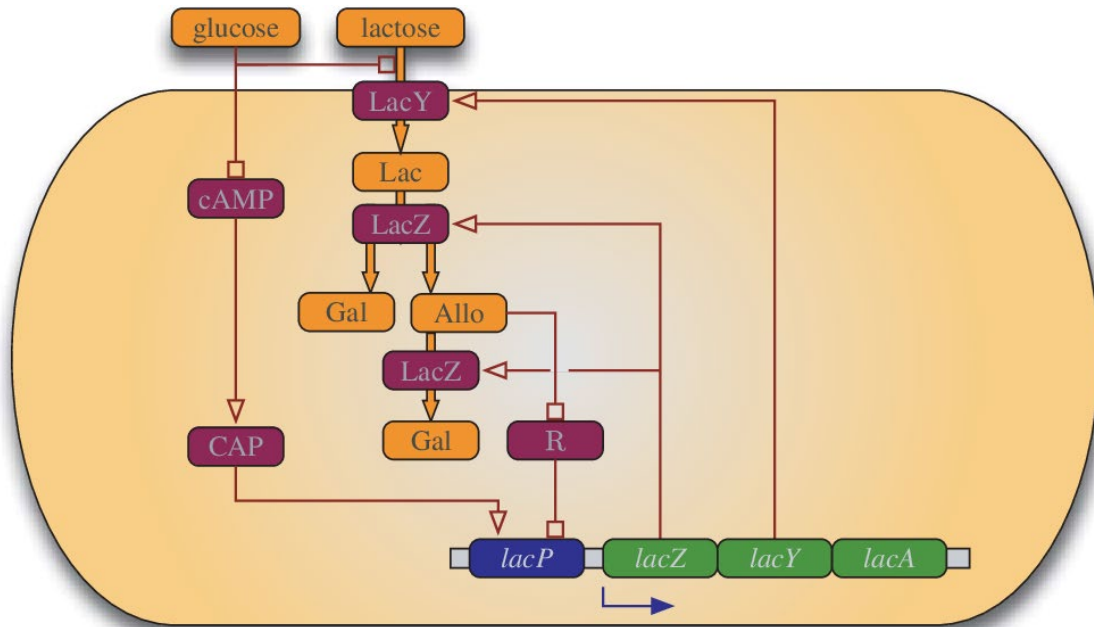


Bistability and oscillations in reaction networks

Chem 163

27 Oct. 2022

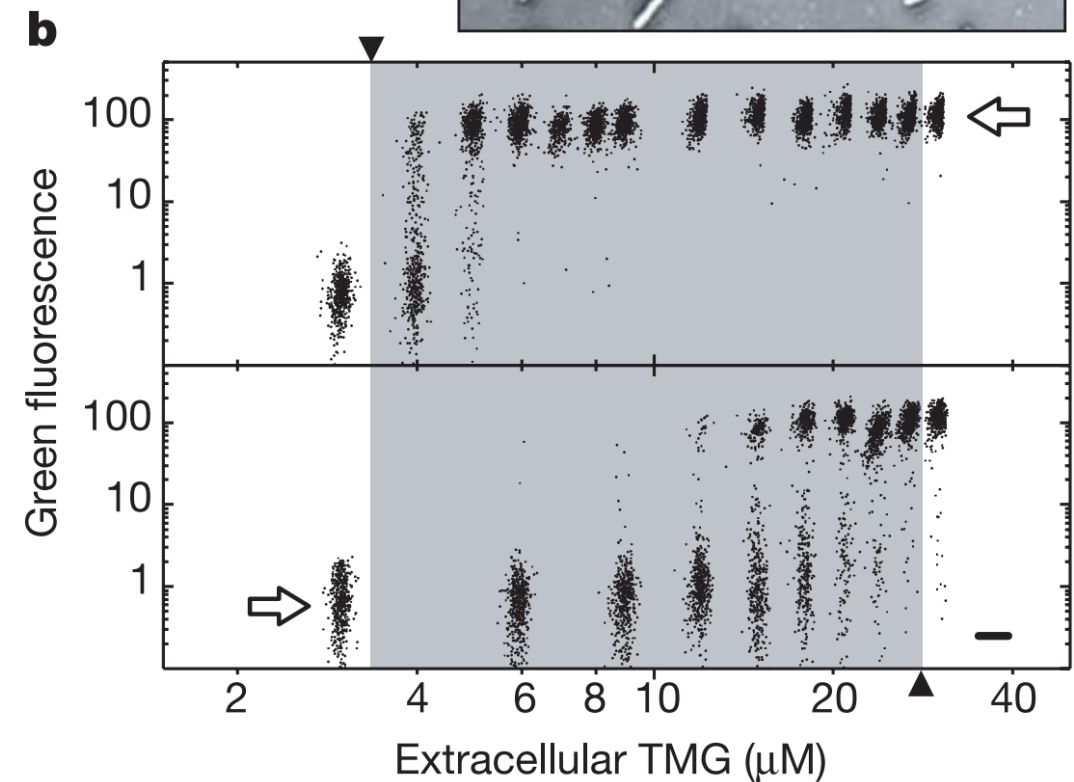
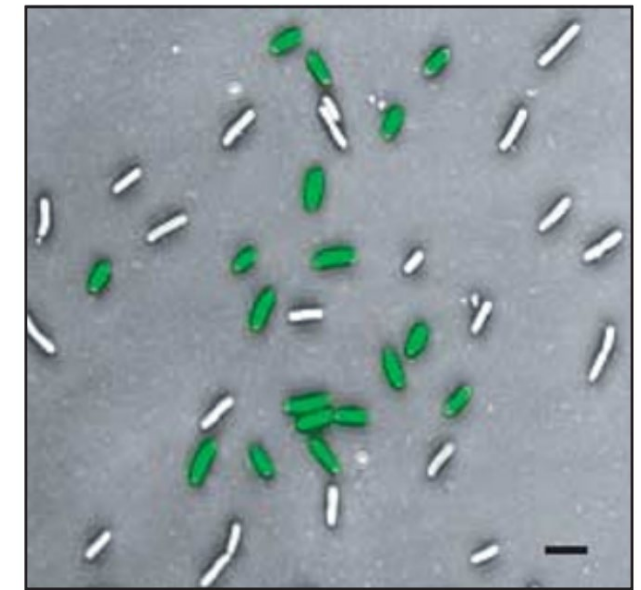
Bistability: *E. coli* Lac operon



