

**Question 1. Branching**

1.0 For the killed end (Dirichlet) boundary condition, we have

$$R_{in} = R_{\infty} \tanh(L)$$

where  $R_{\infty}$  is the input resistance for a semi-infinite cable given by

$$R_{\infty} = \sqrt{\frac{4\tilde{r}_m\tilde{r}_a}{\pi^2 d^3}}$$

and  $L$  is the electrotonic length given by

$$L = \frac{l}{\lambda}$$

where  $\lambda$  is the length constant defined as

$$\lambda = \sqrt{\frac{\tilde{r}_m d}{4\tilde{r}_a}}$$

$\tilde{r}_m$  and  $\tilde{r}_a$  are the specific membrane and axial resistances, respectively. Hence, for the input resistance for compartment 2 we have

$$R_{in,2} = \sqrt{\frac{4 \cdot 1 \cdot 1}{\pi^2 (5 \cdot 10^{-6})^3}} \cdot \tanh(0.089) = 5.05 \text{ M}\Omega$$

For the sealed end (Neumann) we have

$$R_{in} = R_{\infty} \coth(L)$$

Accordingly, for compartment 3 we have

$$R_{in,3} = \sqrt{\frac{4 \cdot 1 \cdot 1}{\pi^2 (4 \cdot 10^{-6})^3}} \cdot \coth(0.1) = 798.45 \text{ M}\Omega$$

Note the following relationship

$$R_{L,1}^{-1} = (R_{in,2}^{-1} + R_{in,3}^{-1})$$

Therefore, the leak resistance for compartment 1 is

$$R_{L,1} = \left( (5.05 \cdot 10^6)^{-1} + (798.45 \cdot 10^6)^{-1} \right)^{-1} = 5.02 \text{ }\mu\Omega$$

1.1 To compute the potential  $V(\infty)$  in response to a constant current  $I_0 = 1 \text{ nA}$  we need to assume that the system has relaxed to a stationary solution and apply the formula for a finite cable potential as shown below

$$V(X) = E_m + R_{\infty} I_0 \frac{R_L \cosh(L - X) + R_{\infty} \sinh(L - X)}{R_L \sinh(L) + R_{\infty} \cosh(L)}$$

where  $R_\infty$  for compartment 1 is computed as shown above and  $X$  is defined as

$$X = \frac{x}{\lambda}$$

where  $x$  is the distance along the compartment. Thus, plugging in the numbers and setting  $t = \infty$  and  $x = 0$  gives

$$X(\infty) = 6.388 \text{ mV}$$

From this we can compute the input resistance  $R_{in,1}$

$$R_{in,1} = \frac{6.338 \cdot 10^{-3}}{10^{-9}} = 6.388 \text{ M } \Omega$$

1.2 To get the current entering compartments 2 & 3,  $I_L$ , we compute

$$V(X = L) = E_m + R_\infty I_0 \frac{R_L \cosh(0) + R_\infty \sinh(0)}{R_L \sinh(L) + R_\infty \cosh(L)} = 4.993 \cdot 10^{-15} \text{ A}$$

And the corresponding  $I_L$  is then

$$I_L = \frac{V(L)}{R_L} = 0.995 \text{ nA}$$

Then we apply the current divider formula for resistors connected in parallel

$$I_X = \frac{R_T}{R_X + R_T} I_T$$

Where  $I_X$  is the current through the resistor with resistance  $R_X$ , and  $I_T$  and  $R_T$  are the total current entering and the total resistance in parallel, respectively. Thus, by substituting the values we get

$$I_2 = 9.883 \text{ nA}, \text{ and } I_3 = 0.0625 \text{ nA}$$

1.3 Assuming that compartment 2 is terminated by a sealed end will change its input resistance and, consequently, the leak resistance for compartment 1. The new input resistance for compartment 2 is thus

$$R_{in,2} = \sqrt{\frac{4 \cdot 1 \cdot 1}{\pi^2 (5 \cdot 10^{-6})^3}} \cdot \coth(0.089) = 641.46 \text{ M}\Omega$$

Hence,  $R_{L,1}$  becomes

$$R_{L,1} = \left( (641.46 \cdot 10^6)^{-1} + (798.45 \cdot 10^6)^{-1} \right)^{-1} = 355.70 \text{ M}\Omega$$

And by applying the above formula for  $V(\infty)$  we get

$$V(\infty) = 104 \text{ mV}$$

**Question 2. Equivalent Cylinder**

- 2.1 No, this branching model cannot be simplified by an equivalent cylinder model, for the branching compartments do not follow the '3/2 diameter rule', which must satisfy

$$(d_1)^{\frac{3}{2}} = (d_2)^{\frac{3}{2}} + (d_3)^{\frac{3}{2}}$$

where  $d_1$ ,  $d_2$ , and  $d_3$  are the corresponding compartment diameters.

