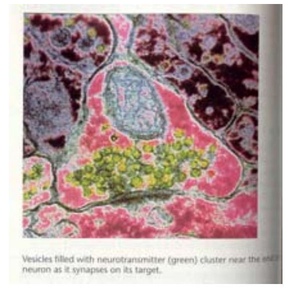
Lecture 6, 30 Jan 2008

Vertebrate Physiology
ECOL 437 (MCB/VetSci 437)
Univ. of Arizona, spring 2008

Kevin Bonine & Kevin Oh



1. Intro Nervous System Fxn
   (slides 32-60 from Mon 28 Jan; Ch10)
2. Neurons & Action Potentials (Ch11)
   (slides in this file)

http://eebweb.arizona.edu/eeb_course_websites.htm

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Housekeeping, 30 January 2008

Upcoming Readings

today: Ch 10&11
LAB Wed 30 Jan: Bisbal & Specker, plus two optional papers
(see website for links to papers; "worksheet" via email)
Fri 01 Feb: Ch11
Mon 04 Feb: Ch 12, Slowinski article

Lab discussion leaders: 30 Jan
1pm – Josh, Seth
3pm – Aaron, Adam

Lab discussion leaders: 06 Feb
1pm – Rittner, Whitney
3pm – Roxanne, Maria

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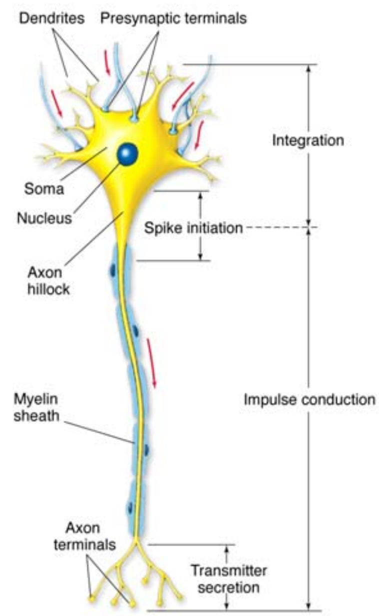
Vertebrate Physiology 437

Chapter 11

1. Neurons
   & Action Potentials

Changing
Membrane
Potentials…



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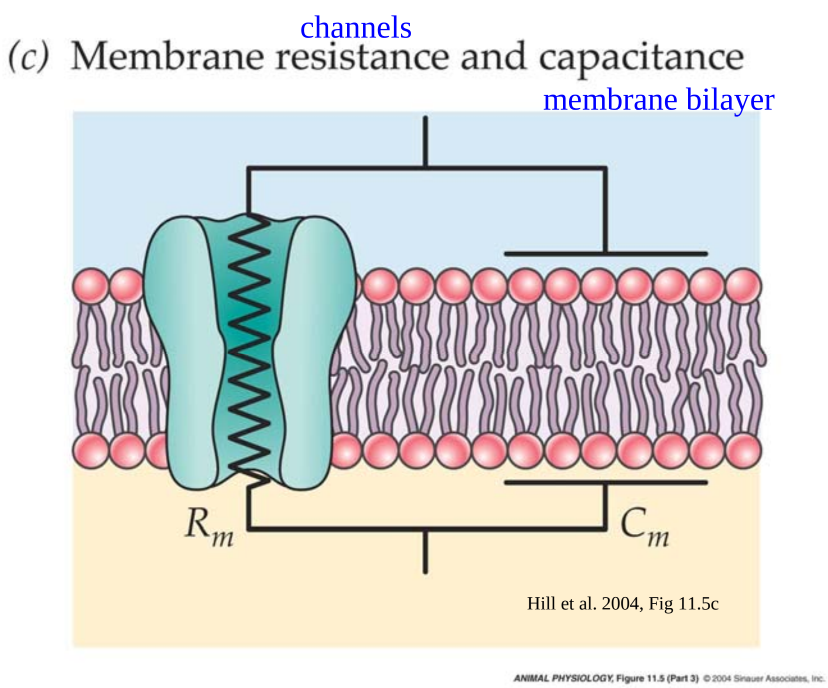
5-2 Randall et al. 2002

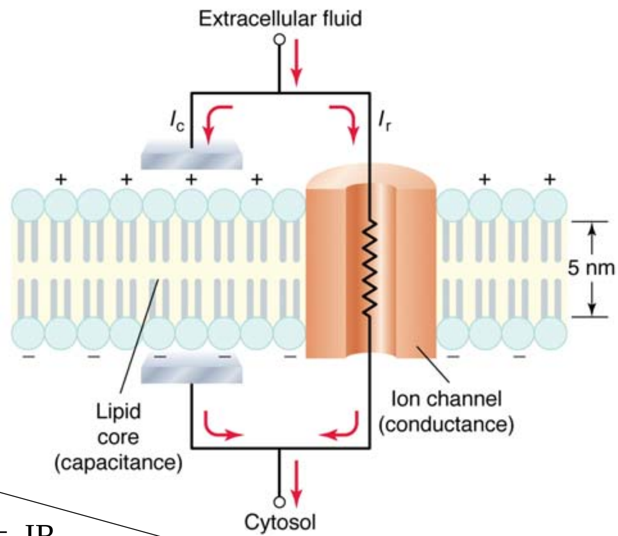


Hill et al. 2004, Fig 11.5c

<u>Membrane Potentials and Electricity</u>

conductance = reciprocal of resistance

vs.
capacitance



deltaV = IR
Change in Voltage = current x resistance

5-10 Randall et al. 2002

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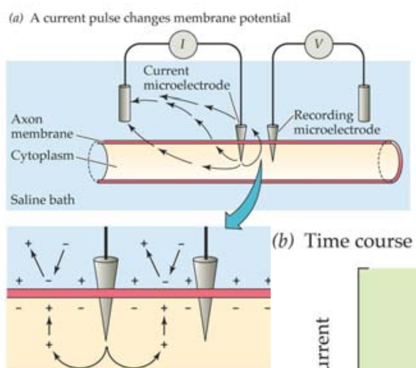
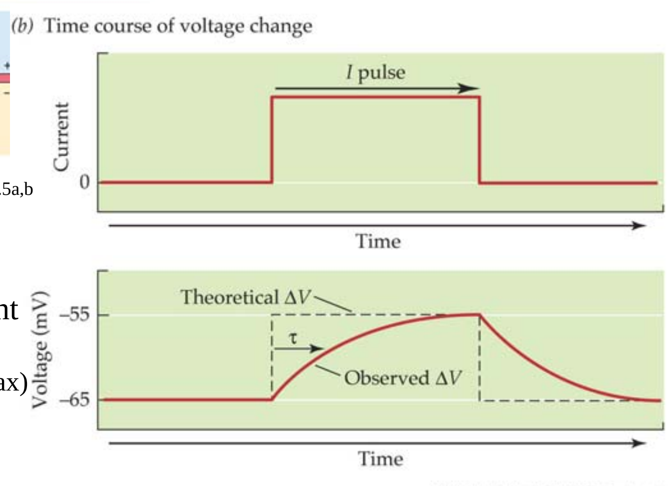
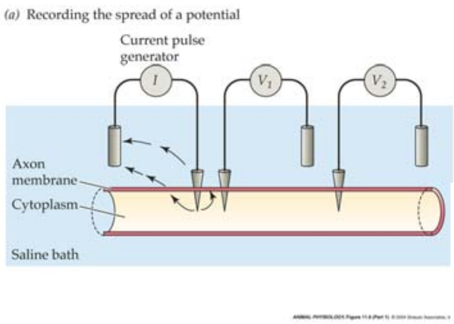


