ELEC ENG 3BB3:

Cellular Bioelectricity

Notes for Lecture 14

Tuesday, February 4, 2014

Dependence of membrane current on V_m*:*

Suppose I is defined as:

$$I = I_i + I_e. \qquad (6.5)$$

From Eqns. (6.3) and (6.4):

$$\frac{\partial I}{\partial x} = \frac{\partial I_i}{\partial x} + \frac{\partial I_e}{\partial x} = -i_m + (i_m + i_p)$$

$$= i_p. \qquad (6.6)$$

That is, any change in the total axial (longitudinal) current must come from the injected current i_p.

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

We now consider the relationship between the transmembrane potential and the extra- and intra-cellular currents and potentials.

Since, by definition $V_m = \Phi_i - \Phi_e$, we have:

$$\frac{\partial V_m}{\partial x} = \frac{\partial \Phi_i}{\partial x} - \frac{\partial \Phi_e}{\partial x} = -r_i I_i + r_e I_e$$

$$= -r_i I_i + r_e (I - I_i) \qquad (6.7)$$

$$= -(r_i + r_e) I_i + r_e I. \qquad (6.8)$$

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:

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

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

Cable equations (cont.):

The resulting relationship between the extracellular potential gradient in the axial direction as a function of the axial current is:

$$\frac{\partial \Phi_e}{\partial x} = -I_e r_e, \tag{6.1}$$

and likewise the intracellular potential gradient is:

$$\frac{\partial \Phi_i}{\partial x} = -I_i r_i. \tag{6.2}$$

Cable equations (cont.):

If current leaves the intracellular space by crossing the membrane, then the intracellular current will show an axial *decrease*, while the transmembrane current will be *positive*. This conservation of current is described by:

$$\frac{\partial I_i}{\partial x} = -i_m, \qquad (6.3)$$

where i_m is the transmembrane current per unit length.

(Note that i_m is a linear function of the membrane potential under passive (subthreshold) conditions but is a nonlinear function under active (suprathreshold) conditions.)

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

In comparison, if Eqn. (6.2) is differentiated with respect to x and Eqn. (6.3) is substituted for $\partial I_i/\partial x$, then:

$$i_m = \frac{1}{r_i}\frac{\partial^2 \phi_i}{\partial x^2}. \qquad (6.13)$$

- Note that Eqn. (6.12) shows the dependence of the transmembrane current i_m on the transmembrane potential, the injected current and the extra- and intra-cellular resistances.
- In contrast, Eqn. (6.13) describes the dependence of the transmembrane current on the intracellular potential and resistance only.

Potentials ϕ_i *and* ϕ_e *from* v_m*:*

From the cable equations, it is possible to work out how a change in the transmembrane potential is split between the changes in the intra- and extra-cellular potentials: from eqn. (6.8)

$$\phi_i(x,t) = \frac{r_i}{r_i + r_e} v_m(x,t) + \frac{r_i r_e}{r_i + r_e} \int_x^\infty I(x)\,\mathrm{d}x. \qquad (6.20)$$

$$\phi_e(x,t) = -\frac{r_e}{r_i + r_e} v_m(x,t) + \frac{r_i r_e}{r_i + r_e} \int_x^\infty I(x)\,\mathrm{d}x. \qquad (6.22)$$

Potentials ϕ_i and ϕ_e from v_m *(cont.):*

If no source exists within the region (x,1), i.e., $i_p = 0$, then I = 0 in that region and the integrals in Eqns. (6.20) and (6.22) drop out.

In such a *source free region*, the extra- and intra-cellular potentials are related to the transmembrane potential via voltage divider type expressions:

$$\phi_i(x,t) = \frac{r_i}{r_i+r_e} v_m(x,t)\,, \qquad (6.23)$$

$$\phi_e(x,t) = -\frac{r_e}{r_i+r_e} v_m(x,t)\,. \qquad (6.24)$$

Local circuit currents:

Propagation of action potentials can be understood qualitatively by considering the patterns of local currents that are produced by an action potential (site A in the figure below).

