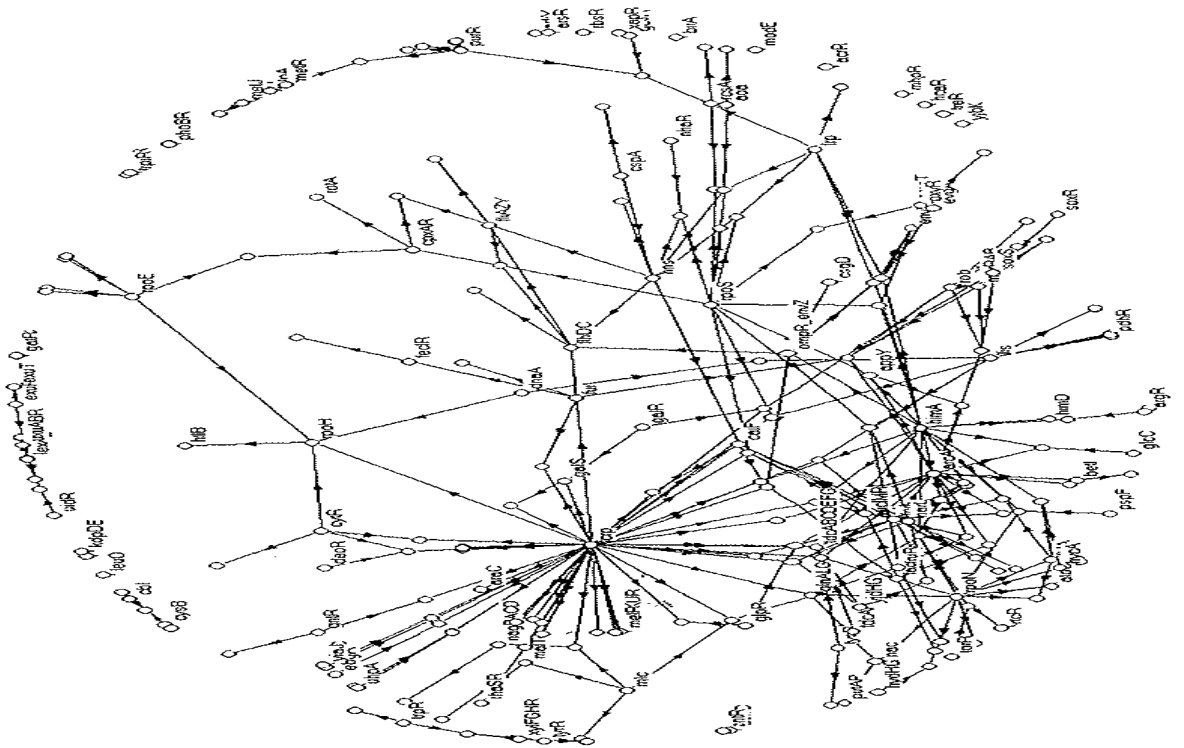
Systems Biology

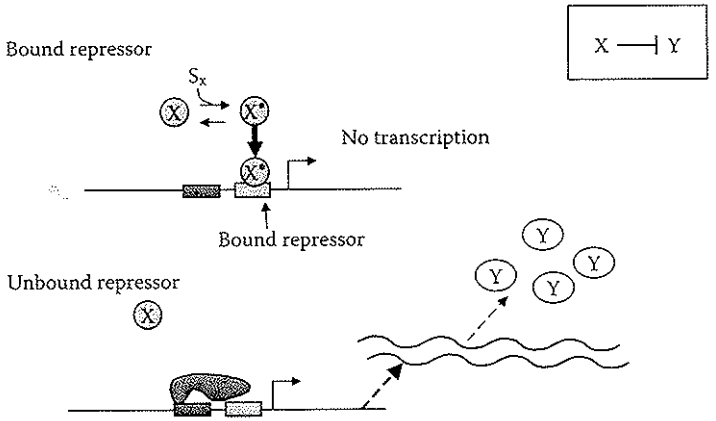


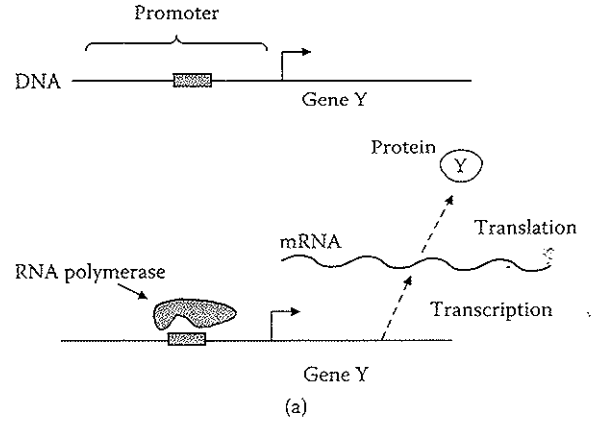
Genome Analysis, 12 Dec 2007

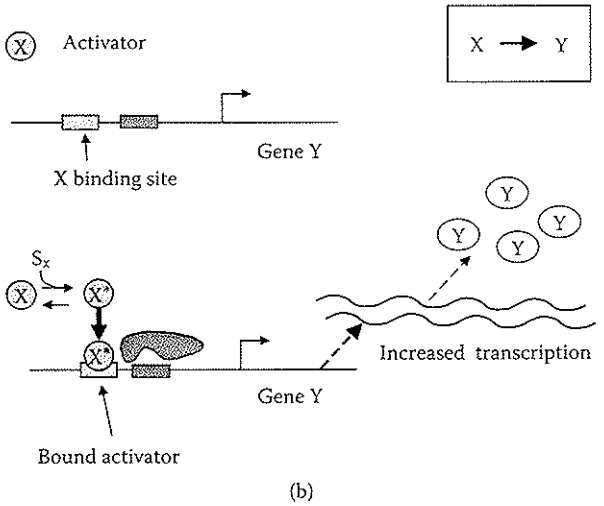
Figures from Uri Alon, An Introduction to Systems Biology

The cell as a dynamic system

- The cell can be seen as a system of interacting components
- Example:
  - transcription regulation:

