

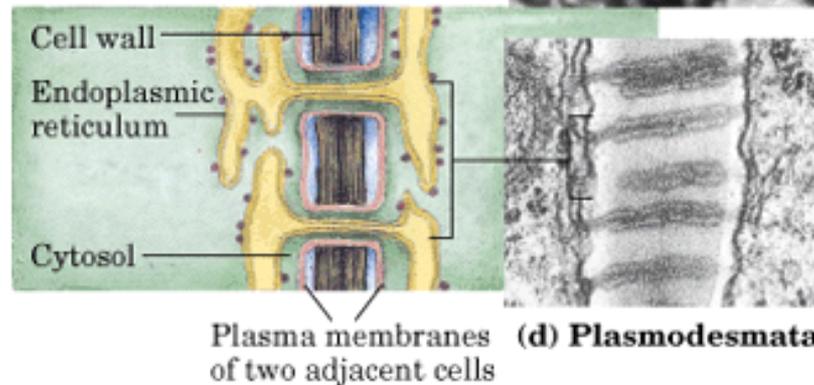
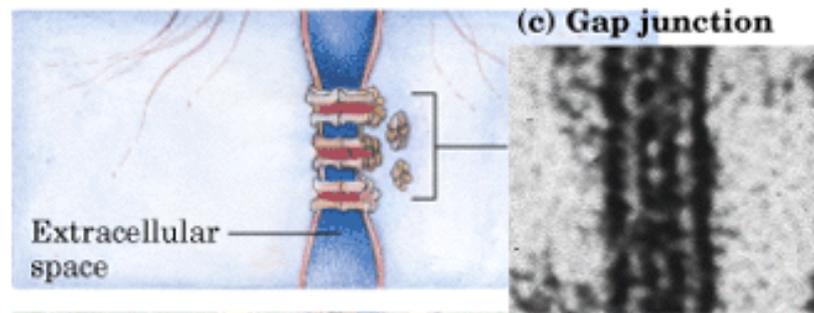
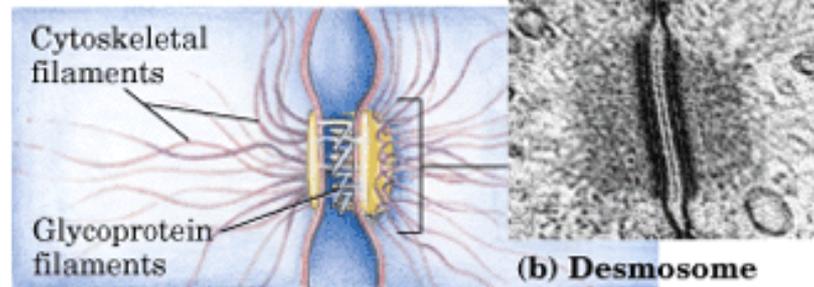
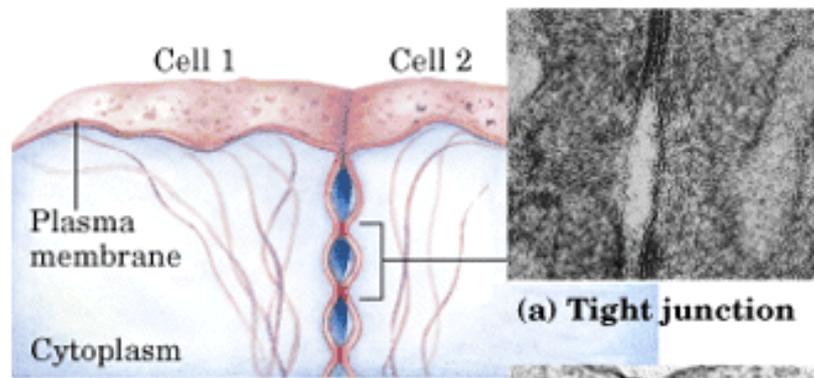


COMUNICACIÓN INTERCELULAR

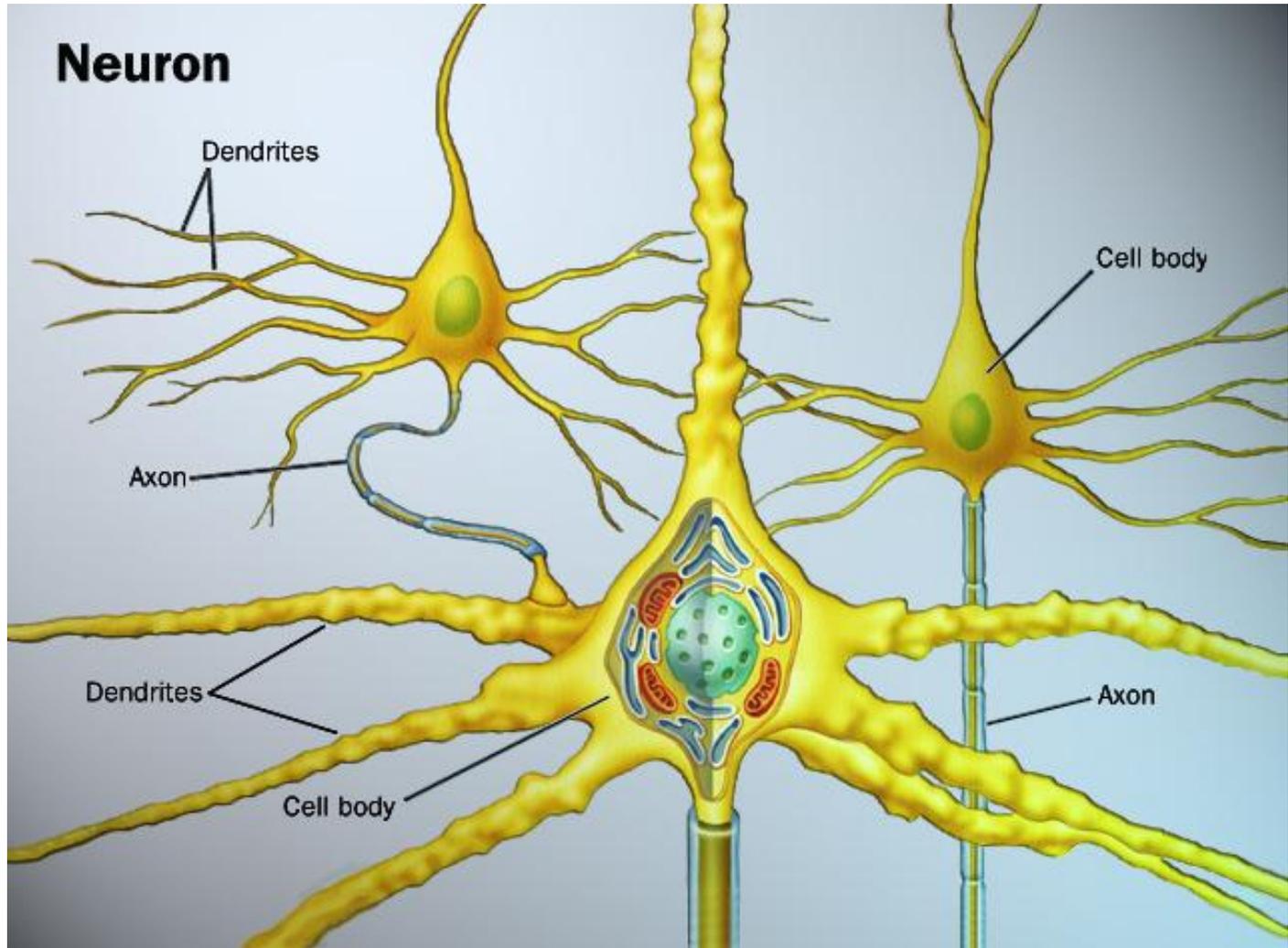
Marco Antonio Galleguillos Caamaño

**Fac. Cs. Veterinarias y Pecuarias
Universidad de Chile**

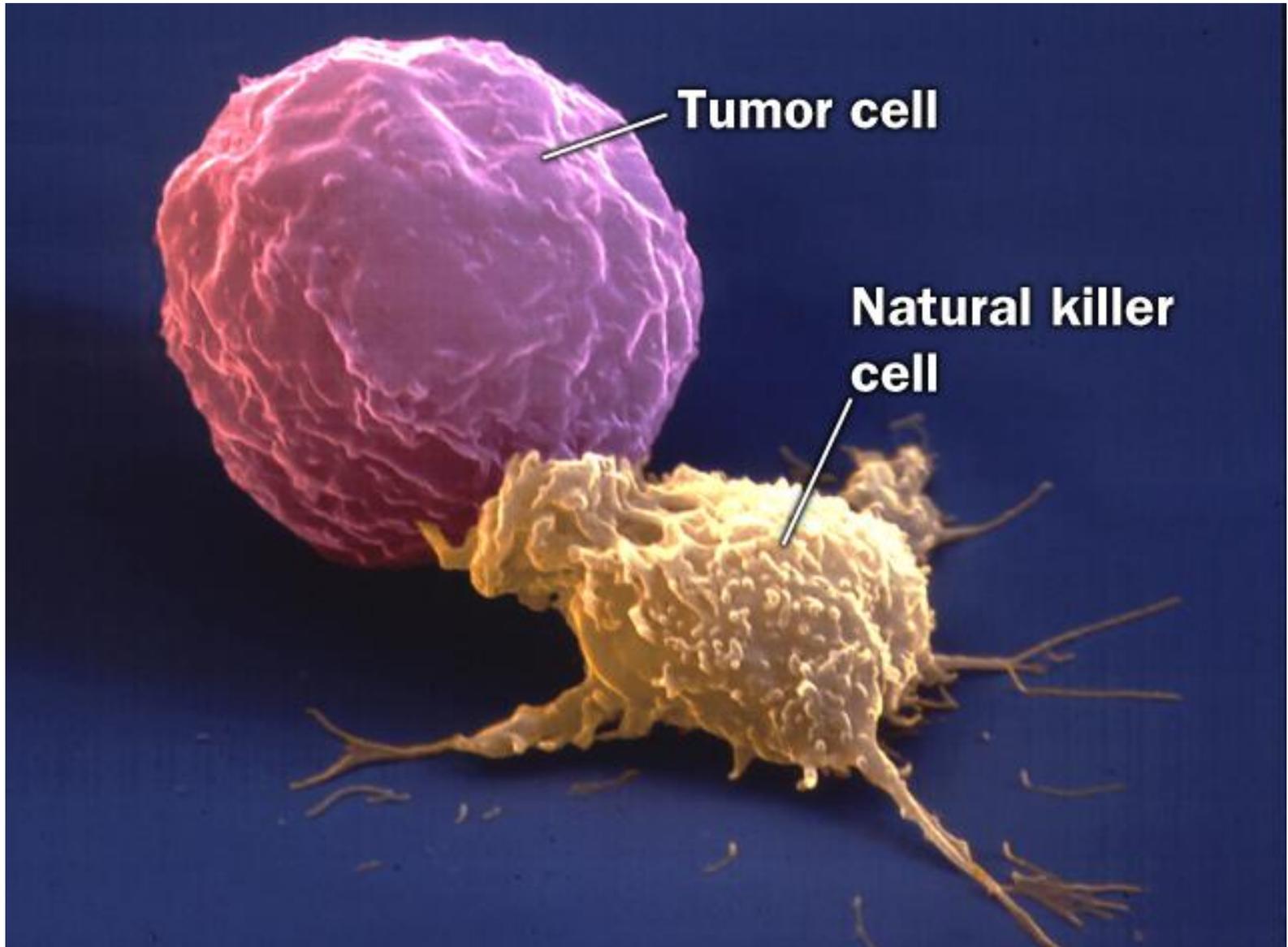
Fuentes: Lehninger 3era Ed.
Alberts B. Ed. 2002



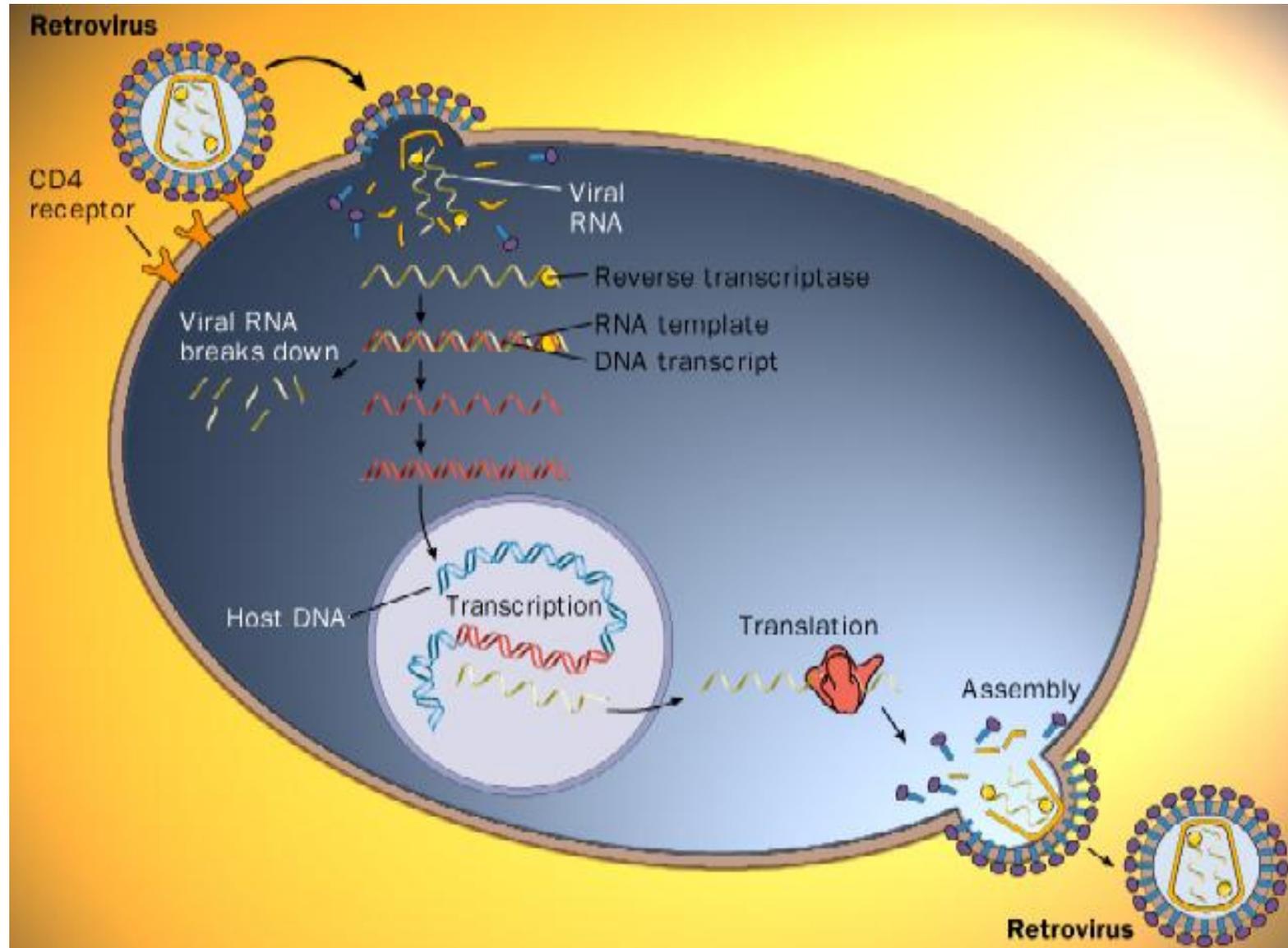
comunicación interneuronal

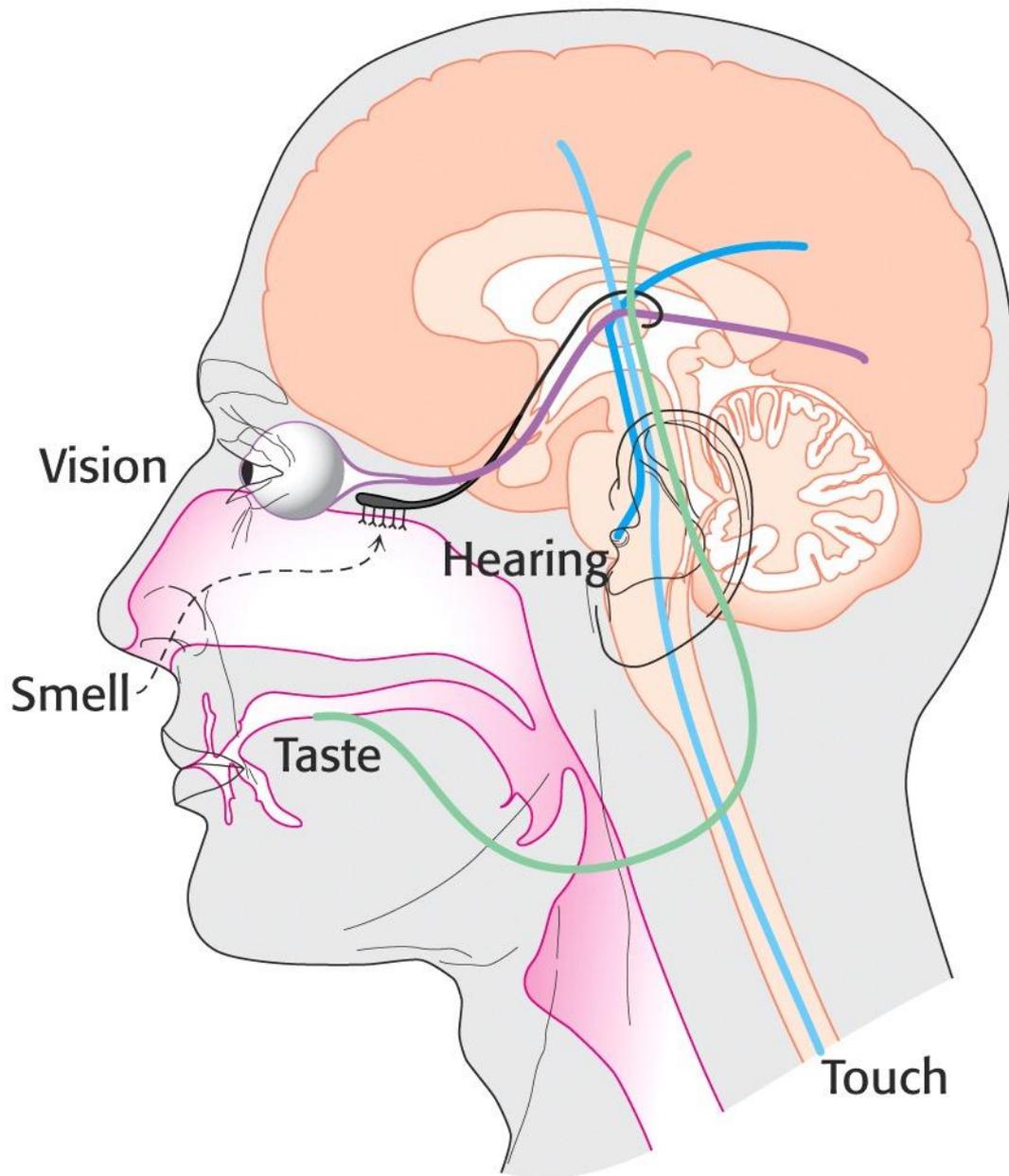


Reconocimiento célula-célula

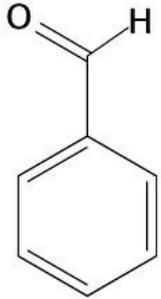


Reconocimiento célula-patógeno (infección viral)



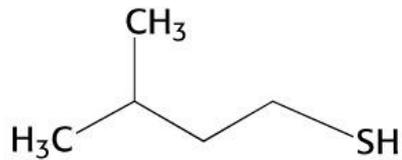


MOLECULAS CON AROMA



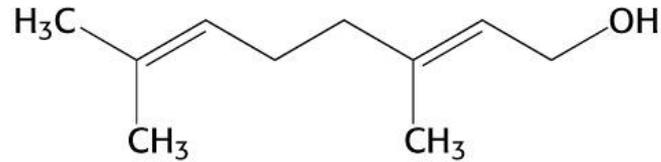
Benzaldehyde
(Almond)

Almendra



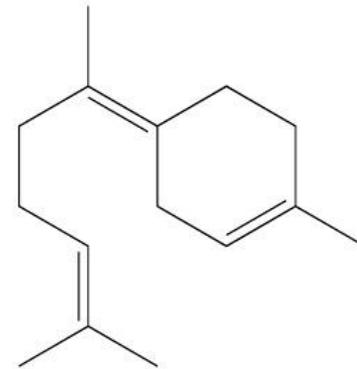
3-Methylbutane-1-thiol
(Skunk)

Mofeta



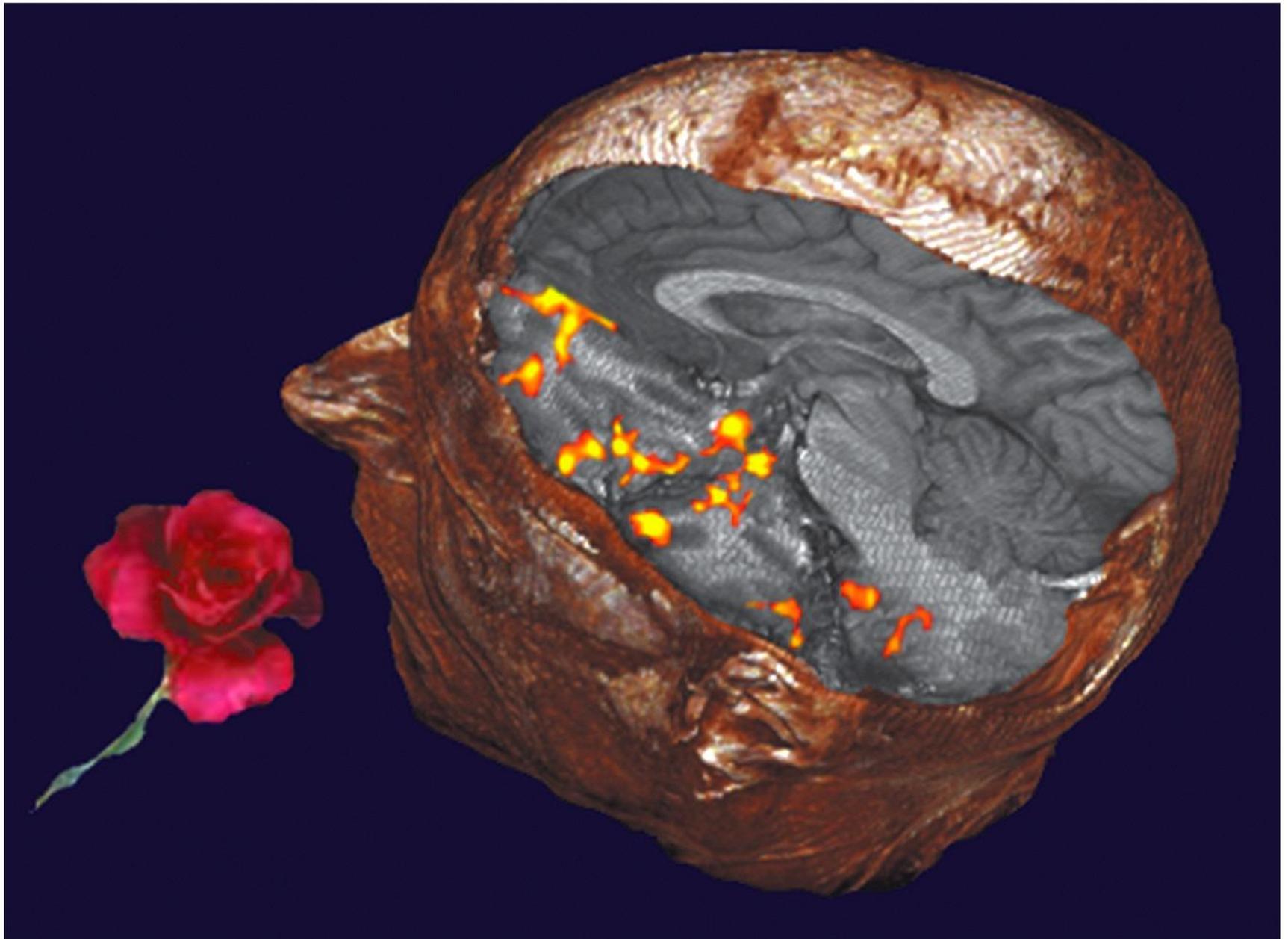
Geraniol
(Rose)

Rosa



Zingiberene
(Ginger)