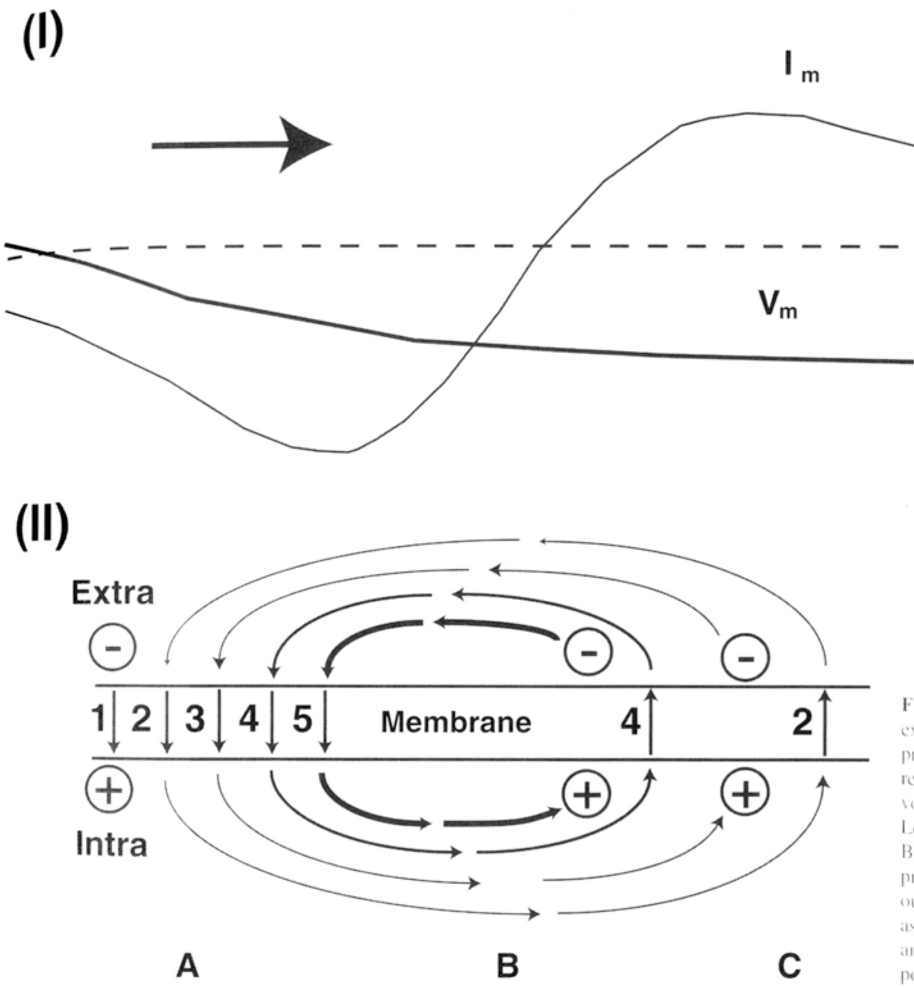

Figure 6.8. Local Circuit Pattern. Panel I (top): The arrow indicates the direction of excitation. Sketches from Figure 6.7 of a segment of the V_m and I_m curves also are present. Panel II (bottom) is a sketch of possible current pathways. The two horizontal lines represent the fiber's membrane, with the extracellular volume above and the intracellular volume below. Five possible current flow pathways are depicted (and discussed in the text). Letters A, B, and C along the axis at bottom identify three major regions as A, sodium influx; B, transition; C, potassium outflux. Along the fiber at the moment depicted, currents of propagation are inward at A, due to the inward movement of sodium ions. At B there is an outward movement of potassium ions. At C there is in effect an outward capacitative current associated with axial current down the longitudinal pathways. Horizontal locations A, B, and C drawn in panel II show currents that correspond approximately to the transmembrane potentials and currents at the same horizontal position.

