Instructions: Submit a short report to answer the questions below, along with your code (either .jl or .ipynb files). Code will be tested using Julia 1.10.5.

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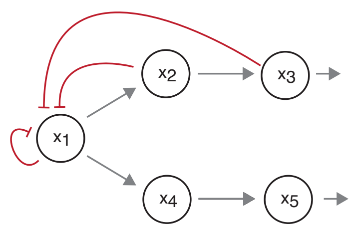
1. Consider the following cell lineage model: a stem cell population, x_1, can differentiate into two progenitor cell populations, x_2 and x_3, which each differentiate further into a terminal cell population, x_4 or x_5, respectively. Feedback interactions exist between the populations as defined in the figure:



This model is defined by the following set of differential equations:

$$
\begin{aligned}
x_1' &= a_1 x_1(1 - x_1 - 0.1x_2 - 0.1x_3) - c_1 x_1 \\
x_2' &= 0.5c_1 x_1 - e_1 x_2 \\
x_3' &= e_1 x_2 - 0.9x_3 \\
x_4' &= 0.5c_1 x_1 - 0.6x_4 \\
x_5' &= x_4 - 0.1x_5,
\end{aligned}
$$

where the parameters (a_1, c_1, e_1) lie in the range $[0, 3]$.

a) Describe the meaning of each term in the first equation (for x_1').

b) Create a model of this system in Julia, given input parameters (a_1, c_1, e_1) and initial conditions. Demonstrate that the model can take different input parameter values.

c) Simulate the model using DifferentialEquations.jl for numerically integration, Simulate this model in the time range $t \in [0, 50]$ for $a_1 = 0.9, c_1 = 0.1, e_1 = 0.5$ and initial conditions $x_1(t_0) = 0.4$, $x_2(t_0) = x_3(t_0) = 0.2$, $x_4(t_0) = x_5(t_0) = 0$. Which species dominate as the system reaches steady state?

2. Can this system be solved at steady state analytically, i.e. in terms of the parameters a_1, c_1, e_1? Why? Solve this system using symbolic computation in Julia. How many fixed points does the model permit? What constraints on the parameters are required to ensure that x_1 will reach a positive value at steady state?

3. The question of whether more than one steady state can be reached for a given set of parameter values (multistability) can be investigated numerically by performing a sweep through a range of

initial conditions. Write a script to simulate the model for different sets of initial conditions (at least 100) in the range $x_i \in [0, 1]$ and analyze the results. Plot the results (you may need to think carefully about the best way to visualize them). Do you find evidence for multistability? Describe approximately the critical initial condition thresholds, if they exist. Discuss briefly what alternative strategies could be used to investigate whether this model permits multistability.

4. Choose a feedback motif that was presented in the Network Motifs paper discussed in class (Alon, 2007). Give a biological system that represents an example of this type of feedback motif. Explain the role of each of the variables/species in the system. Write down a model of this system described by differential equations. Explain your reasoning for the form of each equation. Choose a set of initial conditions and parameter and simulate this model numerically in Julia. Discuss its behavior for different choices of **parameters**. What type of transient and equilibria behaviors does this model display? Could it permit oscillations? Could it permit multistability? Shows plots to explain your reasoning. You are expected to write a short report (2-3 paragraphs) to discuss your investigations and the conclusions you draw.