- 2.2 To find the required diameters, we can use the formula for electrotonic lengths which must hold if we are to simplify this two-branch model. The formula appears below

$$L_i = \frac{l_i}{\lambda_i} = \frac{l_j}{\lambda_j} = L_j \quad \text{for } i, j > 1$$

This can be simplified to (e.g for  $i = 2$  and  $j = 3$ )

$$\begin{aligned} \frac{l_2}{\lambda_2} &= \frac{l_3}{\lambda_3} \\ \implies \lambda_3 &= \frac{l_3 \lambda_2}{l_2} \\ \implies \sqrt{d_3} &= \frac{l_3 \sqrt{d_2}}{l_2} \\ \implies d_3 &= d_2 \left( \frac{l_3}{l_2} \right)^2 \end{aligned}$$

Hence, plugging in the numbers gives us

$$d_3 = 2.04 \mu\text{m}$$

Then applying the '3/2 rule' gives us

$$d_1 = (d_2^{\frac{3}{2}} + d_3^{\frac{3}{2}})^{\frac{2}{3}} = 4.92 \mu\text{m}$$

As regards the length and the diameter of the equivalent cylinder, the entire tree can be modelled by a single cylinder of diameter  $d_1$ , length constant  $\lambda_1$  and  $l_e = (L_1 + L_D)\lambda_1$ , where  $L_D = L_2 = L_3$ . Thus,

$$l_e = l_1 + l_2 \left( \sqrt{\frac{d_1}{d_2}} \right) = 415.3 \mu\text{m}$$

- 2.3 By applying the same two conditions as above, we have

$$\begin{aligned} d_3 &= d_2 \left( \frac{l_3}{l_2} \right)^2 \\ d_4 &= d_2 \left( \frac{l_4}{l_2} \right)^2 \quad (\text{Generalisation of the 3/2 rule}) \end{aligned}$$

Hence, we arrive at

$$\begin{aligned}
 d_1 &= d_2 \left( 1 + \left( \frac{l_3}{l_2} \right)^3 + \left( \frac{l_4}{l_2} \right)^3 \right)^{\frac{2}{3}} \\
 \Rightarrow d_2 &= \frac{d_1}{\left( 1 + \left( \frac{l_3}{l_2} \right)^3 + \left( \frac{l_4}{l_2} \right)^3 \right)^{\frac{2}{3}}} \\
 \Rightarrow d_2 &= 10.78 \mu m
 \end{aligned}$$

We can now solve for the other diameters by the above formulae

$$\begin{aligned}
 d_3 &= 10.78 \left( \frac{100}{150} \right)^2 = 4.79 \mu m \\
 d_4 &= 10.78 \left( \frac{120}{150} \right)^2 = 6.90 \mu m
 \end{aligned}$$

The diameter of the equivalent cylinder will similarly be  $d_1$  and the length can be determined as in 2.2

$$l_e = l_1 + l_2 \left( \sqrt{\frac{d_1}{d_2}} \right) = 392.74 \mu m$$

### Question 3. Simulation of a two-compartment model of the passive membrane

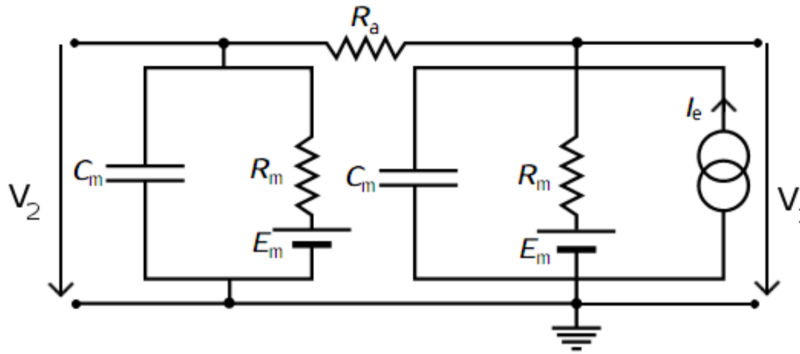


Figure 3: Two compartment model with input current.

