ELEC ENG 3BB3:

Cellular Bioelectricity

Notes for Lecture 9

Thursday, January 23, 2014

4. ACTION POTENTIALS

We will look at:

- Observing action potentials
- Nonlinear membrane behaviour
- Origin of action potential, resting and peak voltages
- Voltage and space clamp
- Hodgkin-Huxley equations
- Simulation of membrane action potential
- Action potential characteristics
- Active transport
- Calcium channels and "other" membrane models

Observing action potentials:

If an adequate current flows between a pair of stimulating electrodes producing a transmembrane current in an excitable cell, an *action potential* (AP) is generated in the membrane at the site of the electrodes.

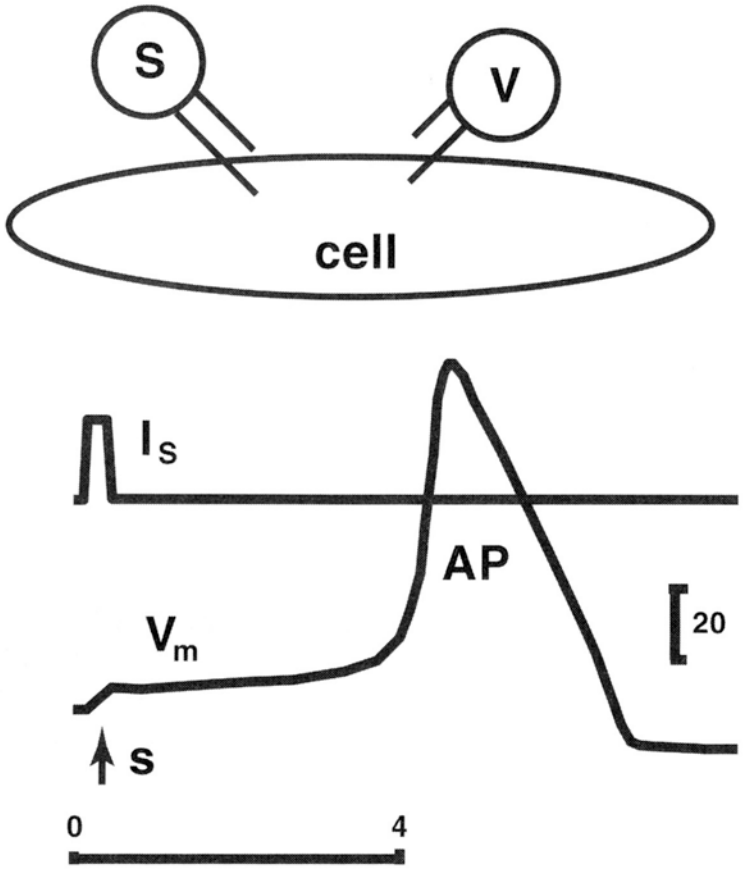


Figure 5.1. Electrical Stimulation of an Excitable Cell. The stimulus elicits an action potential. The top drawing shows a cartoon of a cell with a stimulator S and a voltmeter V attached. The stimulator injects current into the intracellular volume (positive electrode) and removes current from the surrounding extracellular volume. The voltmeter measures transmembrane voltage as a function of time. It is assumed that regions within and around the cell are equipotential, so that a uniform voltage difference exists across all points on the cell membrane. The upper trace shows a stimulus current, I_S, which delivers a short current pulse of 0.3-msec duration, beginning at $t = 0$. The lower trace shows the voltage record, $V_m(t)$. The deflections on the voltage trace are first the direct response to the stimulus, identified with s, and, 4 msec later, a much larger deflection, the action potential (marked AP). The vertical calibration corresponds to 20 μA/cm^2 on the current plot and 20 mV on the voltage plot.

An experimental setup for recording action potentials:

An action potential *propagates* to all parts of the cell.

