CELL COMMUNICATION

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- Cell-to-cell communication is essential for multicellular organisms

- A **signal transduction pathway** is a series of steps by which a signal on a cell's surface is converted into a specific cellular response

TYPES OF CHEMICAL SIGNALING

- Chemical signaling between cells is one of the most important ways that activities of tissues and organs are coordinated.
- The nervous system is the other major coordinating system in animals, but even here chemical signaling is used between adjacent neurons.

Chemical signnal (protein and peptide molecule):

EGF : Epidermal Growth Factor

PDGF:Platelet Derived Growth Factor

FGF : Fibroblast Growth Factor

TNF : Tumor Necrosis Factor

TGFa : Transforming Growth Factor alpha

TGFβ : Transforming Growth Factor beta

G-CSF : granulocyte Colony Stimulating Factor

- M-CSF : Monocyte Colony Stimulating Factor
- IFN-α/β : Interferon α/β
- IFN-γ : Interferon γ
- IL : Interleukin 1 - 12
- Eryp : Erythropoietin
- Ins : Insulin

- Chemical signal (non Peptide molecule/ Neurotransmiter)
- SER : Serotonin
- MEL : Melatonin
- DOP : Dopamin
- NEP : Nor Epinefrin
- EPI : Epinefrin

- ACH : Acetilkolin
- GLU : Asam Glutamat
- GABA: Gama Amino Butyric Acid

- Chemical signal (Steroid)
- EST : estrogen
- TES : Testosteron
- TYX : Tyroksin
- RA : Asam retinoat

Jenis Protein	Gen Struktural
Penyandi faktor pertumbuhan	Int-2, hst, sis
Penyandi reseptor faktor pertumbuhan	Ret, erb, Kit, Fms, Ros, Neu, Met, Trk
Penyandi molekul transduktor membran	Yes, Fgr,Src, Lck,, H-Ras, Ki-Ras, N=Ras
Peyandi molekul transduktor sitosolik	Mos. Pim. Raf

Penyandi faktor transkripsi	Myc, N-Myc, L-Myc. Fos, jun
Penyandi protein pengatur daur sel	PRAD 1

MODES OF CELL-CELL SIGNALING

1. Direct cell-cell or cell-matrix

2. Indirect: Secreted molecules.

A. E The signaling molecules are hormones secreted by endocrine cells and carried through the circulation system to act on target cells at distant body sites.

B. Pa The signaling molecules released by one cell act on neighboring target cells (neurotransmitters).

C. A Cells respond to signaling molecules that they themselves produce (response of the immune system to foreign antigens, and cancer cells).

Autocrine signals
act on the same cell that secretes them.

Paracrine signals
diffuse locally and act on neighboring cells.

Endocrine signals
are hormones carried between cells by blood or other body fluids.

Neural signals
diffuse a short distance between neurons.

Neuroendocrine signals
are released from neurons but act on distant cells.

Pheromones
are released into the environment and act on a different individual.

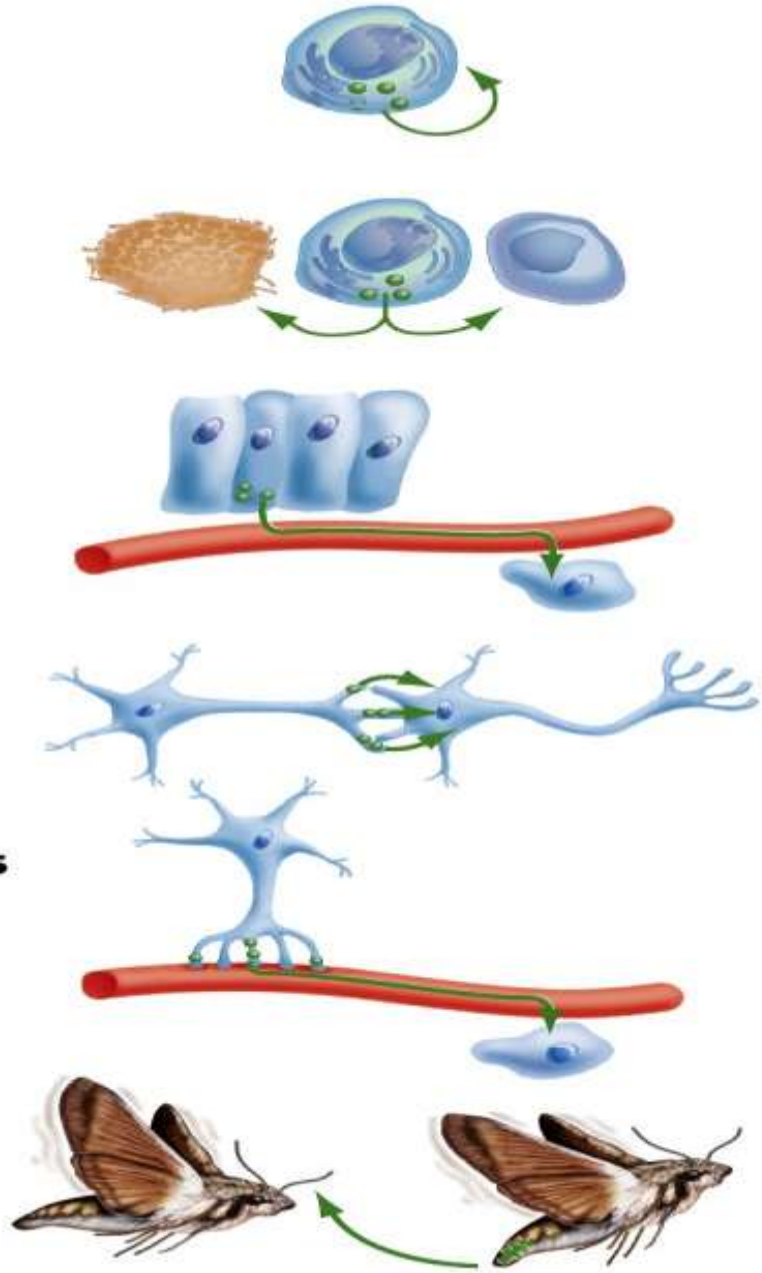
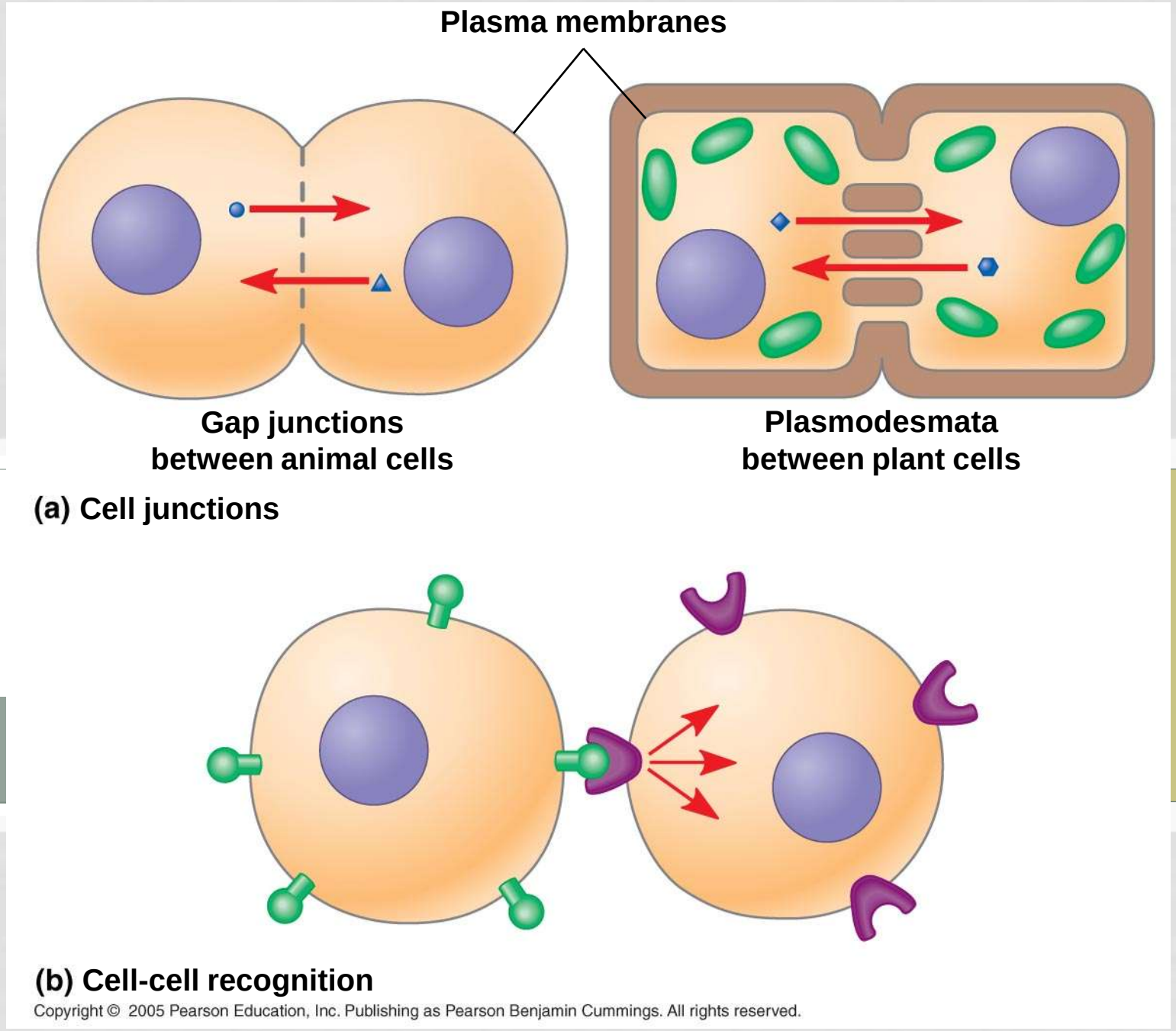
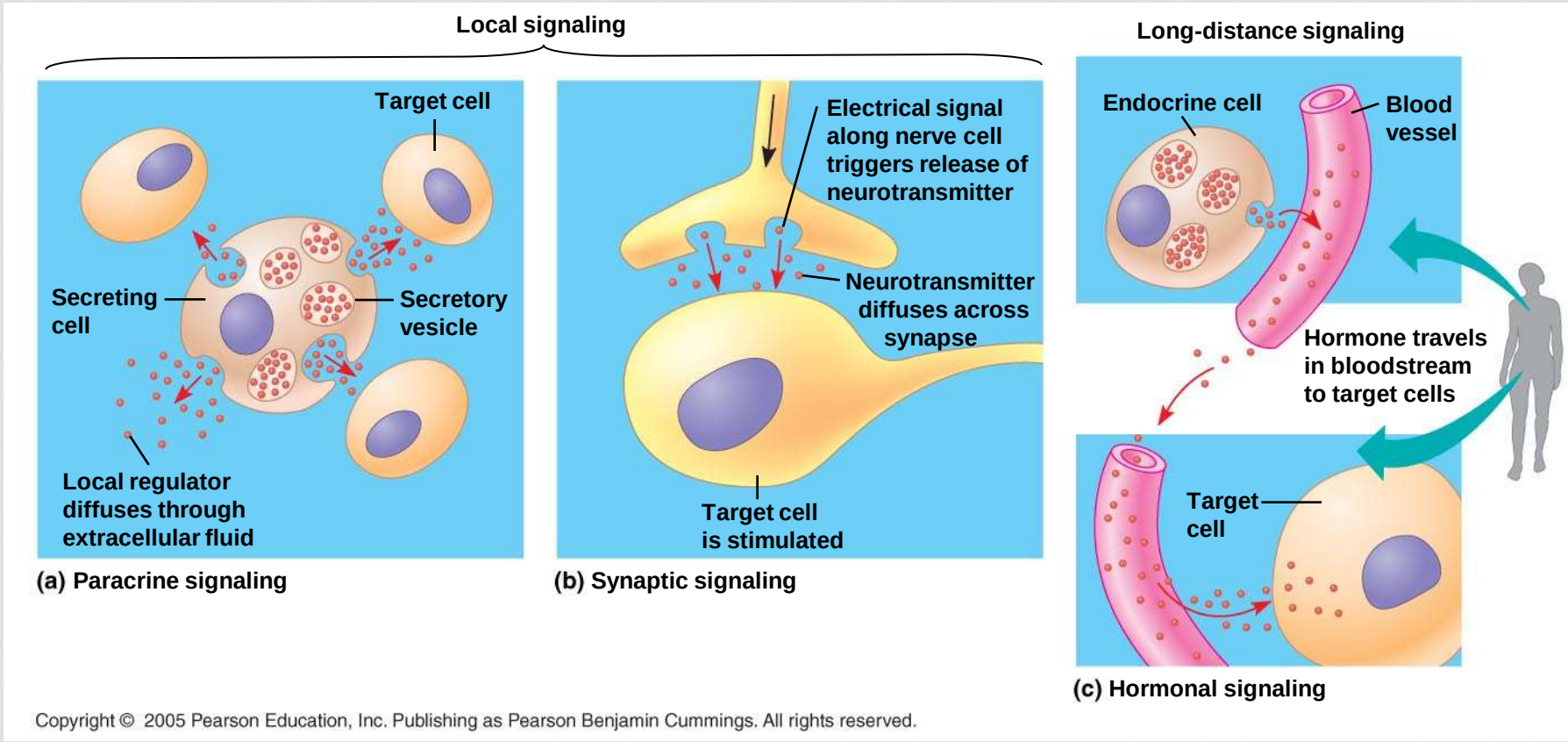


