Chapter 11

Cell Communication

PowerPoint® Lecture Presentations for

Biology

Eighth Edition

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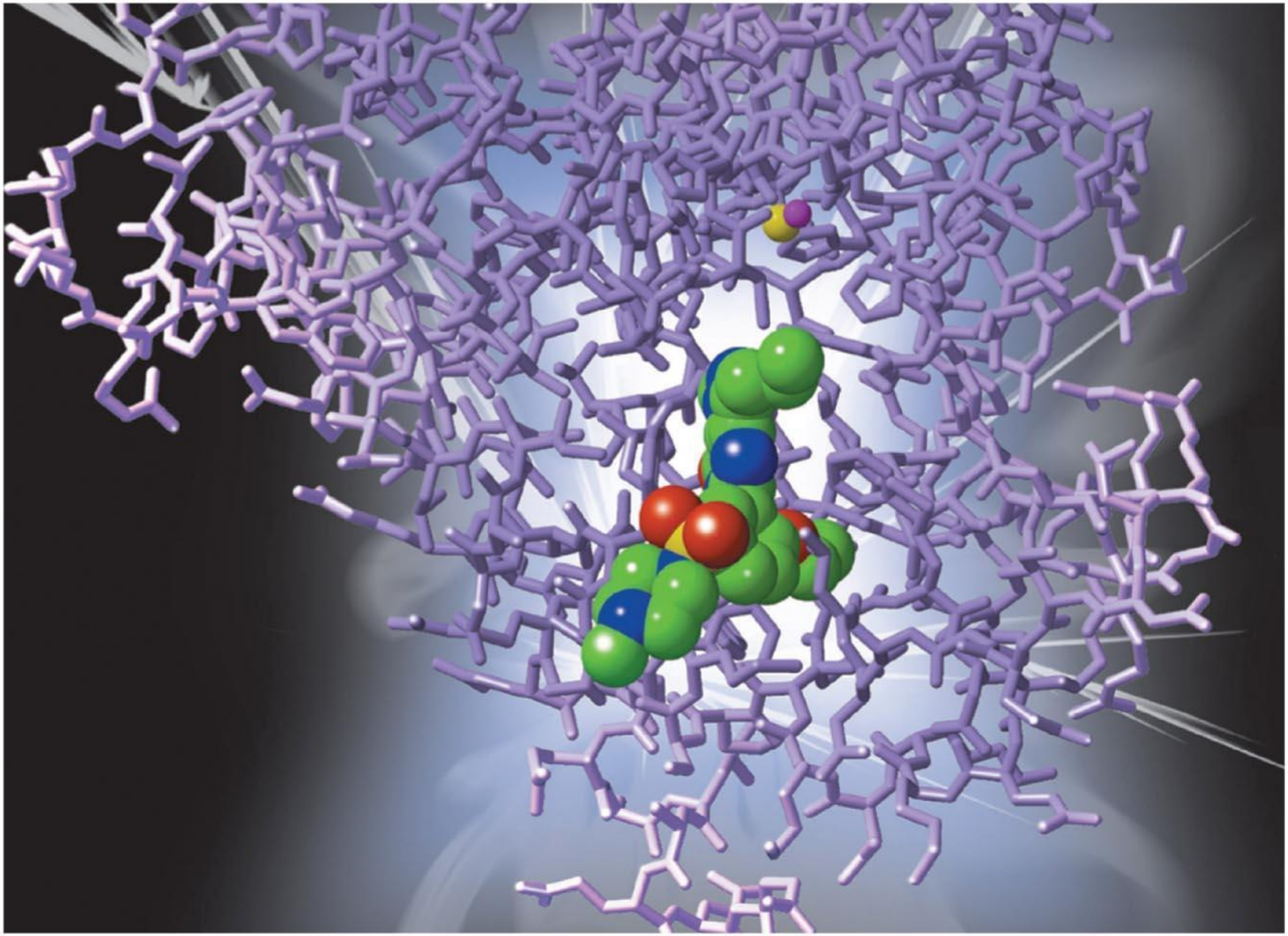
Overview: The Cellular Internet

- Cell-to-cell communication is essential for multicellular organisms
- Biologists have discovered some universal mechanisms of cellular regulation
- The combined effects of multiple signals determine cell response
- For example, the dilation of blood vessels is controlled by multiple molecules

Fig. 11-1



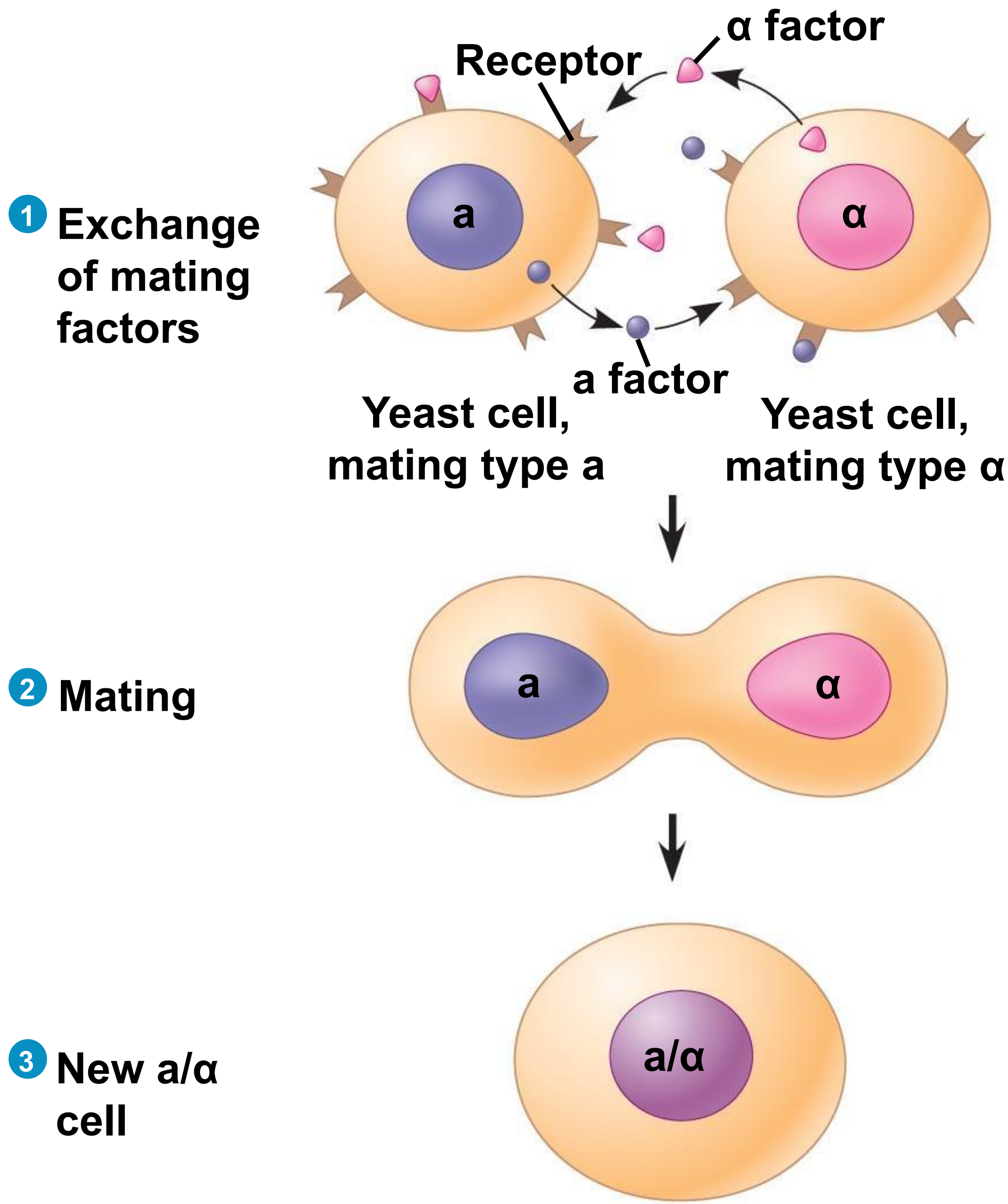
Concept 11.1: External signals are converted to responses within the cell

- Microbes are a window on the role of cell signaling in the evolution of life

Evolution of Cell Signaling

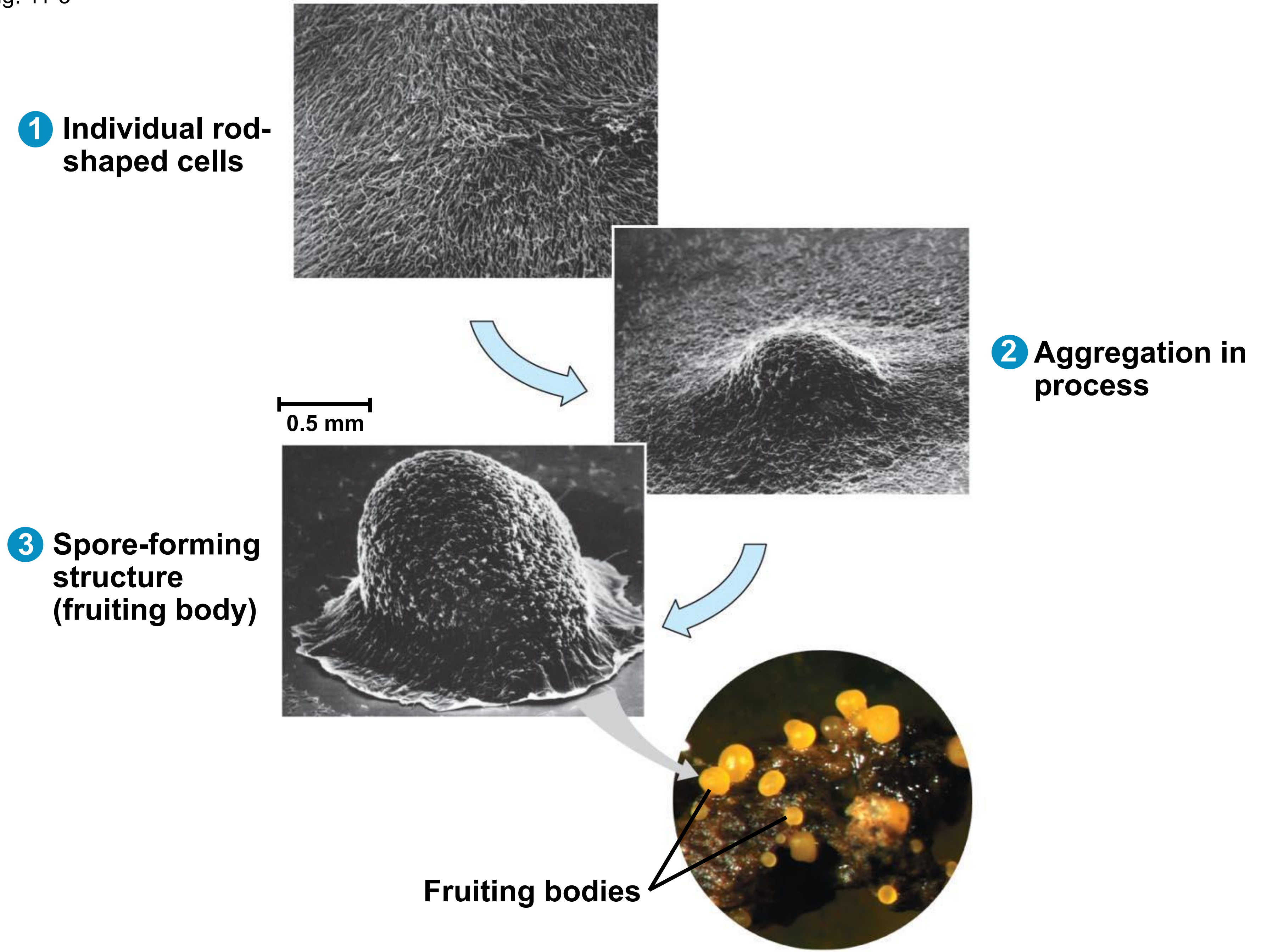
- A **signal transduction pathway** is a series of steps by which a signal on a cell's surface is converted into a specific cellular response
- Signal transduction pathways convert signals on a cell's surface into cellular responses

Fig. 11-2


α factor
Receptor
1 Exchange of mating factors
a
α
a factor
Yeast cell, mating type a
Yeast cell, mating type α
2 Mating
a
α
3 New a/α cell
a/α

- Pathway similarities suggest that ancestral signaling molecules evolved in prokaryotes and were modified later in eukaryotes
- The concentration of signaling molecules allows bacteria to detect population density

