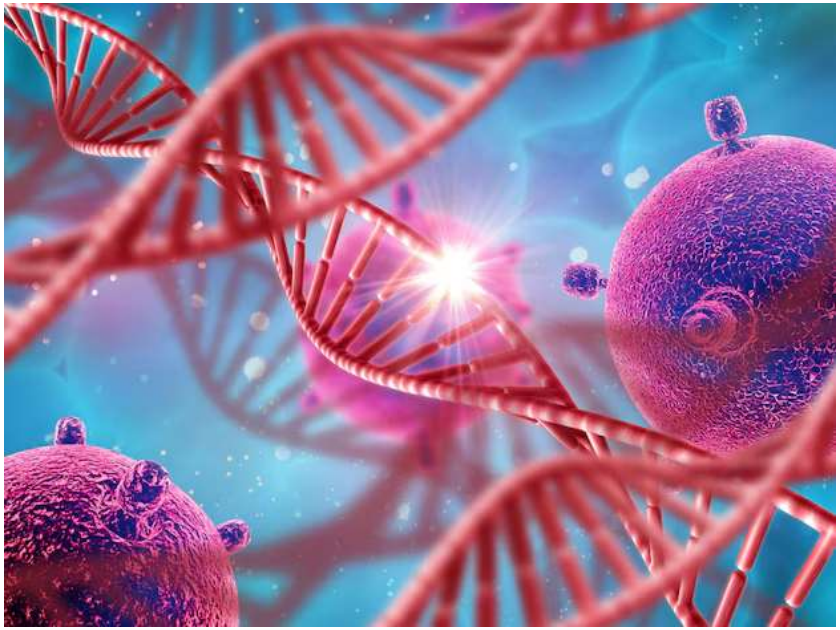
Lecture 10

General Biology & Cytology Course 2301130



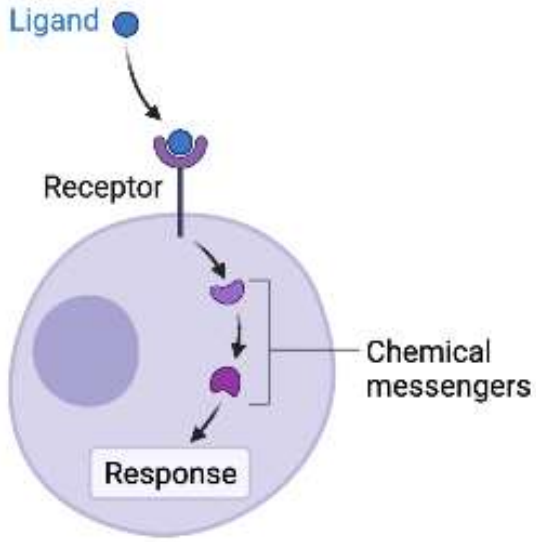
Faculty of Dentistry, Mutah University

Dr. Samer Yousef Alqaraleh

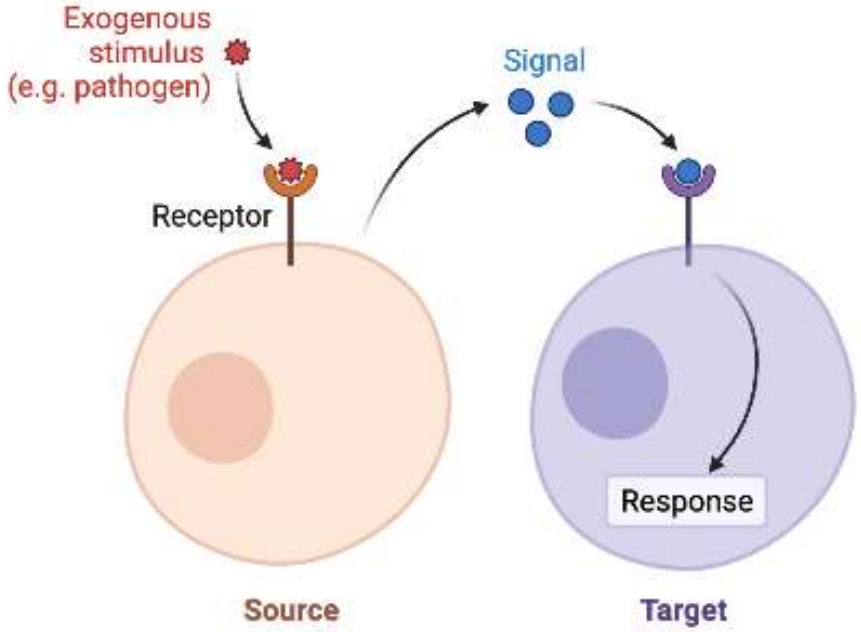
Cell Communication

- Cell-to-cell communication is essential for multicellular organisms.
- Cells typically communicate using chemical signals called **Ligands**. These chemical signals, which are proteins or other molecules produced by a **sending cell**, are often secreted from the cell and released into the extracellular space.

Basic Cell Signaling

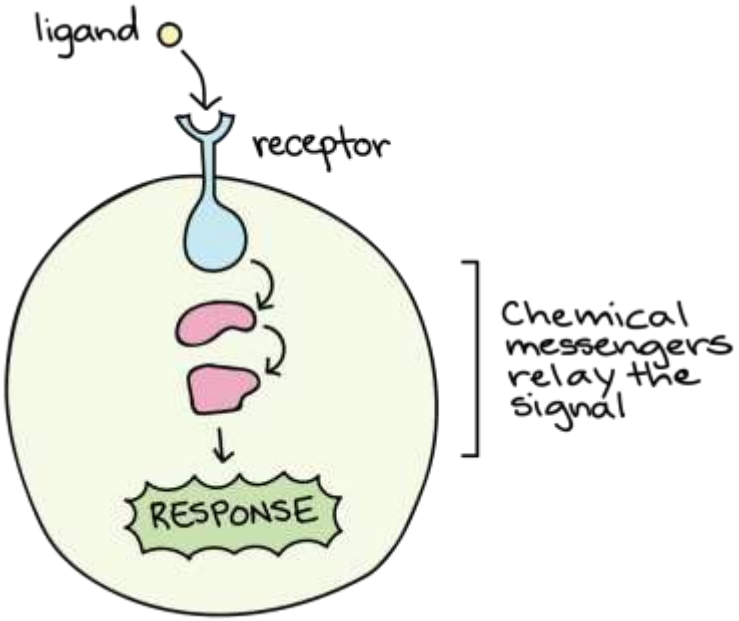


Chemical messengers relay the signal from the ligand and receptor



Cell signaling leads to the production of signals that serve as inputs for other cells

- The message carried by a ligand is often relayed through a chain of chemical messengers inside the cell.
- Ultimately, it leads to a change in the cell, such as alteration in the activity of a gene or even the induction of a whole process, such as cell division.
- Thus, the original **intercellular** (between-cells) signal is converted into an **intracellular** (within-cell) signal that triggers a response.



