Norwegian University of
Science and Technology,
Department of Physics

Exam in TFY4235/FY8904 - Computational Physics

April 29 (7:00) to May 3 (23:59), 2024

Recall that Star tasks do not contribute points directly but can be influential in borderline cases. On the other hand, bonus tasks offer additional points up to the maximum possible points, which are 20% of the final grade in Problem 1 and 80% in Problems 2 and 3.

1 Problem 1

Your suggested solution for Assignment no. 2, **The World of Quantum Mechanics**, should be handed in as first part of the exam. This part will count 20% towards the final grade.

2 Problem 2: Network model of the brain

Understanding the mechanistic processes underlying the functioning of the brain is a goal of tremendous conceptual and practical interest. Every discussion on what intelligence is and how it manifests itself, and any development on artificial devices able to mimic learning and reasoning is greatly affected by the gradual advance of our knowledge of the brain's inner working. The current paradigm on this subject is centered on the physiology and behavior of nerve cells (neurons), and the properties emerging from connecting many of these units into networks of increasing complexity.

In this exam you will do a multiscale computational analysis of systems related to neurons and (to a minor extent) neural networks. In Problem 2, a highly coarse-grained picture is considered, in which neurons are represented as unstructured nodes connected by selective links into a network. It has been shown that the rules that govern the exchange of information among nodes create specific patterns in the time evolution of the network. In Problem 3, the discussion will focus on the real structure and function of neurons; more specifically, on the transmission of electric signals along neurons.

2.1 Systolic Network to model the stochastic dynamics of the brain

As a simple example of the neural network, let us consider a systolic network, consisting of N synchronous nodes connected by links and controlled by a clock. Considering the brain, the relevant quantity to be exchanged is information. For the sake of simplicity, in this exercise, information will be represented as a positive charge, meaning that there is no *negative* information exchanged among the nodes.

Then, the state of each node i is characterized by the positive charge Q_i that resides on it, which can change at every time step dt or tick of the clock. The state of the network at time t is described by a vector $V(t)$ whose N components $V_i(t)$, [i =1, 2,.., N], contain the charge of the nodes:

$$V(t) = V(1, 2, ..., N) = (Q_1, Q_2, ..., Q_N) \tag{1}$$

At the tick of the "clock", that defines the advancing time from t to $t + \mathrm{d}t$, each node transfers its charge in equal parts to the n nodes connected to it.

The step-by-step evolution of the network can be described by the transformation matrix, T.

$$V(t + \mathrm{d}t) = T \cdot V(t) \tag{2}$$

For example, we can consider a network made of three nodes, each connected to the other two. The links in figure 1 define the network topology.

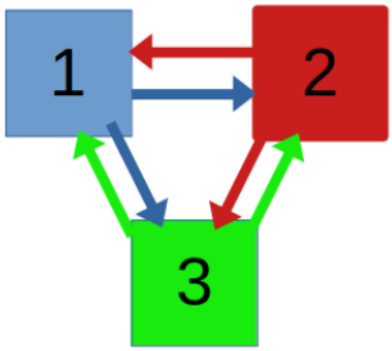

Figure 1: Network scheme with 2 neighbors for each node.

In this simple case, the transformation matrix T describing a single-step evolution can be written as:

$$T = \frac{1}{2}\begin{pmatrix} 0 & 1 & 1 \\ 1 & 0 & 1 \\ 1 & 1 & 0 \end{pmatrix} \tag{3}$$

2.2 Tasks and Questions

a) Generalize the matrix T to the case of a network in which each node is connected to four neighbors, and the total number of nodes $N = 21$. Assume that the set of nodes is ordered in such a way that node i is linked to the two nodes that precede it, i.e. $i - 1$ and $i - 2$, and follow it, i.e. $i + 1$ and $i + 2$ in the list. Apply periodic boundary conditions to the network: the node $N + 1$ is the same as node $N = 1$, etc. Pay attention to the symmetries of matrix T: the diagonal elements are null, and T must

be symmetric, i.e., $T_{ij} = T_{ji}$. Note that the network is simply connected, i.e., any node is connected to any other node through a continuous path of links. In other words, there are not disjoint sub-networks in this case. Include the transformation matrix you have built in to the exam report.

