Question 1. Simulation of a multi-compartment model of a passive neurite.

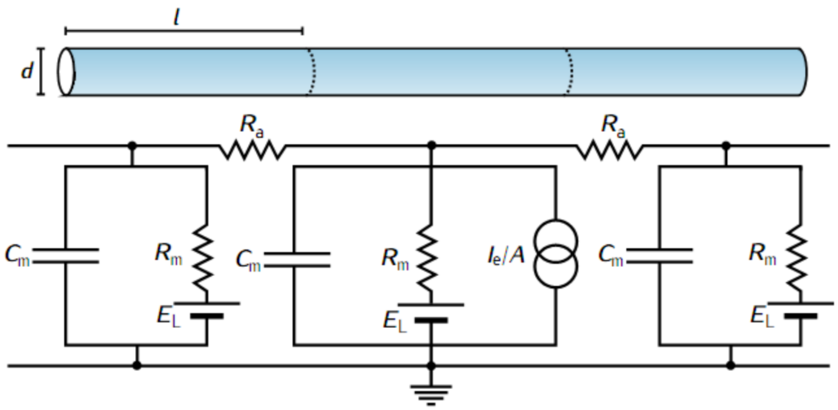

Figure 1: Multi-compartment model.

1.1 In the previous homework we solved for the voltage responses of a two-compartment model. Recall that

$$C_m \frac{dV_1(t)}{dt} = \frac{E_m - V_1(t)}{R_m} + \frac{V_2(t) - V_1(t)}{R_a} + I_e(t)$$
$$C_m \frac{dV_2(t)}{dt} = \frac{V_1(t) - V_2(t)}{R_a} + \frac{E_m - V_2(t)}{R_m}$$

We need to generalise this to an n-compartment model where $n \geqslant 2$ and arbitrary current $I_e(t)$ can be injected into any of the n compartments.

Following the diagram in Figure 1, we observe that

$$I_{e,2}(t) = C_m \frac{dV_2(t)}{dt} + \frac{V_2(t) - E_L}{R_m} + \frac{V_2(t) - V_3(t)}{R_a} + \frac{V_2(t) - V_1(t)}{R_a}$$

Where the compartments are labelled 1-3 starting from the right hand side.

Rearranging yeilds

$$C_m \frac{dV_2(t)}{dt} = \frac{E_L - V_2(t)}{R_m} + \frac{V_3(t) - V_2(t)}{R_a} + \frac{V_1(t) - V_2(t)}{R_a} + I_{e,2}(t)$$

Note that we have the middle compartment 2 expressed in terms of its neighbouring compartments 1 & 3. This can thus be generalised as

$$\frac{dV_j(t)}{dt} = \frac{E_L - V_j(t)}{\tau_m} + \frac{1}{C_m}\left(\frac{V_{j+1}(t) - V_j(t)}{R_a} + \frac{V_{j-1}(t) - V_j(t)}{R_a}\right) + \frac{1}{C_m} I_{e,j}(t) \quad (1)$$

Equation 1 is known as the fundamental equation of a compartmental model. For the compartments without any current injected the response will look the same as in equation 1 but lacking the current term and dependent on the direction of the current flow. Thus, if we use the same numbering scheme, then for compartment i where $0 < i < j$, we have

$$\frac{dV_i(t)}{dt} = \frac{E_L - V_i(t)}{\tau_m} + \frac{1}{C_m}\left(\frac{V_{i-1}(t) - 2V_i(t) + V_{i+1}(t)}{R_a}\right)$$

Similarly, for compartment i where $j < i < N$ where N is the number of compartments, we have

$$\frac{dV_i(t)}{dt} = \frac{E_L - V_i(t)}{\tau_m} + \frac{1}{C_m}\left(\frac{V_{i+1}(t) - 2V_i(t) + V_{i-1}(t)}{R_a}\right)$$

Nota bene for the terminal compartments (i.e. when $i = 0$ or $i = N$ we have to make use of the boundary conditions as shown in Figure 2. For the killed end (Dirichlet)