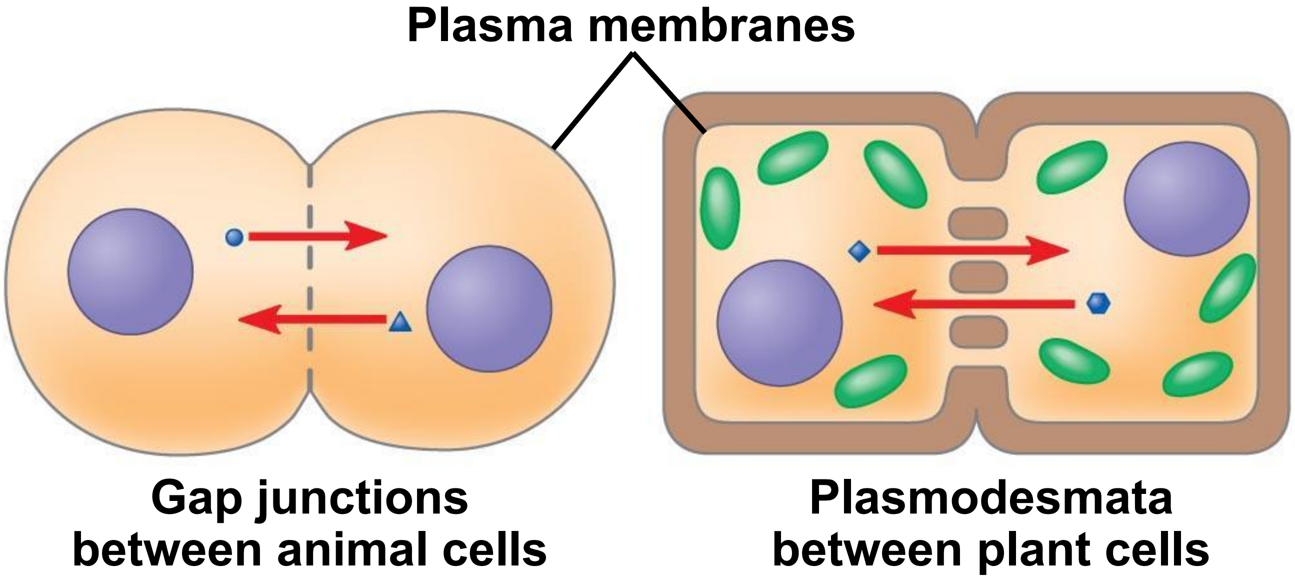
Fig. 11-3


1 Individual rod-shaped cells
2 Aggregation in process
0.5 mm
3 Spore-forming structure (fruiting body)
Fruiting bodies

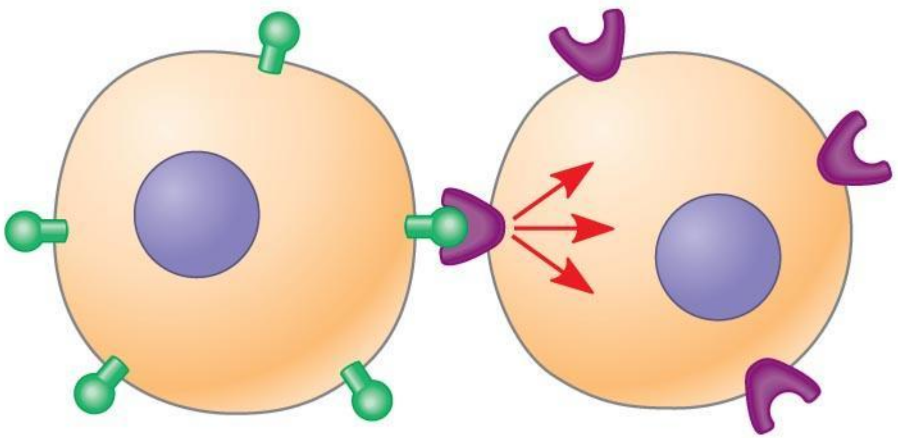
Local and Long-Distance Signaling

- 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

Fig. 11-4



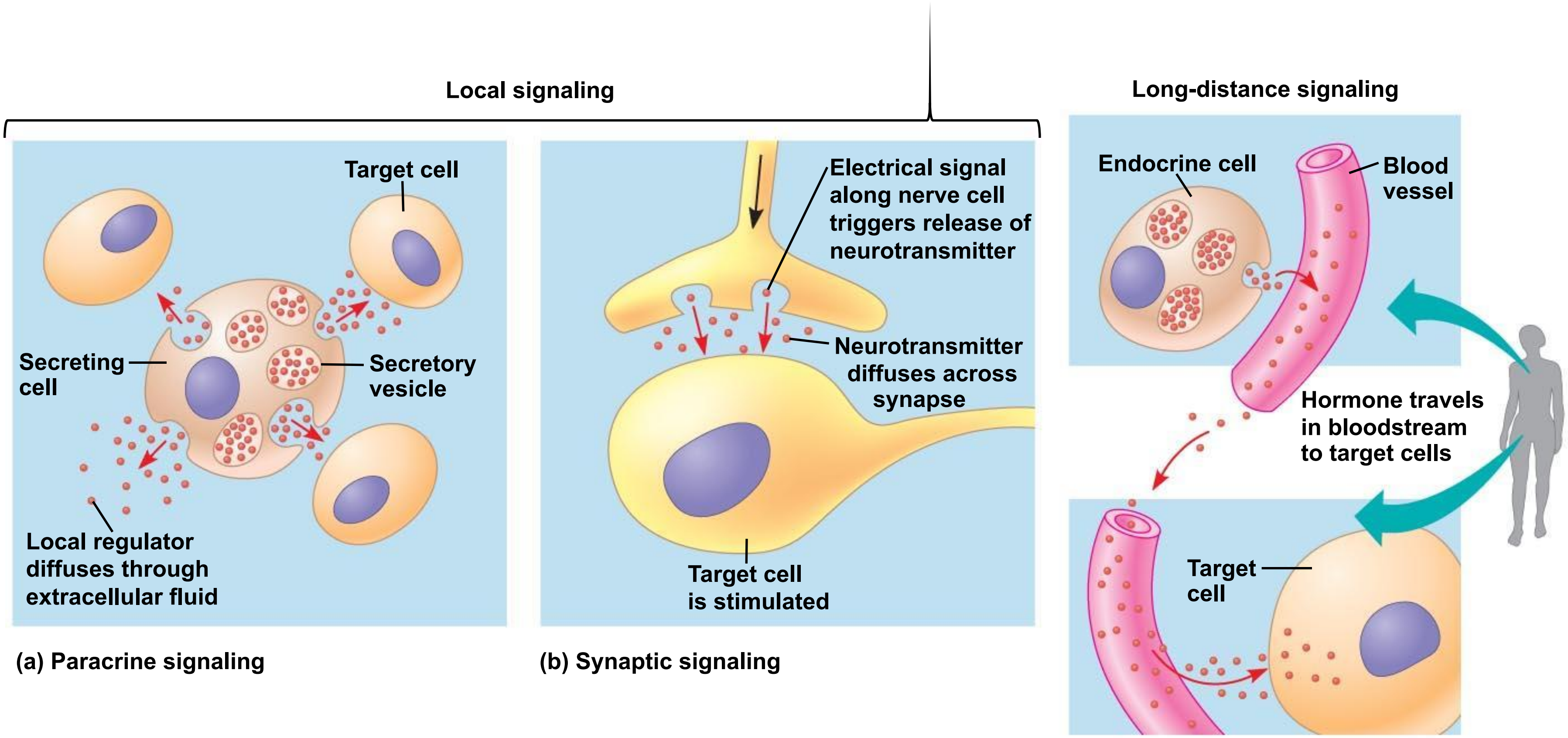
(a) Cell junctions



(b) Cell-cell recognition

- 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**

Fig. 11-5



(a) Paracrine signaling

(b) Synaptic signaling

(c) Hormonal signaling

Fig. 11-5ab

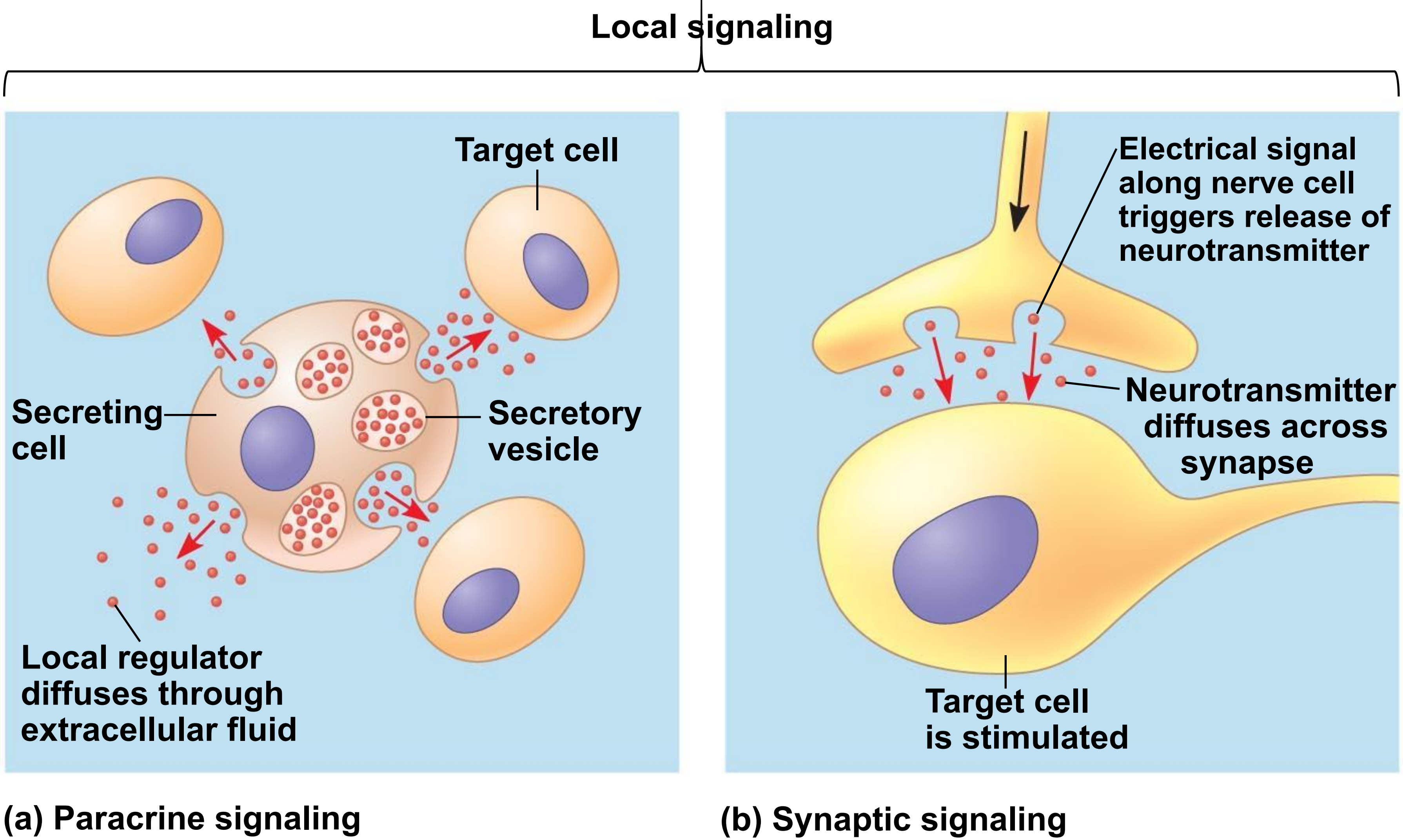
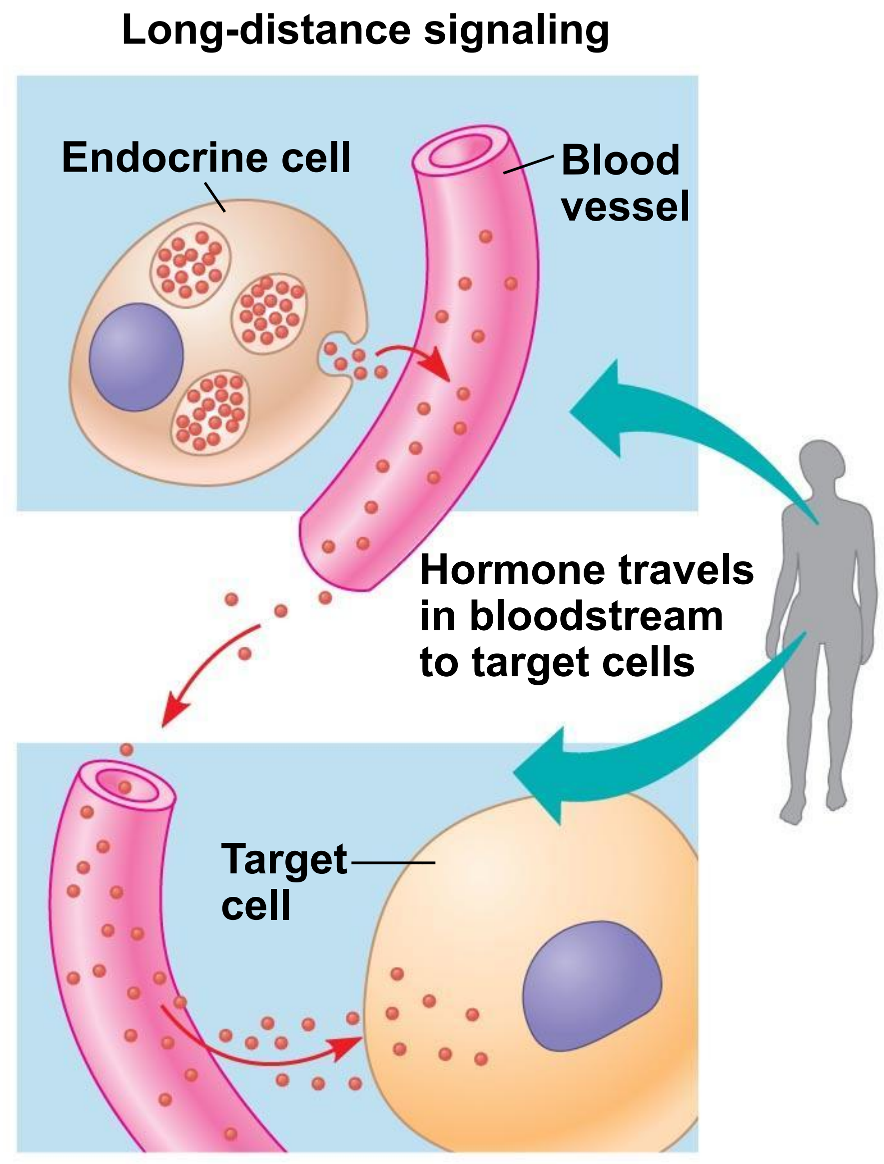

Local signaling
Target cell
Secreting cell
Secretory vesicle
Local regulator diffuses through extracellular fluid
(a) Paracrine signaling
Electrical signal along nerve cell triggers release of neurotransmitter
Neurotransmitter diffuses across synapse
Target cell is stimulated
(b) Synaptic signaling

Fig. 11-5c



(c) Hormonal signaling

The Three Stages of Cell Signaling: *A Preview*

- Earl W. Sutherland discovered how the hormone epinephrine acts on cells
- Sutherland suggested that cells receiving signals went through three processes:
  - **Reception**
  - **Transduction**
  - **Response**

PLAY

Animation: Overview of Cell Signaling

Fig. 11-6-1

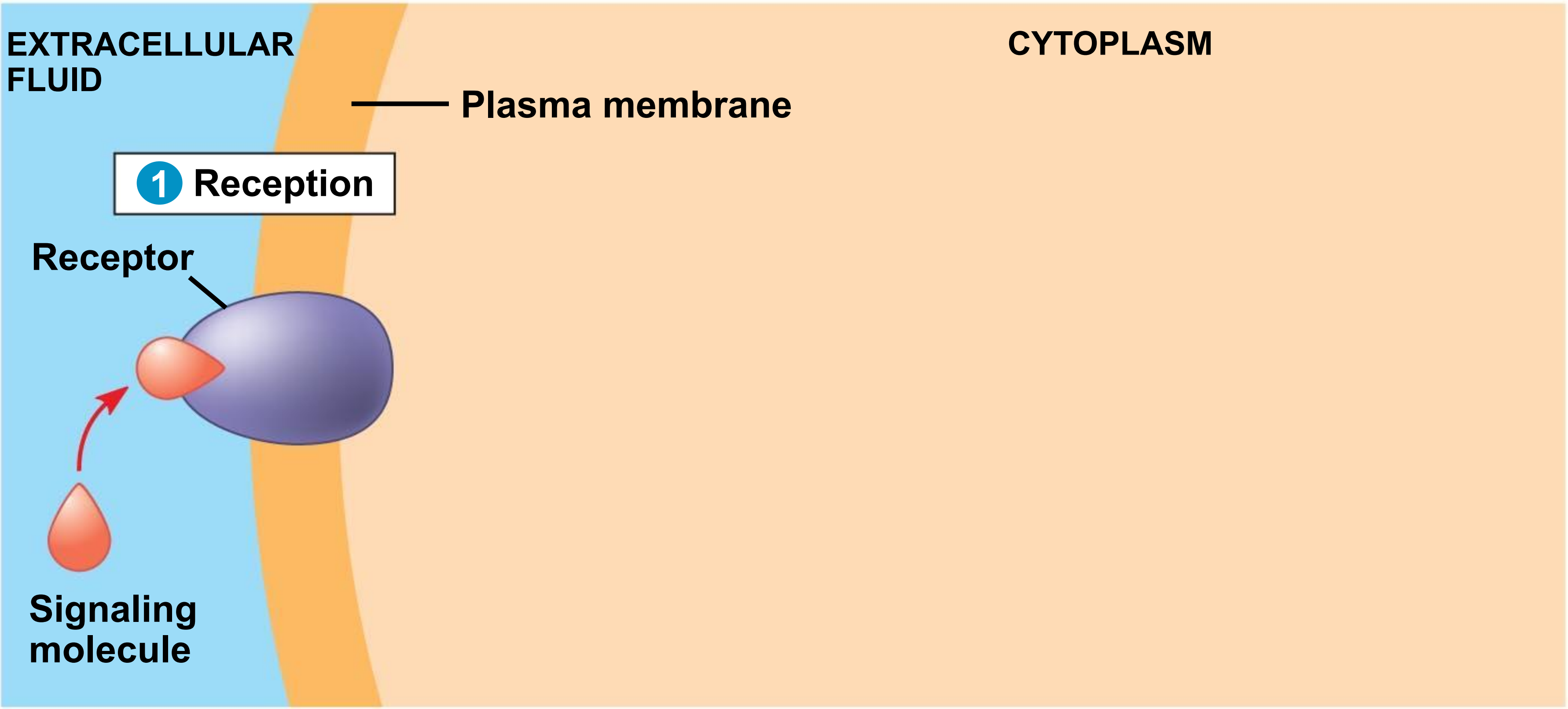

EXTRACELLULAR
FLUID
CYTOPLASM
Plasma membrane
1 Reception
Receptor
Signaling
molecule

Fig. 11-6-2

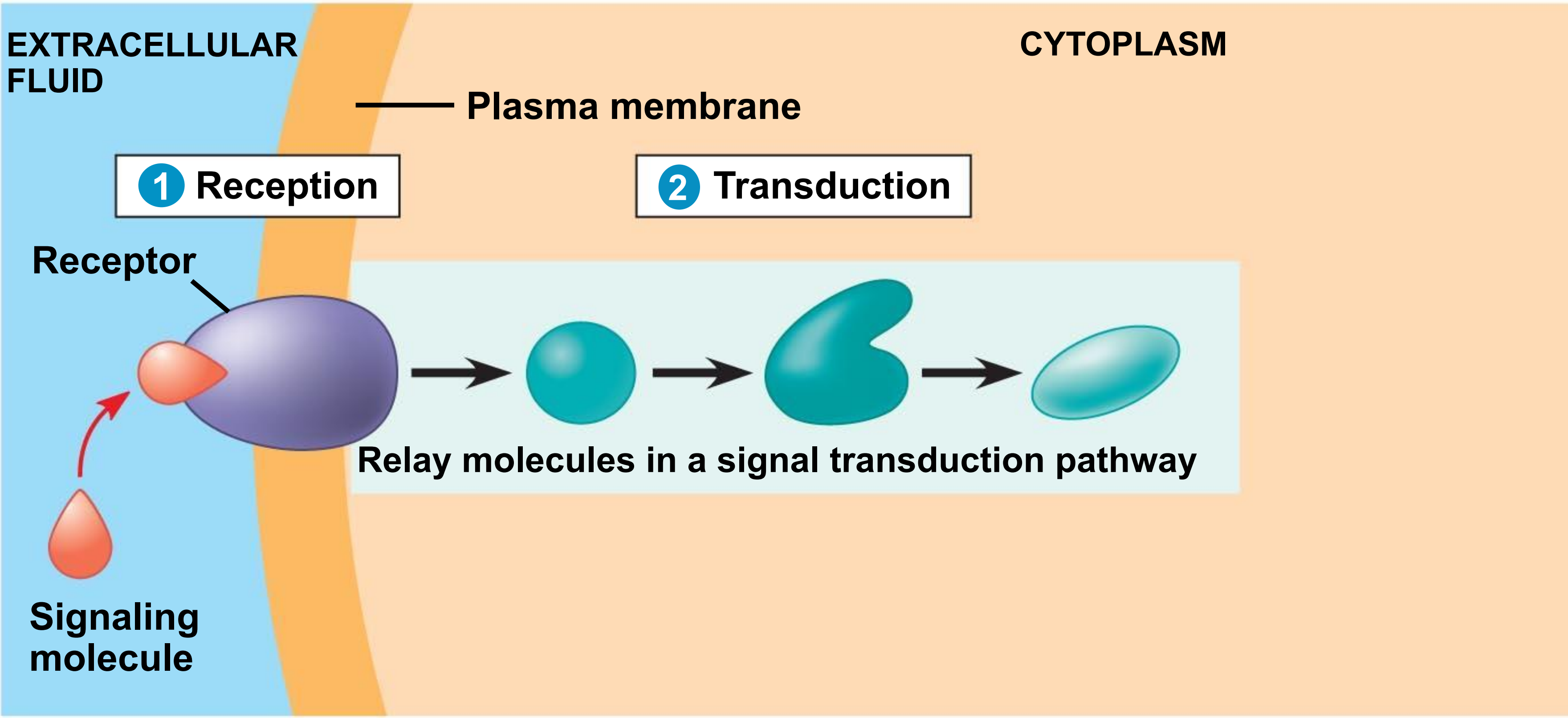
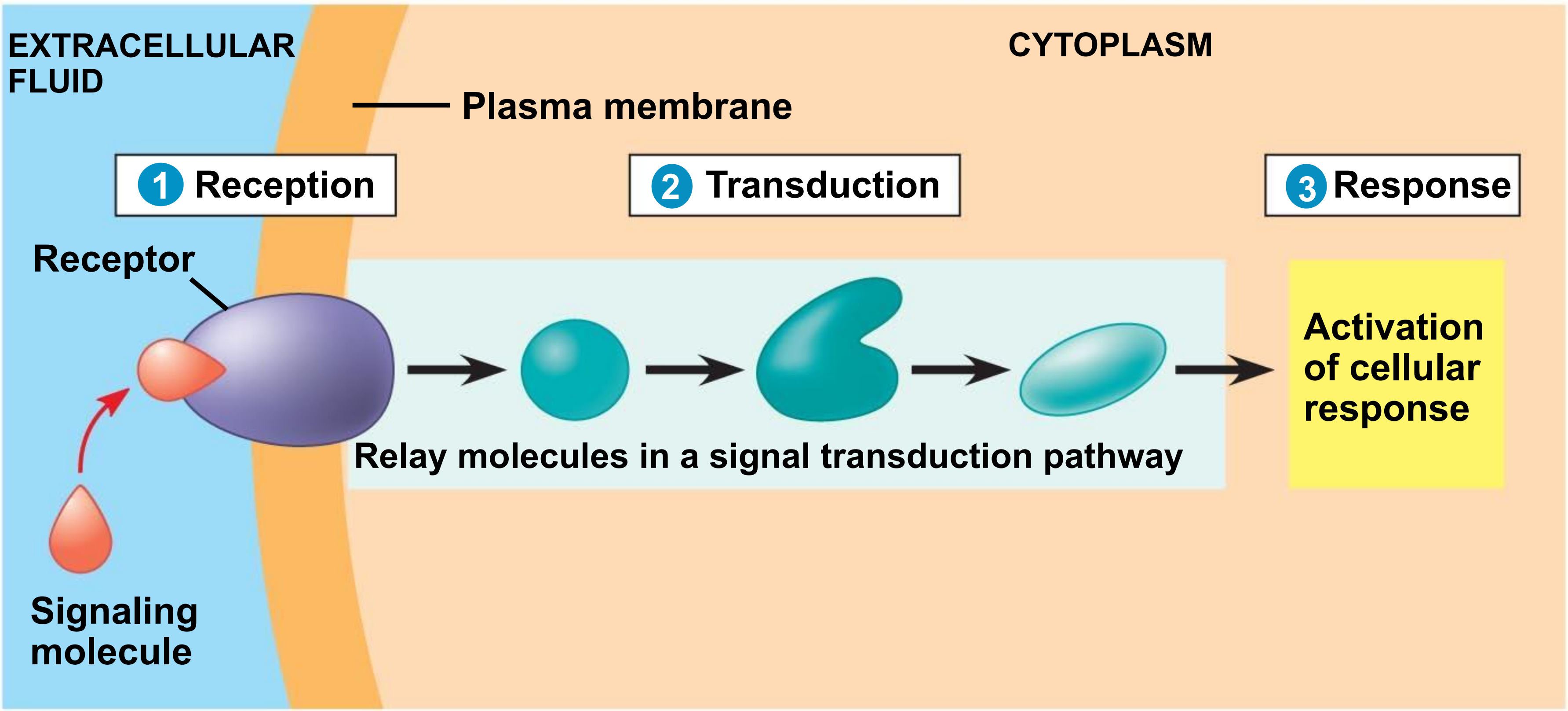

EXTRACELLULAR
FLUID
CYTOPLASM
Plasma membrane
1 Reception
2 Transduction
Receptor
Relay molecules in a signal transduction pathway
Signaling
molecule

Fig. 11-6-3


EXTRACELLULAR FLUID
CYTOPLASM
Plasma membrane
1 Reception
2 Transduction
3 Response
Receptor
Activation of cellular response
Relay molecules in a signal transduction pathway
Signaling molecule

Concept 11.2: Reception: A signal molecule binds to a receptor protein, causing it to change shape

