Cellular Communication

1. Direct cell contact
2. Vesicle-mediated
3. Chemical messengers

Cellular Communication by direct cell-cell contact

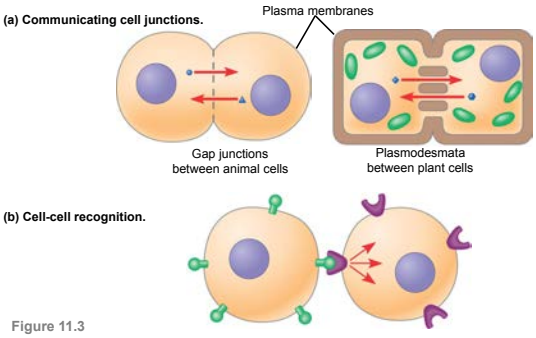
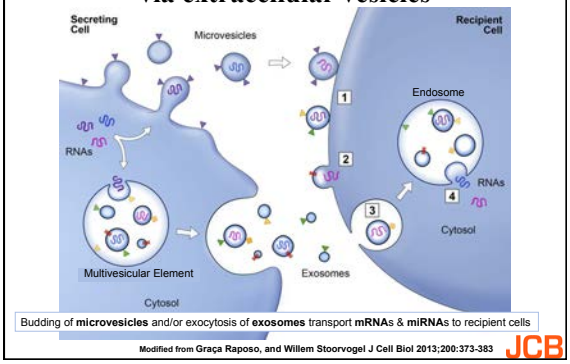
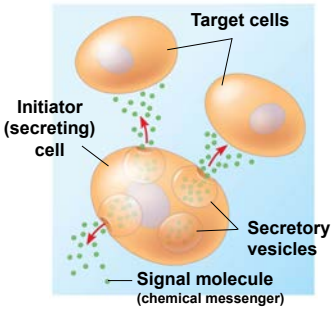


Figure 11.3

Cellular Communication via extracellular vesicles



Cellular Communication via chemical messengers



Cellular Communication via chemical messengers

1. Release: initiator cell secretes (exocytosis) a chemical messenger (signal molecules).
2. Reception: messenger molecules bind to receptors (binding proteins) on target cells.
3. Transduction: binding of signal molecule to receptor causes a change in the structure and activity of the receptor protein.
4. Response: the altered receptor protein initiates a change in the enzymatic and/or transcriptional activity of the target cell.

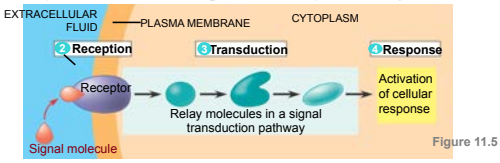
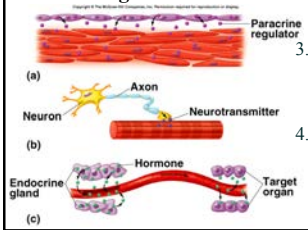


Figure 11.5

Cellular Communication — Chemical Messengers & Receptors

One cell releases a molecule (messenger) that initiates a change in another cell by binding to a protein receptor on that target cell.



1. Synapse: the messenger (neurotransmitter) diffuses across a small gap between a neuron and its target cell.
2. Paracrine: the messenger (local regulator, paracrine factor, growth factor, cytokine) diffuses to nearby target cells.
3. Endocrine: the messenger (hormone) diffuses into the bloodstream to travel to target cells all over the body.
4. Exocrine: the messenger (pheromone) diffuses outside of the organism's body to travel to another organism.

Mechanisms of Messenger Action

- Hydrophilic signal molecules — most amino acid class
  - Amino acids; bioamines; oligopeptides; proteins
  - Water soluble.
  - Short half-life: minutes
  - Do not enter target cells. Act as ligand by binding to protein receptor on cell surface.
- Lipophilic signal molecules — most fatty acid class
  - Steroids; prostaglandins
  - Water insoluble. Must be transported in plasma by carrier proteins.
  - Carrier proteins also protect hormone from degradation. Half-life longer: 1–2 hours.
  - Released from carrier protein to diffuse across cell membrane into target cells. Act by binding to intracellular protein receptors.