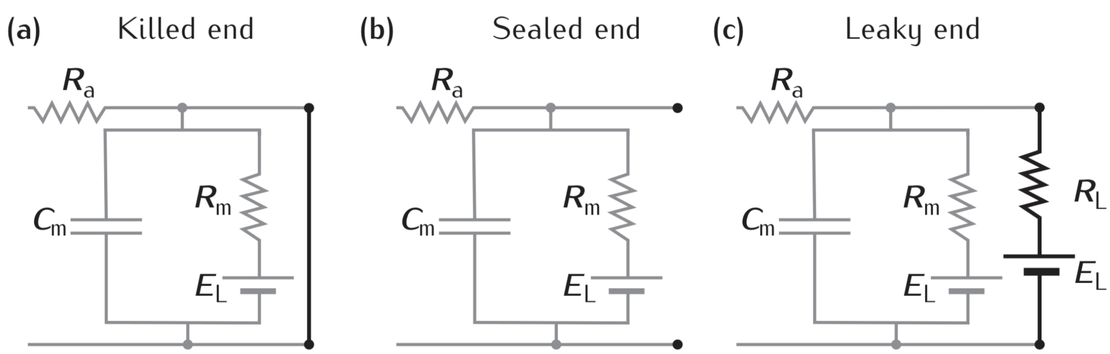

Figure 2: Boundary conditions for the terminal compartments.

boundary condition, the neurite's intracellular environment is in contact with the extracellular medium, and hence the potential V_i for that compartment is set to 0, for it is grounded. For the sealed end (Neumann) boundary condition, we assume that the resistance is so high that no current can pass through the end. Since the axial current is proportional to the gradient of the membrane potential, no current implies zero potential gradient.

$$\frac{V_{i+1} - V_i}{R_a} = C_m \frac{dV_i}{dt} + \frac{V_i - E_L}{R_m}$$
$$\implies \frac{dV_i}{dt} = \frac{E_L - V_i}{\tau_m} + \frac{V_{i+1} - Vi}{C_m R_a}$$

1.2 Equation 1 can be approximated with the forward Euler method as shown below

$$\frac{V_j(t+\Delta t) - V_j(t)}{\Delta t} = \frac{E_L - V_j(t)}{\tau_m} + \frac{1}{C_m}\left(\frac{V_{j+1}(t) - V_j(t)}{R_a} + \frac{V_{j-1}(t) - V_j(t)}{R_a}\right) + \frac{1}{C_m} I_{e,j}(t)$$

$$\implies V_j(t+\Delta t) = V_j(t) + \Delta t\left(\frac{E_L - V_j(t)}{\tau_m} + \frac{1}{C_m}\left(\frac{V_{j+1}(t) - V_j(t)}{R_a} + \frac{V_{j-1}(t) - V_j(t)}{R_a}\right)\right) + \frac{\Delta t}{C_m} I_{e,j}(t)$$

Now, we simulate this with the step current given below

$$I_e(j,t) = \begin{cases} 0, & (t < t_e) \vee (j \neq j_e) \\ 10\,\text{pA}, & (t_e \leqslant t) \wedge (j = j_e) \end{cases}$$

We assume $N = 50$ compartments where the first compartment is terminated as a 'sealed end' and the last compartment is terminated as a 'killed end'. We also assume the following electrical properties

a) Membrane capacitance $C_m = 62.8\,\text{pF}$
b) Membrane resistance $R_m = 1.59\,\text{G}\Omega$
c) Axial resistance $R_a = 0.0318\,\text{G}\Omega$
d) $E_L = E_m = 0\,\text{V}$

The results of the scenario mentioned above appear in Figure 3.