3.1 According to the Kirchhoff's law, total current leaving a node must be equal to total current entering a node. For the compartment on the left hand side (let us call it

compartment 2), we have

$$\begin{aligned}\frac{V_1(t) - V_2(t)}{R_a} &= C_m \frac{dV_2(t)}{dt} + \frac{V_2(t) - E_m}{R_m} \\ \Rightarrow C_m \frac{dV_2(t)}{dt} &= \frac{V_1(t) - V_2(t)}{R_a} + \frac{E_m - V_2(t)}{R_m} \\ \Rightarrow \frac{dV_2(t)}{dt} &= \frac{V_1(t) - V_2(t)}{R_a C_m} + \frac{E_m - V_2(t)}{\tau_m}\end{aligned}$$

Similarly, for compartment 1 we have

$$\begin{aligned}I_e(t) &= C_m \frac{dV_1(t)}{dt} + \frac{V_1(t) - E_m}{R_m} + \frac{V_1(t) - V_2(t)}{R_a} \\ \Rightarrow C_m \frac{dV_1(t)}{dt} &= \frac{E_m - V_1(t)}{R_m} + \frac{V_2(t) - V_1(t)}{R_a} + I_e(t) \\ \Rightarrow \frac{dV_1(t)}{dt} &= \frac{E_m - V_1(t)}{\tau_m} + \frac{V_2(t) - V_1(t)}{R_a C_m} + I_e(t) \frac{1}{C_m}\end{aligned}$$

We can now approximate both with the forward Euler method

$$\frac{dV}{dt} \approx \frac{V(t + \Delta t) - V(t)}{\Delta t}$$

Hence, solving for both  $V_1(t + \Delta t)$  and  $V_2(t + \Delta t)$  we get

$$\begin{aligned}V_1(t + \Delta t) &= V_1(t) + \Delta t \left( \frac{E_m - V_1(t)}{\tau_m} + \frac{V_2(t) - V_1(t)}{R_a C_m} + I_e(t) \frac{1}{C_m} \right) \\ V_2(t + \Delta t) &= V_2(t) + \Delta t \left( \frac{V_1(t) - V_2(t)}{R_a C_m} + \frac{E_m - V_2(t)}{\tau_m} \right)\end{aligned}$$

3.2 Next, I simulated the response of this two-compartment model to the current

$$I_e(t) = \begin{cases} 0, & t < t_e \\ -100 \text{ pA}, & t_e \leq t < t_s \\ 0, & t_s \leq t \end{cases}$$

where  $t_e = 0.4 \text{ s}$  and  $t_s = 0.44 \text{ s}$  with  $E_m = 0 \text{ V}$ ,  $R_m = 265 \text{ M}\Omega$ ,  $R_a = 7 \text{ M}\Omega$ . I also assumed that the initial conditions were  $V_1(t) = 0$  and  $V_2(t) = 0$ . The results appear in Figure 1. With increasing the axial resistance,  $R_a$ , the 'responsiveness' of compartment 2 gradually decreased, as can be seen in Figures 2 and 3. As can be seen from Figure 3, compartment 2 has no response at all to the current injected in compartment 1, for the axial resistance is so high ( $R_a = 30 \text{ G}\Omega$ ) it never reaches it.

3.3 Finally, the model was simulated with an injected sinusoid current  $I_e(t) = 100 \text{ pA} \sin(2\pi f t)$  with all the previous parameters and  $R_a = 300 \text{ M}\Omega$ . An example response for  $f = 20 \text{ Hz}$  is shown in Figure 4 and the resultant Bode diagram appears in Figure 5.

