ELEC ENG 3BB3:

Cellular Bioelectricity

Notes for Lecture 17

Tuesday, February 11, 2014

Linear (subthreshold) response of a cylindrical fiber:

Under subthreshold conditions, the transmembrane current per unit length i_m (mA/cm) in a cylindrical fiber is:

$$i_m = \frac{v_m}{r_m} + c_m \frac{\mathrm{d}v_m}{\mathrm{d}t}, \qquad (7.12)$$

where r_m is the membrane resistance times unit length ($\Omega \cdot$cm) and c_m is the membrane capacitance per unit length (μF/cm).

Dependence of i_m *on* V_m *(cont.):*

If Eqns. (6.8) is differentiated with respect to x, then:

$$\frac{\partial^2 V_m}{\partial x^2} = -(r_i + r_e)\frac{\partial I_i}{\partial x} + r_e \frac{\partial I}{\partial x}. \qquad (6.10)$$

Substituting Eqns. (6.3) and (6.6) gives:

$$\frac{\partial^2 V_m}{\partial x^2} = (r_i + r_e)\, i_m + r_e i_p \qquad (6.11)$$

$$\Rightarrow i_m = \frac{1}{(r_i + r_e)}\left(\frac{\partial^2 V_m}{\partial x^2} - r_e i_p\right). \qquad (6.12)$$

Linear (subthreshold) response of a cylindrical fiber (cont.):

Substituting Eqn. (7.12) into cable equation (6.11) gives:

$$\lambda^2 \frac{\partial^2 v_m}{\partial x^2} - \tau \frac{\partial v_m}{\partial t} - v_m = r_e \lambda^2 i_p \,, \qquad (7.14)$$

where:

$$\lambda = \sqrt{\frac{r_m}{r_i + r_e}} \quad \text{and} \quad \tau = r_m c_m \,. \quad (7.15)$$

Steady-state solution for stimulus current at the origin:

Injection of a small current into the extracellular space at the origin (center) of an infinitely-long cylindrical fiber can be approximated by a spatial delta function source:

$$i_p = I_0 \, \delta(x) \ , \qquad (7.22)$$

where I_0 is the total applied current (mA) and $\delta(x)$ is the unit delta function.

Note that i_p is zero everywhere except at the origin, where it is infinite, and integrating i_p around the origin gives the total current I_0.

Steady-state solution for stimulus current at the origin (cont.):

Solving Eqn. (7.14) under these conditions gives:

$$v_m = -\frac{r_e \lambda I_0}{2} \mathrm{e}^{-|x|/\lambda} \,. \qquad (7.34)$$

In Eqn. (7.34), the constant λ describes the rate of decay of the steady-state membrane potential as a function of *distance* along the cylindrical fiber.

Thus, it is referred to as the **space constant**.

Space constant properties:

For a cylindrical fiber with uniform membrane properties and with r_e ¼ 0:

$$\lambda = \sqrt{\frac{r_m}{r_i + r_e}} \approx \sqrt{\frac{r_m}{r_i}}\,. \qquad (7.19)$$

Substituting for r_i and r_m in Eqn. (7.19) using Eqns. (2.55^0) and (2.56^0) gives:

$$\lambda = \sqrt{\frac{R_m/2\pi a}{R_i/\pi a^2}} \qquad (7.20)$$

$$= \sqrt{\frac{aR_m}{2R_i}}\,. \qquad (7.21)$$

Normalized space and time notation:

To simplify our notation, we introduce the normalized space and time variables:

$$X = \frac{x}{\lambda} \quad \text{and} \quad T = \frac{t}{\tau}, \tag{7.36}$$

such that the homogenous version of Eqn. (7. 14) becomes:

$$\frac{\partial^2 v_m}{\partial X^2} - \frac{\partial v_m}{\partial T} - v_m = 0. \tag{7.37}$$

Step current at origin – general time-varying solution:

If we assume an unbounded extracellular space and an intracellular injected step current, we can assume that r_e ¼ 0.