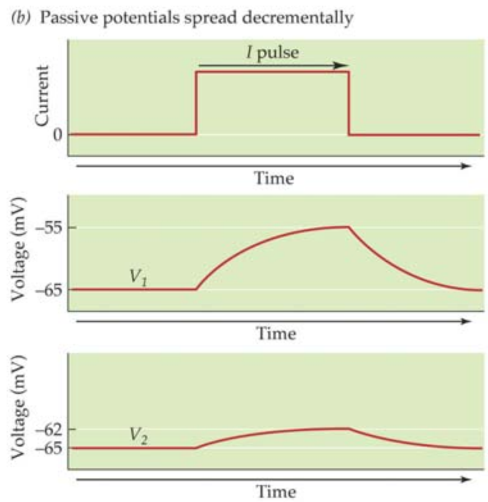
Hill et al. 2004, Fig 11.5a,b

Current from + to –
(follow cations)

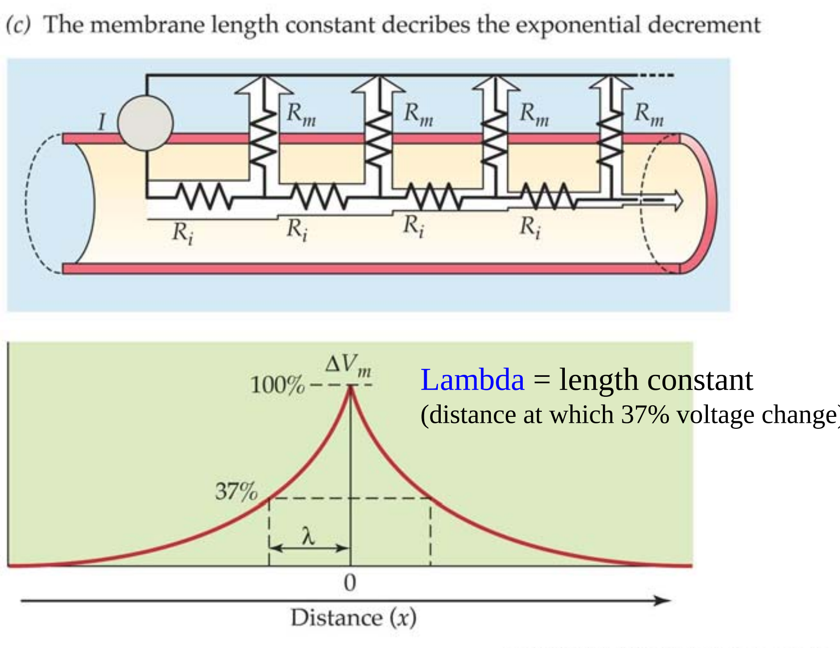


Tau = time constant
(2 - 20 ms)
(time to reach 63% max)





Hill et al. 2004, Fig 11.6a,b



Hill et al. 2004, Fig 11.6c

Nervous System

Synapse

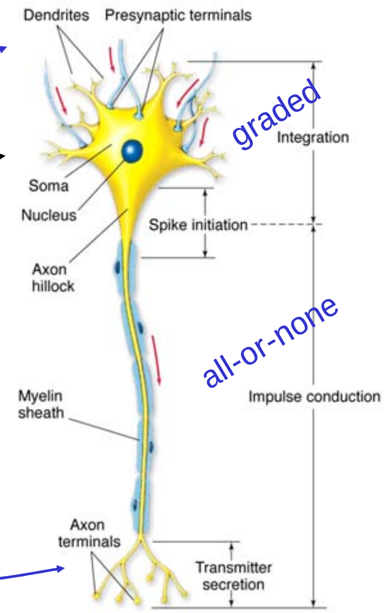
- Presynaptic
- Postsynaptic

1 Sensory Neurons
receive stimuli

2 Interneurons
entirely in CNS

3 Motor Neurons
effector organs
incl. muscle, gland

- Presynaptic
- Postsynaptic



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5-2 Randall et al. 2002

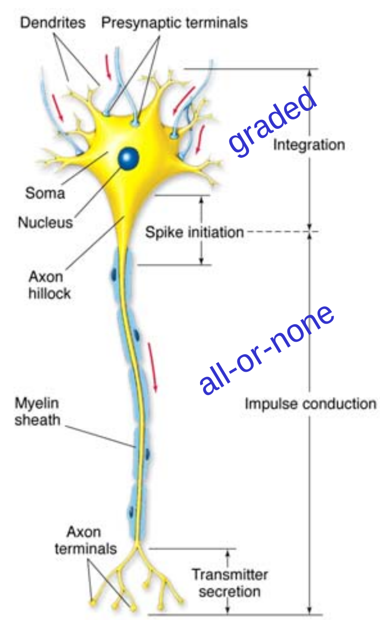
Action Potential

All-or-None from
spike-initiating zone

- Changes in ion permeability...
- Changes in membrane potential

-Voltage-gated ion channels
vs. ligand-gated

- Na^+, K^+, (Ca^{2+})



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5-2 Randall et al. 2002

Frequency and number!

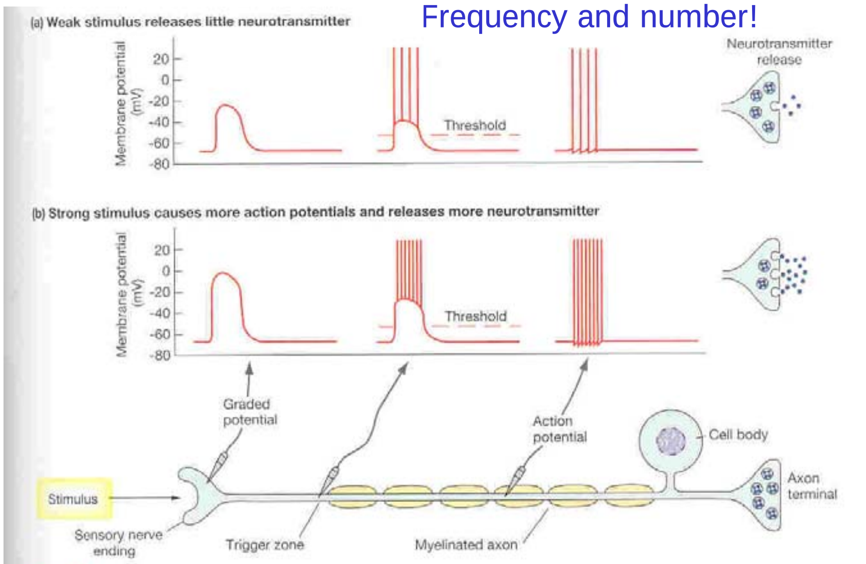

Figure 8-13 Coding for stimulus intensity Stimuli of different intensity change the frequency of action potential firing along the axon. Since all action potentials in a neuron are identical, the strength of the stimulus is indicated by the frequency of action potential firing. (a) A graded potential that is barely above threshold causes a series of action potentials to pass down the axon and release neurotransmitter. (b) A stronger graded potential increases the frequency of action potential firing in the axon and releases more neurotransmitter.

Silverthorn 2001. 2nd ed. Human Physiology. Prentice Hall

Action Potentials

-Moves information; high-speed communication

-Thoughts, Sensations, Memories, Movements etc.