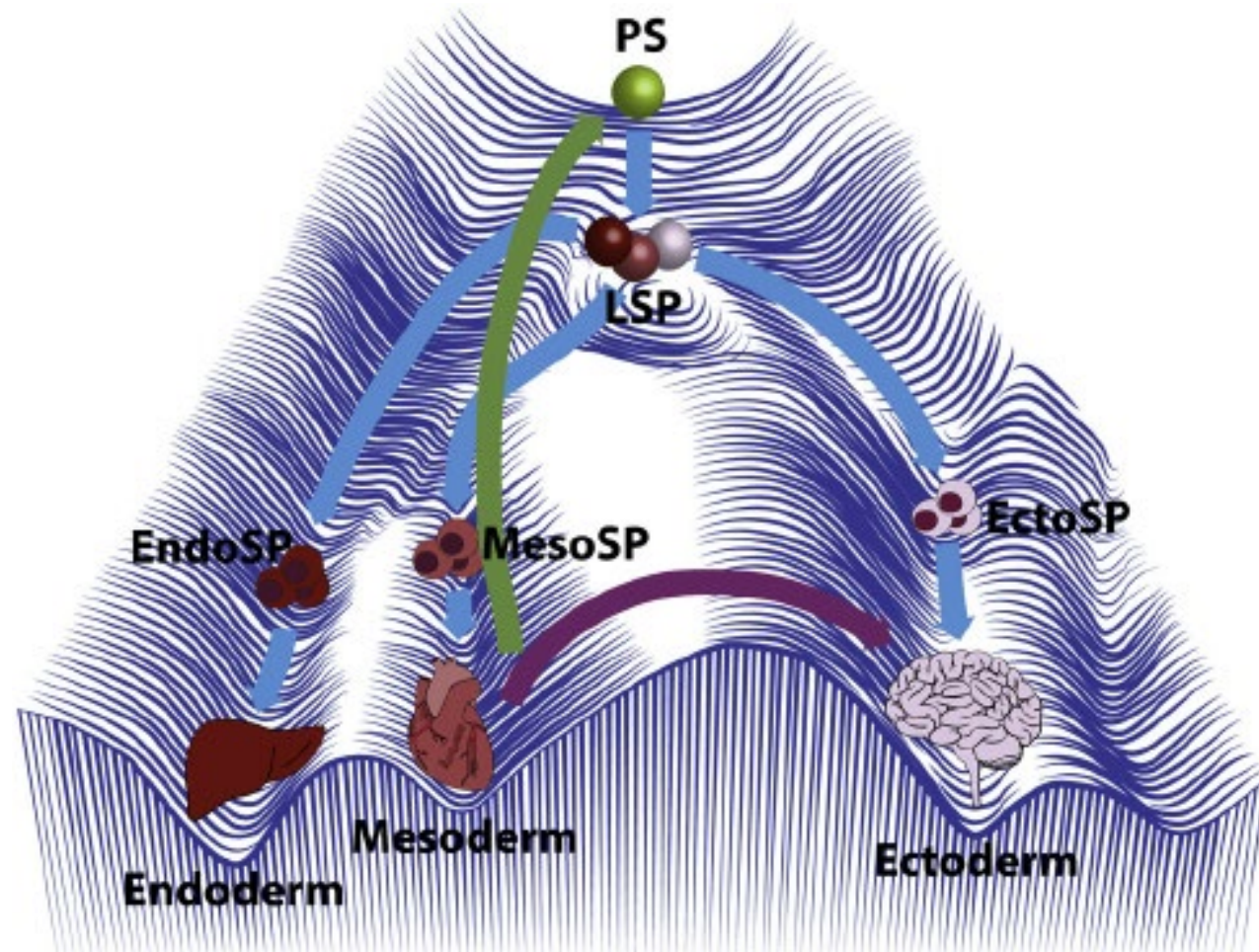
Multistability in the lactose utilization network of *Escherichia coli*

Ertugrul M. Ozbudak^{1*}, Mukund Thattai^{1*}, Han N. Lim¹, Boris I. Shraiman² & Alexander van Oudenaarden¹

