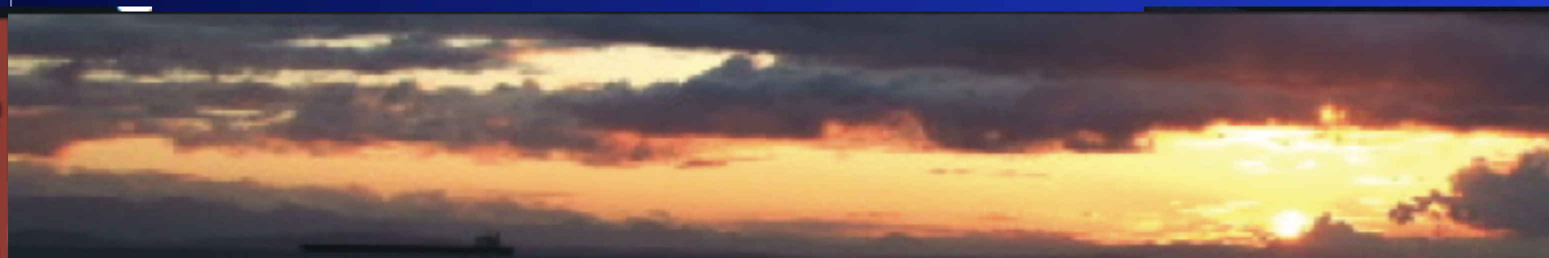
Mathematical Cell Biology Graduate Summer Course

University of British Columbia, May 1-31, 2012

Leah Edelstein-Keshet

Simple biochemical motifs (2.5)



mprime

PIMS

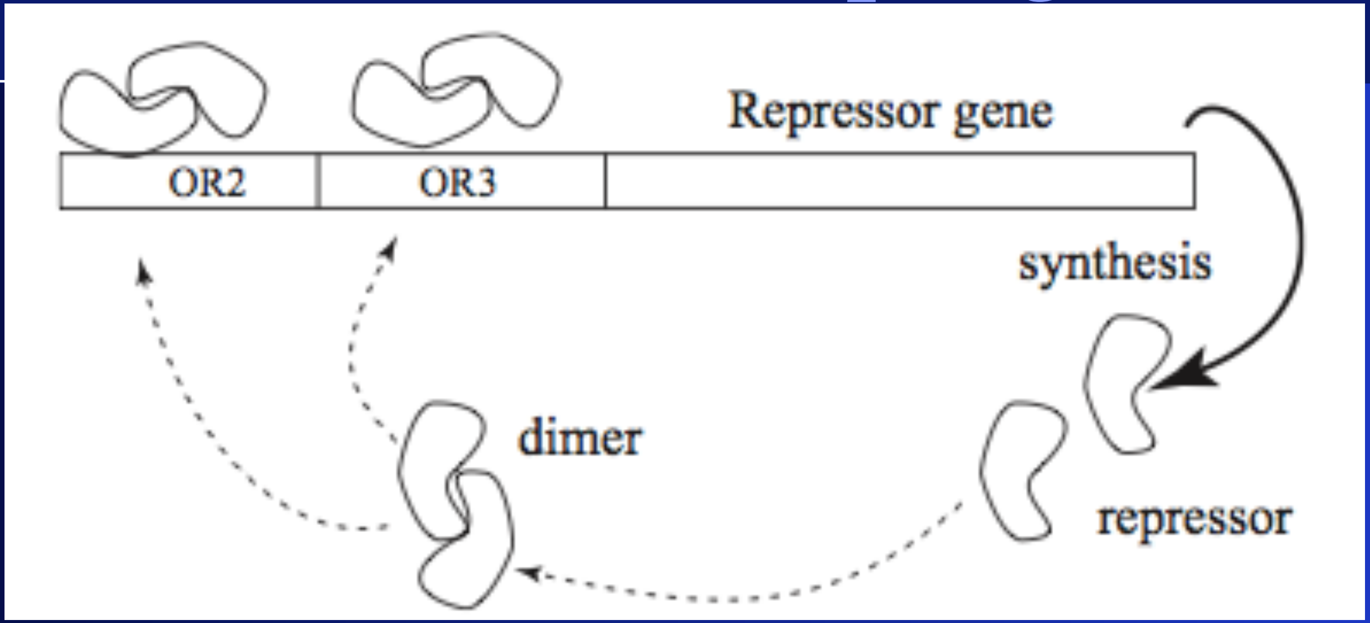
www.math.ubc.ca/~keshet/MCB2012/

Noise-based switches and amplifiers for gene expression

Jeff Hasty*†, Joel Pradines*, Milos Dolnik*‡, and J. J. Collins*

PNAS | February 29, 2000 | vol. 97 | no. 5 | 2075–2080

Dimerization and the phage lambda



- The phage λ gene encodes for protein (conc x)
- Protein dimerizes (conc of dimers y).
- Dimers bind to regulatory sites on the gene.
- Binding to OR2 activates transcription.
- Biding to OR3 inhibits transcription.

