Cell Communication

Multicellular organisms

Cells – comunicate <= chemical language (chemical signals)

- travel across the space between cells;

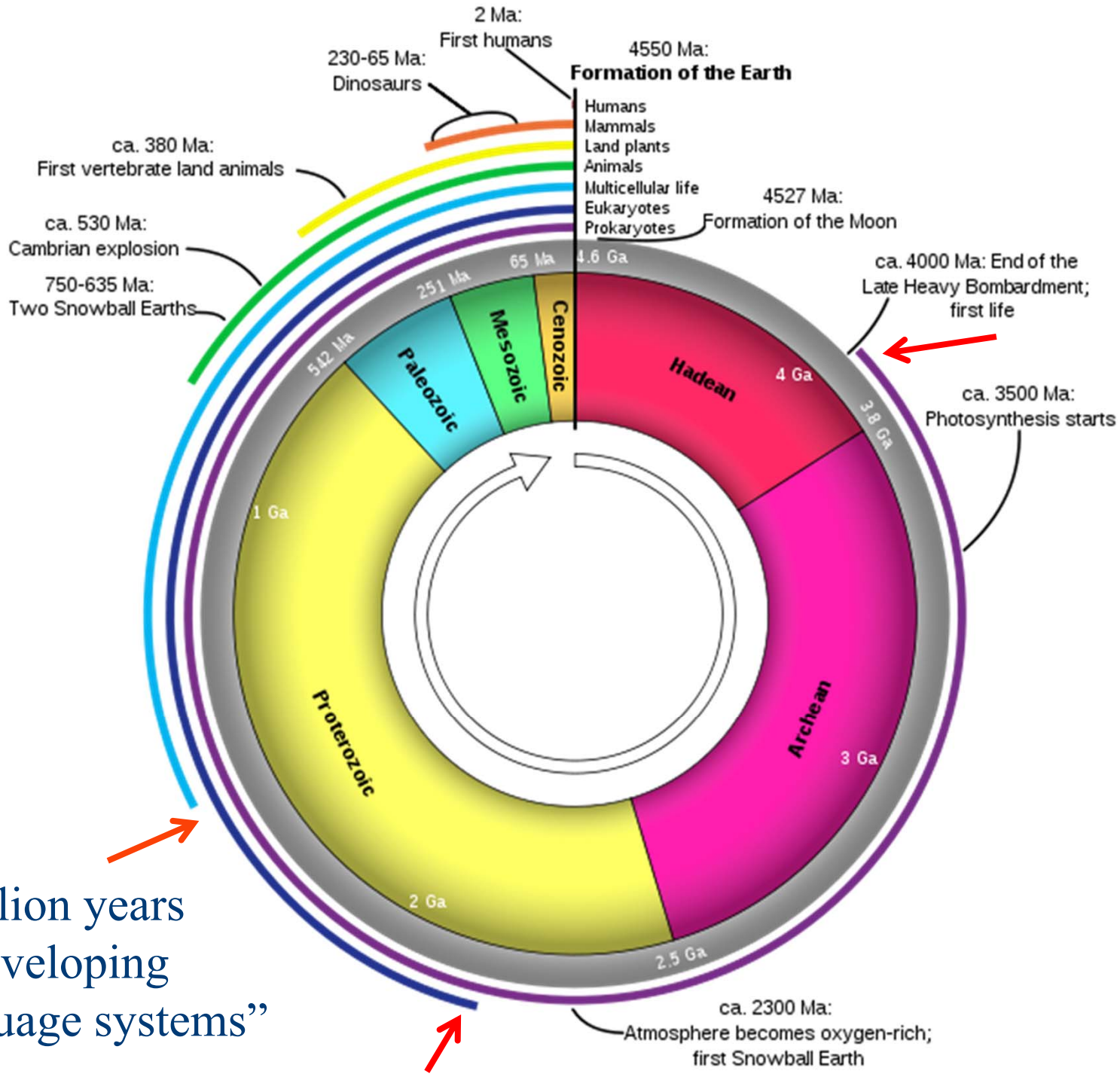
- involves complex intracellular mechanisms:

- which signal?

- how many?

- at what time?

- how to interpret?



2.5 bilion years
for developing
“language systems”

Communication

EMITTING CELL –> SIGNAL –> TARGET CELL -

RECEPTOR –> IC –> SIGNALLING Ps –>

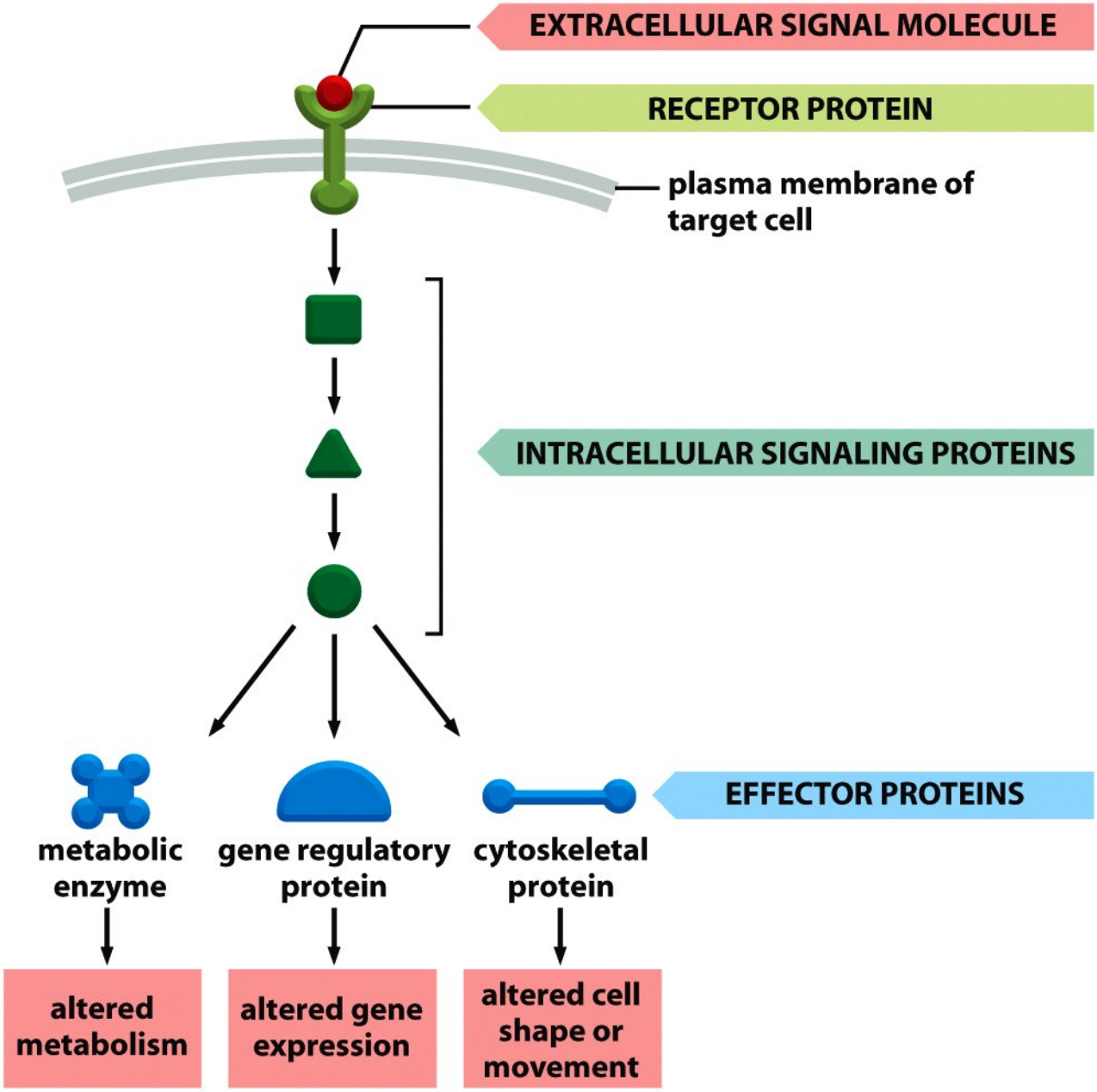
EFFECTOR Ps => EFFECT

SIGNAL MOLECULES:

- ✓ **mainly extracellular;**
- ✓ **long/short distances;**
- ✓ **most cells emit & receive;**

RECEPTOR PROTEINS (cell surface/IC)

- human genome– more than 1500 genes.


EXTRACELLULAR SIGNAL MOLECULE
RECEPTOR PROTEIN
plasma membrane of target cell
INTRACELLULAR SIGNALING PROTEINS
EFFECTOR PROTEINS
metabolic enzyme
gene regulatory protein
cytoskeletal protein
altered metabolism
altered gene expression
altered cell shape or movement

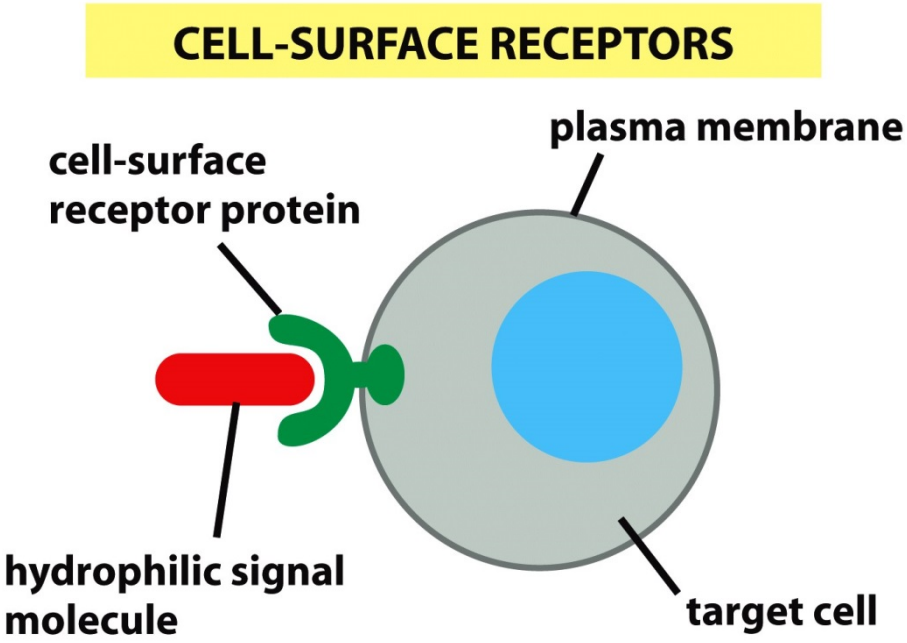
EXTRACELLULAR SIGNAL MOLECULES (hydrophilic/hydrophobic)

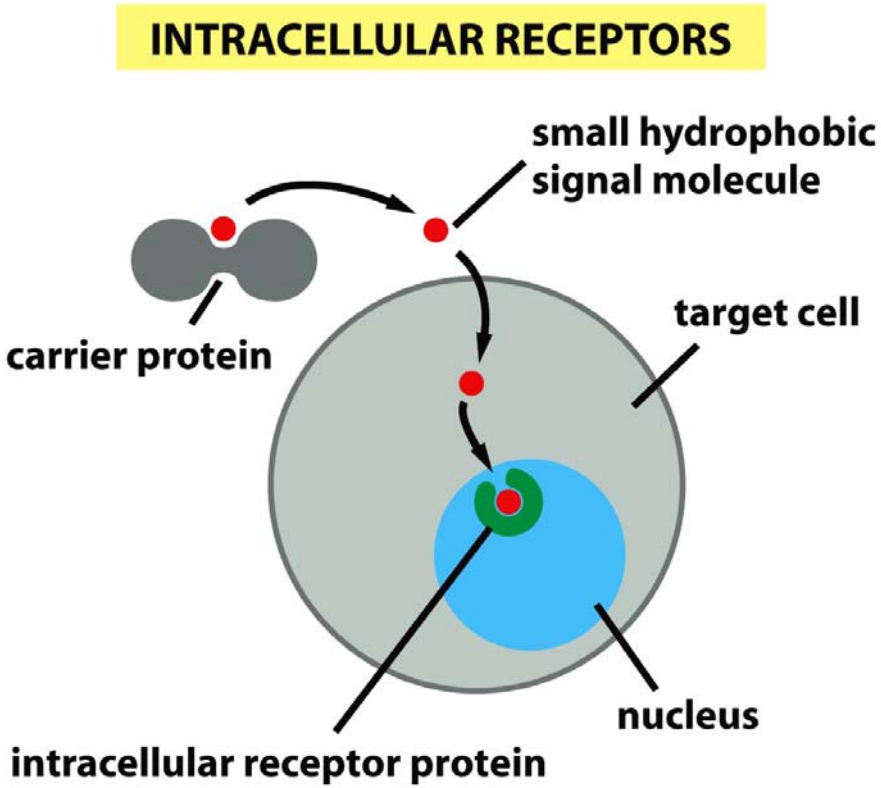
- proteins, small peptides, amino acids;
- nucleotides;
- steroids;
- retinoids;
- fatty acid derivatives;
- dissolved gases (eg: nitric oxide and carbon monoxide).

