Molecular and Cellular Biology (MCB)
BB 101

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Systems and Control Engineering

SysCon iitb Systems & Control

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Welcome to Systems & Control Engineering

Room Booking Status

#103 - Class Room

#104 - Seminar Room

The Systems and Control group, formed in 1977, is a unique interdisciplinary program in the country that offers post-graduate education in the broad area of Systems and Control. The nine faculty members of the group have varied research backgrounds, that includes nonlinear control, robotics, path-planning, embedded control, coordination of autonomous vehicles, multi-agent systems, game theory, information theory, combinatorics, sliding mode control and applications, fractional-order modelling and control, optimization and optimization-based control, and stochastic processes. Other faculty members of the institute with an interest in the field also participate in the activities of the group. The alumni of the group are employed in many reputed academic institutes, ISRO/DRDO and research laboratories, and corporate R & D units of the country.

Feedback & control in complex systems

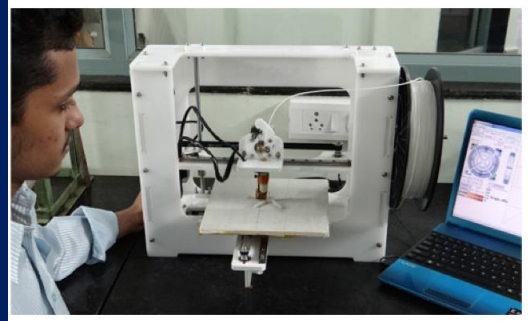
Air planes
Air ships

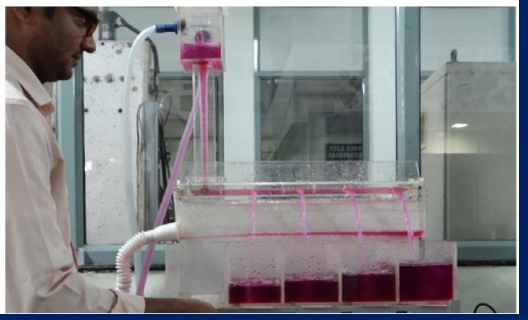
Project Biosynth: Chem Eng @ IITB

convert waste vegetable oil etc. to biodiesel

e-foundry
@ IITB

http://efoundry.iitb.ac.in/efoundry-cells/iitb.html

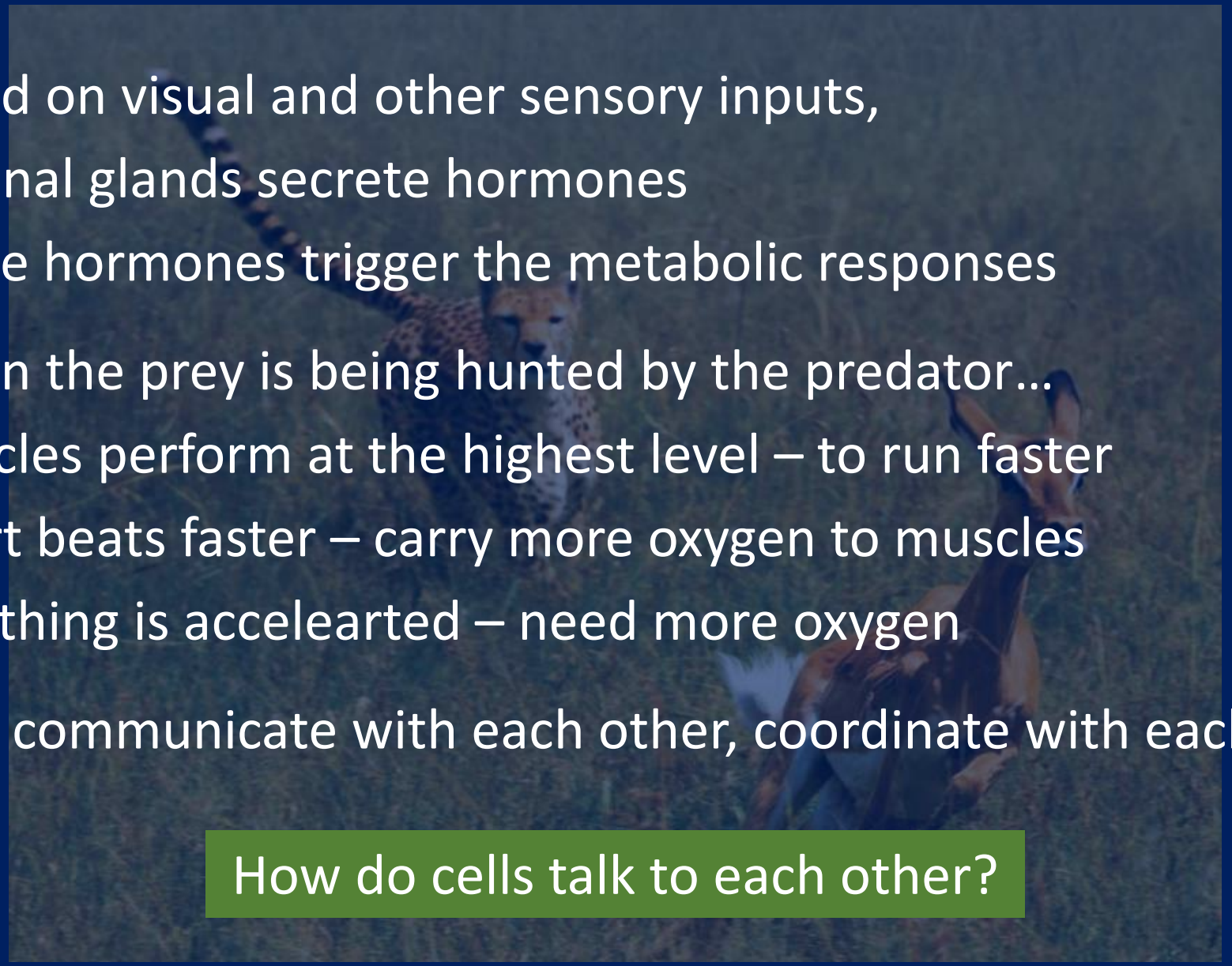




Fight or flight

Figure 11.1
Biology. A global approach

Cellular messaging

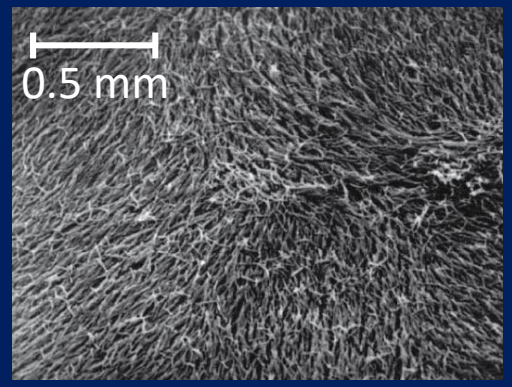


- Based on visual and other sensory inputs,
  Adrenal glands secrete hormones
  These hormones trigger the metabolic responses
- When the prey is being hunted by the predator…
  Muscles perform at the highest level – to run faster
  Heart beats faster – carry more oxygen to muscles
  Breathing is accelearted – need more oxygen
- Cells communicate with each other, coordinate with each other

How do cells talk to each other?

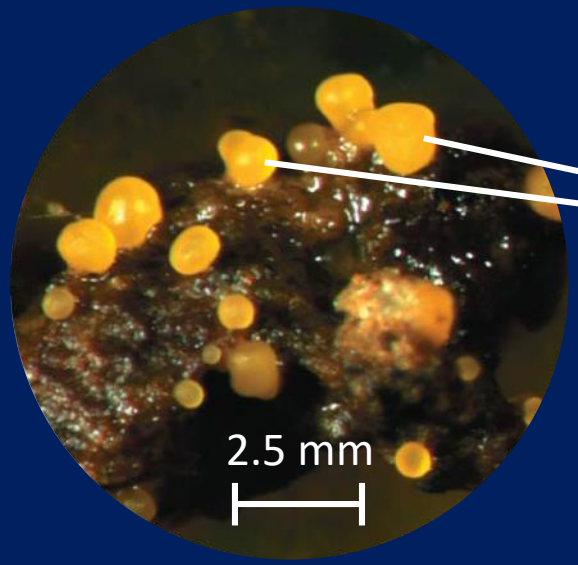
Signaling is not unique to multi-cellular organisms

Figure 11.3



Individual rod shaped cells

favourable conditions

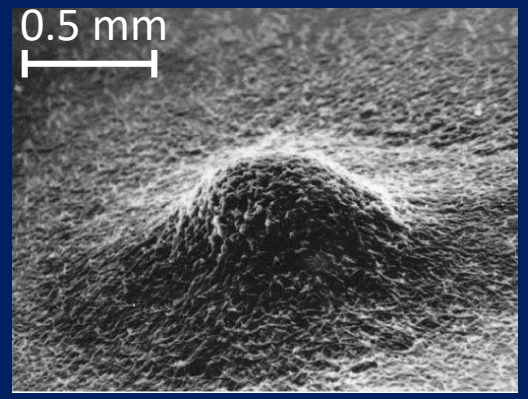


Fruiting bodies (spores)

soil dwelling bacteria
Myxococcus xanthus

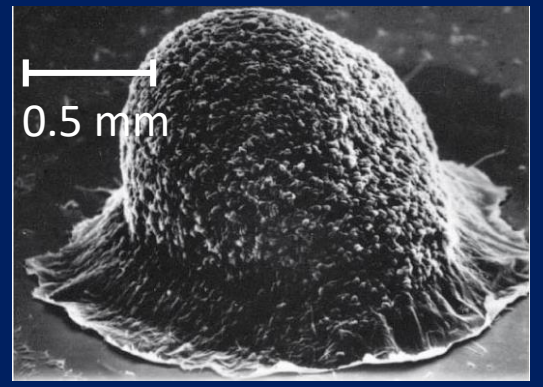
Food scarcity

Starving cells send out a chemical signal



Aggregation in progress

Cells collectively form fruiting body



Spore-forming structure (fruiting body)

Quorum sensing

quorum: the smallest number of people who must be present at a meeting in order for decisions to be made (www.merriam-webster.com)

A concentration of signaling molecules allows bacteria to sense local population density in a process called quorum sensing

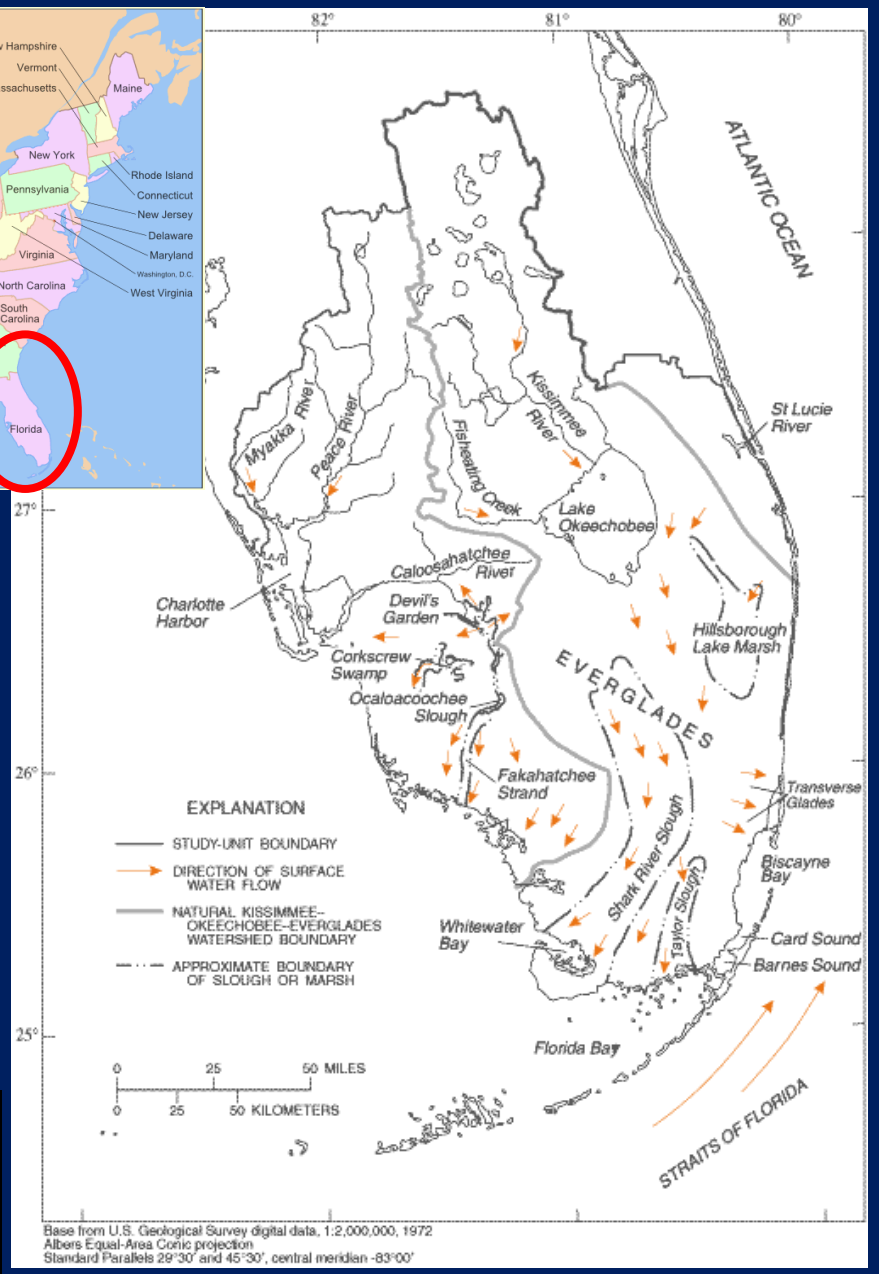
Signaling mechanisms are conserved

Even unicellular organisms talk to each other

Mechanisms by which cells
- send/receive signals
- process the signal
- let other cells know about the signal…

Evolutionarily conserved...
- same mechanisms are encountered again and again
- mechanisms are universal

Inch deep, mile wide



Everglades: a unique ecosystem
Tropical wetlands

An unusual characteristic: very shallow but very wide

Vertical gradient: 2 inches per mile

River flow: half a mile a day

en.wikipedia.org/wiki/Everglades#/media/File:Florida_Everglades_Hydrology.gif

Source: Wikipedia

Class 8: learning objectives

- Cell signaling in yeast – concept of signal transduction
- Local and long distance signaling – illustrative schematics
- Signal transduction – an overview
- Illustrative examples
  - Reception
  - Transduction
  - Response

Cell signaling in yeast

Yeast

Can be haploid or diploid

Saccharomyces cerevisiae

False color electron micrograph

https://www.sciencenews.org/article/yeast-life-span-calorie-restriction-may-be-wash