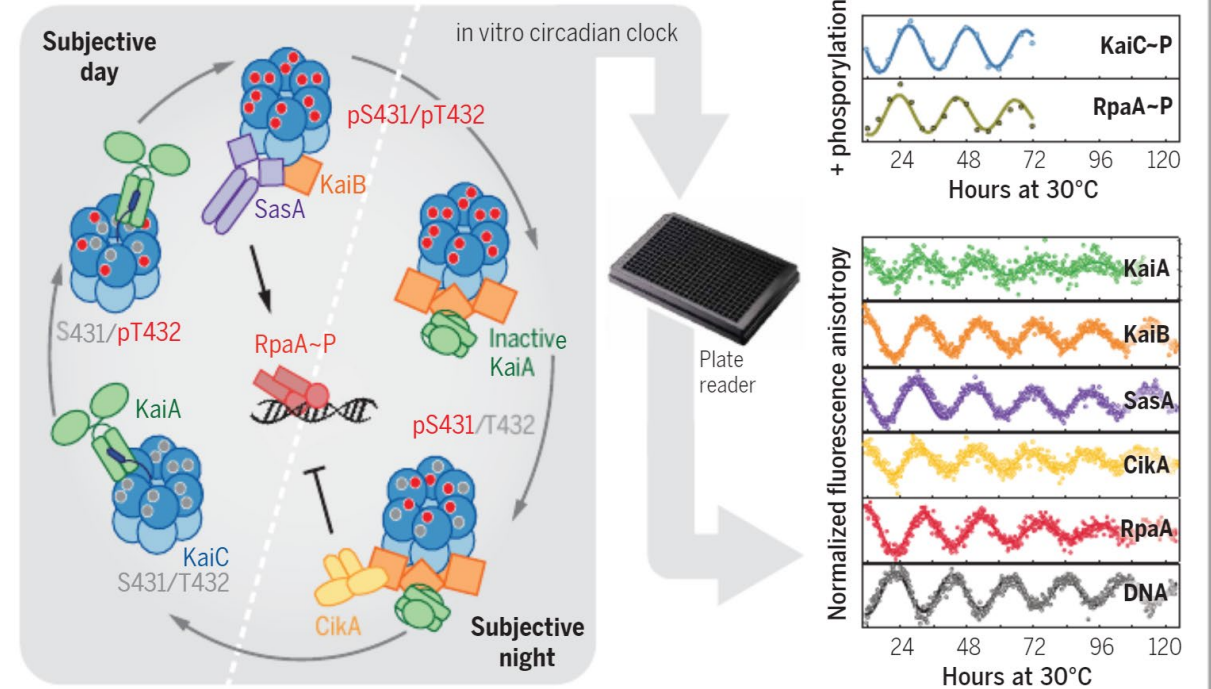
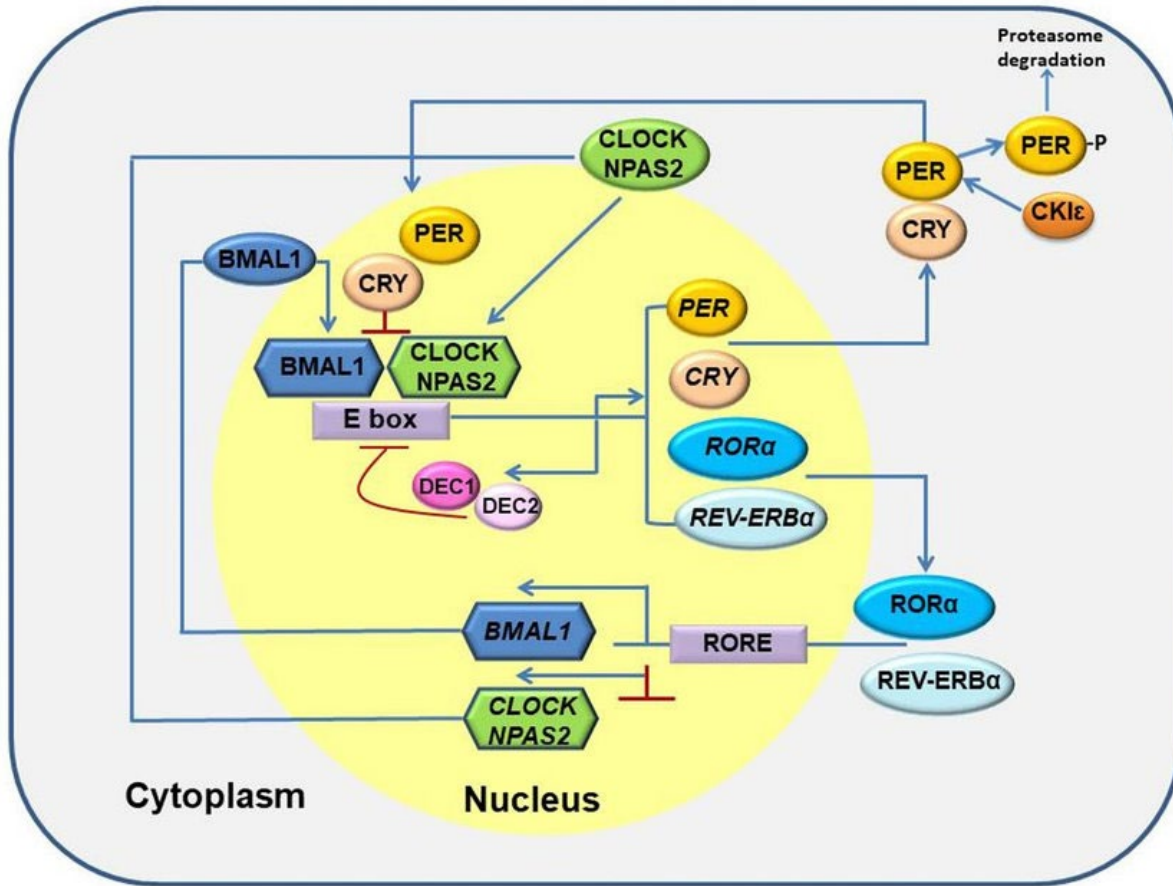
NATURE | VOL 427 | 19 FEBRUARY 2004 | www.nature.com/nature



Multistability: Waddington landscape



Oscillations: Clock genes



RESEARCH ARTICLE

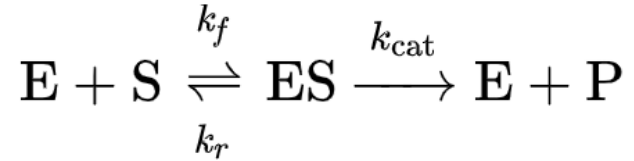
CIRCADIAN RHYTHMS

Reconstitution of an intact clock reveals mechanisms of circadian timekeeping

Chavan *et al.*, *Science* **374**, eabd4453 (2021)