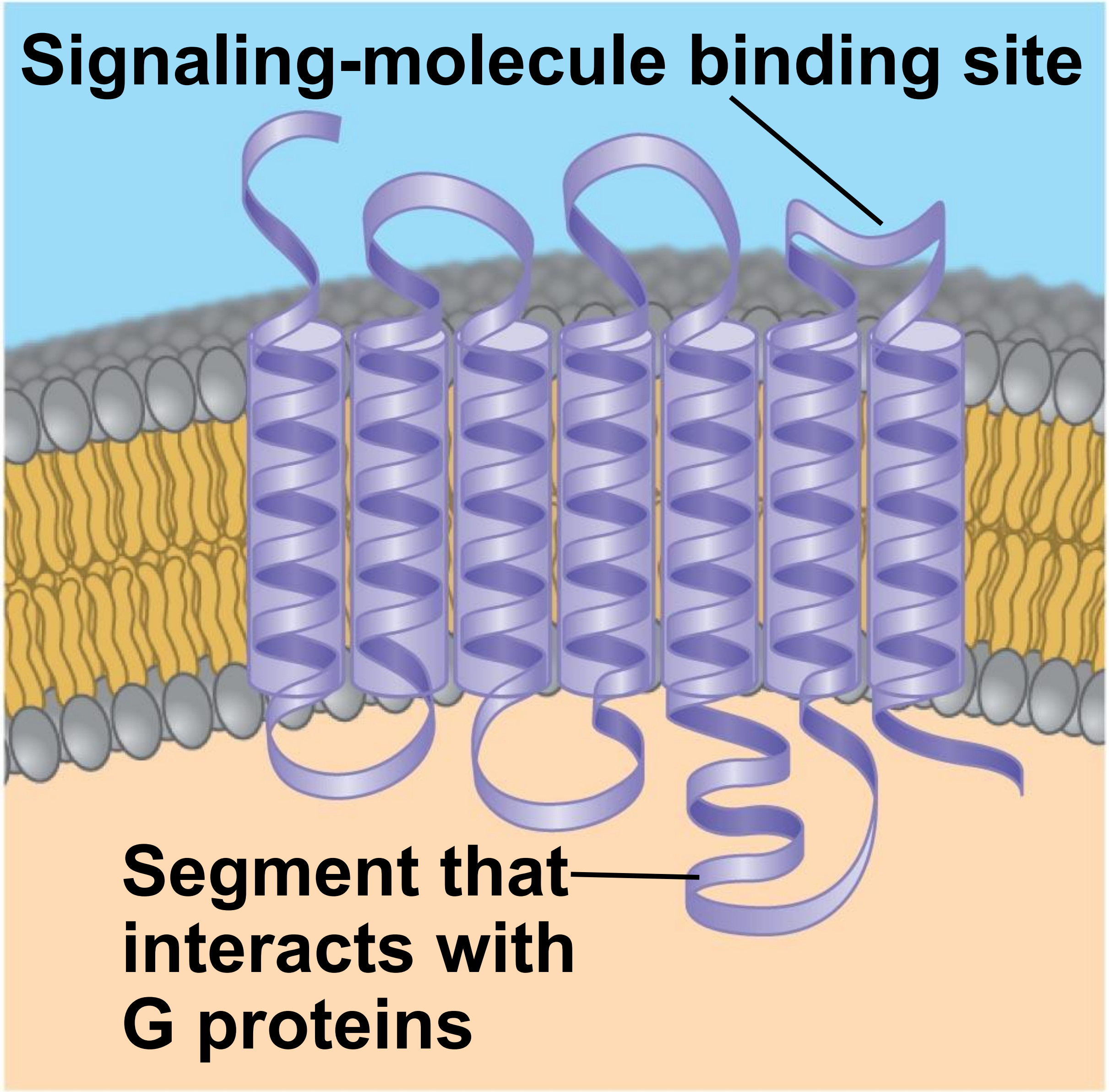
- The binding between a signal molecule (**ligand**) and receptor is highly specific
- A shape change in a receptor is often the initial transduction of the signal
- Most signal receptors are plasma membrane proteins

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-coupled receptors
  - Receptor tyrosine kinases
  - Ion channel receptors

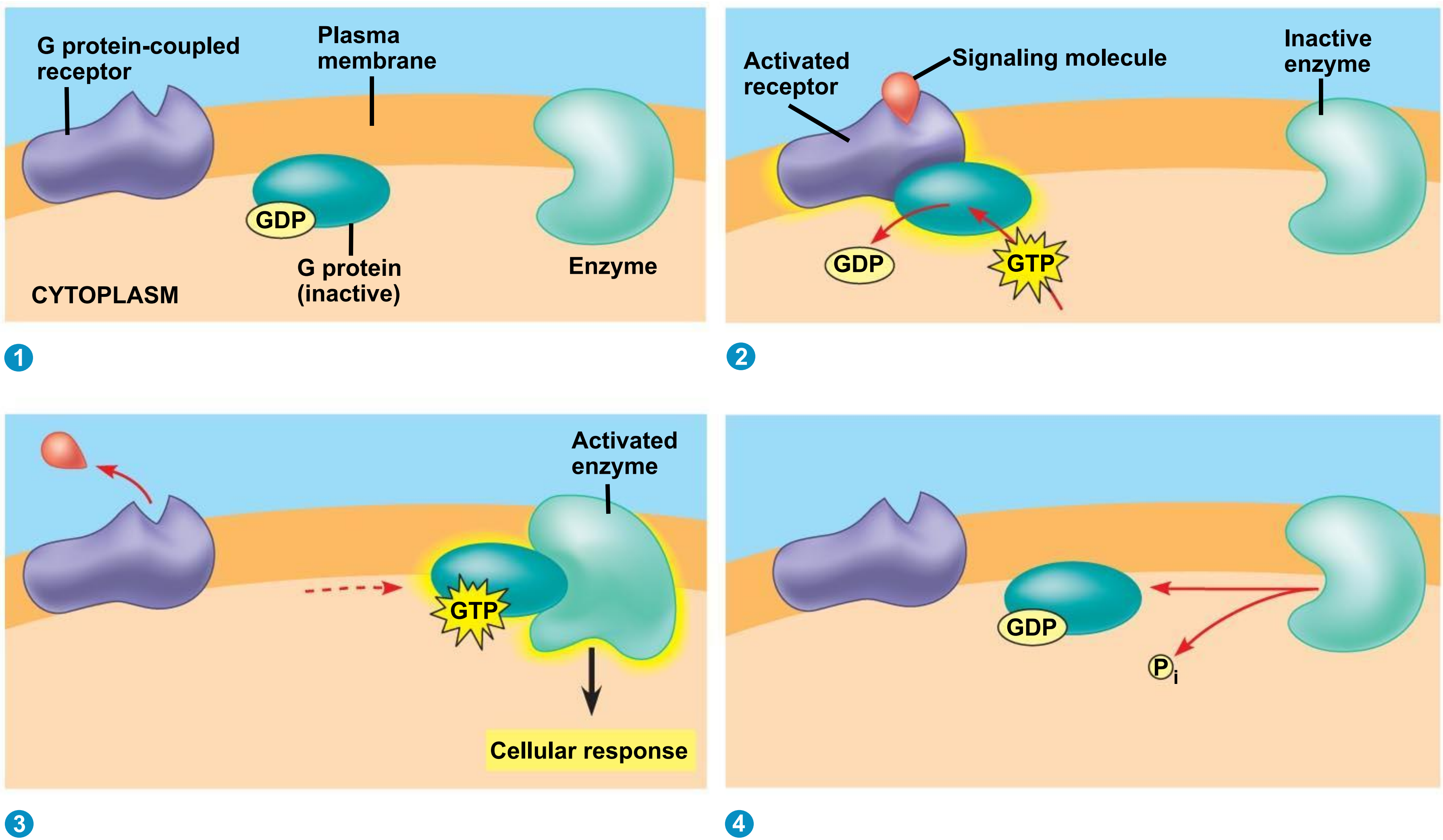
- A **G protein-coupled receptor** is a plasma membrane receptor that works with the help of a **G protein**
- The G protein acts as an on/off switch: If GDP is bound to the G protein, the G protein is inactive

Fig. 11-7a



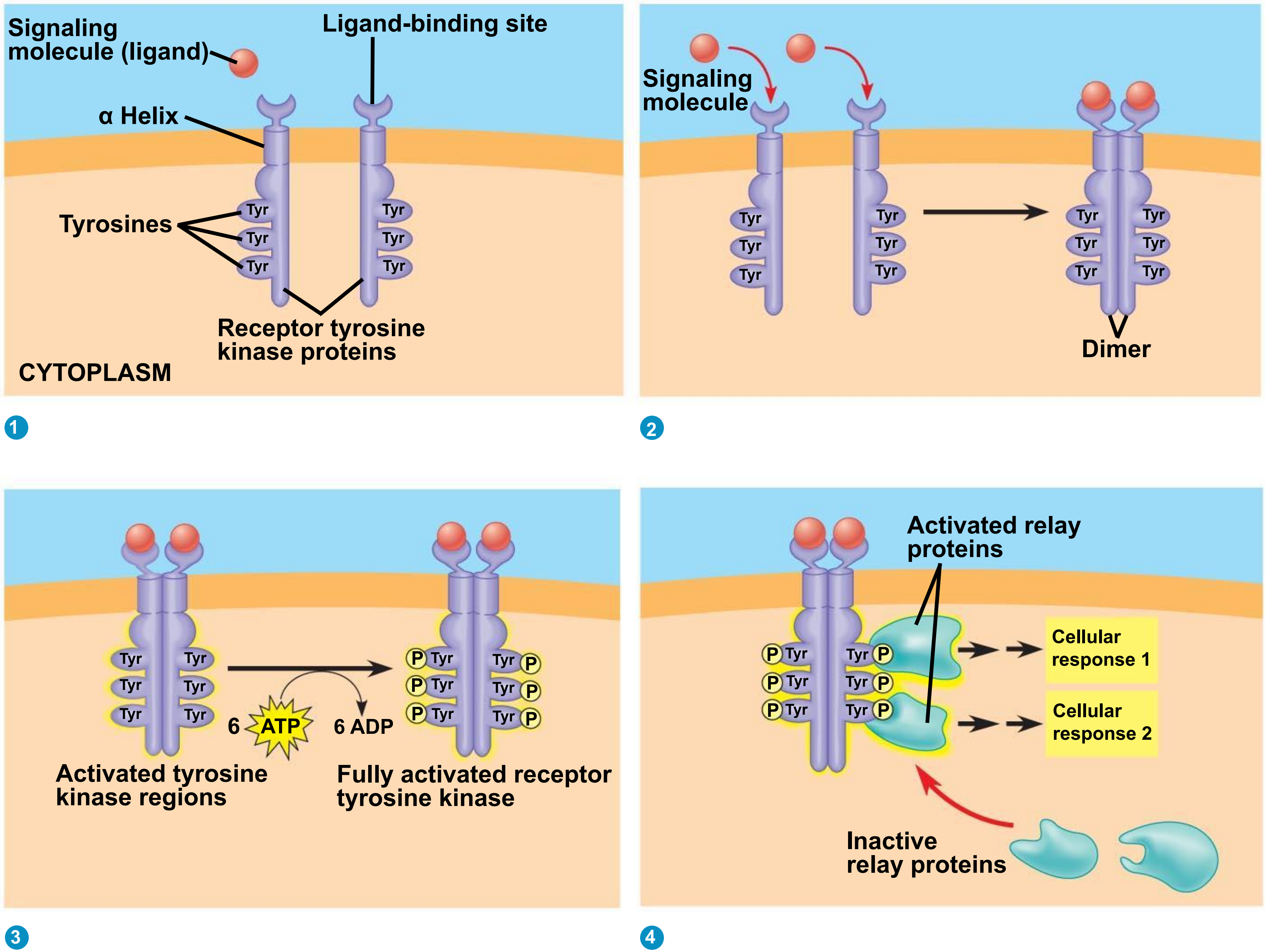
G protein-coupled receptor

Fig. 11-7b


G protein-coupled receptor
Plasma membrane
GDP
G protein (inactive)
Enzyme
CYTOPLASM
1
Activated receptor
Signaling molecule
Inactive enzyme
GDP
GTP
2
Activated enzyme
GTP
Cellular response
3
GDP
P i
4

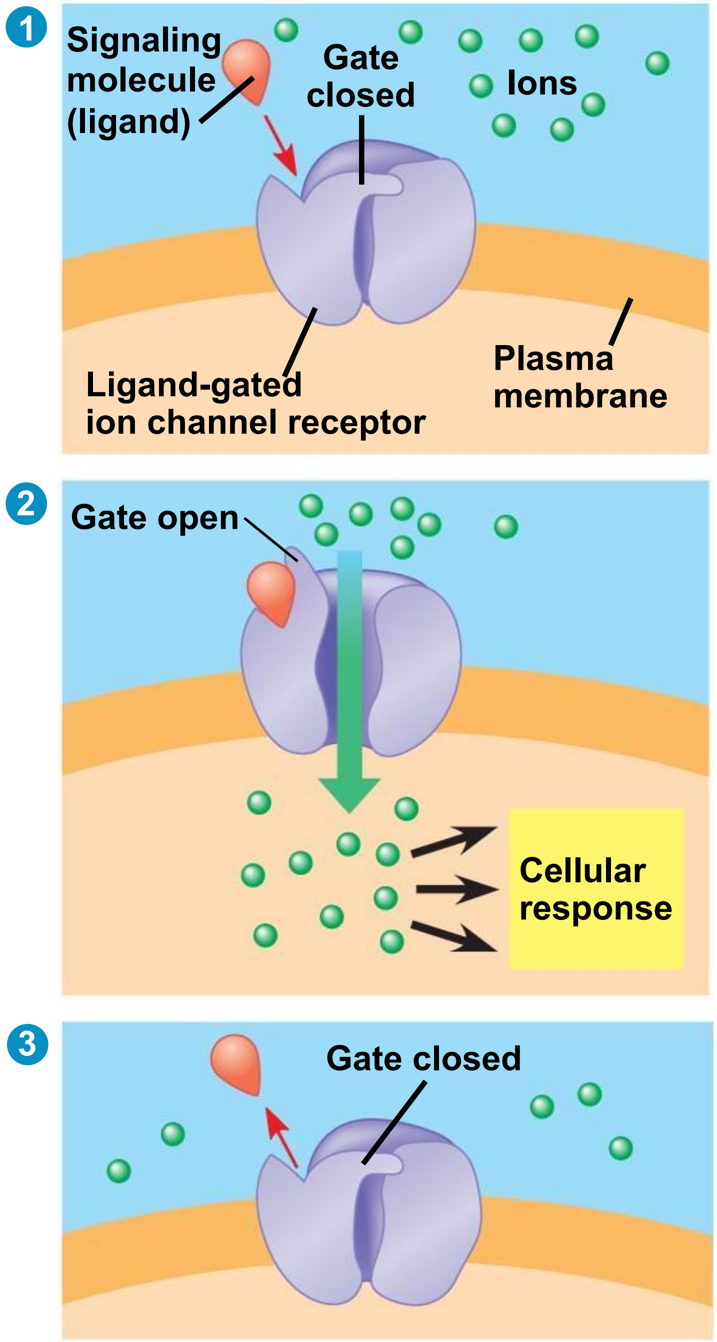
- **Receptor tyrosine kinases** are membrane receptors that attach phosphates to tyrosines
- A receptor tyrosine kinase can trigger multiple signal transduction pathways at once

Fig. 11-7c


Signaling molecule (ligand)
Ligand-binding site
α Helix
Tyrosines
Tyr
Receptor tyrosine kinase proteins
CYTOPLASM
1
Signaling molecule
Dimer
2
Activated tyrosine kinase regions
6 ATP
6 ADP
P
Fully activated receptor tyrosine kinase
3
Activated relay proteins
Cellular response 1
Cellular response 2
Inactive relay proteins
4

- 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

Fig. 11-7d


1
Signaling molecule (ligand)
Gate closed
Ions
Ligand-gated ion channel receptor
Plasma membrane
2
Gate open
Cellular response
3
Gate closed

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

Fig. 11-8-1

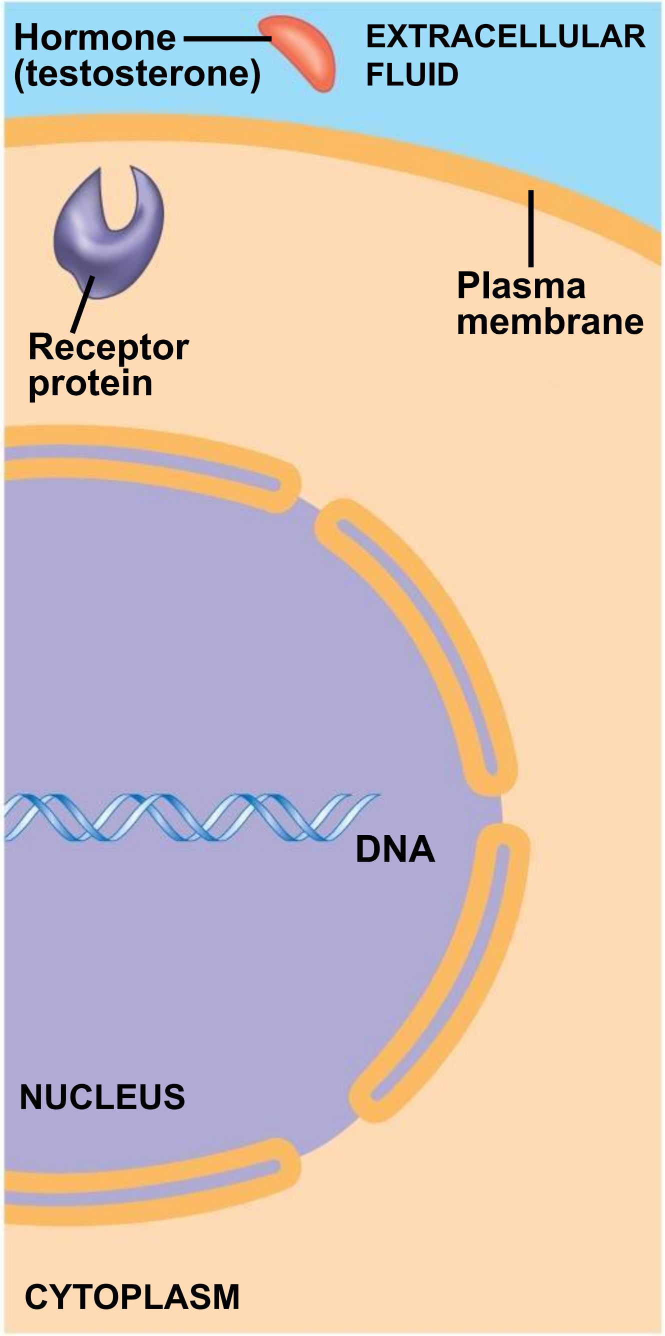

Hormone
(testosterone)
EXTRACELLULAR
FLUID
Receptor
protein
Plasma
membrane
DNA
NUCLEUS
CYTOPLASM