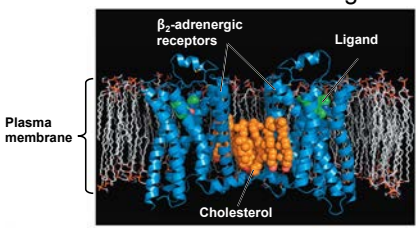
Mechanisms of **Hydrophilic** Signal Molecule Action

- Hydrophilic signal molecules — most amino acid class
  - Water soluble.
  - Short half-life: minutes
  - Do not enter target cells. Act as ligand by binding to protein receptor on cell surface.

1. Since the signal molecule (first messenger) does not enter the cell, the receptor/ligand complex causes a **second messenger** to be produced or released within the cell.
2. This second messenger acts as a coenzyme/cofactor to regulate cellular enzymes ⇒ change the activity of the cell.

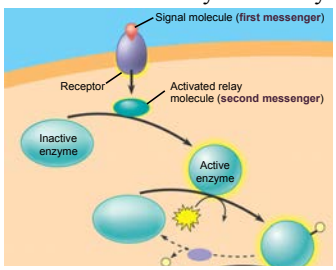
Membrane Receptor Proteins

- The binding between a signal molecule (**ligand**) and receptor is highly specific
- A shape change in a receptor is often the initial transduction of the signal



Signal transduction pathways via **second messengers**

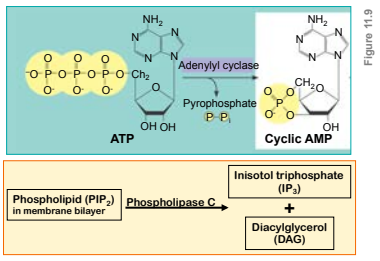
Act as cofactors/coenzymes to modulate intracellular enzyme activity



Common **second messengers**

Act as cofactors/coenzymes to modulate intracellular enzyme activity

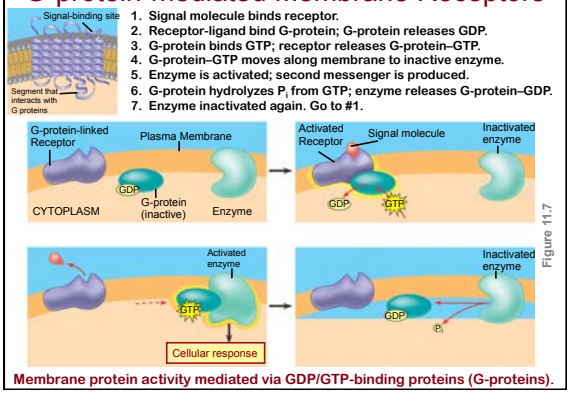
1. Ca^{++}
2. cAMP
3. IP_3
4. DAG



Membrane Receptor Types

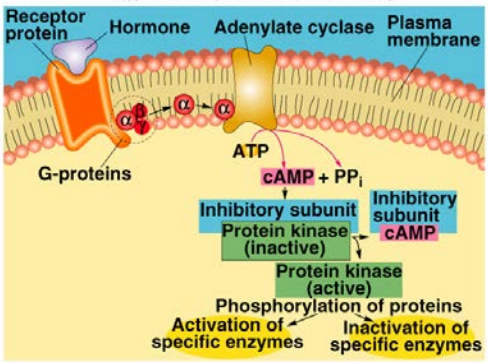
1. G-protein mediated
2. Tyrosine kinase
3. Receptor-ion channels

G-protein-mediated Membrane Receptors

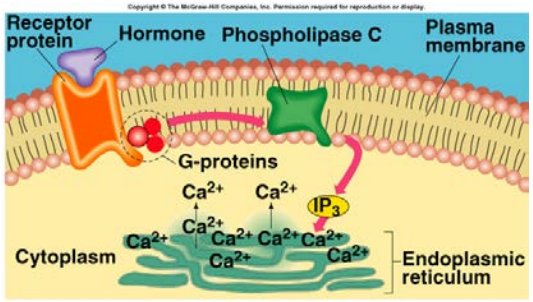


Membrane protein activity mediated via GDP/GTP-binding proteins (G-proteins).

