ZO502 CELL AND MOLECULAR BIOLOGY

BLOCK – I: CELL BIOLOGY

Unit –8 : Cell Communication and Signaling

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Cell Communication

Cells need to be able to communicate to other cells and respond to environment changes

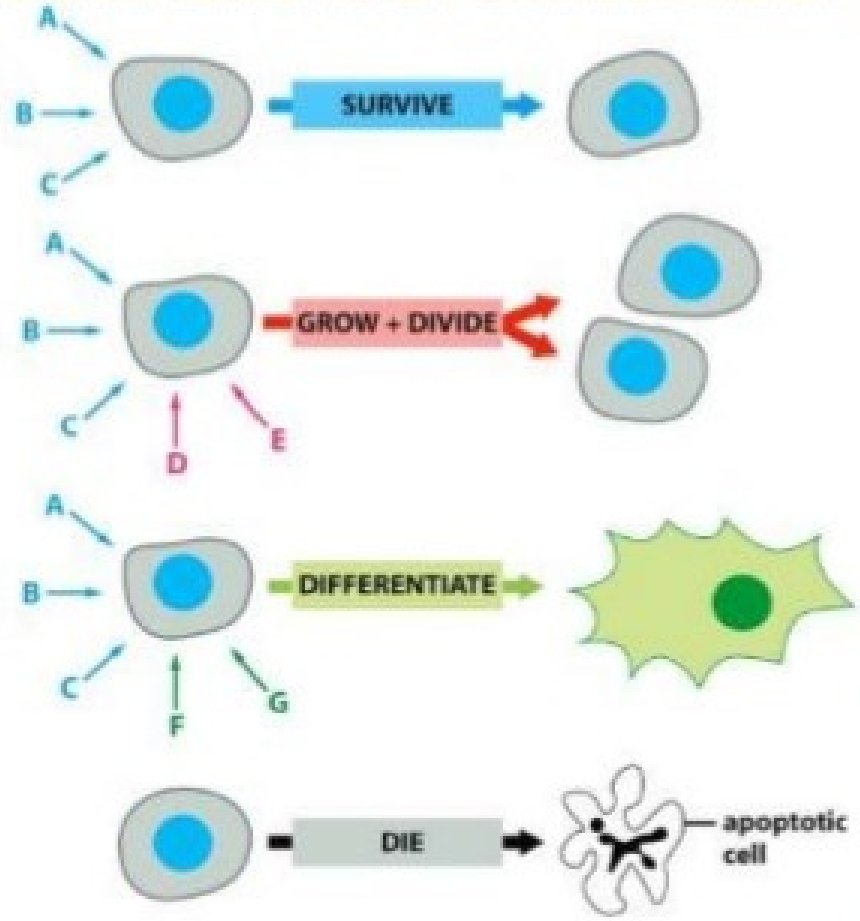
* For multicellular organisms, cell-cell communication is important

* External signals are converted into responses within the cell

For unicellular organisms, they need to be able to respond to physical and chemical changes in their Environment

Unicellular organisms can communicate and influence one another's behavior. Many bacteria can respond to chemical signals that are secreted by their neighbors and increase in concentration with increasing population density (quorum sensing), allowing them to coordinate their behavior, including their mobility, antibiotic production, spore formation, and sexual conjugation.

Each cell is programmed to respond to specific combinations of extracellular signal molecules

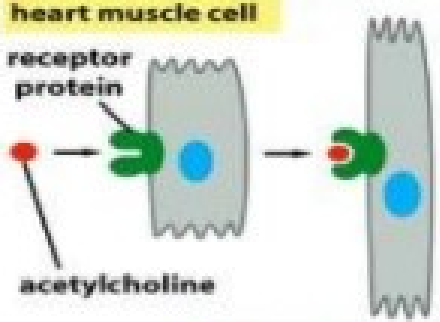


Cells deprived of appropriate survival signal will undergo apoptosis (committ suicide)