8 October 2021

Michaelis Menten kinetics

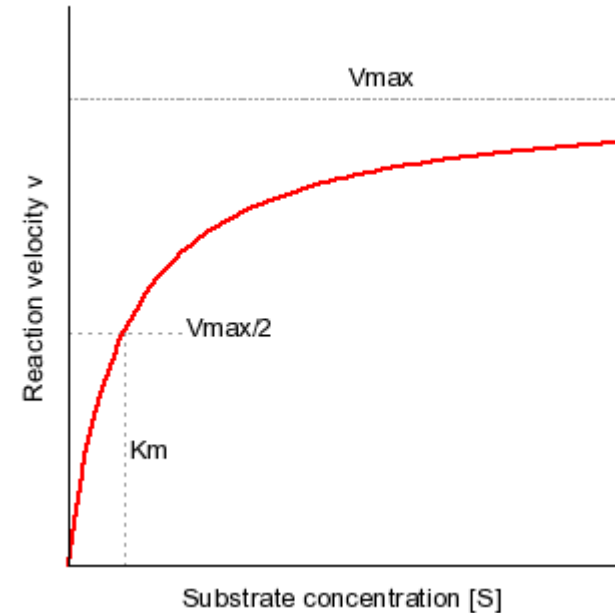


Steady state approximation: $\frac{d}{dt} [\text{ES}] = 0$

Conservation of enzyme: $[\text{E}] + [\text{ES}] = [\text{E}]_0$

$$\frac{d[\text{P}]}{dt} = V_{\text{max}} \frac{[\text{S}]}{K_{\text{M}} + [\text{S}]} = k_{\text{cat}} [\text{E}]_0 \frac{[\text{S}]}{K_{\text{M}} + [\text{S}]}$$

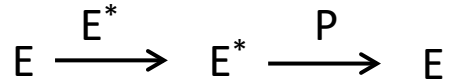
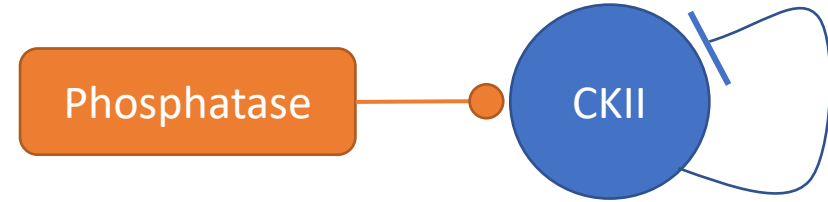
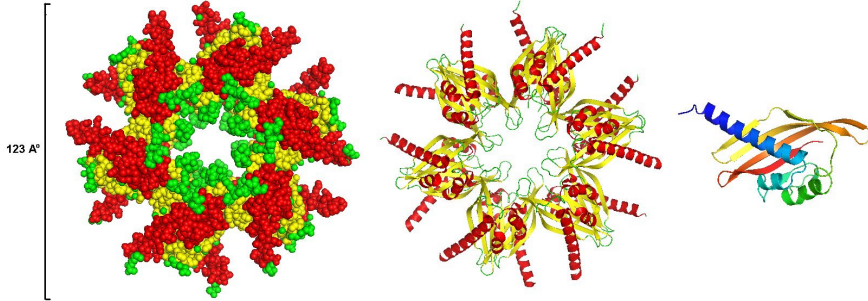
$$K_{\text{M}} = \frac{k_r + k_{\text{cat}}}{k_f}$$



Autocatalytic reaction with first-order decay

CamKII γ

Phosphorylation of Threonine 286 \rightarrow
Constitutive activation



$$\frac{dE^*}{dt} = k_{cat}E^* \frac{E}{K_M + E} - k_p P E^*$$

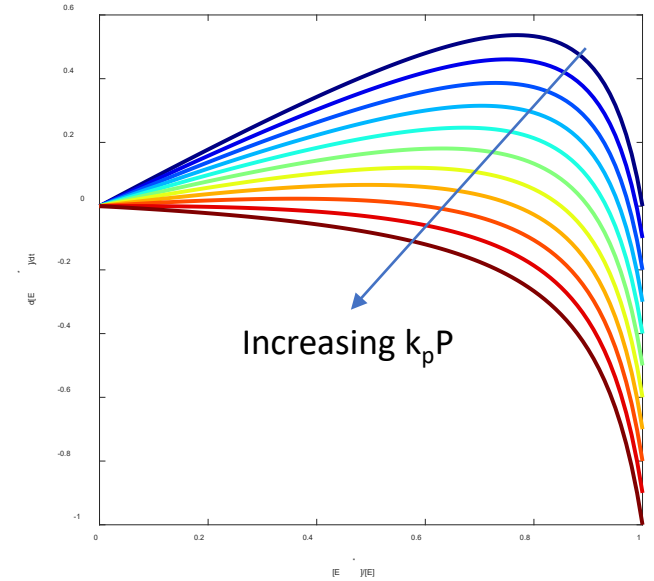
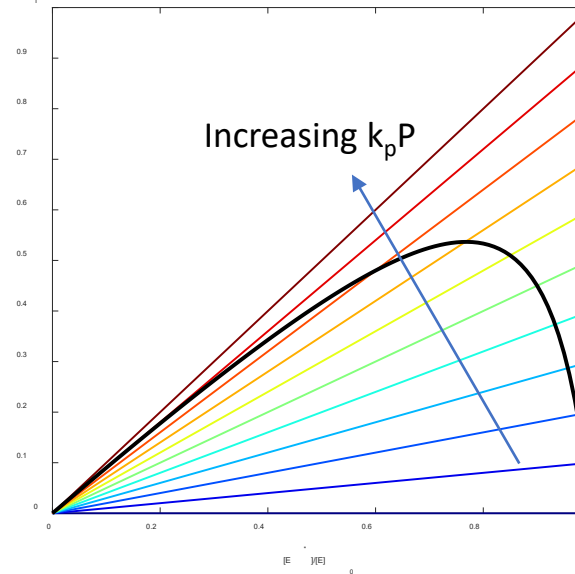
$$E = E_0 - E^*$$

