

1. Together, we shall study I_h , a depolarizing current that is activated by hyperpolarization. To begin we place it in a passive single compartment model. The absolute transmembrane potential, V , obeys,

$$C_m V'(t) + g_L(V(t) - V_L) + g_h h(t)(V - V_h) = I_{stim}(t)/A, \quad V(0) = V_r$$

$$h'(t) = \frac{h_\infty(V(t)) - h(t)}{\tau_h} \quad h_\infty(V) = \frac{1}{1 + \exp((V + 75)/5)}$$

where V_r denotes the resting potential of the cell.

- (a) If the stimulus is small, e.g., $I_{stim}(t) = \varepsilon I_0(t)$, we may search for V and h of the form

$$V(t) = V_r + \varepsilon U(t), \quad h(t) = h_\infty(V_r) + \varepsilon j(t).$$

Derive a linear system of ordinary differential equations of the form

$$\begin{pmatrix} U'(t) \\ j'(t) \end{pmatrix} = \begin{pmatrix} b_{11} & b_{12} \\ b_{21} & b_{22} \end{pmatrix} \begin{pmatrix} U(t) \\ j(t) \end{pmatrix} + \begin{pmatrix} f_1(t) \\ f_2(t) \end{pmatrix}$$

for U and j . Evaluate the B matrix and the f vector in the case that

$$C_m = 1 \mu F/cm^2, \quad g_L = 0.05 mS/cm^2, \quad g_h = 0.5 mS/cm^2,$$

$$\tau_h = 5 ms, \quad V_L = -65 mV, \quad V_h = -45 mV, \quad V_r = -60 mV$$

This can happily be done without the need to evaluate any exponentials. To see this first check the cool identity $h'_\infty(V) = h_\infty(V)(h_\infty(V) - 1)/5$ and then ‘realize’ that $h_\infty(V_r)$ is a product of simple ratios of known conductances and known voltage differences.

- (b) Solve $B\phi = z\phi$ for the eigenvalues and eigenvectors of B . **Derive** a representation for U and j in terms of these eigenvalues and eigenvectors and $I_0(t)$. Compute the associated integrals when

$$I_0(t) = -(t > 1)(t < 2) pA \quad A = 10^{-6} cm^2.$$

Sketch your solution.

- (c) Let us now extend this model to the fiber

$$\frac{a}{2R_2} V_{xx} = C_m V_t + g_L(V - V_L) + g_h h(V - V_h), \quad 0 < x < \ell$$

$$V_x(0, t) = -\frac{R_2}{\pi a^2} I_{stim}(t), \quad V_x(\ell, t) = 0, \quad V(x, 0) = V_r.$$

$$h_t = \frac{h_\infty(V(x, t)) - h}{\tau_h} \quad h_\infty(V) = \frac{1}{1 + \exp((V + 75)/5)}$$

As above, if $I_{stim}(t) = \varepsilon I_0(t)$, then we may search for V and h of the form

$$V(x, t) = V_r + \varepsilon U(x, t), \quad h(x, t) = h_\infty(V_r) + \varepsilon j(x, t).$$

Derive a linear system of equations,

$$\begin{aligned} C_m U_t &= \frac{a}{2R_2} U_{xx} + b_{11}U + b_{12}j \\ j_t &= b_{21}U + b_{22}j \end{aligned}$$

for $U(x, t)$ and $j(x, t)$. Evaluate these b terms using the parameters, $C_m = 1$ etc., specified in part (a). Observe that U and j also satisfy the following boundary and initial conditions

$$U_x(0, t) = -\frac{R_2}{\pi a^2} I_0(t), \quad U_x(\ell, t) = 0, \quad U(x, 0) = j(x, 0) = 0.$$

(d) The associated eigenproblem now reads

$$\begin{aligned} \frac{a}{2R_2} \phi''(x) + b_{11}\phi(x) + b_{12}\psi(x) &= z\phi(x) \\ b_{21}\phi(x) + b_{22}\psi(x) &= z\psi(x) \end{aligned}$$

Solve the latter for ψ in terms of ϕ and plug this into the former and find the eigenvalues, z , and eigenfunctions, ϕ , assuming the end conditions $\phi'(0) = \phi'(\ell) = 0$ and the parameter values $a = 1 \mu m$, $R_2 = 0.1 k\Omega cm$ and $\ell = 1 cm$. (Hint: ϕ , as usual, will be a trig function while z will be the root of a quadratic parametrized by $(n\pi/\ell)^2$. The $n = 0$ case should resemble your findings in part (b) above.) Sketch the location of your eigenvalues in the complex plane.

(e) **Derive** a series representation for $U(x, t)$ and $j(x, t)$ in terms of these eigenvalues and eigenvectors and $I_0(t)$. Compute the associated integrals when

$$I_0(t) = -(t > 1)(t < 2) pA.$$

Sketch the first few individual terms in the series for U .