Theories of Signal Transduction

Bio202

Chaitanya Athale

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Previous Lecture

Simple growth models

Logistic map and transition to chaos

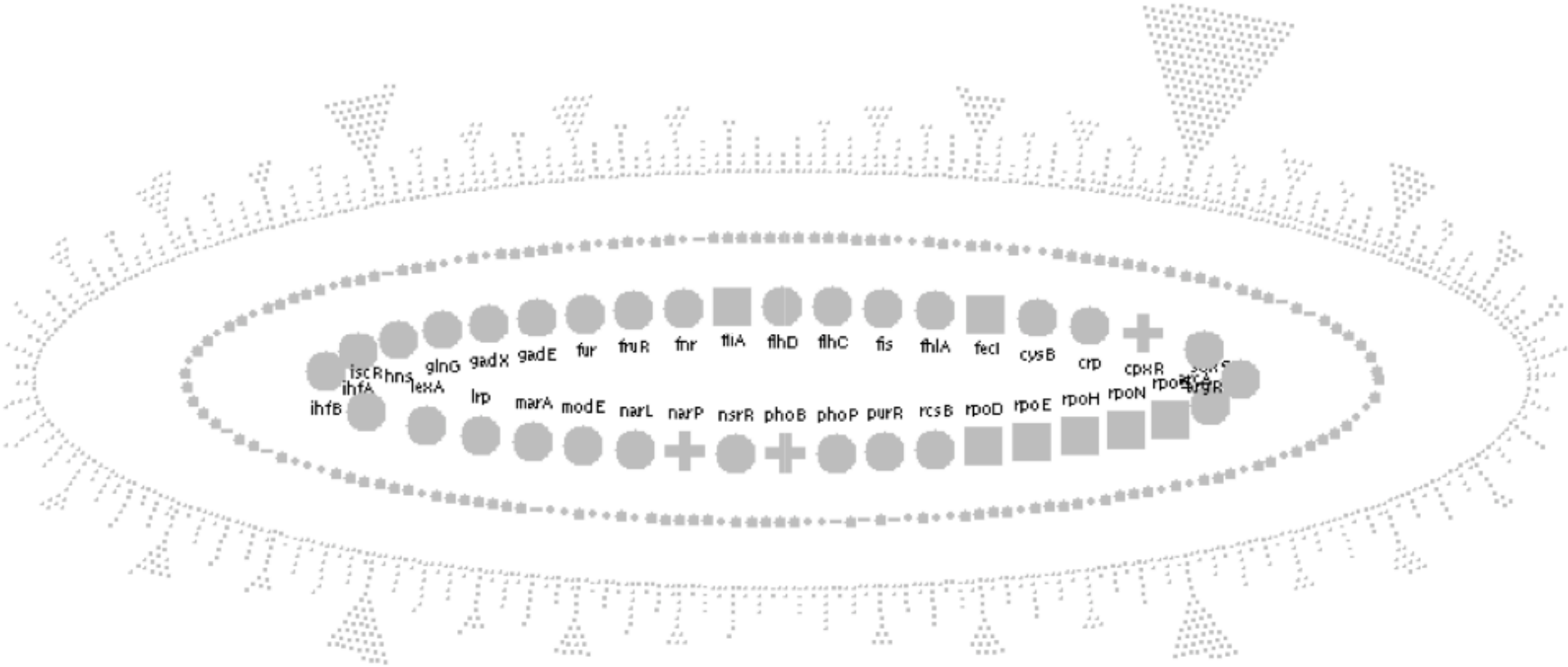