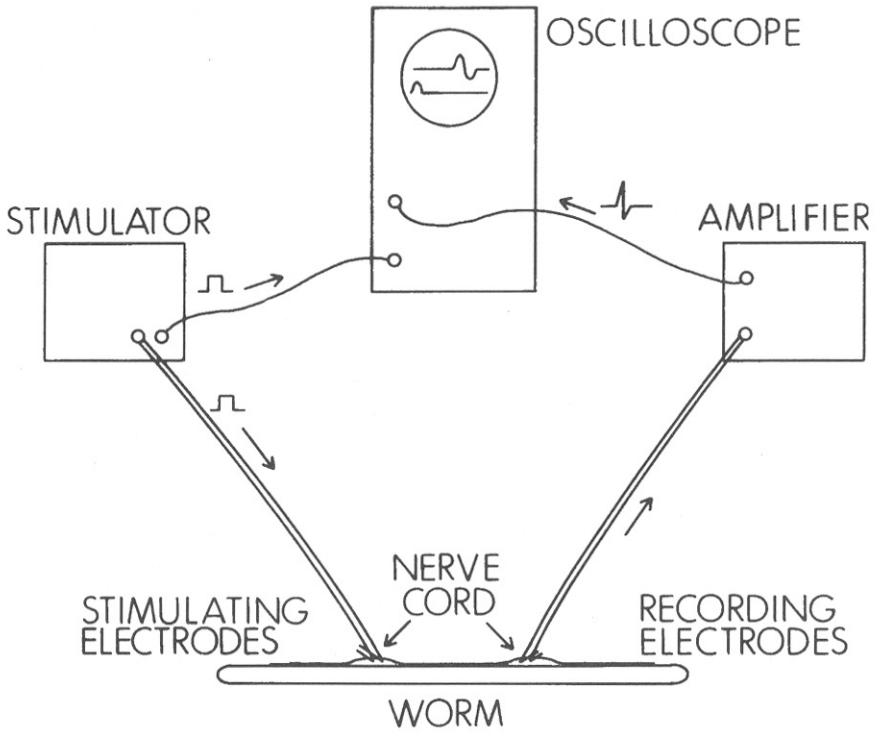


Figure 5.2. Arrangement for recording action potentials from the giant fibers in the nerve cord of the earthworm. (From D. J. Aidley, *The Physiology of Excitable Cells*, Cambridge University Press, Cambridge. 1978. Reprinted with the permission of Cambridge University Press.)

Observing action potentials (cont.):

