Cell Signaling: Communication between cells
Three Stages

Cell Signaling

Receiving Environmental Signals

- Transporters, channels that transport signal across the membrane

- Receptors → bind signals → → endocytosis

- Receptors :
  - Mediate cell-cell recognition : tight junctions
  - ECM - adhesion receptors
  - Signal receivers

Local and Long-Distance Signaling

- Local Signals:
  - **Paracrine** – secreted signal from a neighboring cell. Only nearby cells have receptors – and can respond
    - Ex. development, histamines

  - **Autocrine** – signals affect the same cells that make it

Cell Signaling

Local and Long-Distance Signaling

- **Long Distance**:
  - Hormonal (produced by glands): small protein (ex. Insulin) or small molecules that circulate via the bloods

Signals are recognized by specific receptors on outside the cell HOW?

- Interactions with side chain (R-groups) on amino acids

- Sends signal inside cell
  - Growth
    - Replicate DNA and divide
  - DIE (Apoptosis)
    - Programmed cell death – turn on proteases in cell
  - Turn on genes to do new things
    - Change Metabolism
    - Create new strutures
    - Make a different signal – new response

Cell Signaling

Intracellular Receptors

- Steriods hydrophobic - can cross PM
  - cross the plasma membrane and bind **nuclear receptors** in cytoplasm
  - Transported into nuclues through nuclear pore complex
  - Turn on genes

NOTE: Proteins that can enter the nucleus have signals (nuclear import signals).

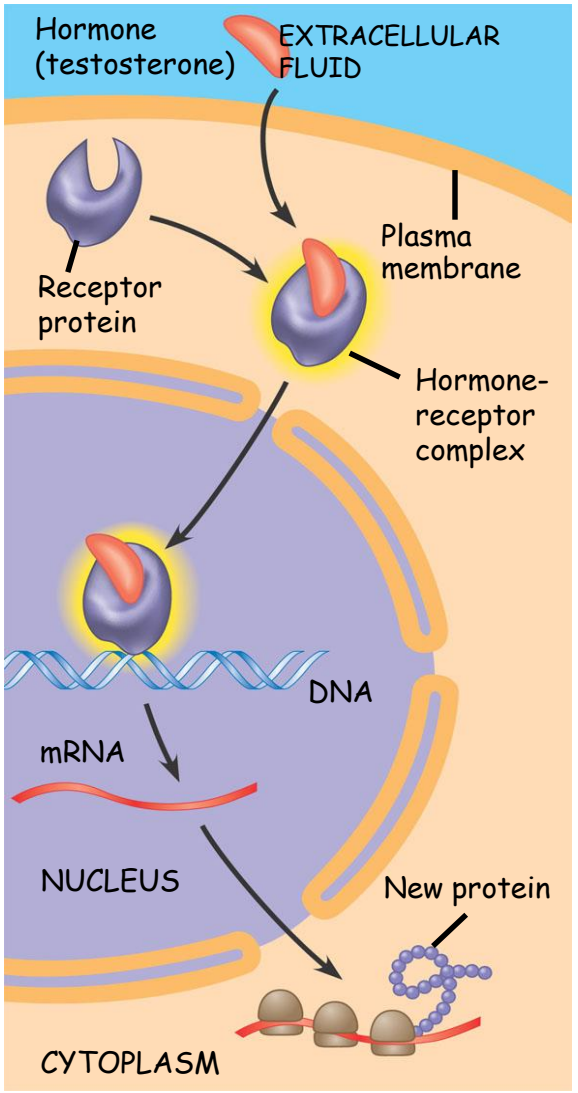


Figure 11.6

Cell Signaling

Three stages of Cell Signaling

- **Reception:**
  - signal binds protein receptor on cell → causes conformational change → signals across membrane.