Self organization

Pattern formation

Turing patterns

E. coli

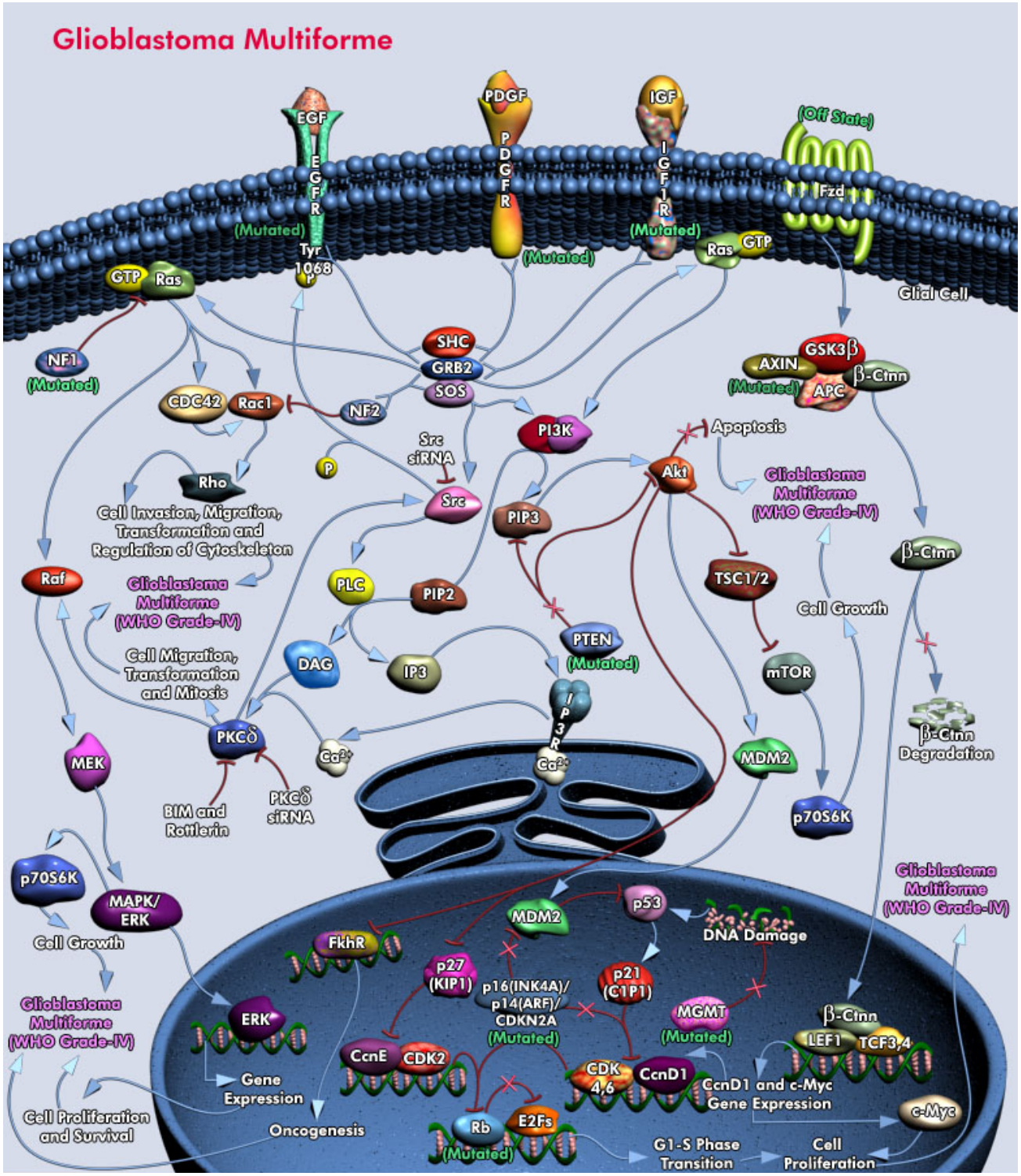
Signal Transduction



ecocyc.org

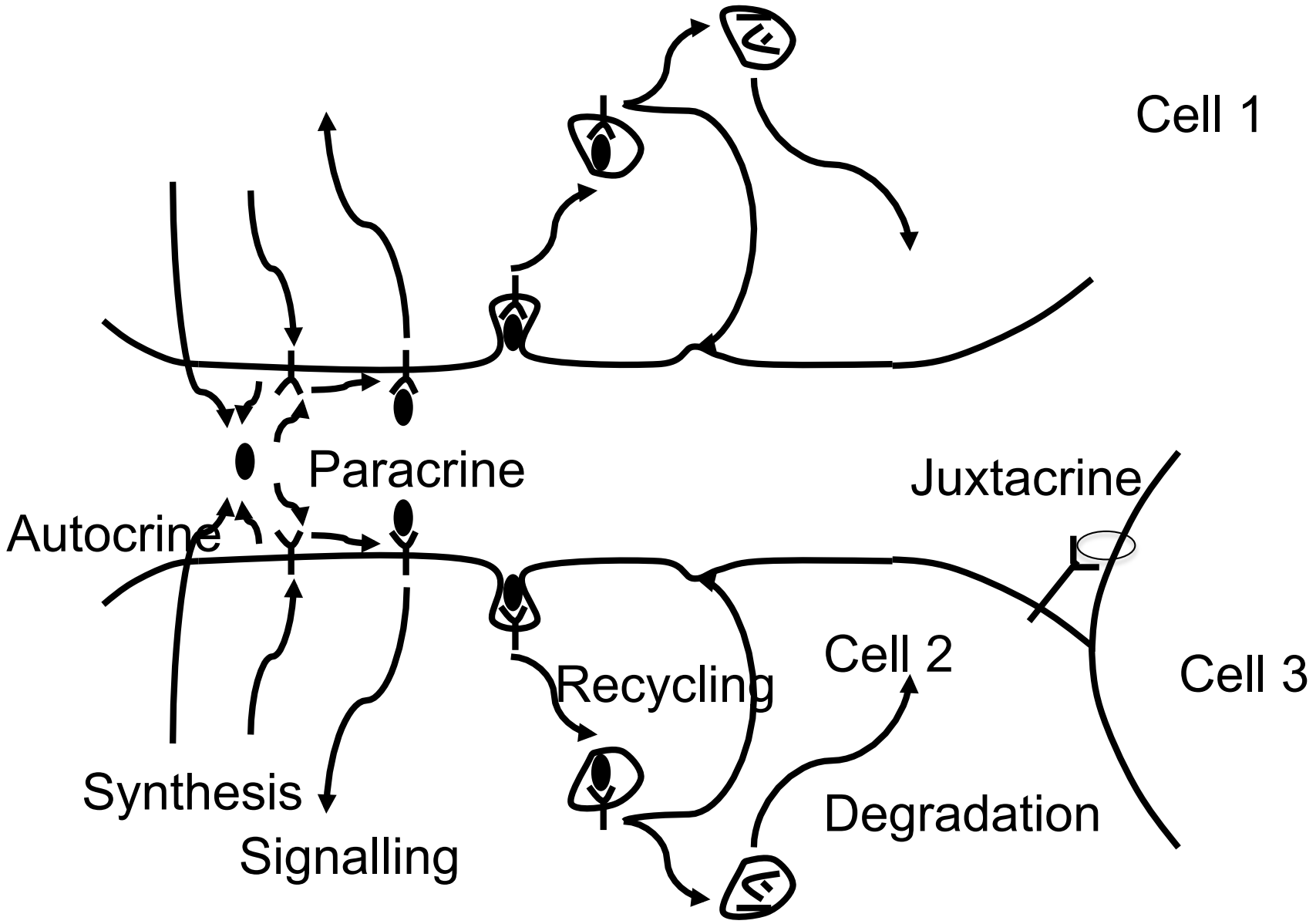
Typical Constraints to Signal Transduction