Fig. 11-8-2

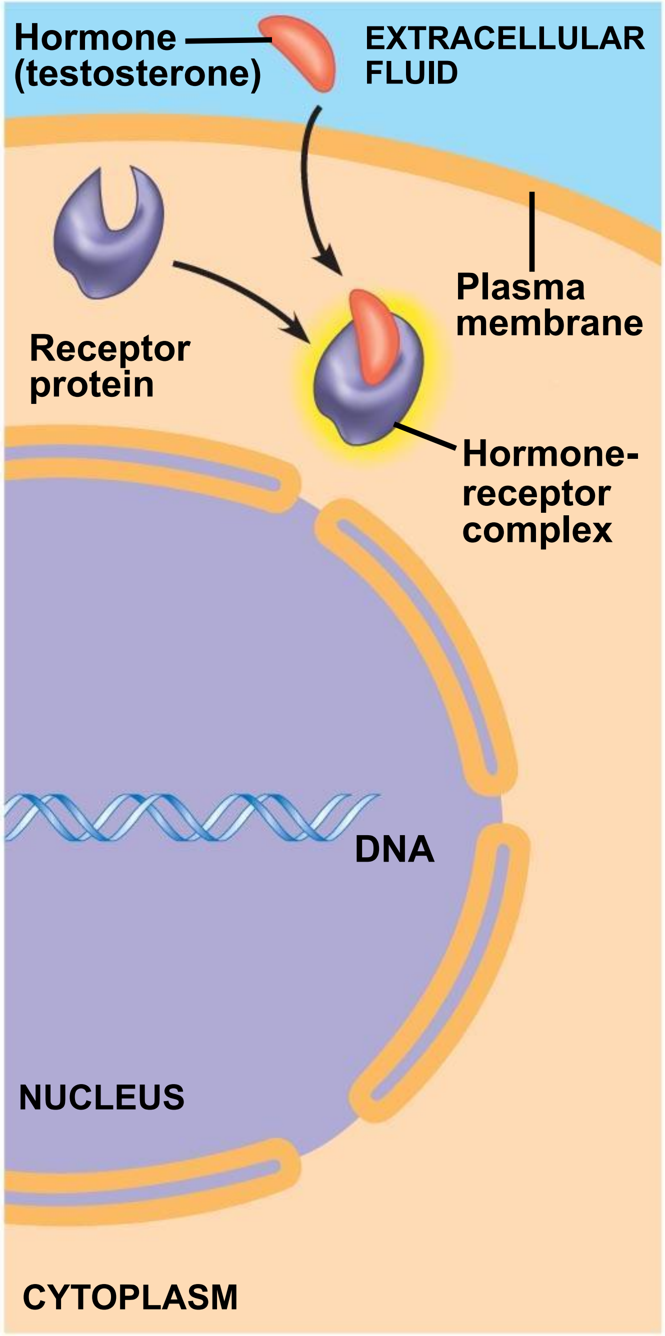
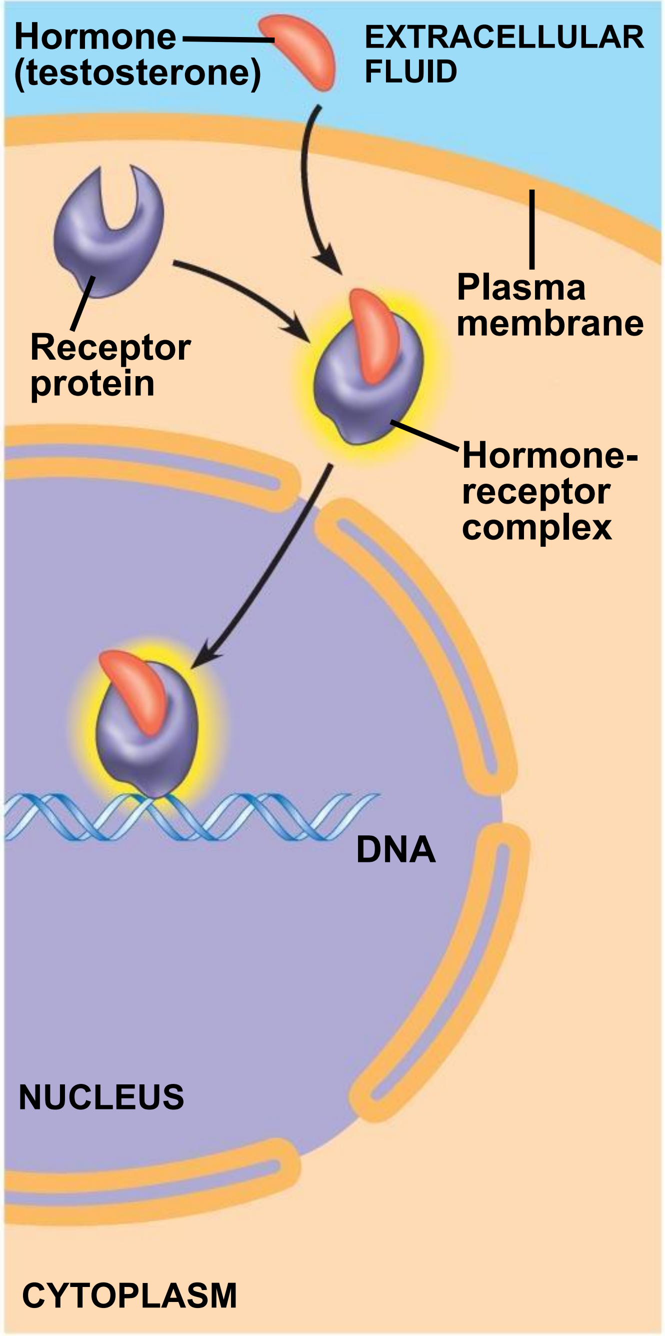
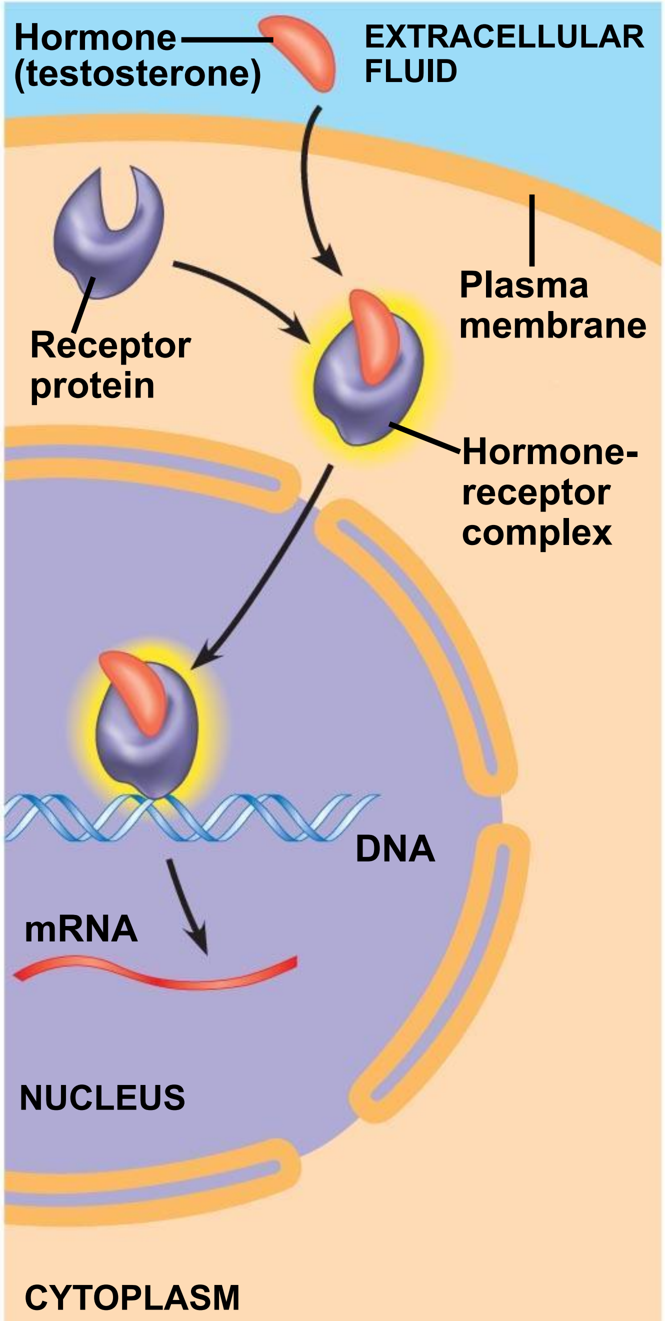

Hormone
(testosterone)
EXTRACELLULAR
FLUID
Receptor
protein
Plasma
membrane
Hormone-
receptor
complex
DNA
NUCLEUS
CYTOPLASM

Fig. 11-8-3



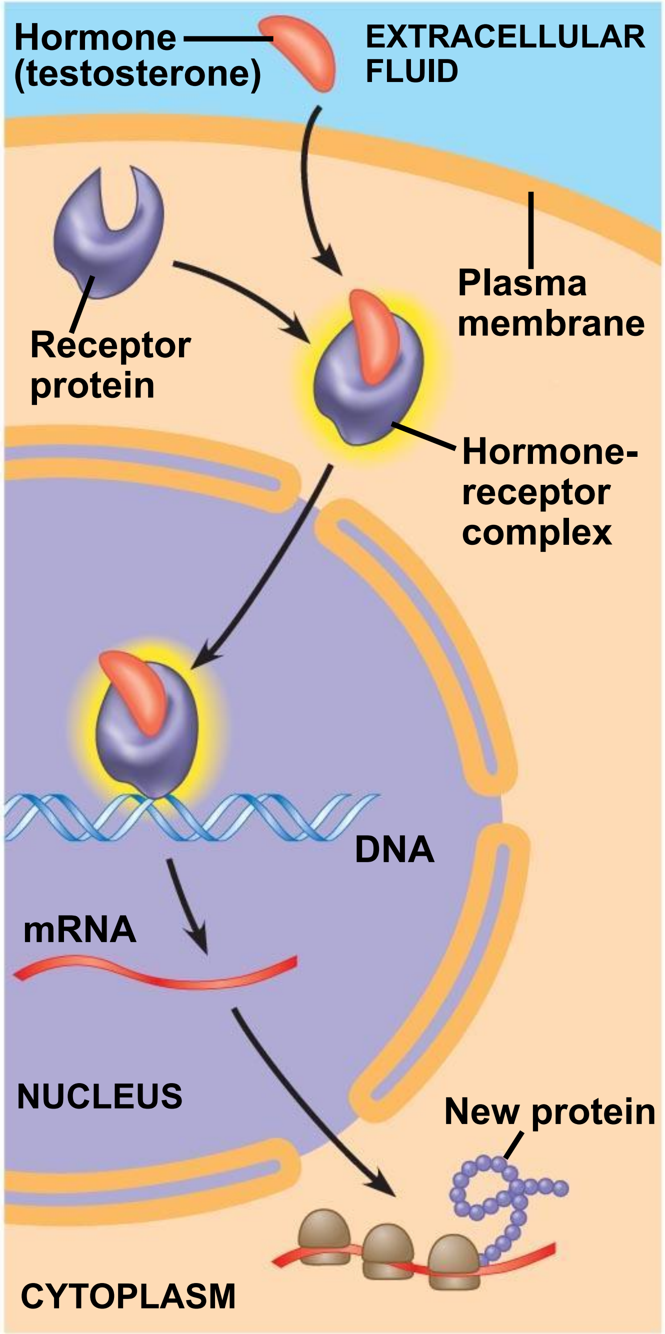
Hormone
(testosterone)
EXTRACELLULAR
FLUID
Receptor
protein
Plasma
membrane
Hormone-
receptor
complex
DNA
NUCLEUS
CYTOPLASM

Fig. 11-8-4



Hormone
(testosterone)
EXTRACELLULAR
FLUID
Receptor
protein
Plasma
membrane
Hormone-
receptor
complex
DNA
mRNA
NUCLEUS
CYTOPLASM

Fig. 11-8-5



Hormone
(testosterone)
EXTRACELLULAR
FLUID
Plasma
membrane
Receptor
protein
Hormone-
receptor
complex
DNA
mRNA
NUCLEUS
New protein
CYTOPLASM

Concept 11.3: Transduction: Cascades of molecular interactions relay signals from receptors to target molecules in the cell

- Signal 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 of the cellular response

Signal Transduction Pathways

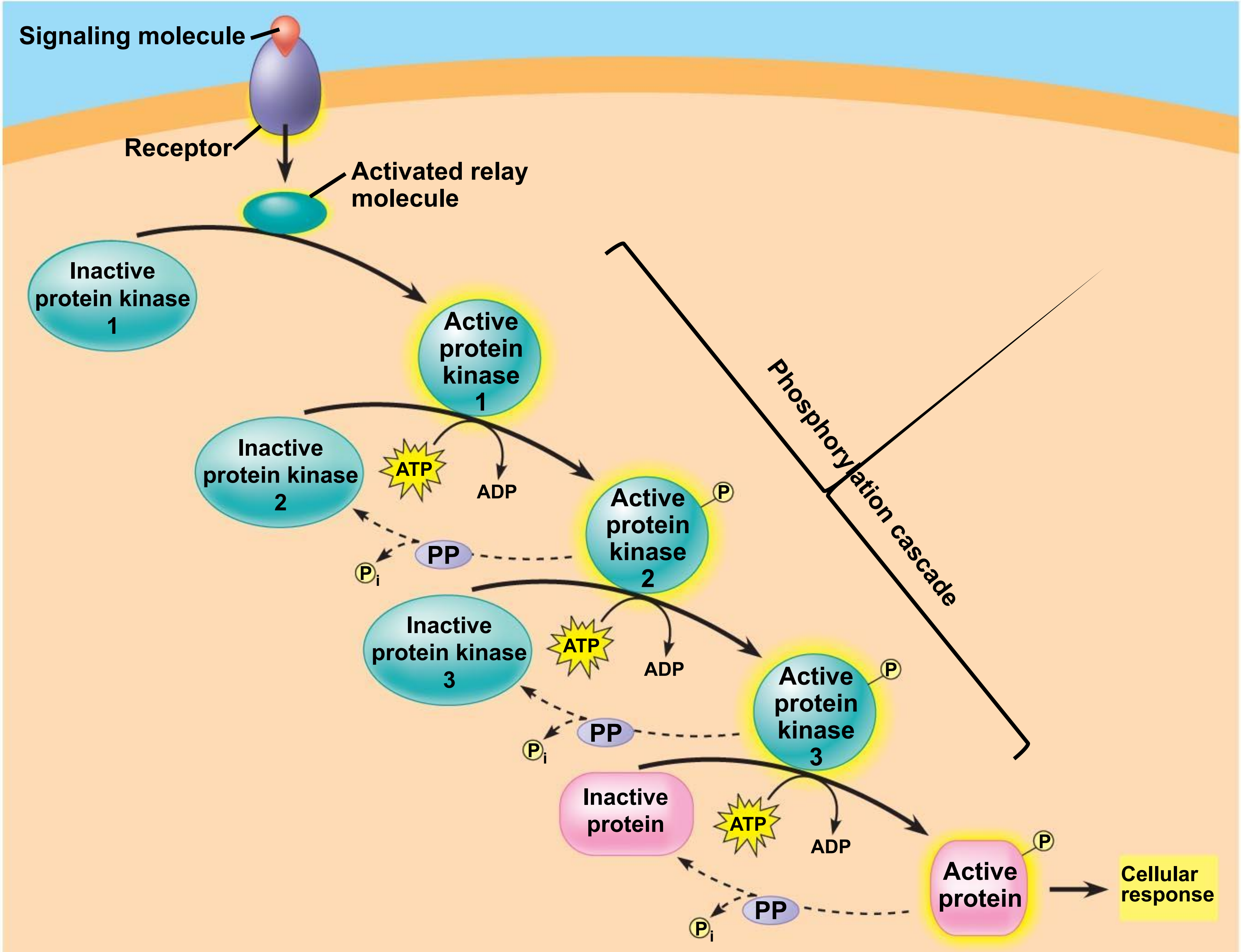
- The molecules that relay a signal from receptor to response are mostly proteins
- Like falling dominoes, the receptor activates another protein, which activates another, and so on, until the protein producing the response is activated
- At each step, the signal is transduced into a different form,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

Protein Phosphorylation and Dephosphorylation

- In many pathways, the signal is transmitted by a cascade of protein phosphorylations
- **Protein kinases** transfer phosphates from ATP to protein, a process called phosphorylation

- **Protein phosphatases** remove the phosphates from proteins, a process called dephosphorylation
- This phosphorylation and dephosphorylation system acts as a molecular switch, turning activities on and off

Fig. 11-9



Signaling molecule
Receptor
Activated relay molecule
Inactive protein kinase 1
Active protein kinase 1
Inactive protein kinase 2
ATP
ADP
Active protein kinase 2
P
PP
Pi
Inactive protein kinase 3
ATP
ADP
Active protein kinase 3
P
PP
Pi
Inactive protein
ATP
ADP
Active protein
P
PP
Pi
Cellular response
Phosphorylation cascade

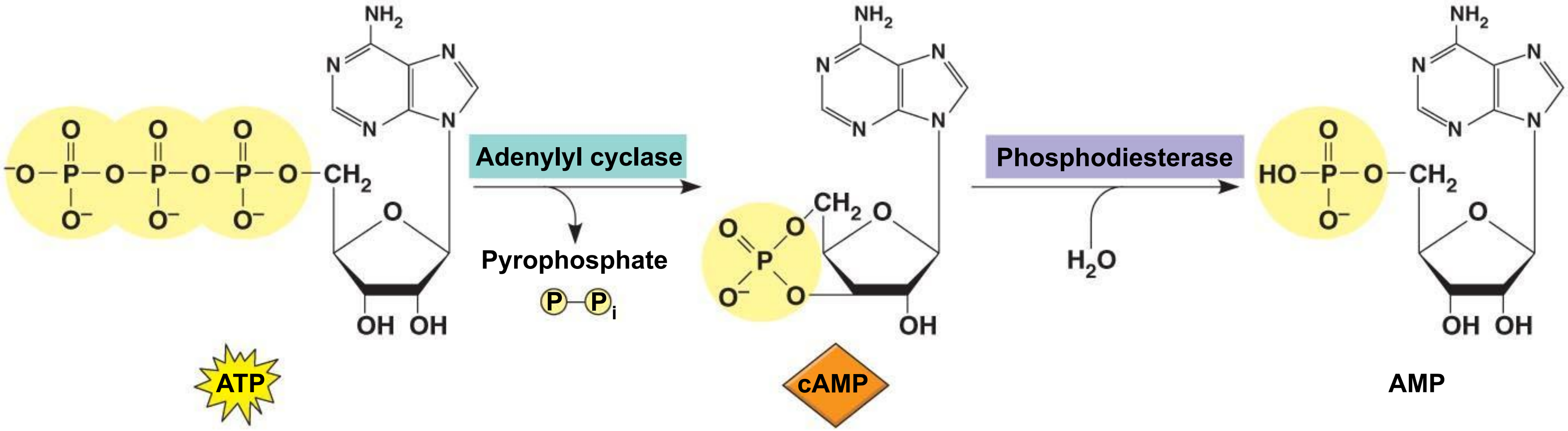
Small Molecules and Ions as Second Messengers

- The extracellular signal molecule 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 G protein-coupled receptors and receptor tyrosine kinases
- Cyclic AMP and calcium ions are common second messengers

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

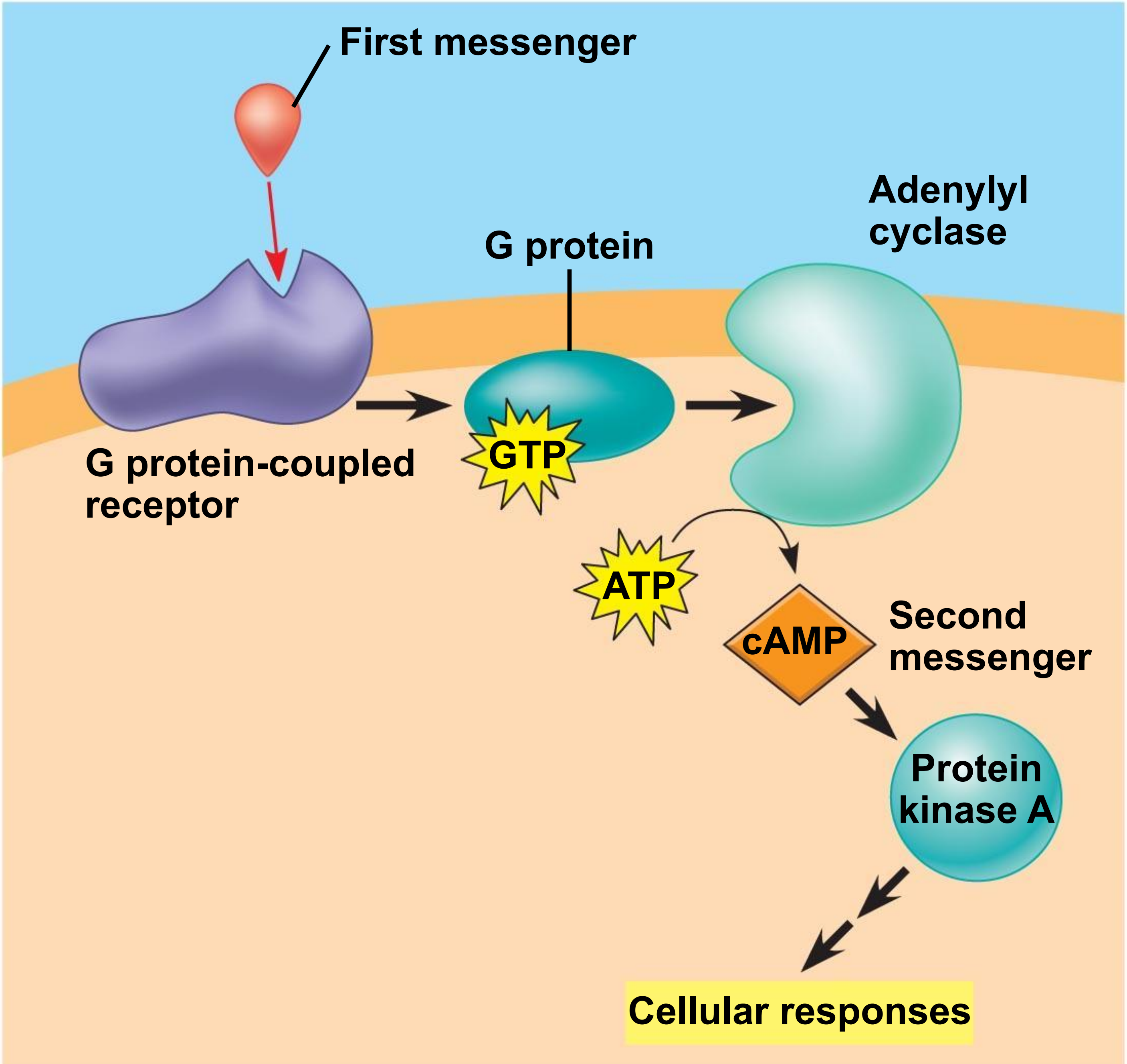
Fig. 11-10



NH2
N
N
N
N
O
O
O
-O
P
O
P
O
P
O
CH2
O-
O-
O-
O
OH
OH
ATP
Adenylyl cyclase
Pyrophosphate
P
P
i
CH2
O
O
P
O-
O
OH
cAMP
Phosphodiesterase
H2O
HO
P
O
CH2
AMP

