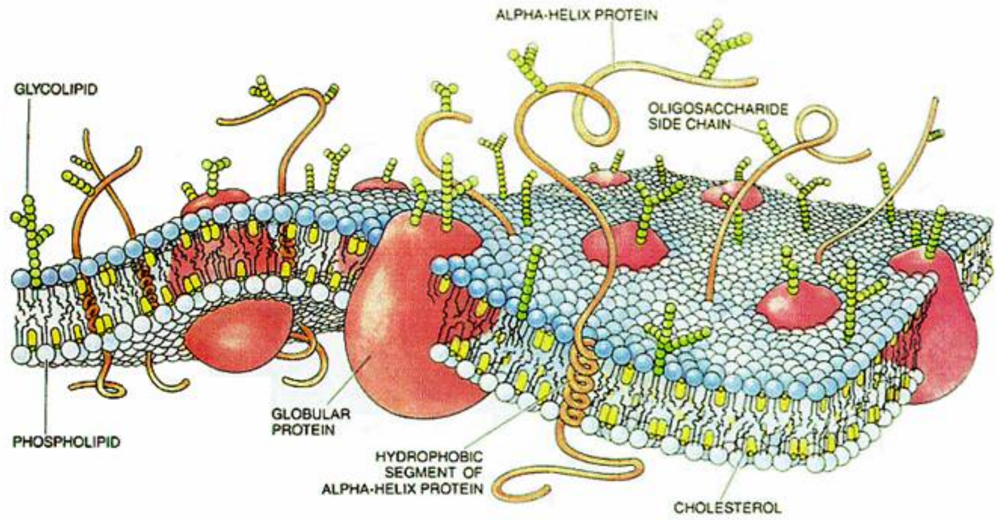
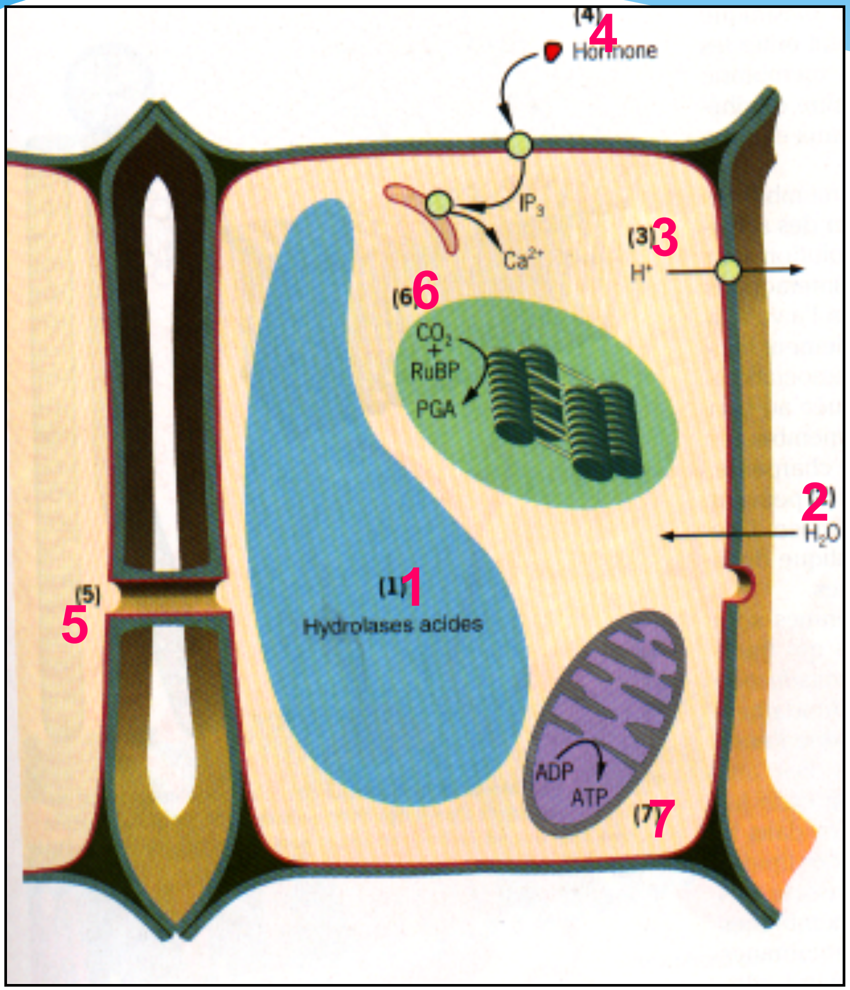
Biomembrane

struktura i funkcija

- Funkcije biomembrane
- Kemijski sastav i plan građe membrana
- Membranski lipidi i fluidnost membrana
- Membranski proteini i šećeri
- Prolaz tvari kroz membranu



Uloga membrana – granica života



1. "Kompartimentizacija" ili odjeljivanje
2. Selektivno-propusna pregrada
3. Transport otopljenih tvari
4. Provođenje signala
5. Interakcija među stanicama
6. Mjesto biokemijskih aktivnosti
7. Pretvorba energije

Sastav membrane

LIPIDI

PROTEINI

UGLJIKOHIDRATI

Membranski lipidi - fosfolipidi

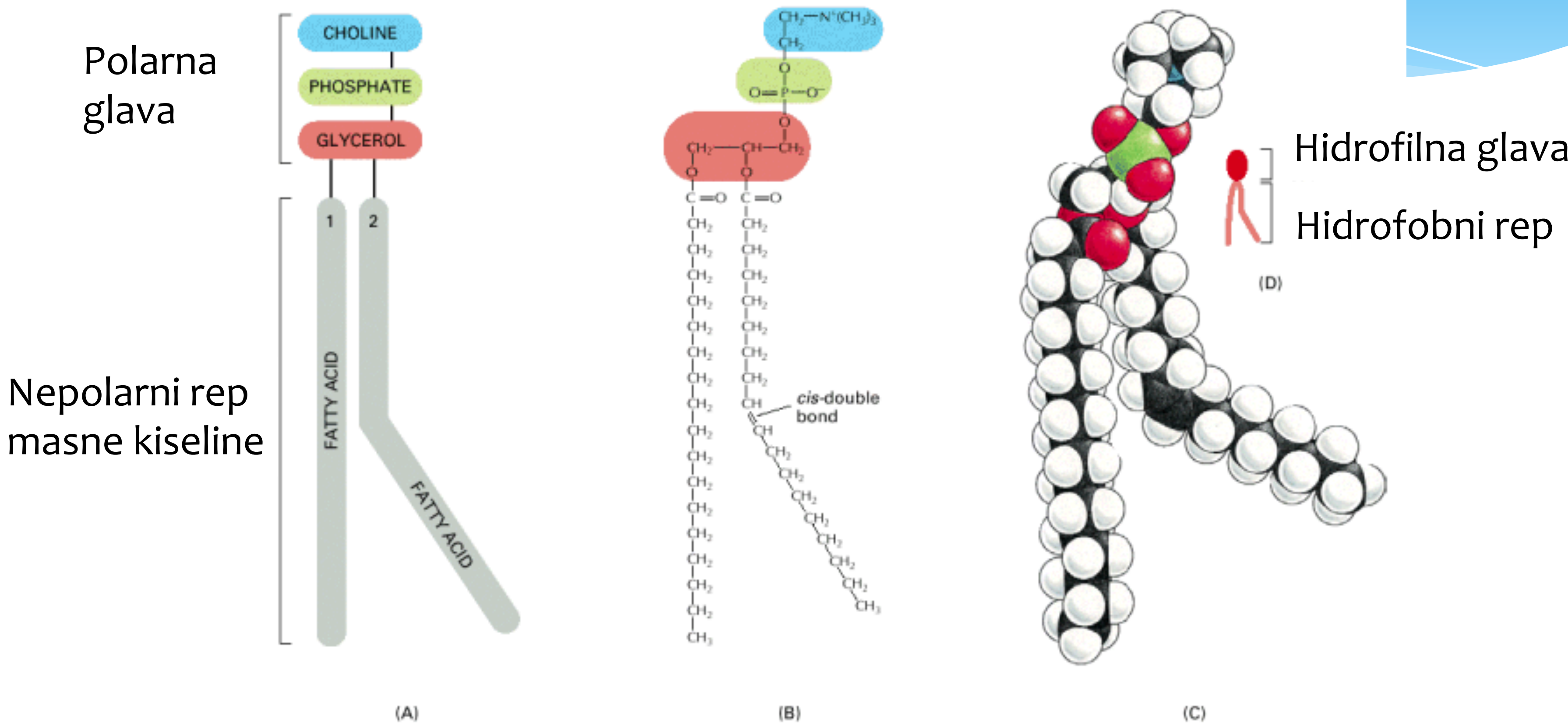
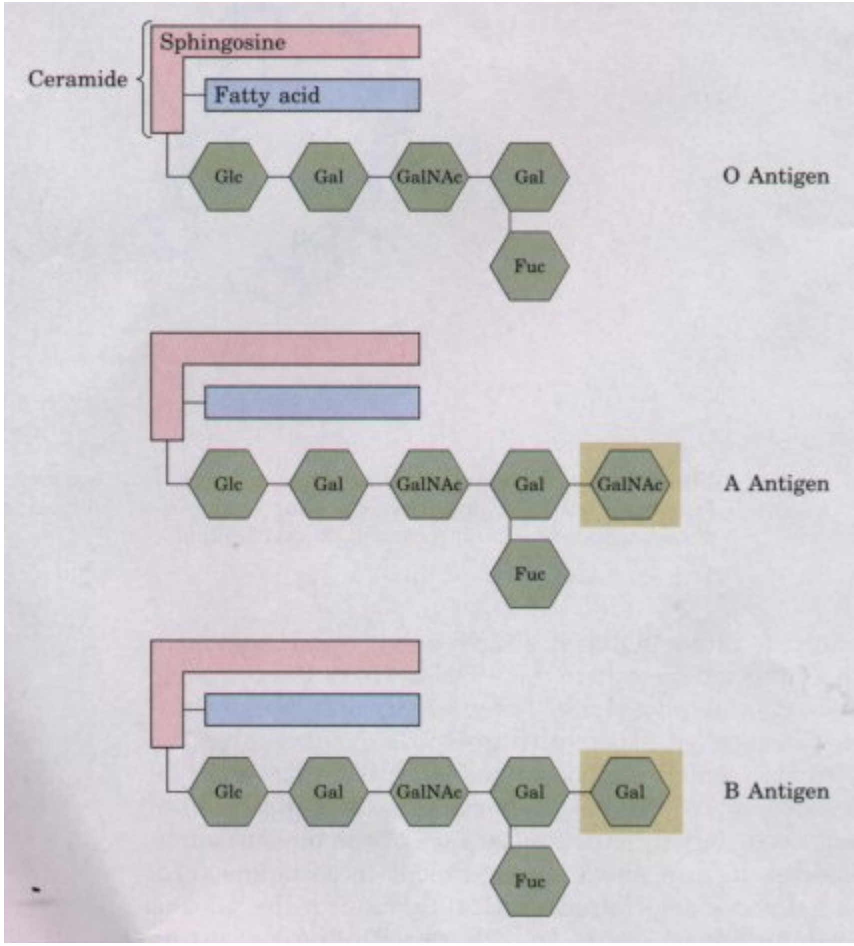


Figure 10-2. Građa fosfolipidne molekule. Primjer fosfatidilkolina. Fosfatidilkolin, (A) shematski, (B) formula, (C) prostorni model, i (D) simbol. 2002 Bruce Alberts, al.

