Membrane Potential (cont)

Two factors create it:

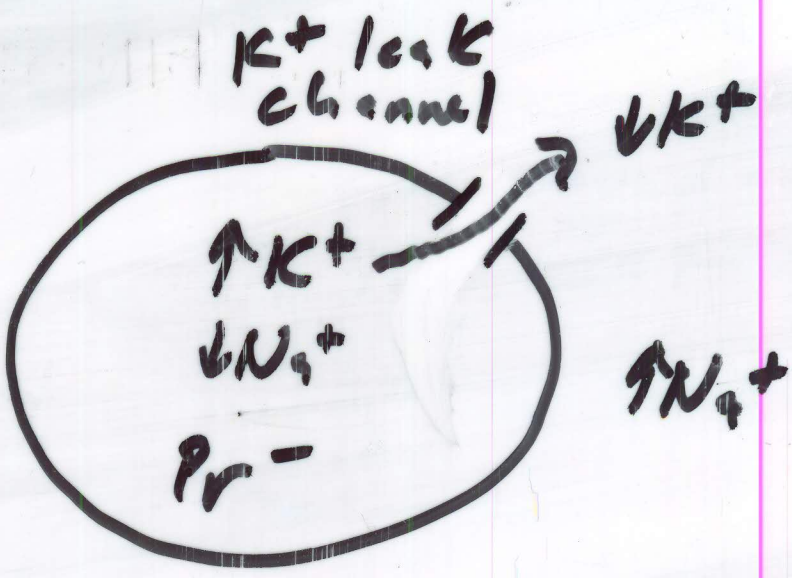
— Differential distribution of ions between the inside + outside of the neurons.

Na^+ ions – most abundant ions in the ECF

K^+ ions – most abundant ions in the ICF

Proteins that are negatively charged (Pr^-), only found in the ICF

– The cell membranes high permeability to K^+, and relatively low permeability to Na^+, and impermeability to Pr^-



K+ moves out down concentration gradient leaving Pr^- behind resulting in ⊖ charge inside relative to outside

Movement of K+ out will continue until conc. gradient forces pushing K+ out are balanced by electrical forces pulling K+ in

At this balance point there is no net movement of K+ across the membrane.

The membrane potential at which this balance is established is called the equilibrium potential for K^+ (E_{K^+})

Nernst equation is used to calculate the equilibrium potential of an ion.

$$E_{ion} = 2.303 \left(\frac{RT}{zF}\right) \log \frac{[ion]_o}{[ion]_i}$$

R = Gas constant (8.31 joules/mole/°K)
F = Faraday's constant
(96,500 coulombs/mole)
T = Temperature (in degrees kelvin)
z = electrical charge of the ion
($K^+ = +1$, $Na^+ = +1$, $Ca^{++} = +2$, $Cl^- = -1$)

$RT/F = 26.72\,mV$

$26.72\,mV \times 2.303 = 61.54\,mV$

$$E_{ion} = \frac{61.54\,mV}{z} \log \frac{[ion]_o}{[ion]_i}$$

$K^+ = +1$ Conc. gradient for K^+ in mammals:

$[K^+]_o = 5\,mM \quad [K^+]_i = 100\,mM$

$$E_{K^+} = \frac{61.54\,mV}{+1} \log \frac{[5\,mM]}{[100\,mM]} \approx -80\,mV$$

The negative sign tells us that at E_{K^+} the membrane potential will be ⊖ inside relative to outside

$Cl^- = -1$, $[Cl^-]_o = 150mM$

$[Cl^-]_i = 13mM$

$$E_{Cl^-} = \frac{61.54mV}{-1} \log \frac{[150]}{[13]} = -65.4mV$$

If the cell membrane were only equal to K^+, then the membrane potential would be equal to the $E_{K^+} = -80mV$.

However, cell membranes are also slightly permeable to Na^+

$$E_{Na^+} = +61.5mV$$

$[Na^+]_i = 15mM$ $[Na^+]_o = 150mM$

membrane potential will depend on which ion the membrane is most permeable to. Membrane potential will be closer to E_{K^+} because the membrane is 50x more permeable to K^+ than to Na^+

Using Goldman Equation the membrane potential for a cell can be calculated. Derived from the Nernst equation with addition of relative permeabilities of ions.

$$\text{membrane potential} = V_m = 61.54\,mV \log \frac{P_{K^+}[K^+]_o + P_{Na^+}[Na^+]_o}{P_{K^+}[K^+]_i + P_{Na^+}[Na^+]_i}$$

P_{ion} = relative permeability of the ion

$$V_m = 61.54mV \log \frac{40[5mM] + 1[150mM]}{40[100mM] + 1[15mM]} = -65mV$$

Actual V_m is closer to $-70mV$ because there is an ion pump in the cell membrane called the Na^+/K^+ ATPase pump

Uses energy from hydrolysis of ATP to move $3Na^+$ out for every $2K^+$ it moves in.