Gengibre



El dolor



Efectos por deficiencia en la hormona LEPTINA



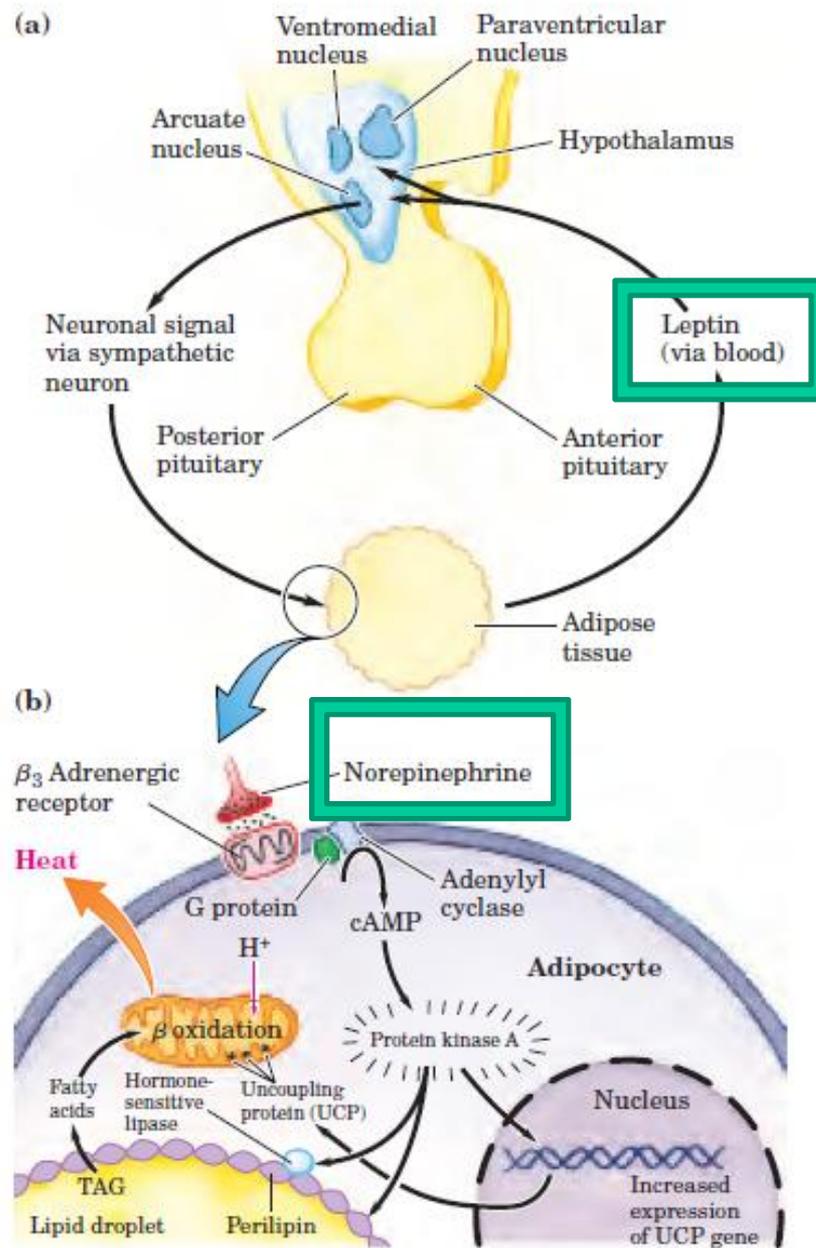
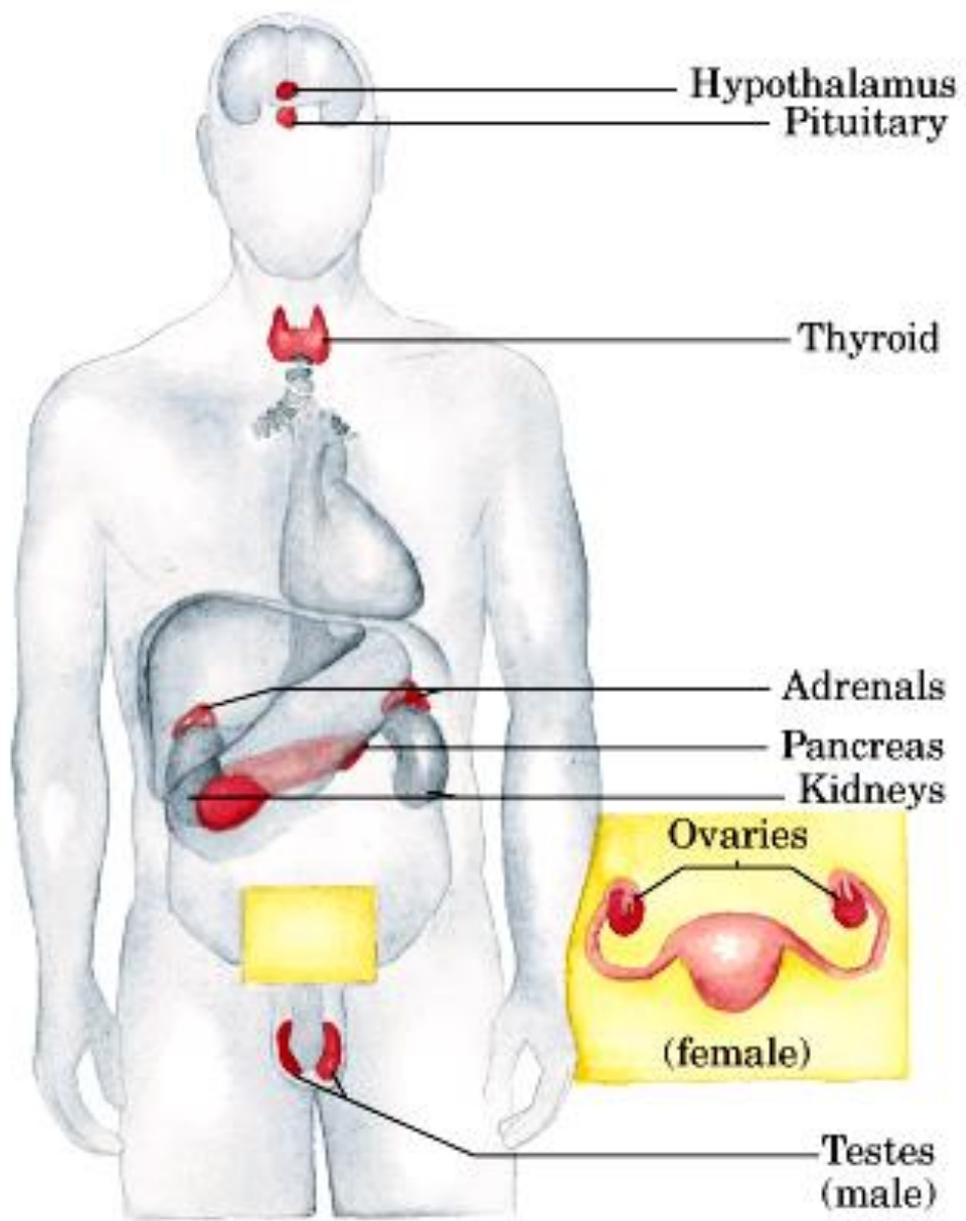
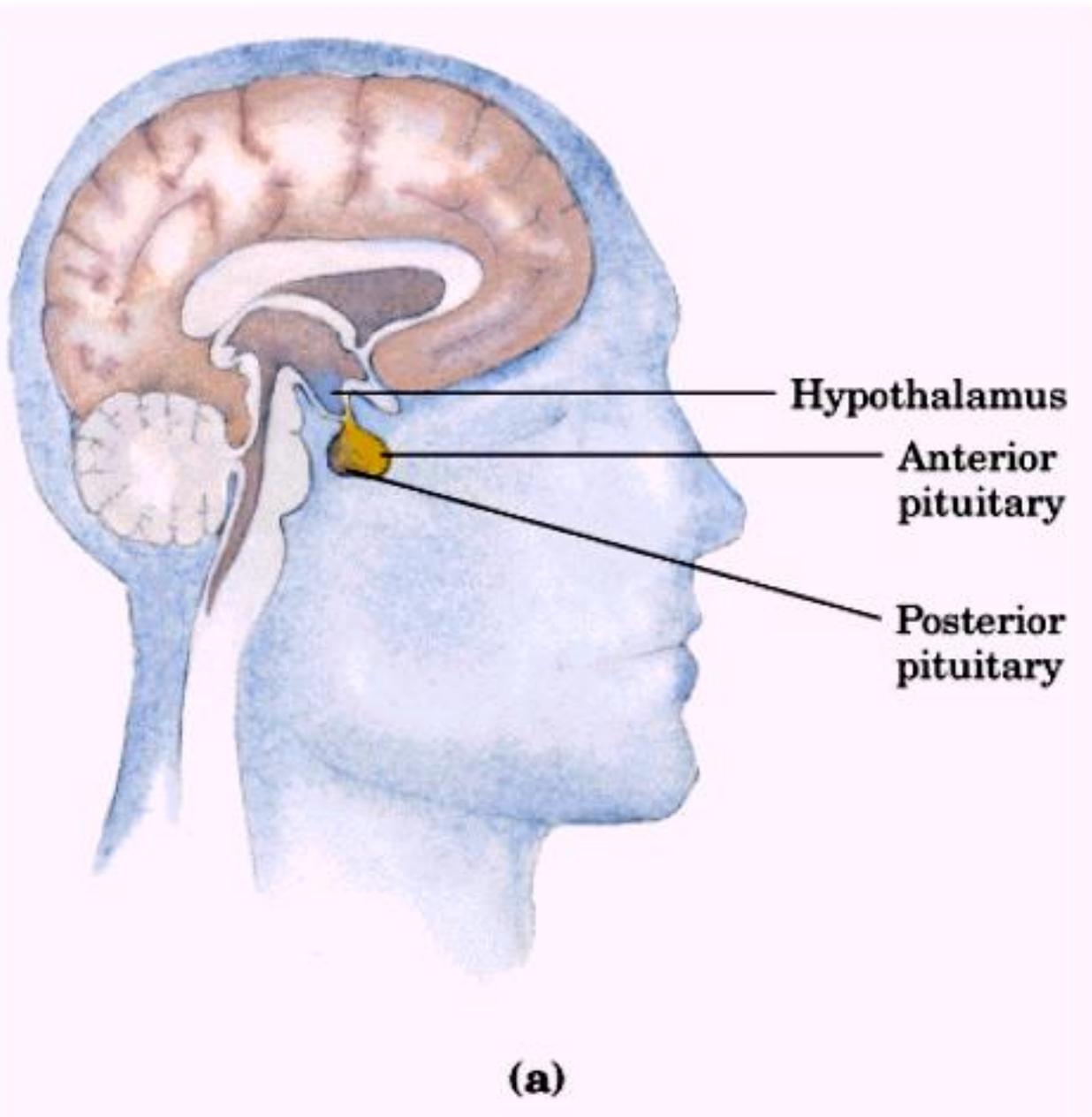
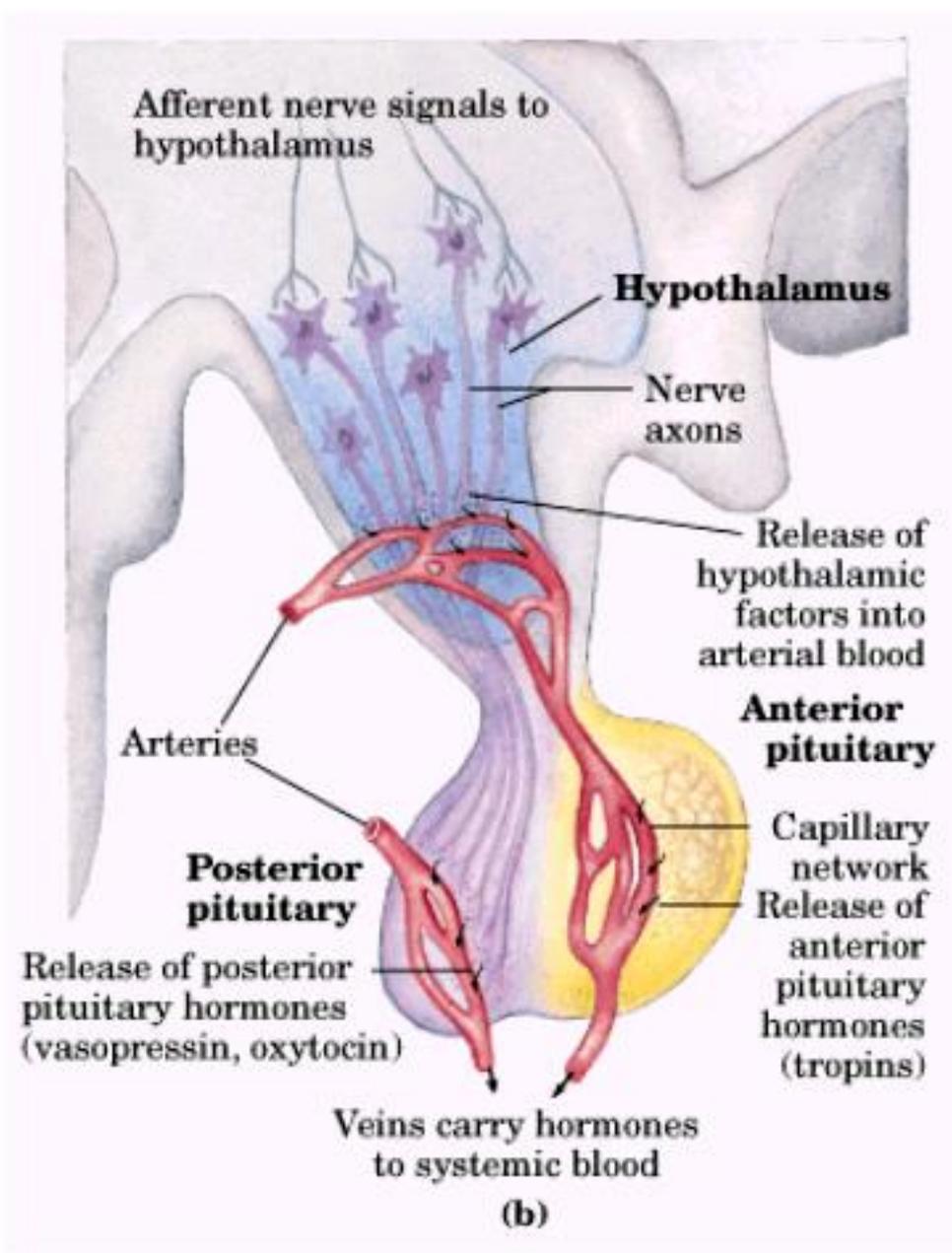
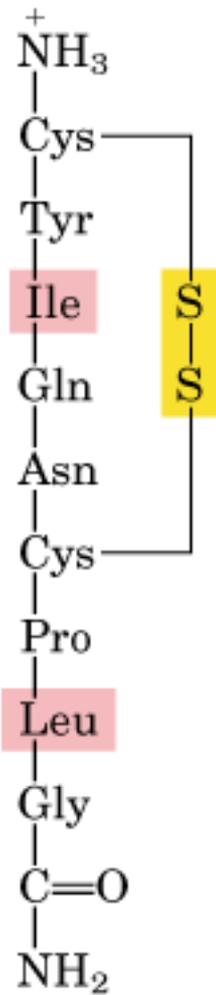


FIGURE 23-32 Hypothalamic regulation of food intake and energy expenditure. (a) Anatomy of the hypothalamus. (b) Interactions between the hypothalamus and an adipocyte, described later in text.

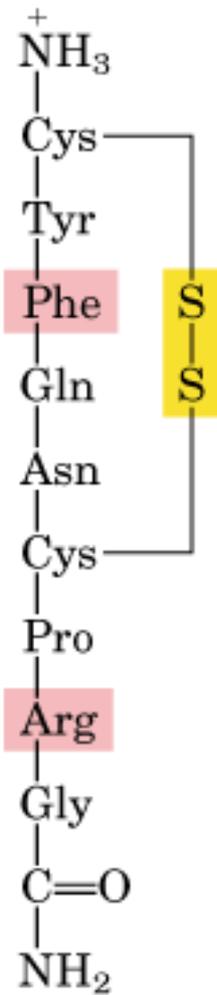






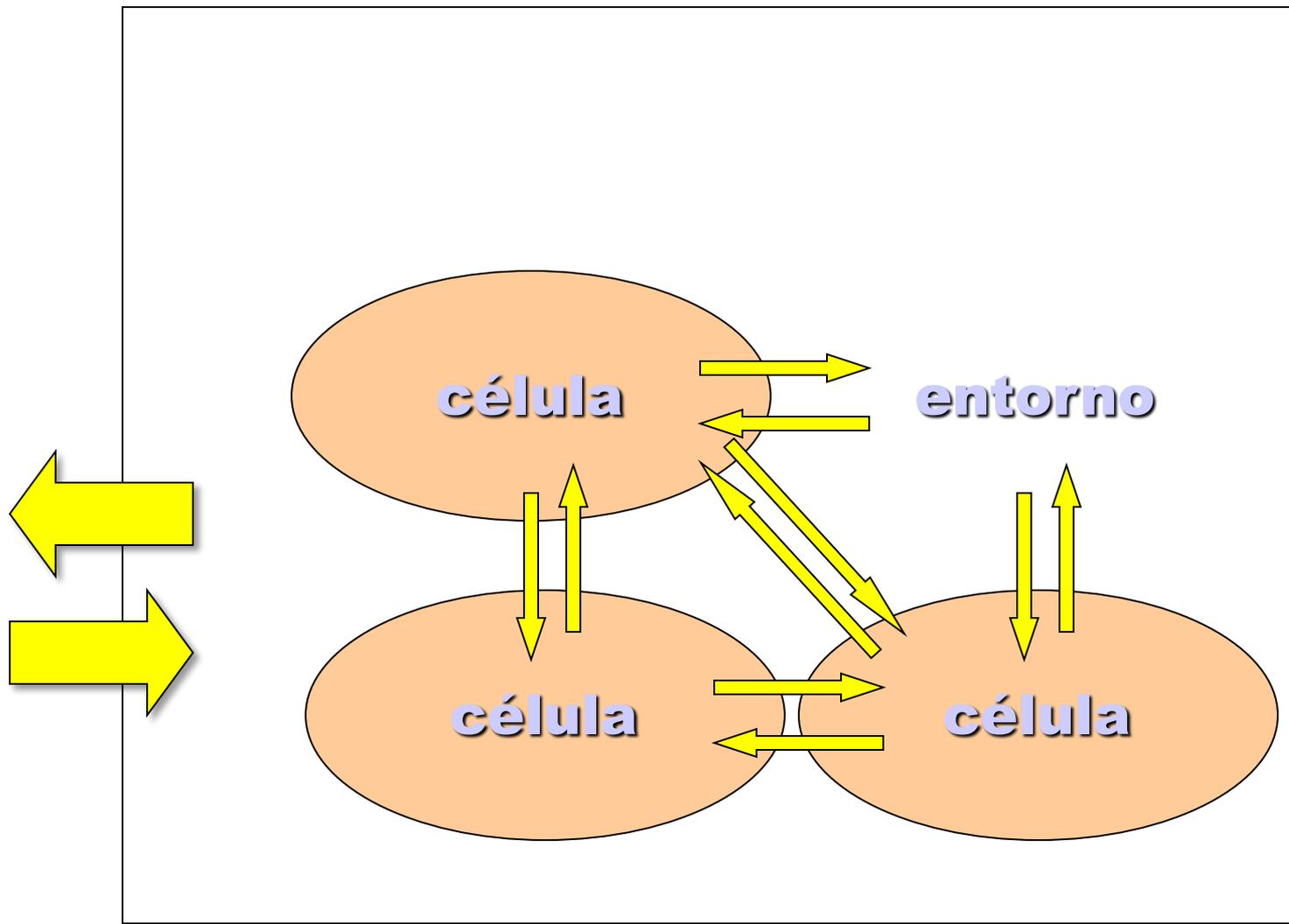


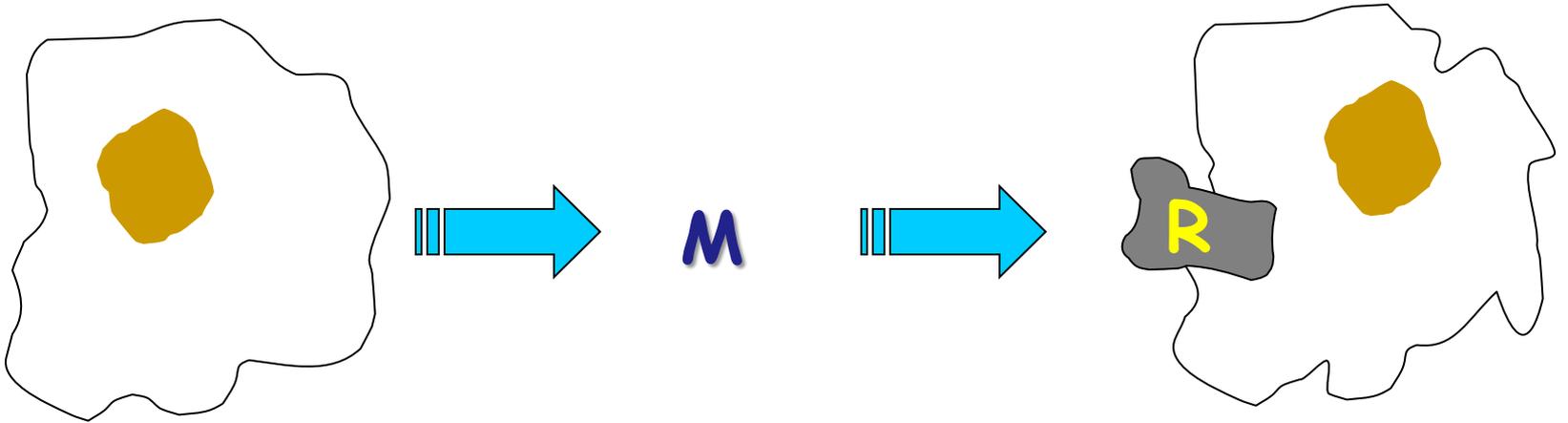
Human oxytocin

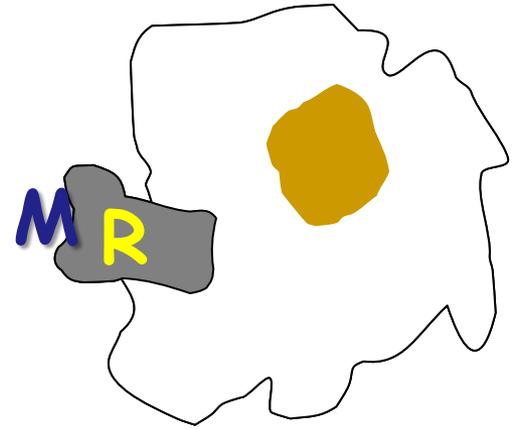
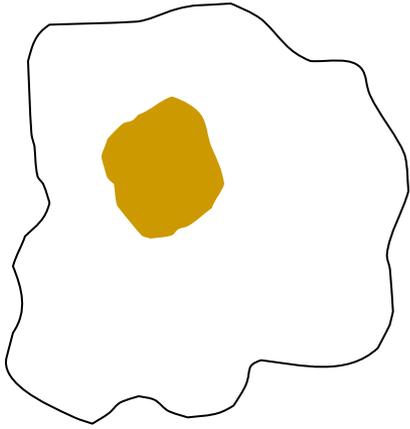


Human vasopressin
(antidiuretic hormone)

“Exterior”

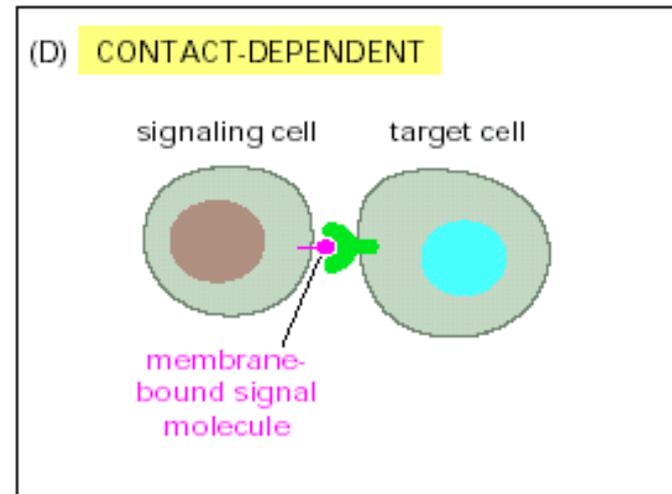
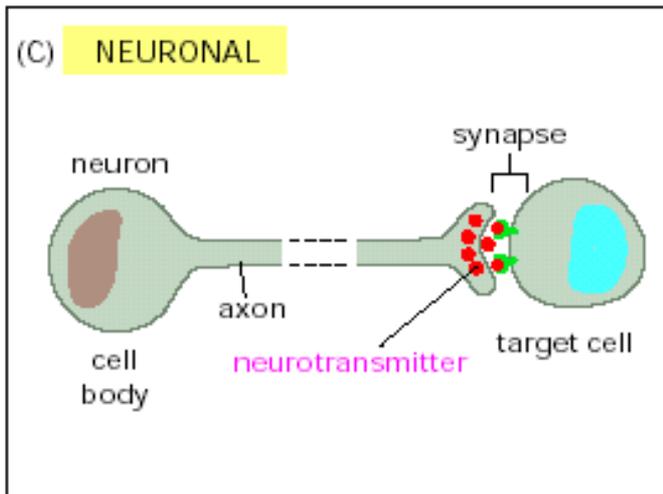
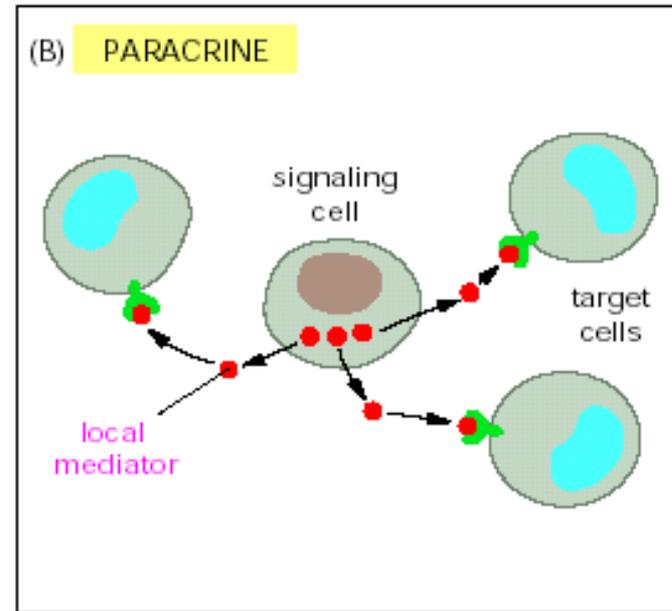
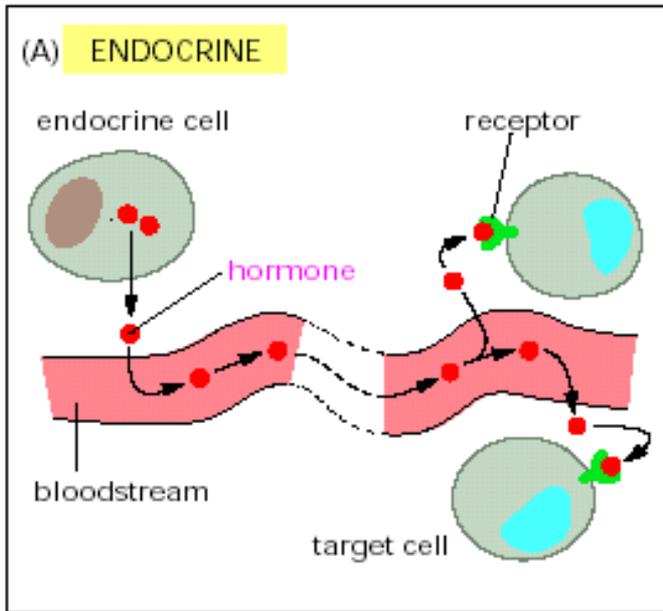


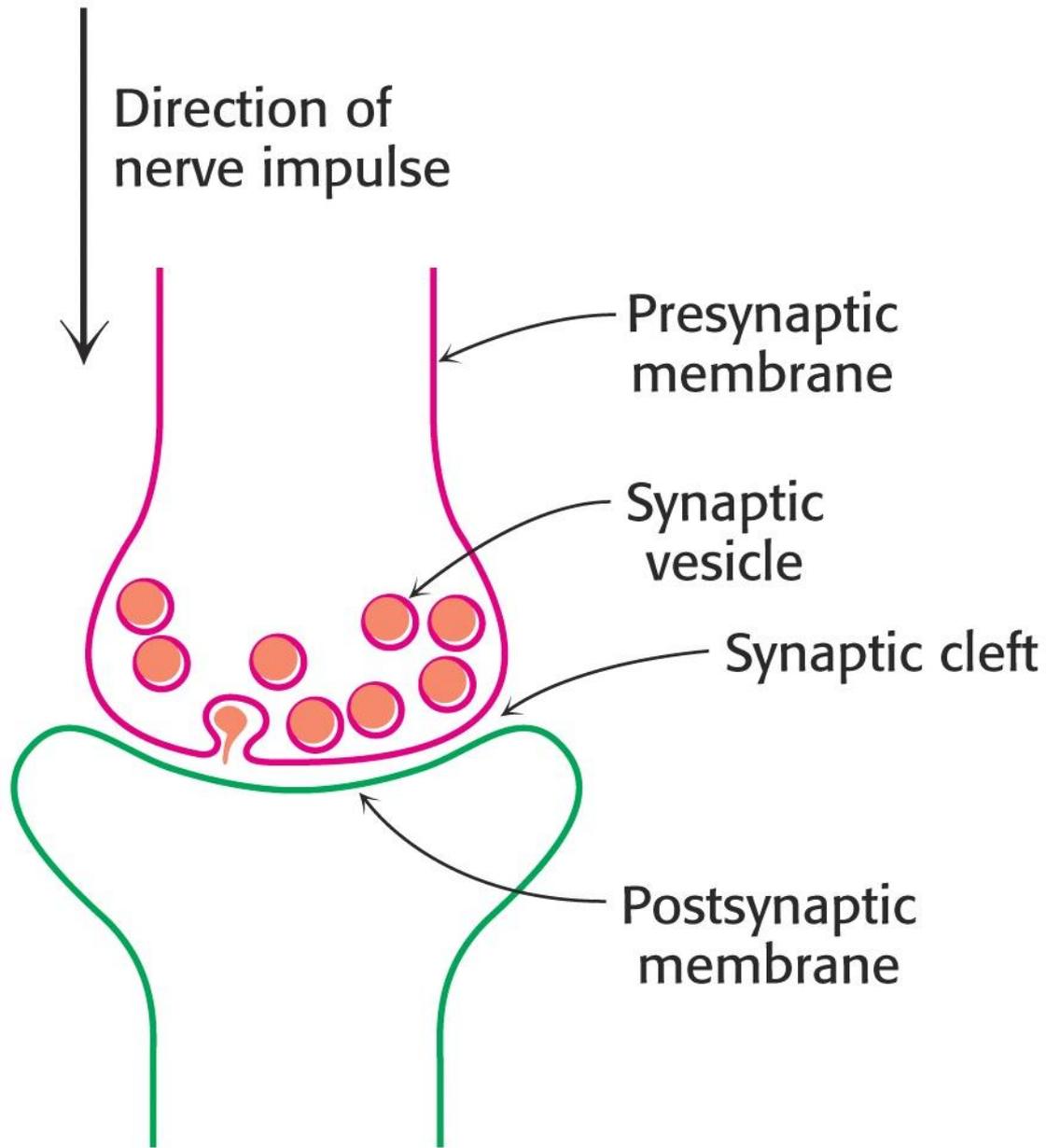




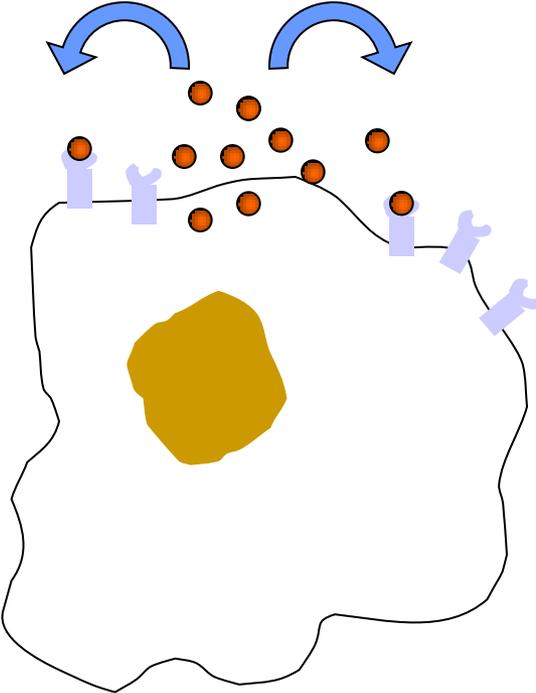
Modos de señal según la distancia entre la célula emisora y la célula blanco:

- **ENDOCRINA**
- **PARACRINA**
- **AUTOCRINA**
- **YUXTACRINA**
- **NEURONAL**





COMUNICACIÓN AUTOCRINA



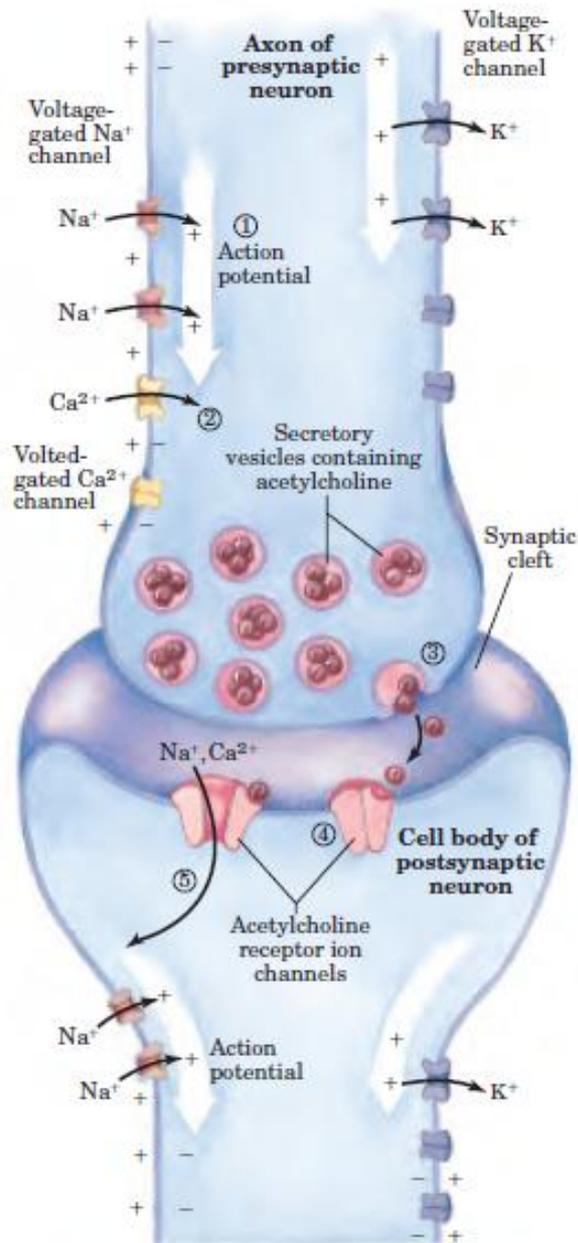
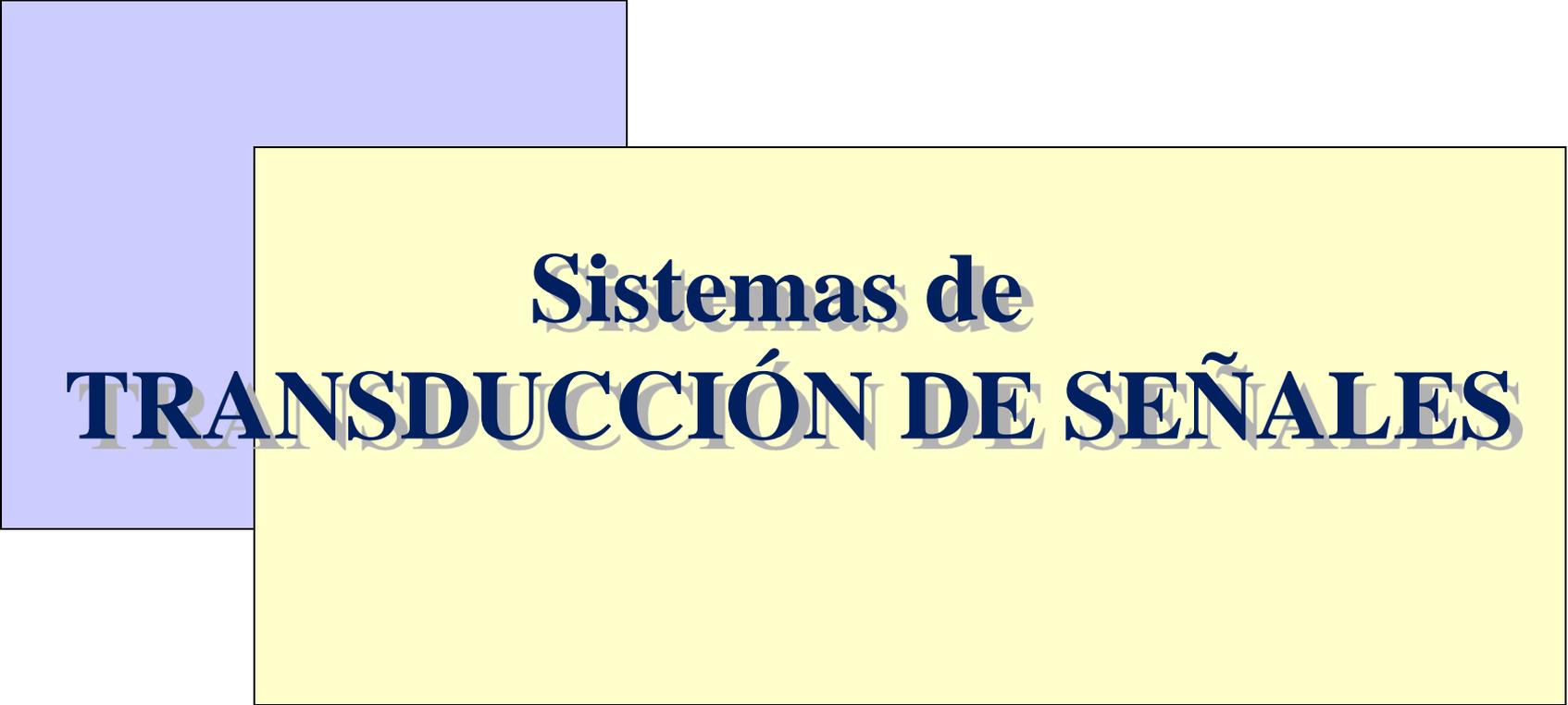


FIGURE 12-5 Role of voltage-gated and ligand-gated ion channels in neural transmission. Initially, the plasma membrane of the presynaptic neuron is polarized (inside negative) through the action of the electrogenic Na^+K^+ ATPase, which pumps 3 Na^+ out for every 2 K^+ pumped into the neuron (see Fig. 12-3). ① A stimulus to this neuron causes an action potential to move along the axon (white arrow), away from the cell body. The opening of one voltage-gated Na^+ channel allows Na^+ entry, and the resulting local depolarization causes the adjacent Na^+ channel to open, and so on. The directionality of movement of the action potential is ensured by the brief refractory period that follows the opening of each voltage-gated Na^+ channel. ② When the wave of depolarization reaches the axon tip, voltage-gated Ca^{2+} channels open, allowing Ca^{2+} entry into the presynaptic neuron. ③ The resulting increase in internal $[\text{Ca}^{2+}]$ triggers exocytic release of the neurotransmitter acetylcholine into the synaptic cleft. ④ Acetylcholine binds to a receptor on the postsynaptic neuron, causing its ligand-gated ion channel to open. ⑤ Extracellular Na^+ and Ca^{2+} enter through this channel, depolarizing the postsynaptic cell. The electrical signal has thus passed to the cell body of the postsynaptic neuron and will move along its axon to a third neuron by this same sequence of events.



Sistemas de TRANSDUCCIÓN DE SEÑALES

Parte de este material fue tomado del Lenhinger 3ª Ed y del Stryer 5ª Ed.

table 13–1

Some Signals to Which Cells Respond

Antigens

Cell surface glycoproteins/oligosaccharides

Developmental signals

Extracellular matrix components

Growth factors

Hormones

Light

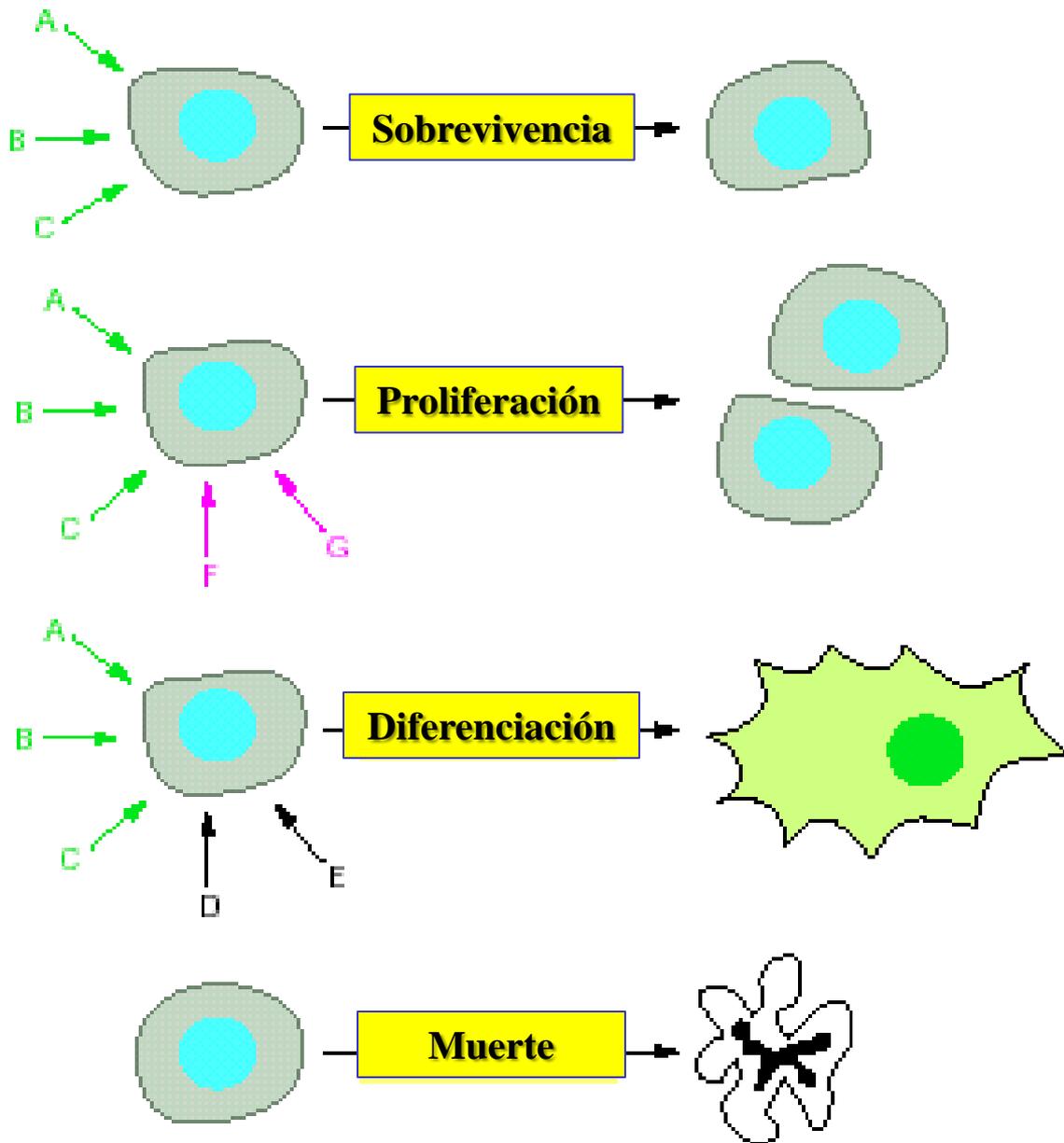
Mechanical touch

Neurotransmitters

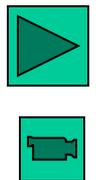
Odorants

Pheromones

Tastants



Apoptosis



En las células eucariontes los primeros mensajeros pueden ser:

- **Proteínas.** (insulina, hormona de crecimiento, prolactina, factores de crecimiento, etc)
- **Pequeños péptidos** (ocitocina, vasopresina, encefalinas, sustancia P, etc.)
- **Aminoácidos o sus derivados** (glutamato, glicina, serotonina, histamina, dopamina, adrenalina)
- **Nucleótidos** (ATP)
- **Esteroides** (cortisol, estradiol, testosterona)
- **Retinoides** (ácido retinoico)
- **Derivados de ácidos grasos** (Prostaglandinas, leucotrienos y tromboxanos)
- **Gases disueltos** (NO y CO)

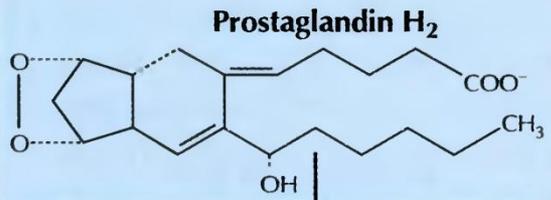
Phospholipids

PLA₂

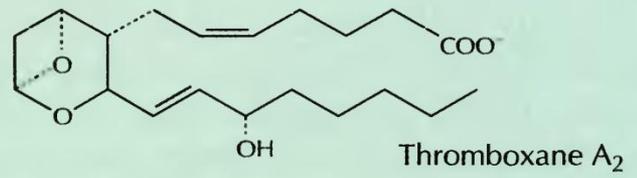
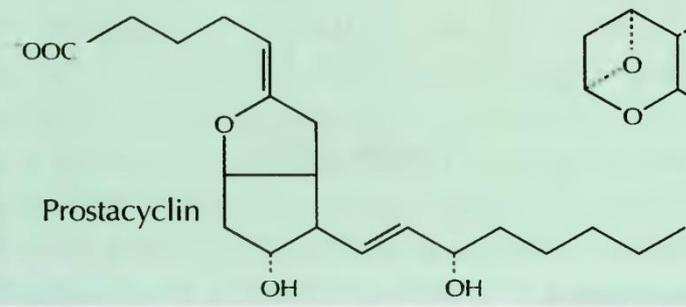
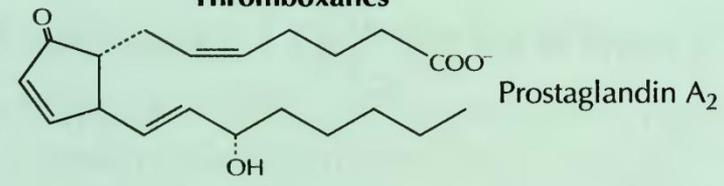
Arachidonic acid

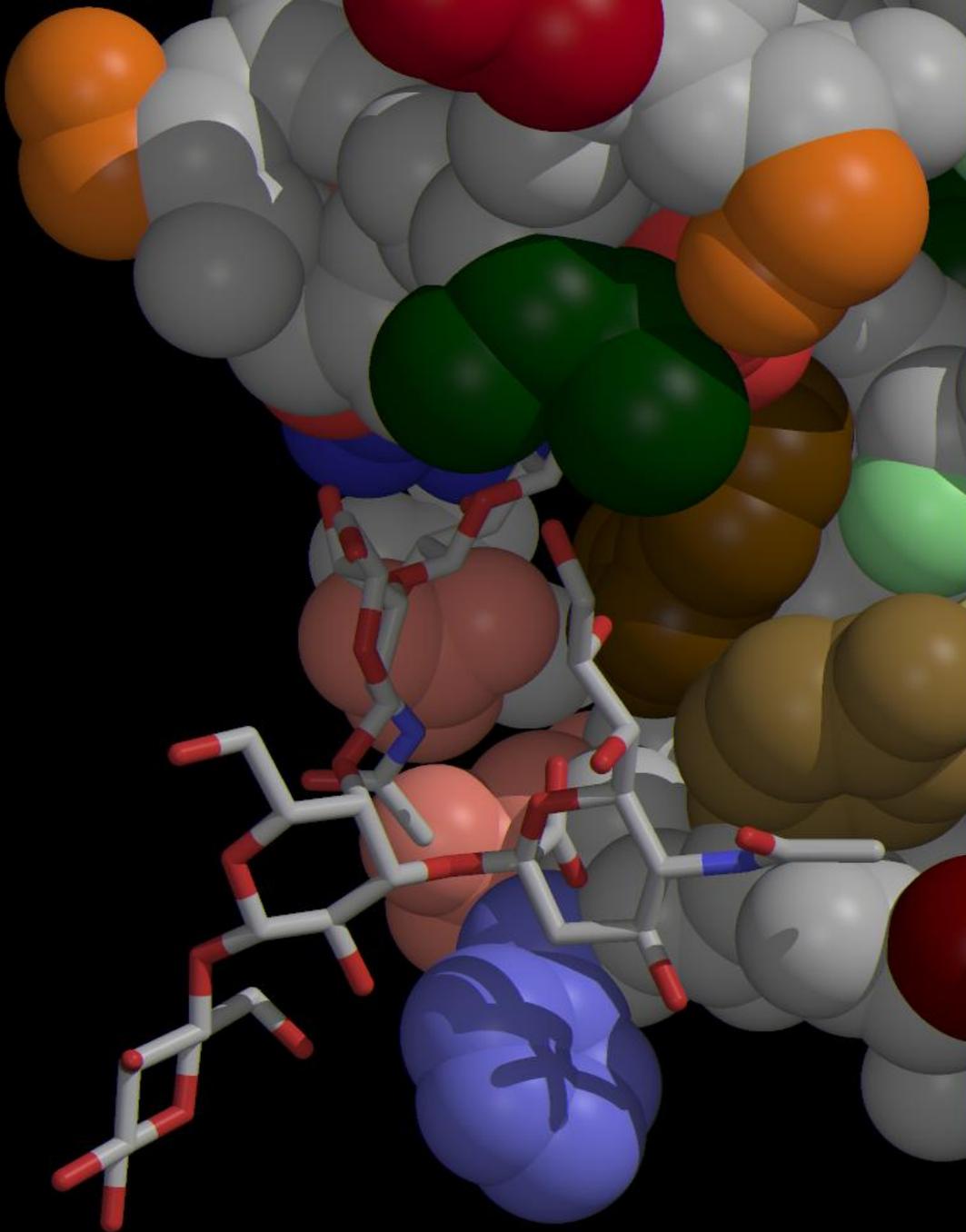


Ciclooxigenasa

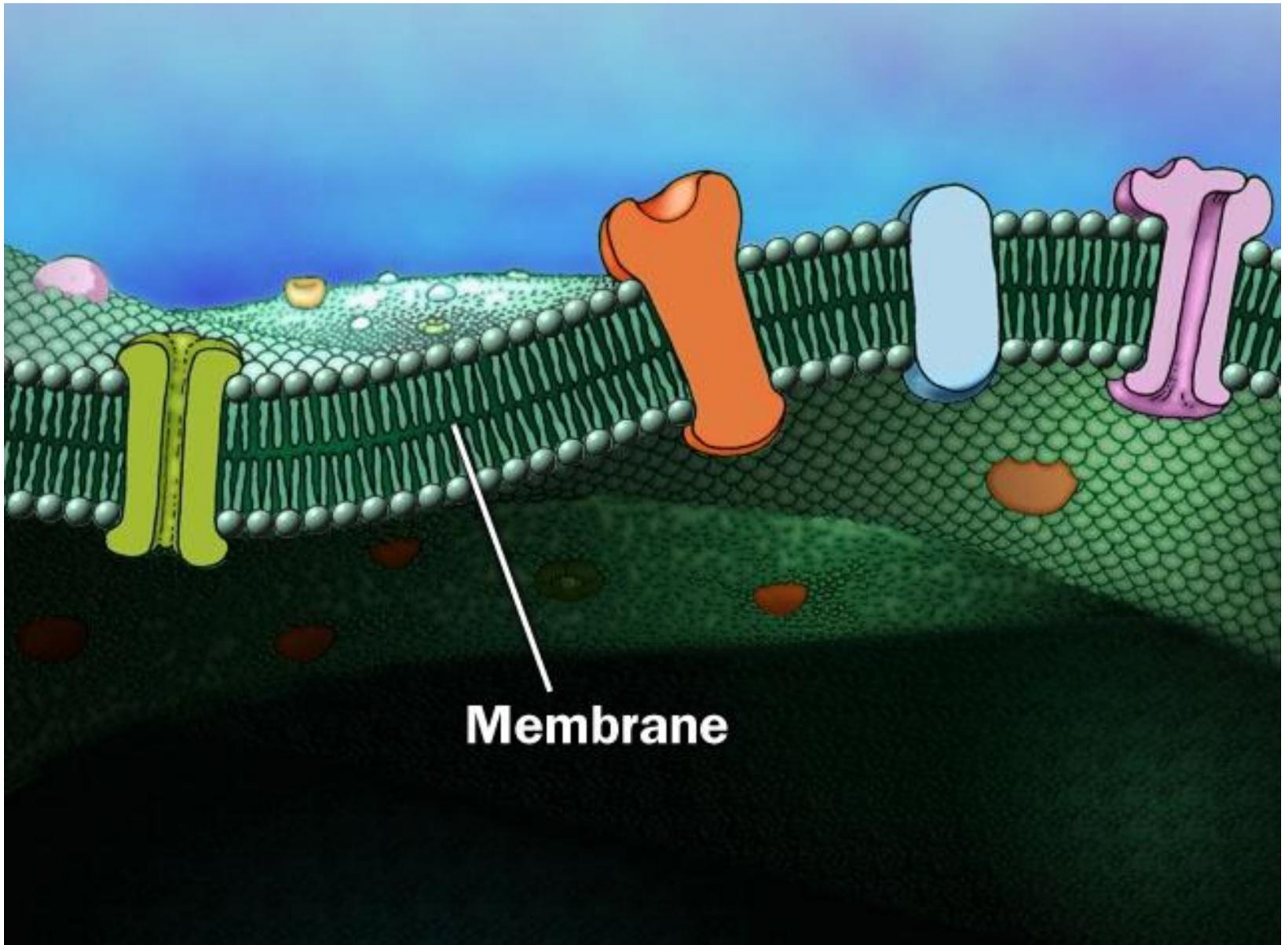


Other prostaglandins
Prostacyclin
Thromboxanes

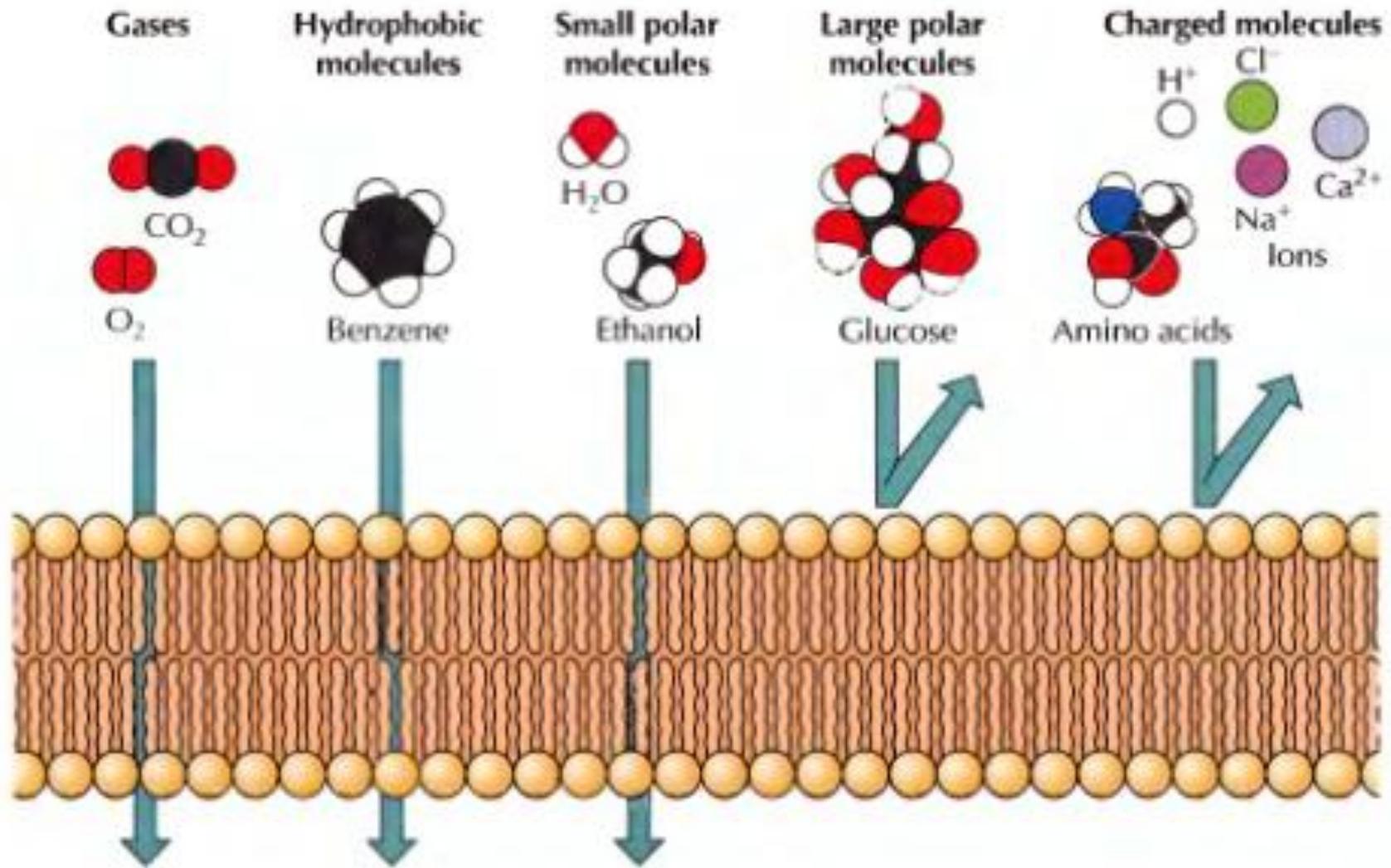


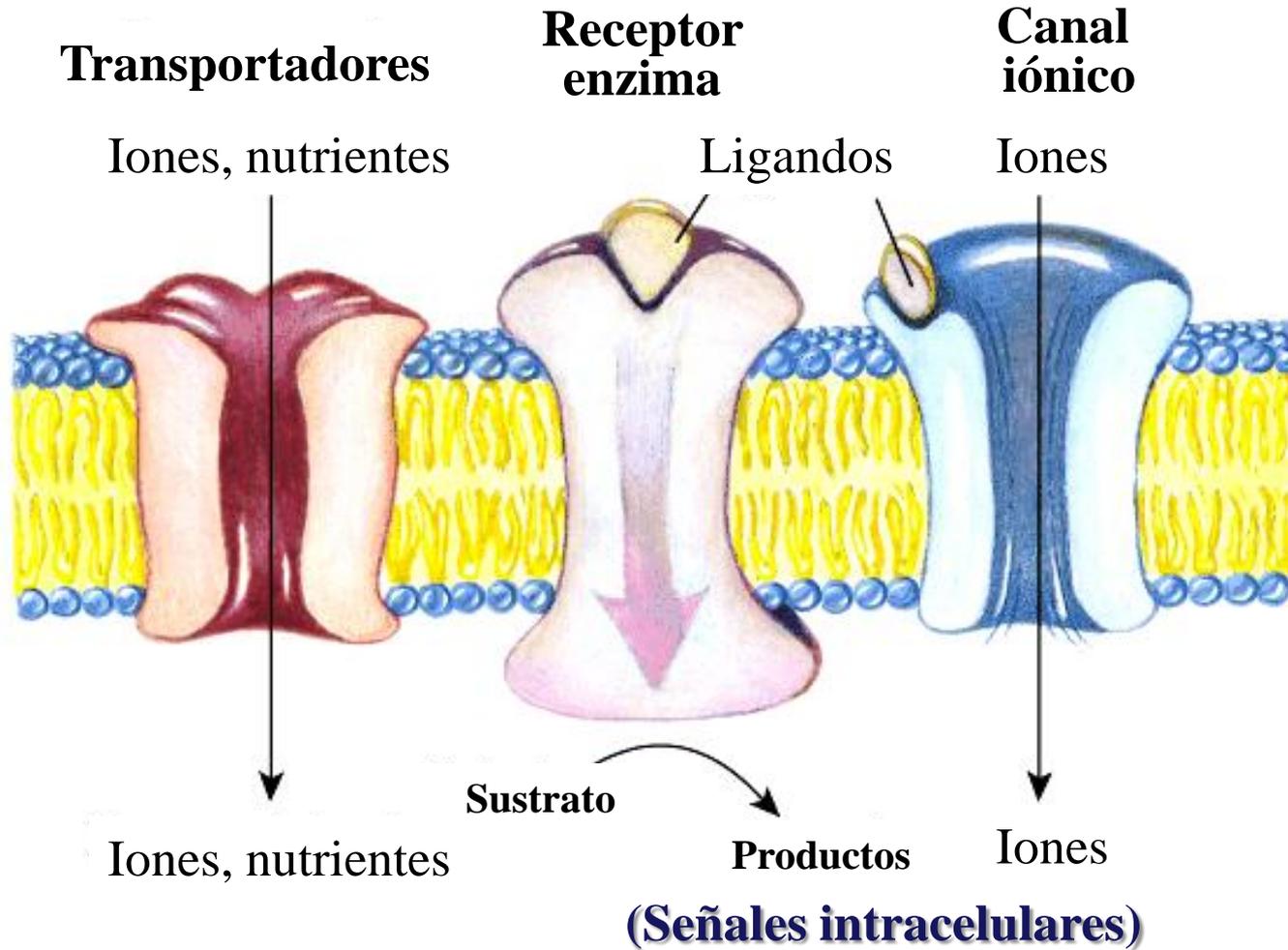


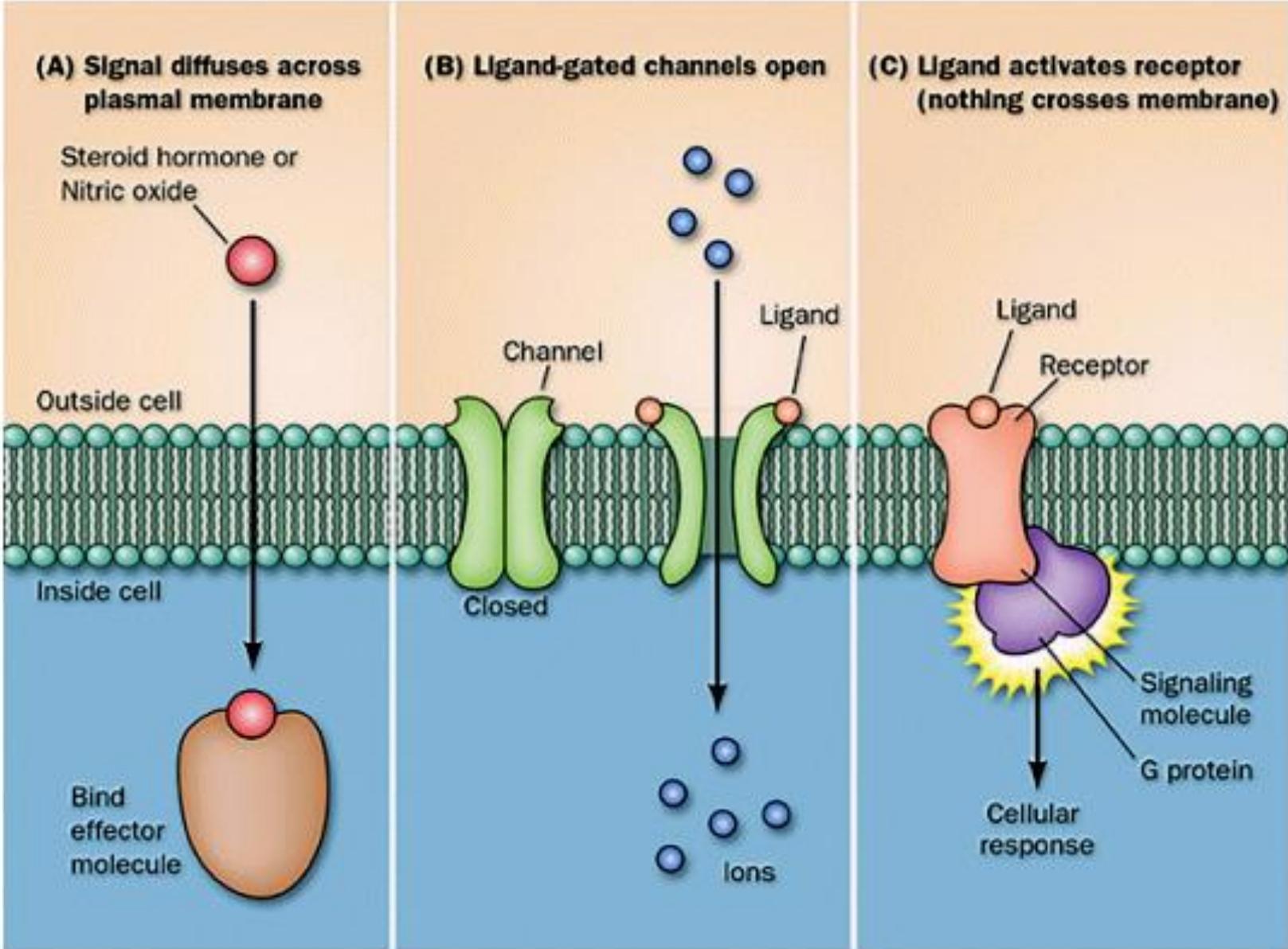
Interacción a nivel molecular



Membrane







La respuesta celular ante un mensajero externo tiene cuatro características:

Es específica

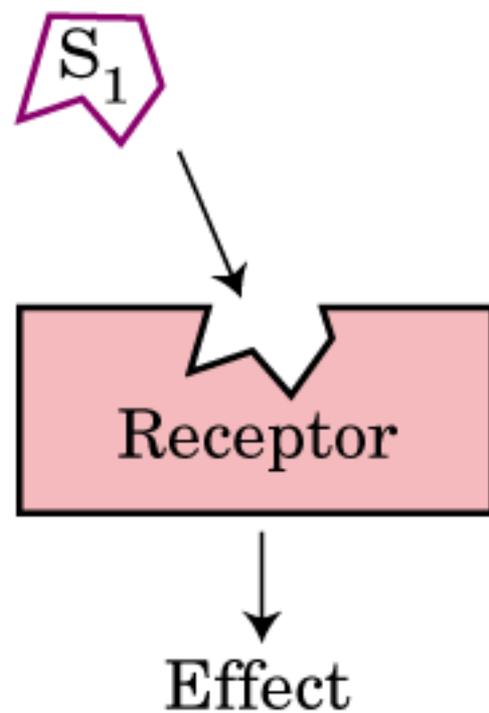
Se amplifica la señal

Se produce adaptación

Se puede integrar con otras señales

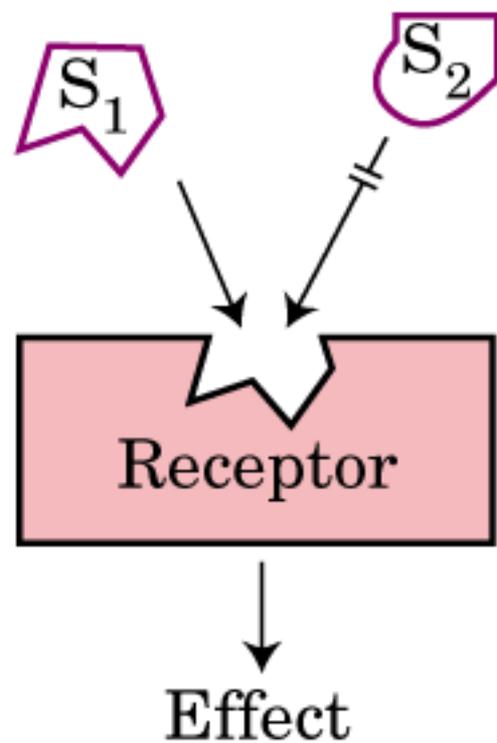
(a) Specificity

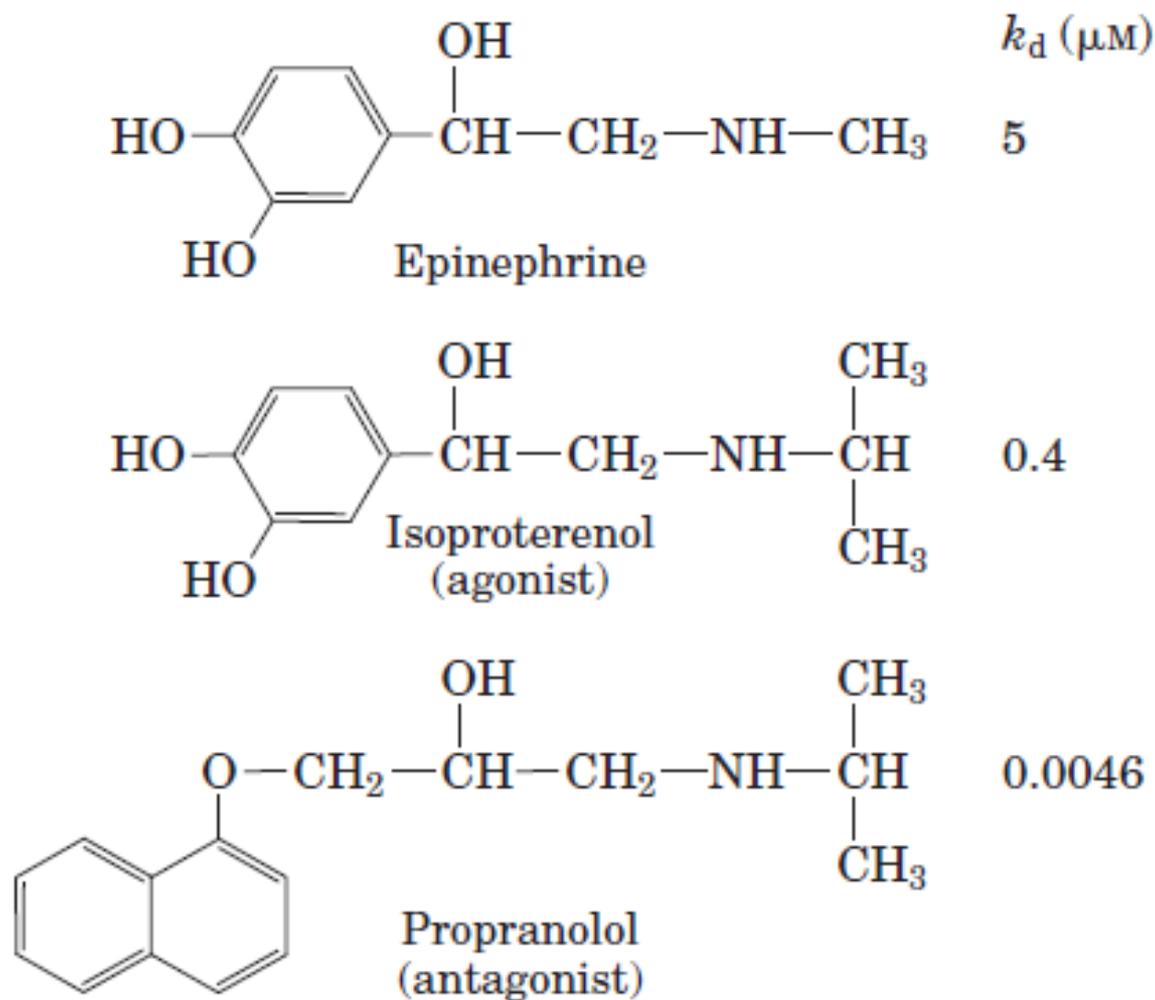
Signal molecule fits binding site on its complementary receptor; other signals do not fit.



(a) Specificity

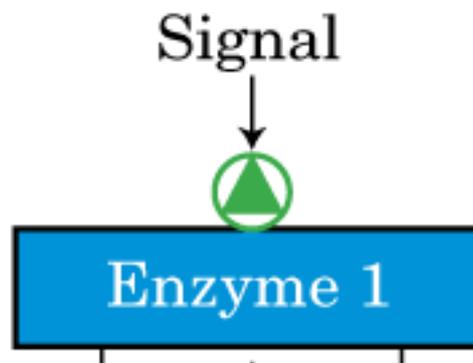
Signal molecule fits binding site on its complementary receptor; other signals do not fit.





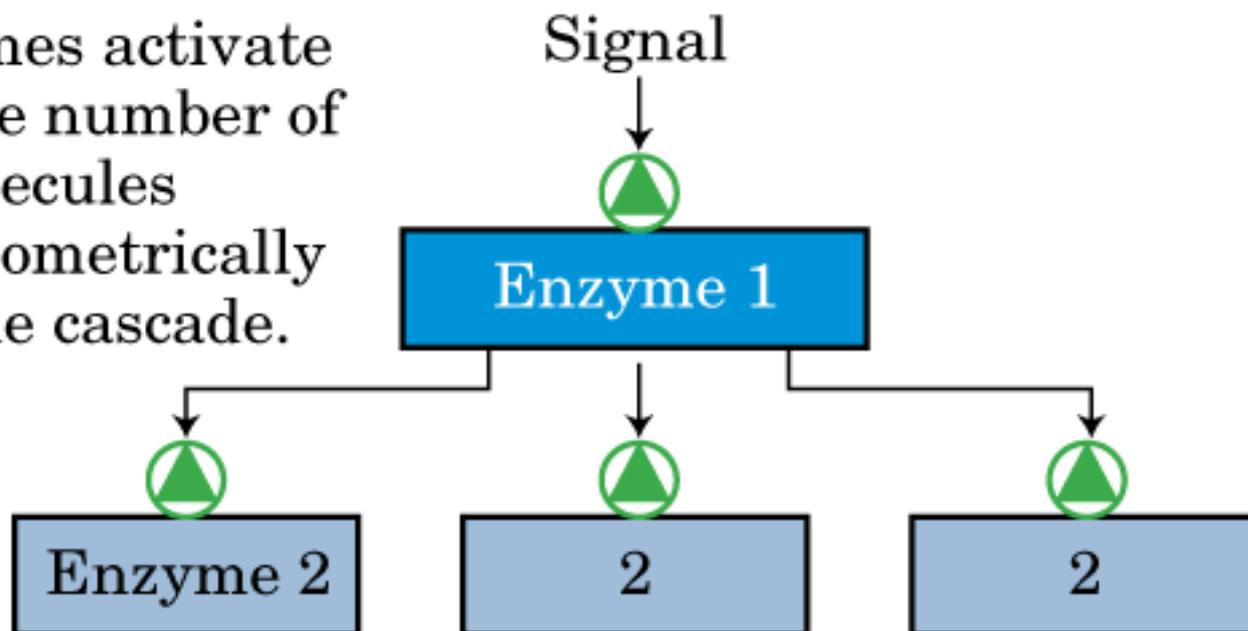
(b) Amplification

When enzymes activate enzymes, the number of affected molecules increases geometrically in an enzyme cascade.



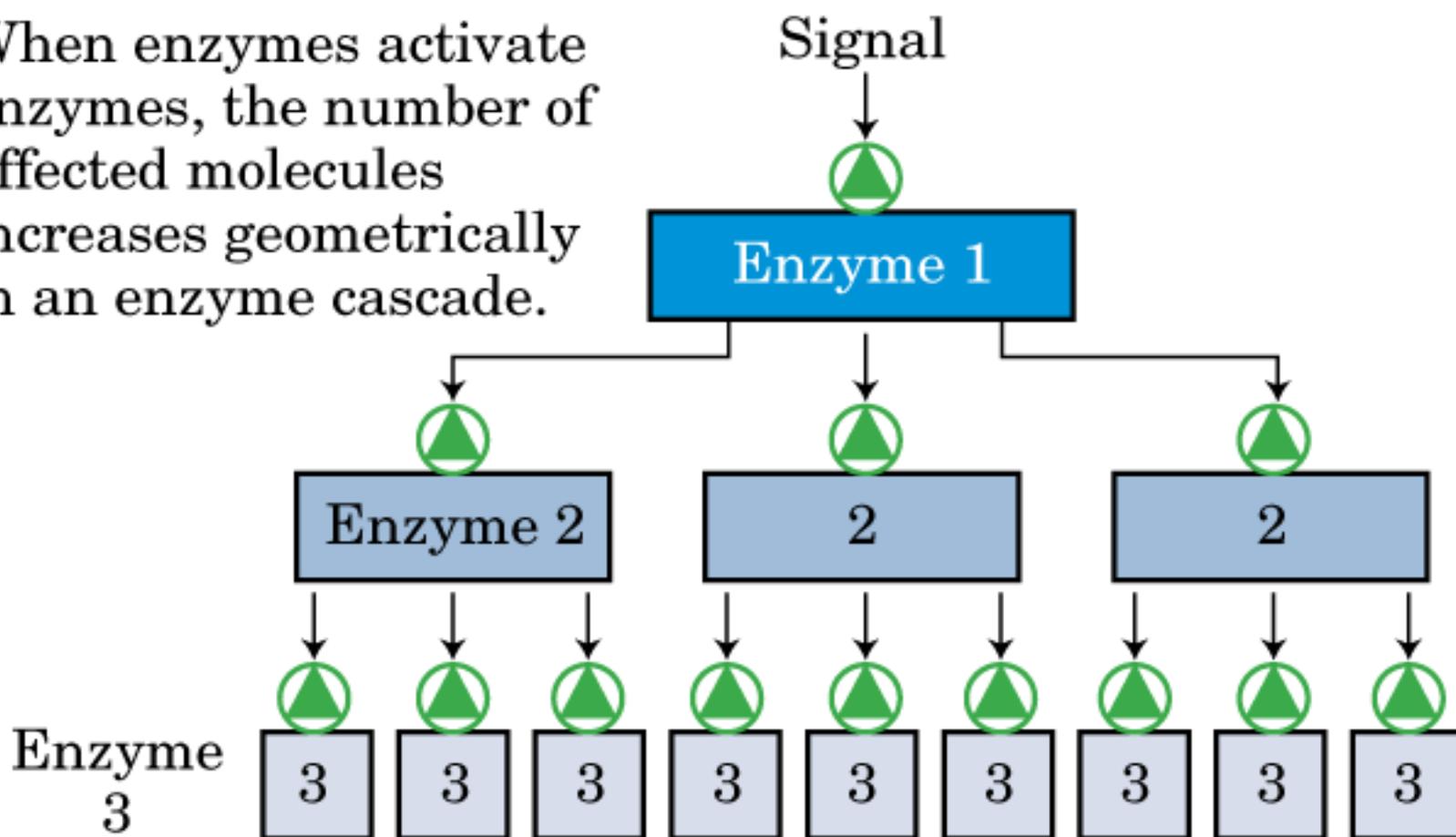
(b) Amplification

When enzymes activate enzymes, the number of affected molecules increases geometrically in an enzyme cascade.



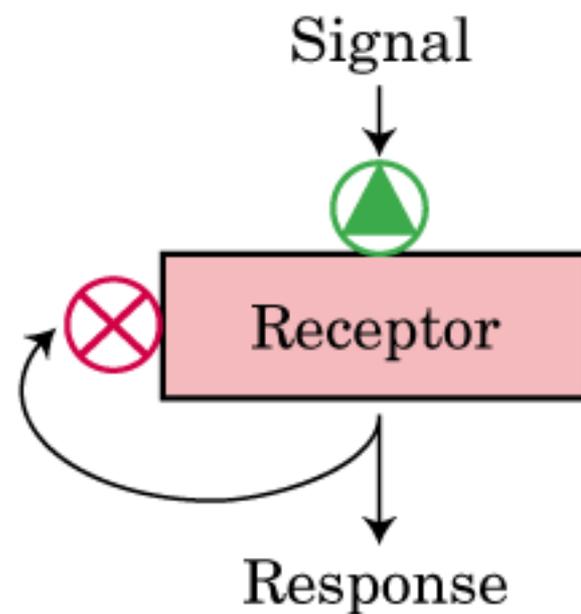
(b) Amplification

When enzymes activate enzymes, the number of affected molecules increases geometrically in an enzyme cascade.



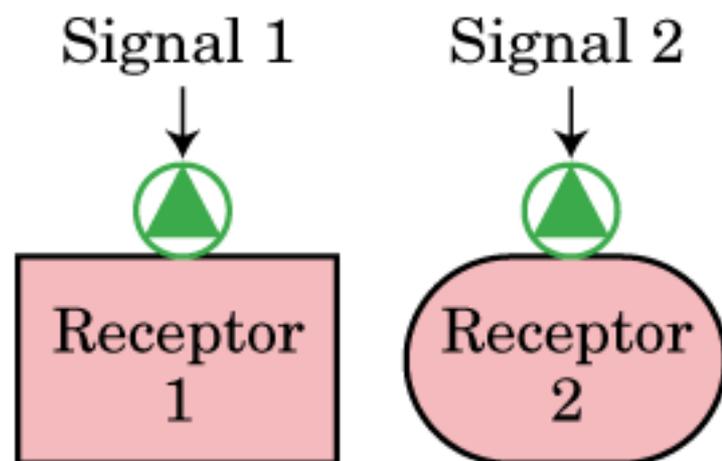
(c) **Desensitization/Adaptation**

Receptor activation triggers a feedback circuit that shuts off the receptor or removes it from the cell surface.



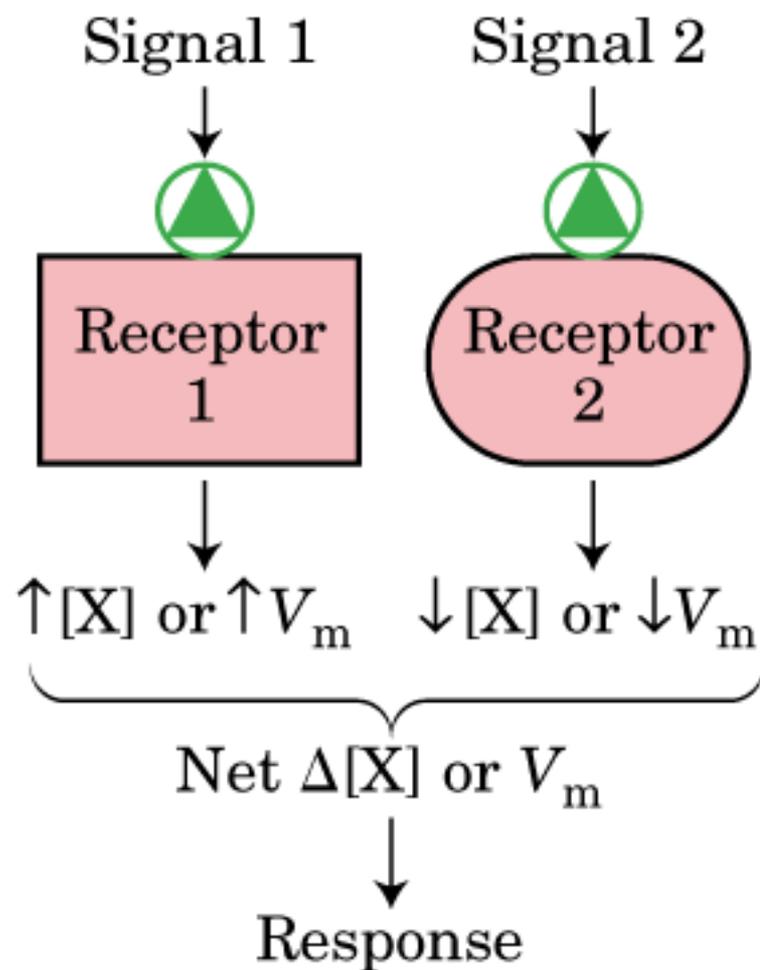
(d) Integration

When two signals have opposite effects on a metabolic characteristic such as the concentration of a second messenger X , or the membrane potential V_m , the regulatory outcome results from the integrated input from both receptors.



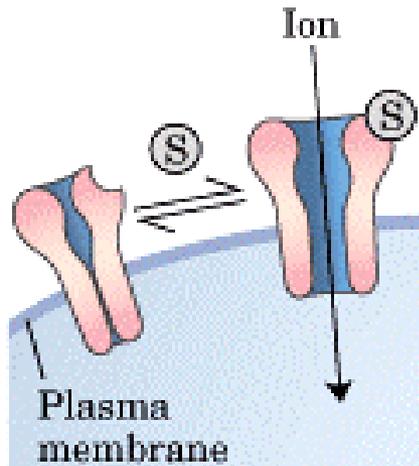
(d) Integration

When two signals have opposite effects on a metabolic characteristic such as the concentration of a second messenger X , or the membrane potential V_m , the regulatory outcome results from the integrated input from both receptors.



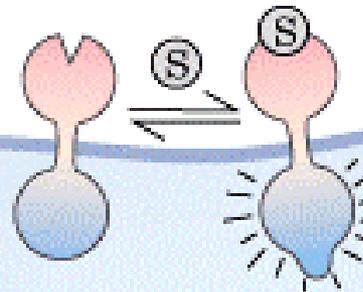
Gated ion channel

Opens or closes in response to concentration of signal ligand (S) or membrane potential.



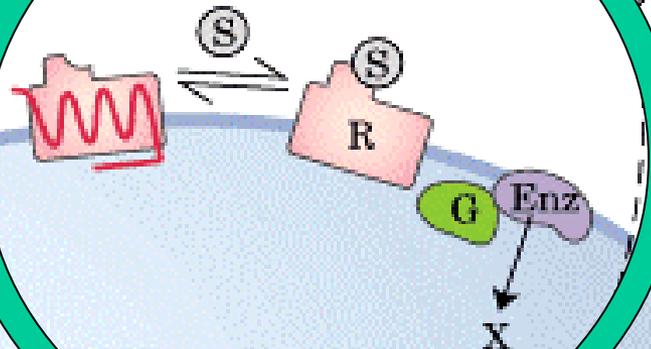
Receptor enzyme

Ligand binding to extracellular domain stimulates enzyme activity in intracellular domain.



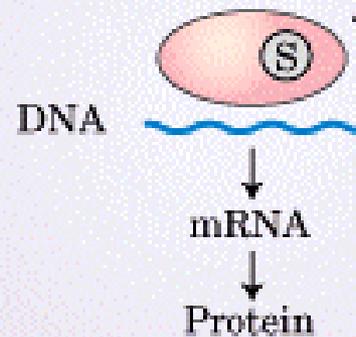
Serpentine receptor

External ligand binding to receptor (R) activates an intracellular GTP-binding protein (G) that stimulates an enzyme (Enz) that generates an intracellular second messenger, X.



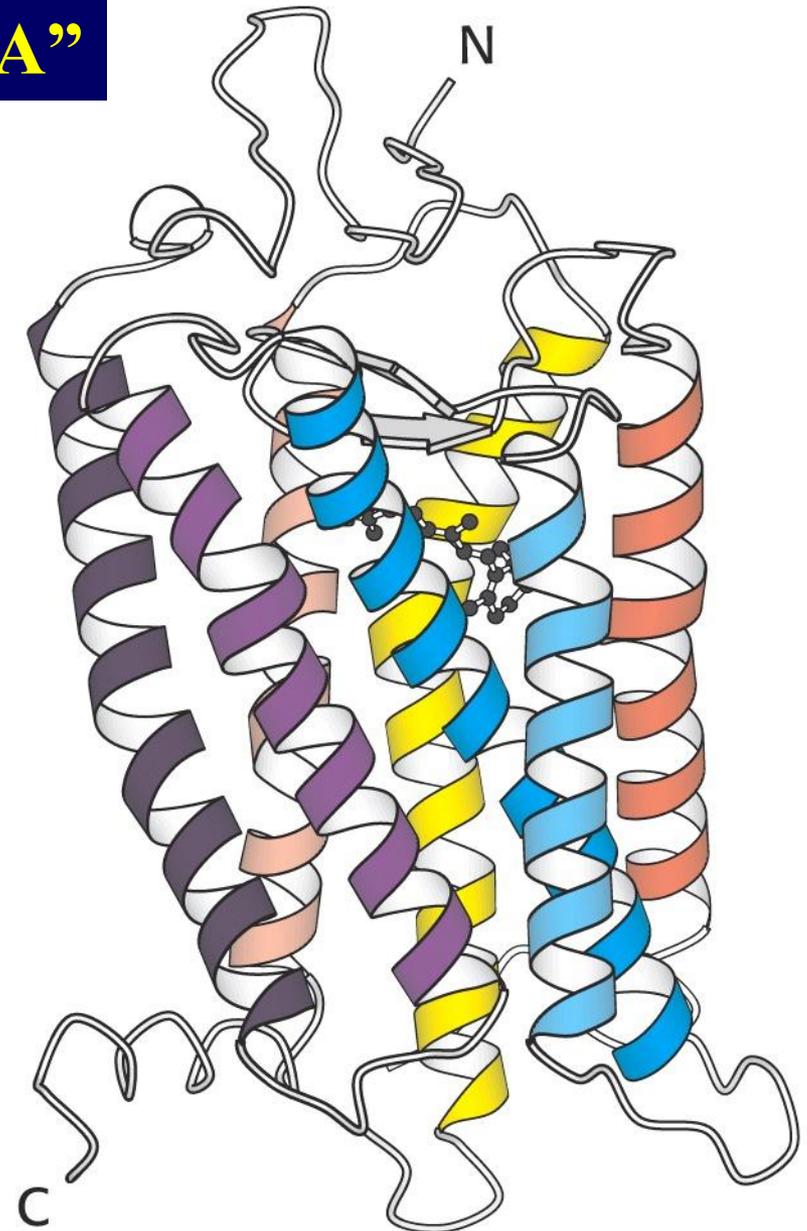
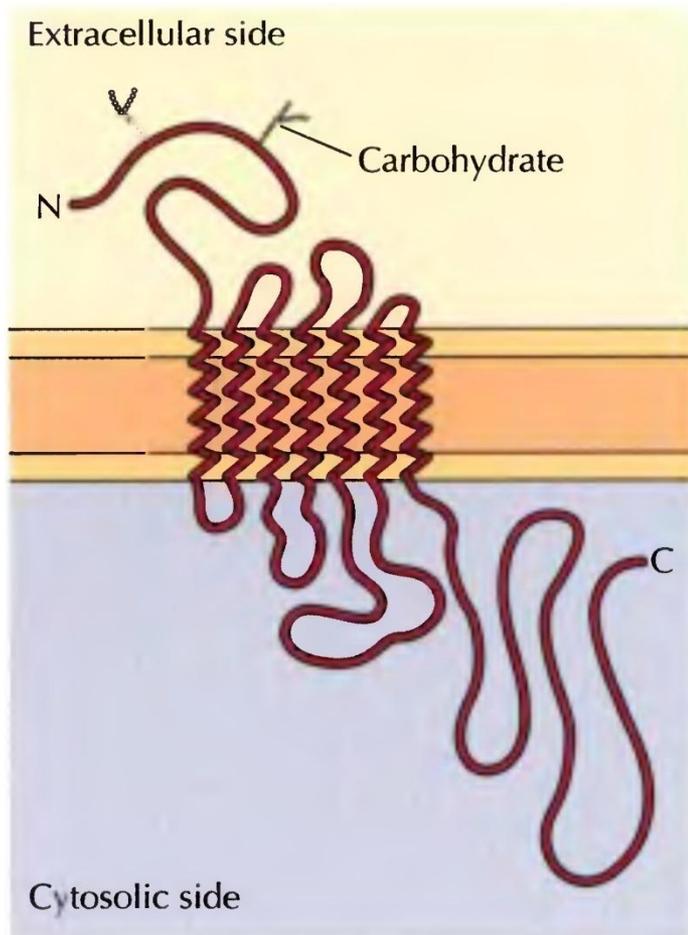
Steroid receptor

Steroid binding to a nuclear receptor protein allows the receptor to regulate the expression of specific genes.

