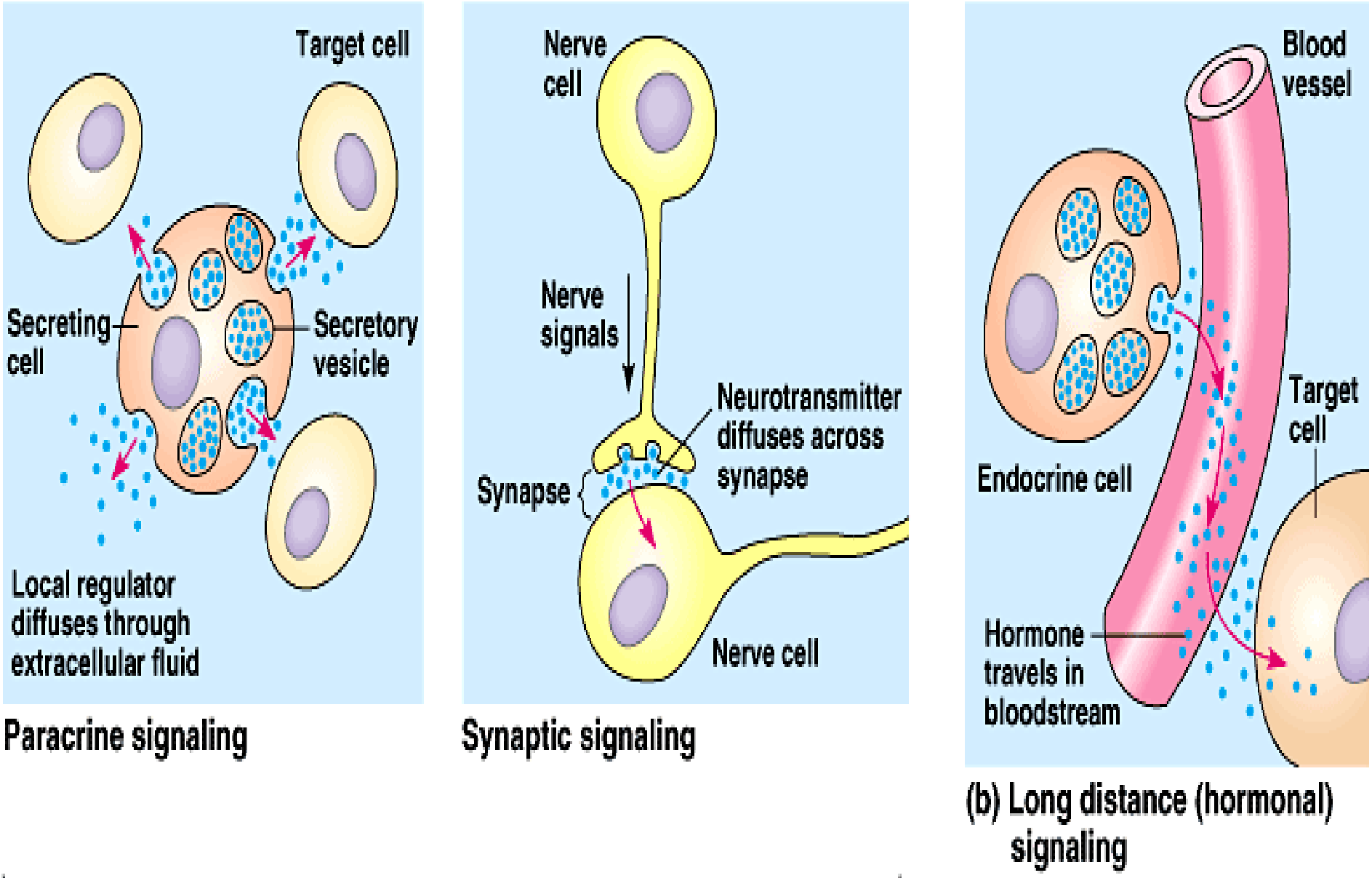
Chapter 11

Cell Communication

Signal Transduction Pathways

Signal-Transduction Pathway

- Signal on a cell's surface is converted into a specific cellular response
- *Local signaling* (short distance) - *Paracrine* (growth factors); *Synaptic* (neurotransmitters)
- *Long distance* - hormones



Stages of Cell Signaling

- Earl Sutherland (Nobel Prize in '71)
- Glycogen depolymerization by epinephrine
- Found epinephrine stimulates glycogen breakdown by activating an enzyme.
- When epinephrine was added to test tube with enzyme and glycogen (substrate) – Nothing happened.
- Epinephrine could ONLY active the enzyme when in solution with intact cells.

What did Sutherland Learn?

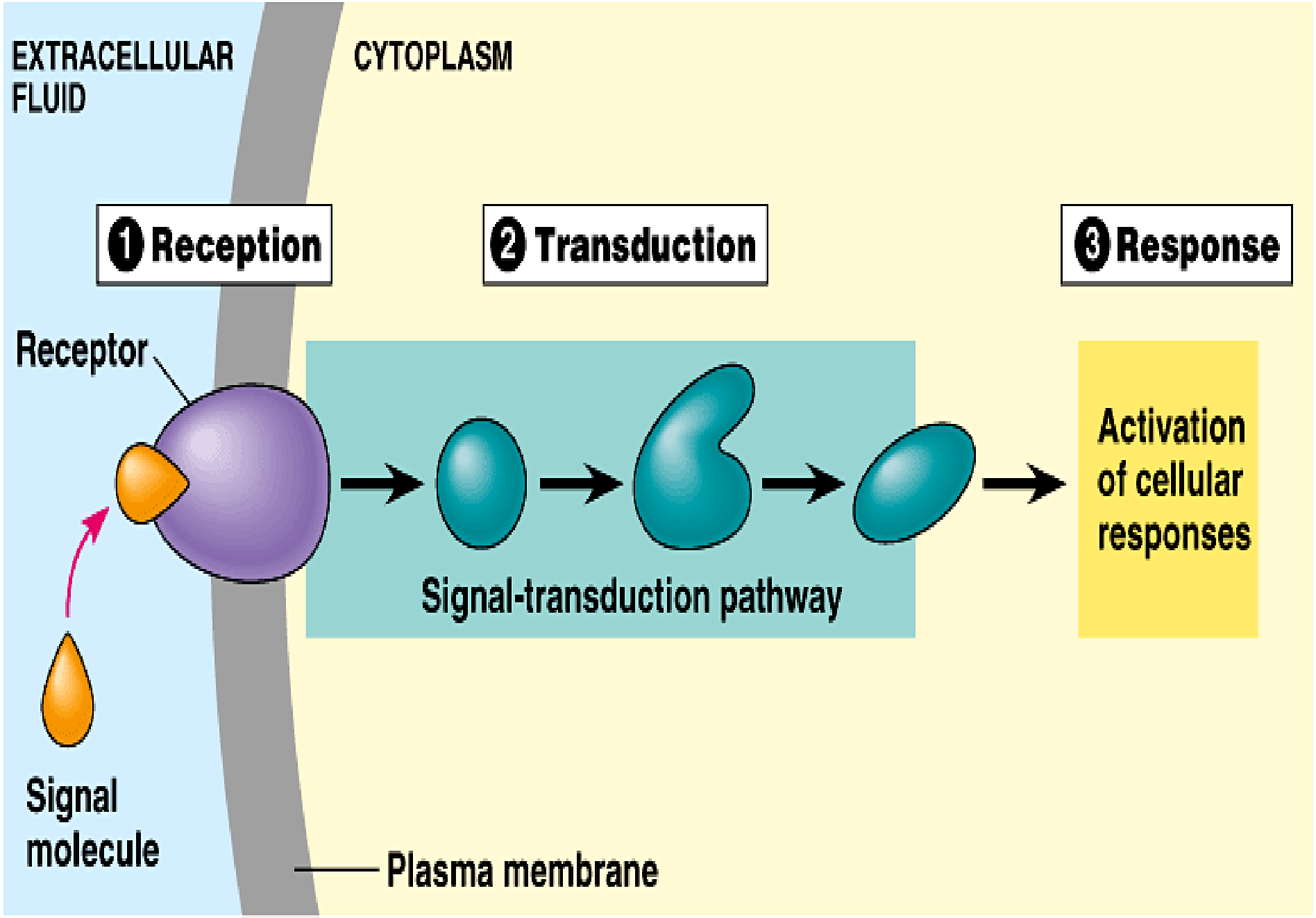
1) Epinephrine does not interact directly with the enzyme responsible for glycogen breakdown and intermediate step or series of steps must occur in cell.