Act at low/high concentrations

Receptors – bind the SMs with high/low affinity

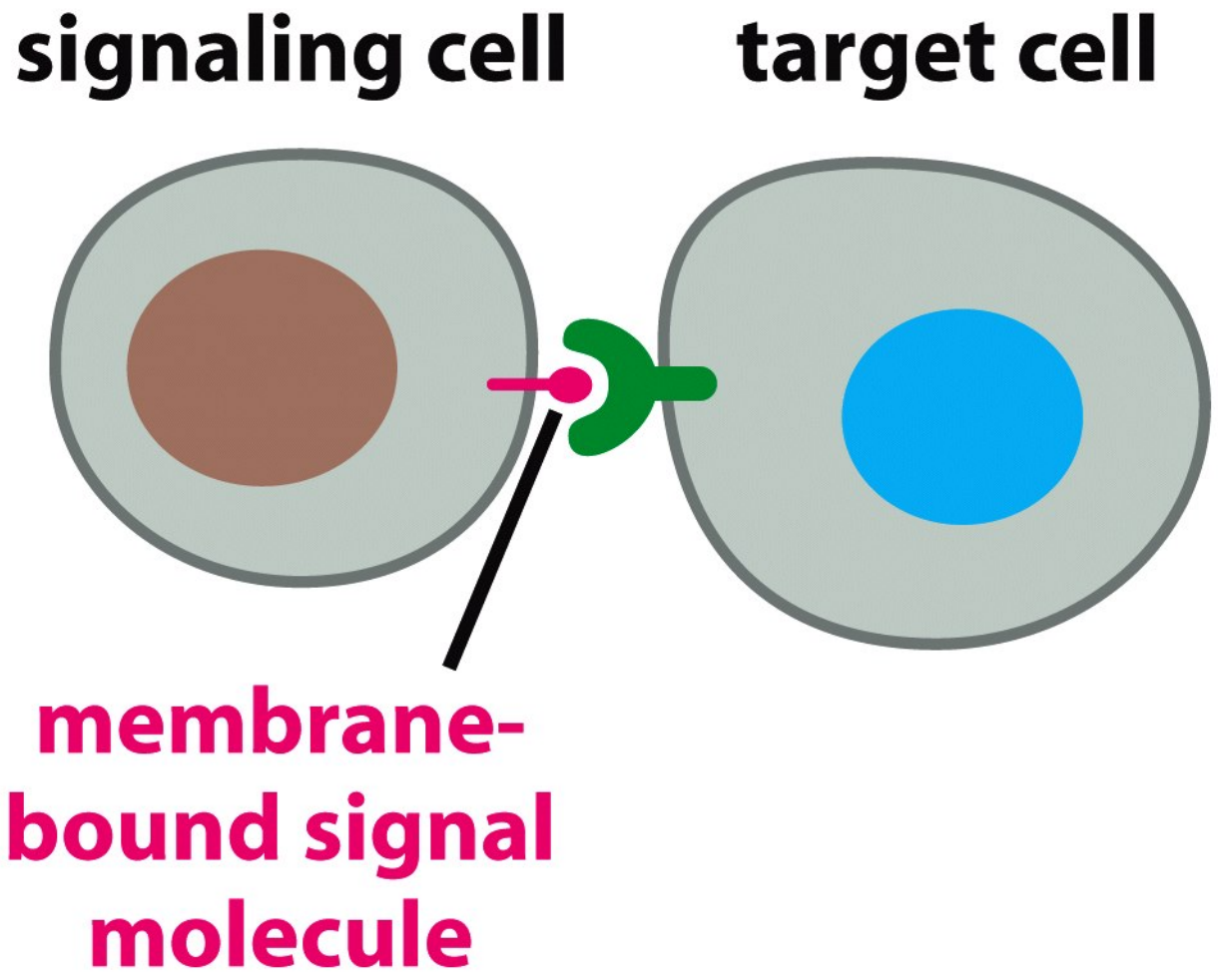
the target cell responds by means of a **RECEPTORS**