Same signal can cause different reactions depending on the target cell

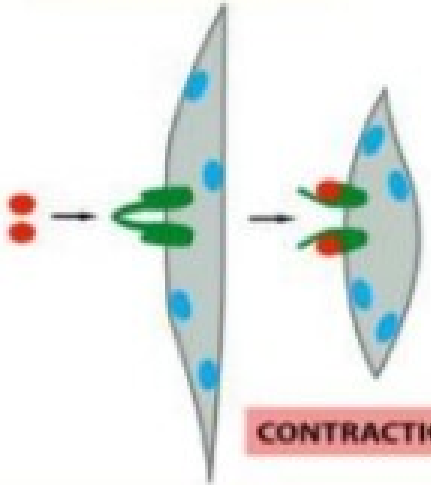
(A) acetylcholine

(B) heart muscle cell



DECREASED RATE AND FORCE OF CONTRACTION

(C) skeletal muscle cell



CONTRACTION

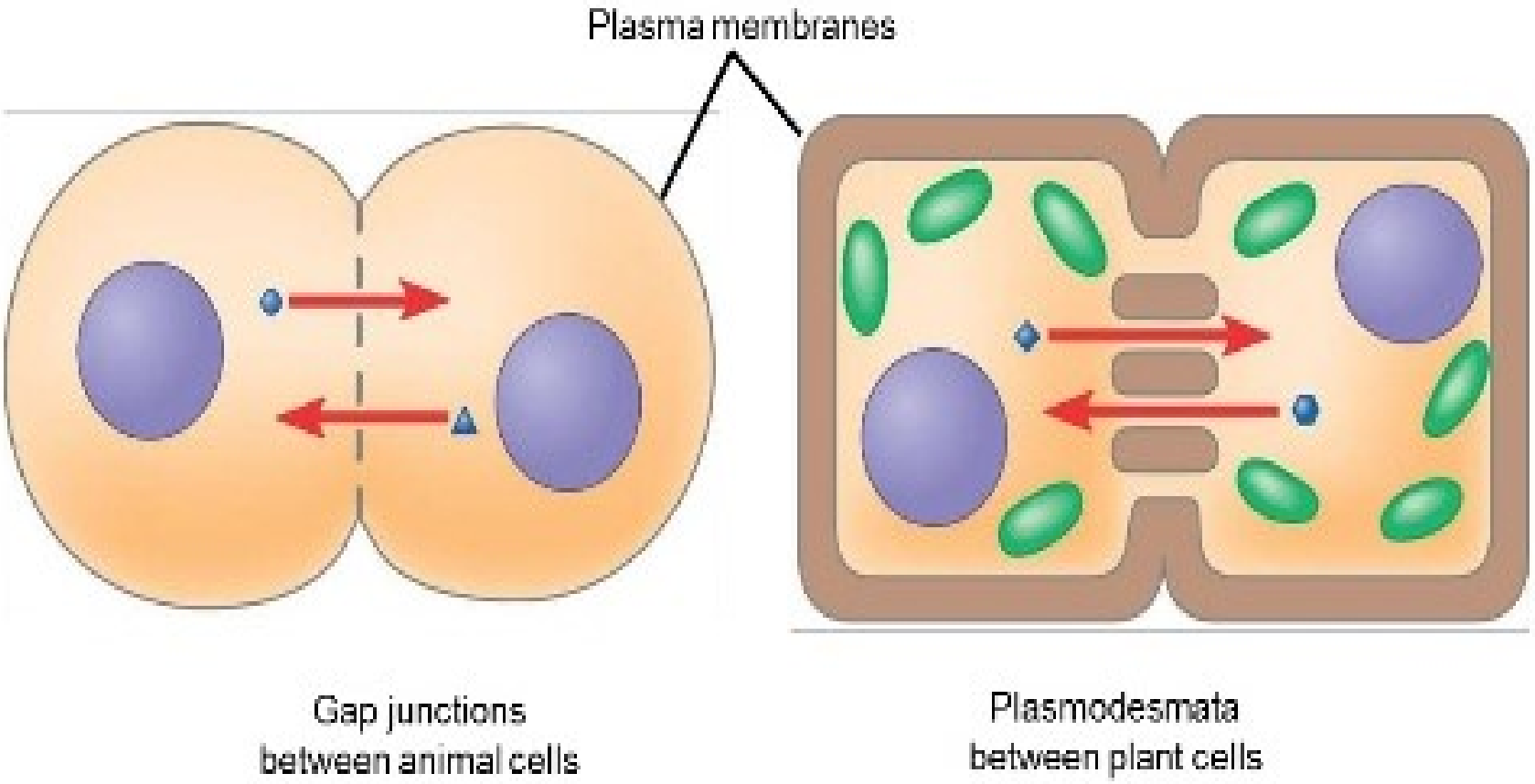
(D) salivary gland cell

SECRETION

Local and Long-Distance Signaling

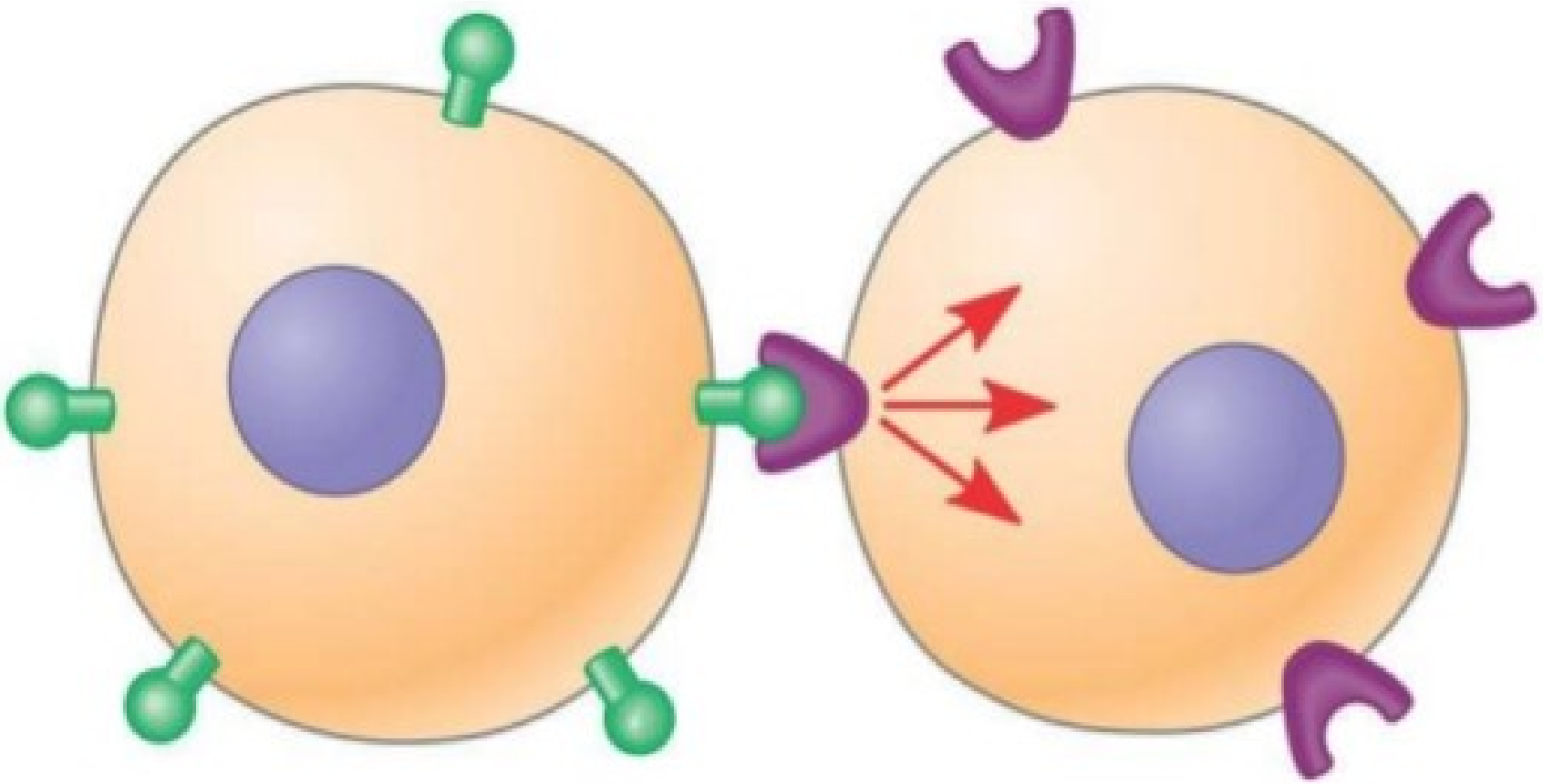
- Cells in a multicellular organism communicate by chemical messengers
- Animal and plant cells have cell junctions that directly connect the cytoplasm of adjacent cells
- In local signaling, animal cells may communicate by direct contact, or cell-cell recognition