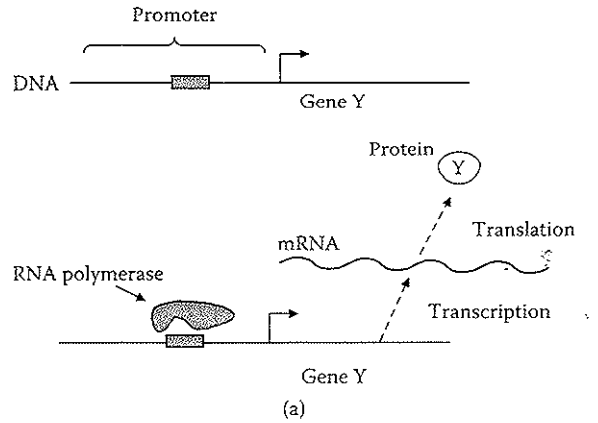


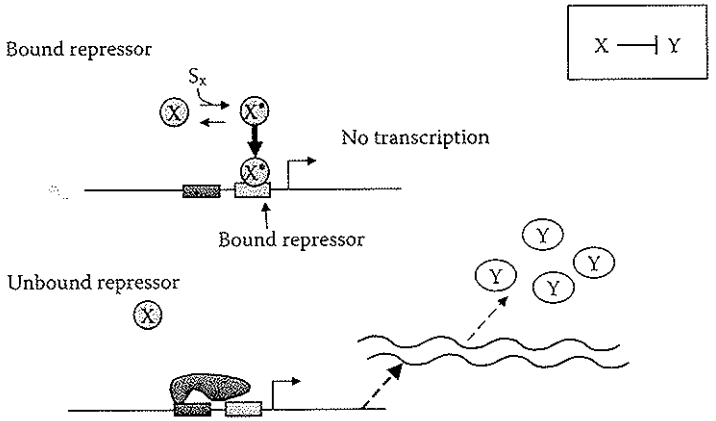


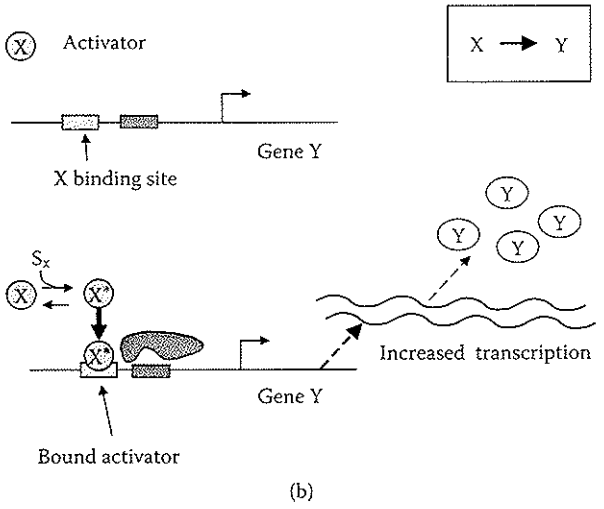


Activation (deactivation)

$$\dot{Y} = \frac{\mathrm{d}\,Y}{\mathrm{d}\,t} = f(X^*) - \alpha Y$$

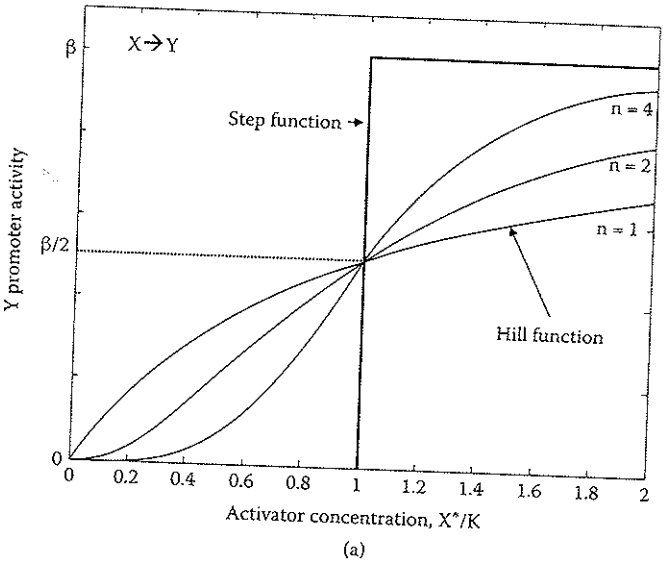






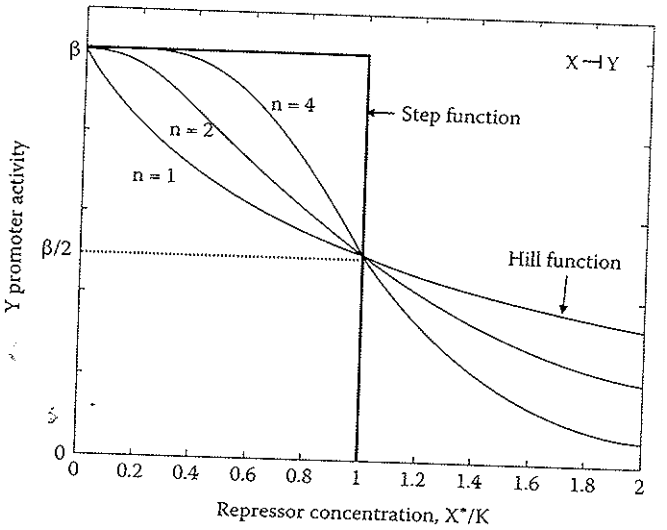
Activation (deactivation)

$$\dot{Y} = \beta \cdot I(X^* > K) - \alpha Y$$



(a)

$$\dot{Y} = \beta \cdot I(X^* < K) - \alpha Y$$



(b)

Activation (deactivation)

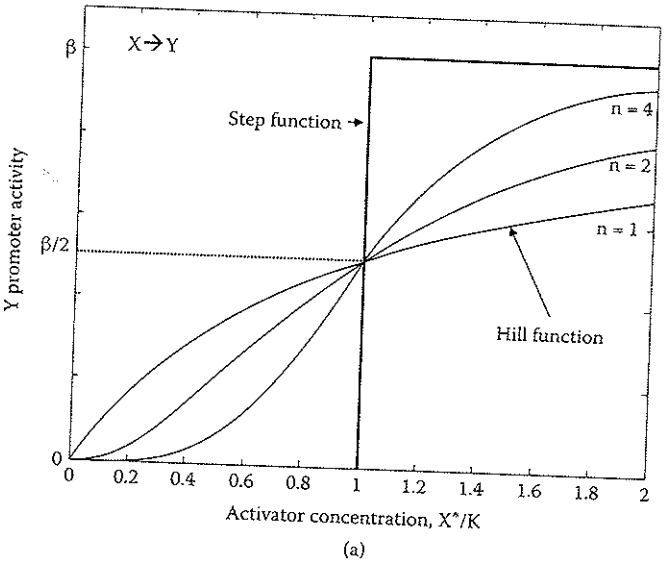
Steady state:

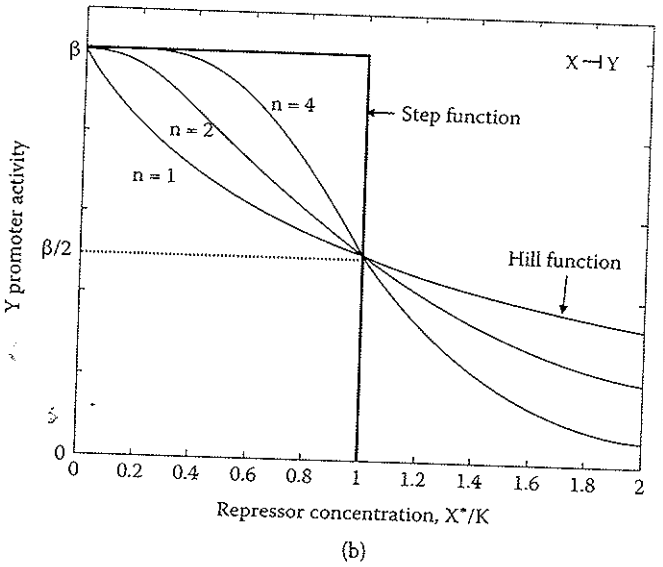
$$\dot{Y} = \beta \cdot I(X^* > K) - \alpha Y = 0$$

$$Y_{\mathrm{st}} = \frac{\beta}{\alpha} \quad \text{or} \quad Y_{\mathrm{st}} = 0$$

depending on

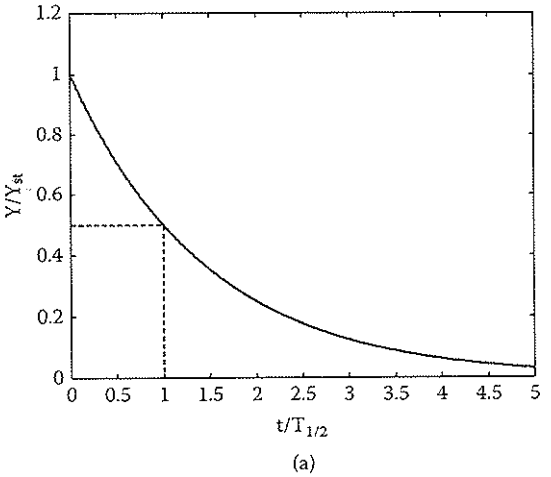
$$I(X^* > K)$$





Activation (deactivation)

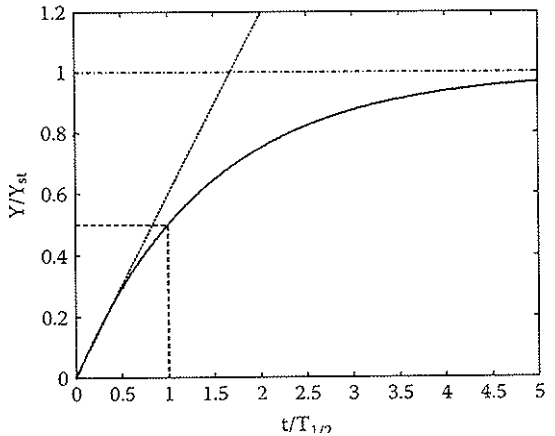
$$\dot{Y} = -\alpha Y \Rightarrow Y(t) = Y_{\mathrm{st}} \exp(-\alpha t)$$



(a)

$$\dot{Y} = \beta - \alpha Y \Rightarrow$$

$$Y(t) = Y_{\mathrm{st}} \left(1 - \exp\left(-\alpha t\right)\right)$$



Network motifs

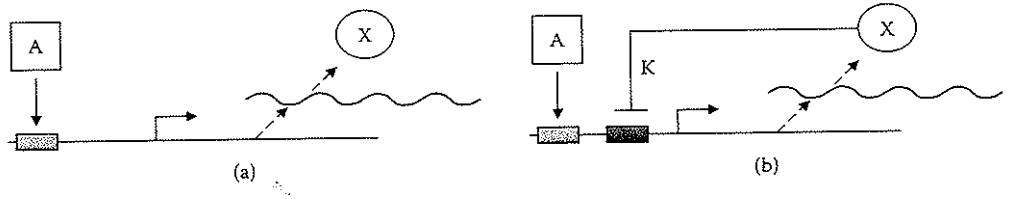
- Some sub-graphs occur again and again in biological networks
  - A motif is a sub-graph that occurs more often than would be expected by chance in a random network (for various definitions of random network)

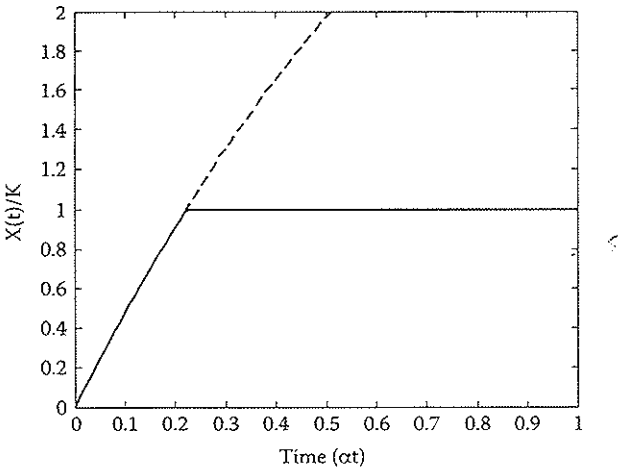
Auto-regulation

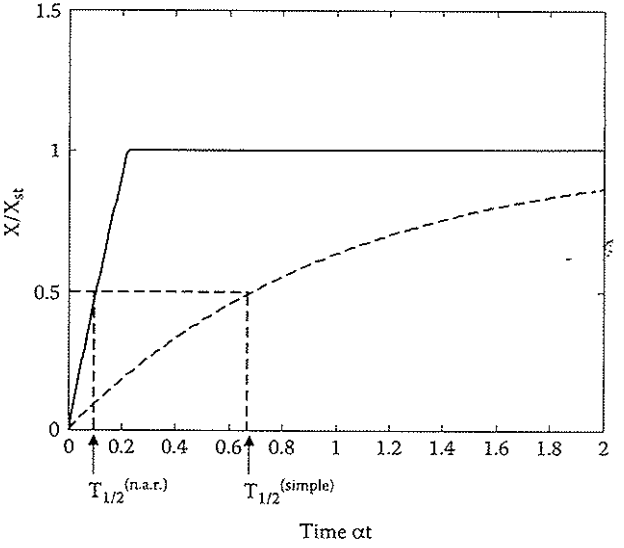
- Negative auto-regulation is a network motif

