M394C - Problem Set 1

due date 02/07/2019

1 Spatial modeling

1.1 Derivation of the cable equation

An axon is modeled as a long cylindrical piece of membrane encapsulating an interior medium. We assume that the membrane voltage across the membrane is only a function of the position along the cylinder x, which represents the distance from the soma of a cell. The cable can be viewed as a succession of iso-potential infinitesimal membrane sections of length dx. There are only three types of ionic currents: the extracellular and intracellular axial currents $I_e(x)$ and $I_i(x)$, and the transmembrane ionic current $I_t(x)$. The transmembrane ionic current $I_t(x)$ is the sum of capacitive currents, ionic currents, and possibly applied currents

$$I_t = p\left(C_m \frac{\partial V}{\partial t} + I_{\text{ion}} + I_{\text{applied}}\right) , \tag{1}$$

where p is the cable perimeter and where C_m, I_{ion} and I_{applied} are the capacitance, the ionic current, and the applied current per unit of surface. Moreover, we assume that both axial currents are Ohmic, i.e. denoting by V_e and V_i the extracellular and intracellular potentials respectively, we have

$$\begin{aligned} V_i(x+dx) - V_i(x) &= -I_i(x) r_i dx \,, & (2) \\ V_e(x+dx) - V_e(x) &= -I_e(x) r_e dx \,, & (3) \end{aligned}$$

where r_i and r_e are the resistance per unit of length of the intracellular and extracellular media, respectively.

1) Using the fact the total axial current $I_e + I_i$ is constant, deduce from Kirchoff's law (i.e., from the conservation of currents) that in the limit $dx \to 0$, one obtains the cable equation under the form

$$I_t = p\left(C_m \frac{\partial V}{\partial t} + I_{\text{ion}} + I_{\text{applied}}\right) = \frac{\partial}{\partial x}\left(\frac{1}{r_i + r_e}\frac{\partial V}{\partial x}\right) . \tag{4}$$

where $V = V_i - V_e$.

Hint: write the transverse current as the derivative the axial current I_e, use the definition of V to express its derivative in terms of I_e and $I_e + I_i$, and combine both results to obtain the desired expression.

2) The intracellular resistivity satisfies $r_i = R_c/A$, where R_c is the cytoplasmic resistivity and where A is the cross-sectional area of the cable. Introducing the membrane resistivity

$$\frac{1}{R_m} = \frac{\partial I_{\text{ion}}}{\partial V}\Big|_{V=V_0}, \tag{5}$$

we define the membrane time constant $\tau_m = R_m C_m$. Neglecting the extracellular resistivity r_e, show that the cable equation takes the dimensionless form

$$\frac{\partial V}{\partial T} = \frac{\partial^2 V}{\partial X^2} + f(V,T)\,, \quad \text{with} \quad X = x/\lambda_m \quad \text{and} \quad T = t/\tau_m\,, \tag{6}$$

and specify the space constant λ_m in terms of R_m and R_c.

1.2 Linear cable equation

Passive electrical conduction in dendrites only involves Ohmic transmembrane currents for which the approximation $f(V,T) = -V$ is valid. This yields the linear cable equation.

3) Find the fundamental solution of the linear cable equation satisfying

$$-\frac{\partial^2 f}{\partial X^2} + f = \delta_a \quad \text{with} \quad \lim_{x\to\pm\infty} f(x) = 0\,, \tag{7}$$

where the Dirac delta function δ_a represents an inward positive current in a. Deduce the solution for an inhomogeneous current input I, seen as an absolutely integrable function of x. Answer the same questions for a finite cylinder with $0 < x < L$ and for sealed-end boundary conditions, i.e., $\partial V/\partial X = 0$, and for short-circuit boundary conditions, i.e., $V = 0$.

4) Consider a branched structure with a cylinder of length L with diameter d branching into two cylinders of lengths L_1 and L_2 and diameters d_1 and d_2, respectively. Find the steady-state solution of the cable equations assuming that $i)$ each component of the branched structure has identical electrical properties, that $ii)$ the terminal boundary conditions are given by

$$\frac{\partial V}{\partial X}\Big|_0 = -r_i \lambda_m I_0\,, \quad V_1(L_1) = V_2(L_2) = 0\,, \tag{8}$$

and that $iii)$ voltages are continuous and currents are conserved at the branching.