HAPLOIDS

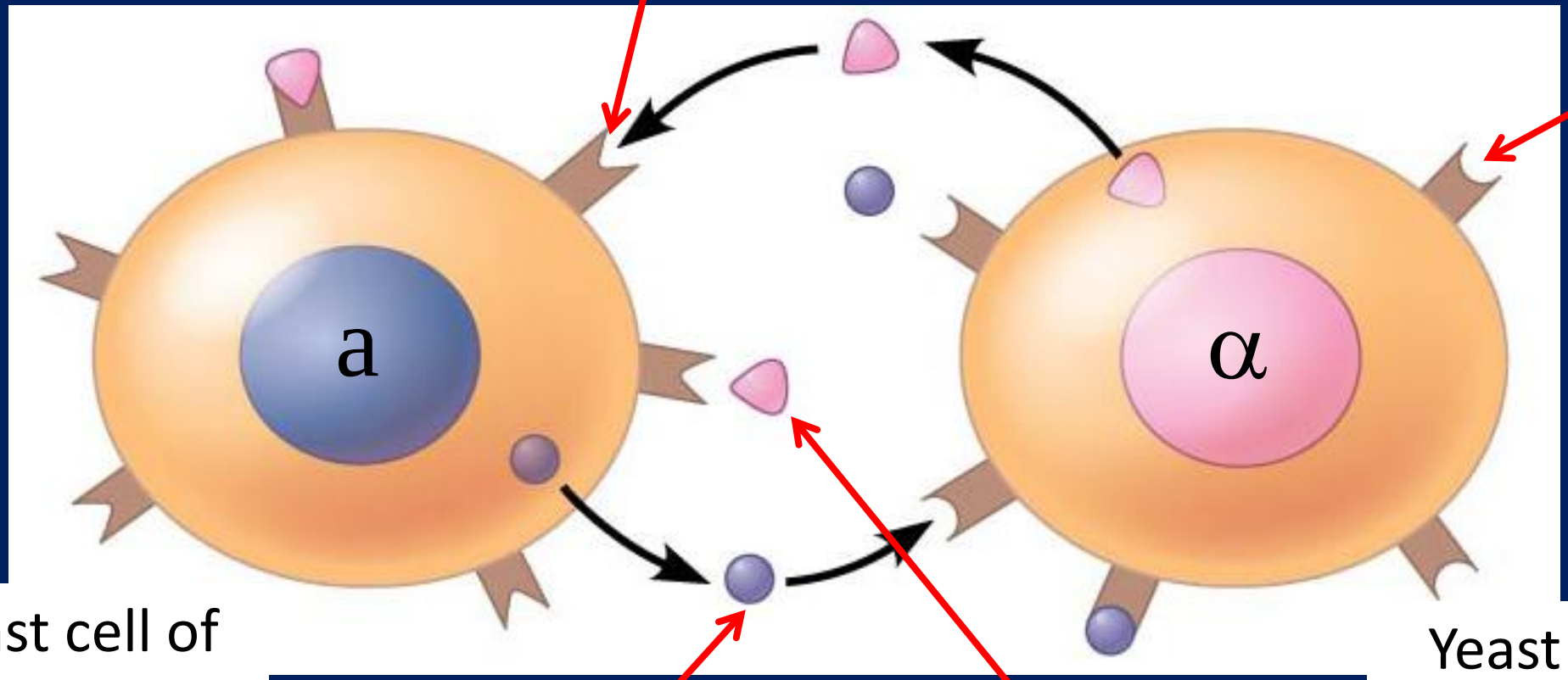
Mating type a

Mating type α

Can switch from a to α during cell division

Exchange of mating factors

Figure 11.2



Mating

a and α factors bind to their respective receptors

Trigger responses inside the cell

Responses lead to fusion of the two yeast cells

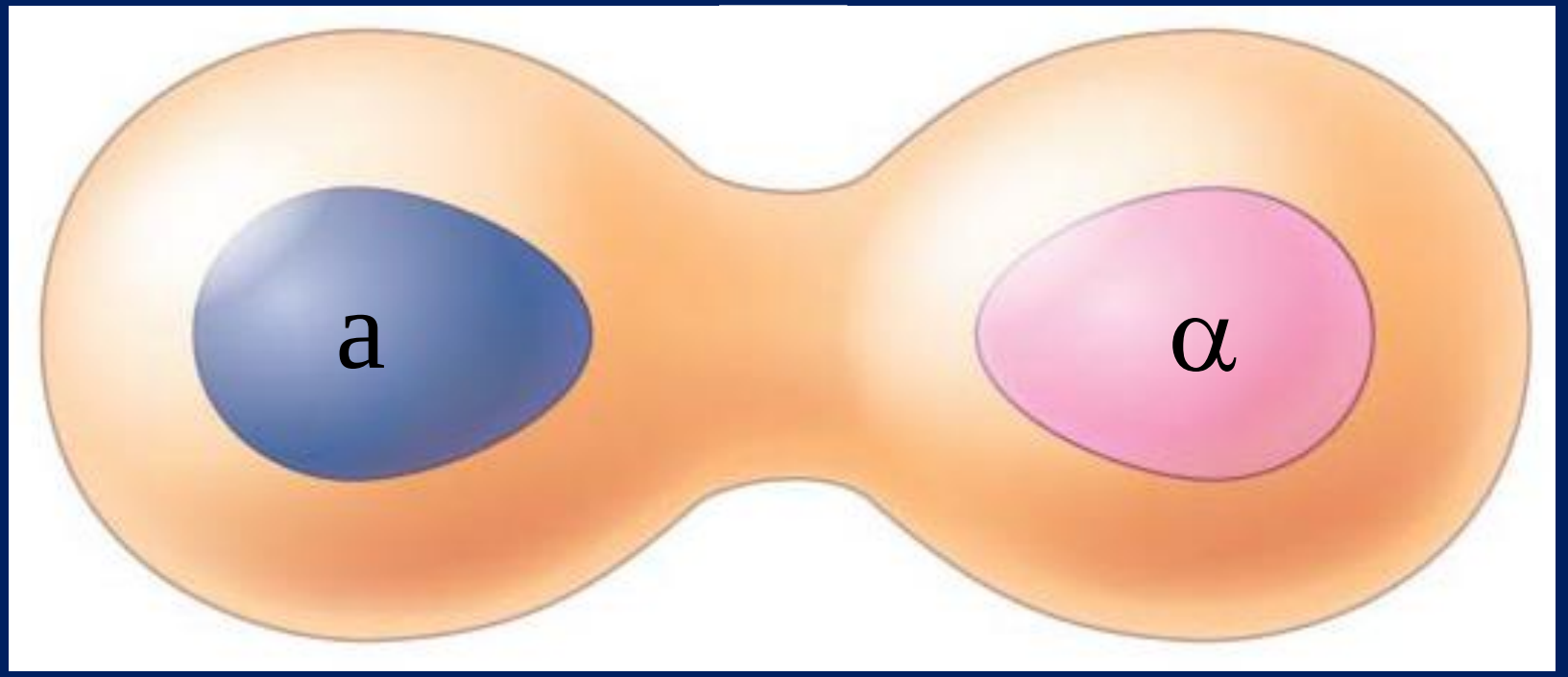
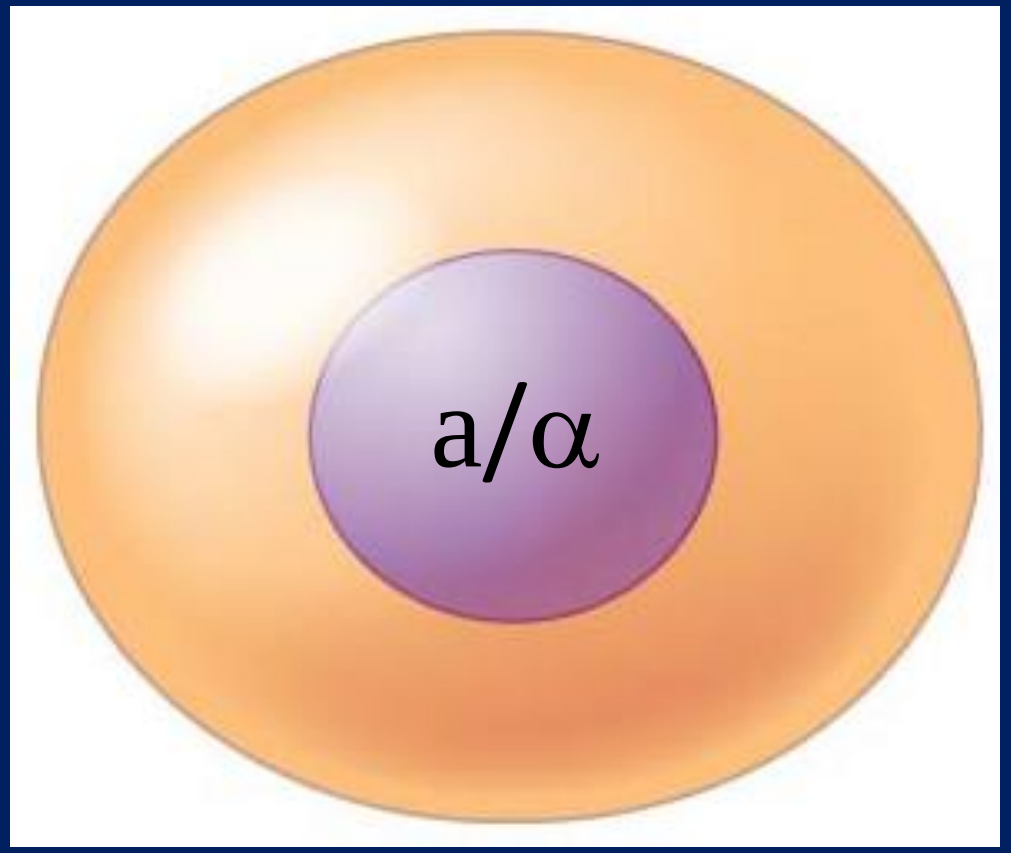


Figure 11.2

Formation of an a/α diploid cell

Nucleus of the fused cell includes all genes from both a and α cells

Can undergo mitosis
Two diploids
Both will be a/α type



Can undergo meiosis
Two type a haploids
Two type α haploids

Figure 11.2

Signal transduction

transduce (*verb*): to convert energy or message into another form (www.merriam-webster.com)

Communication among microbes…
insight into cell communication in multicellular organisms

A chemical outside a cell…
triggers a response inside the cell

Mating in yeast…
illustrates the concept of cell surface receptors
intra-cellular signal transduction in response to an external signal

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Local (neighbor) signaling

Local signaling: cells communicate by direct contact

Animal and plant cells have cell junctions

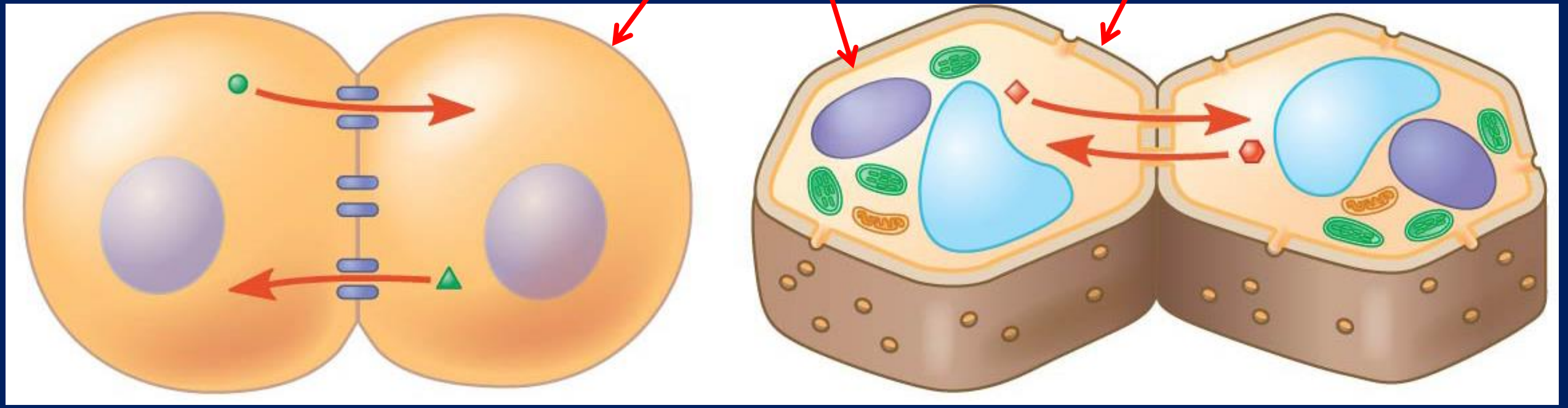
- These junctions directly connect the cytoplasm of adjacent cells
- Signaling substances can pass freely between adjacent cells

Cell junctions

plasma membrane

cell wall

Figure 11.4



gap junctions
(animal cells)

plasmodesmata
(plant cells)

Cell-cell recognition

In embryonic development and immune response

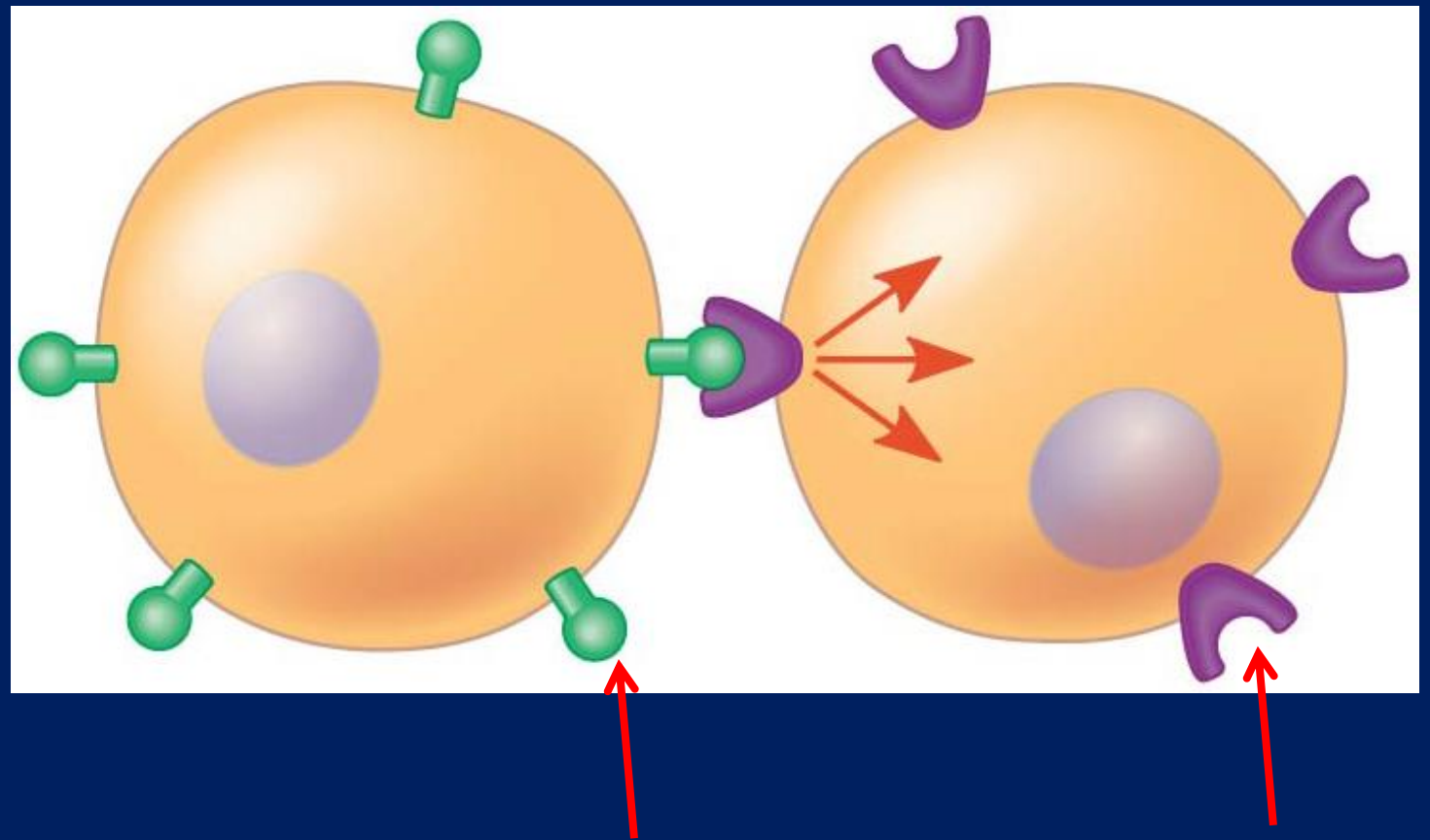


Figure 11.4

Membrane-bound cell surface molecules

Paracrine signaling

- Animal cells communicate using secreted messenger molecules that travel only short distances