2) The Plasma Membrane is involved in transmitting the signal.

STAGES OF CELL SIGNALING

1) **Reception**, a chemical signal binds to a cellular protein, typically at the cell's surface.
2) **Transduction**, binding leads to a change in the receptor that triggers a series of changes along a signal-transduction *pathway.*
3) **Response**, the transduced signal triggers a specific cellular activity.

Fig. 11.5



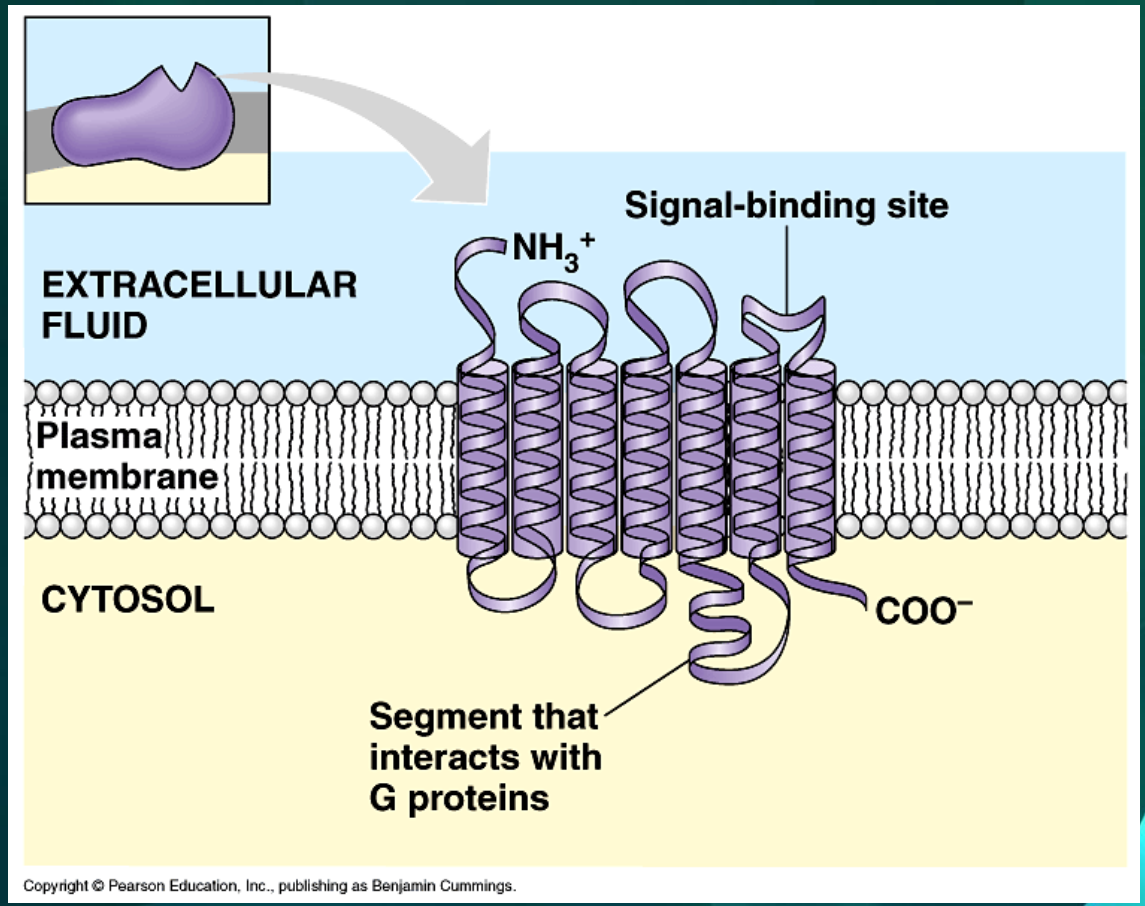
Plasma membrane Receptors

1) G- Protein Linked Receptors
2) Tyrosine-Kinase Receptors
3) Ligand-Gated Ion Receptors