$$\dot{X} = \beta \cdot I(X^* < K) - \alpha X \approx \beta$$

$$X^* < K \qquad X \ll \frac{\beta}{\alpha}$$

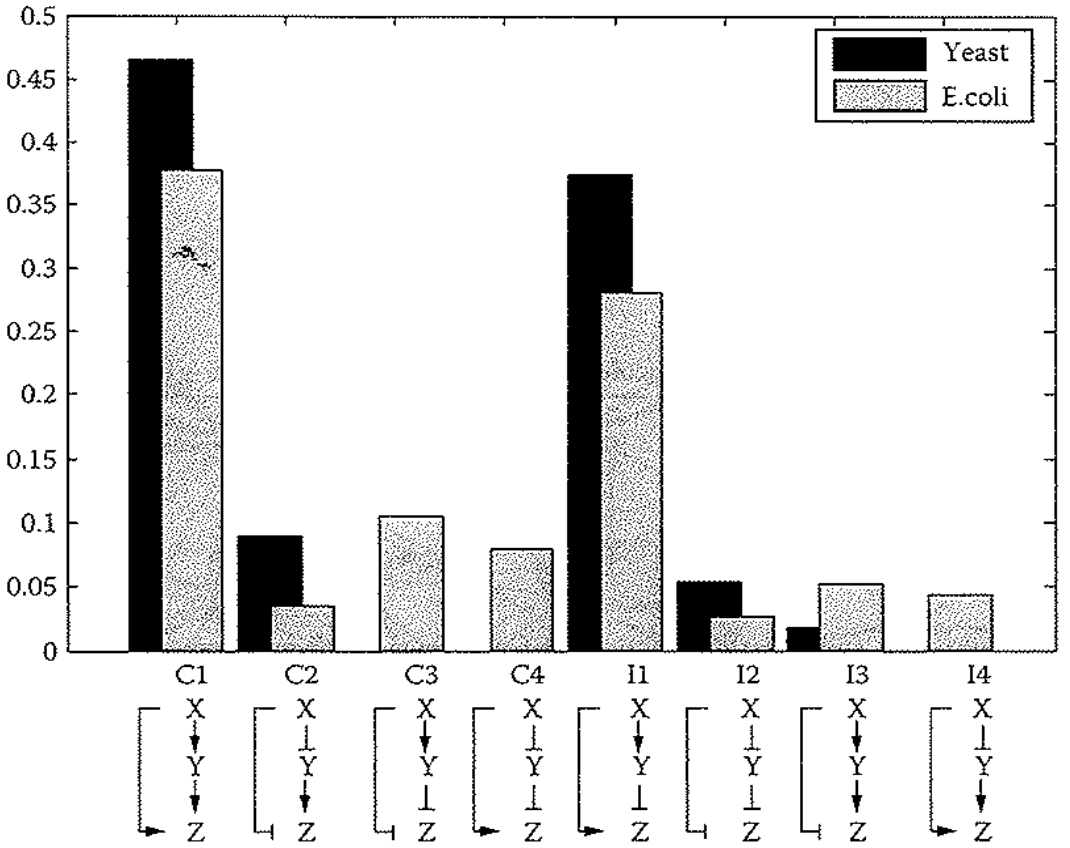




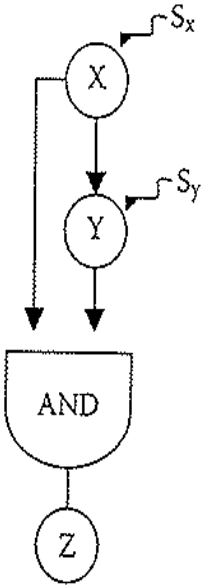


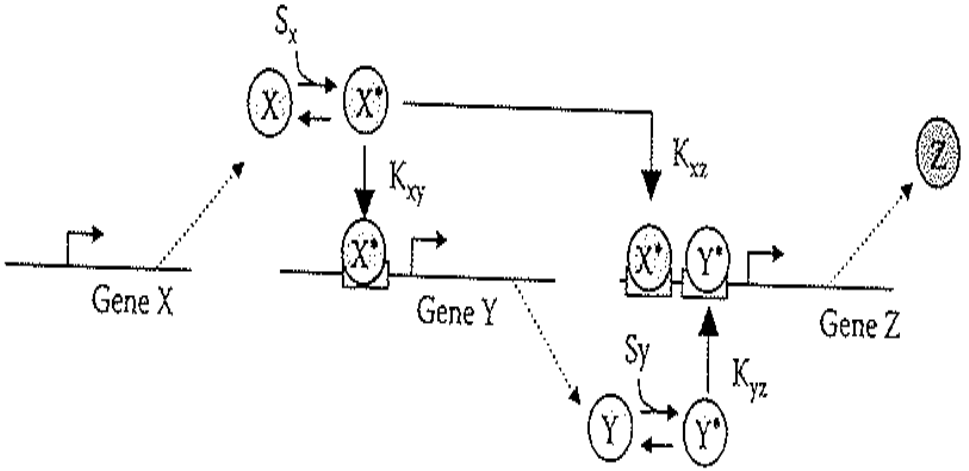
Feed-forward loop

- The feed-forward loop is a network motif



