580.439/639 Homework #8

Due Dec 1, 2014

Problem 1

The cable equation for a non-linear cable can be written as:

$$\frac{1}{r_e + r_i}\frac{\partial^2 V}{\partial x^2} = c_m \frac{\partial V}{\partial t} + I_i(V,x,t) \qquad (1.1)$$

where $I_i(V,x,t)$ is the ionic current density (current/length) through the membrane's voltage dependent channels. For the case of an unmyelinated squid giant axon, I_i can be modeled using the Hodgkin-Huxley equations; then Eqn. 1.1 is a model for action potential propagation in this system. Dimensional analysis of this equation can be used to predict the action potential propagation velocity (Huxley, *J. Physiol.* 148:80, 1959), which is one of the most impressive accomplishments of the Hodgkin-Huxley model.

a) Assuming that $r_e << r_i$, express Eqn. 1.1 in terms of axon radius a, the usual cable electrical constants R_i, R_m, and C_m, and the membrane ion channel current density (current/*area of membrane*) I_i^*. Note that I_i^* is different from $I_i(V,x,t)$.

b) For the special case of a propagating action potential, Eqn. 1.1 can be reduced to an ordinary differential equation by using the experimental observation that the action potential is a propagating wave of constant shape, i.e. that

$$V(x,t) = F(x - \Theta t)$$

where Θ is the propagation velocity. Explain why the equation above is an accurate description of a propagating action potential and why Θ is the conduction velocity. By substituting $F(x\text{-}\Theta t)$ for V in the equation derived in part a), show that Eqn. 1.1 can be written as an ordinary differential equation in $F(u)$, where $u = x - \Theta t$, as

$$\frac{a}{2R_i}\frac{d^2 F}{du^2} = -C_m \Theta \frac{dF}{du} + I_i^* \qquad (1.2)$$

Eqn. 1.2 describes the waveshape F of action potentials propagating along an unmyelinated axon of radius a, with electrical properties R_i and C_m.

c) Eqn. 1.1 is just one of four equations necessary to fully specify this problem; the other three equations being the first-order differential equations for m, n, and h. Write these equations in terms of the variable u in Eqn. 1.2. When written in this form, these equations should not have an explicit dependence on x or t.

d) Show that, with the assumptions of part b) above,

$$\Theta^2 \frac{\partial^2 V}{\partial x^2} = \frac{\partial^2 V}{\partial t^2}$$

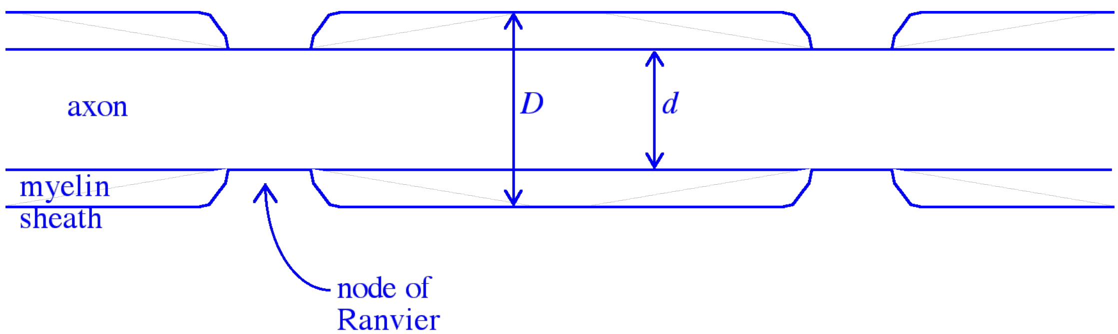
and from this, show that Eq. (1.2) can be written as an ordinary differential equation in time as below for some fixed constant K. Write an equation for K.

$$K\frac{d^2V}{dt^2} = C_m\frac{dV}{dt} + I_i^* \tag{1.3}$$

e) Eqn. 1.3 was found empirically to have stable solutions (i.e. $V(t\rightarrow\infty) = 0$) only for a very narrow range of values of K (Hodgkin and Huxley, *J. Physiol.* 117:500, 1952), regardless of the radius of the axon. Show that a fixed value of K across axons implies that the conduction velocity Θ is proportional to the square root of axon radius a. This is the empirically-determined behavior of conduction velocity in unmyelinated axons. Moreover, for the particular case of the Hodgkin-Huxley model, the solutions are stable for K values which correspond to the experimentally observed conduction velocity in squid giant axon.

Problem 2

Consider the myelinated axon drawn below.