- **Transduction:**
  - Amplify the original signal
    - Phosphorylation Cascade
      - Kinase transfers phosphate from ATP to Proteins
        - **Serine , Threonine, or Tyrosine**
      - Adds a negative charge onto protein
      - Causes conformation change → Turn protein on!
      - Amplify by phosphorylating many other proteins
    - Second Messenger System
      - Turn on a enzyme
      - Synthesizes a small molecule
      - Small molecule acts as a "messenger"
        - Binds and allosterically activates "turns on" other proteins

Cell Signaling

Three stages of Cell Signaling

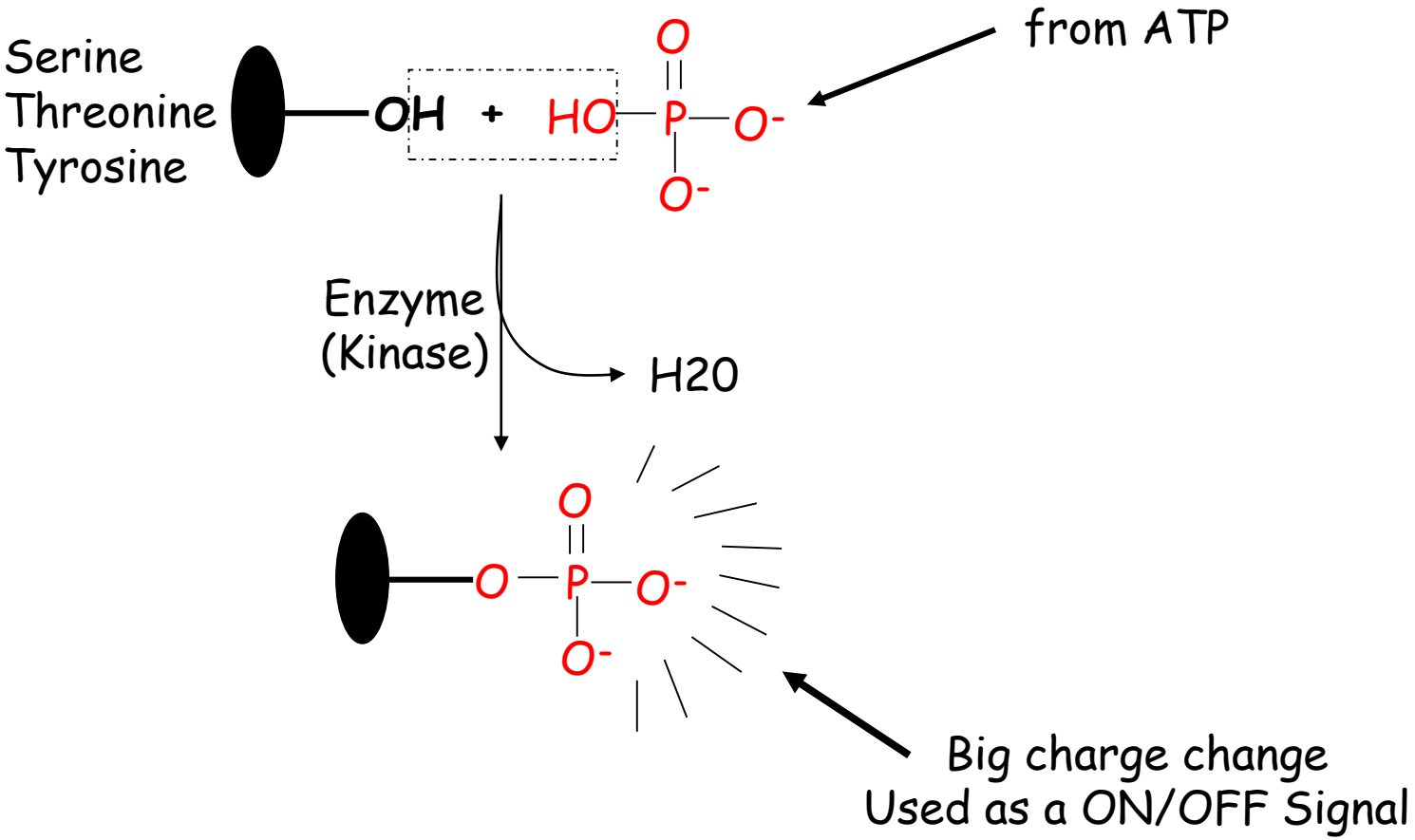
- **Response:**
  - Change an activity in nucleus → by turning genes on
  - Change an activity in cytoplasm
    - Enzyme turned on
    - Change cytoskeleton
  - Open a channel (e.g. brain)

- Opposite can be true also – turn things off
  - Receive signal
  - Amplification
  - Response: unique (specific) to turn a response off!

Examples

Cell Signaling

Phosphorylation: Why is it important in signaling?