Suggestion: Consider a scheme analogous to Fig. 1 for your case and build the transformation matrix T analogous to the Eq. 3.

b) Starting from an arbitrary initial state $V(t = 0)$, describe the network evolution over multiple time steps using a computational method.

c) Calculate the smallest and the biggest eigenvalue and eigenvectors of matrix T with an iterative method and verify your answer using the "linalg" library. How many eigenvectors have eigenvalue 1? Is there any regularity in the distribution of eigenvalues? Discuss your findings.

d) Verify that the network state after $t_{100} = t_0 + 100 \cdot \mathrm{d}t$ is independent of your initial state at t_0, for example using three different choices of your initial network state $V(t_0)$. Is there any relation between the final state and the eigenvectors of the matrix T? Explain.

e) Implement your computational study for a 21-node system consisting of two disjoint sub-networks with 11 and 10 connected nodes each. The disjoint networks are those such that there exist at least two nodes that are not connected by a continuous sequence of links. Calculate bigger and smaller eigenvectors. How many eigenvectors have eigenvalue 1? Can you argue your findings and the performance of your chosen computational method in this case?

f) Consider the state vector:

$$V(t) = (1; 1/2; ...; 1/i; ...; 1/N) \tag{4}$$

What is the charge distribution at $t - \mathrm{d}t$ and at $t - 5\mathrm{d}t$? Solve this last problem using three different solvers of linear equations and compare the efficiency and accuracy of the methods.

2.2.1 Remarks

In this model, the state of the system at time $t+\mathrm{d}t$ is fully determined by its previous state at time t. The sequence of states whose progression in time corresponds to this rule represents a so-called Markov chain. In this context, the general network state V is also known as a stochastic vector, and the transition matrix T is known as a Markov or stochastic matrix. All elements of stochastic matrices and vectors are non-negative by definition. Moreover, the sum of each column of a stochastic matrix is equal to one. Since the T defined above is symmetric, also the sum of each row is equal to 1. By convention, stochastic vectors are normalized in a way that the sum of their components is 1. In comparing eigenvectors, you should take into account that only their direction matters.

Elementary properties:

If V is a stochastic vector, and T is a stochastic matrix, then $(T \cdot V)$ is again a stochastic vector.

Every stochastic matrix has one or more eigenvalue(s) equal to 1, and the remaining eigenvalues are less than 1.

A special class of Markov chains (described by stochastic vectors and matrices) are the so-called *ergodic* Markov chains. The corresponding stochastic matrix has only one unit eigenvalue and describes simply connected networks. Stochastic matrices with more than a unit eigenvector describe disjoint networks, whose number corresponds to the number of unit eigenvectors.

You can use these properties to discuss some of the questions listed above.

3 Problem 3: Transmission of electric impulses

The axon is the part of a neuron (nerve cell) that carries impulses away from the main cell body. In neurons, information can propagate up to 100 m/s from the cell body to the tip of the axon. A neuron typically has one axon that connects it with other neurons, muscle cells, or gland cells. As shown in the scheme of Figure 2, the cell body collects excitatory and inhibitory impulses from other cells, represented by the same arrows ①, which diffuse through the cell membrane towards the axon ②. If the membrane potential reaches a threshold value at the start of the axon, a *so-called* action potential (sharp increase in potential) is generated that transmits the impulse along the axon (towards the right-hand side in the scheme) ③.

This exam will focus on the physics behind the propagation of electrical impulses along nerve cells.

