PHYSIOLOGY OF NERVOUS TISSUE

By

Dr. Hassan Y. Hassan

2nd year/Lecture 2

ELECTRICAL POTENTIALS AND CURRENTS

- electrophysiology – cellular mechanisms for producing electrical potentials and currents
  - basis for neural communication and muscle contraction
- electrical potential – a difference in the concentration of charged particles between one point and another
- electrical current – a flow of charged particles from one point to another
  - in the body, currents are movement of ions, such as Na^+ or K^+ through gated channels in the plasma membrane
  - gated channels are opened or closed by various stimuli
  - enables cell to turn electrical currents on and off
- living cells are polarized
- resting membrane potential (RMP) – charge difference across the plasma membrane
  - -70 mV in a resting, unstimulated neuron
  - negative value means there are more negatively charged particles on the inside of the membrane than on the outside

RESTING MEMBRANE POTENTIAL

- RMP exists because of unequal electrolyte distribution between extracellular fluid (ECF) and intracellular fluid (ICF)

- RMP results from the combined effect of three factors:
  - ions diffuse down their concentration gradient through the membrane
  - plasma membrane is selectively permeable and allows some ions to pass easier than others
  - electrical attraction of cations and anions to each other

CREATION OF RESTING MEMBRANE POTENTIAL

- potassium ions (K^+) have the greatest influence on RMP
  - plasma membrane is more permeable to K^+ than any other ion
  - leaks out until electrical charge of cytoplasmic anions attracts it back in and equilibrium is reached and net diffusion of K^+ stops
  - K^+ is about 40 times as concentrated in the ICF as in the ECF
- cytoplasmic anions can not escape due to size or charge (phosphates, sulfates, small organic acids, proteins, ATP, and RNA)
- membrane much less permeable to high concentration of sodium (Na^+) found outside the cell
  - some leaks and diffuses into the cell down its concentration gradient
  - Na^+ is about 12 times as concentrated in the ECF as in the ICF
  - resting membrane is much less permeable to Na^+ than K^+
- Na^+/K^+ pumps out 3 Na^+ for every 2 K^+ it brings in
  - works continuously to compensate for Na+ and K+ leakage, and requires great deal of ATP
    - 70% of the energy requirement of the nervous system
  - necessitates glucose and oxygen be supplied to nerve tissue (energy needed to create the resting potential)
  - pump contributes about -3 mV to the cell's resting membrane potential of -70 mV

Ionic Basis of Resting Membrane Potential

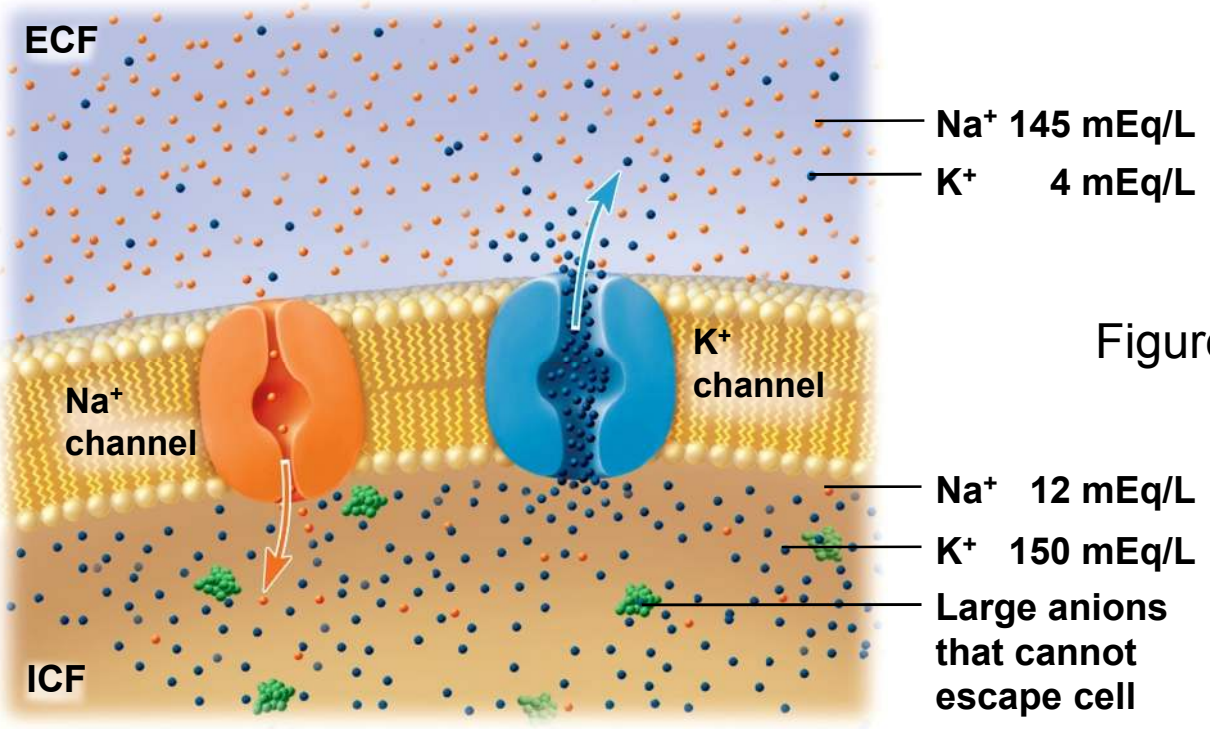


Figure 12.11

- Na^+ concentrated outside of cell (ECF)
- K^+ concentrated inside cell (ICF)