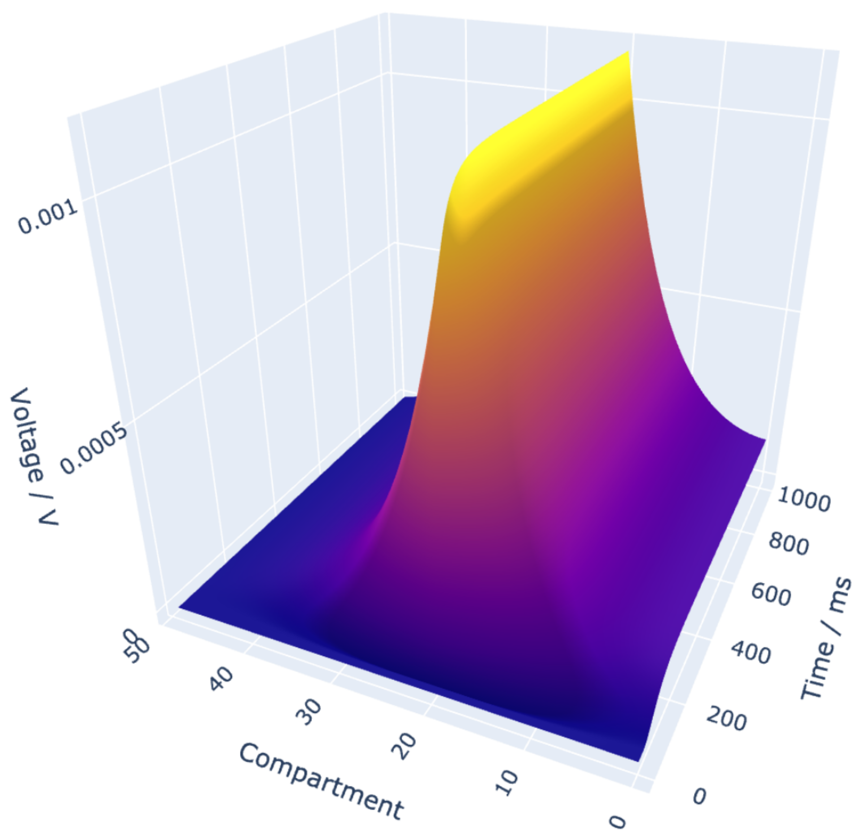

Figure 3: Voltage response over time for 50 compartments.

1.4 Next, the same multi-compartment model was simulated in response to the rectangular current input

$$I_e(j,t) = \begin{cases} 0, & (t < t_e) \vee (t_s \leqslant t) \vee (j \neq j_e) \\ I_0, & (t_e \leqslant t < t_s) \wedge (j = j_e) \end{cases}$$

with $I_0 = 100\,\text{pA}$, $j_e = 14$, $t_e = 20\,\text{ms}$, and $t_s = 200\,\text{ms}$. The results can be seen in Figure 4.

