LECTURE 5: NETWORK MOTIFS (FFL)

Introduction to cellular system modelling

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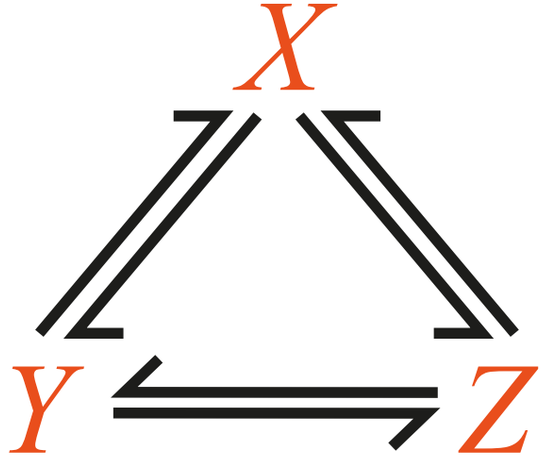
OUTLINE

- 3 node networks
- random network subgraphs
- FFL
- C1 FFL
- AND C1 FFL
- arabinose system example
- OR C1 FFL
- Flagella example
- AND I1 FFL
- Galactose example

3 NODE NETWORKS

There are 13 possible network topologies involving 3 nodes (excluding self loops)



SUBGRAPH PROBABILITY

Probability of a specific subgraph that has n nodes and g edges appearing randomly in a network having N nodes and E edges can be approximated as follows.

$$p = \frac{E}{N^2}$$ prob. of a given edge

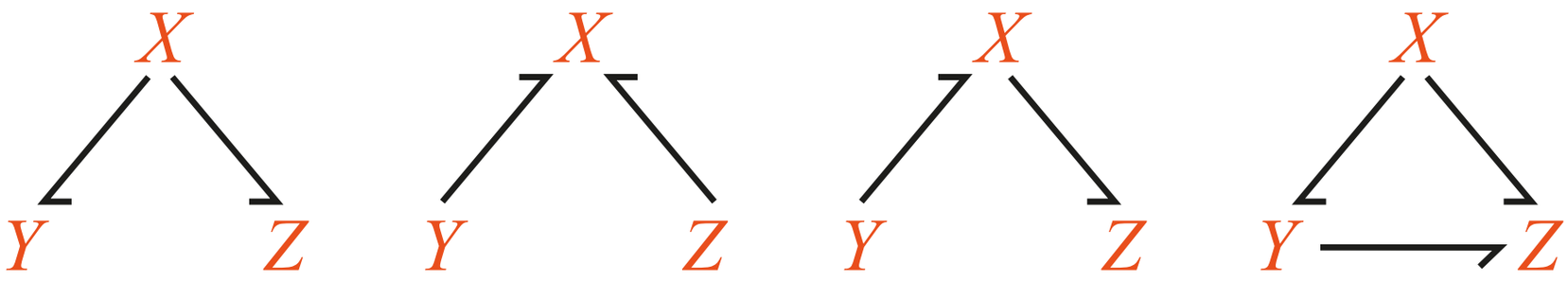
$$\mathbb{E}\left(N_G\right) = \frac{N^n p^g}{a}$$ prob. of a subgraph
a = number of isomorphic permutations

$$\lambda = \frac{E}{N}$$ mean network connectivity

$$\mathbb{E}\left(N_G\right) = \frac{\lambda^g N^{n-g}}{a}$$ prob. of a subgraph expressed in terms of mean connectivity

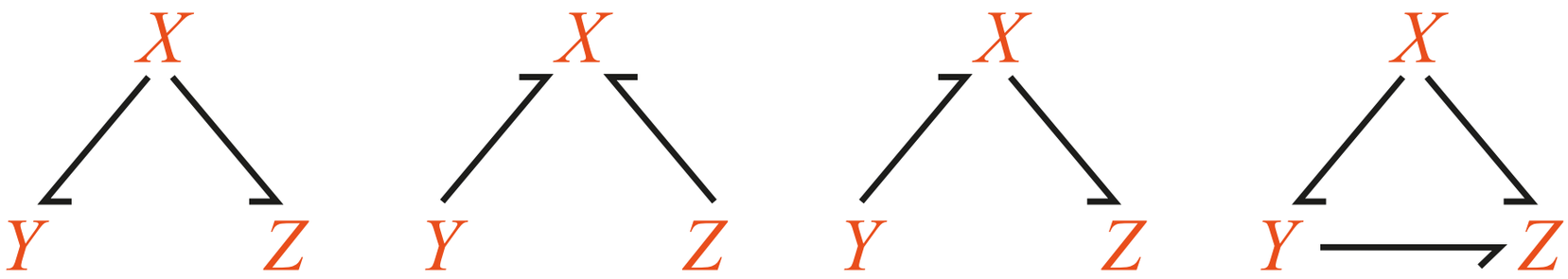
3 NODE MOTIFS

Out of the 13 possibilities, only motifs with two edges and feedforward loops are motifs.



3 NODE MOTIFS

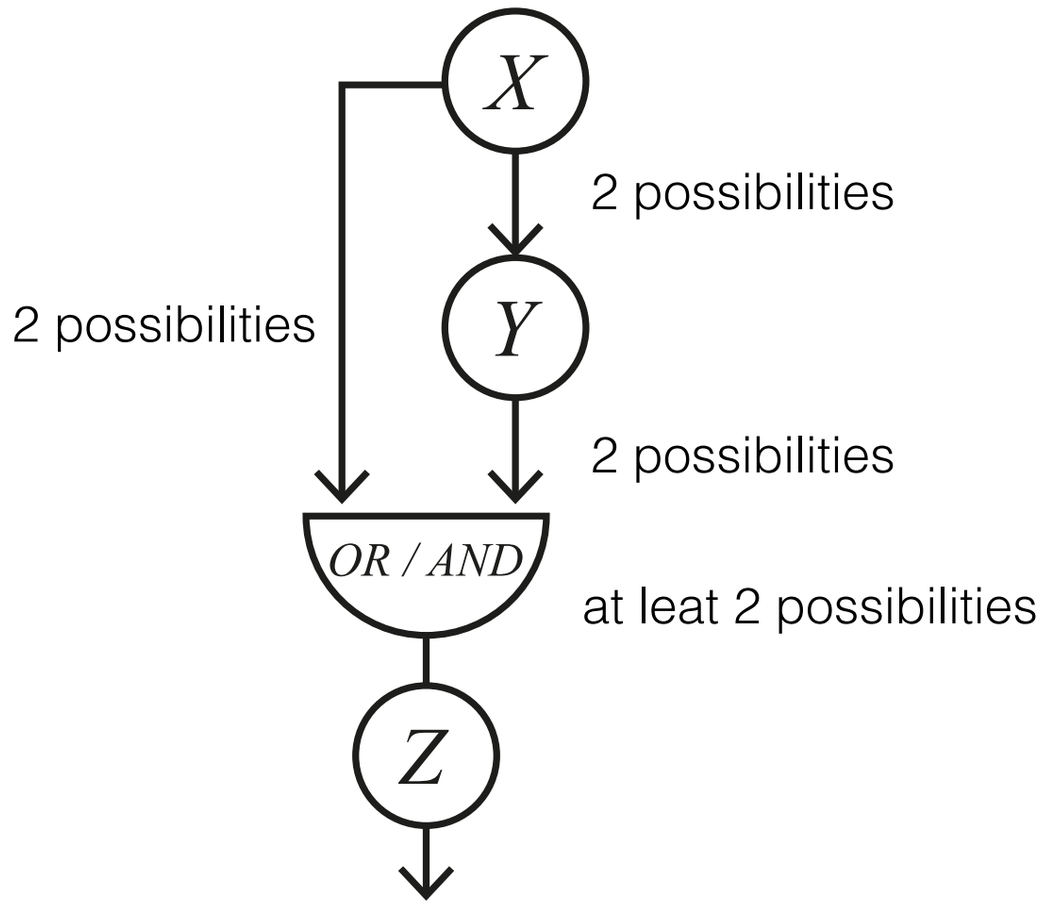
Two edge motifs represent simple activation and repression, which we already discussed.
There is only one three edge motif, the Feedforward Loop (FFL).



