Freie Universität Berlin
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3. Homework (Complex Systems Block)
Introduction to Focus Areas
WS 2024/25

Deadline: December 09, 10:00 (**before** the lecture)

The homework should be worked out in groups. Pen & paper exercises will be discussed on the board. Programming exercises must be submitted via Whiteboard.

Homework 1 (Stochastic simulation: 3 + 2 points)
Expect the Unexpected. Consider the Slögl model.

$$R_1 : 2x_1 \xrightarrow{r_1} 3x_1, \qquad R_2 : 3x_1 \xrightarrow{r_2} 2x_1 + \emptyset, \tag{1}$$

$$R_3 : \emptyset \xrightarrow{r_3} x_1, \qquad R_4 : x_1 \xrightarrow{r_4} \emptyset. \tag{2}$$

with propensities (*stochastic* reaction rates): $r_1 \dots r_4$.

$$r_1 = k_1 \cdot x_1(x_1 - 1) \tag{3}$$

$$r_2 = k_2 \cdot x_1(x_1 - 1)(x_1 - 2) \tag{4}$$

$$r_3 = k_3 \tag{5}$$

$$r_4 = k_4 \cdot x_1 \tag{6}$$

with parameter values are $0.15, 0.0015, 20.0$ and 3.5 for $k_1, \dots, k_4$ respectively. The initial value for x_1 is $x_1(t_0) = 40$. The stoichiometric matrix S is given by:

	r_1	r_2	r_3	r_4
x_1	1	-1	1	-1

a) (**to be uploaded via Whiteboard**) Write a program implementing this model and generate trajectories using the stochastic simulation algorithm. The program reads the input file ("Input.txt") provided in the Whiteboard. The first number in the input file is the 'seed' of the random number generator, the second is the number of trajectories N to be computed. Using this input, compute the trajectories for N simulations up to time $T = 5$. For each simulation, write the time and the values of x_1 into a file "Task1TrajY.txt" as outlined before. Call this program "Exc3Task1.py" and upload via Whiteboard.
b) (**to be discussed in class**) Using the program from the task above, perform $N = 200$ realisations of the Slögl model leading up to $T = 5$. At $T = 5$ plot a histogram of species x_1. Also mark the sample expectation of x_1 on the same figure.

- **Discuss:** is the sample expectation a good statistic to describe the distribution of x_1 for this model?

Troubleshooting. *(i) In case you derive negative results: Make sure all reactions leading out of the state space ($\mathbb{N}$) are zero. (ii) Make sure that you are storing the right state when you cross t_{final}.*

Homework 2 (Programming, 2+3 points)
You are given the following model to describe the pharmacokinetics (concentration-time profile) of a pharmaceutic drug in the 'dosing compartment' x_0 as well as in the 'bloodstream' x_1 after

a single dose intake:

$$x_0 \xrightarrow{r_0} \quad x_1 \ , \ x_1 \xrightarrow{r_1} \quad \varnothing \tag{7}$$

with reaction rates

$$r_0 = \quad x_0 \cdot k_a \ , \ r_1 = \quad x_1 \cdot k_e. \tag{8}$$
$$\tag{9}$$

where k_a and k_e are parameters describing the uptake and elimination of the drug from the body. In our example, let $k_e = 0.3$ and $k_a = 0.5$ and let the dosage of the drug be $x_0(t_0) = 200$ [mg] and the initial concentration in the bloodstream be $x_1(t_0) = 0$. For simplicity, we assumed $V = 1$ [L] and thus x_1 be in units of [mg/L].

a) (**to be uploaded via KVV**) Derive the ODE of this model and write a program that numerically integrates the ODEs with the explicit Euler method using a time step $\Delta t = 1$ up to time $t_{final} = 24$. After simulation, write the time and the values of x_1 into a file "Task2aTraj.txt". The output text-file should be in the comma-separated text format using two digits after the comma (format '%1.2f'), e.g.

$$0.00, 1.00, 2.00, 3.00, ... \tag{10}$$
$$5.00, 6.00, 5.00, 6.00, ... \tag{11}$$

where the first row denotes the times and the second row the corresponding states of x_1. Call this program "Exc3Task2a.py" and submit it via the Whiteboard system.

b) (**to be discussed in class**) The analytical (hence exact) solution of the ODE for the model above is given by:

$$y(t) = x_0(t_0) \cdot \frac{k_a}{k_a - k_e} \cdot \left(e^{-k_e \cdot t} - e^{-k_a \cdot t} \right).$$

Modify your program above in the following way: Use different time steps $\Delta t = 0.01, 0.05, 0.1, 0.5, 1$.

(i) For each time step, superimpose your results from using the explicit Euler method with the analytical solution. What do you see?

(ii) Compute the *average* error between the analytical solution $y(t)$ vs. your numerical solution when using the explicit Euler method with different time-steps. I.e. compute,

$$\bar{\varepsilon}(\Delta t) = \frac{1}{N_t} \sum_{i=0}^{N_t} |x_1(i \cdot \Delta t) - y(t_i)|, \tag{12}$$

where $N_t = t_{final}/(\Delta t)$ denotes the number of time steps in your simulation and $x_1(t_i)$ with $t_i \in (0, \Delta t, 2 \cdot \Delta t, \ldots, N_t \cdot \Delta t)$ denotes your numerical solution with the explicit Euler method. Plot the error vs. the step size. How does the error behave with regards to the step size?

(iii) (**to be discussed in class**) When (at what time) is the maximum concentrations of the drug achieved in the bloodstream? How did you compute it, and how does it depend on the parameters of the model?