Figure 47-1 Biological Science, 2/e

LOCAL AND LONG-DISTANCE SIGNALING

- Cells in a multicellular organisms 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





Some signaling molecules

1. Steroid hormones

This class of molecules diffuse across the plasma membrane and bind to
Receptors in the cytoplasm or nucleus. They are all synthesized from **cholesterol**.
They include sex steroids (estrogen, progesterone, testosterone)corticosteroids
(glucocorticoids and mineralcorticoids)
Thyroid hormone, vitamin D3, and retinoic acid have different structure and
function but share the same mechanism of action with the other steroids.
Steroid Receptor Superfamily. They are transcription factors that function either
as activators or repressors of transcription.

2. Nitric oxide (NO) and Carbon Monoxide (CO)

NO, a simple gas, is able to diffuse across the membrane, and alters the
activity of intracellular target enzymes. It's extremely unstable, so its effects are
local. Ex. It signals the dilation of blood vessels.

3. Neurotransmitters

They signal from neuron to neuron or from neuron to other target cell
(ex. muscle cell).

STEROID HORMONES

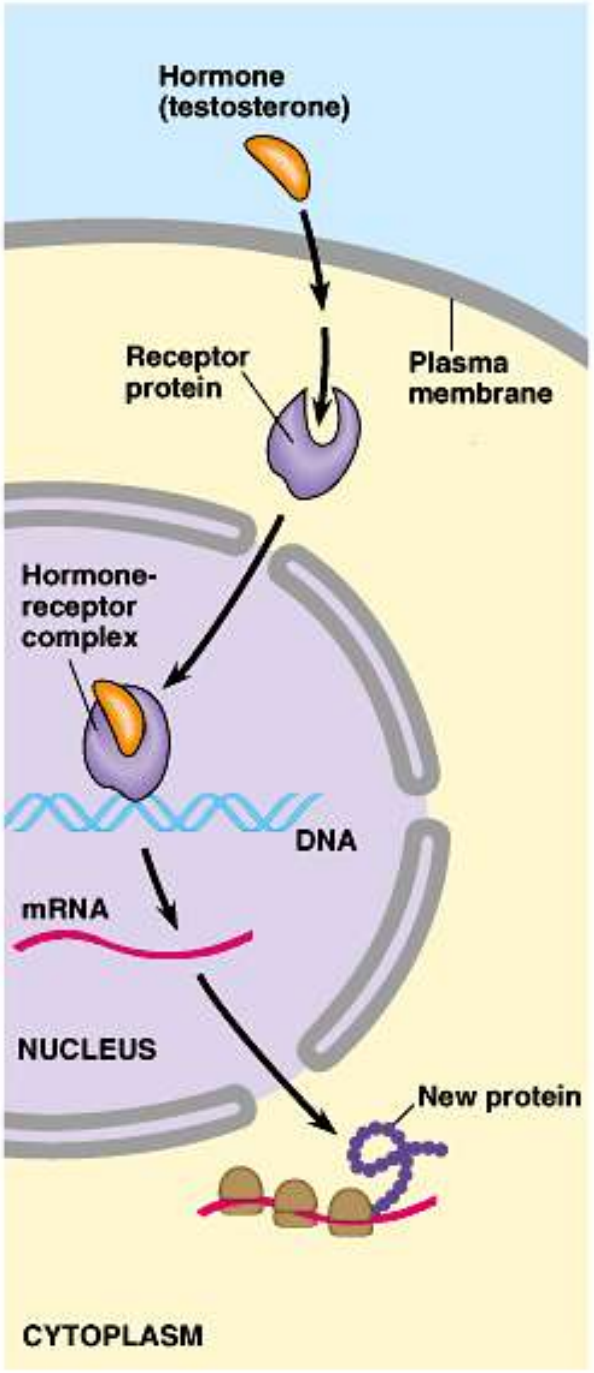
Steroid hormones are soluble in the plasma membrane and readily enter the cytosol where they bind to a mobile receptor.

The hormone-receptor complex enters the nucleus and binds to specific genes where it acts as a transcription factor which turns on the genes.