FFL

42X in E. coli example
1.7 +/- in random nets.

FFL



at least 16 overall possibilities

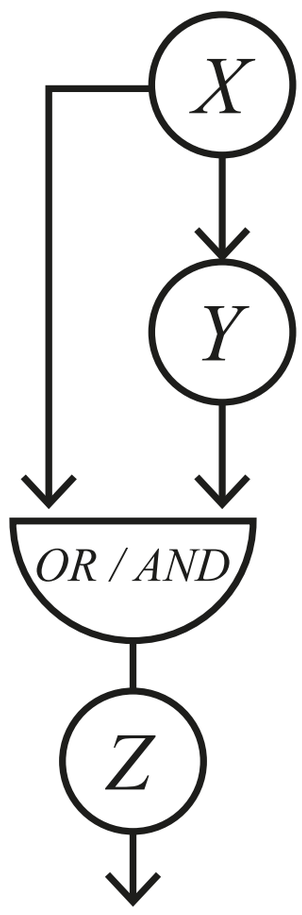
FFL

There are 8 possible feedforward loops that fall into two categories. There are 16 or more possibilities if we consider how the actions of X and Y on Z are aggregated.

Coherent feedforward loops = the delayed and direct paths starting at X both activate or repress the end gene Z.

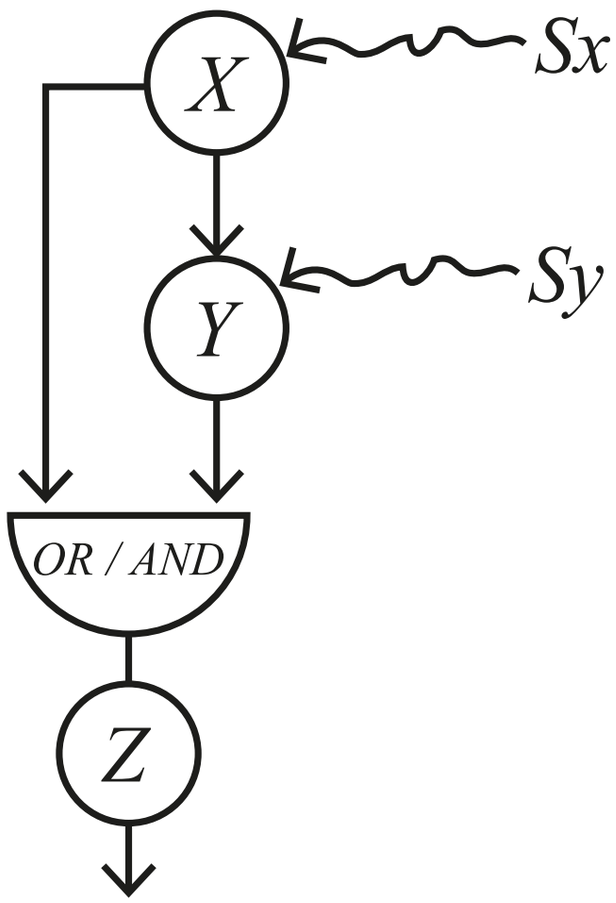
Incoherent feedforward loops = the delayed and direct paths starting at X act oppositely on the end gene Z.

