ELEC ENG 791:

Sensory and Neuromuscular Engineering

Lecture 1

Monday, January 12, 2015

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1. INTRODUCTION TO BIOELECTRICITY AND EXCITABLE CELLS

Historical perspective:

- Bioelectricity first discovered by Luigi Galvani in 1780s
- Originally termed “animal electricity”
- Galvani thought that a special electrical fluid was prepared by the brain, flowing through the nerve tubes into muscles

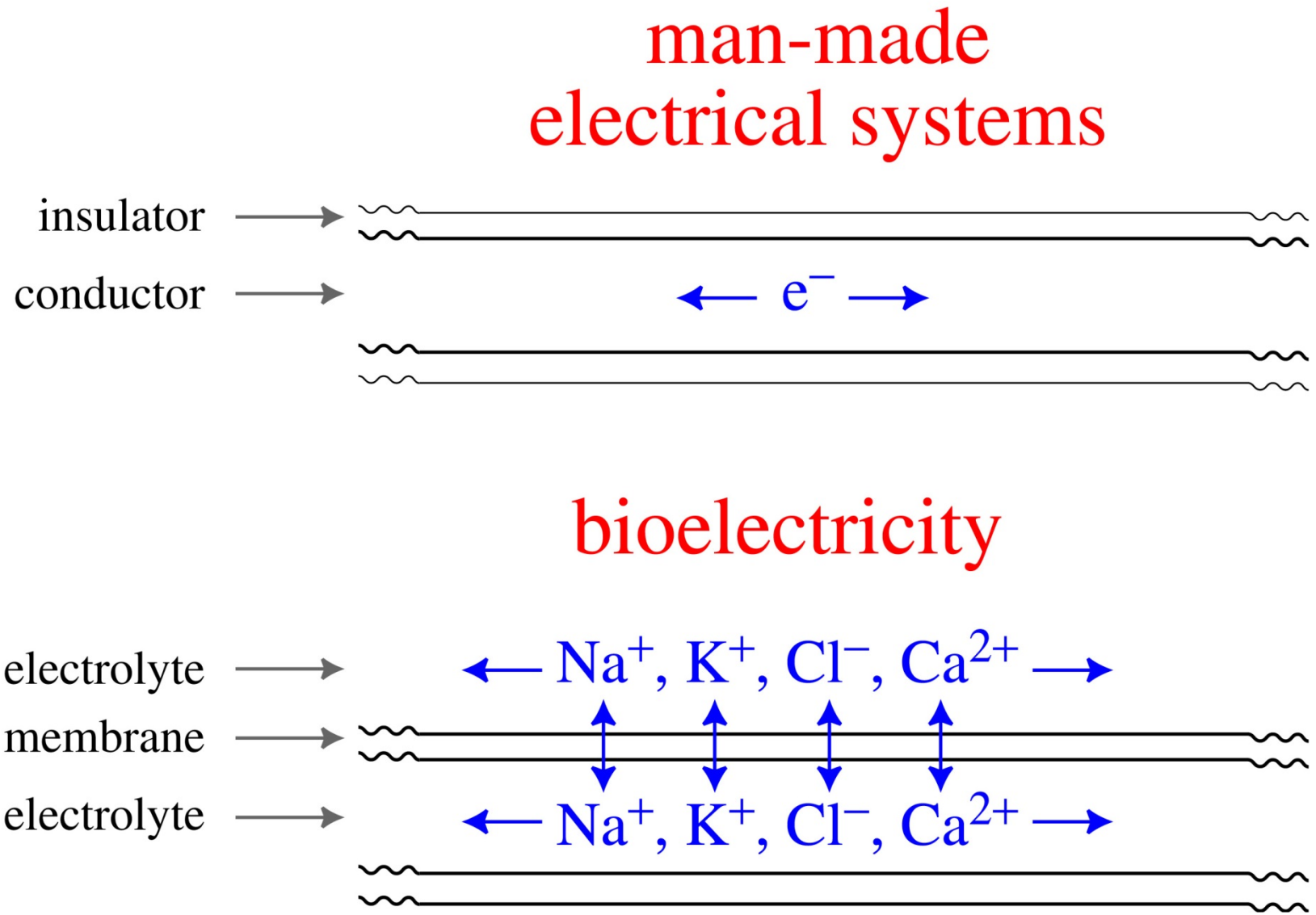
Modern perspective:

- Bioelectricity is now known to obey the same fundamental laws of electricity in the atmosphere, conducting wires, semiconductors, etc.
- However, there are some substantial differences between bioelectrical systems and man-made electrical systems.

Comparison of bioelectricity and man-made electrical systems:

Man-made electrical systems	Charge carriers are electrons within a conductor	Current flow within (insulated) conductors
Bioelectricity	Charge carriers are ions within an electrolyte	Current flow inside *and outside* of (partially-insulated) cell membranes

Comparison (cont.):



Ionic flow in terms of particle movement:

- From the perspective of *chemistry*, ionic movements are described in terms of *moles*, where one mole is:

  $N_A = 6.0225 \times 10^{23}$ molecules,

  Avogadro's number.

- *Ionic flows* are then described in units of moles per second and *fluxes* (here denoted by the lowercase letter j) in units of moles per second per unit area.

Ionic flow in terms of charge movement:

- From the perspective of *electricity*, ionic movements are described in terms of *coulombs*, where an electron (and hence a *univalent ion*) has an electrical charge of 1.6×10^{-19} coulombs.
- *Ionic flows* are then described in units of coulombs per second (or amperes) and *fluxes* (here denoted by the uppercase letter J) in units of amperes per unit area, e.g., amperes per cm^2.

Converting between particle flow and electrical current:

- Ionic movement can be described in terms of either particle flow or electrical current.
- The conversion factor is Faraday's constant:

$$F = \left(6.02 \times 10^{23}\right) \frac{\text{particles}}{\text{mole}} \times \left(1.6 \times 10^{-19}\right) \frac{\text{columbs}}{\text{particle}} = 96,487 \ \frac{\text{columbs}}{\text{mole}}$$

Ionic composition of excitable cells:

- *Sodium* (Na^+) and *potassium* (K^+) are the most important ions for the electrical activity of the majority of excitable cells.
- *Calcium* (Ca^{2+}) and *chloride* (Cl^i) play a significant role in some circumstances.
- Many of the fundamental properties of ionic movement are the same no matter which ion is being considered.

  Consequently, we will often derive mathematical expressions for "the p^{th} ion".

Ionic composition (cont.):

- Example intra- and extra-cellular ionic concentrations are given below.

Table 3.1. Ionic Concentrations[a]

	Concentration (nM/l)			
	Muscle (frog)		Nerve (squid axon)	
	Intracellular	Extracellular	Intracellular	Extracellular
K^+	124	2.2	397	30
Na^+	4	109	50	437
Cl^-	1.5	77	40	556
A^-	126.5			

[a]The A^- ion is large and impermeable.

- Note that the particular ratios of intra- to extra-cellular ionic concentrations are similar across different types of excitable cells.

Nernst-Planck Equation:

- The *Nernst-Planck* equation describes the effects of spatial differences in *concentration* and/or *electric potential* on ion flow.
- The individual effect of a concentration gradient is described by *Fick's law of diffusion*.
- The individual effect of an electric potential gradient is described by *Ohm's law of drift*.

Excitable cells:

- Cells that can generate electrical potentials and currents are referred to as *excitable cells*.
- These potentials and currents can be observed in the cells' interior volume, across their membranes, and in their surrounding conducting volume.
- Excitable cells include *nerve cells* (*neurons*), *muscle fibers*, and *sensory receptor* (*transducer*) *cells*.