Messenger RNA is transcribed, leaves the nucleus, and is translated into a specific protein by ribosomes.

The specific proteins then carry out functions (if they are enzymes) or produce structures in the target cell.

Because steroid hormones initiate protein synthesis, their effects are produced more slowly, but are more long-lasting than those produced by other hormones.



THE THREE STAGES OF CELL SIGNALING

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- Reception
- Transduction
- Response

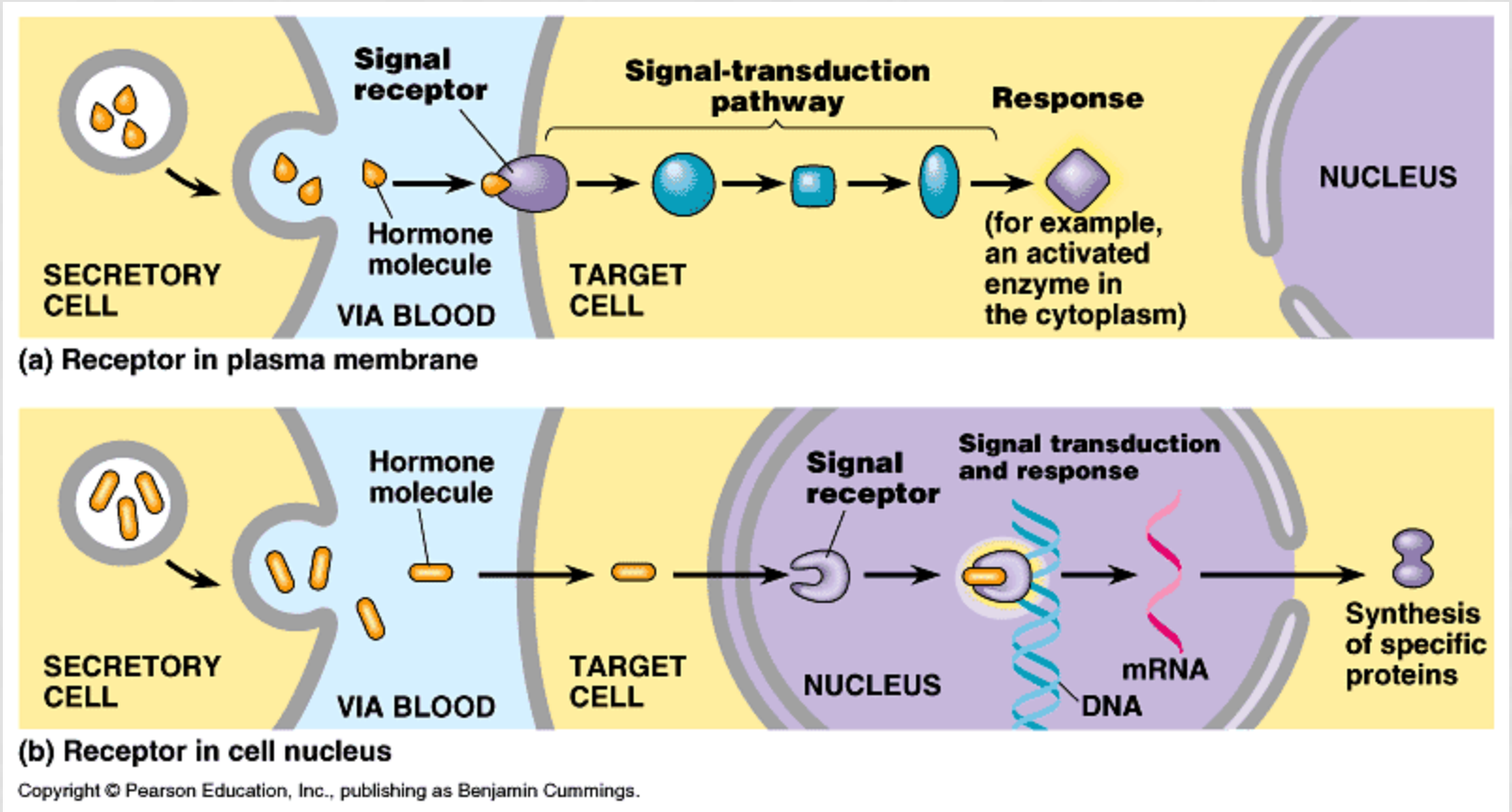
- 1- Reception: A signal molecule binds to a receptor protein, causing it to change shapeThe binding between a signal molecule (ligand) and receptor is highly specific

- Most signal receptors are plasma membrane proteins

THREE STEPS IN CELL SIGNALING

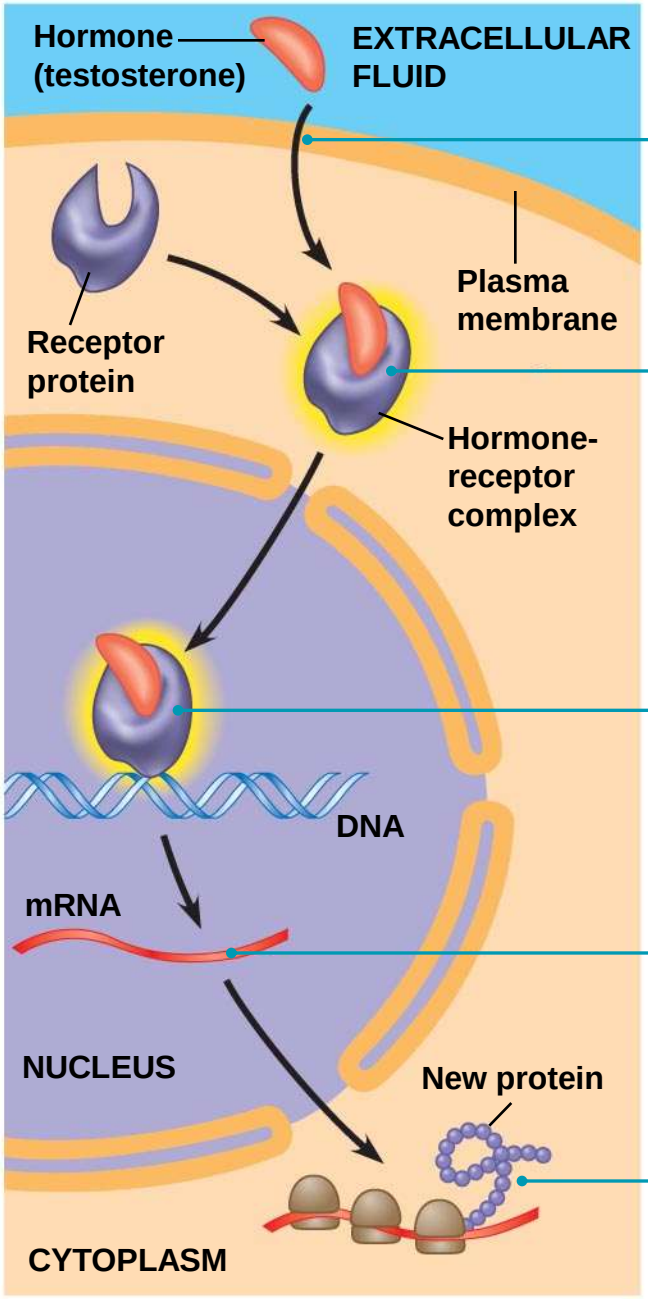
Target organ specificity is the result of specific receptor molecules for the hormone, either on the plasma membrane surface, or in some cases in the cytoplasm, of cells in the target organ.

1) Reception **2) Transduction** **3) Response**



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



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.