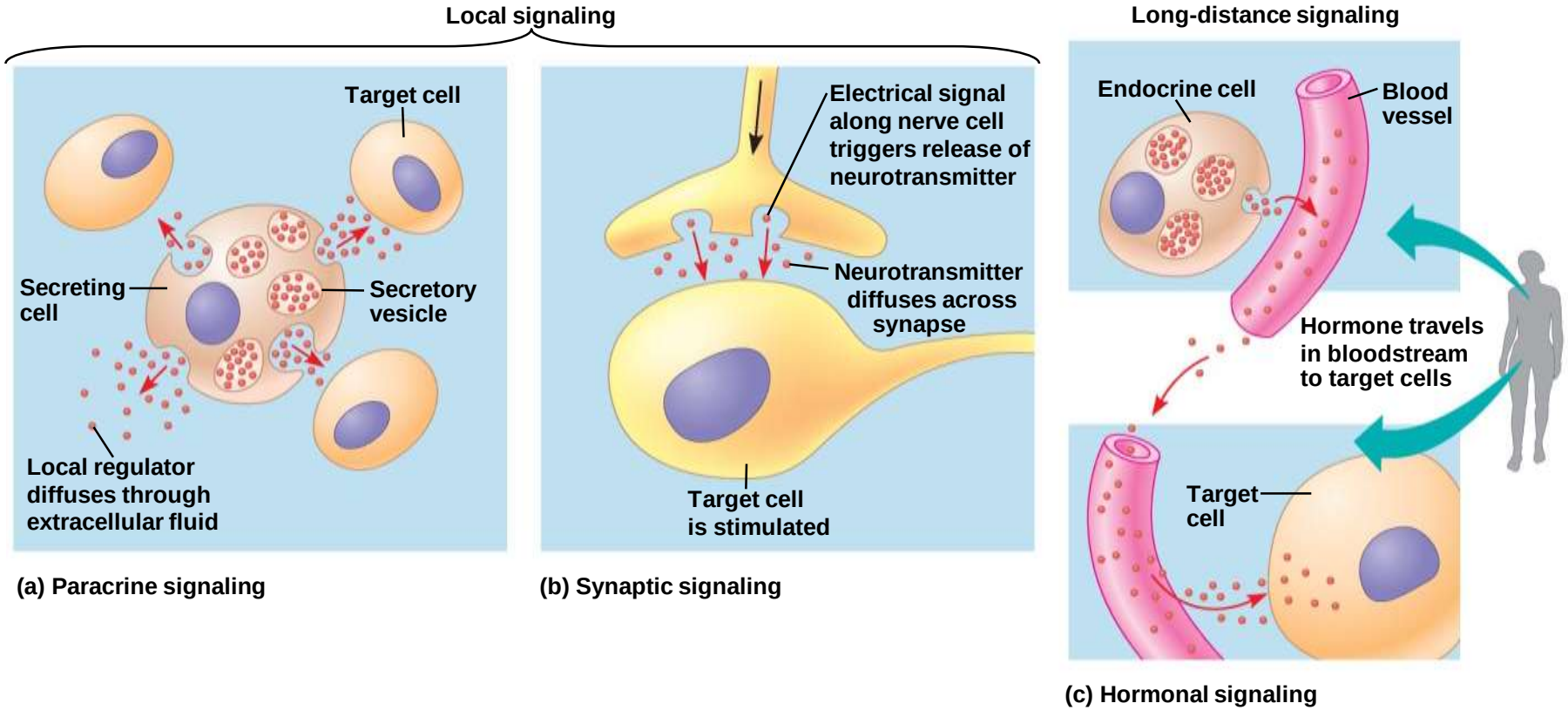
Forms of signaling

- There are **4 basic** categories of chemical signaling found in multicellular organisms:

1. **Paracrine signaling or synaptic.**
2. **Autocrine signaling.**
3. **Endocrine signaling.**
4. **Signaling by direct contact.**

- The main difference between the different categories of signaling is the **distance (Local and Long-Distance Signaling)** that the signal travels through the organism to reach the target cell.

- In many other cases, animal cells communicate using **local regulators**, messenger molecules that travel only short distances
- In long-distance signaling, plants and animals use chemicals called **hormones**.

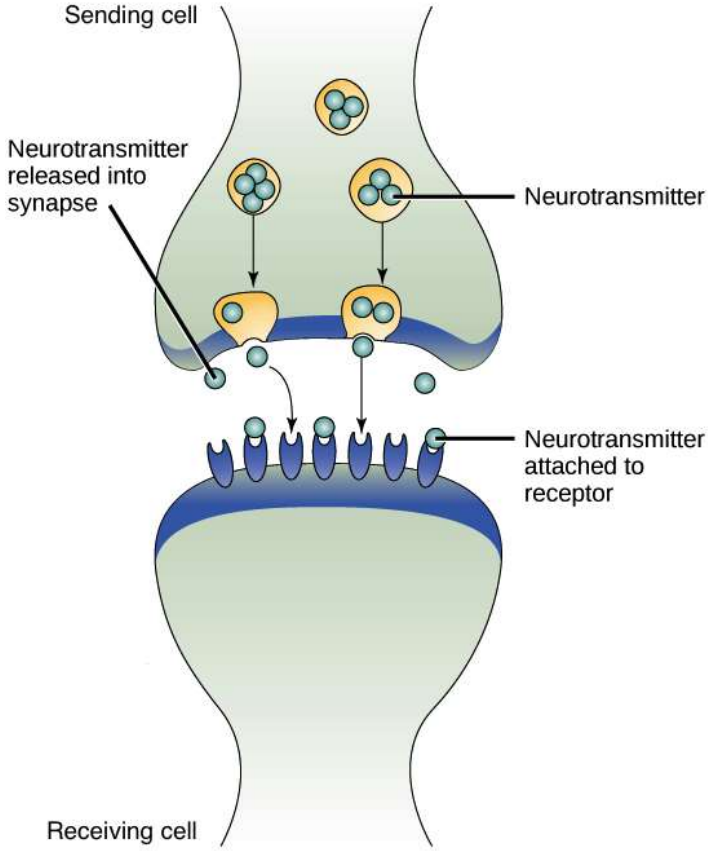


1. Paracrine signaling

- Often, cells that are near one another communicate through the release of chemical messengers (ligands that can diffuse through the space between the cells). This type of signaling, in which cells communicate over relatively short distances, is known as **paracrine signaling**.

- Paracrine signaling allows cells to locally coordinate activities with their neighbors. Although they're used in many different tissues, paracrine signals are especially important during development, when they allow one group of cells to tell a neighboring group of cells what cellular identity to take on.

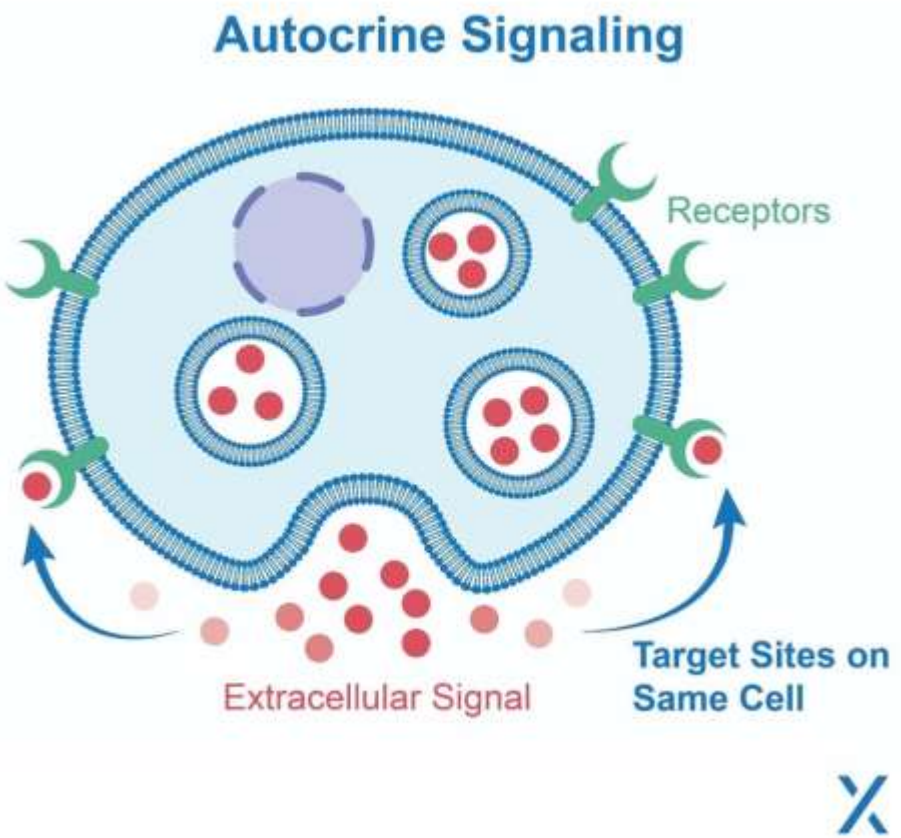
- One unique example of paracrine signaling is **synaptic signaling**, in which nerve cells transmit signals called **neurotransmitters**.
- This process is named for the **synapse**, the junction between two nerve cells where signal transmission occurs.



2. Autocrine signaling

- A cell signals to itself, releasing a ligand that binds to receptors on its own surface.
- This may seem like an odd thing for a cell to do, but autocrine signaling plays an important role in many processes.
- For instance, autocrine signaling is important during development, helping cells take on and reinforce their correct identities.
- From a medical standpoint, autocrine signaling is important in **cancer** and is thought to play a key role in **metastasis**.
- In many cases, a signal may have both autocrine and paracrine effects, binding to the sending cell as well as other similar cells in the area.

For example, in the majority of breast cancer cases, cancer cells express progesterone receptors on their cell surface. These receptors bind to progesterone as signal, released from the cancer cells themselves, thus, acting in an autocrine manner to stimulate cell proliferation



Progesterone: is primarily known as the pregnancy hormone in females, and most of its function relates to maintaining pregnancy.