C1 FFL



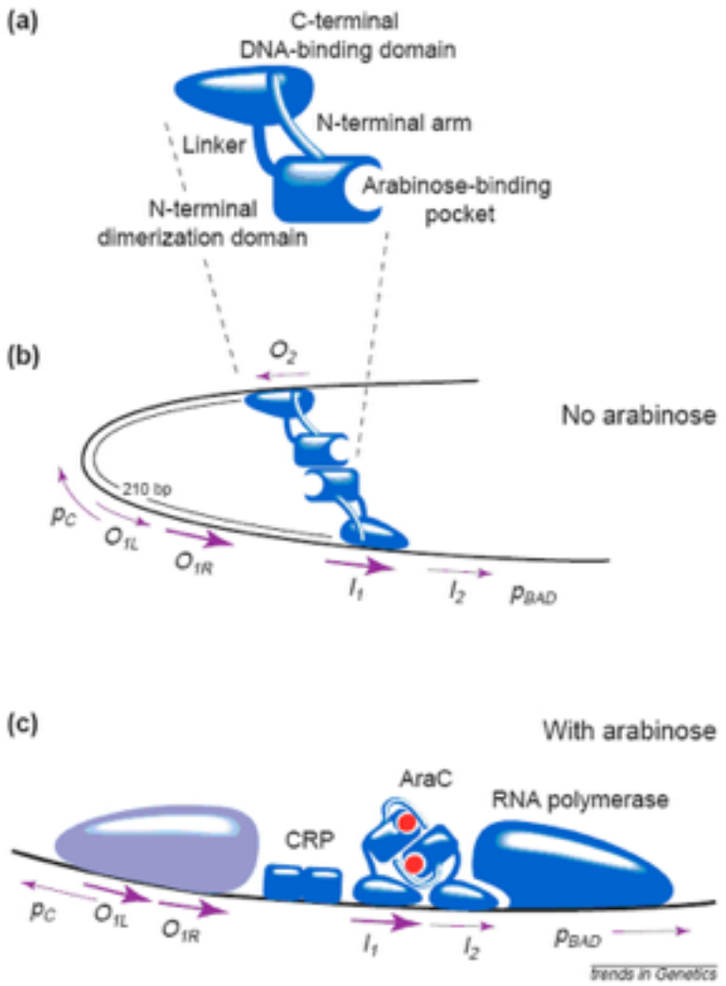
37% of FFLs are C1 FFLs

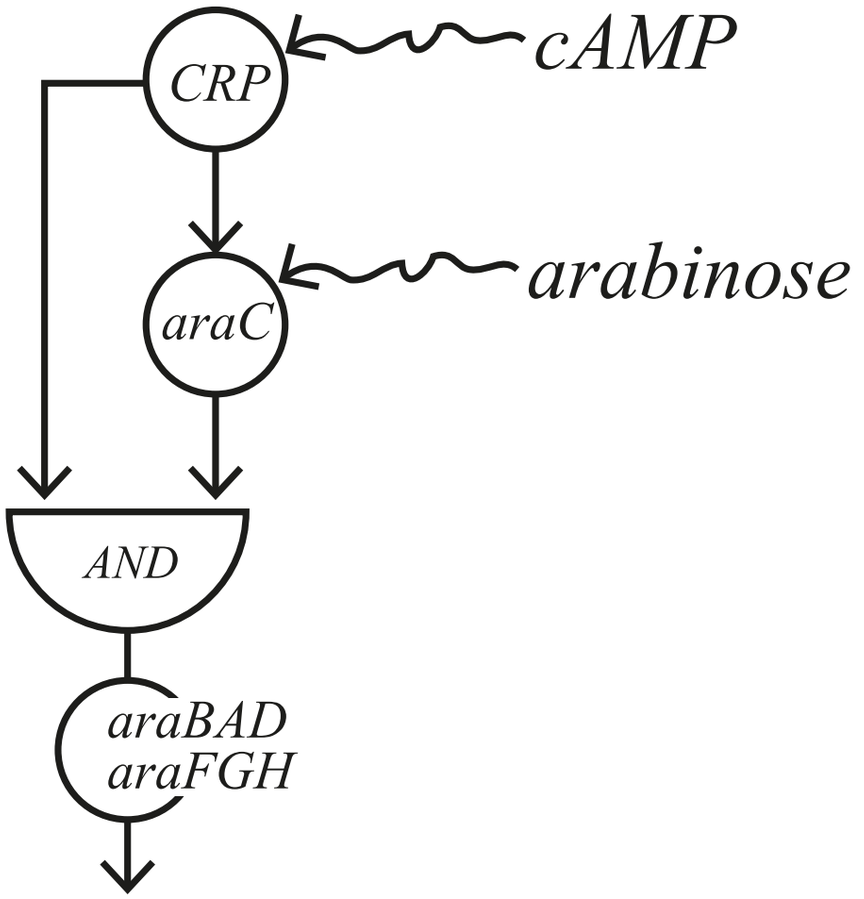
C1 FFL



Implementation of FFLs involves activating signals.

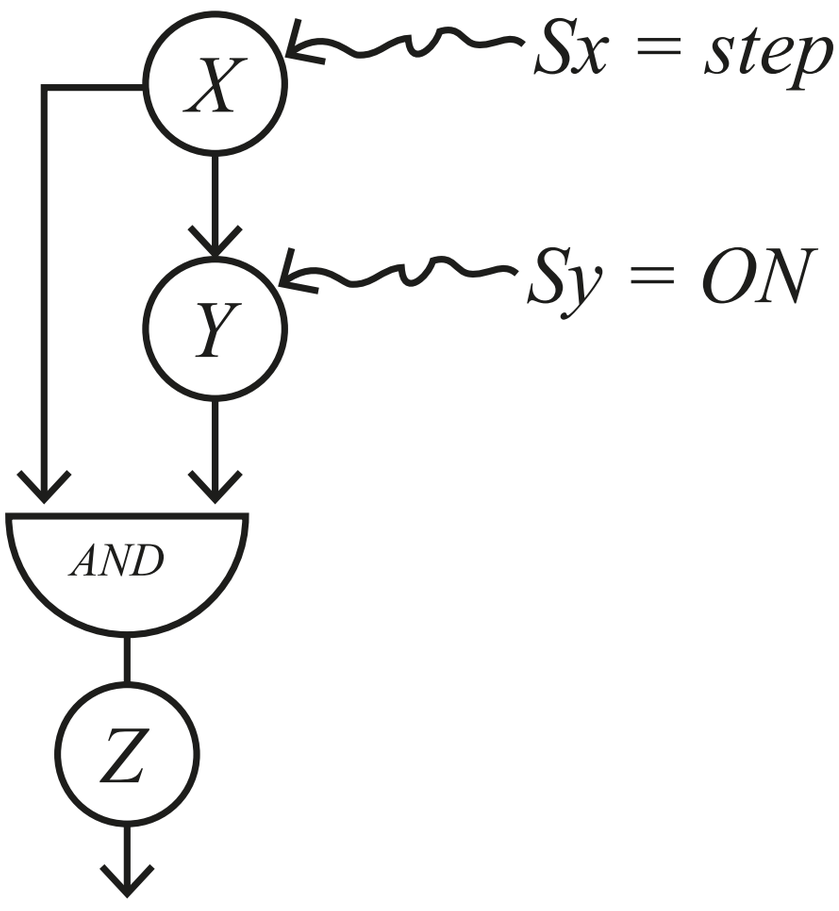
C1 FFL - Arabinose metabolism activation





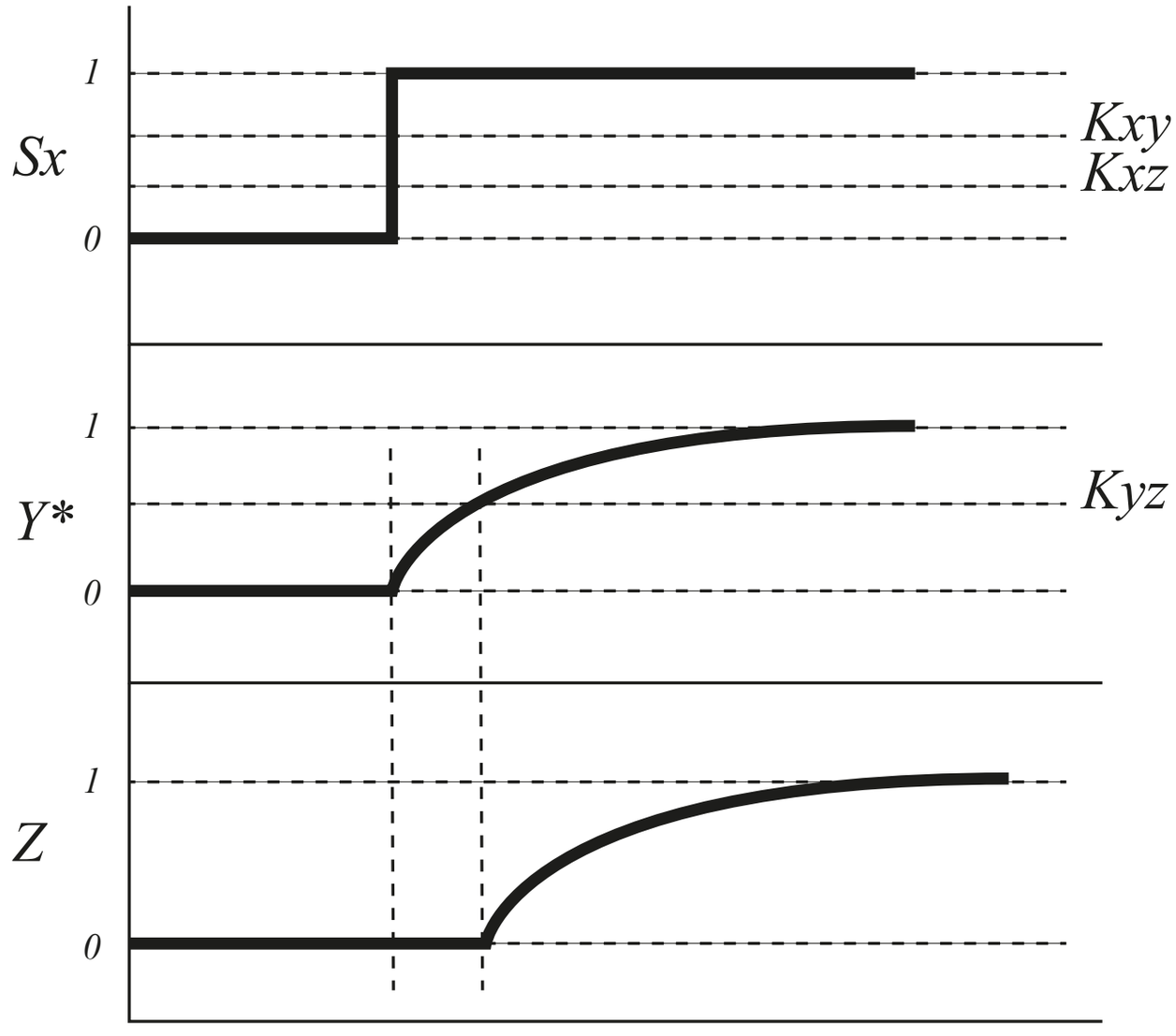
AND C1 FFL is implemented to activate arabinose metabolism.