Cell Signaling

Three main types of membrane receptors

- Tyrosine Kinases
- G-protein linked
- Ion channels

Cell Signaling

Tyrosine Kinase receptors

- Transmembrane protein
- ligand binds outside surface of cell
- Activates kinase inside cell
  - Note: inactive without ligand

- Binds ligand → conformational change
  - 3° → 4°
  - Mononer dimer
  - (inactive) (active)

- Kinase phosphorylates many substrates including itself

- Response: ex. turn genes on (development)
  - Growth hormones use this strategy – signal to divide

To turn OFF: use a phosphatase – removes phosphates from proteins!

Cell Signaling

Tyrosine Kinase receptors – a schematic

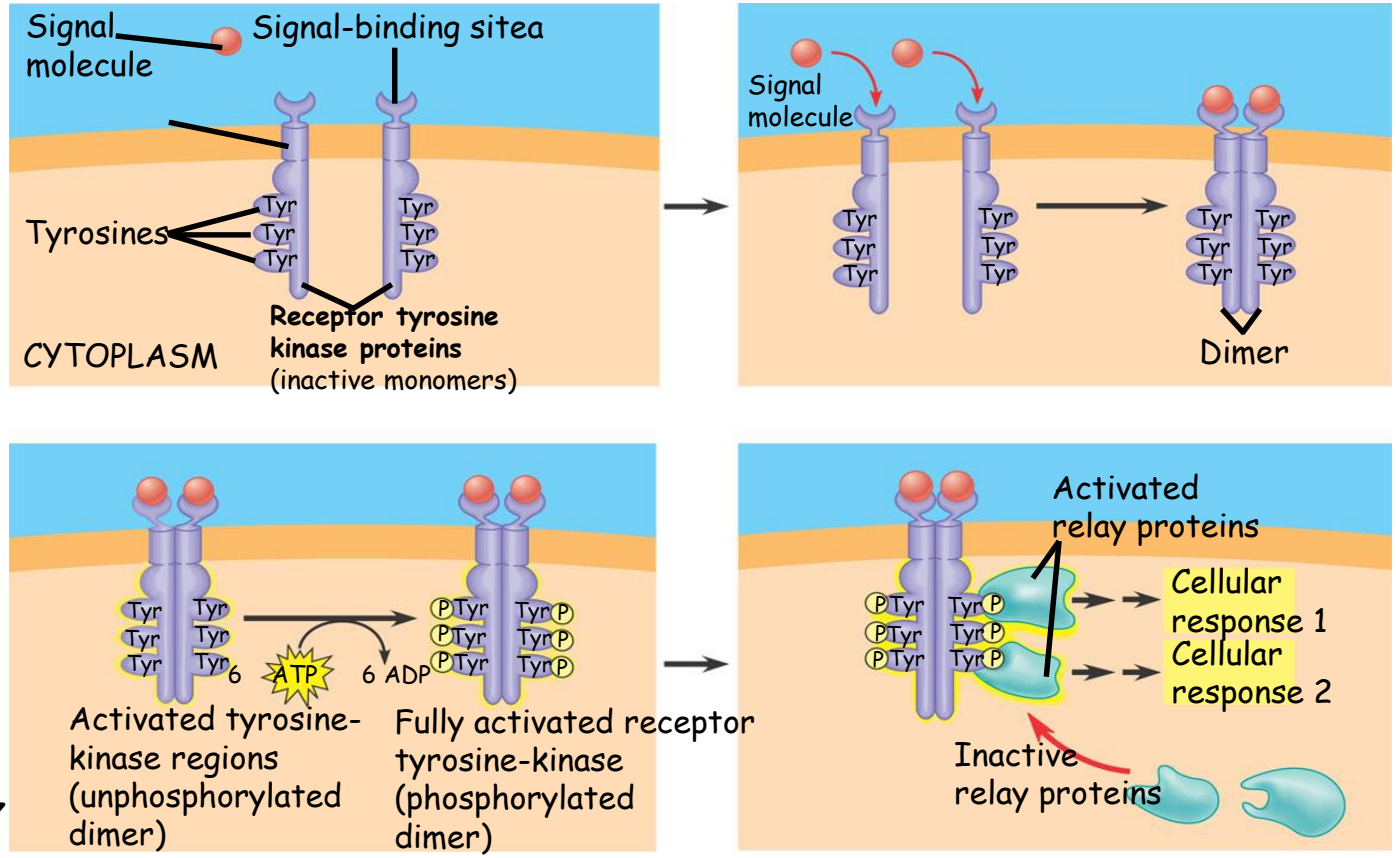


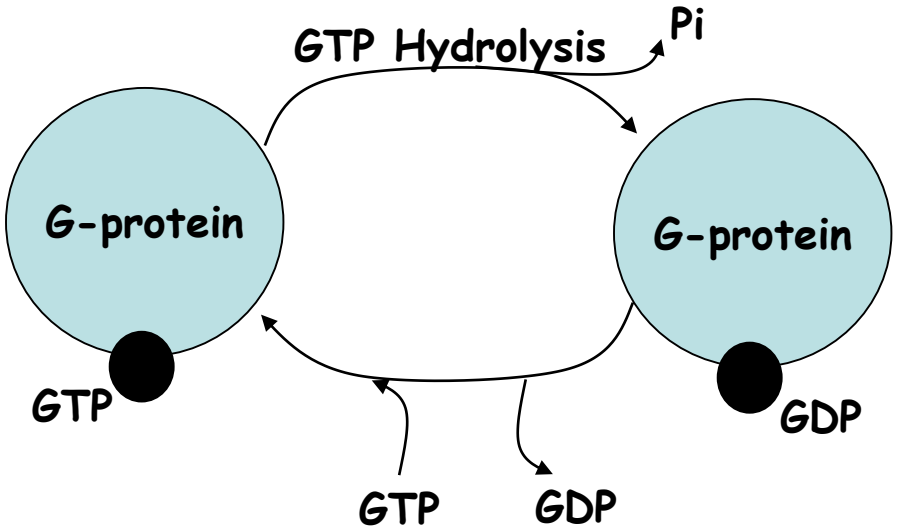
Figure 11.7

Cell Signaling

G-protein coupled receptors

- Seven Transmembrane passing protein
- Ligand binds outside surface of cell
- Binds ligand → conformational change
- Can now bind "G-protein" insides on membrane

- G-Protein
  - Able to bind activated G-protein linked receptors
  - Able to bind GTP