5) Assuming that $L_1 = L_2$, find a condition on the diameters d, d_1, and d_2 such that the solution for the branched structure is equivalent to the solution obtained for a single cylinder. Justify that a branched structure is equivalent to a single cylinder if the following properties are satisfied:

$i)$ If d is the diameter of a parent branch, the diameters $d_1, \ldots, d_n$ of the offspring branches satisfy

$$d_0^{3/2} = d_1^{3/2} + \ldots + d_n^{3/2}\,. \tag{9}$$

$ii)$ All the boundary conditions at the terminal ends are the same.

$iii)$ Each terminal end is the same dimensionless distance L (in units of λ_m) from the origin of the tree.

Hint: Being equivalent to a single cylinder requires that piecewise solutions are smoothly connected at junctions, imposing conditions on the coefficients, which themselves depend on the diameter via the length scale λ_m.

1.3 Rall model

The Rall model consists of a dendritic tree modeled as an equivalent cylinder and of an iso-potential soma that acts as a resistance R_s and a capacitance C_s in parallel. Thus, the dendritic potential V satisfies the same cable equation but with a new boundary condition in 0, at the junction between the soma and the cable. If I_0 denote the applied current to the soma, then the boundary condition in 0 reads

$$I_0 = -\frac{1}{r_i}\frac{\partial V(0,t)}{\partial x} + C_s\frac{\partial V(0,t)}{\partial t} + \frac{V(0,t)}{R_s}\,, \tag{10}$$

so that

$$R_s I_0 = -\gamma\frac{\partial V(0,T)}{\partial X} + \sigma\frac{\partial V(0,T)}{\partial t} + V(0,T)\,, \tag{11}$$

with $\sigma = C_s R_s/\tau_m$ and $\gamma = R_s/(r_i\lambda_m)$. For simplicity, we take $\sigma = 1$. We want to find an expression for the time-dependent response of the Rall model in response to an impulse current $I_0(T) = \delta(T)$ localized at the soma, with sealed terminal boundary conditions $\partial V(L,T)/\partial X = 0$, and with initial condition $V(X,0^-) = 0$.

1) Forgetting about the initial condition, use the method of the separation of the variable for solutions under the form $V(X,T) = \phi(X)e^{-\mu^2 T}$.

2) Justify that the sought-after solutions, with initial condition, can be written as

$$V(X,T) = \sum_{n=0}^{\infty} A_n\left(\cos\left(\lambda_n X\right) - \frac{\lambda_n}{\gamma}\sin\left(\lambda_n X\right)\right)\,, \tag{12}$$

where A_n are some real coefficients.

3) Subsidiary question: Can you specify the unknown coefficients A_n?

2 Traveling wave

It can be shown that the Hodgkin-Huxley cable equation admits traveling wave solutions, modeling spike propagation along the axon. A simpler parabolic partial differential equation that admits traveling wave solutions is the Fisher equation

$$\frac{\partial v}{\partial t} = \frac{\partial^2 v}{\partial x^2} + f(v)\,, \tag{13}$$

where the nonlinear function f is given by $f(v) = v(1-v)$. In the context of the Fisher equation, traveling waves are defined as nonconstant solutions of the form $(x,t) \mapsto v(x,t) = g(x-ct)$ for some real number c and such that $\lim_{x\to\pm\infty} g(x)$ is finite. The Fisher equation prominently features in population dynamics where it models the propagation of a trait in a population.

1) Discuss spatially homogeneous solutions to the Fisher equation.

2) Justify that if $(x,t) \mapsto v(x,t) = g(x-ct)$ is a traveling wave solution of the Fisher equation then f solves the two-dimensional dynamical system

$$\frac{\partial v}{\partial x} = u\,, \quad \frac{\partial u}{\partial x} = -cu - v(1-v)\,. \tag{14}$$

3) Perform the phase portrait analysis of the above two-dimensional system: sketch the vector fields and the nullclines, identify equilibria and discuss their stability.

4) What are possible values for $\lim_{x\to\pm\infty} g(x)$ if $(x,t) \mapsto v(x,t) = g(x-ct)$ is a traveling wave solution to the Fisher equation? Explain that the existence of traveling wave solutions is equivalent to the existence of particular types of trajectories solving the two-dimensional dynamical system (14).

3) Assuming that $c \geq 2$, show that the two-dimensional dynamical system (14) admits heteroclinic orbits. It will be useful to consider the behavior of the trajectories in regions delimited by the curves $u = -v$ and $u = -v(1-v)/c$. Show that traveling wave solutions to the Fisher equation exists for $c > 2$ and that they are positive. What happens if $c < 2$?