Question 1. Simulation of a multi-compartment Hodgkin-Huxley model.

1.1 The Hodgkin-Huxley model for an active neurite with input current $I_e(j,t)$ for a single cylindrical compartment j is given by equations 1-12.

$$V' = \frac{V}{mV} \tag{1}$$

$$I_e(t) = C_m \frac{\mathrm{d}V'_j}{\mathrm{d}t} + g_L\left(V'_j - E_L\right) + g_{\mathrm{Na},j}\left(V'_j - E_{\mathrm{Na}}\right) + g_{\mathrm{K},j}\left(V'_j - E_{\mathrm{K}}\right) + g_{\mathrm{ax}}\left(V'_j - V'_{j-1}\right) + g_{\mathrm{ax}}\left(V'_j - V'_{j+1}\right) \tag{2}$$

$$g_{\mathrm{Na},j} = \bar{g}_{\mathrm{Na}} m_j^3 h_j, \quad g_{\mathrm{K},j} = \bar{g}_{\mathrm{K}} n_j^4 \tag{3}$$

Sodium channels (not writing indices j):

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

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

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

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

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

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

Potassium channel (not writing indices j):

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

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

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

The electrical and geometrical properties are

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

- $g_L = 0.3\,\mathrm{mS}$, leak conductance
- $g_{ax} = 0.5\,\mathrm{mS}$, axial conductance
- $N = 100$, number of compartments

Given the Hodgkin-Huxley model described above, we approximate the DEQs using the Forward Euler method and derive an equation for $V(j,t)$ for an arbitrary compartment j. We assume that the first compartment is terminated as a 'sealed end' and the last compartment is terminated as a 'killed end', as shown in Figure 1.

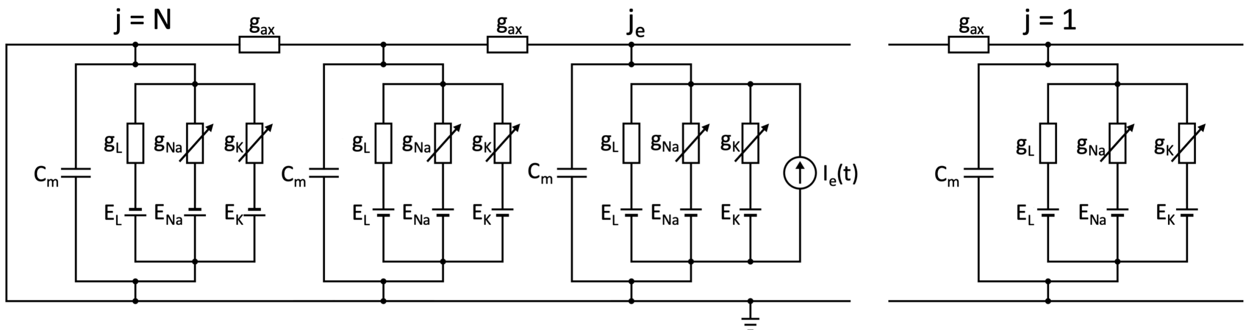

Figure 1: Circuit diagram of a multi-compartment Hodgkin-Huxley model. Compartment 1 is terminated as a 'sealed end' and compartment N is terminated as a 'killed end'. Note that the connection between compartment 1 and compartment j_e is not shown for simplicity.

The approximated DEQ for voltage response of compartment j into which current is injected looks as shown below

$$\begin{aligned}V_j'(t+\Delta t) = V_j'(t) + \frac{\Delta t}{C_m}\Big(I_e(t) &+ g_L\left(E_L - V_j'(t)\right) + \bar{g}_{Na} m_j^3(t) h_j(t)\left(E_{Na} - V_j'(t)\right) \\ &+ \bar{g}_K n_j^4(t)\left(E_K - V_j'(t)\right) + g_{ax}\left(V_{j-1}'(t) - V_j'(t)\right) \\ &+ g_{ax}\left(V_{j+1}'(t) - V_j'(t)\right)\Big)\end{aligned}$$

Following Homework 4, voltage response for compartment i where $0 < i < j$ is

$$\begin{aligned}V_i'(t+\Delta t) = V_i'(t) + \frac{\Delta t}{C_m}\Big(g_L\left(E_L - V_i'(t)\right) &+ \bar{g}_{Na} m_i^3(t) h_i(t)\left(E_{Na} - V_i'(t)\right) \\ &+ \bar{g}_K n_i^4(t)\left(E_K - V_i'(t)\right) + g_{ax}\left(V_{i-1}'(t) - V_i'(t)\right) \\ &+ g_{ax}\left(V_{i+1}'(t) - V_i'(t)\right)\Big)\end{aligned}$$