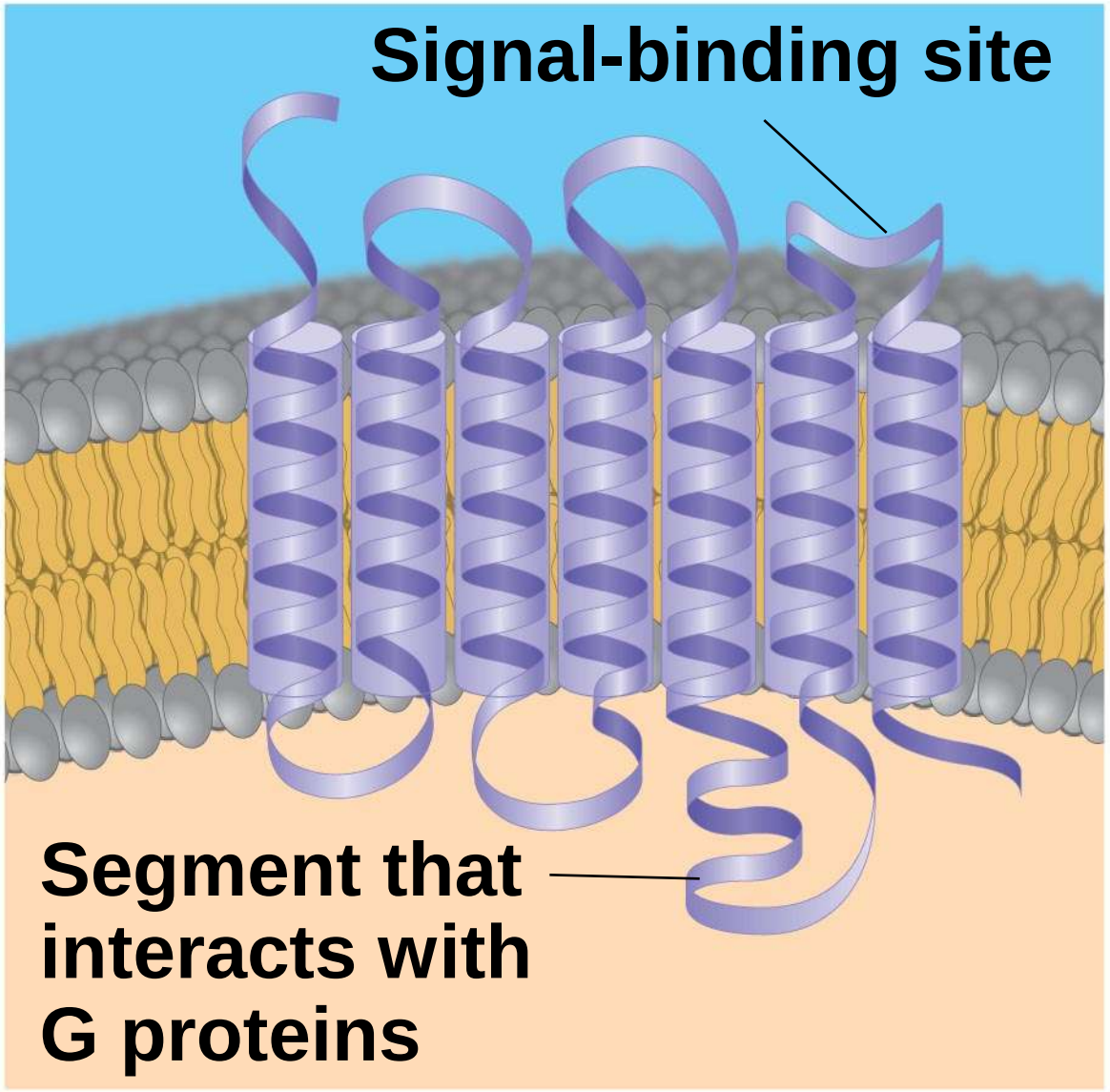
4 The bound protein stimulates the transcription of the gene into mRNA.

5 The mRNA is translated into a specific protein.

RECEPTORS IN THE PLASMA MEMBRANE

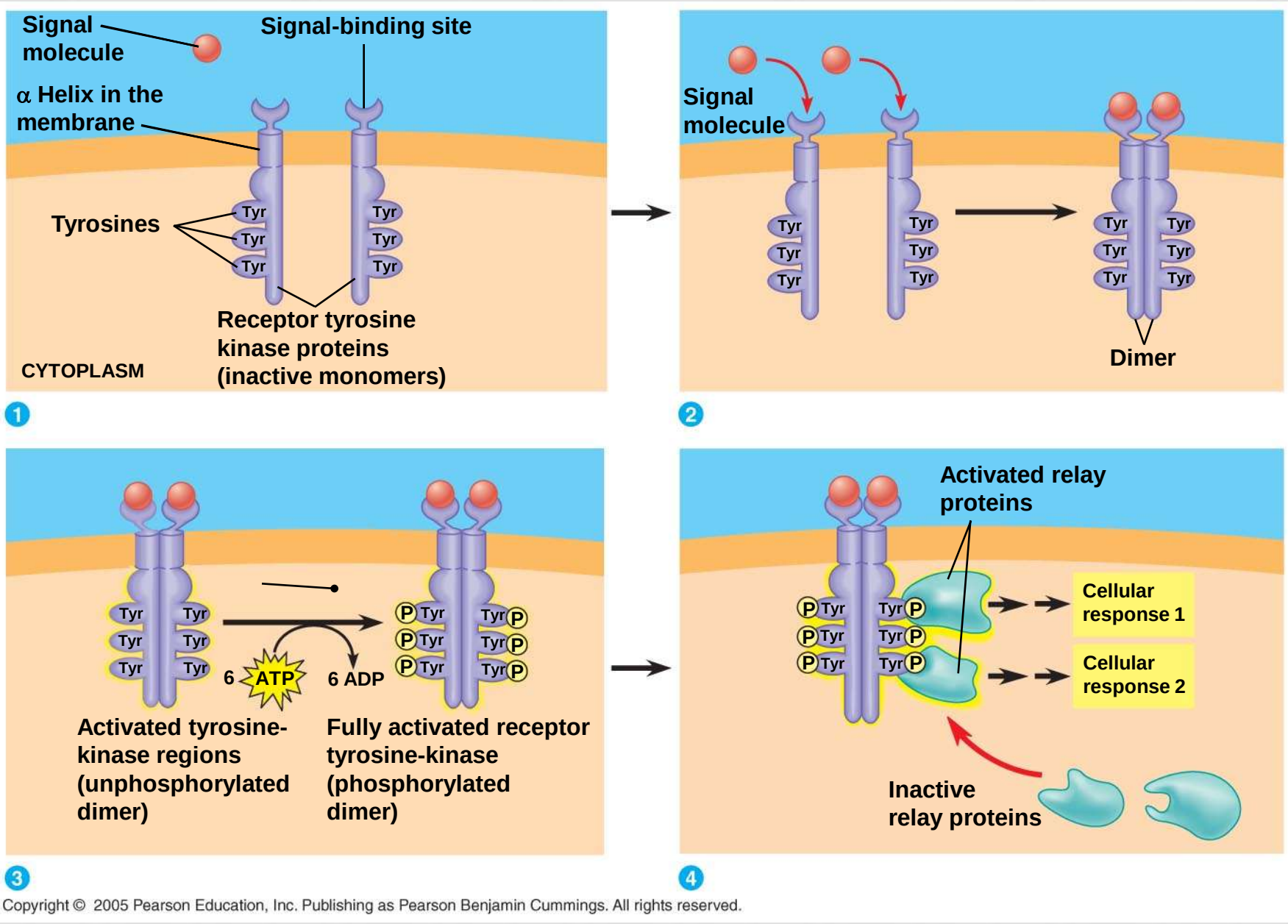
- Most water-soluble signal molecules bind to specific sites on receptor proteins in the plasma membrane
- There are three main types of membrane receptors:
  - G-protein-linked receptors
  - Receptor tyrosine kinases
  - Ion channel receptors