Masne kiseline 14-20C, palmitinska, oleinska, miristinska

Membranski lipidi – sfingolipidi, uloga



- patogeni prepoznaju površinu stanica za napad
- stanična komunikacija
- tkivno prepoznavanje – krvne grupe AB0

Glc – glukoza
Gal – galaktoza
GalNAc - N-Acetylgalactosamine
Fuc - fukoza

Lipidni dvosloj – osim fosfolipida sadrži i kolesterol (1:1)

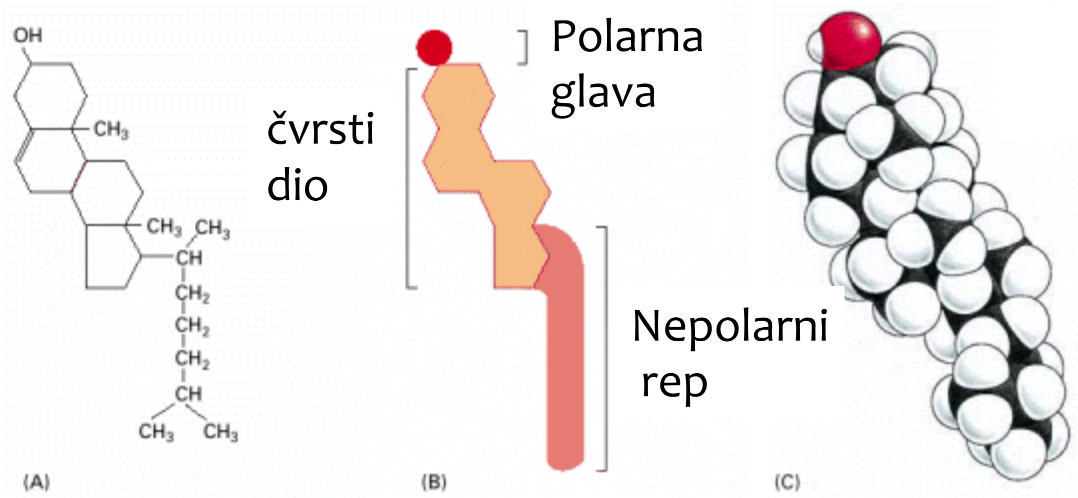


Figure 10-10. struktura kolesterola. (A) formula, (B) shematski prikaz, i (C) prostorni model. © 2002 by Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, and Peter Walter.

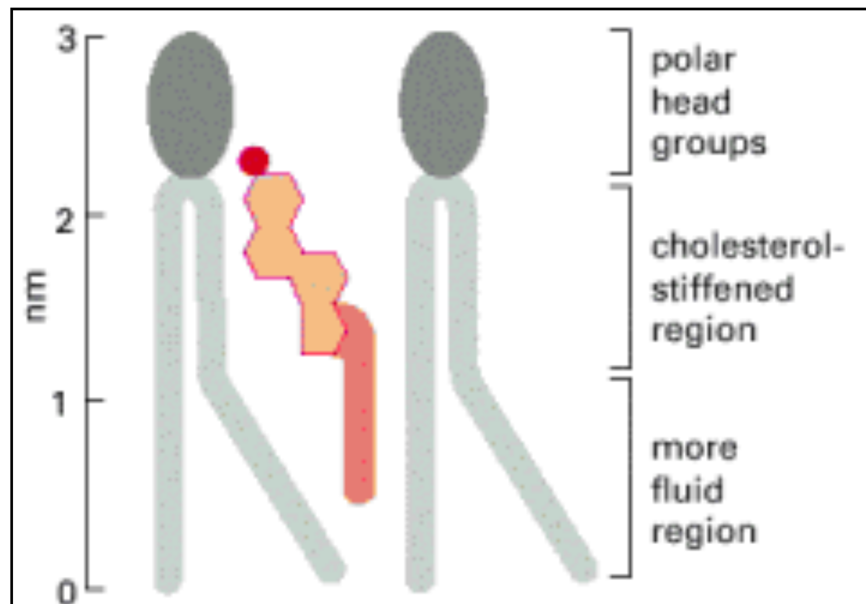
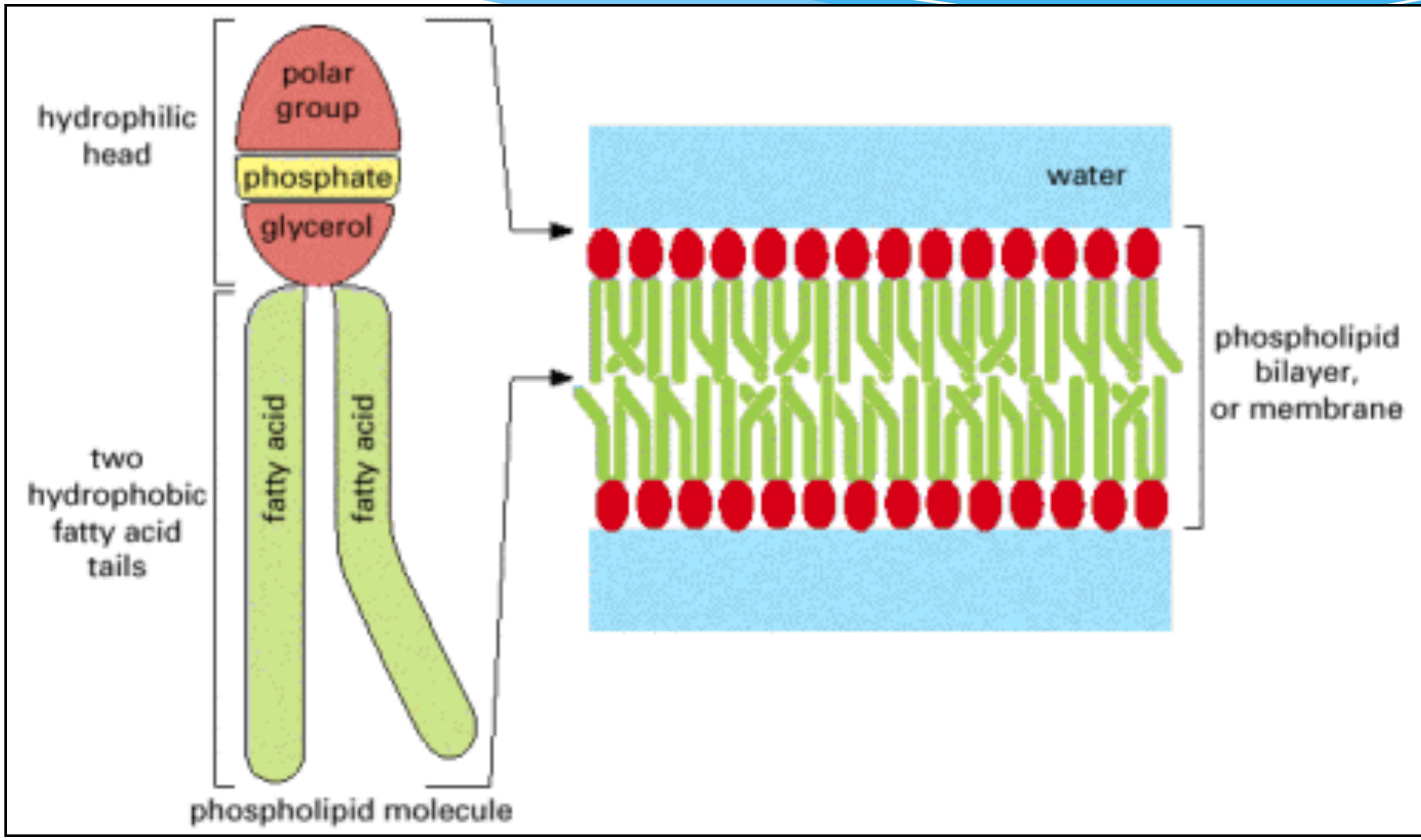