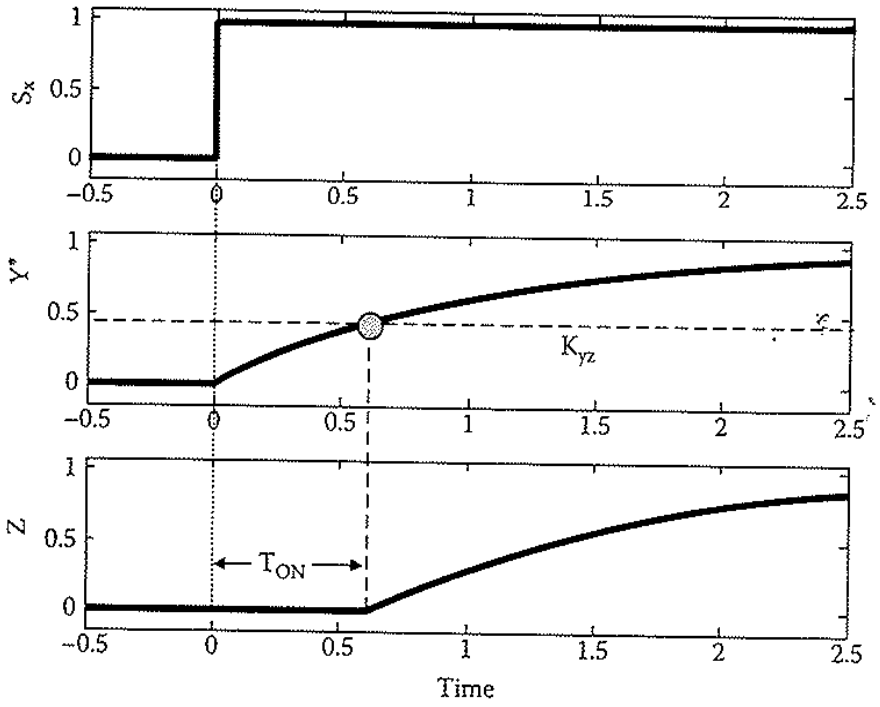
Feed-forward loop

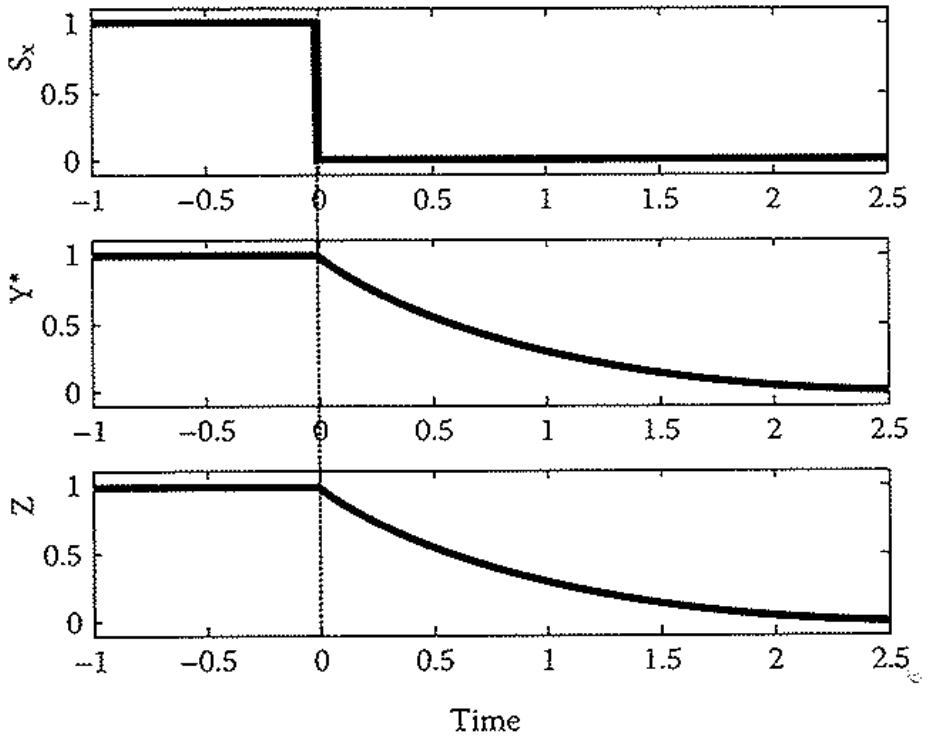




Feed-forward loop

Delayed Z on ON but instant OFF

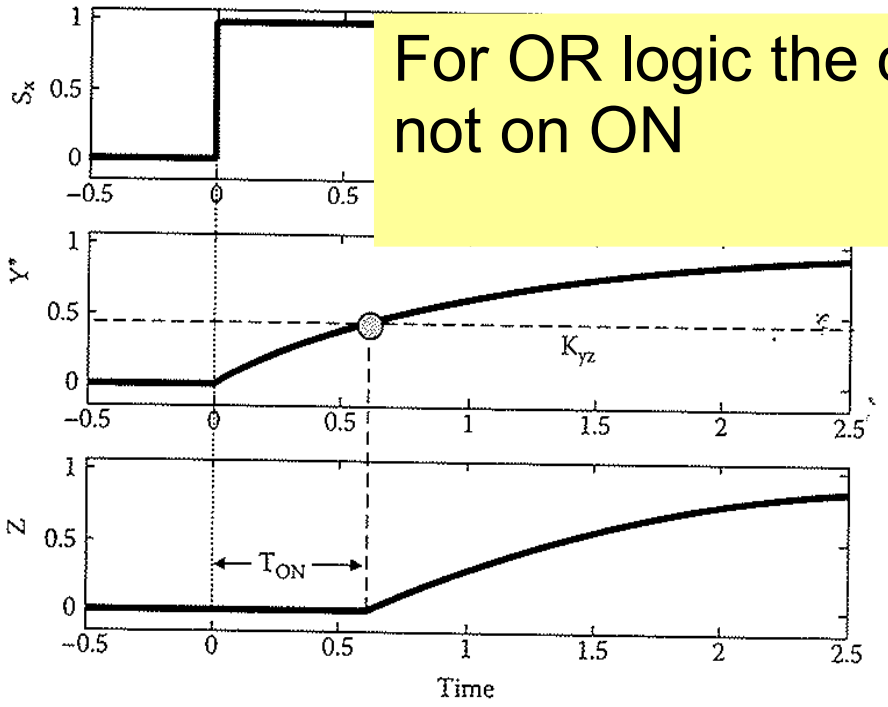


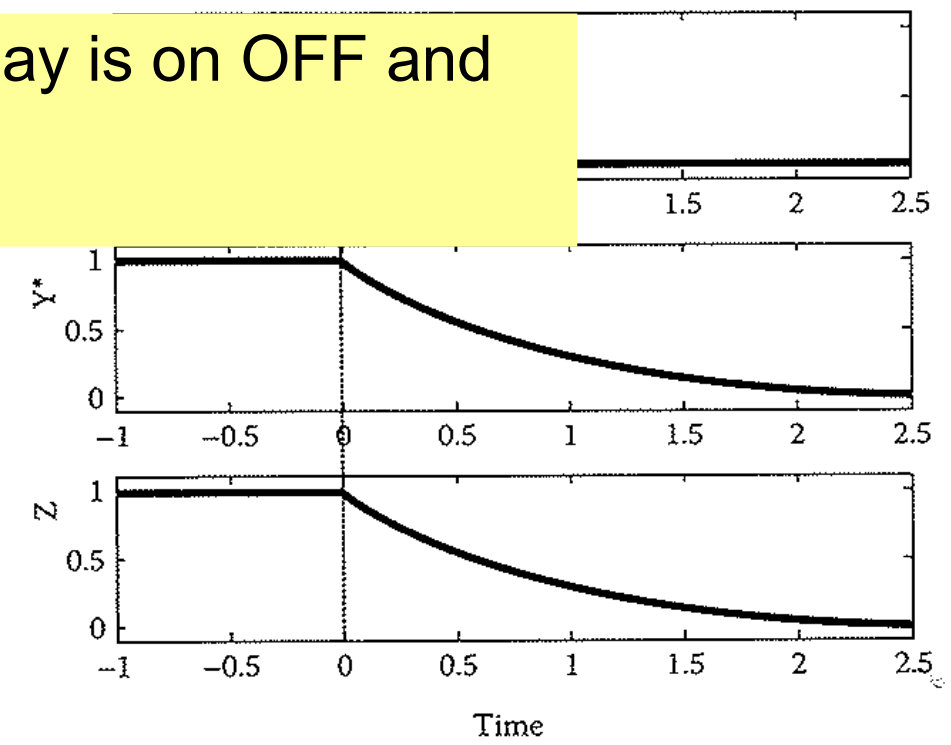


Feed-forward loop

Delayed Z on ON but instant OFF