$$\text{Solve } \frac{dE^*}{dt} = 0$$

$$E^* = 0$$

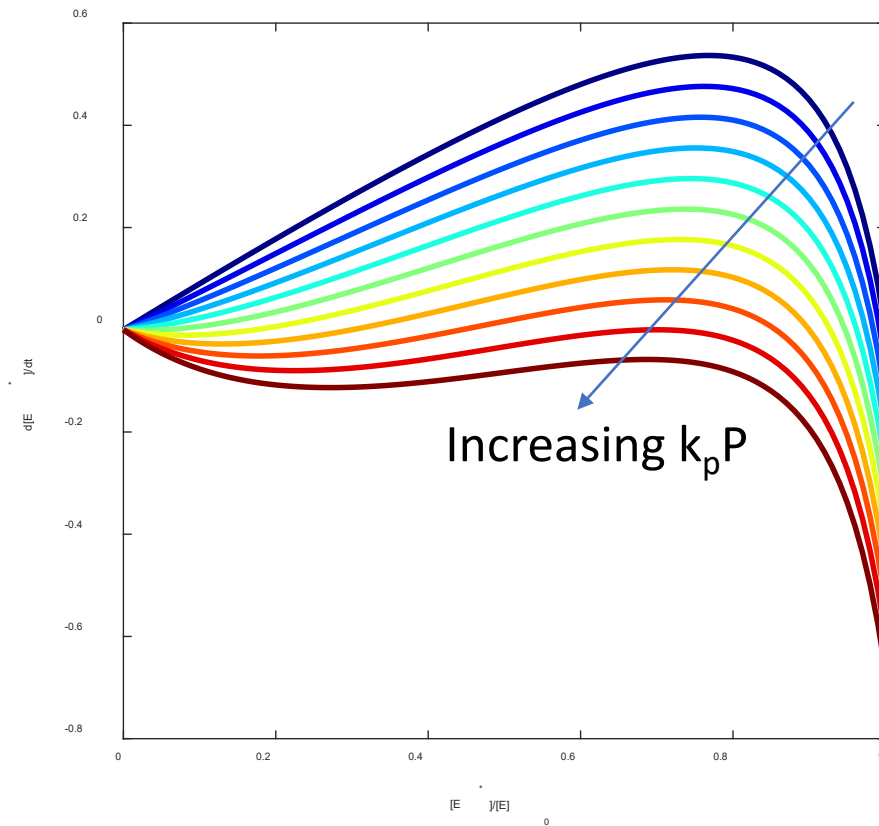
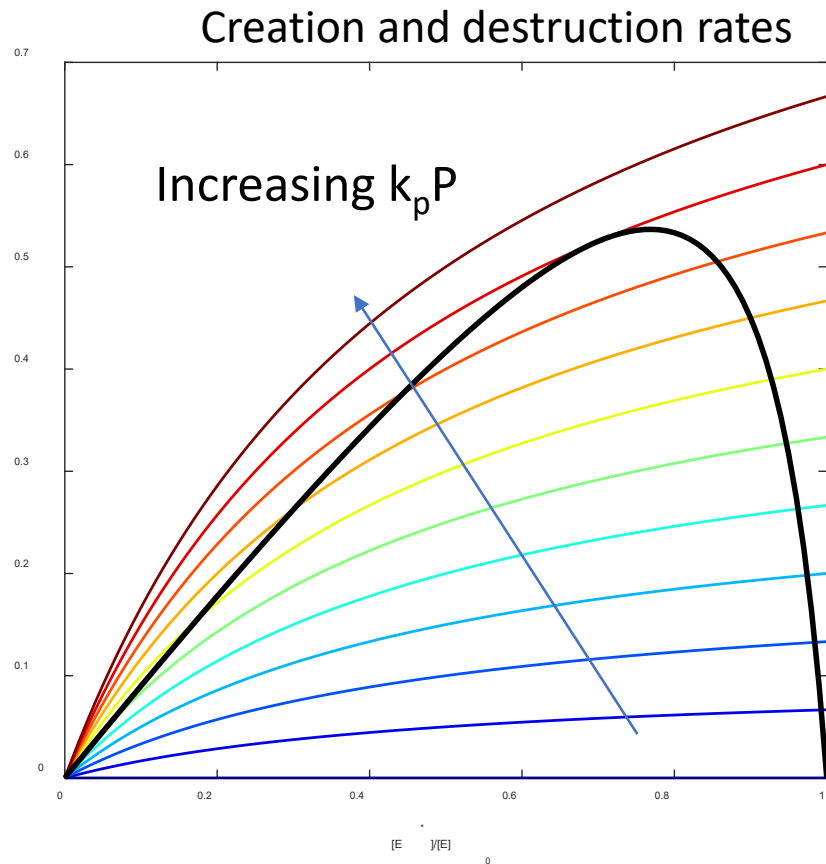
$$E^* = E_0 - \frac{k_p P K_M}{k_{cat} - k_p P}$$

Creation and destruction rates

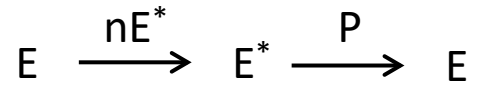


Try again, with Michaelis Menten decay

$$\frac{dE^*}{dt} = k_{cat}E^* \frac{E}{K_M + E} - k_p P \frac{E^*}{K'_M + E^*}$$