Figure 10-11. Kolesterol u lipidnom dvosloju. 2002 Bruce Alberts, et al. →

Struktura i orijentacija fosfolipida u membrani

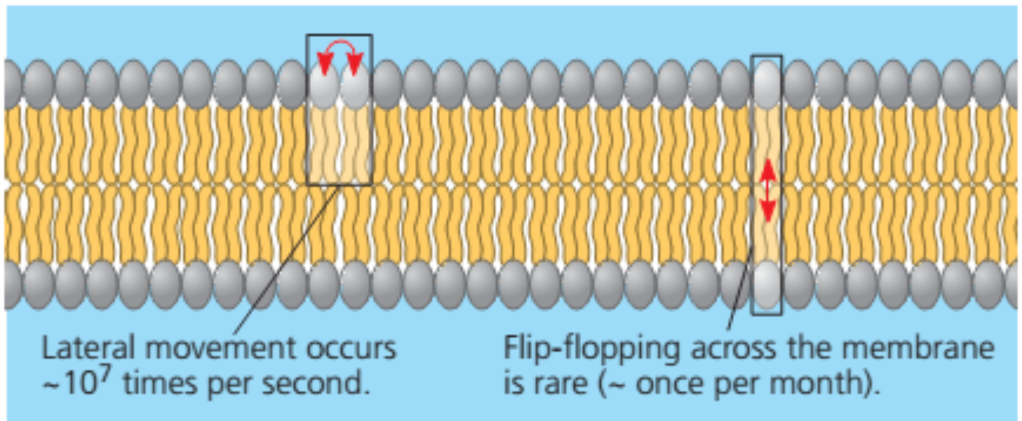


8 nm

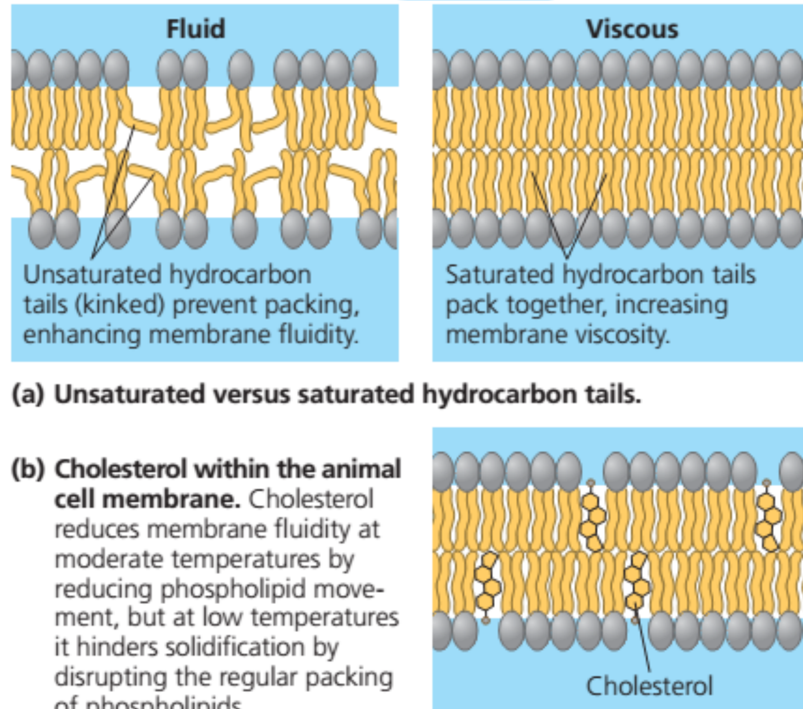
Figure 2-22. Struktura i orijentacija fosfolipida u membrani. U vodenoj sredini hidrofobni repovi fosfolipida približavaju se međusobno, a hidrofilni se orijentiraju prema vodi. Ovdje je nastao dvosloj u kojem su hidrofilni dijelovi izloženi vodi. Lipidni dvosloj je osnovna struktura staničnih membrana.

2002 Bruce Alberts, et al.

Lipidi imaju mogućnosti kretanja kroz membranu



▲ **Figure 7.6 The movement of phospholipids.**



(a) Unsaturated versus saturated hydrocarbon tails.

(b) Cholesterol within the animal cell membrane. Cholesterol reduces membrane fluidity at moderate temperatures by reducing phospholipid movement, but at low temperatures it hinders solidification by disrupting the regular packing of phospholipids.

▲ **Figure 7.8 Factors that affect membrane fluidity.**

Mogući pokreti fosfolipida u membrani, 2 µm/s

Omega 3 masne kiseline ulaze u sastav membrana

Membrane mogu mijenjati fluidnost

Lipidne molekule imaju mogućnost samoorganizacije u vodenoj sredini

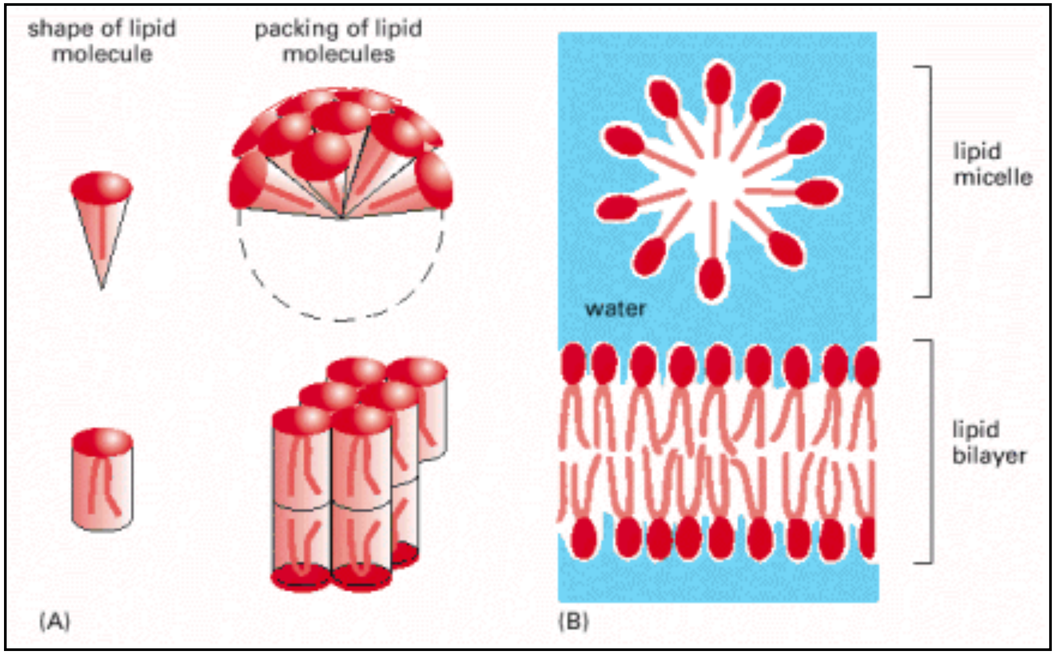


Figure 10-4. Raspored lipidnih molekula u vodenoj sredini. Spontano se slažu u obliku micela ili lipidnog dvosloja.
2002 Bruce Alberts, et al.

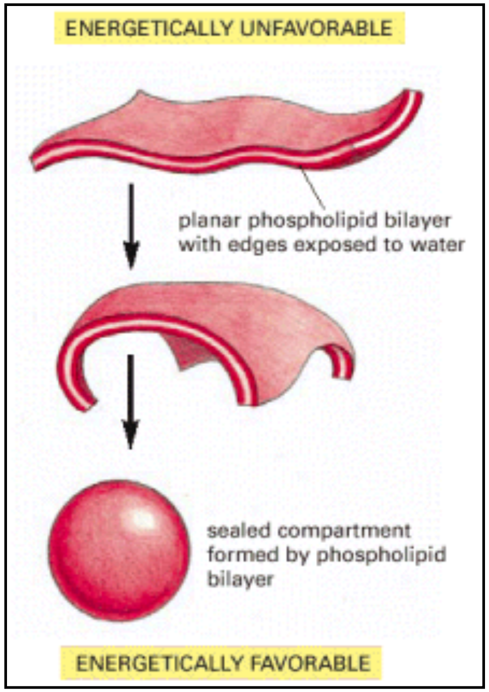
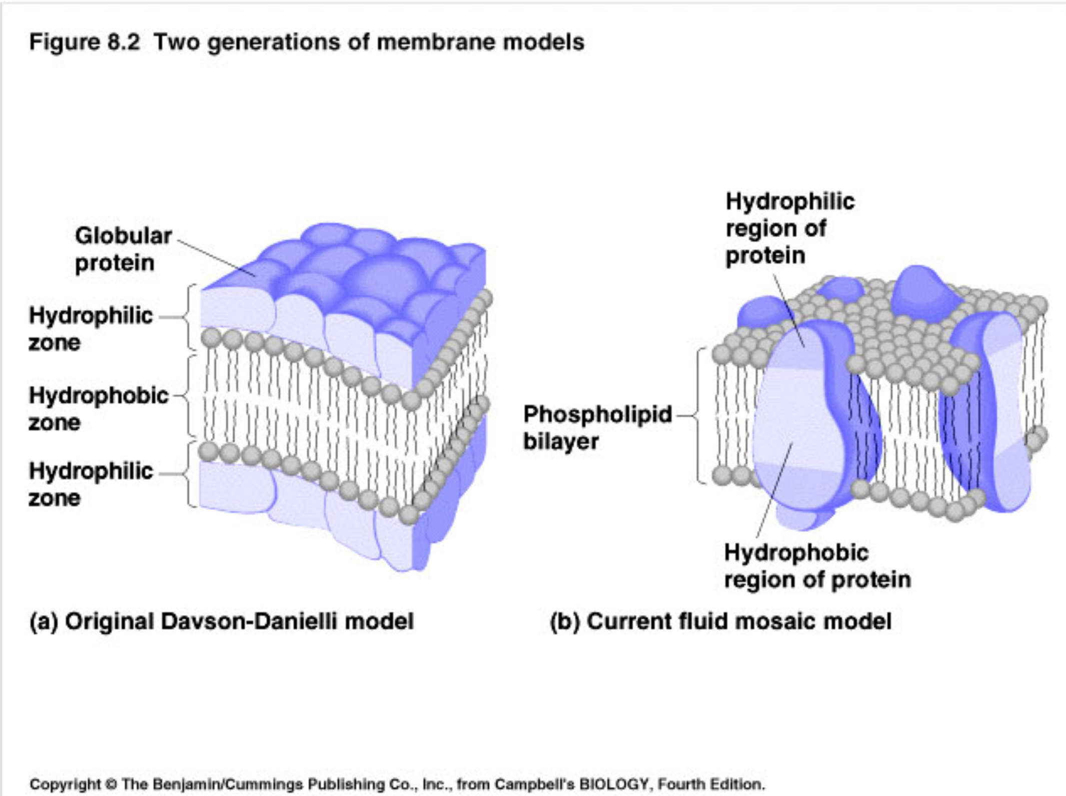


Figure 10-5. Spontano zatvaranje lipidnog dvosloja u membranske mjehuriće

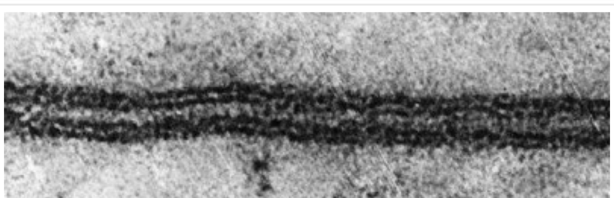
Kako su proteini uključeni u membranu?