Local circuit currents (cont.):

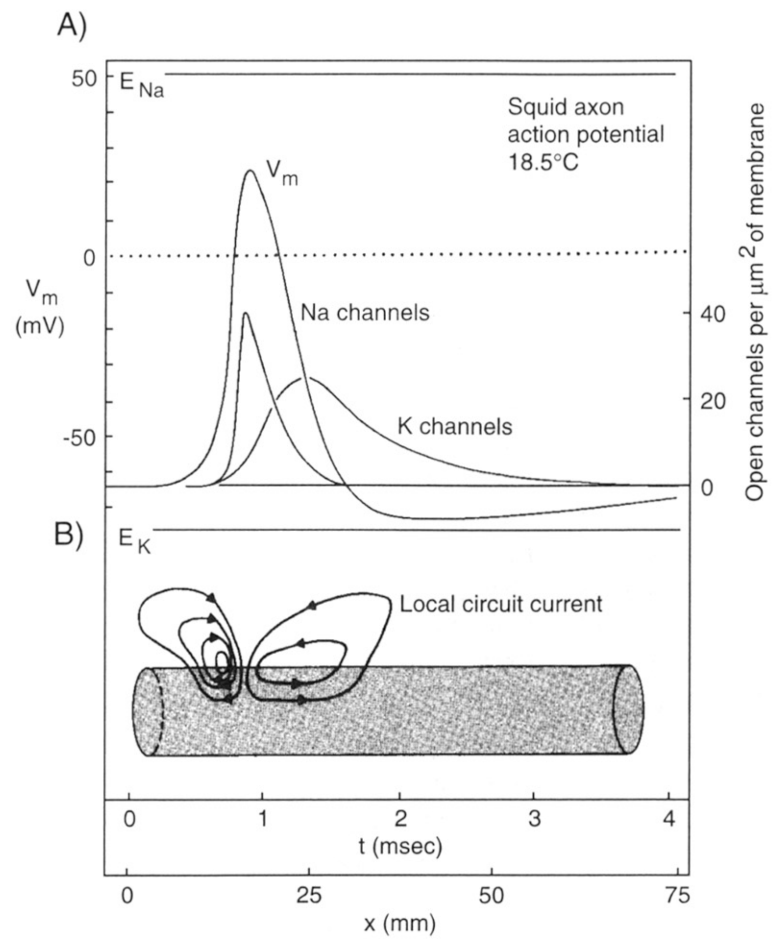

Fig. 6.13 **Local Circuit Current in the Squid Axon** Illustration of the events occurring in the squid axon during the propagation of an action potential. Since the spike behaves like a wave traveling at constant velocity, these two panels can be thought of either as showing the voltages and currents in time at one location or as providing a snapshot of the state of the axon at one particular instant (see the space/time axes at the bottom). **(A)** Distribution of the voltage (left scale) or the number of open channels (right scale) as inferred from the Hodgkin–Huxley model at 18.5° C. **(B)** *Local circuit currents* that spread from an excited patch of the axon to neighboring regions bringing them above threshold, thereby propagating the action potential. The diameter of the axon (0.476 mm) is not drawn to scale. Reprinted by permission from Hille (1992).

(from Koch)

Mathematics of propagating action potentials:

The **cable equations** describe the behaviour of the extra- and intra-cellular (and consequently transmembrane) currents and potentials as a function of **space**, specifically the axial (longitudinal) coordinate x.

In order to describe the **propagation** of transmembrane potentials, i.e., movement in **space** over **time**, we must couple the cable equations with a description of how a patch of membrane behaves as a function of **time**, i.e., the linear (passive) RC circuit equation or the nonlinear (active) HH model equations.