  para- means nearby, beside

- Examples

  Growth factors – stimulate nearby target cells to grow and divide

  Neurotransmitters – transmit signal from one nerve cell to another

Paracrine signaling in plants: not well understood

Paracrine signaling

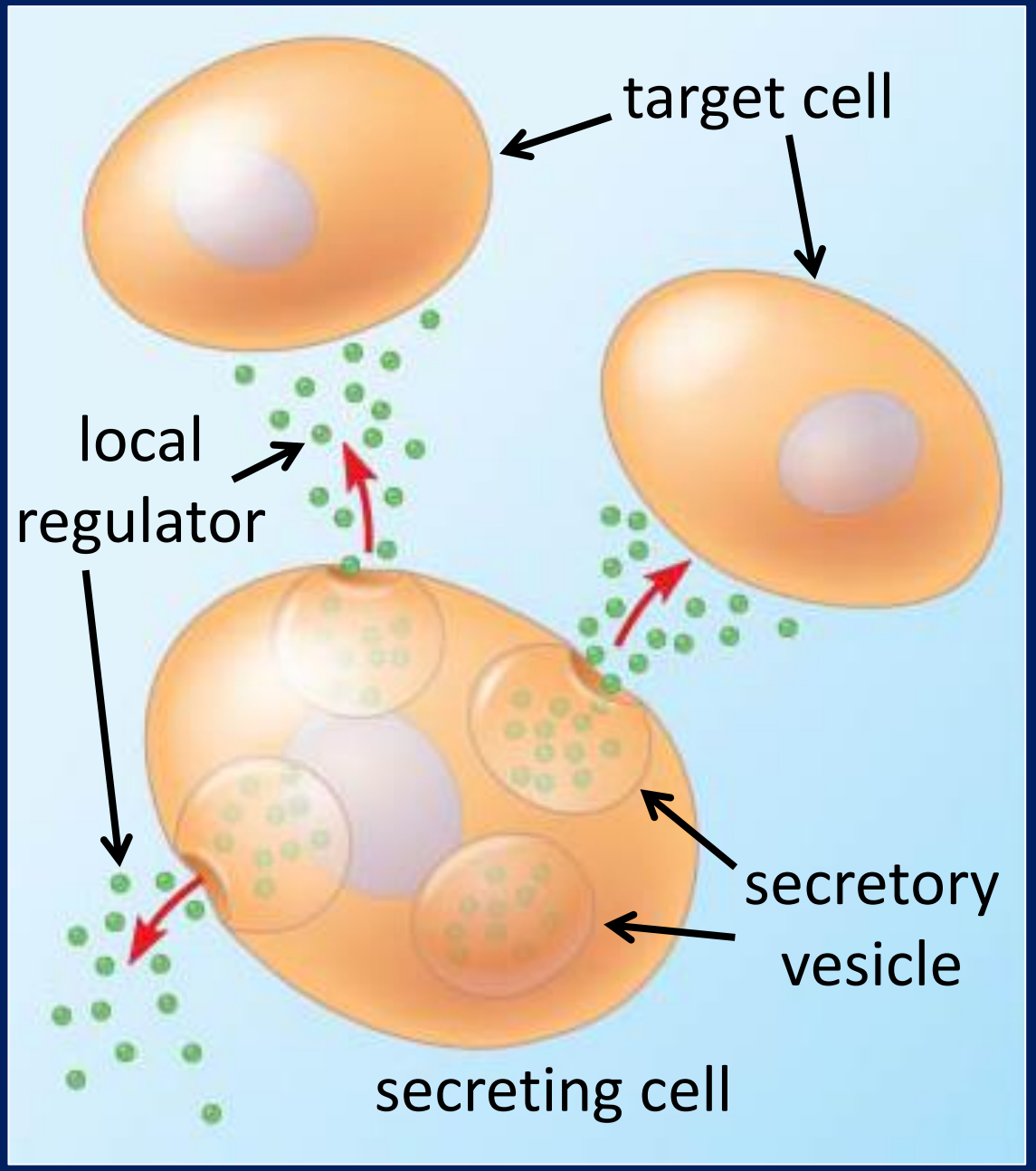


Figure 11.5

Synaptic signaling

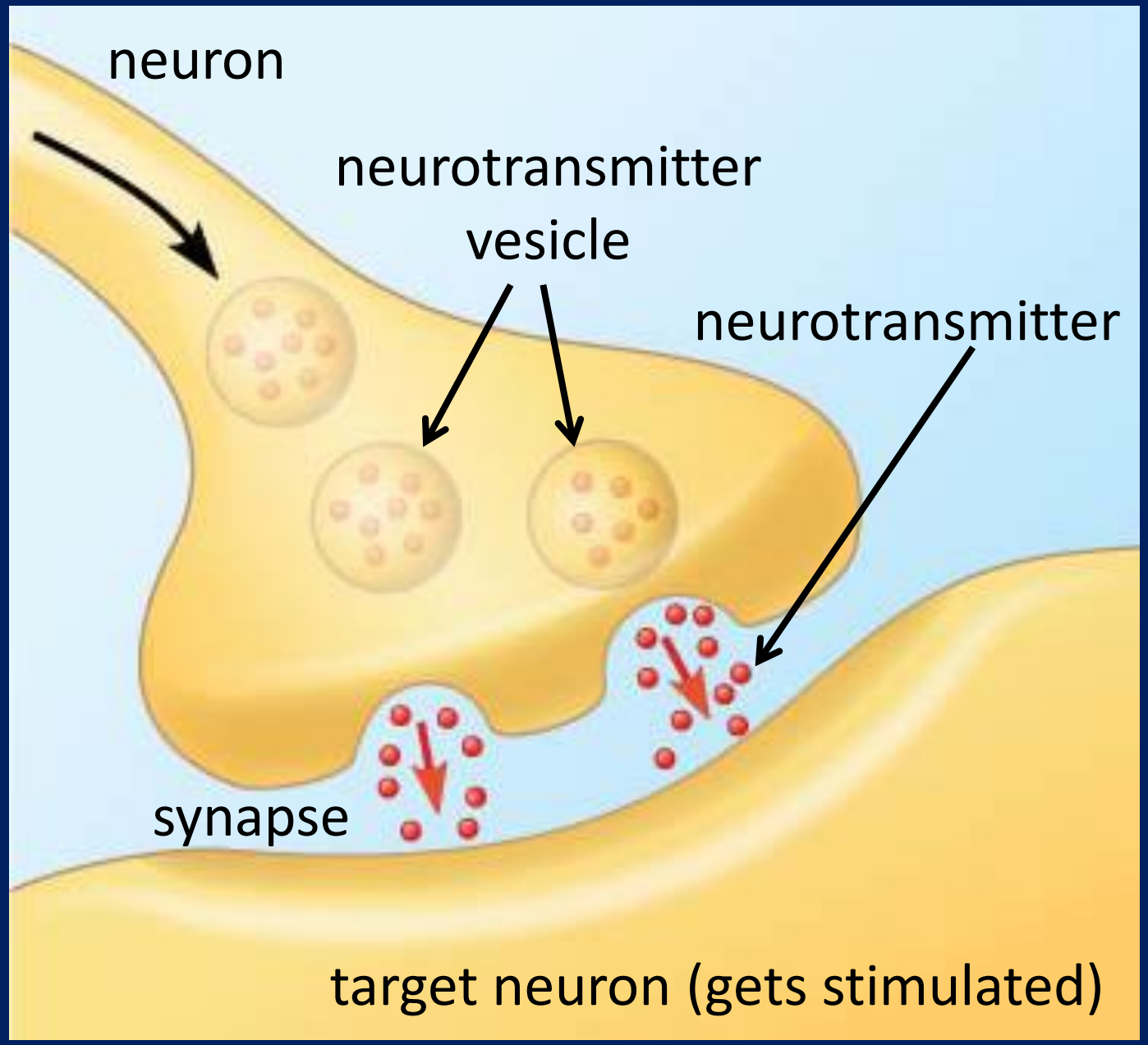


Figure 11.5

Electrical signals trigger release of neuro-transmitters

Long distance signaling: hormones

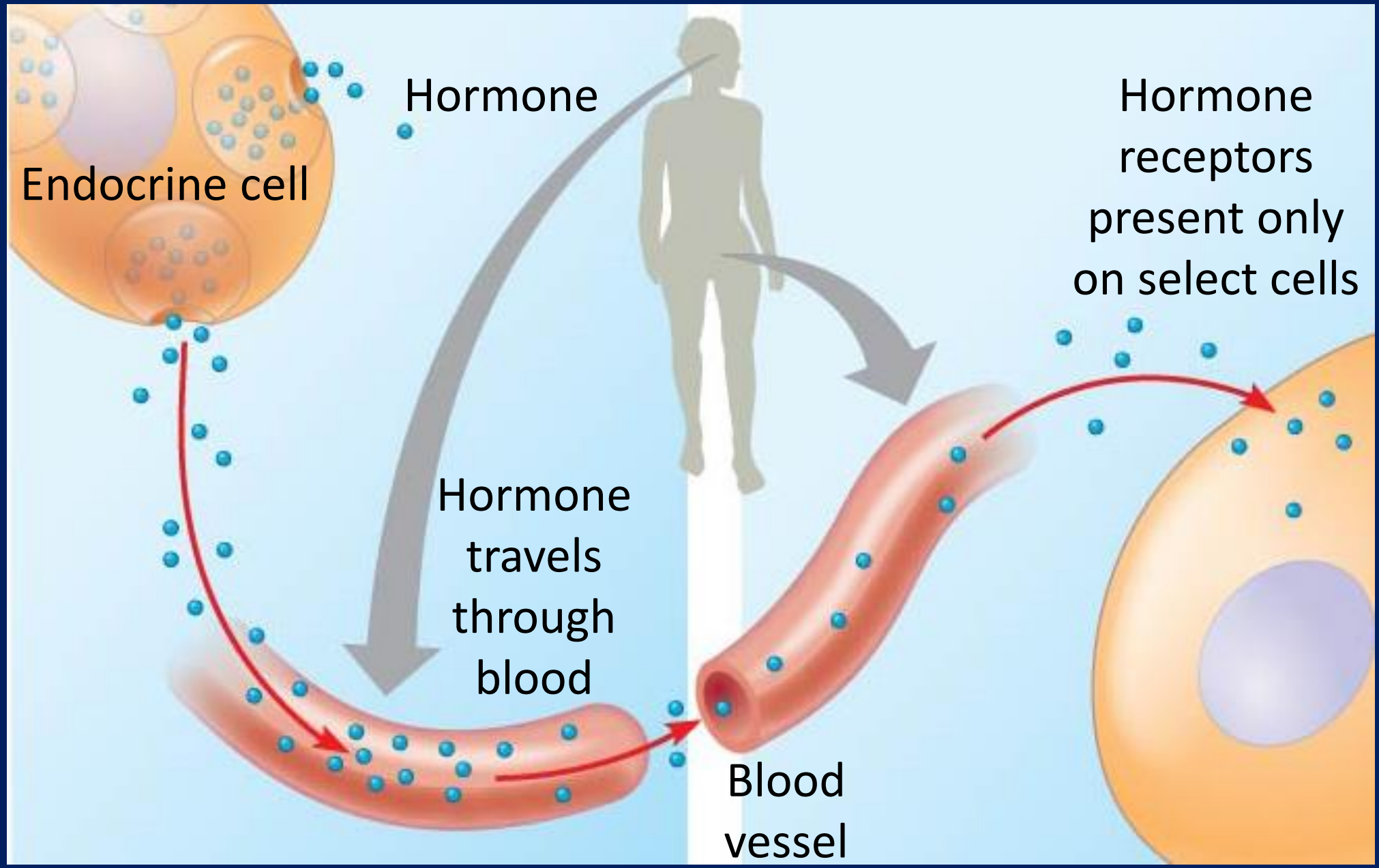
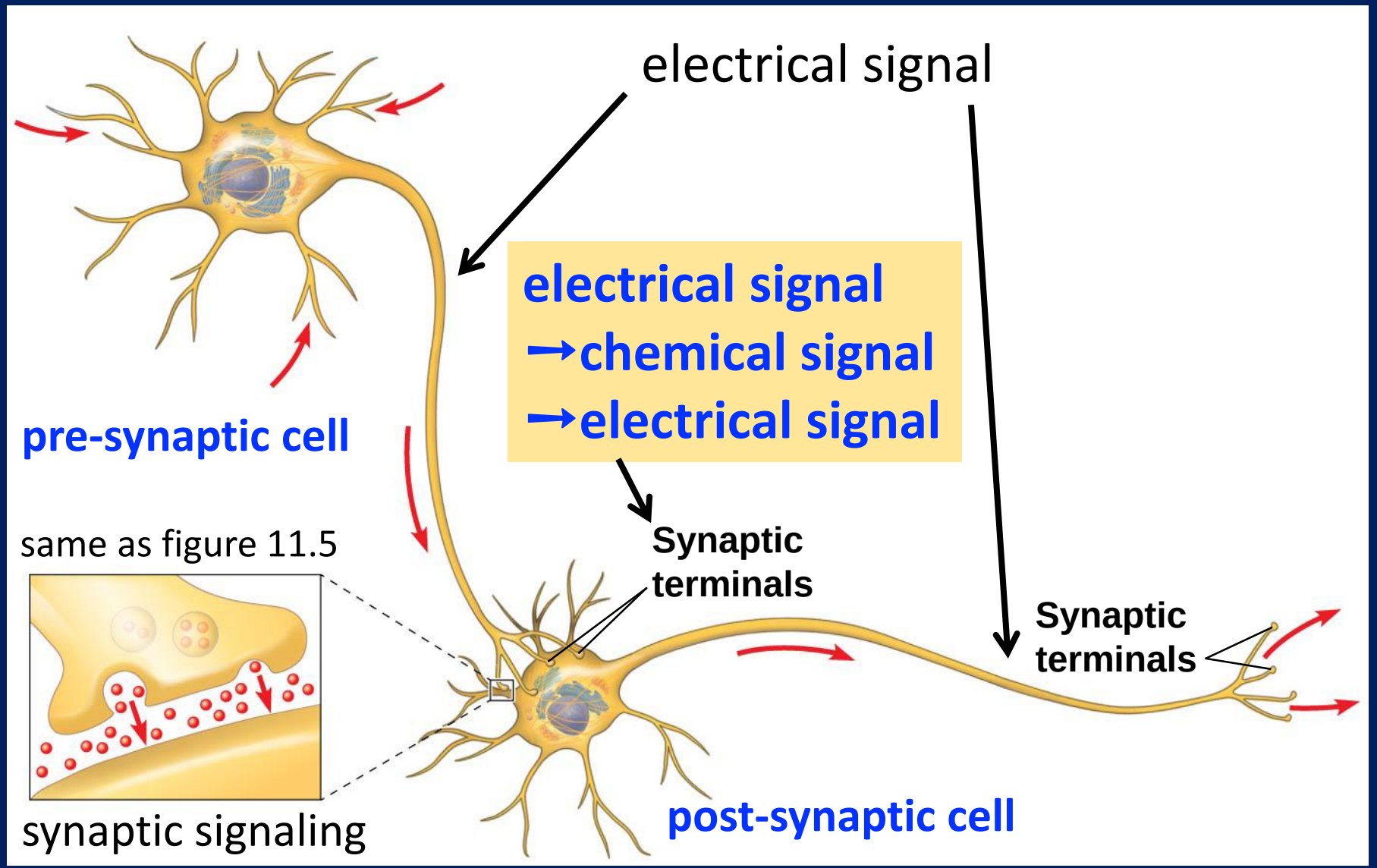


Figure 11.5

Long distance signaling: nerve impulses

Figure 48.4



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How does adrenaline mobilize energy?

Earl W. Sutherland
Nobel prize in 1971
Vanderbilt University

www.nasonline.org

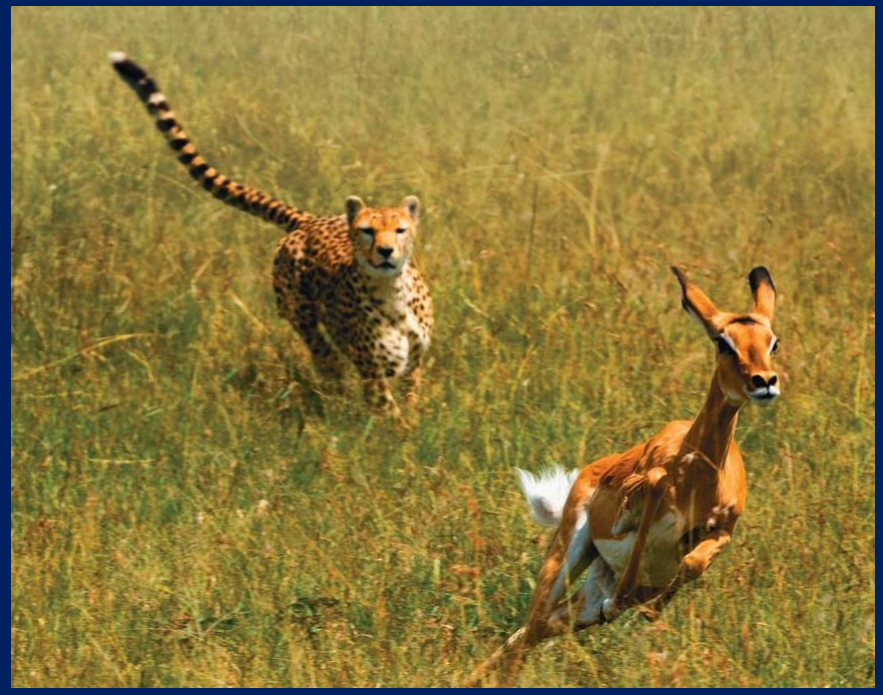
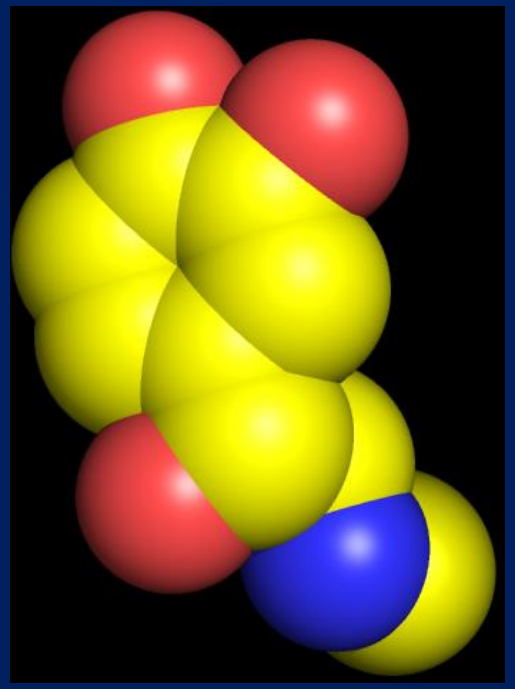


Figure 9.1. Biology. A global approach

from 4LDO.pdb



Molecular model
of adrenaline

Signal transduction: three stages

Reception

knock on the door

Transduction

domestic help opens the door
talks to the visitor

Response

informs the Master of the house
Master acts on the message

Signal transduction: 1. Reception

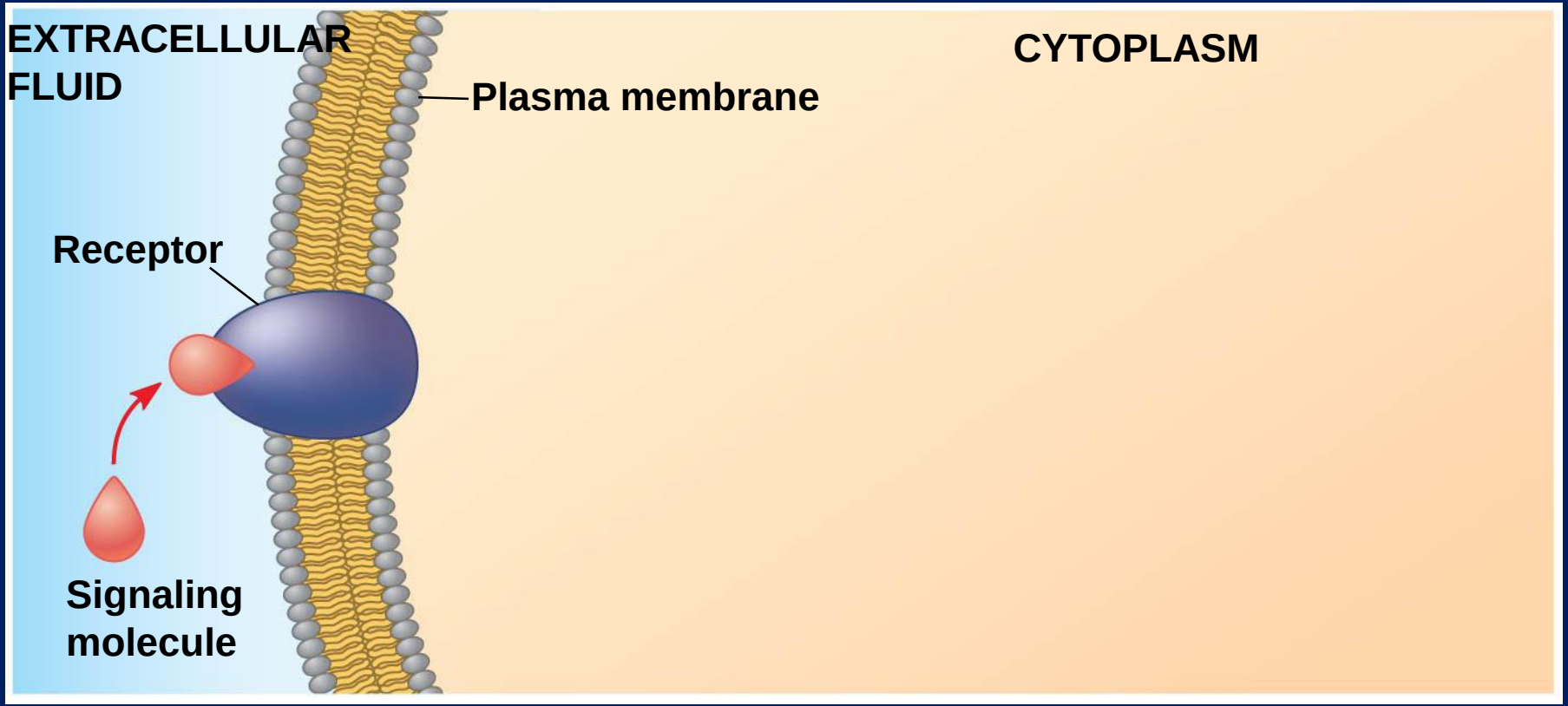


Figure 11.6

A signaling molecule binds to a cell surface receptor
Receptor is on the target cell

Signal transduction: 2. Transduction

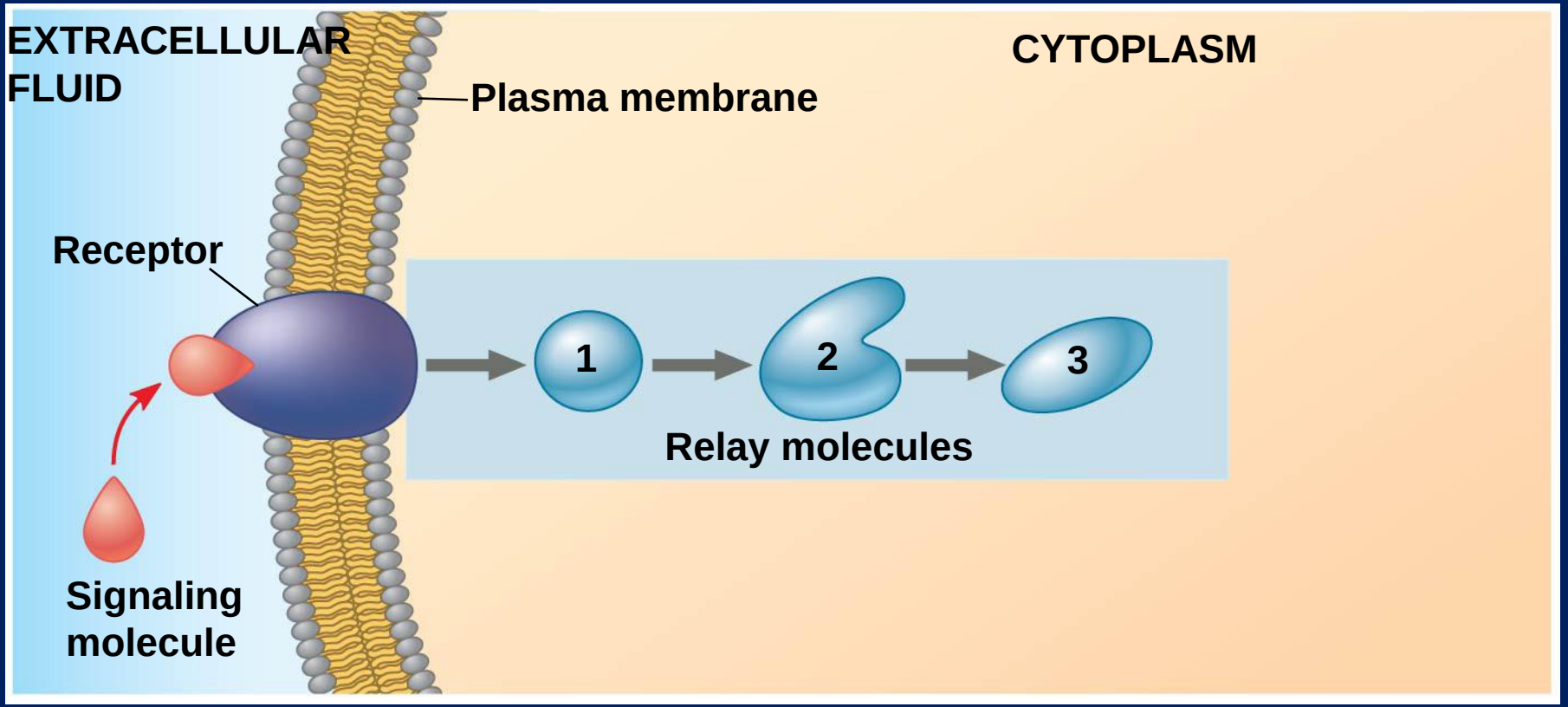


Figure 11.6

Binding leads to a change in the shape of the receptor

Shape change leads to a cellular response

Can be in one step; often, in multiple steps

involves relay molecules

Signal transduction: 3. Response

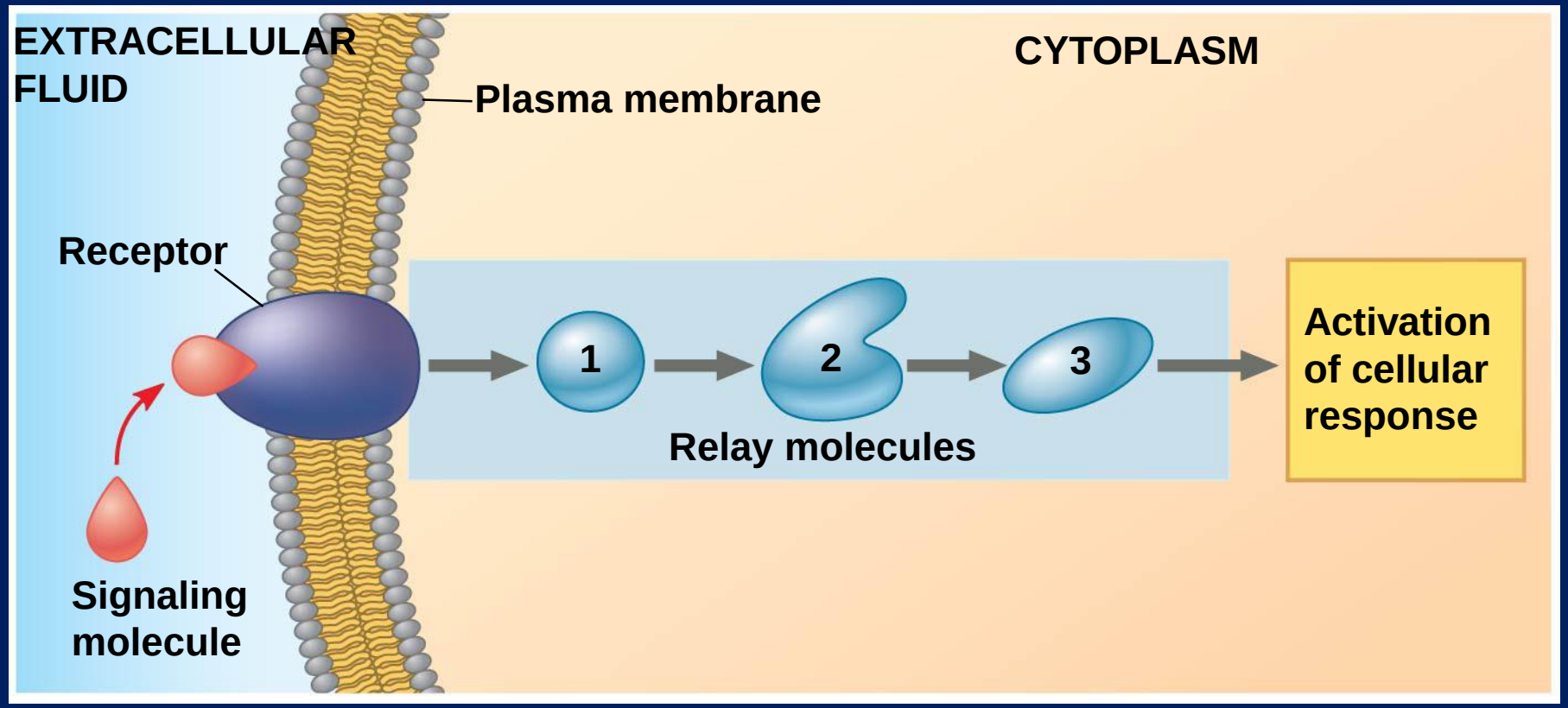


Figure 11.6

Response can be of different types:

1. Catalysis of a reaction by an enzyme
2. Rearrangement of the cytoskeleton
3. Activation of specific genes (gene expression)