This pump is called an electrogenic pump because it is moving more Na^+ out than K^+ in, so contributes a small amount to the V_m

Causes V_m for most neurons to be ~ -70mV, called resting membrane potential because it is stable unless the ion conc. changes or membrane permeability changes.

A couple of mechanisms work to maintain stable K^+ conc. levels in the ECF of the CNS:

- Blood-brain barrier established by the astrocytes. Prevents movement of K^+ out of the ECF of CNS into the blood and vice versa. Effectively isolates the CNS tissues from fluctuations in K^+ concentrations in the blood due to diet, sweating, etc.

- Potassium Spatial Buffering.
  Also involves astrocytes

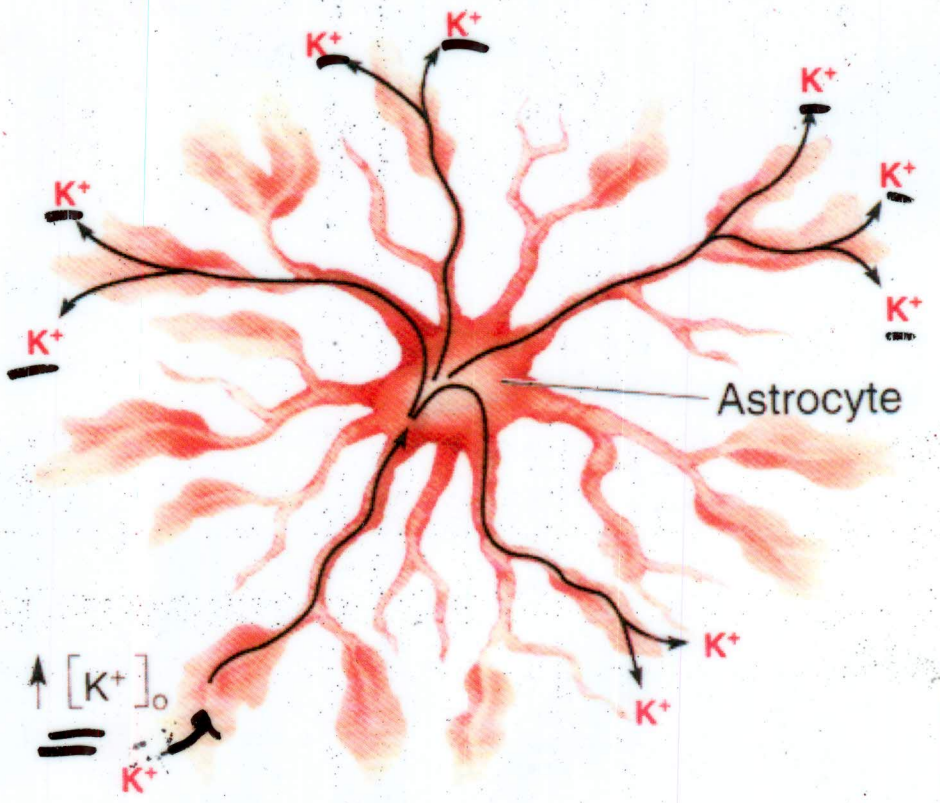
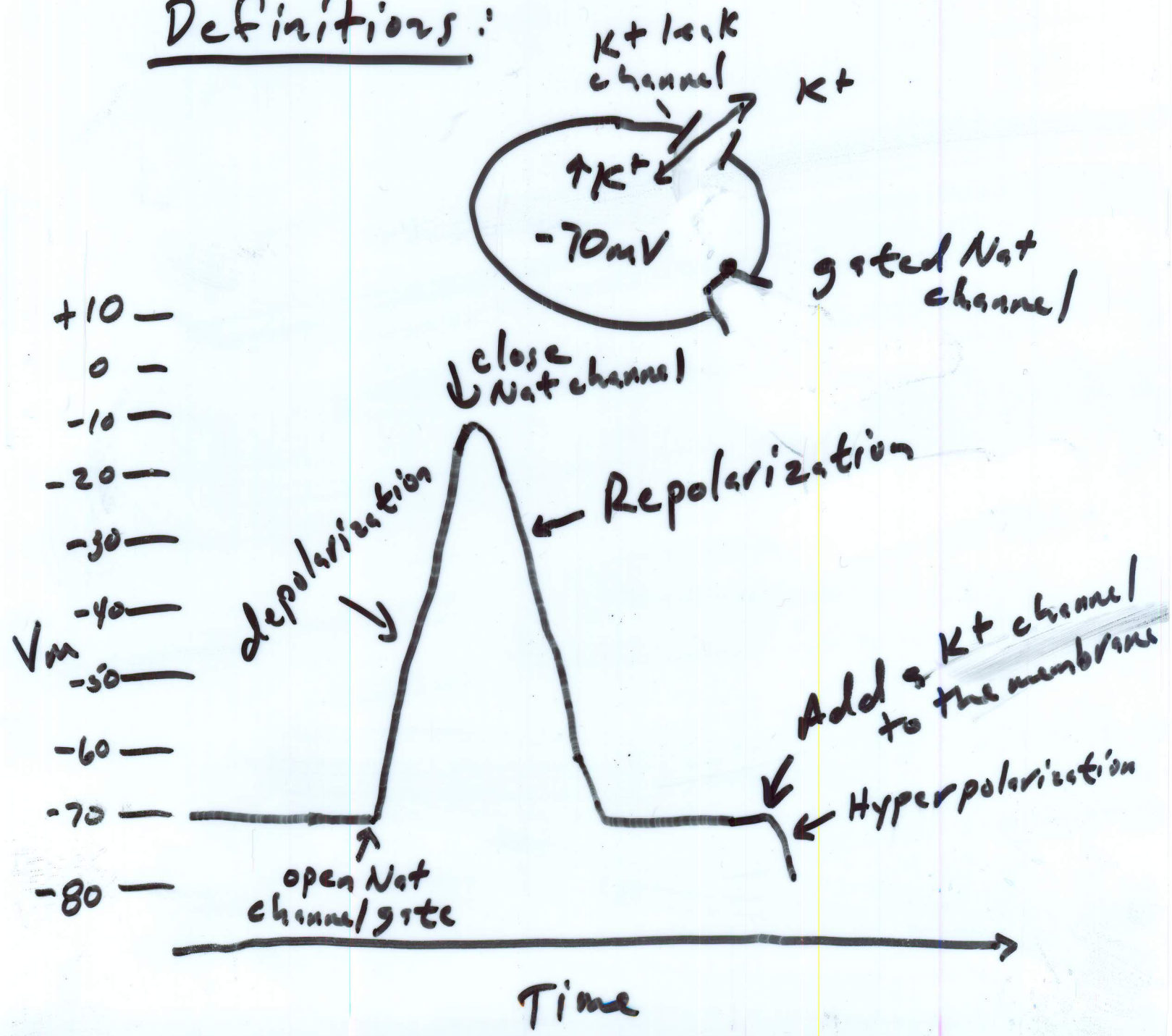