Membrane structure:

- Excitable cells are surrounded by a *plasma membrane* consisting of a lipid bilayer.
- The passage of ions through the membrane is regulated by:

1. Pumps and exchangers

2. Channels

Membrane structure (cont.):

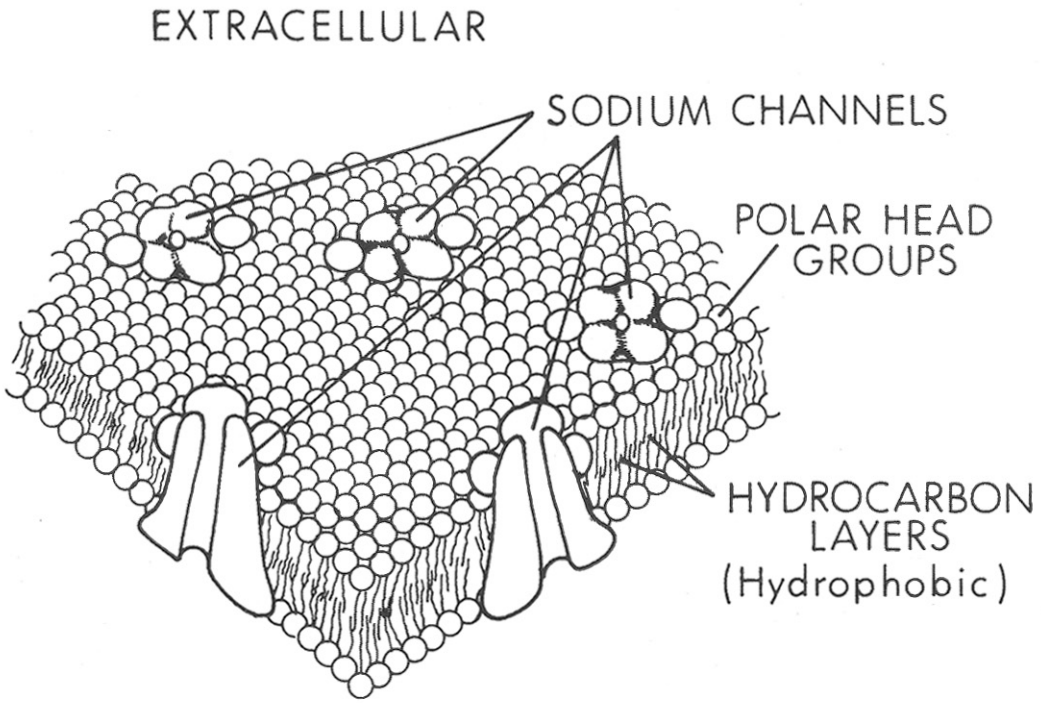


Figure 3.1. Schematic representation of the model of membrane structure showing sodium channel proteins embedded in the lipid bilayer matrix of the membrane. The channel density is unphysiologically high, for illustrative purposes. [Drawing based on W. A. Catterall et al., "Structure and modulation of voltage-gated sodium channels" in "Ion Channels in the Cardiovascular System," P. M. Spooner and A. M. Brown, eds., Futura, Armonk, New York, 1994.

Pumps and exchangers:

- Pumps are active processes (i.e., they consume energy) that move ions against the concentration gradients.
- Exchangers use the concentration gradient of one ion to move another ion against its concentration gradient.
- The purpose of pumps and exchangers is to maintain the different intra- and extra-cellular ionic concentrations.
- The major ion transporters are: Na^+-K^+ pump, Na^+-Ca^{2+} exchanger, Ca^{2+} pump, Bicarbonate-Cl^i exchanger, Cl^i-Na^+-K^+ cotransporter.

Membrane capacitance:

- The lipid membrane itself has a specific resistance of $10^9\ \Omega \cdot cm^2$, i.e., it is effectively an *insulator*.
- Consequently, charge can build up on each side of the membrane in regions where there are no channels or where channels are closed.
  Because of the thinness of the membrane, it acts as a *capacitor*, with a capacitance typically around
  $C_m = 0.9\ \mu F/\ cm^2$.

Ion flow through open channels:

- From the Nernst-Planck equation, the flow of the p^{th} ion will depend on both the concentration gradient of the p^{th} ion and an electric potential gradient.
- For an excitable cell, the unequal concentration of ions in the intra- versus extra-cellular spaces produces ion flow through any open ion channels.
- Ions will accumulate on the membrane because of its capacitance, producing an electrical field across and within the membrane that will in turn exert a force on all charged particles within ion channels.

Nernst equilibrium:

A *Nernst equilibrium* is achieved for a particular ion when the electric field force exactly counteracts the force of the concentration gradient for that ion, such that the net flow through an ion channel is zero:

$$\bar{J}_p = 0 = -D_p F Z_p \left[\nabla C_p + \frac{Z_p C_p F}{RT} \nabla \Phi \right], \quad (3.15)$$

and hence:

$$\nabla C_p = -\frac{Z_p C_p F}{RT} \nabla \Phi. \quad (3.16)$$

Nernst potential:

Thus the potential difference across the membrane at equilibrium, referred to as the **Nernst potential**, is:

$$V_m^{eq} = \Phi_i - \Phi_e = \frac{-RT}{Z_p F} \ln\left(\frac{[C_p]_i}{[C_p]_e}\right), \quad (3.21)$$

where the transmembrane potential V_m is defined as the intracellular potential Φ_i minus the extracellular potential Φ_e.

Equilibrium potentials:

The Nernst potential for a particular ion is often referred to as the *equilibrium potential* and is given the symbol E_p.

For example, the equilibrium potentials for sodium and potassium ions are given the symbols E_{Na} and E_K, respectively.

The equilibrium potential is also sometimes referred to as the *reversal potential*, because at this potential the direction of the ionic current reverses from inwards to outwards, or vice versa.

Example equilibrium potentials:

Table 2.1 Ion concentrations and equilibrium potentials

	Inside (mM)	Outside (mM)	Equilibrium Potential (NE) $E_i = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}}$
Frog muscle (Conway 1957)			$T = 20°C = 293°K$
K^+	124	2.25	$58 \log \frac{2.25}{124} = -101$ mV
Na^+	10.4	109	$58 \log \frac{109}{10.4} = +59$ mV
Cl^-	1.5	77.5	$-58 \log \frac{77.5}{1.5} = -99$ mV
Ca^{2+}	$4.9^\dagger$	2.1	$29 \log \frac{2.1}{10^{-4}} = +125$ mV
Squid axon (Hodgkin 1964)			
K^+	400	20	$58 \log \frac{20}{400} = -75$ mV
Na^+	50	440	$58 \log \frac{440}{50} = +55$ mV
Cl^-	40–150	560	$-58 \log \frac{560}{40-150} = -66 - (-33)$ mV
Ca^{2+}	$0.4^\dagger$	10	$29 \log \frac{10}{10^{-4}} = +145$ mV
Typical mammalian cell			$T = 37°C = 310°K$
K^+	140	5	$62 \log \frac{5}{140} = -89.7$ mV
Na^+	5–15	145	$62 \log \frac{145}{5-15} = +90.7 - (+61.1)$ mV
Cl^-	4	110	$-62 \log \frac{110}{4} = -89$ mV
Ca^{2+}	$1–2^\dagger$	2.5–5	$31 \log \frac{2.5-5}{10^{-4}} = +136 - (+145)$ mV

$^\dagger(10^{-4})$ free

(from Johnston and Wu)

Relative charge depletion and electroneutrality:

The Nernst equilibrium is achieved via movement of ions from the inside to the outside of the membrane, which might (i) deplete a particular ion and (ii) move the electrolyte away from a condition of *electroneutrality*.

However, for typical intra- and extra-cellular volumes found in excitable cells, movement of *less than 0.1%* of available ions is capable of charging up the membrane, i.e., changing the membrane potential by values on the order of 100 mV, and thus charge depletion and loss of electroneutrality are typically negligible.

Parallel conductance model (cont.):

- Simplifying assumptions can be made about the concentration and electric potential gradients, but unfortunately the resulting mathematical expressions do *not* accurately describe the behaviour of most ion channels.
- Consequently, a phenomenological description of current flow in ionic channels is typically used. This **parallel conductance model** does incorporate three earlier results:
  1. the *capacitance* of the plasma membrane,
  2. the *conductive* nature of ion flow, and
  3. the *equilibrium potential* for each ion.

