Ch 8: Neurons: Cellular and Network Properties, Part 1

Objectives:

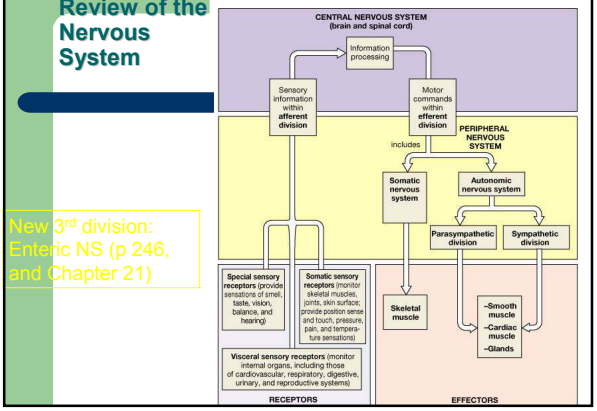
Describe the Cells of the NS

Explain the creation and propagation of an electrical signal in a nerve cell

Outline the chemical communication and signal transduction at the synapse

Review of the Nervous System

New 3rd division: Enteric NS (p 246, and Chapter 21)



The afferent and efferent axons together form the

A. Central nervous system
B. Autonomic division of the nervous system
C. Somatic motor division of the nervous system
D. Peripheral nervous system
E. Visceral nervous system

Autonomic neurons are further subdivided into the

A. Visceral and somatic divisions
B. Sympathetic and parasympathetic divisions
C. Central and peripheral divisions
D. Visceral and enteric divisions
E. Somatic and enteric divisions

Processes or appendages that are part of neurons include

A. Axons
B. Dendrites
C. Neuroglia
D. A and B
E. A, B and C

Cells of NS

Fig 8-2

- **1. Nerve cell = Neuron**
  - **Functional unit of nervous system**
  - **excitable**
  - **can generate & carry electrical signals**
- **Neuron classification either structural or functional (?)**

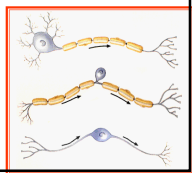


Fig 8-3

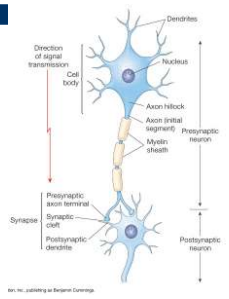
Cells of NS

- 1. Neurons
- 2. Neuroglia = Support cells
  - Schwann Cells (PNS)
  - Oligodendrocytes (CNS)
  - Astrocytes
  - Microcytes
  - Ependymal Cells

Fig 3

Some Terminology

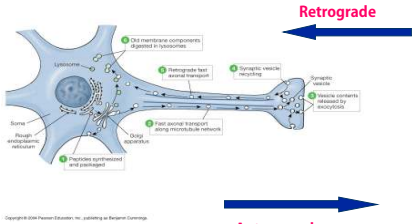
- Pre- and postsynaptic membrane, terminal, neuron, etc.
- Ganglion
- Interneuron
- Synaptic cleft
- Neurotransmitter
- Sensory and Motor



Functional categories of neurons include

A. Afferent neurons
B. Sensory neurons
C. Interneurons
D. Efferent neurons
E. All of these are included as functional categories of neurons

Axonal Transport of Membranous Organelles

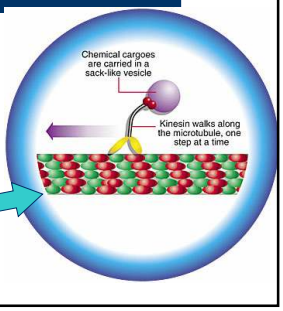


Axonal Transport

What is it? Why is it necessary?

Slow axonal transport (0.2 - 2.5 mm/day)
- Carries enzymes etc. that are not quickly consumed – Utilizes axoplasmic flow

Fast axonal transport (up to 400 mm/day)
- Utilizes kinesins, dyneins and microtubules
- Actively walks vesicle or down axon along a microtubule



2. Neuroglia cells

In CNS:

1. Oligodendrocytes (formation of myelin)
2. Astrocytes (BBB, K^+ uptake)
3. Microglia (modified MΦ)

In PNS:

4. *(Ependymal cells)*
5. Schwann cells (formation of myelin)
6. Satellite cells (support)

What does this mean?

