X/K_{XY})^n} - d_Y Y \qquad (1)$$

$$\frac{dZ}{dt} = \alpha_Z + k_Z \cdot \frac{(X/K_{XZ})^n}{1+(X/K_{XZ})^n} \cdot \frac{(Y/K_{YZ})^n}{1+(Y/K_{YZ})^n} - d_Z Z \qquad (2)$$

↓

AND

Table 1: Parameters

Par.	Description	Value
α_Y	basal transcription rate of Y	0
α_Z	basal transcription rate of Z	0
k_Y	maximal expression level of the promoter Y	1
k_Z	maximal expression level of the promoter Z	1
K_{XY}	activation (or repression) coef. of gene Y by X	0.1
K_{XZ}	activation (or repression) coef. of gene Z by X	0.1
K_{YZ}	activation (or repression) coef. of gene Z by Y	0.5
d_Y	degradation rate of Y	1
d_Z	degradation rate of Z	1
n	Hill coefficient	6

Matlab template files

$$\frac{dZ}{dt} = \alpha_Z + k_Z \cdot \frac{(X/K_{XZ})^n + (Y/K_{YZ})^n}{1+(X/K_{XZ})^n + (Y/K_{YZ})^n} - d_Z Z. \qquad (3)$$

↓

OR

1. Consider the C1FFL motif with an *AND* gate for the Z promoter, and the values of the parameters given in Table 1. Matlab scripts for the simulation of C1FFL motif with *AND* gate for the Z promoter are provided (see C1FFLand, Ex3FFLmain attached).

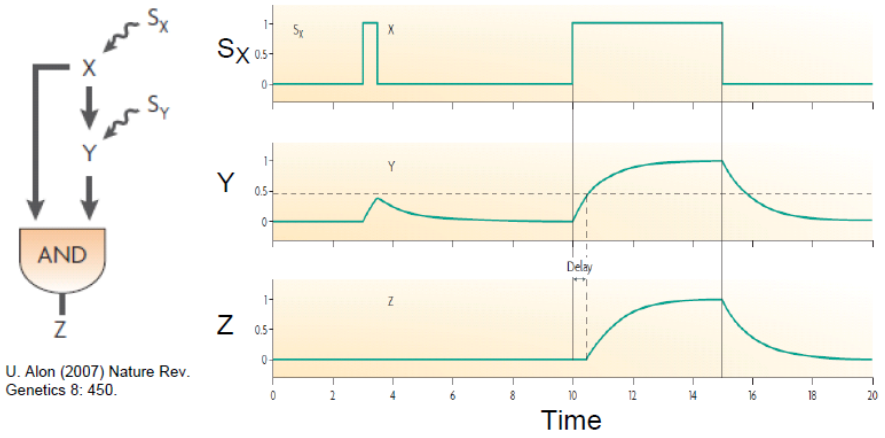
```
function dxdt = C1FFLand(t,x,t_Sx_ON,t_Sx_OFF)

% X activates Y
% Y activates Z
% X activates Z
% type of transcription function for Z: "AND gate„
...
```

1.

a) Does the system show a delay in Z response after addition of the input signal S_X?. And after the removal of the input signal?

b) Perform the analysis in a) for the C1FFL motif with an *OR* logic at the Z promoter.

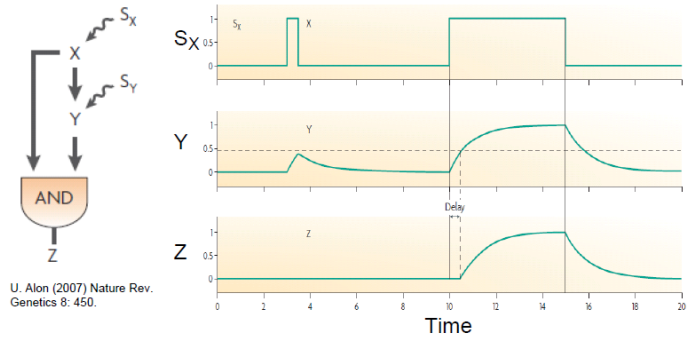


U. Alon (2007) Nature Rev. Genetics 8: 450.

1.

c) The C1FFL motif with *AND* logic is shown to respond only to persistent stimuli. Compute the maximum duration of the signal which can be filtered out by the system dynamics.

d) Repeat the analysis in c) for $K_{YZ} = 0.1$ and $K_{YZ} = 0.9$.



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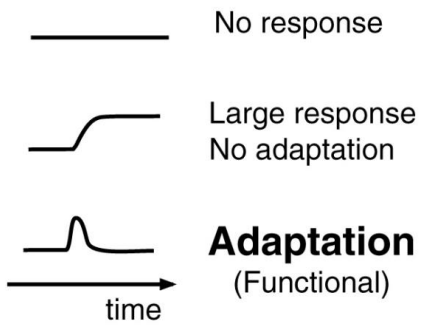
Time delay for Z production: $$\Delta t = \frac{1}{d_Y} \cdot \log\left(\frac{[Y]^{ss}}{[Y]^{ss} - K_{YZ}}\right)$$

2. Biological systems able to respond to a change in input stimulus, and return to its prestimulated output level even when a given stimulus persists, are said to perform *adaptation* (Ma et al., 2009). For the systems under



2. a) Compare the sensitivity to the input stimulus and the adaptation precision of the I1FFL and I4FFL motifs, with the values of the parameters given in Table 1.

b) Repeat the analysis in a) for $K_{YZ} = 0.9$ and $K_{YZ} = 0.01$.

c) Repeat the analysis for the I4FFL motif with $K_{YZ} = 0.01$ and $\alpha_Z = 0.1$.

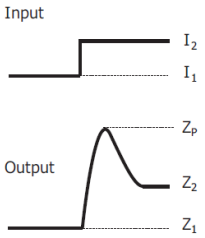


Figure 2: Input-output behaviour defining adaptation, from Ma et al. 2009.

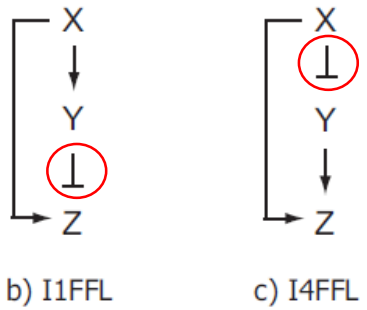
$$\text{Sensitivity} = \left| \frac{(Z_{peak} - Z_1)/Z_1}{(I_2 - I_1)/I_1} \right| \tag{4}$$

$$\text{Precision} = \left| \frac{(Z_2 - Z_1)/Z_1}{(I_2 - I_1)/I_1} \right|^{-1} \tag{5}$$

2. a) Compare the sensitivity to the input stimulus and the adaptation precision of the I1FFL and I4FFL motifs, with the values of the parameters given in Table 1.

b) Repeat the analysis in a) for $K_{YZ} = 0.9$ and $K_{YZ} = 0.01$.

c) Repeat the analysis for the I4FFL motif with $K_{YZ} = 0.01$ and $\alpha_Z = 0.1$.



b) I1FFL c) I4FFL