Animal and Plant Cell



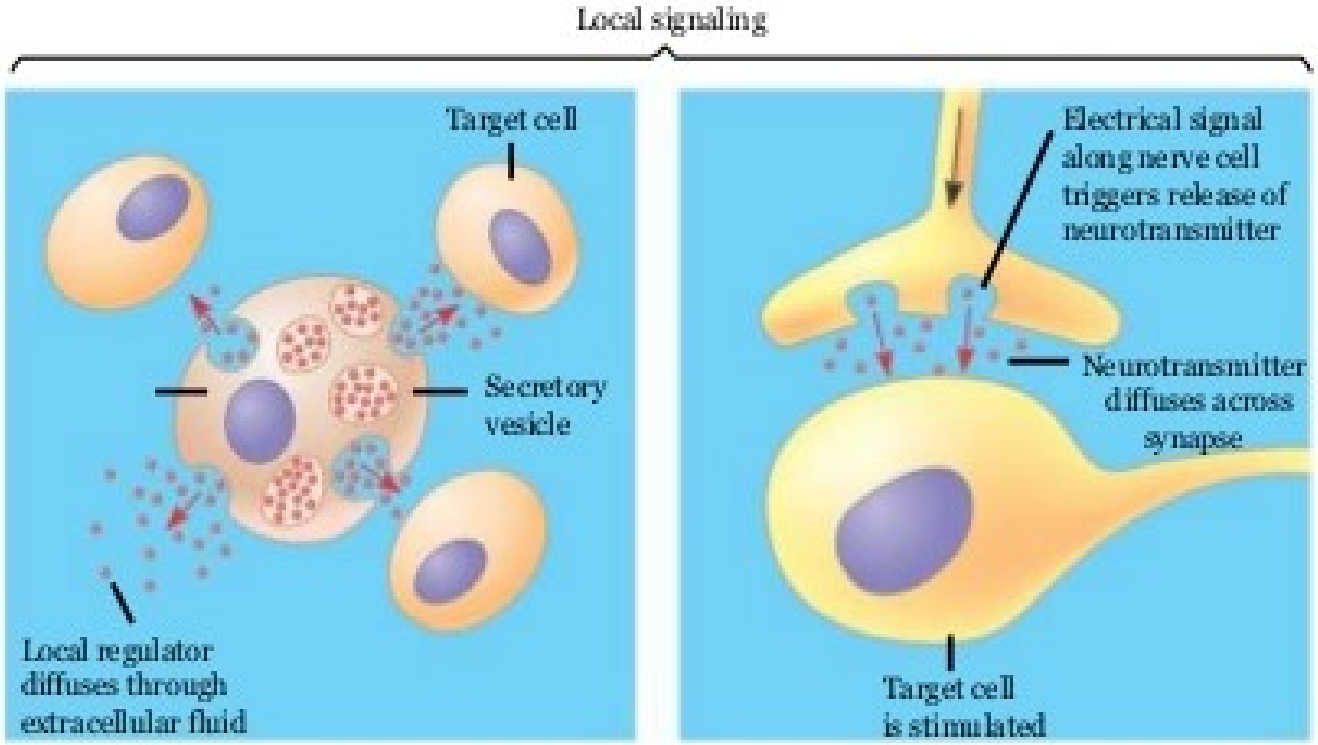
•In local signaling , animal cells

•May communicate via direct contact



•In other cases , animal cells

•Communicate using local regulators



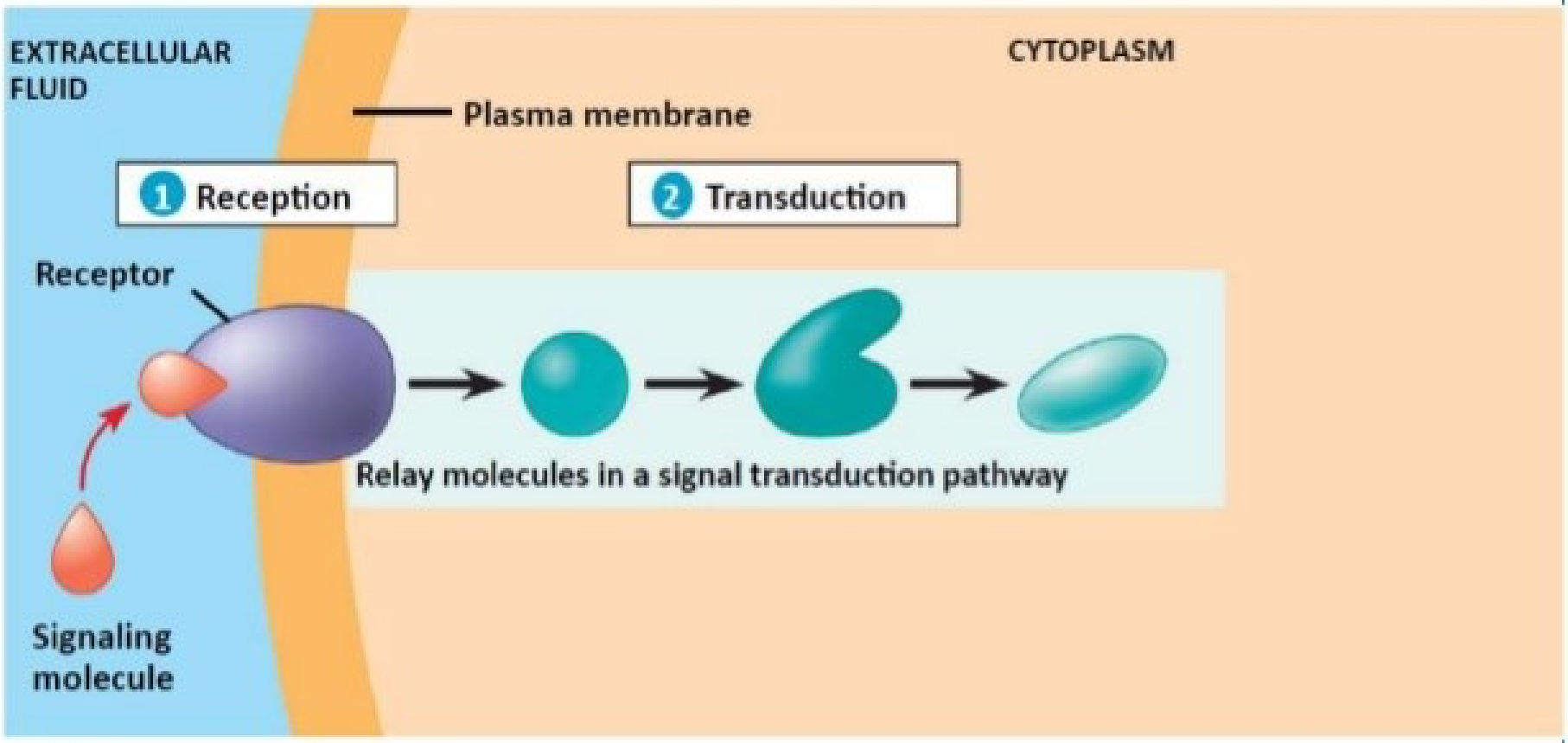
(a) Paracrine signaling. A secreting cell acts on nearby target cells by discharging molecules of a local regulator (a growth factor, for example) into the extracellular fluid.

(b) Synaptic signaling. A nerve cell releases neurotransmitter molecules into a synapse, stimulating the target cell.

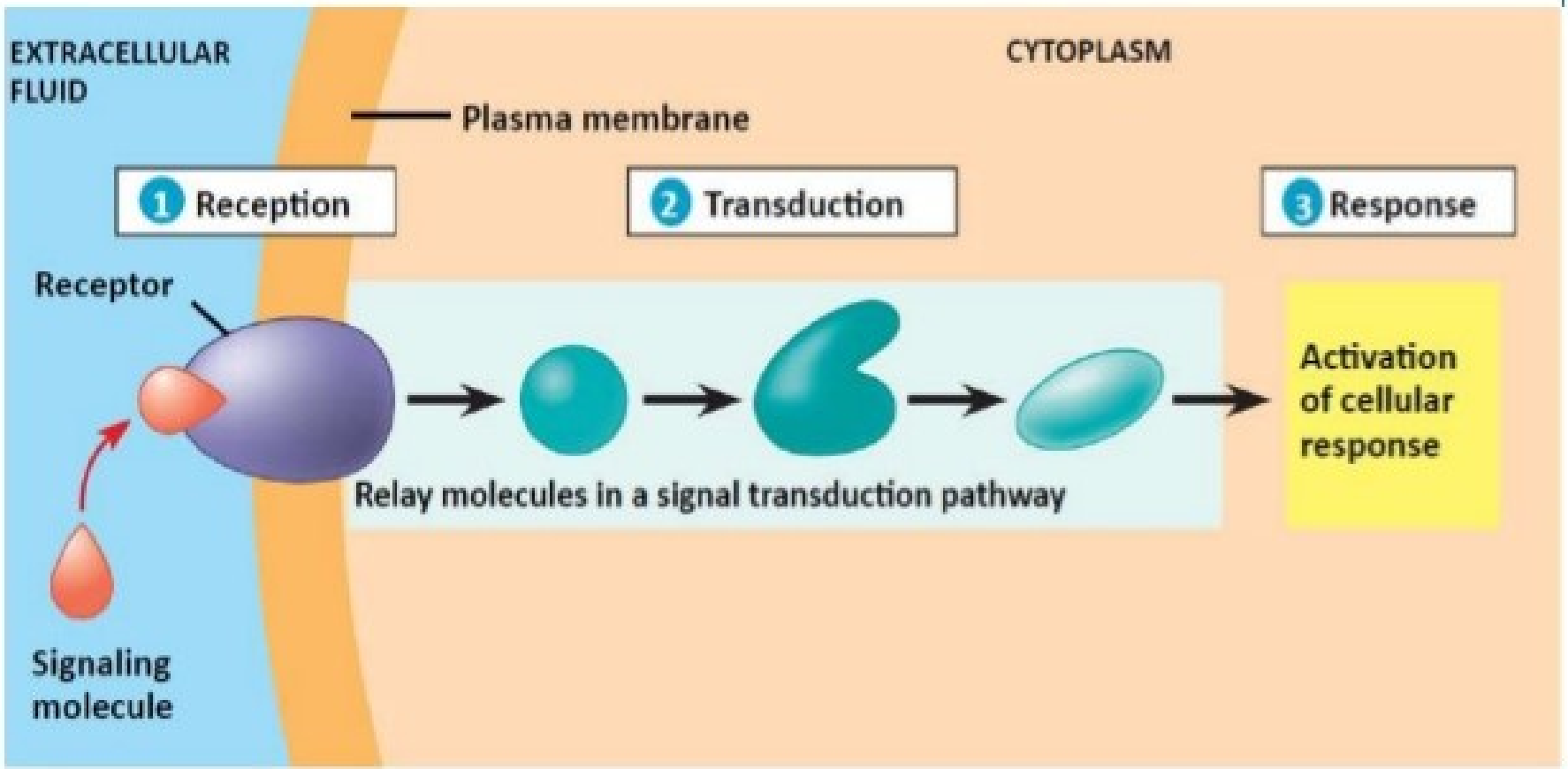
Step 1 of cell signaling: Reception

Usually, two molecules are involved:
- Ligand
- Receptor

Step two of cell signaling Transduction



Step three of cell signaling: Response



Reception

A SIGNAL MOLECULE BINDS TO A RRECEPTOR PROTEIN THAT, CAUSING IT TO CHANGE SHAPE

- The cell target d by a particular chemical signal has a receptor protein on or in the target cell that recognizes the signal molecule