Property	E. coli	Yeast (S. cerevisae)	Mammalian (human fibroblast)
Cell volume	~1 μm^3	~10^3 μm^3	~10^4 μm^3
Proteins/cell	10^6	10^9	10^{10}
Diffusion time of protein across cell	~0.1 s (D=10 $\mu m^2/s$)	~10 s	~100 s
Time to transcribe a gene	1 min	1 min	30 min (incl. mRNA processing)
Time to translate a protein	~2 min	~2 min	~30 min (incl. mRNA export)



Complexity of Signal Transduction

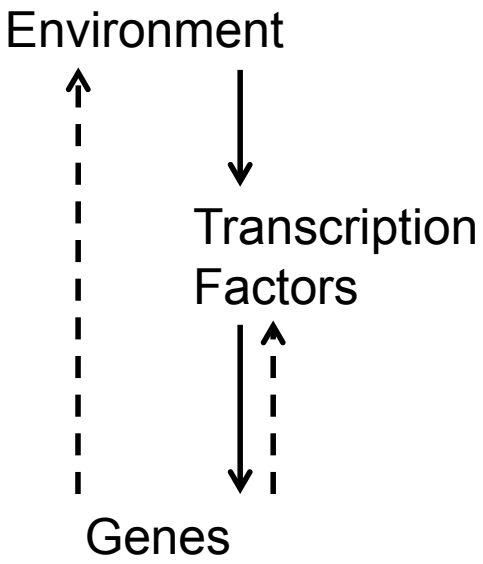
Signalling in a Multicellular context



Types of Signalling Networks

- Transcriptional networks
  - Sensory networks
  - Developmental
- Protein networks
  - Interaction
  - Phosphorylation

Transcription Networks



RNAp
Promoter
Gene
RNA
Protein

Regulation of Gene Transcription

Activators X ⟶ Y

Repressors X ⟞ Y

Activation, Inhibition

Input function

K = Activation coeff.