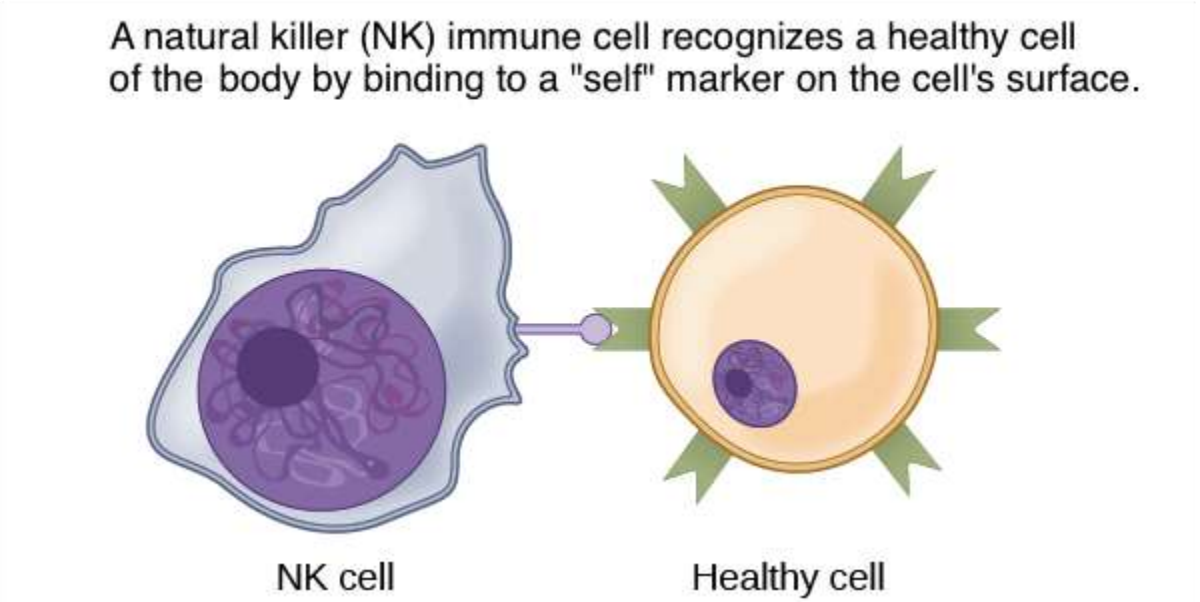
3. Endocrine signaling

- When cells need to transmit signals over long distances, they often use the circulatory system.
- Signals of endocrine are known as **hormones**.
- Each endocrine gland releases one or more types of hormones, many of which are master regulators of development and physiology.
- For example, the pituitary releases **growth hormone** (**GH**), which promotes growth, particularly of the skeleton and cartilage.
- Like most hormones, GH affects many different types of cells throughout the body.
- However, cartilage cells provide one example of how GH functions: it binds to receptors on the surface of these cells and encourages them to divide.

4. Signaling by direct contact.

- Direct signaling (also called juxtacrine signaling) involves communication between cells that are in direct contact with each other.
- This communication is often **mediated by gap junctions** in animal cells and plasmodesmata in plant cells.
- These water-filled channels allow small signaling molecules, called **intracellular mediators**, to diffuse between the two cells.
- Small molecules and ions are able to move between cells, but large molecules like proteins and DNA can’t.
- This allows a group of cells to coordinate their response to a signal that only one of them may have received.

- In another form of direct signaling, two cells may bind to one another because they carry complementary proteins on their surfaces.e.g. MHC1, MHC2
- When the proteins bind to one another, this interaction changes the shape of one or both proteins, transmitting a signal.
- This kind of signaling is especially important in the immune system, where immune cells use cell-surface markers to recognize “self” cells (the body's own cells) and cells infected by pathogens