-Moves SIGNAL without decrement

-AP possible because:

1 Ionic gradients across membrane

2 Creates electrochemical gradient and therefore source of potential energy

3 When ion channels open, ions move down their electrochemical gradients and rapidly change the membrane potential (V_m)

- Na+ and K+ responsible for AP character…

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-Threshold

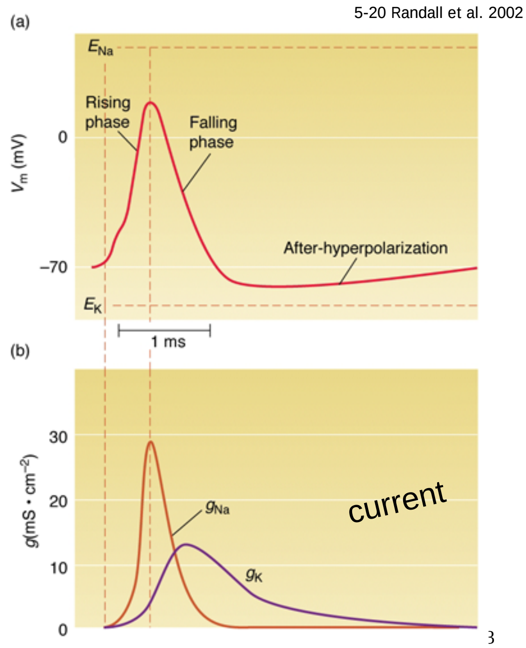
-Voltage gated

-Many channels
for Na+

-Then many
channels for K+

+60 vs. -100

emf



Membrane Potential

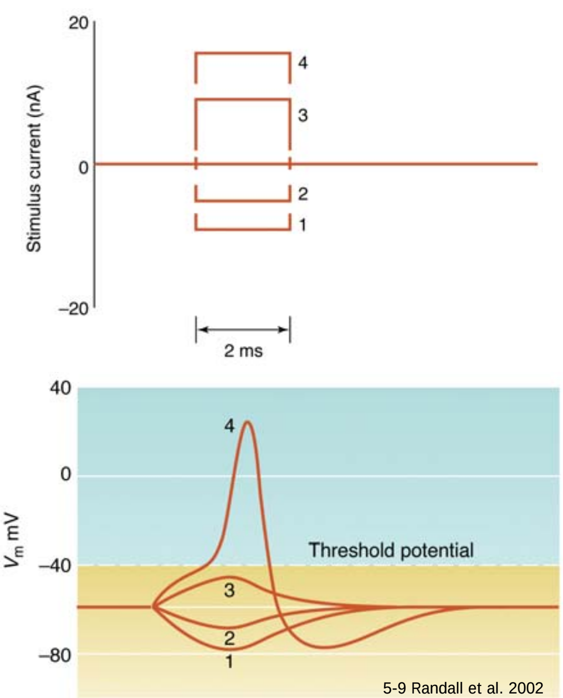
Terms:

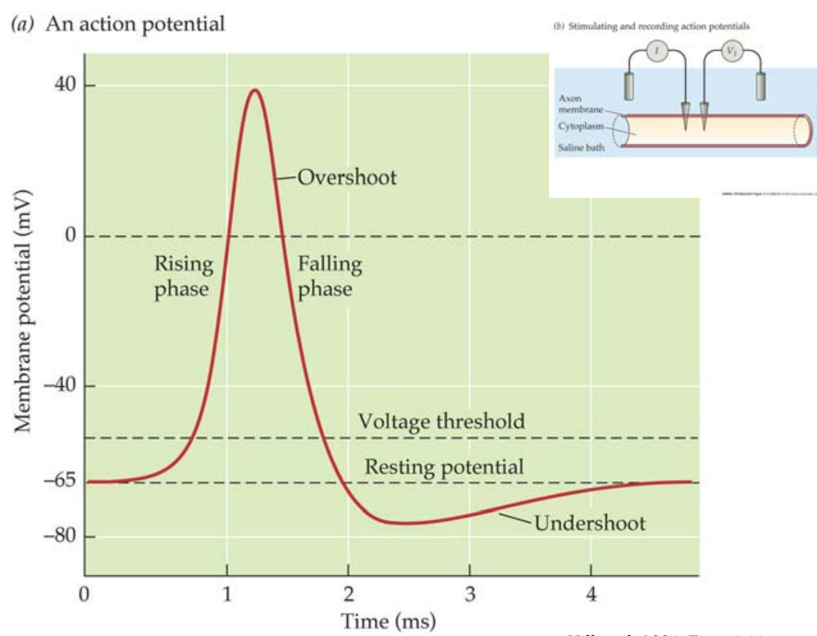
-Hyperpolarization
1 and 2

-Depolarization
3 and 4

-Threshold Potential
see 4 (50% time get AP)

-Repolarization
3 and 4



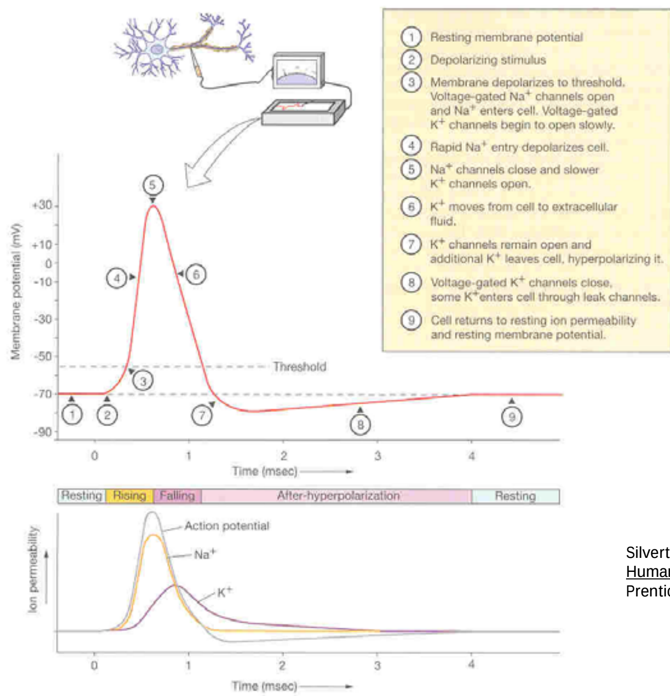


Hill et al. 2004, Fig. 11.11

ANIMAL PHYSIOLOGY, Figure 11.11 (Part 1) © 2004 Sinauer Associates, Inc.