Cell Signaling

G-protein coupled receptors

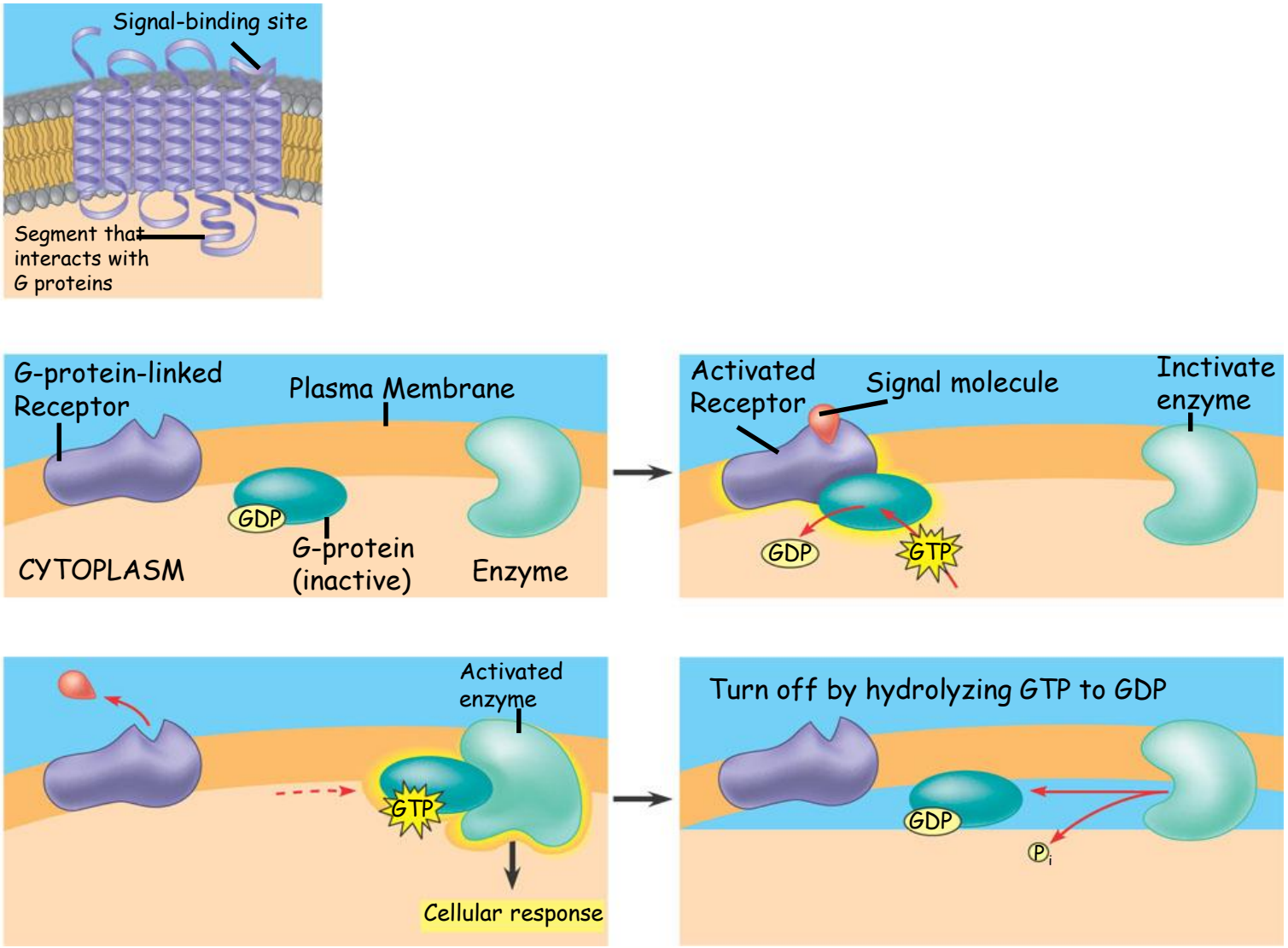


Figure 11.7

Cell Signaling

ION Channels

- Transmembrane protein (usually a pore or channel)
- Closed , waiting for signal
- Ligand binds outside surface of cell (neurotransmitter – secreted by neurons)
- Binds ligand → conformational change
- Opens channel for ion (e.g. Na+) to go thru from High to low concentration
    - FACLITATED DIFFUSION

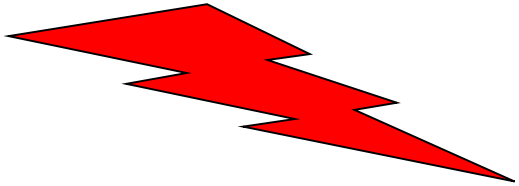
- ACTION POTENTIAL – dramatic change in membrane potential (depolarization) due to the rapid influx of Na+ ions!!

- Turns Off: once channel opens and neurotransmitter released and either digested or reabsorbed