G-Protein Linked Receptors

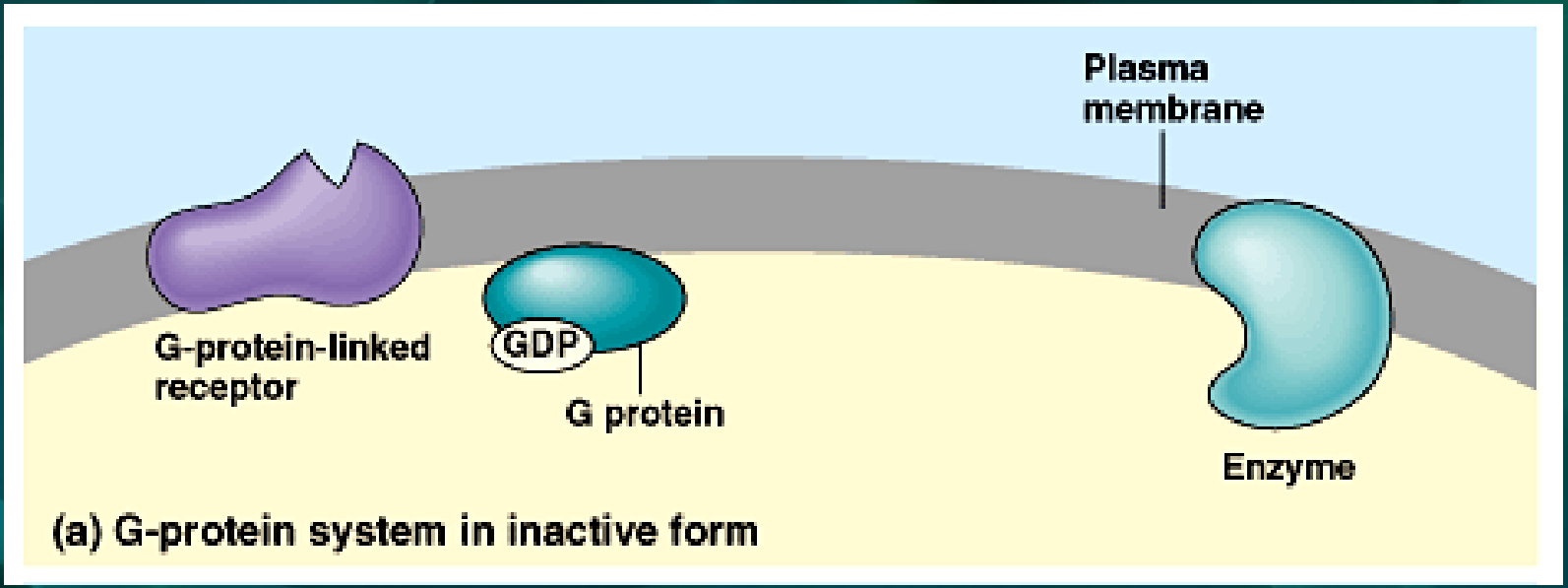
Plasma membrane receptor – works with a G protein.

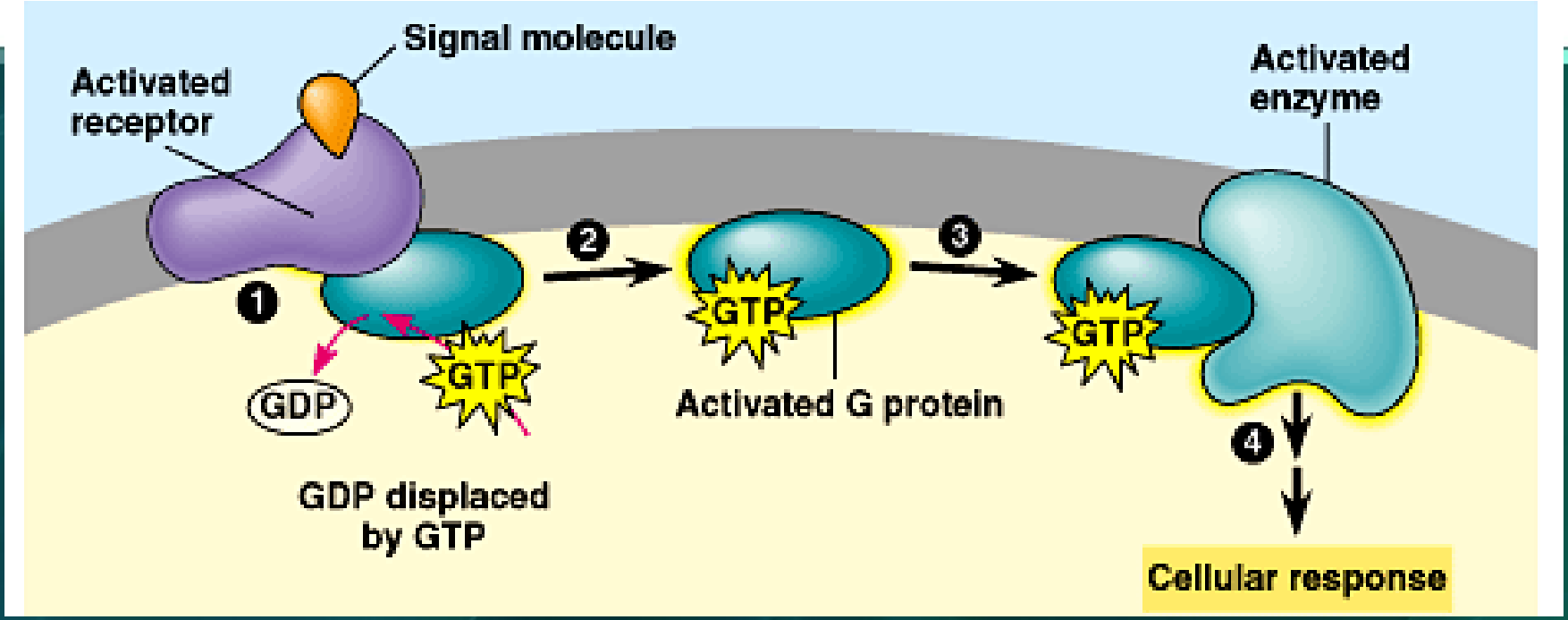
G Proteins are like on/off switches.