Stariji model sendviča (lijevo, Davson-Danielli, 1935) zamjenjen je

modelom **tekućeg mozaika** (Singer i Nicolson, 1972.), koji bolje opisuje strukturu i funkciju membrana

- Molekule lipida i proteina raspoređene u dvije dimenzije
- Proteini slobodno difundiraju u homogenom lipidnom okruženju



Stanična membrana pod TEM

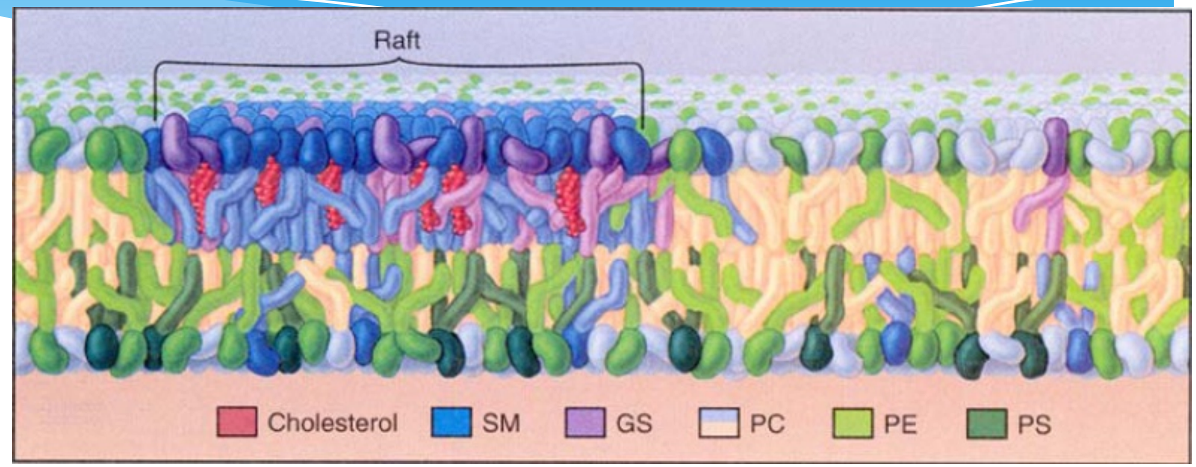
http://www.doctortee.com/cgi/image-lookup.cgi?membrane-tem

Nakon 30-tak godina bez novih vijesti…

- **Lipidne splavi** su male (10-200nm), heterogene, visoko dinamične domene, obogaćene sterolima i sfingolipidima

- Služe za odvajanje membranskih procesa

- Tu se često nalaze proteini uključeni u staničnu signalizaciju i endocitozu



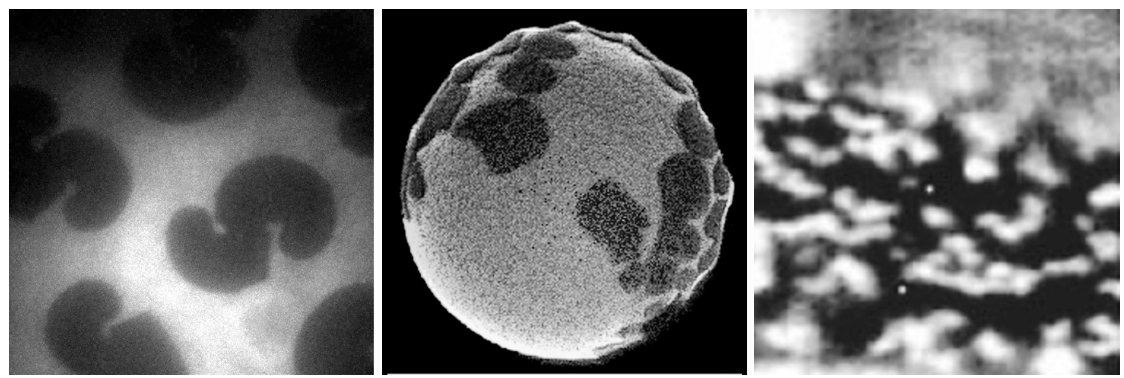
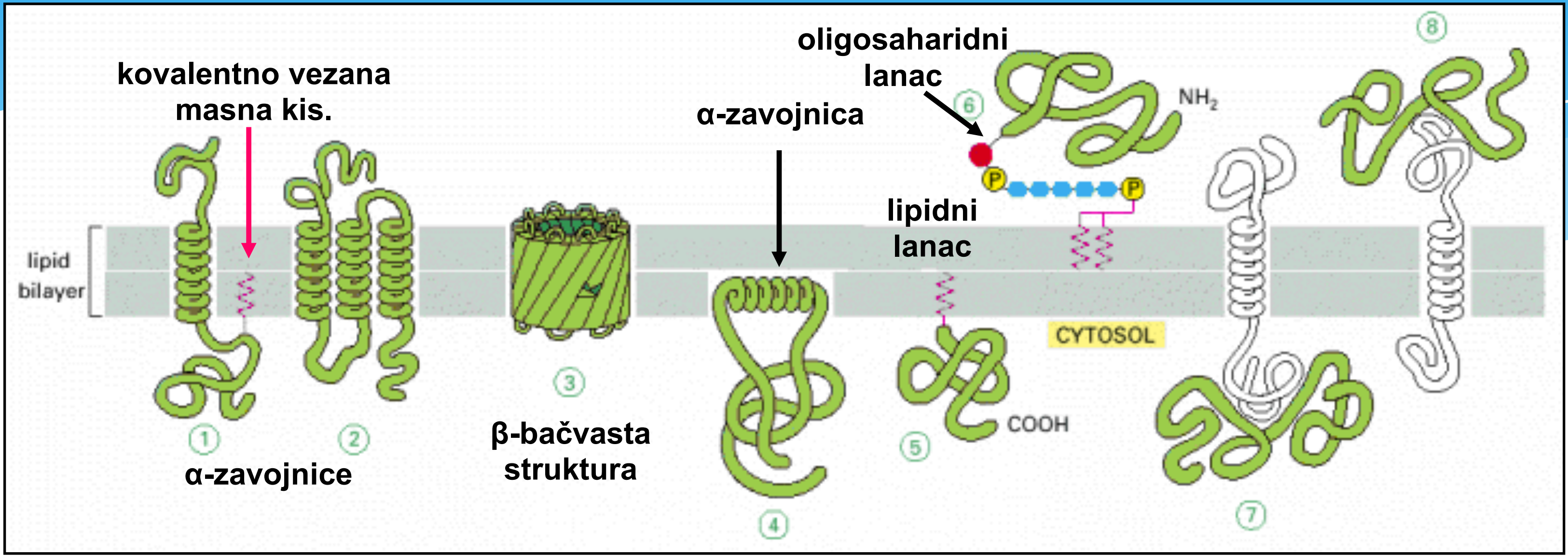


Fig. 1.10 Domain formation in lipid monolayers, bilayers, and in biological cells. Left: Domain formation in the phase coexistence regime of DPPC monolayers. The dimension of the panel is about 100 μm. From Gudmand/Heimburg, NBI Copenhagen. Center: Confocal fluorescence microscopy image of domain formation in a giant lipid vesicle (DLPC:DPPC = 30:70 at room temperature). The size of the vesicle is about 30 μm in diameter. From Fidorra/Heimburg, NBI Copenhagen. Right: Placental alkaline phosphatase distribution in fibroblast. The size of the segment is about 4 μm. From Harder et al. (1998).

Vrste membranskih proteina

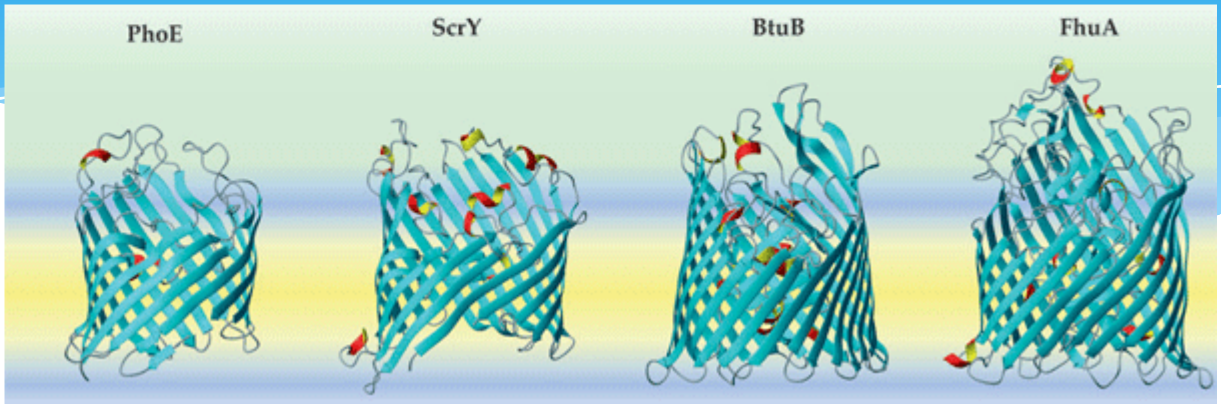


➢ **Figure 10-17. Veza membranskih proteina s lipidnim dvoslojem**

- **1, 2, 3 – transmembranski proteini (amfipatski)**
- **4, 5, 6 – usidreni proteini (izloženi samo s jedne strane)**
- **7 i 8 – periferni proteini (vezani slabim nekovalentnim vezama)**

2002 Bruce Alberts, et al.

Primjeri transmembranskih proteina



Porini – membrane mitohondrija ili bakterija

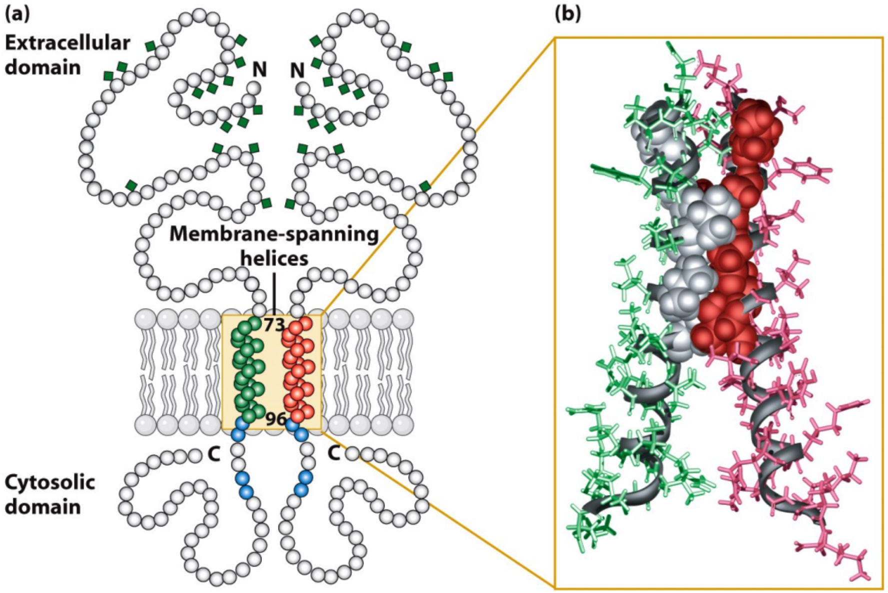
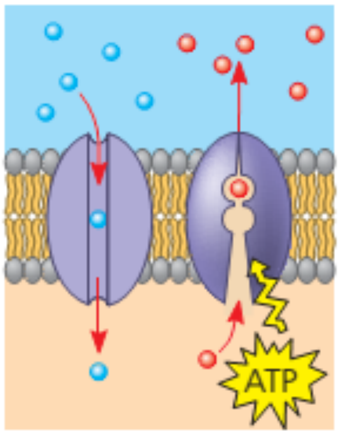