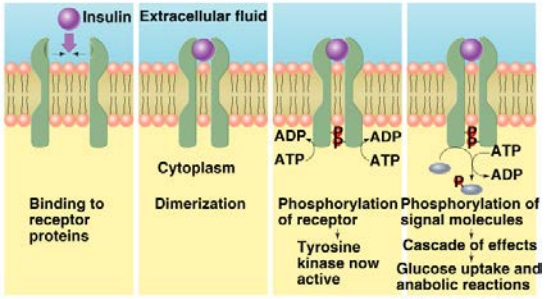
Second messenger: cyclic-AMP



Second messengers: IP_3 / DAG / Ca^{++}

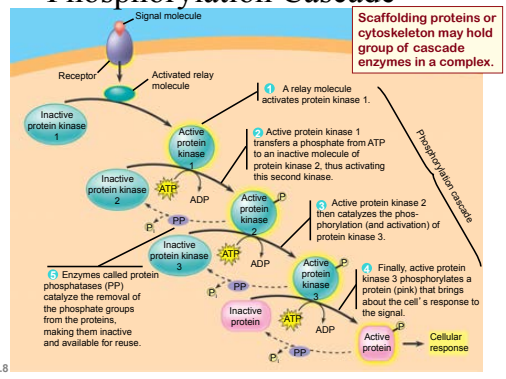


Tyrosine Kinase Receptors



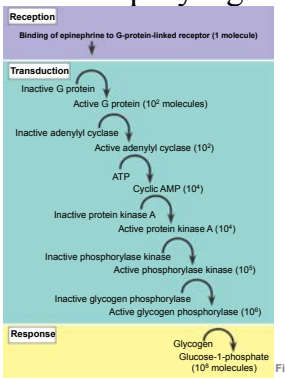
- Kinase ("enzyme activation enzyme"): phosphorylase
- Tyrosine kinase: phosphate added to tyrosine residues of enzyme proteins

Phosphorylation Cascade



Cascade reactions amplify signal

- One epinephrine signal molecular momentarily binding to the membrane receptor
- Results in the production of 100,000,000 glucose-1-phosphate molecules in the cell.



Receptor-ion channels

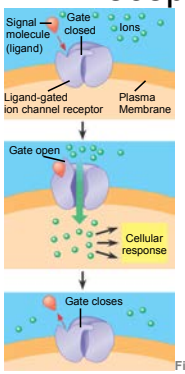
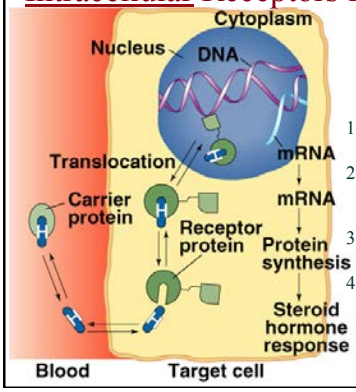


Figure 11.7

- Chemically-mediated ion gates
- Signal molecule binds receptor; gated channel opens or closes
  - Direct: receptor is the gate.
  - Indirect: receptor opens/closes separate gate protein via G-proteins.
- Opening gates causes voltage change in cell.
  - Na^+ gate: depolarizes
  - K^+ or Cl^- gate: hyperpolarizes

Intracellular Receptors for **Lipophilic** Signal Molecules



1. Steroid diffuses across membrane into cell
2. Intracellular receptor/ steroid complex binds to DNA
3. Transcription factor — turns genes on/off
4. Change nature of the cell (Longer-lasting effect)

Mechanisms of Messenger Action

- Hydrophilic signal molecules — most amino acid class
  - Bind to membrane receptors on cell surface
  - Primary effect: turn enzymes on/off → Δ activity of cell.
  - Secondary effect: enzymes may produce or activate transcription factors → turn genes on/off.

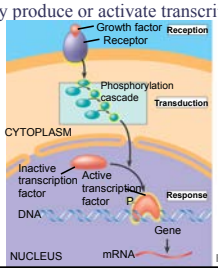


Figure 11.14

Mechanisms of Messenger Action

- Hydrophilic signal molecules — most amino acid class
  - Bind to membrane receptors on cell surface
  - Primary effect: turn enzymes on/off → Δ activity of cell.
  - Secondary effect: enzymes may produce or activate transcription factors → turn genes on/off.
- Lipophilic signal molecules — most fatty acid class
  - Bind to intracellular receptors in cytoplasm or nucleoplasm
  - Primary effect: turn genes on/off → Δ nature of cell.
  - Secondary effect: gene expression may produce or activate enzymes → turn metabolic pathways on/off.