AND C1 FFL (ASSUMPTIONS)



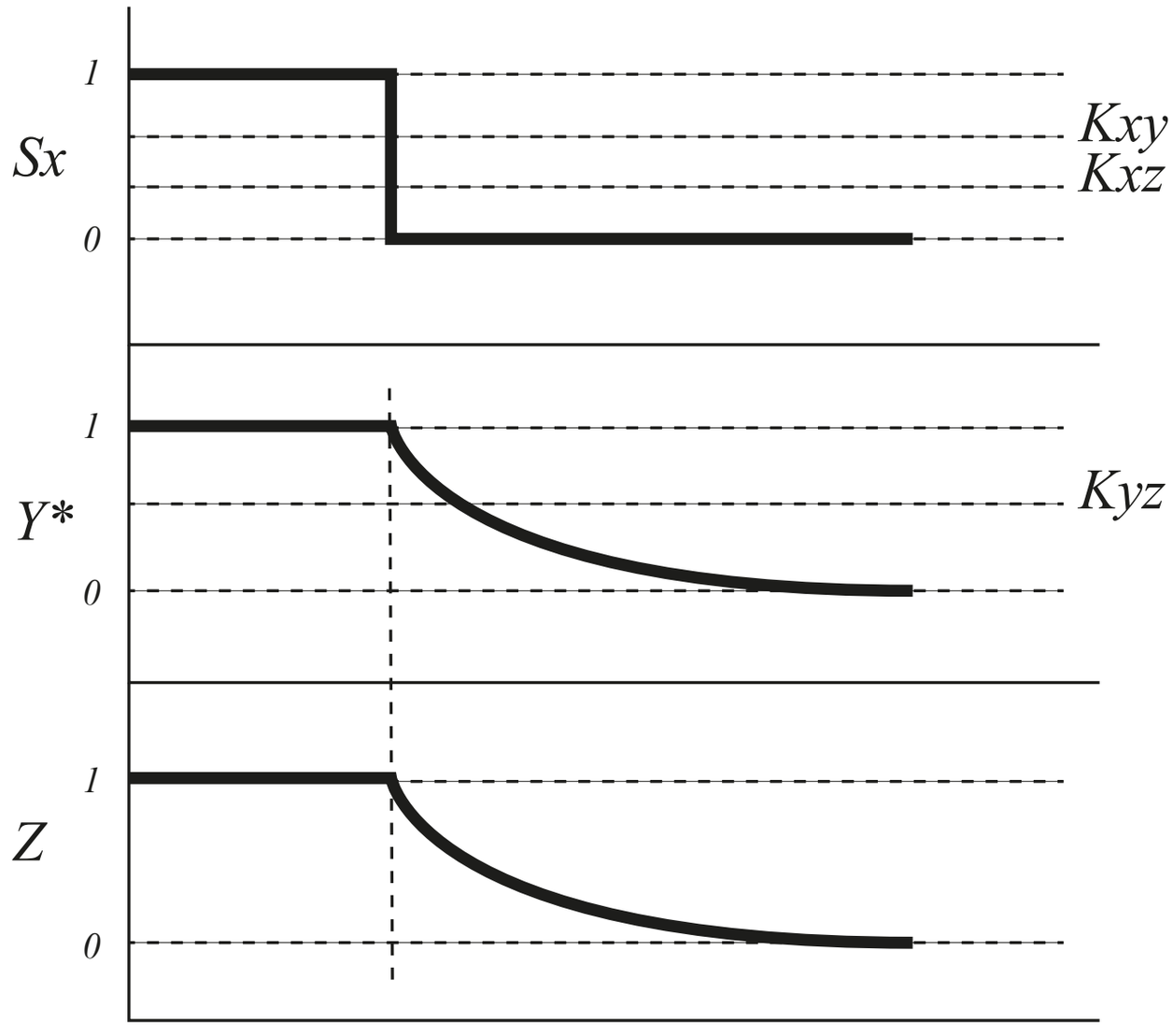
Signal activate transcription factors immediately. Production rates are approximated by boolean functions with prescribed activation thresholds, K_{XY}, K_{XZ}, K_{YZ}. Production rate of Z is boolean AND.

AND C1 FFL (ON)



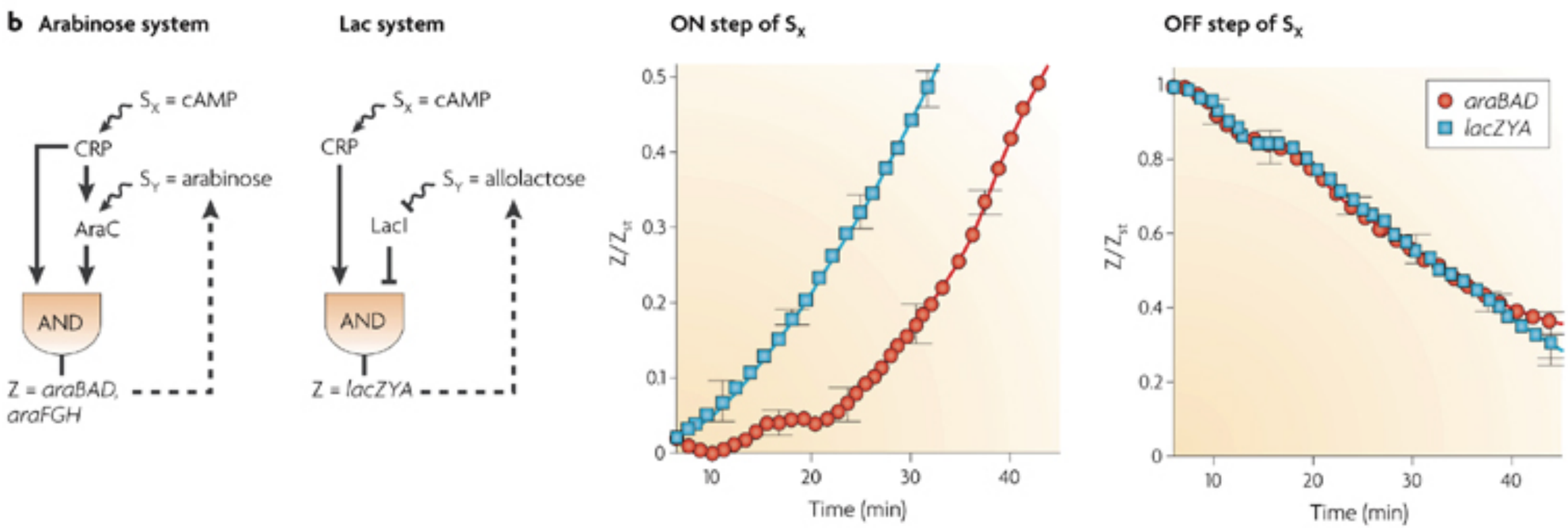
AND C1 FFL generates a delay in turning ON the circuit

AND C1 FFL (ON)