In the normalized space and time variables the time-varying solution is:

$$v_m(X,T) = \frac{r_i \lambda I_0}{4}\left\{ \mathrm{e}^{-|X|}\left[1 - \mathrm{erf}\left(\frac{|X|}{2\sqrt{T}} - \sqrt{T}\right)\right] - \mathrm{e}^{|X|}\left[1 - \mathrm{erf}\left(\frac{|X|}{2\sqrt{T}} + \sqrt{T}\right)\right]\right\}, \quad (7.48)$$

Step current at origin – general time-varying solution (cont.):

Converting back to the original coordinates gives:

$$v_m(x,t) = \frac{r_i \lambda I_0}{4}\left\{ \mathrm{e}^{-|x|/\lambda}\left[1 - \mathrm{erf}\left(\frac{|x|}{2\lambda}\sqrt{\frac{\tau}{t}} - \sqrt{\frac{t}{\tau}}\right)\right] - \mathrm{e}^{|x|/\lambda}\left[1 - \mathrm{erf}\left(\frac{|x|}{2\lambda}\sqrt{\frac{\tau}{t}} + \sqrt{\frac{t}{\tau}}\right)\right]\right\} \quad (7.49)$$

where:

$$\mathrm{erf}(y) \triangleq \frac{2}{\sqrt{\pi}}\int_0^y \mathrm{e}^{-z^2}\mathrm{d}z. \quad (7.50)$$

Step current at origin – general time-varying solution (cont.):

For a given value of time, the spatial behaviour is exponential-like. For $t > \tau$, $v_m(x)$ tends towards a true exponential, as was obtained for the steady-state response described by Eqn. (7.34).

This continuous decrement of $v_m(x)$ with increasing jxj is due to the leakage of current through the membrane, while λ describes the rate of this effect.

Step current at origin – general time-varying solution (cont.):

For a given position x along a fiber, the membrane potential reaches its steady-state in an exponential-like manner over time.

Only at $x = \lambda$ is it truly exponential, i.e., the fraction of the steady-state potential that is achieved at $t = \tau$ is $1 - 1/e$.

Table 7.2. Temporal Morphology at Different Values of x Due to Current Step at $x = 0$

x	Fraction of steady-state value reached at $t = \tau$
0	0.843
λ	0.632
2λ	0.372
3λ	0.157
4λ	0.0453
5λ	0.00862

Step current at origin – general time-varying solution (cont.):