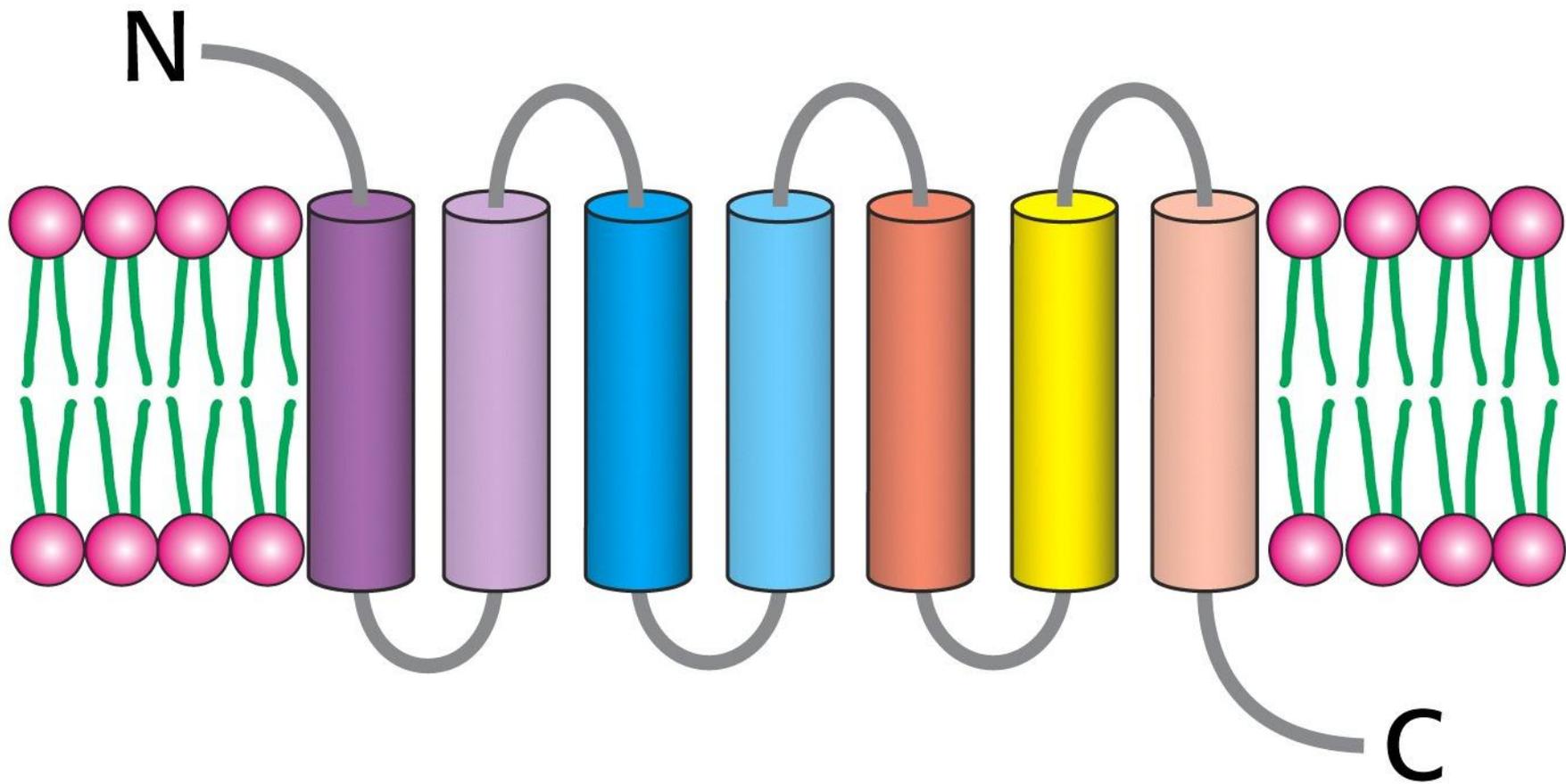


Nuclear envelope

RECEPTORES “SERPENTINA”



(A)

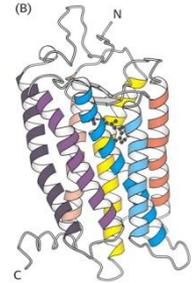


RECEPTORES “SERPENTINA”

TABLE 15.1 Biological functions mediated by 7TM receptors

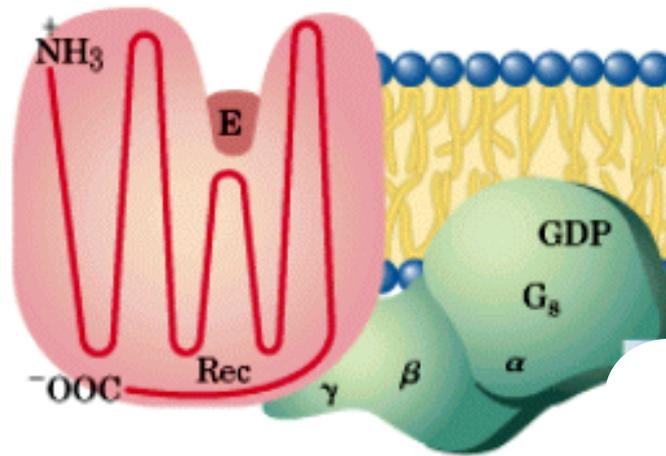
- Smell
- Taste
- Vision
- Neurotransmission
- Hormone secretion
- Chemotaxis
- Exocytosis
- Control of blood pressure
- Embryogenesis
- Cell growth and differentiation
- Development
- Viral infection
- Carcinogenesis

Source: After J. S. Gutkind, *J. Biol. Chem.* 273(1998):1839.



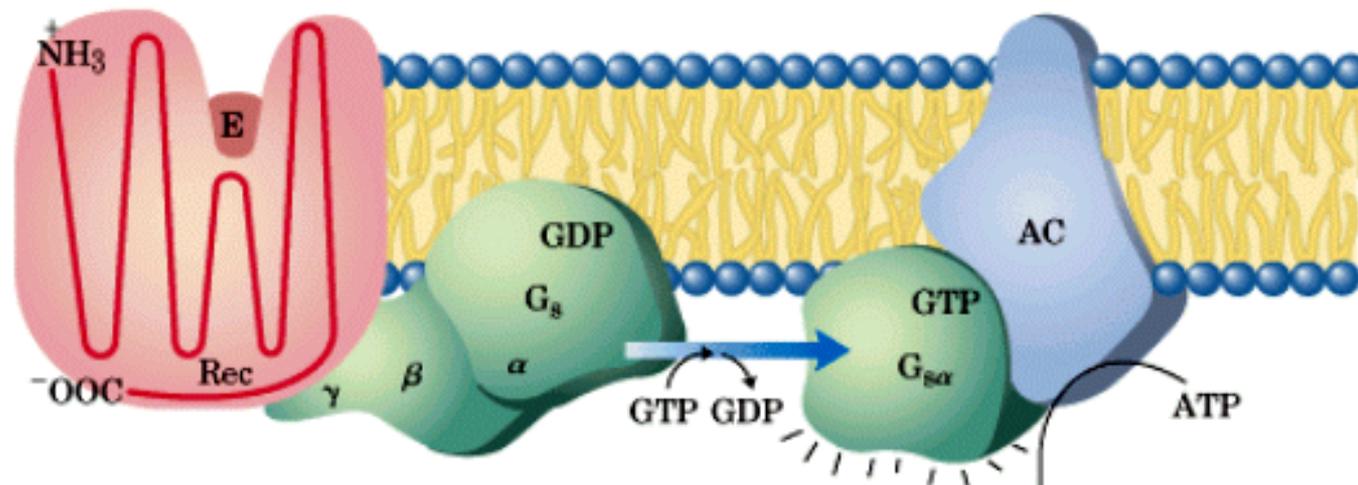
①

Epinephrine binds to its specific receptor.



①

Epinephrine binds to its specific receptor.



②

The occupied receptor causes replacement of the GDP bound to G_s by GTP, activating G_s .

③

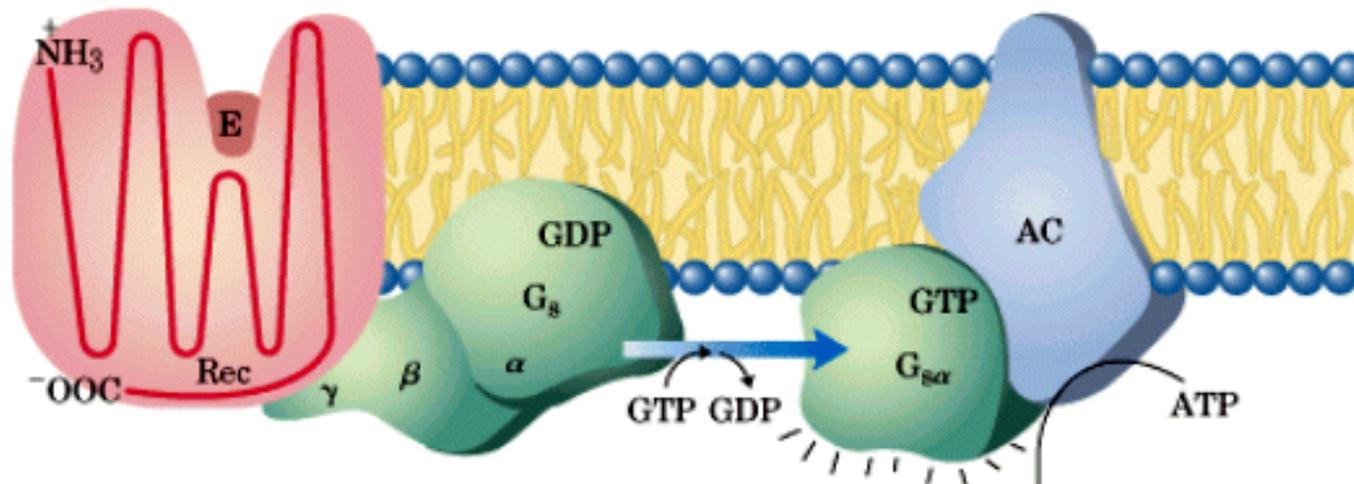
G_s (α subunit) moves to adenylyl cyclase and activates it.

④

Adenylyl cyclase catalyzes the formation of cAMP.

①

Epinephrine binds to its specific receptor.



②

The occupied receptor causes replacement of the GDP bound to G_s by GTP, activating G_s .

③

G_s (α subunit) moves to adenylyl cyclase and activates it.

④

Adenylyl cyclase catalyzes the formation of cAMP.

⑤

PKA is activated by cAMP.

cAMP

cyclic nucleotide phosphodiesterase

5'-AMP

⑥

Phosphorylation of cellular proteins by PKA causes the cellular response to epinephrine.

⑦

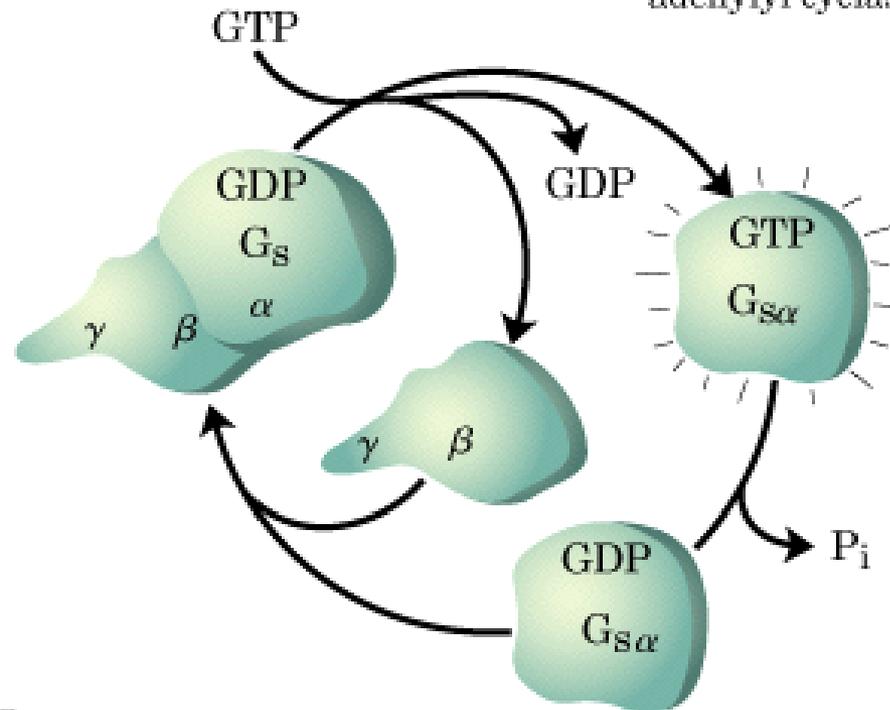
cAMP is degraded, reversing the activation of PKA.



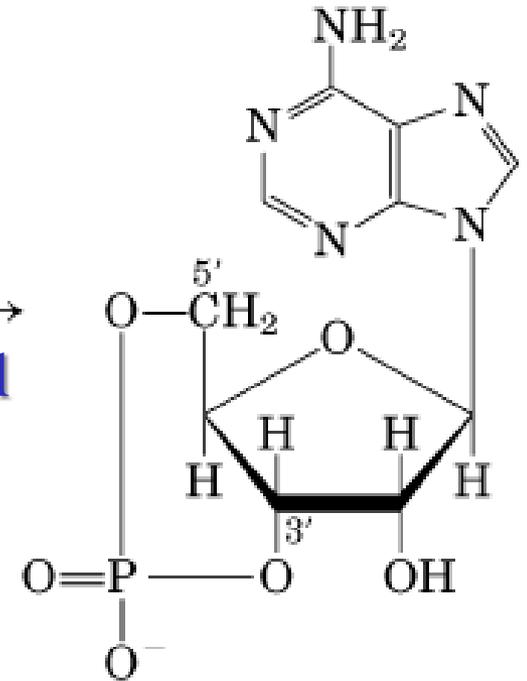
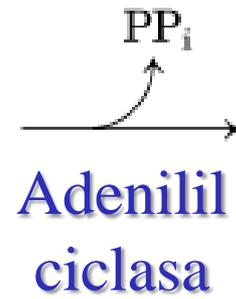
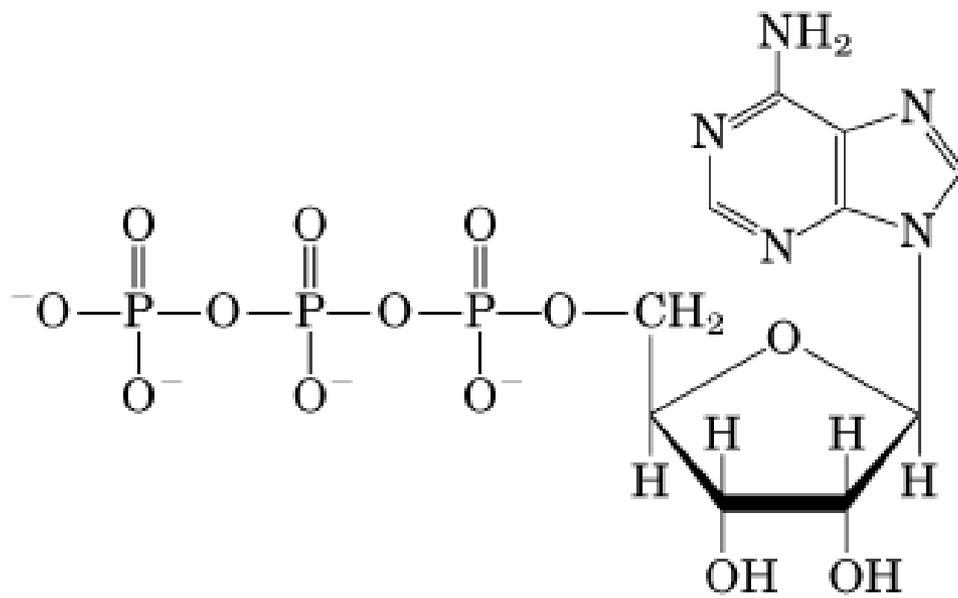
① G_s with GDP bound is turned off; it cannot activate adenylyl cyclase.

② Contact of G_s with hormone-receptor complex causes displacement of bound GDP by GTP.

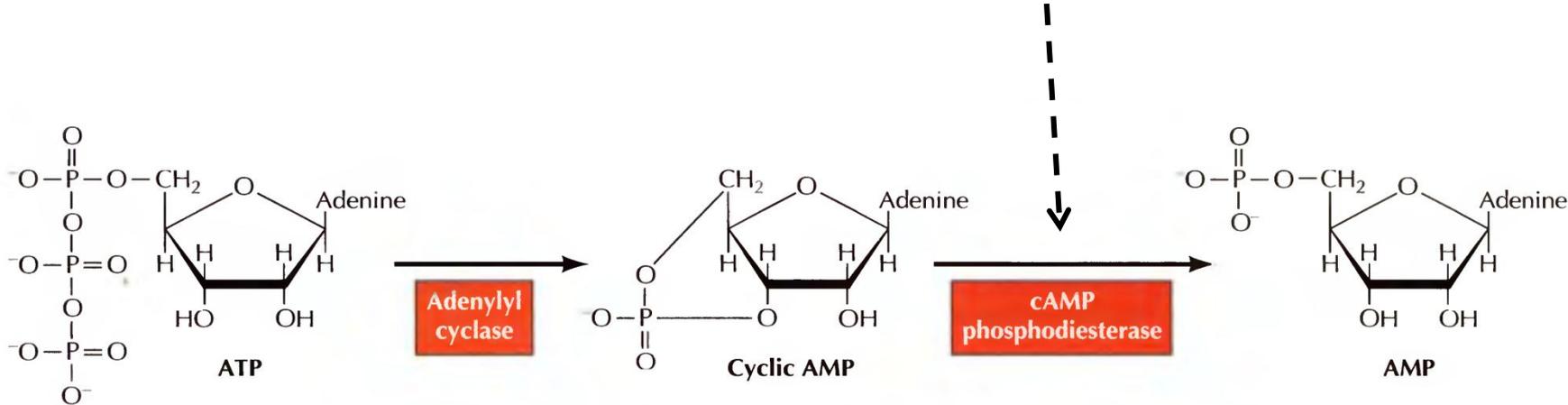
③ G_s with GTP bound dissociates into α and $\beta\gamma$ subunits. $G_{s\alpha}$ -GTP is turned on; it can activate adenylyl cyclase.



④ GTP bound to $G_{s\alpha}$ is hydrolyzed by the protein's intrinsic GTPase; $G_{s\alpha}$ thereby turns itself off. The inactive α subunit reassociates with the β , γ subunits.



FOSFODIESTERASA

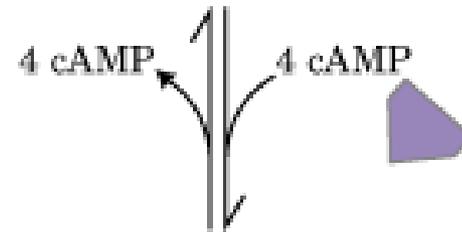
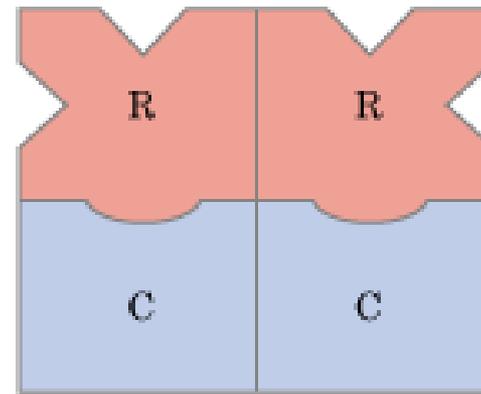


Proteína quinasa
o
Proteína cinasa
(PKA)

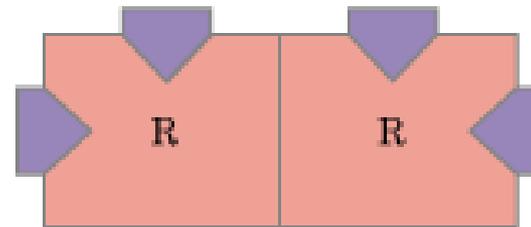
Inactive PKA

Regulatory subunits:
empty cAMP sites

Catalytic subunits:
substrate-binding
sites blocked by
autoinhibitory
domains of R subunits

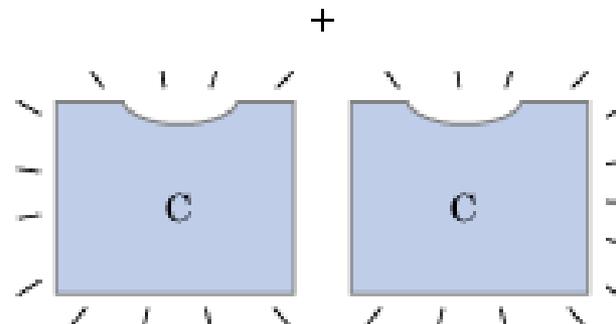


Regulatory subunits:
autoinhibitory
domains buried

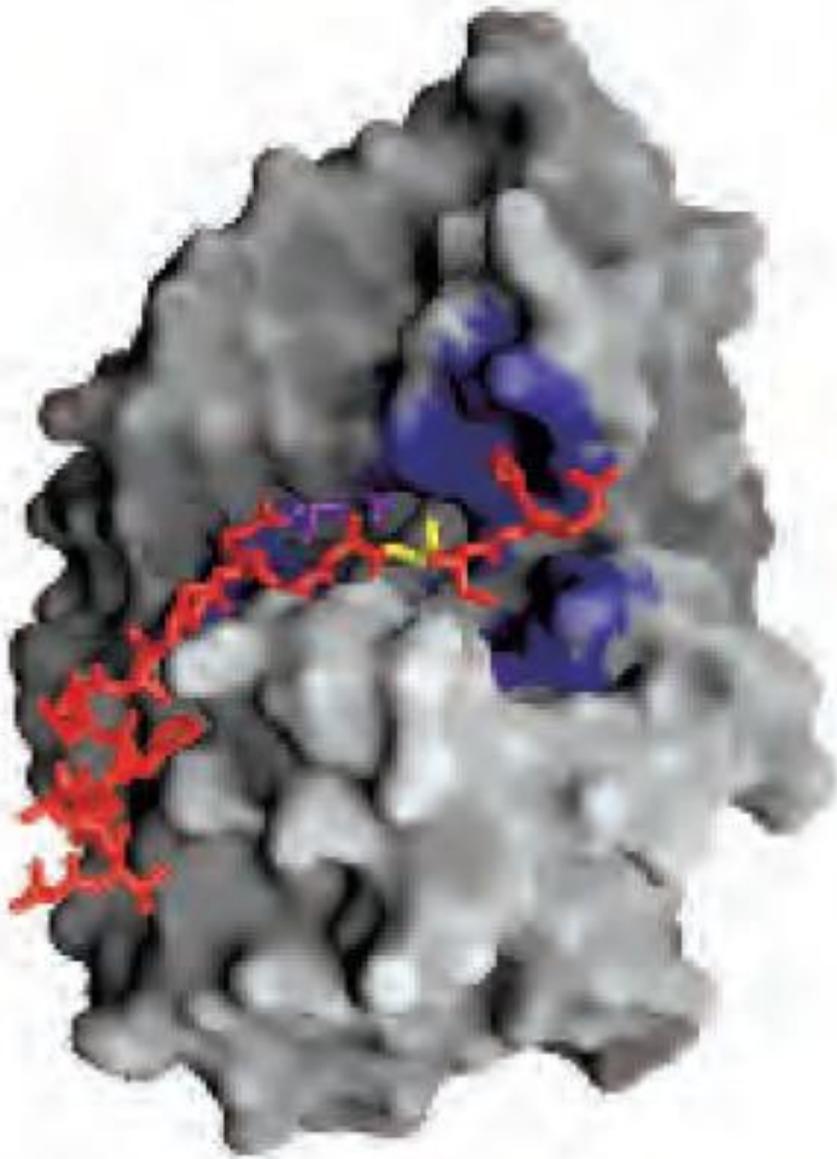


Active PKA

Catalytic subunits:
open substrate-
binding sites



(a)



Región de unión al sustrato de la subunidad catalítica. Péptido sustrato (**rojo**), cadenas laterales de los residuos de aminoácidos críticos para la unión del sustrato (**azul**), residuo de serina (**amarillo**)

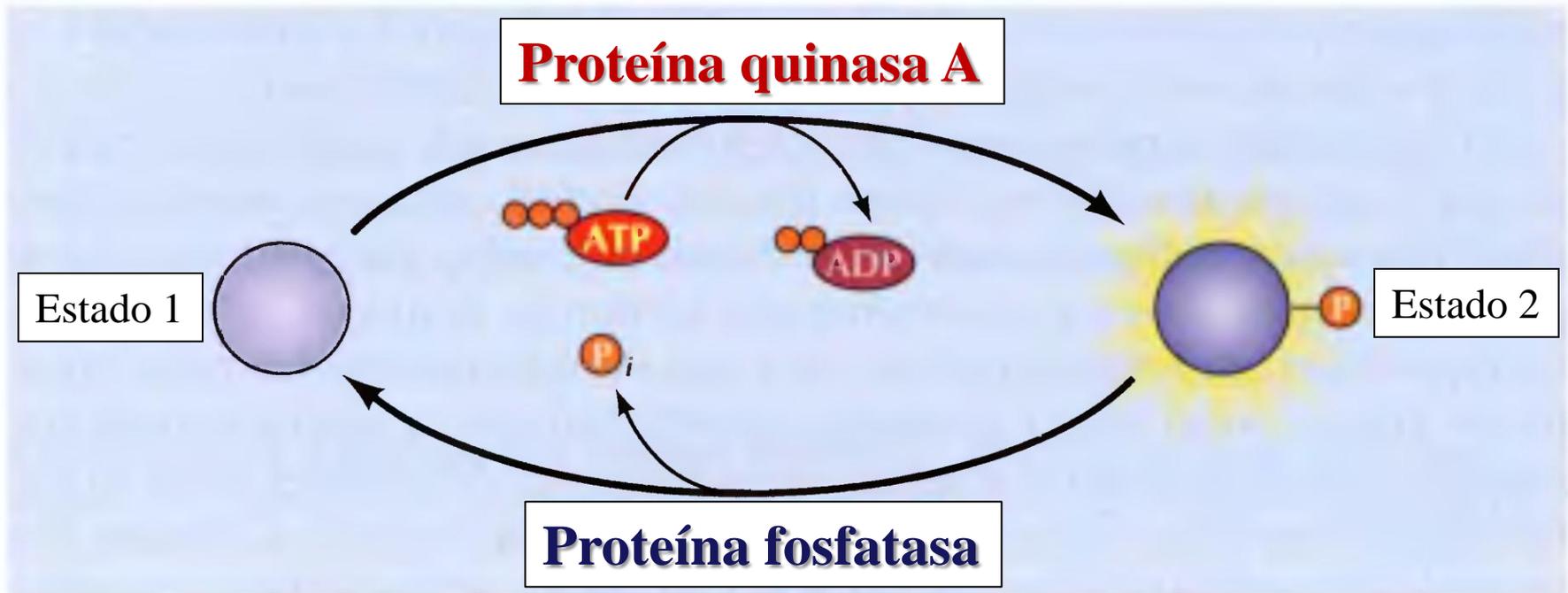
Proteínas fosforiladas por PKA

TABLE 12-3 Some Enzymes and Other Proteins Regulated by cAMP-Dependent Phosphorylation (by PKA)

<i>Enzyme/protein</i>	<i>Sequence phosphorylated*</i>	<i>Pathway/process regulated</i>
Glycogen synthase	RASCTSSS	Glycogen synthesis
Phosphorylase <i>b</i> kinase		
α subunit	VEFRRLSI	Glycogen breakdown
β subunit	RTKRSGSV	
Pyruvate kinase (rat liver)	GVLRRASVAZL	Glycolysis
Pyruvate dehydrogenase complex (type L)	GYLRRASV	Pyruvate to acetyl-CoA
Hormone-sensitive lipase	PMRRSV	Triacylglycerol mobilization and fatty acid oxidation
Phosphofructokinase-2/fructose 2,6-bisphosphatase	LQRRRGSSIPQ	Glycolysis/gluconeogenesis
Tyrosine hydroxylase	FIGRRQSL	Synthesis of L-DOPA, dopamine, norepinephrine, and epinephrine
Histone H1	AKRKASGPPVS	DNA condensation
Histone H2B	KKAKASRKESYSVYVK	DNA condensation
Cardiac phospholamban (cardiac pump regulator)	AIRRAST	Intracellular [Ca ²⁺]
Protein phosphatase-1 inhibitor-1	IRRRRPTP	Protein dephosphorylation
PKA consensus sequence [†]	XR(R/K)X(S/T)B	Many

*The phosphorylated S or T residue is shown in red. All residues are given as their one-letter abbreviations (see Table 3-1).

[†]X is any amino acid; B is any hydrophobic amino acid.



Al menos el 10% de las proteínas en una célula eucarionte sufren modificación covalente por fosforilación. Se han descrito 2000 kinasas y unas 1000 fosfatasas.