LOCAL POTENTIALS

- local potentials - disturbances in membrane potential when a neuron is stimulated
- neuron response begins at the dendrite, spreads through the soma, travels down the axon, and ends at the synaptic knobs
- when neuron is stimulated by chemicals, light, heat or mechanical disturbance
  - opens the Na^+ gates and allows Na^+ to rush in to the cell
  - Na^+ inflow neutralizes some of the internal negative charge
  - voltage measured across the membrane drifts toward zero
  - depolarization - case in which membrane voltage shifts to a less negative value
  - Na^+ diffuses for short distance on the inside of the plasma membrane producing a current that travels towards the cell's trigger zone – this short-range change in voltage is called a local potential

CHARACTERISTICS OF LOCAL POTENTIALS

- differences of local potentials from action potentials
  - are graded - vary in magnitude with stimulus strength
    - stronger stimuli open more Na^+ gates
  - are decremental - get weaker the farther they spread from the point of stimulation
    - voltage shift caused by Na^+ inflow diminishes rapidly with distance
  - are reversible - when stimulation ceases, K^+ diffusion out of cell returns the cell to its normal resting potential
  - can be either excitatory or inhibitory - some neurotransmitters (glycine) make the membrane potential more negative – hyperpolarize it – becomes less sensitive and less likely to produce an action potential

EXCITATION OF A NEURON BY A CHEMICAL STIMULUS

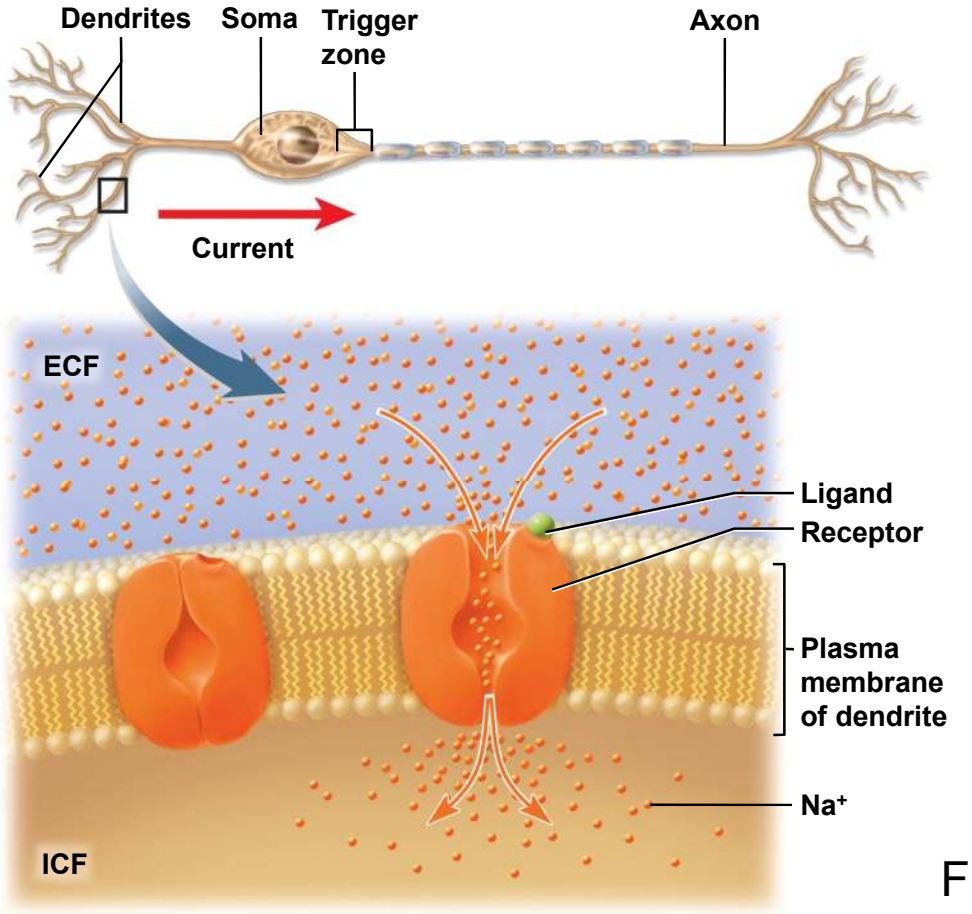


Figure 12.12

ACTION POTENTIALS

- action potential – more dramatic change produced by voltage-regulated ion gates in the plasma membrane
  - only occur where there is a high enough density of voltage-regulated gates
  - soma (50 -75 gates per μm^2) - cannot generate an action potential
  - trigger zone (350 – 500 gates per μm^2) – where action potential is generated
    - if excitatory local potential spreads all the way to the trigger zone, and is still strong enough when it arrives, it can open these gates and generate an action potential
- action potential is a rapid up-and-down shift in the membrane voltage
  - sodium ions arrive at the axon hillock
  - depolarize the membrane at that point
  - threshold – critical voltage to which local potentials must rise to open the voltage-regulated gates
    - -55mV