FIGURE 3.20
Potassium spatial buffering by astrocytes. When brain $[K^+]_o$ increases as a result

Prevents localized accumulations of K+ in the ECF of the CNS.

Neurons have ion channels in their cell membrane that can be opened and closed.

Definitions:



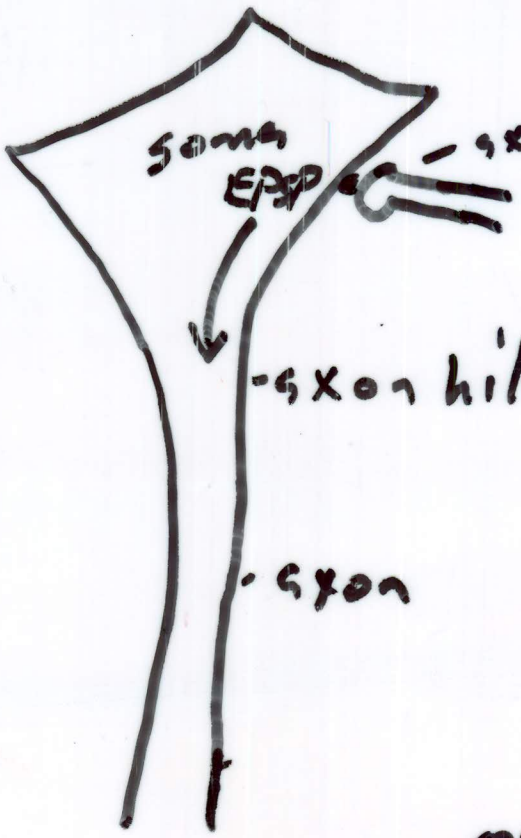
Two types of electrical signals generated by neurons:

- Action potentials (APs)
- Post-synaptic Potentials (PSPs)
  aka "Graded Potentials"
  because they vary in amplitude

Characteristic	APs	PSPs
Where they occur	Axon	occur primarily in dendrites + soma
How Vm is affected	Involve depolarization followed by repolarization and then hyperpolarization	Involve either depolerization or hyperpolarization
Amplitude of change in Vm	Always have same amplitude of change in VM	Amplitude of change in Vm depends on # of ion channels that open in response to an initiating signal
How they spread through neuron	Actively conducted without changing in amplitude	Passively spread through the cytosol diminishing in amplitude
How the signal is initiated	Initiated by opening of voltage-gated Nat channels that open in response to axonal membrane depol.	Initiated by channels that respond to binding of neurotransmitter on neuronal cell membrane "chemically gated channels"

EPSPs - Excitatory Post-synaptic potentials

Initiated at synapses in response to the binding of neurotransmitter to a receptor on the post-synaptic membrane - invoked a depolarization of Vm at the site of initiation