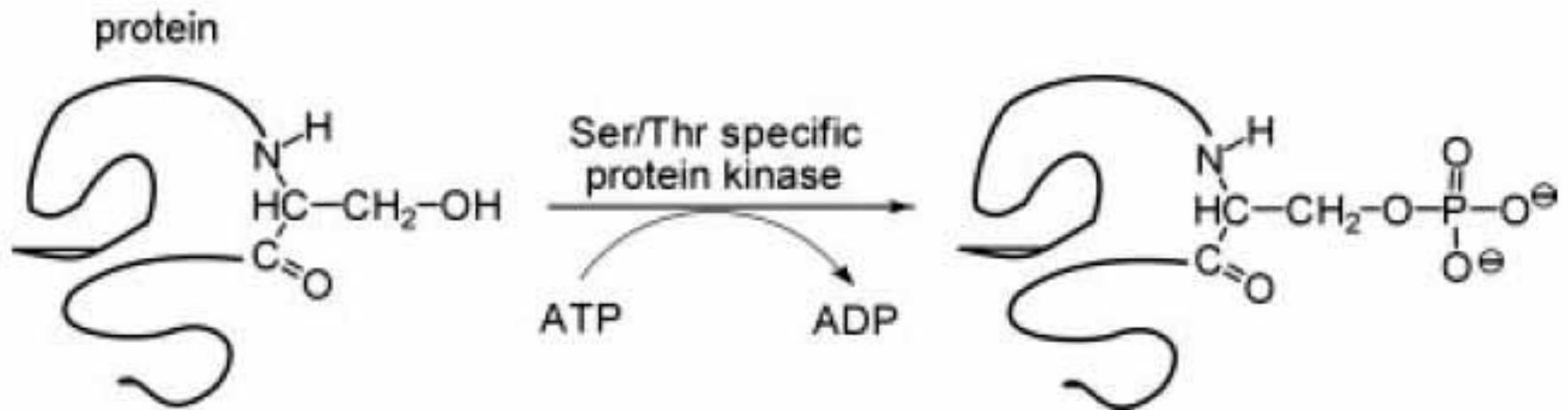
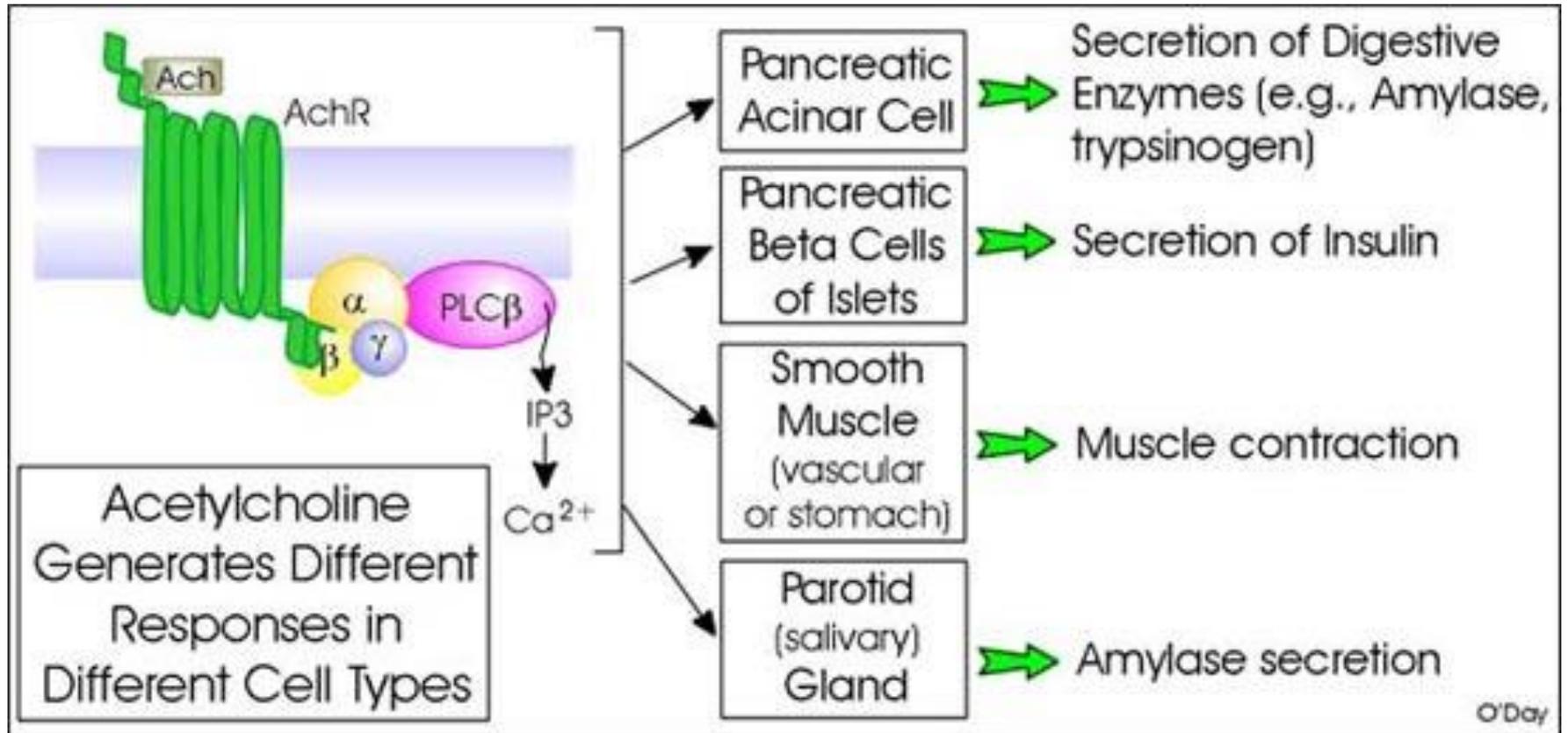
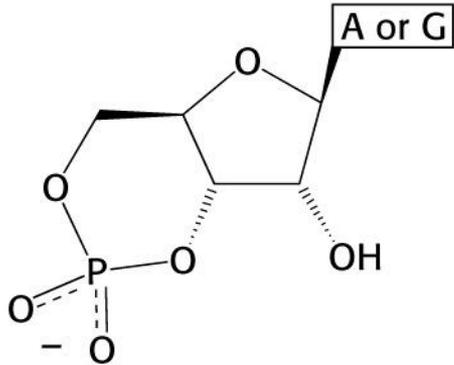


Fig. 2.5 Change in charge state of proteins via phosphorylation. The phosphorylation of Ser residues is catalyzed by a Ser/Thr-specific protein kinase that utilizes ATP as the phosphate group donor. The product of the reaction is a Ser-phosphate ester which carries a net charge of -2 at physiological pH.

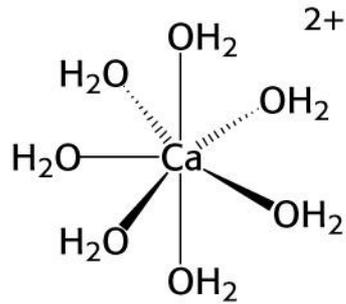
La Acetilcolina actúa vía proteína G



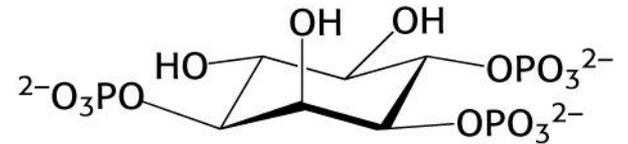
SEGUNDOS MENSAJEROS



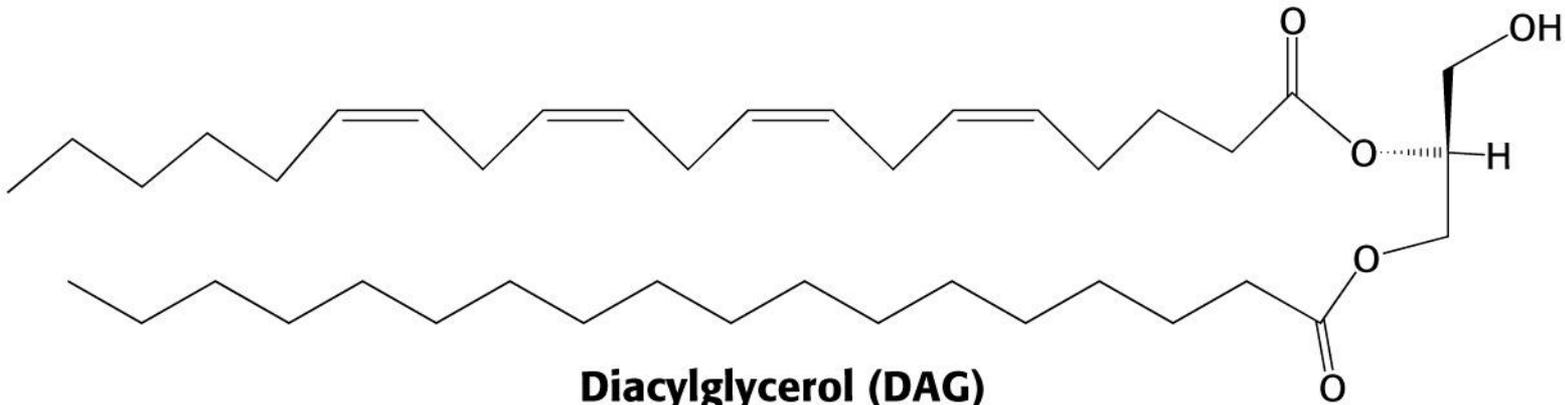
cAMP, cGMP



Calcium ion



Inositol 1,4,5-trisphosphate (IP₃)



Diacylglycerol (DAG)

Class or Type	Stimulus	Effector	Effect
G_s α_s  α_{olf}	Glucagon, β -adrenergics Odorant	\uparrow Adenylyl cyclase \uparrow Cardiac Ca^{2+} , Cl^- , and Na^+ channels \uparrow Adenylyl cyclase	Gluconeogenesis, lipolysis, glycogenolysis Olfaction
G_i $\alpha_{1,2,3}$  α_0 α_t	Acetylcholine, α_2 -adrenergics M_2 cholinergics Opioids, endorphins Light	\downarrow Adenylyl cyclase \uparrow Potassium channels \downarrow Calcium channels \uparrow Potassium channels \uparrow cGMP phosphodiesterase	Slowed heart rate Neuronal electrical activity Vision
G_q α_q  α_{11}	M_1 cholinergics α_1 -Adrenergics α_1 -Adrenergics	\uparrow Phospholipase C- β_1 \uparrow Phospholipase c- β_2	\uparrow Muscle contraction and \uparrow Blood pressure

Extracelular

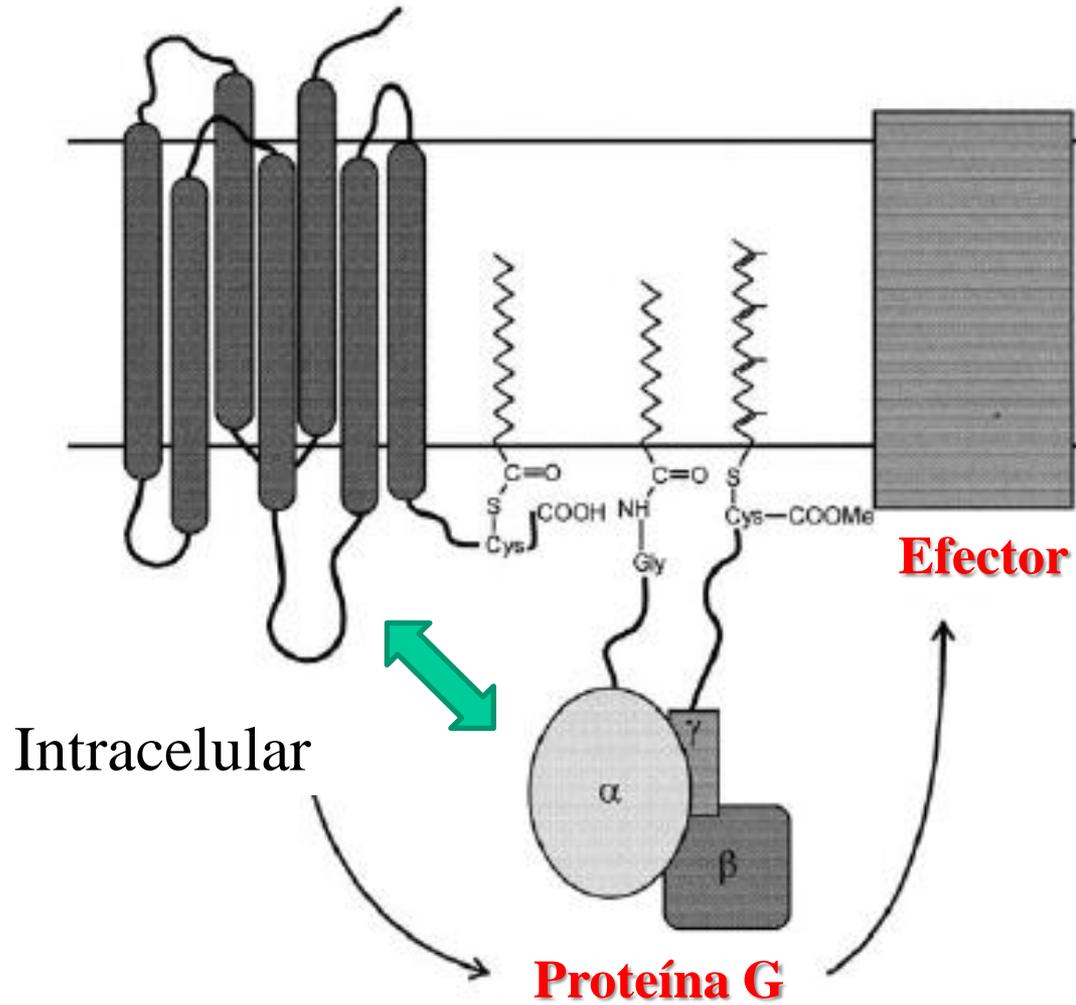
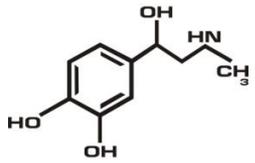
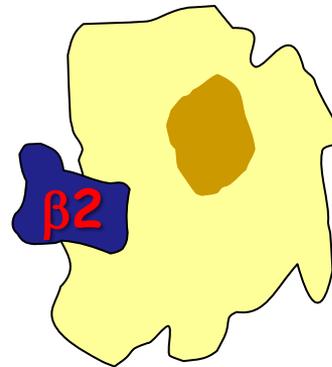
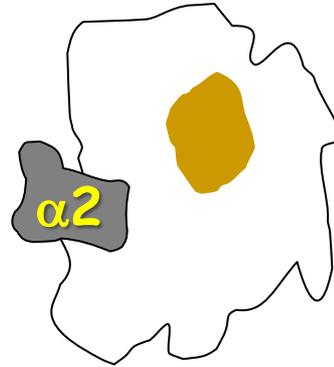


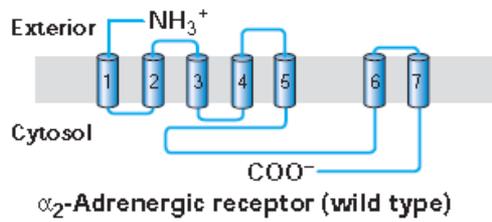
Table 43–2. Subclassification of group II.A hormones.

Hormones That Stimulate Adenylyl Cyclase (H_s)	Hormones That Inhibit Adenylyl Cyclase (H_i)
ACTH ADH β -Adrenergics Calcitonin CRH FSH Glucagon hCG LH LPH MSH PTH TSH	Acetylcholine α_2 -Adrenergics Angiotensin II Somatostatin



Adrenalina



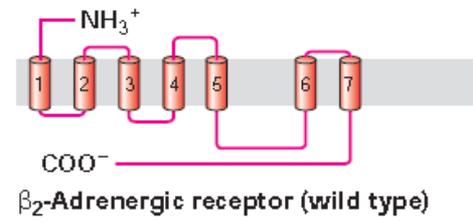


Effect on
adenylyl cyclase

Inhibits (binds G_i)



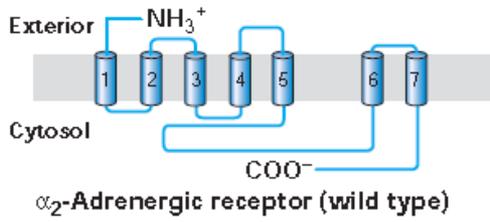
\downarrow $[\text{AMP}_c]$



Activates (binds G_s)



\uparrow $[\text{AMP}_c]$

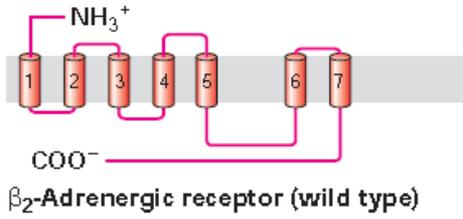


Effect on
adenylyl cyclase

Inhibits (binds **Gi**)



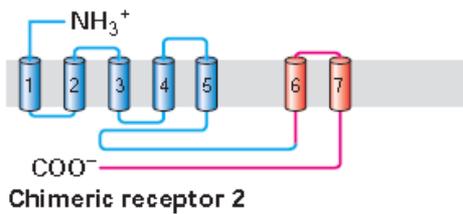
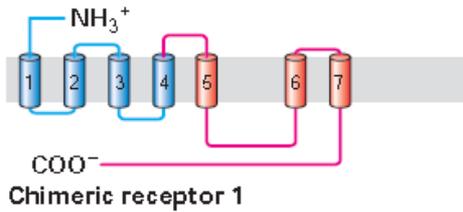
↓ [AMP_c]



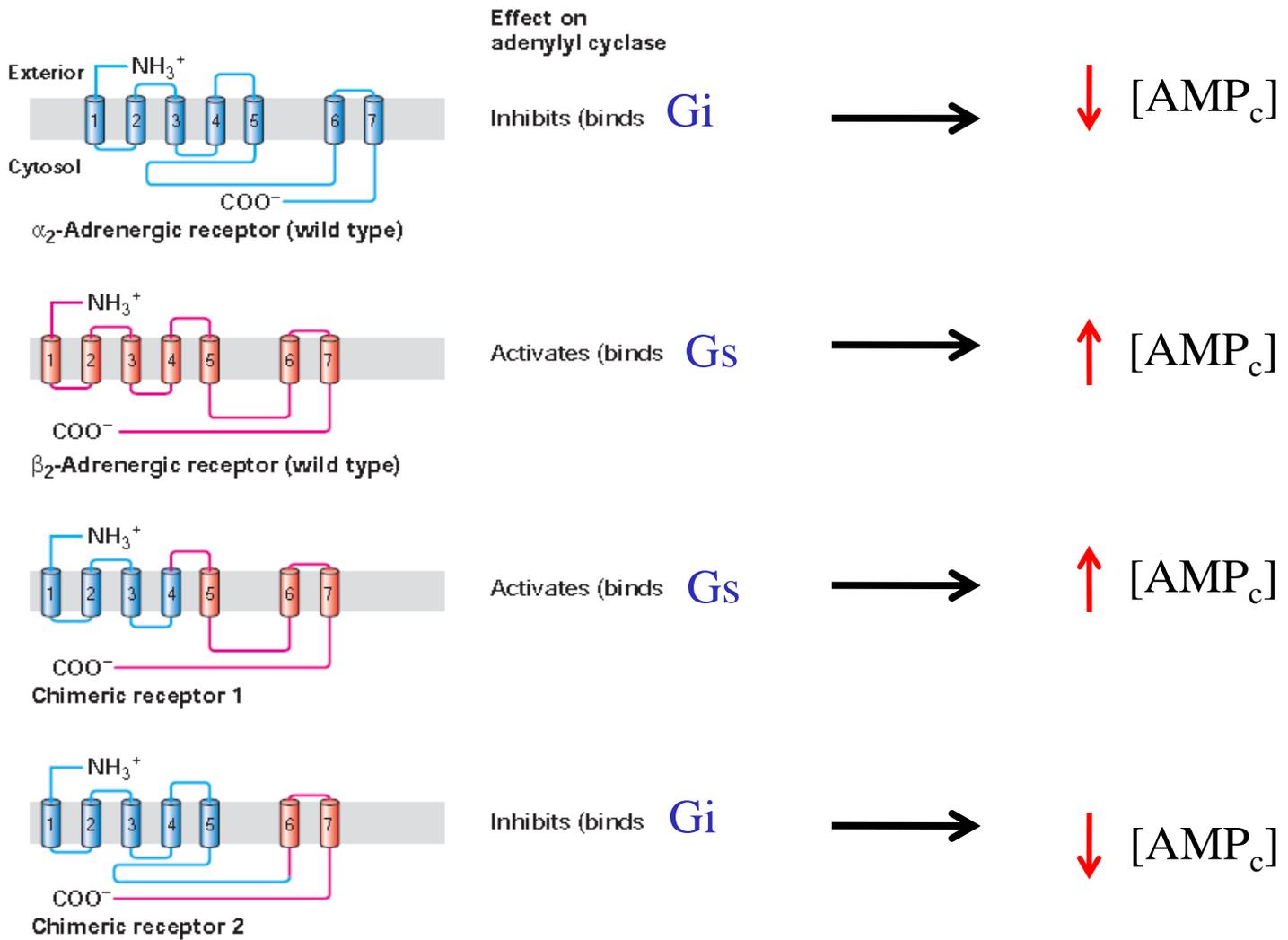
Activates (binds **Gs**)

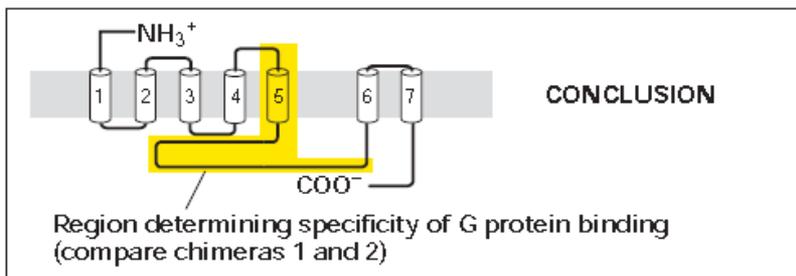
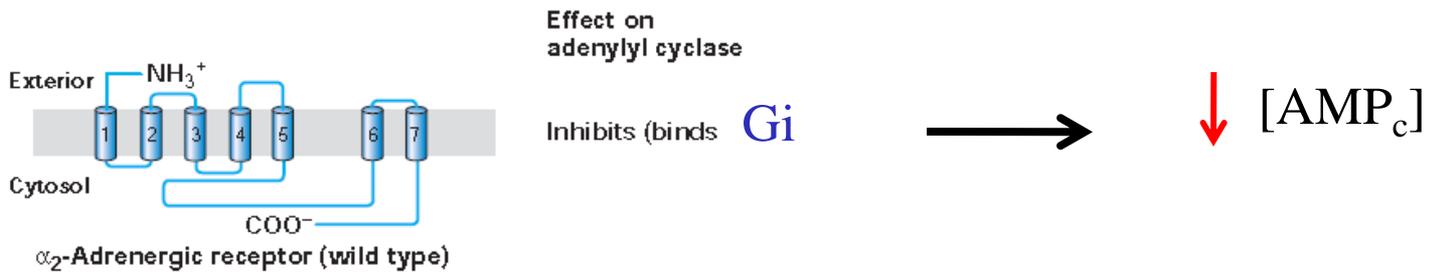


↑ [AMP_c]