Table 5-1 **Examples of ion channels found in axons** Randall et al. 2002

Channel	Current through channel	Characteristics	Selected blockers	Function
Leak channel (open in resting axon)	I_K (leak)	Produces relatively high P_K of resting cell	Partially blocked by tetraethylammonium (TEA)	Largely responsible for V_{rest}
Voltage-gated Na^+ channel	I_{Na}	Rapidly activated by depolarization; becomes inactivated even if V_m remains depolarized	Tetrodotoxin (TTX)	Produces rising phase of AP
Voltage-gated Ca^{2+} channel	I_{Ca}	Activated by depolarization but more slowly than Na^+ channel; inactivated as function of cytoplasmic $[Ca^{2+}]$ or V_m	Verapamil, D600, Co^{2+}, Cd^{2+}, Mn^{2+}, Ni^{2+}, La^{3+}	Produces slow depolarization; allows Ca^{2+} to enter cell, where it can act as second messenger
Voltage-gated K^+ channel ("delayed rectifier")	$I_{K(V)}$	Activated by depolarization but more slowly than Na^+ channel; inactivated slowly and not completely if V_m remains depolarized	Intra- and extracellular TEA, amino pyridines	Carries current that rapidly repolarizes the membrane to terminate an AP
Ca^{2+}-dependent K^+ channel	$I_{K(Ca)}$	Activated by depolarization plus elevated cytoplasmic $[Ca^{2+}]$; remains open as long as cytoplasmic $[Ca^{2+}]$ is higher than normal	Extracellular TEA	Carries current that repolarizes the cell following APs based on either Na^+ or Ca^{2+} and that balances I_{Ca}, thus limiting depolarization by I_{Ca}



■ Figure 8-9 The action potential

Silverthorn 2001. 2[nd] ed.
Human Physiology.
Prentice Hall

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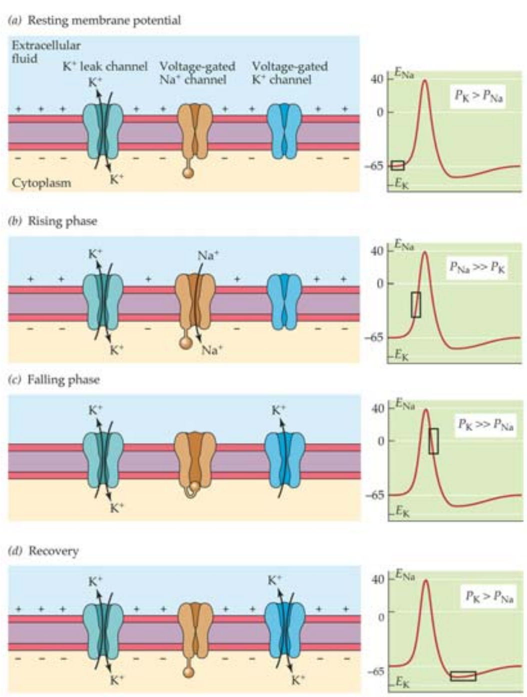

Action Potential

Hill et al. 2004, Fig. 11.12

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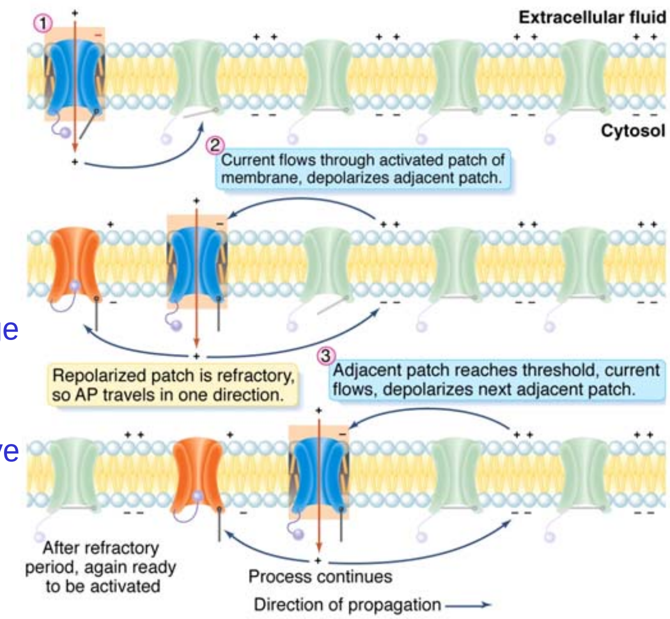
Voltage-gated Na+ channels

local current flow causes Vm change

AP is regenerative



6-4 Randall et al. 2002

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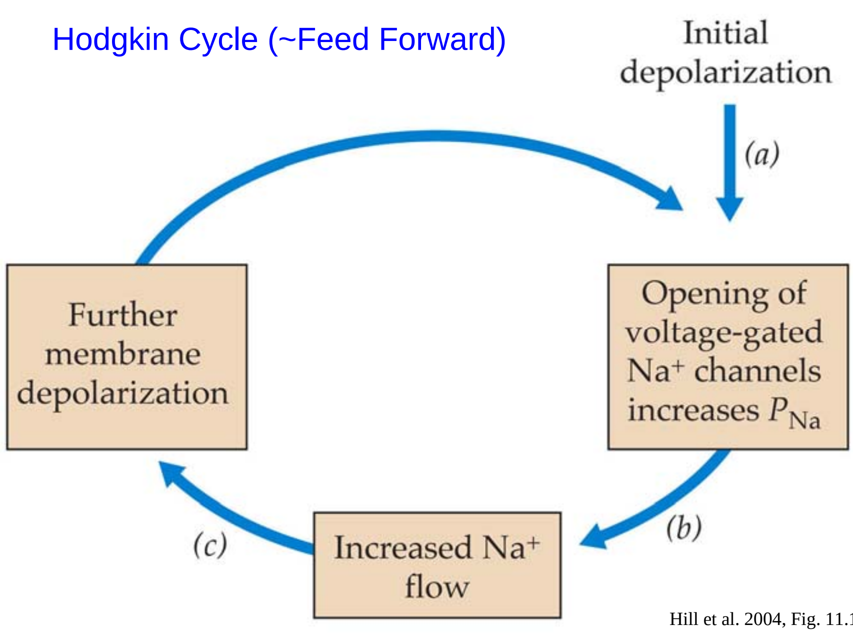
Hodgkin Cycle (~Feed Forward)



Hill et al. 2004, Fig. 11.13

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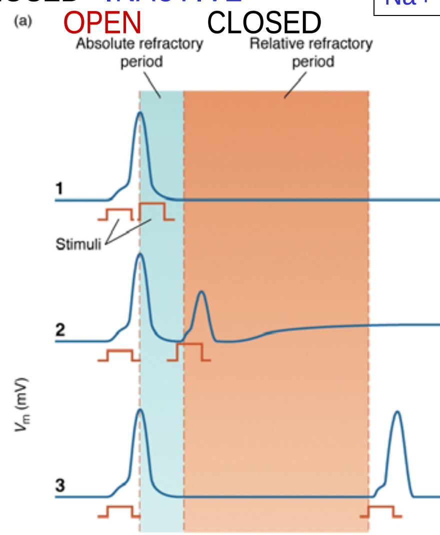
-Refractory Periods

Voltage-gated Na+ channels

CLOSED INACTIVE

OPEN CLOSED



-Absolute

-Relative

~ Toilet Analogy...

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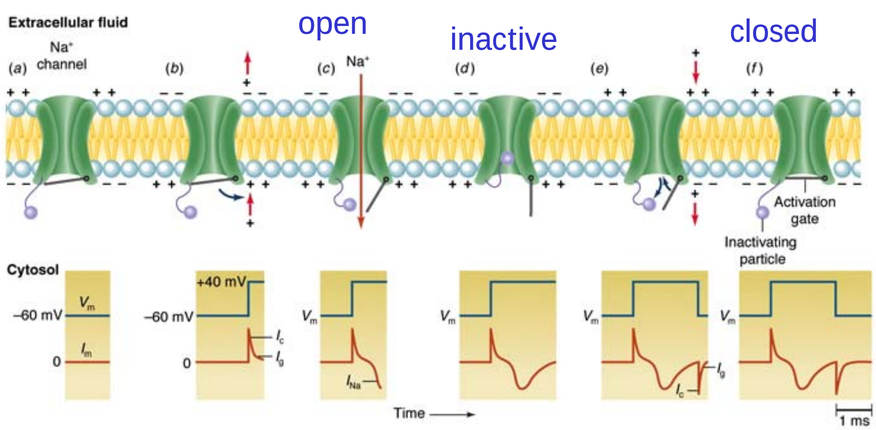
5-17 Randall et al. 2002

closed

open

inactive

closed



Voltage -top

Current- bottom

5-22 Randall et al. 2002

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How would you make the membrane in the axon hillock/spike initiation zone more, or less, likely to send an AP?