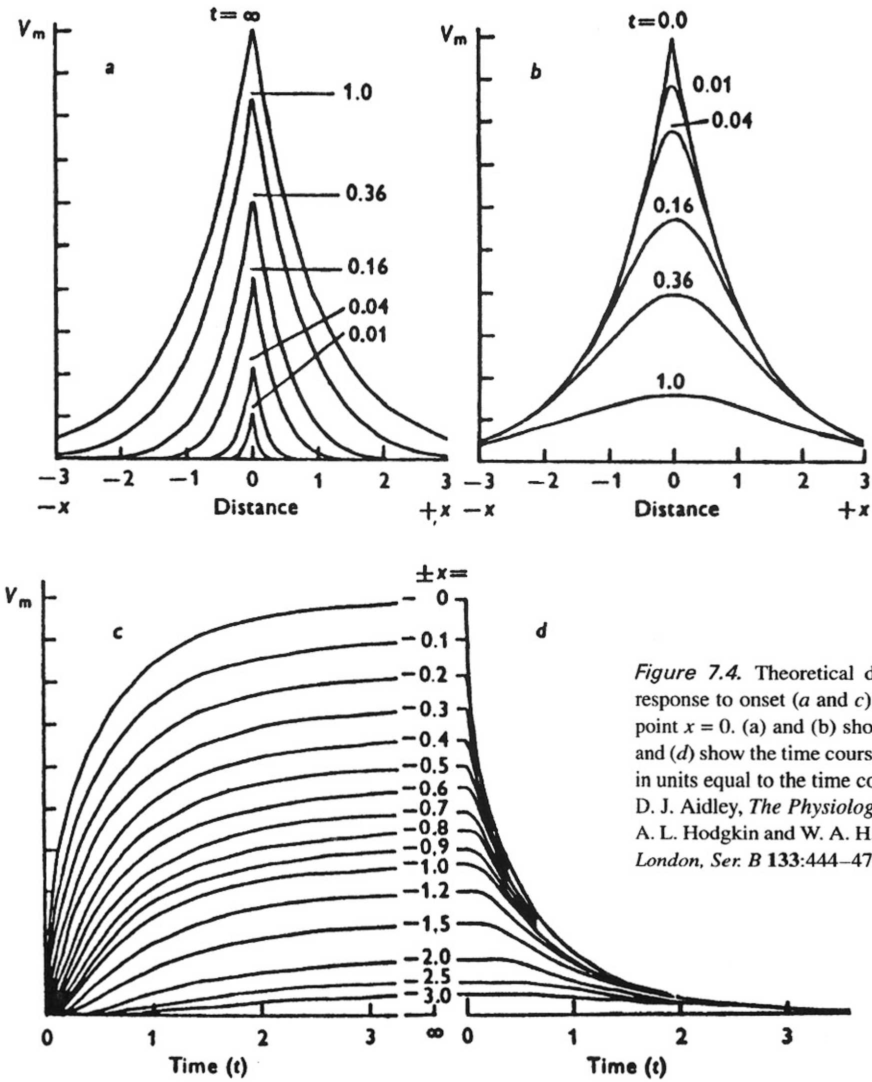

Figure 7.4. Theoretical distribution of potential difference across a passive nerve membrane in response to onset (*a* and *c*) and cessation (*b* and *d*) of a constant current applied intracellularly at the point $x = 0$. (a) and (b) show the spatial distribution of potential difference at different times, and (*c*) and (*d*) show the time course of the potential at different distances along the axon. Time (t) is expressed in units equal to the time constant, τ, and distance (x) is expressed in units of space constant, λ. [From D. J. Aidley, *The Physiology of Excitable Cells*, Cambridge University Press, Cambridge, 1978. After A. L. Hodgkin and W. A. H. Rushton, The electrical constants of a crustacean nerve fiber, *Proc. R. Soc. London, Ser. B* **133**:444–479 (1946). Reprinted with permission of Cambridge University Press.]

Subthreshold response to an external point current stimulus:

Consider the source-fiber geometry shown to the right.

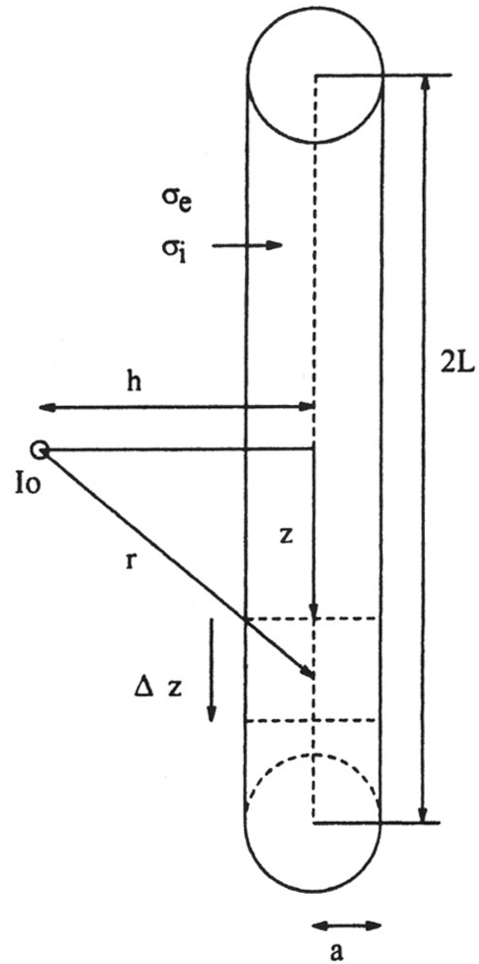

Figure 7.5. Geometry of source and fiber. A single current point source of magnitude I_0 is placed at a distance h from a circular cylindrical fiber of length $2L$. The extracellular region is unbounded, uniform, and has a conductivity σ_e. The fiber radius is a and its intracellular conductivity is σ_i. The fiber's centerline lies along the coordinate z axis. The length is divided into elements Δz for numerical calculations.

Subthreshold response to an external point current stimulus (cont.):

The resulting extracellular field is:

$$\phi_a = \frac{I_0}{4\pi\sigma_e r}, \qquad (7.55)$$

where I_0 is the current strength, σ_e is the conductivity of the extracellular medium, and r is the distance from the source to an arbitrary field point.

Note that the effect of the fiber on the field is typically ignored.