- 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

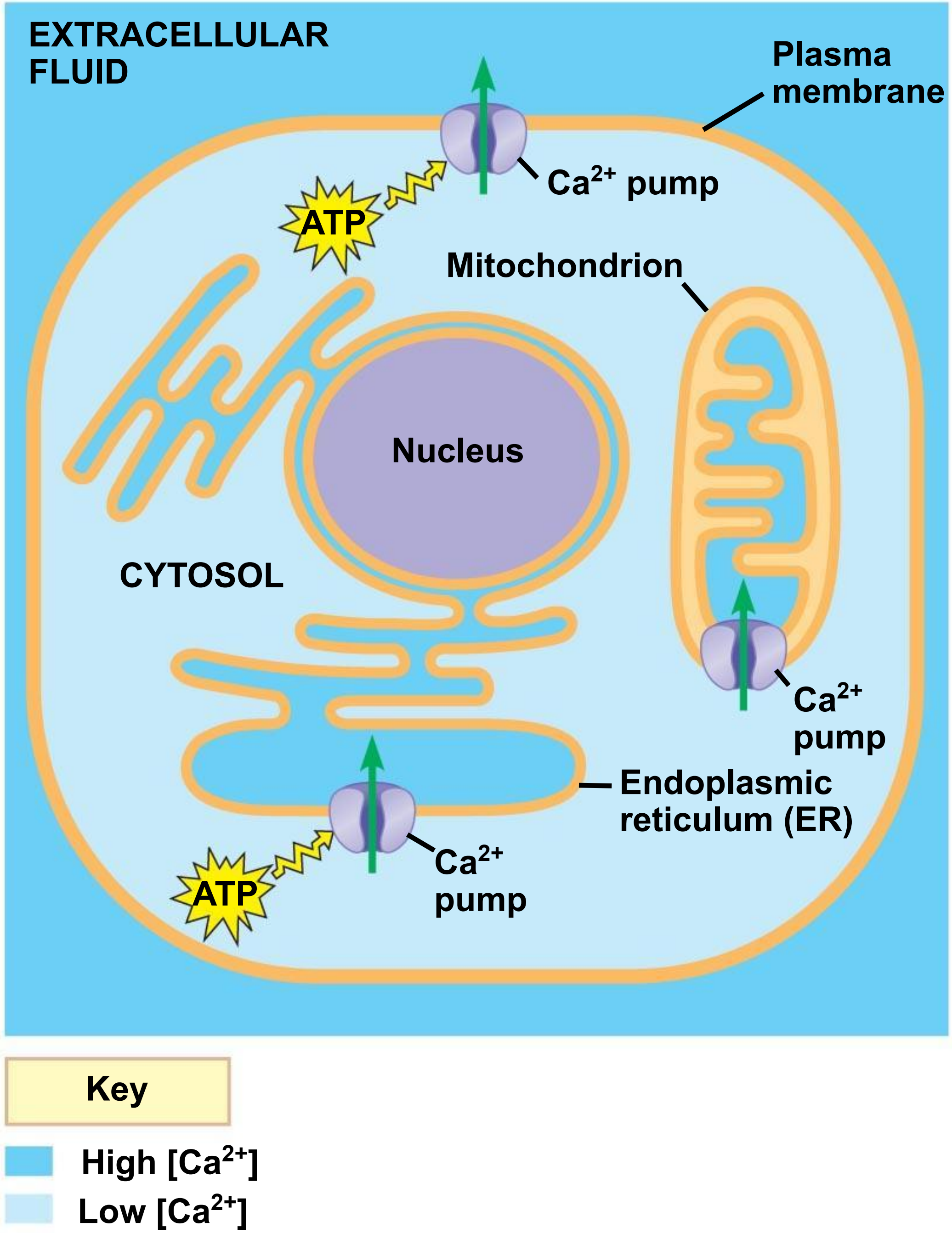
Fig. 11-11


First messenger
G protein
Adenylyl cyclase
G protein-coupled receptor
GTP
ATP
cAMP
Second messenger
Protein kinase A
Cellular responses

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

Fig. 11-12

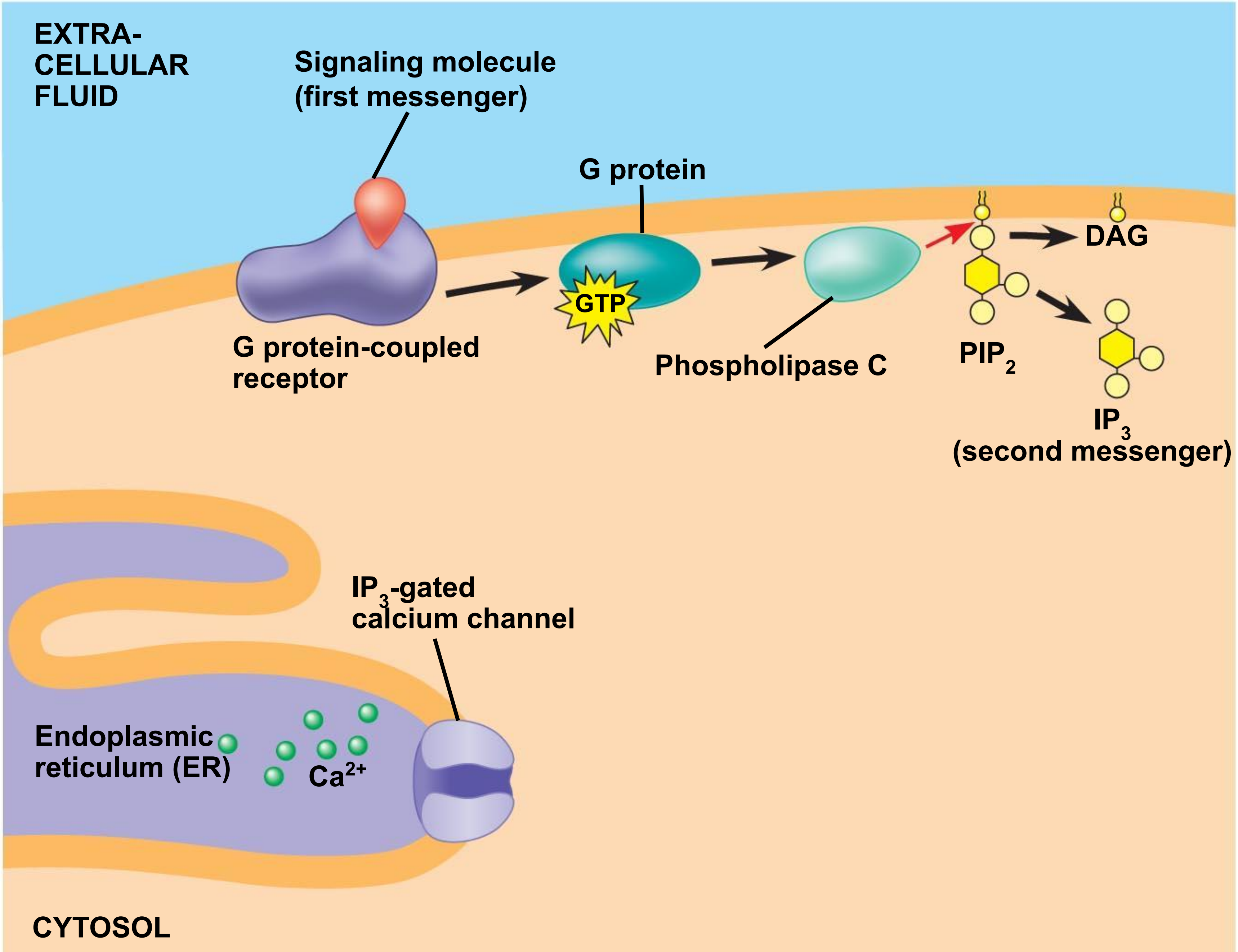


EXTRACELLULAR FLUID
Plasma membrane
Ca2+ pump
ATP
Mitochondrion
Nucleus
CYTOSOL
Ca2+ pump
Endoplasmic reticulum (ER)
Ca2+ pump
ATP
Key
High [Ca2+]
Low [Ca2+]

- 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 additional second messengers

PLAY Animation: Signal Transduction Pathways

Fig. 11-13-1



EXTRA-
CELLULAR
FLUID
Signaling molecule
(first messenger)
G protein
GTP
DAG
G protein-coupled
receptor
Phospholipase C
PIP2
IP3
(second messenger)
IP3-gated
calcium channel
Endoplasmic
reticulum (ER)
Ca2+
CYTOSOL

Fig. 11-13-2

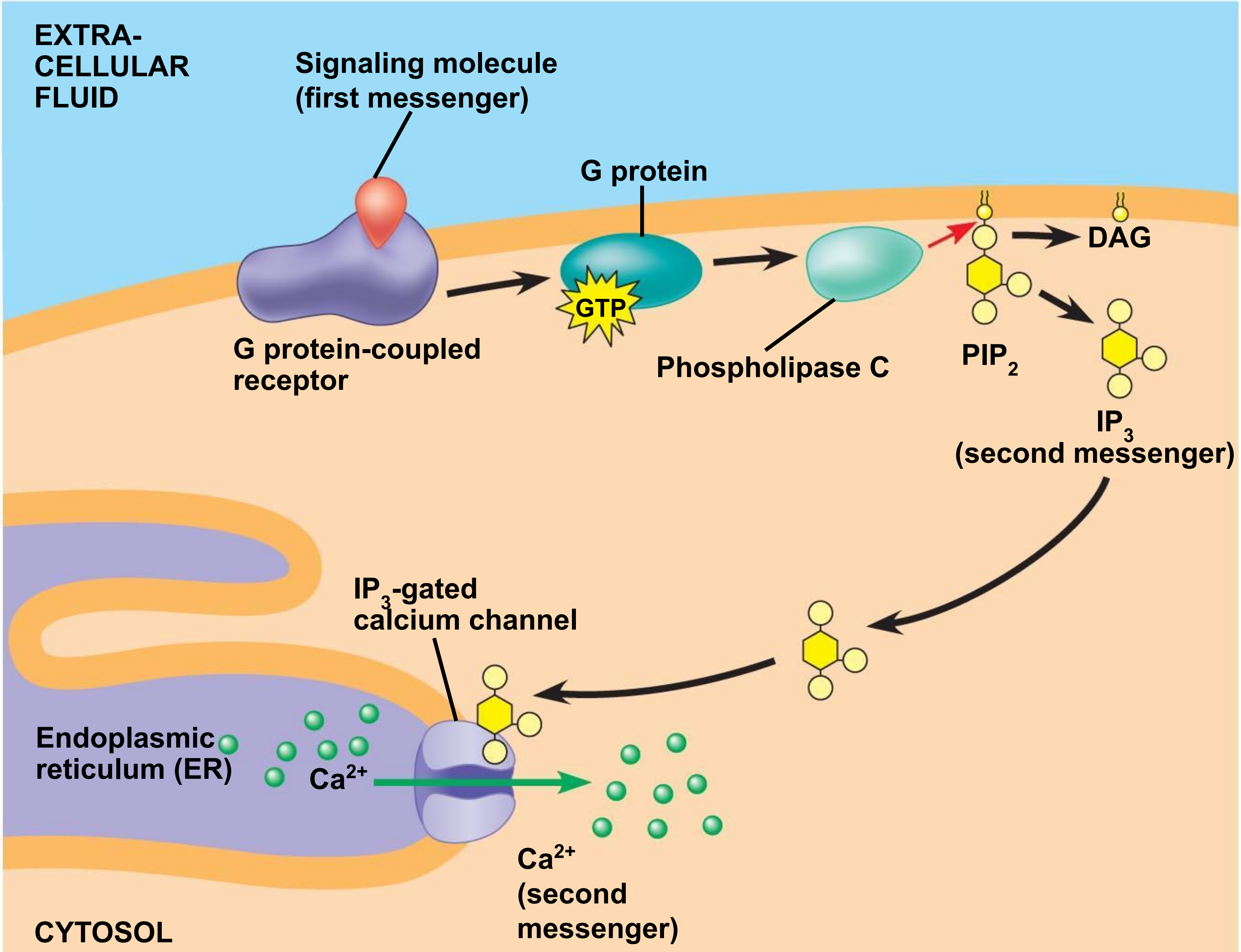
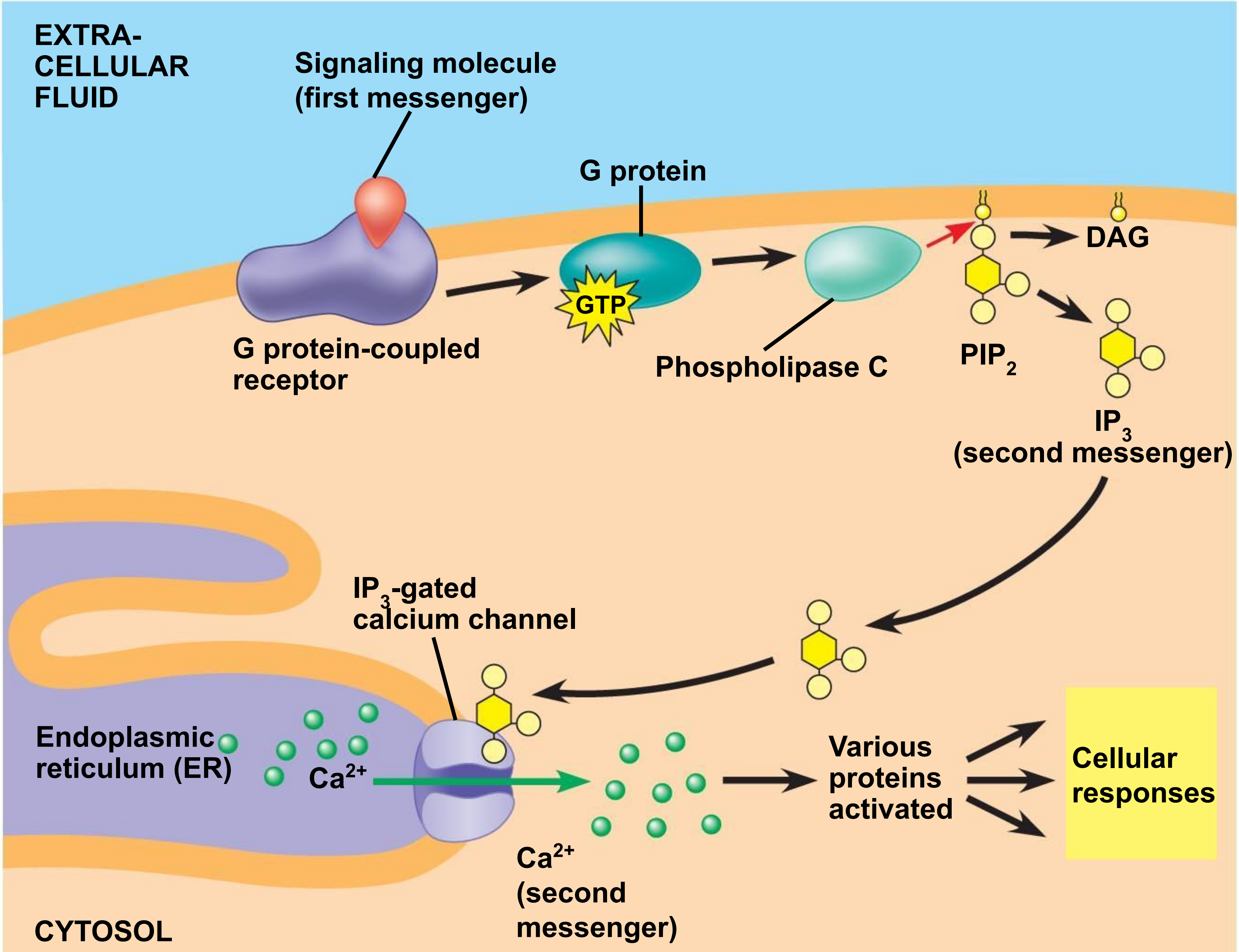

EXTRA-
CELLULAR
FLUID
Signaling molecule
(first messenger)
G protein
GTP
DAG
G protein-coupled
receptor
Phospholipase C
PIP$_2$
IP$_3$
(second messenger)
IP$_3$-gated
calcium channel
Endoplasmic
reticulum (ER)
Ca^{2+}
Ca^{2+}
(second
messenger)
CYTOSOL

Fig. 11-13-3


EXTRA-
CELLULAR
FLUID
Signaling molecule
(first messenger)
G protein
GTP
DAG
G protein-coupled
receptor
Phospholipase C
PIP$_2$
IP$_3$
(second messenger)
IP$_3$-gated
calcium channel
Endoplasmic
reticulum (ER)
Ca^{2+}
Various
proteins
activated
Cellular
responses
Ca^{2+}
(second
messenger)
CYTOSOL