G Protein linked Receptor

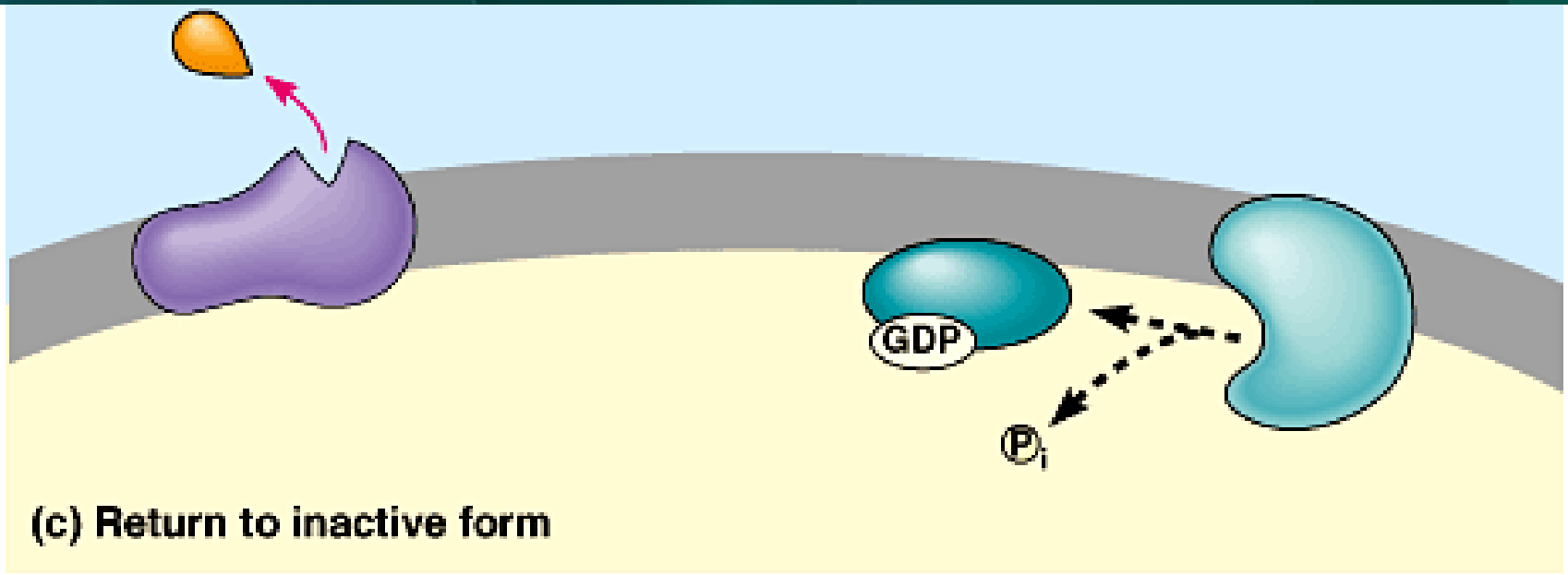
- No extracellular signal = INACTIVE





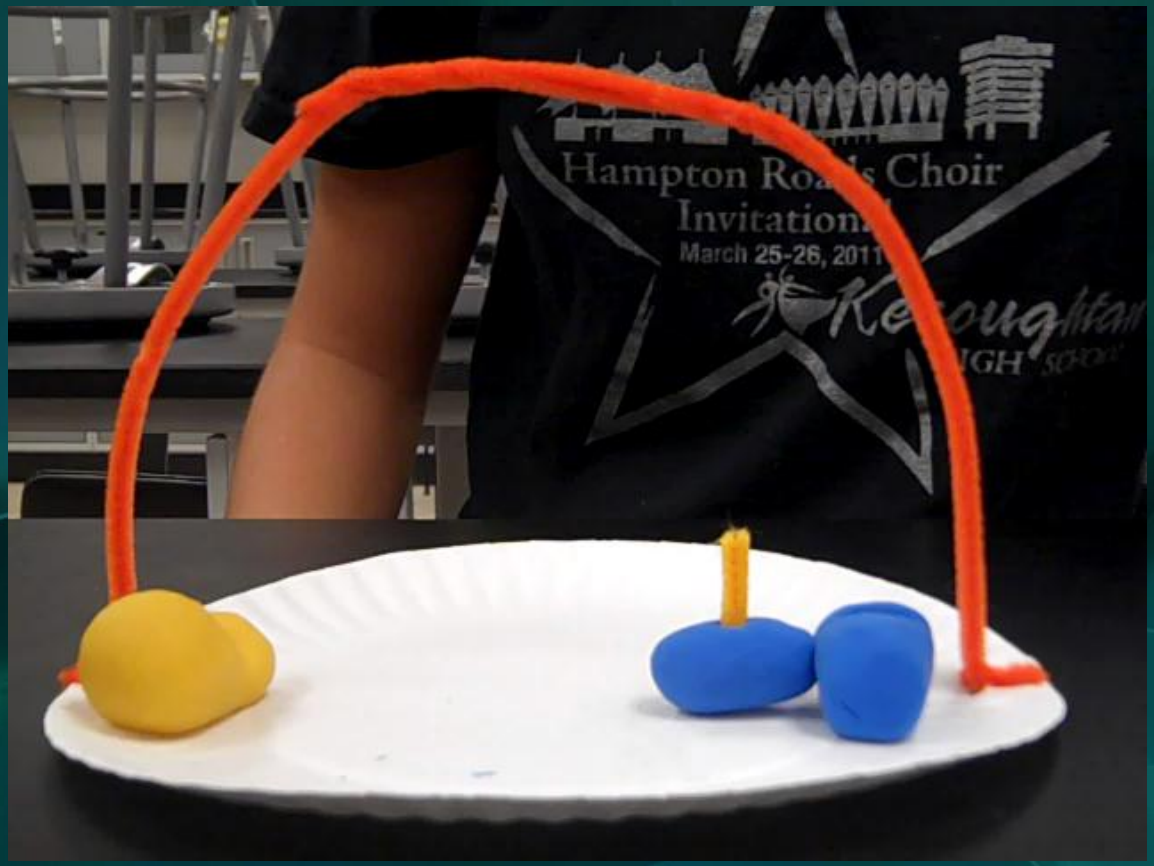
1) Signal molecule binds to receptor protein – changes shape and binds to G protein.
2) GTP molecule displaces GDP on G protein – activating the protein.
3) Active G protein moves along membrane and activates an enzyme.
4) Triggers next step in pathway – leads to cell response.

G protein catalyzes hydrolysis of GTP back to GDP - Inactive



- All three proteins remain ATTACHED to the cell membrane.