β = Maximal expression level

n = Hill coefficient

Logic Input Functions

Logic approximation

OFF $f(X^*)=0$

ON $f(X^*)=\beta$

K = threshold

Several Inputs

AND

OR

SUM

Dynamics and Response Times

$X \longrightarrow Y$

β= const. production rate

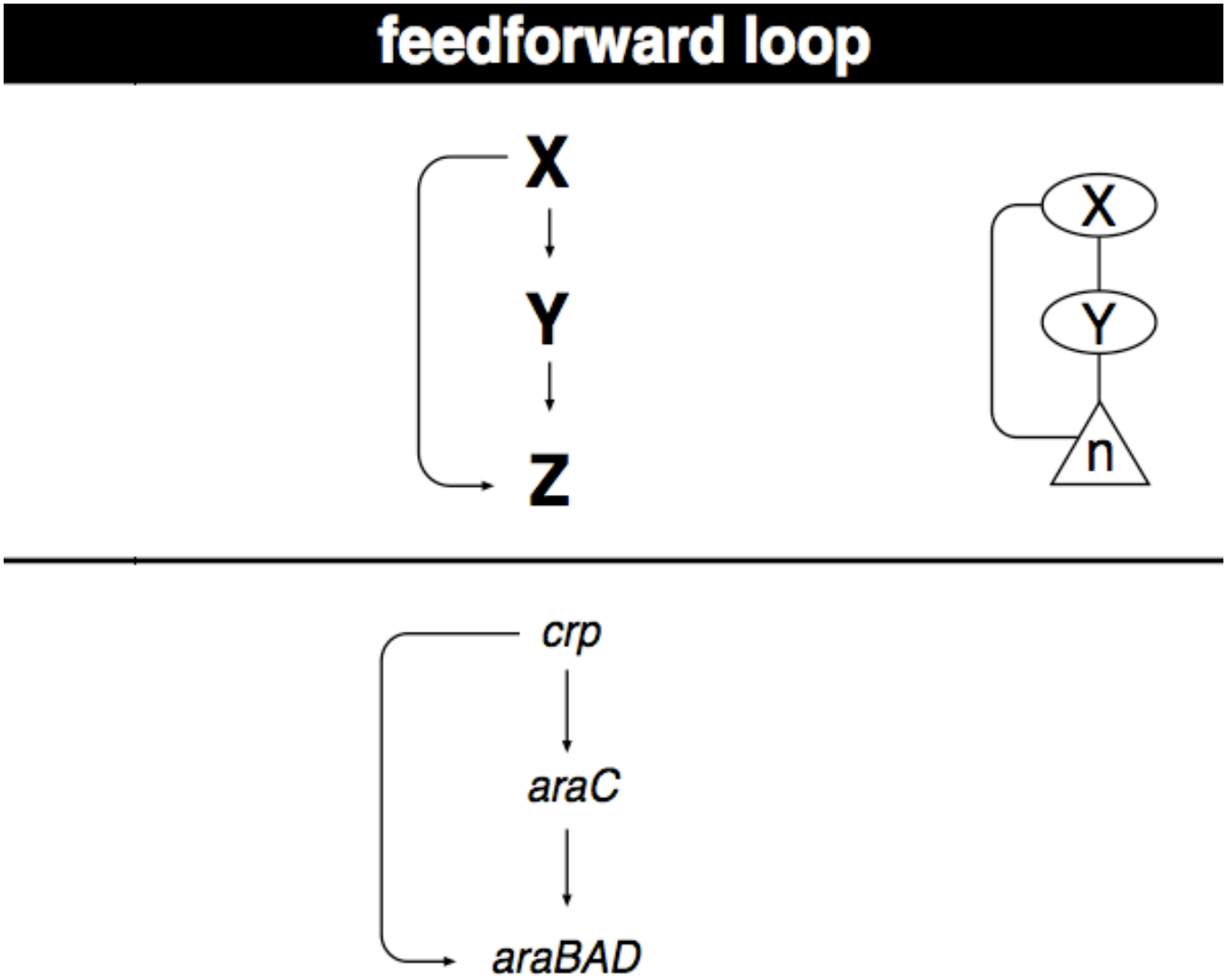
$\alpha = \alpha_{deg} + \alpha_{dil}$

α_{deg}

α_{dil}

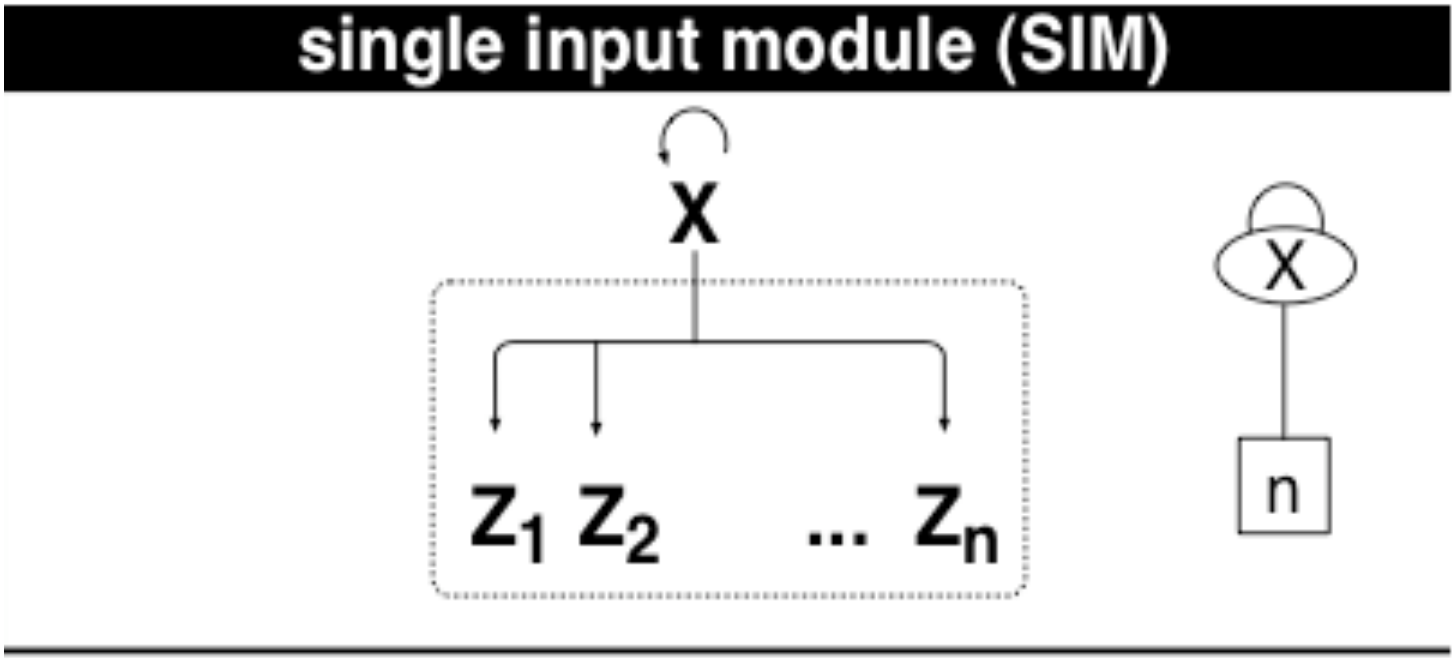
Comparison to Randomized Directed Graphs