EPSP spreads into the axon hillock

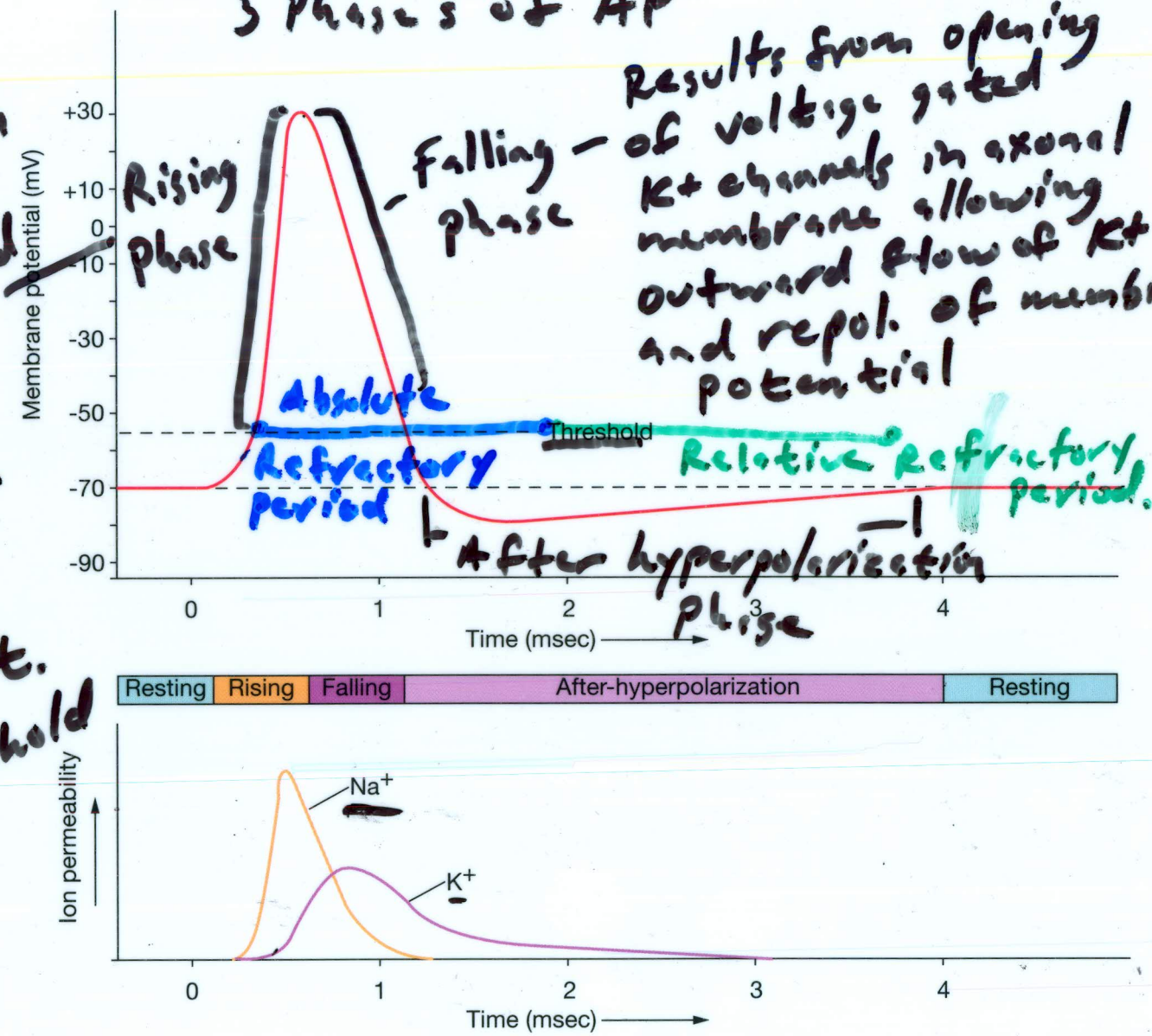
has an abundance of voltage gated Na+ channels and voltage gated K+ channels

open in response to depolarization of membrane potential ≥ threshold

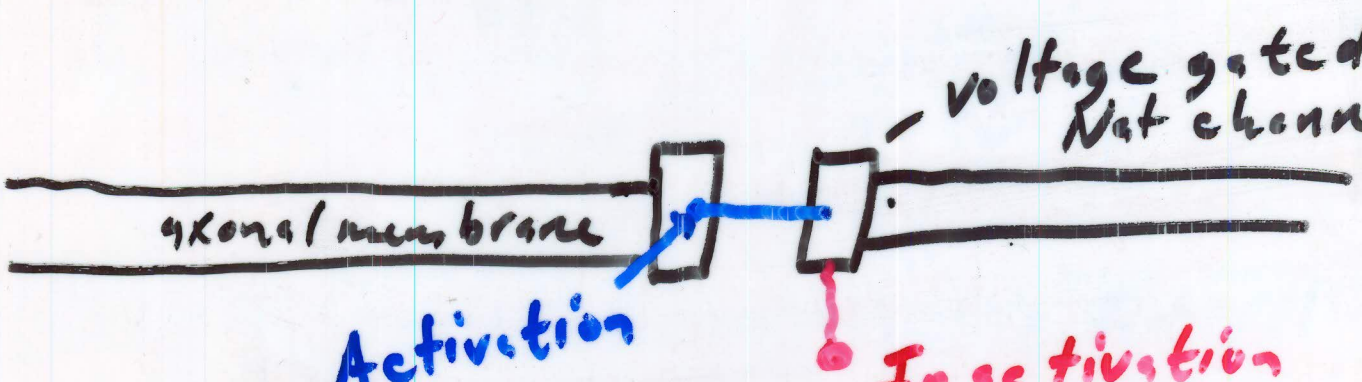
If the EPSP is not $\geq$ threshold then the voltage gated channels will not open and no AP will be initisted