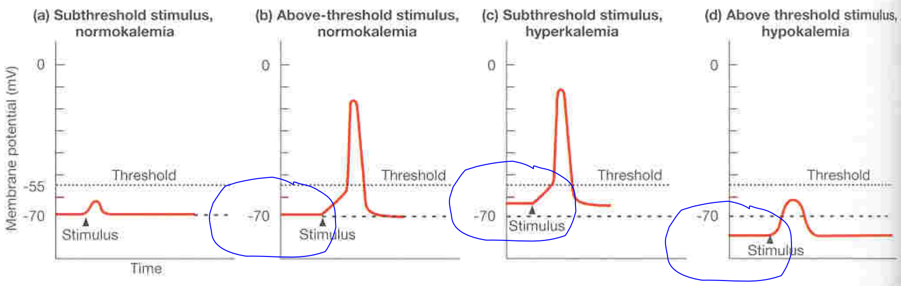
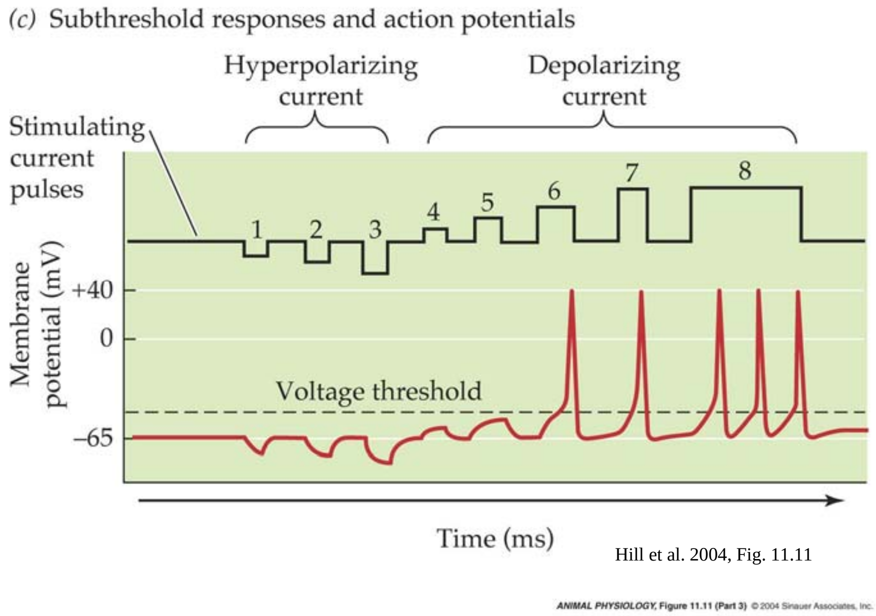


Figure 8-18 Effect of changing extracellular potassium concentration on the excitability of neurons If the extracellular concentration of K^+ changes, the resting membrane potential of cells changes. (a) A subthreshold graded potential does not fire an action potential when blood K^+ concentration is in the normal range (normokalemia). (b) An above-threshold (suprathreshold) stimulus will fire an action potential when K^+ concentration is normal. (c) Hyperkalemia, increased blood K^+ concentration, brings the membrane closer to threshold. Now a subthreshold stimulus can trigger an action potential. (d) Hypokalemia, decreased blood K^+ concentration, hyperpolarizes the membrane and makes the neuron less likely to fire an action potential in response to a stimulus that would normally be above threshold.

Silverthorn 2001. 2nd ed. Human Physiology. Prentice Hall



Hill et al. 2004, Fig. 11.11

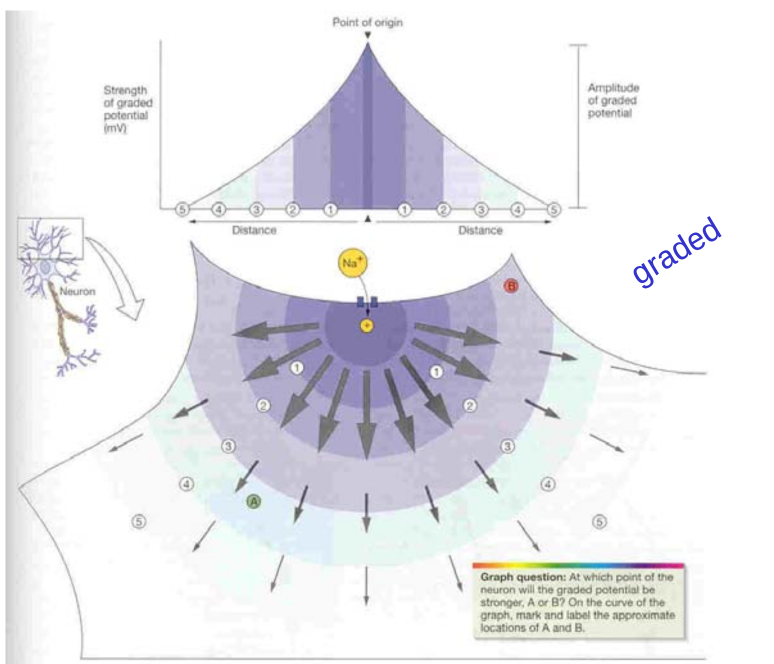


Figure 8-7 Graded potentials decrease in strength as they spread out from the point of origin

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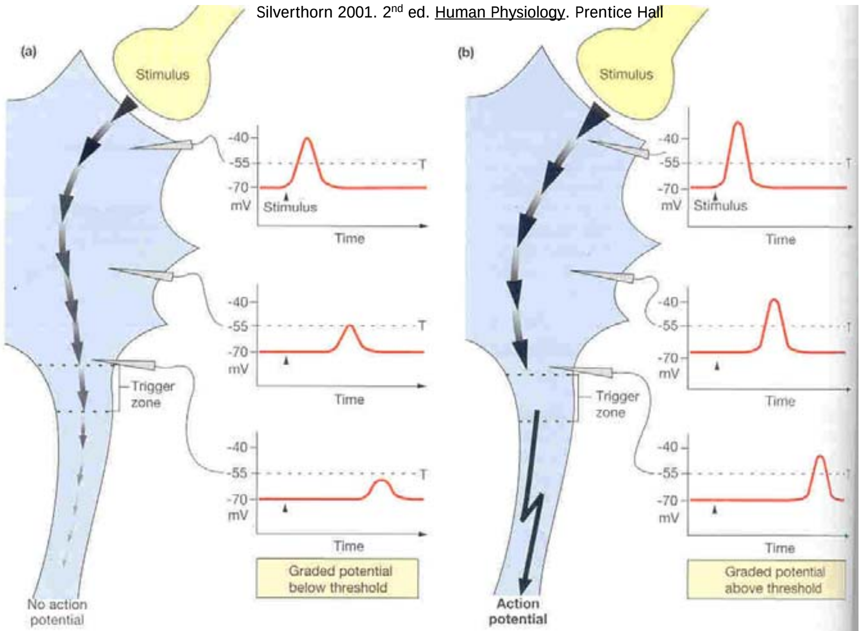
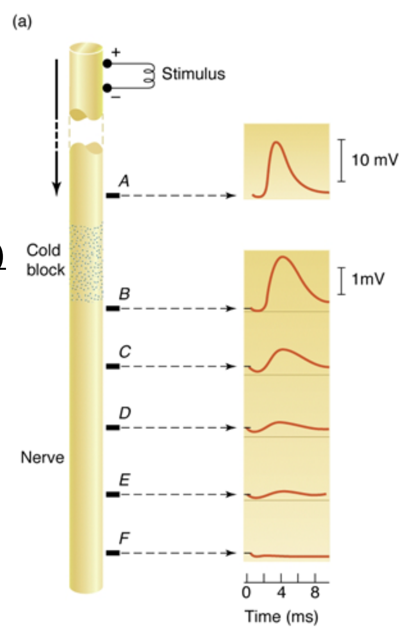