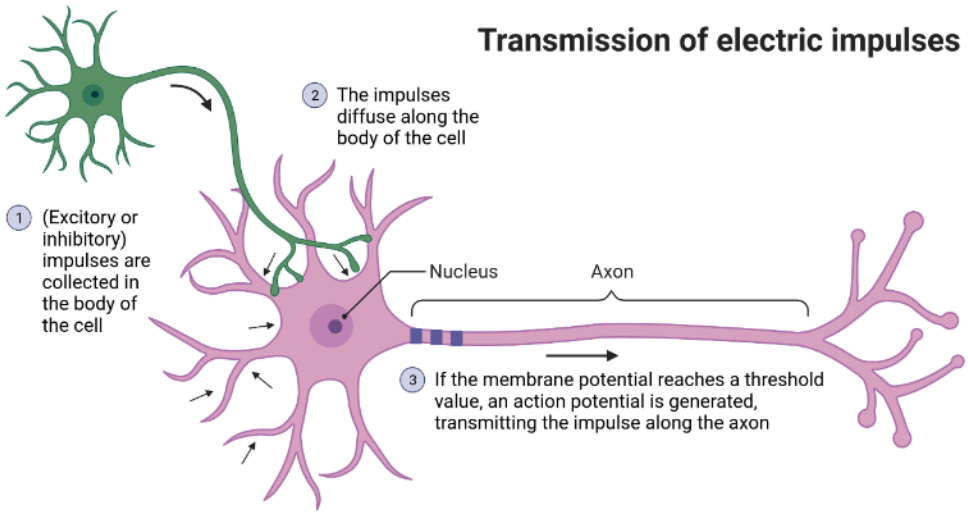

Figure 2: Scheme of transmission of electric impulses along a nerve cell. Created with BioRender.com.

3.1 Ion transport across the cell membrane

Cells are surrounded by a lipid membrane that functions as a permeability barrier, preventing the spontaneous movement of (most) molecules into and out of the cells. Ions, in particular,

can only cross the membrane through protein channels embedded in the membrane. These channels are ion-specific.

In part due to this permeability barrier, there are large differences in the concentration of most common ions inside and outside of the cell, as shown in Table 1.

Table 1: Intracellular (C_{intra}) and extracellular (C_{extra}) ion concentrations (given in millimolar (10^{-3} mol·dm^{-3})) and the Nernst potential ($\mathcal{V}^{\text{Nernst}}$) for three different ions. Other ion species, including macroions like DNA, make the interior and exterior overall neutral. The numbers are typical of a squid axon, which have a membrane resting potential, $V_{\text{mem}} \approx -60\,\text{mV}$. From *Biological Physics. Energy, Information, Life* by P. Nelson, Chiliagon Science, 2020.

Ion species	C_{intra} (mM)	C_{extra} (mM)	$\mathcal{V}^{\text{Nernst}}$ (mV)
K^+	380	20	–76
Na^+	50	440	56
Cl^-	50	560	–62

The presence of potassium ion (K^+) channels that are constantly open (allowing for free flow of K^+ across the membrane, out of the cell due to its Nernst potential) leads to a small unbalance of charges on each side of the membrane, allowing a **nonzero membrane potential**, as depicted in Figure 3. This is called the **resting membrane potential**, denoted V_{mem}, corresponding to a difference in potential inside and outside the cell ($V_{\text{in}} - V_{\text{out}}$), when the cell is *at rest* (in 'equilibrium').

In addition to these *leaky* K^+-channels, there are channels that use chemical energy (ATP hydrolysis) to transport K^+ and Na^+ against their **electrochemical gradient**, maintaining the imbalance in ion concentrations shown in Table 1. A third important class of ion channels are voltage-gated ion channels that, as the name suggests, open (allowing ion flow) when the membrane potential reaches some threshold V^*. The most relevant of this class are the voltage-gated Na^+ channels.

3.2 The Nernst equation, ion flow, and action potential

The flow of an organic ion through a membrane channel is driven by the electrochemical gradient for that ion. This gradient represents the combination of two influences: the voltage gradient and the concentration of ions across the membrane. At the point when these balance each other the electrochemical gradient of the ion is zero, and there is no net flow of the ion through the channel. The equilibrium potential for the ion is called the Nernst potential and is defined according to:

$$\mathcal{V}^{\text{Nernst}} = \frac{k_{\text{B}}T}{ze} \ln \frac{C_{\text{extra}}}{C_{\text{intra}}}\,, \tag{5}$$

where k_{B} is the Boltzmann constant, T is the temperature, z is the valence (charge) of the ion, and e is the elementary charge.

For example, when Na^+ channels in the membrane open, Na^+ ions will rush into the cell. This happens because there is both an excess of Na^+ ions outside the cell and the potential is 'more negative' inside the cell. This leads to a change in the membrane potential that propagates along the axon, as depicted in Figure 4.