Figure 10-15
Molecular Cell Biology, Sixth Edition

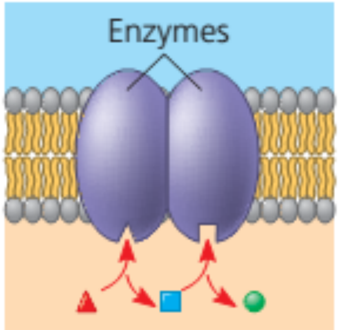
Glikoforin, membrana eritrocita – bogati ugljikohidratima – ne vežu se za krvne žile

Uloge membranskih proteina



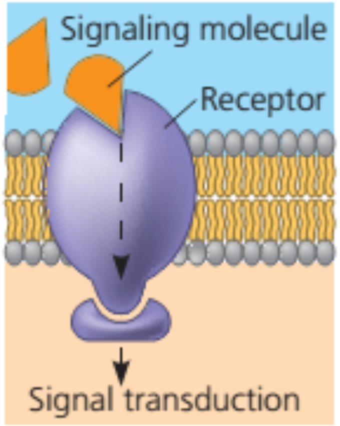
Pasivni ili aktivni prijenos molekula: hidrofilni kanali koji propuštaju određene molekule, neki hidroliziraju ATP kao izvor energije za aktivni prijenos tvari

Npr. glukoze ili steroidnih hormona.



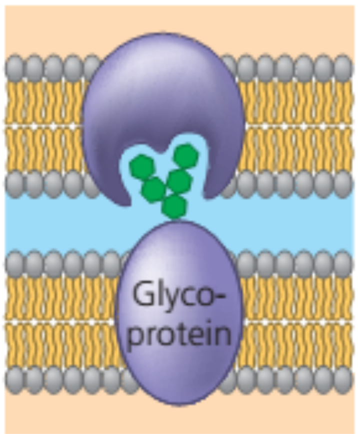
Kataliziranje reakcija: aktivna strana enzima u kontaktu s tvarima otopine koja okružuje membranu, nekoliko enzima u skupini može biti odgovorno za odvijanje jednog koraka u metaboličkom putu

Npr. enzimi za dobivanje energije u mitohondriju



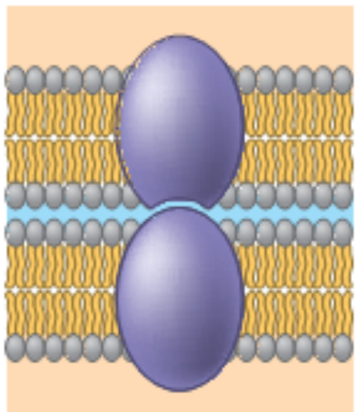
Prijenos signala: proteini na vanjskoj strani plazmatske membrane djeluju kao receptori za npr. hormone, antitijela, viruse i sl., signali iz okoliša stanice mogu potaknuti promjene u konformaciji proteina na unutarnjoj strani membrane što može dovesti do lančane reakcije kemijskih promjena u stanici

Uloge membranskih proteina



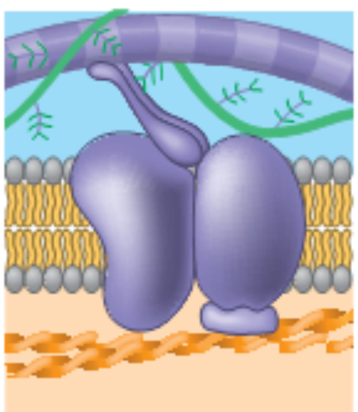
Prepoznavanje stanica: neki glikoproteini služe kao identifikacijski dodatak koji specifično prepoznaju drugu stanicu

Npr. u imunološkom sustavu



Povezivanje stanica: membranski proteini susjednih stanica mogu biti povezani različitim vrstama međustaničnih veza

Npr. u tkivima



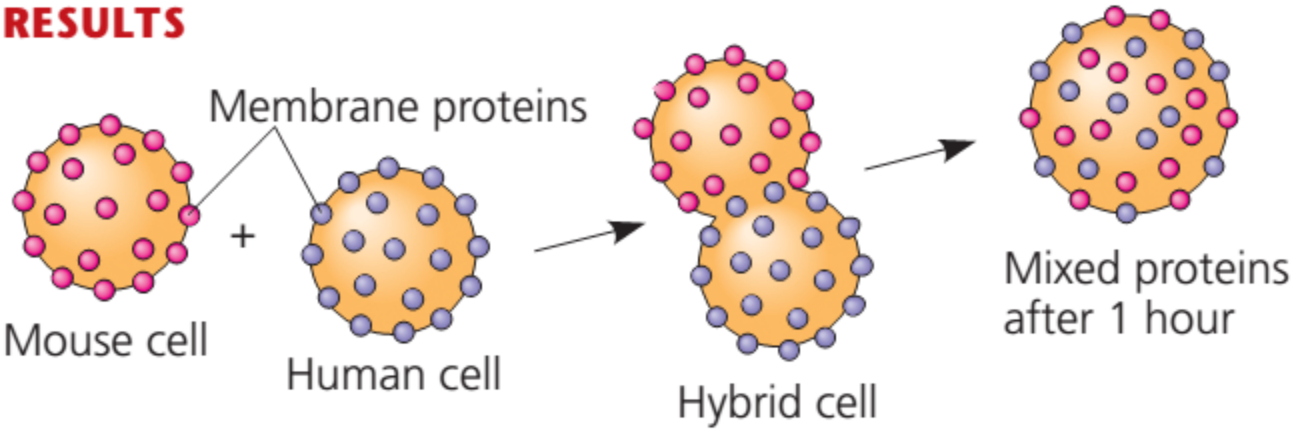
Učvršćivanje citoskeleta na izvanstanični matrix: mikrofilamenti ili elementi citoskeleta mogu biti vezani za membranske proteine što omogućuje održavanje oblika stanice i kotvljenje membranskih proteina. Oni mogu koordinirati izvanstanične i unutarstanične promjene

Npr. u tkivima

Membranski proteini su također pokretni u membrani

EXPERIMENT Larry Frye and Michael Edidin, at Johns Hopkins University, labeled the plasma membrane proteins of a mouse cell and a human cell with two different markers and fused the cells. Using a microscope, they observed the markers on the hybrid cell.

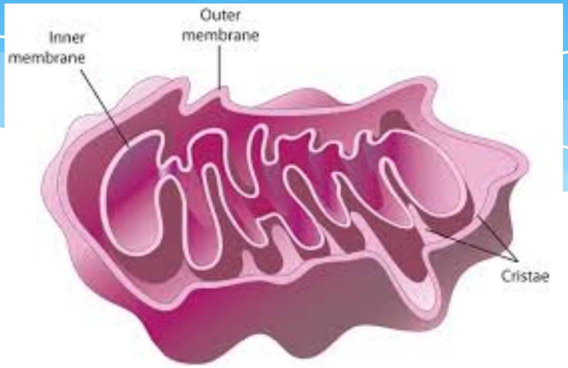
RESULTS



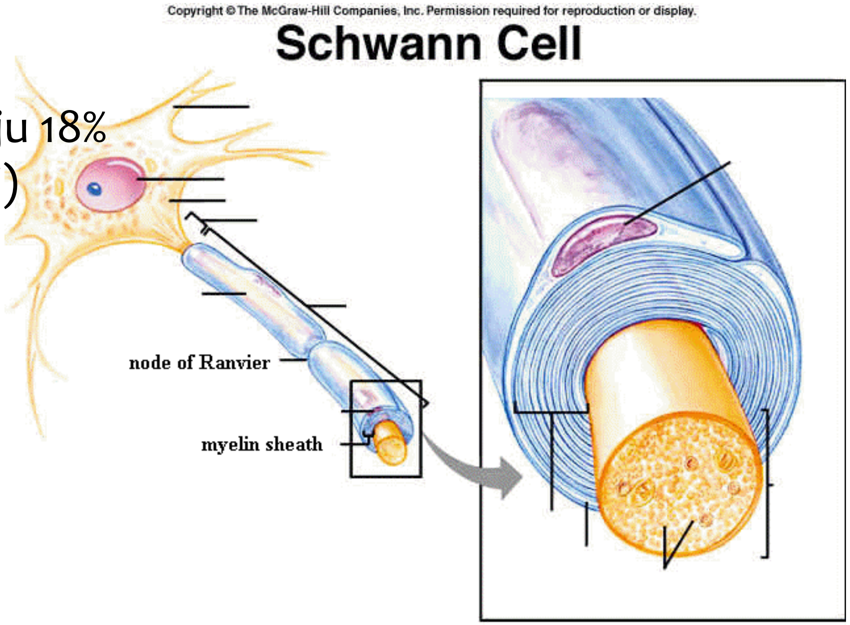
https://www.youtube.com/watch?v=Qqsf_UJcfBc

Omjer proteina i lipida ovisi o tipu i funkciji membrane

Mitohondrijske unutarnje membrane imaju oko 75% proteina (proteini oksidativne fosforilacije)