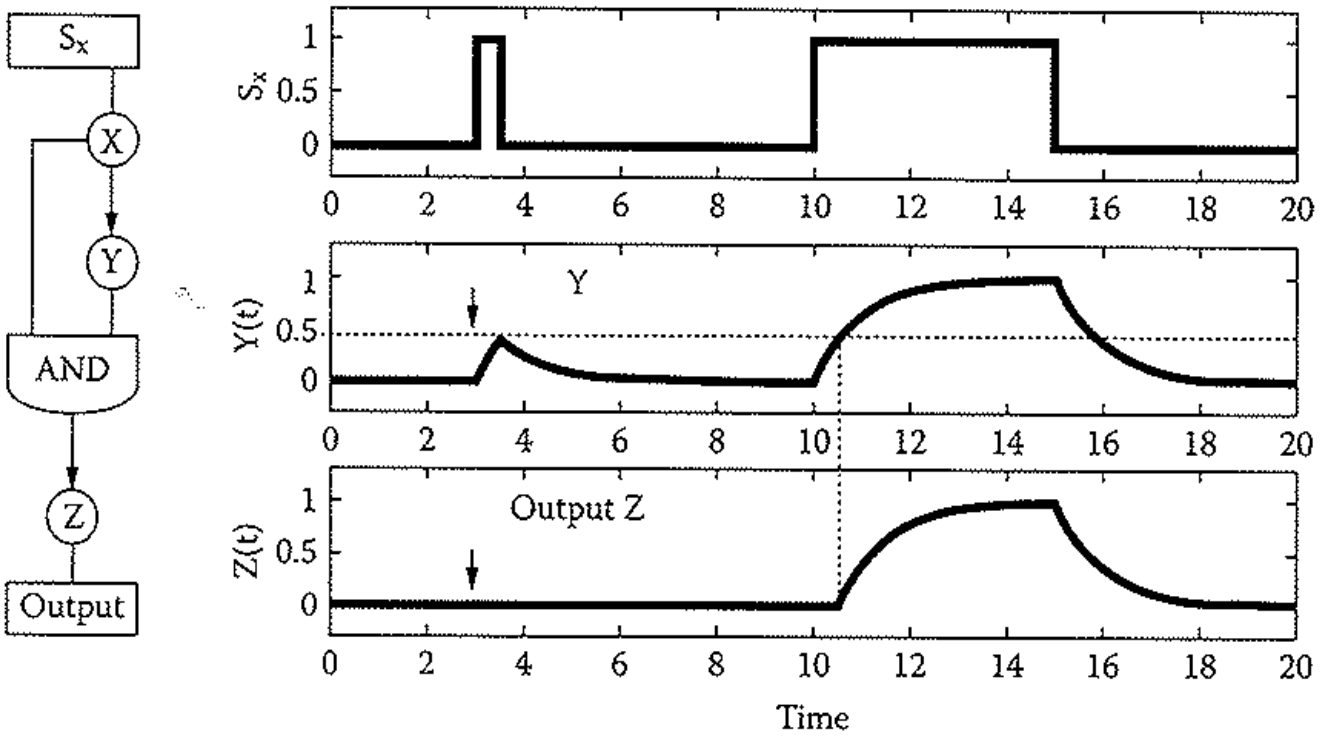
For OR logic the delay is on OFF and not on ON



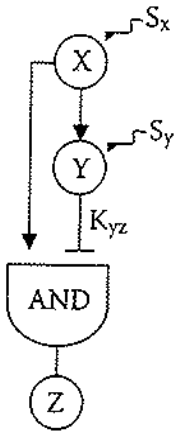


Feed-forward loop

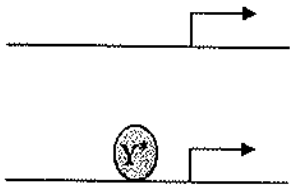
Dampening



Feed-forward loop



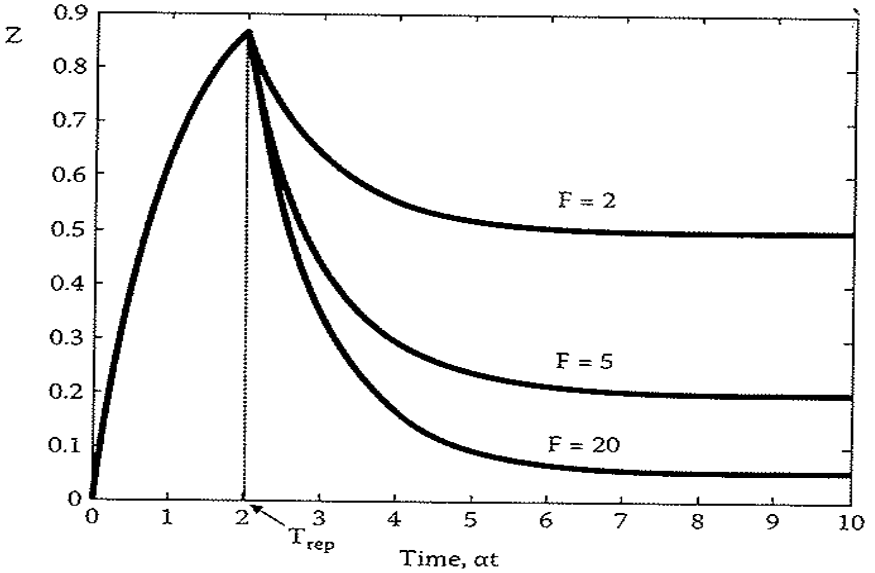
(a)