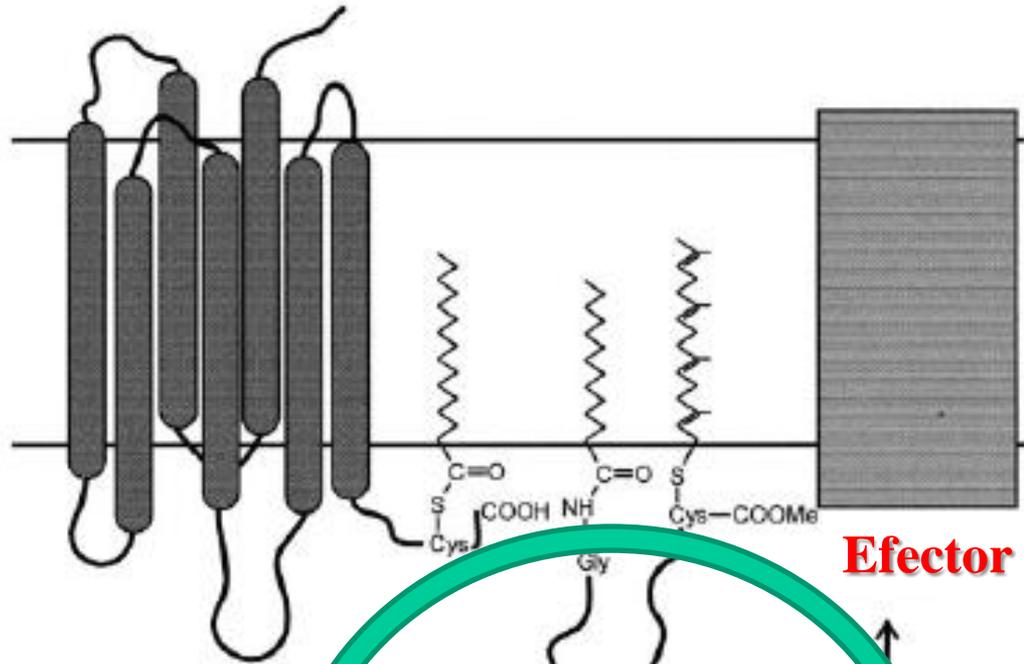


Receptores
quiméricos

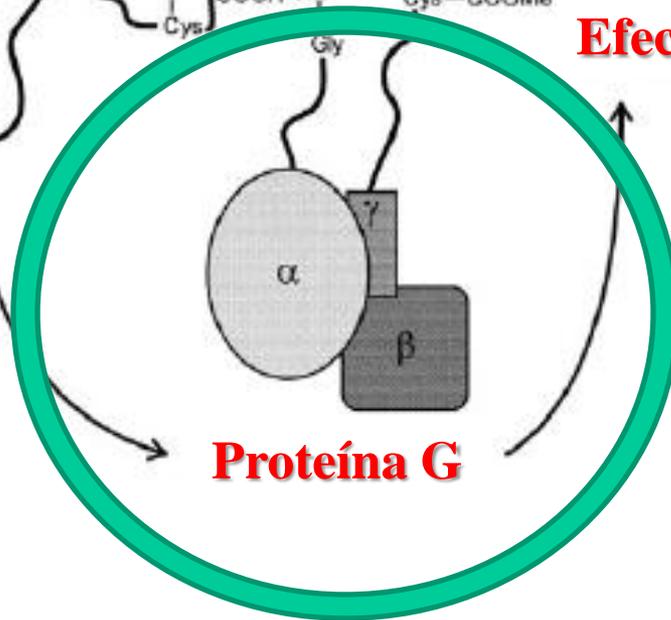




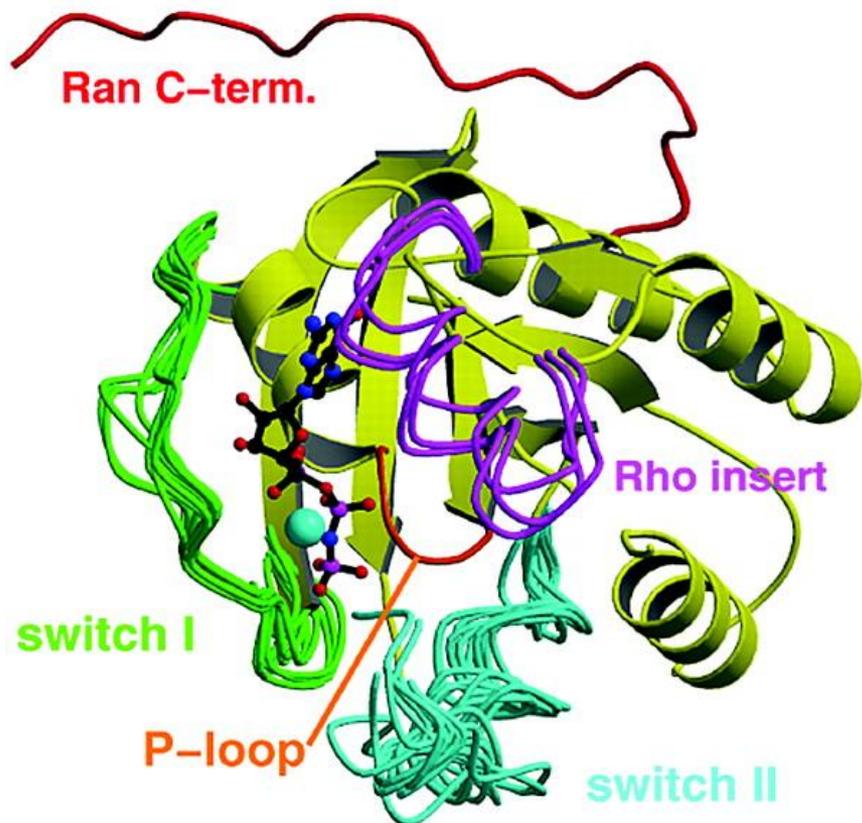
Extracelular



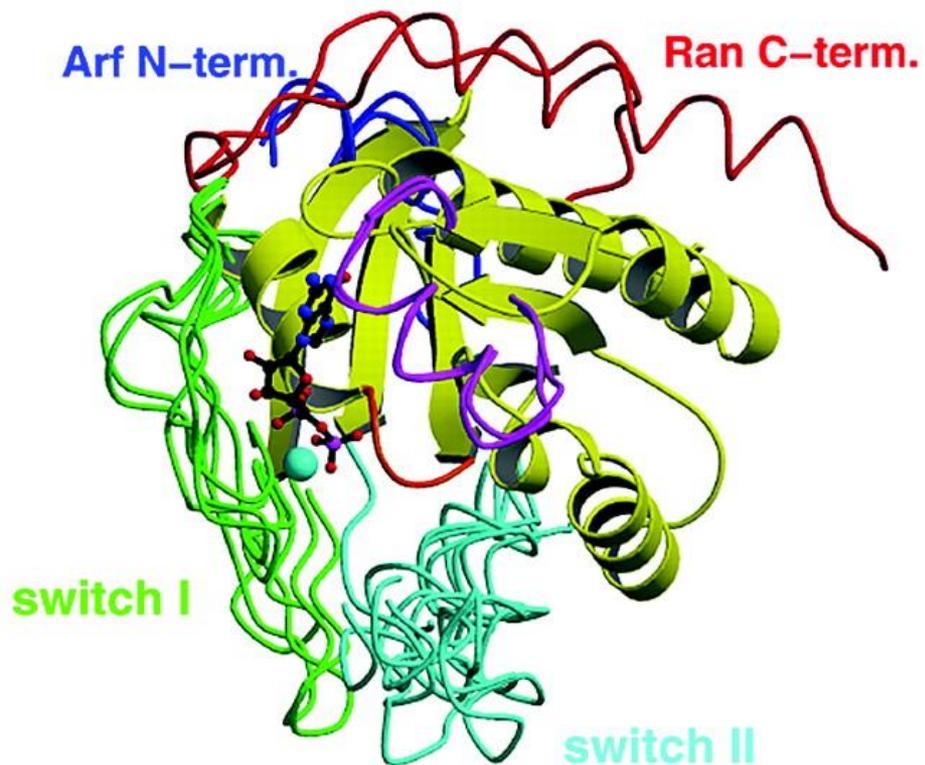
Intracelular



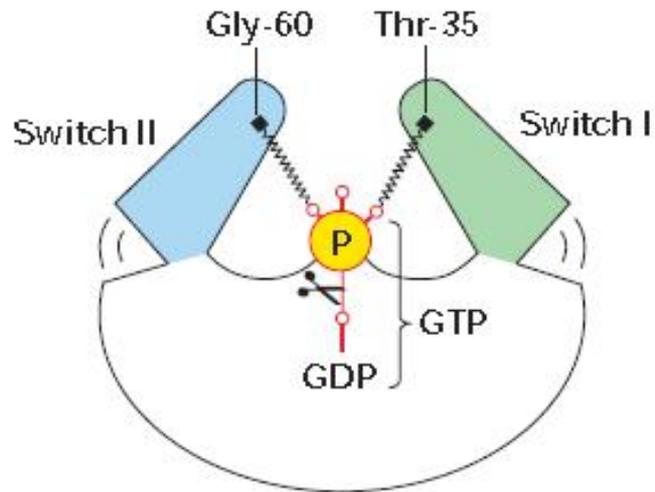
GTP-form



GDP-form



(a) GTP-bound "on" state



(b) GDP-bound "off" state

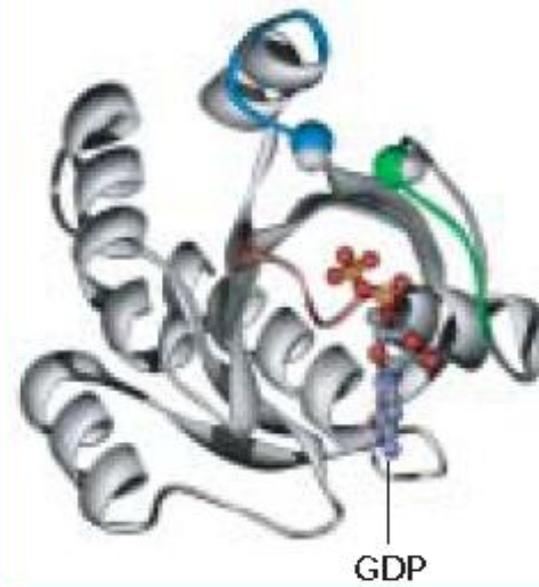
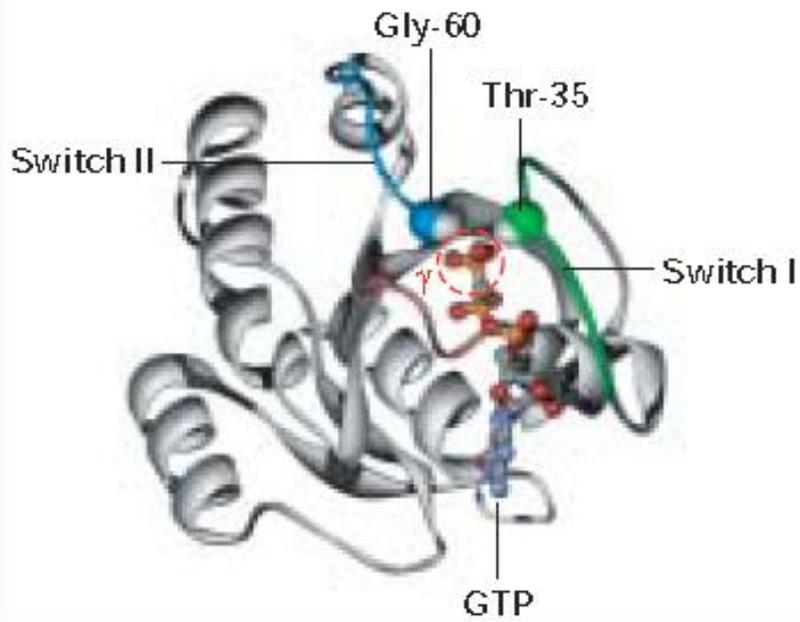
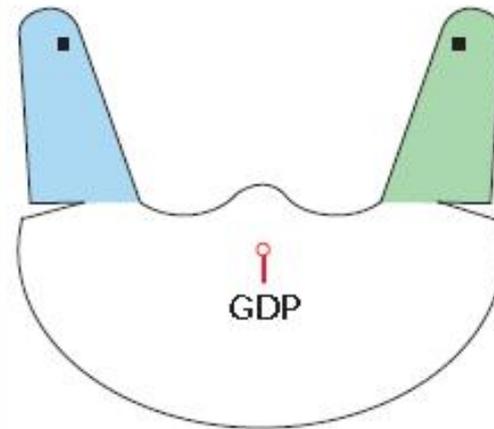
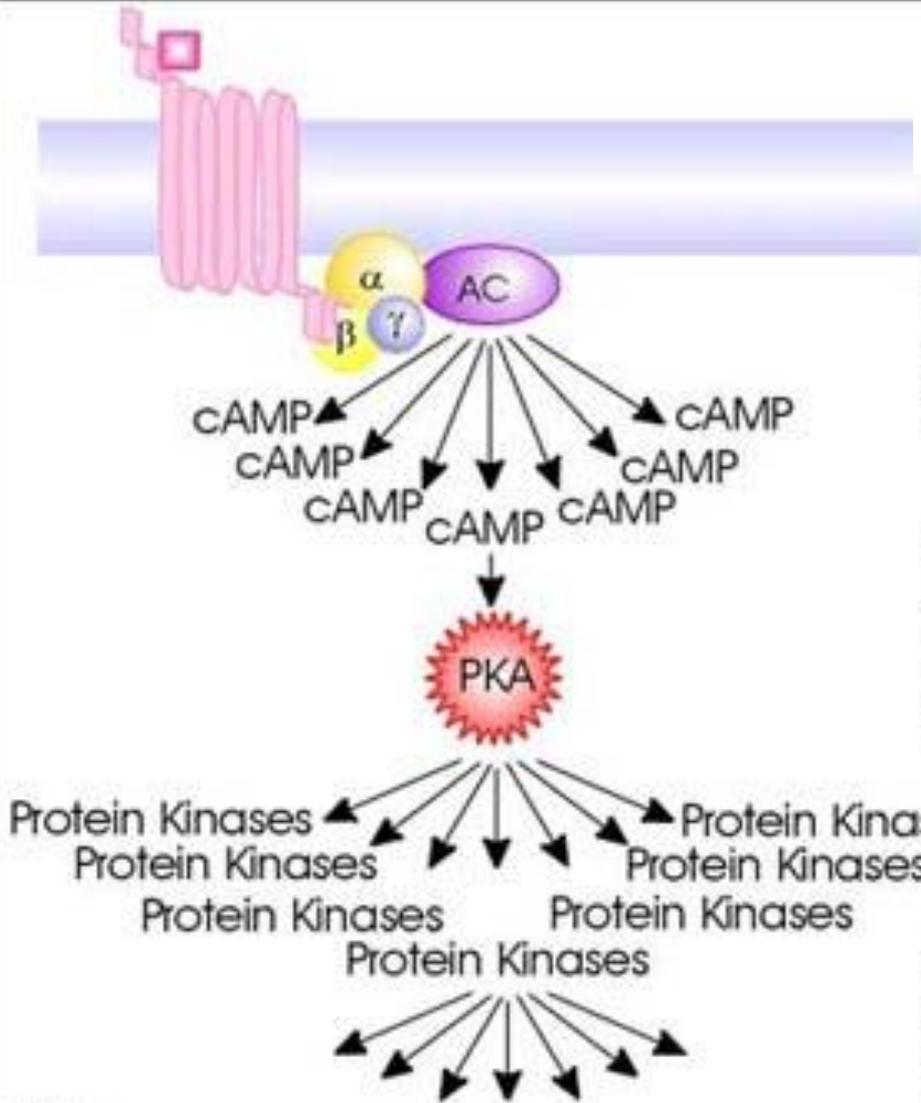


TABLE 12-4 Some Signals That Use cAMP as Second Messenger

Corticotropin (ACTH)
Corticotropin-releasing hormone (CRH)
Dopamine [D_1 , D_2]*
Epinephrine (β -adrenergic)
Follicle-stimulating hormone (FSH)
Glucagon
Histamine [H_2]*
Luteinizing hormone (LH)
Melanocyte-stimulating hormone (MSH)
Odorants (many)
Parathyroid hormone
Prostaglandins E_1 , E_2 (PGE_1 , PGE_2)
Serotonin [5-HT-1a, 5-HT-2]*
Somatostatin
Tastants (sweet, bitter)
Thyroid-stimulating hormone (TSH)

*Receptor subtypes in square brackets. Subtypes may have different transduction mechanisms. For example, serotonin is detected in some tissues by receptor subtypes 5-HT-1a and 5-HT-1b, which act through adenylyl cyclase and cAMP, and in other tissues by receptor subtype 5-HT-1c, acting through the phospholipase C- IP_3 mechanism (see Table 12-5).

Amplificación de la señal



Each activated AC generates many cAMP molecules

Amplification

cAMP molecules stimulate PKA; Each PKA phosphorylates many kinases

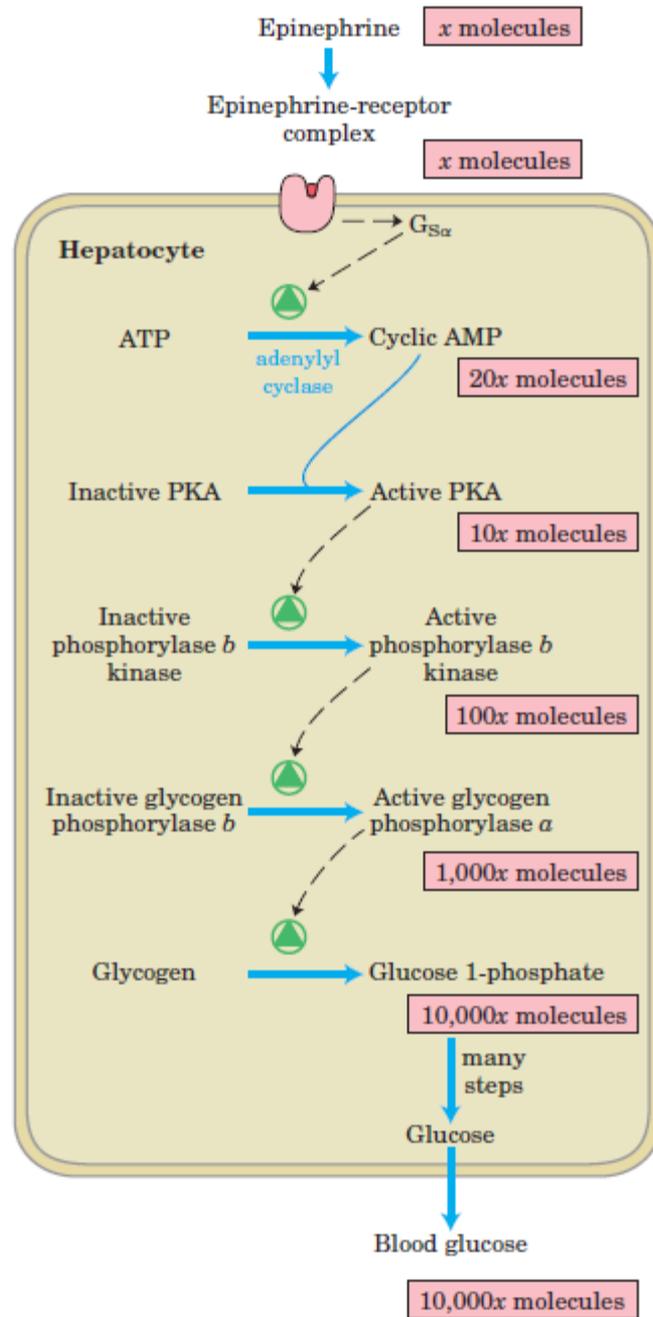
Amplification

Each kinases phosphorylates more targets (including kinases)

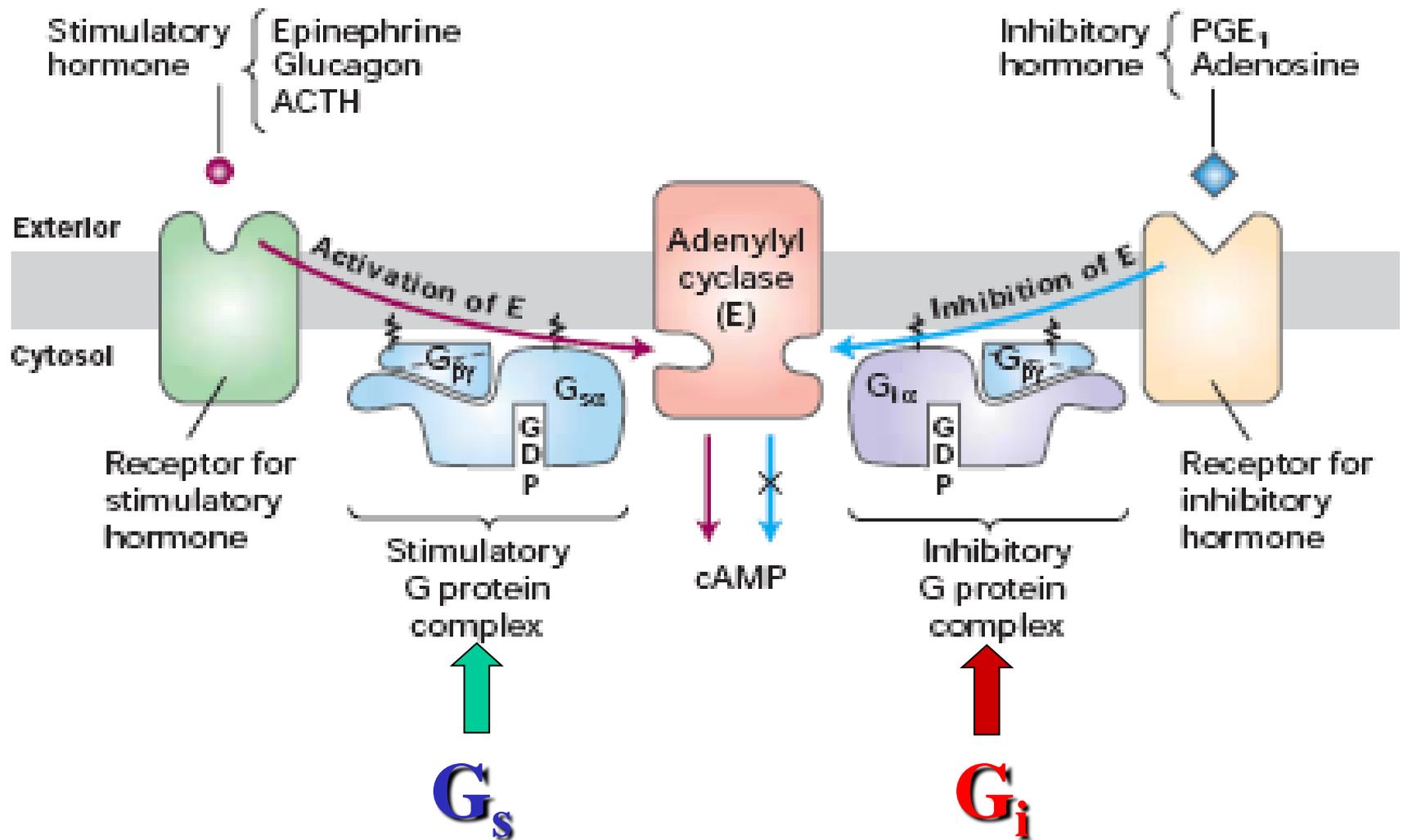
Amplification

Amplification?

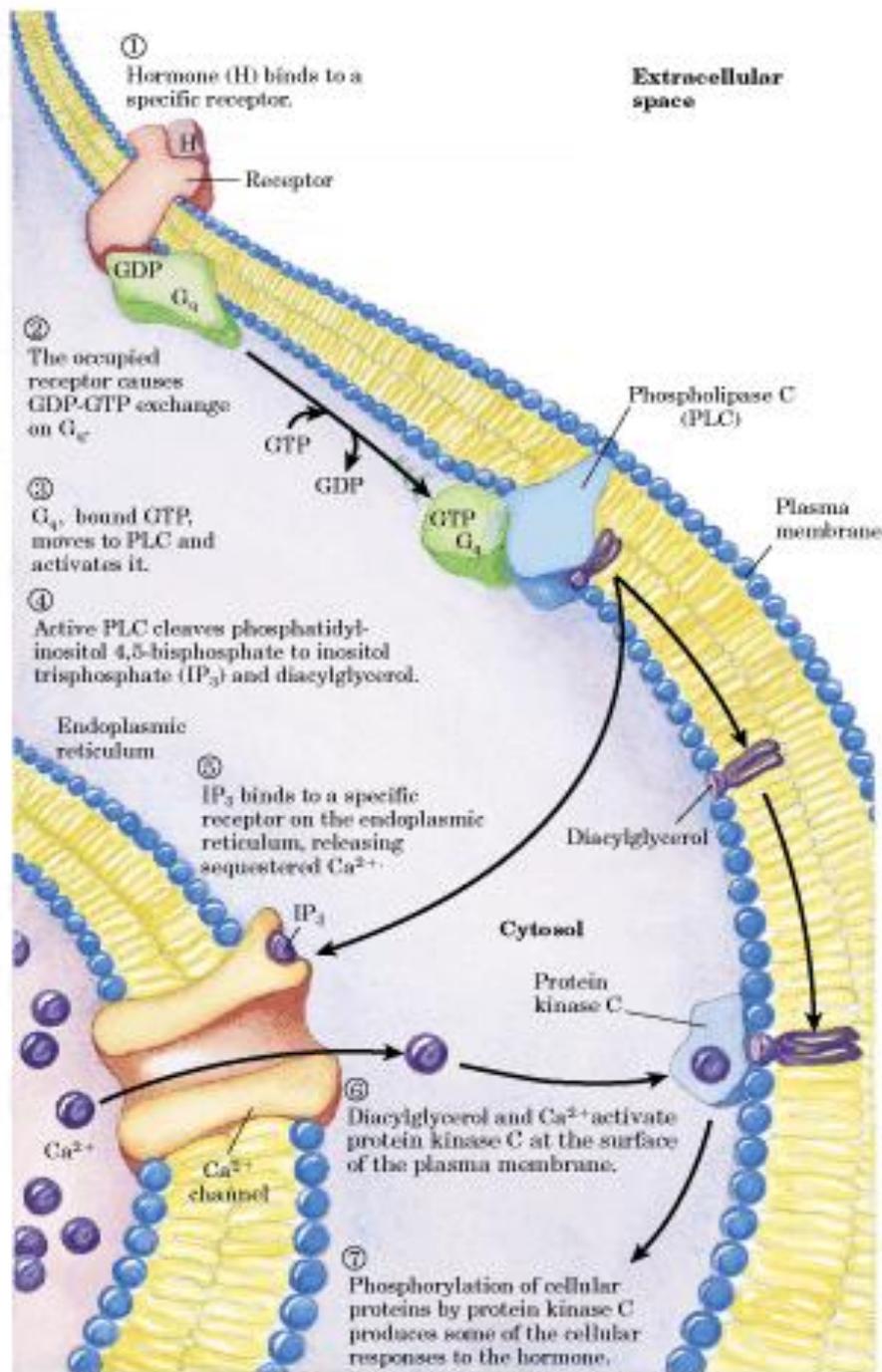


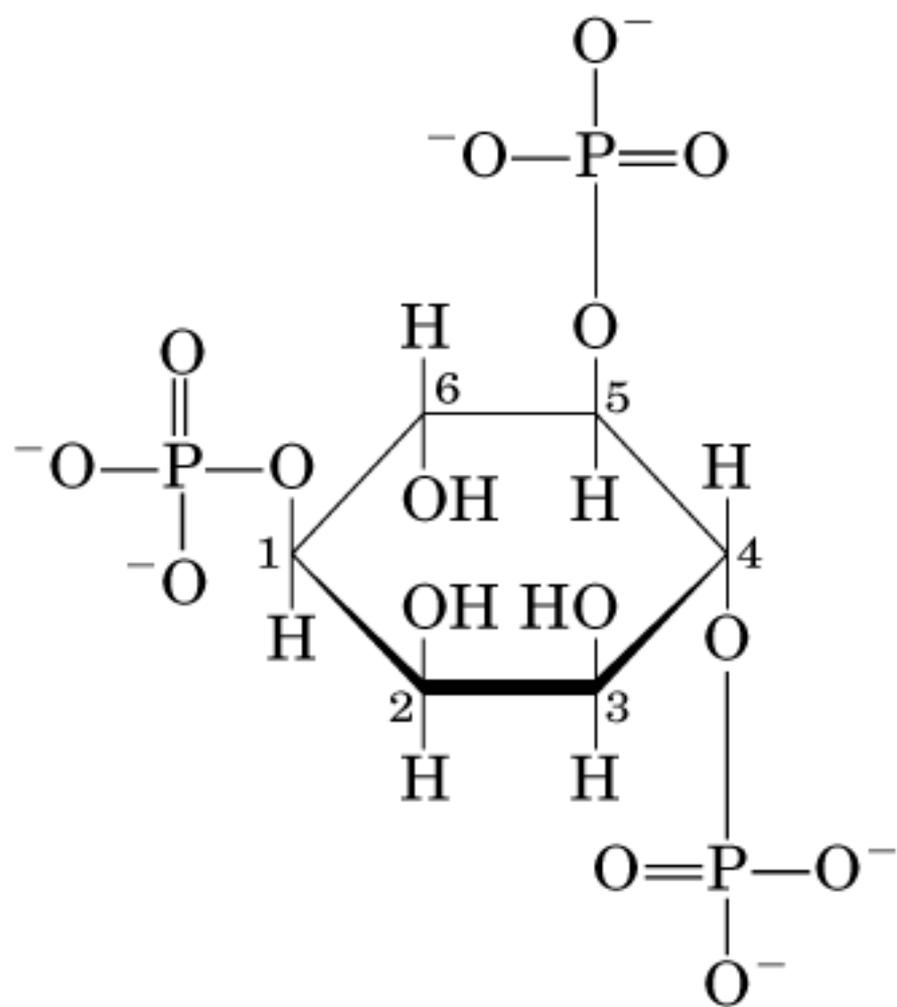


Class or Type	Stimulus	Effector	Effect
G_s α_s  α_{olf}	Glucagon, β -adrenergics Odorant	\uparrow Adenylyl cyclase \uparrow Cardiac Ca^{2+} , Cl^- , and Na^+ channels \uparrow Adenylyl cyclase	Gluconeogenesis, lipolysis, glycogenolysis Olfaction
G_i $\alpha_{1,2,3}$  α_0 α_t	Acetylcholine, α_2 -adrenergics M_2 cholinergics Opioids, endorphins Light	\downarrow Adenylyl cyclase \uparrow Potassium channels \downarrow Calcium channels \uparrow Potassium channels \uparrow cGMP phosphodiesterase	Slowed heart rate Neuronal electrical activity Vision
G_q α_q  α_{11}	M_1 cholinergics α_1 -Adrenergics α_1 -Adrenergics	\uparrow Phospholipase C- β_1 \uparrow Phospholipase c- β_2	\uparrow Muscle contraction and \uparrow Blood pressure