Reaction scheme

Dimerization: $2X \underset{}{\overset{K_1}{\rightleftarrows}} X_2$

Binding to DNA (OR2): $D + X_2 \underset{}{\overset{K_2}{\rightleftarrows}} DX_2$

Binding to DNA (OR3): $D + X_2 \underset{}{\overset{K_3}{\rightleftarrows}} DX_2^*$

Double binding (OR2 and OR3): $DX_2 + X_2 \underset{}{\overset{K_4}{\rightleftarrows}} DX_2X_2$

DX_2= the dimerized repressor bound to site OR2
DX_2 = the dimerized repressor bound to site OR3,*
DX_2X_2 = both OR2 and OR3 are bound by dimers

QSS

$$
\begin{aligned}
y &= K_1 x^2, \\
u &= K_2 d y = K_1 K_2 d x^2, \\
v &= \sigma_1 K_2 d y = \sigma_1 K_1 K_2 d x^2, \\
z &= \sigma_2 K_2 u y = \sigma_2 (K_1 K_2)^2 d x^4.
\end{aligned}
$$

The "fast variables" assumed to equilibrate rapidly with the variable x.

Slower timescale

Protein synthesis: $DX_2 + P \xrightarrow{k_1} DX_2 + P + nX$

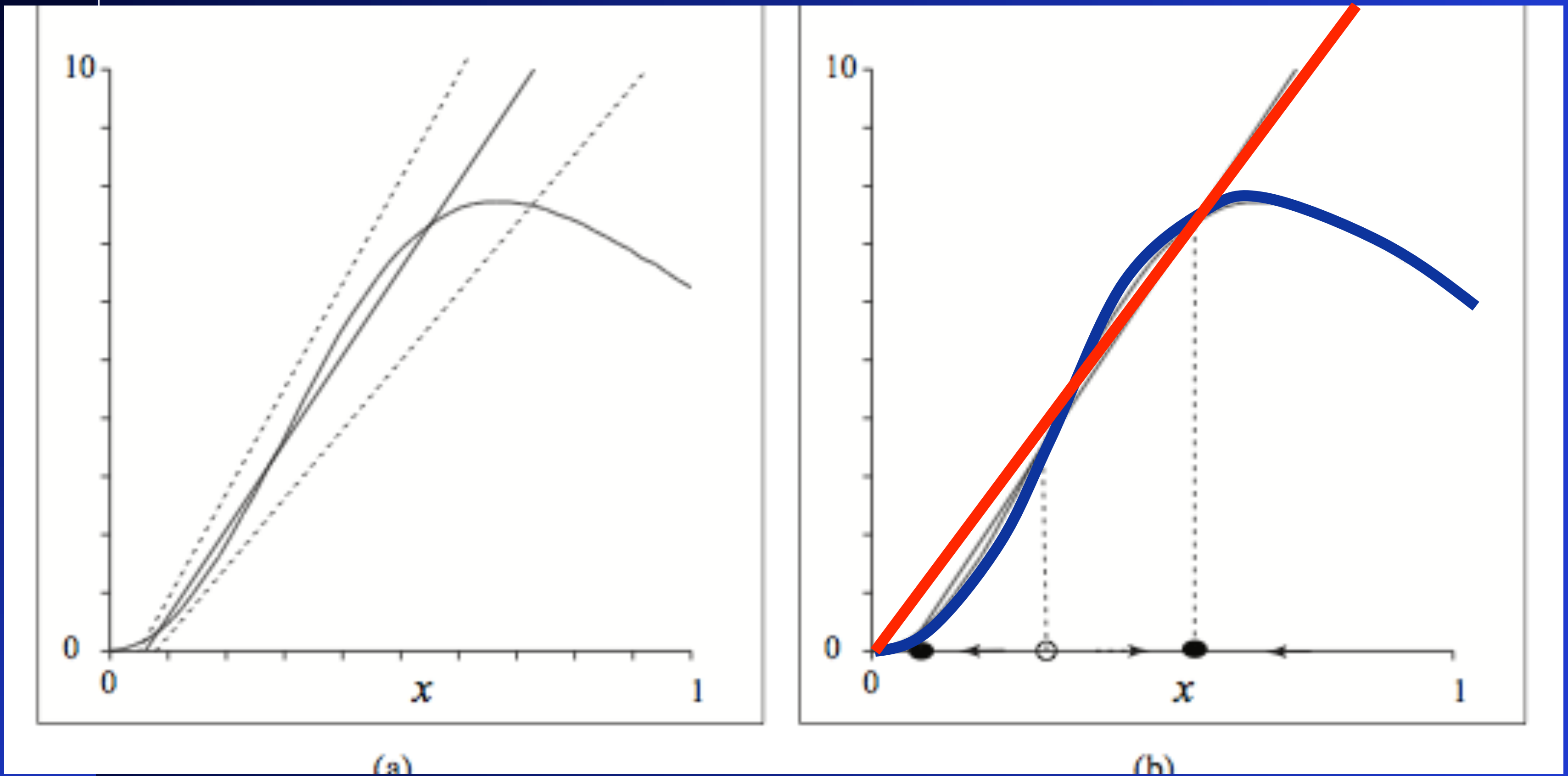
Protein degradation: $X \xrightarrow{k_d} A$