Parallel conductance model (cont.):

Assuming independent conductance channels for K^+, Na^+ and Cl^i, the electric circuit for a *membrane patch* is:

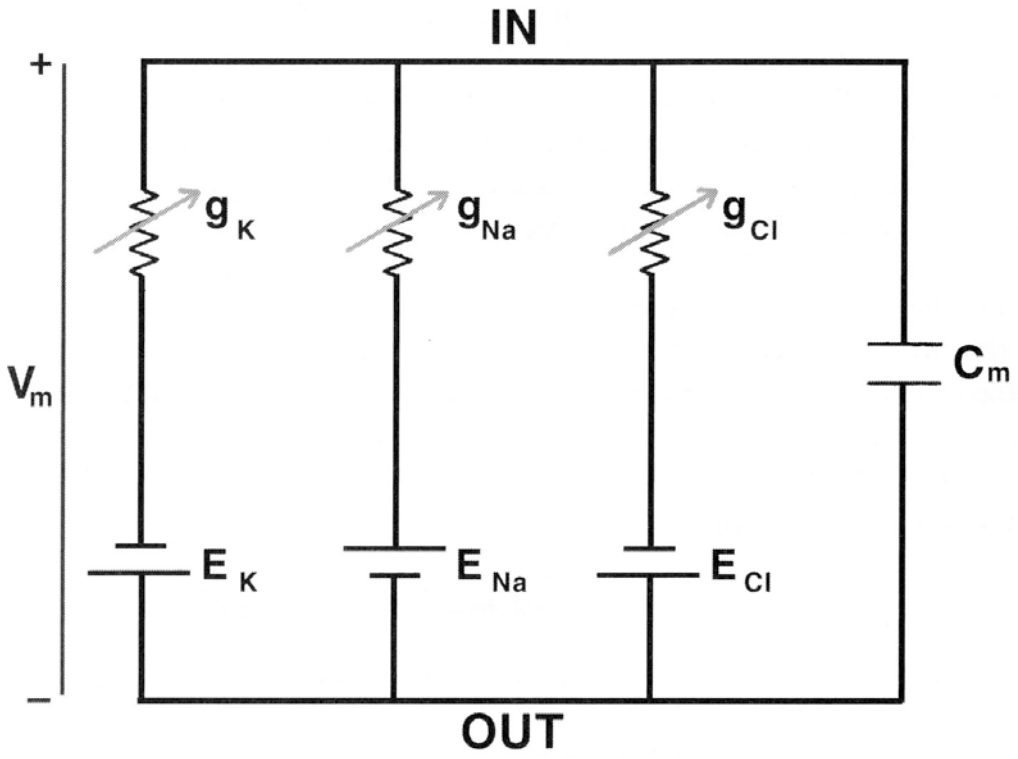


Figure 3.3. The Parallel-Conductance Model of an Excitable Membrane (IN = intracellular, OUT = extracellular). Independent conductance channels are present for K^+, Na^+, and Cl^-. Transmembrane potential V_m is positive when the inside has higher potential than the outside. The battery polarity is chosen to show that usually the Nernst potentials of E_K and E_{Cl} are negative (inside more negative than outside) and that of E_{Na} is positive (inside more positive than outside).

Ionic currents:

The current for the p^{th} ion is assumed to be proportional to how far the membrane potential V_m deviates from the equilibrium potential E_p, with the constant of proportionality g_p corresponding to the instantaneous conductance of the channel.

For the three ionic channels shown in Fig. 3.3, we have:

$$I_{\mathrm{K}} = g_{\mathrm{K}} (V_m - E_{\mathrm{K}}) \tag{3.26}$$

$$I_{\mathrm{Na}} = g_{\mathrm{Na}} (V_m - E_{\mathrm{Na}}) \tag{3.27}$$

$$I_{\mathrm{Cl}} = g_{\mathrm{Cl}} (V_m - E_{\mathrm{Cl}}) \tag{3.28}$$

Capacitive current:

The capacitive current is:

$$I_C = C\frac{\mathrm{d}V_m}{\mathrm{d}t}, \qquad (3.29)$$

where C is the capacitance for the patch of membrane.

Importantly, at rest (i.e., at steady state), $I_C = 0$ because $dV_m/dt = 0$.

Resting V_m *at steady-state:*

The total transmembrane current is:

$$I_m = I_C + I_{\mathsf{K}} + I_{\mathsf{Na}} + I_{\mathsf{Cl}}.$$

Assuming that no current is being injected into the intra- or extra-cellular space, the total transmembrane current must be zero, such that at steady state:

$$I_m = 0 = 0 + I_{\mathsf{K}} + I_{\mathsf{Na}} + I_{\mathsf{Cl}}$$

$$\Rightarrow g_{\mathsf{K}}\left(V_m - E_{\mathsf{K}}\right) + g_{\mathsf{Na}}\left(V_m - E_{\mathsf{Na}}\right) + g_{\mathsf{Cl}}\left(V_m - E_{\mathsf{Cl}}\right) = 0. \qquad (3.30)$$

Resting V_m *at steady-state (cont.):*

Solving for V_m to obtain the *resting transmembrane potential* V_{rest} gives:

$$V_{\text{rest}} = \frac{g_{\text{K}} E_{\text{K}} + g_{\text{Na}} E_{\text{Na}} + g_{\text{Cl}} E_{\text{Cl}}}{g_{\text{K}} + g_{\text{Na}} + g_{\text{Cl}}}. \quad (3.31)$$

That is, the resting membrane potential is the weighted sum of the equilibrium potentials, where the weightings depend on the resting values of the ionic conductances.

Example resting V_m*:*

Assuming the following equilibrium potentials and resting ionic conductances for the squid axon:

$$\begin{aligned} E_{\mathrm{K}} &= -74.7\ \mathrm{mV}, & g_{\mathrm{K}} &= 0.367\ \mathrm{mS/cm^2}, \\ E_{\mathrm{Na}} &= \ \ 54.2\ \mathrm{mV}, & g_{\mathrm{Na}} &= 0.010\ \mathrm{mS/cm^2}, \\ E_{\mathrm{Cl}} &= -65.8\ \mathrm{mV}, & g_{\mathrm{Cl}} &= 0.582\ \mathrm{mS/cm^2}, \end{aligned}$$

from Eqn. (3.31) we find that the resting membrane potential is $V_m = -68.0$ mV.

Contributions from chloride:

Although the resting membrane potential in the previous example is quite close to the chloride equilibrium potential, it is primarily potassium that determines the resting potential (which would be ¼ ¡ 71.0 mV if the chloride channel were ignored).

This is because the intracellular chloride concentration is so small that it undergoes large percentage changes with just small amounts of chloride influx or efflux.

Consequently, the chloride equilibrium potential tends to track the resting potential determined by potassium.

Effect of I_m *and* I_{ion} *on* V_m*:*

The total transmembrane current I_m can change because of current injected into a patch of membrane by an electrode in a physiological experiment or by a propagating potential under normal physiological operation.

Alternatively, the net ionic current I_{ion} can change because of ion channel gating, i.e., changes in g_p giving rise to a change in the membrane resistance R.

How do each of these factors contribute to changes in the transmembrane potential V_m?

Effect of I_m *and* I_{ion} *on* V_m *(cont.):*

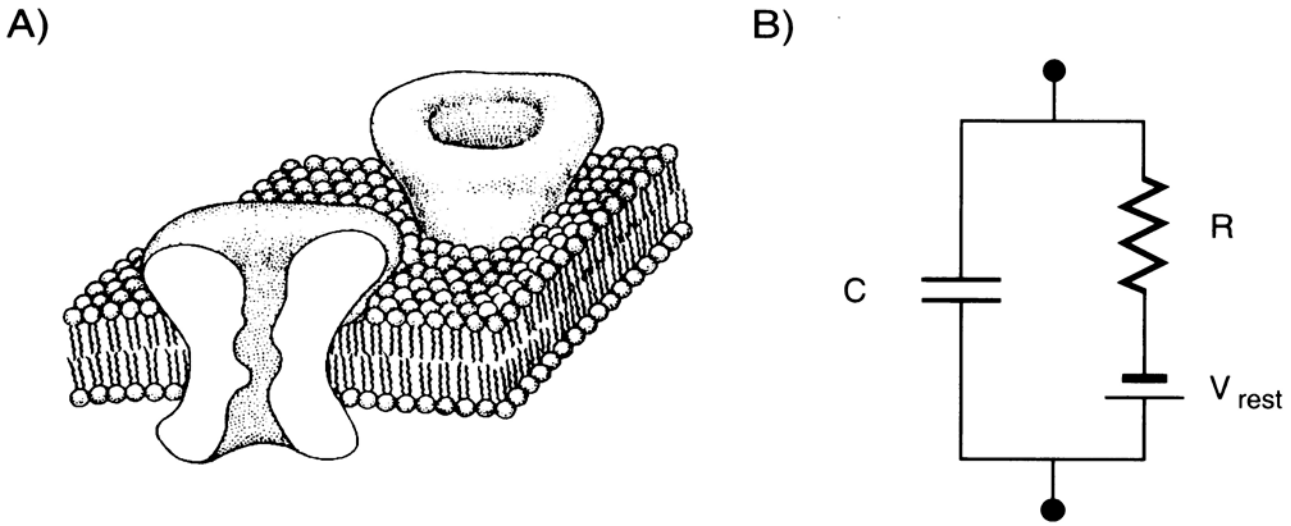


Fig. 1.1 NATURE OF THE PASSIVE NEURONAL MEMBRANE **(A)** Schematic representation of a small patch of membrane of the types enclosing all cells. The 30–50 Å thin bilayer of lipids isolates the extracellular side from the intracellular one. From an electrical point of view, the resultant separation of charge across the membrane acts akin to a capacitance. Proteins inserted into the membrane, here ionic channels, provide a conduit through the membrane. Reprinted by permission from Hille (1992). **(B)** Associated lumped electrical circuit for this patch, consisting of a capacitance and a resistance in series with a battery. The resistance mimics the behavior of voltage-independent ionic channels inserted throughout the membrane and the battery accounts for the cell's resting potential V_{rest}.