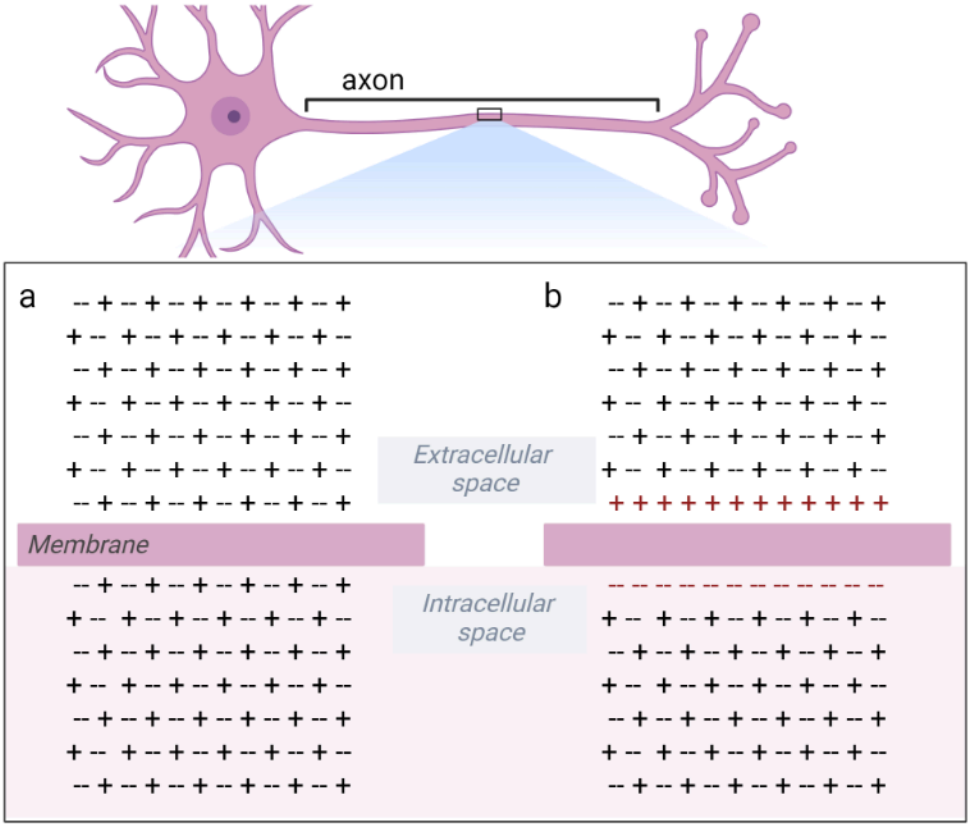

Figure 3: The ionic basis of a membrane potential. Panel (a) shows an exact balance of charges on each side of the membrane, $\Delta V = 0$. In panel (b) a small flow of ions through an ion channel carries enough charge to cause a change in the electric potential across the membrane, setting a nonzero membrane potential. Created with BioRender.com.

3.3 Question

a) If Cl^- channels open, will the ions move into or out of the cell? Justify.

3.4 A patch of the cell membrane can be modeled as an electric circuit

Within the context of biological electricity, it is useful to define a cell membrane as a collection of resistors, batteries and capacitors, as shown in Figure 5. Considering that the interior of the cell membrane has a low dielectric constant, the membrane is well approximated to a capacitor with a capacitance C. The upper capacitor plate, corresponding to the inside of the cell (see Fig. 5) carries a charge $-q$. The lower capacity plate (the side of the membrane facing outside) has charge $+q$. The charge of the membrane is related to the potential difference across the membrane, $\Delta V = V_2 - V_1$, by

$$q = C\Delta V\,. \tag{6}$$

In addition, the membrane patch is equivalent to a battery with potential drop $\mathcal{V}^{\text{Nernst}}$ in series with a resistor of resistance $R = 1/(gA)$, with g the conductance per area A, which is related to the ion permeability that is controlled by the ion channels. Note that the figure