As for compartment i where $j < i < N$, we have

$$\begin{aligned}V_i'(t+\Delta t) = V_i'(t) + \frac{\Delta t}{C_m}\Big(g_L\left(E_L - V_i'(t)\right) &+ \bar{g}_{Na} m_i^3(t) h_i(t)\left(E_{Na} - V_i'(t)\right) \\ &+ \bar{g}_K n_i^4(t)\left(E_K - V_i'(t)\right) + g_{ax}\left(V_{i+1}'(t) - V_i'(t)\right) \\ &+ g_{ax}\left(V_{i-1}'(t) - V_i'(t)\right)\Big)\end{aligned}$$

As regards the termini, membrane potential for compartment $j = N$ is set to 0 and for compartment $j = 1$ we assume no axial current flowing out, and hence all membrane potential difference is due to current flowing through the membrane

$$\begin{aligned} V_1'(t+\Delta t) = V_1'(t) + \frac{\Delta t}{C_m} \big(&+ g_L \left(E_L - V_1'(t)\right) + \bar{g}_{Na} m_1^3(t) h_1(t) \left(E_{Na} - V_1'(t)\right) \\ &+ \bar{g}_K n_1^4(t) \left(E_K - V_1'(t)\right) + g_{ax} \left(V_2'(t) - V_1'(t)\right)\big) \end{aligned}$$

For the approximations of m, h, n gating variables please refer to Homework 4.

1.2 Now, we turn on simulating the above model for an input current $I_e(j,t)$

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

with $j_e = 14$, $t_e = 60\,\text{ms}$, $t_s = 260\,\text{ms}$ and different amplitudes $I_0 = 6\,\mu\text{A}$, $I_0 = 8\,\mu\text{A}$, $I_0 = 15\,\mu\text{A}$, and $I_0 = 20\,\mu\text{A}$. The results of this simulation appear in Figures 2, 3, 4, 5.