If the EPSP is $\geq$ threshold then the voltage gated channels will open and an AP will be initiated.

Fig. 8-14 The action potential



Voltage gated Nat channels have two gates



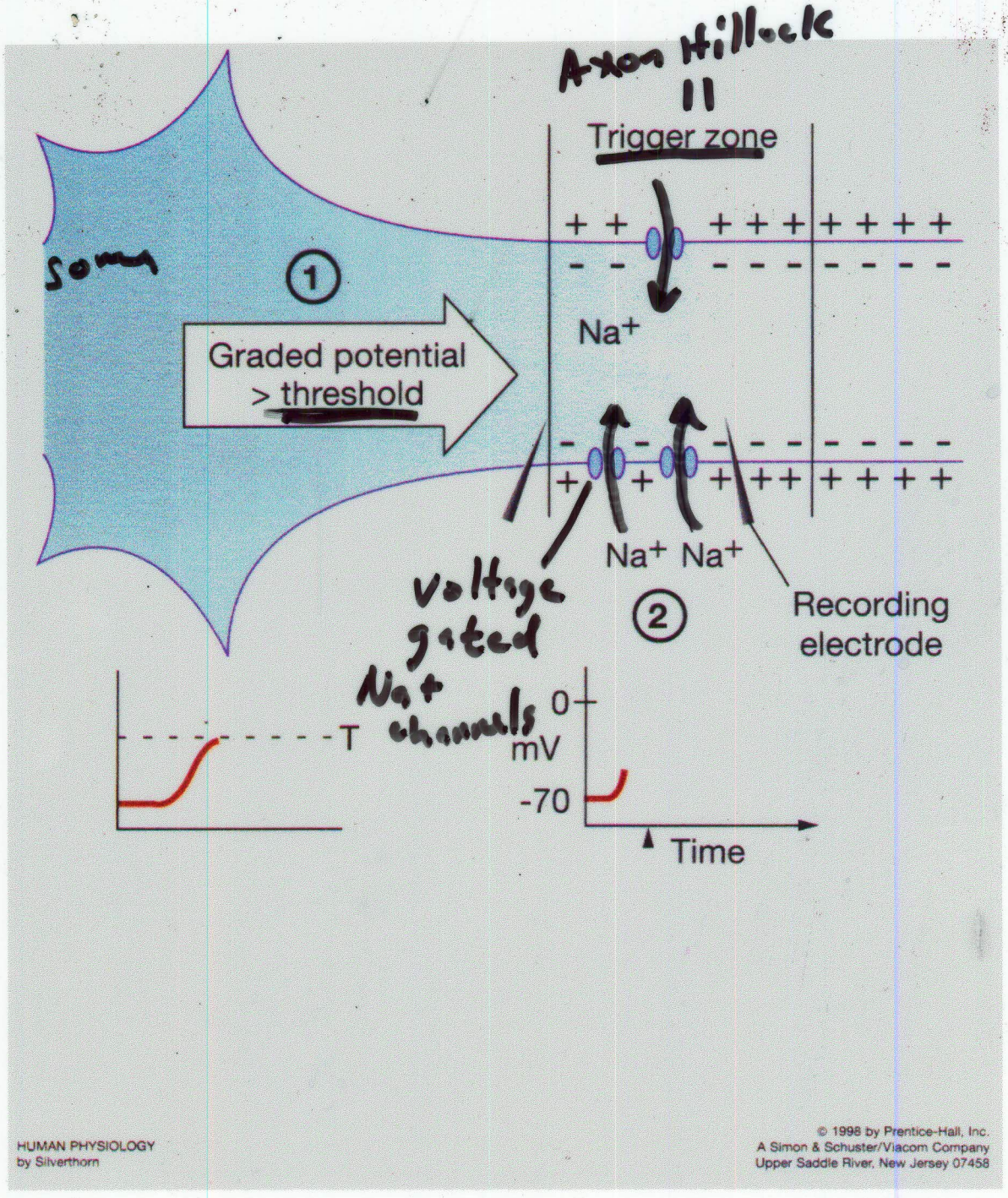
Activation gate opens when V_m is depol. $\geq T$