Motifs in E. coli-1

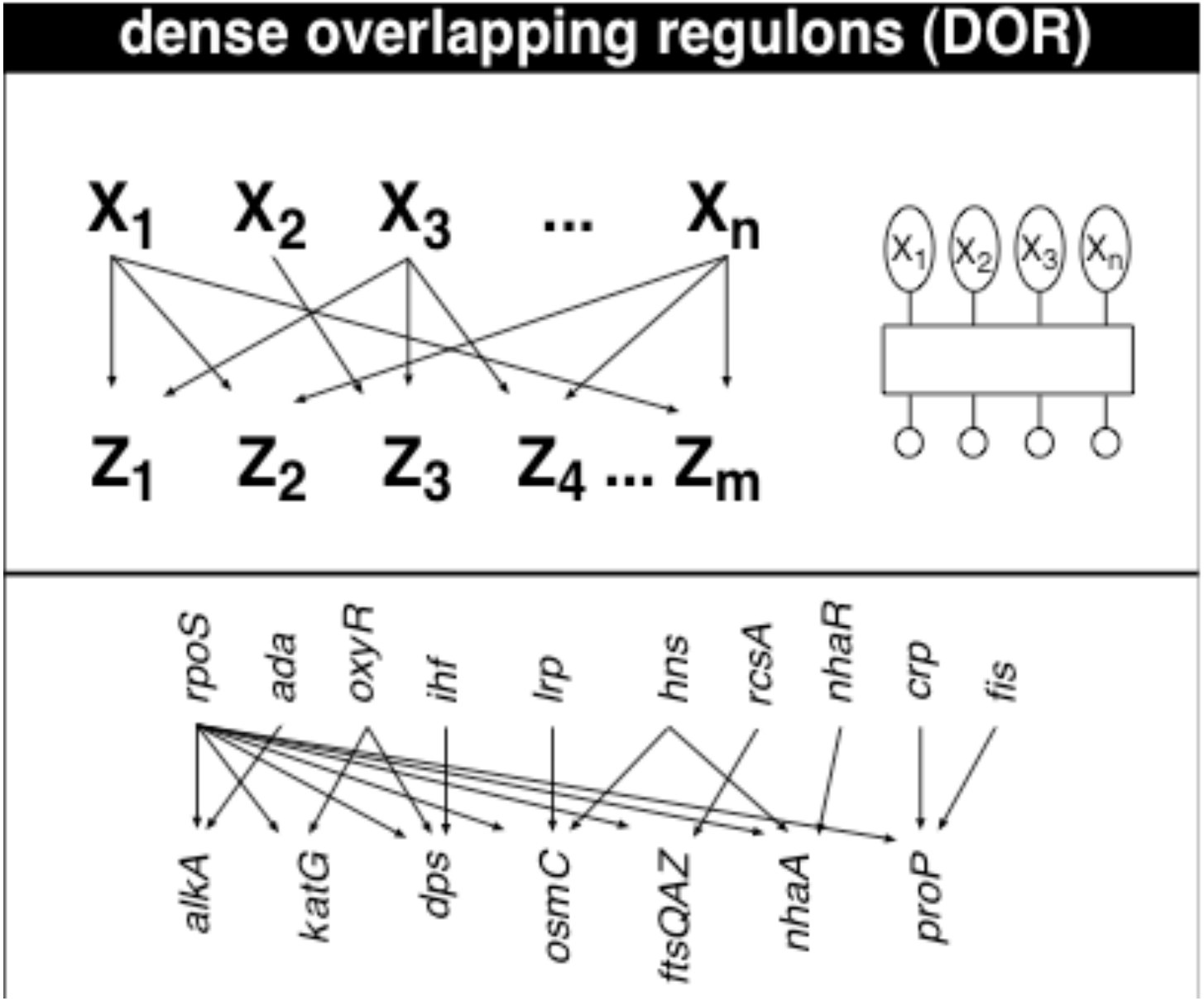


Shen-Orr et al. (2002)