See Fig 5

Resting Membrane Potential (Electrical Disequilibrium)

Ch 5, p160-167

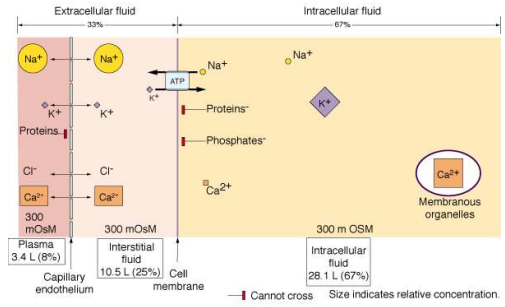
- Recall that most of the solutes, including proteins, in a living system are ions
- Recall also that we have many instances of chemical disequilibrium across membranes
- Opposite (+ vs. -) charges attract, thus energy is required to maintain separation
- The membrane is an effective insulator

Resting Membrane Potential (Electrical Disequilibrium)

Ch 5, p160-167

- Membrane potential = unequal distribution of charges (ions) across cell membrane
- K^+ is major intracellular cation
- Na^+ is major extracellular cation
- Water = conductor
- Cell membrane = insulator

Review of Solute Distribution in Body Fluids

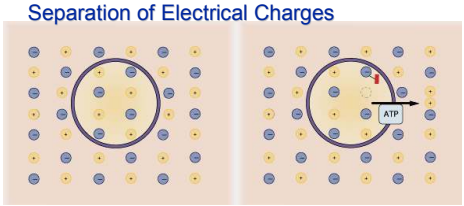


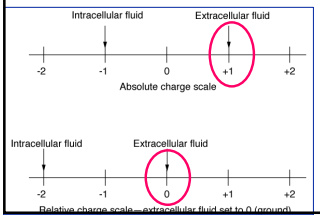
Electro-Chemical Gradients

- Allowed for, and maintained by, the cell membrane
- Created via
  - Active transport (Na^+ pump)
  - Selective membrane permeability to certain ions and molecules

Fig 5-36

Separation of Electrical Charges





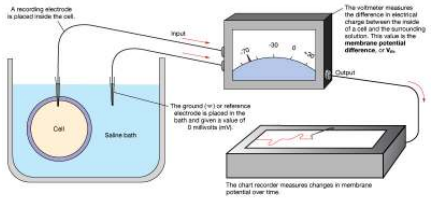
These Measurements are on a relative scale !

Resting Membrane Potential Difference

- All cells have it
- Resting ⇒ cell at rest
- Membrane Potential ⇒ separation of charges creates potential energy
- Difference ⇒ difference between electrical charge inside and outside of cell (ECF by convention 0 mV)

Fig 5-33

Measuring Membrane Potential Differences



Equilibrium Potential for K^+ (Ch 5, p 163)

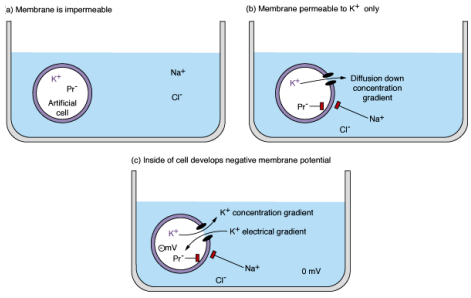
= Membrane potential difference at which movement down concentration gradient equals movement down electrical gradient

Fig 5-34

Definition: electrical gradient equal to and opposite concentration gradient

Equilibrium potential for K^+ = -90 mV

Potassium Equilibrium Potential

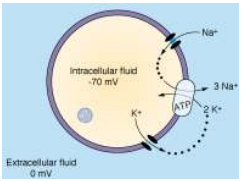


Resting Membrane Potential (Ch 5, p 160)

of most cells is between -50 and -90 mV (average ~ -70 mV)