ACTION POTENTIALS

- when threshold is reached, neuron 'fires' and produces an action potential
- more and more Na^+ channels open in in the trigger zone in a positive feedback cycle creating a rapid rise in membrane voltage – spike
- when rising membrane potential passes 0 mV, Na^+ gates are inactivated
  - begin closing
  - when all closed, the voltage peaks at +35 mV
  - membrane now positive on the inside and negative on the outside
  - polarity reversed from RMP - depolarization
- by the time the voltage peaks, the slow K^+ gates are fully open
  - K^+ repelled by the positive intracellular fluid now exit the cell
  - their outflow repolarizes the membrane
    - shifts the voltage back to negative numbers returning toward RMP
- K^+ gates stay open longer than the Na^+ gates
  - slightly more K^+ leaves the cell than Na^+ entering
  - drops the membrane voltage 1 or 2 mV more negative than the original RMP – negative overshoot – hyperpolarization or afterpotential
- Na^+ and K^+ switch places across the membrane during an action potential

ACTION POTENTIALS

- only a thin layer of the cytoplasm next to the cell membrane is affected
  - in reality, very few ions are involved
- action potential is often called a spike – happens so fast
- characteristics of action potential versus a local potential
  - follows an all-or-none law
    - if threshold is reached, neuron fires at its maximum voltage
    - if threshold is not reached it does not fire
  - nondecremental - do not get weaker with distance
  - irreversible - once started goes to completion and can not be stopped