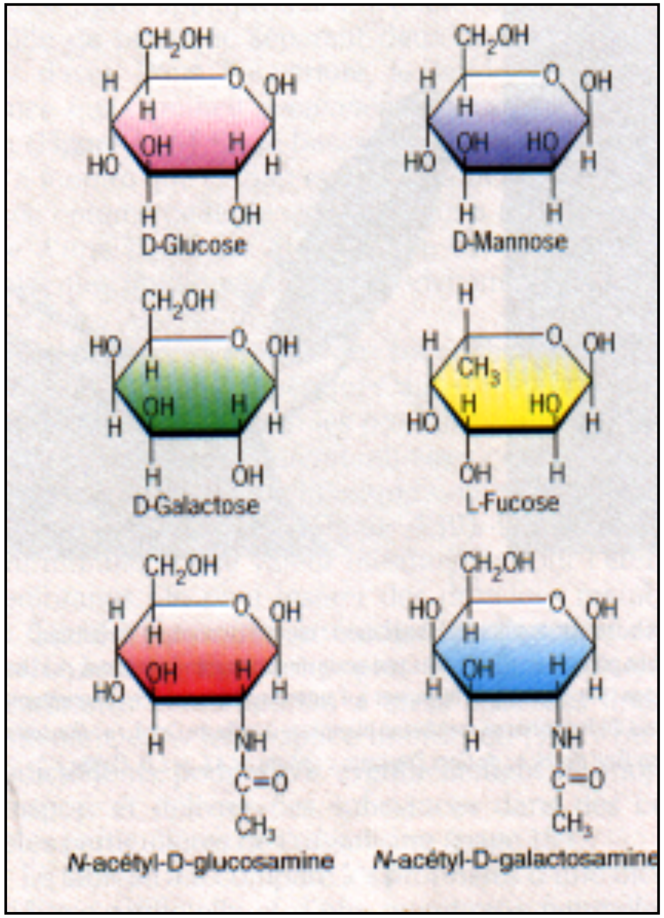


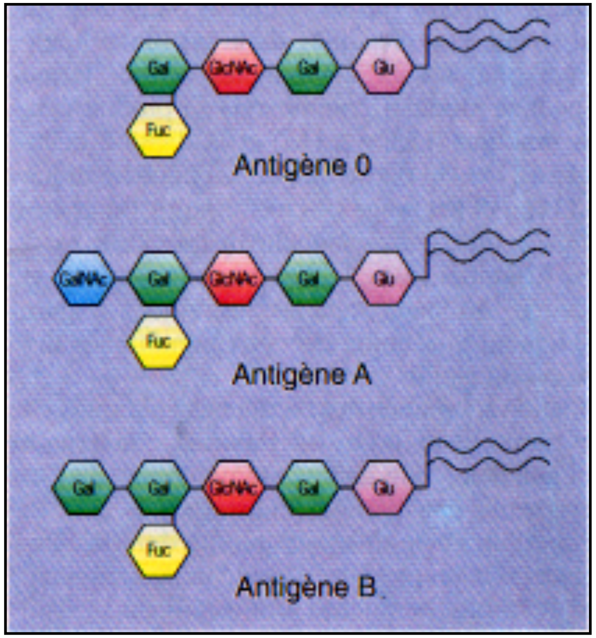
Membrane Schwannovih stanica imaju 18% proteina (fosfolipidi su dobri izolatori)



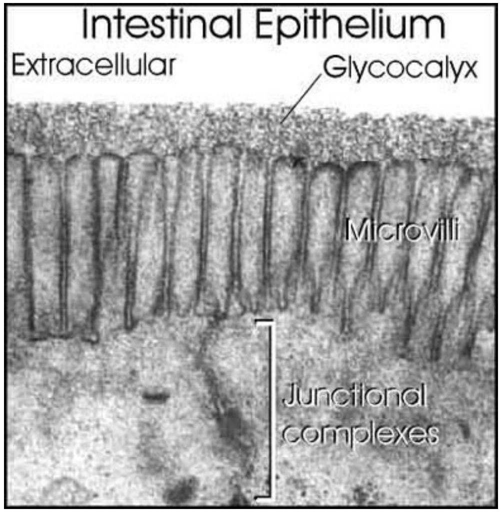
Membranski ugljikohidrati

- šećeri koji su vezani za <u>proteine</u> ili <u>lipide</u> u membranama
- samo u <u>necitoplazmatskom</u> (vanjskom) sloju lipidnog dvosloja
- **Glikokaliks** – ugljikohidratni pokrov od oligosaharida lipida i proteina



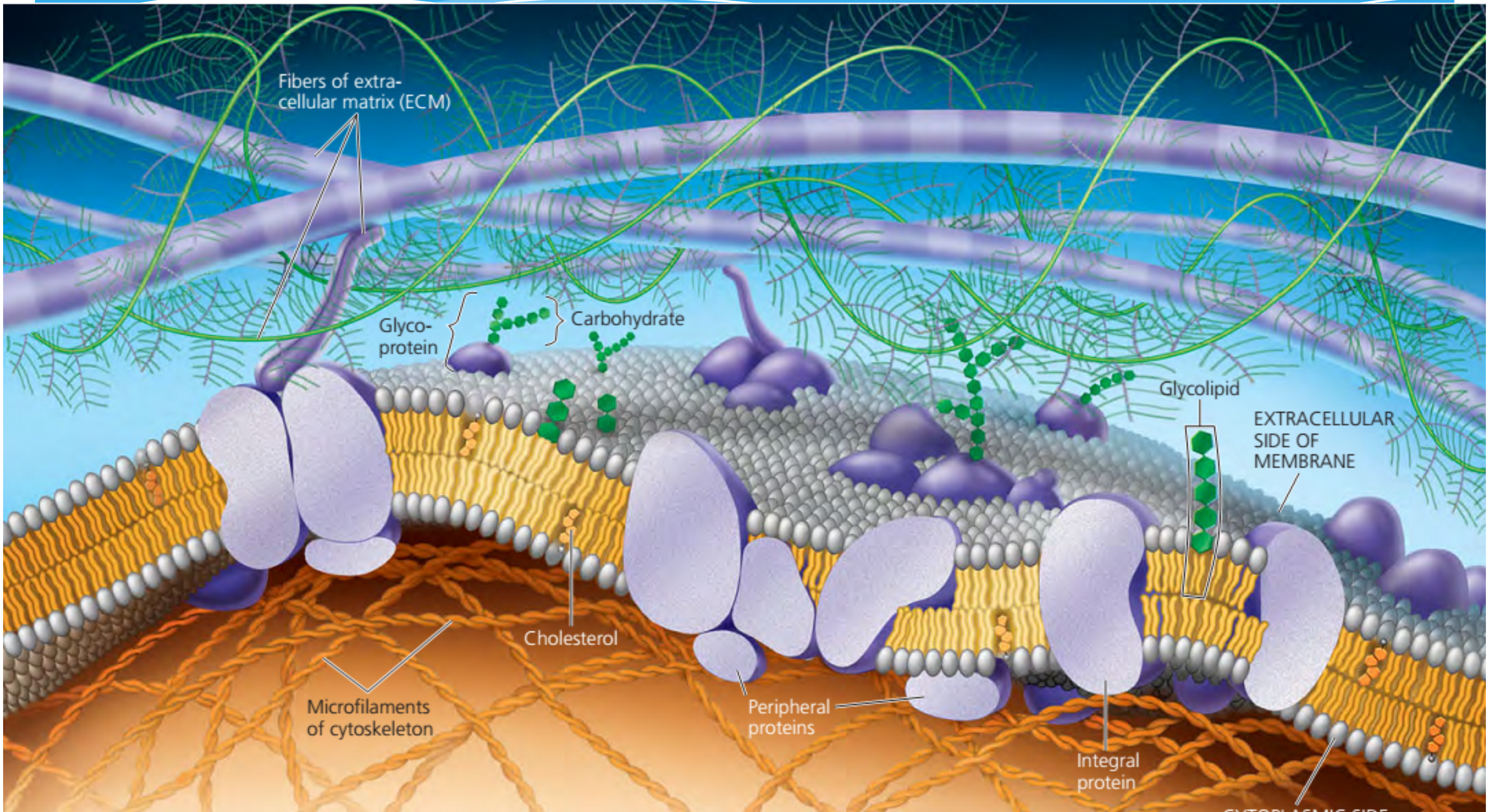


Antigeni krvnih grupa



Glikokaliks u stanicama Probavnog sustava

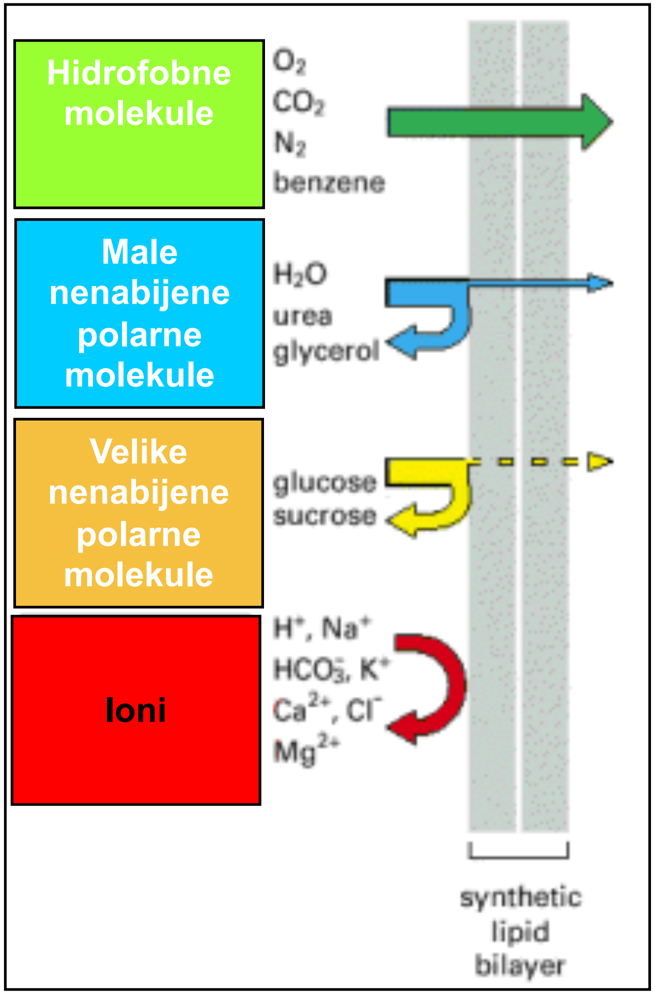
Stanična membrana je kompleksni sustav lipida, proteina i ugljikohidrata



▲ **Figure 7.5 Updated model of an animal cell's plasma membrane (cutaway view).**

Drugi, slatki, model stanične membrane

Relativna propusnost *sintetskog* lipidnog dvosloja za različite skupine molekula.



Što je molekula manja i bolje topiva u mastima brže prolazi kroz lipidni dvosloj.

Lijekovi moraju biti topivi u mastima!