Reasons:

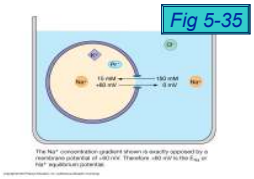
- Membrane permeability: $K^+ > Na^+$ at rest
- Small amount of Na^+ leaks into cell
- Na^+/K^+-ATPase pumps out 3 Na^+ for 2 K^+ pumped into cell



Equilibrium Potential for Na+

- Assume artificial cell with membrane permeable to Na^+ but to nothing else
- Redistribution of Na^+ until movement down concentration gradient is exactly opposed by movement down electrical gradient
- Equilibrium potential for Na^+ = + 60 mV

Fig 5-35



Ions Responsible for Membrane Potential

Cell membrane
- impermeable to Na^+, Cl^- & Pr^-
- permeable to K^+

⇒ K^+ moves down concentration gradient (from inside to outside of cell)

⇒ Excess of neg. charges inside cell

⇒ Electrical gradient created

Neg. charges insic cell

TABLE 8-2 Ion Concentrations and Equilibrium Potentials

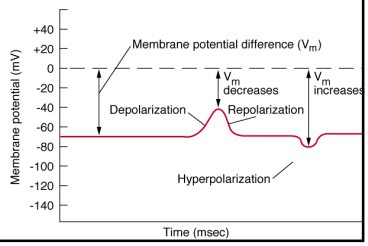
ION	EXTRACELLULAR FLUID (mM)	INTRACELLULAR FLUID (mM)	E_{ion} AT 37° C
K^+	5 mM (normal range: 3.5–5)	150 mM	−90 mV
Na^+	145 mM (normal range: 135–145)	15 mM	+60 mV
Cl^-	108 mM (normal range: 100–108)	10 mM (range: 5–15)	−63 mV
Ca^{2+}	1 mM	0.0001 mM	see Concept Check question 6

Change in Ion Permeability

- leads to change in membrane potential
- *Terminology:*

Stimulus
↓
Depolarization
↓
Repolarization
↓
Hyperpolarization

Fig 7-37

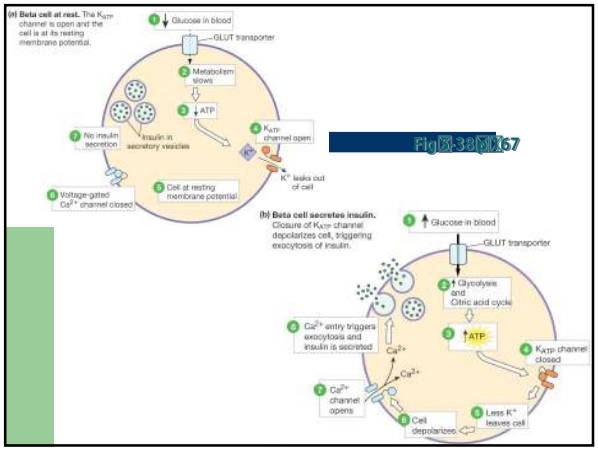


Explain

- Increase in membrane potential
- Decrease in membrane potential
- What happens if cell becomes more permeable to potassium
- Maximum resting membrane potential a cell can have

- **Membrane potential changes play important role also in non-excitable tissues!**
- Insulin Secretion p 166
  - β-cells in pancreas have two special channels:
    - Voltage-gated Ca^{2+} channel
    - ATP-gated K^+ channel

Fig 7-38



Return to Ch 8: p. 252

Electrical Signals in Neurons

Changes in membrane potential are the basis for electrical signaling

Only nerve and muscle cells are excitable (= able to propagate electrical signals)

GHK Equation:
Resting membrane potential = combined contributions of the conc. gradients and membrane permeability for Na^+, K^+ *(and Cl)*

Control of Ion Permeability

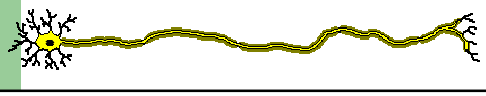
- Gated ion channels – alternate between open and closed state
  - Mechanically gated channels
  - Chemically gated channels
  - Voltage-gated channels
- Net movement of ions de- or hyperpolarizes cell