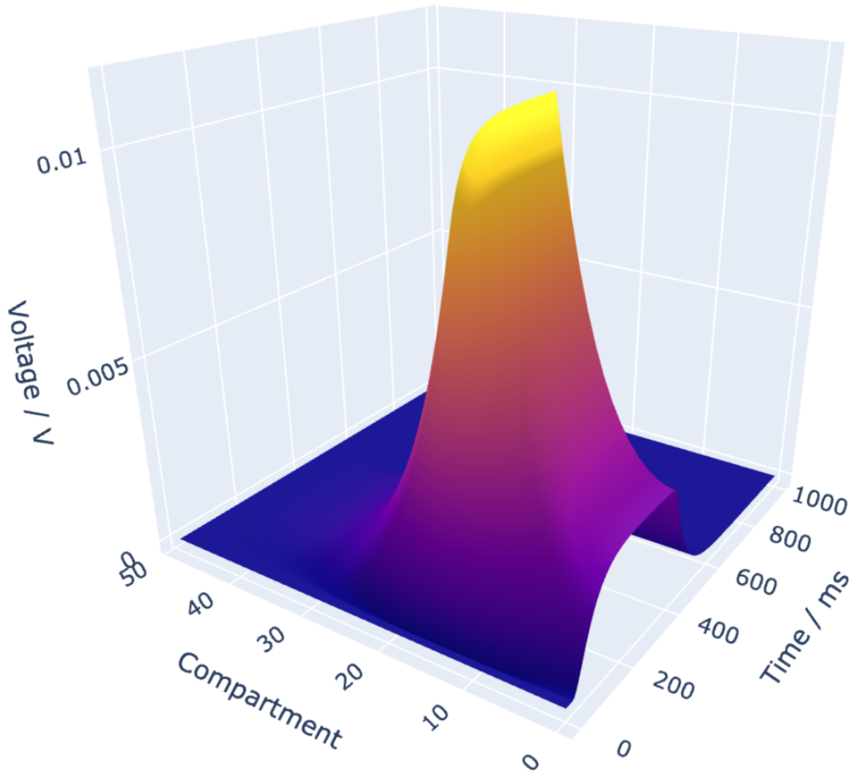

Figure 4: Voltage response over time for 50 compartments.

Question 2. Simulation of a single-compartment Hodgkin-Huxley model of an active neurite.

2.1 The equations (3-12) give the Hodgkin-Huxley model of an imaginary single-compartment (i.e. no axial current) active neurite with input current $I_e(t)$. The electric properties for this neurite are

- $C_m = 1\,\mu\text{F}$, membrane capacitance
- $E_{Na} = 115\,\text{mV}$, sodium equilibrium potential
- $E_K = -12\,\text{mV}$, potassium equilibrium potential
- $E_L = 10.6\,\text{mV}$, leak equilibrium potential
- $V(0) = 0\,\text{mV}$, initial membrane potential
- $\bar{g}_{Na} = 120\,\text{ms}$, maximum sodium channel conductance
- $\bar{g}_K = 36\,\text{ms}$, maximum potassium channel conductance
- $\bar{g}_L = 0.3\,\text{ms}$, maximum leak conductance

$$C_m \frac{\mathrm{d}\,V}{\mathrm{d}\,t} = I_e(t) - \bar{g}_L(V - E_L) - \bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}}) - \bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}}) \tag{3}$$

$$\frac{\mathrm{d}\,m}{\mathrm{d}\,t} = \alpha_m(1-m) - \beta_m m \tag{4}$$

$$\alpha_m = \begin{cases} 0.1 \frac{V-25}{1-\exp\left(-\frac{V-25}{10}\right)} & V \neq 25mV \\ 1 & V = 25mV \end{cases} \tag{5}$$

$$\beta_m = 4\exp\left(-\frac{V}{18}\right) \tag{6}$$

$$\frac{\mathrm{d}\,h}{\mathrm{d}\,t} = \alpha_h(1-h) - \beta_h h \tag{7}$$

$$\alpha_h = 0.07\exp\left(-\frac{V}{20}\right) \tag{8}$$

$$\beta_h = \frac{1}{1+\exp\left(-\frac{V-30}{10}\right)} \tag{9}$$

$$\frac{\mathrm{d}\,n}{\mathrm{d}\,t} = \alpha_n(1-n) - \beta_n n \tag{10}$$

$$\alpha_n = \begin{cases} 0.01 \frac{V-10}{1-\exp\left(-\frac{V-10}{10}\right)} & V \neq 10mV \\ 0.1 & V = 10mV \end{cases} \tag{11}$$

$$\beta_n = 0.125\exp\left(-\frac{V}{80}\right) \tag{12}$$

To approximate the given DEQs we will use the Forward Euler method

$$V(t+\Delta t) = V(t) + \frac{\Delta t}{C_m}\left(I_e(t) - \bar{g}_L(V(t) - E_L) - \bar{g}_{Na} m^3 h (V(t) - E_{Na}) - \bar{g}_K n^4 (V(t) - E_K)\right)$$
$$m(t+\Delta t) = m(t) + \Delta t\,(\alpha_m(1-m) - \beta_m m)$$
$$h(t+\Delta t) = h(t) + \Delta t\,(\alpha_h(1-h) - \beta_h h)$$
$$n(t+\Delta t) = n(t) + \Delta t\,(\alpha_n(1-n) - \beta_n n)$$

Now, we implement this model with an input current $I_e(t)$.