Signal reception by mobiles

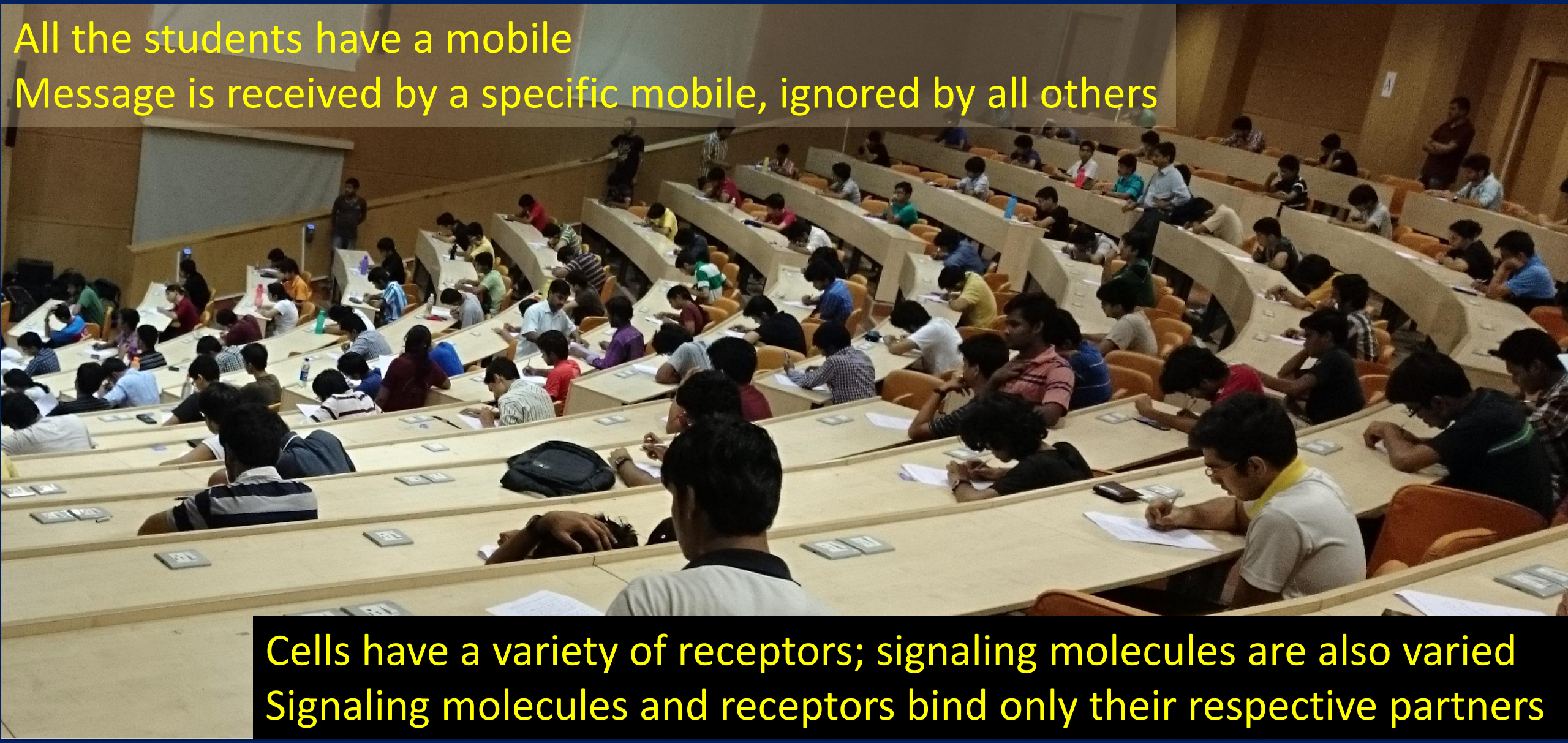
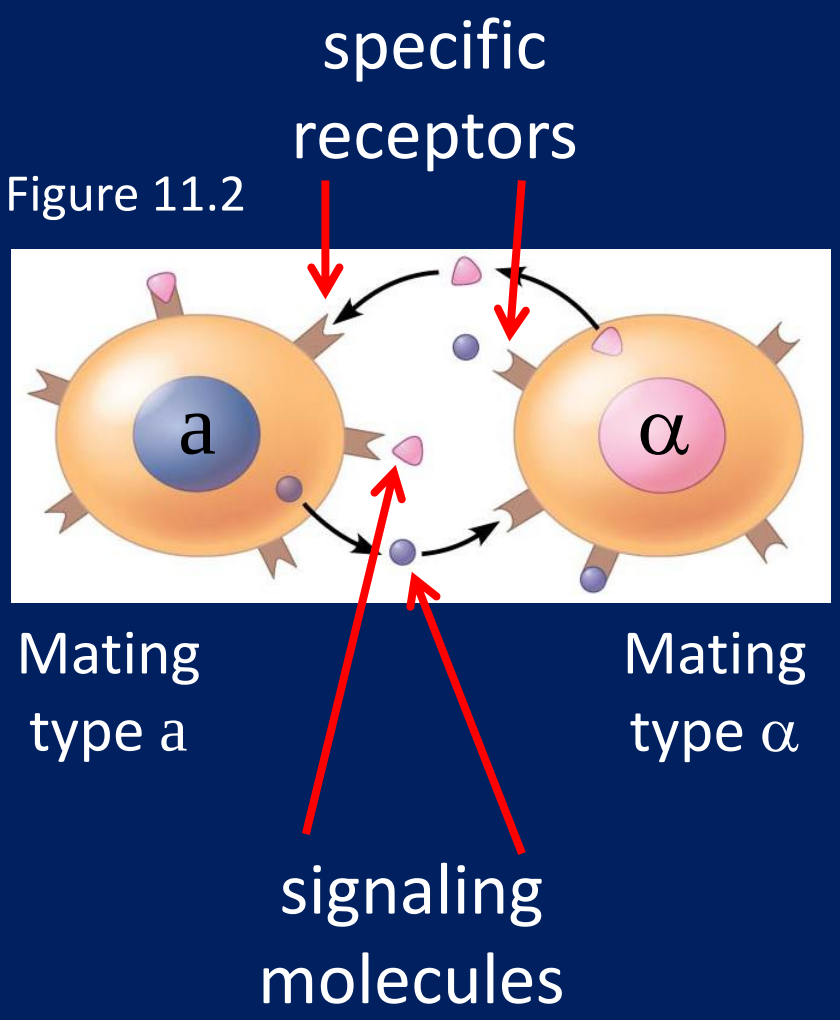


Photo courtesy: Prof M S Balakrishna

Exchange of mating factors

Figure 11.2



Signaling molecule = LIGAND

Receptor and ligand have complementarity
This ensures specificity

Receptors are cell surface molecules

Ligand binding induces shape change

Shape change can
a) directly trigger a response
b) relay the signal to trigger a response

Class 8: learning objectives

- Cell signaling in yeast – concept of signal transduction
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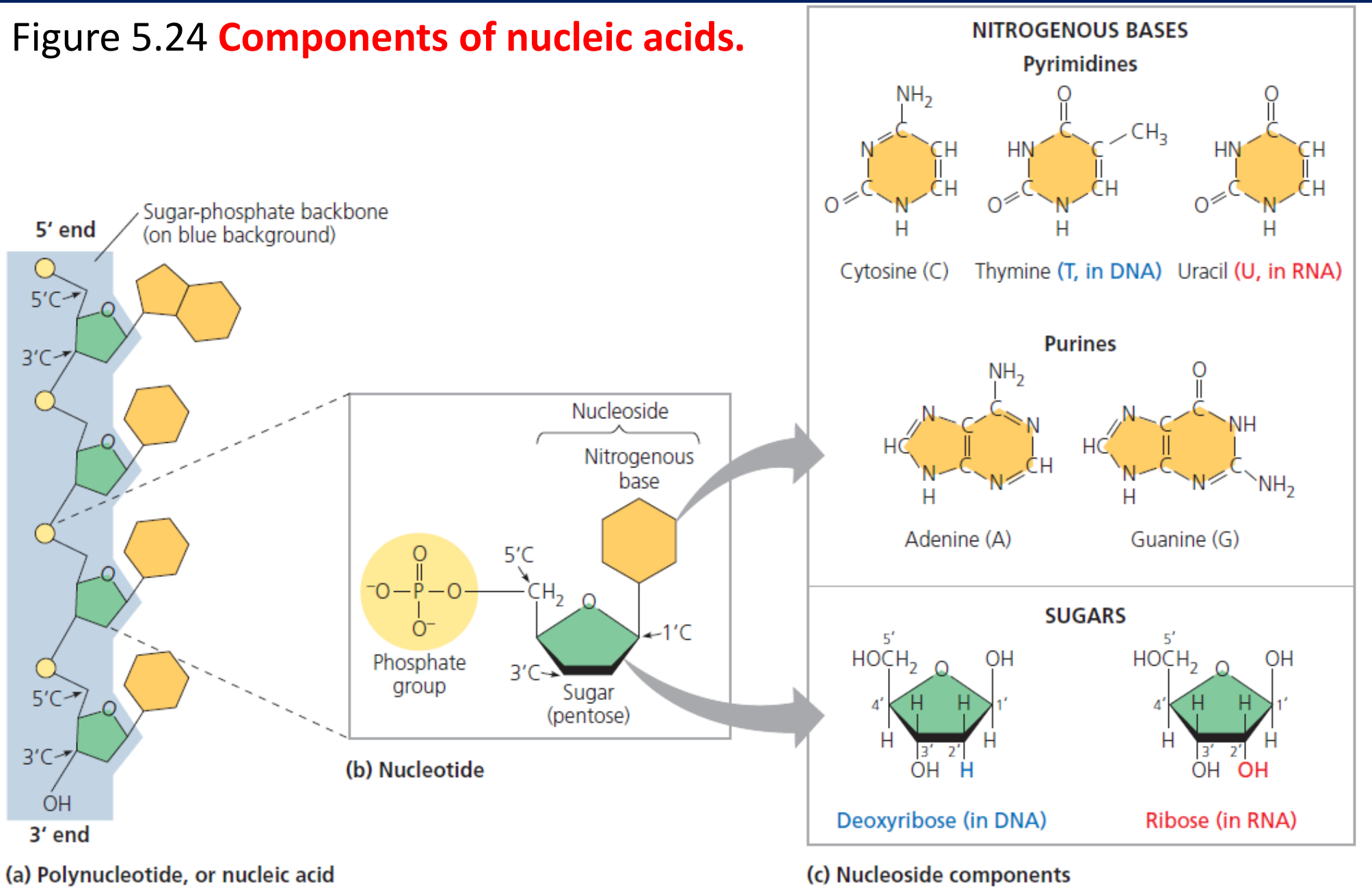
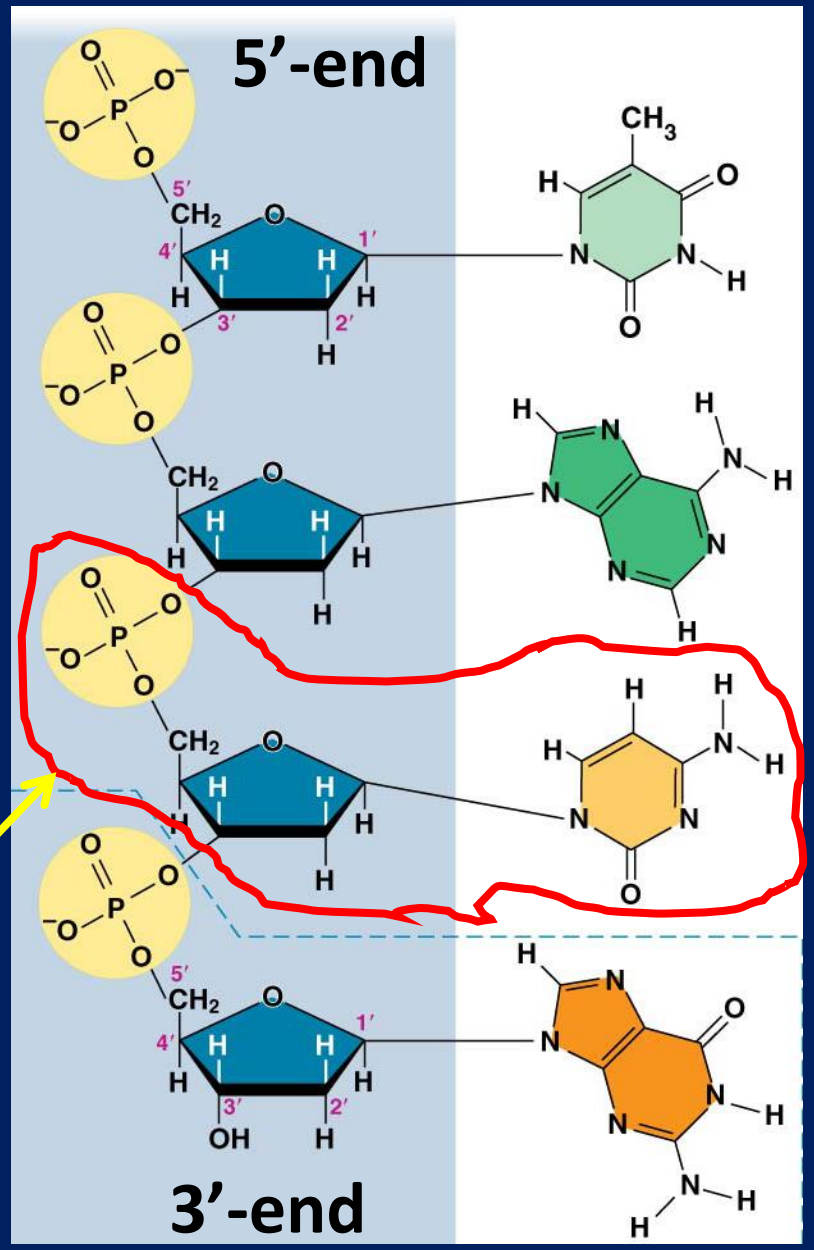
Figure 5.24 **Components of nucleic acids.**



Nucleotides in DNA

Figure 16.5



Thymine (T)

Adenine (A)

Cytosine (C)

Guanine (G)

Nitrogenous bases

Sugar phosphate backbone

A nucleotide

Dual role of nucleotides

Nucleotides have other roles also

ATP is an energy currency

GTP, CTP, TTP, UTP (from uracil) are also energy currencies, but far less widely used than ATP

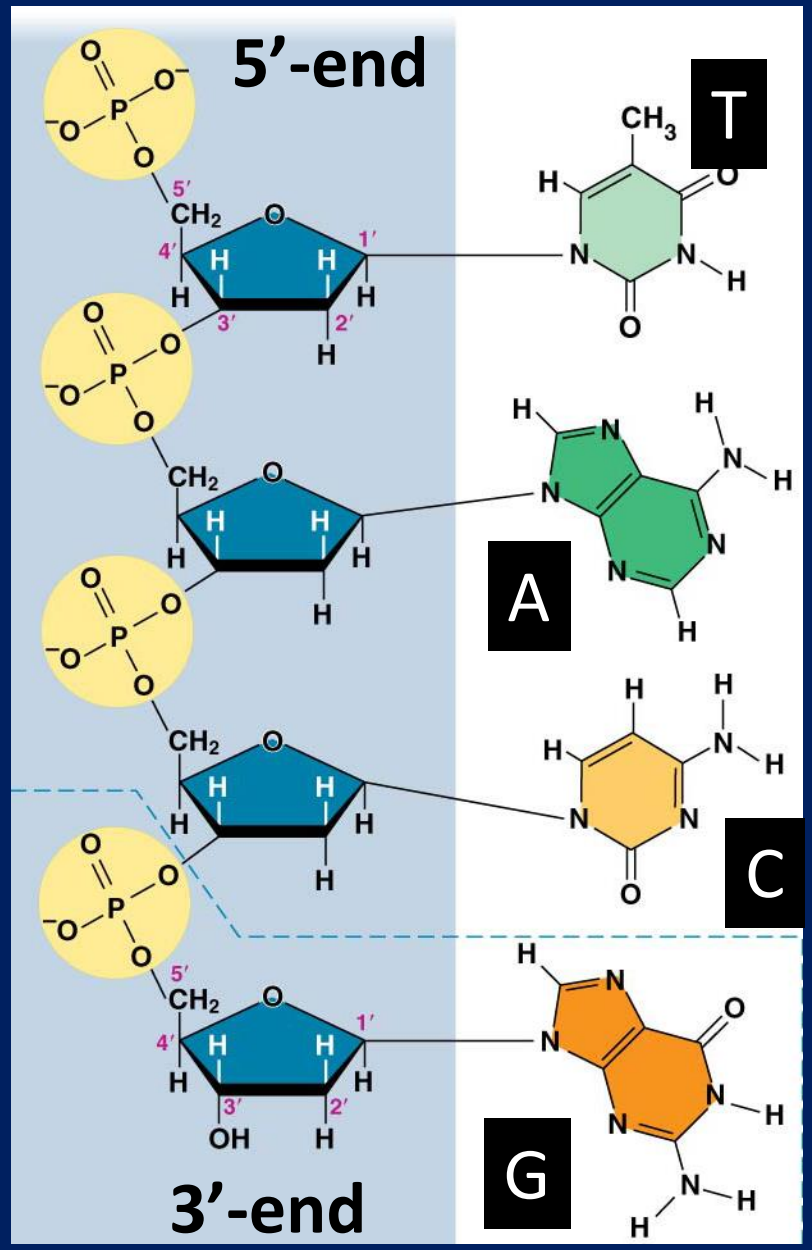
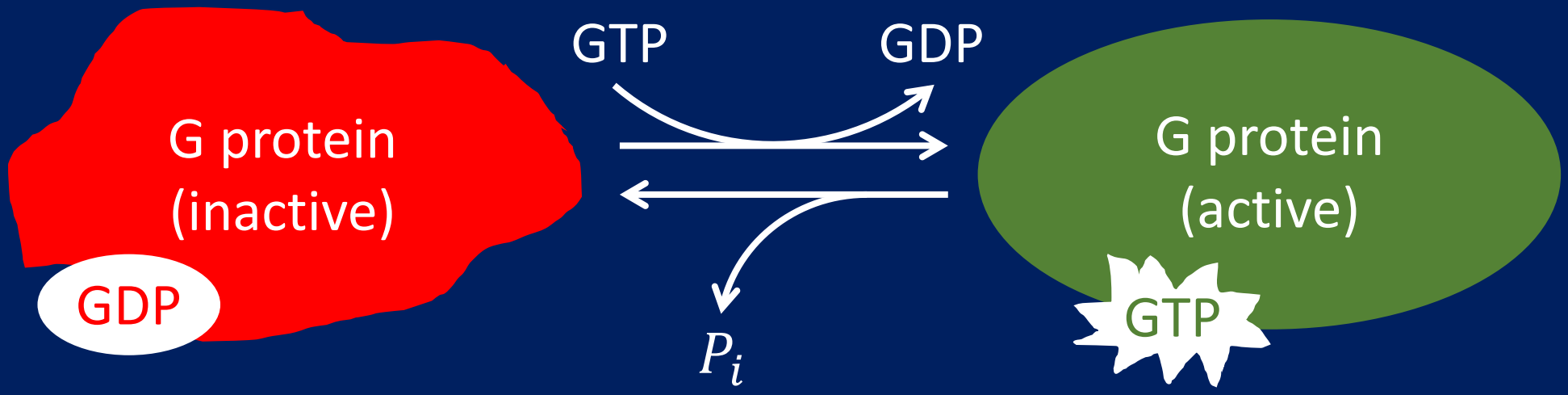


Figure 16.5

GTP plays an important role in signal transduction

G proteins

- G proteins are a large family of proteins found ubiquitously
- They act as molecular switches
- Exchange GTP/GDP as part of signaling events



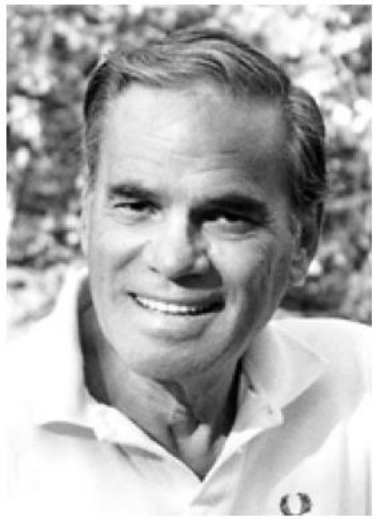
Energy is spent in conversion from active to inactive state

Change in shape or conformation

G proteins

The Nobel Prize in Physiology or Medicine 1994

Alfred G. Gilman
Prize share: 1/2



Martin Rodbell
Prize share: 1/2

Discovered while working with impure ATP

The Nobel Prize in Physiology or Medicine 1994 was awarded jointly to Alfred G. Gilman and Martin Rodbell *"for their discovery of G-proteins and the role of these proteins in signal transduction in cells"*

G protein-coupled receptors (GPCRs)