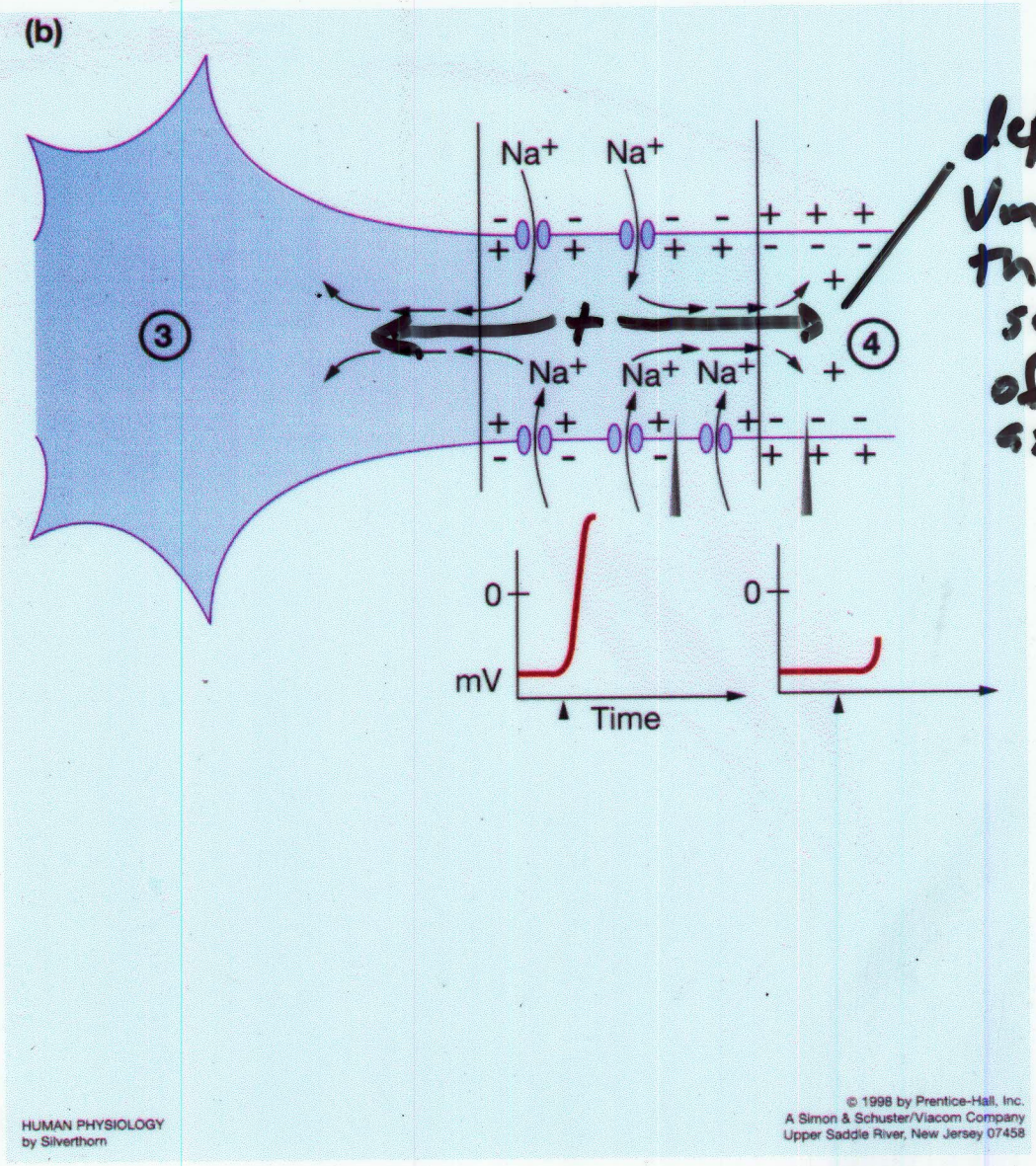
Inactivation gate
Time sensitive
closes channel
1/2 - 3/4 msec after activation gate opens
keeps the channel closed for ~1msec after closing