(from Koch)

Effect of I_m *and* I_{ion} *on* V_m *(cont.):*

The response of the transmembrane potential V_m for a patch of membrane with constant membrane resistance R initially at V_{rest} and then subjected to an intracellularly-injected current step of amplitude I_0 is:

$$V_m(t) = I_0 R \left(1 - e^{-t/\tau}\right) + V_{rest}$$

$$= V_0 \left(1 - e^{-t/\tau}\right) + V_{rest},$$

where $\tau = RC$ and $V_0 = I_0 R = V_m(t! \ 1) - V_{rest}$.

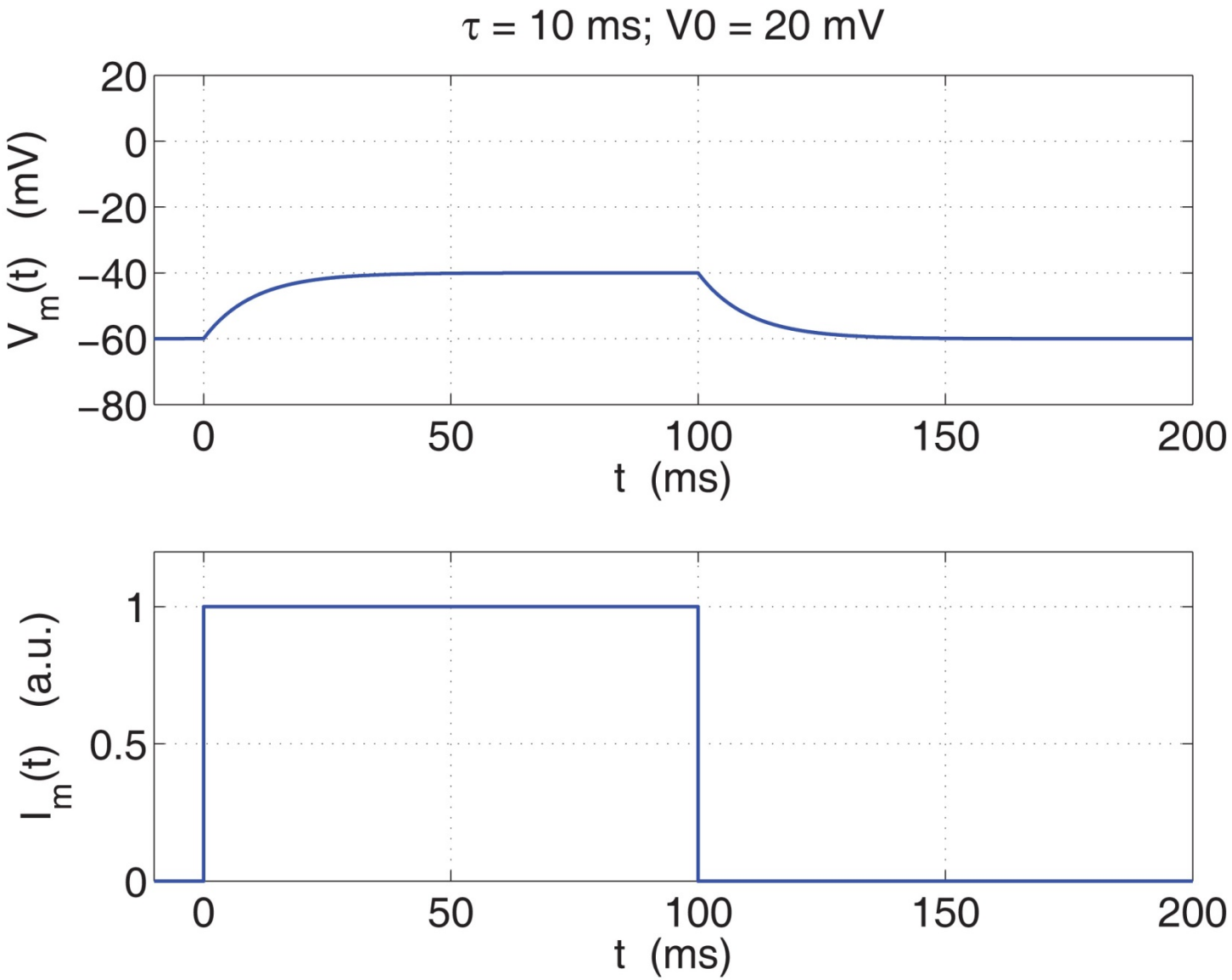
Effect of I_m *and* I_{ion} *on* V_m *(cont.):*

The transmembrane potential V_m for a patch of membrane with constant membrane resistance R initially at $V_m(t=0)$ and with no current injection returns to the resting potential according to:

$$V_m(t) = [V_m(0) - V_{\text{rest}}]\, e^{-t/\tau} + V_{\text{rest}},$$

where $\tau = RC$.

Effect of I_m *and* I_{ion} *on* V_m *(cont.):*



Effect of I_m *and* I_{ion} *on* V_m *(cont.):*

Consider a parallel conductance model with sodium and potassium ionic channels. The response of the transmembrane potential V_m for a patch of membrane initially at V_{rest} and then subjected to an instantaneous change in the sodium conductance to g_{Na}^0 is:

$$V_m(t) = V_0\left(1 - e^{-t/\tau'}\right) + V_{rest},$$

where $\tau^0 =$ R℃ and $V_0 =$ V_m(t! 1)–V_{rest}.

Effect of I_m *and* I_{ion} *on* V_m *(cont.):*

The new membrane conductance G^0 or its reciprocal the membrane resistance R^0 is given by:

$$G' = \frac{1}{R'} = g_{\mathrm{K}} + g'_{\mathrm{Na}},$$

and the new steady-state potential $V_m(t! \ 1)$ is:

$$V_m(t \to \infty) = \frac{g_{\mathrm{K}} E_{\mathrm{K}} + g'_{\mathrm{Na}} E_{\mathrm{Na}}}{g_{\mathrm{K}} + g'_{\mathrm{Na}}}.$$

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:

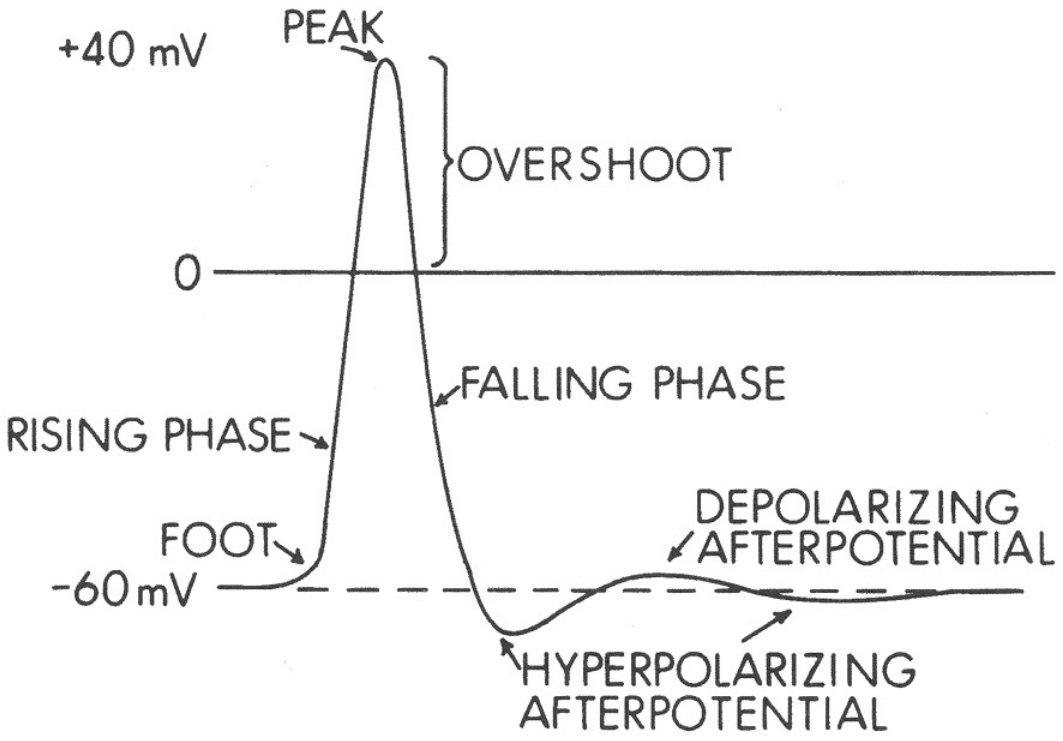


Figure 5.4. Diagram to show the nomenclature applied to an action potential and the afterpotentials that may follow it.