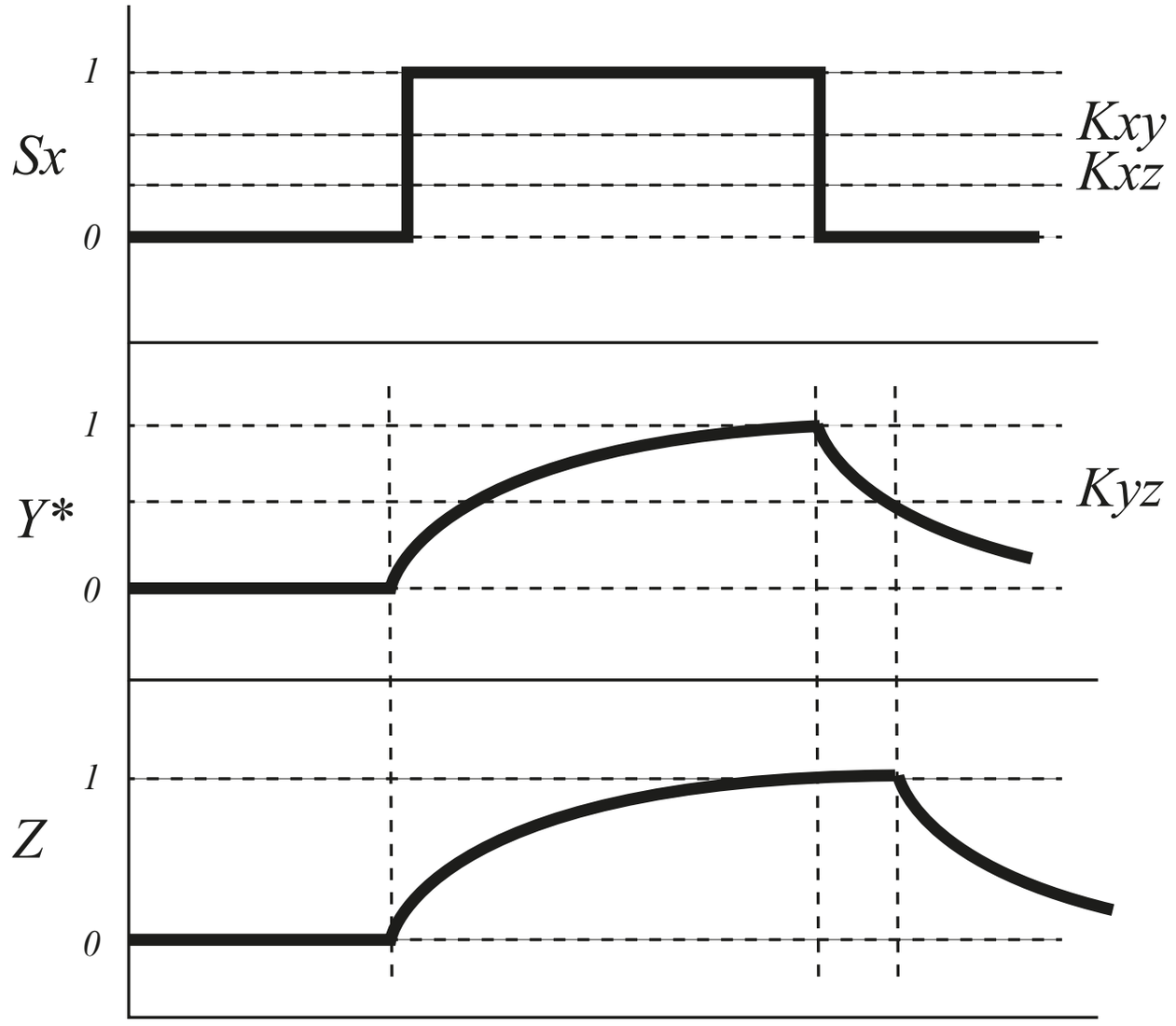
AND C1 FFL generates NO delay in turning OFF the circuit

AND C1 FFL (ON and OFF) - arabinose



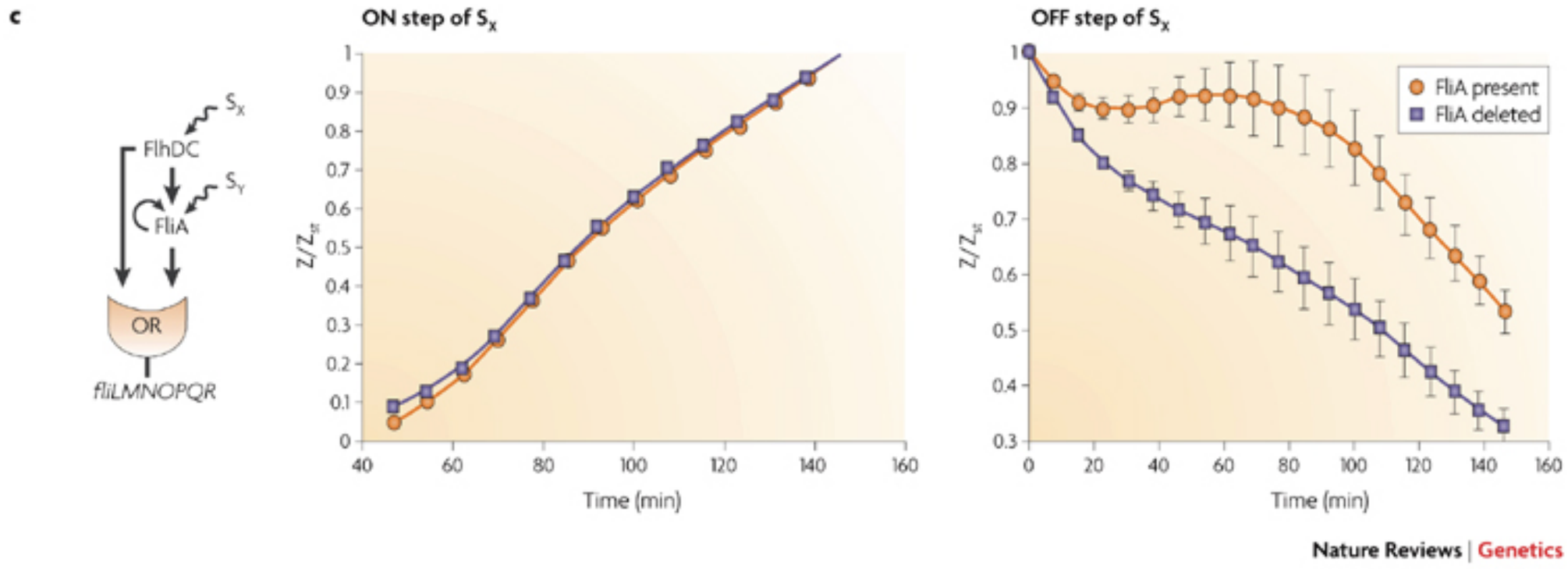
AND C1 FFL generates a delay in turning ON the circuit

OR C1 FFL



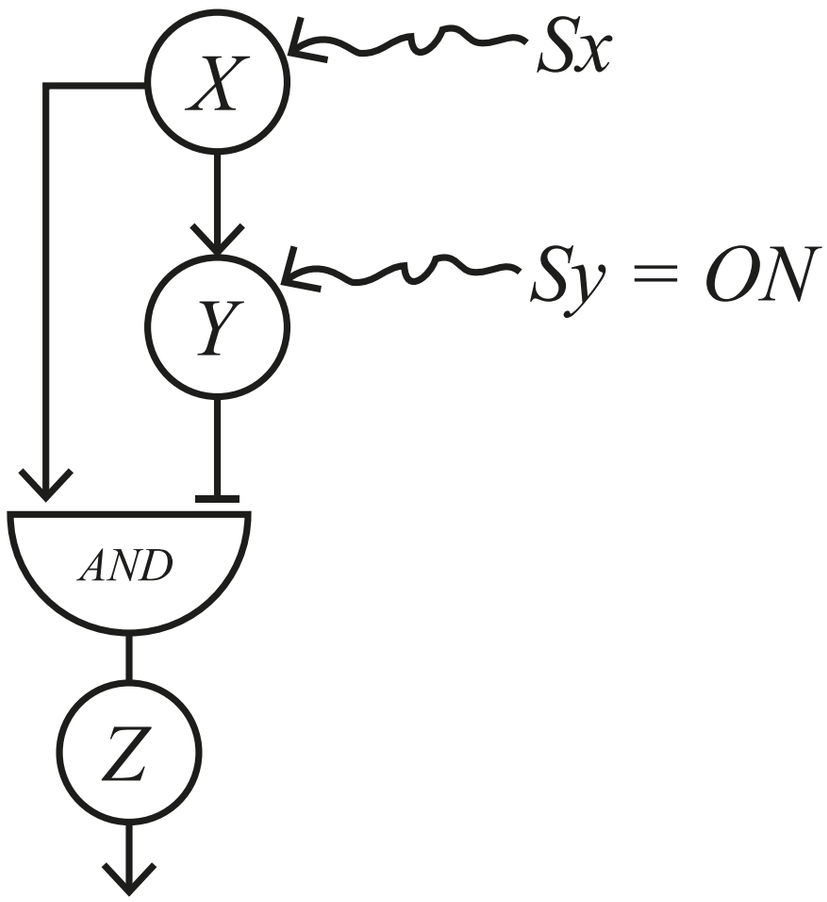
OR C1 FFL generates NO delay in turning ON tand a positive delay in turning OFF the circuit.