Subthreshold response to an external point current stimulus (cont.):

Reformulating Eqn. (6.13) gives:

$$r_i i_m = \frac{\partial^2 \phi_i}{\partial z^2}, \qquad (7.56)$$

where z now defines the axial (longitudinal) coordinate.

The transmembrane current i_m must also equal the intrinsic ionic plus capacitive current of the membrane.

Subthreshold response to an external point current stimulus (cont.):

Replacing ϕ_i by $v_m + \phi_e$ and i_m by $i_{ion} + c_m \partial v_m / \partial t$ in Eqn. (7.56) gives:

$$r_i \frac{\partial v_m}{\partial t} = \frac{1}{c_m}\left(-i_{\text{ion}} r_i + \frac{\partial^2 v_m}{\partial z^2} + \frac{\partial^2 \phi_e}{\partial z^2}\right). \quad (7.57)$$

At rest, $v_m = 0$ for all z) $\partial^2 v_m / \partial z^2 = 0$ and $i_{ion} = v_m / r_m = 0$. Consequently, when the stimulus is first applied:

$$r_i \frac{\partial v_m}{\partial t} = \frac{1}{c_m} \frac{\partial^2 \phi_e}{\partial z^2}. \quad (7.59)$$

Subthreshold response to an external point current stimulus (cont.):

Thus, the region where excitation is possible is where $\partial^2\phi_e/\partial z^2$ is positive, because this will make $\partial v_m/\partial t$ initially positive.

Conversely, regions where $\partial^2\phi_e/\partial z^2$ is negative will hyperpolarize, because this will make $\partial v_m/\partial t$ initially negative.

Consequently, the function $\partial^2\phi_e/\partial z^2$ has been named the *activating function*.

Subthreshold response to an external point current stimulus (cont.):

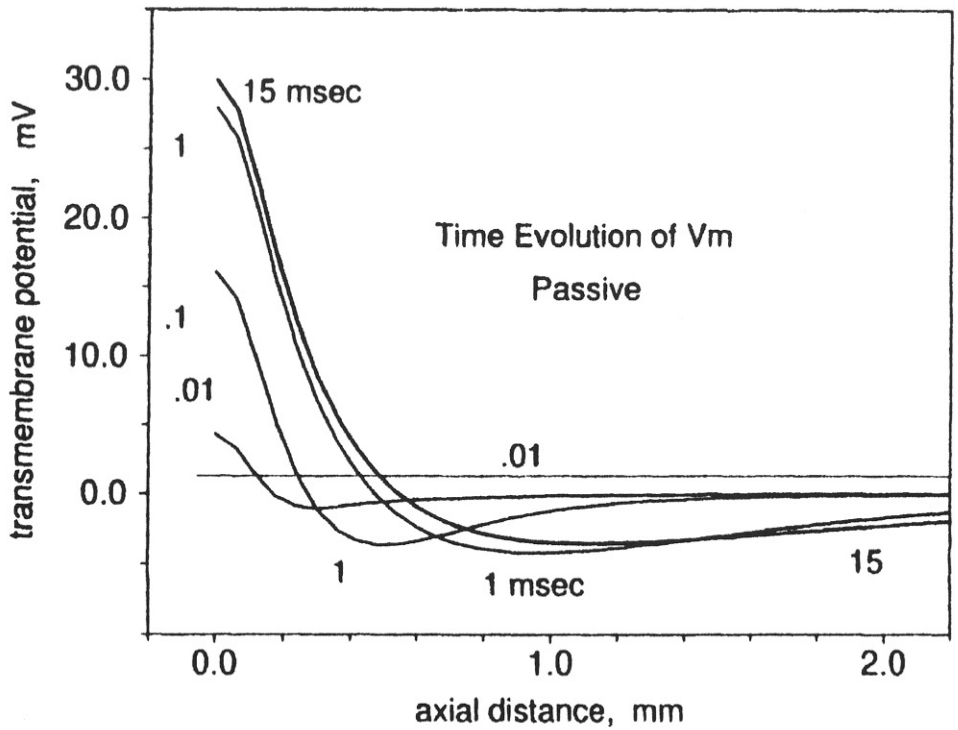

Figure 7.6. Time evolution of the induced transmembrane voltage along a fiber. Stimulus duration is shown in milliseconds. The point current stimulus is at distance $h = 0.02$ cm from a fiber described in Fig. 7.5. Other parameters are $\lambda = 0.086$ cm, $\tau = 1.5$ msec, $\sigma_e = 33.3$ mS/cm, and $I_0 = -0.44$ mA. Note the region which is initially hyperpolarized but becomes depolarized. The activating function is similar to the 0.01-msec curve. [From R. Plonsey and R. C. Barr, Electric field stimulation of excitable tissue, *IEEE Trans. Biomed. Eng.* **42**:329–336 (1995). Copyright 1995, IEEE.]