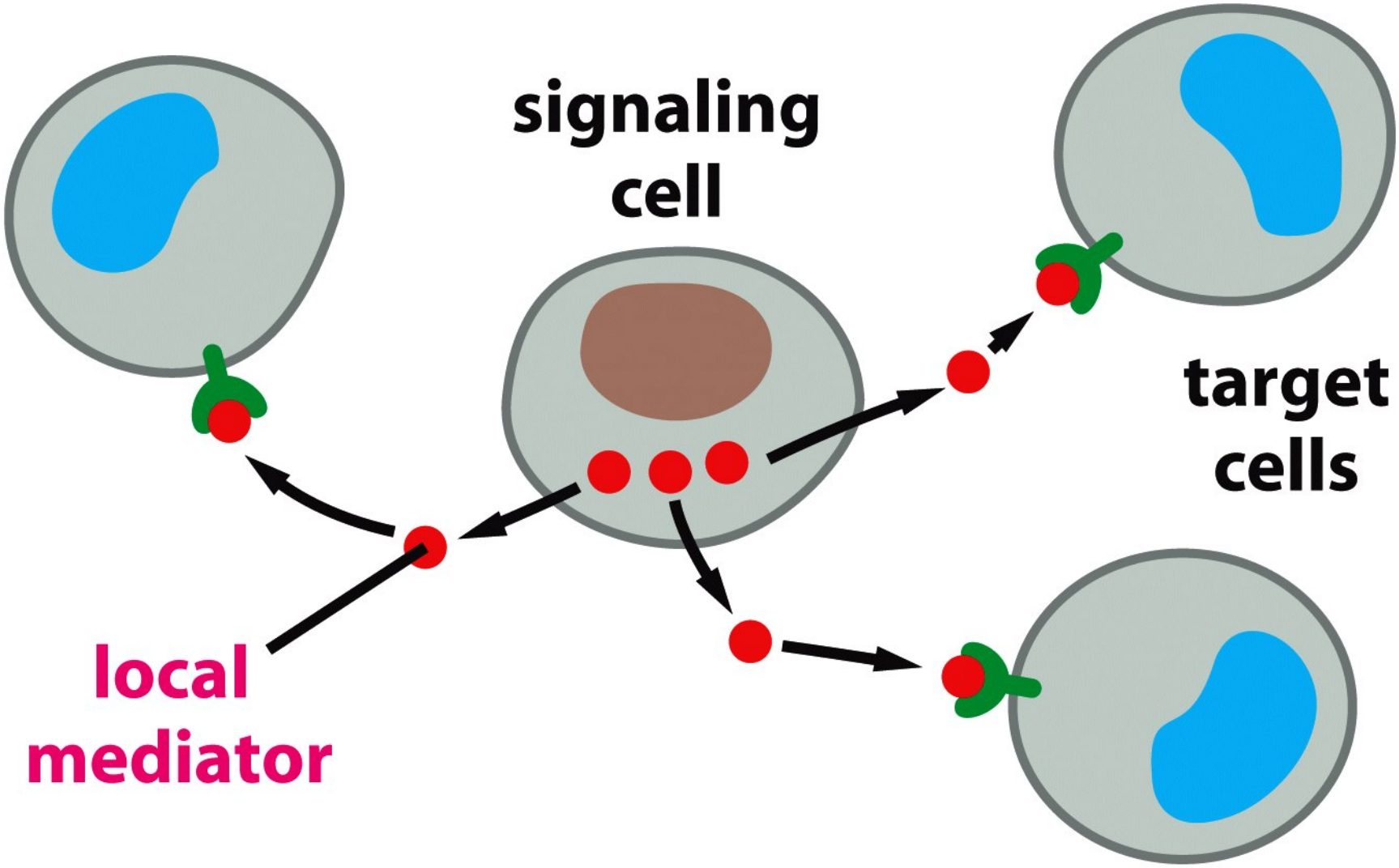


Extracellular Signal Molecules Can Act Over Either Short or Long Distances

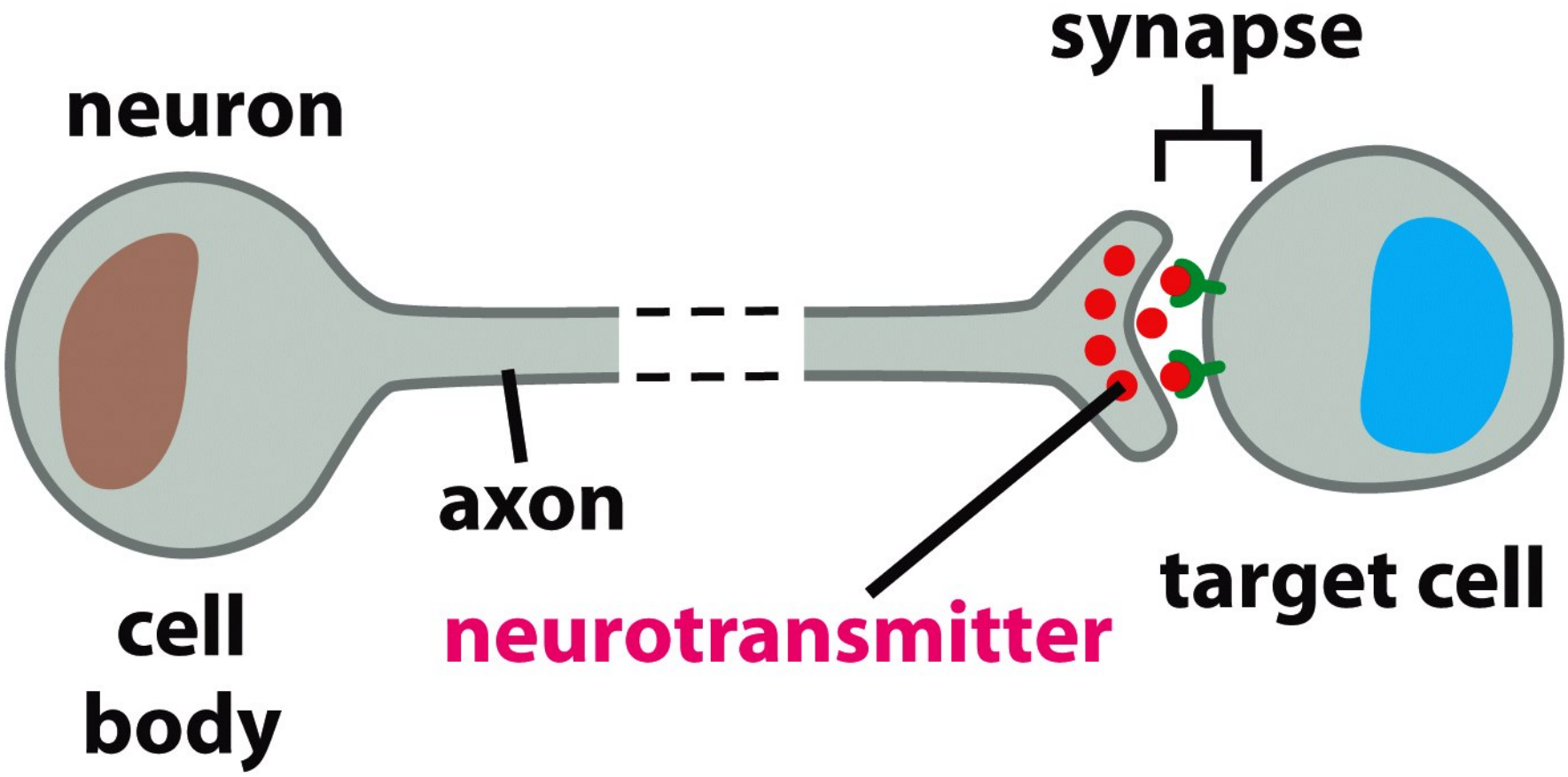
CONTACT-DEPENDENT



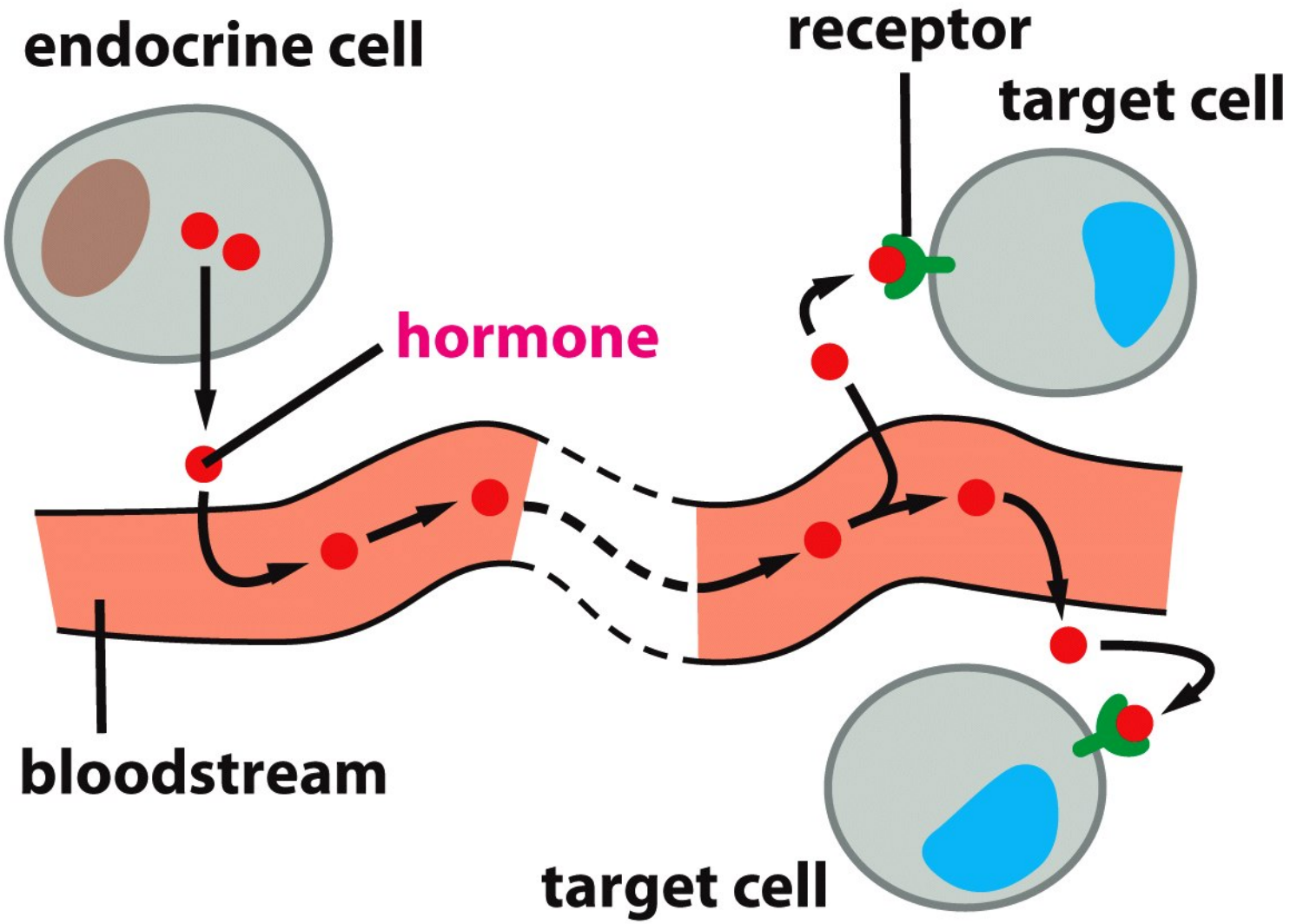
PARACRINE

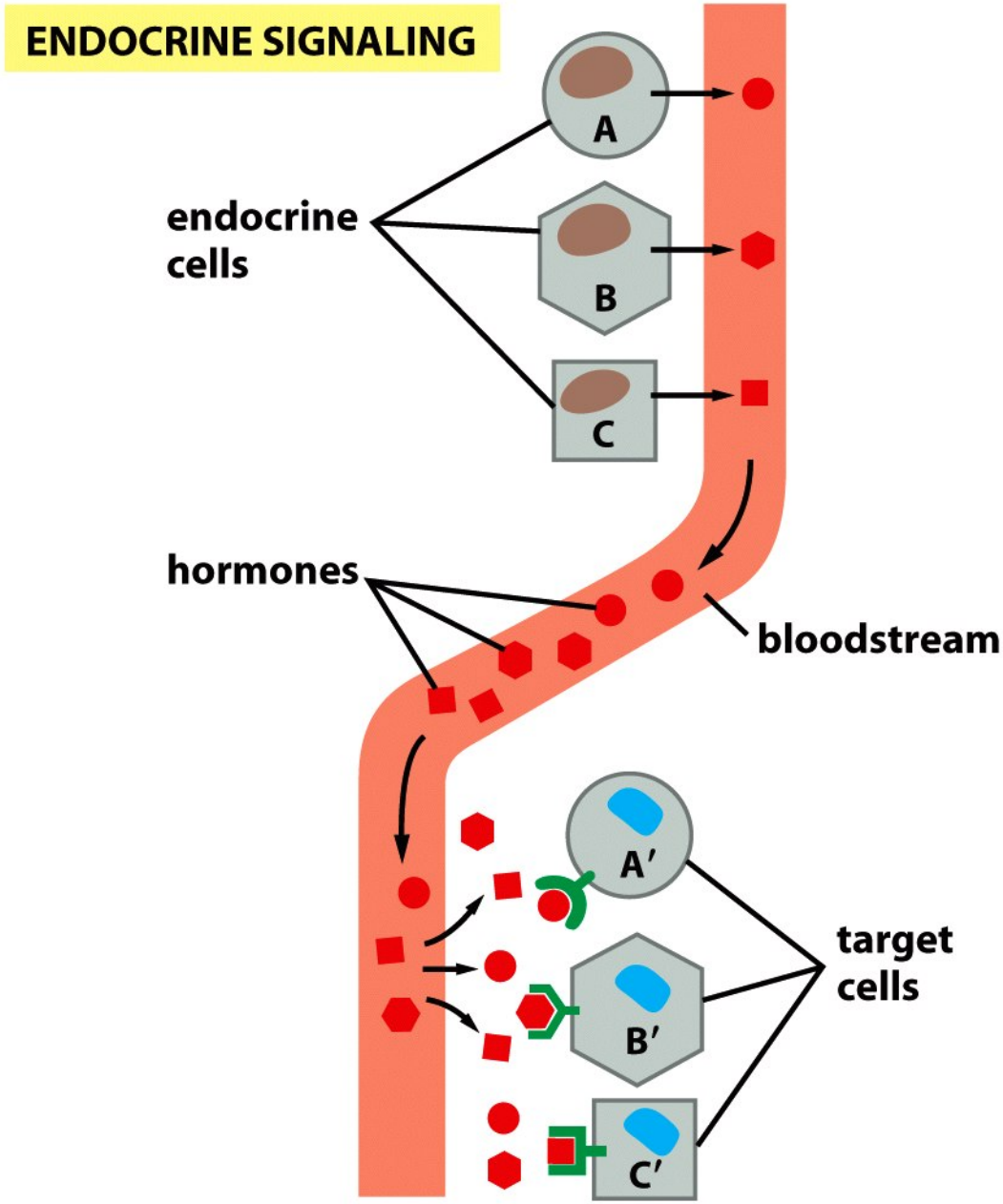


SYNAPTIC

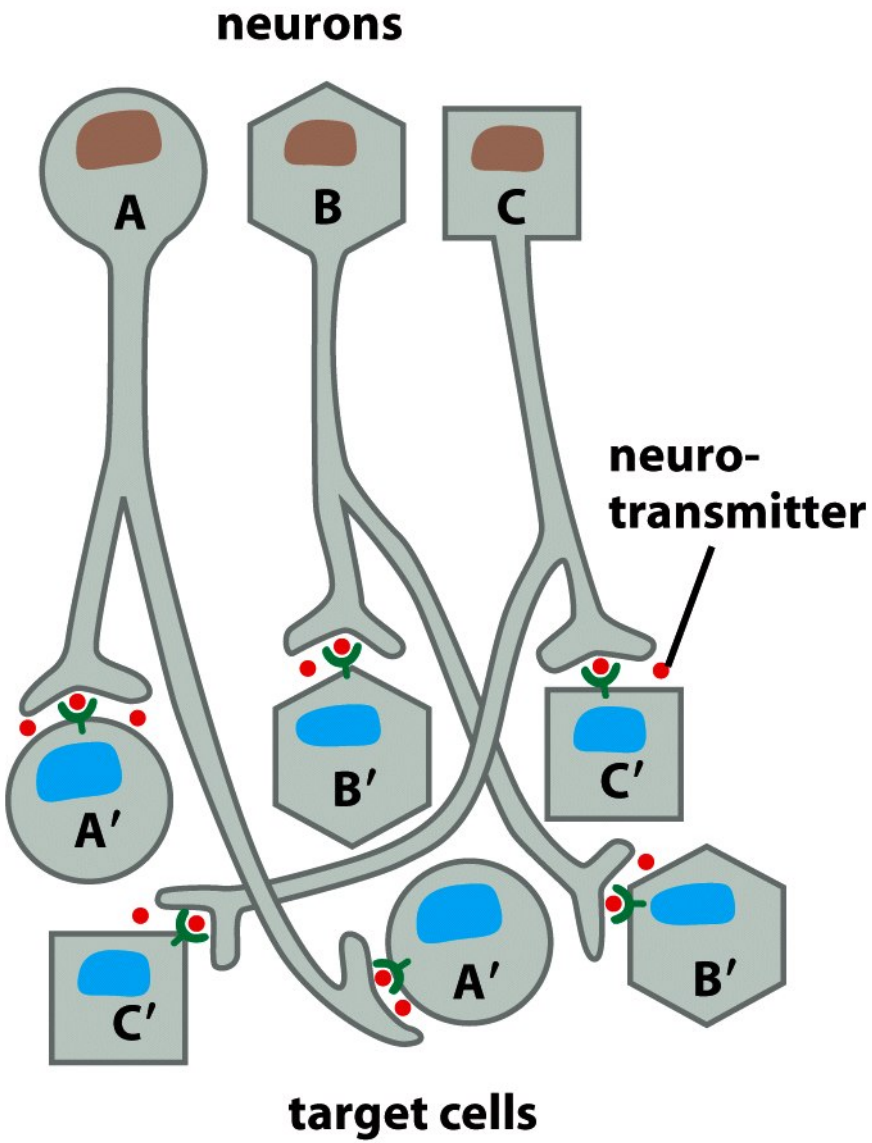

neuron
synapse
axon
cell body
neurotransmitter
target cell

ENDOCRINE

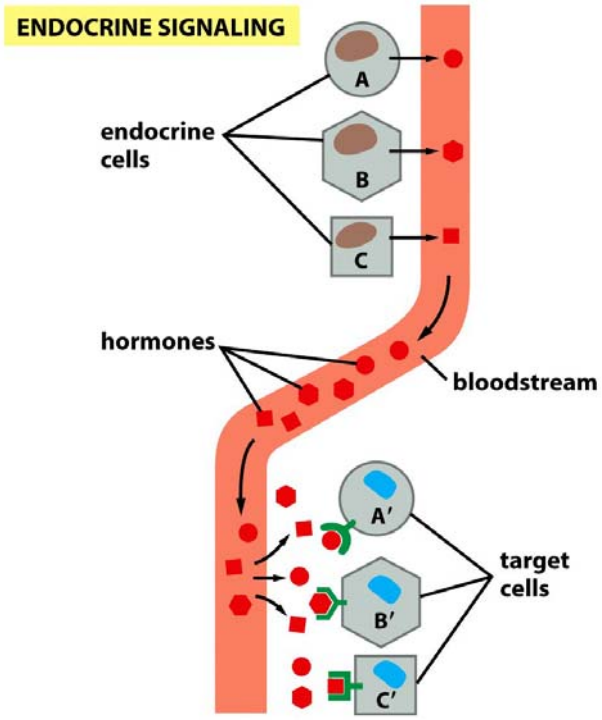

endocrine cell
receptor
target cell
hormone
bloodstream
target cell


ENDOCRINE SIGNALING
A
endocrine
cells
B
C
hormones
bloodstream
A′
target
cells
B′
C′

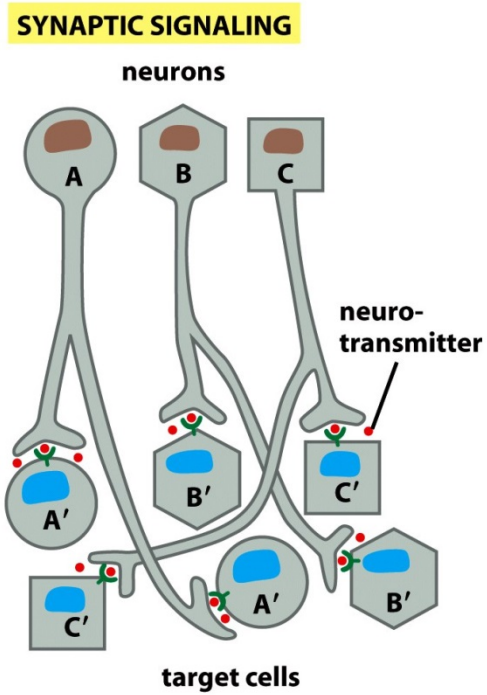
SYNAPTIC SIGNALING



Synaptic *vs* Endocrine SIGNALING

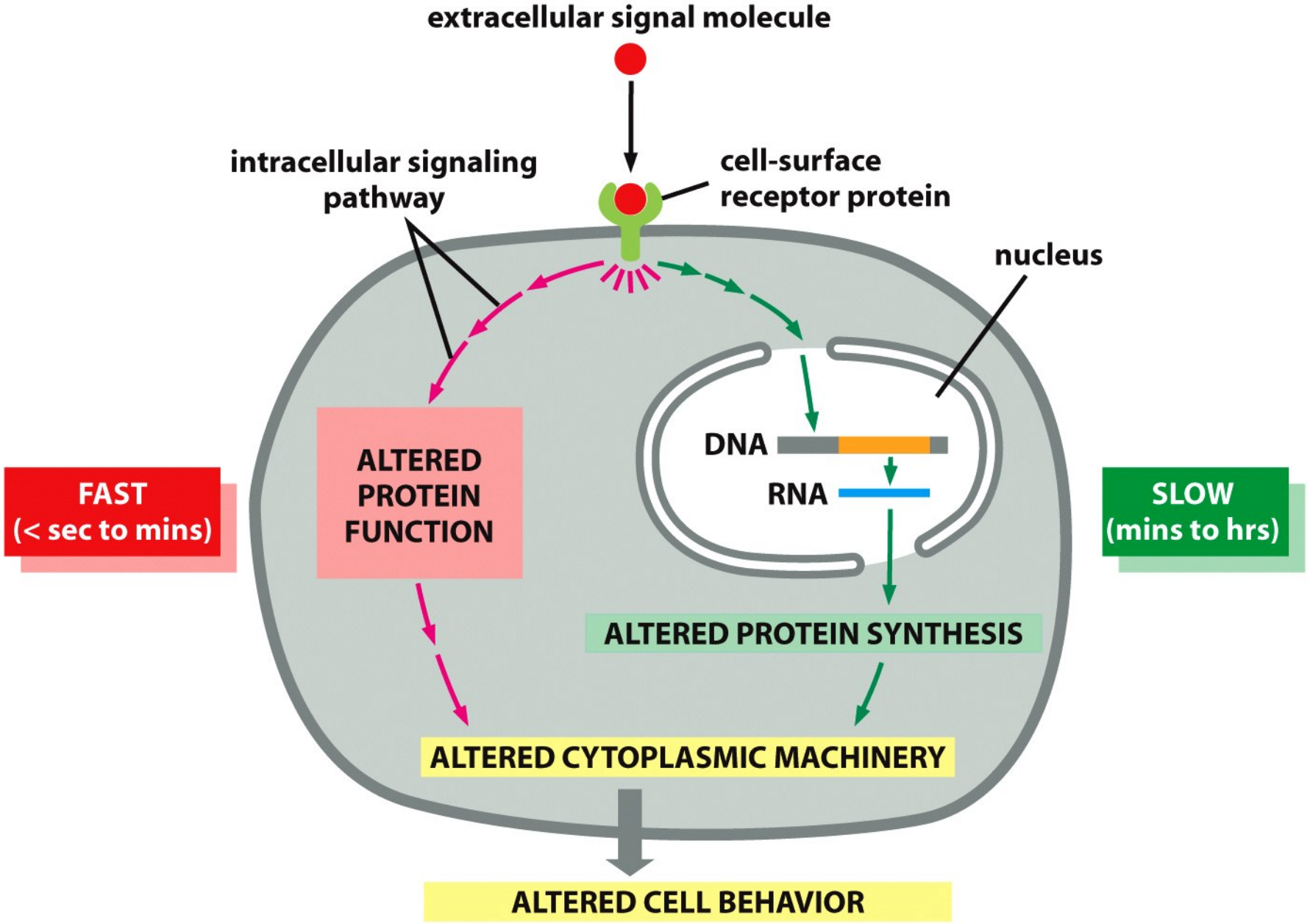


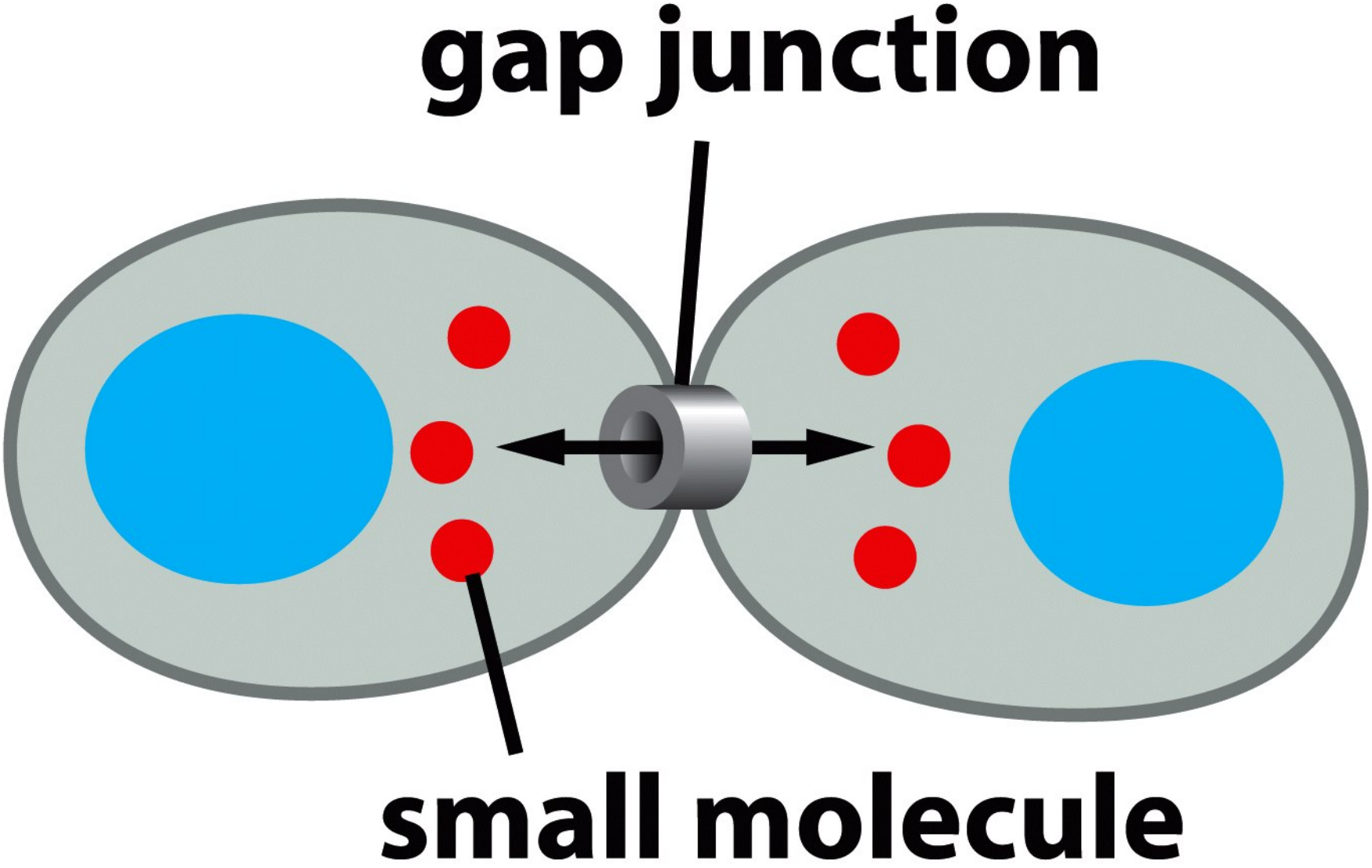
- different endocrine cells must use different hormones to communicate specifically with their target cells;
- specificity – receptor dependent;
- must act at low concentrations (diluted in blood)



- the same neurotransmitter;
- specificity – synaptic contact: neuron – target cell;
- much faster response;
- higher concentration;
- receptors - low affinity for neurotransmitters – help terminate a response.