G protein Rap

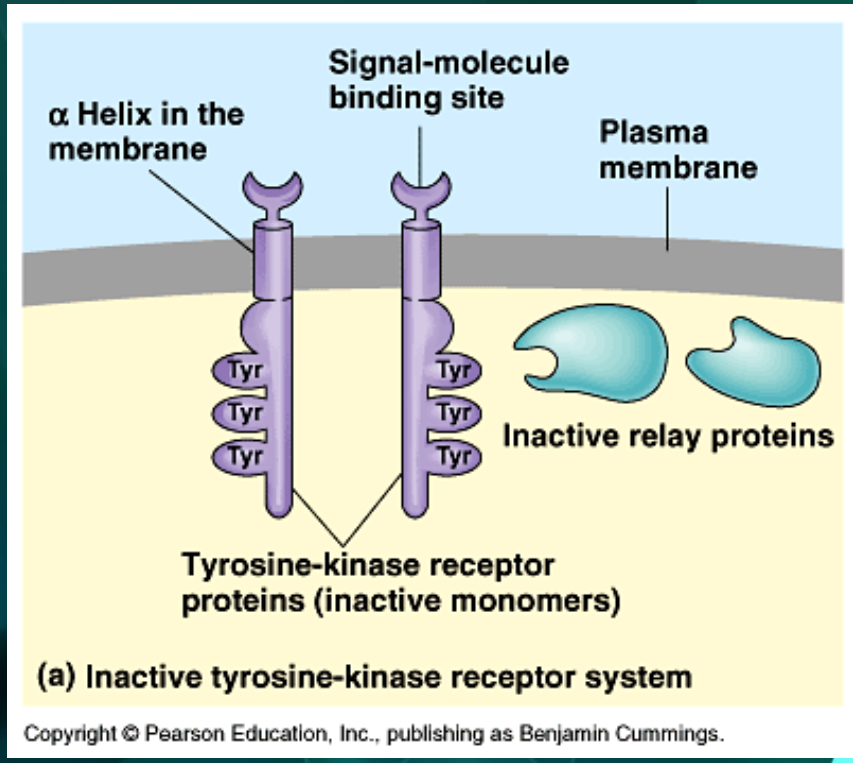


G Protein Modeling

- Use the play dough provided to make a quick model of the G protein.
- Use the handout as a guide.

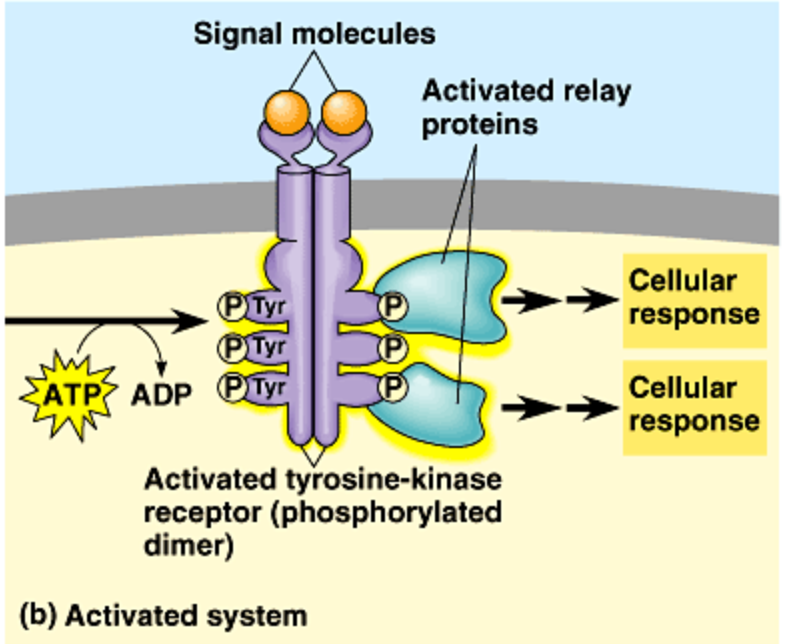
Tyrosine-Kinase Receptors

- When no ligand signal molecules are bound to the receptors – receptor is inactive.
- Tyrosine receptors that extend into the cytoplasm are monomers and inactive.



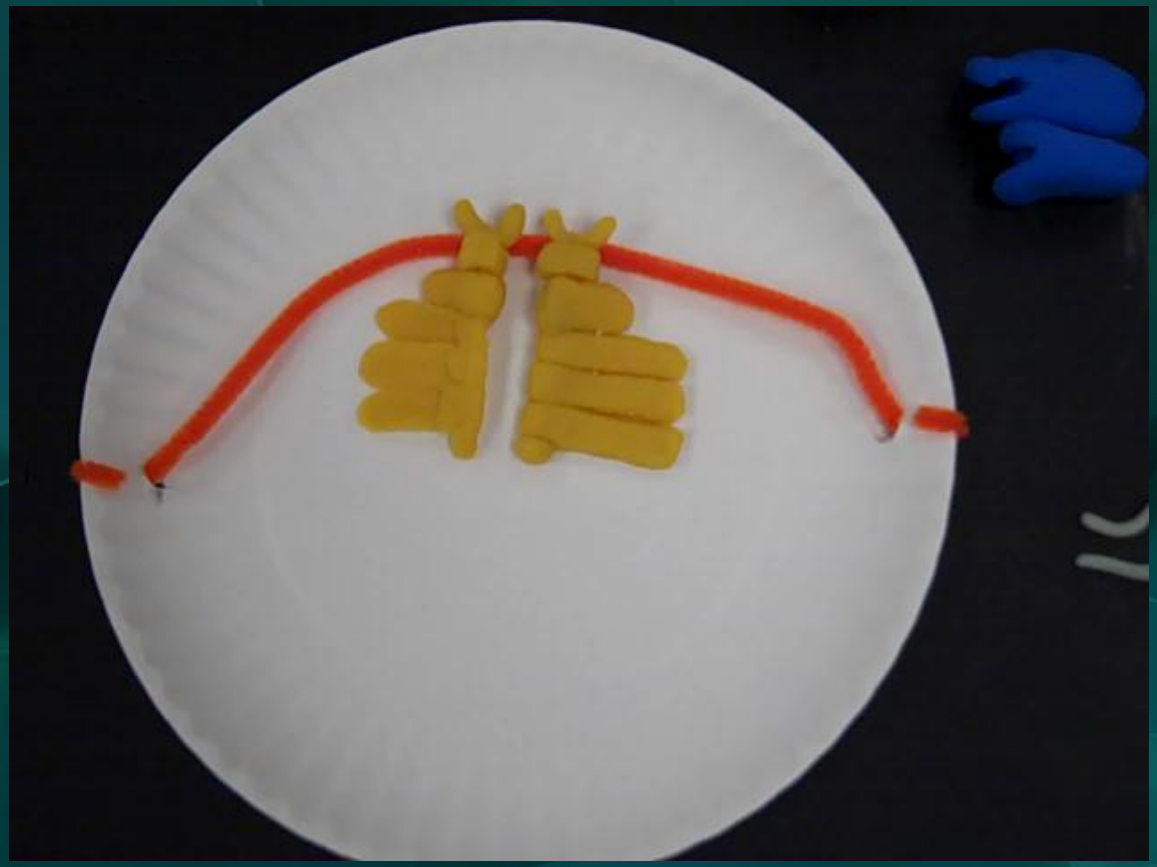
Tyrosine-Kinase Receptors

1) Signal molecules attach to binding sites – to monomers join and form dimer.
2) 6 ATP phosphorylate the tyrosines – ACTIVE
3) Receptor protein binds to relay proteins which actives the relay proteins
4) Relay proteins initiate a signal transduction pathway causing a cellular response.