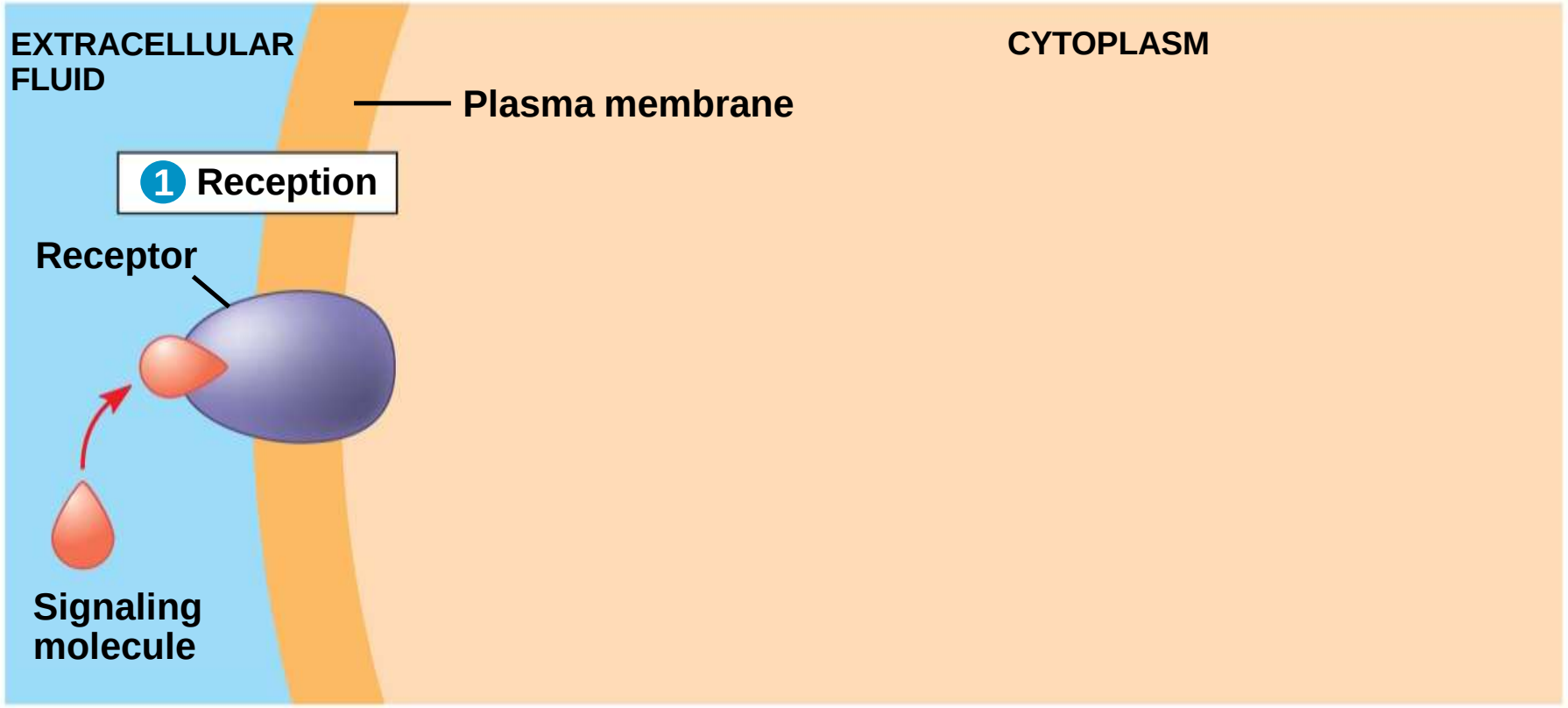
Signaling Pathways and Steps

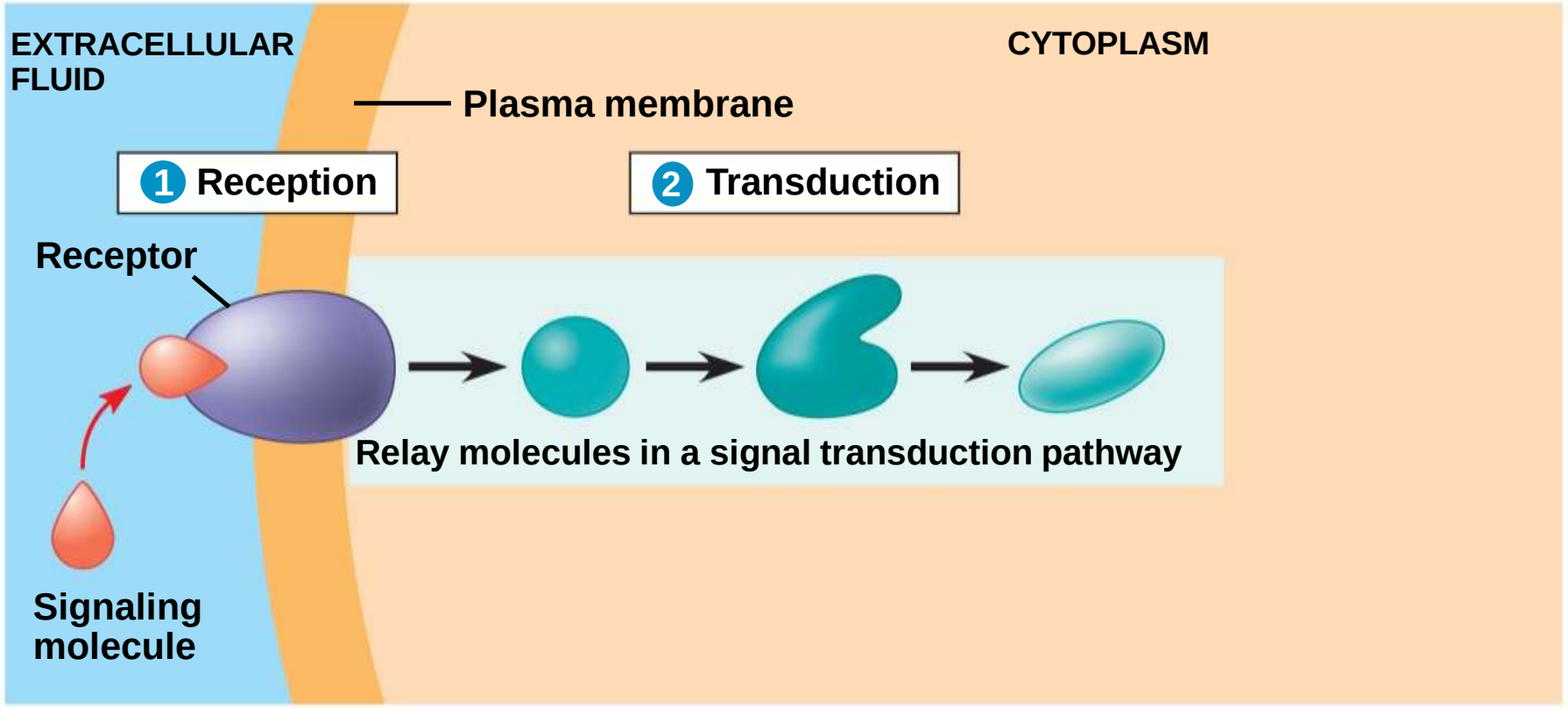
- Sutherland suggested that cells receiving signals went through three processes:

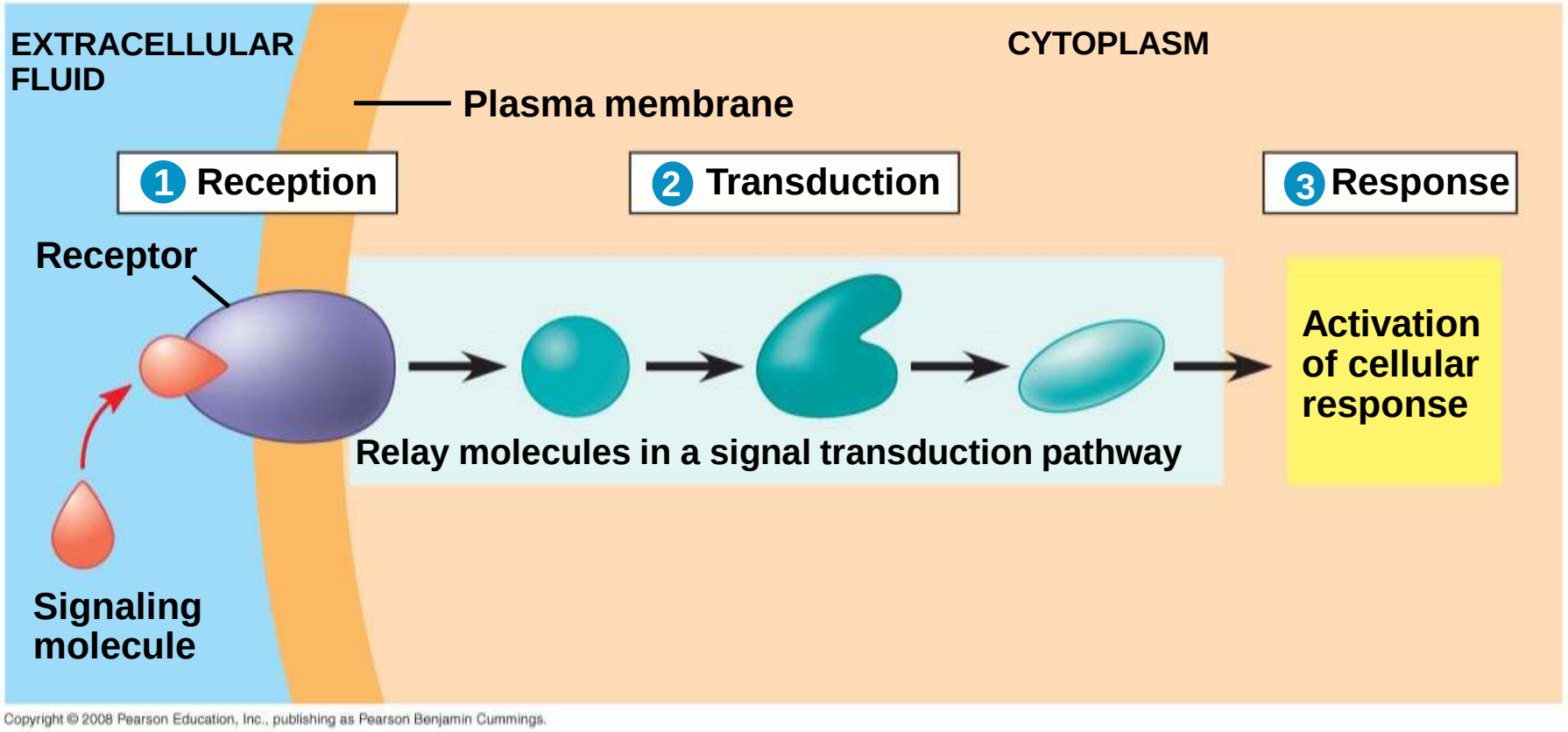
  1- Reception

  2- Transduction

  3- Response





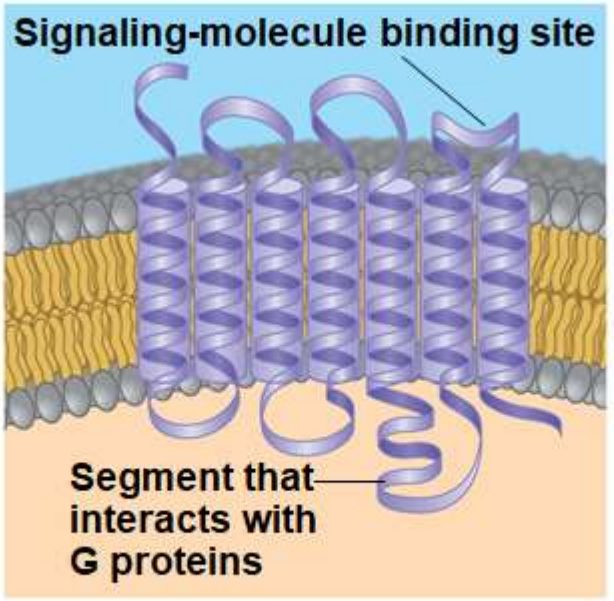


1- Reception

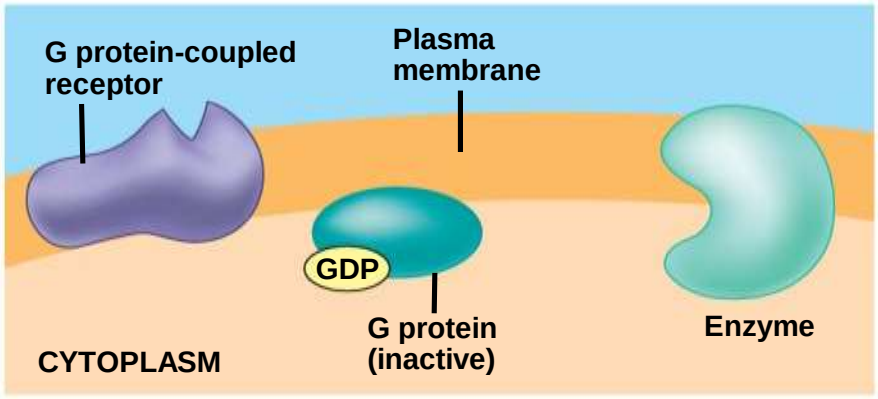
- The binding between a signal molecule (**ligand**) and receptor is highly specific
- A shape change in a receptor is often the initial transduction of the signal
- Most signal receptors are plasma membrane proteins.
- Most water-soluble signal molecules bind to specific sites on receptor proteins in the plasma membrane
- There are three main types of membrane receptors:
  - G protein-coupled receptors
  - Receptor tyrosine kinases
  - Ion channel receptors