The myelin sheath is an insulating cylinder around the axon whose inner and outer diameters are d (the axon diameter) and D (the outer diameter of the myelin). Action potentials in a myelinated axon jump from one node of Ranvier to the next; the active channels necessary to generate an action potential are concentrated in the nodes. Propagation of potentials through the myelin sheath region occurs by passive propagation down the cable formed by the sheath. Because the sheath has considerable thickness, the resistance per unit length of the myelin (r_m) and capacitance per unit length (c_m) are best written in terms of equations for cylindrical resistors and capacitors:

$$r_m = \frac{R_{my}}{2\pi}\ln\frac{D}{d} \quad \text{and} \quad c_m = \frac{2\pi\kappa\varepsilon_0}{\ln\frac{D}{d}}$$

where R_{my} is the bulk resistivity of the myelin (i.e. the resistance between the faces of a unit cube of myelin). π, κ, and ε_0 are constants. r_i is related to the bulk resistivity of axoplasm, R_i, in the usual way.

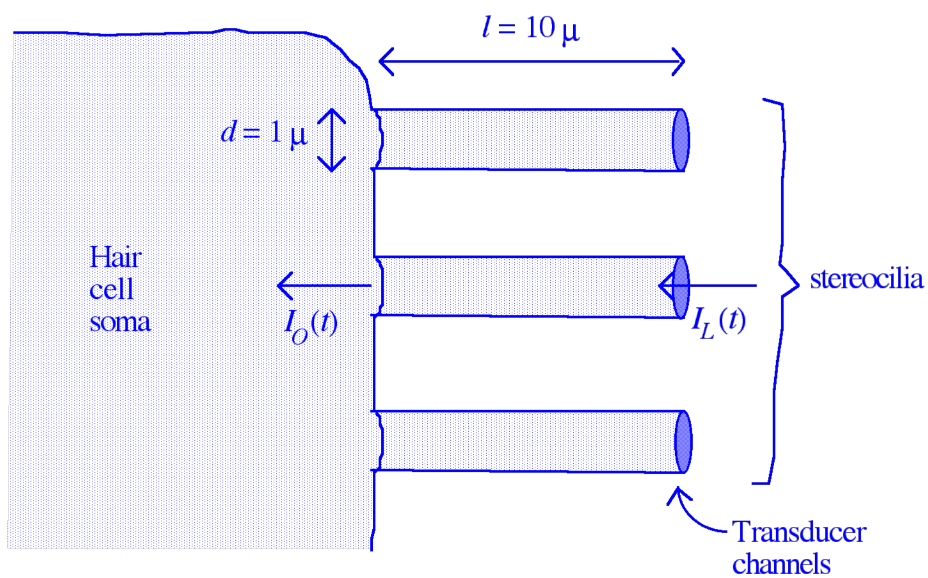
a) Derive the equation for r_m above by considering the myelin to be a sequence of shells of inner radius r and thickness dr. Current flow through the myelin is exclusively radial and passes through the shells in series, so the resistance r_m is the sum of the resistances of all the shells from radius $d/2$ to radius $D/2$.

b) Write an equation for the length constant λ of the myelin in terms of the diameters d and D and the electrical parameters R_{my} and R_i (ignore r_e for this calculation). Show that for a fixed value of D, λ is maximized by $d = 0.61D$. It turns out that many axons have diameter ratios $d/D \; \varepsilon \; (0.5{,}0.7)$.

c) Assume that the propagation velocity of disturbances through the myelin is proportional to λ/τ_{my}, where τ_{my} is the membrane time constant of the myelin sheath. Argue that the propagation velocity through the myelin region is maximized, for fixed D, when $d/D = 0.61$.

Problem 3

The figure below is a sketch of the apical end of a vertebrate hair cell.



The stereocilia are long membrane cylinders which protrude from the apical surface of hair cells. Their membrane is continuous with the hair cell membrane and their cytoplasm is continuous with the inside of the hair cell. At the end of the cilia are transducer channels which inject current $I_L(t)$ when the cilia are displaced. The current I_L is the input to the cable formed by the cilia and the current I_O delivered at the base of the cilia into the hair cell soma is the output. When evidence that the transducer channels are at the ends of the cilia was first put forward, there was concern that the cilia would act as a low pass filter between I_L and I_O and prevent the hair cell from working at audio frequencies (up to 100 kHz in animals like bats and dolphins). For this problem, assume the following electrical constants for hair cell membrane:

$$R_m = 12000 \; \Omega\text{-cm}^2 \qquad R_i = 150 \; \Omega\text{-cm} \qquad C_m = 1.2 \; \mu\text{fd/cm}^2$$

a) What are the values of time constant and space constant for one stereocilium? What is L, their electrotonic length?

b) Write the cable equation with suitable boundary conditions for a cilium driven by current I_L which dumps current I_O into a load impedance $1/Y_L = 0$, i.e. assume that the hair cell soma is so large compared to a cilium that the output end of the cilia are short circuited. Write the equations in a form that is suitable for the sinusoidal steady state, which is reasonable since hair cells are frequently tested with sinusoidal inputs (hint: $q^2 = 1+j\omega$)

c) Solve for current $I_O(j\omega)$ in terms of current $I_L(j\omega)$, i.e. for the transfer function through a cilium. What is the gain I_0/I_L of the cilium at 0 Hz and at 1000 Hz? At what frequency does the gain equal 0.5?