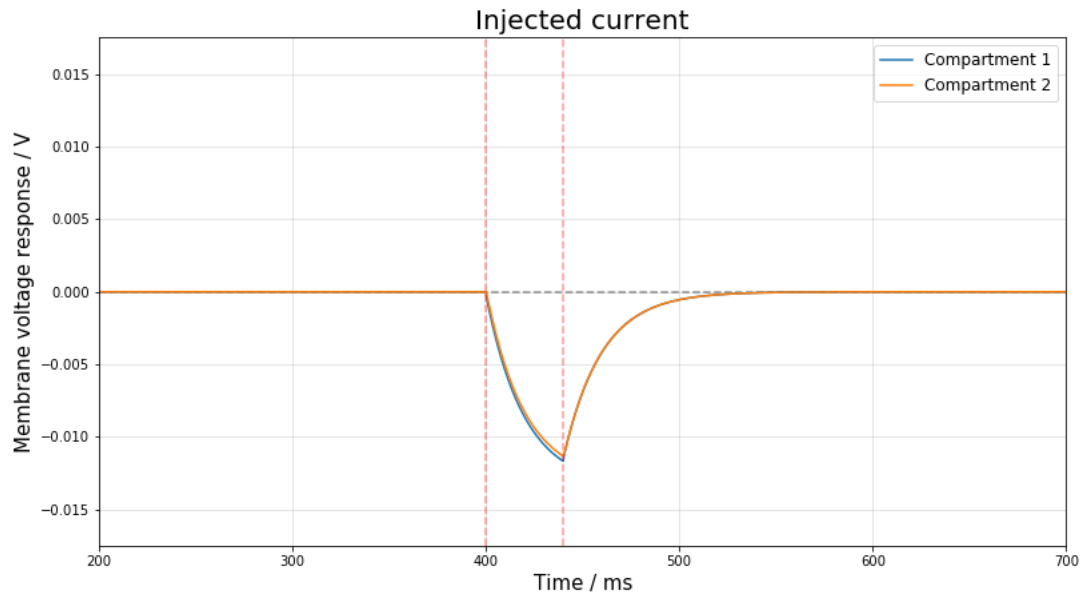


Figure 1: Voltage responses for compartments 1 and 2 with  $R_a = 7 \text{ M}\Omega$ .

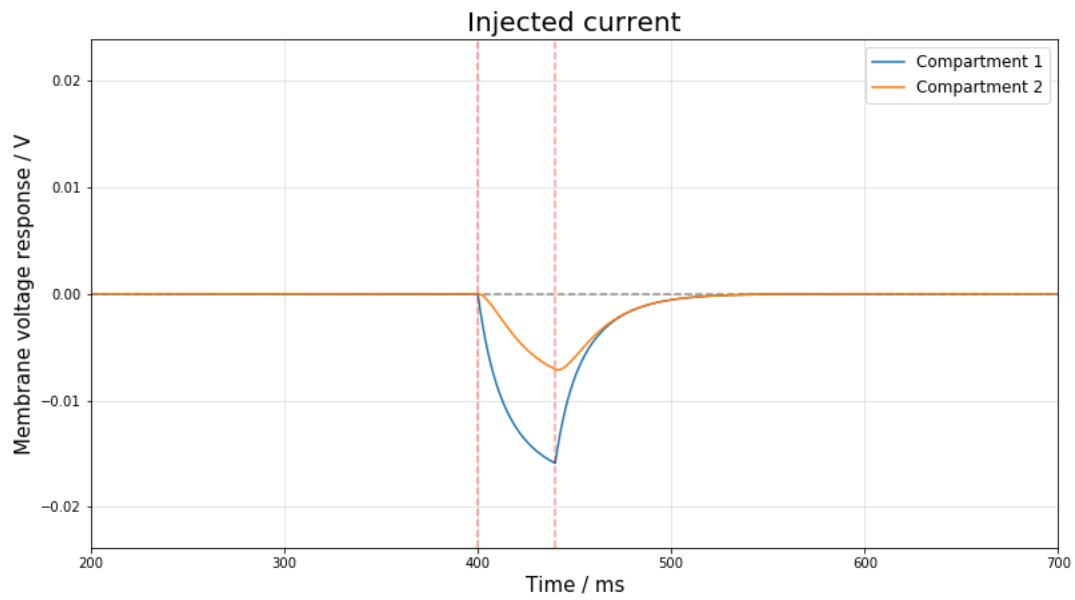


Figure 2: Voltage responses for compartments 1 and 2 with  $R_a = 265 \text{ M}\Omega$ .