- A **G protein-coupled receptor** is a plasma membrane receptor that works with the help of a **G protein**
- The G protein acts as an on/off switch: If GDP is bound to the G protein, the G protein is inactive

Fig. 11-7a



G protein-coupled receptor



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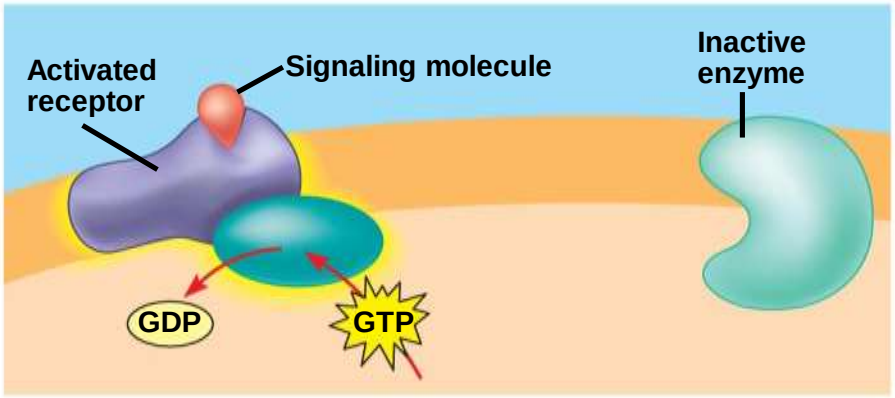

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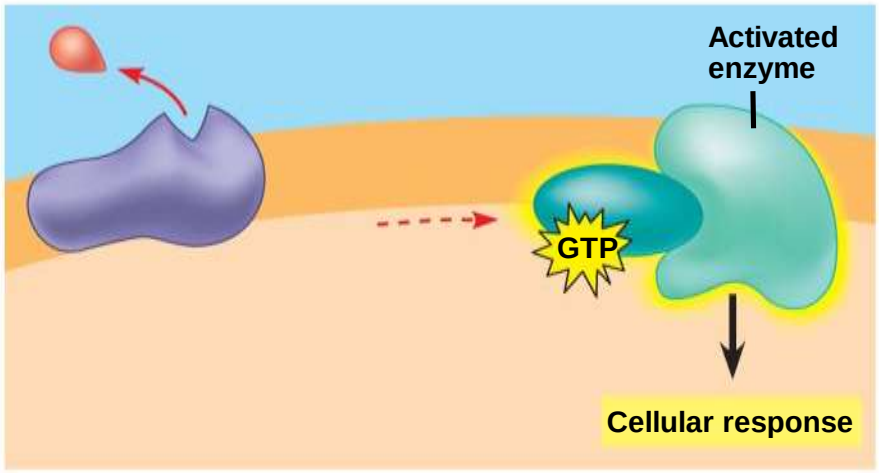

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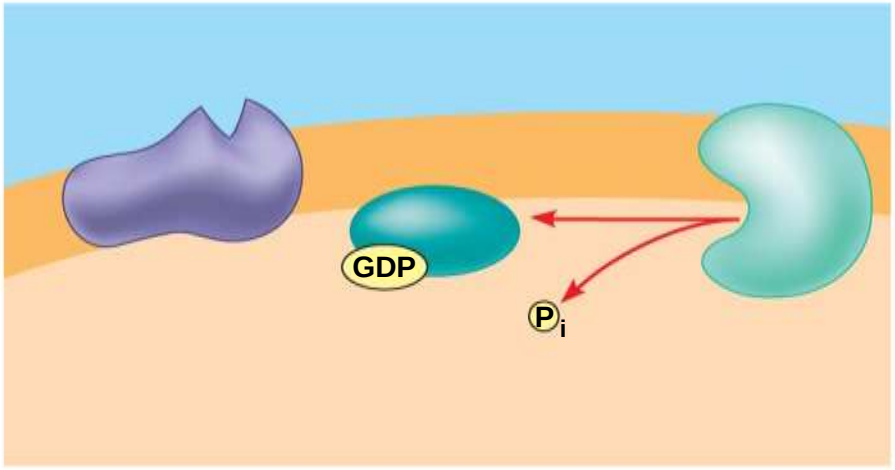

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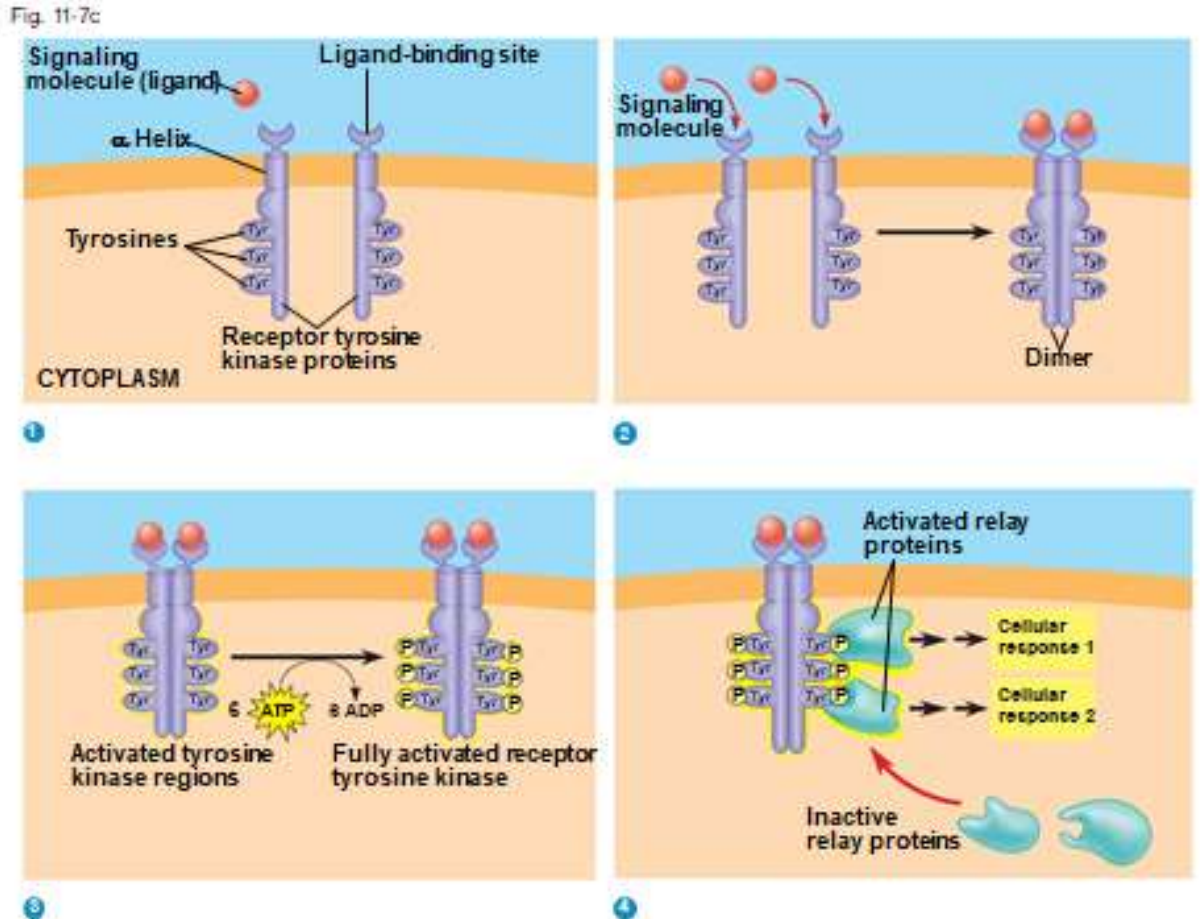
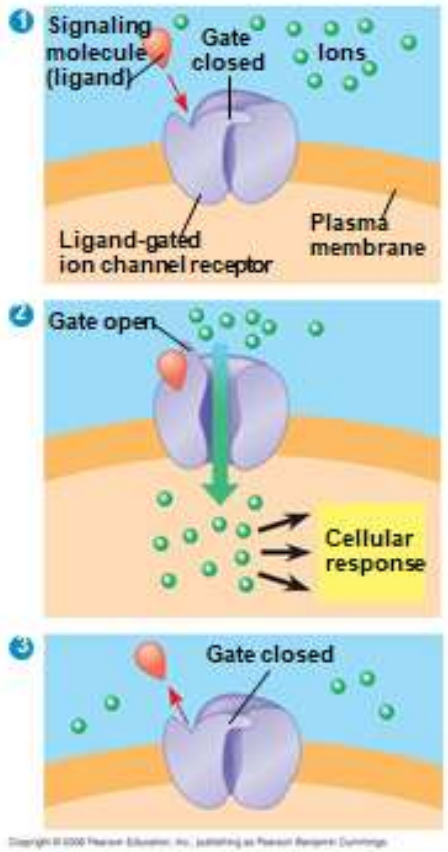
- **Receptor tyrosine kinases** are membrane receptors that attach phosphates to tyrosines
- A receptor tyrosine kinase can trigger multiple signal transduction pathways at once

