Athermal dynamics of strongly coupled stochastic three-state oscillators

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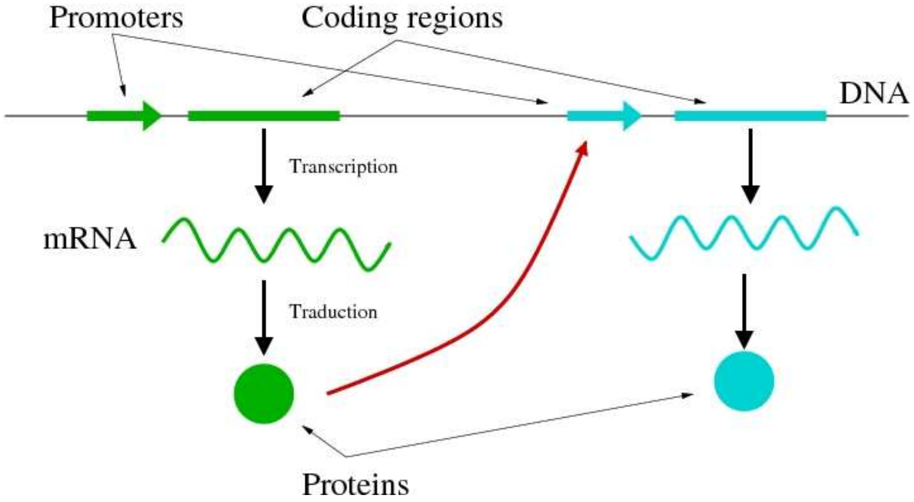
Principles and modeling of gene regulation



Gene expression level: $x_i^t \in \{0,1\}$

Dynamical rules:

activation: A → B

$x_A^t = 1 \longrightarrow x_B^{t+1} = 1$

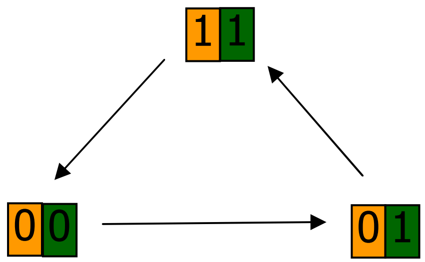
$x_A^t = 0 \longrightarrow x_B^{t+1} = 0$

inhibition: A ⊣ B

$x_A^t = 1 \longrightarrow x_B^{t+1} = 0$

$x_A^t = 0 \longrightarrow x_B^{t+1} = 1$

Three-state oscillator:

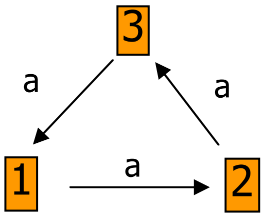


= Gene A

= Gene B

Single stochastic three-state unit:

[extensions to d-state units]



probability rate to switch from i to i+1: $a = 1$

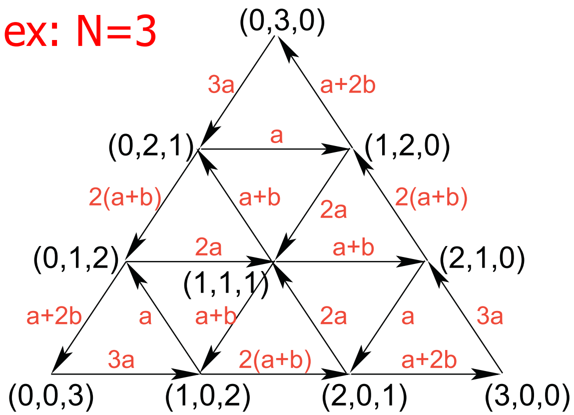
p_i = probability to be in state i

$$\dot{p}_i = -p_i + p_{i-1}, i = 1,2,3 \longrightarrow p_i^s = 1/3, i = 1,2,3$$

+ decay rate

Globally coupled three-state oscillators:

ex: N=3



(a)