No action potentials

Action potentials

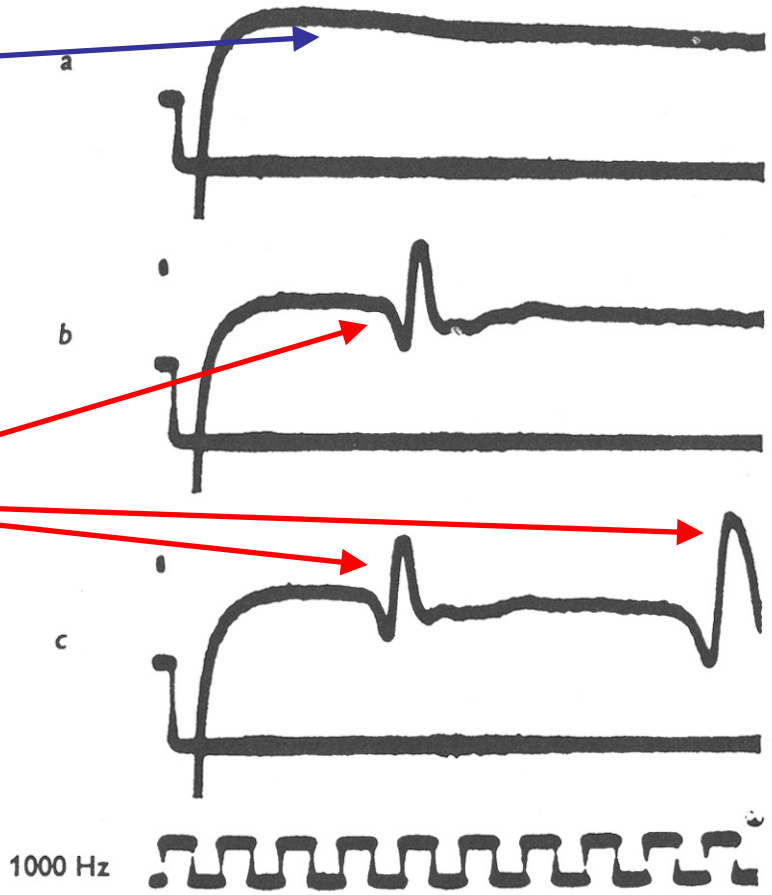
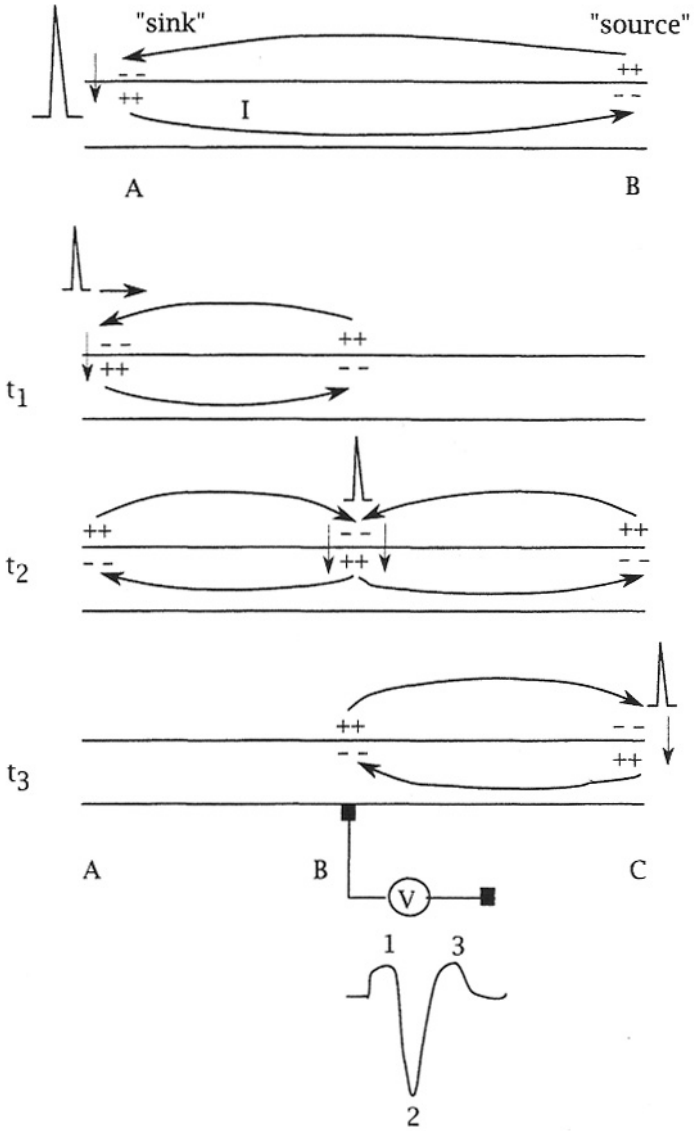


Figure 5.3. Oscilloscope records from the experiment shown in Fig. 5.2. In each case the upper trace is a record of the potential changes at the recording electrode and the lower trace (at a much lower amplification) monitors the stimulus pulse. (From D. J. Aidley, *The Physiology of Excitable Cells*, Cambridge University Press, Cambridge. 1978. Reprinted with the permission of Cambridge University Press.)

Observing action potentials (cont.):



(from Johnston and Wu)

Figure 14.1 Action potential propagation along an axon. In the upper diagram an action potential is initiated at A and the current flow (I) from A to B is indicated. The bottom three diagrams illustrate a time sequence ($t_1 < t_2 < t_3$) for the propagation of an action potential from A to B to C. The recording at B indicates a positivity (1), a negativity (2), and a positivity (3) corresponding to this time sequence of AP propagation (see text for further explanation).

Action potentials are:

- *all-or-nothing* events,
- *regenerative*,
- generated when a *threshold* is reached,
- *propagating* potentials, and
- also known as nerve *spikes* or *impulses*.