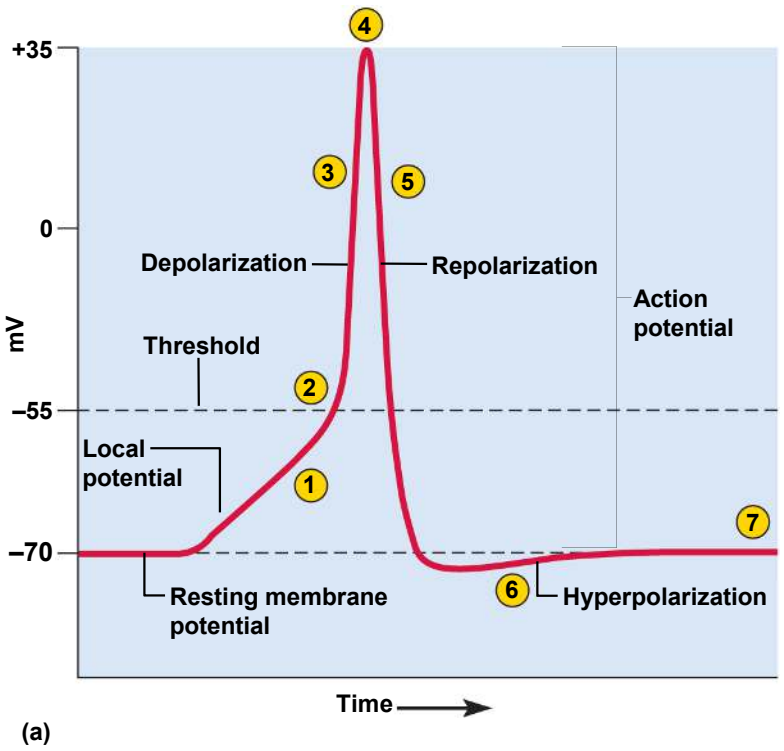


Figure 12.13a

ACTION POTENTIAL VS. LOCAL POTENTIAL

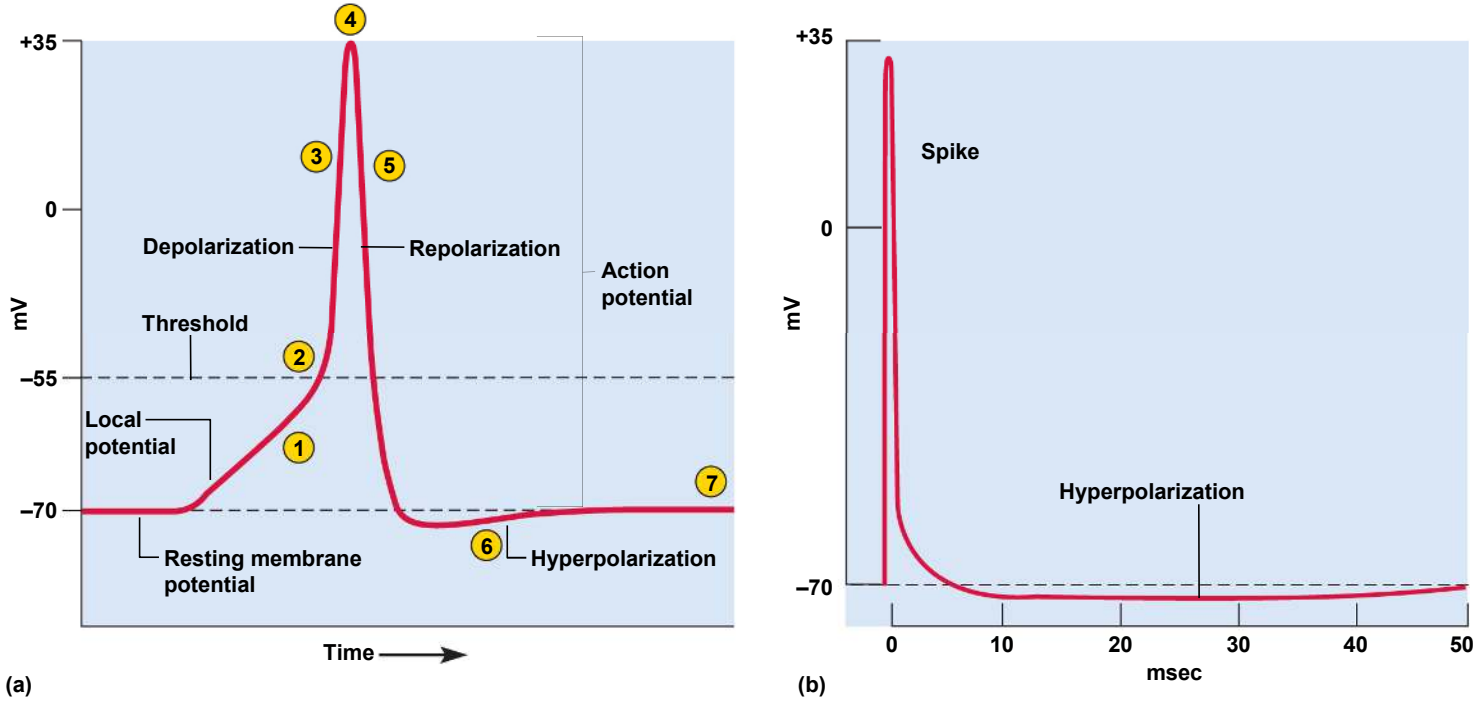


Figure 12.13 a-b

SODIUM AND POTASSIUM GATES

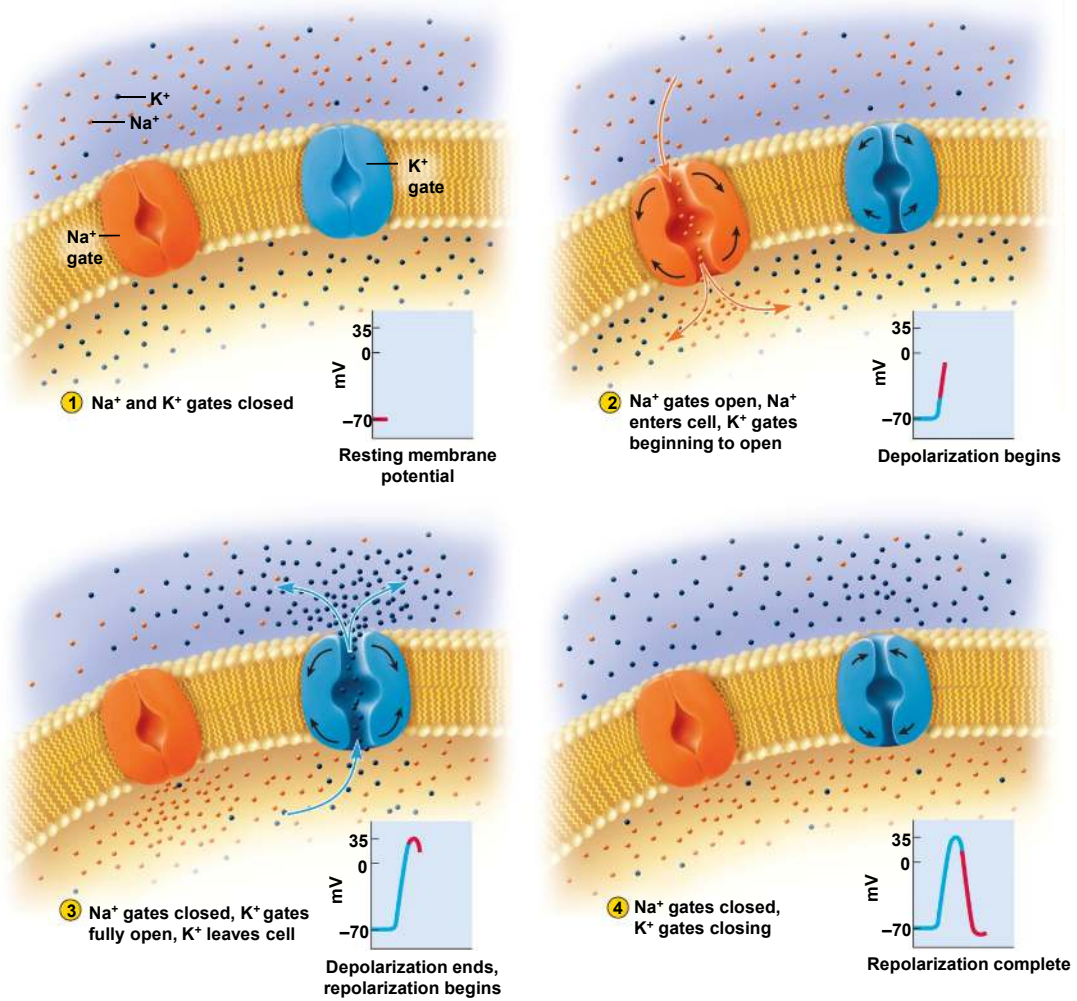


Figure 12.14

THE REFRACTORY PERIOD

- during an action potential and for a few milliseconds after, it is difficult or impossible to stimulate that region of a neuron to fire again.
- refractory period – the period of resistance to stimulation
- two phases of the refractory period
  - absolute refractory period
    - no stimulus of any strength will trigger AP
    - as long as Na^+ gates are open
    - from action potential to RMP
  - relative refractory period
    - only especially strong stimulus will trigger new AP
      - K^+ gates are still open and any affect of incoming Na^+ is opposed by the outgoing K^+
- refractory period is occurring only at a small patch of the neuron's membrane at one time
- other parts of the neuron can be stimulated while the small part is in refractory period