Figure 15-5a&b *Molecular Biology of the Cell* (© Garland Science 2008)


extracellular signal molecule
intracellular signaling pathway
cell-surface receptor protein
nucleus
DNA
RNA
ALTERED PROTEIN FUNCTION
FAST (< sec to mins)
SLOW (mins to hrs)
ALTERED PROTEIN SYNTHESIS
ALTERED CYTOPLASMIC MACHINERY
ALTERED CELL BEHAVIOR


gap junction
small molecule

Gap junctions

- ✓ narrow water-filled channels that directly connect the cytoplasms of adjacent epithelial cells, as well as of some other cell types;
- ✓ allow the exchange of inorganic ions and other small water soluble molecules (cyclic AMP and Ca2+);
- ✓ for the most intimate of all forms of cell communication (cytoplasmic bridges or cell fusion);
- ✓ their typical effect is to homogenize conditions in the communicating cells.

SIGNAL MOLECULES

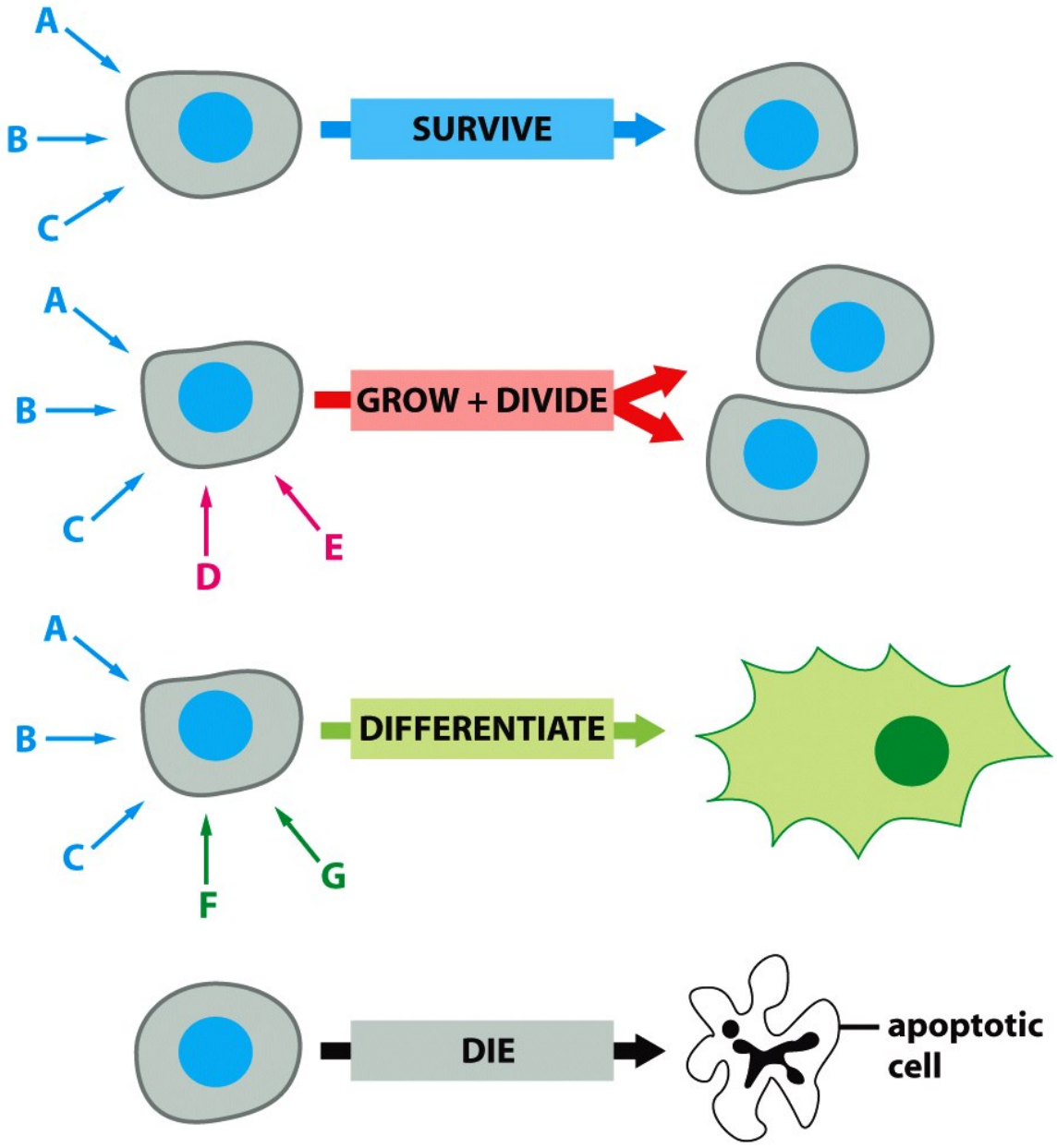
- a typical cell in a multicellular organism may be exposed to hundreds of different signal molecules;

- molecules can be soluble, bound to the ECM, or bound to the surface of a neighboring cell;

- can be stimulatory or inhibitory;

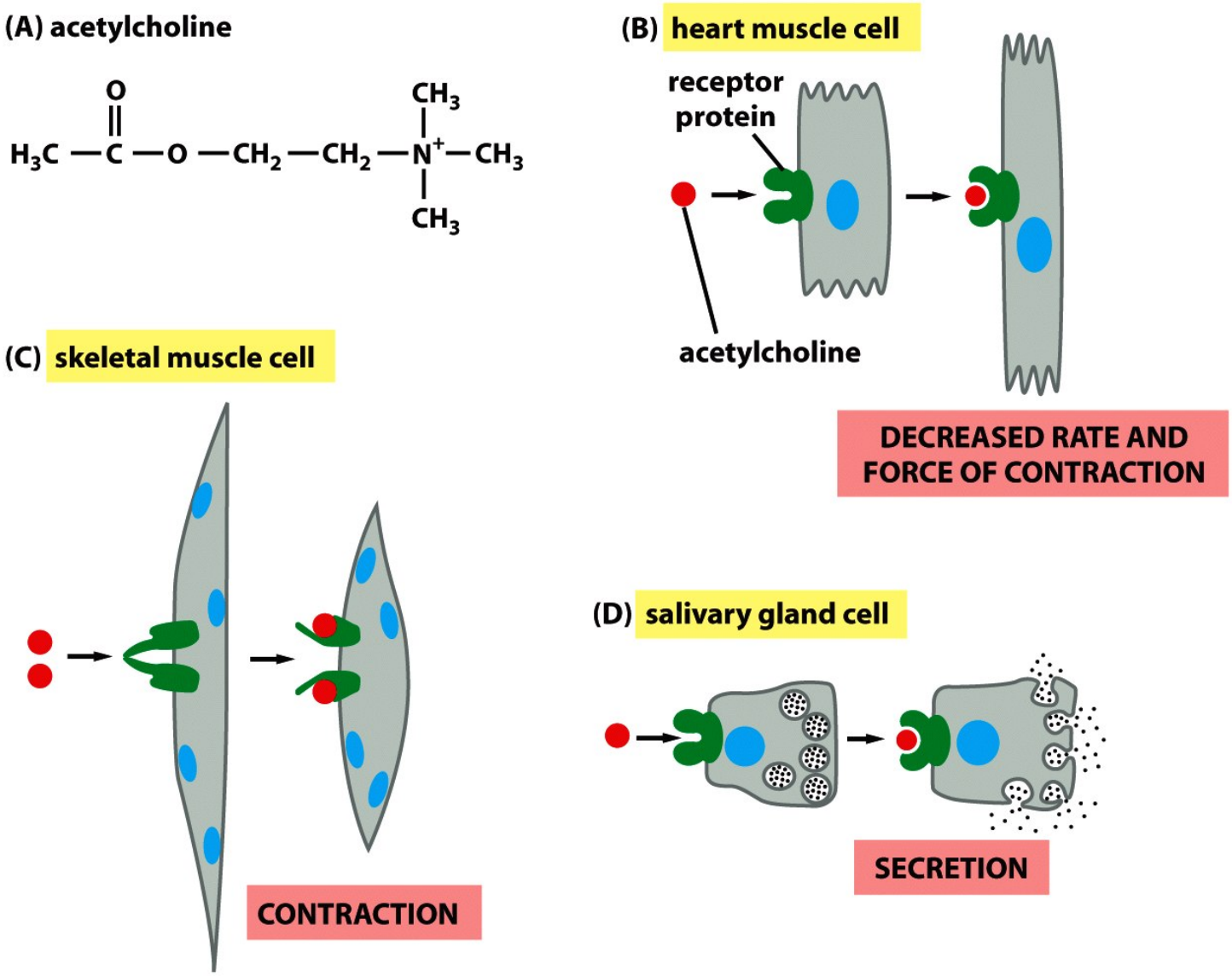
- can act in innumerable different combinations;

- can influence almost any aspect of cell behavior.



Cell's dependence on multiple extracellular signal molecules

The same signal on different cell types => Different responses



The cell's responses reflects the differences in:

- intracellular signaling proteins activated;
- effector proteins or genes activated;

=> Extracellular signal:

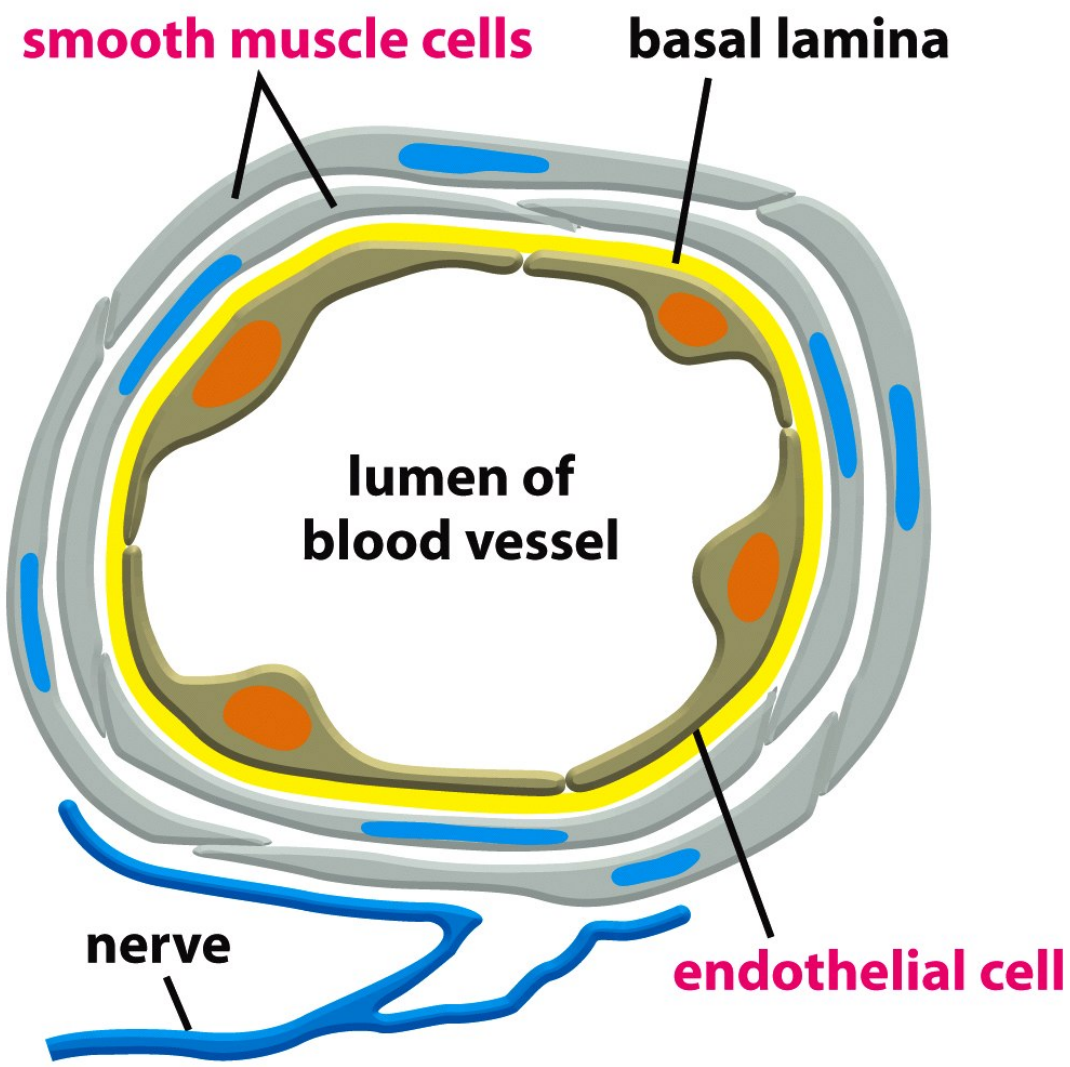
- has little information content;
- it simply induces the cell to respond according to its predetermined state;

=> Response depends on:

- the cell's developmental history;
- the specific genes it expresses.