Transmembrane action potential morphology:

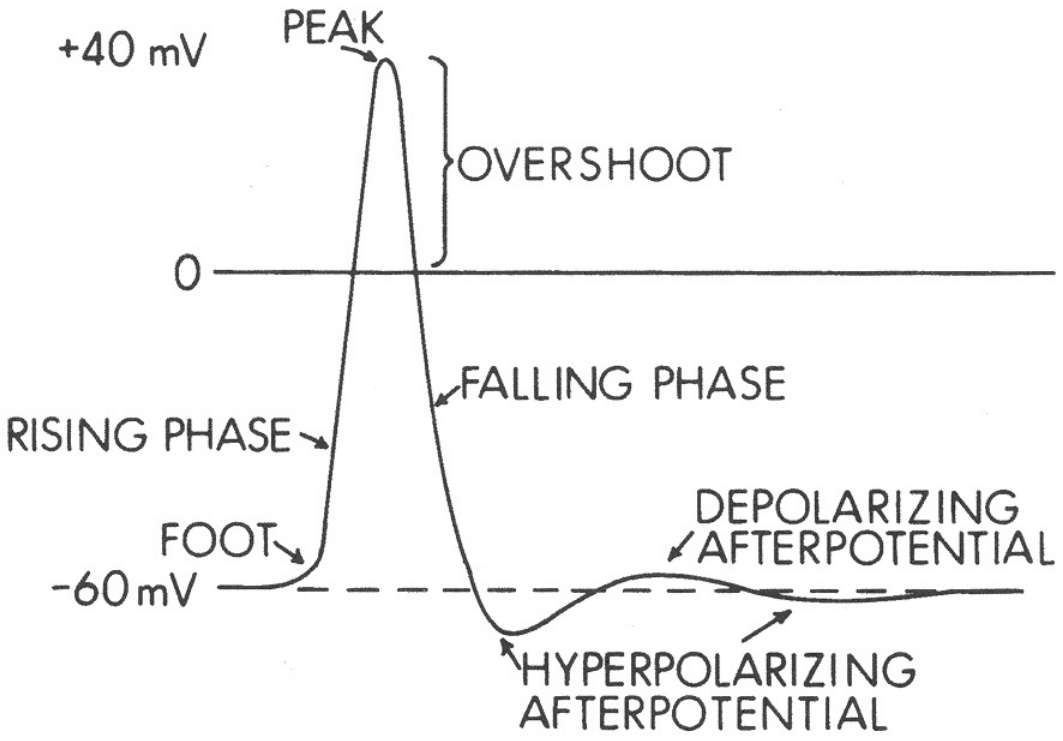


Figure 5.4. Diagram to show the nomenclature applied to an action potential and the afterpotentials that may follow it.

Observing action potentials (cont.):