Figure 8-8 Subthreshold and suprathreshold graded potentials in a neuron (a) A graded potential starts above threshold at the point where it is initiated but decreases in strength as it travels through the cell body. At the trigger zone it is below threshold (T) and therefore does not initiate an action potential. (b) A stronger stimulus at the same point on the cell body creates a graded potential that is still above threshold by the time it reaches the trigger zone, so an action potential results.

-Role of local current flow

(no APs past here)

-But can see local graded potential diminishing



p.161 Randall et al. 2002

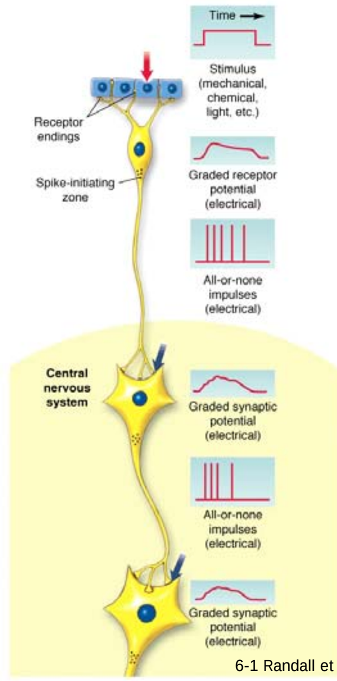
-Receptor potential is graded and decremental

-Magnitude of graded receptor potential determines frequency of APs (~all of the same size)

-Neurotransmitter Release

-Alternate between graded psps and all-or-none APs

psp =
postsynaptic potential



6-1 Randall et al. 2002

TABLE 8-2 Comparison of Graded Potential and Action Potential

	Graded Potential	*Action Potential*
Type of signal	Input signal	Conduction signal
Where occurs	Usually dendrites and cell body	Trigger zone through axon
Types of gated ion channels involved	Mechanically, chemically, or voltage-gated channels	Voltage-gated channels
Ions involved	Usually Na^+, Cl^-, Ca^{2+}	Na^+ and K^+
Type of signal	Depolarizing (e.g., Na^+) or hyperpolarizing (e.g., Cl^-)	Depolarizing
Strength of signal	Depends on initial stimulus; can be summed	Is always the same (all-or-none phenomena); cannot be summed
What initiates the signal	Entry of ions through channels	Above-threshold graded potential at the trigger zone
Unique characteristics	No minimum level required to initiate Two signals coming close together in time will sum	Threshold stimulus required to initiate Refractory period; two signals too close together in time cannot sum Initial stimulus strength is indicated by frequency of a series of action potentials

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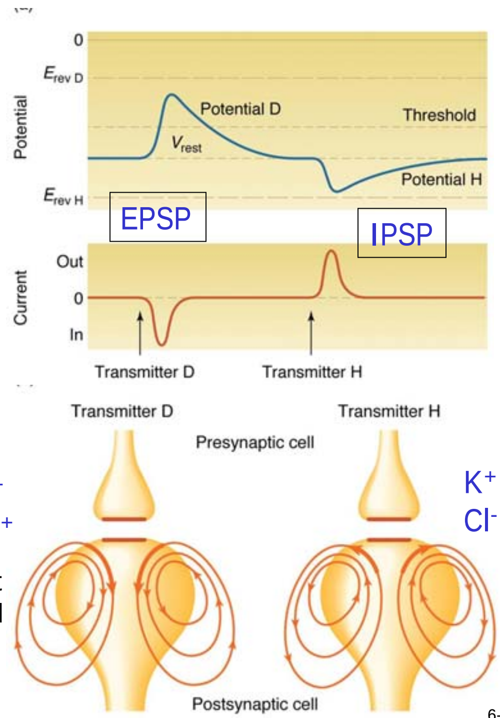
EPSP and IPSP

Excitatory or Inhibitory Postsynaptic Potentials



psp

psc

Na^+
Ca^{2+}

K^+
Cl^-

Graded current causing graded potential:

psc

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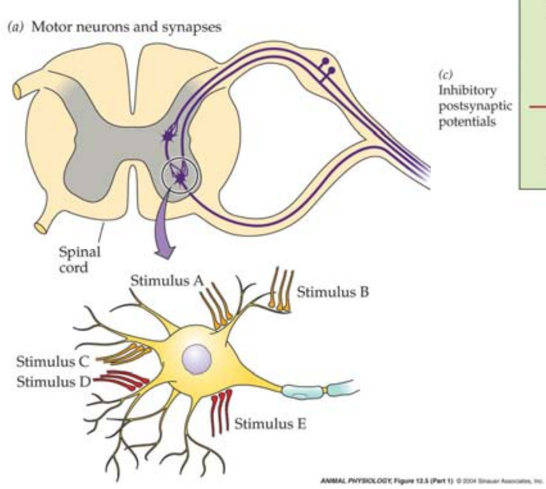
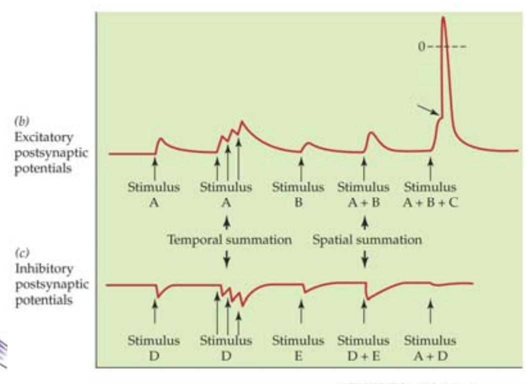
6-19 Randall et al. 2002