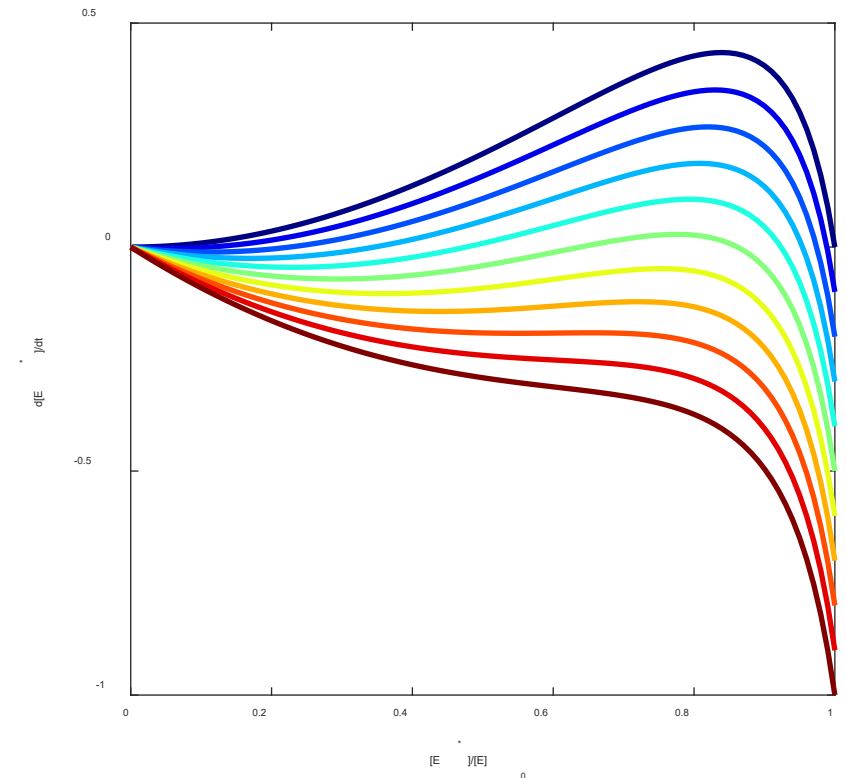
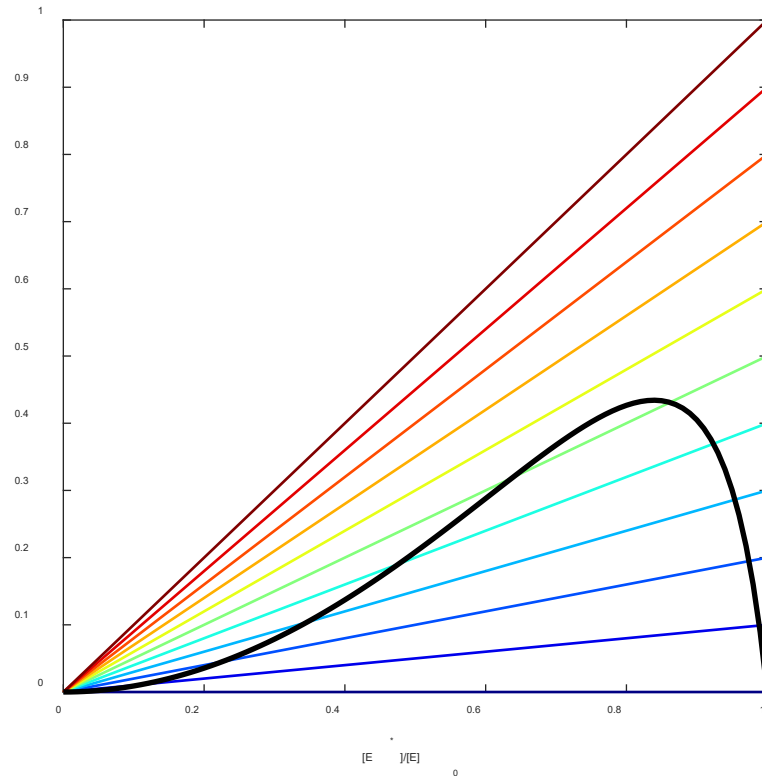