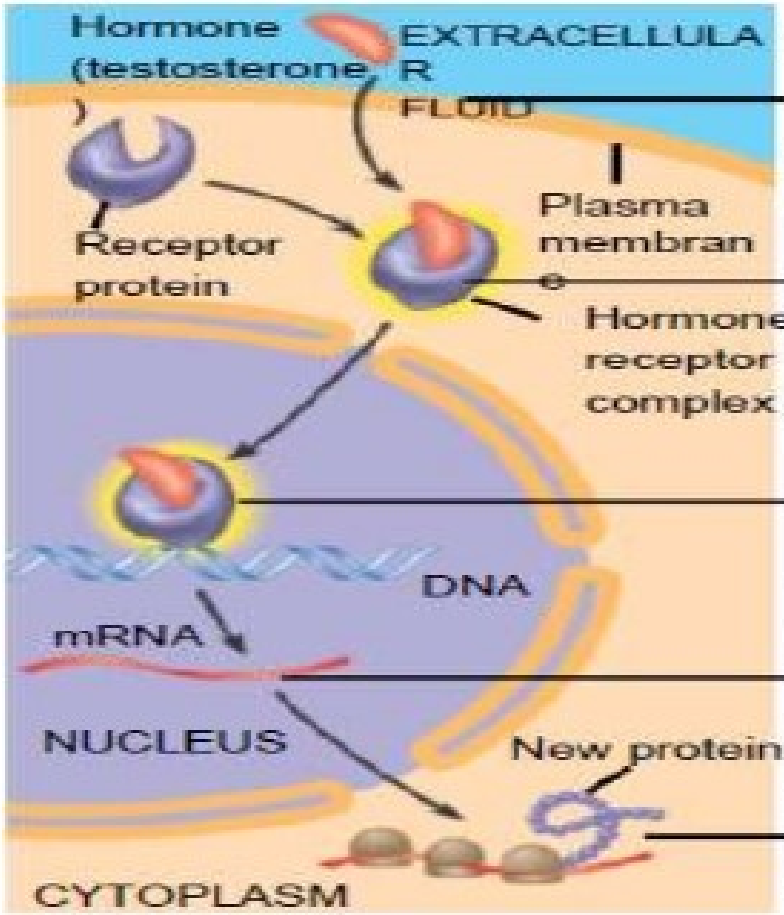
- Recognition occurs when the signal binds to a specific site on the receptor that is the complementary in shape to the signal.

- Ligand binding causes the receptor protein to undergo a change in shape that may activate the receptor so that it can interact with other molecules

Intracellular Receptors

- Some ligands are small hydrophobic molecules that can cross cell membranes (Ex. Testosterone).
- Receptors that detect such ligand are intracellular , found in the cytosol or nucleus of target cells.
- An activated hormone-receptor complex can act as a transcription factor. Turning on specific genes

Hydrophobic messengers include the steriod and thyroid hormones



1. The steroid hormone testosterone passes through the plasma membrane.
2. Testosterone binds to a receptor protein in the cytoplasm, activating it.
3. The hormone–receptor complex enters the nucleus and binds to specific genes.
4. The bound protein stimulates the transcription of the gene into mRNA.
5. The mRNA is translated into a specific protein.

Receptors in the plasma membrane

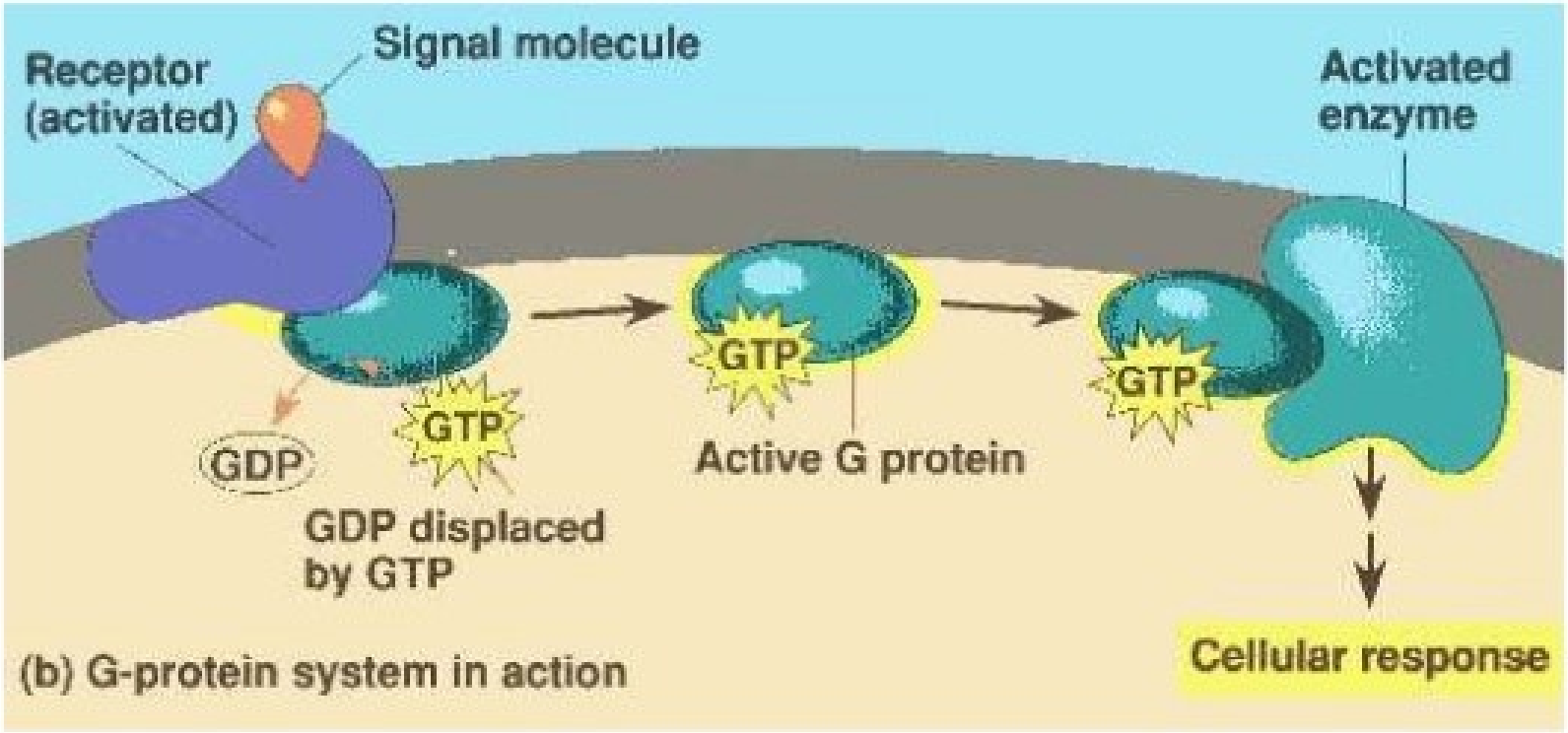
- There are three main types of membrane receptors