Modulation of signal effect

- Priming (upregulation)
  Signal binds→ more receptors synthesized
  ↓
  more hormone can bind cell
- Desensitization (downregulation)
  Prolonged exposure to high signal molecule levels can reduce receptor expression.
  ☛Downregulation may be avoided by pulsatile secretion of the messenger.
- Receptor-mediated endocytosis
  Receptor-ligand complex internalized on vesicle to enhance duration of effect.

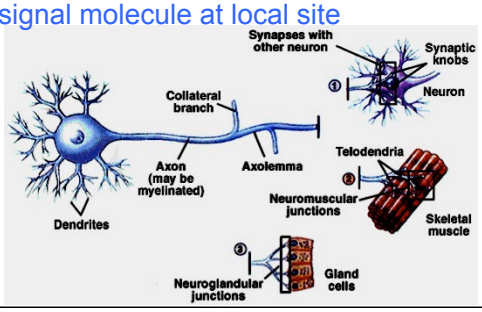
Compound messenger effects

- Antagonistic:
  - Insulin stimulates lipogenesis; glucagon stimulates lipolysis.
- Synergistic:
  - Both glucagon and epinephrine receptors cause the production of cAMP second messenger in the same cell.
- Complementary:
  - FSH and testosterone stimulate different parts of spermatogenesis.
- Permissive:
  - Glucocorticoids stimulate the synthesis of enzymes that are regulated by epinephrine.

Electrochemical communication

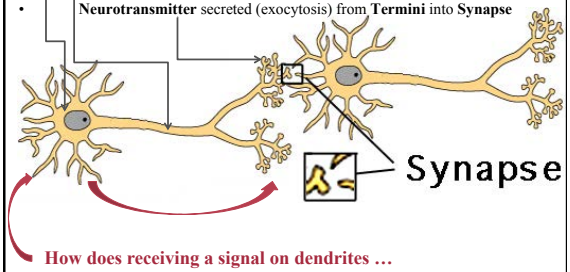
Rapid signaling to specific targets

Neuron — cell extends axon to release signal molecule at local site



Neurons & Specific Long-distance Communication

- **Neurotransmitter** molecules produced in **vesicles** by **rER** & **Golgi** in **Cell Body**
- **Vesicles** transported along **cytoskeleton** from **Cell Body** to **Axon Termini**
- **Neurotransmitter** secreted (exocytosis) from **Termini** into **Synapse**



How does receiving a signal on dendrites …

- **… result *rapidly* in releasing signal molecules into synapse?**

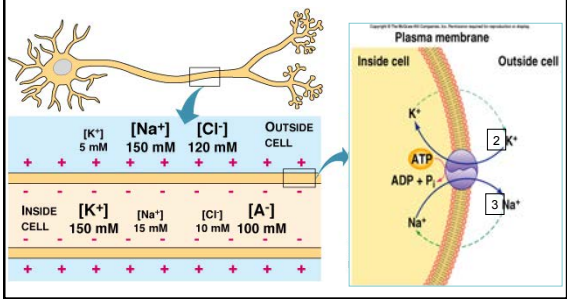
Neuron Requirements

Function requires:

1. **Membrane potential**:
   – Voltage (millivolts) across plasma membrane
2. **Excitability**:
   – The ability to undergo rapid changes in membrane potential in response to stimuli
3. **Conduction**:
   – Propagation of a series of excitations along the plasma membrane
4. **Transmission**:
   – Release and reception of signal molecules (neurotransmitters)

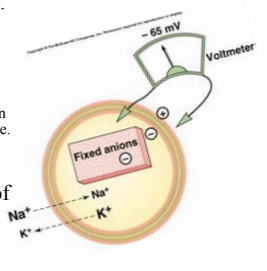
Membranes of cells are electrically polarized

- Ion concentration gradients → electrical gradient



Resting Membrane Potential

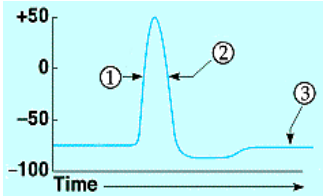
- At equilibrium, inside of the cell membrane would have a higher [negative charges] than the outside.
- Potential difference:
  - Magnitude of difference in charge on the 2 sides of the membrane..
- Depends upon 2 factors:
  - Ratio of the concentrations of each ion on the 2 sides of the plasma membrane.
  - Specific permeability of membrane to each different ion.
- Resting membrane potential of most cells ranges from - 65 to – 85 mV.