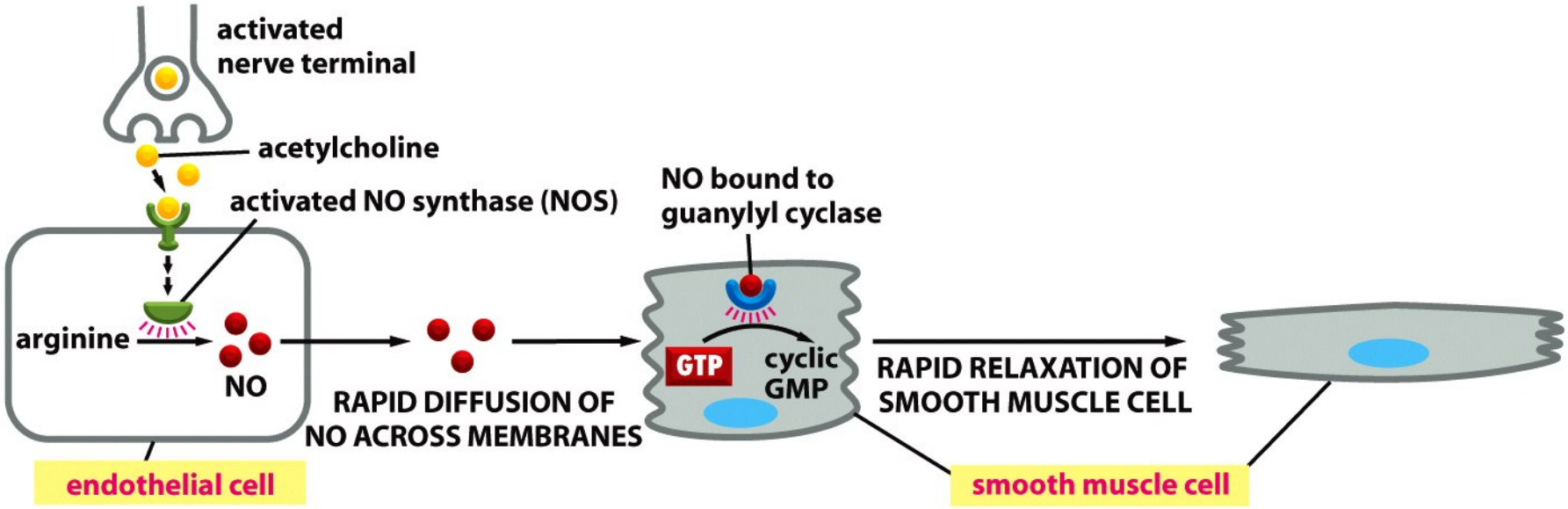
SIGNAL MOLECULES THAT ACTIVATE INTRACELLULAR RECEPTORS

-nitric oxide and steroid hormones-



The role of nitric oxide (NO) in smooth muscle relaxation in a blood vessel wall

Explains the mechanism of action of nitroglycerine treatment of patients with angina.



The role of nitric oxide (NO) in smooth muscle relaxation in a blood vessel wall

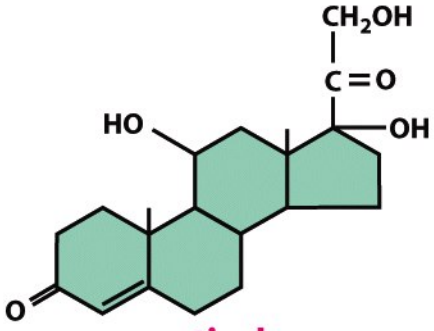
The role of nitric oxide (NO)

- dissolved NO passes readily across membranes;
- it acts only locally because it has a short;
- oxygen and water convert it to nitrates and nitrites;
- **NO reversibly binds to iron** in the active site of the enzyme **guanylyl cyclase** *(IC receptor for NO and IC signaling protein)*;

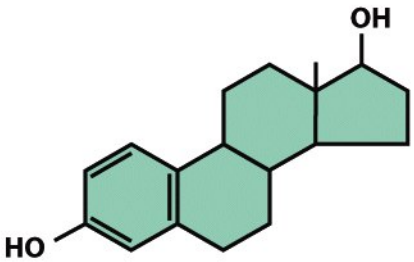
→ **cyclic GMP** *(intracellular signaling molecule)*
degraded by a phosphodiesterase (Inhibit by Viagra)

Nuclear Receptors Are Ligand-Modulated Gene Regulatory Proteins

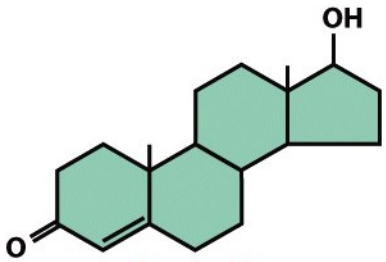
- small hydrophobic signal molecules diffuse directly across the plasma membrane of target cells and bind to intracellular receptors that are gene regulatory proteins;
- include steroid hormones, thyroid hormones, retinoids, and vitamin D;
- similar mechanism: alter the ability receptor proteins to control the transcription of specific genes;
- ICR proteins: both intracellular receptors and as intracellular effectors for the signal.