Try again, with cooperative kinetics

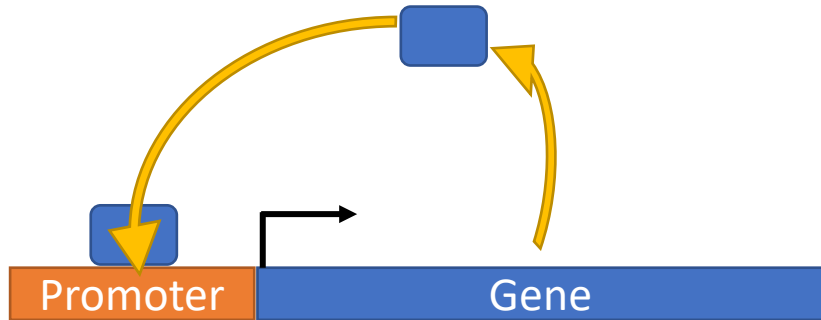


$$\frac{dE^*}{dt} = k_{cat}(E^*)^n \frac{E}{K_M + E} - k_p P E^*$$

$$E = E_0 - E^*$$

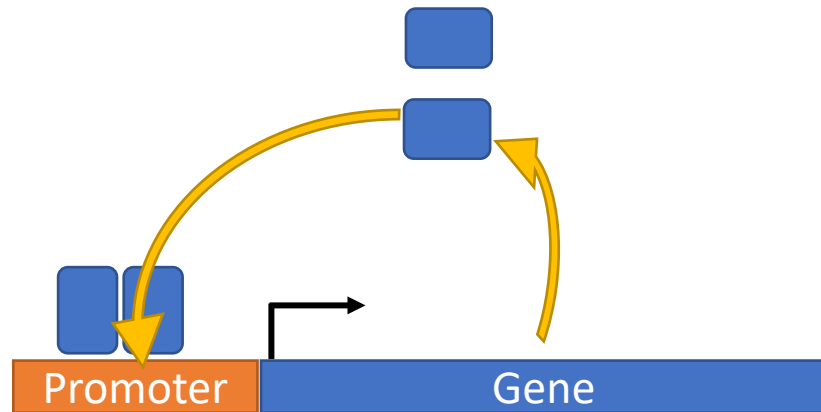


Self-induced transcription



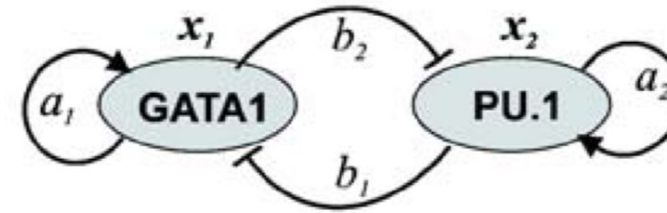
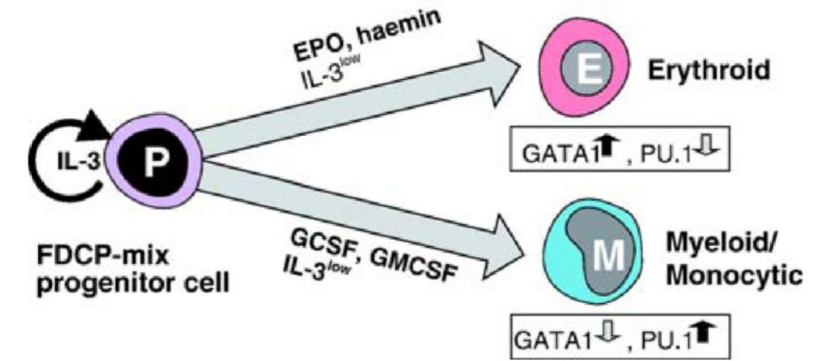
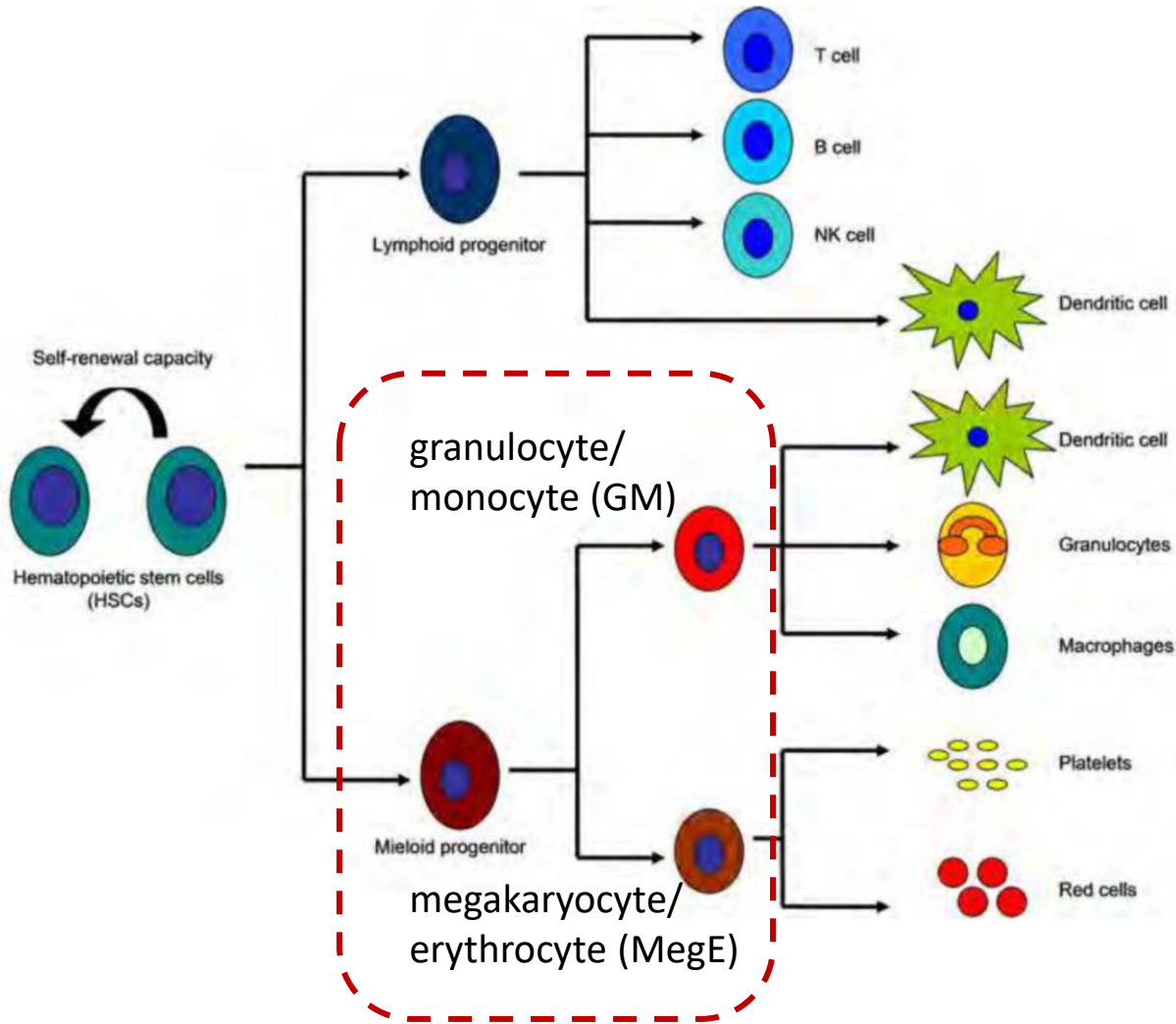
$$\frac{dG}{dt} = \frac{kG}{G + M} - k_P P G$$

vs



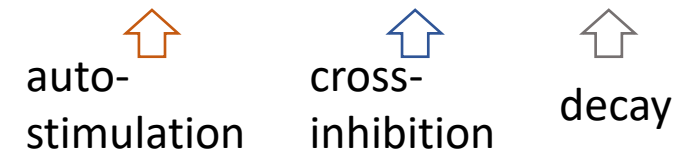
$$\frac{dG}{dt} = \frac{kG^n}{G^n + M^n} - k_P P G$$