2 types of electrical signals
Graded potentials, travel over short distances
Action potentials, travel very rapidly over longer distances

Chapter 8: Neurons, Part I

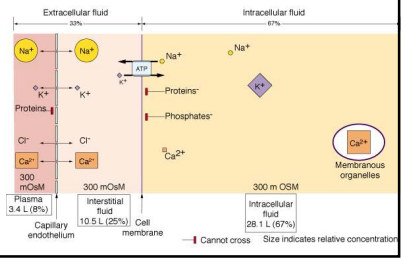
Four Basic Components of Signal Movement Through Neuron

1. Input signal (graded potential)
2. Integration of input signal at trigger zone
3. Conduction signal to distal part of neuron (= Action Potential)
4. Output signal (usually neurotransmitter)



Review of Solute Distribution in Body Fluids

- The [ ] gradient of K^+ is the main source of the membrane potential
- Change in permeability ot Na^+ can allow influx of Na^+
  - Depolarization
  - Electric signal created
  - Controlled by gated channels



Graded Potentials

Trigger Zone

- Usually Axon Hillock
- and/or Initial segment of axon
- Many Na^+ Channels

- Some stimuli may be inhibitory
  - Hyperpolarizing effect

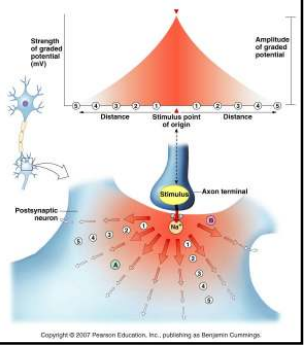


Fig 8-7

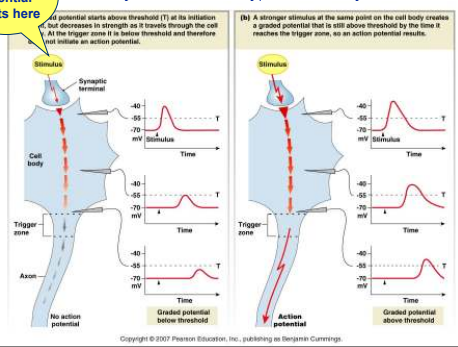
Graded Potentials

- Location: Any receptor
- Strength (= amplitude) ~ strength of triggering event
- Travel over short distances to trigger zone
  - Amount of local current flow is variable
- Diminish in strength as they travel
- May be depolarizing (EPSP) or hyperpolarizing (IPSP)

Fig 8-7

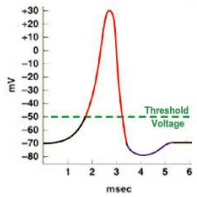
Graded potential starts here

reshold potential vs. Suprathreshold potential



Conduction Signals: Action Potentials (AP)

- Travel over long distances
- Do not lose strength as they travel
- Are all identical (all-or-none principle): 100mV amplitude
- Represent movement of Na^+ and K^+ across membrane



Ability to propagate the AP = Excitability

Ion Movement across Cell Membrane During AP

- Sudden increase in Na^+ permeability
- Na^+ enters cell down electrochemical gradient (+ feedback loop for ~ .5 msec)
- Influx causes depolarization of membrane potential = electrical signal
- *What stops + feedback loop? The* Na^+ inactivation gate closes.

Na^+ Channels in Axon Have 2 Gates

- Activation gate and Inactivation gate
- Na^+ entry based on pos. feedback loop ⇒ needs intervention to stop
- Inactivation gates close in delayed response to depolarization
- ⇒ stops escalating pos. feedback loop