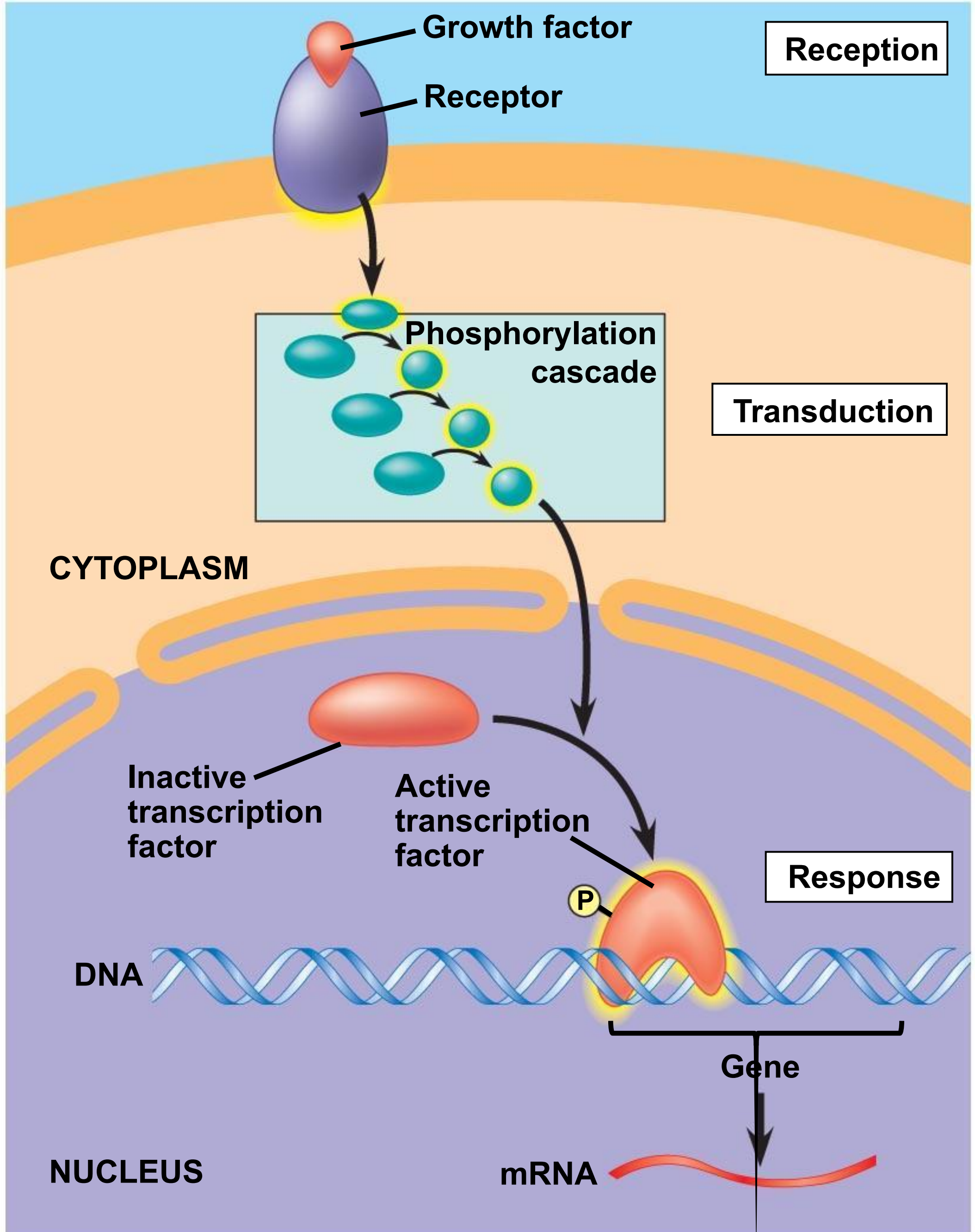
Concept 11.4: Response: Cell signaling leads to regulation of transcription or cytoplasmic activities

- The cell's response to an extracellular signal is sometimes called the "output response"

Nuclear and Cytoplasmic Responses

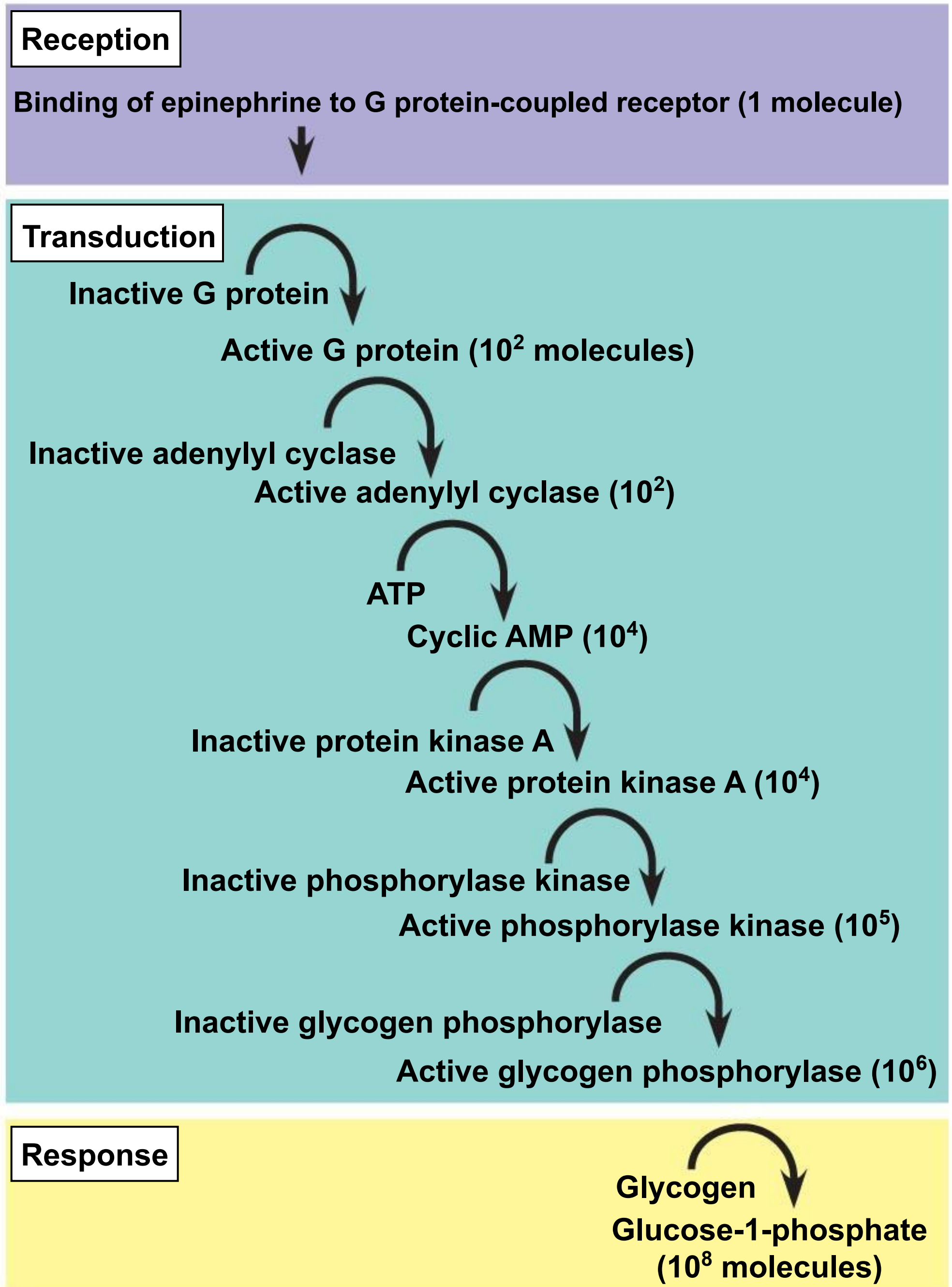
- Ultimately, a signal transduction pathway leads to regulation of one or more cellular activities
- The response may occur in the cytoplasm or may involve action in the nucleus
- Many signaling pathways regulate the *synthesis* of enzymes or other proteins, usually by turning genes on or off in the nucleus
- The final activated molecule may function as a transcription factor

Fig. 11-14


Growth factor
Receptor
Reception
Phosphorylation cascade
Transduction
CYTOPLASM
Inactive transcription factor
Active transcription factor
P
Response
DNA
Gene
NUCLEUS
mRNA

- Other pathways regulate the *activity* of enzymes

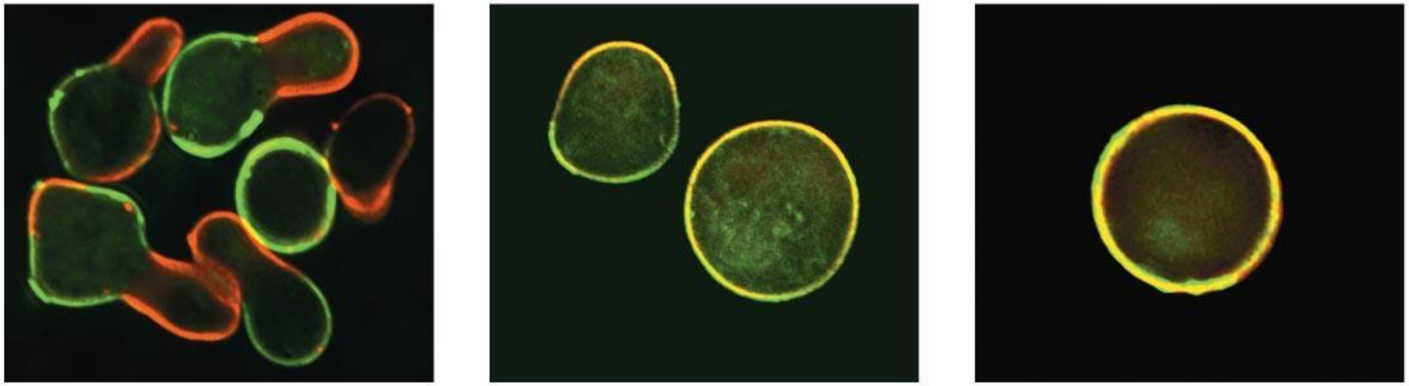
Fig. 11-15


Reception
Binding of epinephrine to G protein-coupled receptor (1 molecule)
Transduction
Inactive G protein
Active G protein (10^2 molecules)
Inactive adenylyl cyclase
Active adenylyl cyclase (10^2)
ATP
Cyclic AMP (10^4)
Inactive protein kinase A
Active protein kinase A (10^4)
Inactive phosphorylase kinase
Active phosphorylase kinase (10^5)
Inactive glycogen phosphorylase
Active glycogen phosphorylase (10^6)
Response
Glycogen
Glucose-1-phosphate
(10^8 molecules)

- Signaling pathways can also affect the physical characteristics of a cell, for example, cell shape

Fig. 11-16

RESULTS



Wild-type (shmoos) ∆Fus3 ∆formin

CONCLUSION

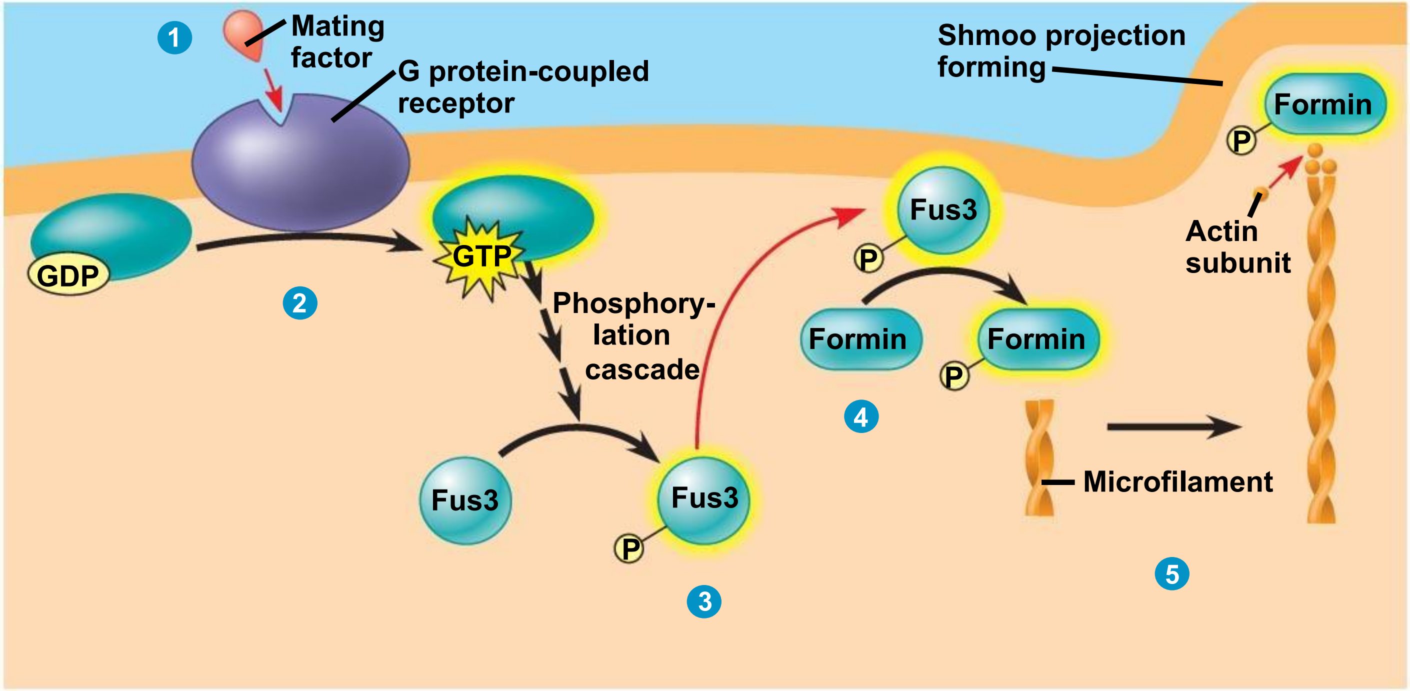
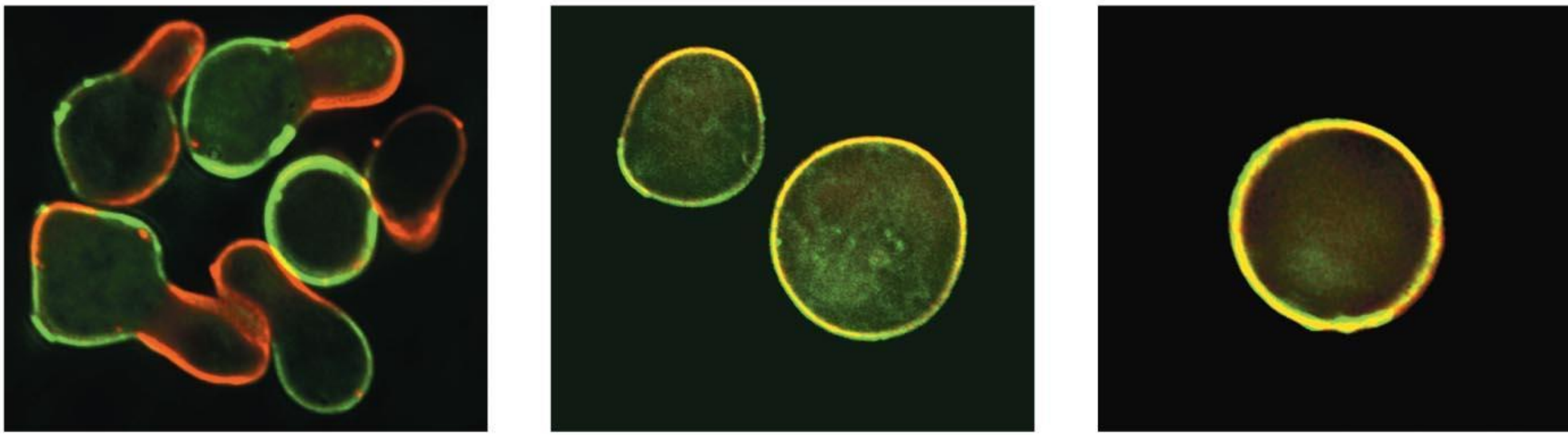


Fig. 11-16a

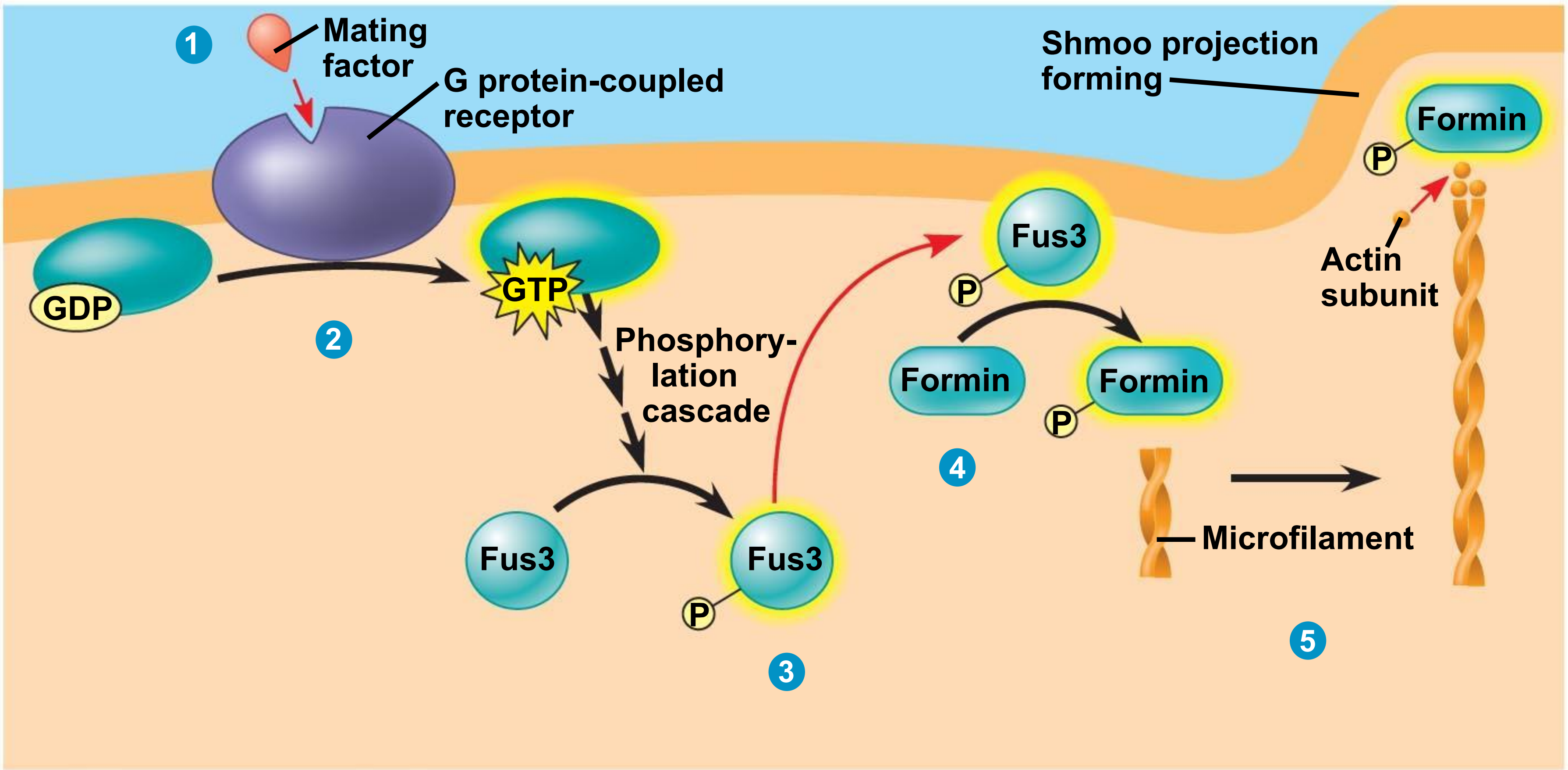
RESULTS



Wild-type (shmoos) **ΔFus3** **Δformin**

Fig. 11-16b

CONCLUSION



Fine-Tuning of the Response

- Multistep pathways have two important benefits:
  - Amplifying the signal (and thus the response)
  - Contributing to the specificity of the response