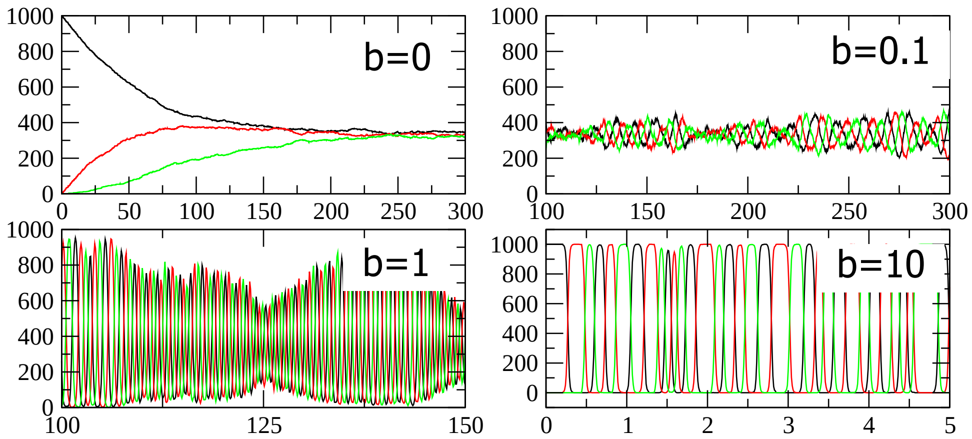
N oscillators

state: (n_1, n_2, n_3) n_i number of oscillators in state i

switching i to i+1 prob. rate for one oscillator: $\pi_{i,i+1} = a + bn_{i+1}$

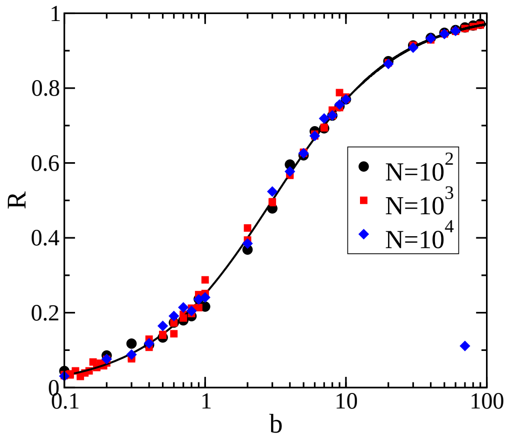
Gillespie simulations:

N = 1000



Order parameter: R (degree of synchrony)

$n_1 = n_2 = n_3 = N/3 \Rightarrow R = 0$ $n_i = N \Rightarrow R = 1$



Mean field approximation: $x_i = n_i / N$ real variable

$\dot{x}_i = x_{i-1}(1 + bNx_i) - x_i(1 + bNx_{i+1})$ ⟶ $(x_1, x_2, x_3) = (\frac{1}{3}, \frac{1}{3}, \frac{1}{3})$ stable stationary point for all b

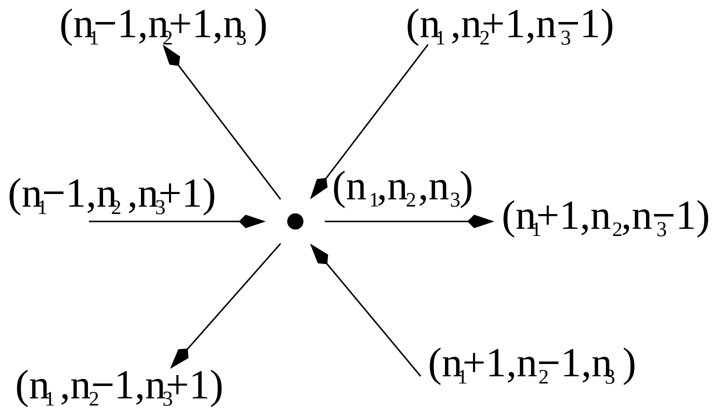
No oscillations for large b = unappropriate approximation

Rem: appropriate for other coupling functions $\pi_{i,i+1} = \Pi(x_{i+1})$ $Ex: \Pi(x) = 1 + bNx$

⟶ Hopf bifurcation to regular oscillations if $\Pi'(1/3) > 3\Pi(1/3)$

Stochastic description:

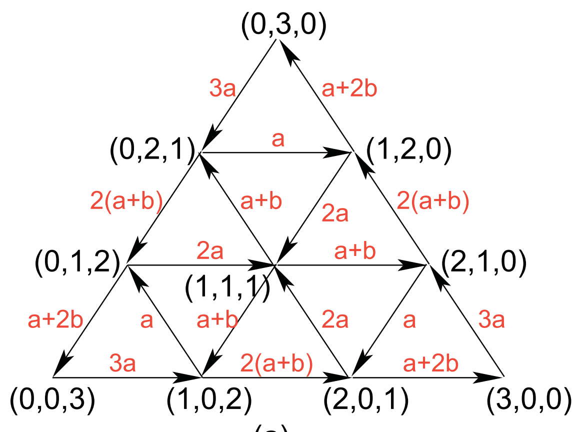
$$
\begin{aligned}
\dot{p}(n_1,n_2,n_3) = &(n_1+1)[1+b(n_2-1)]p(n_1+1,n_2-1,n_3) \\
&+(n_2+1)[1+b(n_3-1)]p(n_1,n_2+1,n_3-1) \\
&+(n_3+1)[1+b(n_1-1)]p(n_1-1,n_2,n_3+1) \\
&-[N+b(n_1n_2+n_2n_3+n_3n_1)]p(n_1,n_2,n_3)
\end{aligned}
$$