- 1- A G-protein-linked 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

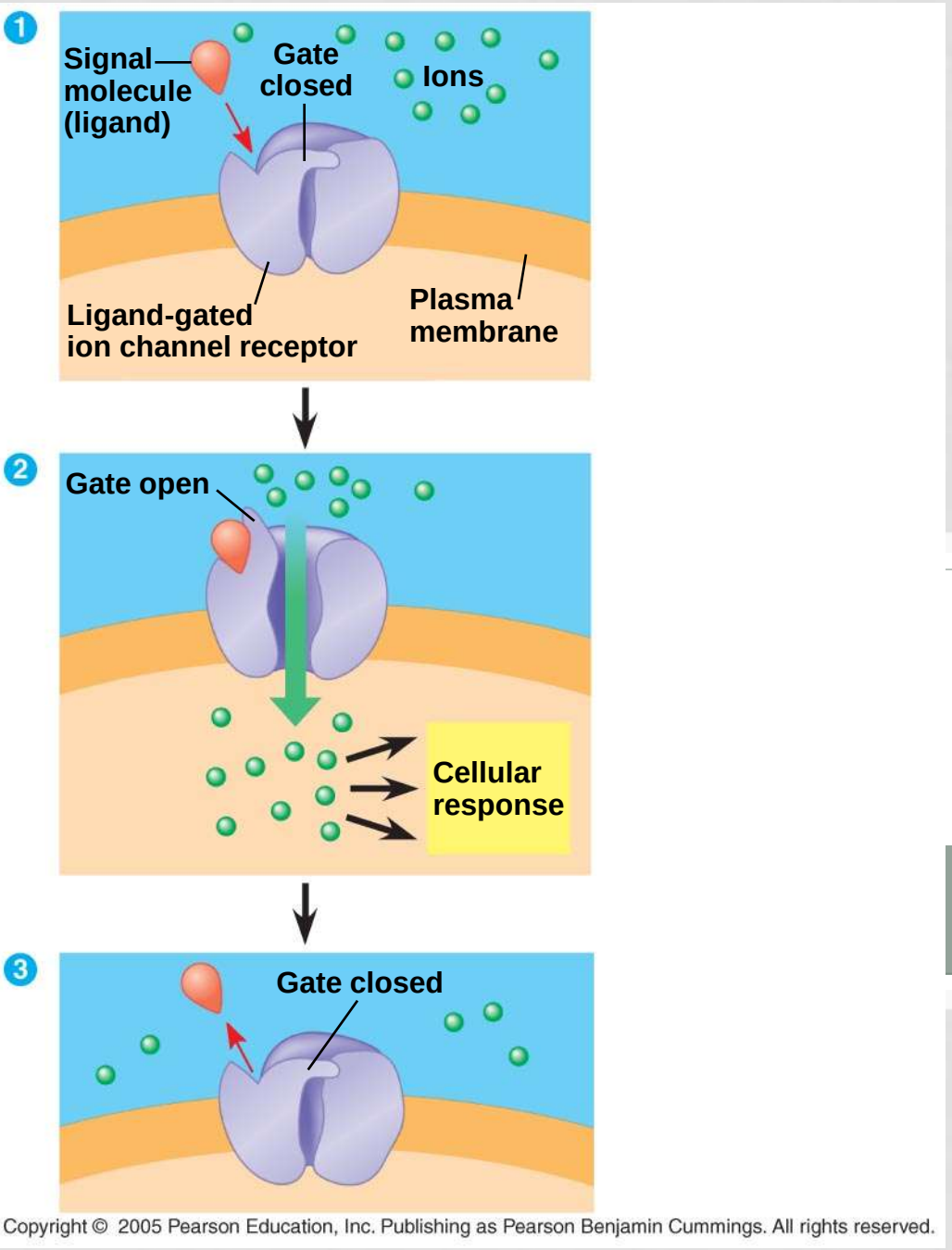


G-protein-linked receptor

- 2- Receptor tyrosine kinases are membrane receptors that attach phosphates to tyrosines
- A receptor tyrosine kinase can trigger multiple signal transduction pathways at once
- A kinase, alternatively known as a phosphotransferase, is a type of enzyme that transfers phosphate groups from high-energy donor molecules, such as ATP, to specific substrates. The process is referred to as *phosphorylation*.



- 3- An 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



2- TRANSDUCTION: CASCADES OF MOLECULAR INTERACTIONS RELAY SIGNALS FROM RECEPTORS TO TARGET MOLECULES IN THE CELL

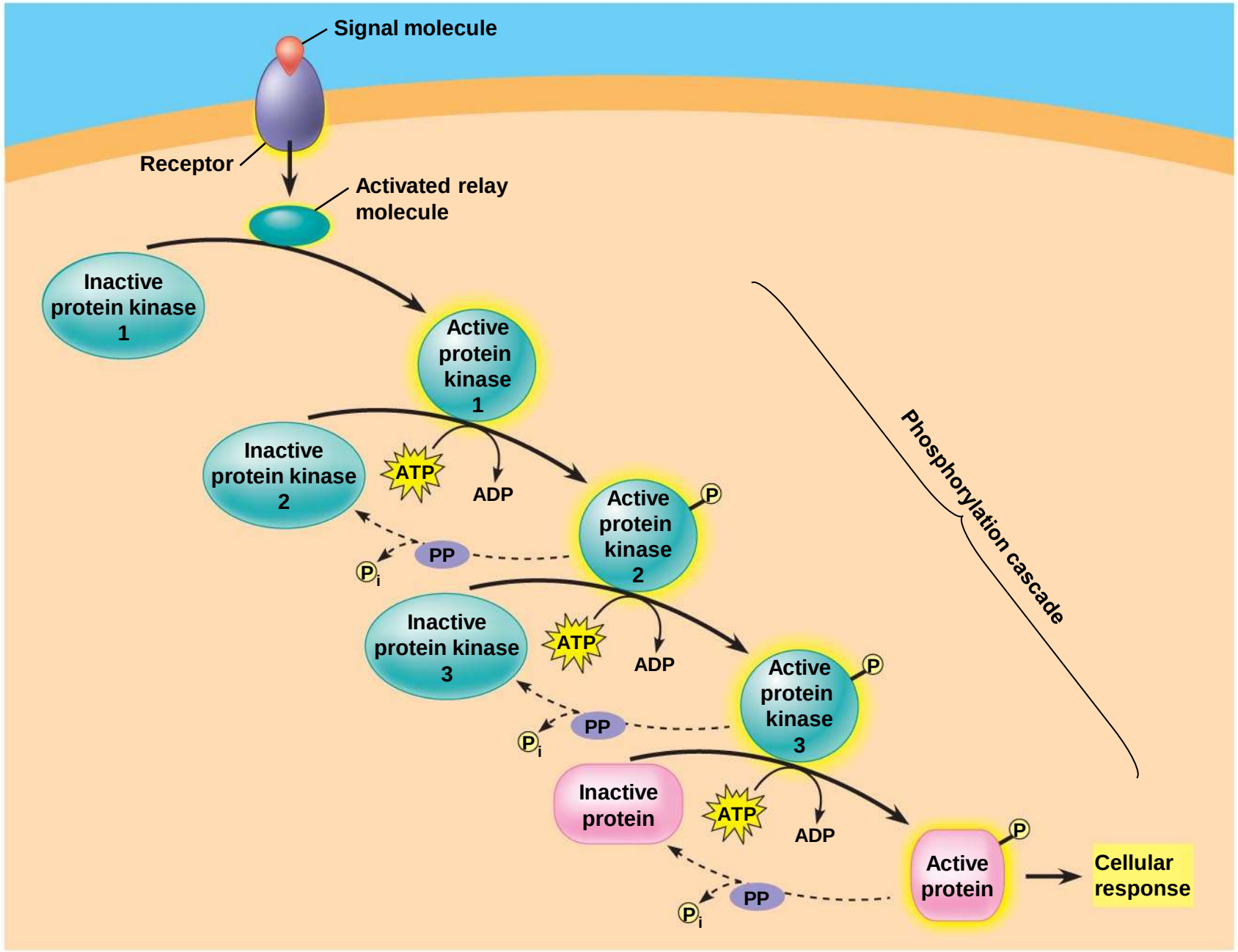
- Transduction usually involves multiple steps
- Multistep pathways can amplify a signal: A few molecules can produce a large cellular response
- Multistep pathways provide more opportunities for coordination and regulation

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 conformational change

PROTEIN PHOSPHORYLATION AND DEPHOSPHORYLATION

- In many pathways, the signal is transmitted by a cascade of protein phosphorylations
- Phosphatase enzymes remove the phosphates
- This phosphorylation (kinases) and dephosphorylation (phosphotases) system acts as a molecular switch, turning activities on and off



PHOSPHORYLATION CASCADE

Signal transduction pathways often involve an enzyme phosphorylation cascade.

A series of protein kinases each activate the next in a series by phosphorylating the inactive precursor.

Because each protein kinase is an enzyme it catalyzes activation of a number of the inactive kinases of the next member in the series.

The result is a large amplification of the original signal, binding of a hormone to the external receptor.