  1. G-protein-linked

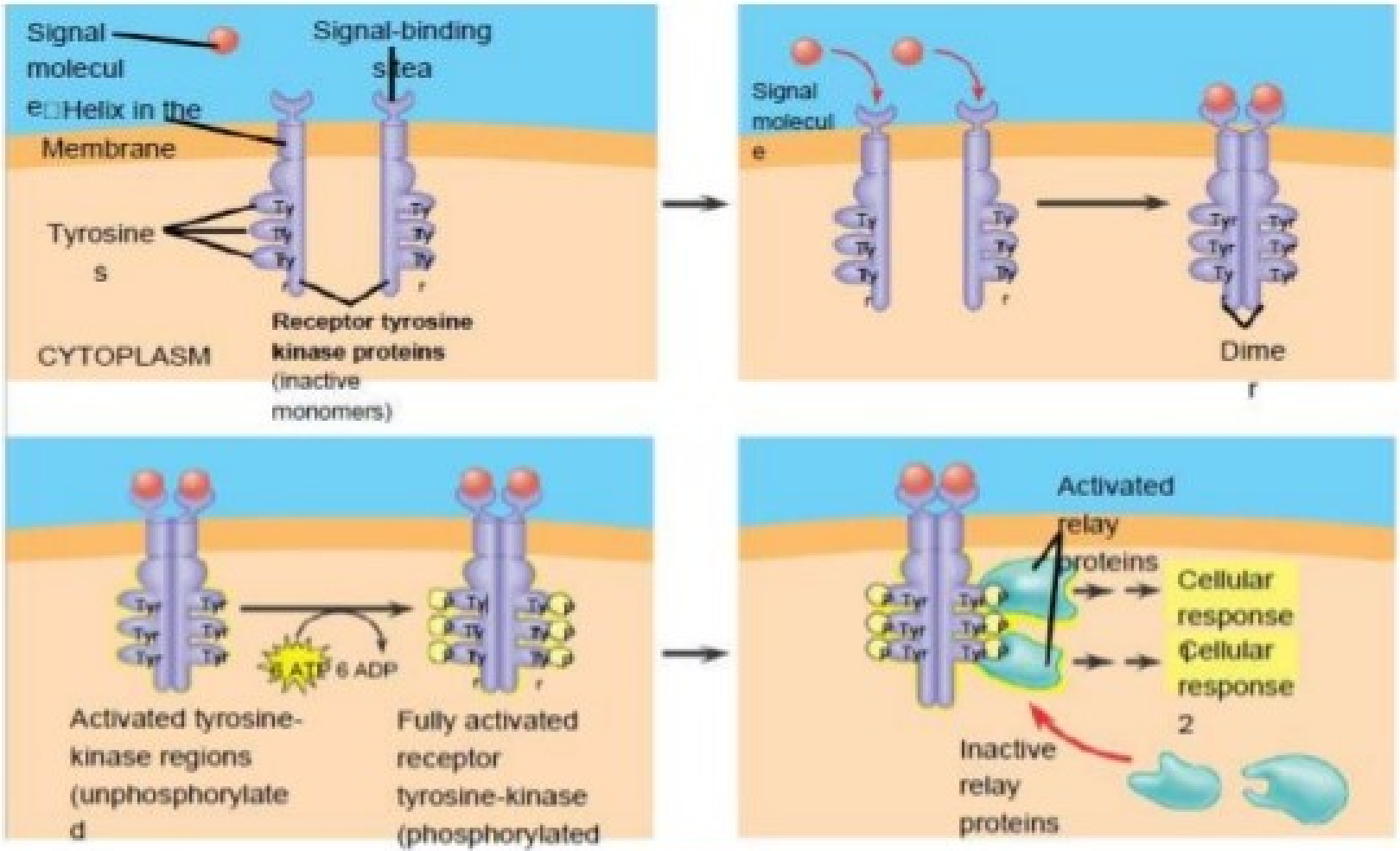
  2. Tyrosine kinases

  3. Ion channel

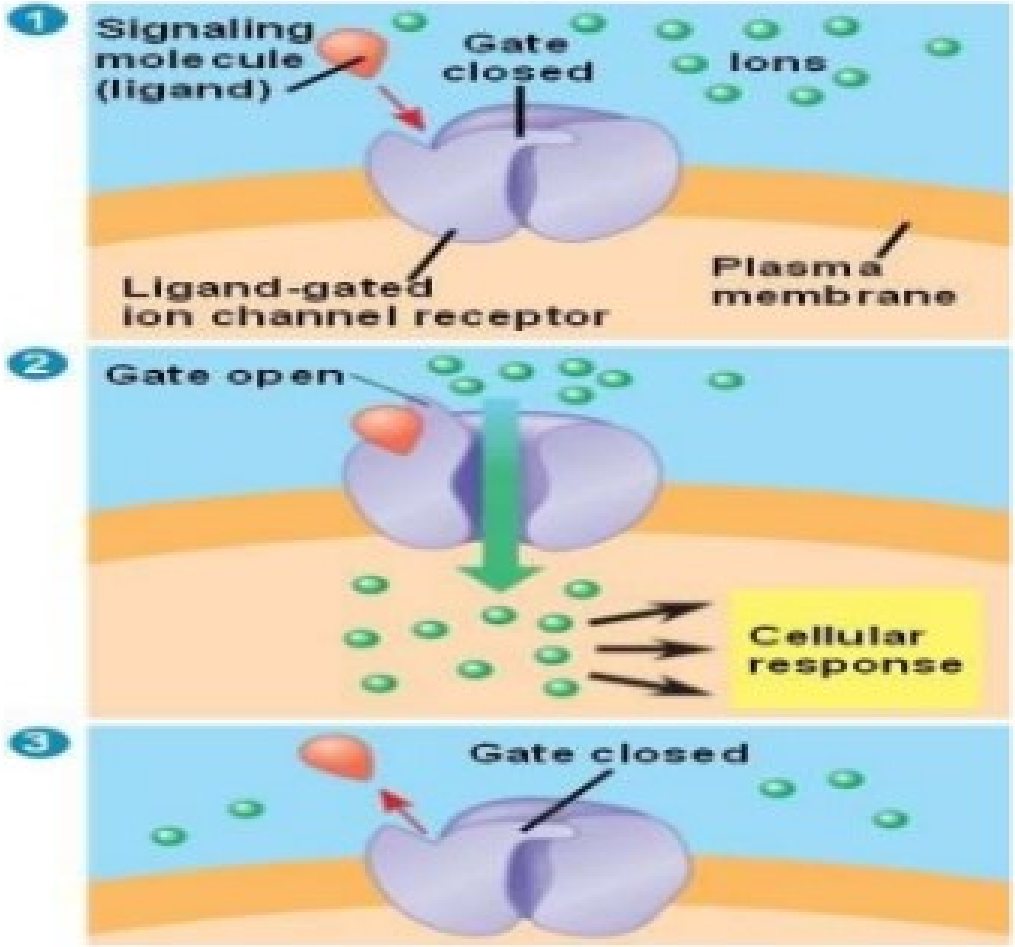
G- protein –linked receptors



Receptor tyrosine kinase



Ion Channel Receptors



Transduction

- **CASCADES OF MOLECULAR INTERACTIONS RELAY SIGNALS FROM THE RECEPTORS TO TARGET MOLECULES IN THE CELL**

- The transduction stage of signaling is usually a multi step pathway and these pathways amplify the signal and provide more opportunities for coordination and regulation.
- If some molecules in a pathway transmit a signal to multiple molecules of the next component in the series, the result can be large numbers of activated molecules at the end of the pathway.
- A small number of signal molecules can produce a large cellular response.

Signal Transduction Pathways

- The molecules that relay a signal from receptor to response are mostly proteins.
- Like falling dominoes, the receptor activates another protein, which activates another, and so on, until the protein producing the response is activated.
- At each step, the signal is transduced into a different form, usually a shape change in a protein.

Protein Phosphorylation and Dephosphorylation

- In many pathways, the signal is transmitted by a cascade of protein phosphorylation.
- **Protein kinases** transfer phosphates from ATP to protein, a process called phosphorylation (activation) .
- **Protein phosphatases** remove the phosphates from proteins, a process called dephosphorylation (deactivation) .