Suprathreshold response to an external point stimulus (cont.):

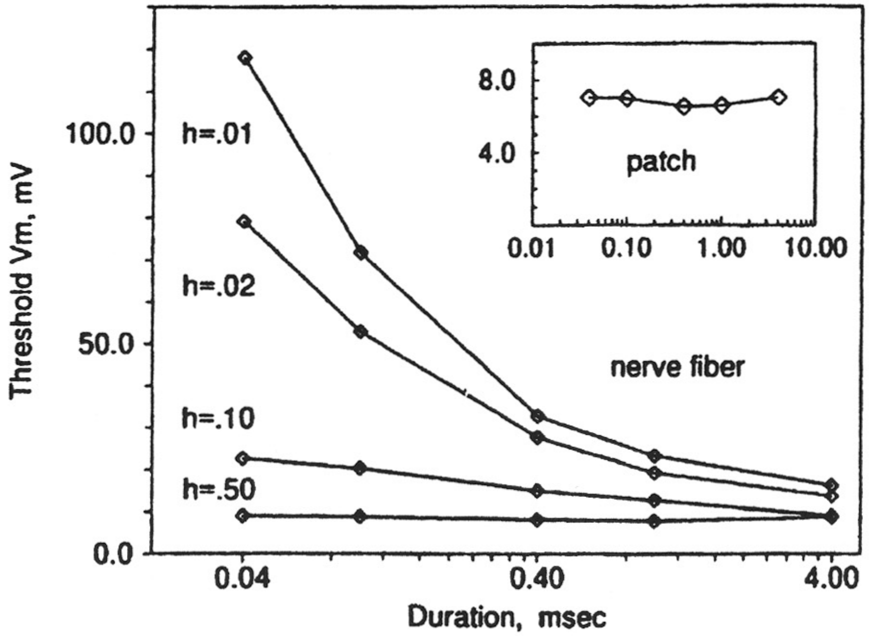

Figure 7.7. Threshold values of v_m versus stimulus duration. **Inset**: Patch geometry. The transmembrane voltage at the end of the stimulus is shown for a stimulus condition that is just below threshold. Patch data are for the condition of no spatial variation. All potentials shown are relative to a baseline of −57 mV. **Outer**: Each curve is for a different source–fiber distance as shown (h given in cm). Results shown are for $z = 0$, the shortest fiber–stimulus distance. Membrane properties are: $E_K = -72.1$ mV, $E_{Na} = 52.4$ mV, $\bar{g}_{Na} = 120$ mS/cm^2, $\bar{g}_K = 36$ mS/cm^2, $g_l = 0.30$ mS/cm^2. Fiber properties are: $R_m = 0.148$ Ωcm^2, $\lambda = 0.086$ cm, $C_m = 1.0$ μF/cm^2. [From R. C. Barr and R. Plonsey, Threshold variability in fibers with field stimulation of excitable membranes. *IEEE Trans. Biomed. Eng.* **42**:1185–1191 (1995). Copyright 1995, IEEE.]

Suprathreshold response to an external point stimulus (cont.):