Observing action potentials (cont.):

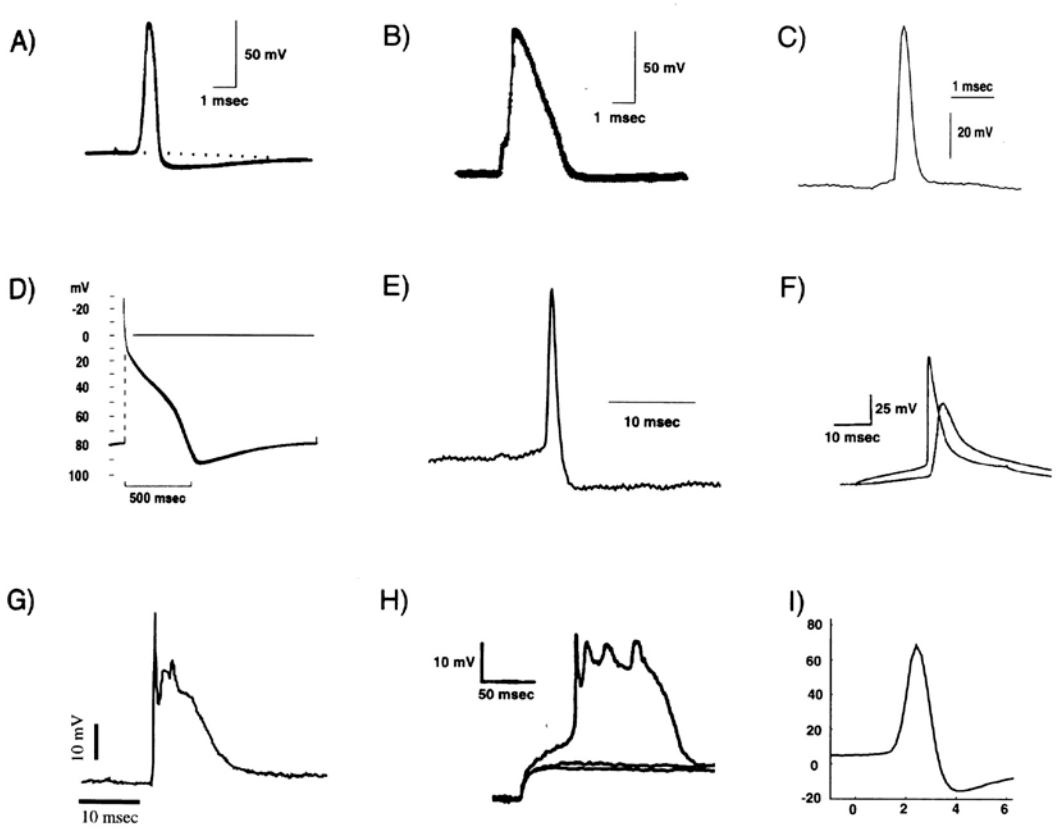


Fig. 6.1 ACTION POTENTIALS OF THE WORLD Action potentials in different invertebrate and vertebrate preparations. Common to all is a threshold below which no impulse is initiated, and a stereotypical shape that depends only on intrinsic membrane properties and not on the type or the duration of the input. **(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.

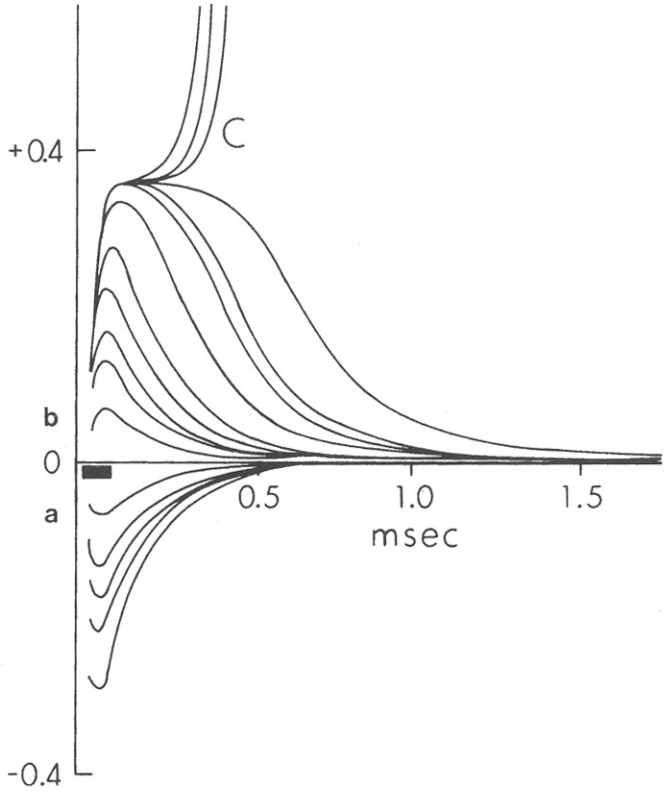


Figure 5.5. Subthreshold responses recorded extracellularly from a crab axon in the vicinity of the stimulating electrodes. The axon was placed in paraffin oil, and, consequently the measured extracellular potential is directly related to the transmembrane potential (according to the linear core-conductor 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.):

For the squid axon:-

- C_m ¼ 1 $\mu F / cm^2$ throughout the entire action potential
- R_m ¼ 1000 Ω¢cm^2 at rest
- R_m ¼ 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**.

Parallel conductance model (cont.):

Assuming independent conductance channels for K^+, Na^+ and Cl^-, the electric circuit for a *membrane patch* is:

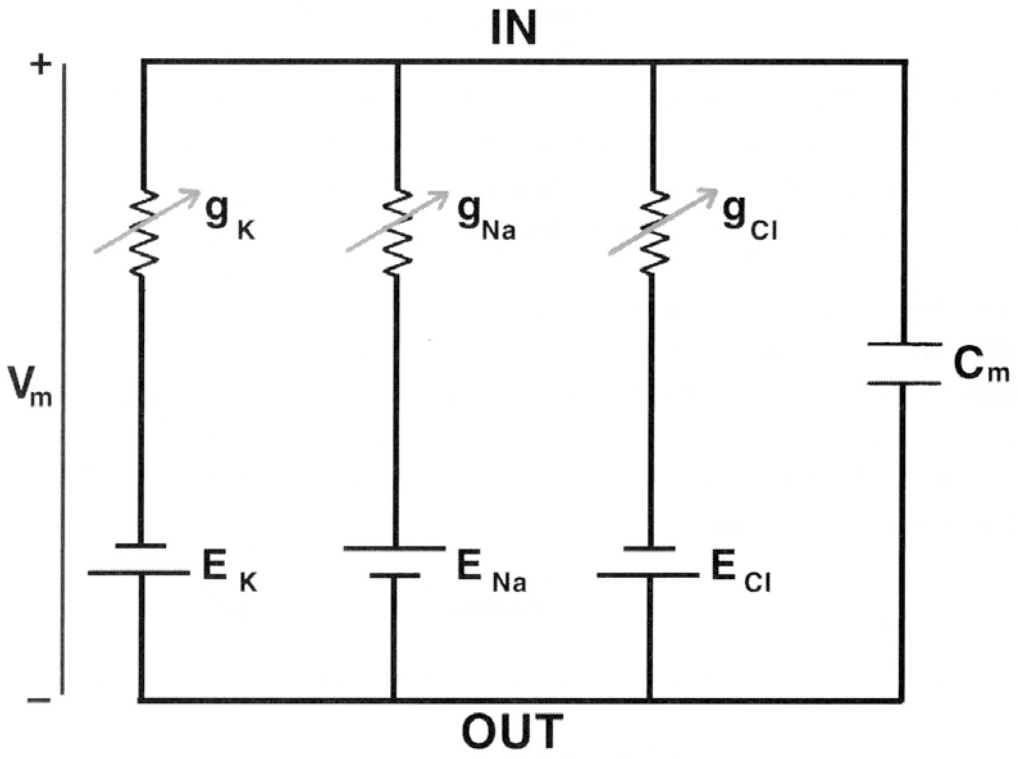


Figure 3.3. The Parallel-Conductance Model of an Excitable Membrane (IN = intracellular, OUT = extracellular). Independent conductance channels are present for K^+, Na^+, and Cl^-. Transmembrane potential V_m is positive when the inside has higher potential than the outside. The battery polarity is chosen to show that usually the Nernst potentials of E_K and E_{Cl} are negative (inside more negative than outside) and that of E_{Na} is positive (inside more positive than outside).