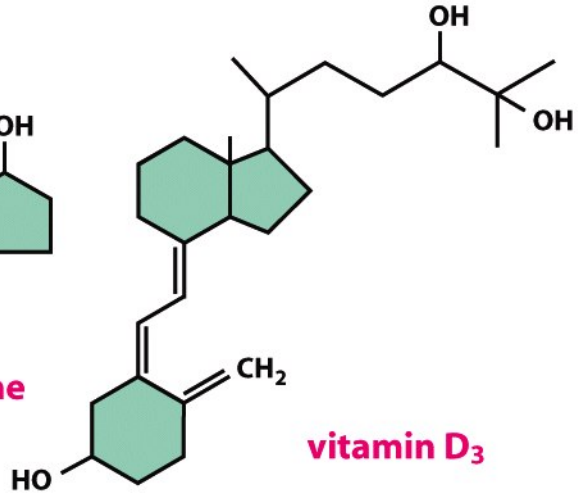
cortisol



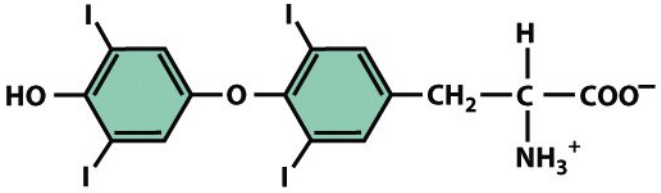
estradiol



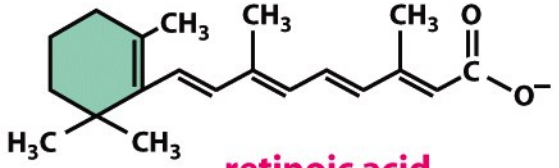
testosterone



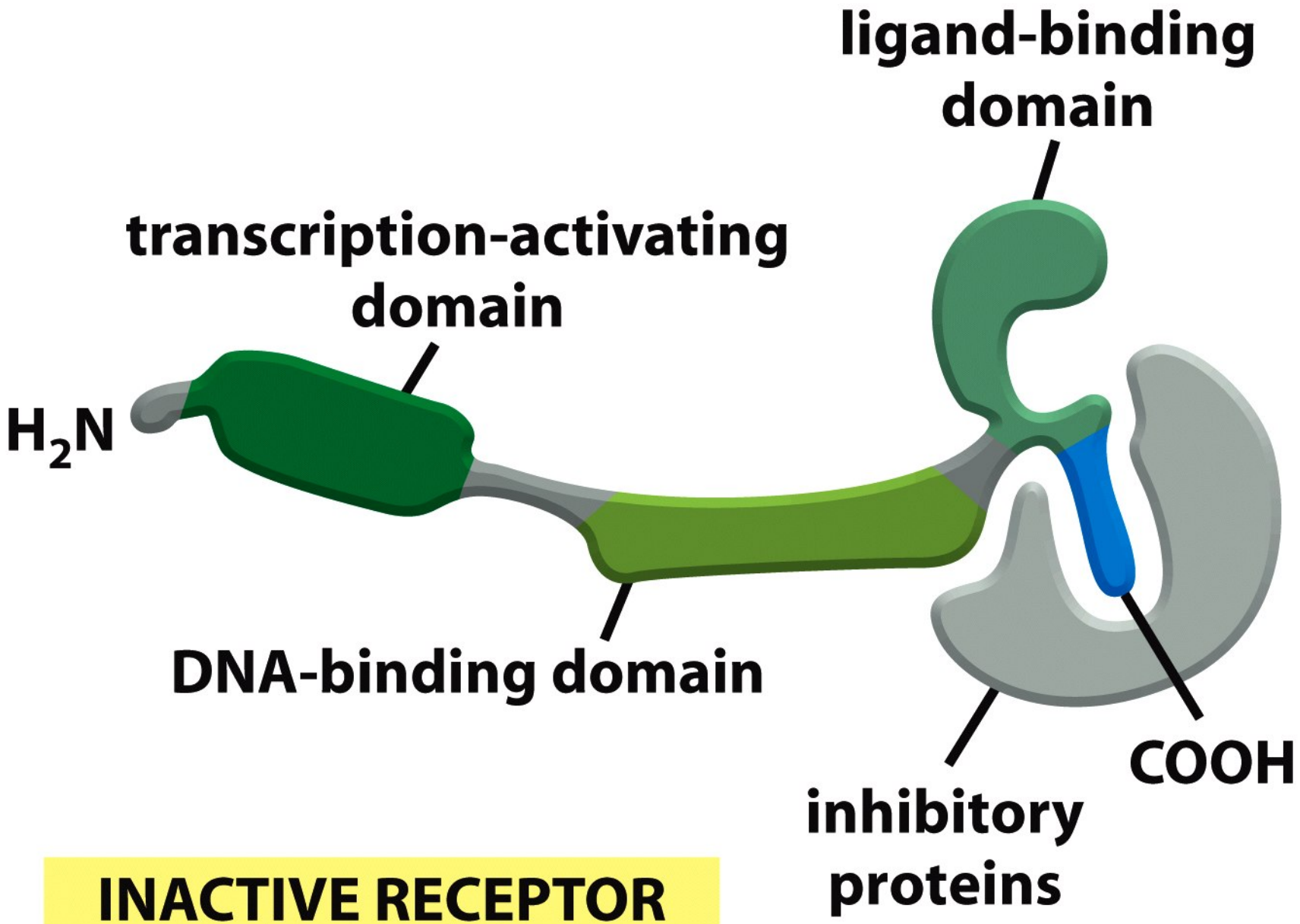
vitamin D_3

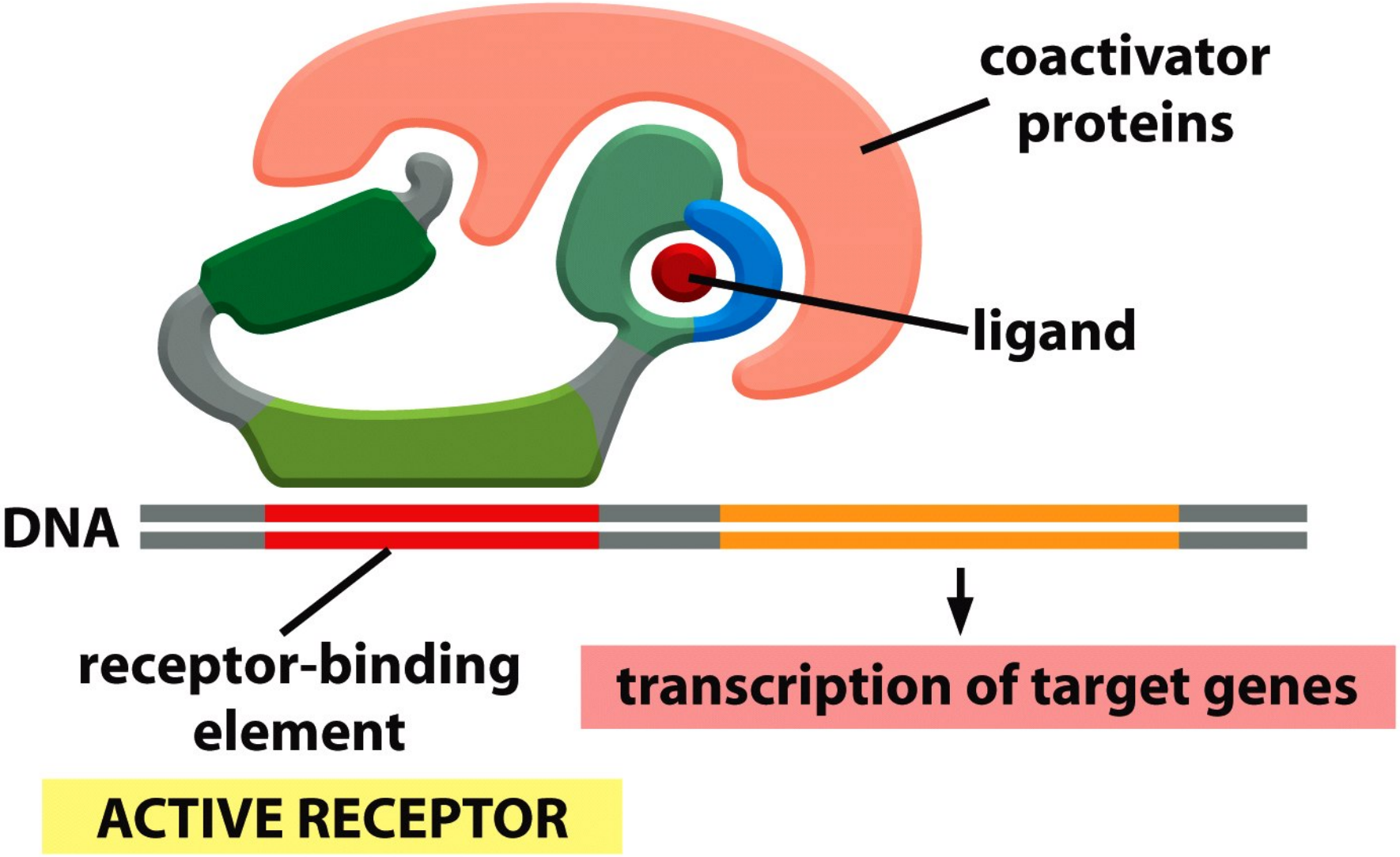


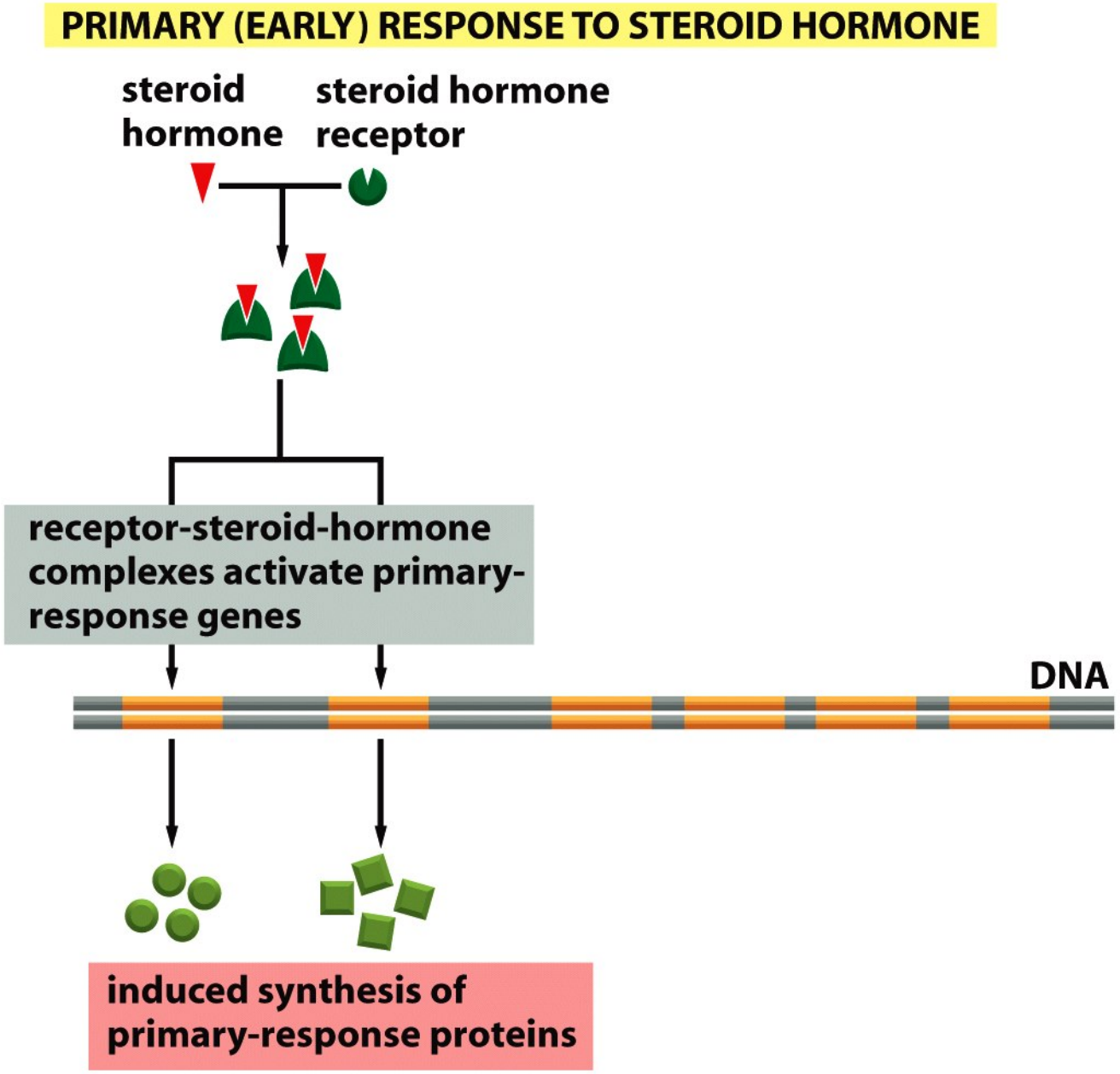
thyroxine



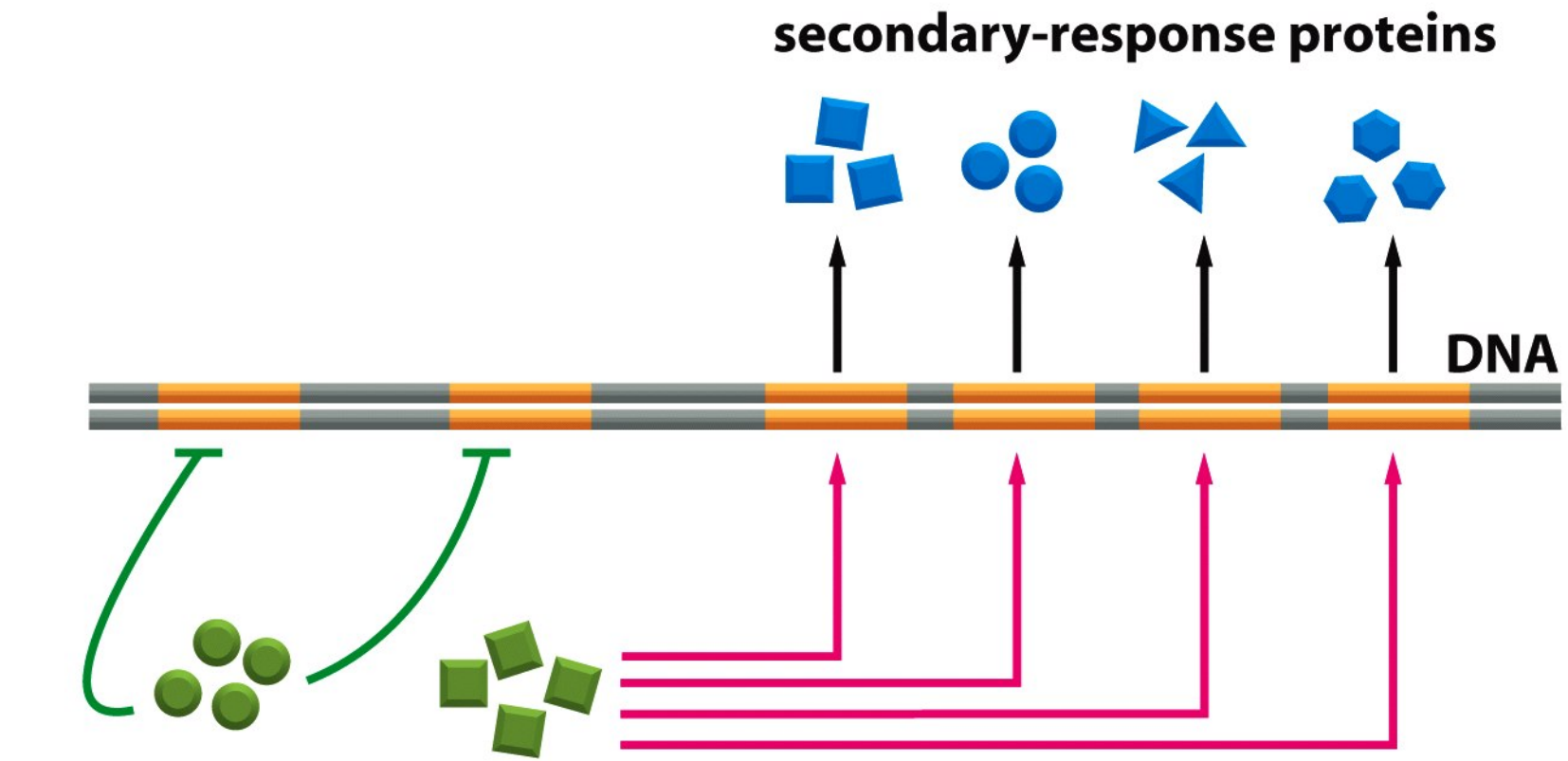
retinoic acid


ligand-binding domain
transcription-activating domain
H_2N
DNA-binding domain
COOH
inhibitory proteins
INACTIVE RECEPTOR


coactivator proteins
ligand
DNA
receptor-binding element
transcription of target genes
ACTIVE RECEPTOR


PRIMARY (EARLY) RESPONSE TO STEROID HORMONE
steroid hormone
steroid hormone receptor
receptor-steroid-hormone complexes activate primary-response genes
DNA
induced synthesis of primary-response proteins

SECONDARY (DELAYED) RESPONSE TO STEROID HORMONE

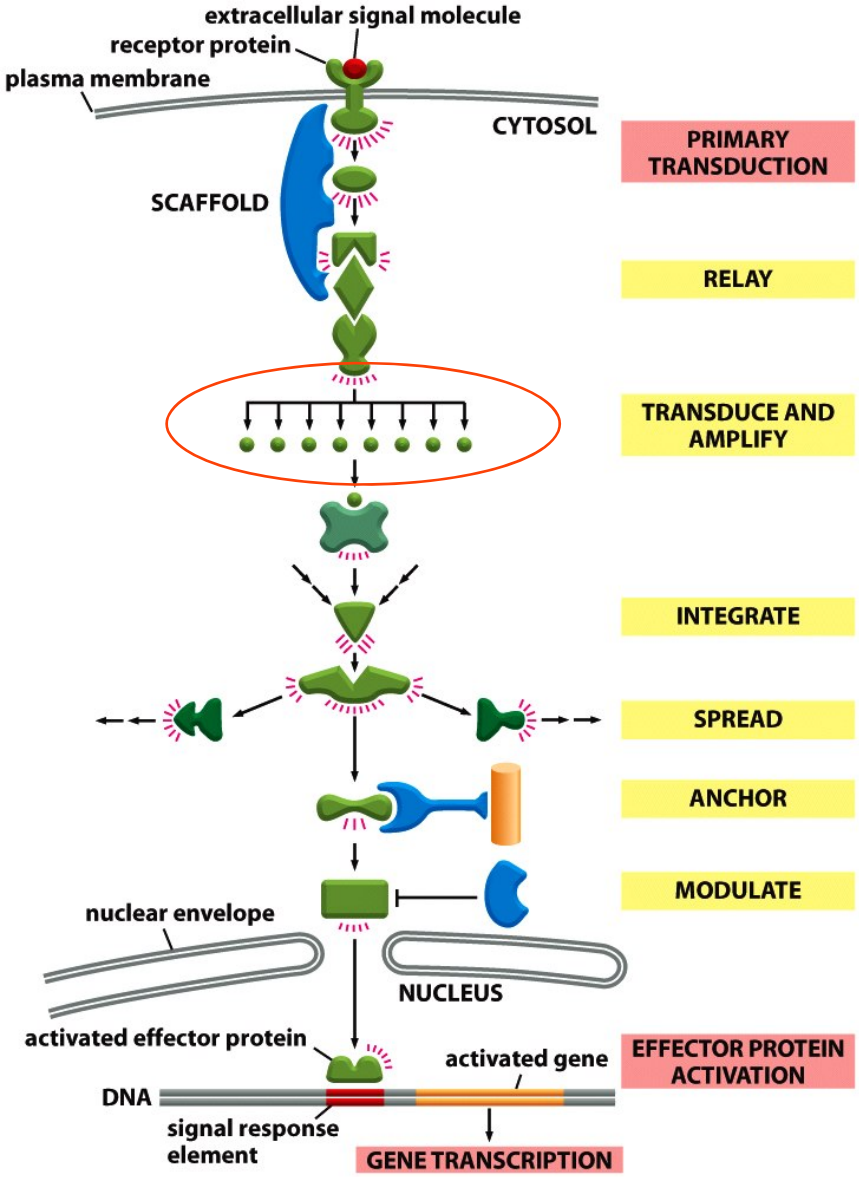


SIGNAL MOLECULES THAT ACTIVATE

Cell-Surface Receptor Proteins

- Ion-Channel-Coupled, G-Protein-Coupled and Enzyme-Coupled Receptors -

Cell-Surface Receptor Proteins



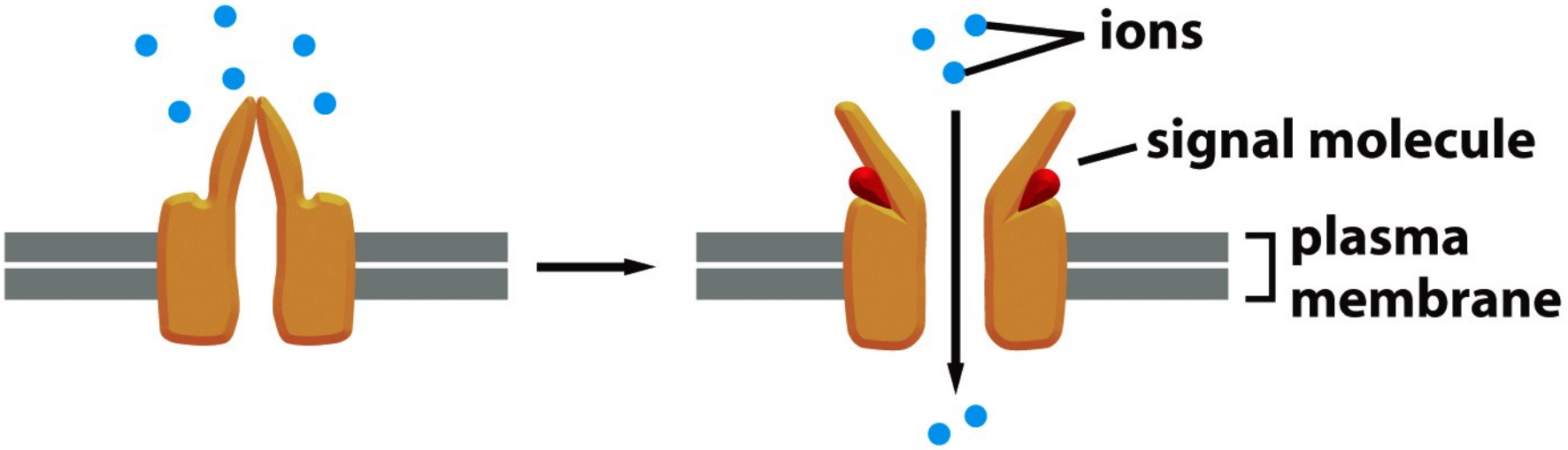
Cell-Surface Receptor Proteins

- act as signal transducers by converting an extracellular ligand-binding event into intracellular signals that alter the behavior of the target cell;

1. - Ion-channel-coupled receptors (transmitter-gated ion channels or ionotropic receptors):

- rapid synaptic signaling between nerve cells and other electrically excitable target cells (eg: nerve and muscle cells)

ION-CHANNEL-COUPLED RECEPTORS



Cell-Surface Receptor Proteins

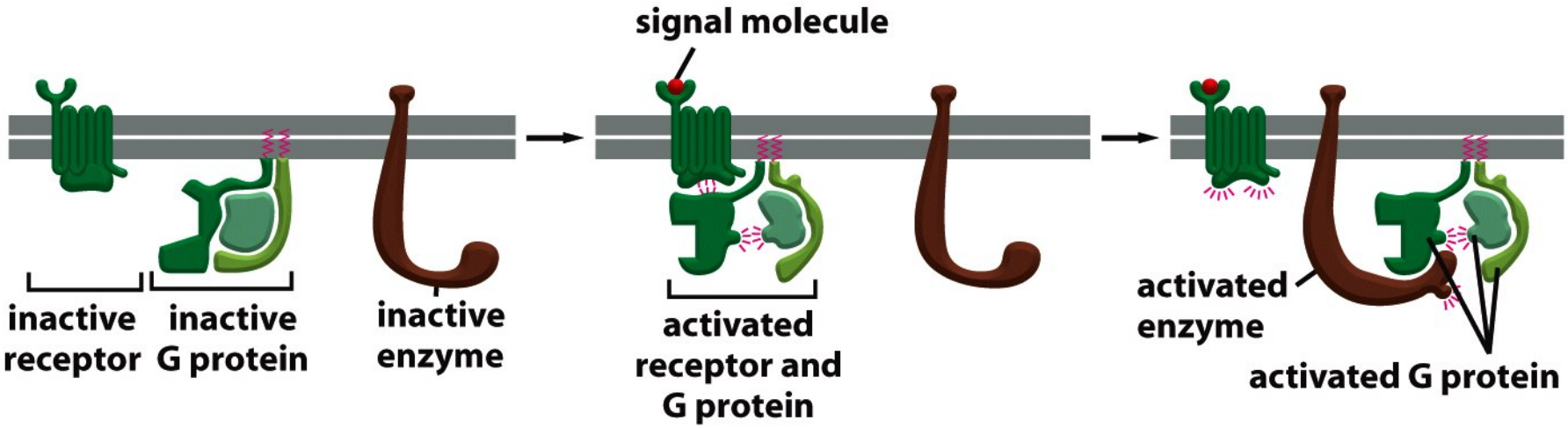
2. - G-protein-coupled receptors:

- act by indirectly regulating the activity of a separate plasma-membrane-bound target protein (enzyme or an ion channel);

- a trimeric GTP-binding protein (G protein) mediates the interaction between the activated receptor and this target protein;

- the activation of the target protein can change:
  - the concentration of one or more small intracellular mediators (if the target protein is an enzyme);
  or - the ion permeability of the plasma membrane (if the target protein is an ion channel).