Model tekućeg mozaika daje sposobnost regulacije prijenosa (transporta) tvari

❖plazmatske membrane su selektivno propusne za različite molekule

❖Neprestani prijenos tvari

-šećeri, aminokiseline i druge hranjive tvari ulaze u stanicu

-otpadne tvari (metabolički produkti) izlaze iz stanice

-kisik potreban za stanično disanje ulazi u stanicu, ugljikov dioksid izlazi iz stanice

-kontrola koncentracije anorganskih iona, Na^{+}, K^{+}, Ca^{2+}, Cl^{-}

Tvar	Izvanstanična	Unutarstanična
Na+	140 mmol/L	10 mmol/L
K+	4 mmol/L	140 mmol/L
Ca2+	2.5 mmol/L	0.1 micromol/L
Mg2+	1.5 mmol/L	30 mmol/L
Cl-	100 mmol/L	4 mmol/L
HCO3-	27 mmol/L	10 mmol/L
PO4	2 mmol/L	60 mmol/L
Glukoza	5.5 mmol/L	0-1 mmol/L
Protein	2g/dL	16g/dL

Kako tvari prolaze kroz membranu?

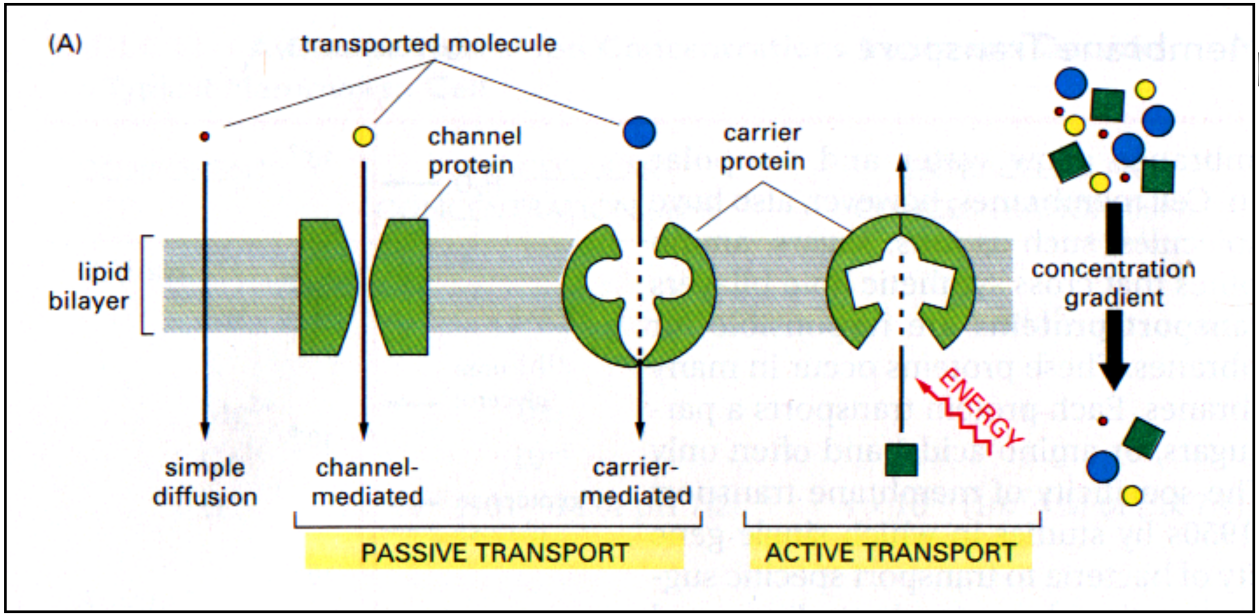


Figure 11-4.

Pasivni transport:
jednostavna difuzija ili olakšana difuzija kroz kanale ili pasivne prenositelje.

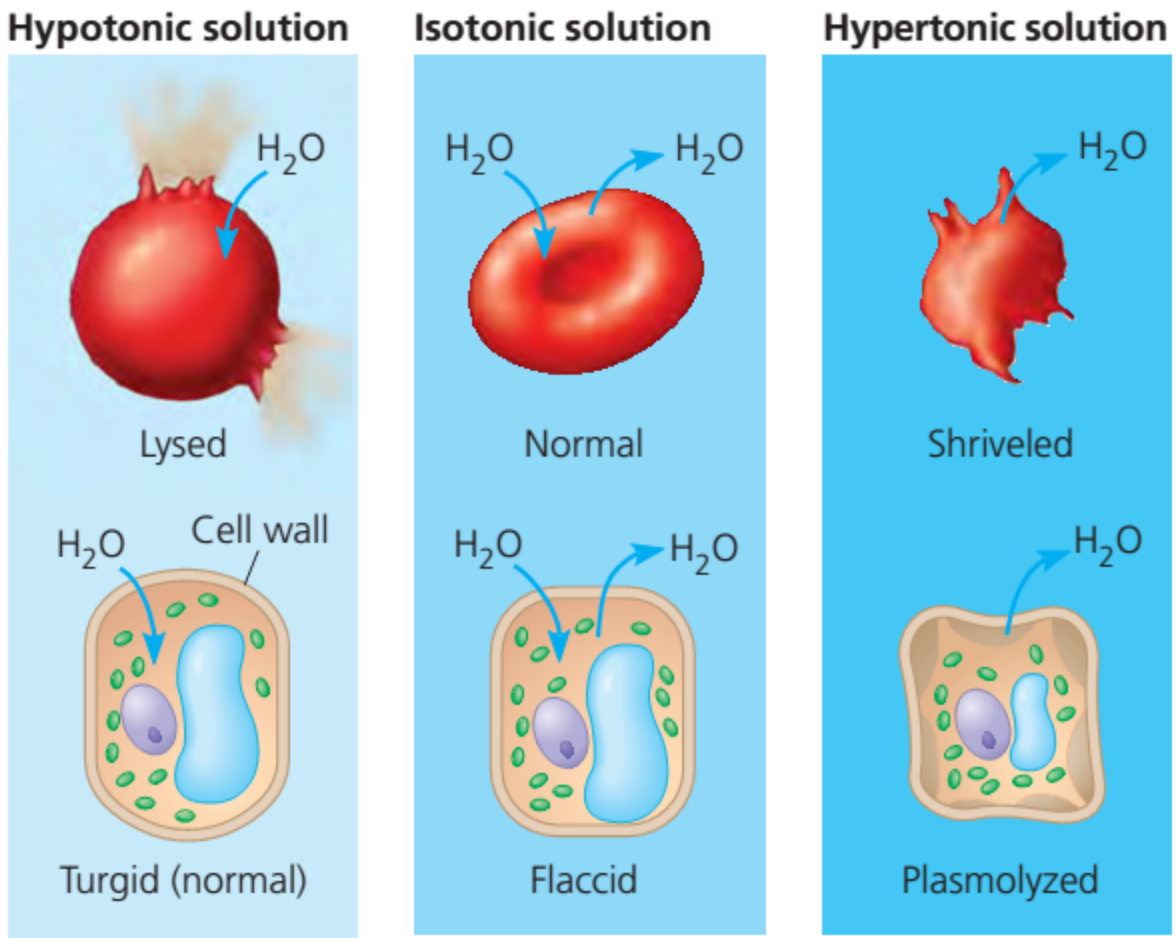
Aktivni transport: ide protiv koncentracijskog gradijenta i treba dodatnu energiju.

2002 Bruce Alberts, et al.

Održavanje vodne ravnoteže – vitalno za život

(a) Animal cell. An animal cell fares best in an isotonic environment unless it has special adaptations that offset the osmotic uptake or loss of water.

(b) Plant cell. Plant cells are turgid (firm) and generally healthiest in a hypotonic environment, where the uptake of water is eventually balanced by the wall pushing back on the cell.

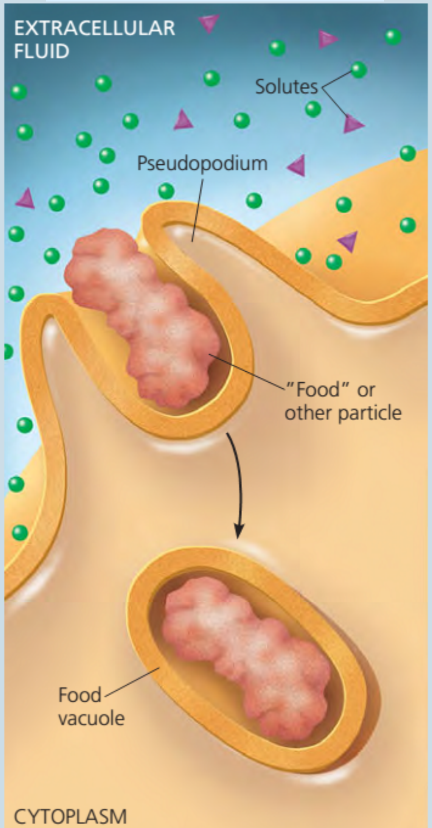


▲ **Figure 7.15 The water balance of living cells.** How living cells react to changes in the solute concentration of their environment depends on whether or not they have cell walls. **(a)** Animal cells, such as this red blood cell, do not have cell walls. **(b)** Plant cells do. (Arrows indicate net water movement after the cells were first placed in these solutions.)

Prijenos „teškog i velikog” tereta preko membrane (proteini, polisaharidi, itd.)

Endocitoza

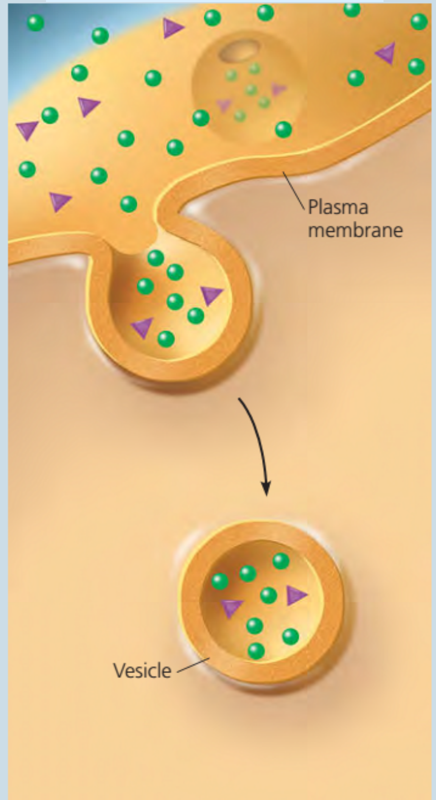
FAGOCITOZA



In **phagocytosis,** a cell engulfs a particle by wrapping pseudopodia (singular, *pseudopodium*) around it and packaging it within a membranous sac called a food vacuole. The particle will be digested after the food vacuole fuses with a lysosome containing hydrolytic enzymes (see Figure 6.13a).