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:

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

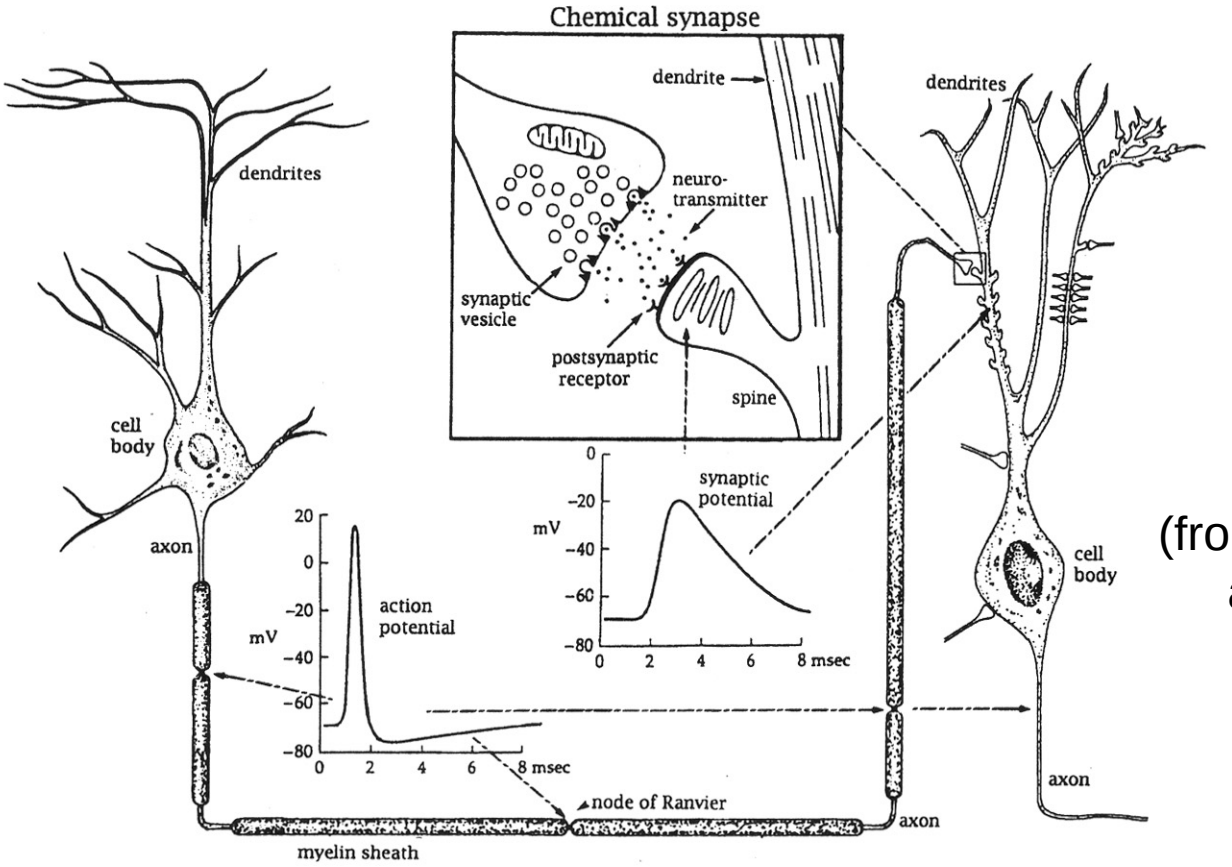
$$\text{At the peak: } V_m \approx E_{\mathsf{Na}} = \frac{RT}{F}\ln\left(\frac{[\mathsf{Na}]_o}{[\mathsf{Na}]_i}\right) \qquad (5.8)$$

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

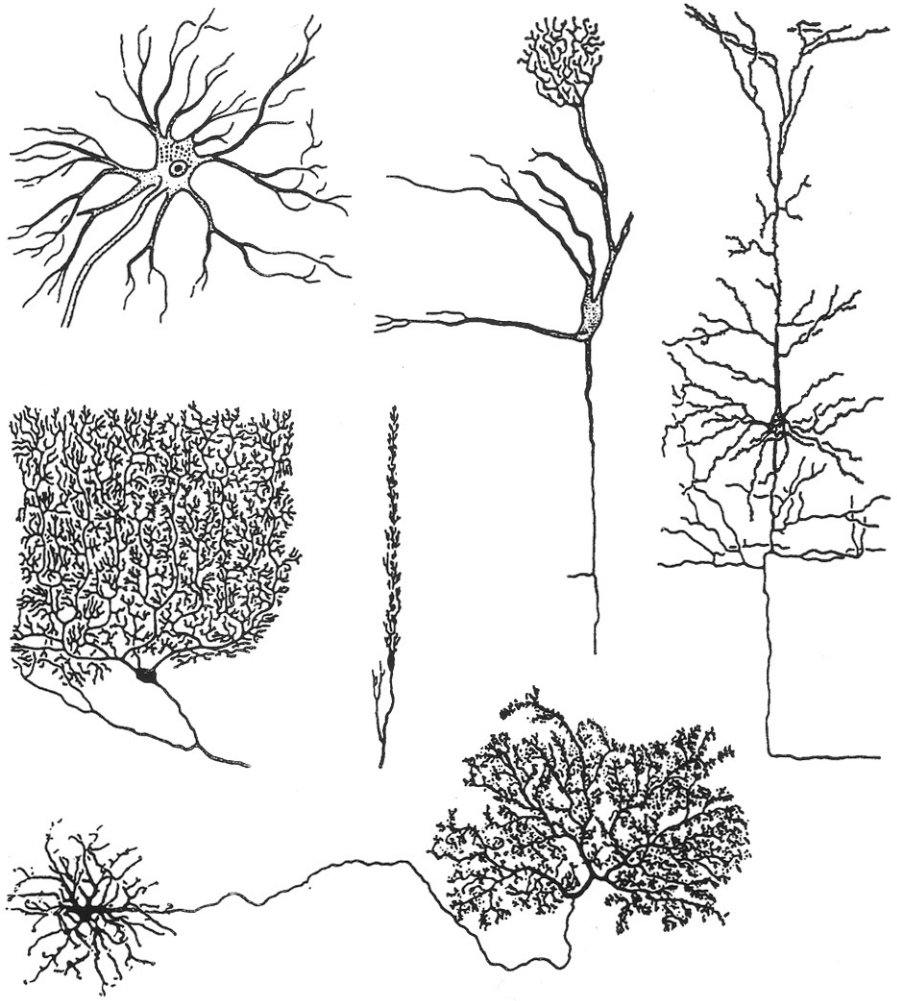
Nerve cells:



(from Johnston and Wu)

Figure 1.2 Neurons convey information by electrical and chemical signals. Electrical signals travel from the cell body of a neuron (left) to its axon terminal in the form of action potentials. Action potentials trigger the secretion of neurotransmitters from synaptic terminals (upper insert). Neurotransmitters bind to postsynaptic receptors and cause electric signals (synaptic potential) in the postsynaptic neuron (right). Synaptic potentials trigger action potentials, which propagate to the axon terminal and trigger secretion of neurotransmitters to the next neuron. (Adapted from Kandel et al. 1991 and from L.L. Iversen, copyright © 1979 by Scientific American, Inc. All rights reserved.)

