Format for delivery of report and programs

The format of the project is that of a printed file or hand-written report. The programs should also be included with the report. Write only your candidate number on the first page of the report and state clearly that this is your report for project 5 of FYS3150, fall 2011. There will be a box marked 'FYS3150' at the reception of the Department of Physics (room FV128).

Project 5, Diffusion of neurotransmitters in the synaptic cleft, deadline December 12, 3pm

The dominant way of transporting signals between neurons (nerve cells) in the brain is by means of diffusion of particular signal molecules called *neurotransmitters* across the synaptic cleft separating the cell membranes of the two cells. A drawing of a synapse is given in Fig. 1.
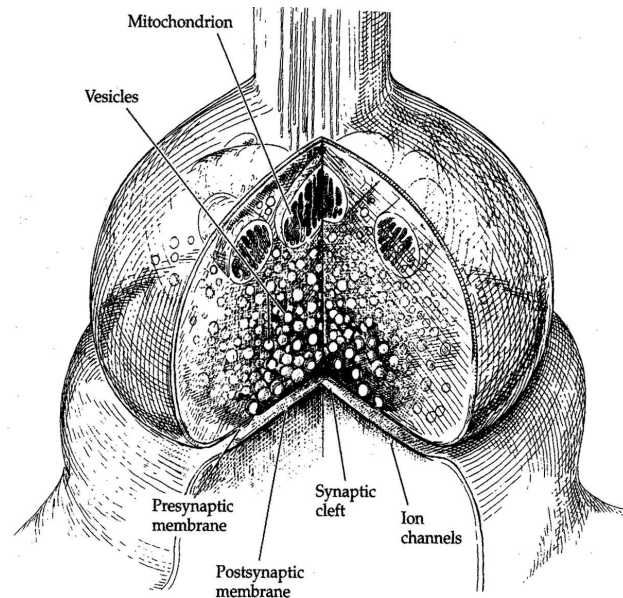

Figure 1: Drawing of a synapse. The axon terminal is the knoblike structure and the spine of the receiving neuron is the bottom one. The synaptic cleft is the small space between the presynaptic (axon) and postsynaptic (dendritic spine) membrane. (From Thompson: "The Brain", Worth Publ., 2000)

Following the arrival of an action potential in the axon terminal a process is initiated in which (i) vesicles inside the axon terminal (filled with neurotransmitter molecules) merge with the presynaptic (axon) membrane and (ii) release neurotransmitters into the synaptic cleft. These neurotransmitters diffuse across the synaptic cleft to receptors on the postsynaptic side which "receives" the signal. A schematic illustration of this process is shown in Fig. 2(left). Since the transport process in the synaptic cleft is governed by diffusion, we can describe it mathematically by

$$\frac{\partial u}{\partial t} = D\nabla^2 u, \tag{1}$$

where u is the concentration of the particular neurotransmitter, and D is the diffusion coefficient of the neurotransmitter in this particular environment (solvent in synaptic cleft).

If we assume (i) that the neurotransmitter is released roughly equally on the "presynaptic" side of the synaptic cleft, and (ii) that the synaptic cleft is roughly equally wide across the whole synaptic terminal, we can, given the large area of the synaptic cleft compared to its width, assume that the neurotransmitter concentration only varies in the direction across the synaptic cleft (from presynaptic to postsynaptic side).
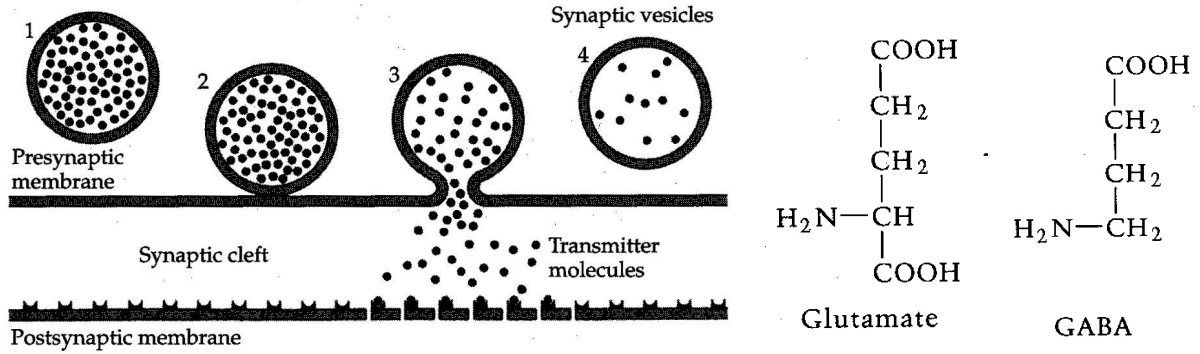
Figure 2: Left: Schematic drawing of the process of vesicle release from the axon terminal and release of transmitter molecules into the synaptic cleft. (From Thompson: "The Brain", Worth Publ., 2000). Right: Molecular structure of the two important neurotransmitters *glutamate* and *GABA*.