Mathematics of propagating action potentials (cont.):

Consider the membrane current equation generalized to axial position x on a uniform cable:

$$I_m(x,t) = I_{\text{ion}}(x,t) + I_C(x,t)\,. \qquad (6.25)$$

Because of the nature of the capacitive current, Eqn. (6.25) can be reformulated to give:

$$\frac{\partial V_m(x,t)}{\partial t} = \frac{1}{C_m}\left(I_m(x,t) - I_{\text{ion}}(x,t)\right)\,. \quad (6.27)$$

Mathematics of propagating action potentials (cont.):

The transmembrane current per unit area, I_m, is related to i_m (the current per unit length) via the cylindrical geometry, such that:

$$I_m = \frac{i_m}{2\pi a}, \qquad (6.30)$$

and consequently from Eqn. (6.12):

$$I_m = \frac{1}{2\pi a(r_i + r_e)}\left(\frac{\partial^2 V_m}{\partial x^2} - r_e i_p\right). \qquad (6.31)$$

Mathematics of propagating action potentials (cont.):

Eqn. (6.27) gives the partial derivative of the membrane potential with respect to time t, whereas Eqn. (6.31) gives the (2^{nd}) partial derivative with respect to space x.

A single PDE describing the membrane potential behaviour in time and space can be obtained by substituting Eqn. (6.31) into Eqn. (6.27):

$$\frac{\partial V_m}{\partial t} = \frac{1}{C_m}\left[\frac{1}{2\pi a(r_i + r_e)}\left(\frac{\partial^2 V_m}{\partial x^2} - r_e i_p\right) - I_{\text{ion}}(x,t)\right].$$

Mathematics of propagating action potentials (cont.):

To model the propagation of action potentials, the ionic current term from Eqn. (6.27) can be found from the HH model current equations:

$$\begin{aligned} I_{\text{ion}}(x,t) &= g_{\text{K}}(x,t)\,[V_m(x,t)-E_{\text{K}}] \\ &+ g_{\text{Na}}(x,t)\,[V_m(x,t)-E_{\text{Na}}] \\ &+ g_L\,[V_m(x,t)-E_L]\,. \end{aligned} \qquad (6.28)$$

Example propagating action potential:

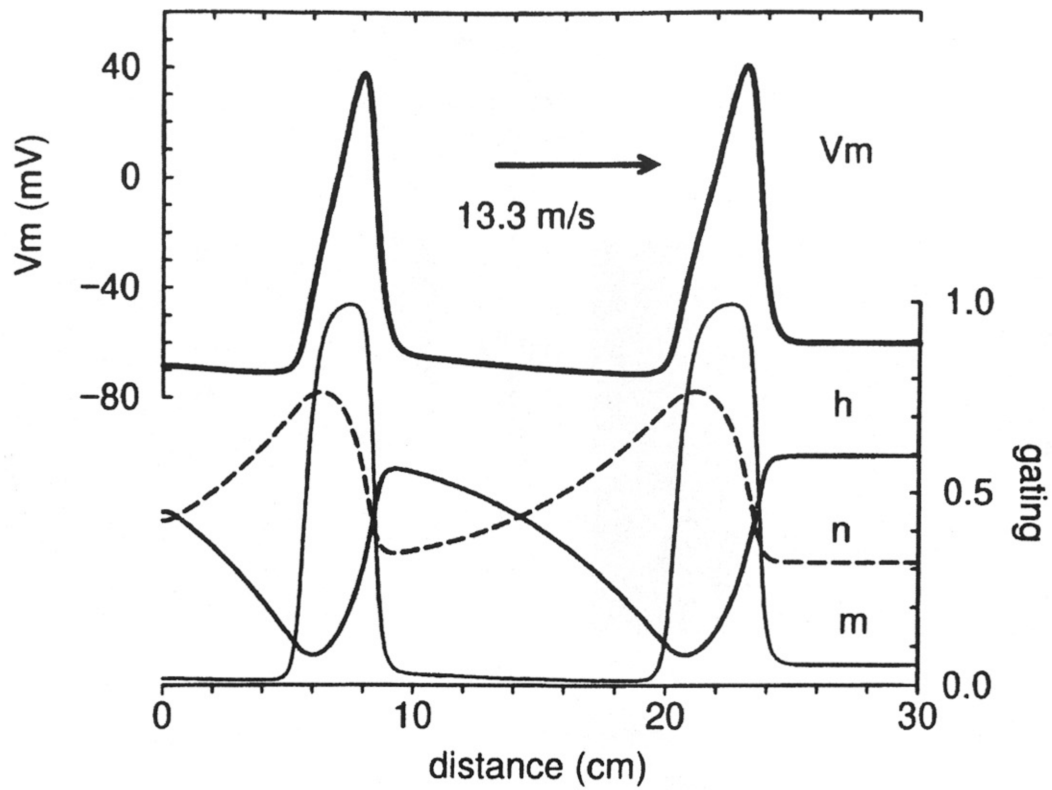

Figure 6.10. Simulation of Propagation on squid axon of diameter 600 μm at $T = 6.3°$C. Hodgkin–Huxley membrane parameters and equations are utilized. The Figure describes the behavior of *gating variables* and transmembrane potential as functions of the axial coordinate. The velocity of propagation is 13.3 m/sec. Following Hodgkin–Huxley, $R_i =$ 30 and $R_e = 20\ \Omega$cm.

Example propagating action potential (cont.):

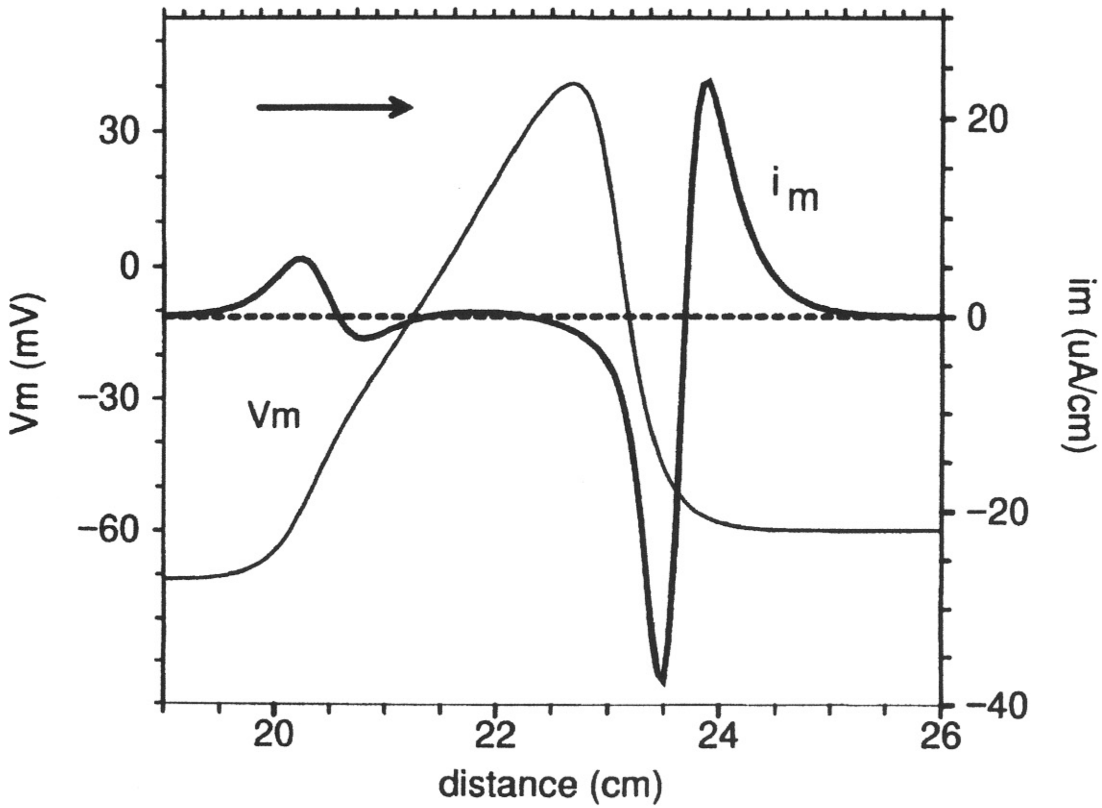

Figure 6.7. Propagating Action Potential and Transmembrane Current. The data come from a simulation of propagation on squid axon of diameter 600 μm at $T = 6.3°$C. The parameter values follow those of Hodgkin–Huxley, whose equations are utilized.