Integration





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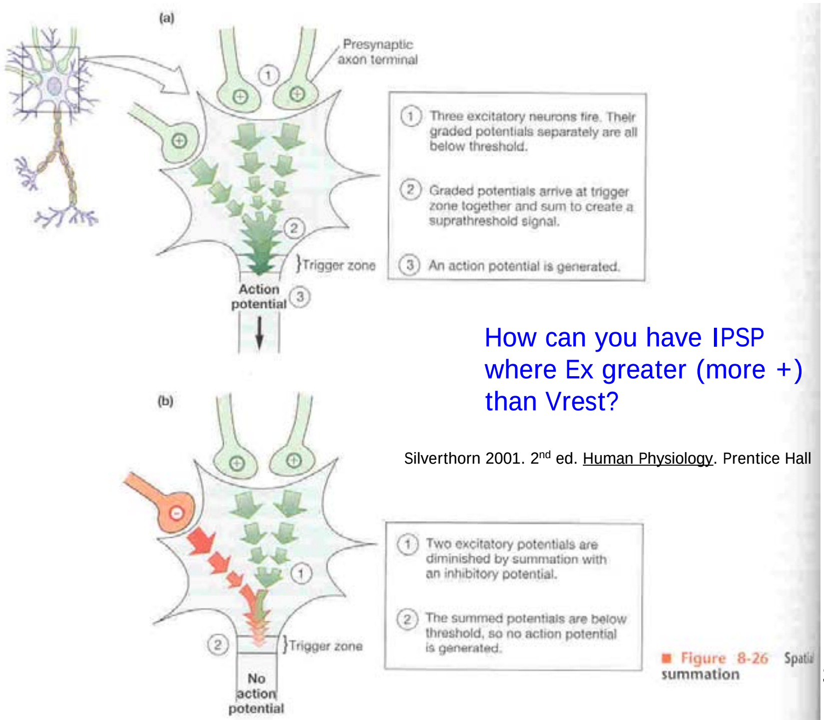
Hill et al. 2004, Fig 12.5



How can you have IPSP where Ex greater (more +) than Vrest?

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Reversal Potential

Opening channel for a given ion species X means Vm will move toward *E*x

*E*rev is the reversal potential

Can’t change membrane potential beyond *E*rev for a given ion(s) and its channels

Use Nernst to calculate for one ion species

Goldman equation for multiple ions

ACh opens for K+ and Na+, so *E*rev between E_K and E_{Na}

EPSP and IPSP

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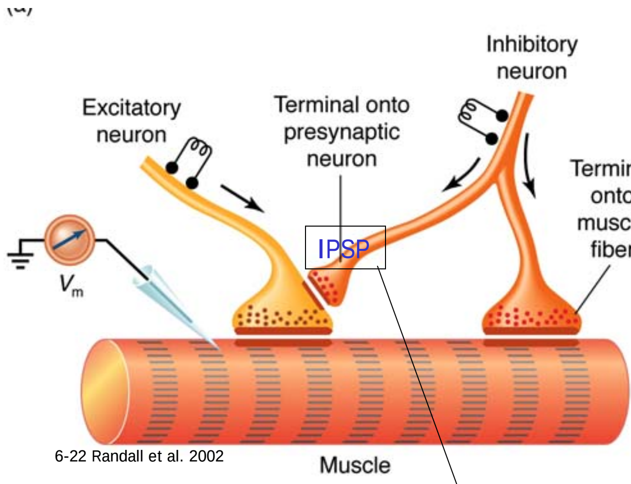
Presynaptic inhibition



Synaptic Efficacy

e.g., Cl^-, K^+ or alter Ca^{2+}

NT release via exocytosis: the role of Ca^{2+}

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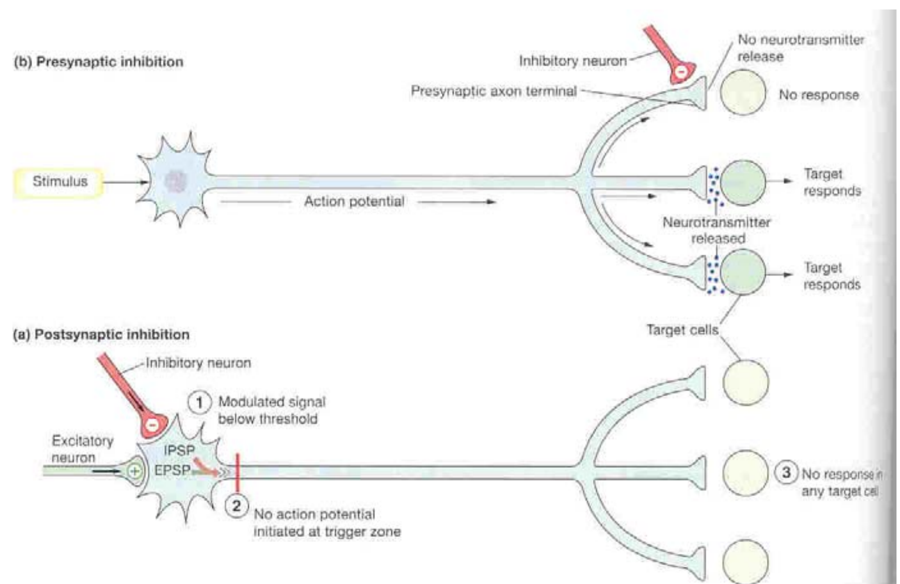

■ Figure 8-28 **Presynaptic and postsynaptic inhibition** (a) In presynaptic inhibition, a modulatory neuron synapses on one collateral of the presynaptic neuron. In this way, one target of the neuron can be selectively inhibited. (b) In postsynaptic inhibition, all targets of the postsynaptic cell will be inhibited equally.

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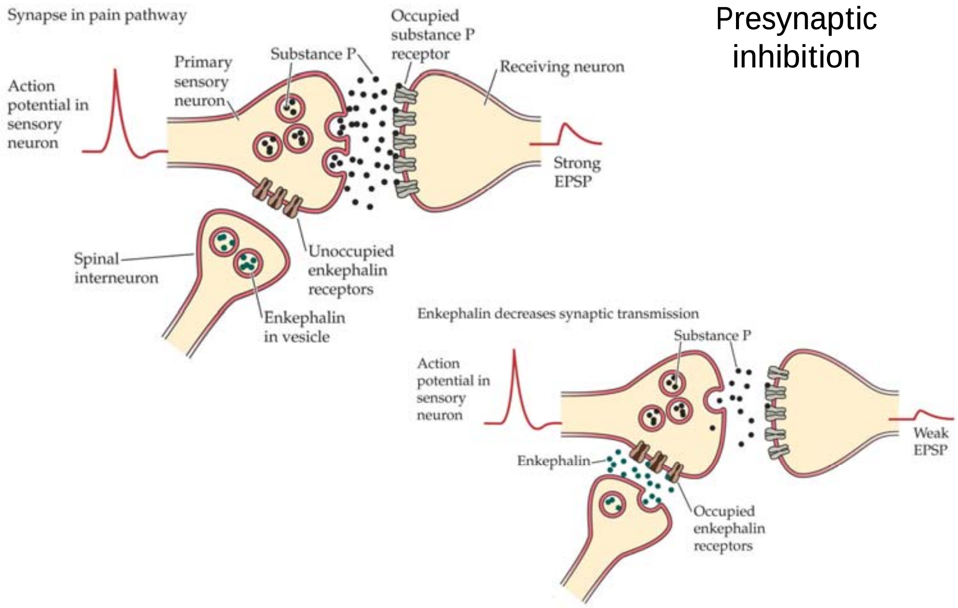
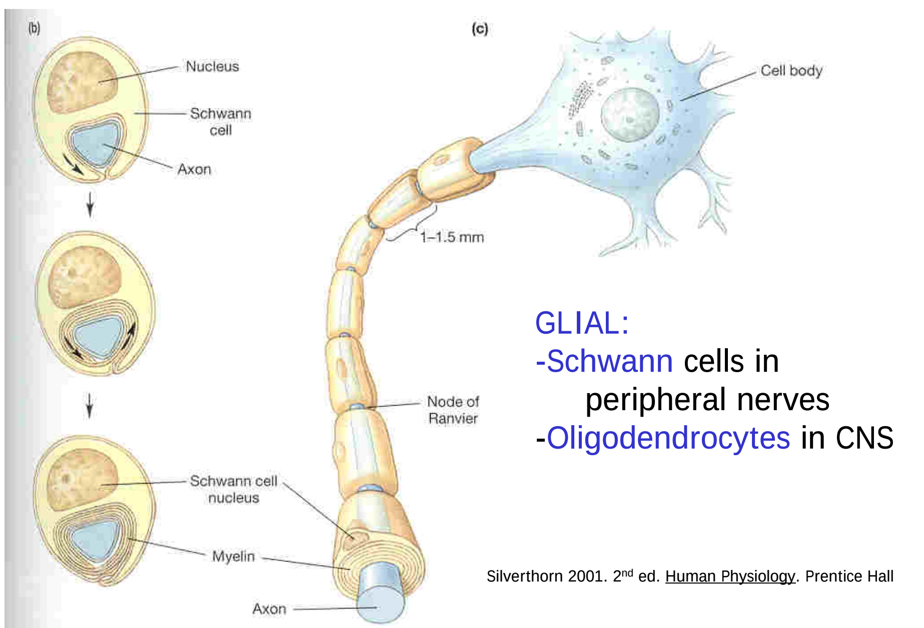
Presynaptic inhibition