We choose this direction to be the x-direction (see Fig. 3). In this case $u(\mathbf{r}) = u(x)$, the diffusion equation reduces to

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

Immediately after the release of a neurotransmitter into the synaptic cleft ($t = 0$) the concentration profile in the x-direction is given by

$$u(x, t = 0) = N\,\delta(x), \tag{3}$$

where N is the number of particle released into the synaptic cleft per area of membrane.

To get an idea over the time-dependence of the neurotransmitter concentration at the postsynaptic side ($x = d$), we can look at the solution of a "free" random walk (i.e., no obstacles or particle absorbers in either direction). The solution of Eq. (2) with the initial condition in Eq. (3) is given by (see Nelson: *Biological Physics*, p. 143 or Lectures notes chapter 12.3)

$$u(x, t) = \frac{N}{\sqrt{4\pi Dt}}e^{-x^2/4Dt}\ . \tag{4}$$

The concentration at the postsynaptic side $u(d, t)$ approaches 0 in the limit $t \to 0$ and $t \to \infty$.

The above assumption regarding the neurotransmitter molecules undergoing a "free" random walk, is obviously a simplification. In the true diffusion process in the synaptic cleft the neurotransmitter molecules will, for example, occasionally bump into the presynaptic membrane they came from. Also at the postsynaptic side the neurotransmitters are absorbed by receptors located on the postsynaptic cell membrane and are thus (temporally) removed from the solution.

To approach this situation in our mathematical model we can impose the following boundary and initial conditions with $x \in [0, d]$

$$u(x = 0, t > 0) = u_0,\ \ u(x = d, \text{all } t) = 0,\ \ u(0 < x < d, t < 0) = 0\ . \tag{5}$$
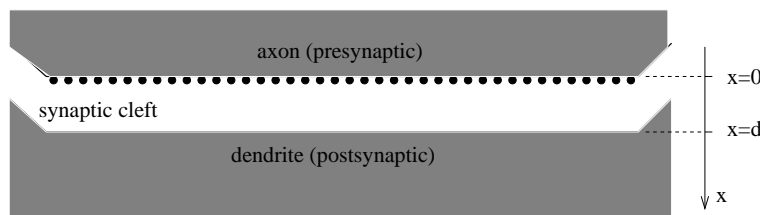

Figure 3: Schematic drawing of the synaptic cleft in our model. The black dots represent neurotransmitter molecules, and the situation shown corresponds to the situation immediately after neurotransmitter release into the synaptic cleft.

Hereafter we set $d = 1$. This corresponds to that (i) for $t < 0$ there are no neurotransmitters in the synaptic cleft, (ii) for $t > 0$ the concentration of neurotransmitters at the presynaptic boundary of the synaptic cleft ($x = 0$) is kept *fixed* at $u = u_0 = 1$ in our case, and (iii) that the postsynaptic receptors immediately absorb nearby neurotransmitters so that $u = 0$ on the postsynaptic side of the cleft ($x = d = 1$).

The full solution of the diffusion equation with boundary/initial conditions in Eq. (5) can be found in a closed form. We will use this solution to test our numerical calculations.