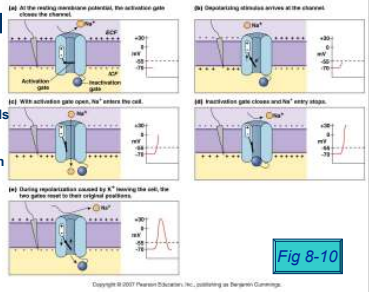
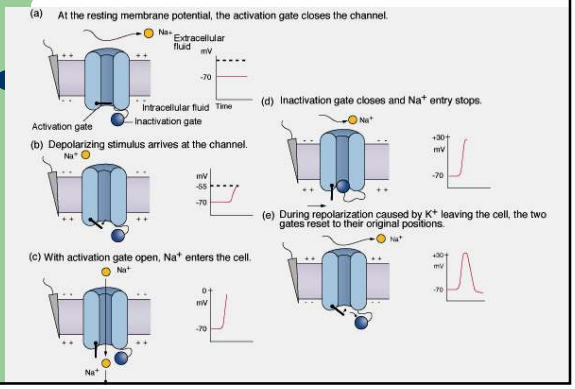


Fig 8-10

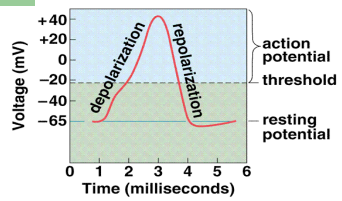
Model of Activation and Inactivation Gates



AP-Graph

has 3 phases

1. Rising (Na^+ permeability ↑)
2. Falling (K^+ permeability ↑)
3. "Undershoot" or Hyperpolarization



Graded potentials

A. Produce an effect that increases with distance from the point of stimulation
B. Produce an effect that spreads actively across the entire membrane surface
C. May involve either depolarization or hyperpolarization
D. Are all-or-none
E. All of the above

The principal cause of early repolarization of a nerve fiber after an adequate stimulus has been applied is:

A. An increase in the diffusion of K^+ into the neuron
B. An increase in the diffusion of Na^+ out of the neuron
C. And increase in the diffusion of Na^+ into the neuron
D. And increase in the diffusion of K^+ out of the neuron
E. A decrease in the diffusion of Na^+ into the neuron

Absolute & Relative Refractory Periods

No movement of Na^+ possible

Na^+ channels reset to resting state, K^+ channels still open higher stimulus necessary

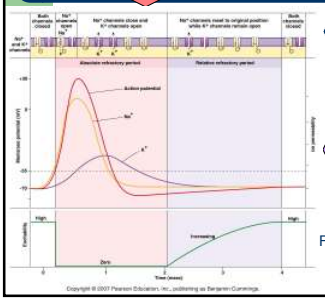
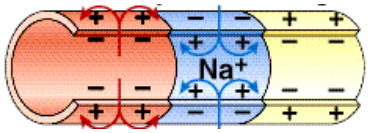


Fig 8-12

Refractory Periods

1. **Limit signal transmission rate (no summation!)**

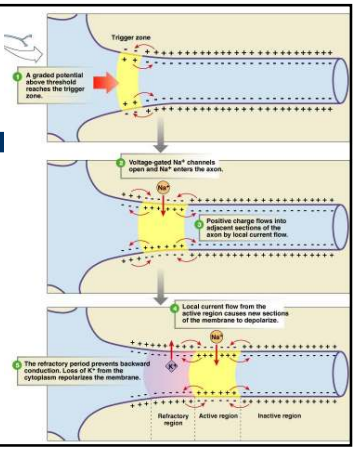
3. **Remember that the Na^+ and K^+ concentration gradients remain nearly unchanged!** Animation



Forward current excites, backward current does NOT re-excite !

Conduction of AP

- Graded Potential
  - Cytoplasmic flow
- AP starts at Axon Hillock
- Na^+ gates open
  - Na^+ into axon
- K^+ moves out
  - Hyperpolarizes membrane briefly
  - "resets" membrane for next AP



Conduction speed depends on . . . .