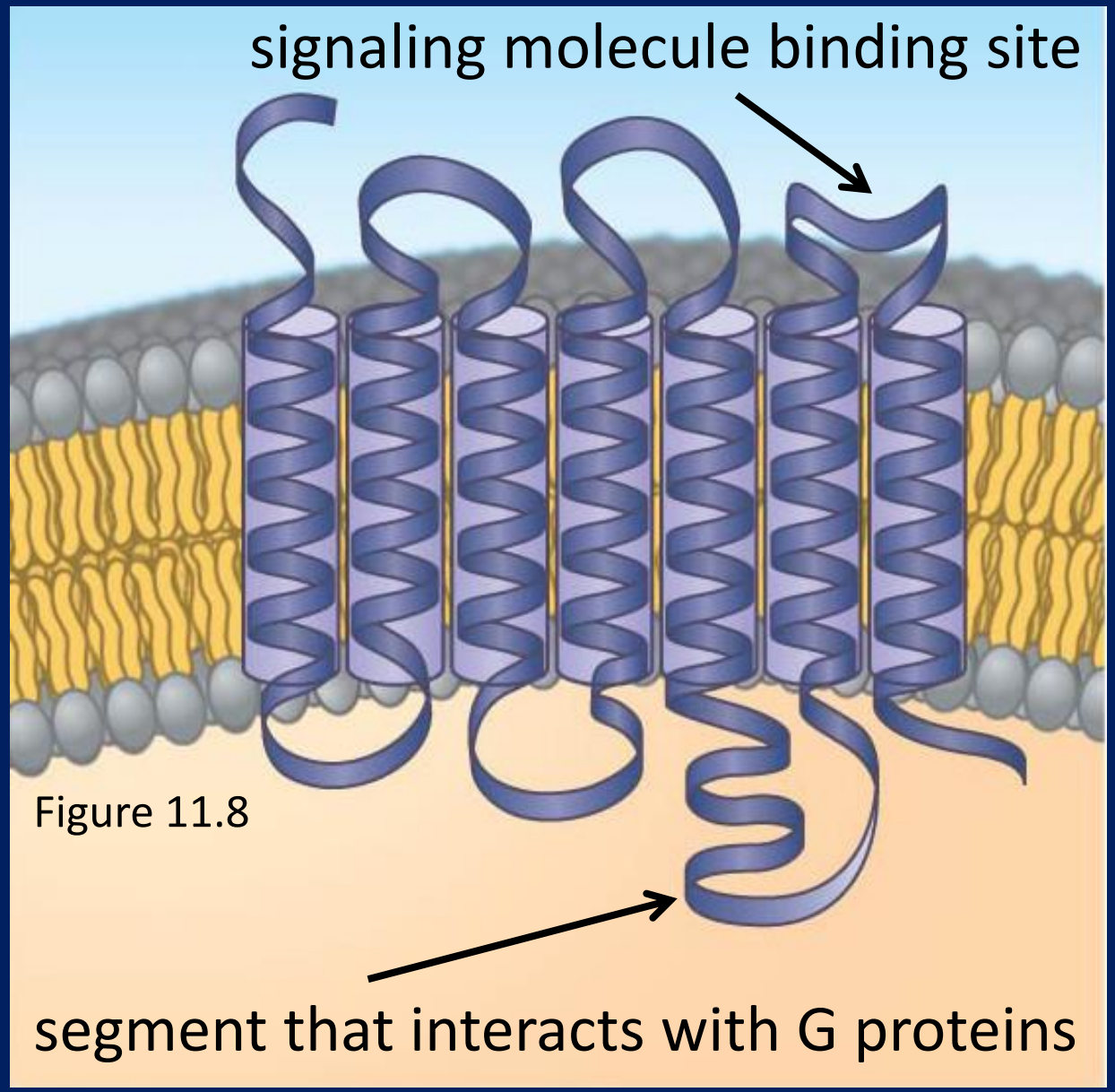
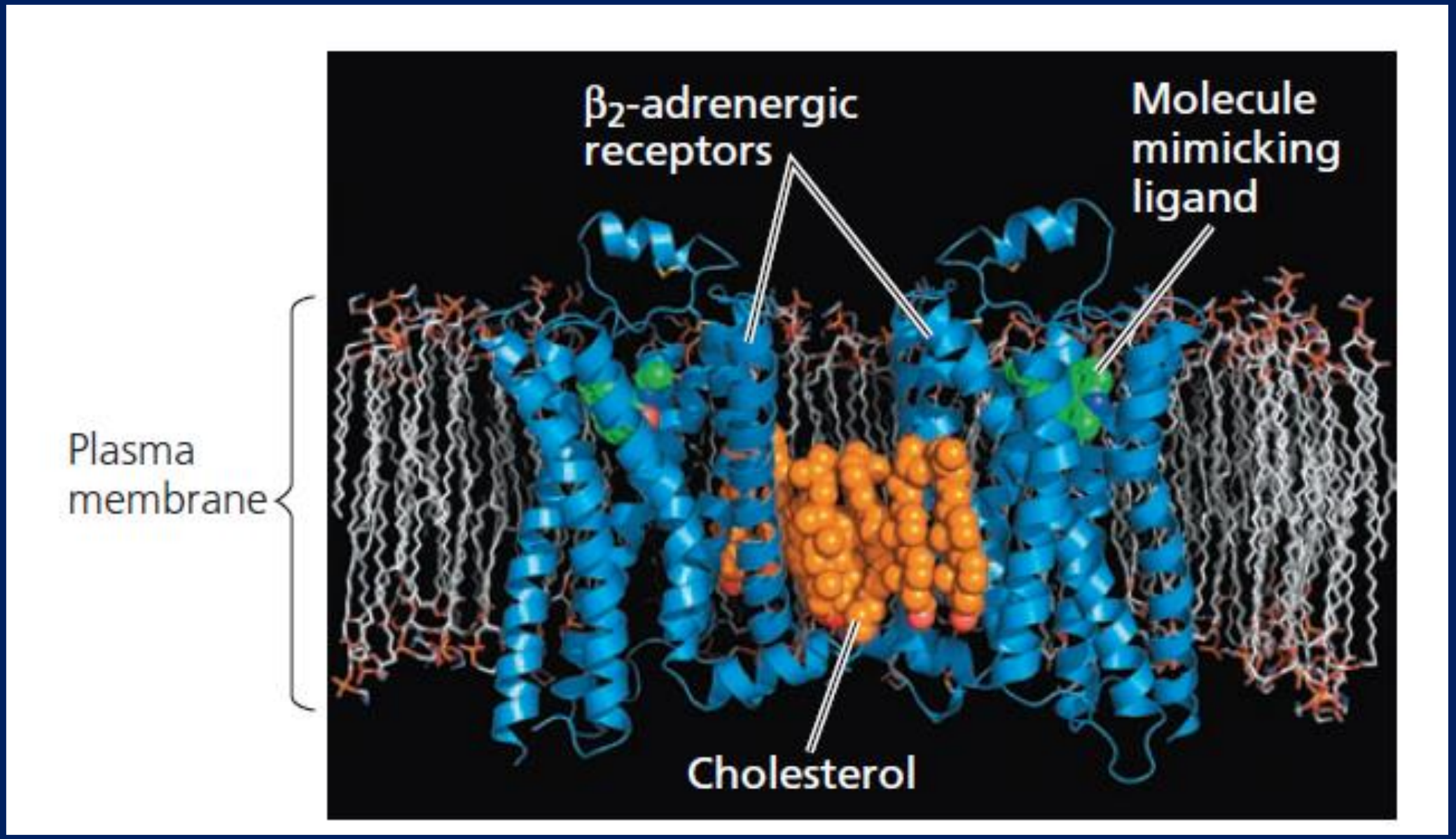


Figure 11.8

- Extremely widespread
- Involved in a variety of processes
  embryonic development
  vision, taste, smell, …
- Involved in several human diseases
  e.g., cholera, pertussis, botulism
- ~60% of all medicines used today
  target GPCRs
- Share a common architecture
  seven transmembrane receptors

G protein-coupled receptors (GPCRs)



How GPCRs receive and transduce signal

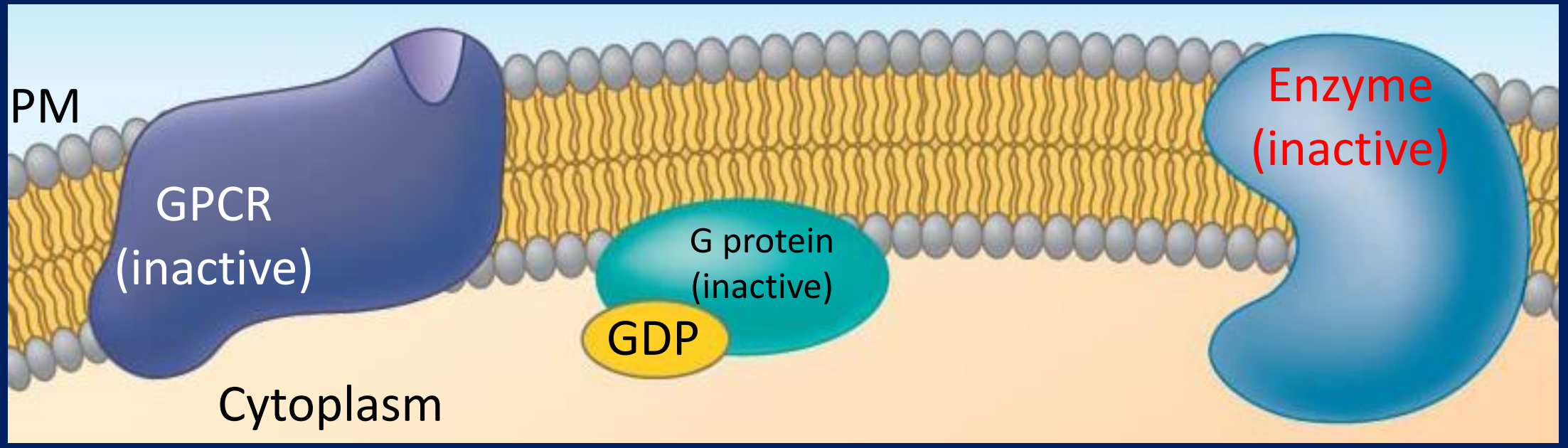


Figure 11.8

GPCR is in an inactive conformation
G protein is also inactive (since it is bound to GDP)
Enzyme is also inactive (since it is NOT bound by G protein)

PM: plasma membrane

Ligand binding site of GPCR is on the outside
G protein binding site of GPCR is on the inside

How GPCRs receive and transduce signal

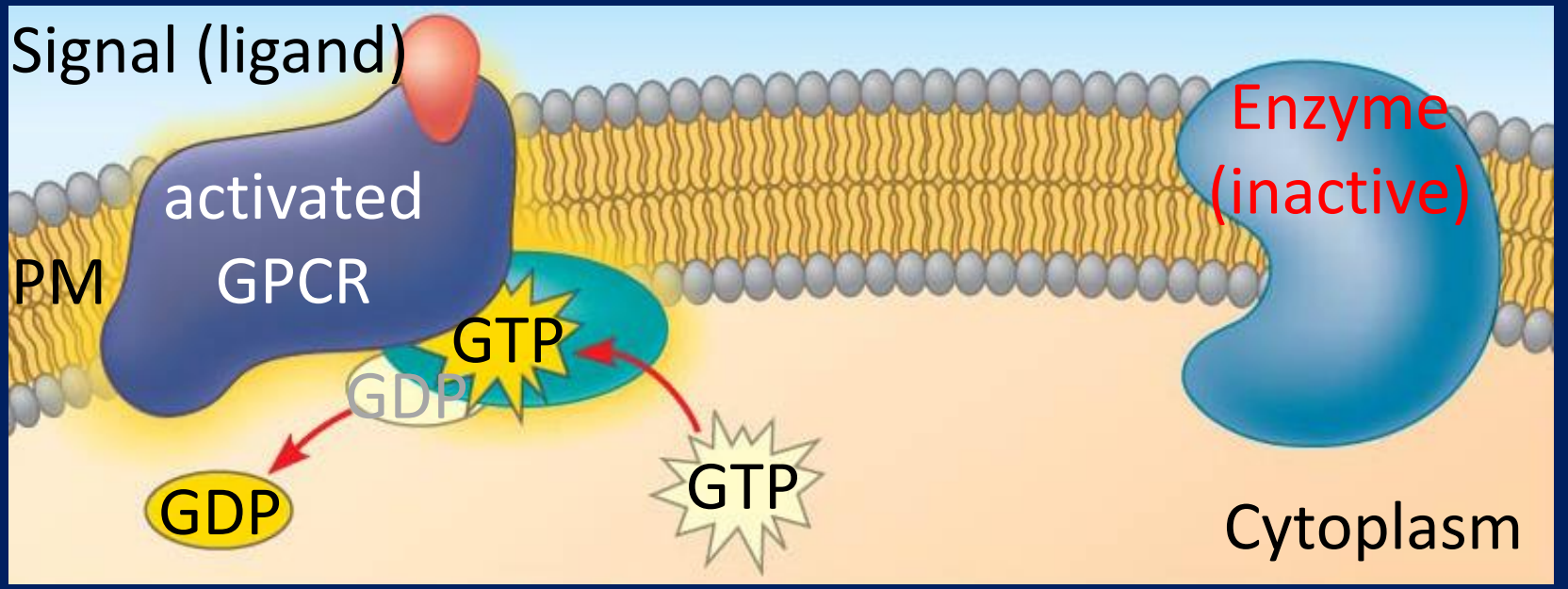


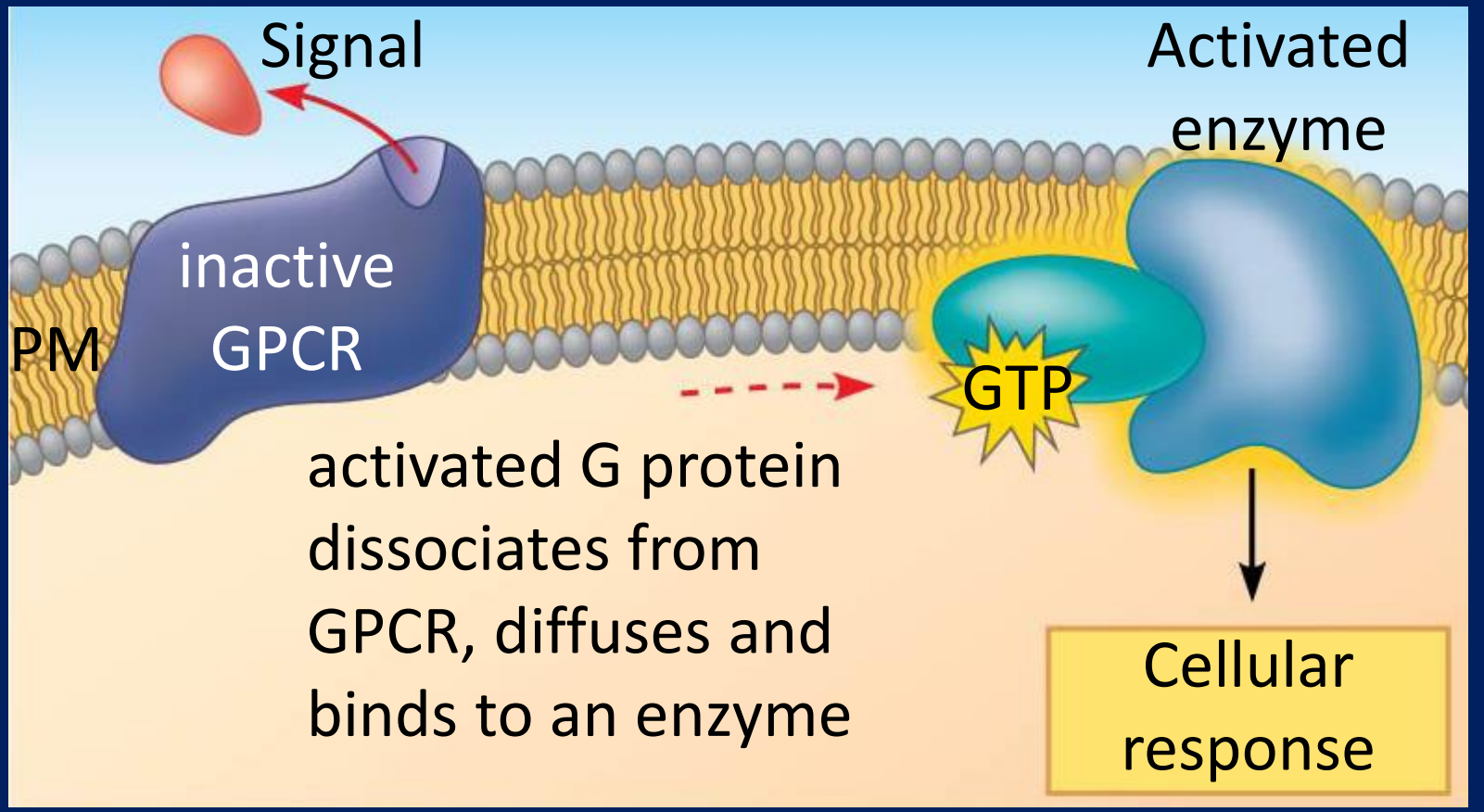
Figure 11.8

1. Signaling molecule (ligand) binds to GPCR on the outside
2. Binding induces change of shape (conformation)
3. Change of shape leads to binding of G-protein on the inside
4. Binding leads to exchange of GDP with GTP
5. GTP binding activates the G protein

How GPCRs receive and transduce signal

Reversible binding of the signal (ligand)
$[ligand]$ determines $binding \rightleftarrows dissociation$

Figure 11.8



Activated enzyme triggers a cellular response

How GPCRs receive and transduce signal

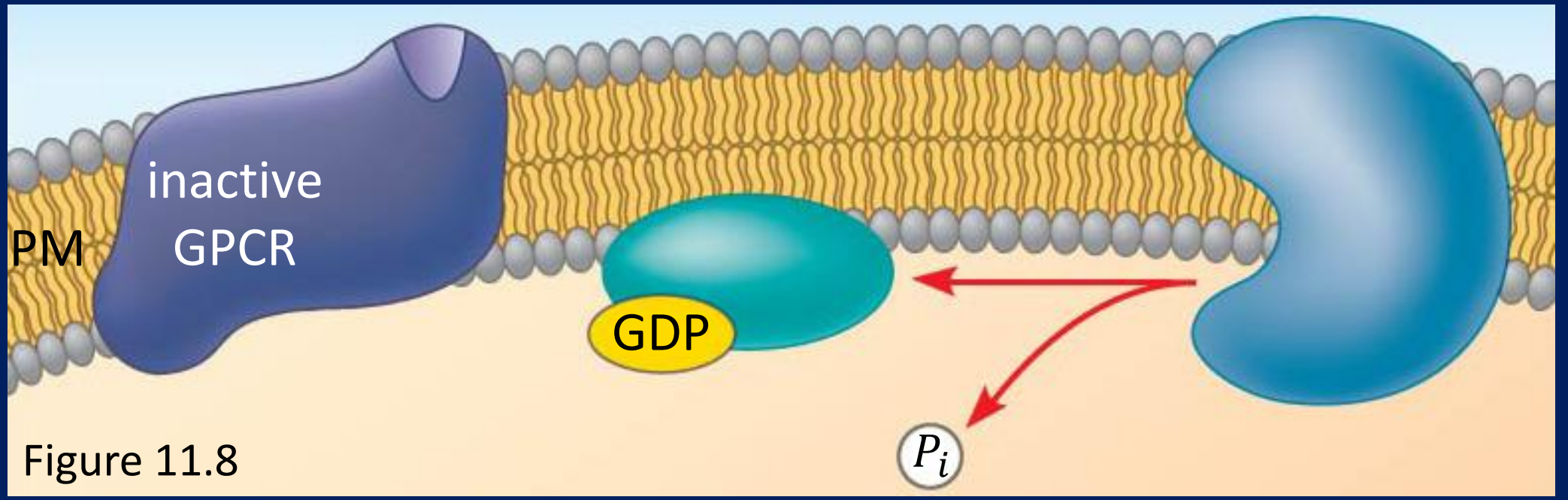


Figure 11.8

- Changes in the enzyme and G protein are transient
- G protein has GTPase activity – hydrolyzes GTP to GDP and P_i
- G protein is now GDP-bound – dissociates from the enzyme