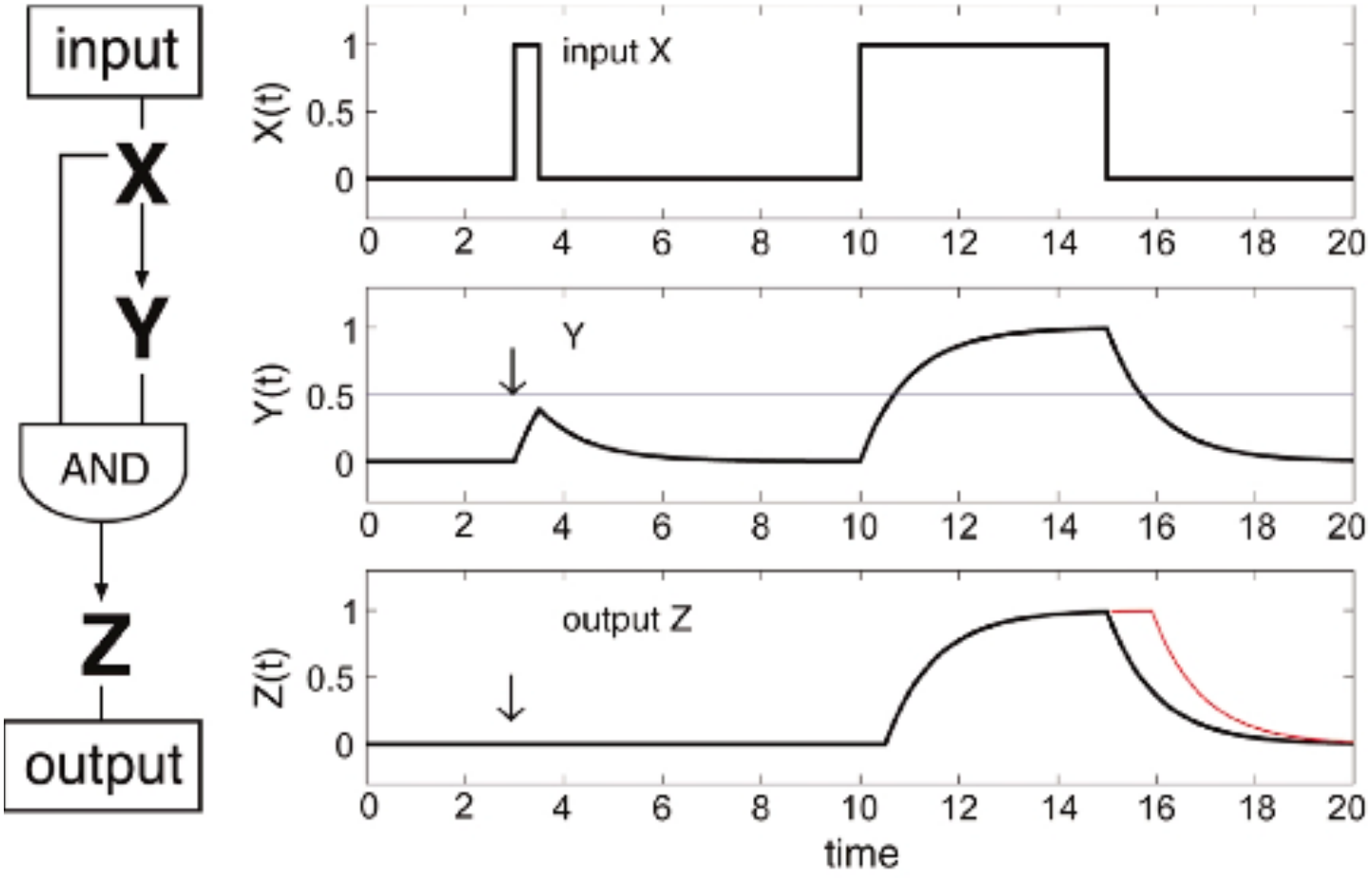
Motifs in E. coli-2



Motifs in E. coli-3



Dynamics of Feed Forward Loop