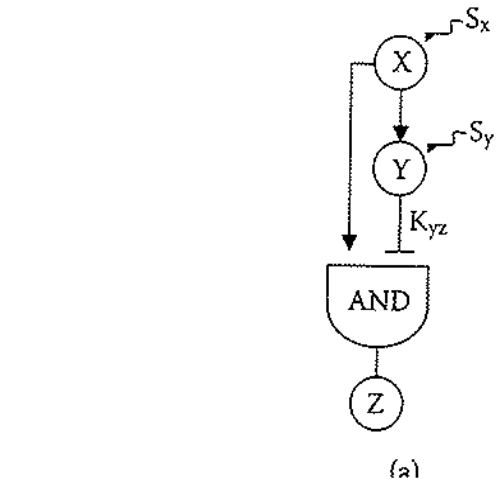
→ β Strong transcription

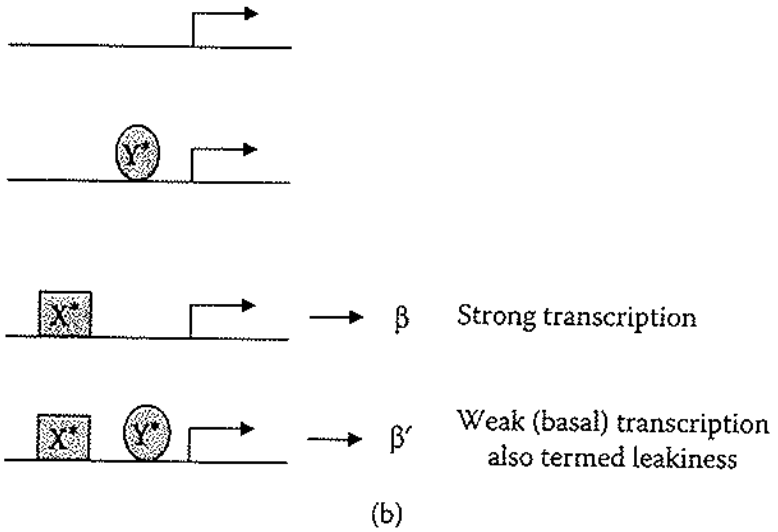
→ β′ Weak (basal) transcription also termed leakiness

(b)