This is a built-in controlling mechanism

Ligand-gated ion channel

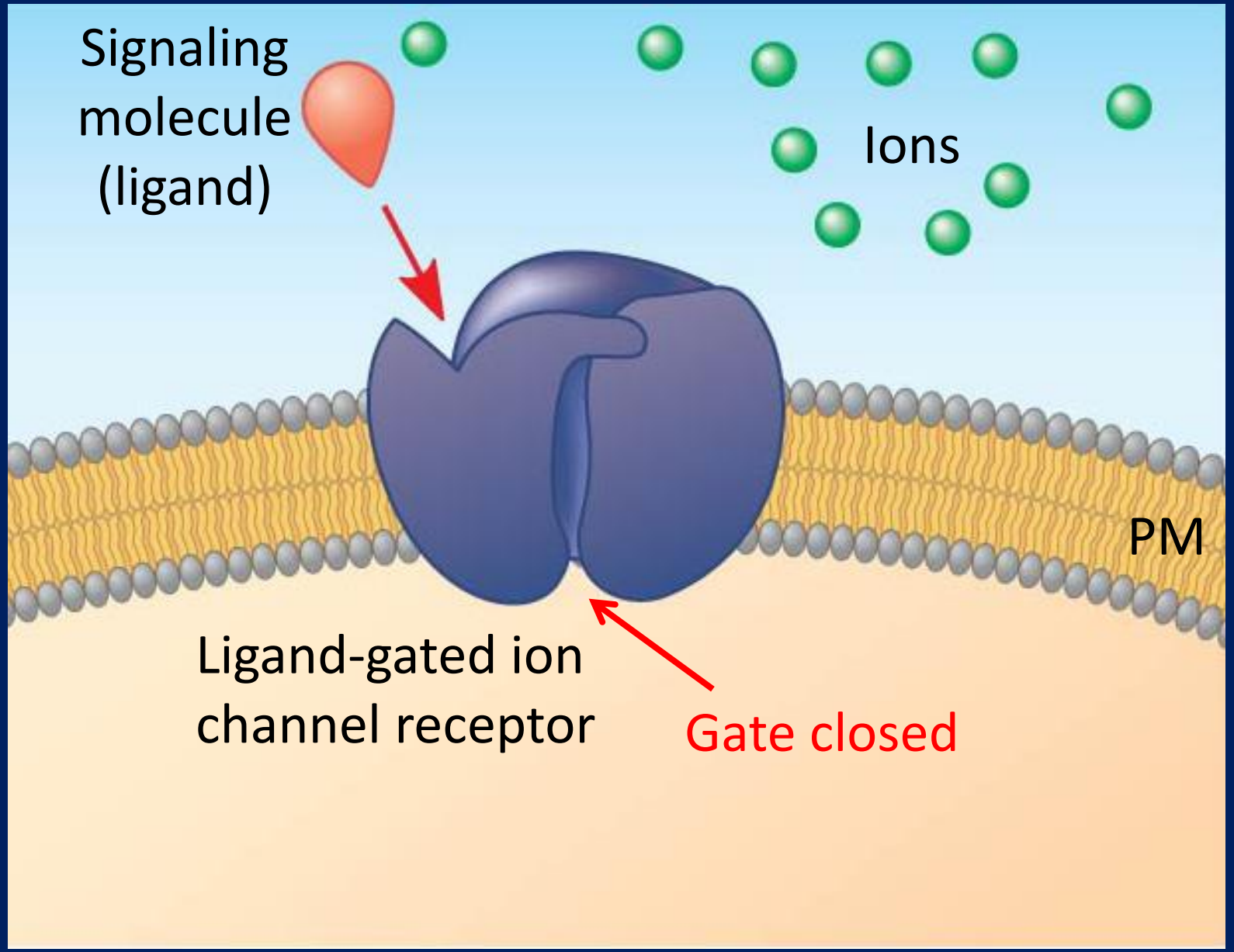


Figure 11.8

Ligand-gated ion channel

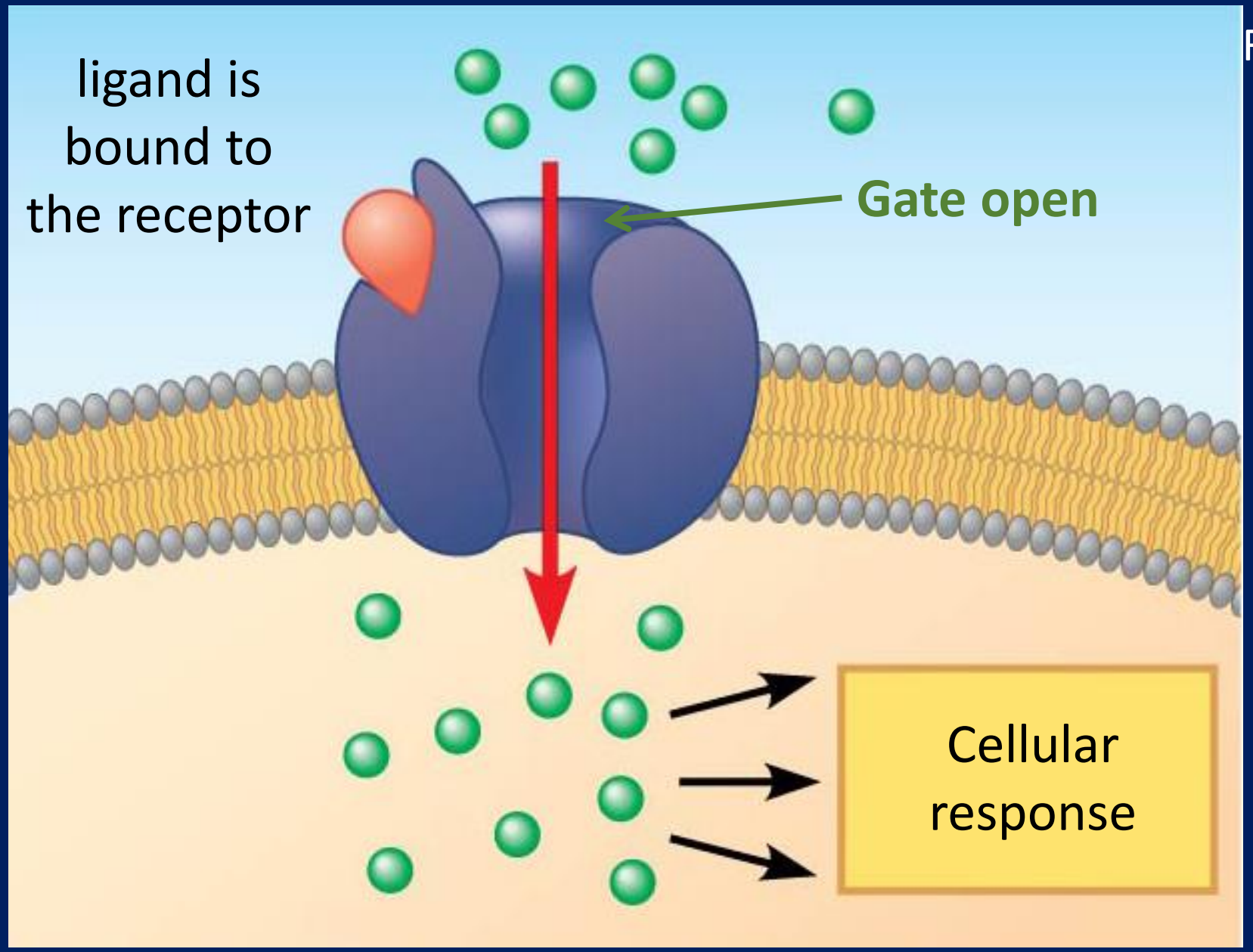
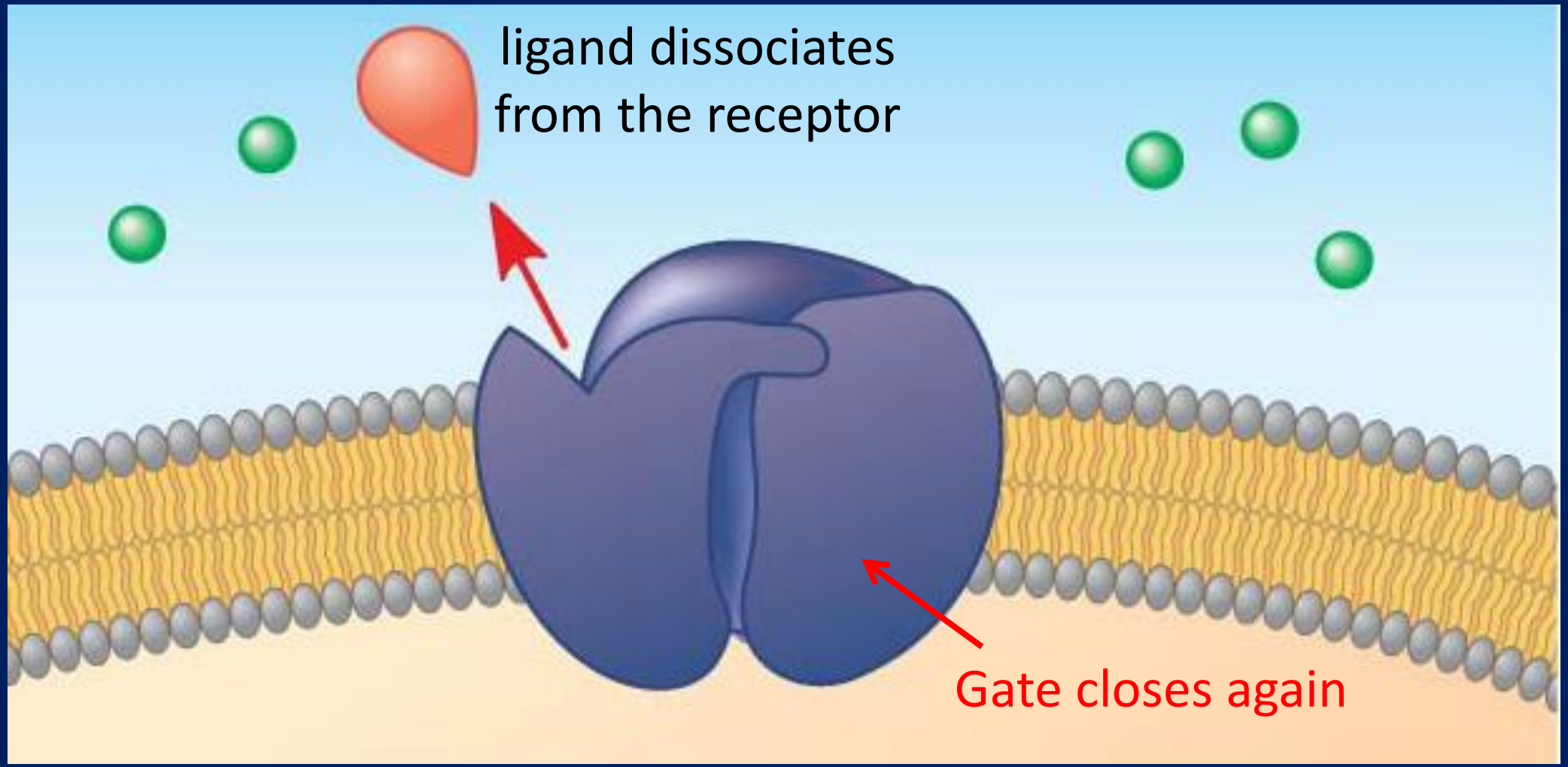


Figure 11.8

Ligand-gated ion channel

Figure 11.8



Signals that enter the cell

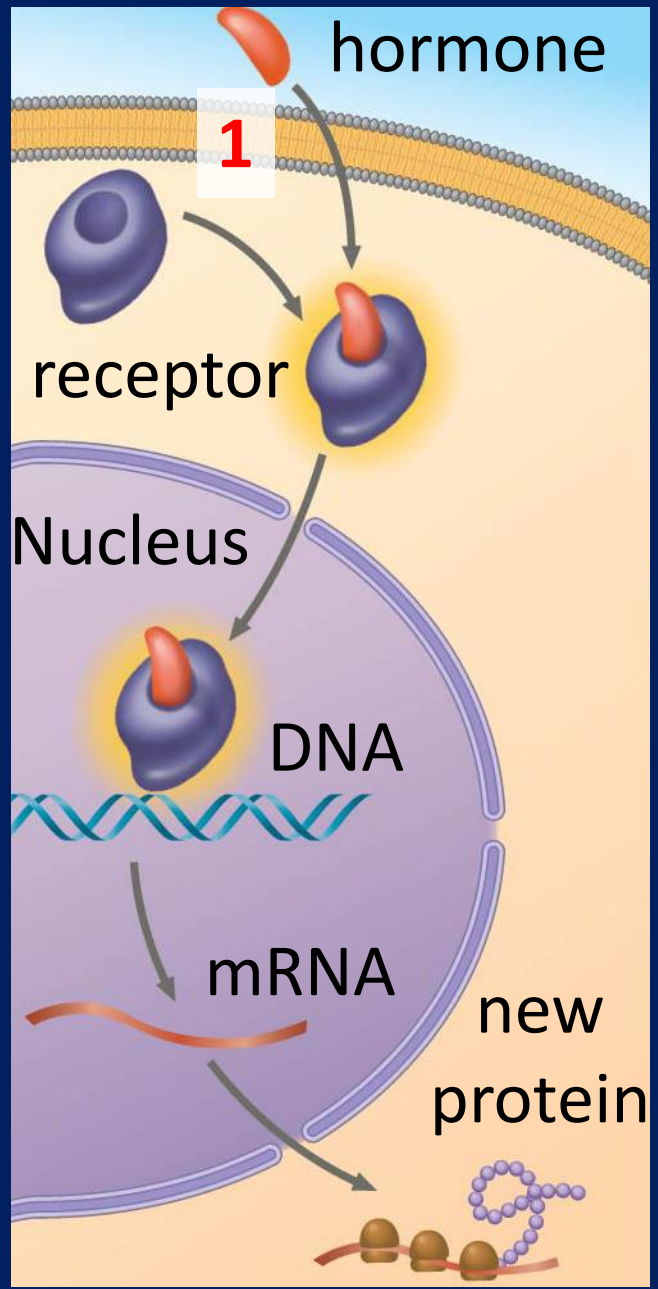


Figure 11.9

1. The steroid hormone passes through the cell membrane

Signals that enter the cell

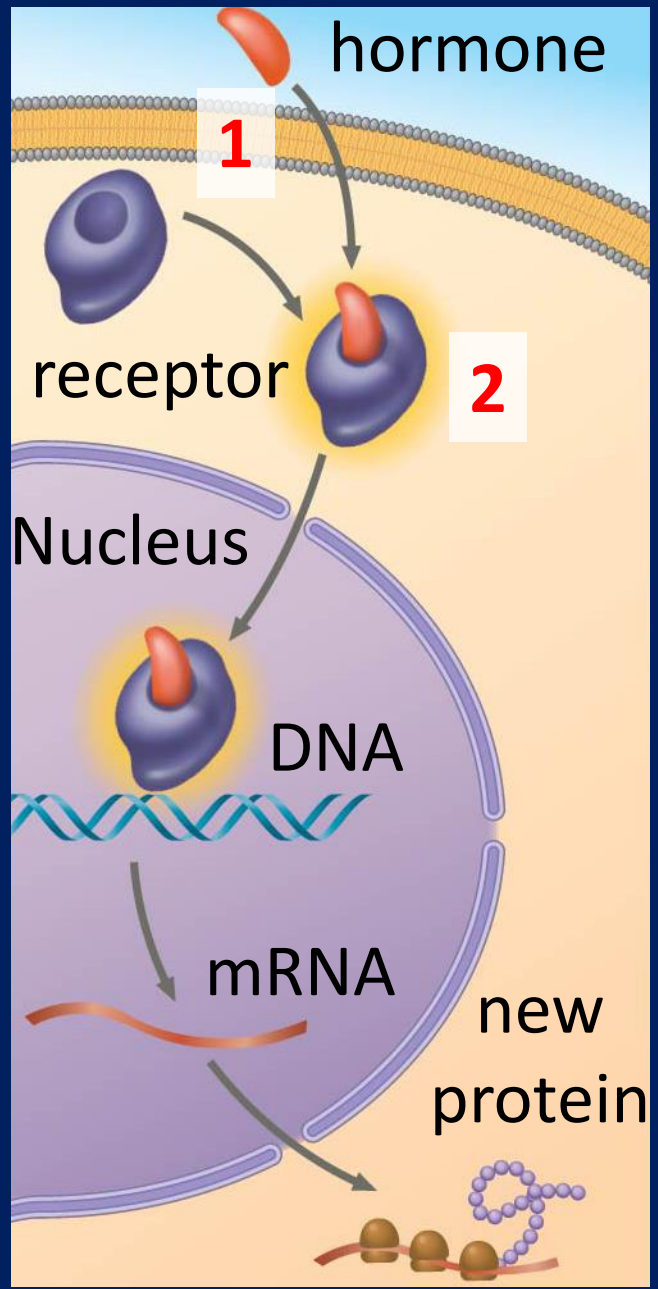


Figure 11.9

2. Hormone binds to its specific receptor in the cytoplasm

Binding activates the receptor

Signals that enter the cell

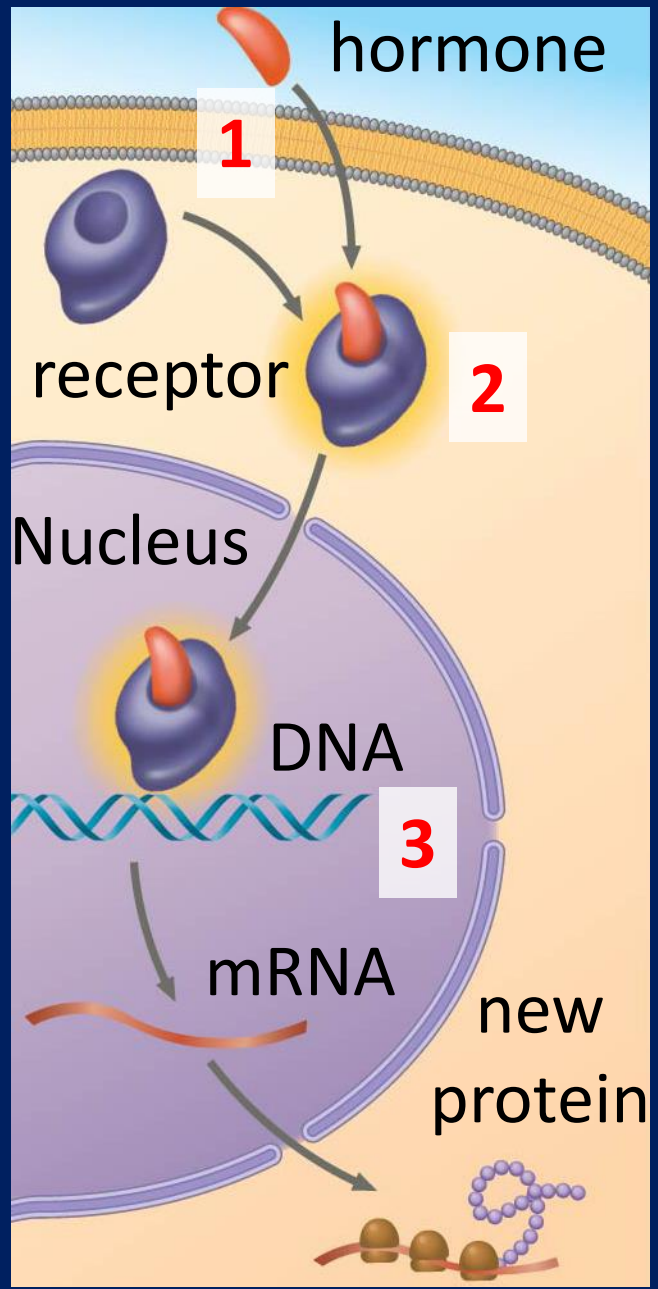


Figure 11.9

3. Hormone – receptor complex enters the nucleus

Binds to specific genes on the chromosome

Binding triggers transcription

Signals that enter the cell

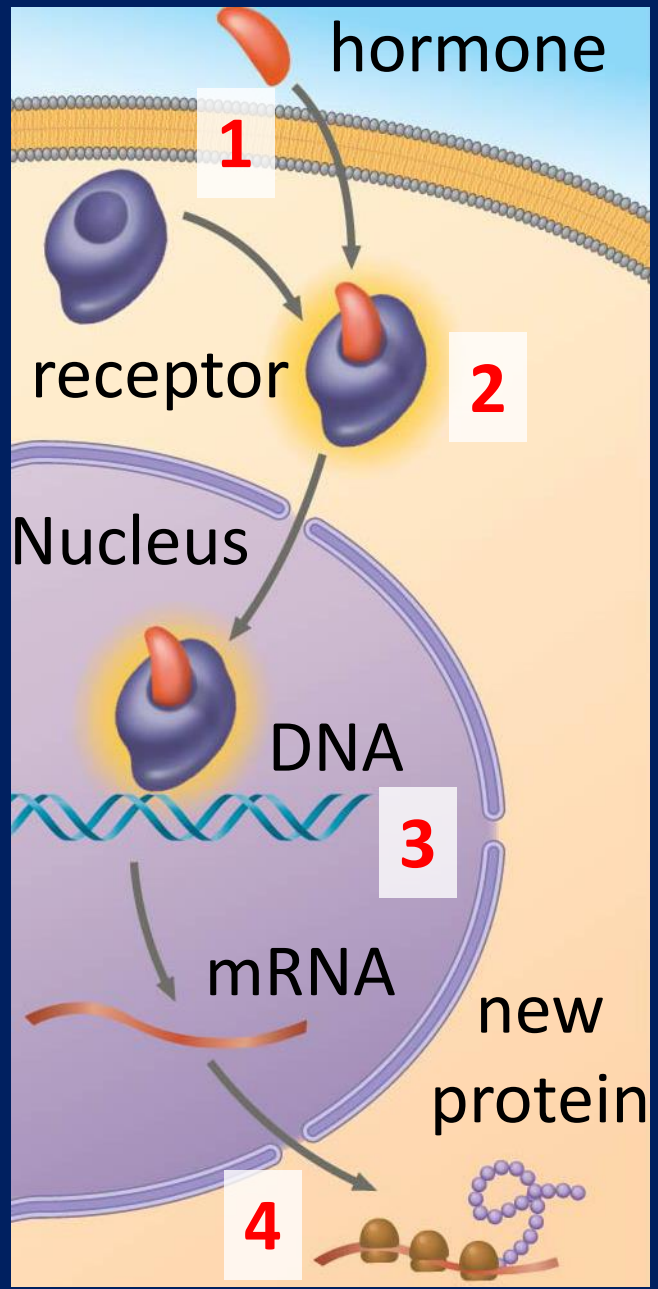


Figure 11.9

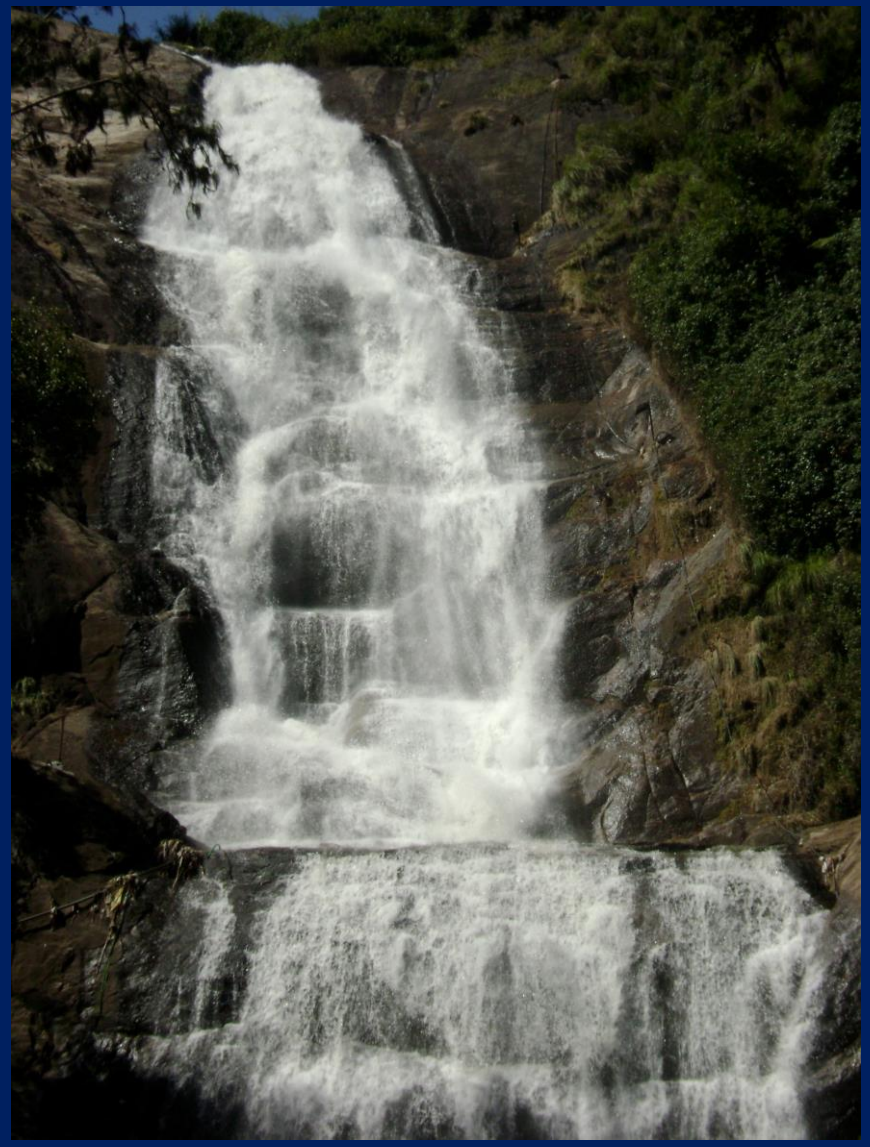
4. Specific protein is synthesized

With the synthesis of the protein, signaling is complete

Class 8: learning objectives

- Cell signaling in yeast – concept of signal transduction
- Local and long distance signaling – illustrative schematics
- Signal transduction – an overview
- Illustrative examples
  - Reception
  - Transduction
  - Response

