Practical Assignment Part 1

Systems Biology Models (8BM050)

This document outlines the practical assignment part 1 for the systems biology models course of academic year 2024-2025. This assignment has to be completed **individually**.

Assignment Description

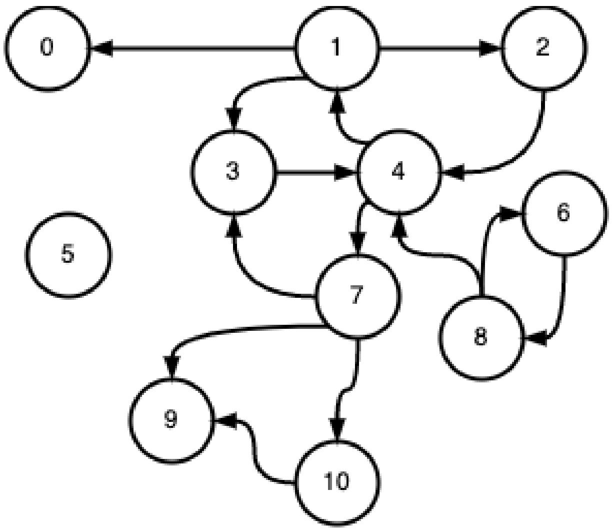
This practical assignment part contains various questions. Each question has a designated number of points that you can score.

Questions

Question 1

a)

Consider the following unweighted directed graph:



Define a python variable `adjacency_matrix` that is a `numpy array` representing the adjacency matrix of the graph. The element index `(i, j)` should correspond to the edge from node `i` to node `j`. If there is no edge between the nodes, the element should be zero.

b)

Define two functions: `in_degree` and `out_degree`, that receive the adjacency matrix and a node index and return the in-degree and out-degree of the node, respectively.

c)

Create a plot of the in-degree and out-degree distribution of the graph. The x-axis should represent the degree and the y-axis the number of nodes with that degree.

d)

Use the adjacency matrix to compute the amount of walks of length 6 that exist in the graph that start and end in the same node.

Question 2

Consider the following description of a differential equation model:

We have two molecules A and B. The molecule A is spontaneously converted into a molecule B with a rate k_1. In the presence of a molecule X, the rate of conversion of A into B is increased with

$k_{\mathrm{stim}}X$. The molecule B is spontaneously converted back into A with a rate k_2. The molecule X does not affect the conversion of B into A. Additionally, the molecule X is not produced, but degrades with a rate k_{deg}.

a)

Draw a diagram of the system. Indicate the reactions and the rates of each reaction.

b)

Write down the system of differential equations that describes the system.

c)

Given are the following parameter values and initial conditions.

- $k_1 = 0.002$
- $k_2 = 0.05$
- $k_{\mathrm{stim}} = 0.03$
- $k_{\mathrm{deg}} = 0.05$

Use the initial conditions:

- $A_0 = 100$ mM
- $B_0 = 0$ mM
- $X_0 = 1$ mM

Derive the units of the rate constants.

d)

Implement the system of differential equations and simulate it for 100 minutes. Plot the values of A, B and X over time.

Question 3

In [1], Shi et al. defined a differential equation model of caffeine in the body. Their model looked like this:

$$\begin{aligned}\frac{\mathrm{d}C^{\mathrm{pl}}(t)}{\mathrm{d}t} &= -k_{12}C^{\mathrm{pl}}(t) + k_{21}C^{\mathrm{int}}(t) - k_{10}C^{\mathrm{pl}}(t) \\ \frac{\mathrm{d}C^{\mathrm{int}}(t)}{\mathrm{d}t} &= k_{12}C^{\mathrm{pl}}(t) - k_{21}C^{\mathrm{int}}(t)\end{aligned}$$

Where $C^{\mathrm{pl}}(t)$ is the concentration of caffeine in the blood plasma, $C^{\mathrm{int}}(t)$ is the concentration of caffeine in the interstitial compartment. The parameters are given by k_{12}, k_{21}, and k_{10}.

a)

Draw a diagram of the model showing the direction of the fluxes and the state variables.

b)

The model was calibrated by Shi et al., the parameter values for the given parameters are:

- $k_{12} = 1.64\ \mathrm{h}^{-1}$
- $k_{21} = 1.91\ \mathrm{h}^{-1}$
- $k_{10} = 0.34\ \mathrm{h}^{-1}$

Use the following initial conditions:

- $C^{\mathrm{pl}}(0) = 13.0\ \mu\mathrm{g} \cdot \mathrm{mL}^{-1}$
- $C^{\mathrm{int}}(0) = 0.0\ \mu\mathrm{g} \cdot \mathrm{mL}^{-1}$

Simulate the model from 0 to 24 hours and create a figure of the result.

c)

Shi et al. reported variability in the k_{10} parameter as a standard deviation of $\sigma_{10} = 0.069 \text{ h}^{-1}$. Simulate the model for k_{10} values of $0.34 - \sigma_{10}$ and $0.34 + \sigma_{10}$ and plot the results in a single figure. Describe the effect of the variability of the k_{10} parameter on the observed concentration values of caffeine.

Bibliography

[1] J. Shi, N. L. Benowitz, C. P. Denaro, and L. B. Sheiner, "Pharmacokinetic-pharmacodynamic modeling of caffeine: Tolerance to pressor effects," *Clinical Pharmacology and Therapeutics*, vol. 53, no. 1, pp. 6–14, Jan. 1993, doi: 10.1038/clpt.1993.3.