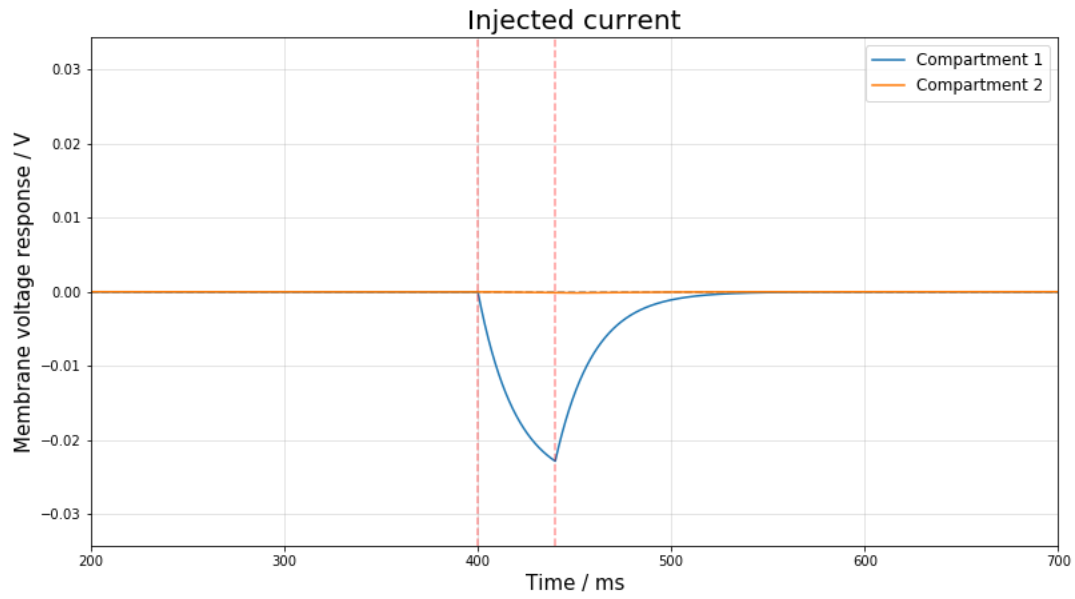


Figure 3: Voltage responses for compartments 1 and 2 with  $R_a = 30 \text{ G}\Omega$ .

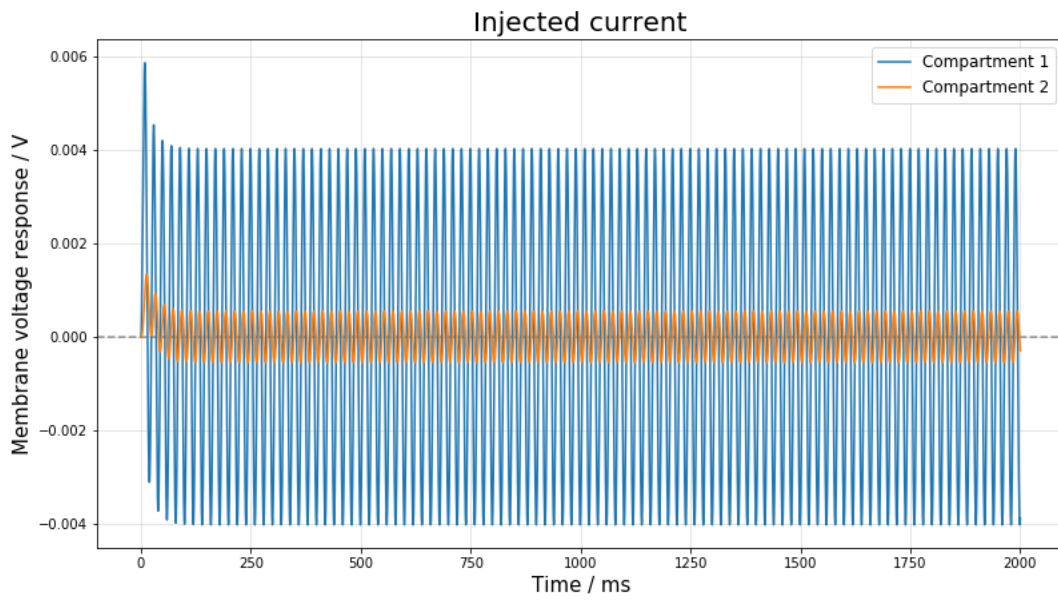


Figure 4: Voltage responses for compartments 1 and 2 for a sinusoid current.

