MT5855 Take-home assignment

Instructions:

This assignment contains questions that require coding and questions that require responses in text. For your final submissions please provide

1. Your solutions containing written text as one pdf file. Handwritten submissions, such as those that you submit to exams, or typeset solutions will both be accepted.

2. One python file containing all code needed for the assignment. Please annotate your file with comments, such that it is clear which question each section of the file belongs to. The python file should not import any modules other than `numpy`, `math` and `matplotlib`.

3. Pdf files for all figures generated by your code. This is in particular necessary for any questions that specifically ask for visualisations. These pdf files can be uploaded individually, or as part of the pdf file containing your text solutions. For all figures that you provide, please ensure both axes are labelled, and a figure title is provided. The figure title should include the number of the question that it answers.

Since this is a take-home assignment, you can use any resources that are available to you, provided you cite your sources. If you use a book, paper or online resource such as stackoverflow in your answers or your code, explicitly state this and include links where appropriate. Specifically useful may be the book *Stochastic Modelling of Reaction-Diffusion processes* by Radek Erban and Jonathan Chapman (2019), chapters 4 and 6.

Part I: Compartment-based models of diffusion

In the lecture notes, we have learned about modelling diffusion and Brownian motion via stochastic differential equations. Specifically, Brownian motion with the diffusion coefficient D is modelled by the stochastic differential equation

$$\frac{\mathrm{d}X}{\mathrm{d}t} = \sqrt{2D}\xi. \tag{1}$$

It can be shown that the probability $p(x,t)$ to find the particle at position x at time t fulfills the diffusion equation

$$\frac{\partial p}{\partial t} = D\frac{\partial^2 p}{\partial x^2}. \tag{2}$$

If many independent random walkers are present, an equivalent equation holds for the expected concentration $c(x,t)$ of walkers per space interval

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}. \tag{3}$$

In such situations where a large number of random walkers is considered, it may be computationally expensive to precisely model the position of each walker. An approach to simulate these situations more efficiently is to subdivide the domain into compartments (i.e. bins), and to only keep track of the number of particles in each compartment.

In the following, we will model particles of a chemical species A diffusing on a domain $[0, L]$. To do so, we subdivide the domain into K compartments of length $h = L/K$. Hence, the i^{th} compartment will cover the domain $[(i-1)h, ih)$, with $i \in [1, 2, ..., K]$. We denote the number of A molecules in the i^{th} compartment by A_i. As a result of Brownian motion, molecules will jump between neighbouring compartments. A suitable approach to to model diffusion on this compartmentalised domain may be to consider a chain of mock chemical reactions

$$A_1 \underset{d}{\overset{d}{\rightleftarrows}} A_2 \underset{d}{\overset{d}{\rightleftarrows}} A_3 \underset{d}{\overset{d}{\rightleftarrows}} ... \underset{d}{\overset{d}{\rightleftarrows}} A_K, \tag{4}$$

where $A_i \underset{d}{\overset{d}{\rightleftarrows}} A_{i+1}$ is a shorthand for the reactions $A_i \xrightarrow{d} A_{i+1}$ and $A_{i+1} \xrightarrow{d} A_i$. For this approach to work as intended, we need to relate the reaction rate d to the diffusion coefficient D describing the motility of the random walkers. This is what we will explore in the first assignment questions.

1. Use the system of chemical reactions (4) to derive a system of ODEs for the mean molecule number in each compartment, $M_i(t)$, $i \in [1, ..., K]$.

   Hint: It may be beneficial to express the chemical master equation on the probability to be in state $\boldsymbol{n} = [n_1, ..., n_K]$ using the operators $R_j\boldsymbol{n} = [n1, ..., n_j + 1, n_{j+1} - 1, ..., n_K]$ and $L_j\boldsymbol{n} = [n1, ..., n_{j-1} - 1, n_j + 1, ..., n_K]$ **[6]**

2. The concentration $c(x_i, t)$ of particles at the centre of compartment i can be approximated as

   $$c(x_i, t) = M_i(t)/h. \tag{5}$$

   Derive a PDE on $c(x, t)$ by applying a Taylor expansion to your result from question one. From the resulting PDE, what is the required relationship between D and d?