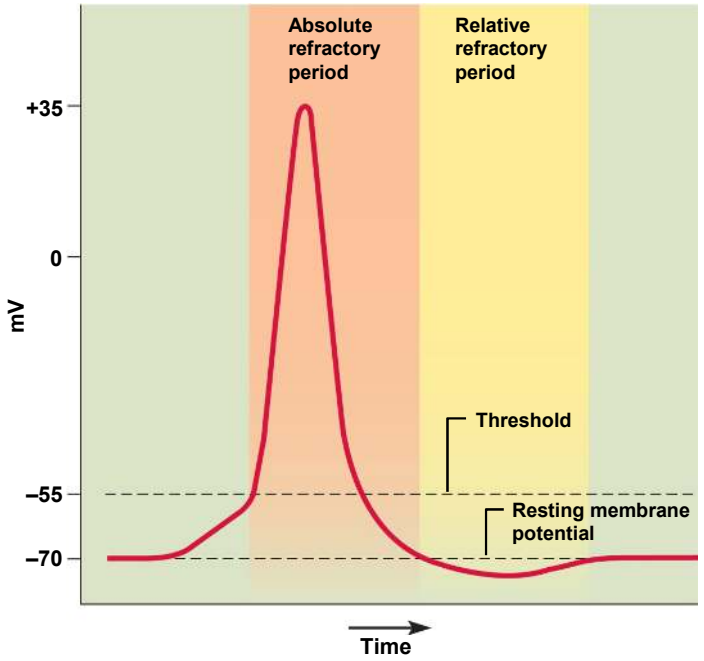


Figure 12.15

SIGNAL CONDUCTION IN UNMYELINATED FIBERS

- for communication to occur, the nerve signal must travel to the end of the axon
- unmyelinated fiber has voltage-regulated ion gates along its entire length
- action potential from the trigger zone causes Na^+ to enter the axon and diffuse into adjacent regions beneath the membrane
- the depolarization excites voltage-regulated gates immediately distal to the action potential.
- Na^+ and K^+ gates open and close producing a new action potential
- by repetition the membrane distal to that is excited
- chain reaction continues to the end of the axon

NERVE SIGNAL CONDUCTION UNMYELINATED FIBERS

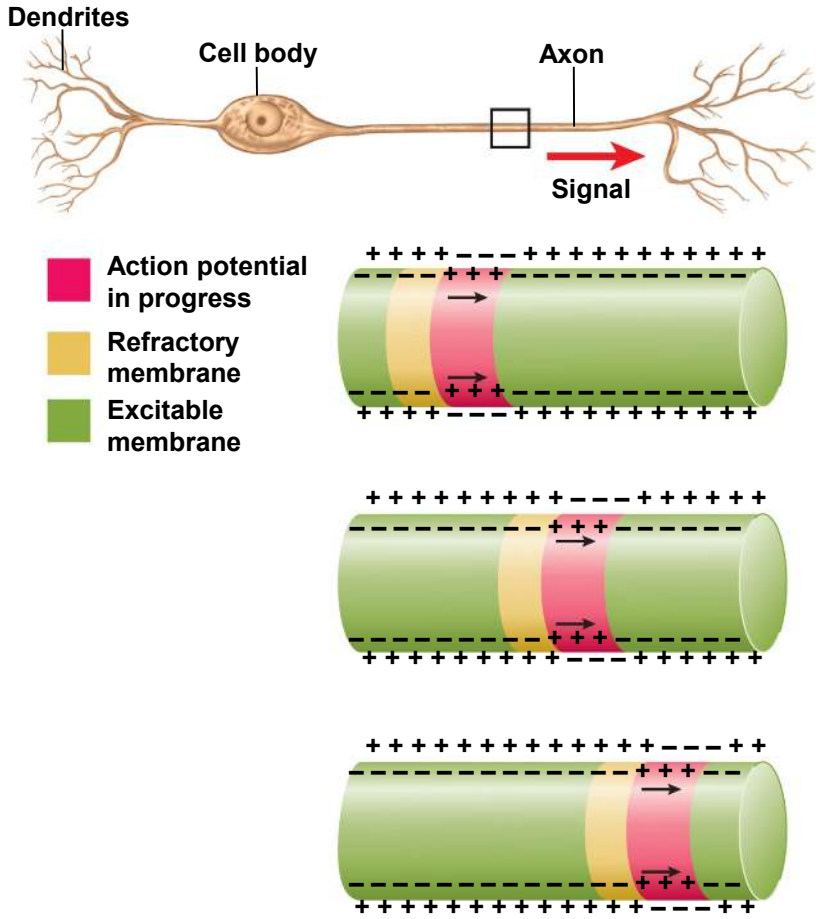


Figure 12.16

SALTATORY CONDUCTION MYELINATED FIBERS

- voltage-gated channels needed for APs
  - fewer than 25 per μm^2 in myelin-covered regions (internodes)
  - up to 12,000 per μm^2 in nodes of Ranvier
- fast Na^+ diffusion occurs between nodes
  - signal weakens under myelin sheath, but still strong enough to stimulate an action potential at next node
- saltatory conduction – the nerve signal seems to jump from node to node

