

ADVANCED SUMMER SCHOOL ON APPLIED DYNAMICS IN SYSTEMS AND SYNTHETIC BIOLOGY

EXERCISES - GENE REGULATORY CIRCUITS

1. Consider the following activator-repressor model discussed in class:

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

Use the tools that you have learned in the different courses of this school to analyze this dynamical system in the plane, as the basal expression rate a_1 of x varies, as shown in the slides. Use these values for the other parameters to perform simulations if necessary: $a_2=0.025$ nM/s, $b_1=15$ nM/s, $b_2=0.8$ nM/s, $d_1=d_2=5 \cdot 10^{-5}$ s⁻¹, $g=2.5 \cdot 10^{-7}$ nM⁻¹s⁻¹, $K_1=3000$ nM, $K_2=750$ nM, and $n=m=2$.

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

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

Again, use the tools that you have learned in the different courses of this school to analyze this dynamical system in the plane, as the parameters α_k , α_s and β_s vary (one at a time or in pairs). Reproduce and study the response of the system in the different dynamical regimes studied in class. Consider the following baseline parameter values:

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

3. 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.
4. 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).