Hill et al. 2004 pg. 330



GLIAL:
- Schwann cells in peripheral nerves
- Oligodendrocytes in CNS

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Figure 8-6 Formation of myelin (a) In the CNS, oligodendrocytes form myelin around portions of several interneuron axons. Astrocytes contact both neurons and blood vessels, but do not form myelin. (b) During myelin formation in the peripheral nervous system, the Schwann cell wraps around the axon many times while its nucleus is pushed to outside of the myelin sheath. (c) A Schwann cell forms myelin around a small segment of one axon.

-How increase conduction velocity?

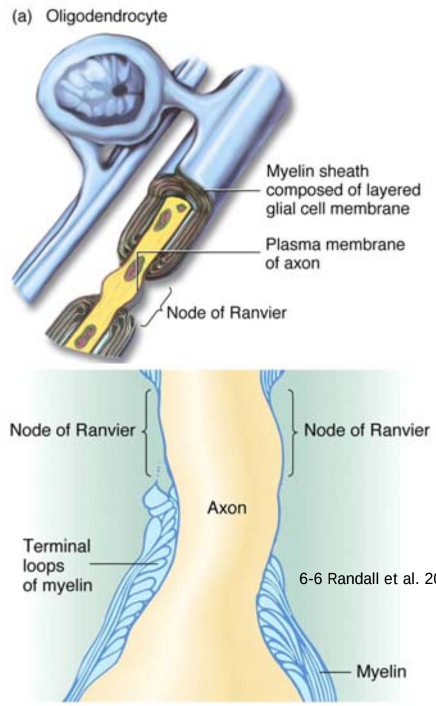
1 –Diameter

2 -Insulation

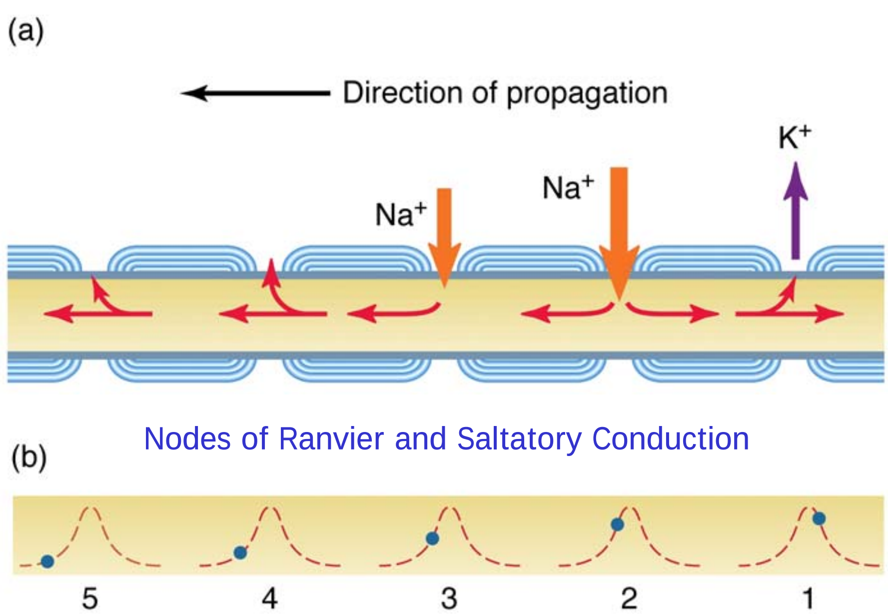
-Long axons require insulation (support cells)

-glial cells for myelination (fatty tissue) aka:

-Schwann cells in peripheral nerves
-Oligodendrocytes in CNS



6-6 Randall et al. 2002



Nodes of Ranvier and Saltatory Conduction

6-7 Randall et al. 2002

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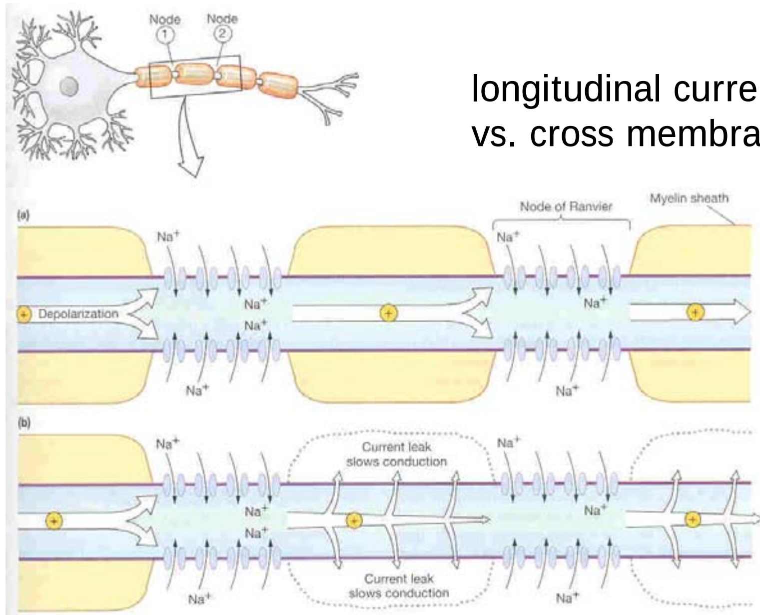

■ Figure 8-17 **Saltatory conduction** (a) Action potentials appear to jump from one node of Ranvier to the next when local current flow moves rapidly through the myelinated sections between the nodes. Voltage-gated Na^+ channels are scarce between the nodes. (b) In demyelinating diseases, conduction slows down as current leaks out of the previously insulated regions between the nodes. Since there are few Na^+ channels in those regions, the action potentials are not conducted as strongly between the nodes.

longitudinal current
vs. cross membrane

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Table 6-1 **The diameter of frog axons and the presence or absence of myelination control the conduction velocity.**

Fiber type	Average axon diameter (μm)	Conduction velocity ($m \cdot s^{-1}$)
Myelinated fibers		
Aα	18.5	42
Aβ	14.0	25
Aγ	11.0	17
B	Approximately 3.0	4.2
Unmyelinated fibers		
C	2.5	0.4–0.5

Source: Erlanger and Gasser, 1937.

Randall et al. 2002

Multiple sclerosis caused by demyelination

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