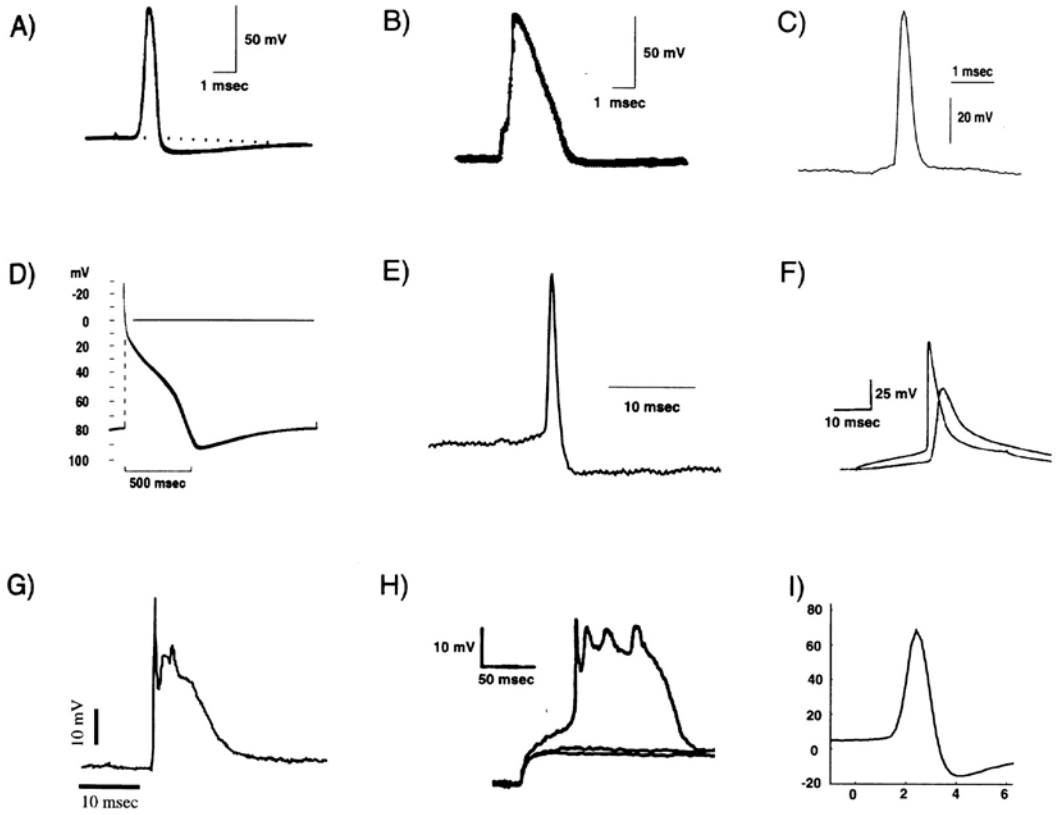


Fig. 6.1 ACTION POTENTIALS OF THE WORLD Action potentials in different invertebrate and vertebrate preparations. Common to all is a threshold below which no impulse is initiated, and a stereotypical shape that depends only on intrinsic membrane properties and not on the type or the duration of the input. **(A)** Giant squid axon at 16° C. Reprinted by permission from Baker, Hodgkin, and Shaw (1962). **(B)** Axonal spike from the node of Ranvier in a myelinated frog fiber at 22° C. Reprinted by permission from Dodge (1963). **(C)** Cat visual cortex at 37° C. Unpublished data from J. Allison, printed with permission. **(D)** Sheep heart Purkinje fiber at 10° C. Reprinted by permission from Weidmann (1956). **(E)** Patch-clamp recording from a rabbit retinal ganglion cell at 37° C. Unpublished data from F. Amthor, printed with permission. **(F)** Layer 5 pyramidal cell in the rat at room temperatures. Simultaneous recordings from the soma and the apical trunk. Reprinted by permission from Stuart and Sakmann (1994). **(G)** A complex spike—consisting of a large EPSP superimposed onto a slow dendritic calcium spike and several fast somatic sodium spikes—from a Purkinje cell body in the rat cerebellum at 36° C. Unpublished data from D. Jaeger, printed with permission. **(H)** Layer 5 pyramidal cell in the rat at room temperature. Three dendritic voltage traces in response to three current steps of different amplitudes reveal the all-or-none character of this slow event. Notice the fast superimposed spikes. Reprinted by permission from Kim and Connors (1993). **(I)** Cell body of a projection neuron in the antennal lobe in the locust at 23° C. Unpublished data from G. Laurent, printed with permission.

(from Koch)

Nonlinear membrane behaviour:

Subthreshold and action potential responses to a brief stimulating current.

