computational systems biology

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Assignment 7

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Stability Analysis of a Genetic Toggle Switch

We want to perform a linear stability analysis of a genetic toggle switch, the core of which consists of two repressors and two (strong) promoters as shown in Figure 1.

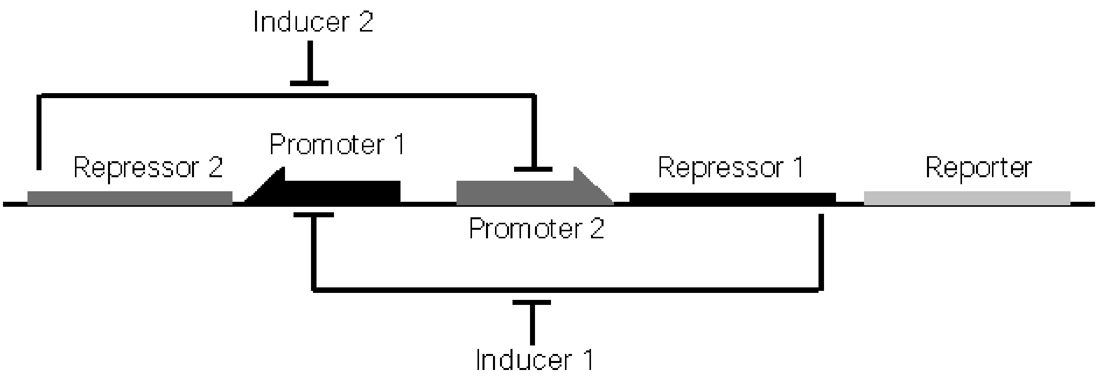

Figure 1: Sketch of the genetic toggle switch (from Gardner et al., 2000).

The dynamics of the two repressor concentrations (u_1 for repressor 1 and u_2 for repressor 2) can be described by the following ODE model:

$$\frac{du_1}{dt} = \frac{\alpha_1}{1+u_2^{\beta}} - u_1 \tag{1}$$

$$\frac{du_2}{dt} = \frac{\alpha_2}{1+u_1^{\gamma}} - u_2 \tag{2}$$

Here, u_1 and u_2 are dimensionless concentrations, while α_1 and α_2 denote effective synthesis rates of repressor 1 and 2, respectively, also in dimensionless form. Both synthesis rates implicitly incorporate the effect of the inducers shown in Figure 1, but are considered constant for sake of simplicity. Also, the reporter activity has been neglected in this scenario. The constants β and γ indicate the degree of cooperativity in the mutual repression of both repressors. Both of these coefficients are assumed greater than 1.
For the given system, please perform the following:

a) Calculate the nullclines of the system ($u_{10}(u_2)$ and $u_{20}(u_2)$) and plot them in a phase plane (u_1, u_2) diagram in MATLAB. Let $u_2 \in [0, 12]$ for the plot and assume the following values for this purpose: $\alpha_1 = \alpha_2 = 10, \beta = \gamma = 2$. **Hint**: *In both Python and MATLAB define the system of equation symbolically and solve it. You may find inspiration in computational assignment 6.* How many steady states does the system have under these conditions? Visualize the velocity field (du_1/dt, du_2/dt) in the same diagram using the MATLAB commands `meshgrid` and `quiver`. In Python you may use `numpy.meshgrid` and `matplotlib.quiver`.

b) We are interested in the dependence of the system stability on the values of α_1 and α_2 in the vicinity of the steady states. Using the general formulas given in equations (1) and (2), determine the eigenvalues of the *linearized* system as $\lambda = f(\alpha_1, \alpha_2, \beta, \gamma)$. Make use of the MATLAB commands `jacobian` and `eig`. In Python you may use the `sympy` module.

Some useful MATLAB commands and help entries for this exercise:

`meshgrid, quiver, jacobian, eig, subs, solve, eval, ezplot, function handles (@)`

Some useful Python commands and help entries for this exercise:

`numpy.meshgrid, matplotlib.quiver, sympy.Matrix, sympy.Matrix.jacobian, scipy.linalg.eigvals`

Submission:

Please address any questions to

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