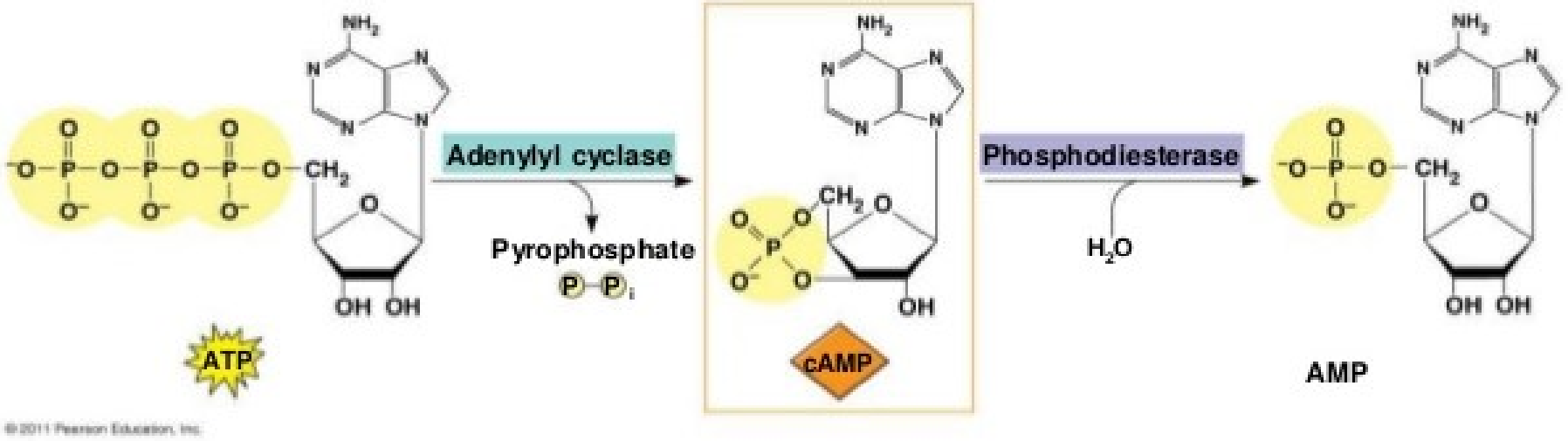
Small Molecules and Ions as Second Messengers

- The extracellular signal molecule (ligand) that binds to the receptor is a pathway's "first messenger".
- **Second messengers** are small, nonprotein, water-soluble molecules or ions that spread throughout a cell by diffusion.
- Second messengers participate in pathways initiated by GPCRs and RTKs.
- Cyclic AMP and calcium ions are common second messengers.

Cyclic AMP

- **Cyclic AMP (cAMP)** is one of the most widely used second messengers
- **cAMP** is made from **ATP** by **Adenylyl cyclase**
- **Adenylyl cyclase**, an enzyme in the plasma membrane, converts ATP to cAMP in response to an extracellular signal

Cyclic AMP – made from ATP



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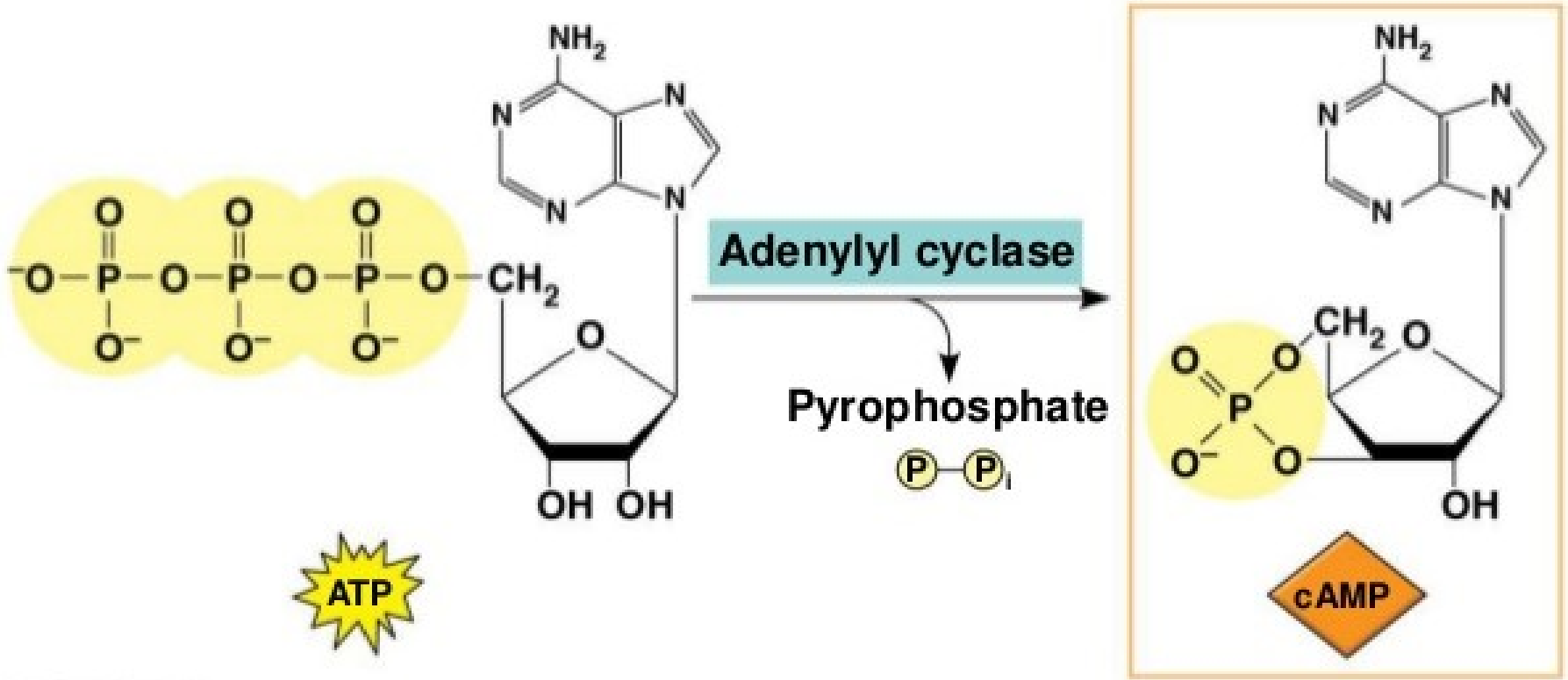

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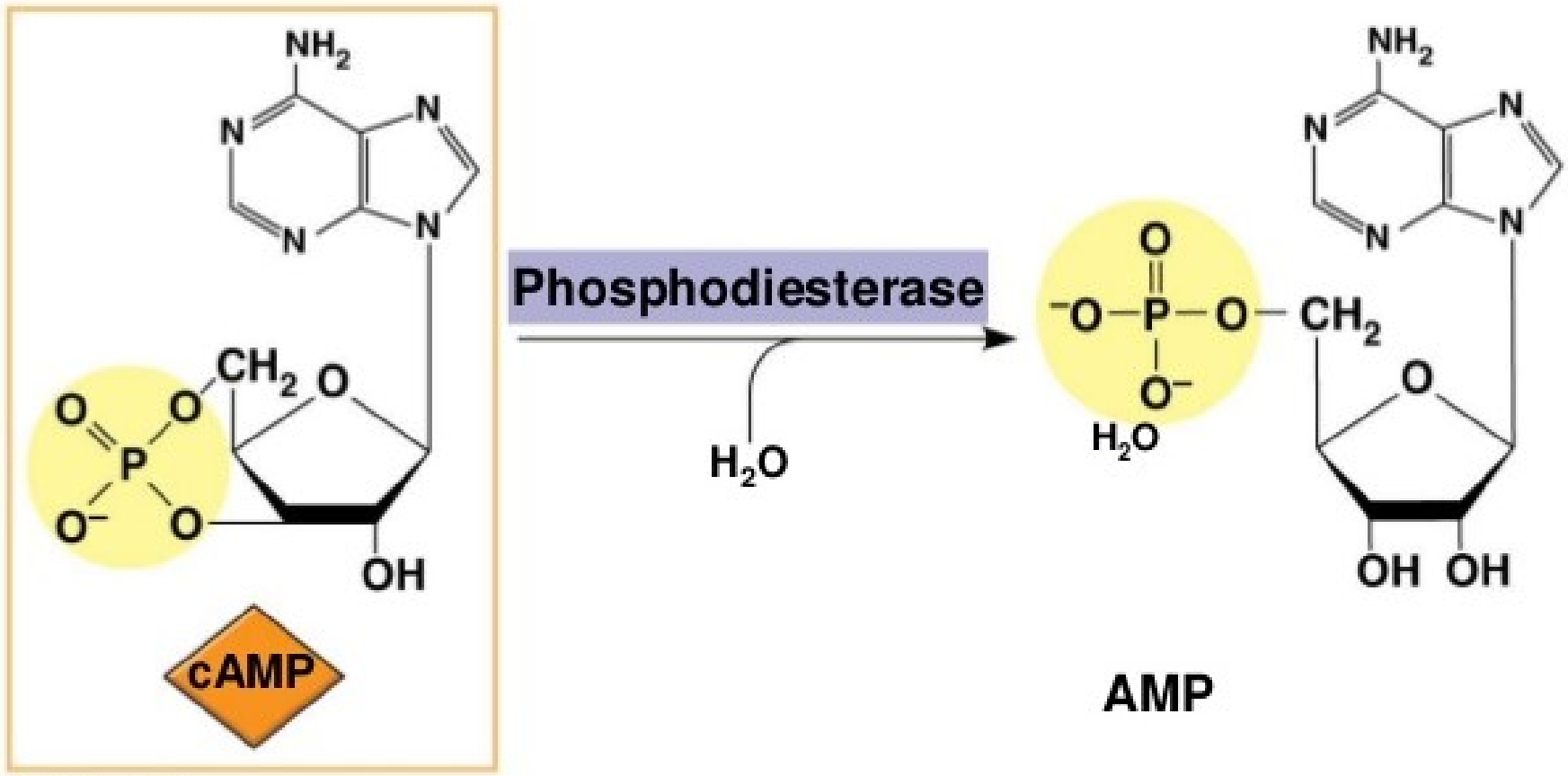