OR C1 FFL - Flagella example



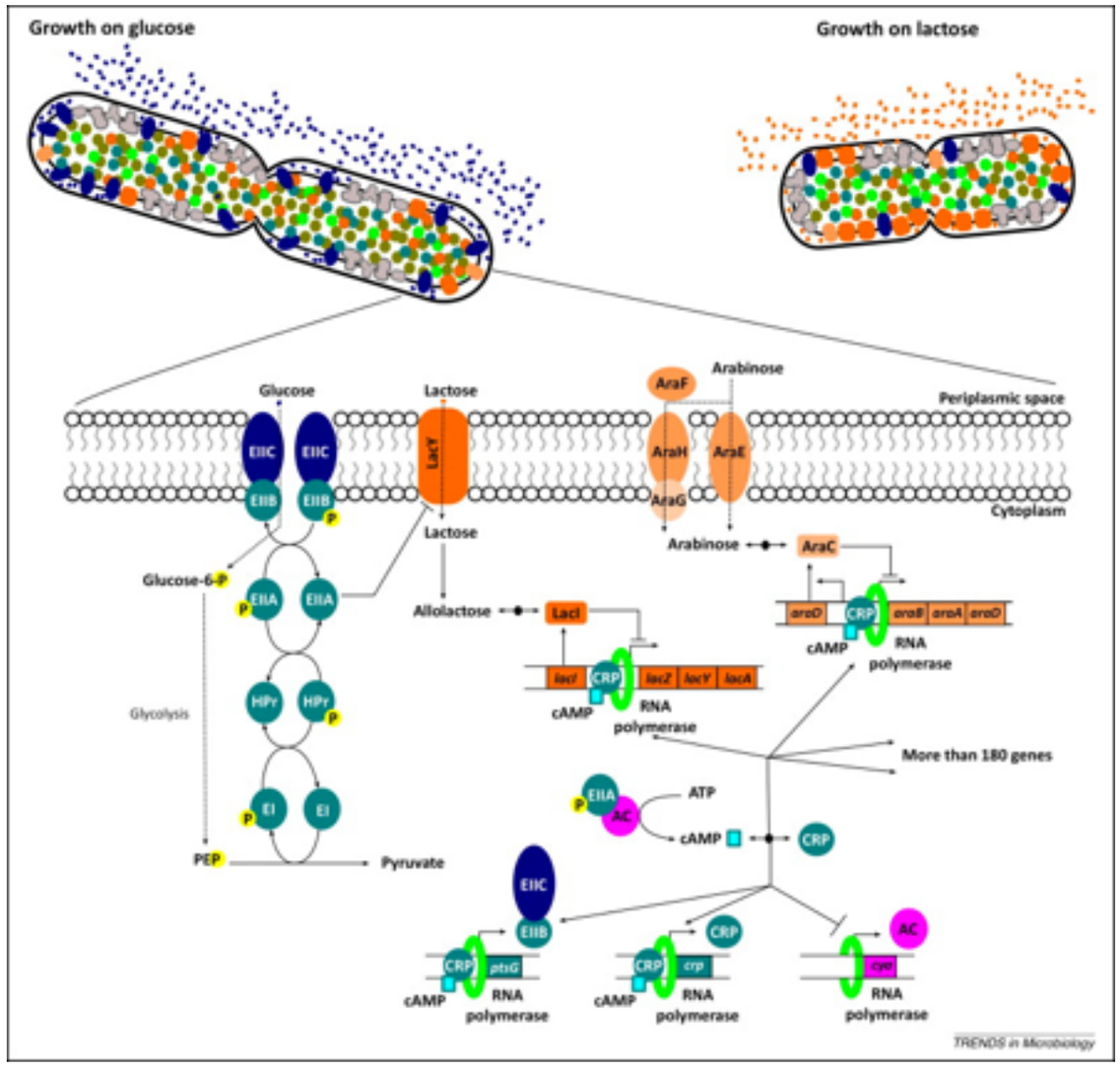
OR C1 FFL generates a delay in turning OFF the circuit