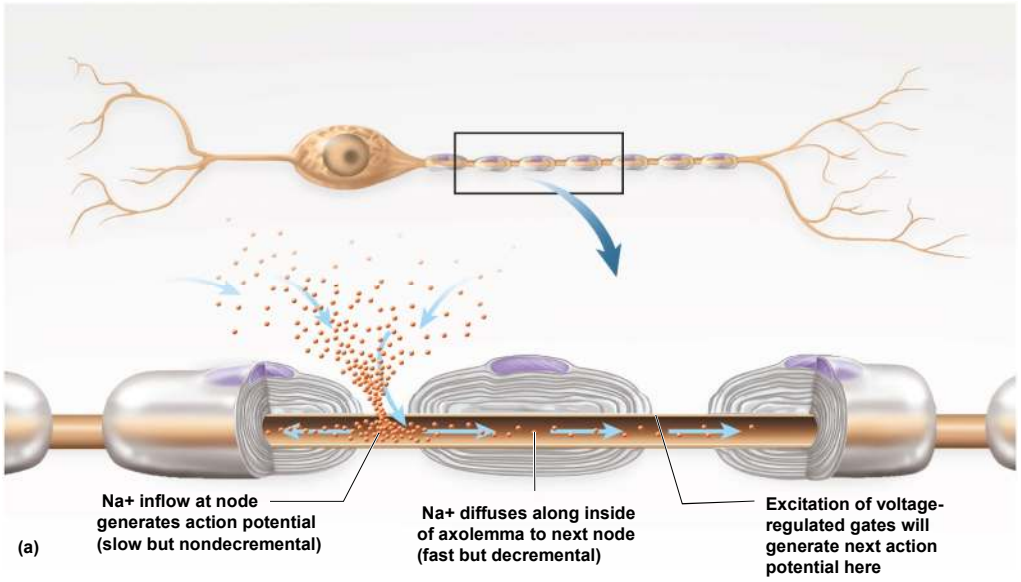


Figure 12.17a

SALTATORY CONDUCTION

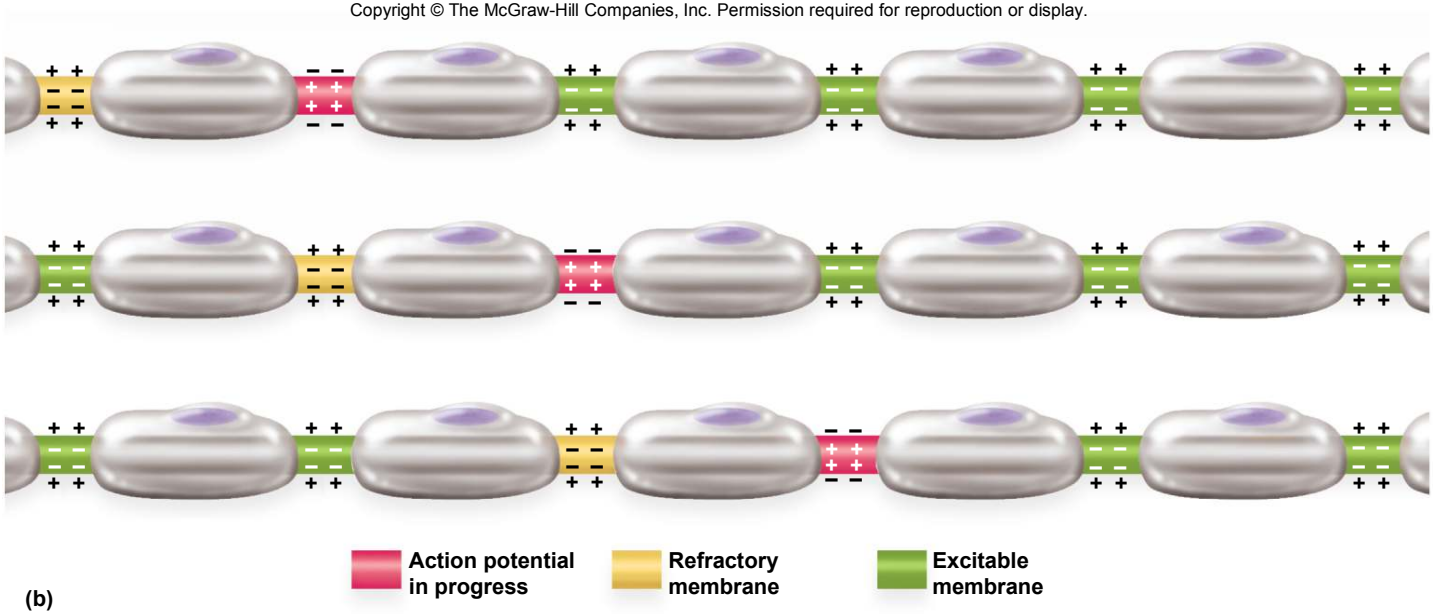


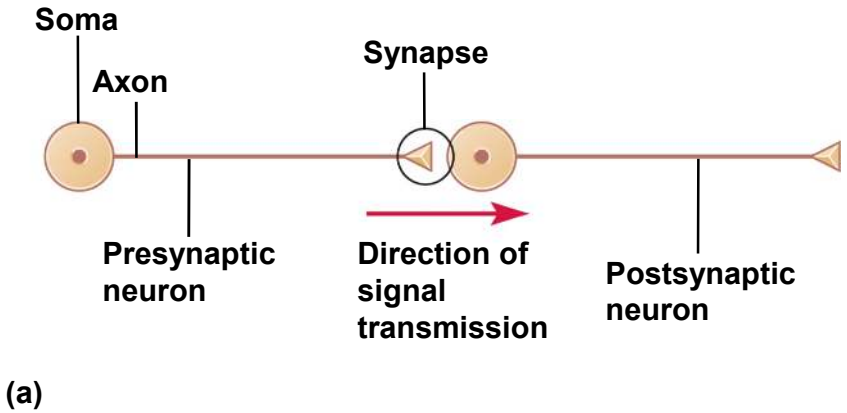
Figure 12.17b

- much faster than conduction in unmyelinated fibers

SYNAPSES

- a nerve signal can go no further when it reaches the end of the axon
  - triggers the release of a neurotransmitter
  - stimulates a new wave of electrical activity in the next cell across the synapse
- synapse between two neurons
  - 1st neuron in the signal path is the presynaptic neuron
    - releases neurotransmitter
  - 2nd neuron is postsynaptic neuron
    - responds to neurotransmitter
- presynaptic neuron may synapse with a dendrite, soma, or axon of postsynaptic neuron to form axodendritic, axosomatic or axoaxonic synapses
- neuron can have an enormous number of synapses
  - spinal motor neuron covered by about 10,000 synaptic knobs from other neurons
    - 8000 ending on its dendrites
    - 2000 ending on its soma
- in cerebellum of brain, one neuron can have as many as 100,000 synapses

SYNAPTIC RELATIONSHIPS BETWEEN NEURONS



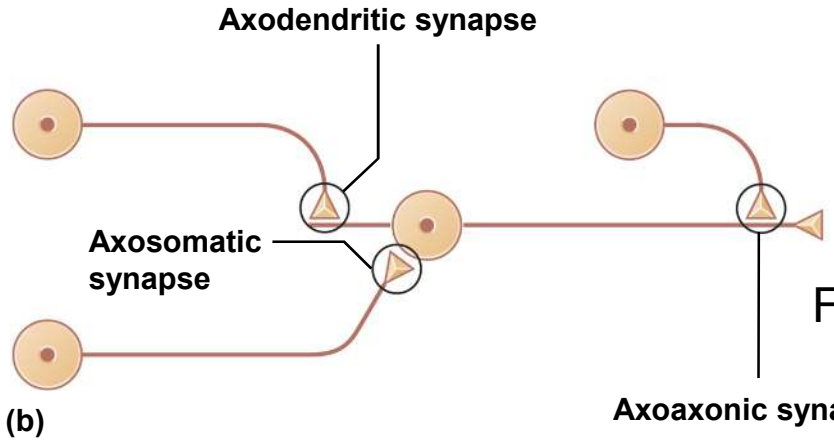


Figure 12.18

DISCOVERY OF NEUROTRANSMITTERS

- synaptic cleft -gap between neurons was discovered by Ramón y Cajal through histological observations
- Otto Loewi, in 1921, demonstrated that neurons communicate by releasing chemicals – chemical synapses
  - he flooded exposed hearts of two frogs with saline
  - stimulated vagus nerve of the first frog and the heart slowed
  - removed saline from that frog and found it slowed heart of second frog
  - named it Vagusstoffe ("vagus substance")
    - later renamed acetylcholine, the first known neurotransmitter
- electrical synapses do exist
  - some neurons, neuroglia, and cardiac and single-unit smooth muscle
  - gap junctions join adjacent cells
    - ions diffuse through the gap junctions from one cell to the next
  - advantage of quick transmission
    - no delay for release and binding of neurotransmitter
    - cardiac and smooth muscle and some neurons
  - disadvantage is they cannot integrate information and make decisions
    - ability reserved for chemical synapses in which neurons communicate by releasing neurotransmitters