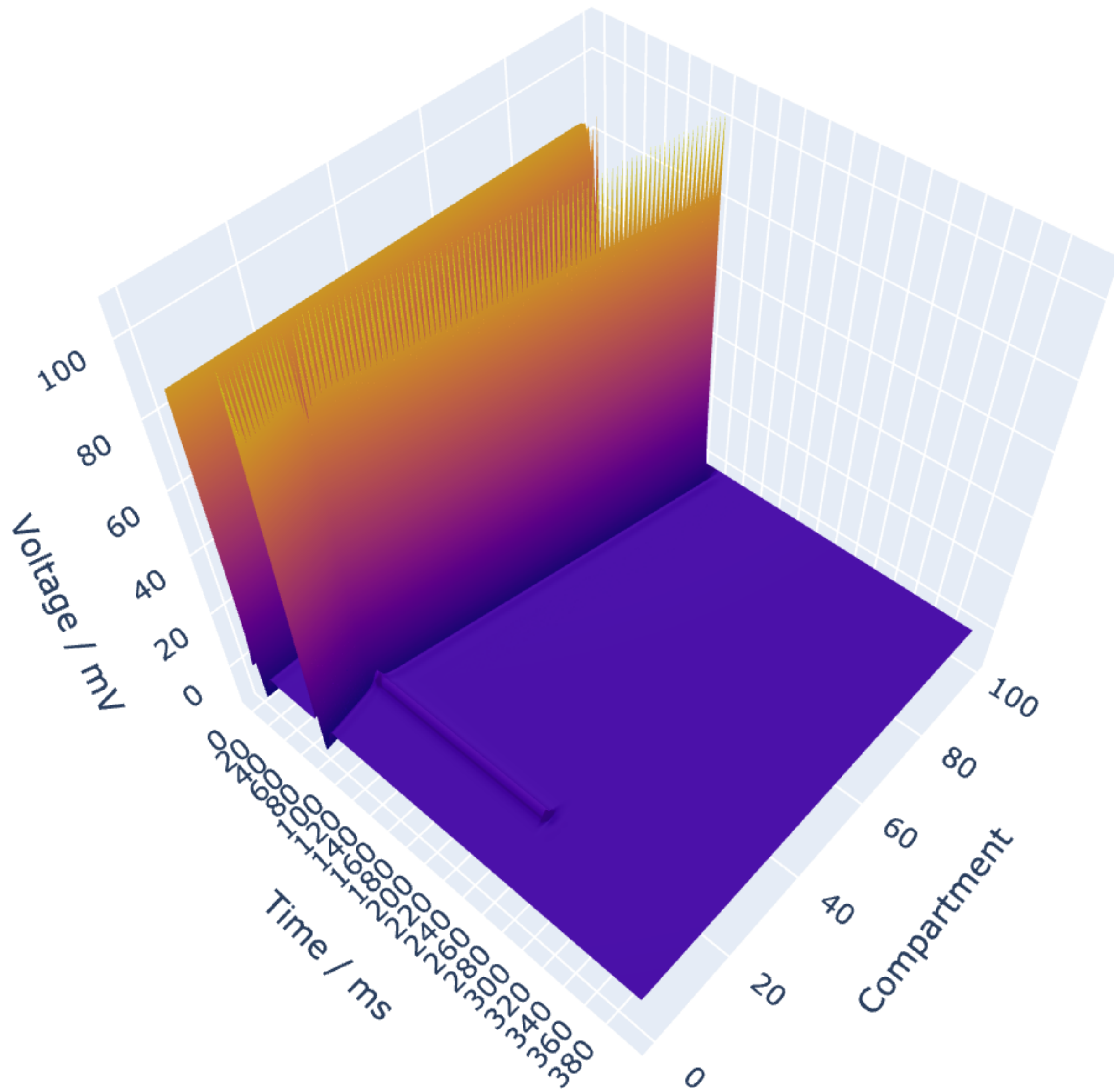

Figure 2: Voltage response to $I_e(14, t)$ of $6\,\mu$A amplitude.