Cell Signaling

ION Channels

ACTION Potential



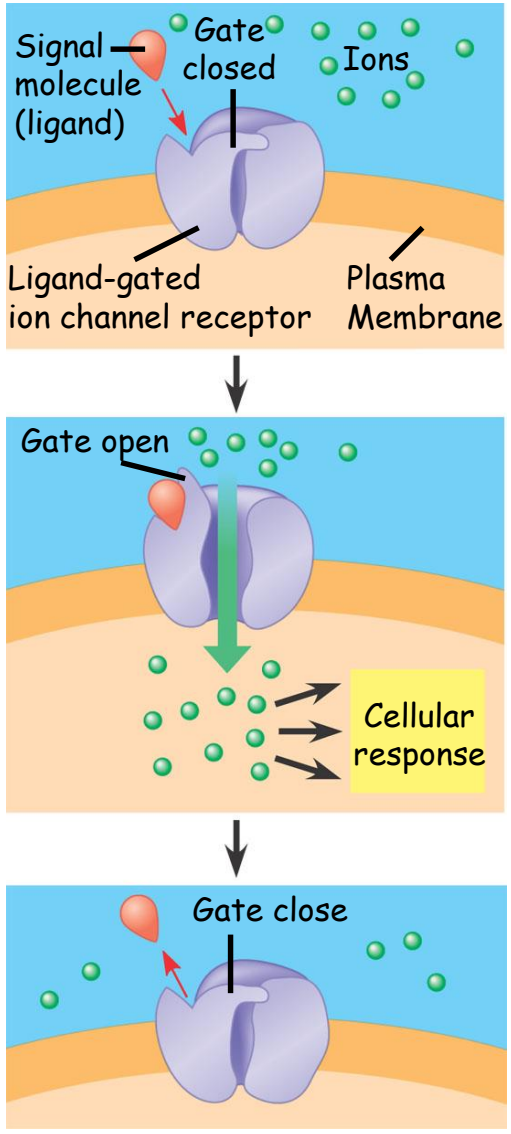
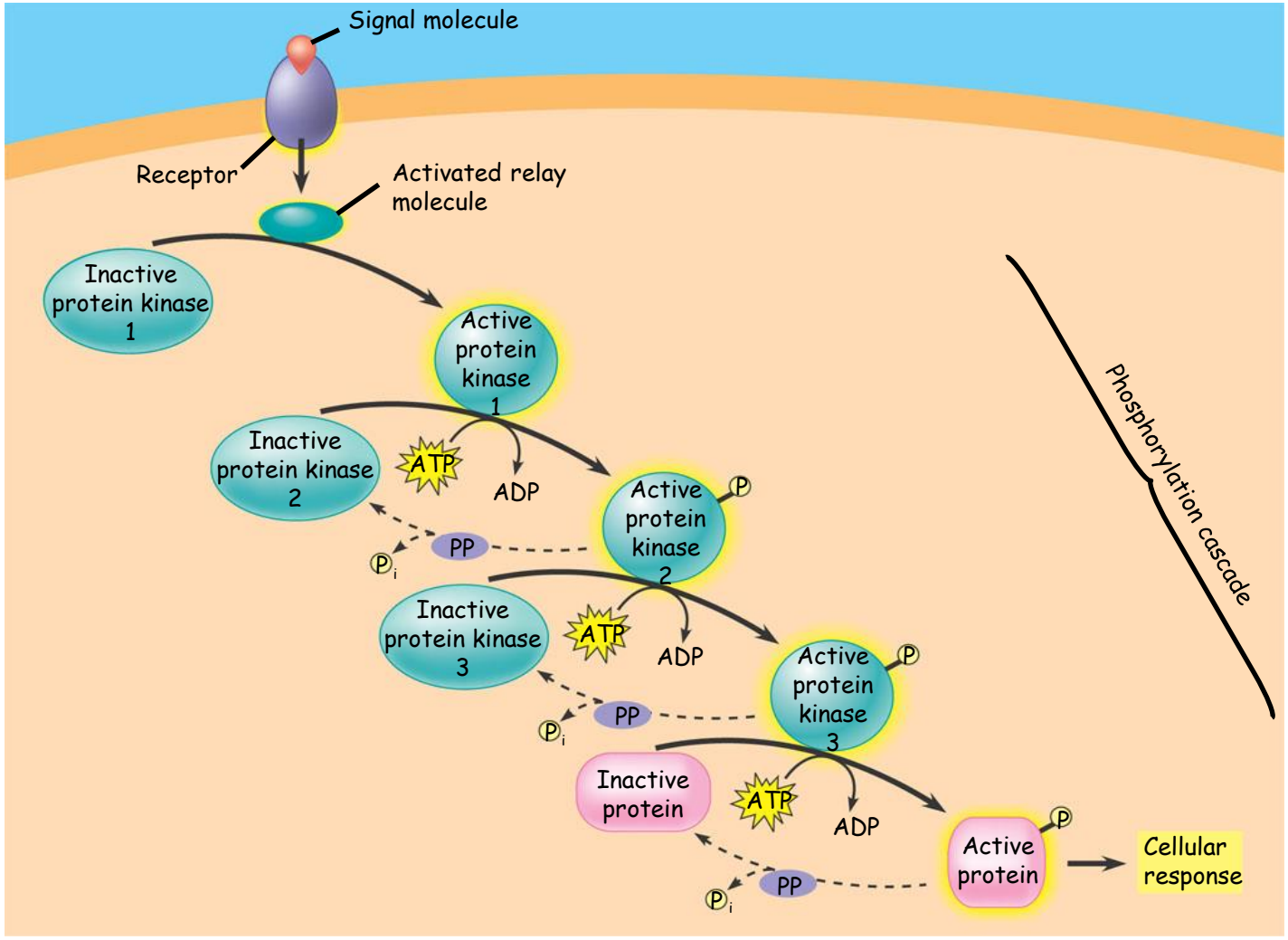