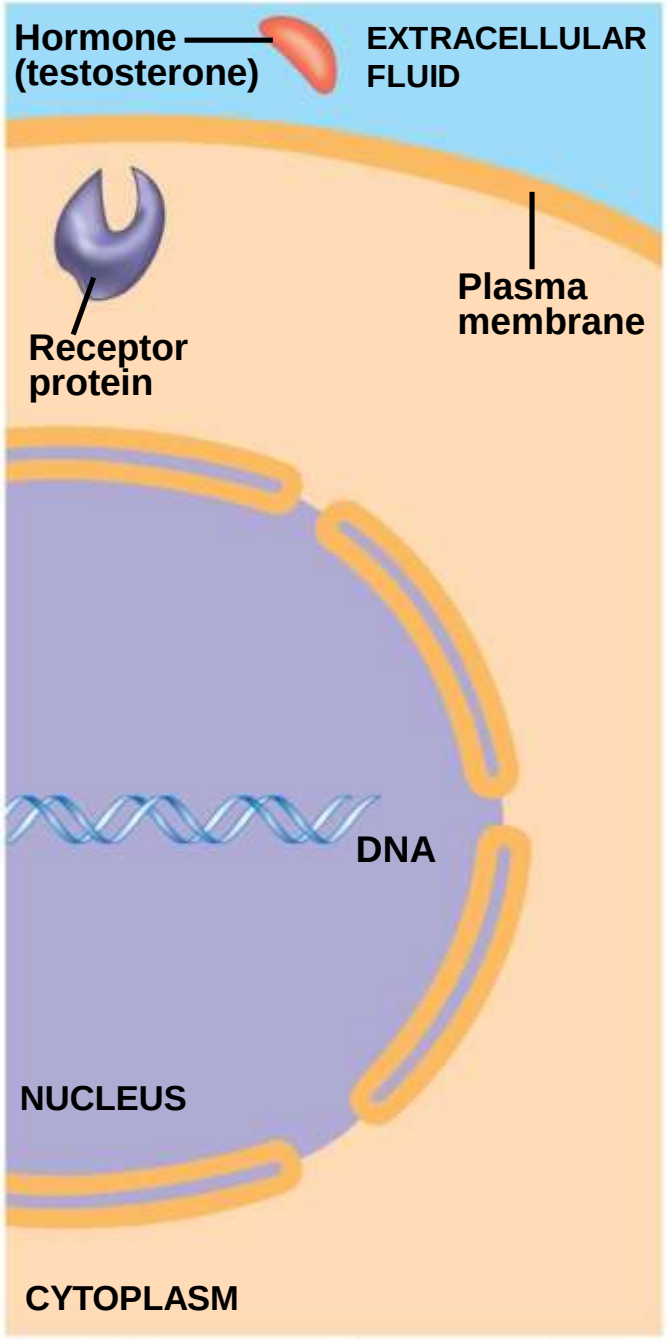


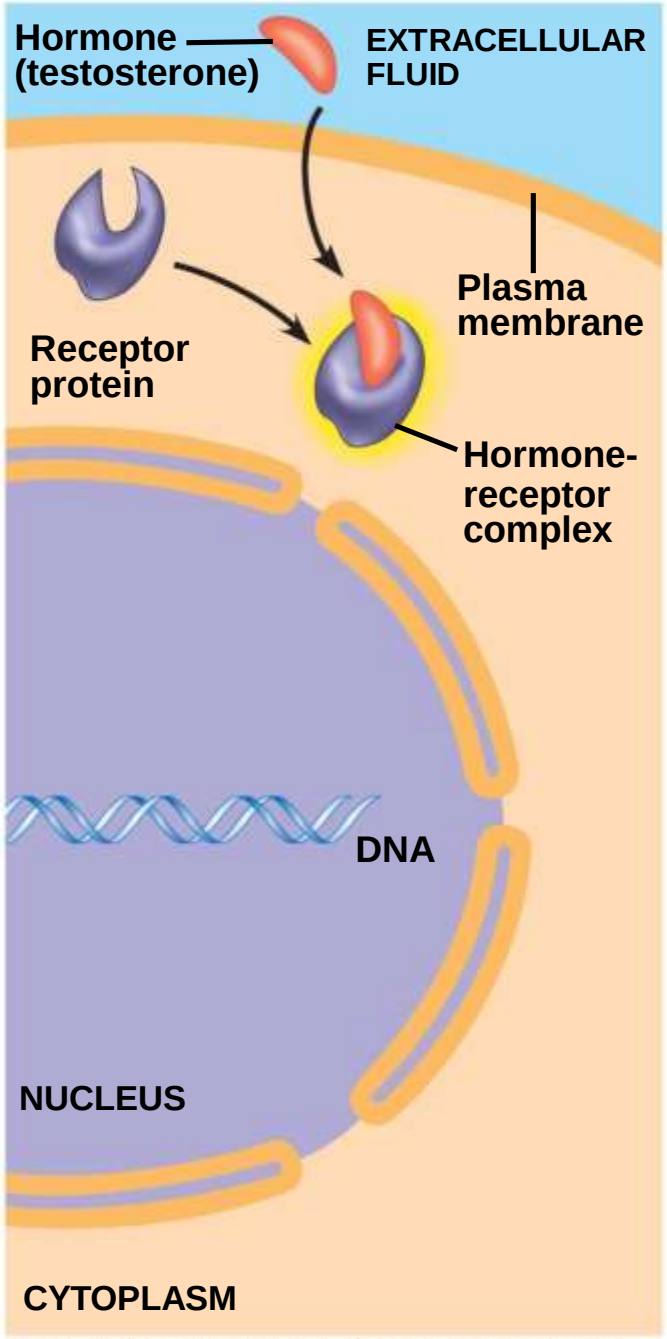
- A **ligand-gated ion channel** receptor acts as a gate when the receptor changes shape
- When a signal molecule binds as a ligand to the receptor, the gate allows specific ions, such as Na^+ or Ca^{2+}, through a channel in the receptor.