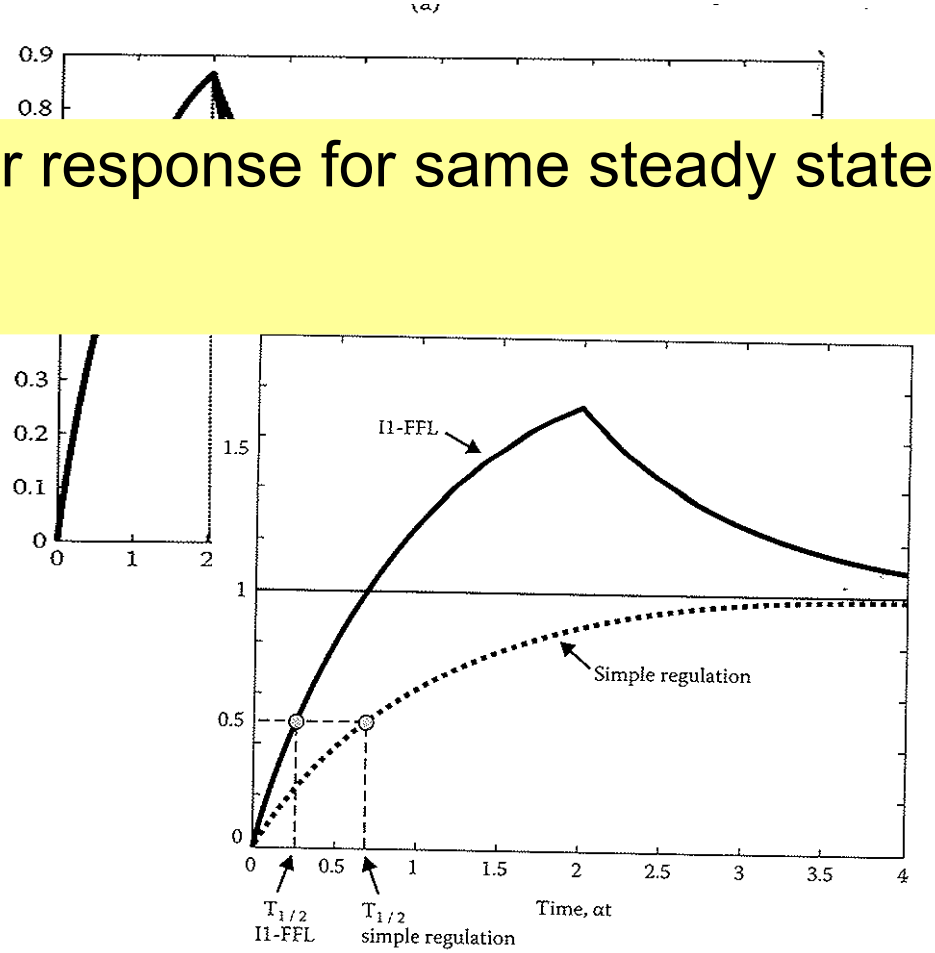


Feed-forward loop

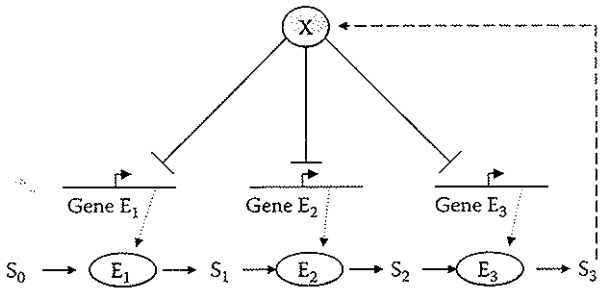


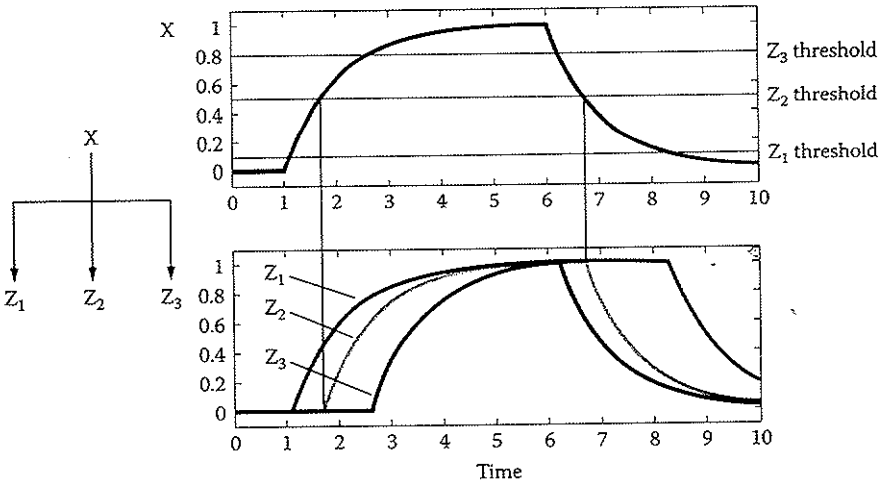


Faster response for same steady state

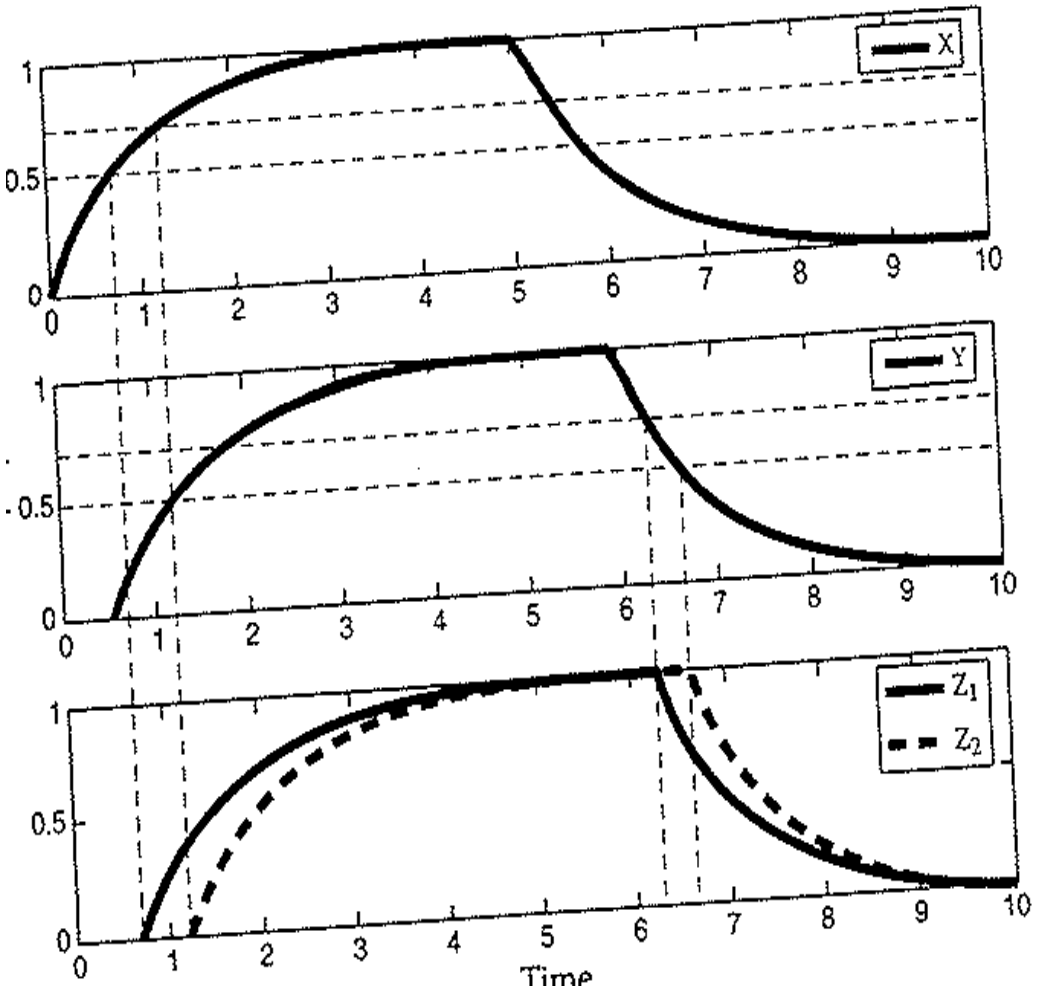


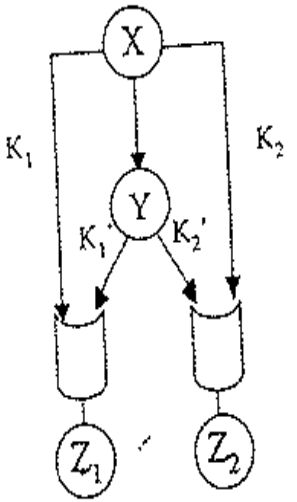
Single Input Module (SIM)





Multi-output FFL



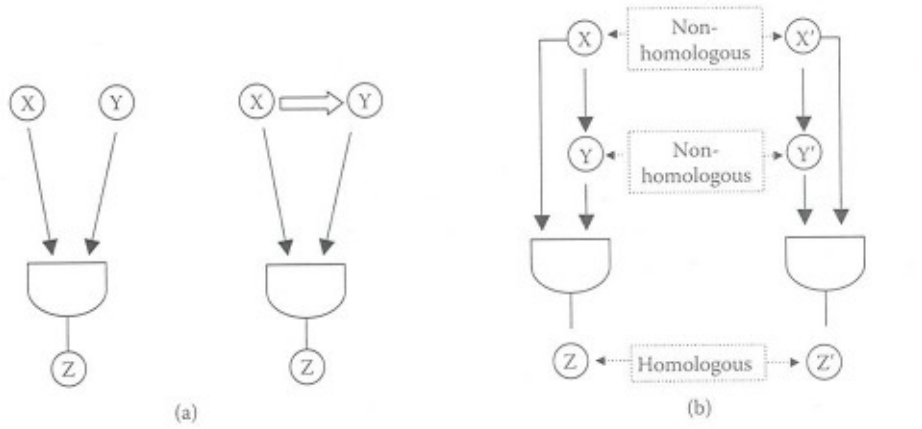


$K_1 < K_2$

$K_1' > K_2'$

Evolution

- Connections in networks seem to evolve faster than genes
- Motifs are typically results of convergent evolution rather than homology



Summary

The cellular system is a dynamic system of interacting component.

As an example we considered the transcription network

We saw various motifs from transcription networks and their dynamic/functional behaviour

Systems Biology Q3 2008

Much much more in the class *Systems Biology* the coming spring.