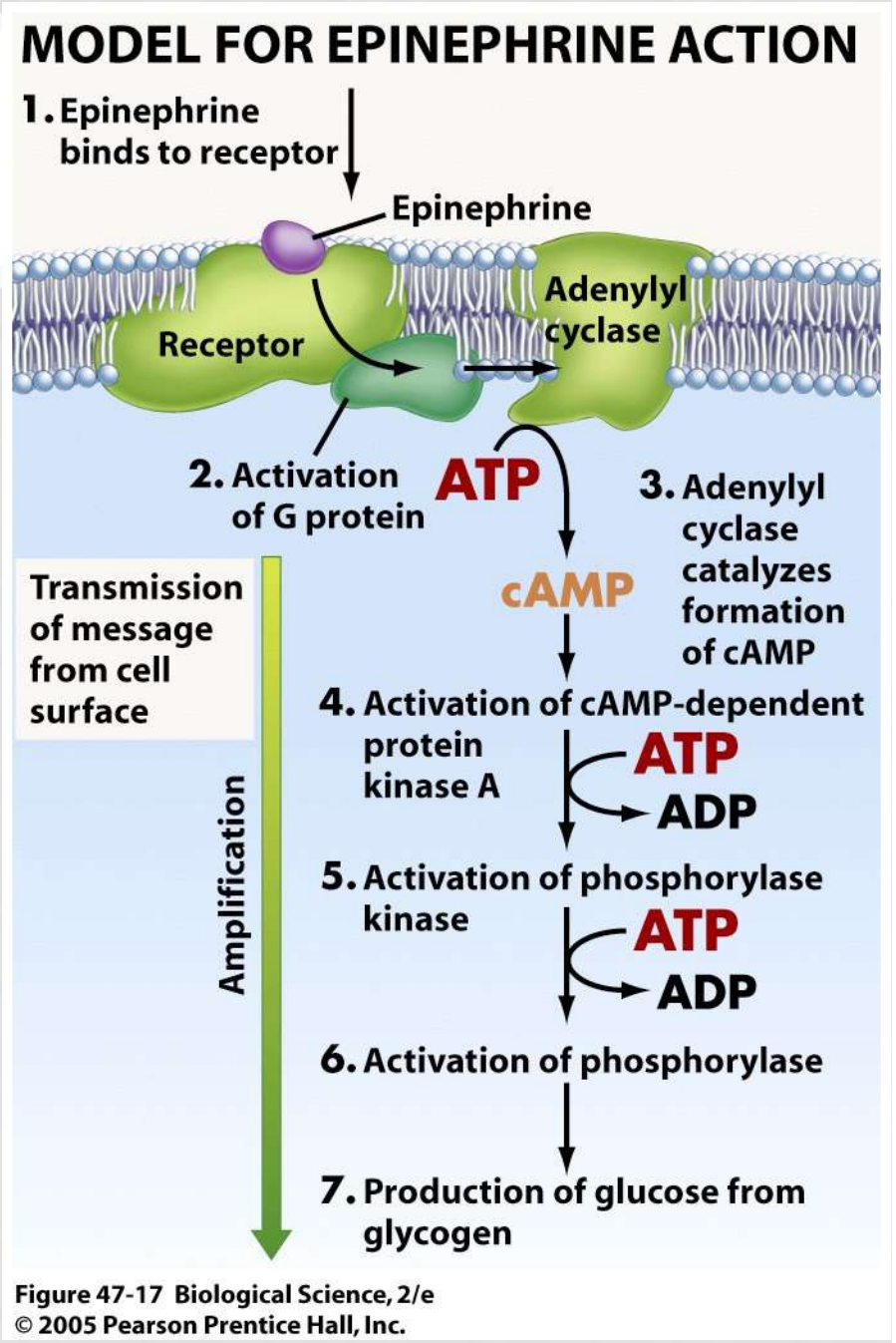


Figure 47-17 Biological Science, 2/e

SMALL MOLECULES AND IONS AS SECOND MESSENGERS

- Second messengers are small, nonprotein, water-soluble molecules or ions
- The extracellular signal molecule that binds to the membrane is a pathway's "first messenger"
- Second messengers can readily spread throughout cells by diffusion
- Second messengers participate in pathways initiated by G-protein-linked receptors and receptor tyrosine kinases

CYCLIC AMP

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

CYCLIC AMP AS A SECOND MESSENGER

Most water-soluble hormones do not readily enter the target cell - they bind to a surface receptor.

In many cases, a G protein is activated which then activates an enzyme, adenylyl cyclase which converts ATP to cyclic AMP (cAMP).

cAMP then serves as a second messenger which activates another enzyme in the cell.

cAMP initiates a chain of events (the signal transduction pathway) that results in some specific response of the cell to the first messenger (hormone).

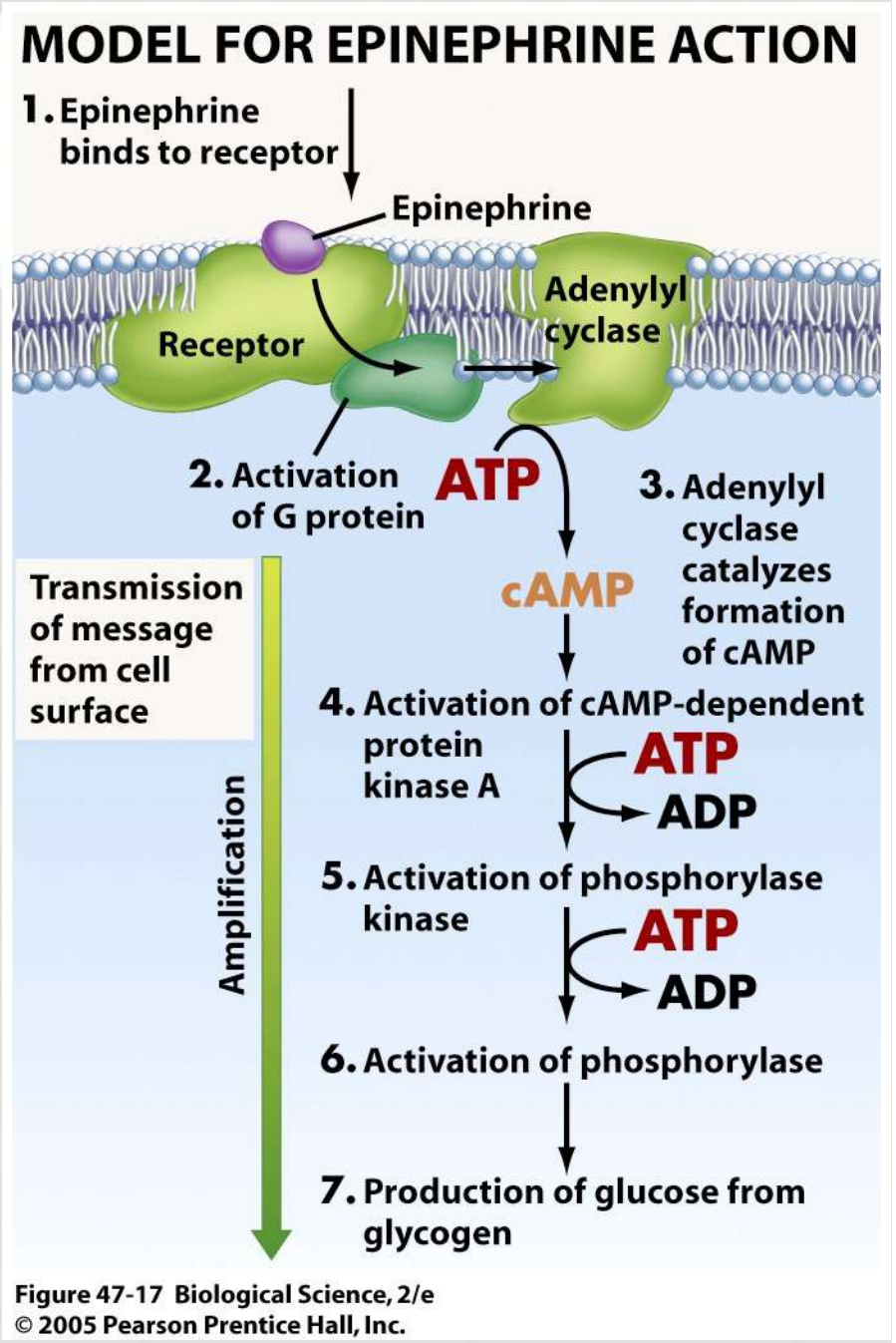
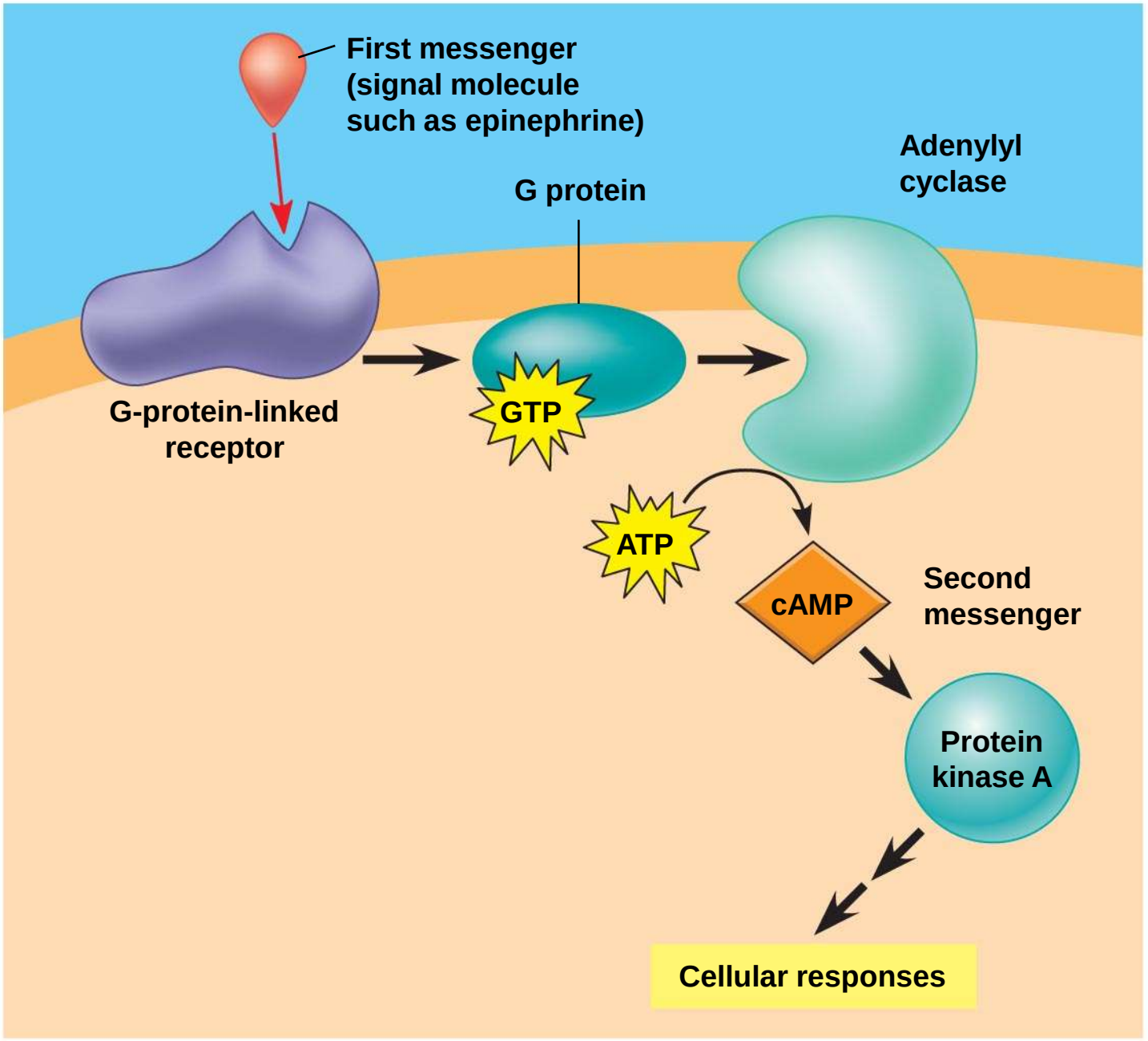