SYNAPTIC KNOBS

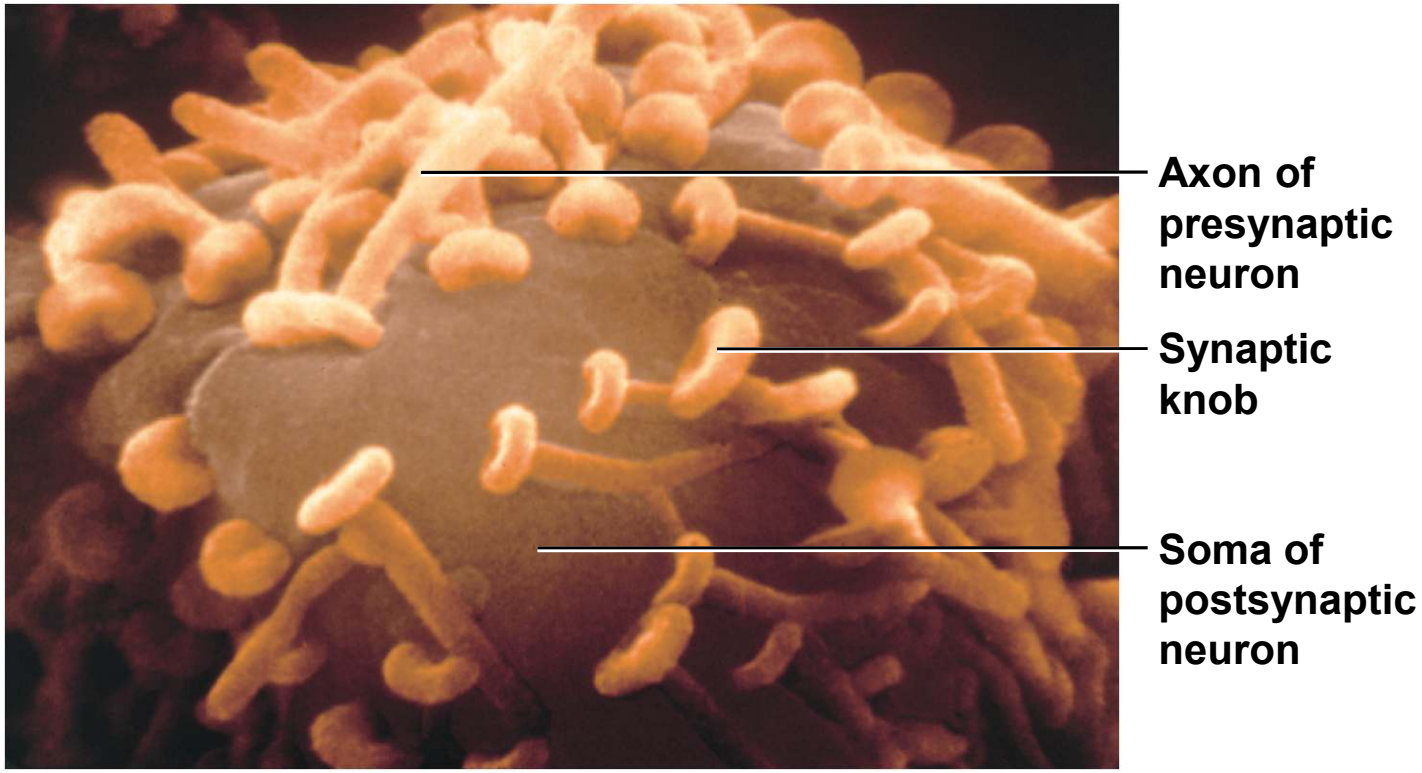


Figure 12.19

STRUCTURE OF A CHEMICAL SYNAPSE

- synaptic knob of presynaptic neuron contains synaptic vesicles containing neurotransmitter
  - many docked on release sites on plasma membrane
    - ready to release neurotransmitter on demand
  - a reserve pool of synaptic vesicles located further away from membrane
- postsynaptic neuron membrane contains proteins that function as receptors and ligand-regulated ion gates

STRUCTURE OF A CHEMICAL SYNAPSE

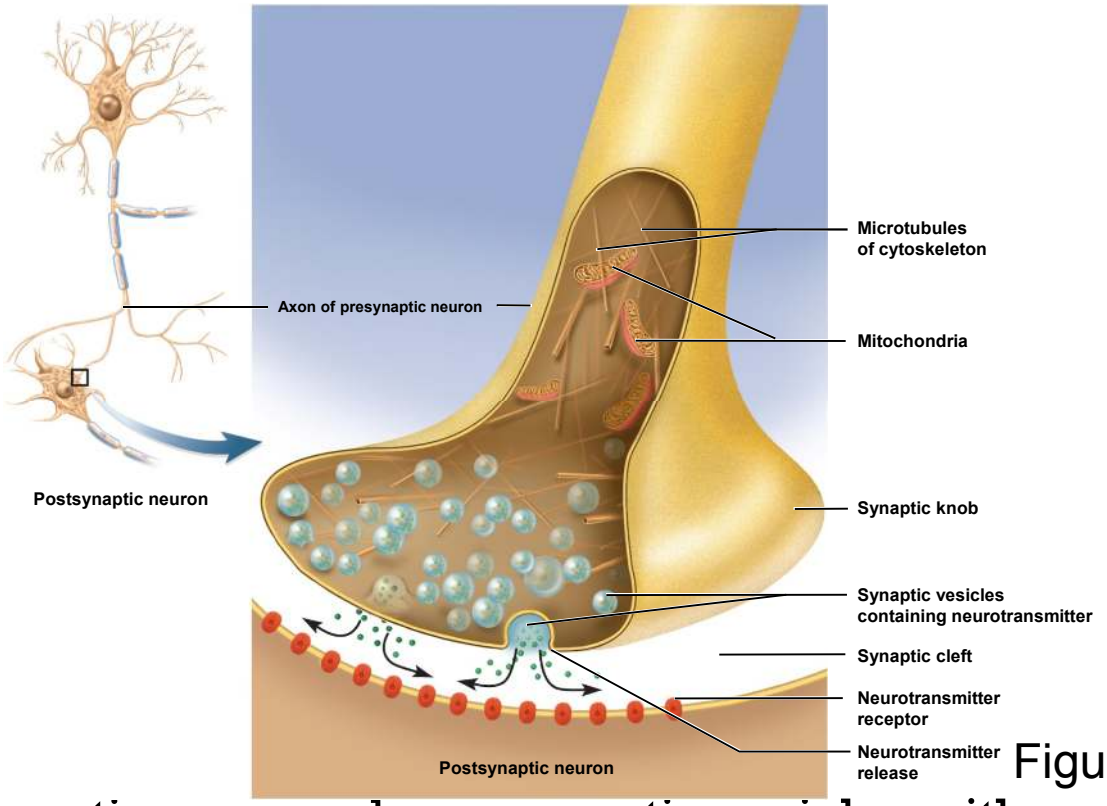


Figure 12.20

- presynaptic neurons have synaptic vesicles with neurotransmitter and postsynaptic have receptors and ligand-regulated ion channels