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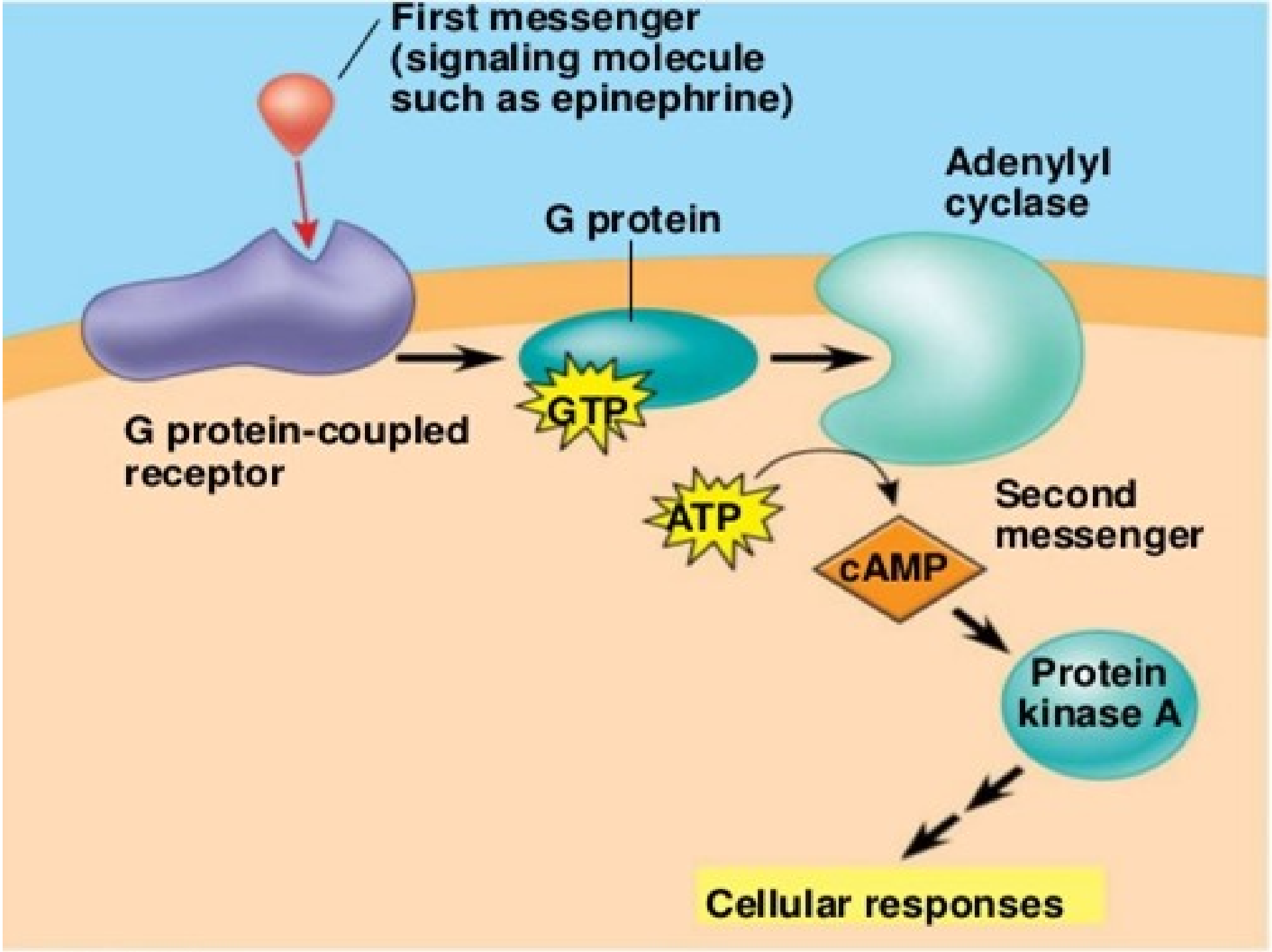
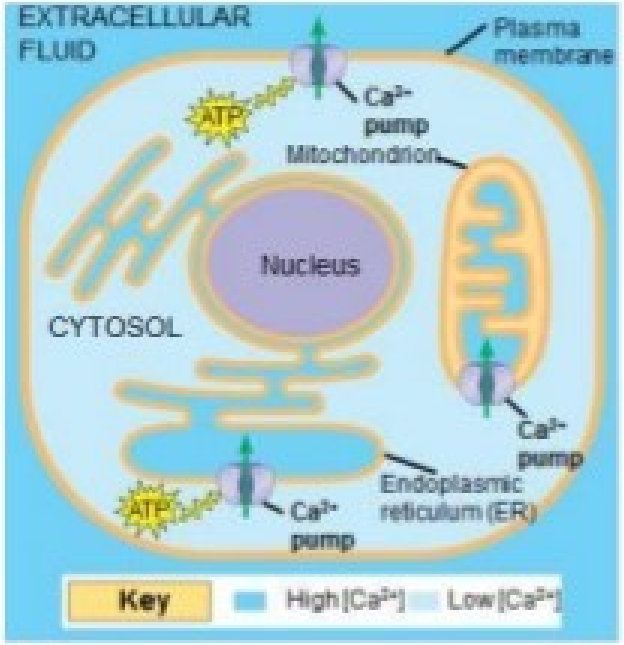
- Many signal molecules trigger formation of cAMP
- Other components of cAMP pathways are G proteins, G protein-coupled receptors, and protein kinases
- cAMP usually activates protein kinase A, which phosphorylates various other proteins
- Further regulation of cell metabolism is provided by G-protein systems that inhibit adenylyl cyclase


First messenger
(signaling molecule
such as epinephrine)
Adenylyl
cyclase
G protein
G protein-coupled
receptor
GTP
ATP
Second
messenger
cAMP
Protein
kinase A
Cellular responses

Calcium ions and Inositol Triphosphate (IP3)

- **Calcium ions (Ca^{2+})** act as a second messenger in many pathways
- Calcium is an important second messenger because cells can regulate its concentration



Inositol triphosphate and diacyglycerol

- The pathways leading to the release of calcium involve diacylglycerol (DAG) and inositol triphosphate (IP3) as second messengers.
- Can trigger an increase in calcium in the cytosol.

Cytoplasmic and Nuclear Responses

- Ultimately, a signal-transduction pathway leads to the regulation of one or more cellular activities.
- The response may occur in the cytoplasm or may involve action in the nucleus.
- Many pathways regulate the activity of enzymes

Other Pathways – Nuclear response

- Many signaling pathways regulate the synthesis of enzymes or other proteins, usually by turning genes on or off in the nucleus.