Cascade



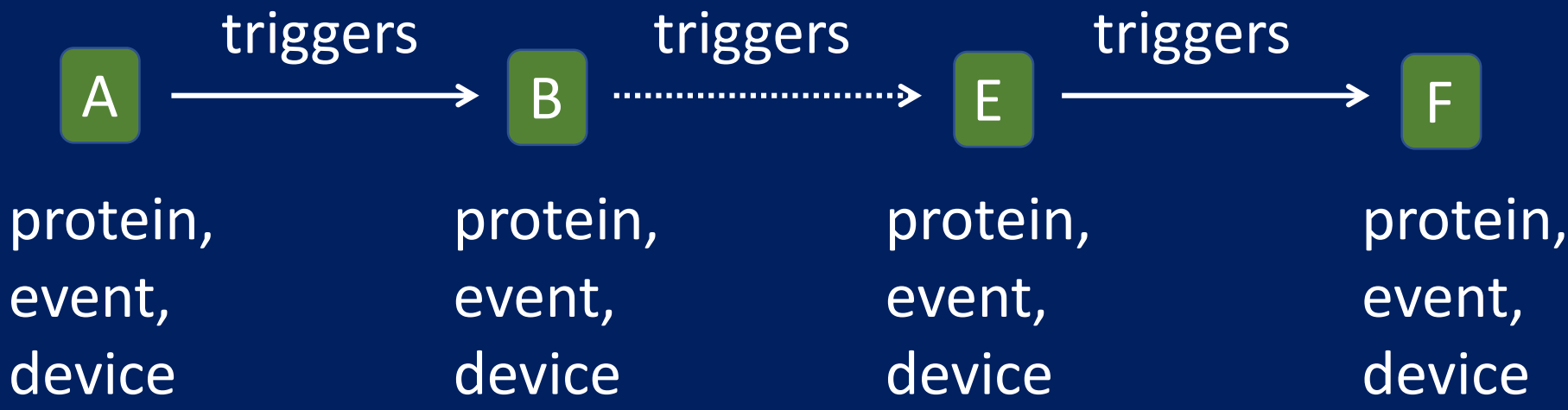
https://upload.wikimedia.org/wikipedia/en/5/55/Silver_Cascade_3-4.JPG

cascade (*noun*)

- A small, steep waterfall
- A large number of things that happen quickly in a series

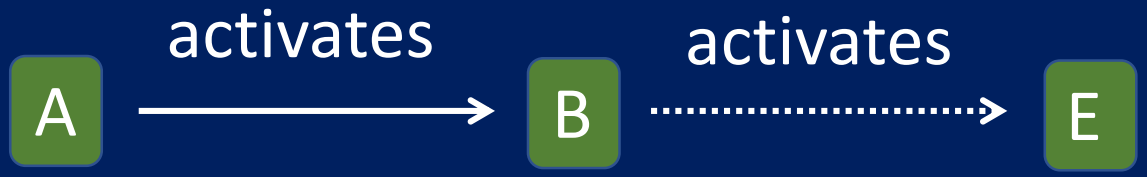
(www.merriam-webster.com)

Cascade



What is the advantage?

Cascade



protein is activated by ligand (signal)

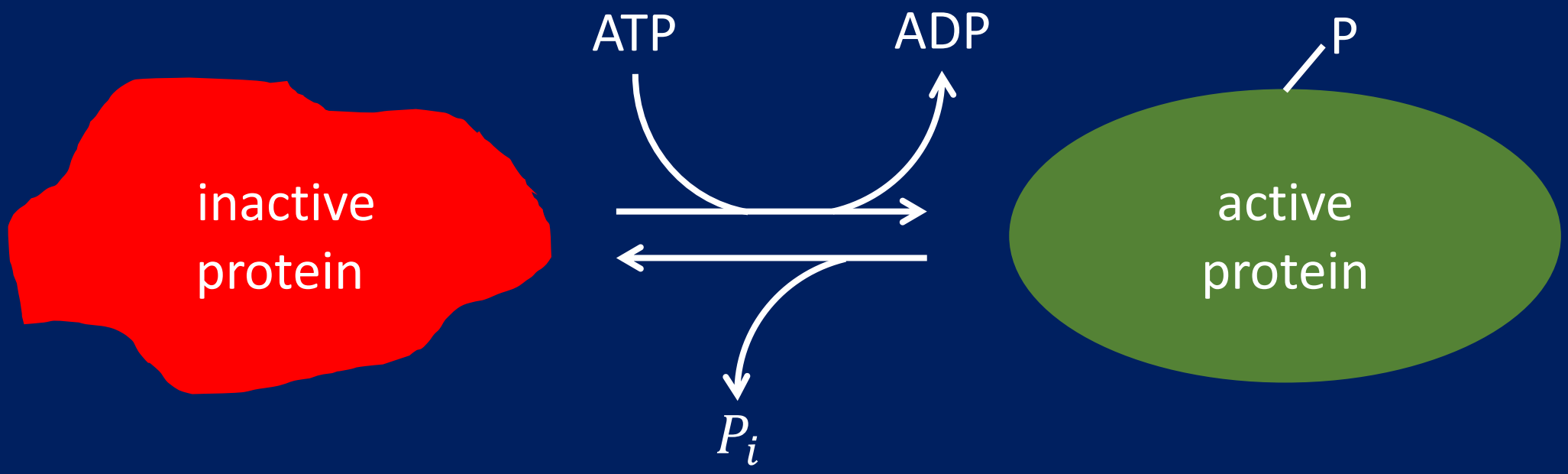
Remains active only for a short duration

e.g., by phosphorylation

is deactivated by a phosphatase

Kinase and phosphatase

Kinase (an enzyme which phosphorylates the protein)

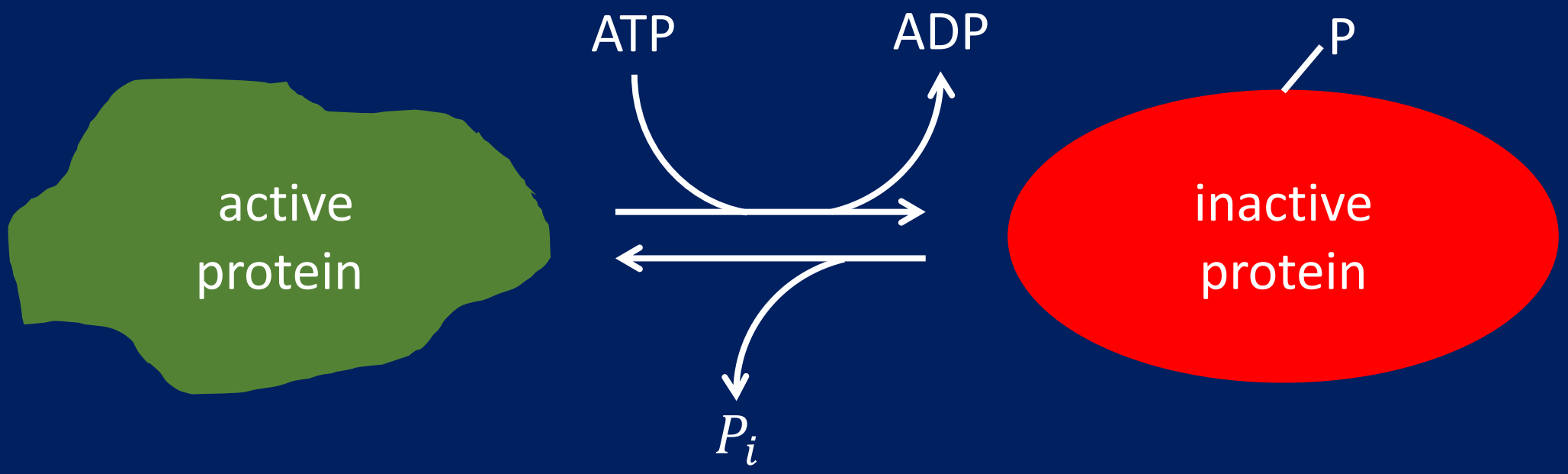


Phosphatase (an enzyme which dephosphorylates the protein)

Phosphorylation – dephosphorylation bring about shape (conformation) changes

Kinase and phosphatase

Kinase (an enzyme which phosphorylates the protein)



Phosphatase (an enzyme which dephosphorylates the protein)

Phosphorylation – dephosphorylation bring about shape (conformation) changes

Phosphorylation cascade

Dominos

- Signal transduction usually involves multiple steps
- Multistep pathways can greatly amplify a signal
- Binding of ligand to the receptor triggers the first step
- Domino effect: sequential activation of proteins
- Each step involves signal transduction – usually, a change in the shape of a protein

http://dataquarks.com/am-i-alright-jack-the-domino-effect-of-brexit

Phosphorylation cascade

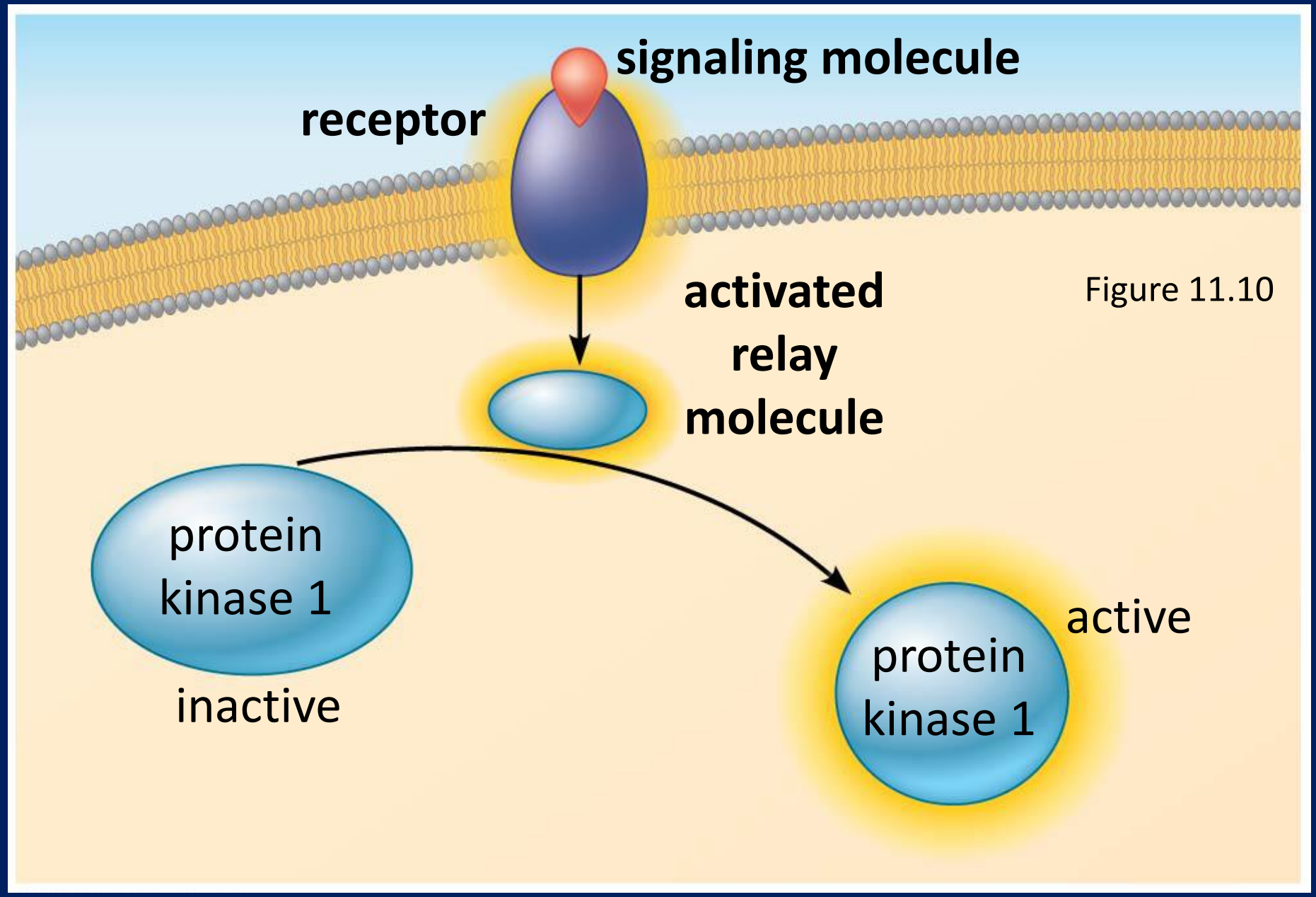
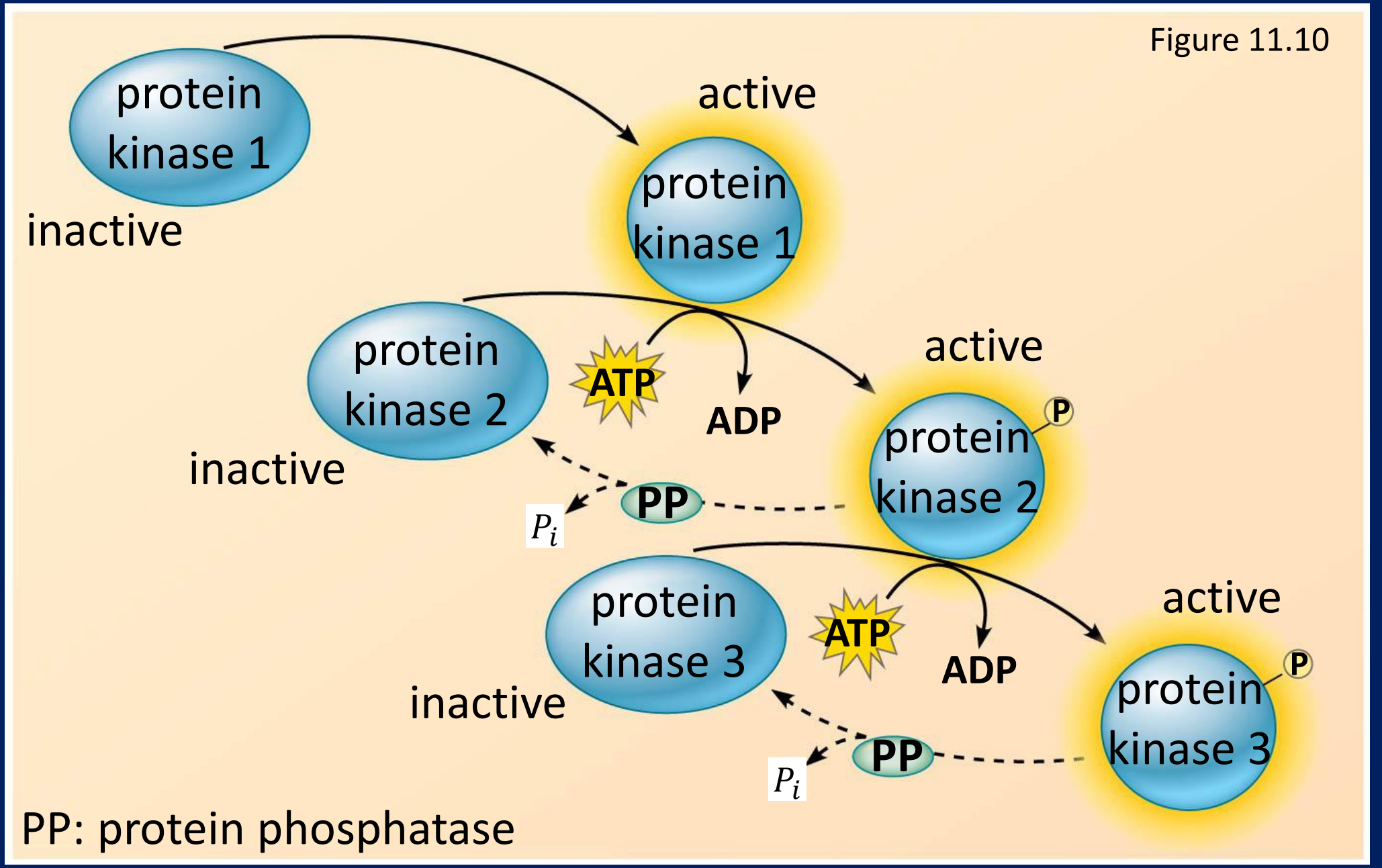
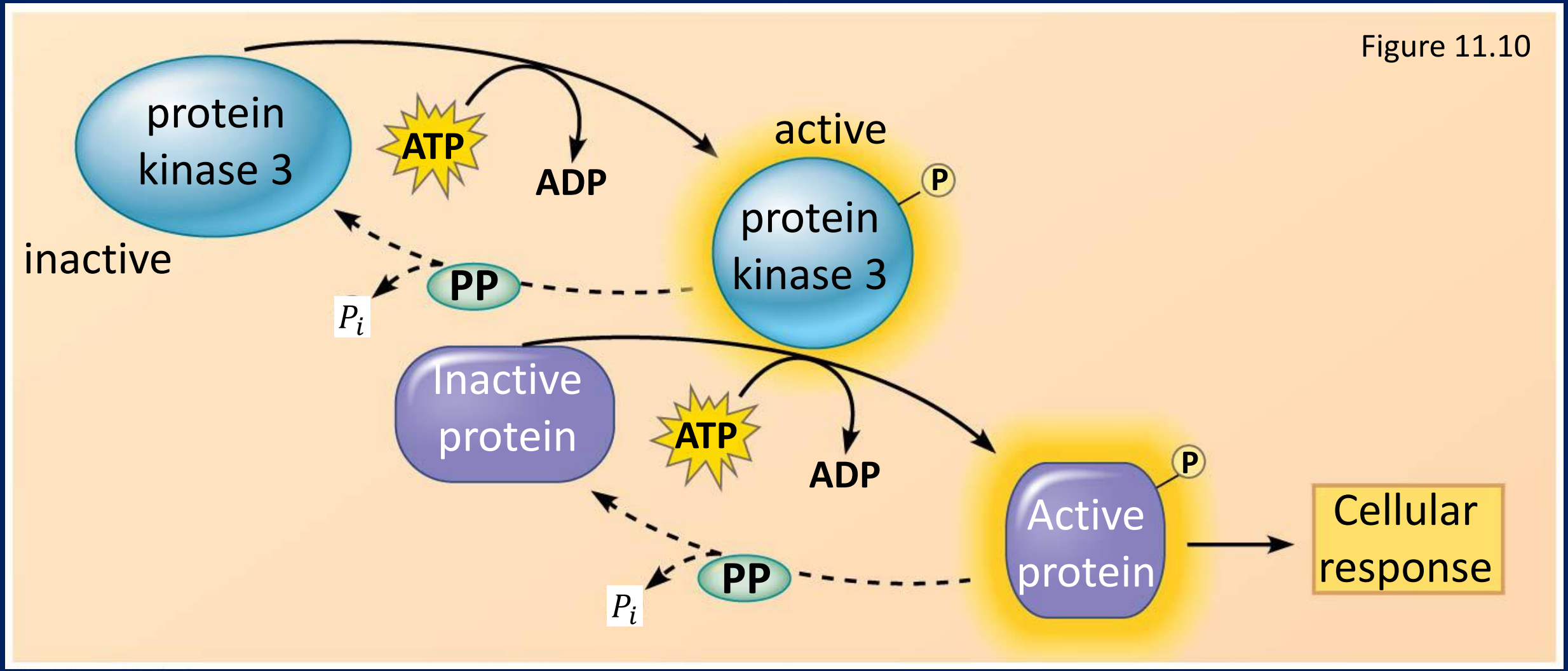