G-PROTEIN-COUPLED RECEPTORS



Cell-Surface Receptor Proteins

3. - Enzyme-coupled receptors:

- either function directly as enzymes or associate directly with enzymes that they activate;

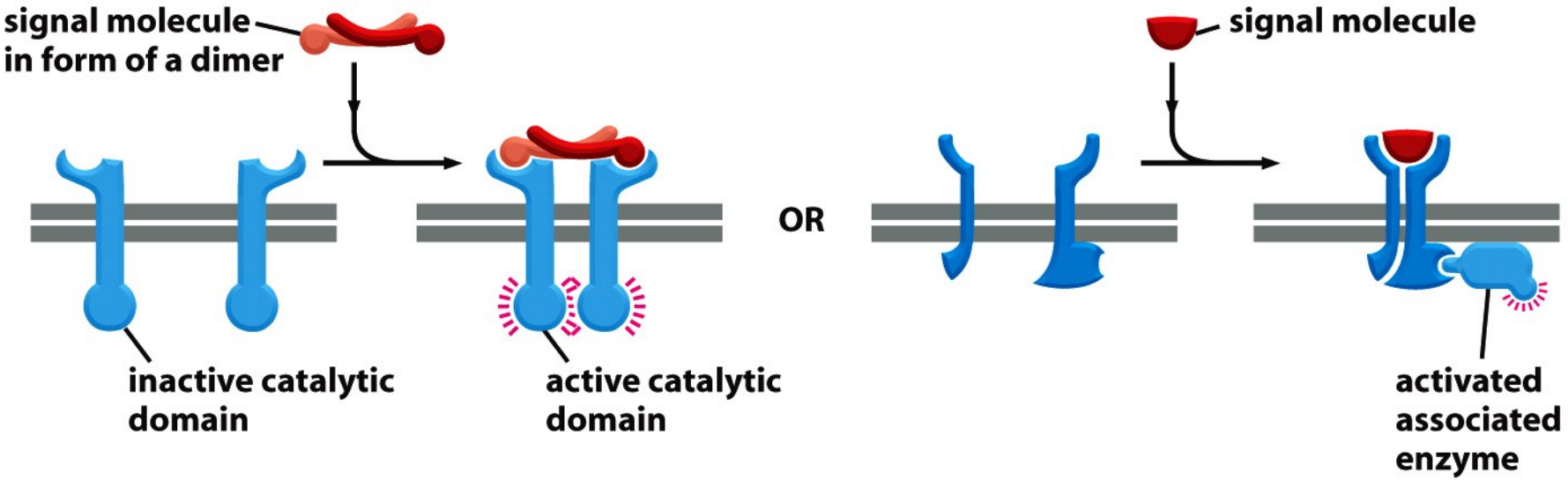
- usually single pass transmembrane proteins;

- have their ligand-binding site outside the cell and their catalytic or enzyme-binding site inside;

- enzyme-coupled receptors are heterogeneous in structure compared with the other two classes;

- The great majority: protein kinases or associate with protein kinases, which phosphorylate specific sets of proteins in the target cell when activated.

ENZYME-COUPLED RECEPTORS



SECOND MESSENGERS

- cell-surface receptors relay signals via small molecules and a network of intracellular signaling proteins

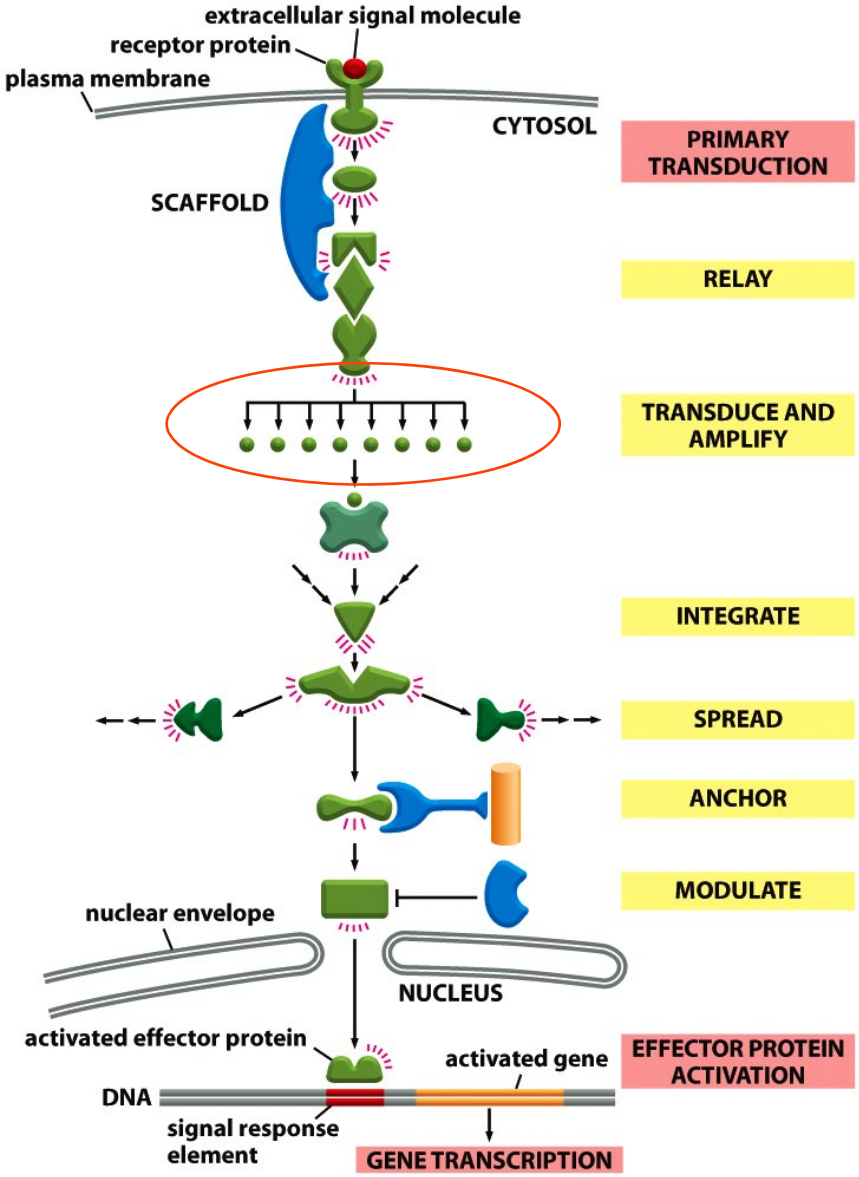
- away from their source (if water-soluble), spreading the signal to other parts of the cell.

- pass the signal on by binding to and altering the conformation and behavior of selected signaling proteins or effector proteins.

- water-soluble (cAMP, Ca^{2+});

- lipid-soluble (diacylglycerol-DAG);

Cell-Surface Receptor Proteins



Cell-Surface Receptor Proteins

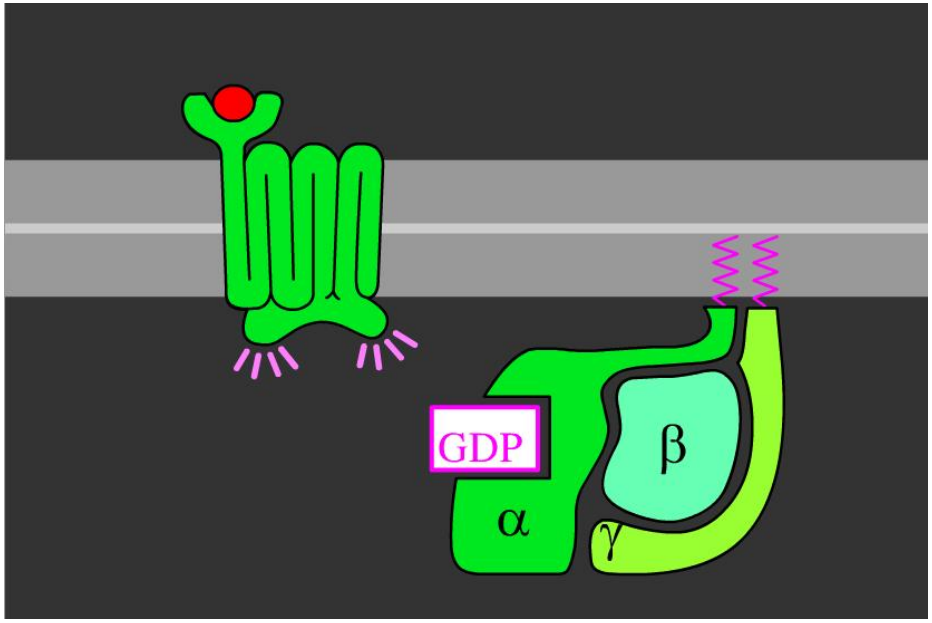
G-protein-coupled receptors:

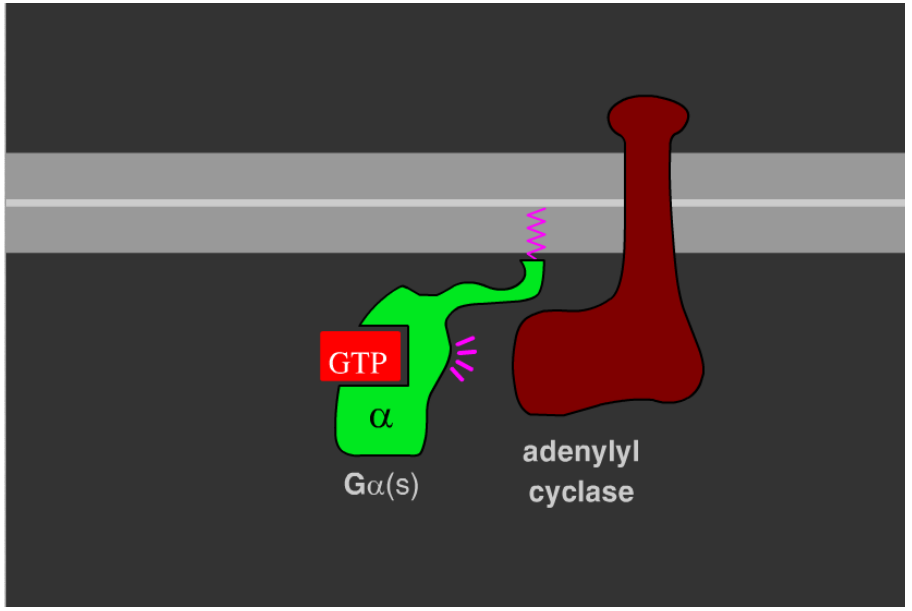
1. - SIGNAL (LIGAND);

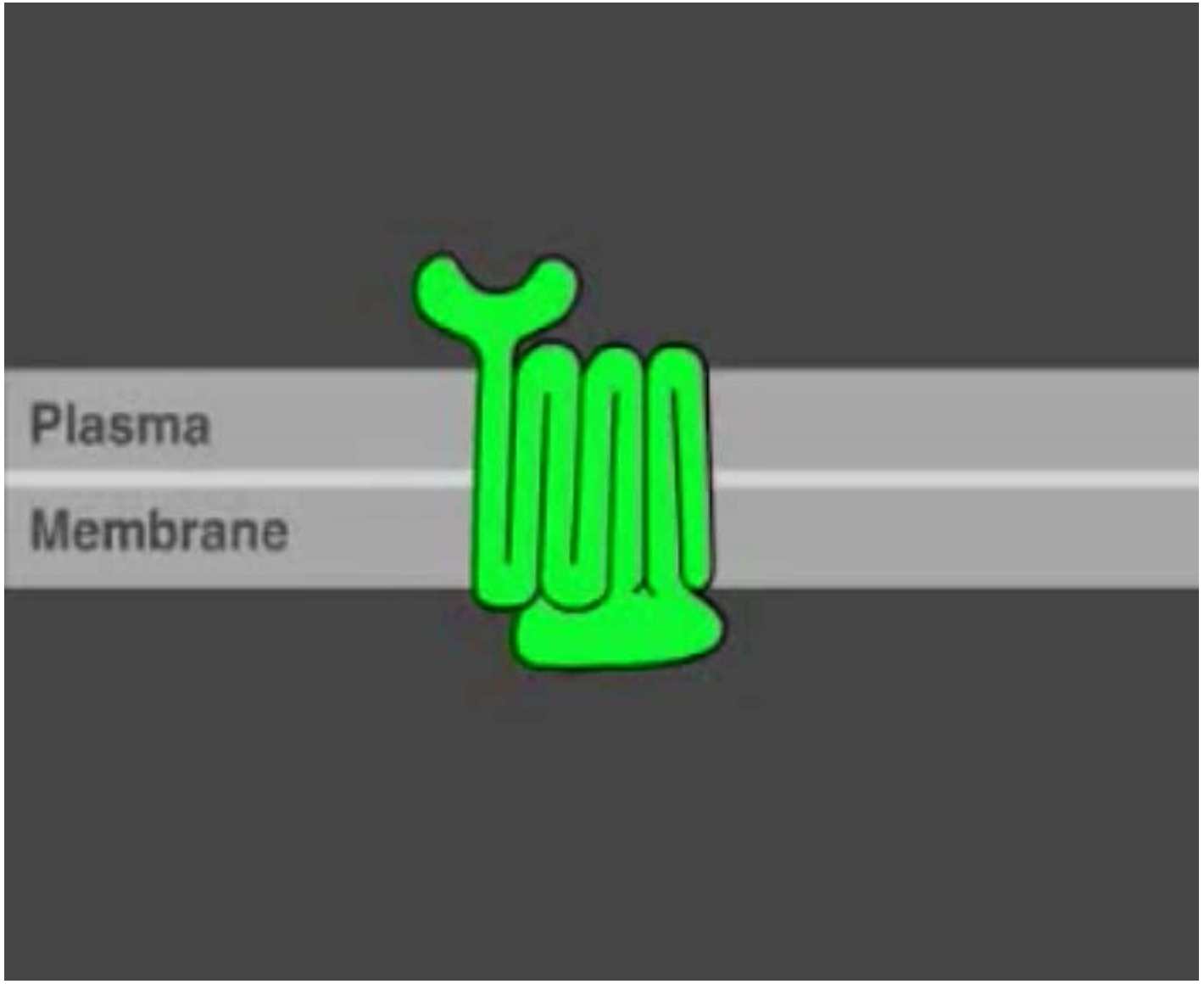
2. – RECEPTOR;

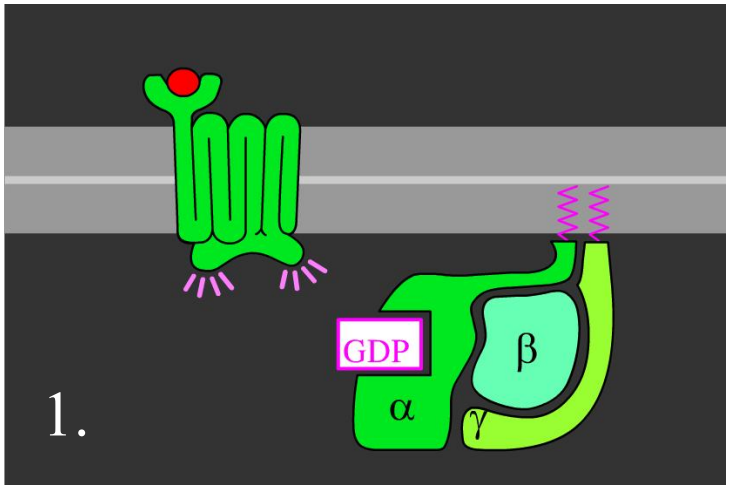
3. - G PROTEIN - a trimeric GTP-binding protein;

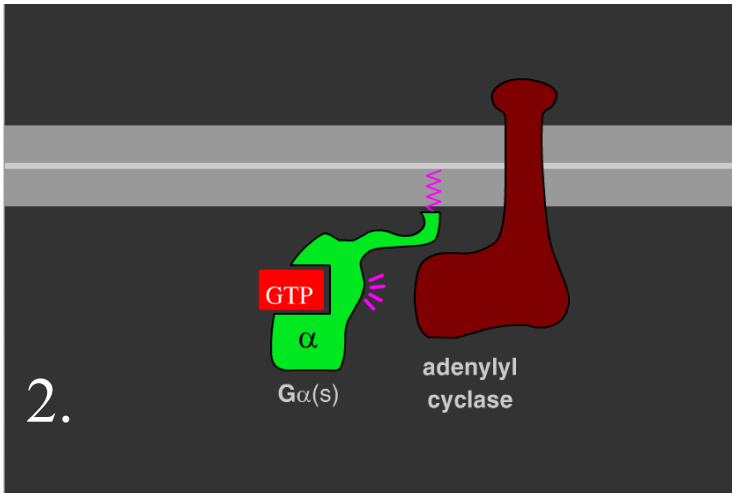
4. – TARGET PROTEIN.

