

ADVANCED SUMMER SCHOOL ON APPLIED DYNAMICS IN SYSTEMS AND SYNTHETIC BIOLOGY

EXERCISES - GENE REGULATORY CIRCUITS

1. Consider a gene whose expression is affected by a direct positive feedback, with Hill coefficient 2, maximum expression rate 1 nM/s, activation threshold 100 nM, and degradation rate 0.001 s^{-1} . Integrate the differential equation that represents the dynamics of the concentration of the expressed protein, and determine the threshold value of the initial condition that separates the basins of attraction of the two coexisting equilibrium states of the system.
2. Consider the following activator-repressor model discussed in class (slide titled “From oscillations to pulses”):

$$\begin{aligned}\frac{dx}{dt} &= a_1 + \frac{b_1 x^n}{K_1^n + x^n} - gxy - d_1 x \\ \frac{dy}{dt} &= a_2 + \frac{b_2 x^m}{K_2^m + x^m} - d_2 y\end{aligned}$$

Simulate this model for the following parameter values: $a_2=0.025 \text{ nM/s}$, $b_1=15 \text{ nM/s}$, $b_2=0.8 \text{ nM/s}$, $d_1=d_2=5 \cdot 10^{-5} \text{ s}^{-1}$, $g=2.5 \cdot 10^{-7} \text{ nM}^{-1}\text{s}^{-1}$, $K_1=3000 \text{ nM}$, $K_2=750 \text{ nM}$, and $n=m=2$. Vary a_1 as shown in the slides. Reproduce the dynamics obtained there.

3. The following model describes genetic competence in *B. subtilis*:

$$\begin{aligned}\frac{dK}{dt} &= \alpha_k + \frac{\beta_k K^n}{k_k^n + K^n} - \frac{\gamma_k K}{1 + \frac{K}{\Gamma_k} + \frac{S}{\Gamma_s}} - \delta_k K \\ \frac{dS}{dt} &= \alpha_s + \frac{\beta_s}{1 + (K/k_s)^p} - \frac{\gamma_s S}{1 + \frac{K}{\Gamma_k} + \frac{S}{\Gamma_s}} - \delta_s S\end{aligned}$$

Simulate this model for the parameter values given in the table below:

Parameter	Value	Parameter	Value	Parameter	Value
α_k	0.00875 molec/s	γ_k, γ_s	0.001 s^{-1}	k_k	5000 molec
α_s	0.0004 molec/s	δ_k, δ_s	10^{-4} s^{-1}	k_s	833 molec
β_k	7.5 molec/s	Γ_k	25000 molec	n	2
β_s	0.06 molec/s	Γ_s	20 molec	p	5

Next, vary the parameters α_k , α_s and β_s (one at a time) and study the response of the system in the different situations. Reproduce the different dynamical regimes studied in class.



4. Implement a model of a constitutively expressed gene in a single step combining transcription and translation (with expression rate 0.01 nM/s and decay rate 10^{-4} s^{-1}), and simulate it using a stochastic algorithm. Examine the effect of noise on the dynamics of gene expression, by plotting the stochastic time traces and the corresponding histogram of the protein number in stationary state.
5. Implement a model of a constitutively expressed gene, separating now transcription and translation. Consider the following parameter values: transcription rate 0.1 nM/s, translation rate 0.1 s^{-1} , mRNA decay rate 0.01 s^{-1} , and protein decay rate 0.001 s^{-1} . Simulate the model using a stochastic algorithm. Examine the effect on the expression noise of compensatory variations in the transcription and translation rates (increasing one and decreasing the other by the same factor, for instance, so that the average protein concentration remains constant).