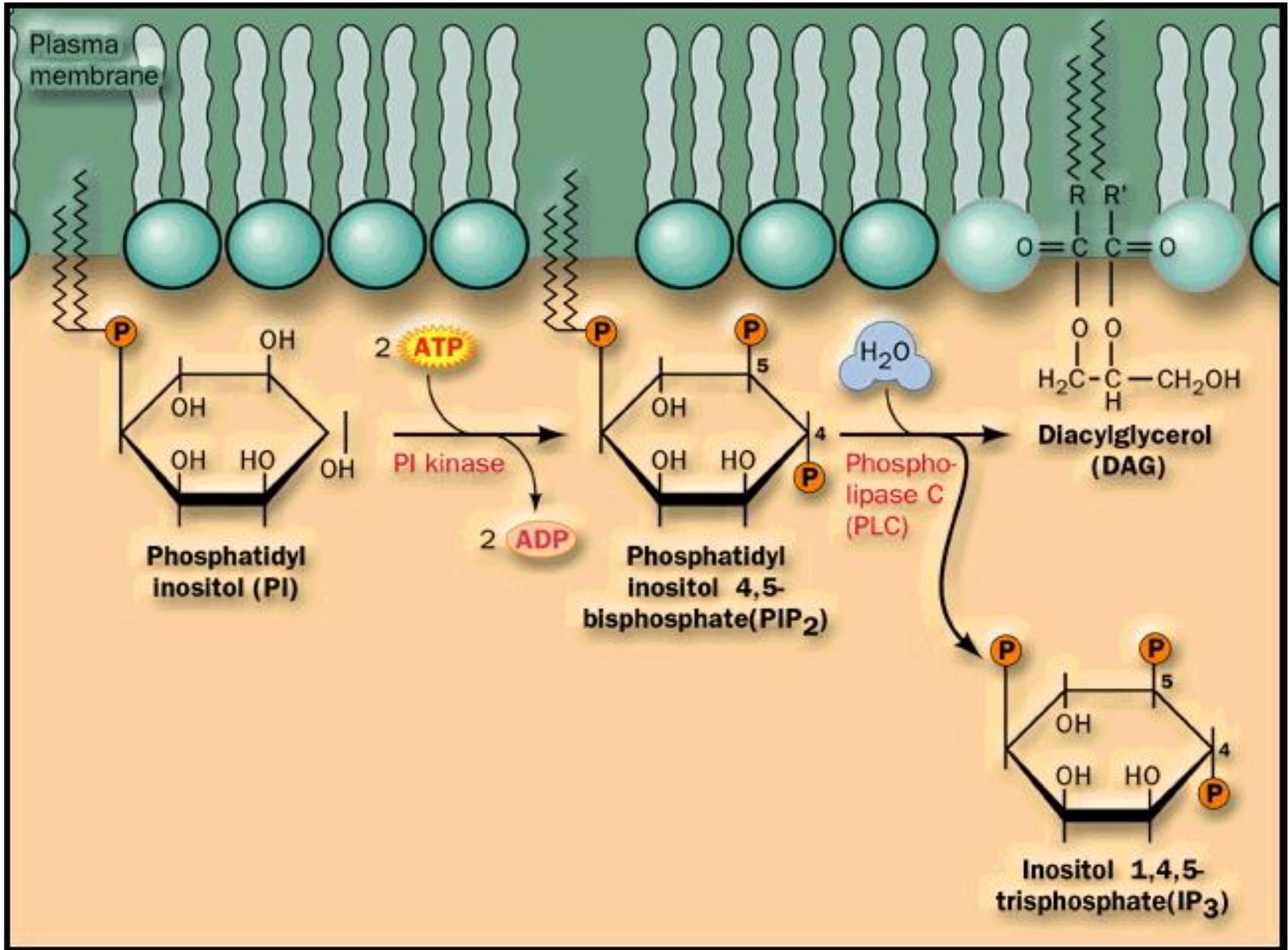


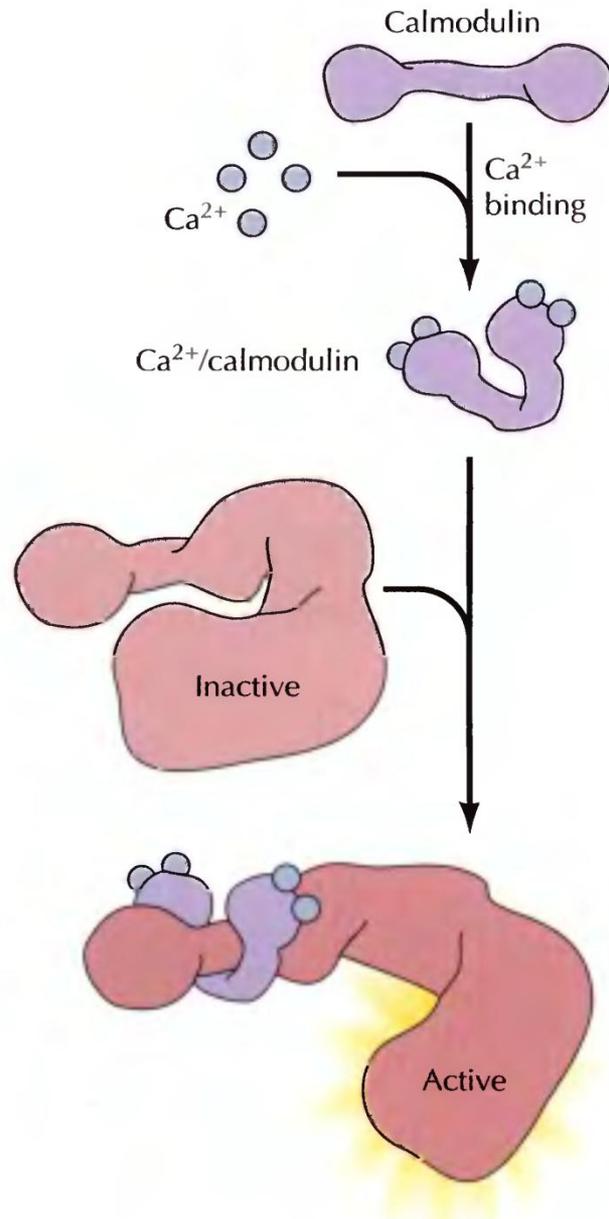
G_q



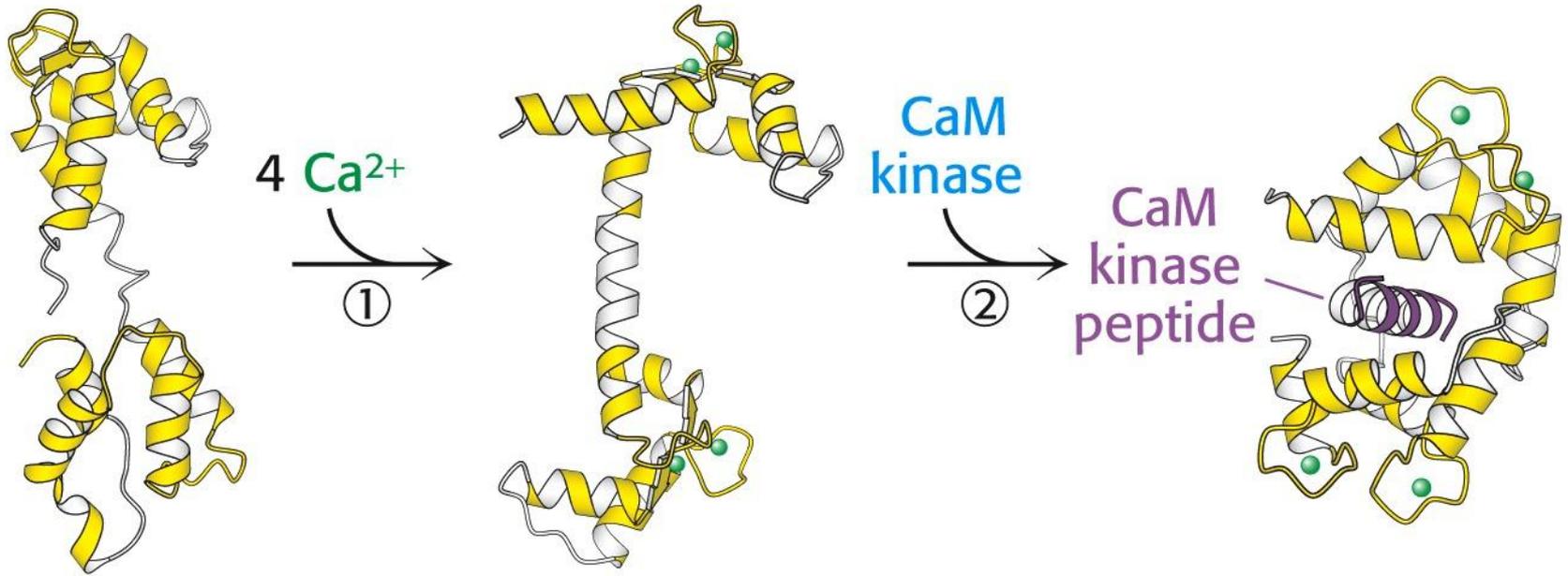


Inositol 1,4,5-trisphosphate



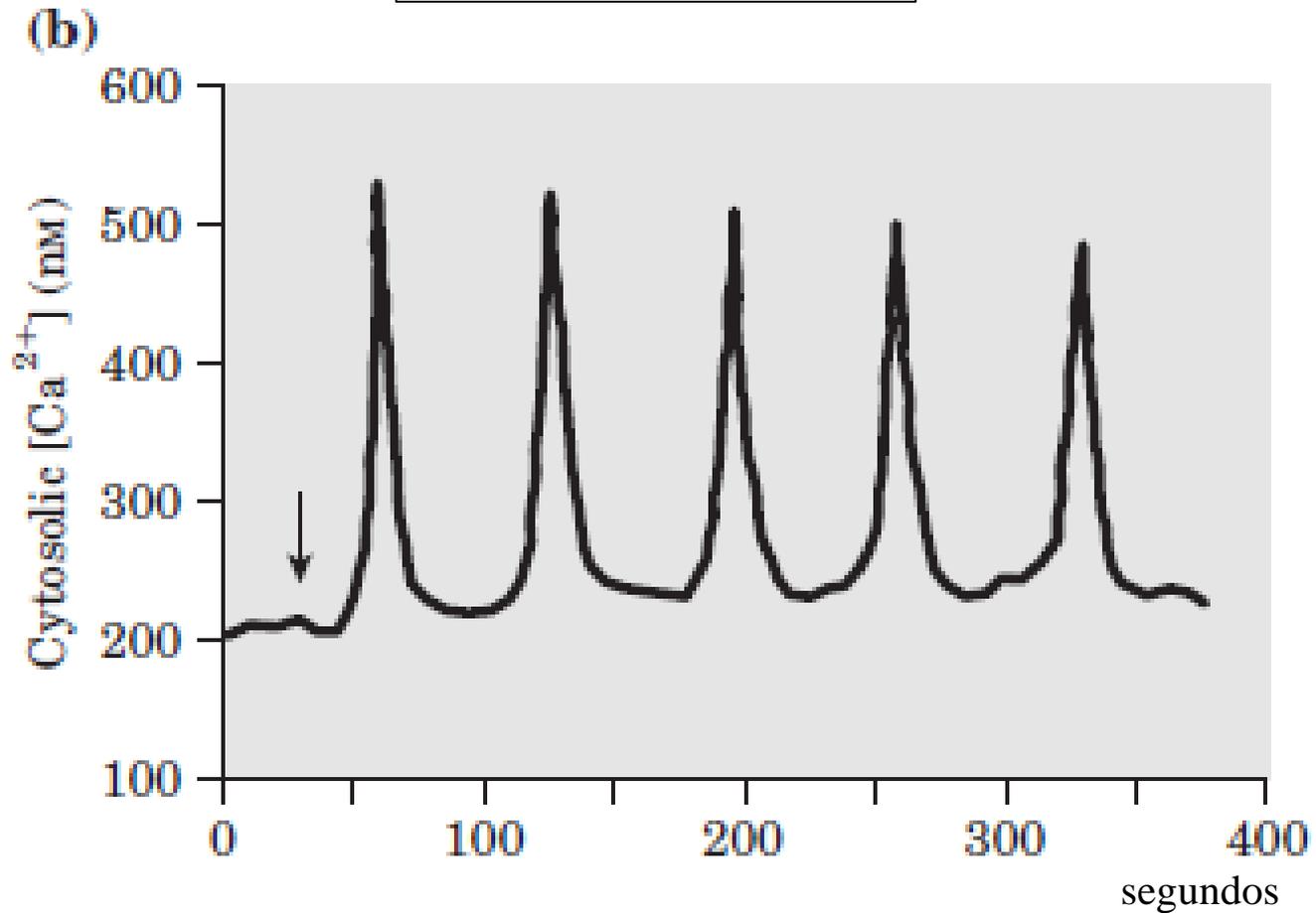


(B)



Calmodulin (apo)

Ondas de calcio



Se estimuló una célula (hepatocito) con un agonista de norepinefrina (flecha)



Table 43–4. Enzymes and proteins regulated by calcium or calmodulin.

Adenylyl cyclase

Ca²⁺-dependent protein kinases

Ca²⁺-Mg²⁺ ATPase

Ca²⁺-phospholipid-dependent protein kinase

Cyclic nucleotide phosphodiesterase

Some cytoskeletal proteins

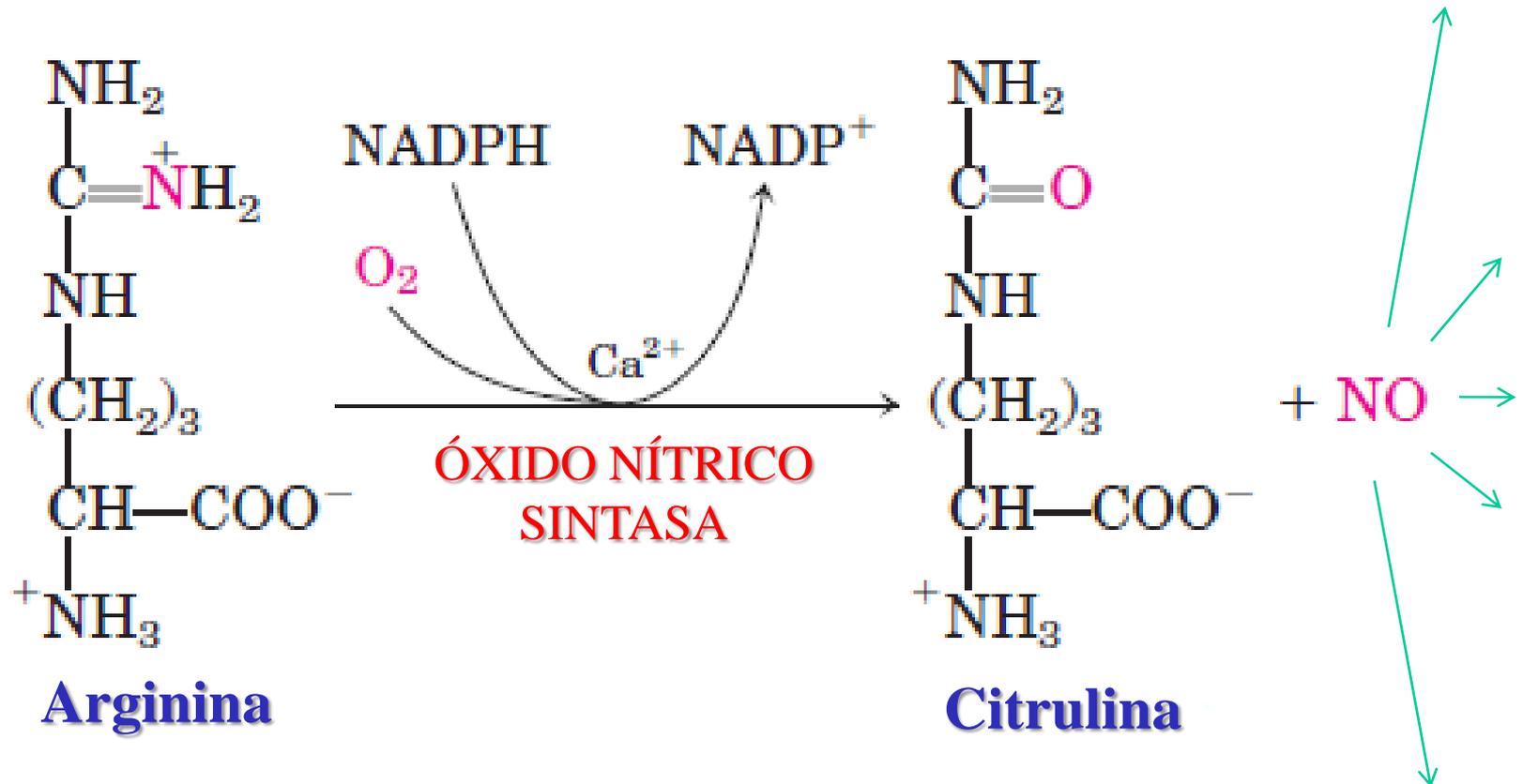
Some ion channels (eg, L-type calcium channels)

Nitric oxide synthase

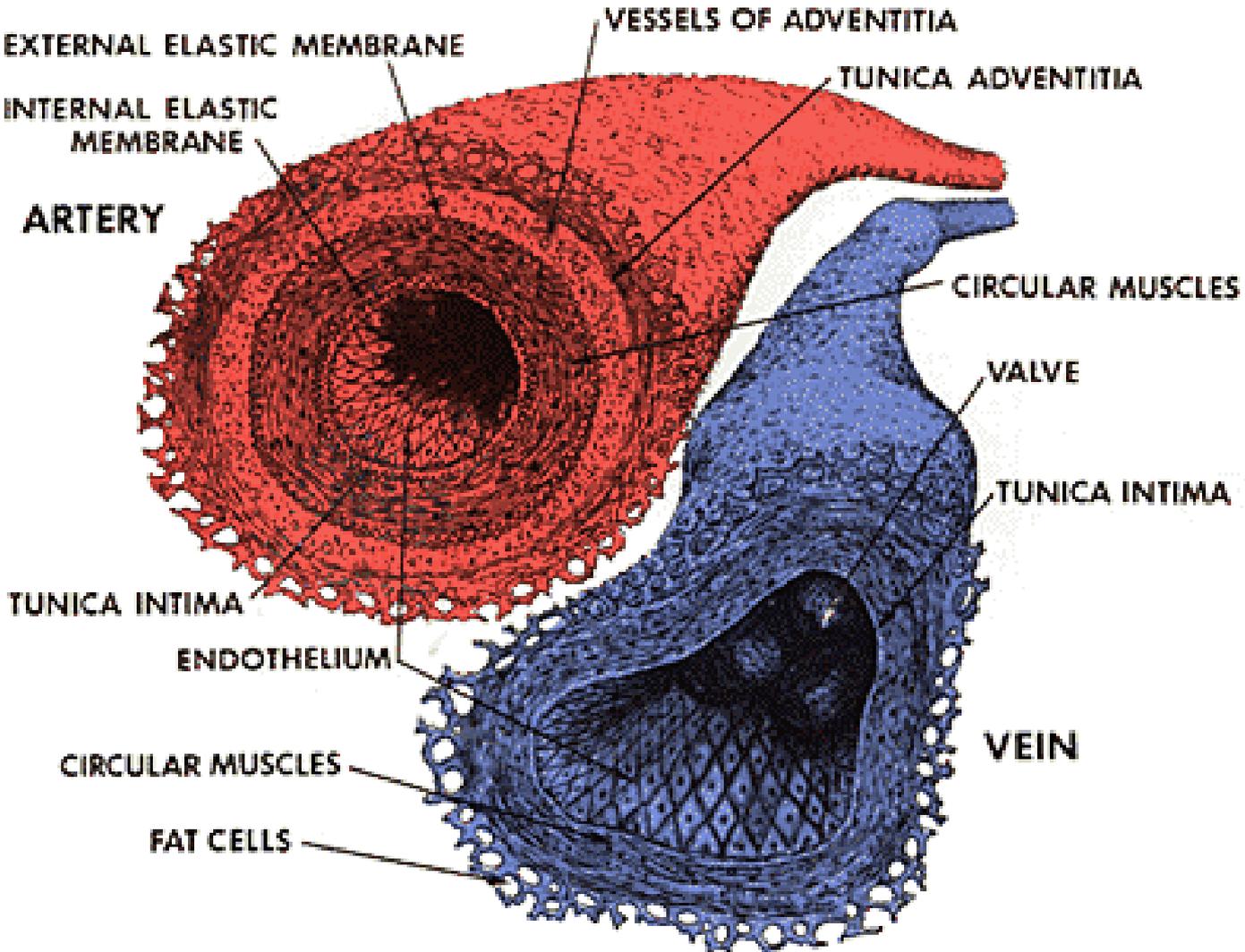
Phosphorylase kinase

Phosphoprotein phosphatase 2B

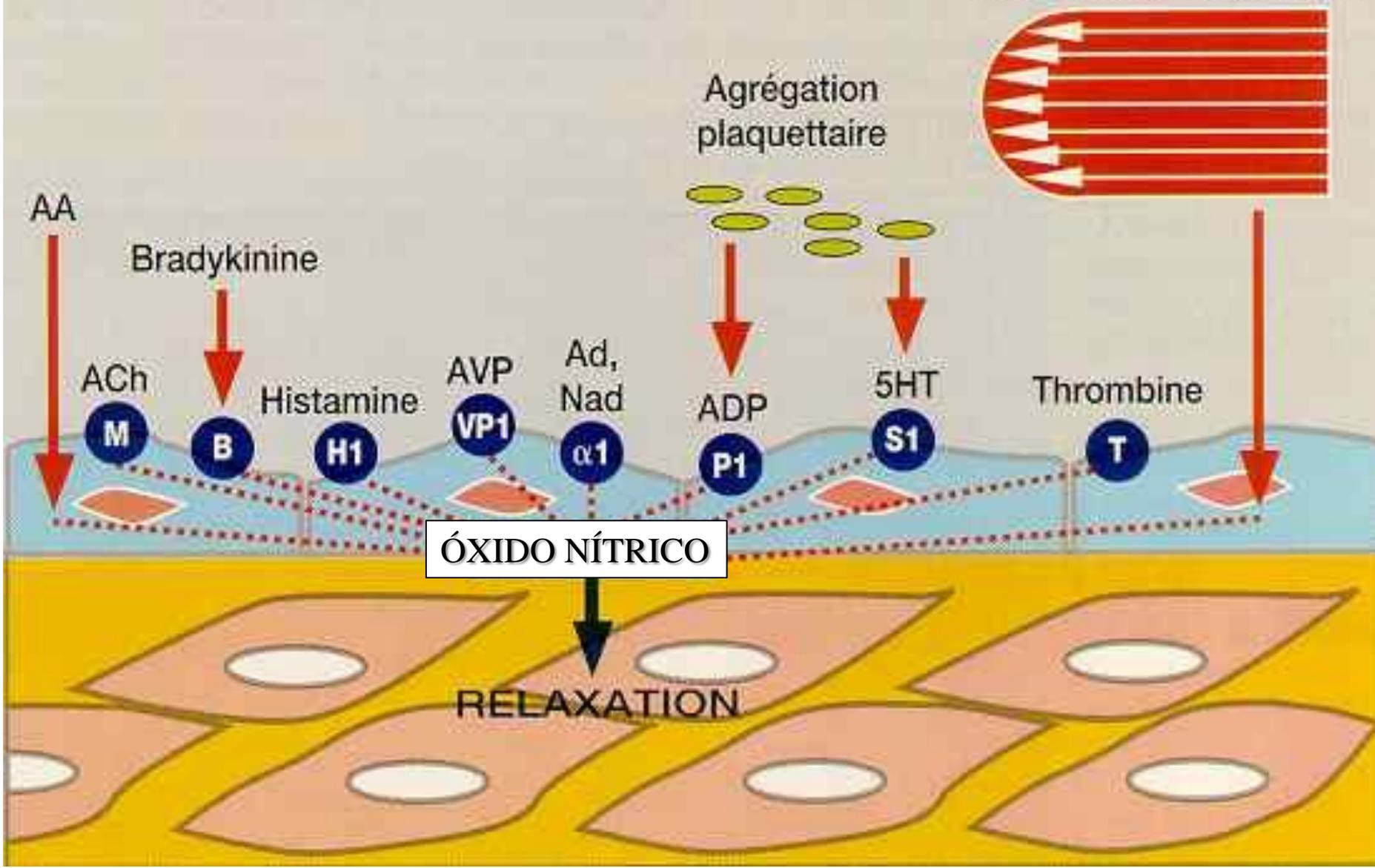
Some receptors (eg, NMDA-type glutamate receptor)



Endotelio vascular



Contraintes mécaniques



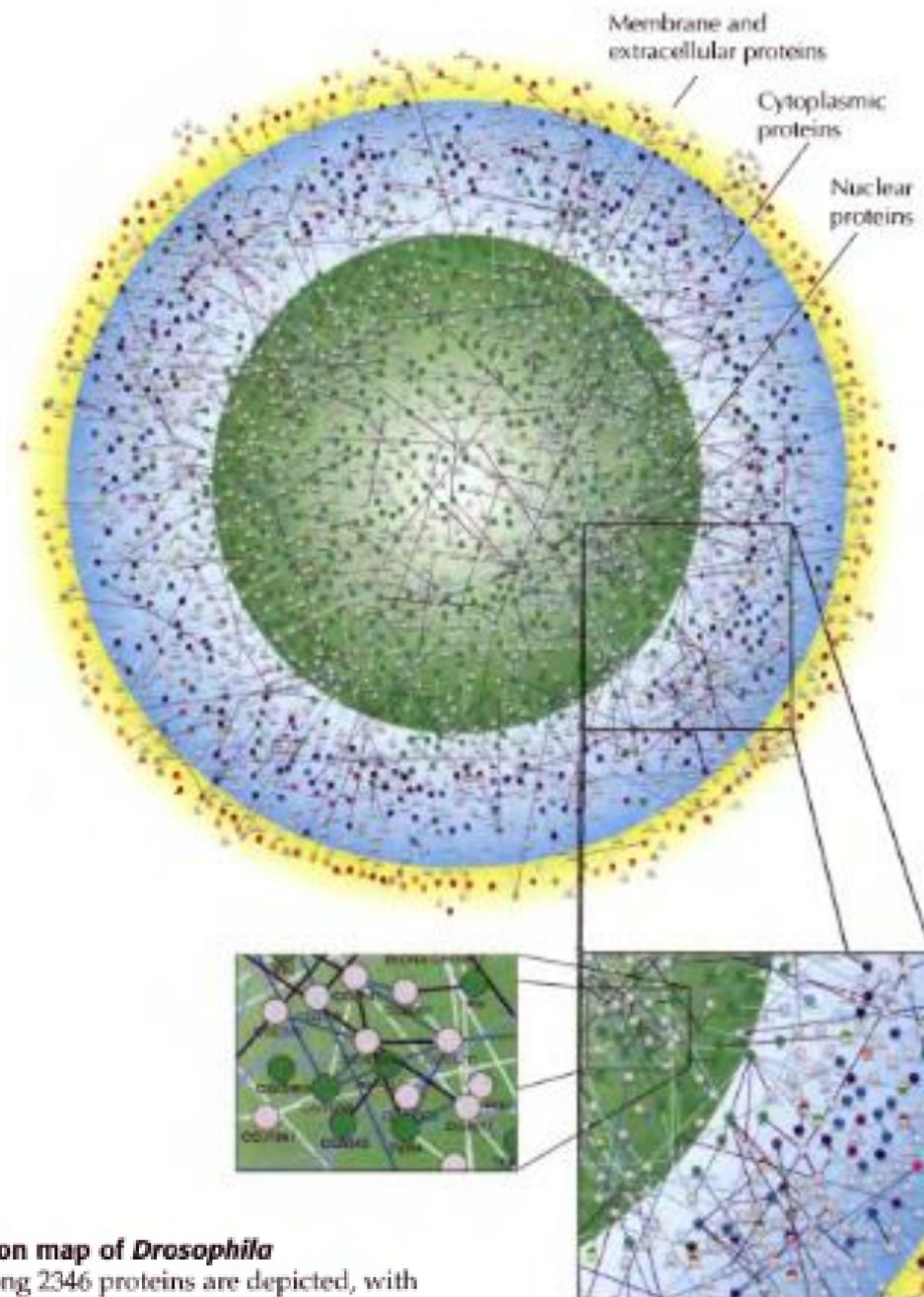


FIGURE 2.33 A protein interaction map of *Drosophila melanogaster*. Interactions among 2346 proteins are depicted, with each protein represented as a circle placed according to its subcellular localization. (From L. Glot et al., 2003. *Science* 302: 1727).

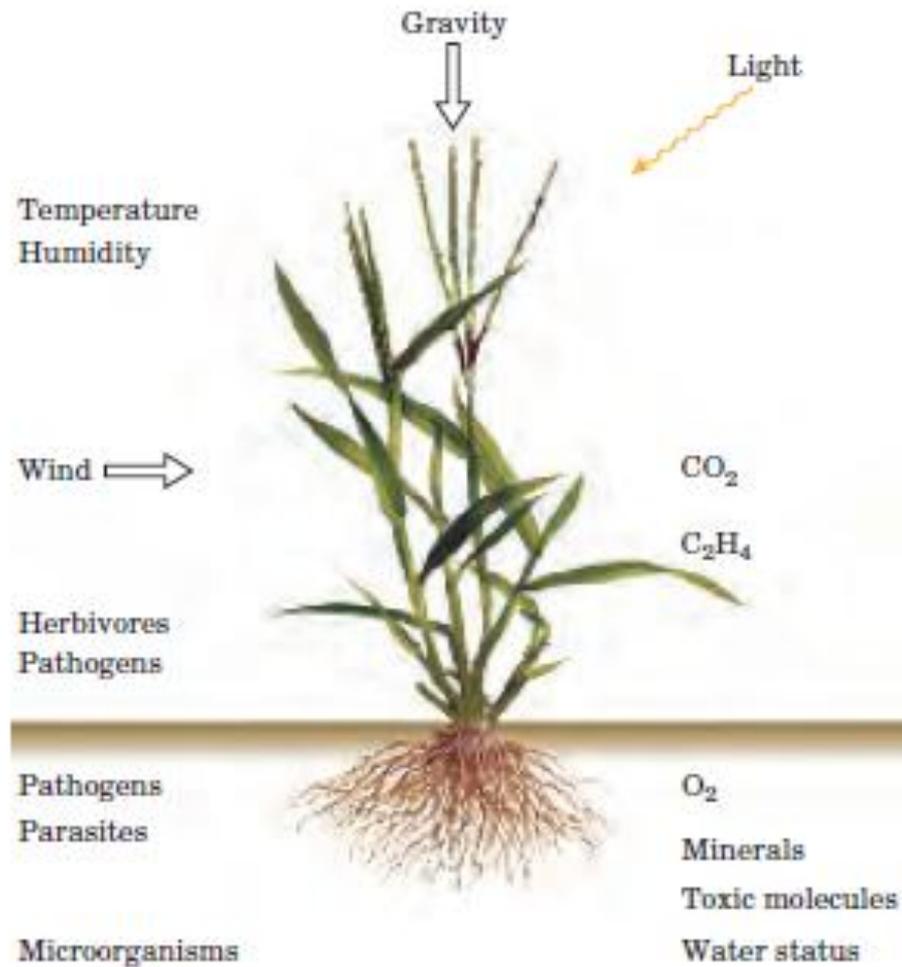
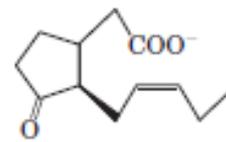
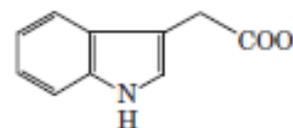


FIGURE 12-27 Some stimuli that produce responses in plants.

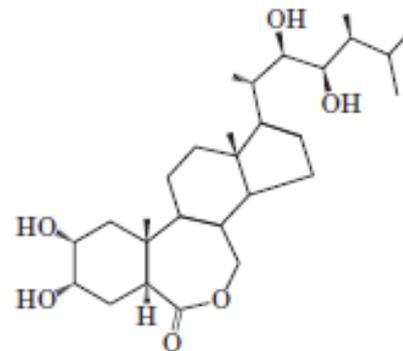
Plants



Jasmonate

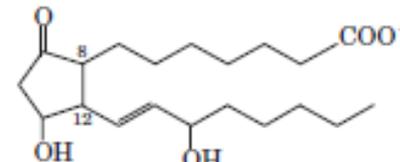


Indole-3-acetate
(an auxin)

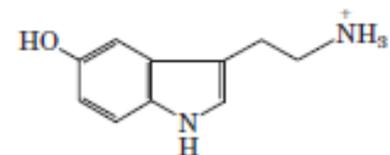


Brassinolide
(a brassinosteroid)

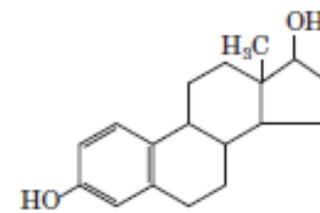
Animals



Prostaglandin E₁



Serotonin
(5-hydroxytryptamine)



Estradiol

FIGURE 12-28 Structural similarities between plant and animal signals. The plant signals jasmonate, indole-3-acetate, and brassinolide resemble the mammalian signals prostaglandin E₁, serotonin, and estradiol.

TABLE 12-7 Signaling Components Present in Mammals, Plants, or Bacteria

<i>Signaling protein</i>	<i>Mammals</i>	<i>Plants</i>	<i>Bacteria</i>
Ion channels	+	+	+
Electrogenic ion pumps	+	+	+
Two-component His kinases	+	+	+
Adenylyl cyclase	+	+	+
Guanylyl cyclase	+	+	?
Receptor protein kinases (Ser/Thr)	+	+	?
Ca ²⁺ as second messenger	+	+	?
Ca ²⁺ channels	+	+	?
Calmodulin, CaM-binding protein	+	+	—
MAPK cascade	+	+	—
Cyclic nucleotide-gated channels	+	+	—
IP ₃ -gated Ca ²⁺ channels	+	+	—
Phosphatidylinositol kinases	+	+	—
Serpentine receptors	+	+/-	+
Trimeric G proteins	+	+/-	—
PI-specific phospholipase C	+	?	—
Tyrosine kinase receptors	+	?	—
SH2 domains	+	?	?
Nuclear steroid receptors	+	—	—
Protein kinase A	+	—	—
Protein kinase G	+	—	—