Figure 11.7

Cell Signaling

Phosphorylation Cascade Widely used by cells



Cell Signaling

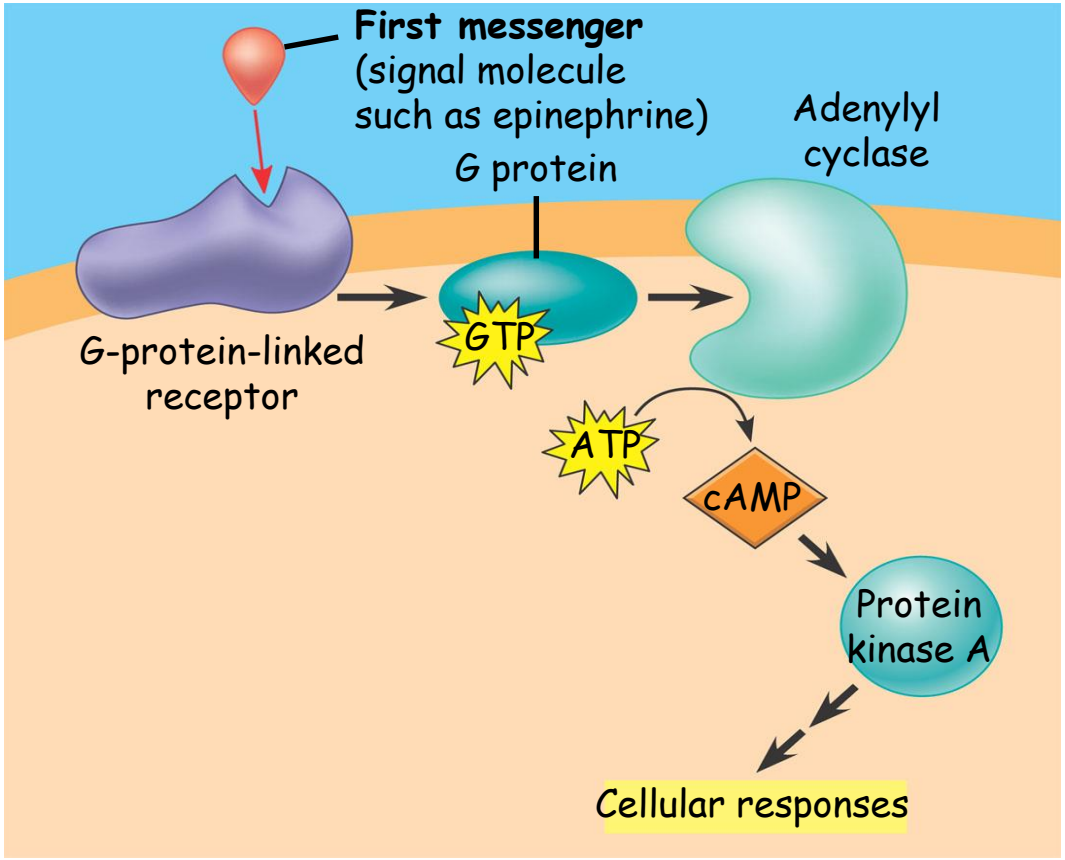
Second Messenger Signaling

- Cyclic adenosine monophosphate (**cAMP**)
  - Produced via G-protein coupled receptor signaling

- Ca^{2+} influx into the cell
  - Via channel opening (classic and very important example – ION Channels – via ACTION Potential)

Cell Signaling

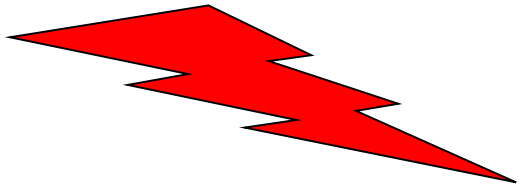
cAMP – a simplified view



Cell Signaling

Ca2+ :

ACTION Potential



Action potential causes Ca^{2+} to enter cell from outside and from intracellular stores

