Prof. Jörg Stelling
D-BSSE
ETH Center UNG H14
Universitätstrasse 19
CH-8092 Zürich
https://www.csb.ethz.ch

Computational Systems Biology
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Assignment 10

(Issue: 28-Nov-2025)

1 Sensitivity Analysis & Identification

You want to study a linear biochemical pathway with two molecular species S_1 and S_2 as shown below:

$$\xrightarrow{k_1} S_1 \xrightarrow{k_2} S_2 \xrightarrow{k_3}$$

and we assume constant influx k_1 and mass-action kinetics for the two other reactions.

a) Determine the steady-state solutions for the concentrations of S_1 and S_2.

b) Write down the matrix of steady-state parameter sensitivities for the system.

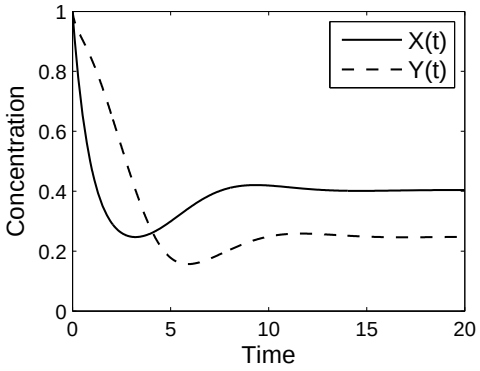
c) Assume you can either perturb k_1 or k_2 by the same amount to elicit the highest absolute response in the steady-state concentration of S_1. Which parameter would you choose and why?

d) You have experimentally determined the steady-state concentrations of S_1 and S_2 as $x_1^{ss} = 5$ mM and $x_2^{ss} = 2$ mM, respectively. Now you want to estimate the system's parameters using a least-squares approach. The corresponding optimization problem is $\Phi(\mathbf{k}) = \mathbf{e^2} \rightarrow \mathbf{min}$, where $\mathbf{e} = \mathbf{x} - \mathbf{x^M}$ is the error with model states $\mathbf{x}$ and measured states $\mathbf{x^M}$, $\Phi(\mathbf{k})$ is the objective function, and $\mathbf{k} = [\mathbf{k_1}\,\mathbf{k_2}\,\mathbf{k_3}]^\mathbf{T}$ is the unknown parameter vector. Are all parameters practically identifiable (justify your answer with a derivation)?

e) Assume you know that $k_3 = 5$ mM/min. Can you determine the parameter values now (and what are they)?

2 Qualitative dynamics

You want to analyze the qualitative dynamic behavior of a circuit with two components X and Y; their concentrations are $X(t)$ and $Y(t)$. You know that the system (i) has a dynamic behavior like the one shown in the figure below, and (ii) has a single, stable steady-state.



a) What does this information tell you about the eigenvalues of the system matrix?

b) Draw a (qualitative) phase portrait that contains (i) the nullclines, (ii) the steady-state, and (iii) one representative trajectory.

c) Label the n regions of identical qualitative behavior in the diagram from b) by $R_1 ... R_n$ and tabulate the derivative sign patterns $\pi(R_i)$ for all regions.

d) Draw the transition graph for the system (only transitions between different regions need to be included).

Submission:

These exercises can be solved by hand. Please address any questions to

alix.moawad@bsse.ethz.ch