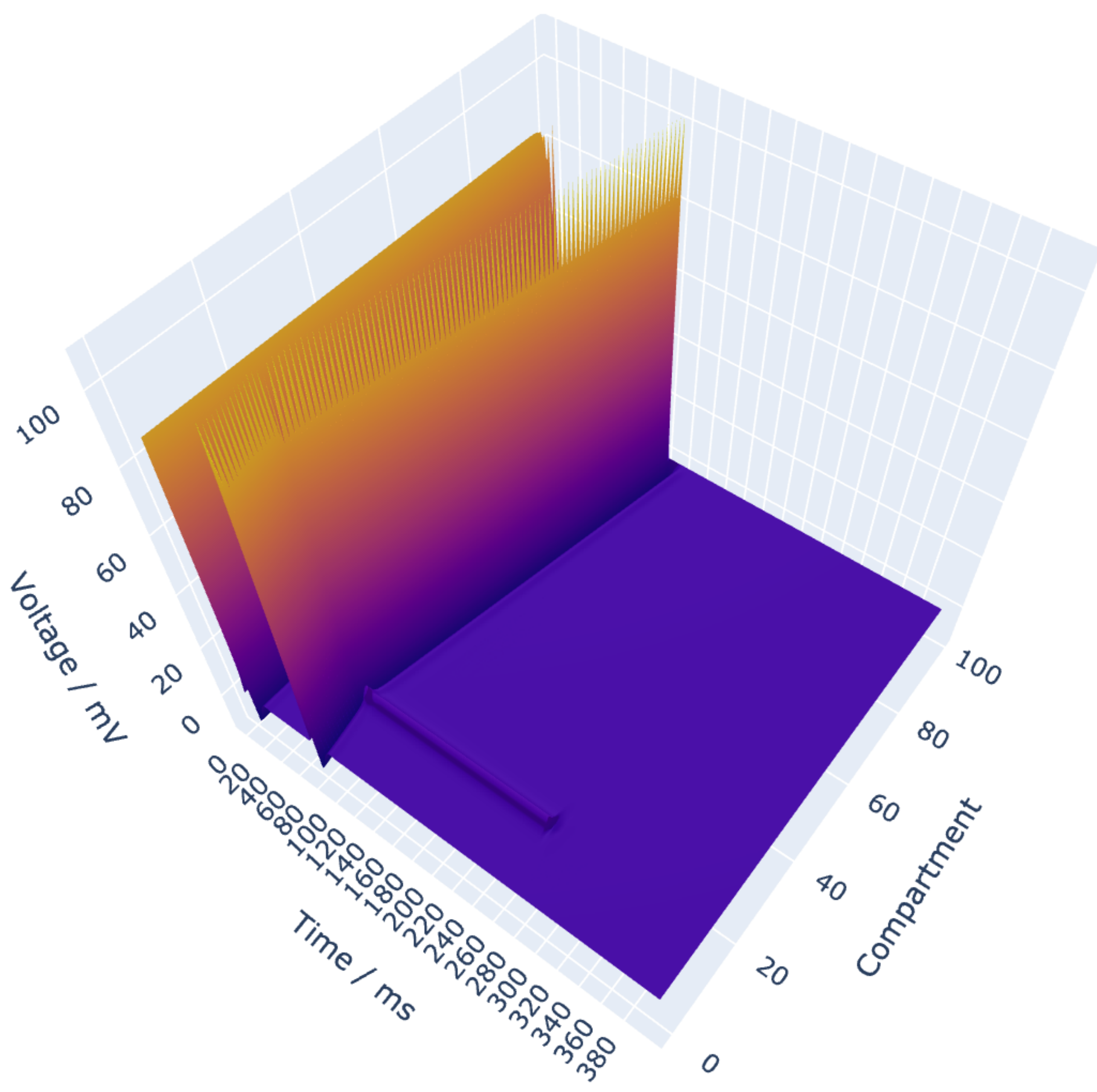

Figure 3: Voltage response to $I_e(14, t)$ of $8\,\mu$A amplitude.

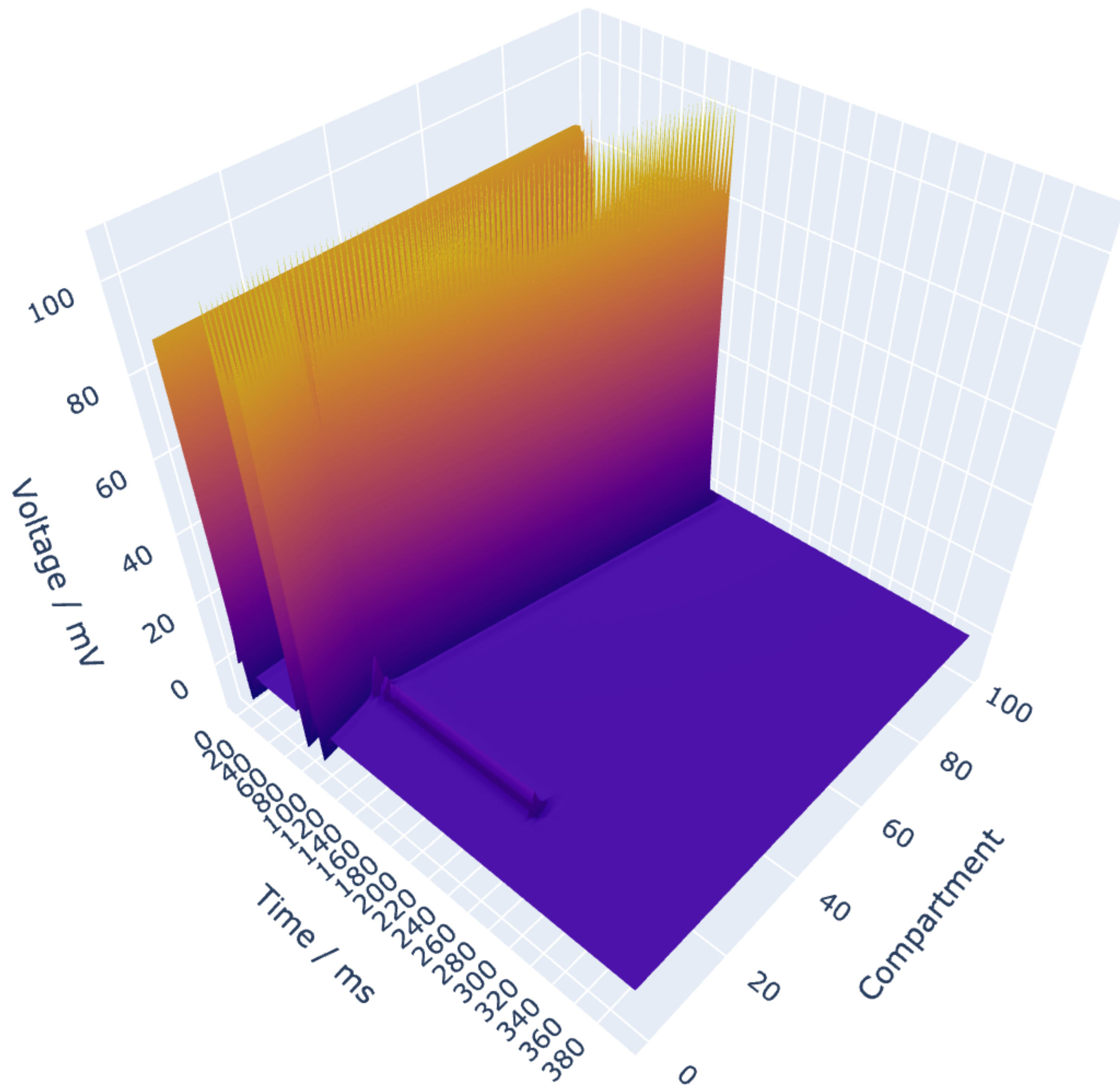

Figure 4: Voltage response to $I_e(14, t)$ of $15\,\mu$A amplitude. Note the second wave of spikes.