ON/OFF switch for other proteins

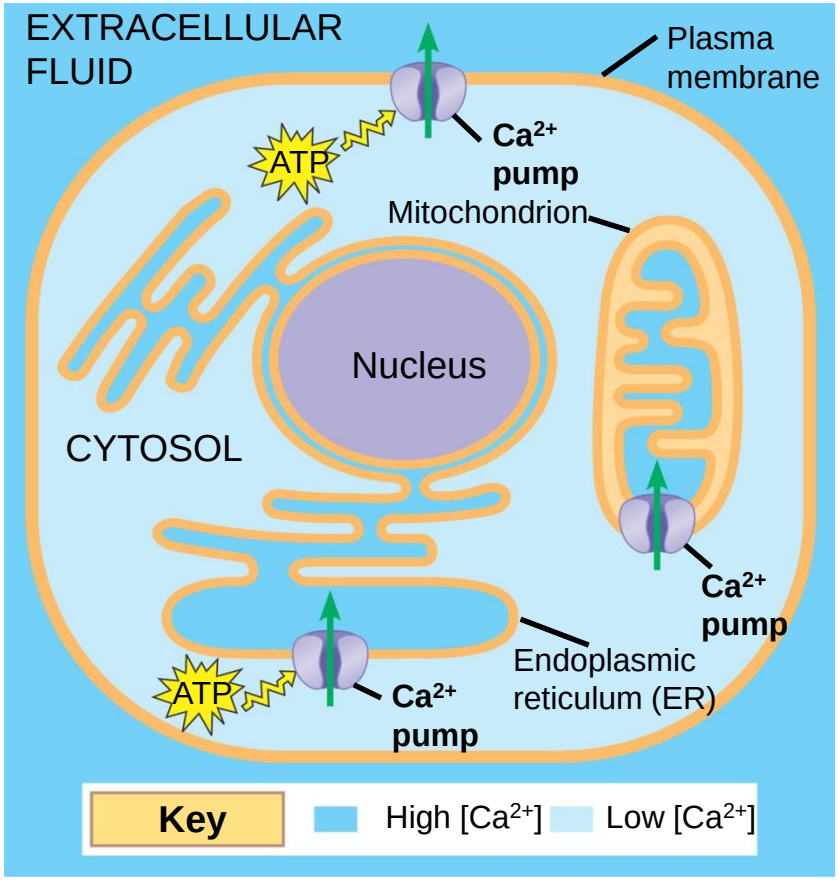


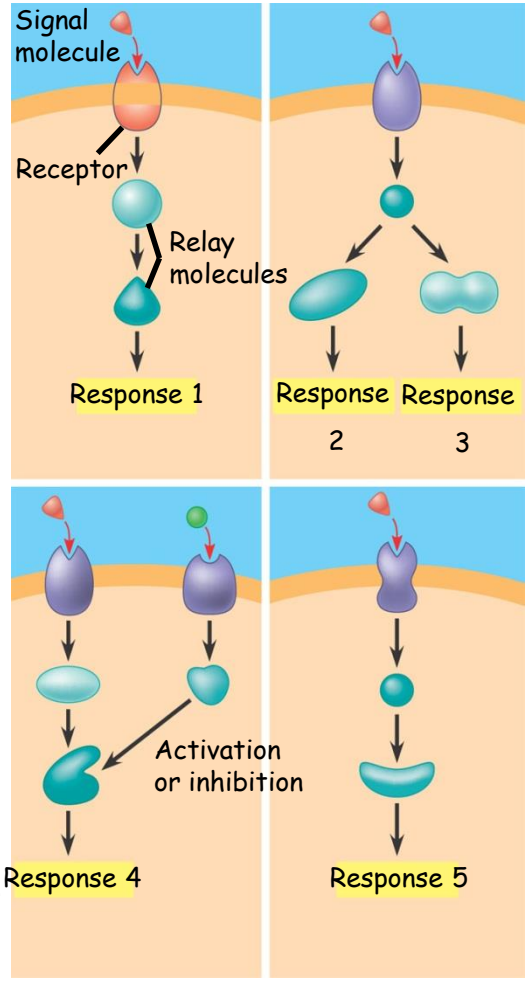
Figure 11.11

Cell Signaling – SPECIFITY!

- Many different types of cells
- Many signals
- Many proteins involved
- Many, many responses

- How does the cell accomplish all this?

Cell Signaling – SPECIFITY!



Cell A. Pathway leads to a single response

Cell B. Pathway branches, leading to two responses

Cell C. Cross-talk occurs between two pathways

Cell D. Different receptor leads to a different response

Figure 11.15