Question 1. Branching

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

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

where R_∞ 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 λ 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

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

For the sealed end (Neumann) boundary condition we have

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

Acccordingly, for compartment 3 we have

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

Note the following relationship

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

Therefore, the leak resistance for compartment 1 is

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

1.1 To compute the potential $V(\infty)$ in response to constant current $I_0 = 1\,\mathrm{nA}$ 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

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

where R_∞ 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

$$X(\infty) = 6.388\,\mathrm{mV}$$

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

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

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

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

And the corresponsing I_L is then

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

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 flowing 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

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

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

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

Hence, $R_{L,1}$ becomes

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

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

$$V(\infty) = 104\,\mathrm{mV}$$

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 lenghts 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 λ_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

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

Hence, we arrive at

$$d_1 = d_2 \left(1 + \left(\frac{l_3}{l_2}\right)^3 + \left(\frac{l_4}{l_2}\right)^3\right)^{\frac{2}{3}}$$
$$\implies d_2 = \frac{d_1}{\left(1 + \left(\frac{l_3}{l_2}\right)^3 + \left(\frac{l_4}{l_2}\right)^3\right)^{\frac{2}{3}}}$$
$$\implies d_2 = 10.78\mu m$$

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

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

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

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

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

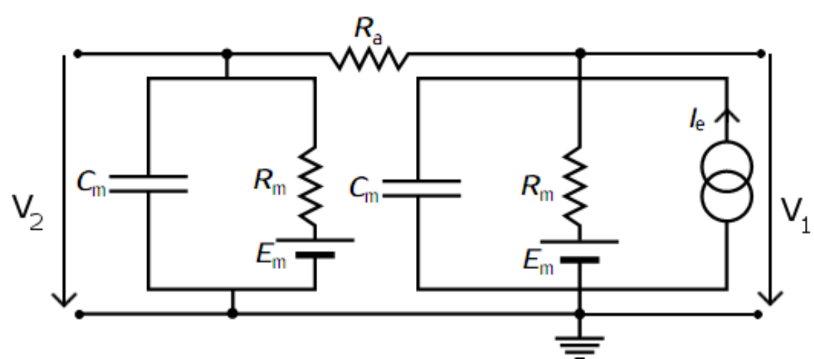

Figure 3: Two compartment model with input current.

3.1 According to the Kirchoff's law, total current leaving a node must be equal to total current entering that node. For the compartment on the left hand side (let us call it compartment 2), we have

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

Similarly, for compartment 1 we have

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

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

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

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. Wtih increasing the axial resistance, R_a, the 'responsiveness' of compartment 2 gradually decreased, as can be seen in Figures 2 and 3. Figure 3 shows voltage responses at $R_a = 30\,\text{G}\Omega$. In this case, compartment 2 has no response at all, for the axial resistance is so high the current hardly ever reaches it.