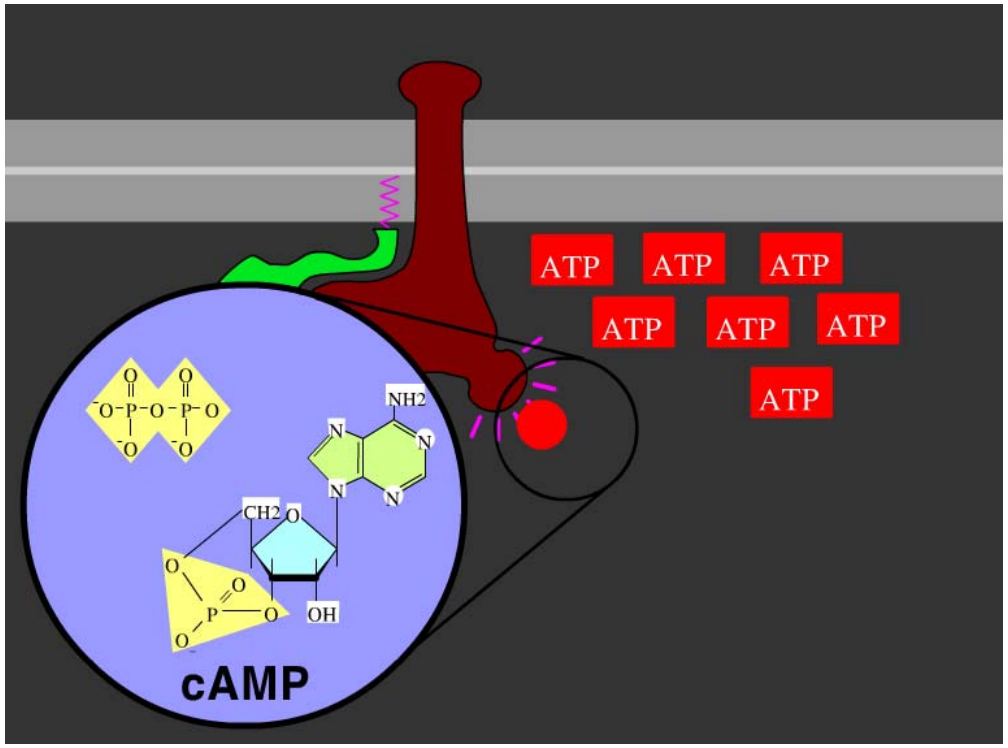

GDP
α
β
γ

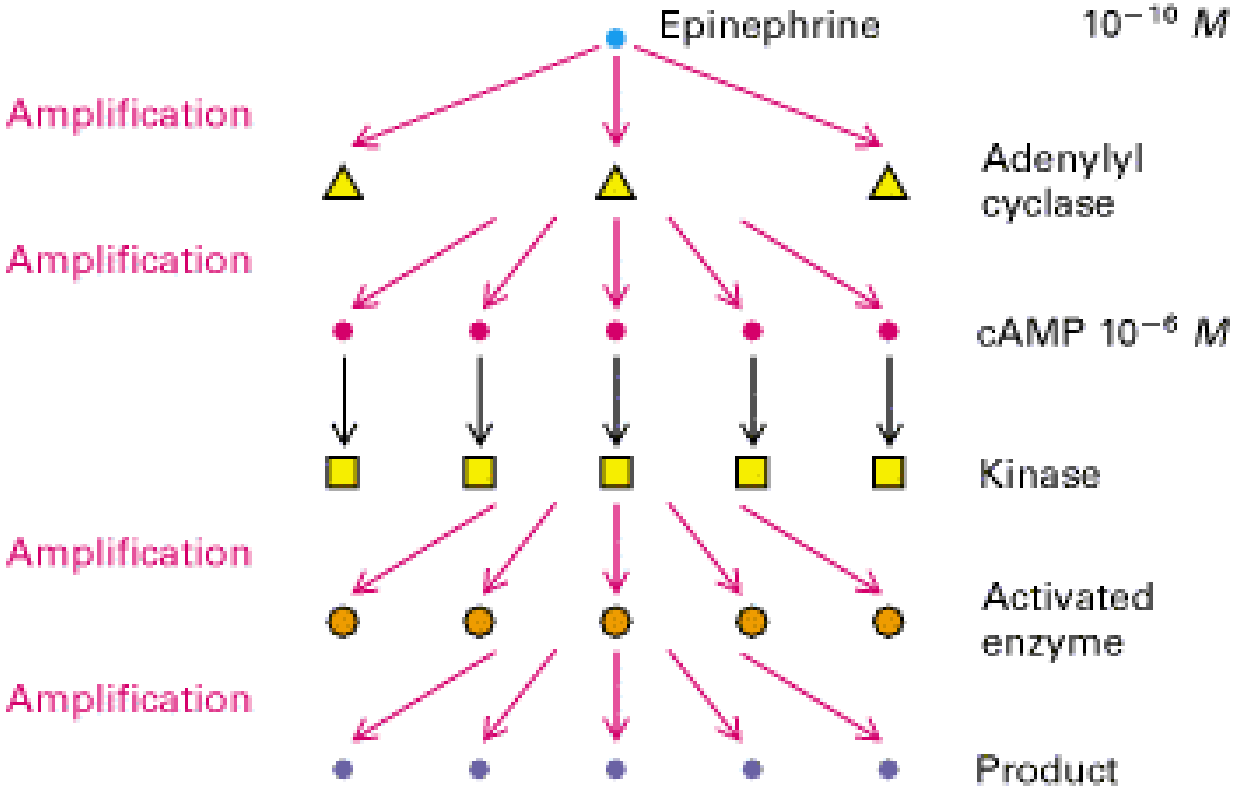

GTP
α
Gα(s)
adenylyl
cyclase

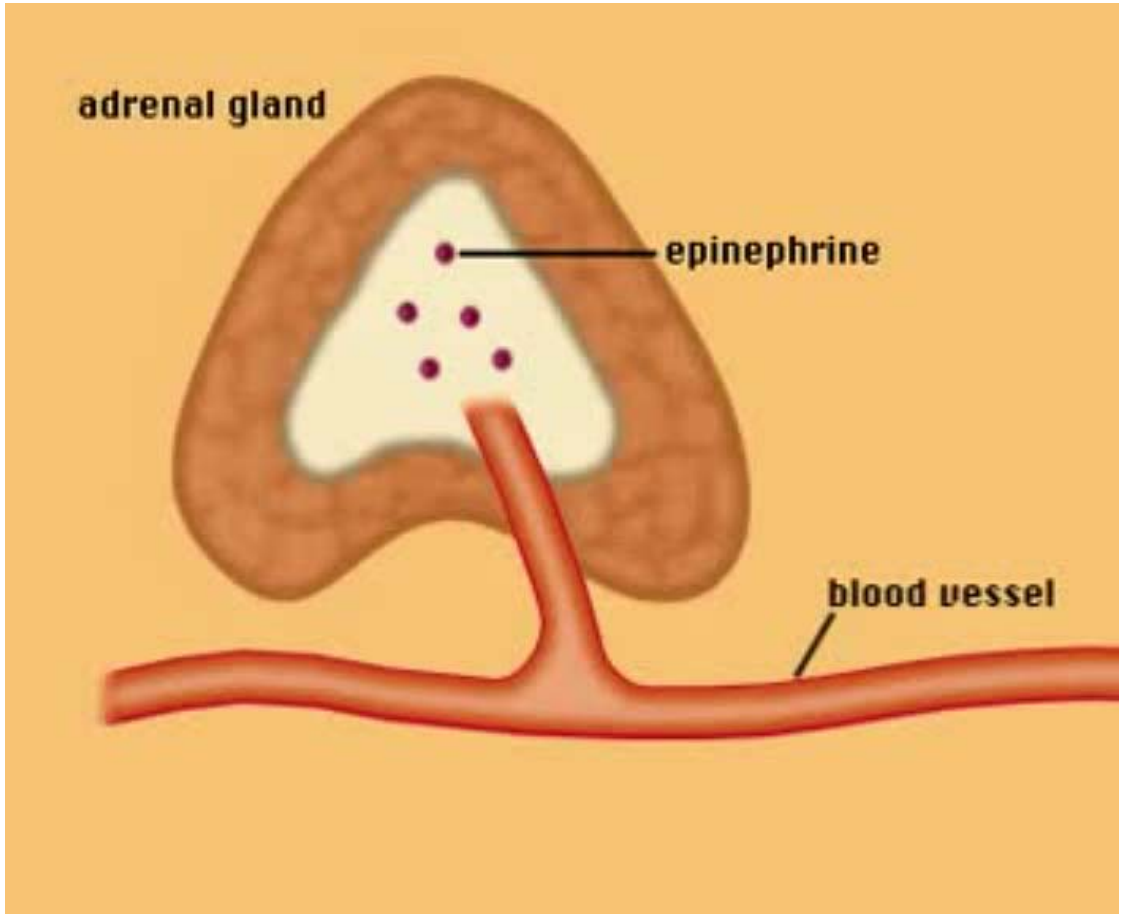

Plasma
Membrane

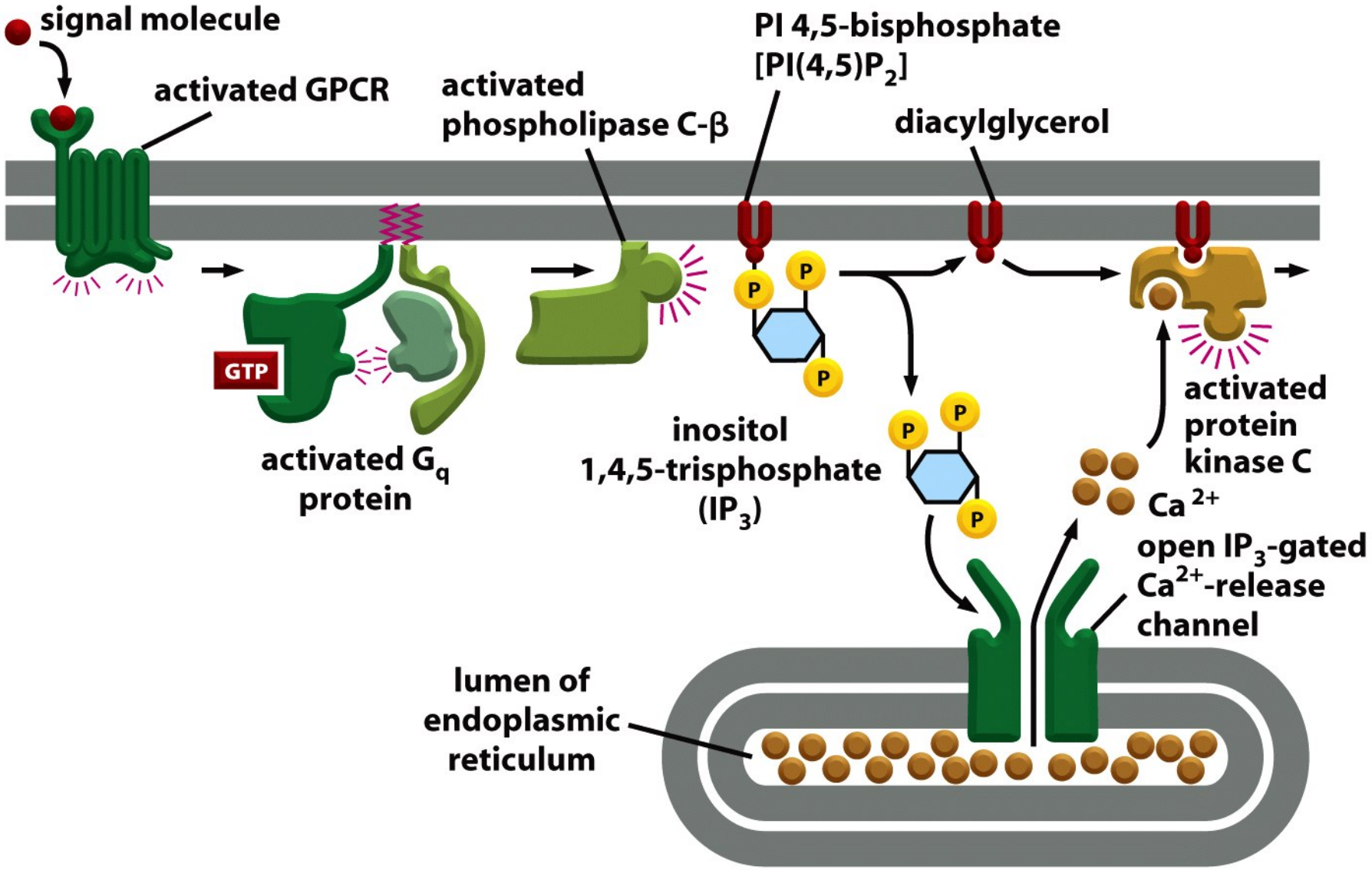

GDP
α
β
γ
1.


GTP
α
Gα(s)
adenylyl
cyclase
2.


ATP
ATP
ATP
ATP
ATP
ATP
ATP
NH2
N
N
N
N
CH2
O
O
O
P
O
O
OH
cAMP


Epinephrine
10^{-10} M
Amplification
Amplification
Amplification
Amplification
Adenylyl cyclase
cAMP 10^{-6} M
Kinase
Activated enzyme
Product


adrenal gland
epinephrine
blood vessel


signal molecule
activated GPCR
activated phospholipase C-β
PI 4,5-bisphosphate [PI(4,5)P2]
diacylglycerol
GTP
activated Gq protein
inositol 1,4,5-trisphosphate (IP3)
activated protein kinase C
Ca 2+
open IP3-gated Ca2+-release channel
lumen of endoplasmic reticulum
P

Vă mulțumesc!