1. **Axon diameter** ***(the larger the faster)***
   1. Size constraints on axons become problem with increasing organismal complexity

   Fig 8-17
2. **Membrane resistance**
   1. High resistance of myelin sheath reduces leakage of current (ion) flow between axon and ECF
   2. Saltatory Conduction from node to node

Fig 8-18

1. Axon Diameter

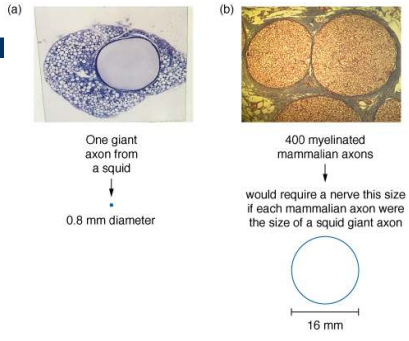
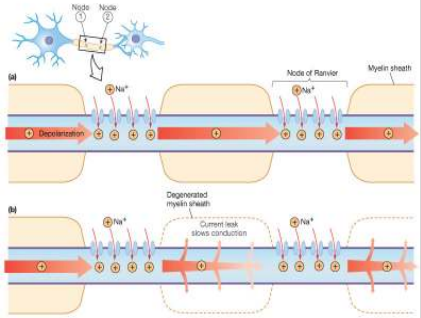


Fig 8-17

Fig. 8-18

2. Signal Transduction in Myelinated Axon:

Animation



Demyelination diseases *(E.g. ?)*

The primary problem in hypokalemia is that

A. [illegible] potential is hyperpolarized
B. Neurons are hyper-excitable because their resting potential is closer to threshold
C. Neurons respond too quickly to smaller graded potentials
D. A and C
E. B and C

The basis of neural integration is

A. Addition of postsynaptic potentials overlapping in time and space
B. Command signals from central pattern generators
C. Spontaneous activity in pacemaker neurons
D. The area under the curve of postsynaptic potentials overlapping in time and space
E. All of the above

How would blocking the ability for retrograde transport in an axon affect the activity of a neuron?

A. The neuron would not be able to produce NT
B. The neuron would not be able to have APs
C. The cell body would not be able to export products to the axon terminal
D. The cell body would not be able to respond to changes in the distal end of the axon
E. The neuron would be unable to depolarize when stimulated.

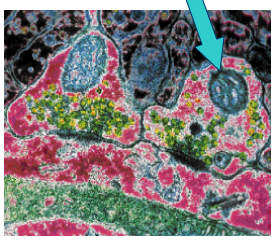
Output Signal: Communication at Synapses

What's this?

Synapse = point where neuron meets target cell *(e.g. ?)*

2 types
- chemical
- electrical

3 components of chemical synapse
- presynaptic cell
- synaptic cleft
- postsynaptic cell

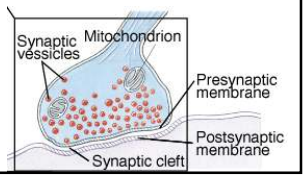


Chemical Synapses

= Majority of synapses

neurotransmitters [illegible] cell to cell

Axon terminals have mitochondria & synaptic vesicles containing neurotransmitter



Events at the Synapse

AP reaches axon terminal

↓

Voltage-gated Ca^{2+} channels open

↓

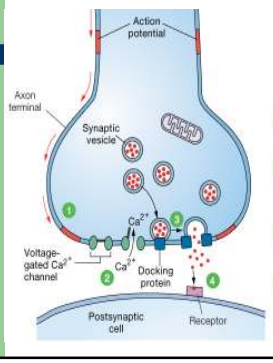
Ca^{2+} entry

↓

Exocytosis of neurotransmitter containing vesicles

Ca^{2+} = Signal for Neurotransmitter Release

Synapse



1. An action potential depolarizes the axon terminal.
2. The depolarization opens voltage-gated Ca^{2+} channels and Ca^{2+} enters the cell.
3. Calcium entry triggers exocytosis of synaptic vesicle contents.
4. Neurotransmitter diffuses across the synaptic cleft and binds with receptors on the postsynaptic cell.