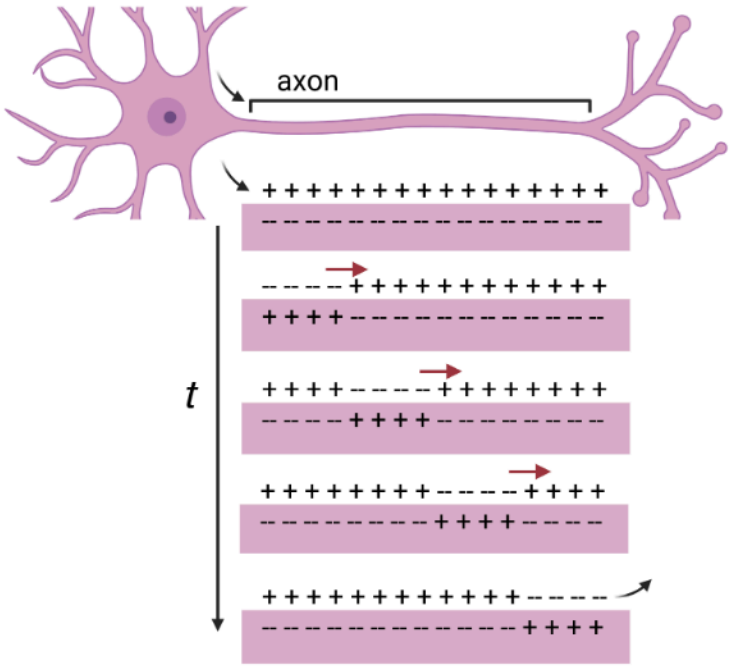

Figure 4: Scheme of the propagation of an action potential along the axon of a nerve cell. Created with BioRender.com

does not imply that all three Nernst potentials are equal. Instead, it can be written that

$$\Delta V = I_i R_i + \mathcal{V}_i^{\text{Nernst}}\,, \tag{7}$$

where i refers to each ionic specie, $I_i = j_{q,i}A$ are the currents through a patch of membrane, considered positive if the ion current flows from the inside to the outside.

Taking the time derivative of Eq. 6 we obtain

$$I_r = C\frac{\mathrm{d}(\Delta V)}{\mathrm{d}t}\,, \tag{8}$$

with I_r the total radial (outward) electric current.

So far, our analysis has been restricted to either a small patch of membrane or a large membrane whose potential is uniform along its length. Let us now consider a non-uniform potential along the length of the axon. If the potential varies along the axon, so will the current. Such axial flow corresponds to a current I_x flowing through the ends of the top and bottom horizontal wires, as depicted in Figure 6. We will adopt the convention that I_x is positive when positive ions flow in the $+x$ direction.

To obtain the equation for the development of the potential along the axon, we first state the condition of charge neutrality for the (cylindrical) slice of the axon, that is, the net current into the ends of the slice, $I_x(x) - I_x(x + \mathrm{d}x)$ must balance the total rate at which charge flows radially, out of the cell, $I_r(x)$ (see Fig. 6), according to:

$$I_x(x) - I_x(x + \mathrm{d}x) = -\frac{\mathrm{d}I_x}{\mathrm{d}x} \cdot \mathrm{d}x = I_r(x)\,. \tag{9}$$

The total radial current $I_r(x)$ equals the sum of the charge permeating *through* the membrane, $2\pi a\mathrm{d}x \cdot j_{q,r}$, plus the rate at which charge *accumulates* at the membrane, $2\pi a\mathrm{d}x \cdot \mathcal{C}\mathrm{d}V_2/\mathrm{d}t$, according to

$$I_r(x) = 2\pi a\left(j_{q,r}(x) + \mathcal{C}\frac{\mathrm{d}V_2}{\mathrm{d}t}\right)\mathrm{d}x\,, \tag{10}$$

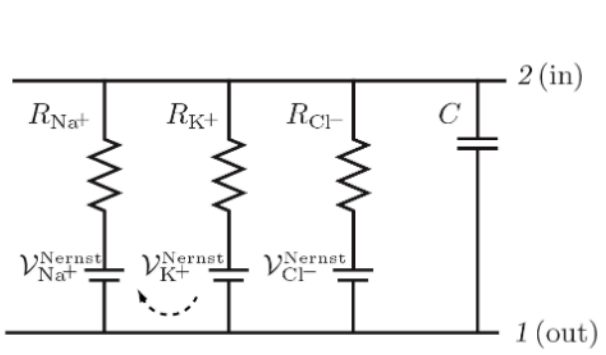

Figure 5: Discrete element model of a small patch of cell membrane of area A. Three representative ions can flow between the interior and the exterior of the cell. Each ion channel has its own resistance R_i and 'driving force' $\mathcal{V}_i^{\text{Nernst}}$. The dashed arrow depicts the circulating flow of sodium and potassium ions expected from data in Table 1. From *Biological Physics. Energy, Information, Life* by P. Nelson, Chiliagon Science, 2020.

where Eq. 6 and $C = A\mathcal{C}$ were used.