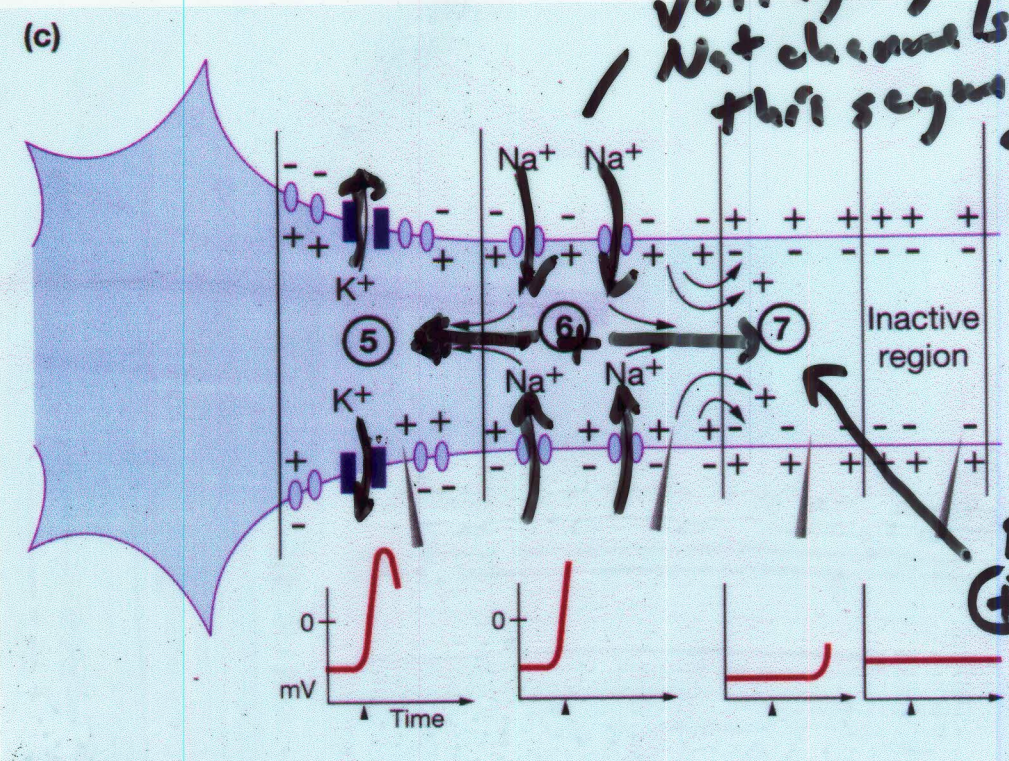
Activation gate opens when EPSP $\geq T$ allowing Nat to move inward through the channel.

After 1/2 - 3/4 msec the inactivation gate swings in to close the channel blocking further

inflow of Na^+, holds channel closed for ~1msec. Then the gates reset and the activation gate can reopen if membrane potential is again depol. to or greater T.




(b)
Na+
Na+
Na+
Na+
Na+
3
4
0
mV
Time
0
depolarizes Vm in the next segment of axon
HUMAN PHYSIOLOGY
by Silverthorn
© 1998 by Prentice-Hall, Inc.
A Simon & Schuster/Viacom Company
Upper Saddle River, New Jersey 07458



voltage gated Na+ channels in this segment open initiating AP in this segment

Flow of ⊕ charge into this segment opens voltage gated Na+ channels initiating AP in this segment

The speed of action potential conduction depends on how far down along the axon the ⊕ current produces depol. of great enough amplitude to reach T and open the voltage gated Nat channels in the axonal membrane.

Spread of ⊕ current along the axon diminishes in amplitude as a result of two factors

- Resistance to current flow with in the axon (r_i), determined by axon diameter and resistance to current flow in cytosol.

↑ diameter of axon → ↓ r_i

- Leak of ⊕ charge out across the axonal membrane (r_m)

The greater the resistance of the membrane to leak of current, the further down the axon the current will flow without diminishing in amplitude

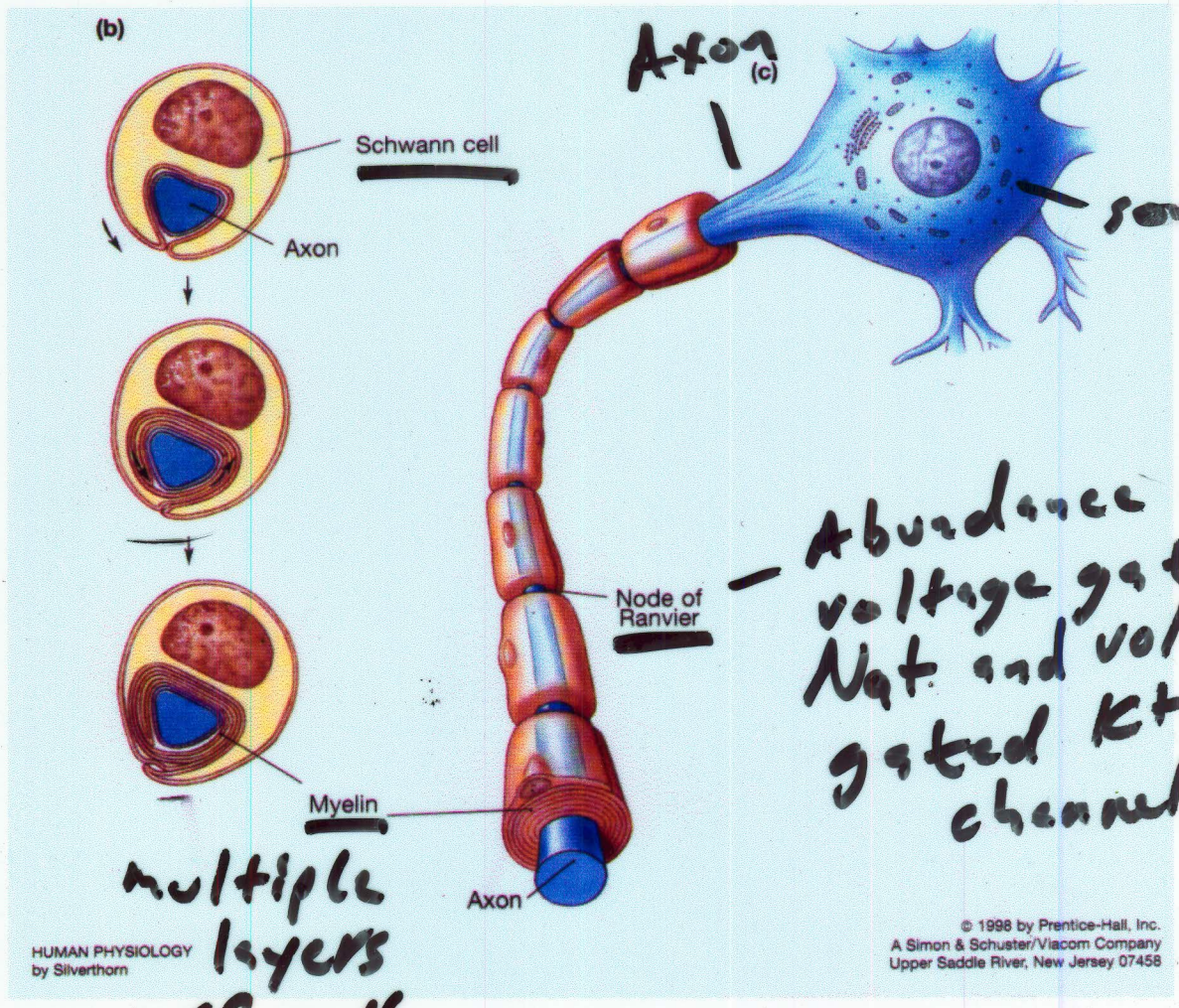
To maximize the distance the ⊕ current will spread requires that r_m be high and r_i be low.