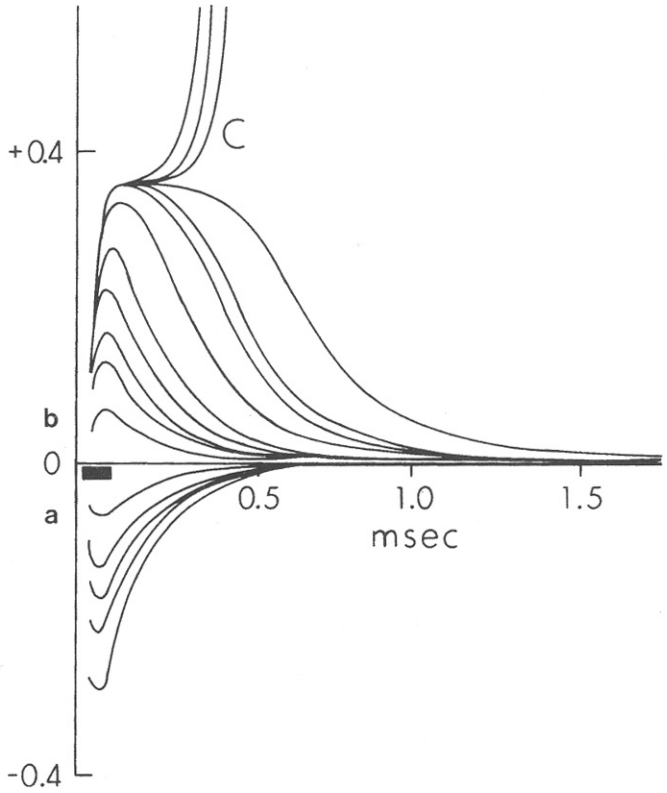


Figure 5.5. Subthreshold responses recorded extracellularly from a crab axon in the vicinity of the stimulating electrodes. The axon was placed in paraffin oil, and, consequently the measured extracellular potential is directly related to the transmembrane potential (according to the linear core-conductor model described in Chapter 6). The heavy bar indicates the stimulus period, which was approximately 50 μsec in duration. The ordinate is a voltage scale on which the height of the action potential is taken as one unit. [From A. L. Hodgkin, The subthreshold potentials in a crustacean nerve fibre, *Proc. R. Soc. London, Ser. B* **126**:87–121 (1938).]

Nonlinear membrane behaviour (cont.):