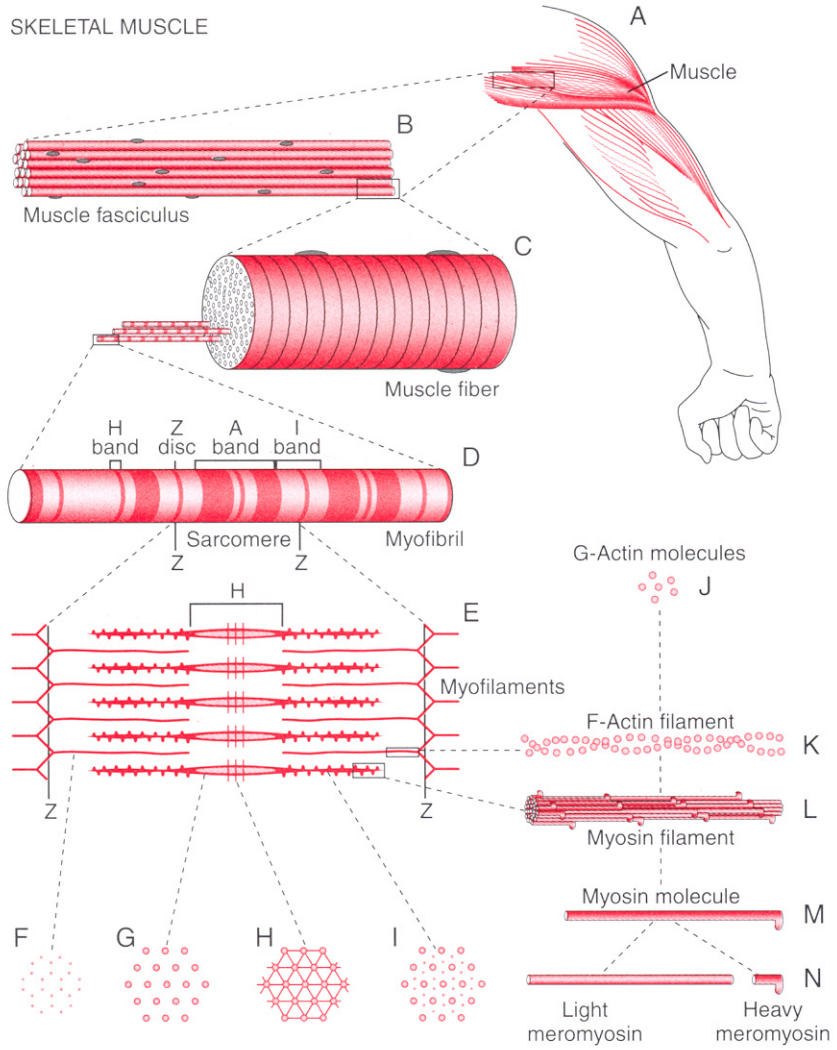
Examples of neuron morphologies:



(from Johnston and Wu)

Figure 1.1 Examples of neurons in the nervous system exhibiting various morphology. From the upper left in clockwise order: motor neuron from the spinal cord, mitral cell from olfactory bulb, pyramidal cell from cortex, horizontal cell from retina, and Purkinje cell (front and side views) from cerebellum. (From Nicholls et al. 1992 and Fisher and Boycott 1974.)

Skeletal muscle cells:

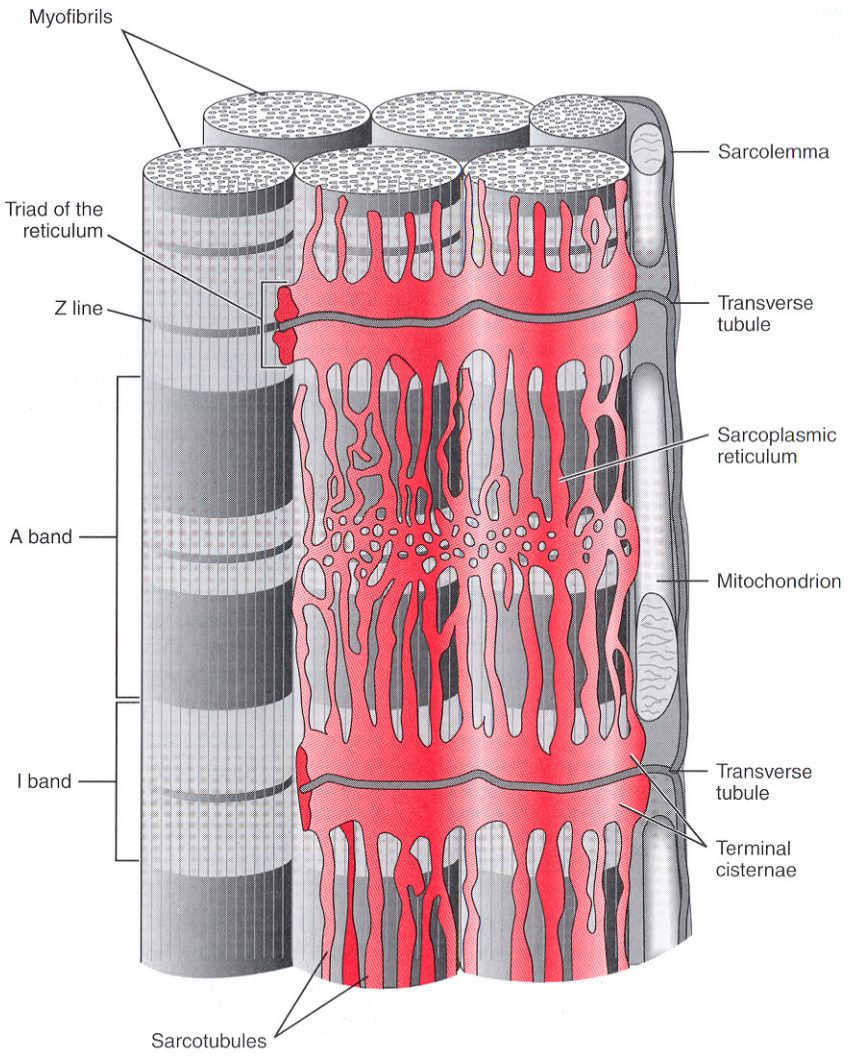


(from Guyten)

FIGURE 6–1

Organization of skeletal muscle, from the gross to the molecular level. *F, G, H,* and *I* are cross sections at the levels indicated. (Drawing by Sylvia Colard Keene. Modified from Fawcett DW: Bloom and Fawcett: A Textbook of Histology. Philadelphia: WB Saunders Co, 1986.)

Transverse tubule-sarcoplasmic reticulum system for excitation-contraction coupling:



(from Guyten)

FIGURE 7–5

Transverse (T) tubule-sarcoplasmic reticulum system. Note the *longitudinal tubules* that terminate in large *cisternae*. The cisternae in turn abut the T tubules. Note also that the T tubules communicate with the outside of the cell membrane. This illustration was drawn from frog muscle, which has one T tubule per sarcomere, located at the Z line. A similar arrangement is found in mammalian heart muscle, but mammalian skeletal muscle has two T tubules per sarcomere, located at the A-I junctions. (Redrawn from Bloom W, Fawcett DW: A Textbook of Histology. Philadelphia: WB Saunders Co, 1986. Modified after Peachey LD: J Cell Biol 25:209, 1965. Drawn by Sylvia Colard Keene.)

Cardiac muscle cells are interconnected via electrical "gap junctions":

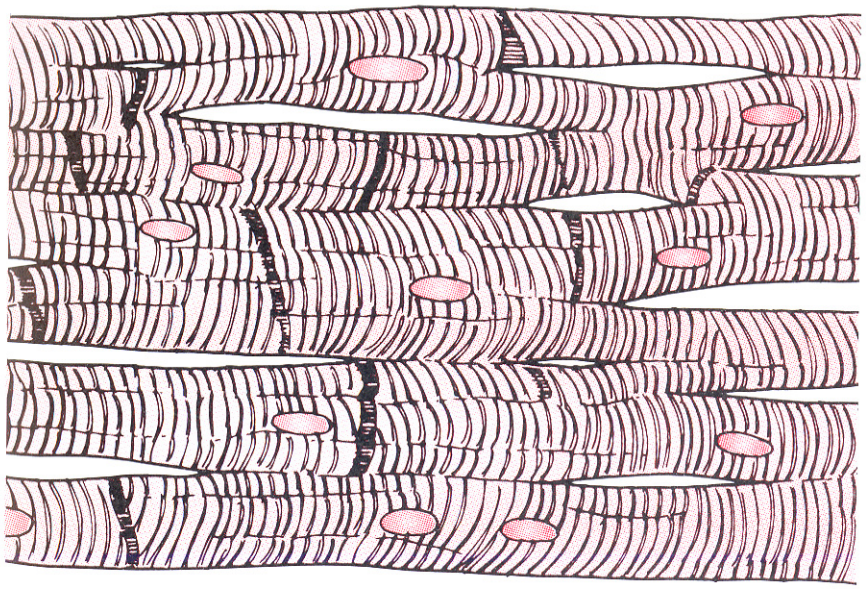


FIGURE 9 – 2

"Syncytial," interconnecting nature of cardiac muscle fibers.