Invertebrates - ex. squid use giant diameter axons to maximize AP conduction velocity

Vertebrates – Ex. humans

rely on maximizing r_m to the leak of ⊕ current out of the axon. to maximize AP conduction velocity.

Achieved by wrapping segments of axons in myelin sheath.



Abundance of voltage gated Na^+ and voltage gated K^+ channels

multiple layers of cell membrane prevents leak of ⊕ current

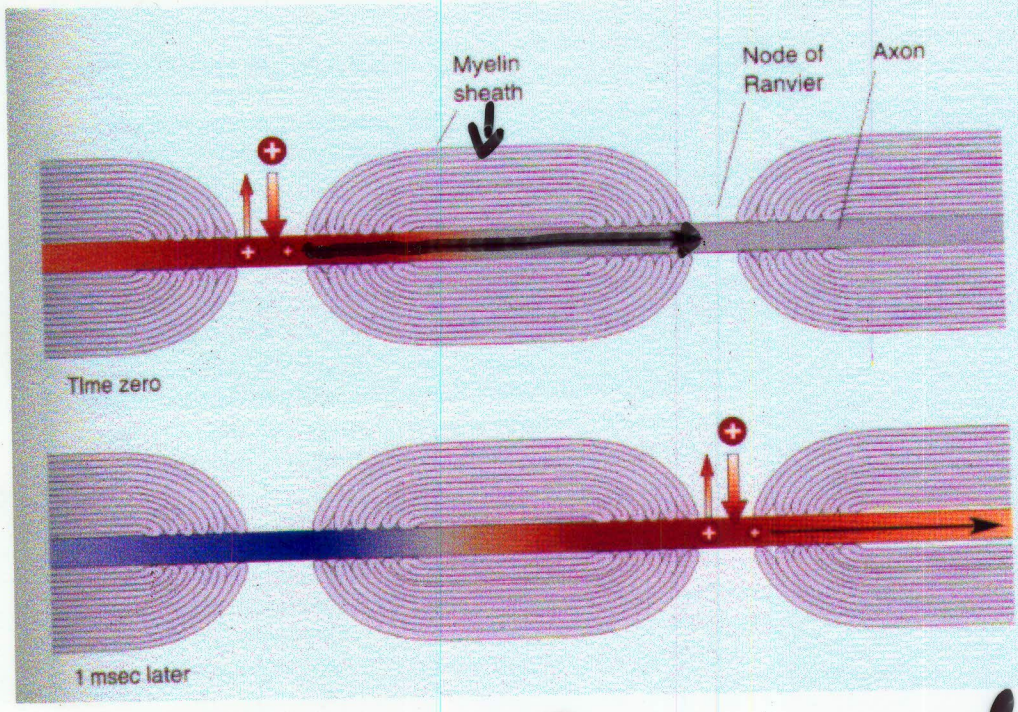


Figure 4.13
Saltatory conduction. Myelin allows current to spread farther and faster between nodes, thus speeding action potential conduction. Compare this figure with Figure 4.11.

AP jumps from one node to the next down the length of the axon. — Saltatory Conduction