Hint:
Kinase = Phosphorylation

Tyrosine-Kinase with strange, really bad Italian accent

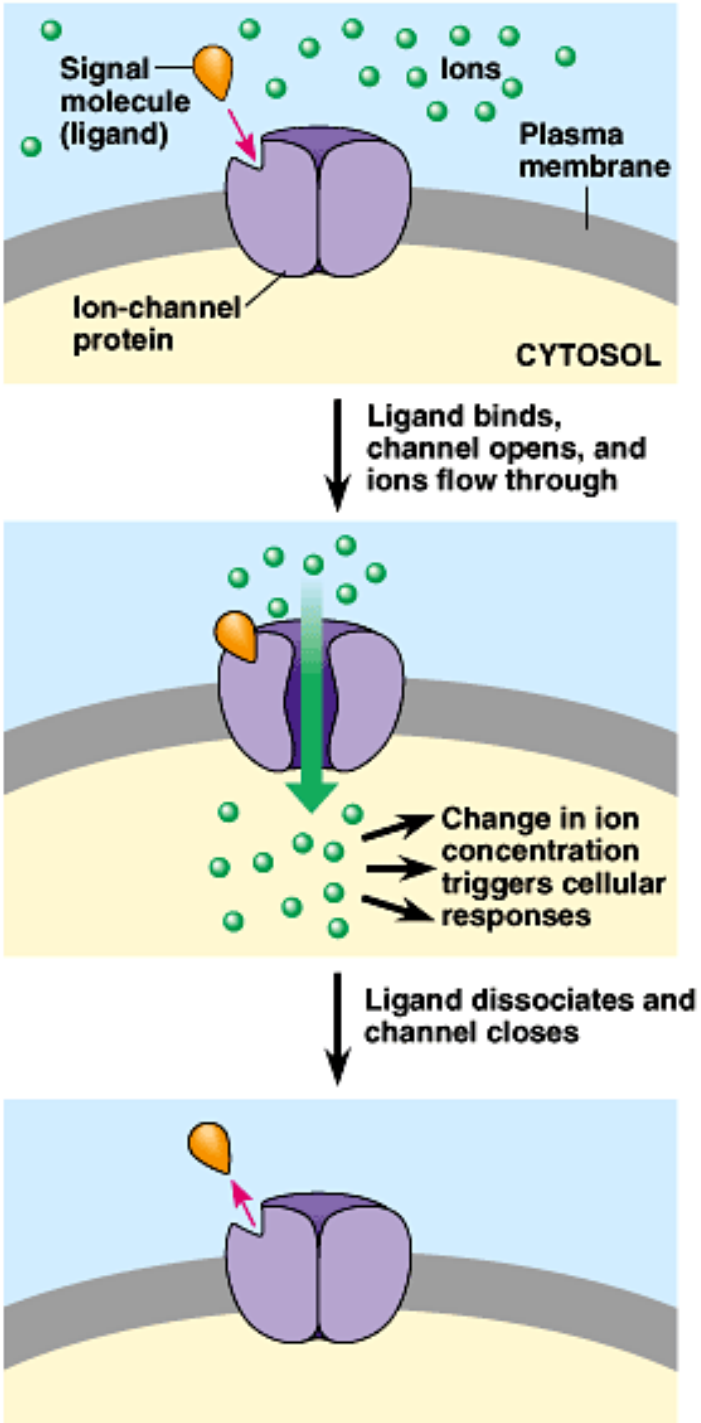


Remember Action Potentials!!!

Ion-Channel Receptors

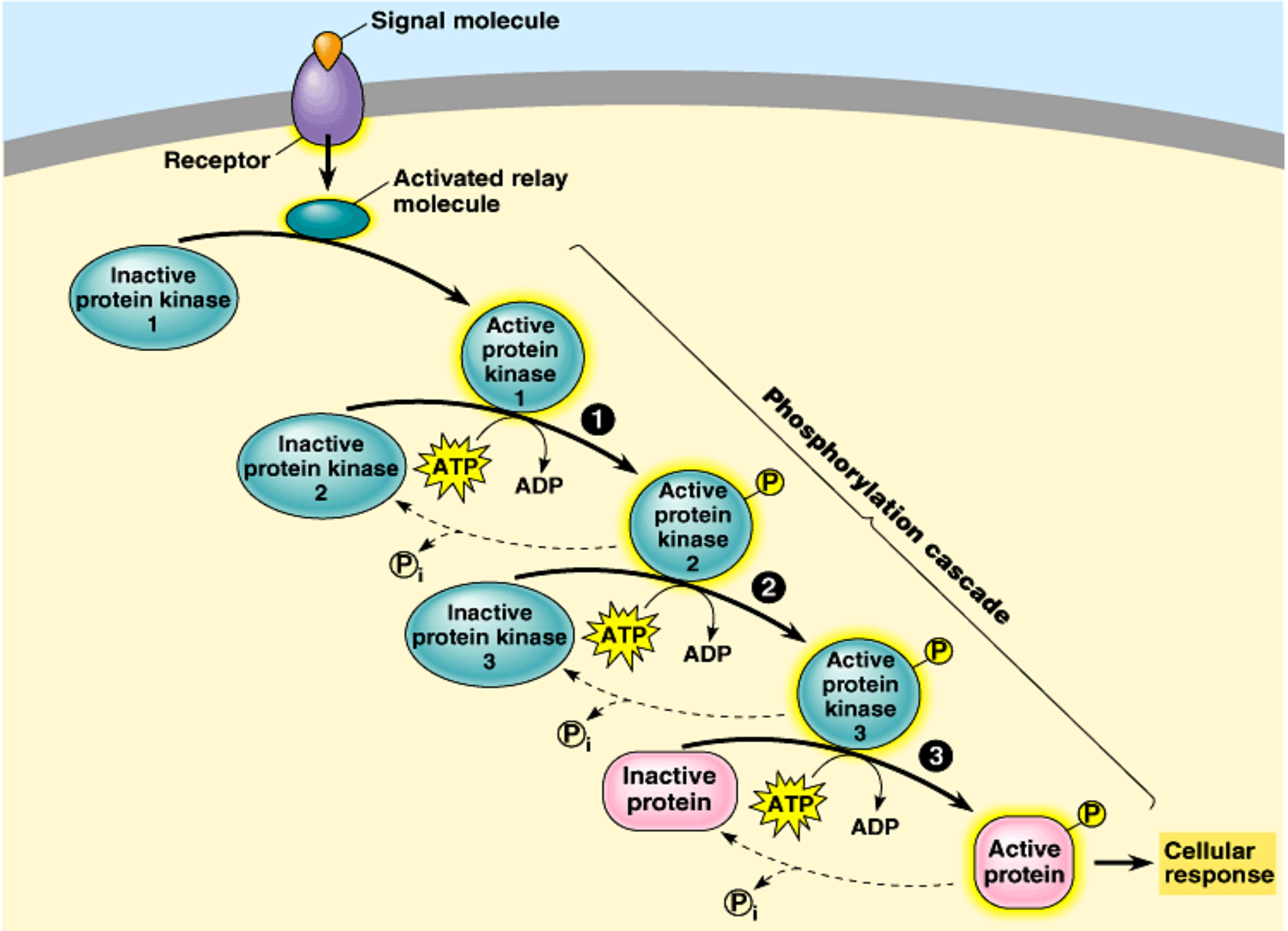
Bound ligand opens ion-channel.