Figure 11.10

Phosphorylation cascade



Phosphorylation cascade



Signal amplification by cascades

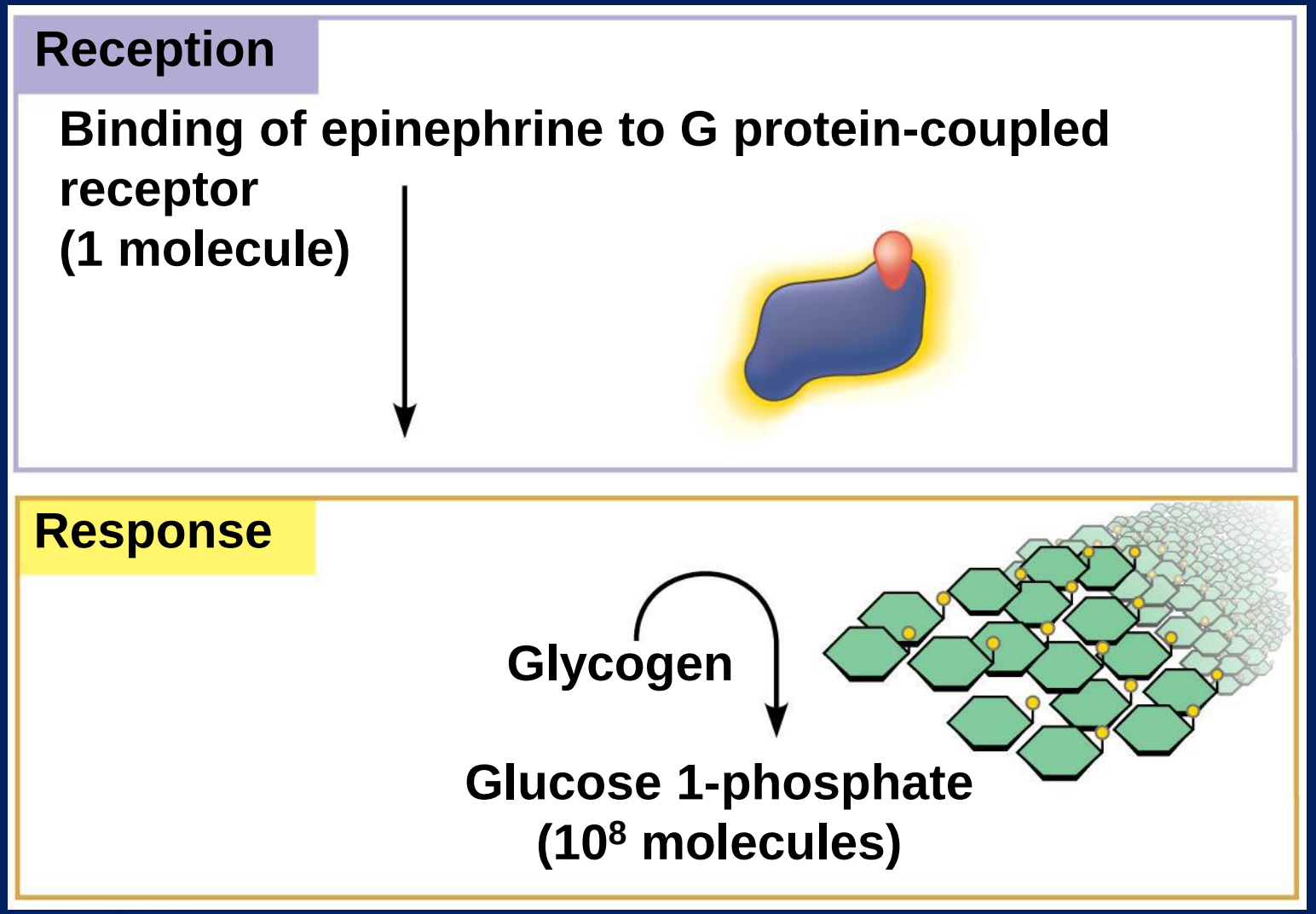


Figure11.16

Signal amplification by cascades

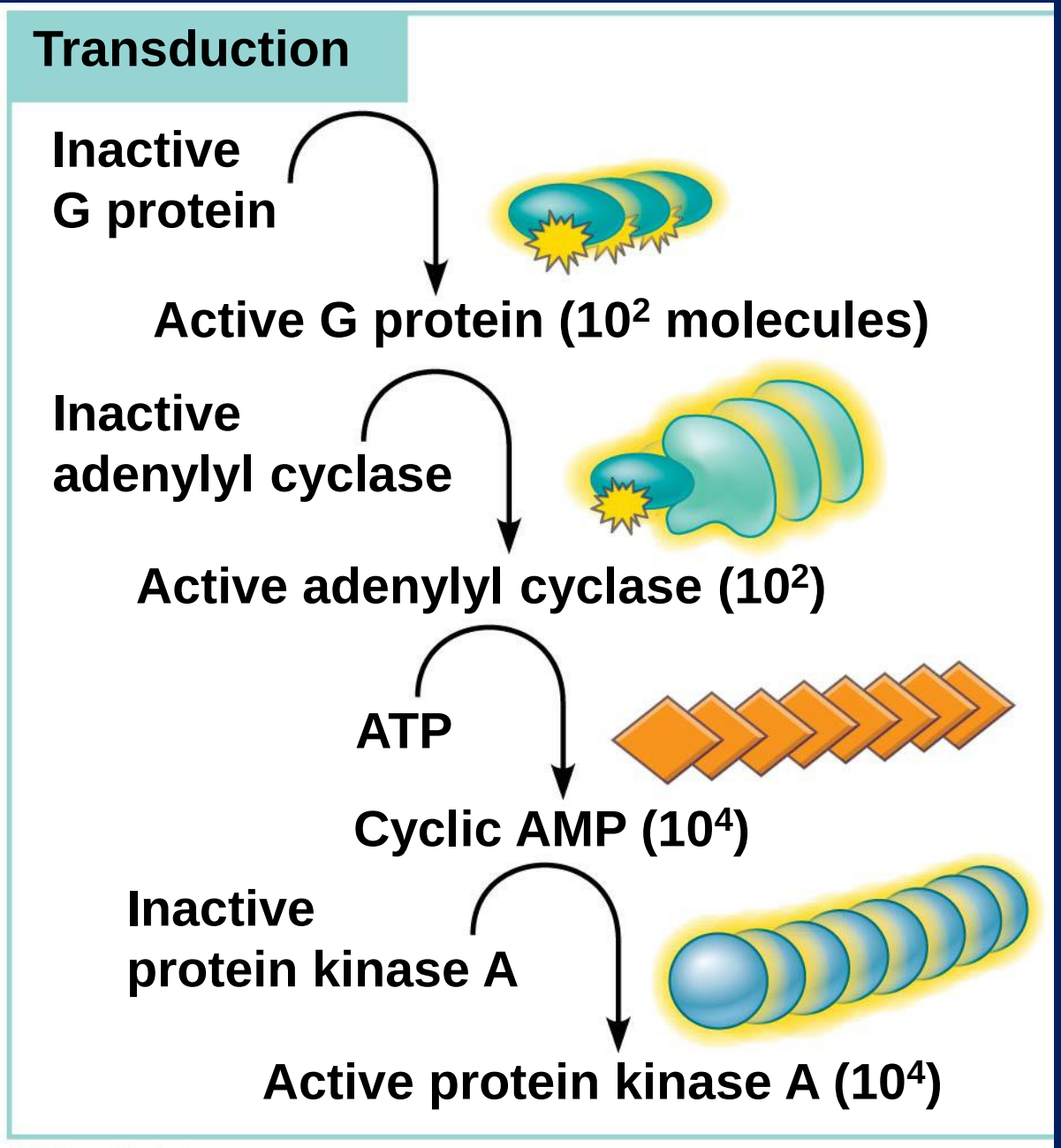


Figure 11.16

Signal amplification by cascades

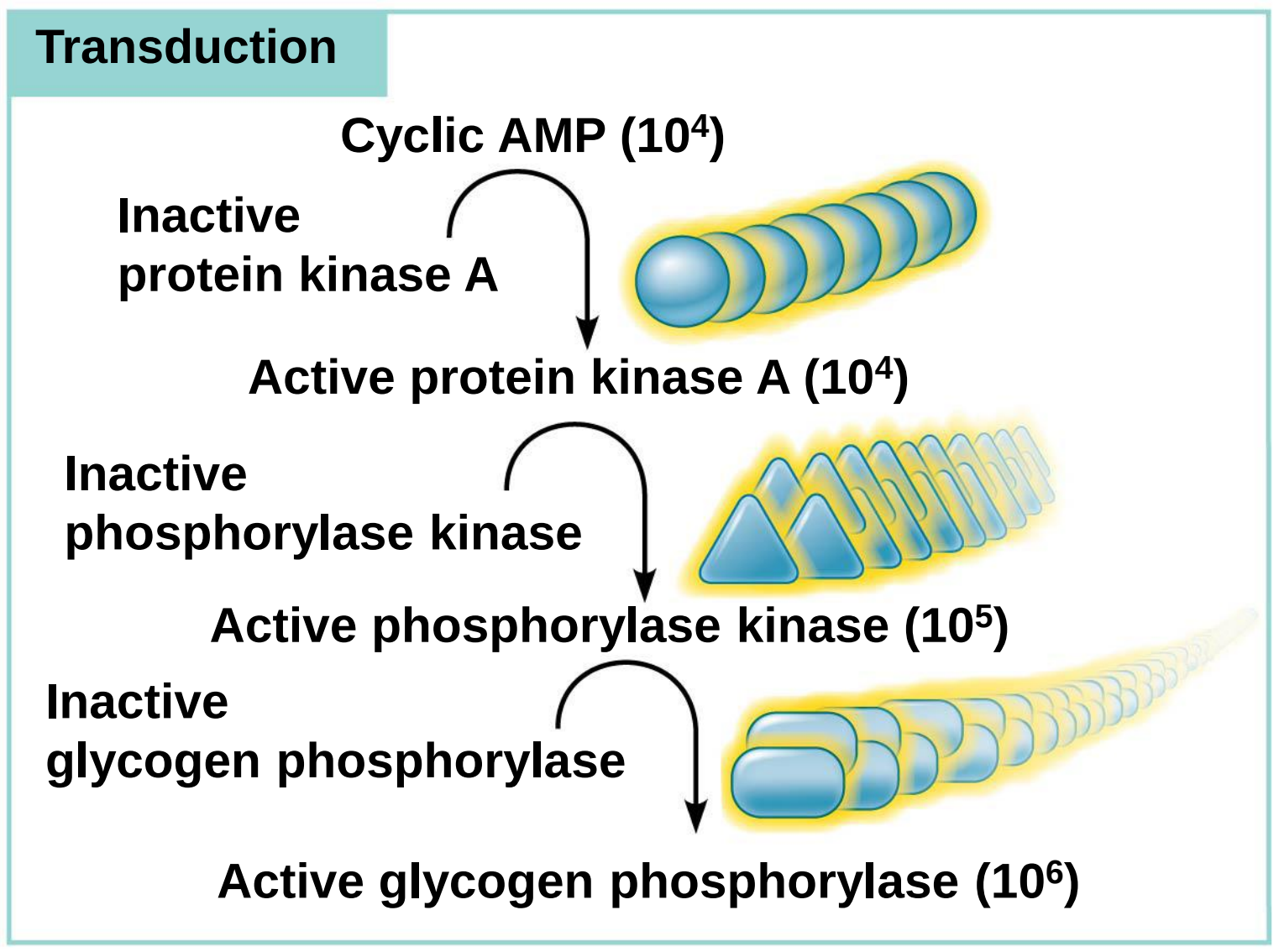


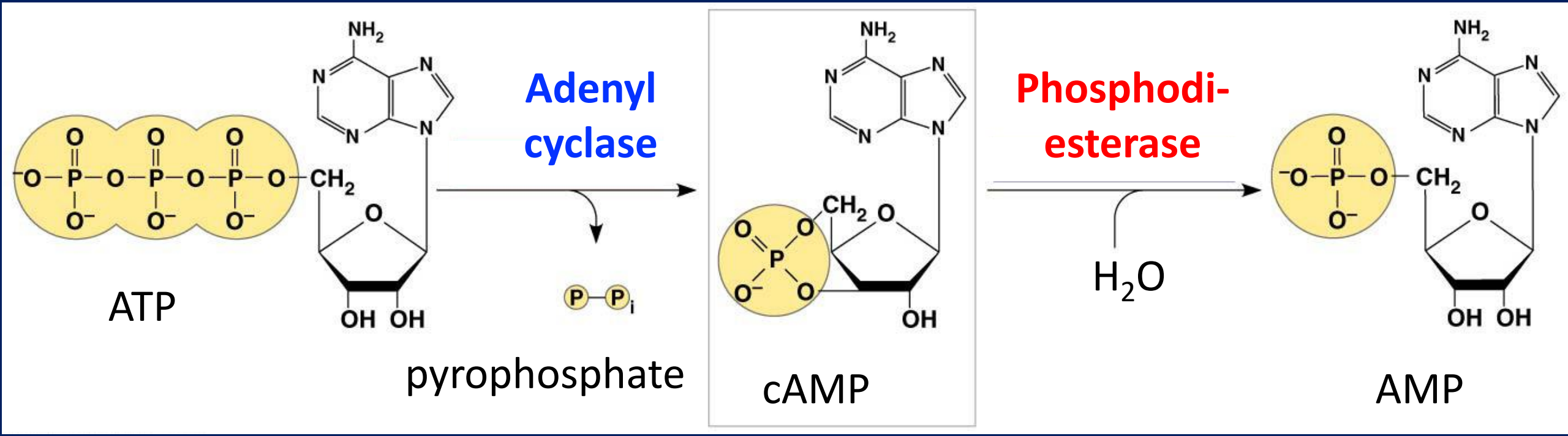
Figure 11.16

Second messenger

AMP: adenosine monophosphate

cyclic AMP: cAMP

Figure 11.11



cAMP and G protein signaling pathway

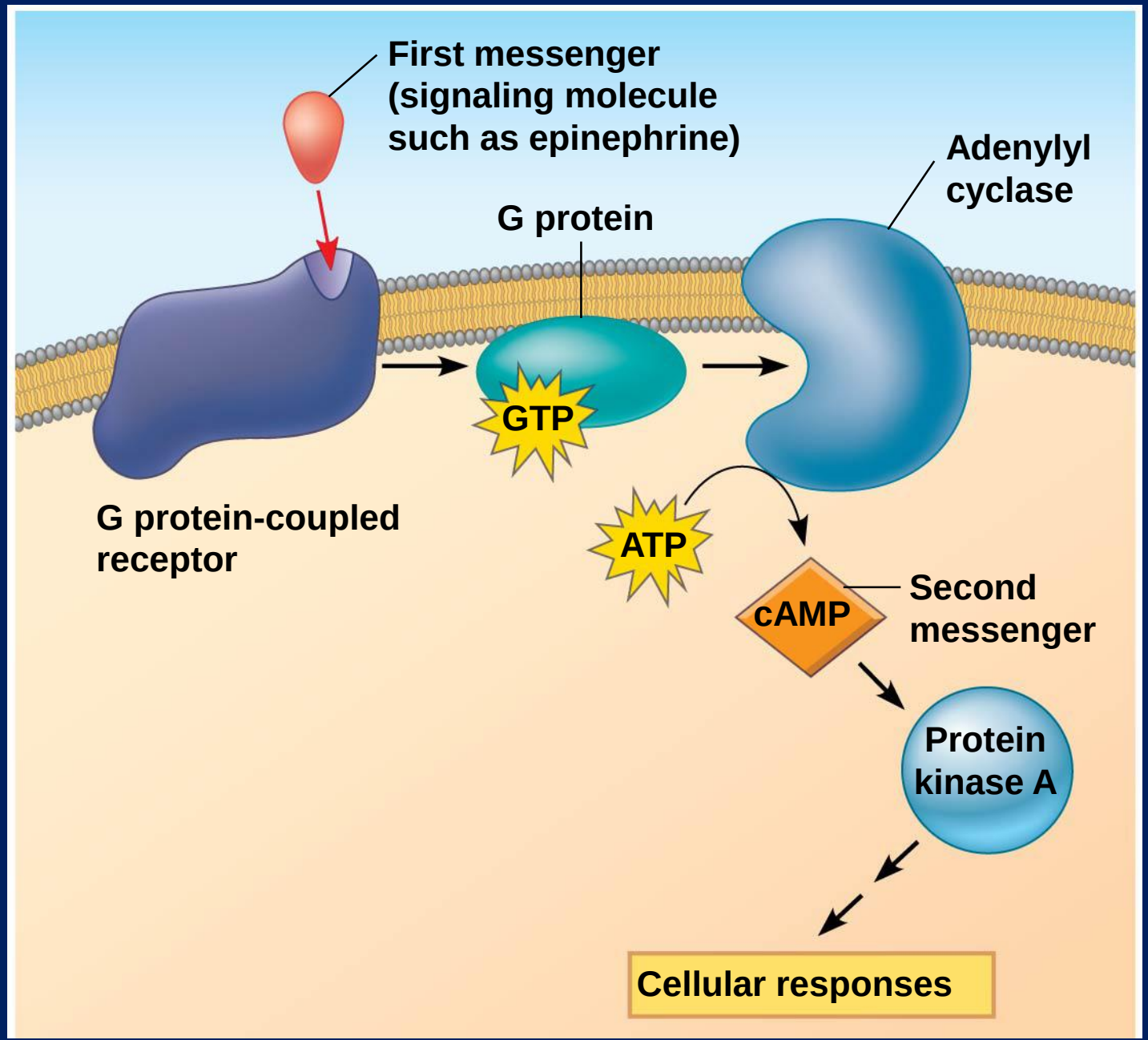
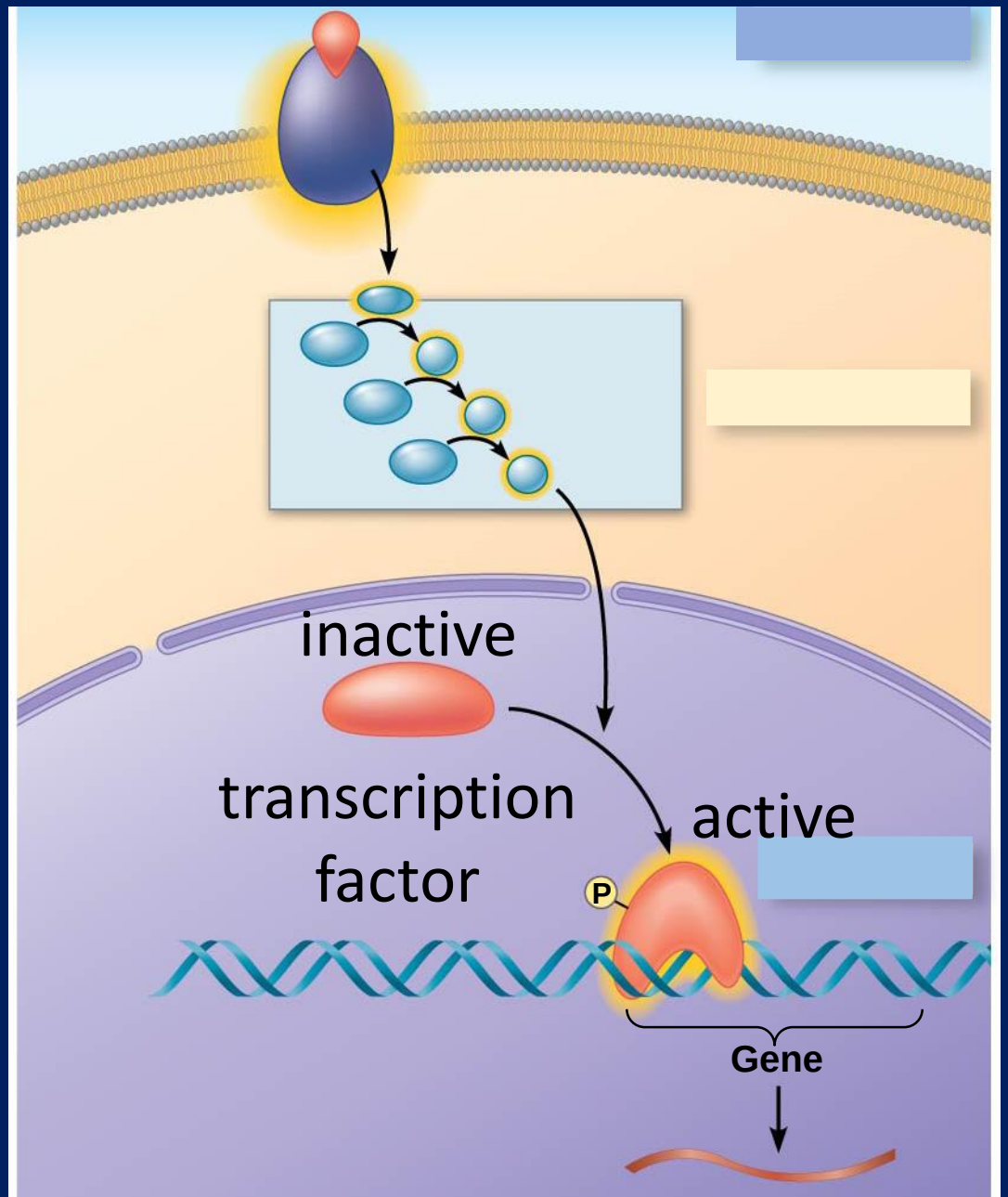


Figure 11.12

Class 8: learning objectives

- Cell signaling in yeast – concept of signal transduction
- Local and long distance signaling – illustrative schematics
- Signal transduction – an overview
- Illustrative examples
  - Reception
  - Transduction
  - Response

Figure 11.15



Reception

Transduction

Response