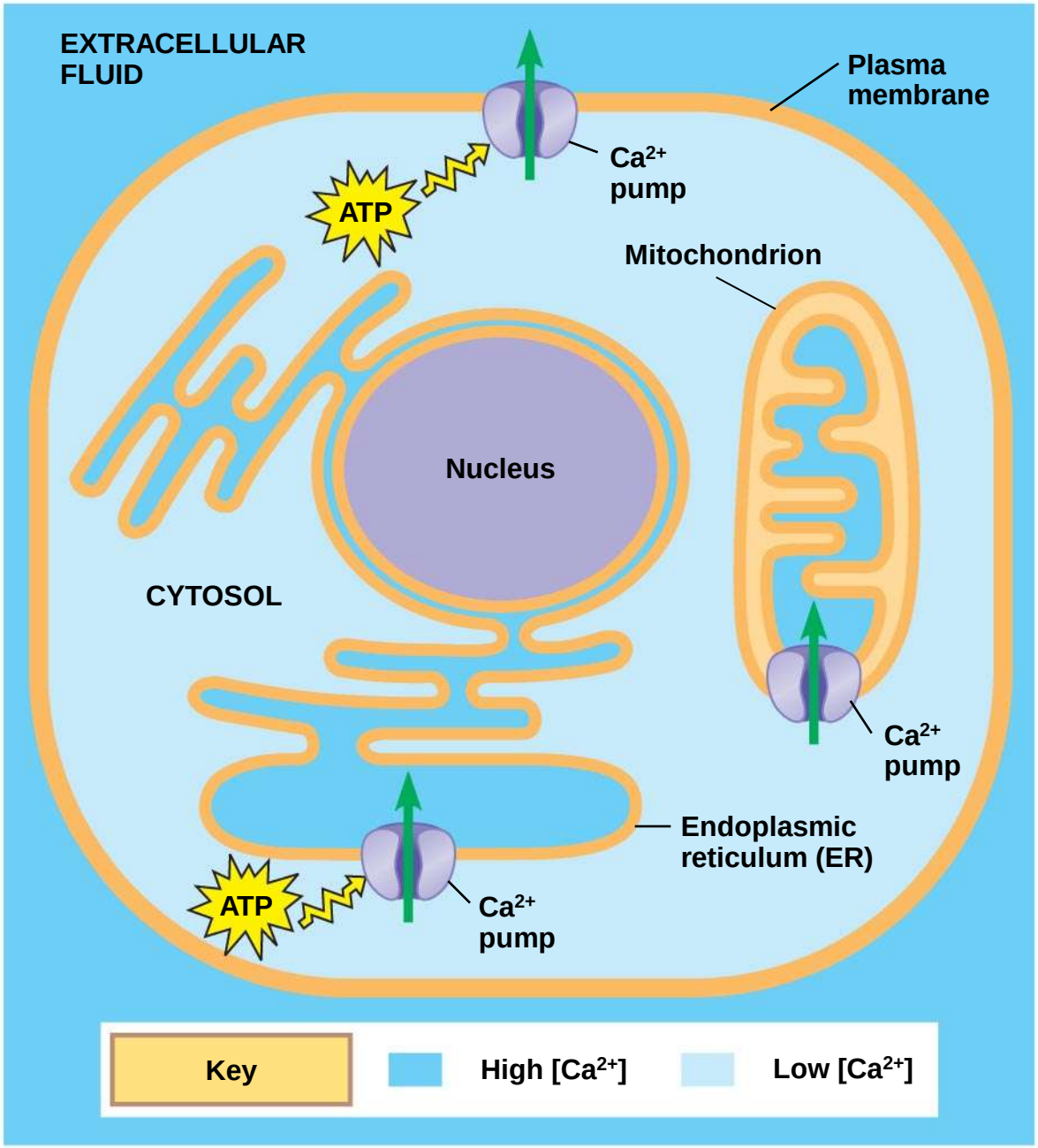
Figure 47-17 Biological Science, 2/e

- Many signal molecules trigger formation of cAMP
- Other components of cAMP pathways are G proteins, G-protein-linked 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

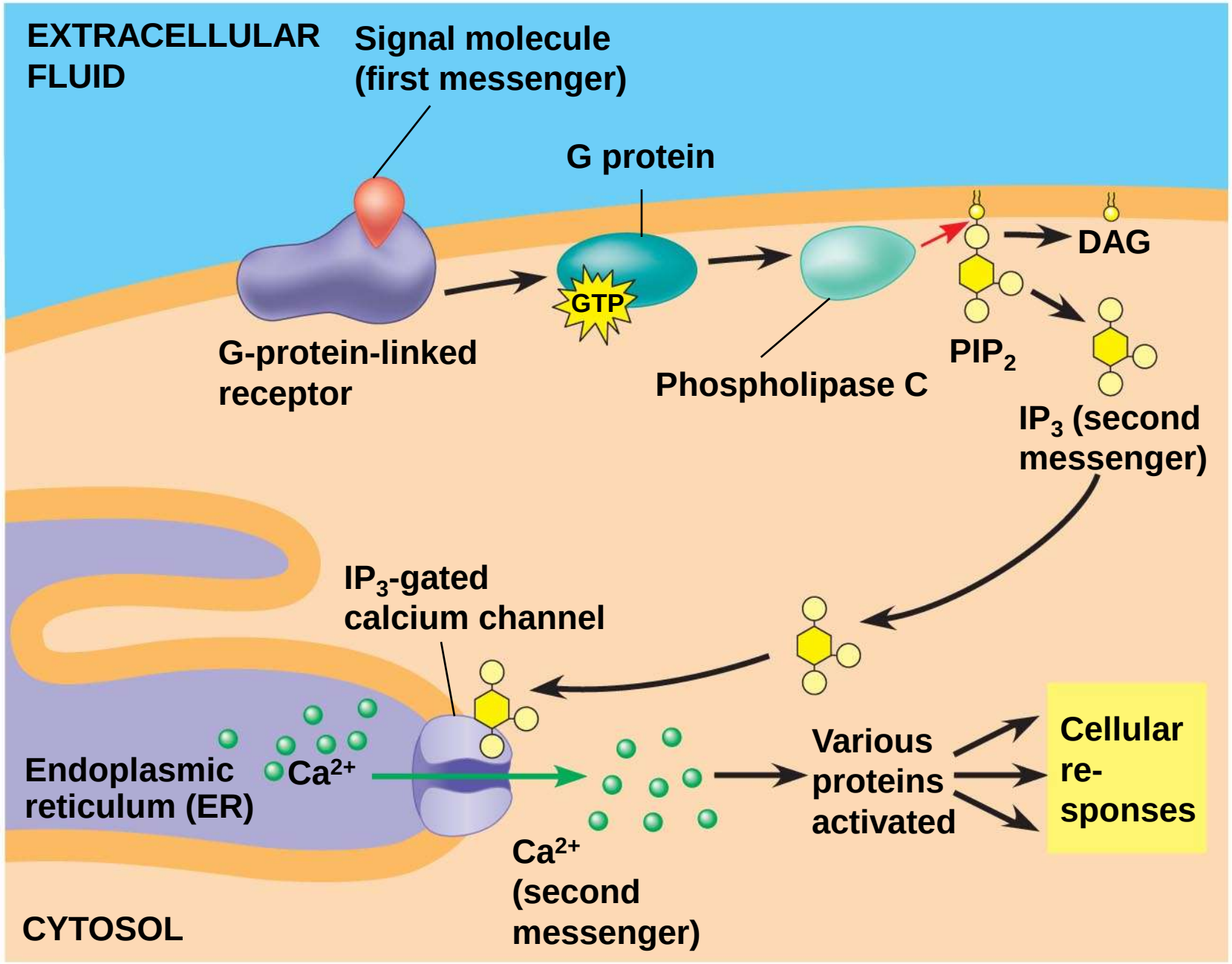


CALCIUM IONS AND INOSITOL TRIPHOSPHATE (IP_3)