Remove of ligand closes the channel



Protein Phosphorylation

- G protein or Tyrosine kinase start a protein phosphorylation cascade.
- Protein activity regulation
- Adding phosphate from ATP to a protein (activates proteins)
- Enzyme: protein kinases (2% of all our genes)
- Example: cell reproduction
- Reversal enzyme: protein phosphatases

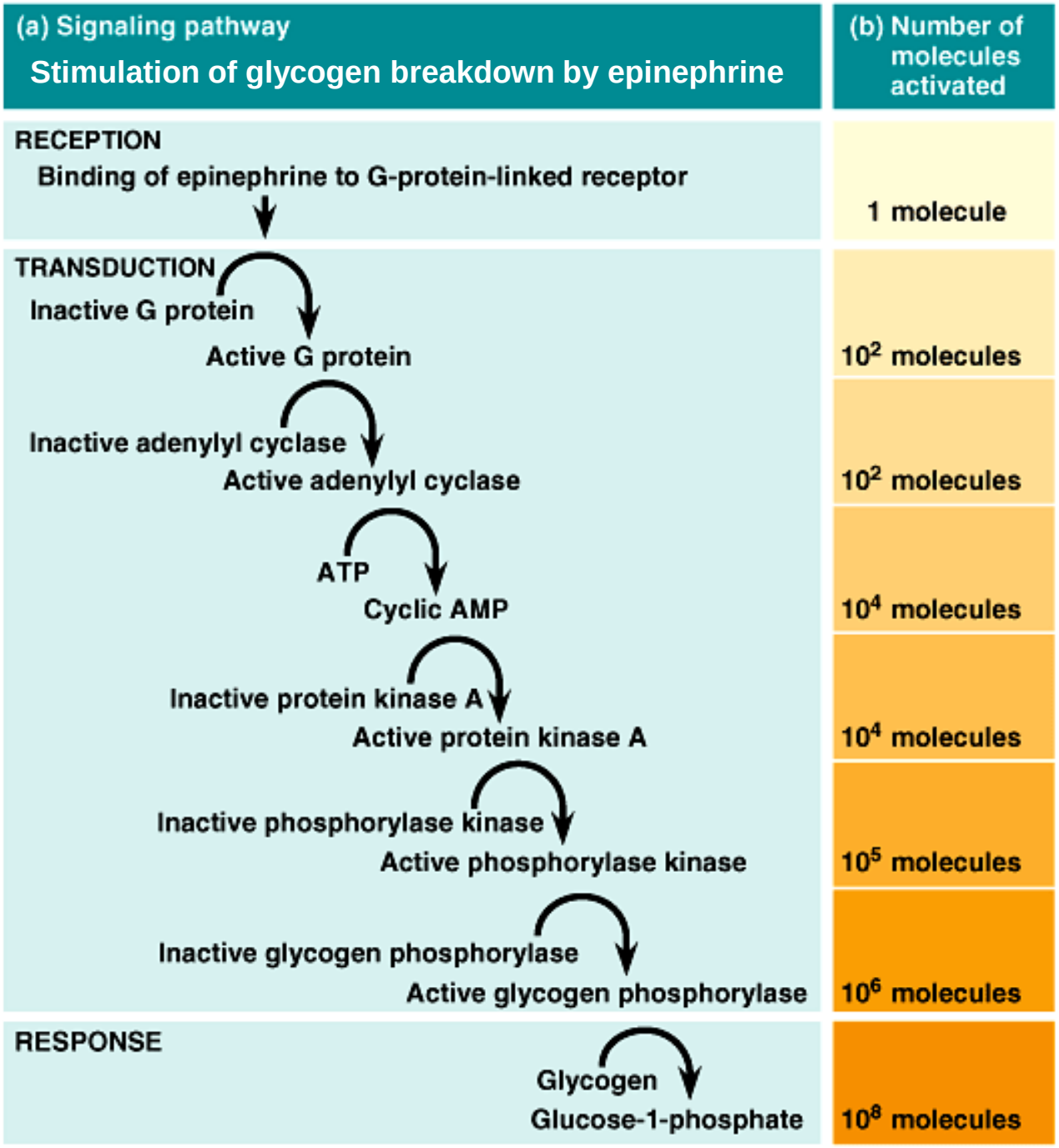


Phosphorylation Cascade

- A series of different molecules in a pathway are phosphorylated.
- The phosphorylated proteins are now active and can catalyze the phosphorylation of another protein in the pathway.
- The cascade continues until a cellular response is produced.
- The removal of phosphate groups then deactivates the proteins.

Purpose of Signal Transduction pathways

- Series of **chain reactions**
- Each reaction in the series **amplifies** the signal being sent.
- The molecules that are activated in each step, **activate many molecules** that in **turn activate many molecules.**
- So **one molecule** at the beginning creates a **huge cellular response** due to the signal transduction pathways.