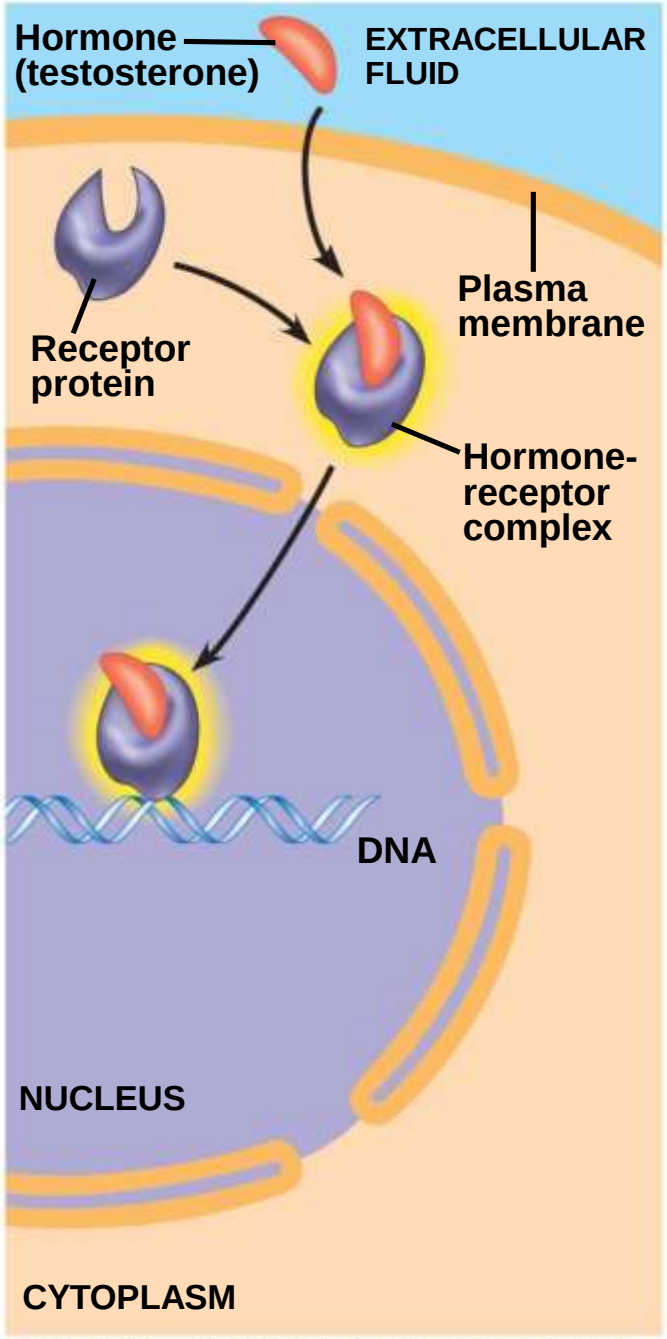


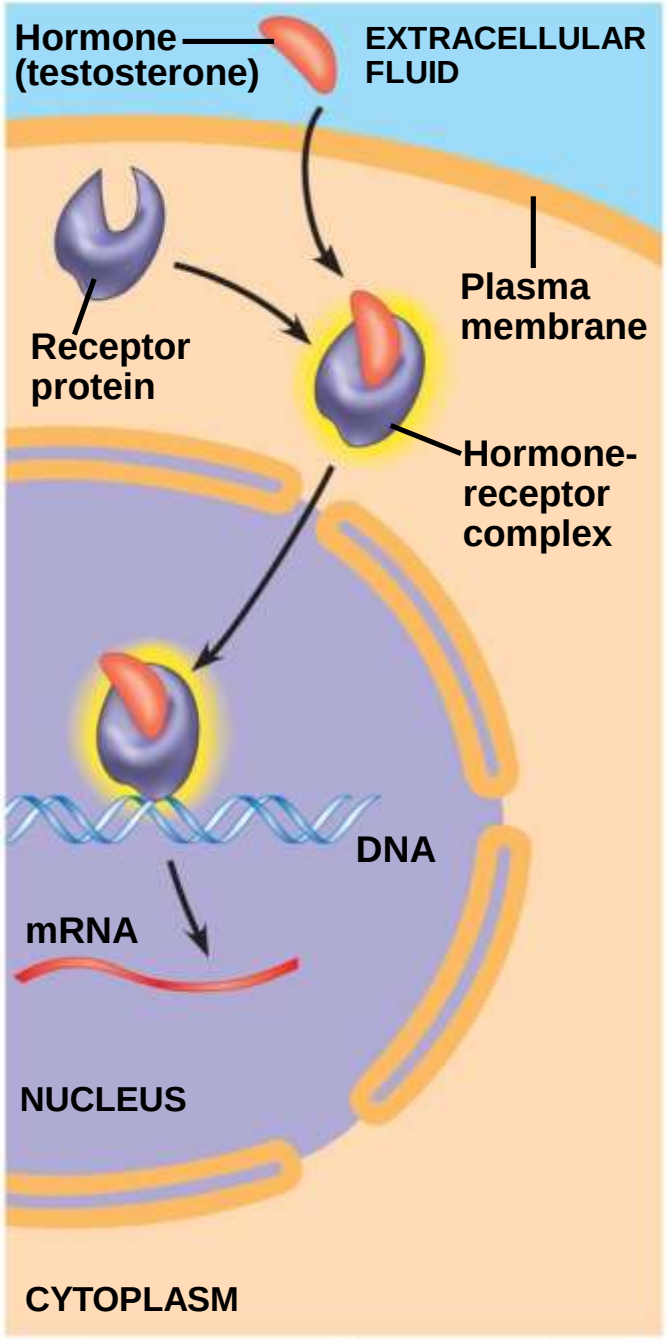
Intracellular Receptors

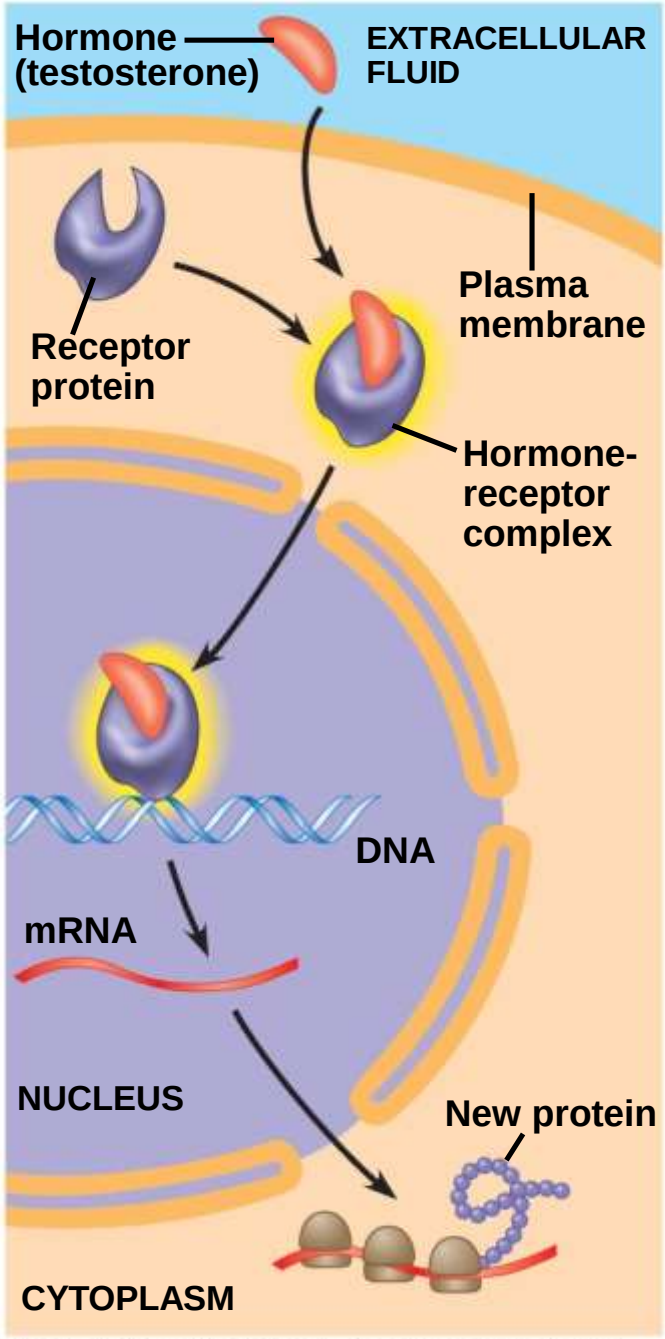
- Some receptor proteins are intracellular, found in the cytosol or nucleus of target cells
- Small or hydrophobic chemical messengers can readily cross the membrane and activate receptors
- Examples of hydrophobic messengers are the **steroid** and **thyroid hormones** of animals
- An activated hormone-receptor complex can act as a transcription factor, turning on specific genes