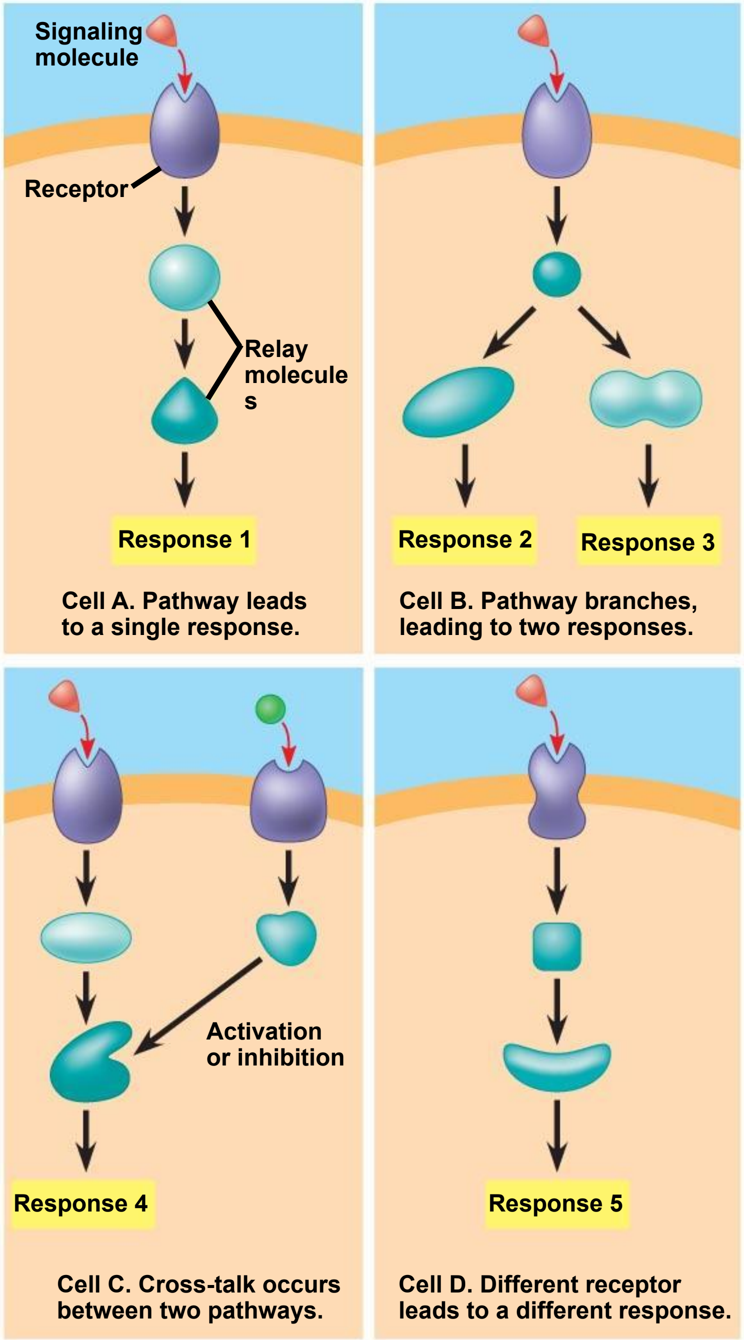
Signal Amplification

- 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 and Coordination of the Response

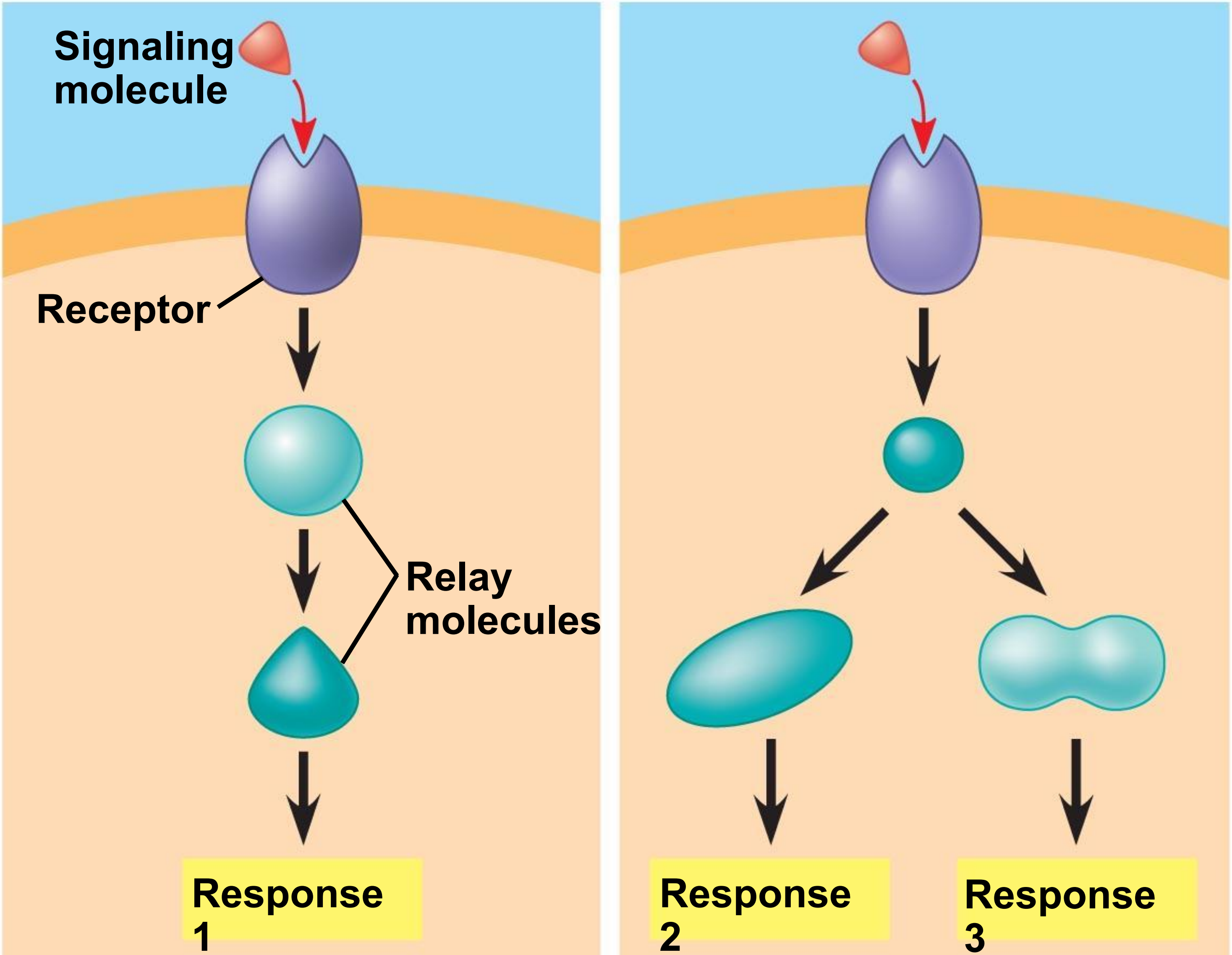
- Different kinds of cells have different collections of proteins
- These different proteins allow cells to detect and respond to different signals
- Even the same signal can have different effects in cells with different proteins and pathways
- Pathway branching and "cross-talk" further help the cell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

Fig. 11-17



Signaling molecule
Receptor
Relay molecule
s
Response 1
Cell A. Pathway leads to a single response.
Response 2
Response 3
Cell B. Pathway branches, leading to two responses.
Activation or inhibition
Response 4
Cell C. Cross-talk occurs between two pathways.
Response 5
Cell D. Different receptor leads to a different response.

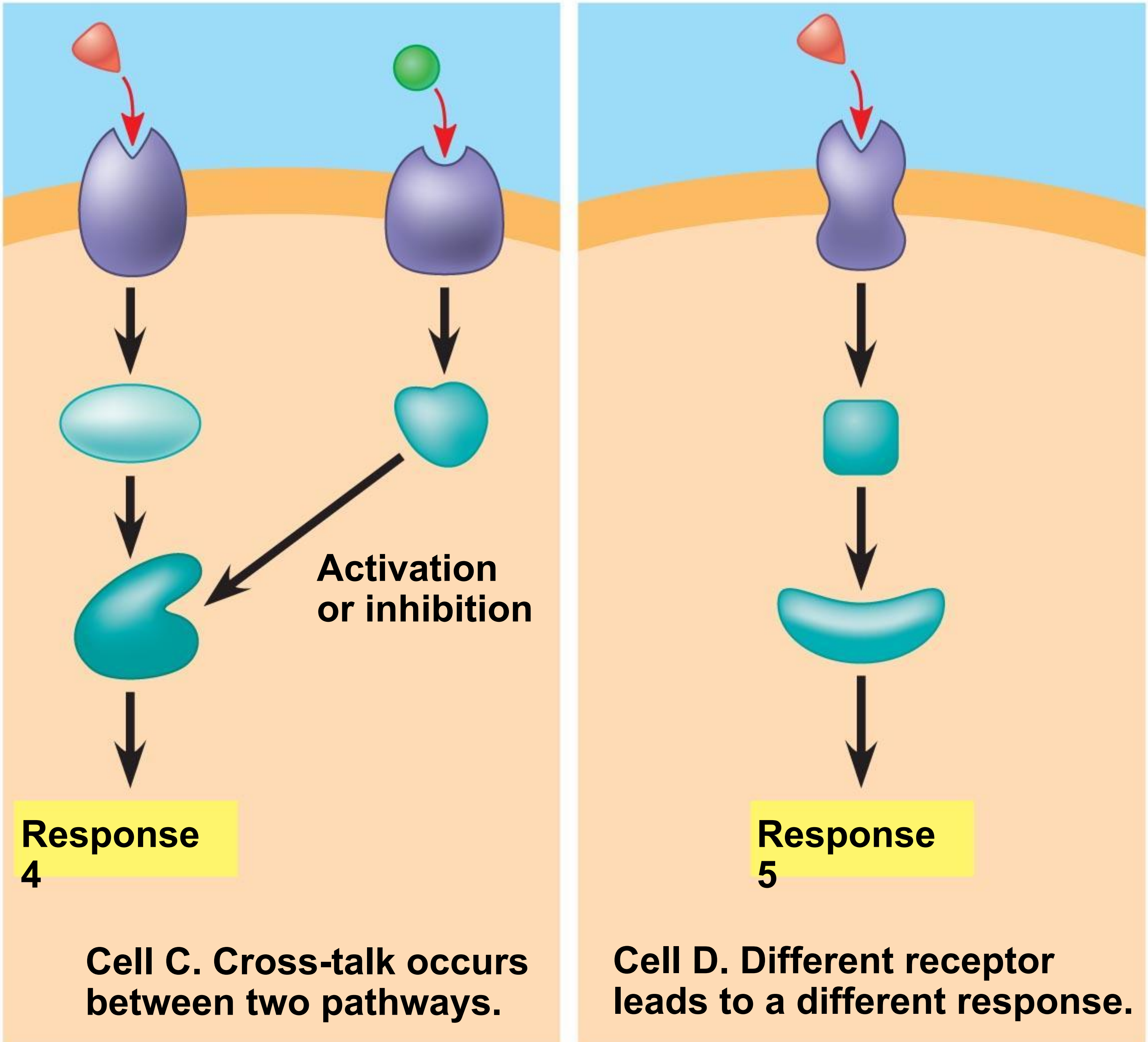
Fig. 11-17a



Cell A. Pathway leads to a single response.

Cell B. Pathway branches, leading to two responses.

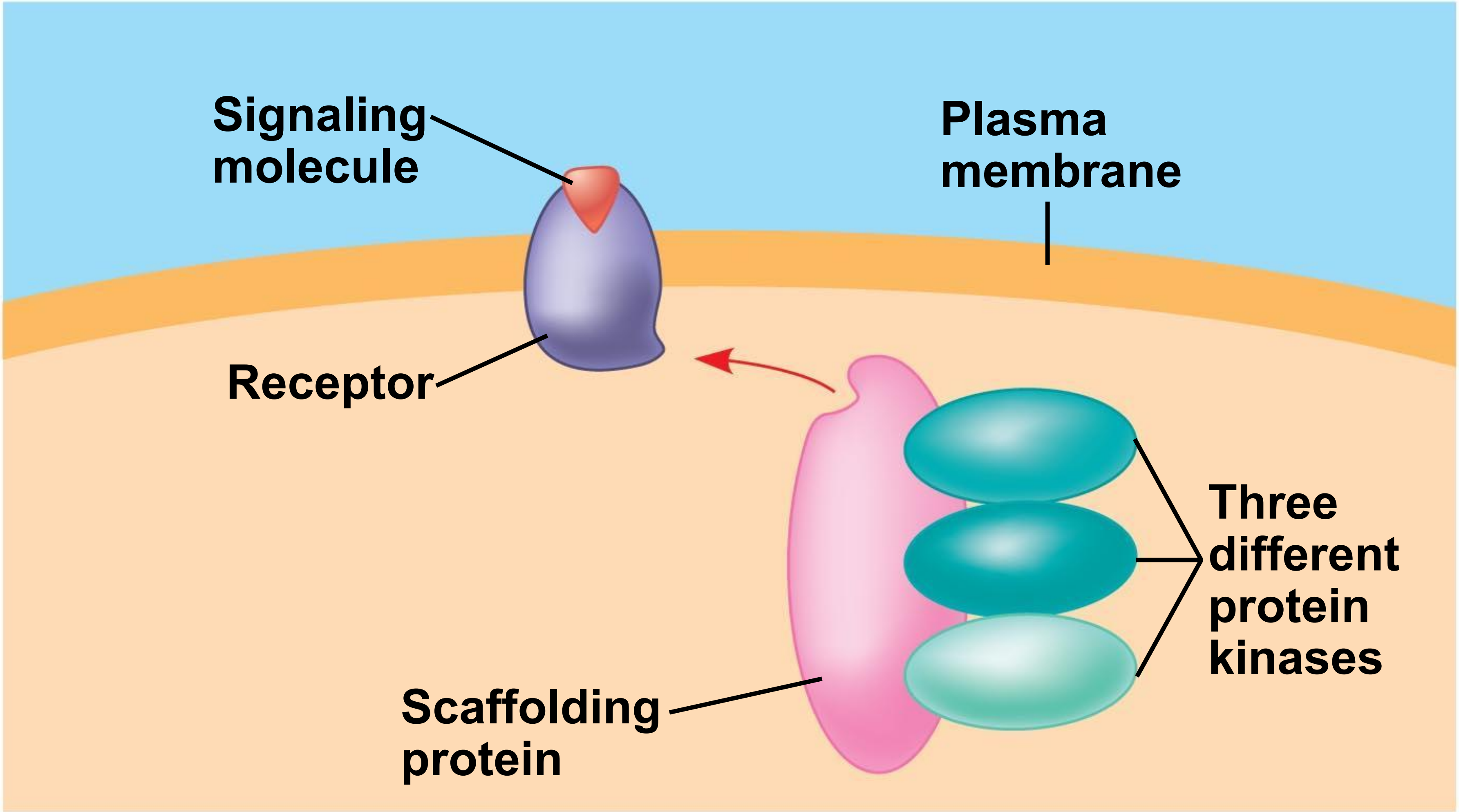
Fig. 11-17b


Activation
or inhibition
Response
4
Response
5
Cell C. Cross-talk occurs
between two pathways.
Cell D. Different receptor
leads to a different response.

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

Fig. 11-18


Signaling molecule
Plasma membrane
Receptor
Three different protein kinases
Scaffolding protein

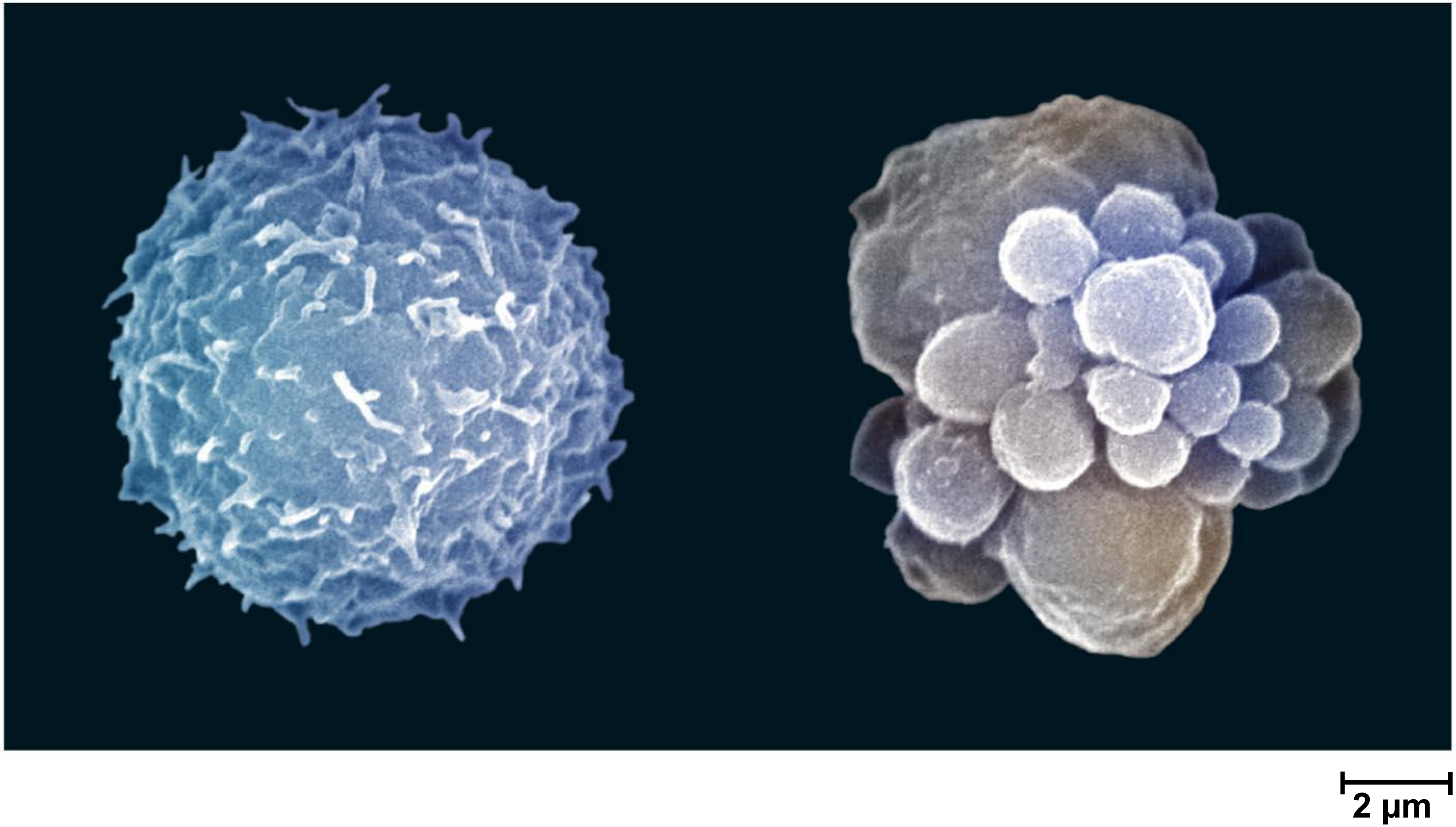
Termination of the Signal

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

Concept 11.5: Apoptosis (programmed cell death) integrates multiple cell-signaling pathways

- **Apoptosis** is programmed or controlled cell suicide
- A cell is chopped and packaged into vesicles that are digested by scavenger cells
- Apoptosis prevents enzymes from leaking out of a dying cell and damaging neighboring cells