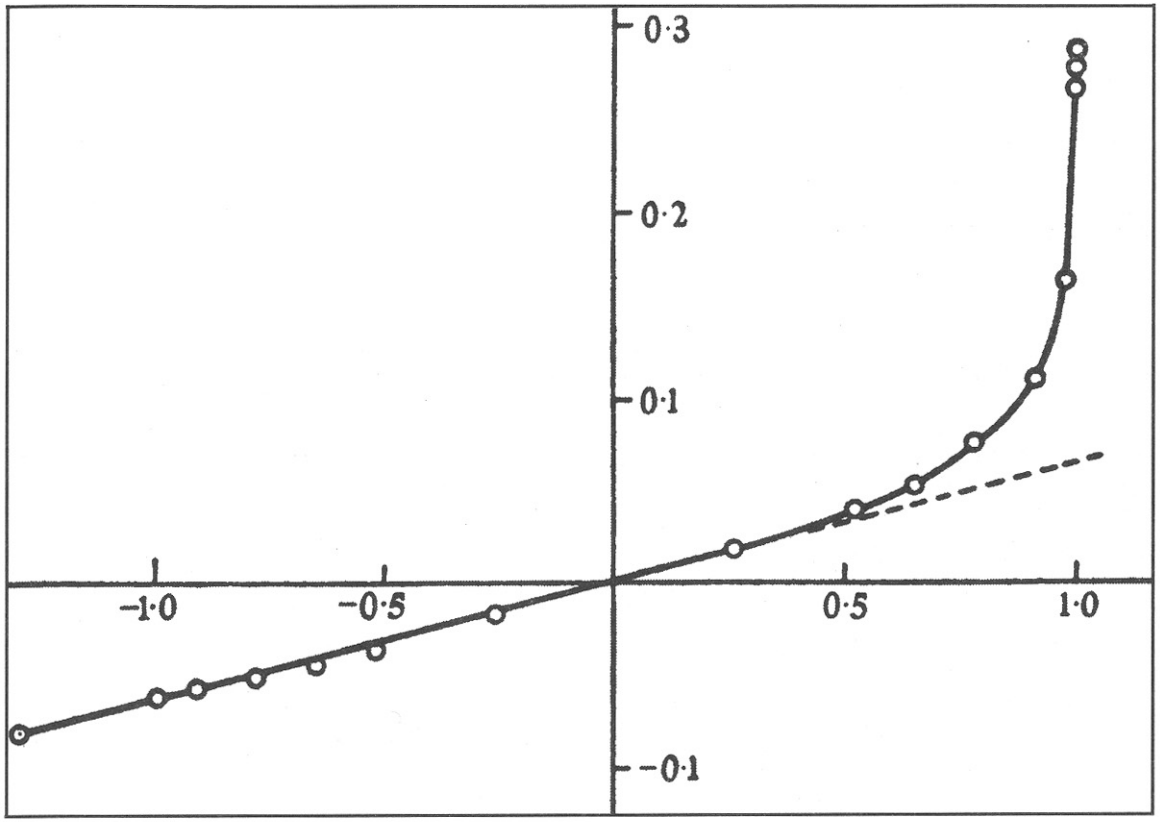


Figure 5.6. The relation between stimulus and response in a crab axon. This figure was derived from Fig. 5.5. The abscissa shows the stimulus intensity, measured as a fraction of the threshold stimulus. The ordinate shows the recorded potential 0.29 msec after the stimulus, measured as a fraction of the action potential peak. [Reprinted with permission from A. L. Hodgkin, The subthreshold potentials in a crustacean nerve fibre, *Proc. R Soc. London, Ser. B* **126**:87–121 (1938).]

Nonlinear membrane behaviour (cont.):

For the squid axon:-

- C_m = 1 μF/cm^2 throughout the entire action potential
- R_m = 1000 Ω cm^2 at rest
- R_m = 25 Ω cm^2 at the peak of the action potential

Origin of action potential, resting and peak voltages:

In the classic studies by Hodgkin and Huxley, the results were related to the Goldman-Hodgkin-Katz (GHK) equation for the transmembrane potential:

$$V_m = \frac{RT}{F} \ln \left[\frac{P_{\mathrm{K}}[\mathrm{K}]_e + P_{\mathrm{Na}}[\mathrm{Na}]_e + P_{\mathrm{Cl}}[\mathrm{Cl}]_i}{P_{\mathrm{K}}[\mathrm{K}]_i + P_{\mathrm{Na}}[\mathrm{Na}]_i + P_{\mathrm{Cl}}[\mathrm{Cl}]_e} \right], \quad (5.1)$$

where P_p is the *permeability* of the p^{th} ion channel.

(The GHK equation is derived from the Nernst-Planck equation, making simplifying assumptions about the electric potential and concentration gradients inside the channel.)

Origin of action potential, resting and peak voltages (cont.):

As we have observed previously, the **resting transmembrane potential** is slightly higher than the **potassium equilibrium potential**.

Looking at the action potential waveform, we see that the **peak transmembrane potential** approaches but never exceeds the **sodium equilibrium potential**.

Origin of action potential, resting and peak voltages (cont.):

This result is consistent with an elevated sodium permeability in the rising phase and peak of the action potential.

Good agreement between theory and experimental data from the squid axon is obtained with:

$$P_{\mathrm{K}}{:}P_{\mathrm{Na}}{:}P_{\mathrm{Cl}} = 1.0{:}0.04{:}0.45 \quad \text{for membrane at rest}$$

$$P_{\mathrm{K}}{:}P_{\mathrm{Na}}{:}P_{\mathrm{Cl}} = 1.0{:}20.0{:}0.45 \quad \text{at an action potential peak}$$

Origin of action potential, resting and peak voltages (cont.):

To a first approximation:

$$\text{At rest: } V_m \approx E_{\mathsf{K}} = \frac{RT}{F} \ln\left(\frac{[\mathsf{K}]_o}{[\mathsf{K}]_i}\right) \qquad (5.7)$$

$$\text{At the peak: } V_m \approx E_{\mathsf{Na}} = \frac{RT}{F} \ln\left(\frac{[\mathsf{Na}]_o}{[\mathsf{Na}]_i}\right) \qquad (5.8)$$

Origin of action potential, resting and peak voltages (cont.):

In an experiment using radioactive tracers, it was found for the cuttlefish *Sepia* giant axon that:

- at rest, there is steady influx of sodium and efflux of potassium, consistent with $E_K < V_{rest} < E_{Na}$
- during an action potential there is an influx of 3.7 pmoles/cm^2 of sodium
- during an action potential there is an efflux of 4.3 pmoles/cm^2 of potassium

Origin of action potential, resting and peak voltages (cont.):

These results can be compared with the charge movement required to depolarize the transmembrane potential by around 125 mV:

$$Q = CV = 1.0 \times 10^{-6} \times 0.125$$
$$= 1.25 \times 10^{-7}\ \mathrm{C/cm^2}$$

$$\Rightarrow \text{number of mole} = Q/F$$
$$= 1.25 \times 10^{-7}/96487$$
$$= 1.3\ \mathrm{pmol/cm^2}$$