(from Guyten)

Electrical "gap junctions" in cardiac cells:

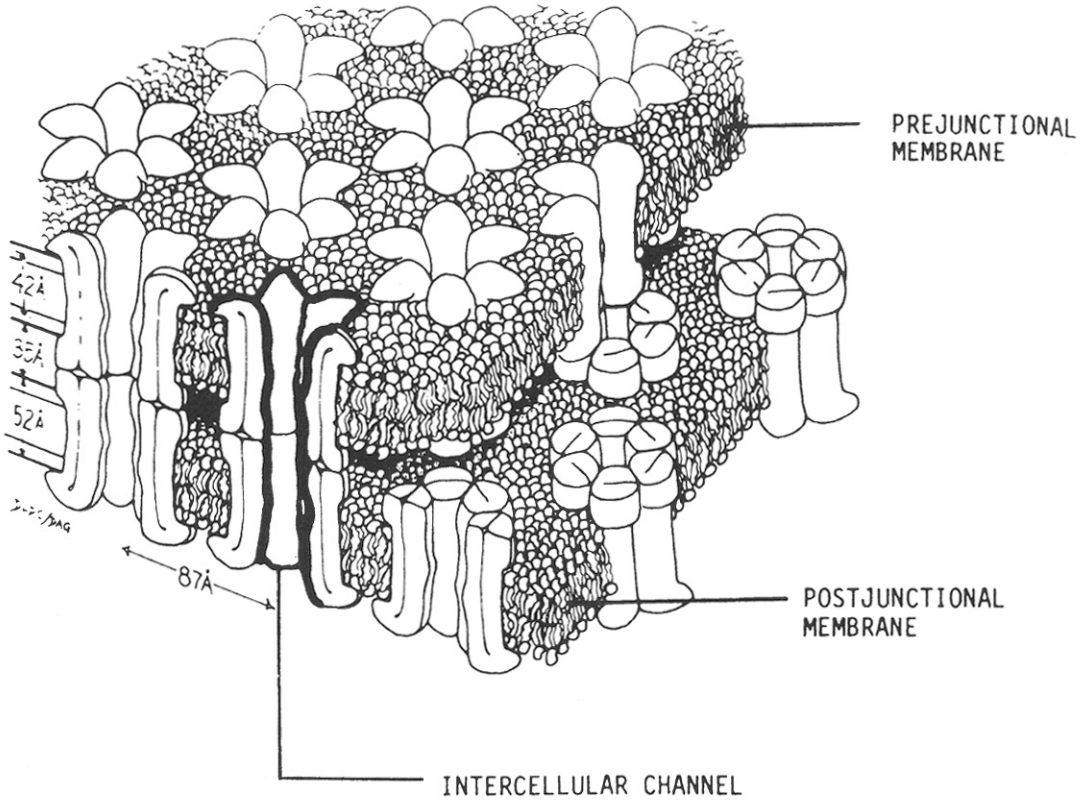


Figure 9.4. Details of the communicating-type intercellular cardiac junction (connexon array) is shown. Each unit (connexon) is a protein channel running transverse to the opposing membranes. Connexons from abutting cells align themselves to form structural continuity. The structural detail shown is based on morphometry obtained from X-ray diffraction, electron microscopy, and chemical studies. The gap spacing is given as 35 Å. [R. Plonsey, The use of a bidomain model for the study of excitable media, *Lectures on Mathematics in the Life Sciences* **21**:123–149 (1989). From L. Makowski, D. L. D. Caspar, W.C. Phillips, and D. A. Goodenough, Gap junctional structures II. Analysis of x-ray diffraction, *J. Cell Biol.* **74**:629–645 (1977). Reproduced from the Journal of Cell Biology, 1977, vol. 74, pp. 629–645 by copyright permission of the Rockefeller University Press.]

Sensory receptors:

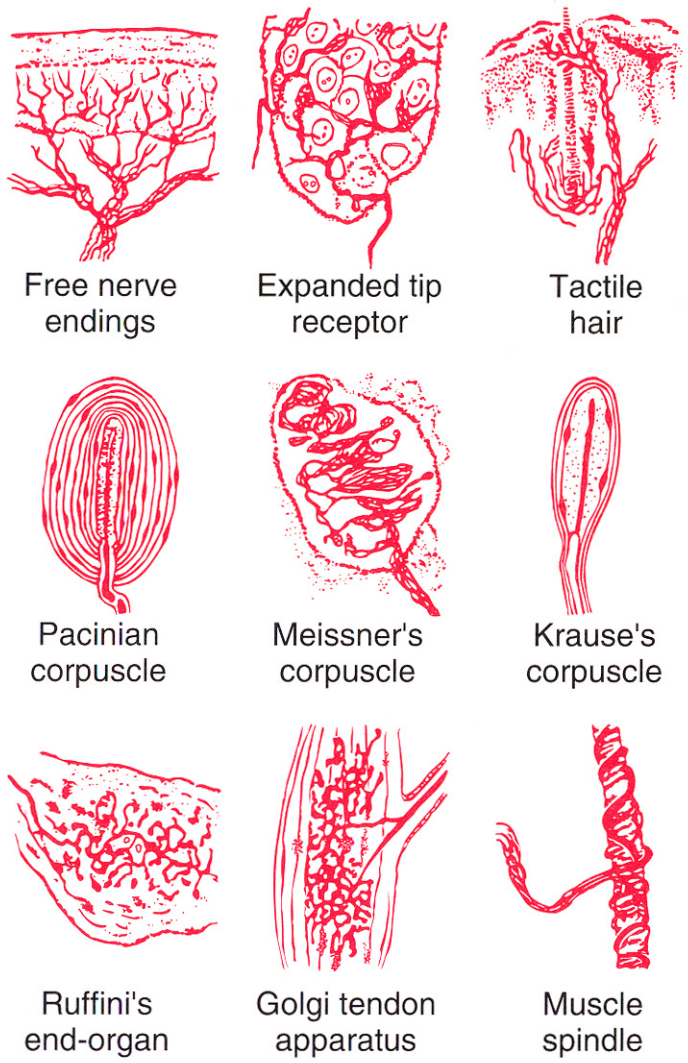


FIGURE 46–1

Several types of somatic sensory nerve endings.

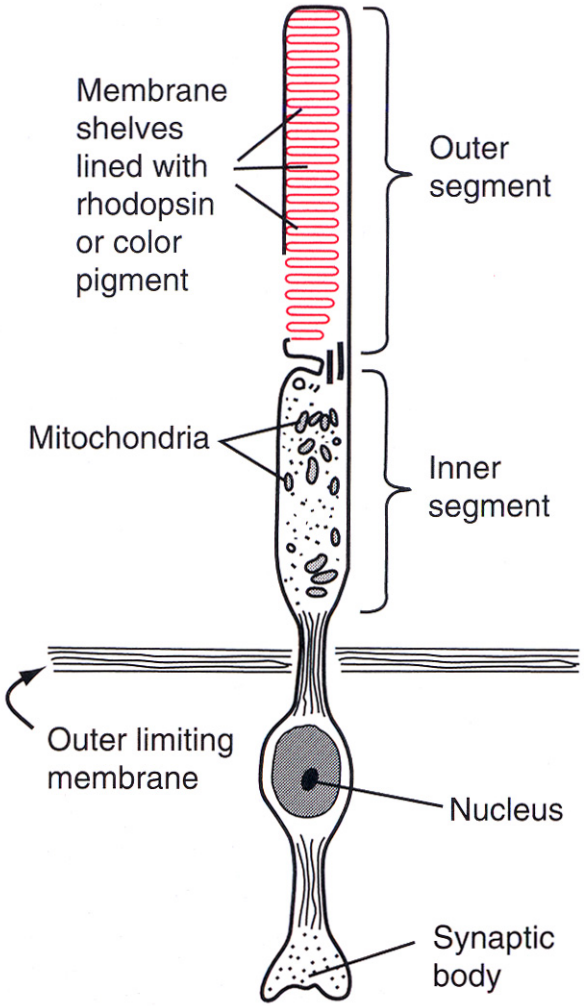


FIGURE 50–3

Schematic drawing of the functional parts of the rods and cones.

(from Guyten)