Example propagating action potential (cont.):

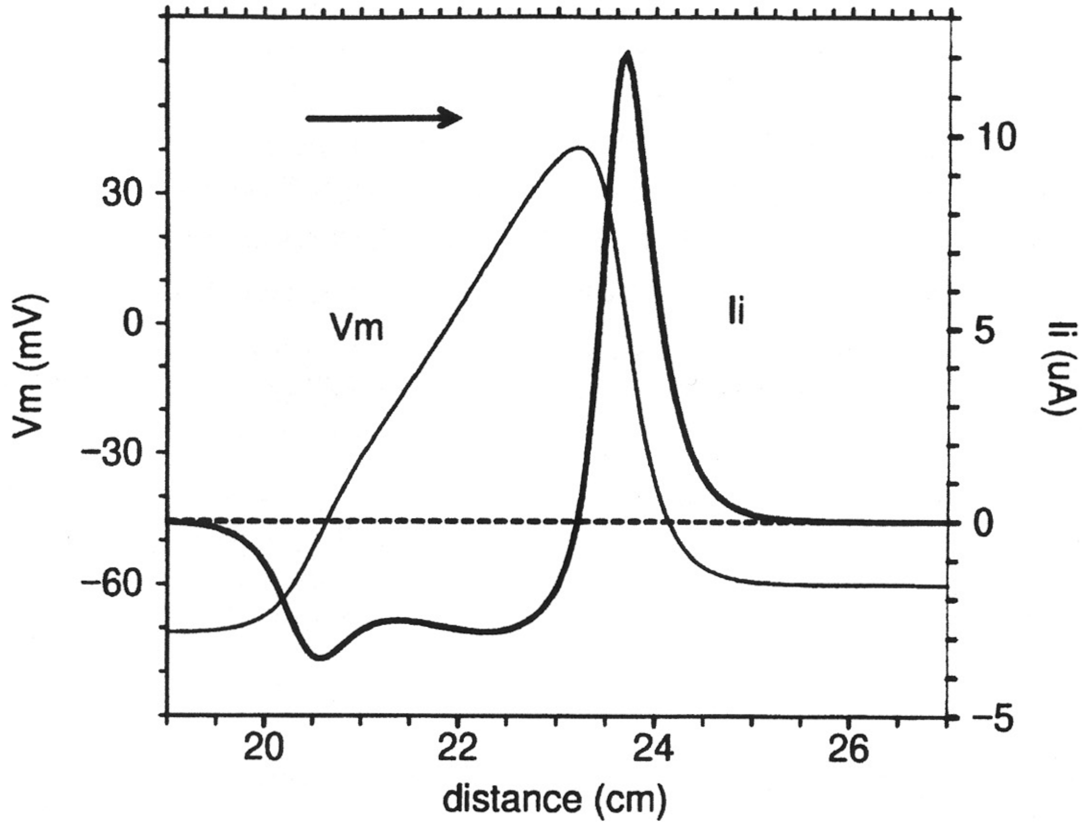

Figure 6.6. Transmembrane Potential and Axial Current from simulation of propagation on squid axon of diameter 600 μm at $T = 6.3°$C. Hodgkin–Huxley membrane parameters and equations are utilized. $R_i = 30\ \Omega$cm and $R_e = 20\ \Omega$cm. The Figure describes the spatial behavior of the transmembrane potential (scale on the left) and the intracellular axial current (scale on the right). The lines overlap so that the time relationships are evident. V_m is given in mV and I_i in μA.