1 molecule

100,000,000 molecules

Second Messengers

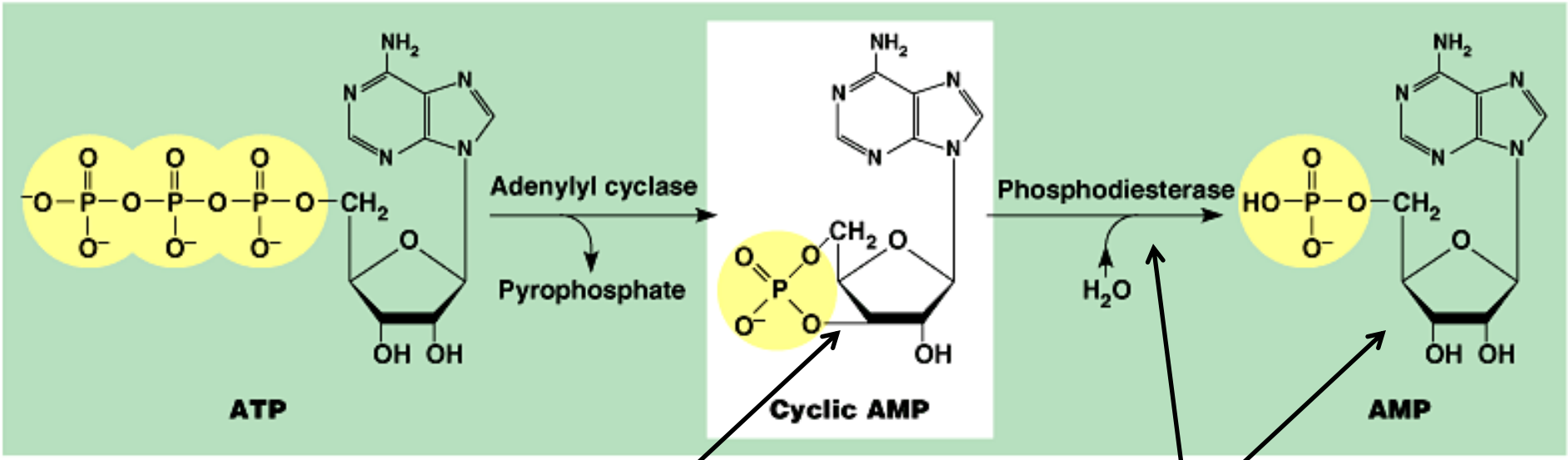
- Non-protein signaling pathway
- Small, non-protein, water-soluble molecules or ions. – spread through the cell by diffusion
- Participate in pathways initiated by **G protein-coupled receptors** and **tyrosine kinases**.
- Two most widely used 2nd messengers are cAMP and Ca^{2+}

Second Messengers

- Example: *cyclic AMP (cAMP)*
- Ex: Glycogen breakdown with epinephrine
- Enzyme: *adenylyl cyclase*

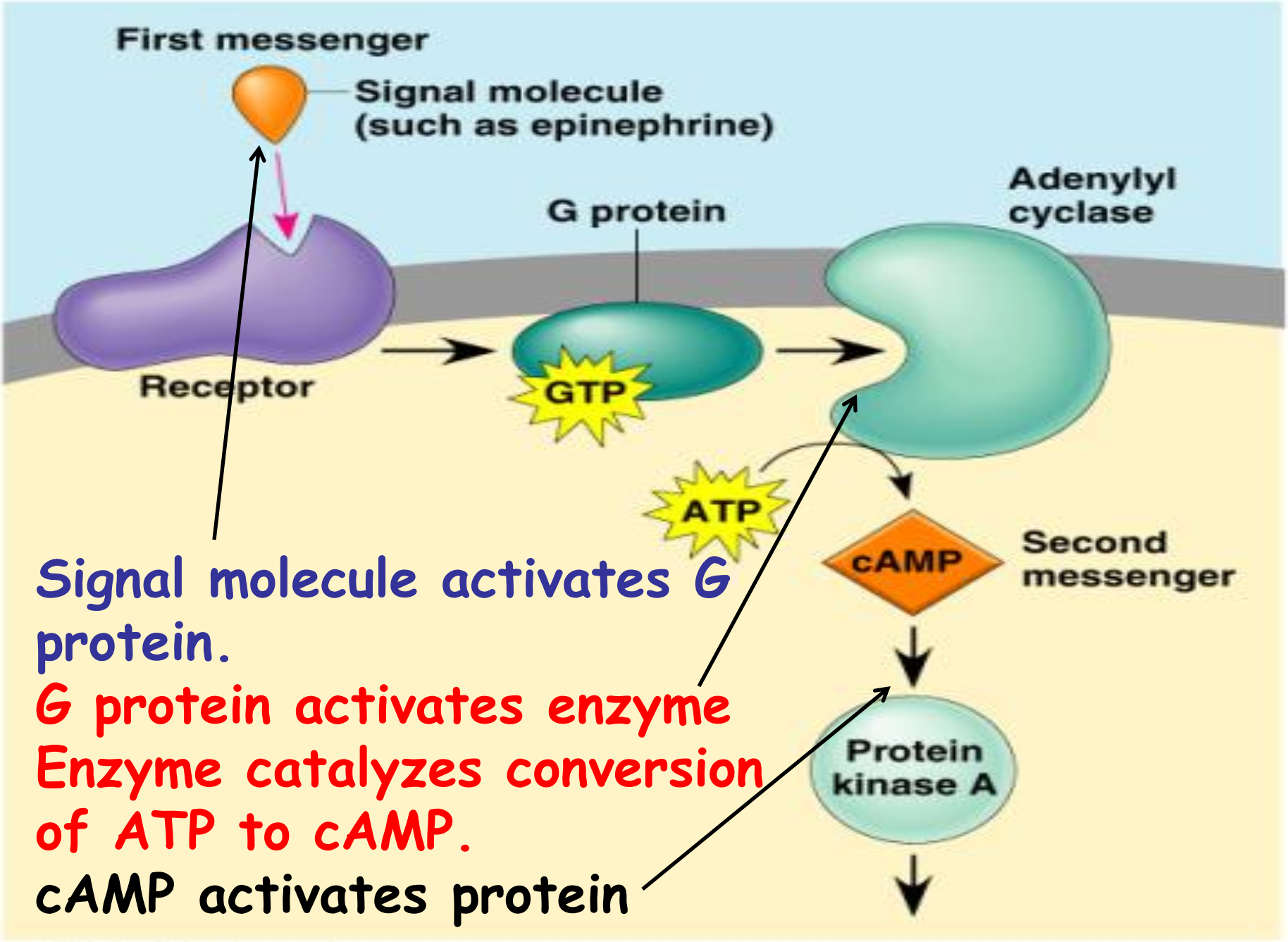
- *Epinephrine* activates G protein → G protein activates *adenylyl cyclase* → Adenylyl cyclase dephosphorylates ATP to make cAMP → cAMP activates many protein kinases amplifying the original signal.

cAMP



Notice the bond and the removal of 2 phosphates

Hydrolysis occurs, now bond is broken



Signal molecule activates G protein.

G protein activates enzyme

Enzyme catalyzes conversion of ATP to cAMP.

cAMP activates protein

Calcium ions as 2nd messenger

- More widely used than cAMP
- Increasing calcium ion concentration in cytosol occurs:
  - in muscle contraction
  - secretion of some neurotransmitters
  - Cell division

Cellular Responses to Signals

- Cytoplasmic activity regulation
- Cell metabolism regulation
- Nuclear transcription regulation