Model GATA1-PU.1 Gene Regulatory Circuit



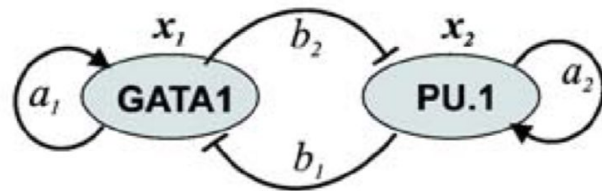
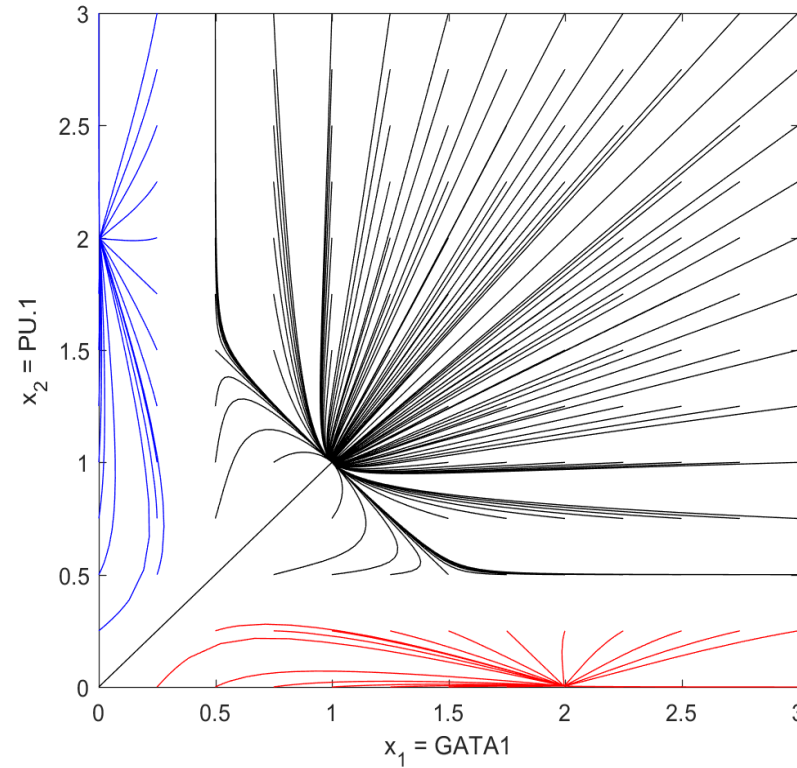
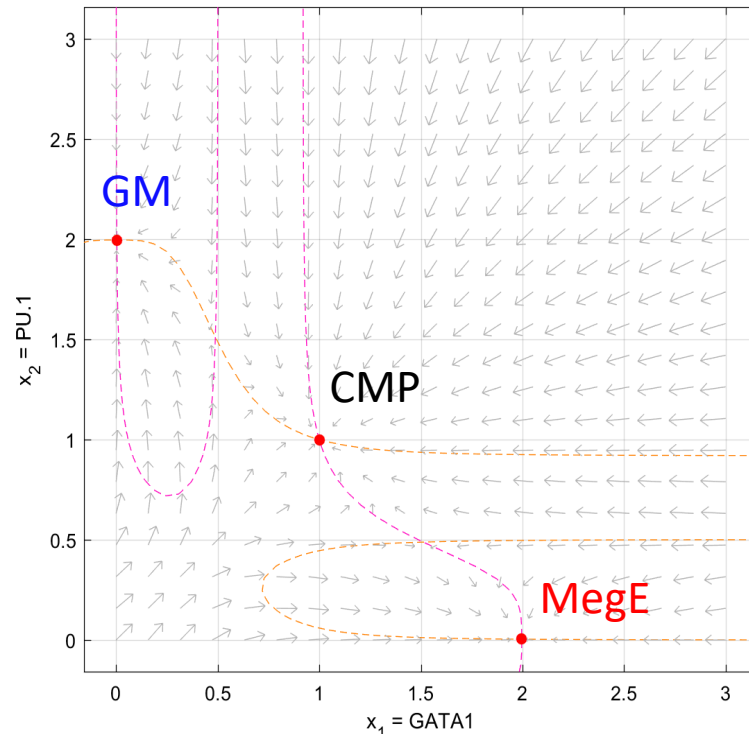
$$\frac{dx_1}{dt} = a_1 \frac{x_1^n}{\theta^n + x_1^n} + b_1 \frac{\theta^n}{\theta^n + x_2^n} - k_1 x_1$$

$$\frac{dx_2}{dt} = a_2 \frac{x_2^n}{\theta^n + x_2^n} + b_2 \frac{\theta^n}{\theta^n + x_1^n} - k_2 x_2$$



Huang, Sui, et al. "Bifurcation dynamics in lineage-commitment in bipotent progenitor cells." *Developmental biology* 305.2 (2007): 695-713.

Tristability corresponds to steady states of progenitor and differentiated lineages



$$a_1 = a_2 = 1, b_1 = b_2 = 1, k_1 = k_2 = 1, n = 4, \theta = 0.5$$

Types of symmetry breaking