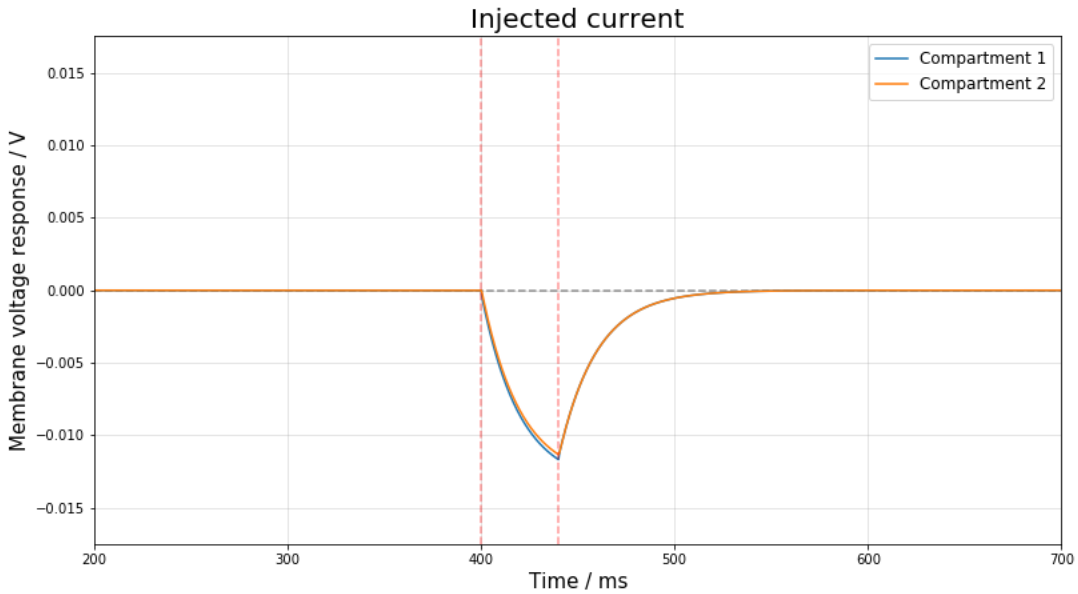

Figure 1: Voltage resposes for compartments 1 and 2 with $R_a = 7\,\mathrm{M\Omega}$.

3.3 Finally, the model was simulated for 2 seconds with injected sinusoid current $I_e(t) = 100\mathrm{pA}\sin(2\pi f t)$ having all the parameters as before and $R_a = 300\,\mathrm{M\Omega}$. An example response for $f = 20\,\mathrm{Hz}$ is shown in Figure 4 and the resultant Bode diagram for a range of frequencies appears in Figure 5. Amplitudes for the bode diagram were conputed after 1s of stimulation to ensure the voltages have relaxed to sinusoidal output.

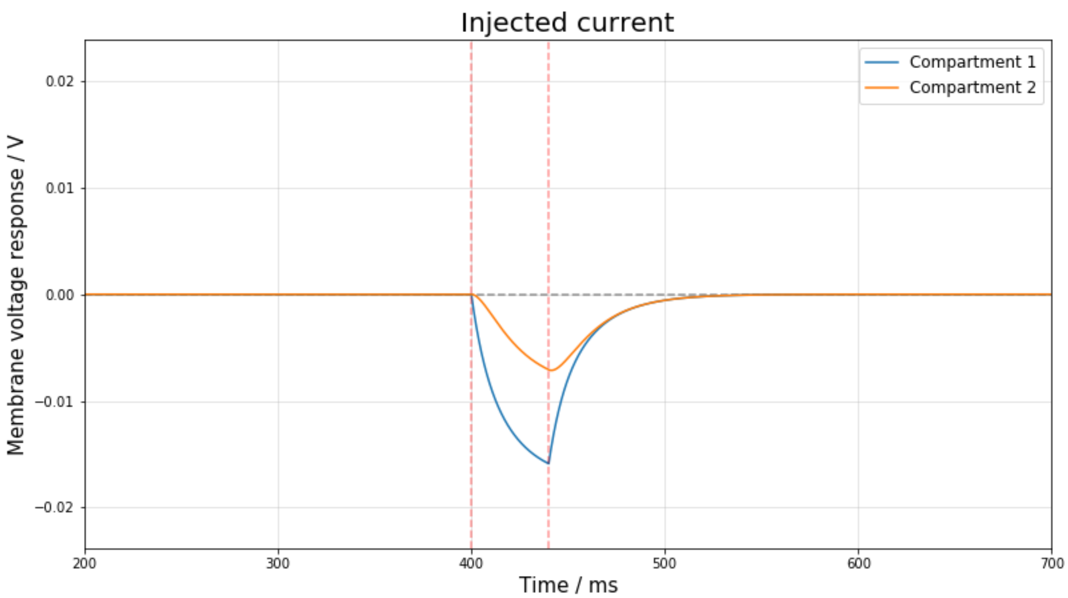

Figure 2: Voltage resposes for compartments 1 and 2 with $R_a = 265\,\mathrm{M}\Omega$.