QSS and scaling the equations: system collapses to one variable, amt of synthesized protein, *x*:

$$\frac{dx}{dt} = \frac{\alpha x^2}{1 + (1+\sigma_1)x^2 + \sigma_2 x^4} - \gamma x + 1.$$

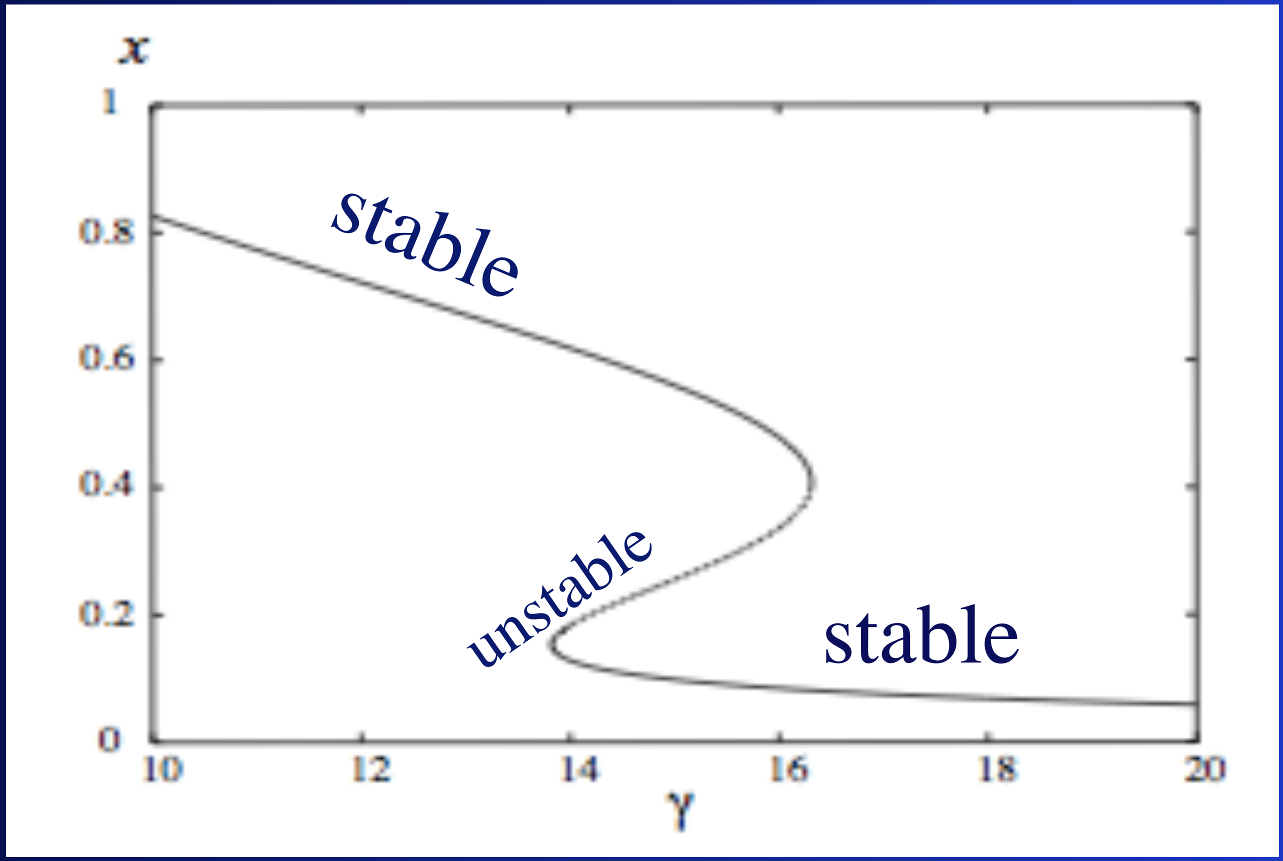
bistability

$$\frac{dx}{dt} = \frac{\alpha x^2}{1+(1+\sigma_1)x^2+\sigma_2 x^4} - \gamma x + 1.$$



Bifurcation:

$$\frac{dx}{dt} = \frac{\alpha x^2}{1+(1+\sigma_1)x^2+\sigma_2 x^4} - \gamma x + 1.$$



Comments

Combination of scaling, time scale considerations, and various simplifications can often reduce larger networks to effective dynamics of simpler systems.

Other examples will be provided.