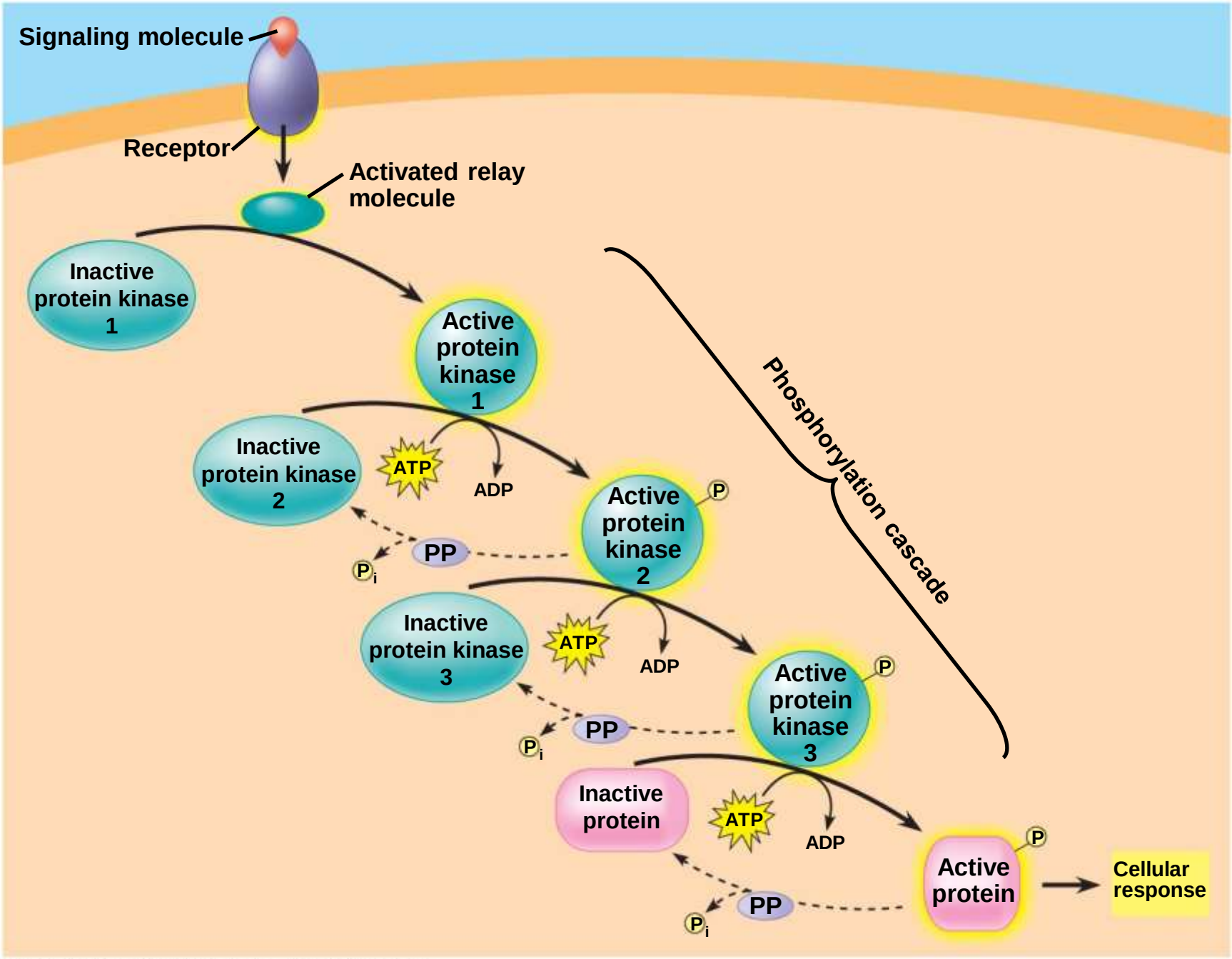
2- Transduction

- This step is necessary only for hydrophilic ligands (Peptide hormones such as **oxytocin** and **GH**) that must bind extracellular receptors because they cannot cross the plasma membrane.
- Once a hormone binds to the extracellular portion of the cell-surface receptor, the intracellular portion of the receptor changes shape, resulting in activation of a chain of events that is called a **signaling pathway** or **signaling cascade**.

Signal Transduction Pathways

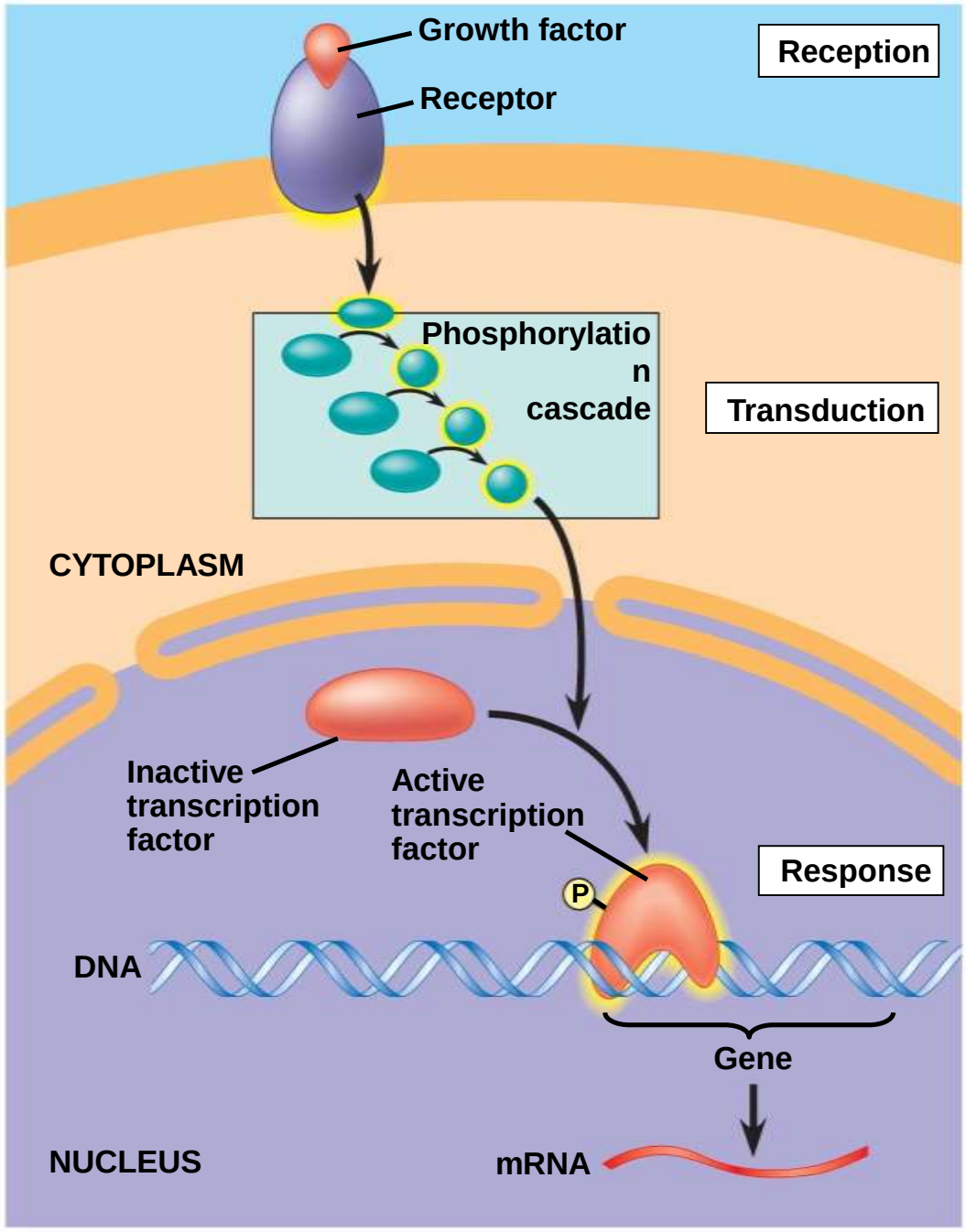
- The events in the **cascade** occur in a defined series of events. Many different enzymes are activated by different specific receptors, but in general this activated enzyme then activates other proteins which carry the signal into the cell to elicit a response.
- Like **falling dominoes**, the receptor activates another protein, which activates another, and so on, until the protein producing the response is activated

- Pathways activated by cell surface receptors might include either:
  - Synthesis of **second messengers** (non-protein signaling molecules) such as calcium or cyclic AMP which propagate throughout the cell to spread the signal, or
  - Initiation of a **phosphorylation cascade** where a series of proteins are activated by having a phosphate group added to them, which changes their activity.
- **Protein kinases** transfer phosphates from ATP to protein, a process called phosphorylation



3- Response and Feedback Loops:

- The last stage of a signaling pathway is the **signal response**.
- There are many different types of cellular responses to a hormone, including changes in gene expression, changes in cell metabolism, and/or changes in cell growth and division.
- These responses are often carried out in one of two types of **feedback loops**:

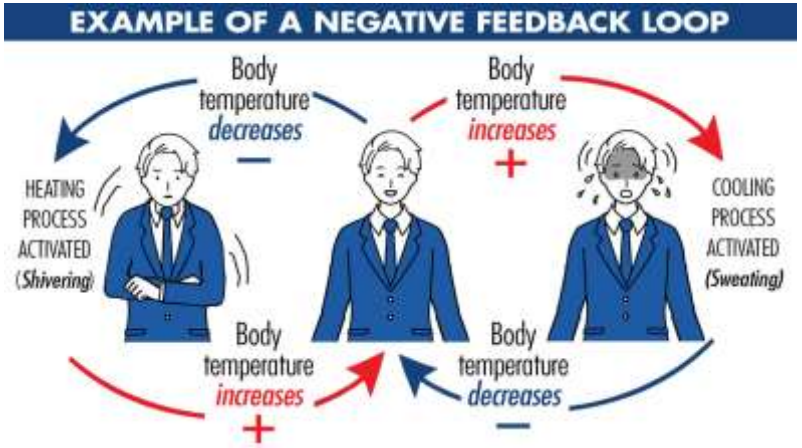


• **Positive feedback loop** occurs when the response to a hormone causes the original signal to be *amplified* or *increase*. The signal in this scenario has *increased* in a positive feedback loop. Example:

- **Oxytocin** from the posterior pituitary gland during labor

• **Negative feedback loop** occurs when the response to a hormone causes the original signal to be *decreased*. The signal in this scenario has *decreased* in a negative feedback loop.

•Example:



The Specificity of Cell Signaling and Coordination of the Response

- Different kinds of cells have different collections of proteins (Receptors).
- 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

Fine Tuning 2: The Specificity of Cell Signaling and Coordination of the Response