Action Potential

by voltage-gated ion channels

1 Na^+ channels open
   - Na^+ rushes in (making inside positive)
2 Na^+ channels close. K^+ channels open
   - K^+ rushes out (making it negative)
3 K^+ channels close. Na^+ / K^+ pumps resegregate ions.



c.f., Fig. 48.10

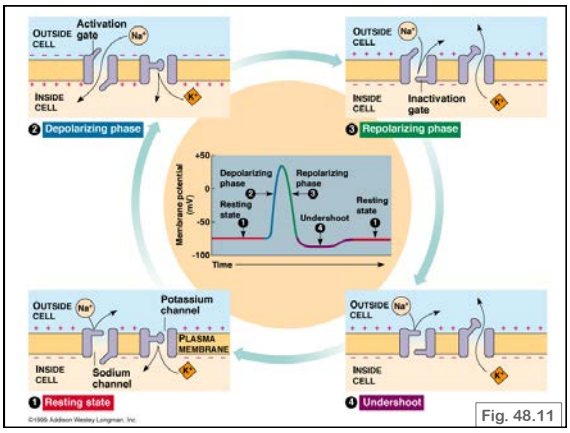


Fig. 48.11

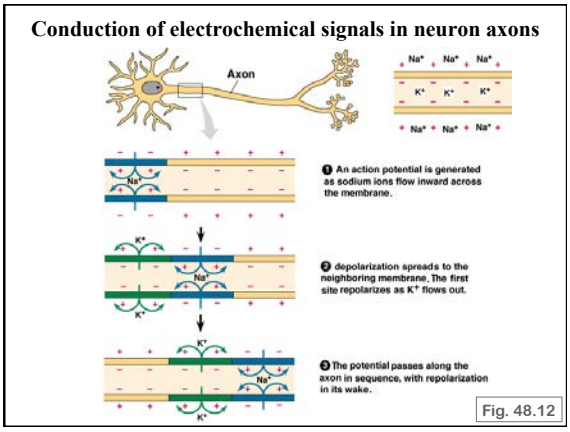


Fig. 48.12

Synaptic Transmission: release of signal molecule

- Action potentials conducted down axon to terminus.
- Voltage-Gated **Ca^{2+} channels** open.
  - Ca^{2+} rapidly enters terminus
    - (down concentration and charge gradient).
  - Ca^{2+} acts as cofactor for enzymes to trigger rapid fusion of synaptic vesicles ➔ exocytosis of neurotransmitter (NT) into synaptic cleft.
- NT release is rapid because many vesicles form fusion-complexes at "docking sites."

Synaptic Transmission: Reception

- Released NTs (signal molecules) diffuse across synaptic cleft.
- NT (ligand) binds to specific **receptor-ion channels** in postsynaptic cell membrane.
- Ligand-gated ion channels open.
  - **If Na^+ gates ➔ depolarization ➔ stimulation**.
  - **If K^+ or Cl^- gates ➔ hyperpolarization ➔ inhibition**.
- Neurotransmitter inactivated to end transmission.

Synaptic Transmission: release & reception

- NT receptors open **ion channels**, allowing in Na^+
  - this initiates a response in the target cell
- NTs are broken down & recycled by enzymes.

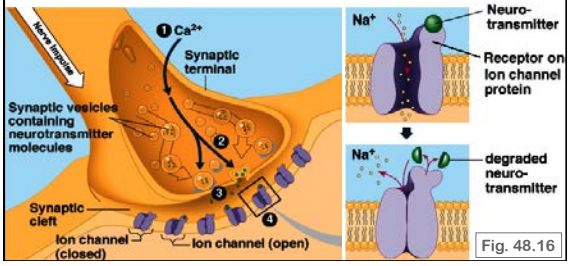


Fig. 48.16

Neurotransmitters

- Different types used by different neurons.
  - dopamine, serotonin, endorphins, even NO
- They can excite or inhibit transmission.
- Chemicals (e.g., LSD, insecticides, opiates)
  - mimic neurotransmitters
  - block neurotransmitters
  - block receptor sites
  - block breakdown enzymes