   Hint: Consider that $x_{i+1} = x_i + h$ and $x_{i-1} = x_i - h$. **[4]**

3. Now use this compartment-based algorithm to simulate diffusion. Specifically, set $L = 1$, $K = 40$, $D = 10^{-4}$ and assume that initially there are 10000 walkers all starting at position $x = 0.4$. This initial condition can be approximated by starting 5000 random walkers each in compartment 16 and 17. Implement a Gillespie SSA to simulate this diffusion process for $t \in [0, 300]$. Visualise the final occupancy of each compartment at $t = 300$ as a histogram. **[10]**

   Hint: You may wish to consider the following points to make the algorithm more computationally efficient.

   (i) The chemical reaction system (4) is a system of $(2K - 2)$ chemical reactions that have only K different propensities that can each be expressed as $\alpha_i = dA_i(t)$.

   (ii) Each reaction only changes two propensities.

   (iii) The base propensity α_0 fulfills $\alpha_0 = 2dN - \alpha_1(t) - \alpha_K(t)$ and hence only changes if the first or last compartment changes.

Part II: Stochastic simulations of patterning formation

Next, we are going to consider systems in which the involved chemical species can diffuse and also react with each other. In the lectures so far, we have considered reaction systems in which all species are well mixed across the reaction volume, and learned how to use the Gillespie SSA to simulate the resulting dynamics. We can attempt to simulate systems in which concentrations are spatially varying by using the compartment based approach introduced in Part I. Specifically, we can again subdivide the spatial domain into compartments, and assume that chemical species in each compartment are well mixed, and that molecules can only react with other molecules in the same compartment, not other compartments. It will then be possible to apply the Gillespie SSA on each compartment individually, in addition to applying the compartment-based simulation for diffusion introduced above. This combination allows to simultaneously model diffusion as well as chemical reactions.

4. When modelling diffusion, it is possible to see from our derivations in question 2 that the solution will become more accurate the smaller the chosen compartments are. Do you expect the same statement to hold true if reactions are also involved? Explain your response. **[3]**

In the following, we are going to simulate a reaction-diffusion system that can be shown to generate patterns, i.e. spatially inhomogenous solutions, when the system is modelled deterministically using PDEs. Our aim will be to explore whether patterns can still be formed if stochastic effects are taken into account. Specifically, we a are going to investigate two interacting molecular species A and B that can diffuse and which are subject to the the *Schnakenberg system* of chemical reactions defined by

$$2A + B \xrightarrow{k_1} 3A, \qquad \emptyset \underset{k_3}{\overset{k_2}{\rightleftarrows}} A, \qquad \emptyset \xrightarrow{k_4} B. \tag{6}$$

When implementing these reactions, we need to consider that, if space is taken into account, reaction propensities need to be provided relative to the spatial volume. To help us correctly account for this dependency, we will use dimensional quantities in the next question.

5. Simulate the Schnakenberg system in on the spatial domain $[0, L]$, with $L = 1\text{mm}$. Divide the domain into $K = 40$ compartments of length $h = L/K$. Assume A can diffuse with diffusion coefficient $D_A = 10^{-5}\text{mm}^2\text{s}^{-1}$, and B can diffuse with diffusion coefficient $D_B = 10^{-3}\text{mm}^2\text{s}^{-1}$. Assume $k_1 = 10^{-4}h^2s^{-1}$, $k_2 = 0.1h^{-1}s^{-1}$, $k_3 = 0.02s^{-1}$, $k_4 = 0.3h^{-1}s^{-1}$. Simulate the system for 30 minutes. Assume that every compartment is initially occupied by 200 molecules of A, and 75 molecules of B. Plot a histogram each of the distributions of A and B molecules across compartments at the end of the simulation duration. **[10]**

6. Using your simulation results, discuss pattern formation under the simulated stochastic Schnakenberg system. **[1]**