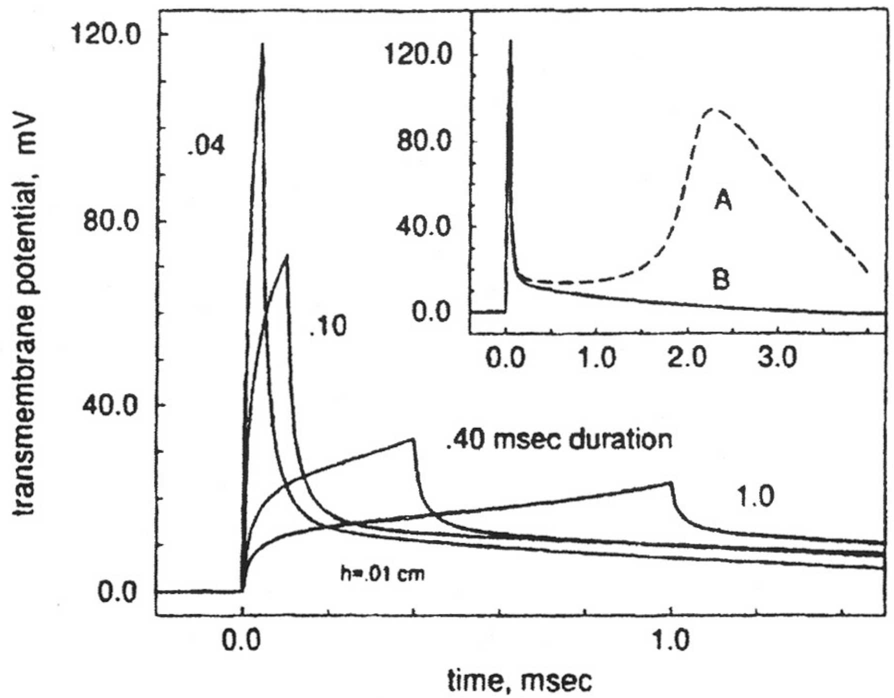

Figure 7.8. Transmembrane potential as a function of time for stimuli which are just below and just above threshold. **Inset**: Curve A is for a just transthreshold stimulus and B for a just subthreshold stimulus. The source–fiber distance is 0.01 cm. Stimulus magnitudes were 1.40 mA (A) and 1.30 mA (B). **Outer**: Temporal responses for just subthreshold stimuli for stimulus duration as shown (in msec). [From R. C. Barr and R. Plonsey, Threshold variability in fibers with field stimulation of excitable membranes, *IEEE Trans. Biomed. Eng.* **42**:1185–1191 (1995) Copyright 1995 IEEE.]

Suprathreshold response to an external point stimulus (cont.):

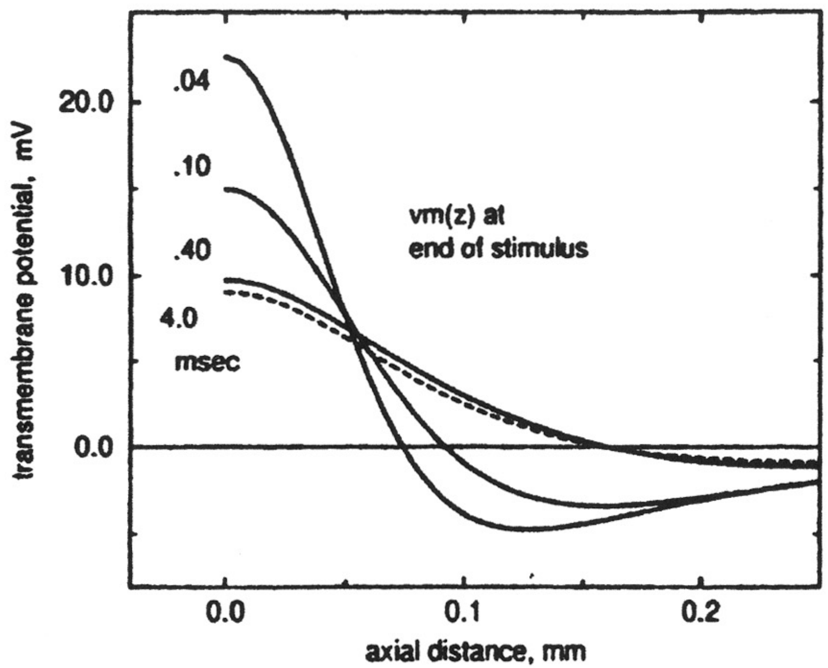

Figure 7.9. Spatial distribution of transmembrane potential, $v_m(z)$, at the end of the stimulus. Each curve is labeled with the duration of the stimulus. The source–fiber distance is 0.10 cm. In each case the stimulus magnitude is for a just subthreshold response. [From R. C. Barr and R. Plonsey, Threshold variability in fibers with field stimulation of excitable membranes. *IEEE Trans. Biomed. Eng.* **42**:1185–1191 (1995). Copyright 1995 IEEE.]