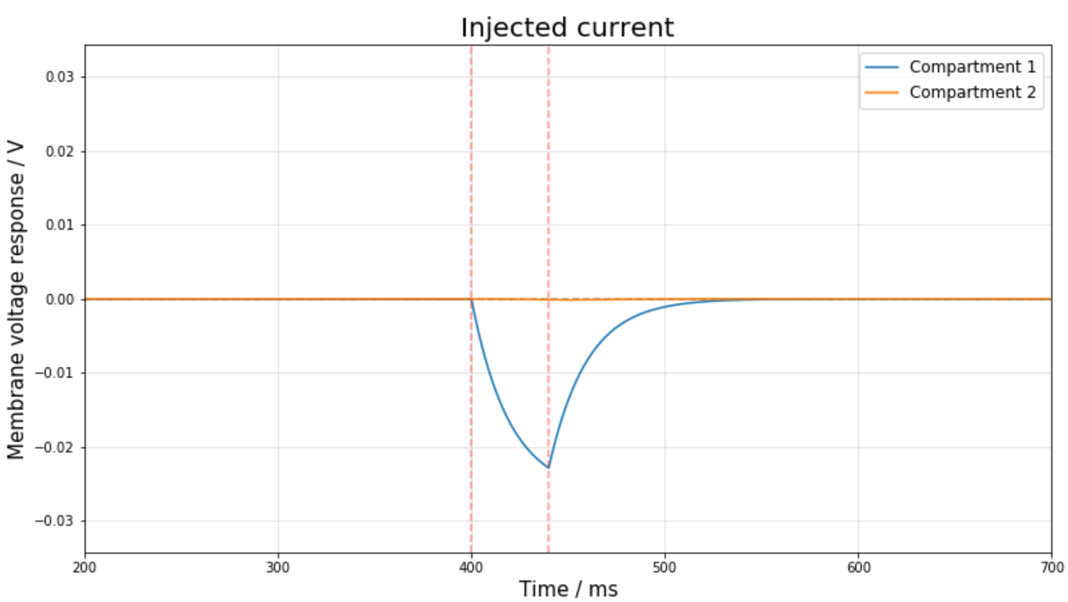

Figure 3: Voltage resposes for compartments 1 and 2 with $R_a = 30\,\mathrm{G}\Omega$.

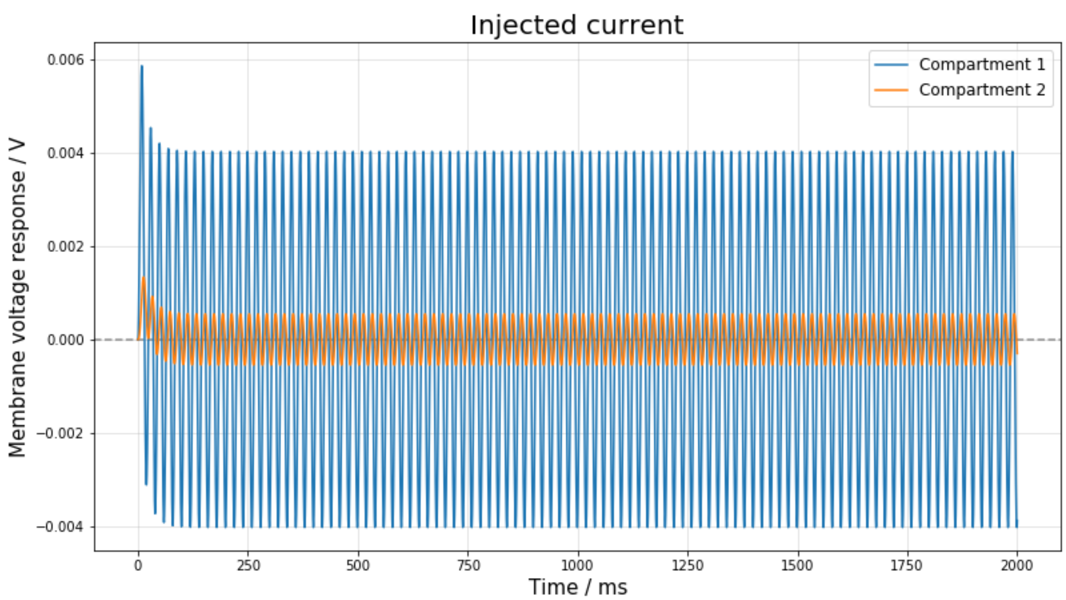

Figure 4: Voltage resposes for compartments 1 and 2 for a sinusoid current.