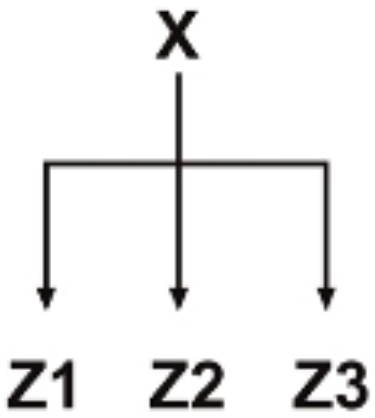
AND gate

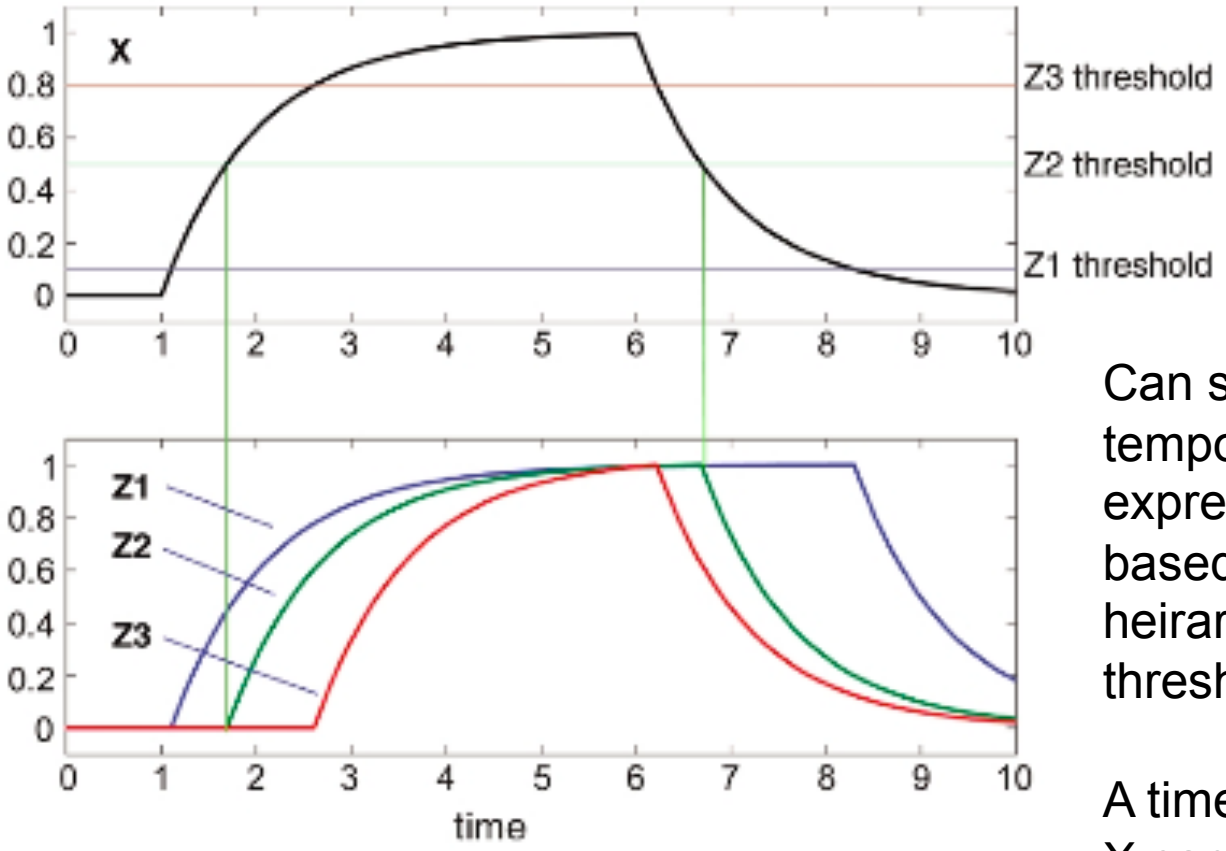
Capable of rejecting rapid variations in input X