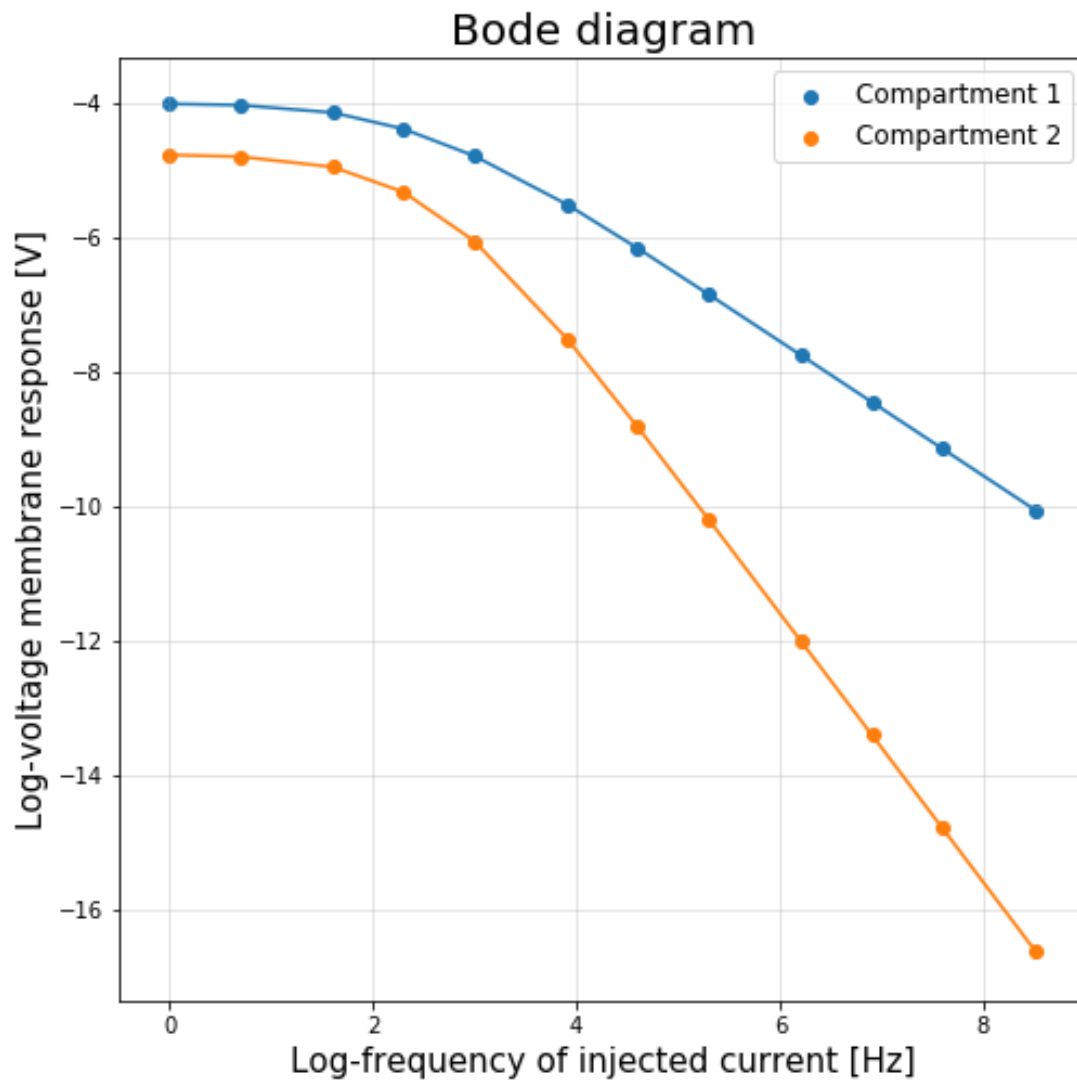


Figure 5: Stationary log-voltage responses for compartments 1 and 2 for different log-frequencies of the injected current.