We are thus looking at a one-dimensional problem

$$\frac{\partial^2 u(x,t)}{\partial x^2} = \frac{\partial u(x,t)}{\partial t}, t > 0, x \in [0,d]$$

or

$$u_{xx} = u_t,$$

with initial conditions, i.e., the conditions at $t = 0$,

$$u(x,0) = 0 \quad 0 < x < d$$

with $d = 1$ the length of the x-region of interest. The boundary conditions are

$$u(0,t) = 1 \quad t > 0,$$

and

$$u(d,t) = 0 \quad t > 0.$$

In this project we want to study the numerical stability of three methods for partial differential equations (PDEs). These methods are

1. The explicit forward Euler algorithm with discretized versions of time given by a forward formula and a centered difference in space resulting in

$$u_t \approx \frac{u(x, t + \Delta t) - u(x,t)}{\Delta t} = \frac{u(x_i, t_j + \Delta t) - u(x_i, t_j)}{\Delta t}$$

and

$$u_{xx} \approx \frac{u(x + \Delta x, t) - 2u(x,t) + u(x - \Delta x, t)}{\Delta x^2},$$

or

$$u_{xx} \approx \frac{u(x_i + \Delta x, t_j) - 2u(x_i, t_j) + u(x_i - \Delta x, t_j)}{\Delta x^2}.$$

2. The implicit Backward Euler with

$$u_t \approx \frac{u(x,t) - u(x, t - \Delta t)}{\Delta t} = \frac{u(x_i, t_j) - u(x_i, t_j - \Delta t)}{\Delta t}$$

and

$$u_{xx} \approx \frac{u(x + \Delta x, t) - 2u(x,t) + u(x - \Delta x, t)}{\Delta x^2},$$

or

$$u_{xx} \approx \frac{u(x_i + \Delta x, t_j) - 2u(x_i, t_j) + u(x_i - \Delta x, t_j)}{\Delta x^2},$$

3. Finally we use the implicit Crank-Nicolson scheme with a time-centered scheme at $(x, t + \Delta t/2)$

$$u_t \approx \frac{u(x, t + \Delta t) - u(x,t)}{\Delta t} = \frac{u(x_i, t_j + \Delta t) - u(x_i, t_j)}{\Delta t}.$$

The corresponding spatial second-order derivative reads

$$u_{xx} \approx \frac{1}{2} \left(\frac{u(x_i + \Delta x, t_j) - 2u(x_i, t_j) + u(x_i - \Delta x, t_j)}{\Delta x^2} + \right.$$

$$\left. \frac{u(x_i + \Delta x, t_j + \Delta t) - 2u(x_i, t_j + \Delta t) + u(x_i - \Delta x, t_j + \Delta t)}{\Delta x^2} \right).$$

Note well that we are using a time-centered scheme wih $t + \Delta t/2$ as center.

a) Find the closed form solution to this problem. You will need this in order to study the numerical accuracy of your results. To find the closed-form solution, we will need the stationary solution (steady-state solution). The solution to the steady-state problem is on the form $u(x) = Ax + b$. The solution for the steady-state case u_s that obeys the above boundary conditions is

$$u_s(x) = 1 - x.$$

You can use this solution to define a new function $v(x) = u(x) - u_s(x)$ with boundary conditions $v(0) = v(d) = 0$. The latter is easier to solve both numerically and on a closed form.

b) Write down the algorithms for these three methods and the equations you need to implement. For the implicit schemes show that the equations lead to a tridiagonal matrix system for the new values.

c) Find the truncation errors of these three schemes and investigate their stability properties.

d) Implement the three algorithms in the same code and perform tests of the solution for these three approaches for $\Delta x = 1/10$, $h = 1/100$ using Δt as dictated by the stability limit of the explicit scheme. Study the solutions at two time points t_1 and t_2 where $u(x, t_1)$ is smooth but still significantly curved and $u(x, t_2)$ is almost linear, close to the stationary state. Remember that for solving the tridiagonal equations you can use your code from project 1.

e) Compare the solutions at t_1 and t_2 with the analytic result for the continuous problem. Which of the schemes would you classify as the best?

f) This part is optional but gives you an additional 20% on the final score! The above problem can be solved using Monte Carlo methods and random walks. We follow here Farnell and Gibson in Journal of Computational Physics, volume **208**, pages 253-265 (2005). Choose a constant step length $l_0 = \sqrt{2D\Delta t}$ and equal probability for jumping left and right. Set up the algorithm for solving the above diffusion problem and write a code to do it. Compare your results with those from the partial differential equation solution and comment the results.

g) This part is also optional, and together with f) gives an additional 10% score. Change the above stepsize by using a Gaussian distribution with mean value 1 and standard deviation 0. The step length of the random walker is now $l_0 = \sqrt{2D\Delta t}\xi$, where ξ is random number chosen from the above Gaussian distribution. Implement this stepsize to the program from f) and compare the results and comment.