⟶ $$p_s(n_1,n_2,n_3) = C_b \frac{G(b,n_1)G(b,n_2)G(b,n_3)}{n_1!n_2!n_3!}$$

$$G(x,n) = \prod_{k=0}^{n-1}(1+kx)$$

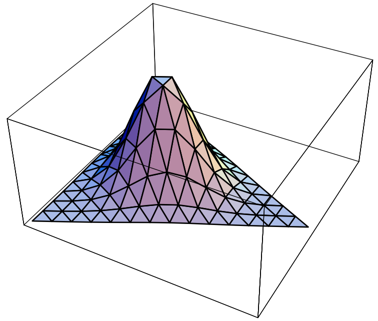
C_b normalisation constant



(a)

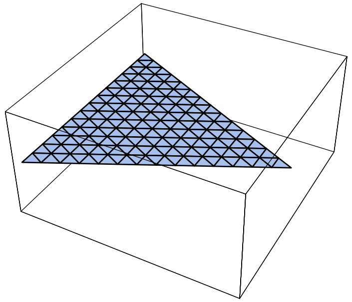
Stochastic description: $$p_s(n_1,n_2,n_3)=C_b\frac{G(b,n_1)G(b,n_2)G(b,n_3)}{n_1!n_2!n_3!}$$ $$G(x,n)=\prod_{k=0}^{n-1}(1+kx)$$

Uncoupled limit (b=0): $$p_s(n_1,n_2,n_3)=\frac{N!}{3^N n_1!n_2!n_3!}$$ (trinomial distrib.)



Convexity transition (b=1):

$$p_s(n_1,n_2,n_3)=cst$$

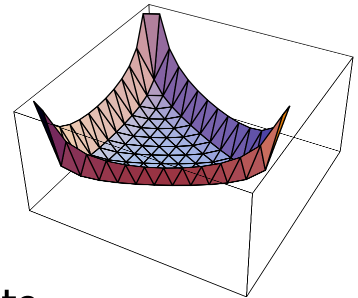


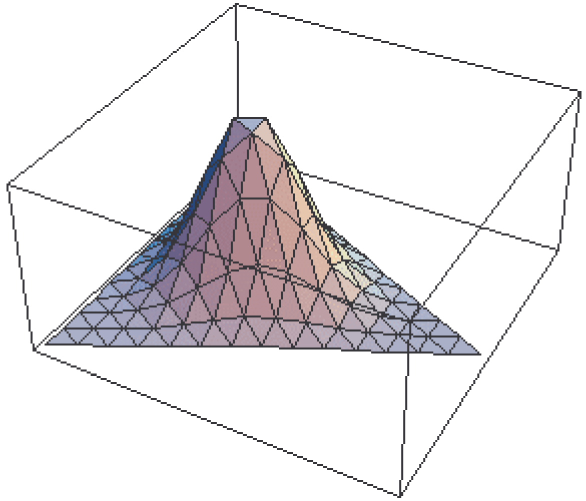
Strong coupling (b large):

$$p_s(0,0,N)=\frac{1}{3}-\frac{2}{3b}\sum_{k=1}^{N-1}\frac{1}{k}+O(1/b^2)$$

$$p_s(n,0,N-n)=\frac{N^2}{3bn(N-n)}+O(1/b^2),n=1,\ldots,N$$

$$p_s(n_1,n_2,n_3)=O(1/b^2),n_1n_2n_3>0$$





+ decay rate

Large N behaviour:

Stirling formula

→ $$p_s(n_1,n_2,n_3)\cong C_b\frac{b^N}{\Gamma^3(1/b)}(n_1n_2n_3)^{1/b-1}$$ if n_1,n_2 and n_3 large

→ $$R=\frac{b}{b+3}$$

$$\left(R=\frac{1}{2N^2}\sum_{n_i\geq 0:n_1+n_2+n_3=N}\left((n_1-n_2)^2+(n_2-n_3)^2+(n_3-n_1)^2\right)p_s(n_1,n_2,n_3)\right)$$