According to Ohms law, the axial current at a point x of the axon is equal to the potential drop along a short distance, divided by the axial resistance $\mathrm{d}R_x = \mathrm{d}x/(\kappa\pi a^2)$, where κ is the fluid's electrical conductivity:

$$I_x(x) = -\frac{V_2(x + \frac{1}{2}\mathrm{d}x) - V_2(x - \frac{1}{2}\mathrm{d}x)}{\mathrm{d}x/(\pi a^2\kappa)} = -\pi a^2\kappa\frac{\mathrm{d}V_2}{\mathrm{d}x}\,. \tag{11}$$

The minus sign indicates that if V_2 increases as we move to the right, then the positive ions will be driven to the left. Replacing the derivative of Eq. 11 and Eq. 10 in Eq. 9 yields the so-called cable equation.

$$\pi a^2\kappa\frac{\mathrm{d}^2V_2}{\mathrm{d}x^2} = 2\pi a\left(j_{q,r}(x) + \mathcal{C}\frac{\mathrm{d}V_2}{\mathrm{d}t}\right)\,. \tag{12}$$

It is interesting to note that the cable equation, describing the propagation of signals along a wire, or 'cable', was first derived by Kelvin in 1854 while he studied the feasibility of the transatlantic telegraph cable. Much later, in the 1930s, Rushton developed the analogy to axons.

By defining $V(x,t) \equiv V_2(x,t) - V_{\text{mem}}$, representing the membrane depolarization, and as the current through the membrane is $j_{q,r} = g_{\text{tot}}V$, we obtain the so-called linear cable equation:

$$\lambda^2\frac{\partial^2V(x,t)}{\partial x^2} - \tau\frac{\partial V(x,t)}{\partial t} = V(x,t)\,, \tag{13}$$

where $\lambda \equiv \sqrt{a\kappa/(2g_{\text{tot}})}$ and $\tau \equiv \mathcal{C}/g_{\text{tot}}$ are the axon's space and time constants, respectively.

3.5 Questions and tasks

a) Implement the Euler explicit, Euler implicit, and Crank-Nicholson schemes to solve numerically the time-dependent cable equation (Eq. 13). Explain the method implementation in the context of the problem. Use a narrow Gaussian impulse as the initial condition and a system bounded to $[a, b]$, where $a, b \in \mathbb{R}$, $a < b$ with Neumann boundary conditions. For simplicity use $\lambda = 1.0\,\text{m}$ and $\tau = 1.0\,\text{s}$. Plot the time evolution of