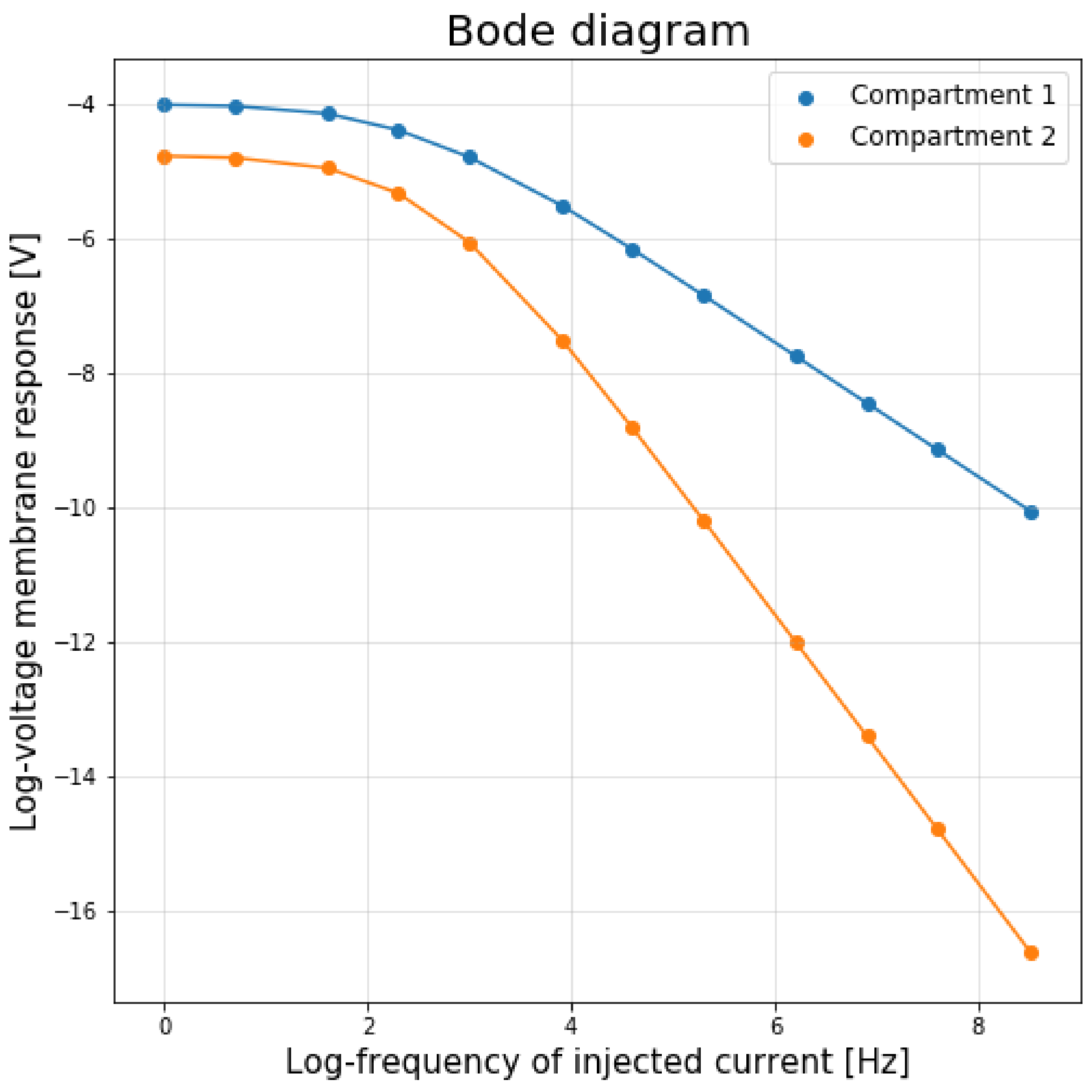

Figure 5: Stationary log-voltage resposes (after 1s) for compartments 1 and 2 for different log-frequencies of the injected current.