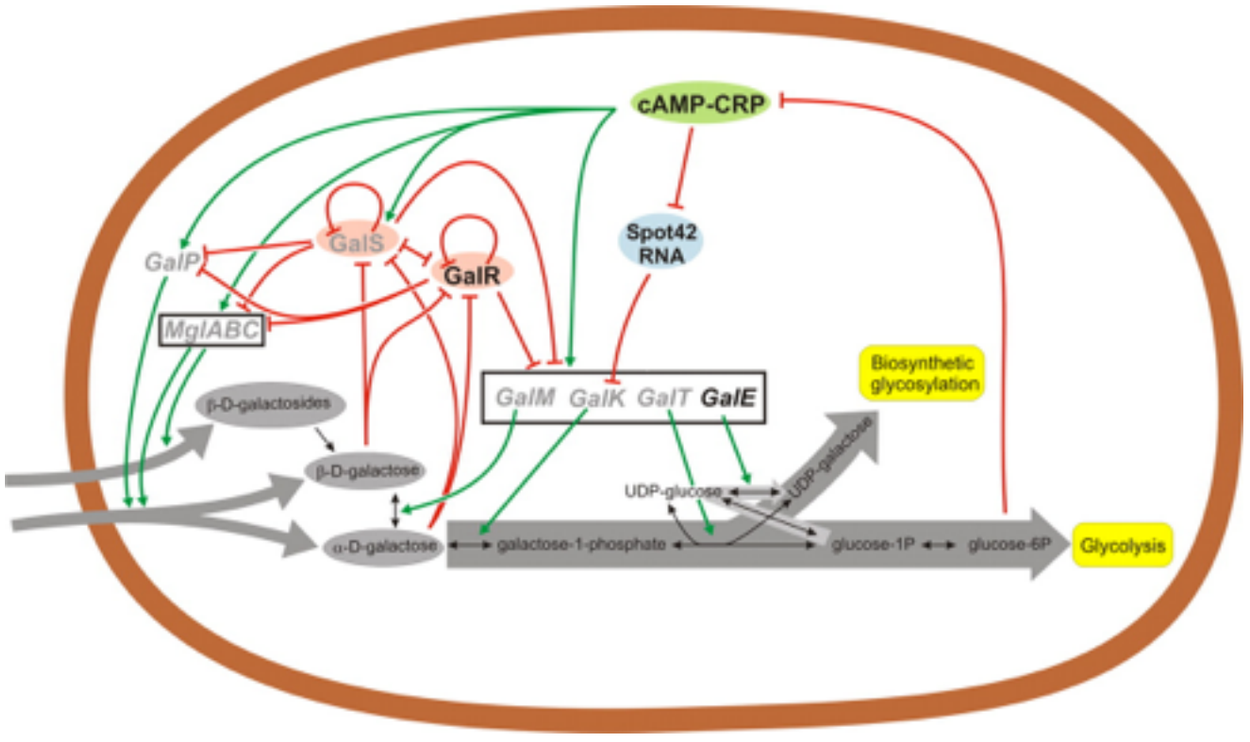
I1 FFL



30% of FFLs are I1 FFLs

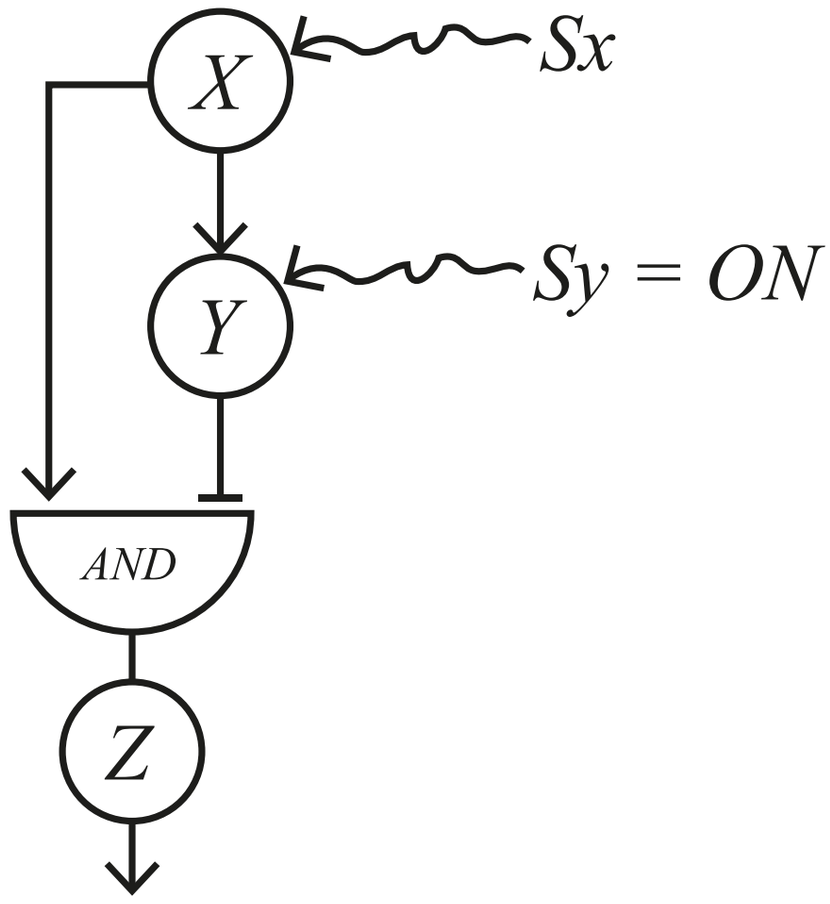
I1 FFL - Galactose metabolism activation





AND i1 FFL is implemented to activate galactose metabolism.

AND I1 FFL (ASSUMPTIONS)



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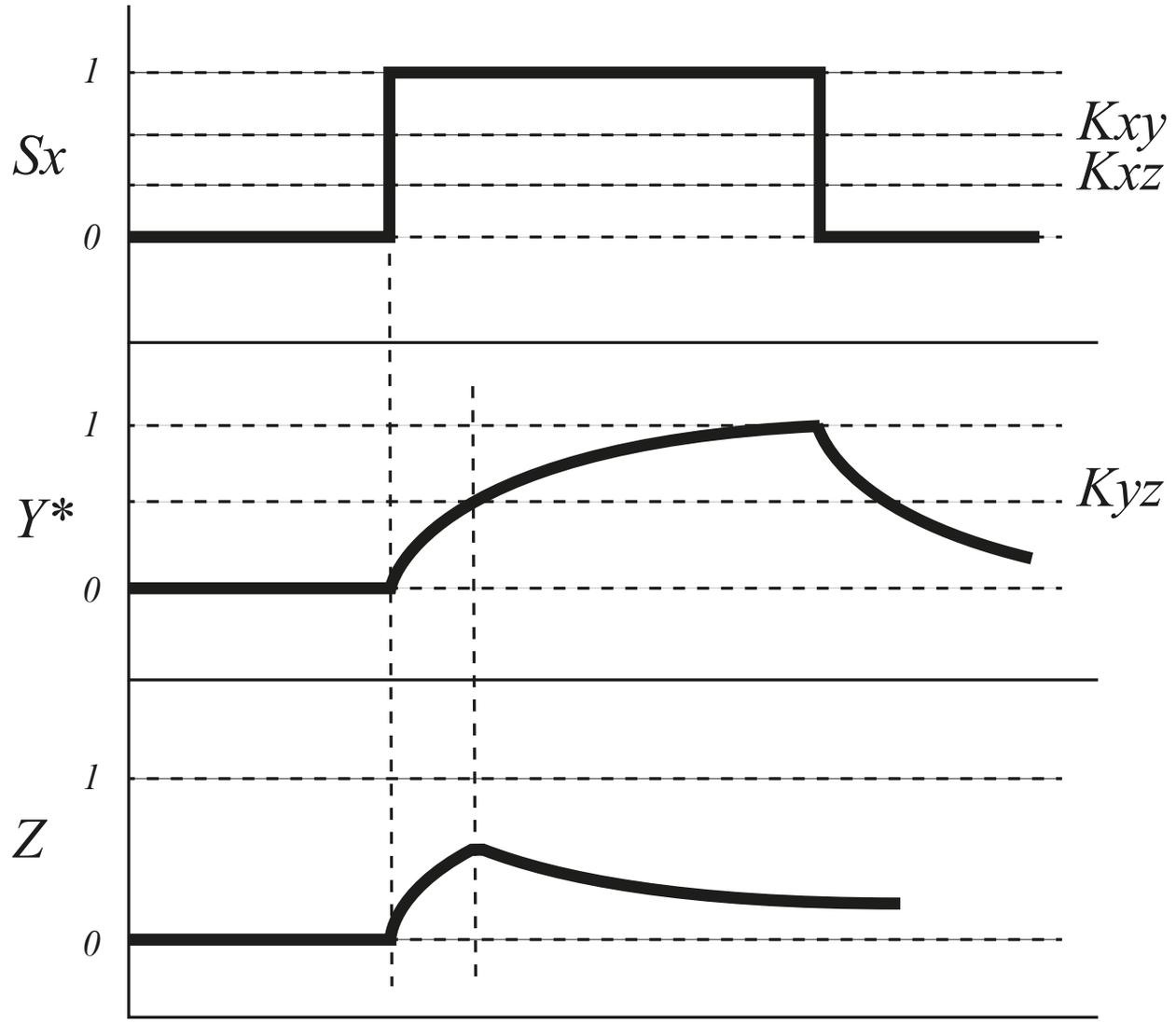
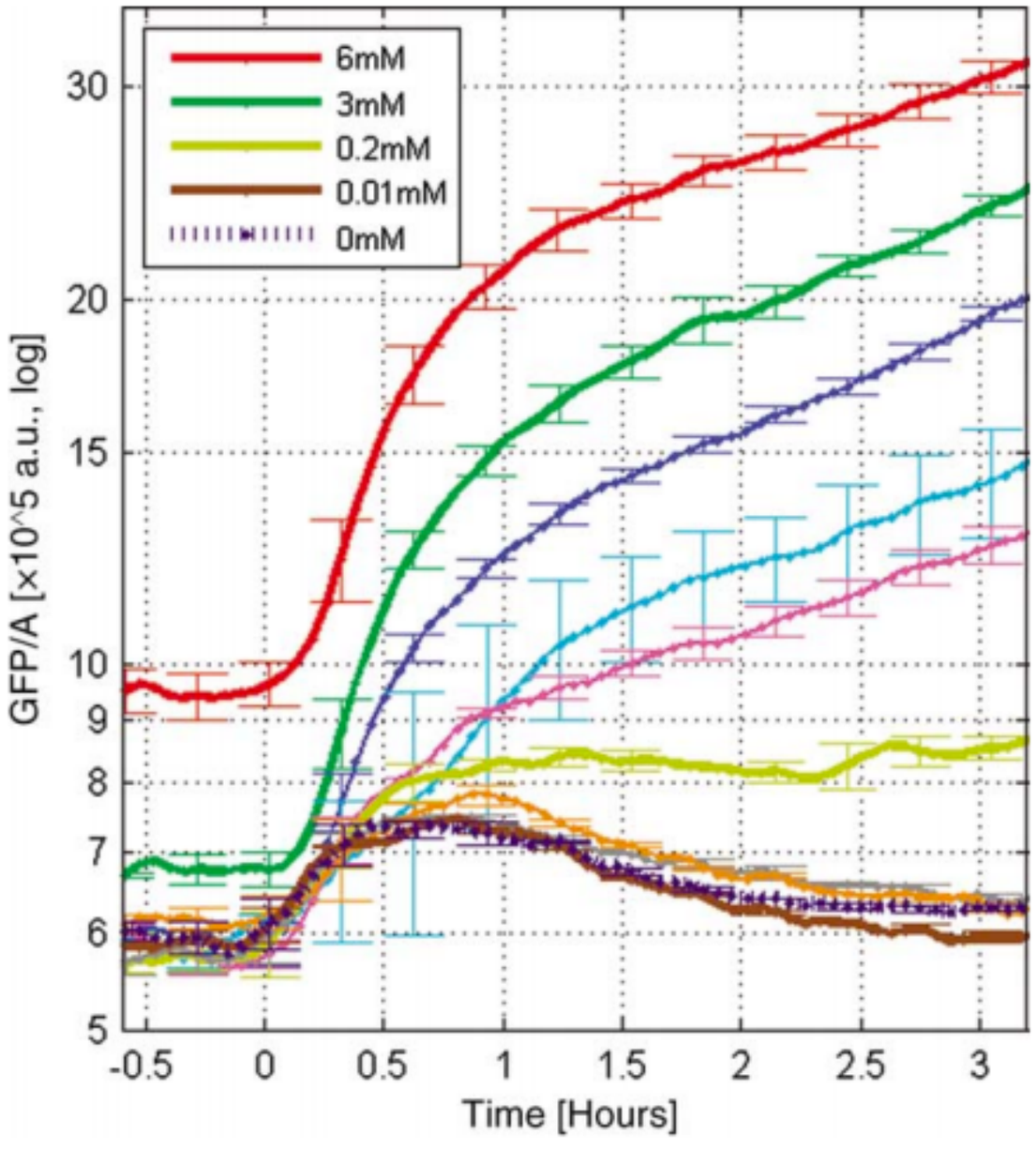
AND C1 FFL (ON)