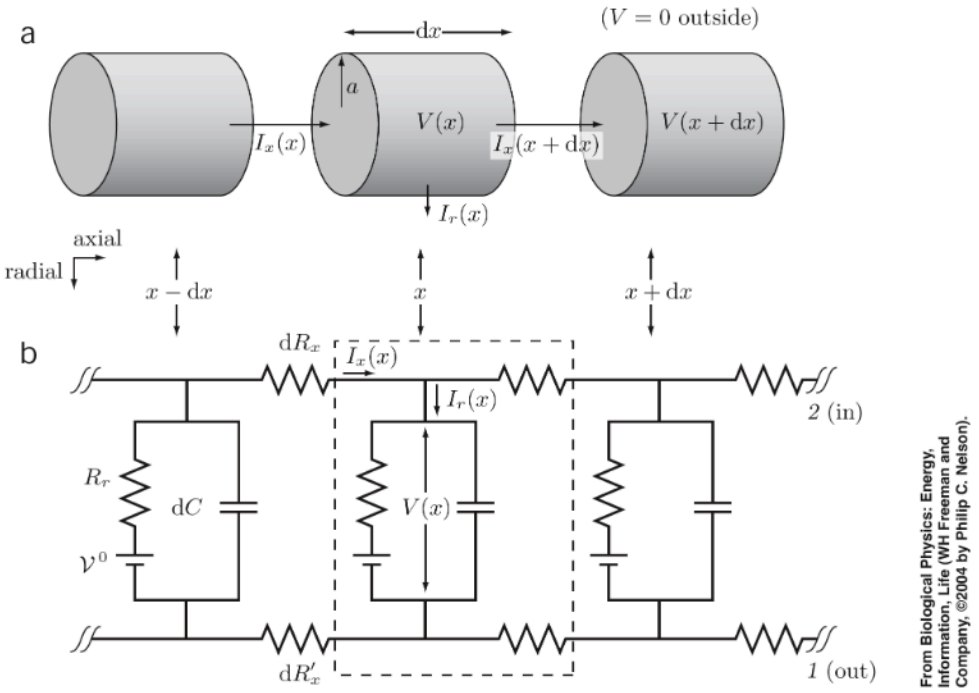

Figure 6: Discrete-element model of an axon. (a) The axon is seen as a chain of cylindrical elements of length $\mathrm{d}x$ and radius a, and surface area $\mathrm{d}A = 2\pi a \mathrm{d}x$. (b) Each cylindrical element is viewed as electrical networks, each containing a battery of voltage $\mathcal{V}_0 = \Sigma_i \frac{g_i}{g_{\mathrm{tot}}} \mathcal{V}_i^{\mathrm{Nernst}}$. The 'radial' resistor with resistance $R_r = 1/(g_{\mathrm{tot}} \mathrm{d}A)$ represents ion permeation through the axon membrane. The axial resistors $\mathrm{d}R_x$ and $\mathrm{d}R'_x$ represent the fluid inside and outside the axon, respectively. For simplicity, it is assumed that $\mathrm{d}R'_x = 0$ and $V_1 = 0$. From *Biological Physics. Energy, Information, Life* by P. Nelson, Chiliagon Science, 2020.

the membrane voltage along the membrane.

b) An analytical solution for an unbounded problem is given by

$$V(x,t) = \frac{\tilde{V}_0}{\sqrt{4\pi(\lambda^2/\tau)t}} \exp\left[\frac{-(x-x_0)^2}{4(\lambda^2/\tau)t} - \frac{t}{\tau}\right]. \tag{14}$$

What are the units of the normalization term, $\tilde{V}_0$?

c) Check if your results are satisfactory by comparing them with the analytical solution.

d) For what values of t do you expect the analytical solution of the unbounded problem to be a good approximation to the numerical solution with Neumann boundary conditions?

e) Study and discuss the numerical stability and accuracy of the schemes.

f) **Bonus:** Discuss the equation you arrive at when defining new dimensionless variables $t' = t/\tau$ and $x' = x/\lambda$.

You will find out that one obtains a passive-spread solution, and not a traveling wave solution. In other words, Eq. (13) is unable to model the action potential.

3.6 Transmission of impulses along a nerve cell

Let us now consider the effect of ion channels on the membrane potential evolution along the cell axon. Equation 13 is expanded to include the permeability of the membrane to Na^+ and K^+ ions, according to

$$\lambda^2 \frac{\partial^2 V(x,t)}{\partial x^2} - \tau \frac{\partial V(x,t)}{\partial t} = \frac{g_{\mathrm{Na}}(V(x,t))}{g_{\mathrm{K}}} \left[V(x,t) - \mathcal{V}_{\mathrm{Na}}^{\mathrm{Nernst}}\right] + \left[V(x,t) - \mathcal{V}_{\mathrm{K}}^{\mathrm{Nernst}}\right]. \quad (15)$$

For simplicity we will only consider *leaky* K^+ channels, which impose a constant permeability $g_K = 5.0\,\Omega^{-1}\mathrm{m}^{-2}$, and voltage-gated Na^+ channels whose permeability varies with the voltage according to

$$g_{\mathrm{Na}}(V) = \left(\frac{100}{1 + \mathrm{e}^{\gamma(V^* - V)}} + \frac{1}{5}\right) \quad [\Omega^{-1}\mathrm{m}^{-2}], \quad (16)$$

where V^* is the threshold potential and γ is a constant. $\mathcal{V}_{\mathrm{Na}}^{\mathrm{Nernst}}$ and $\mathcal{V}_{\mathrm{K}}^{\mathrm{Nernst}}$, in Eq. 15, are the Nernst potential of sodium and potassium ions, respectively, which represents the equilibrium distribution of the ions inside and outside of the cell, as explained above.