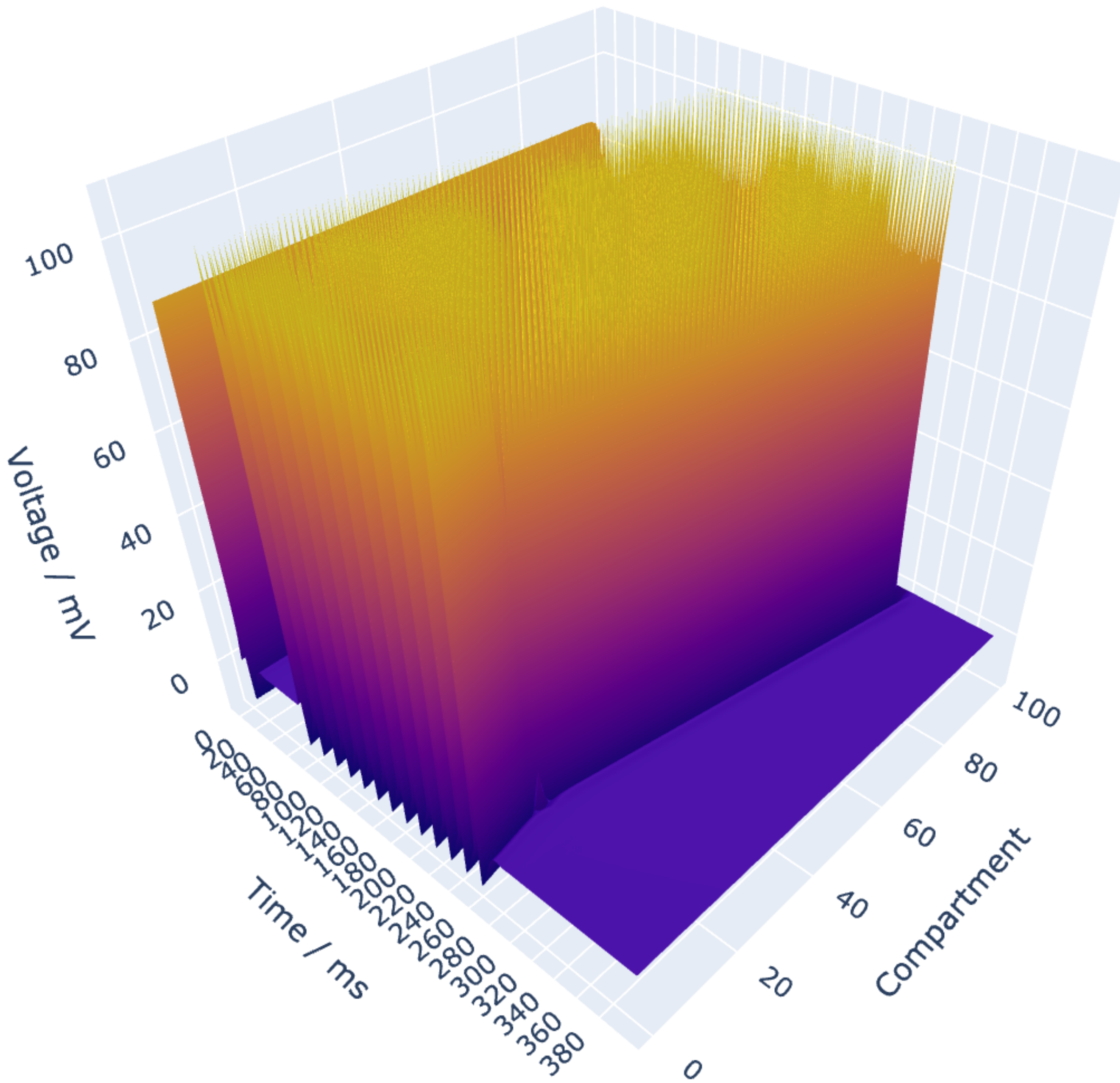

Figure 5: Voltage response to $I_e(14, t)$ of $20\,\mu$A amplitude.