- The final activated molecule in the signaling pathway may function as a **transcription factor**

Fine-Tuning of the Response

- Multistep pathways have two important benefits:

  I. **Amplifying the signal** (and thus the response)

  II. **Contributing to the specificity of the response**

Signal Amplification

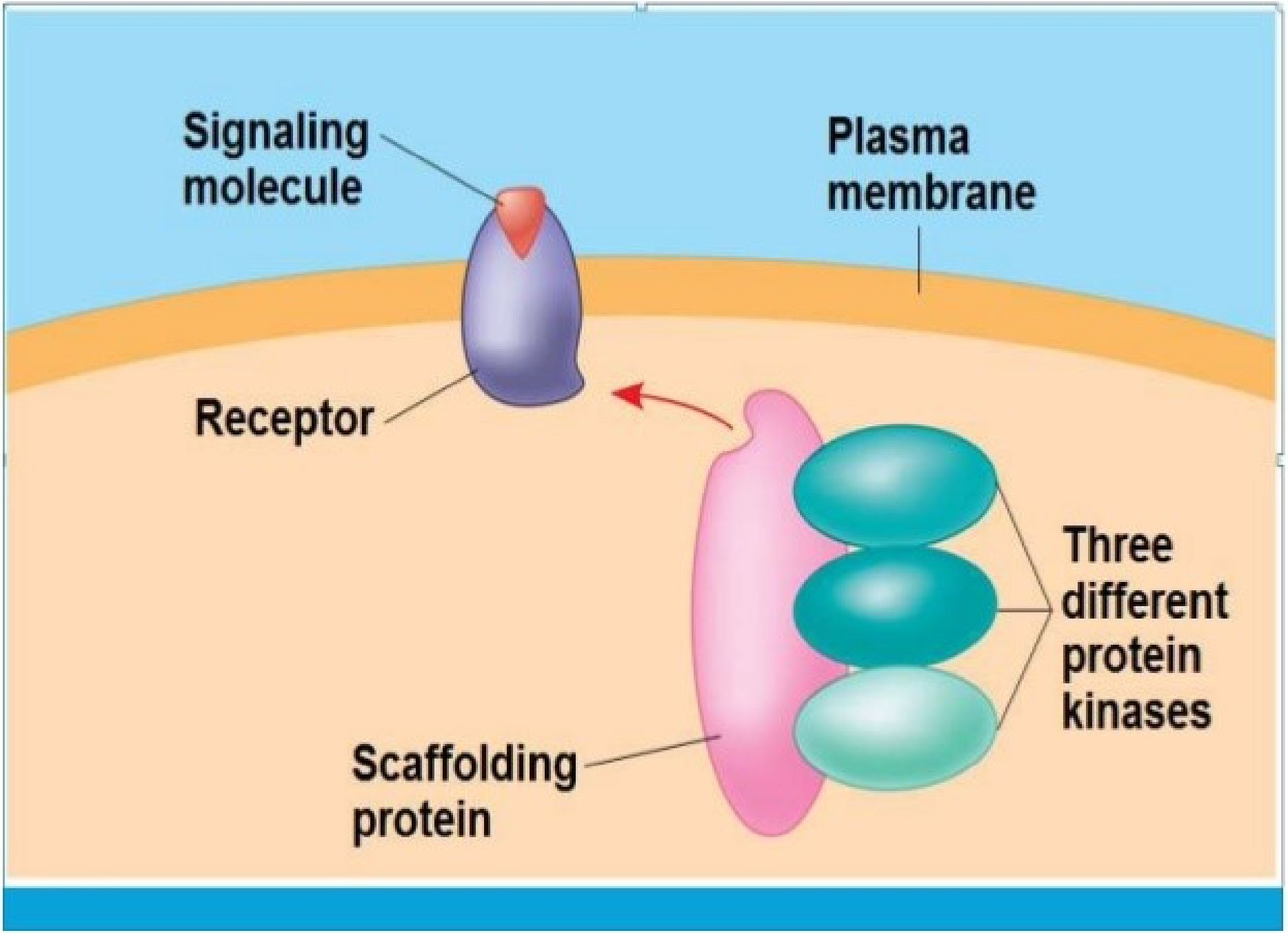
- Enzyme cascades amplify the cell's response to signal.
- At each step, the number of activated products is much greater than in the preceding step

The Specificity of Cell Signaling

- Different kinds of cells have different collections of proteins
- These different proteins allow cells to detect and respond to different signals
- Even the same signal can have different effects in cells with different proteins and pathways
- Pathway branching and "cross-talk" further help the cell coordinate incoming signals.

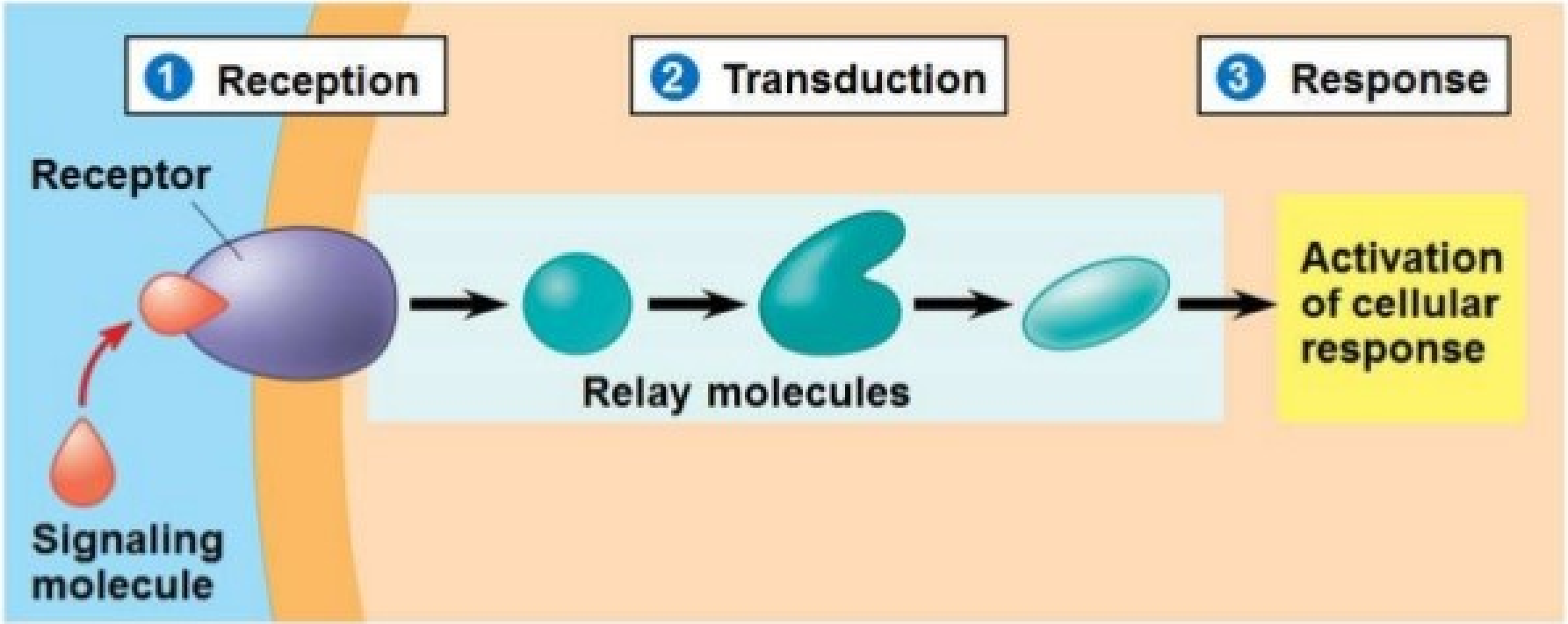
Signaling Efficiency: Scaffolding Proteins and Signaling Complexes

- **Scaffolding proteins** are large relay proteins to which other relay proteins are attached
- Scaffolding proteins can increase the signal transduction efficiency by grouping together different proteins involved in the same pathway
- In some cases, scaffolding proteins may also help activate some of the relay proteins


Signaling molecule
Plasma membrane
Receptor
Three different protein kinases
Scaffolding protein

Termination of Signal

- Signal response is terminated quickly by reversal of ligand binding.
- Inactivation mechanisms are an essential aspect of cell signaling.
- Unbound receptors revert to an inactive state.


1 Reception
2 Transduction
3 Response
Receptor
Signaling molecule
Relay molecules
Activation of cellular response

Thanku very Much