Fig 8-21

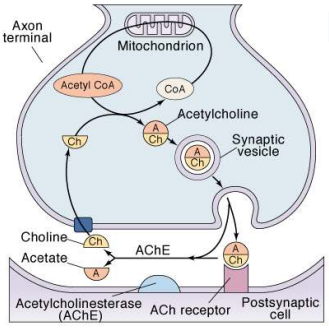
3 Classes of Neurotransmitters (of 7)

Fig 8-22

1. **Acetyl Choline (ACh)**
   - Synthesized in axon terminal
   - Quickly degraded by ACh-esterase
   - Cholinergic neurons and receptors – Nicotinic (agonistic) and muscarinic (antagonist)
2. **Amines**
   - **Serotonin** (tryptophane) and Histamine (histidine)
     - SSRI = antidepressants
   - **Dopamine and Norepinephrine** (tyrosine)
   - Widely used in brain, role in emotional behavior (NE used in ANS)
   - Adrenergic neurons and receptors - α and β
3. **Gases**
   - NO (nitric oxide) and CO
4. **Others: AA, (e.g., GABA), lipids, peptides, purines**

Synthesis and Recycling of ACh at Synapse

Fig 8-22



Postsynaptic Responses

Can lead to either EPSP or IPSP *(p.277)*

Fast synaptic potentials

Opening of chemically gated ion channel

Rapid & of short duration

Slow synaptic potentials

Involve G-proteins and 2nd messengers

Can open or close channels or change protein composition of neuron

Integration of Neural Informati

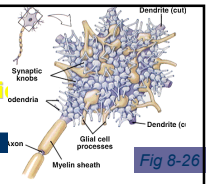
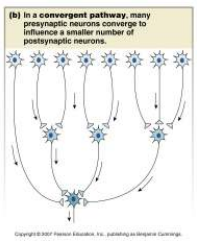


Fig 8-26

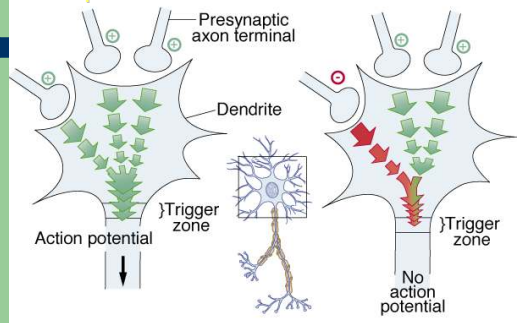
Multiple graded potentials are integrated at axon hillock to evaluate necessity of AP

1. Spatial Summation: stimuli from different locations are added up
2. Temporal Summation: sequential stimuli added up

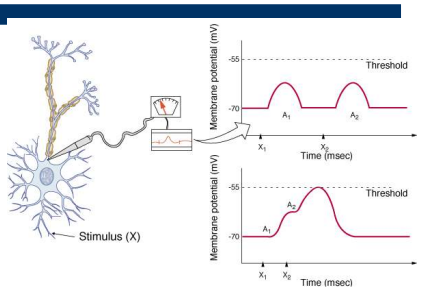
Fig 8-25



1. Spatial Summation



2. Temporal Summation



Synapse: most vulnerable step in signal propagation

Many disorders of synaptic transmission, *e.g.*:

- **Myasthenia gravis** (PNS)
- **Parkinson's** (CNS)
- **Schizophrenia** (CNS)
- **Depression** (CNS)
- **Many toxins**

Chapter 9, The CNS

- Blood Brain Barrier
- Diencephalon ("between-brain")
- Integration of sensory information

Blood Brain Barrier (p299)

- Allows careful selection of what substances can cross to neurons
- Capillary walls are different
  - Fewer pores
  - Tight junctions
  - Special carriers
- Water soluble substances do not cross easily.
  - Lipophilic molecules can cross
- Vomiting Center in medulla oblongata and posterior pituitary have no BBB. Why??

Diencephalon ("between-brain")

- Between brainstem and cortex
- Thalamus is a relay station
  - Like spinal cord, can modify information
- Hypothalamus is center of maintenance
  - Autonomic integration and output
  - RH to anterior pituitary

Integration of sensory information

- Functional Areas (like compartmentation)
  - Sensory (becomes perception)
  - Motor
  - Association (for integration)
    - Both brain and spinal cord
- Modulation of Output
  - Reticular formation (p 303)
    - Group of nuclei in brain stem
  - State of arousal
  - Specific NT