Respond only to persistent activation

Linear x-y-z also shows but slower shutdown

Dynamics of Single Input Module





Can show temporal expresison based on heirarchy of thresholds

A timed spike in X can cause early, mid and late expression

Synthetic Biology

Understanding

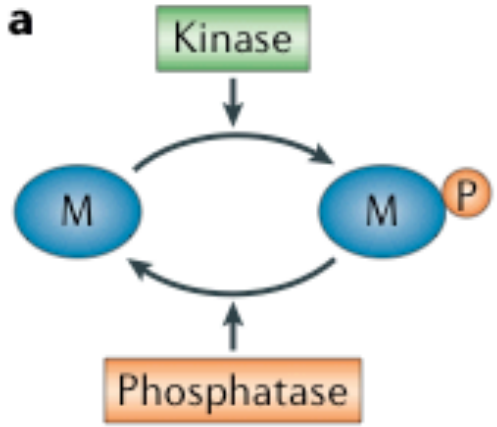
Synthesis

Biological problems

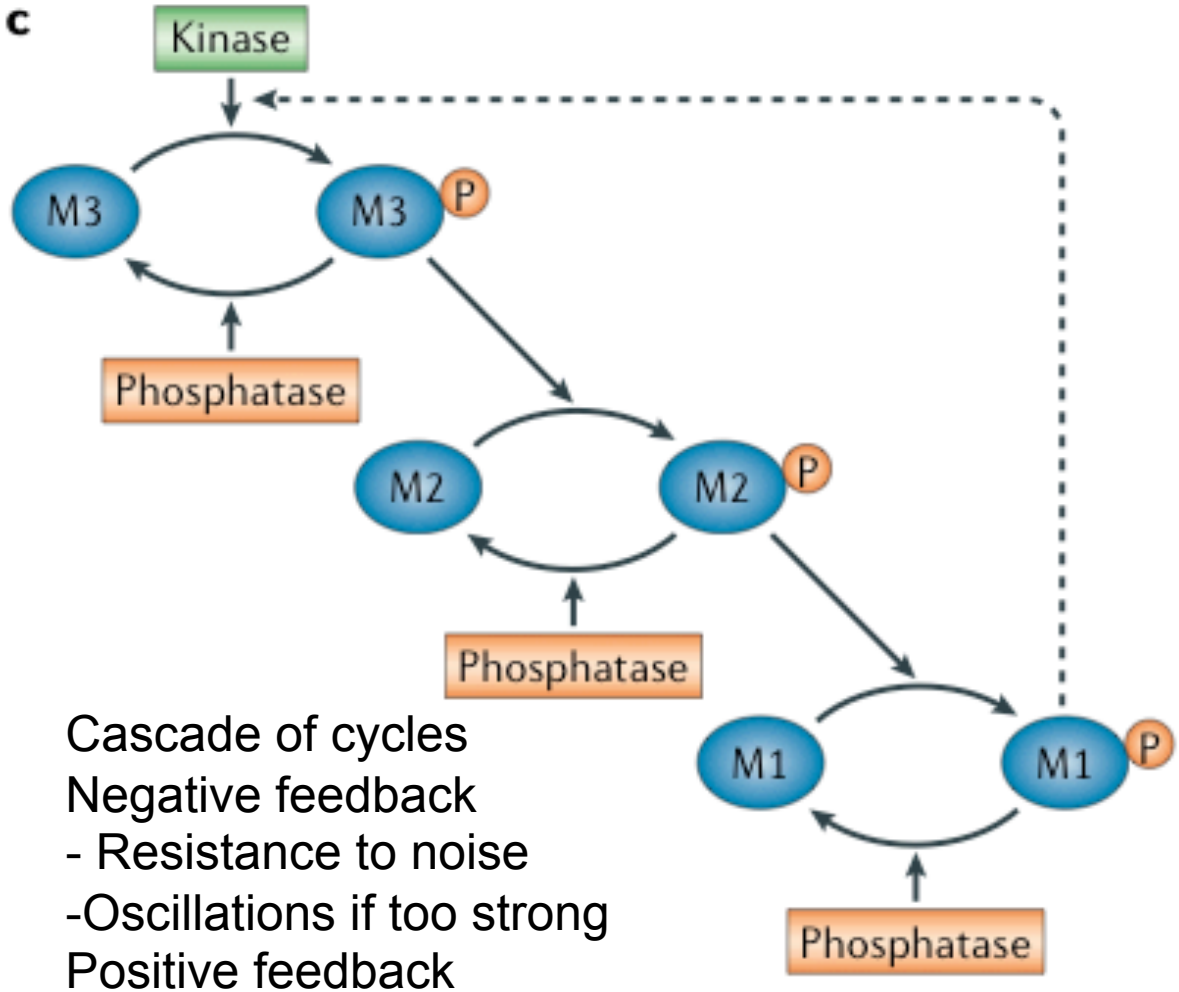
iGem

Motifs in Cellular Signalling

One site phosphorylation



GDP-GTP exchange



Cascade of cycles
Negative feedback
- Resistance to noise
-Oscillations if too strong
Positive feedback
-Increases target sensitivity
-Relaxation oscillations

References

- Shen-Orr (2002) Network motifs in the transcriptional regulatory network of E. coli
- Alon Introduction to Systems Biology
- Kholodenko (2006) Cell signalling dynamics in space and time

Next

Models of Development