3.7 Questions and tasks

a) Solve numerically Eq. 15 using Eq. 16 and one of the above listed methods. Use now the following (biologically relevant) values: $\lambda = 0.18$ mm, $\tau = 2.0$ ms, $\gamma = 0.5\,\mathrm{mV}^{-1}$, $V^* = -40$ mV, $\mathcal{V}_{\mathrm{Na}}^{\mathrm{Nernst}} = 56$ mV and $\mathcal{V}_{\mathrm{K}}^{\mathrm{Nernst}} = -76$ mV.

Consider an initial condition of the form

$$V(x,0) = (V_{\mathrm{appl}} - V_{\mathrm{mem}}) \exp\left(-\frac{(x - x_0)^2}{2\lambda^2}\right) + V_{\mathrm{mem}}\,, \quad (17)$$

that describes an impulse applied to the membrane that results in a potential difference V_{appl} at x_0. Use $V_{\mathrm{mem}} = -70$ mV. For this problem only, set $V_{\mathrm{appl}} = -50$ mV.

b) Study the effect of the strength of the applied impulse (V_{appl}) on the spreading of the voltage along the membrane. Plot again the time evolution of the membrane voltage along the cell.

c) In your opinion, does this model describe well the transmission of electric signals in nerve cells? Justify.

As depicted in Figure 2, neurons collect different impulses, some excitatory and others inhibitory. The impulses spread through the body of the cell and initiate an action potential at the start of the axon (where a larger number of voltage-gated Na^+ channels are located) if the membrane potential is equal or larger than the threshold potential of the ion channels.

d) To model this, modify your program such that the sodium ion channel (where the conductance greatly increases if $V \geq V^*$) is at, for example, a distance 0.25 mm to the right of the impulse. How large must the impulse be to induce an action potential?

e) Compare (qualitatively) your results with experimental data, as that shown in Figure 7, where the membrane potential is measured as a function of time. Suggest modifications to your program such that the numerical solution approaches the experimentally observed signals.

f) Returning to the first question in this problem, if a Cl^- ion channel opens, is the current of ions across the membrane an excitatory impulse or an inhibitory process for the transmission of an action potential along the nerve cell? Justify.

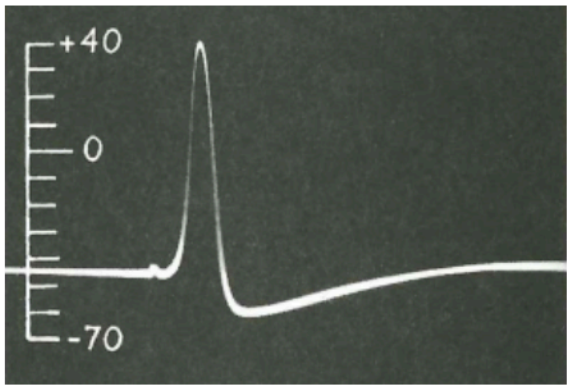

Figure 7: Potential recorded between the inside and the outside of the axon of a nerve cell, as a function of time. It can be seen that the resting membrane potential of this cell is $V_{\text{mem}} \sim -45\,\text{mV}$. From *Physical Biology of the Cell* (2nd ed.) by R. Philips, J. Kondev, J. Theriot, and H.G. Garcia, Garland Science, 2013 and adapted from Hodgkin, A., Huxley, A. Action Potentials Recorded from Inside a Nerve Fibre. Nature 144, 710-711 (1939).

4 Further reading

- Here is a video with an overview of mechanisms involved in formation of action potentials: `https://www.youtube.com/watch?v=iBDXOt_uHTQ`. The first 3:40 are the most relevant to the exam.
- Some of the figures and text were extracted from Chapter 12 of *Biological Physics. Energy, Information, Life* by P. Nelson, Chiliagon Science, 2020. Available in the Realfagbiblioteket.
- Another good textbook that includes the topic of biological electricity (Chapter 17) is from *Physical Biology of the Cell* (2nd ed.) by R. Philips, J. Kondev, J. Theriot, and H.G. Garcia, Garland Science, 2013. Available in the Realfagbiblioteket.