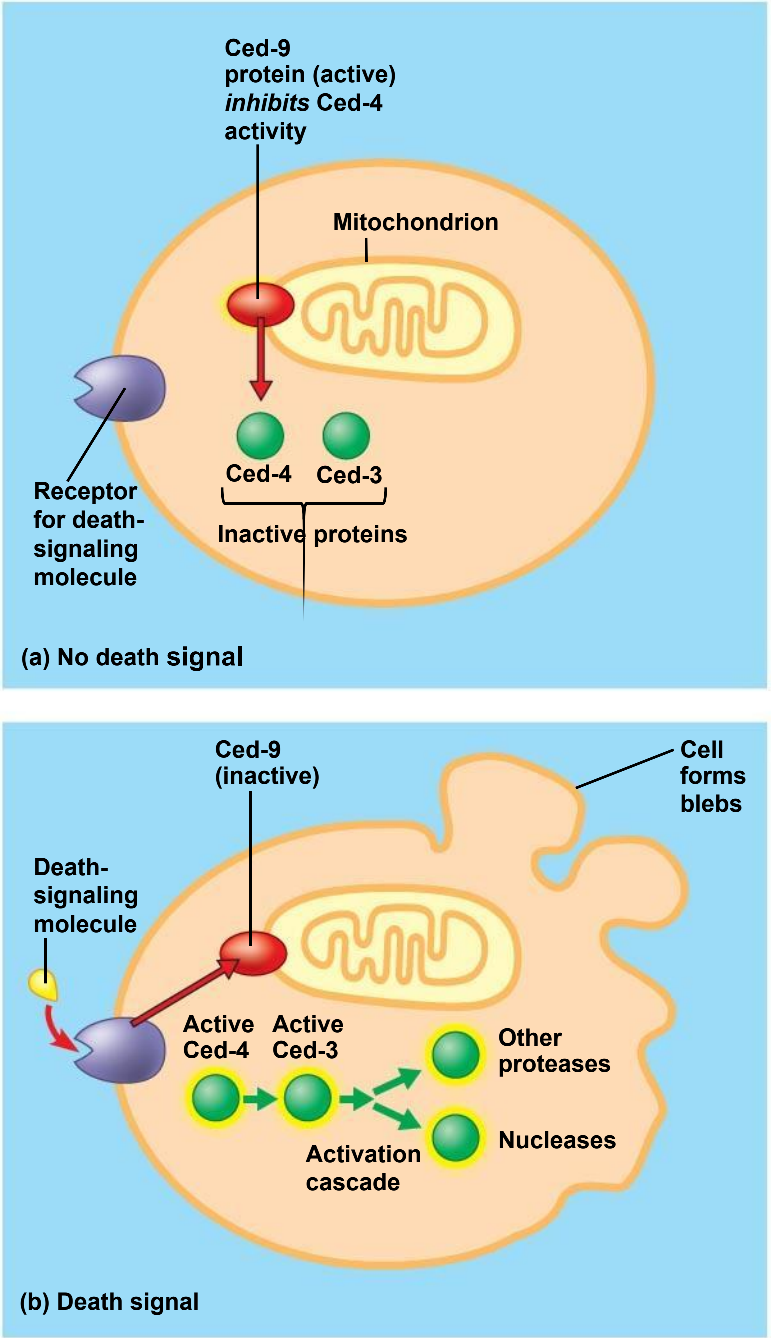
Fig. 11-19



Apoptosis in the Soil Worm *Caenorhabditis elegans*

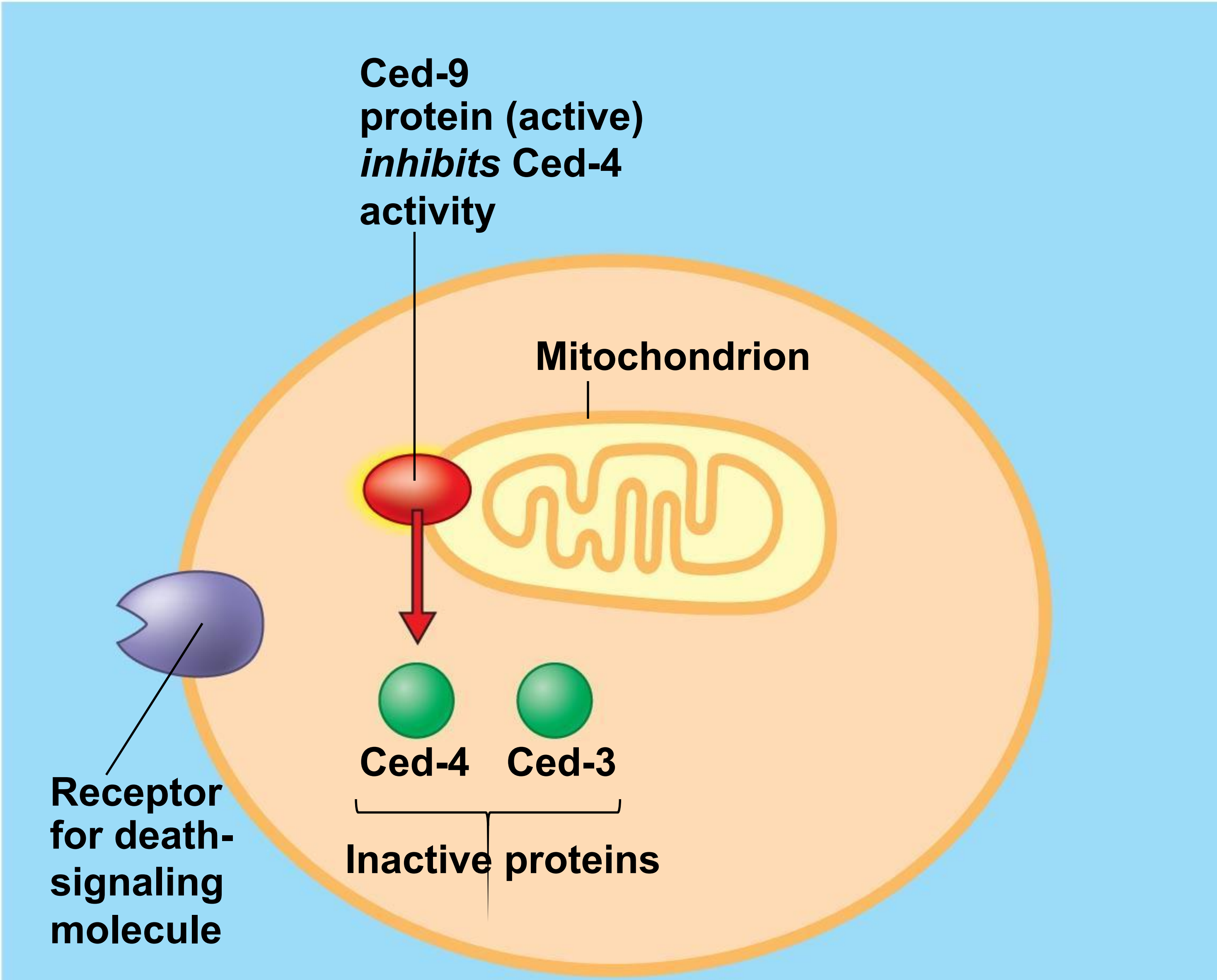
- Apoptosis is important in shaping an organism during embryonic development
- The role of apoptosis in embryonic development was first studied in *Caenorhabditis elegans*
- In *C. elegans*, apoptosis results when specific proteins that “accelerate” apoptosis override those that “put the brakes” on apoptosis

Fig. 11-20



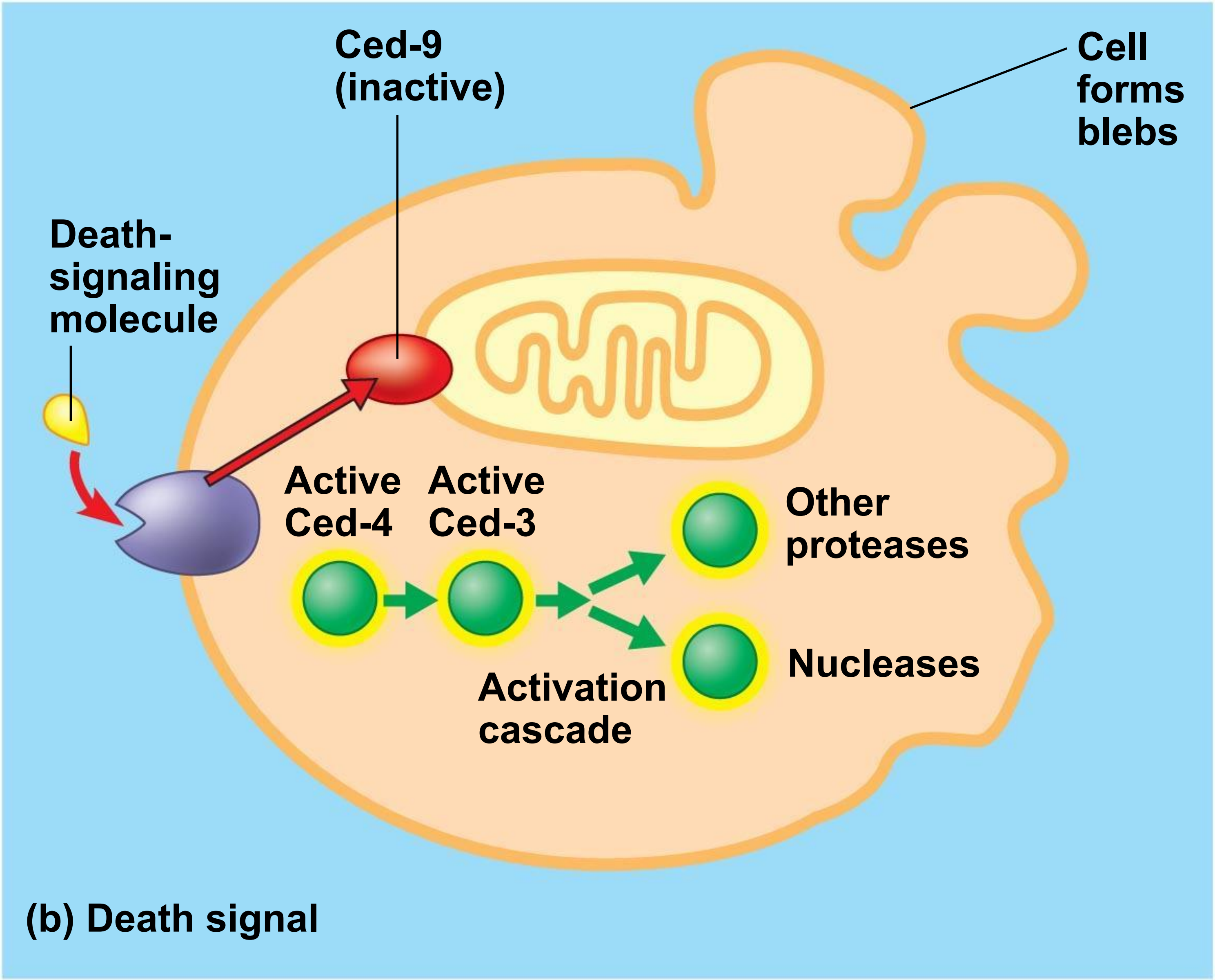
Ced-9
protein (active)
inhibits Ced-4
activity
Mitochondrion
Receptor
for death-
signaling
molecule
Ced-4
Ced-3
Inactive proteins
(a) No death signal
Ced-9
(inactive)
Cell
forms
blebs
Death-
signaling
molecule
Active
Ced-4
Active
Ced-3
Other
proteases
Nucleases
Activation
cascade
(b) Death signal

Fig. 11-20a



(a) No death signal

Fig. 11-20b


Ced-9
(inactive)
Cell
forms
blebs
Death-
signaling
molecule
Active
Ced-4
Active
Ced-3
Other
proteases
Nucleases
Activation
cascade
(b) Death signal

Apoptotic Pathways and the Signals That Trigger Them

- Caspases are the main proteases (enzymes that cut up proteins) that carry out apoptosis
- Apoptosis can be triggered by:
  - An extracellular death-signaling ligand
  - DNA damage in the nucleus
  - Protein misfolding in the endoplasmic reticulum

- Apoptosis evolved early in animal evolution and is essential for the development and maintenance of all animals
- Apoptosis may be involved in some diseases (for example, Parkinson’s and Alzheimer’s); interference with apoptosis may contribute to some cancers

Fig. 11-21

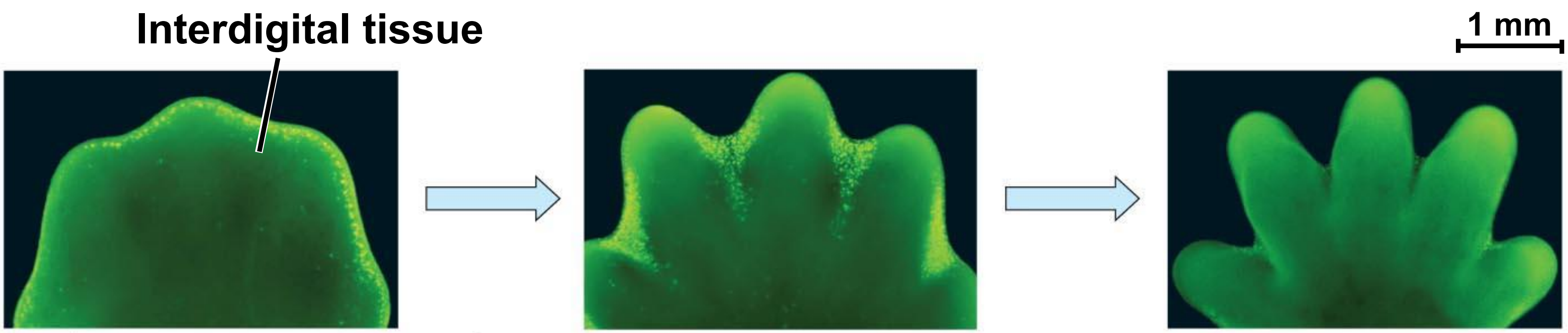


Fig. 11-UN1

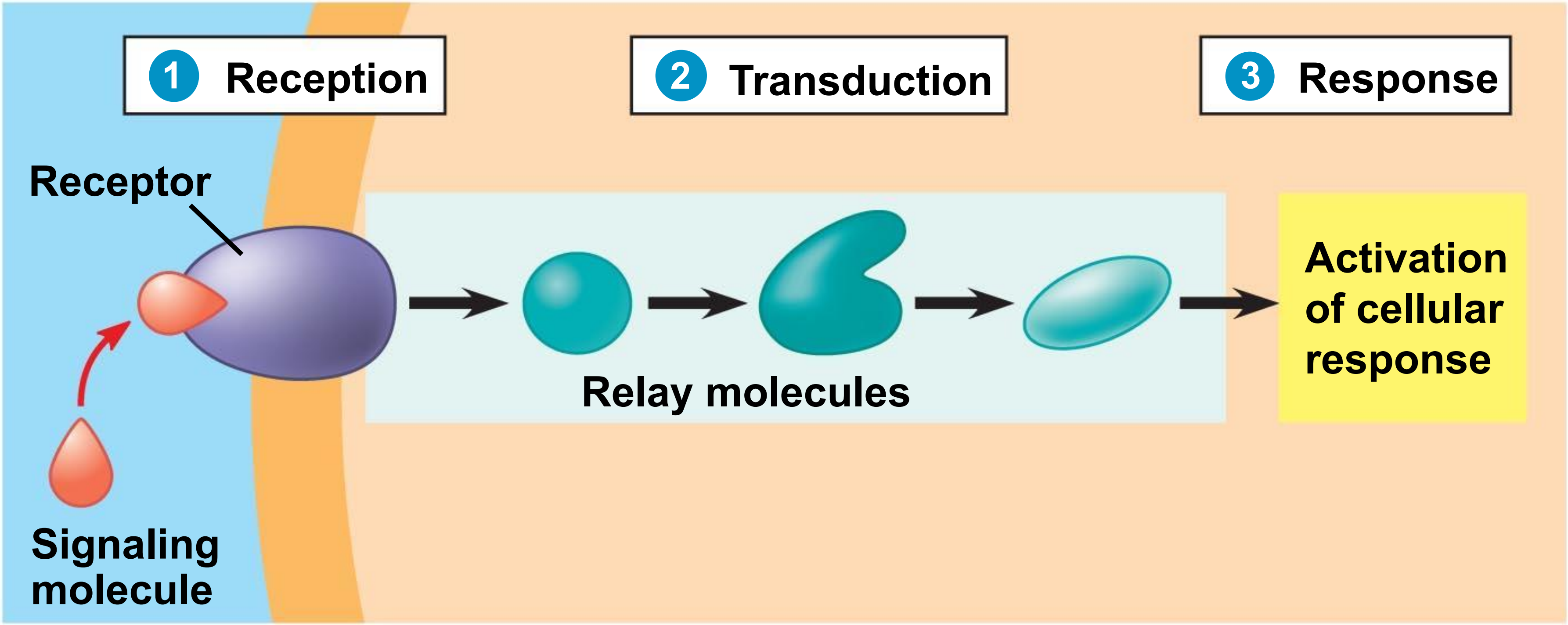
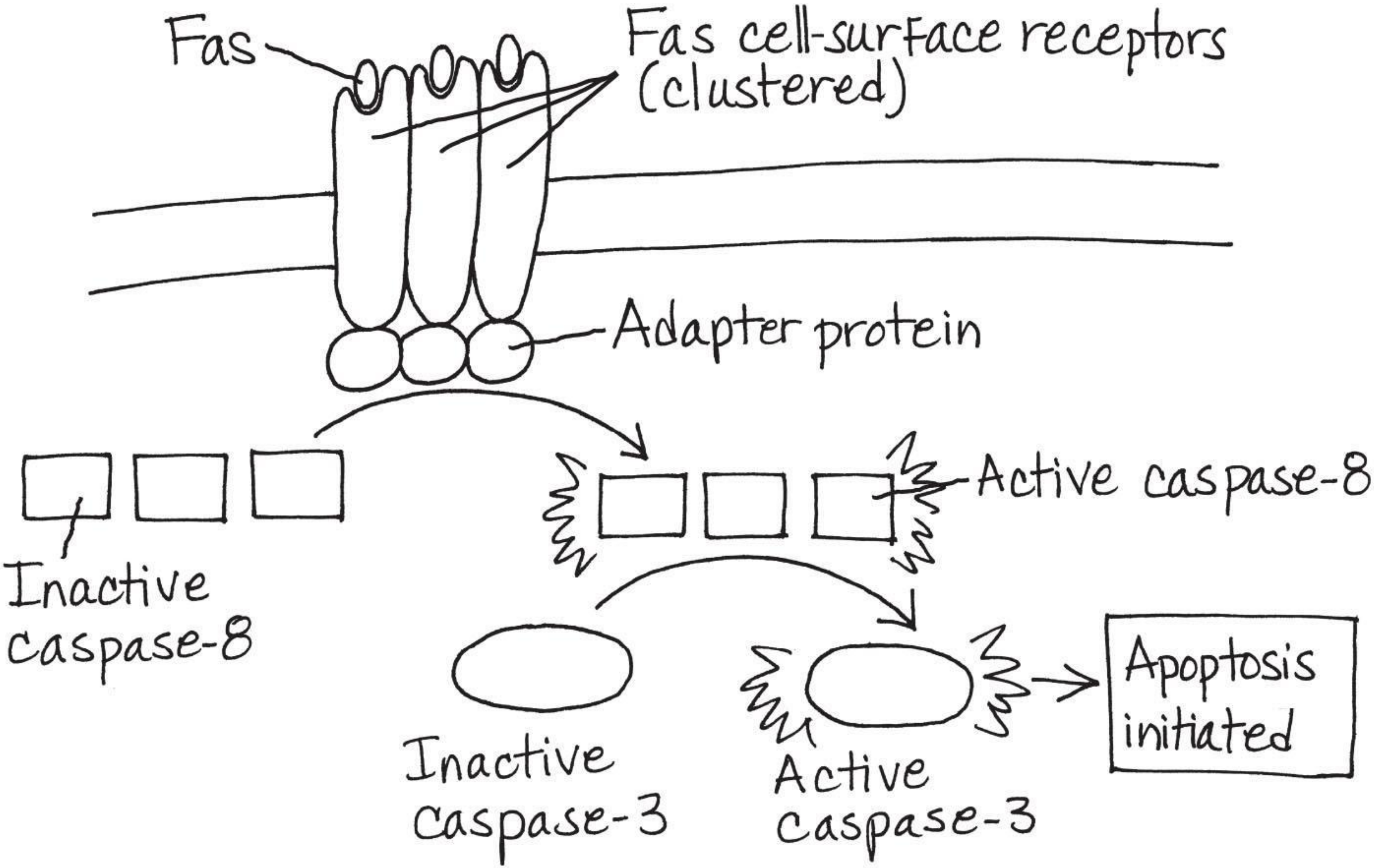

1 Reception
2 Transduction
3 Response
Receptor
Relay molecules
Activation of cellular response
Signaling molecule

Fig. 11-UN2



Fas
Fas cell-surface receptors (clustered)
Adapter protein
Active caspase-8
Inactive caspase-8
Inactive caspase-3
Active caspase-3
Apoptosis initiated

You should now be able to:

1. Describe the nature of a ligand-receptor interaction and state how such interactions initiate a signal-transduction system
2. Compare and contrast G protein-coupled receptors, tyrosine kinase receptors, and ligand-gated ion channels
3. List two advantages of a multistep pathway in the transduction stage of cell signaling
4. Explain how an original signal molecule can produce a cellular response when it may not even enter the target cell

5. Define the term *second messenger*; briefly describe the role of these molecules in signaling pathways
6. Explain why different types of cells may respond differently to the same signal molecule
7. Describe the role of apoptosis in normal development and degenerative disease in vertebrates