Freie Universität Berlin
Prof. Dr. Max von Kleist
Dr. Alexia Raharinirina

3. Assignment
Complex Systems for Bioinformaticians
SS 2025

Deadline: May 6, 12:00 (**before** the lecture)

The homework should be worked out individually, or in groups of 2 students. Pen & paper exercises should be handed at the designated deadline. Each solution sheet must contain the names and 'Matrikulationnummer' of all group members and the name of the group. The name of the group must include the last names of the group members, in alphabetic order, e.g. "AlbertRamakrishnanRastapopoulos", for group members Mandy Albert, Mike Ramakrishnan, and Marcus Rastapopoulos. Please staple all sheets.
Programming exercises must be submitted via Whiteboard.

Homework 1 (Convergence (pen & paper), 1 (+1) points)
You have sampled a Poisson process $\left\{X^{(1)}, X^{(2)}, \ldots, X^{(p)}\right\}$ all taken at a fixed time point t using the stochastic simulation algorithm with $p = 1000$ times. Let's assume that this Poisson process has an inherent variance $\sigma^2 = 2.5$. Subsequently, you computed the sample mean $\bar{X}^{(p)}$ and you observed that the standard deviation of the sample mean $\sigma_p = \left(\mathbb{E}\left[|\bar{X}^{(p)} - \mu|^2\right]\right)^{\frac{1}{2}} = 0.05$, where μ is the true mean the Poisson process also at the time-point t. How often would you have had to sample to achieve half the precision, $\sigma_p = 0.1$? (Can you do the derivation? [+1])

Homework 2 (Analytical Solution (pen & paper), 1+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:

$$x_0 \xrightarrow{r_0} x_1 \, , \, x_1 \xrightarrow{r_1} \varnothing \tag{1}$$

with reaction rates

$$r_0 = x_0 \cdot k_a \, , \, r_1 = x_1 \cdot k_e. \tag{2}$$

where k_a and k_e are parameters describing the uptake and elimination of the drug from the body. In our example, let $k_a = 0.5$ and $k_e = 0.3$.
a) (**pen & paper**) Derive the ordinary differential equations for this model.
b) (**pen & paper**) Analytically solve this model using the method of 'integrating factors' with initial condition: $x_0(t_0) = \text{dose}$ and $x_1(t_0) = 0$ and $t_0 = 0$.
Hint: First solve the ODE for $x_0(t)$ and then substitute it into the ODE for x_1 and solve.

Homework 3 (Implementation, 1+1+1+2 points)
a) (**to be uploaded via Whiteboard**) Write a program implementing the model from the previous task and generate trajectories using the stochastic simulation algorithm. The program reads the input file ("Input.txt") provided in 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. Let the initial condition be $x_0(t_0) = 100$ and $x_1(t_0) = 0$. Using this input, compute the trajectories for N simulations up to time $t_{final} = 24$. Store the population of x_0 and x_1 every 1 time unit until you reach $t_{final} = 24$ and write them into the file "Task3aTrajYTimed.txt",

where 'Y' $= 1 \ldots N$ denotes the respective simulation. The output text-file should be in the comma-separated text format using two digits after the comma (format '%1.2f'), e.g.

$$0.00, 1.00, 2.00, 3.00, ... \tag{3}$$
$$5.00, 6.00, 5.00, 6.00, 7.00, ... \tag{4}$$
$$7.00, 12.00, 4.00, 13.00, 9.00, ... \tag{5}$$

where the first row are the storage times (i.e. every 1 time units), second- and third correspond to the states of x_0, x_1 respectively at these time points. Call this program "Ex3a.py" and submit it via the Whiteboard system.
b) (**to be printed**) Perform 100 simulations and plot the sample mean of $x_1 \pm$ standard deviation, akin to the figure below.
c) (**to be uploaded via Whiteboard**) Change the program above: Let N be the number of simulations. From different numbers of simulations $N \in \{10, 40, 160\}$, compute the sample mean of x_1 at time $t = 5$,

$$\bar{x_1}^{(N)} := \sum_{i=1}^{N} \frac{x_1^{(i)}}{N}.$$

Save three numbers into a file "SampleMeans.txt" in comma-separated text format using 2 digits after the comma (format '%1.2f') e.g.

$$3.50, 7.06, 11.00$$

Call this program "Ex3c.py" and upload via the whiteboard.
d) (**to be printed and discussed**) Using the specifications in c), repeat the procedure at least 10 times (i.e. compute 10 'sample means' respectively for $N \in \{10, 40, 160\}$). Plot on a log–log scale (or any suitable scaling) and make e.g. scatter plot of

$$\epsilon_j^{(N)} = \left| \bar{x}_1^{(N)}(t = 5) - \mathbb{E}[x_1(t = 5] \right| \text{ versus } N,$$

where $\mathbb{E}[x_1(t = 5)]$ is the expectation of x_1 at the time point $t = 5$, which you computed analytically in the previous task (alternatively: solve the ODE numerically). **Discuss:** what is the order at which the error ϵ tends to zero as a function of N, e.g. $\mathcal{O}(?)$?

Homework 4 (Implementation (upload via Whiteboard), 4 points)
Implement the EXTRANDE method for the model from Homework 2 (this assignment) with the following modification:

$$r_1(t) = x_1(t) \cdot k_e \cdot 0.5 \cdot (\sin(t \cdot 180) + 2)$$

where 'sin' denotes the sinus function.
a) (**to be uploaded via Whiteboard**) Write a program implementing this model and generate trajectories using the EXTRANDE algorithm. The program reads the input file ("Input.txt") provided in Whiteboard. The first number in the input file is the 'seed' of the random number generator, and the second is the number of trajectories N to be computed. Compute the trajectories for N simulations up to time $T = 24$. For each simulation, write the time and the values X_1 into a file "Task4TrajY.txt". The output textfile should be in the comma-separated text format using 2 digits after the comma (format '%1.2f'). Name your program "Ex4.py" and submit via Whiteboard. **Hint:** First, explore the value of $k_e \cdot 0.5 \cdot (\sin(t \cdot 180) + 2)$ over the time horizon $t \in [0, \infty]$ and compute its maximum for computing the upper bound B.

Good luck!

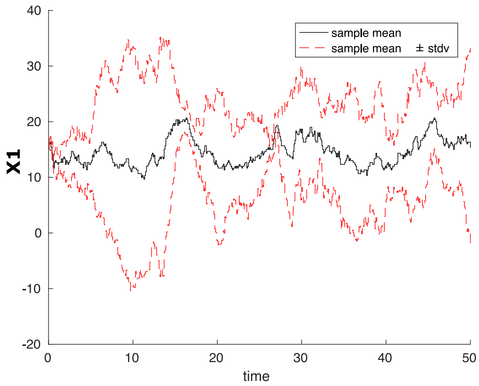

Figure 1: How to plot x_1 in Ex.3b. The black line indicates the sample mean $\bar{x}(t)$ and the red dotted lines mark the sample mean $\pm$ one standard deviation.