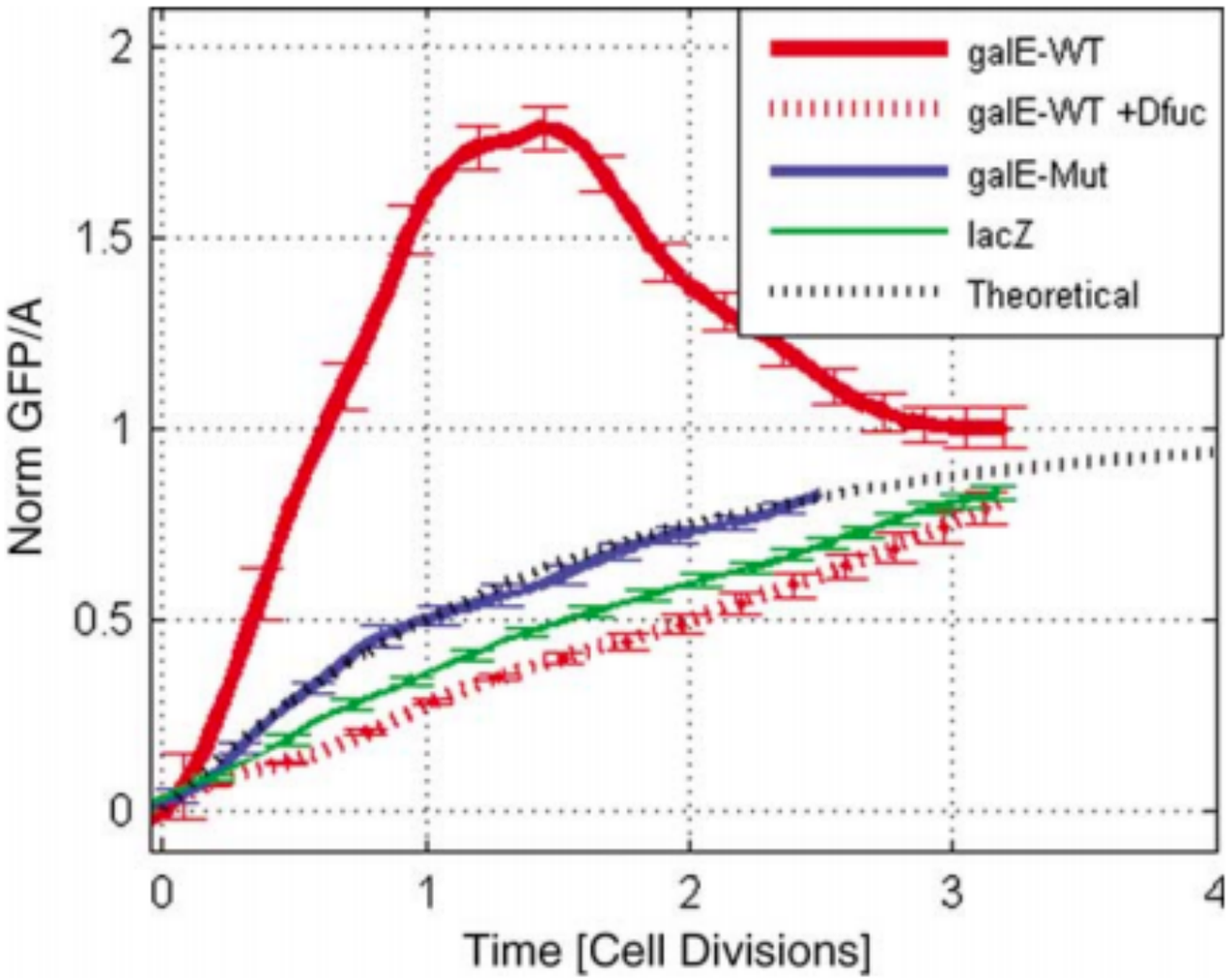
AND I1 FFL generates an impulse and also speeds up the response.

AND I1 FFL- galactose



AND I1 FFL speeds up the activation of galactose metabolism to glucose starvation.

AND I1 FFL- galactose



AND I1 FFL speeds up the activation of galactose metabolism to glucose starvation.