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



- A signal relayed by a signal transduction pathway may trigger an increase in calcium in the cytosol
- Pathways leading to the release of calcium involve inositol triphosphate (IP_3) and diacylglycerol (DAG) as second messengers

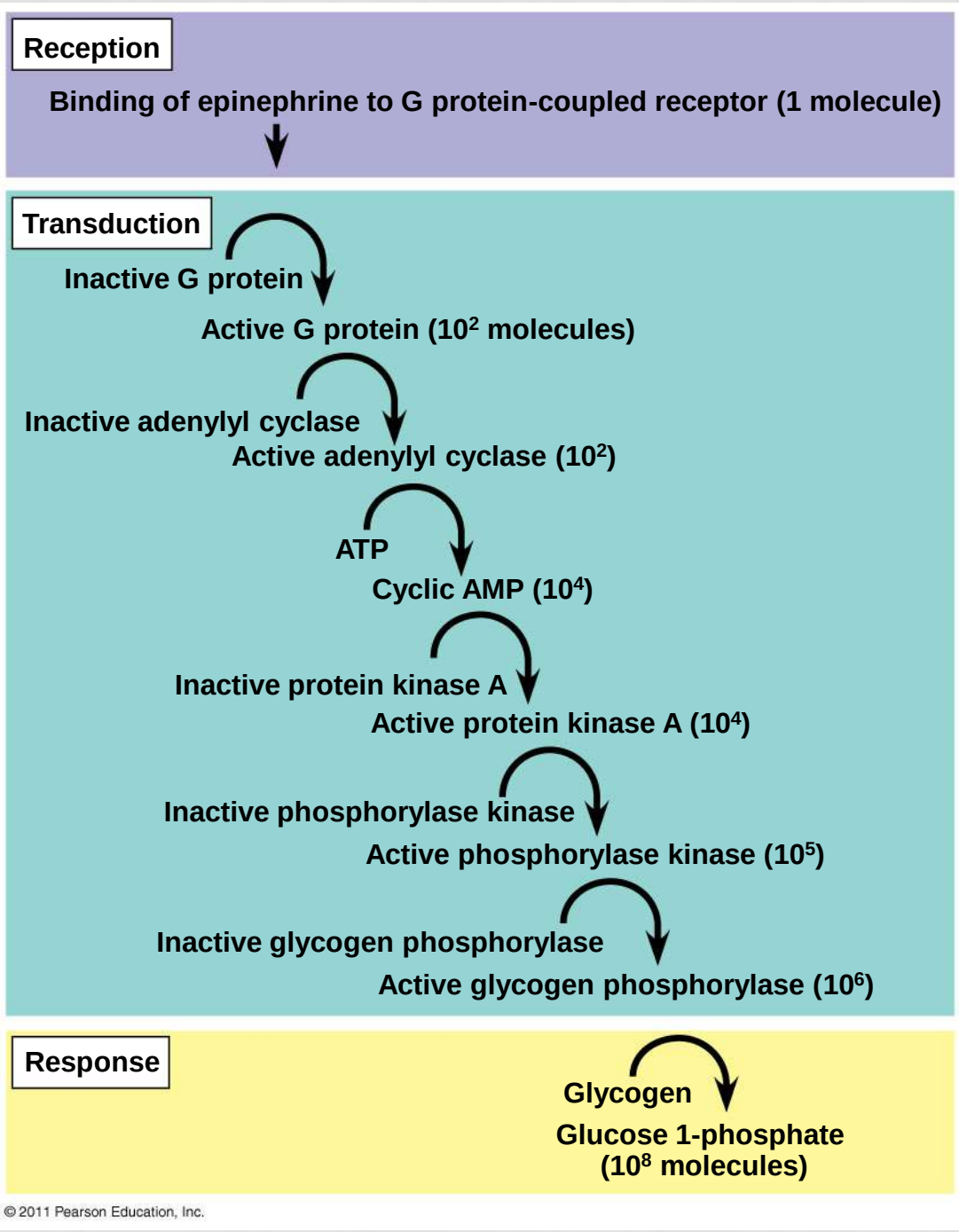


3- CYTOPLASMIC AND NUCLEAR RESPONSES

- **Ultimately, a signal transduction pathway leads to regulation of one or more cellular activities**
- **The response may occur in the cytoplasm or in the nucleus**
- **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**

- Many other signaling pathways regulate the *synthesis* of enzymes or other proteins, usually by turning genes on or off in the nucleus
- The final activated molecule may function as a transcription factor

FIGURE 11.16



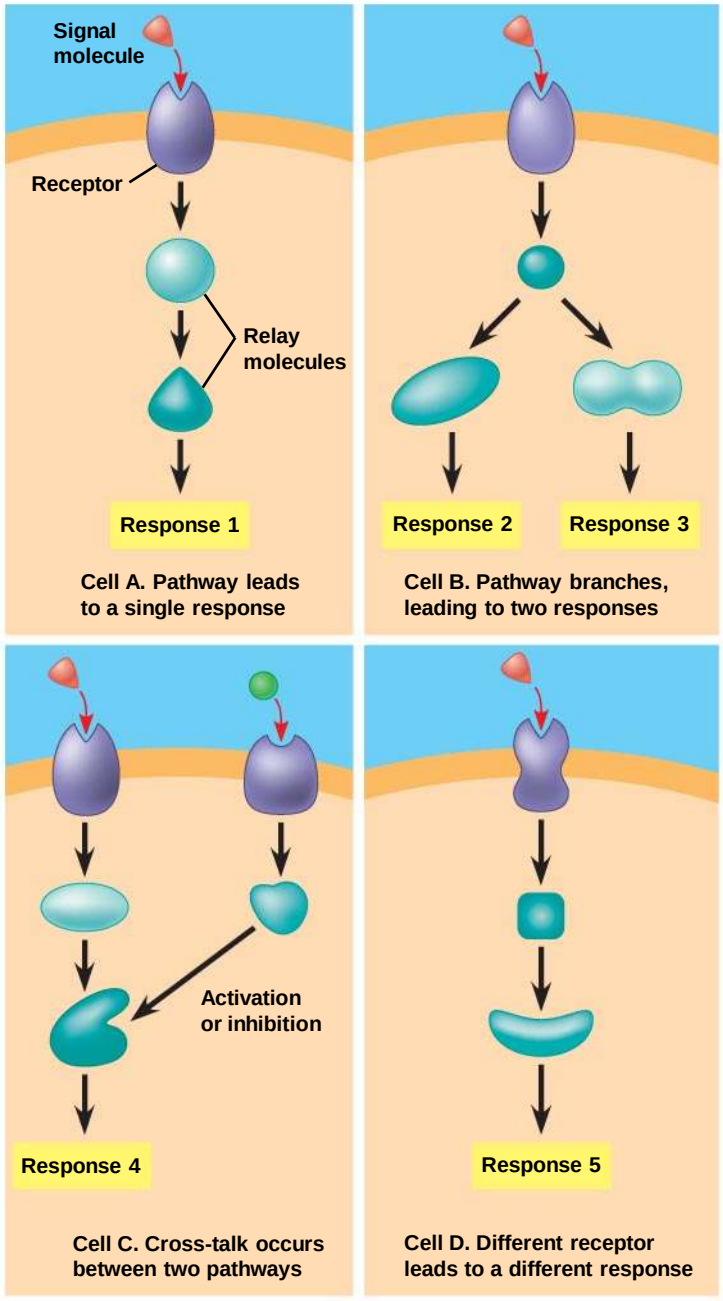
- There are four aspects of fine-tuning to consider
  - Amplifying the signal (and thus the response)
  - Specificity of the response
  - Overall efficiency of response, enhanced by scaffolding proteins
  - Termination of the signal

SIGNAL AMPLIFICATION

- Enzyme cascades amplify the cell's response
- 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 differences in proteins give each kind of cell specificity in detecting and responding to signals
- The response of a cell to a signal depends on the cell's particular collection of proteins
- Pathway branching and "cross-talk" further help the cell coordinate incoming signals



TERMINATION OF THE SIGNAL

- Inactivation mechanisms are an essential aspect of cell signaling
- When signal molecules leave the receptor, the receptor reverts to its inactive state


Thank
You