Npr. makrofagi, amebe,...

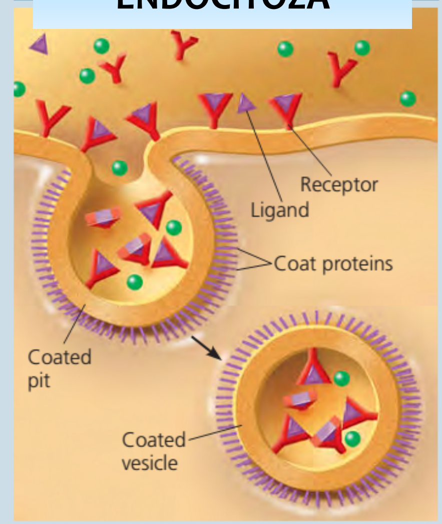
PINOCITOZA



In **pinocytosis,** the cell "gulps" droplets of extracellular fluid into tiny vesicles. It is not the fluid itself that is needed by the cell, but the molecules dissolved in the droplets. Because any and all included solutes are taken into the cell, pinocytosis is nonspecific in the substances it transports.

Npr. stanice tankog crijeva

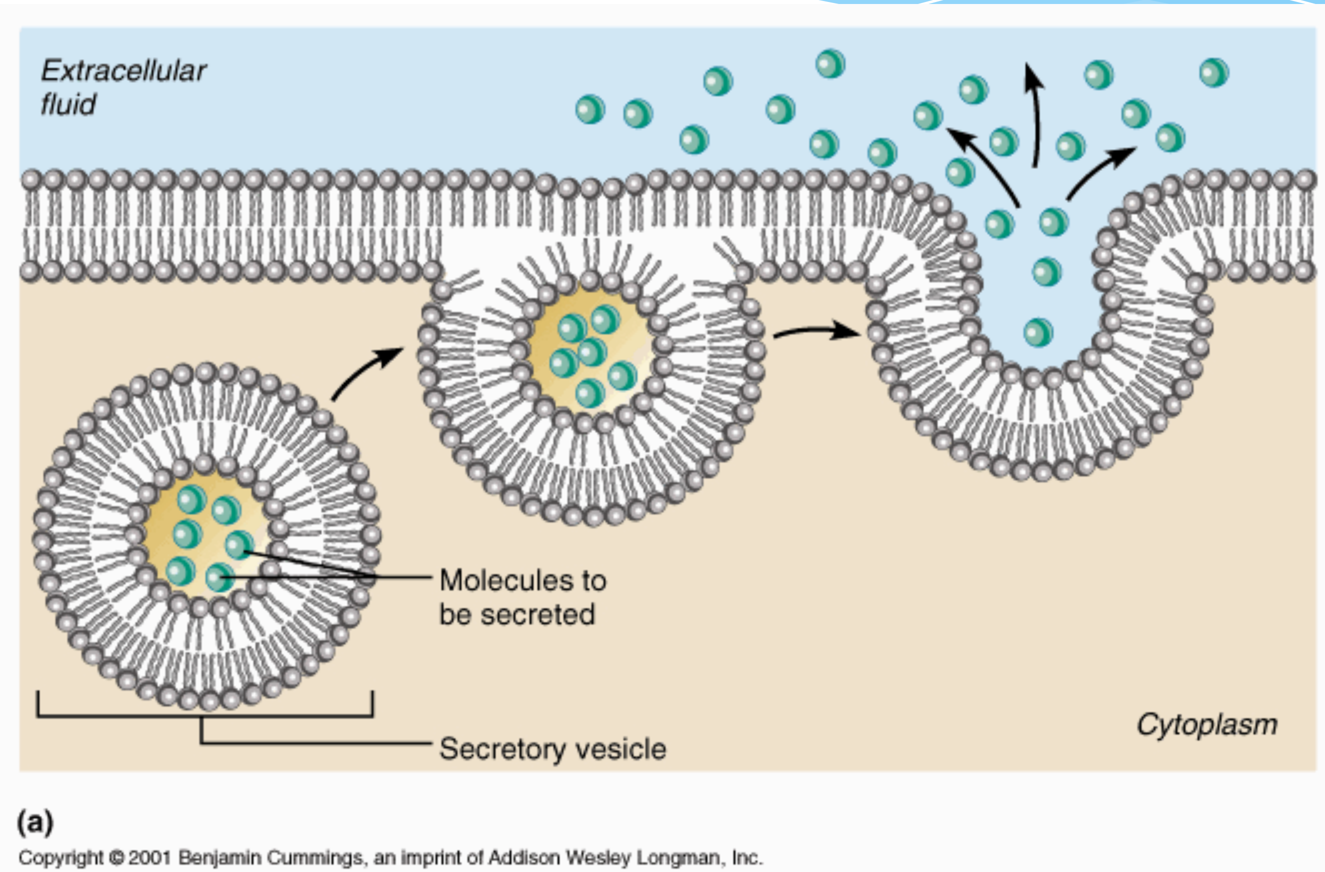
RECEPTORSKA ENDOCITOZA



Receptor-mediated endocytosis enables the cell to acquire bulk quantities of specific substances, even though those substances may not be very concentrated in the extracellular fluid. Embedded in the membrane are proteins with specific receptor sites exposed to the extracellular fluid, to which specific substances (ligands) bind. The receptor proteins then cluster in regions of the membrane called coated pits, which are lined on their cytoplasmic side by a fuzzy layer of coat proteins. Next, each coated pit forms a vesicle containing the ligand molecules. Notice that there are relatively more bound molecules (purple) inside the vesicle, but other molecules (green) are also present. After the ingested material is liberated from the vesicle, the emptied receptors are recycled to the plasma membrane by the same vesicle.

Npr. stanice uzimaju kolesterol iz LDL čestica

Egzocitozom, stanice izbacuju tvari iz stanice



Stanice gušterače izbacuju inzulin u krvotok
Stanice se mogu rješavati nepotpuno razgrađenog materijala

Sažetak:

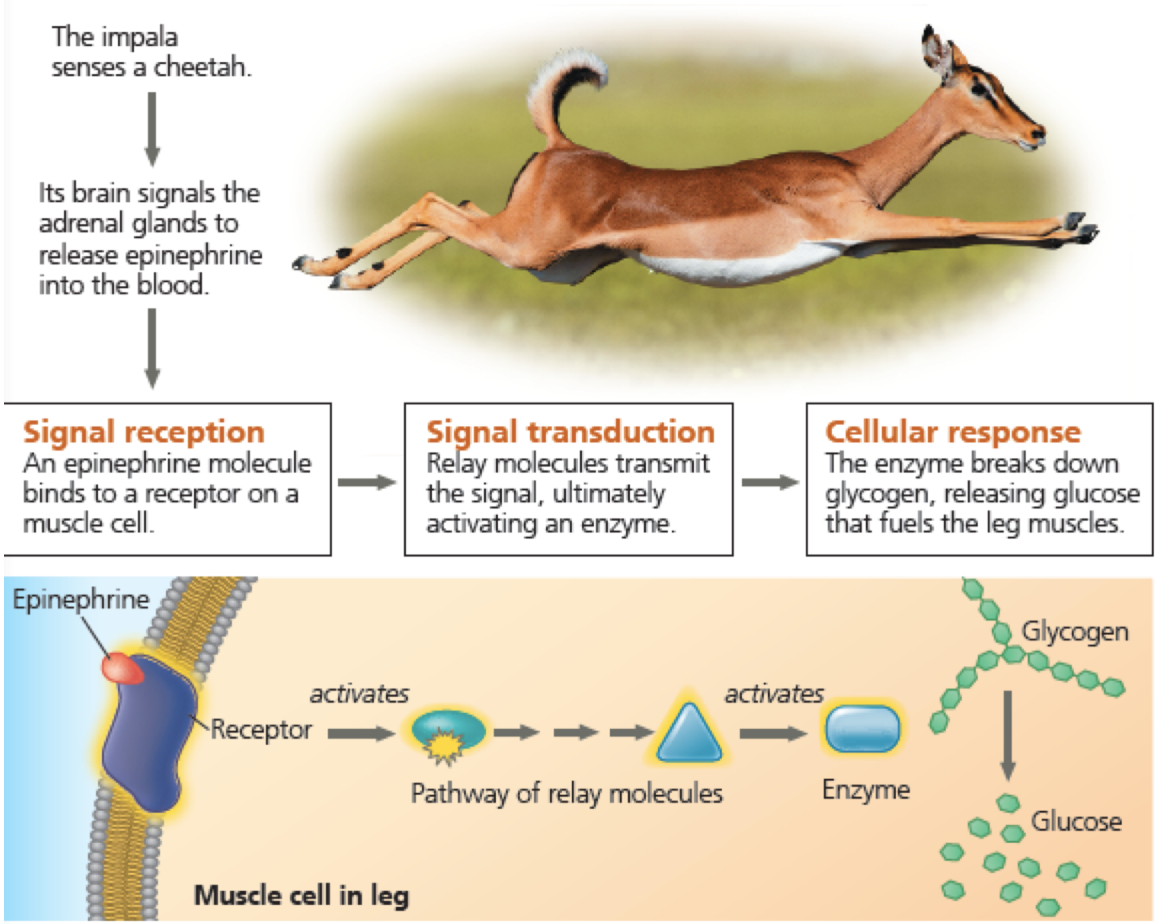
- Membrane se sastoje od lipida, proteina i ugljikohidrata
- Trenutni model membrane je tekući mozaik
- Lipidi čine strukturnu osnovu membrane
- Proteini proširuju funkciju membrane
- Ugljikohidrati služe za stanično prepoznavanje
- Membrana je polupropusna
- Molekule ulaze difuzijom, pasivnim ili aktivnim transportom
- Ostale tvari mogu ući fagocitozom, pinocitozom ili receptorskom endocitozom
- Tvari se izbacuju egzocitozom

Pitanja za ponavljanje:

1. Što je hipotonična, hipertonična i izotonična otopina?
2. Kako objašnjavamo mogućnost samoorganizacije membrana?
3. Što znači model tekućeg mozaika (Singer i Nicolson 1972.)? Zašto mozaik, a zašto tekući?
4. Što su polarne molekula, a što amfipatske?
5. Na čemu se zasniva hidrofilnost, a na čemu hidrofobnost?
6. Kakav je biokemijski sastav membrana?
7. Koju ulogu imaju pojedine molekularne skupine u membrani?

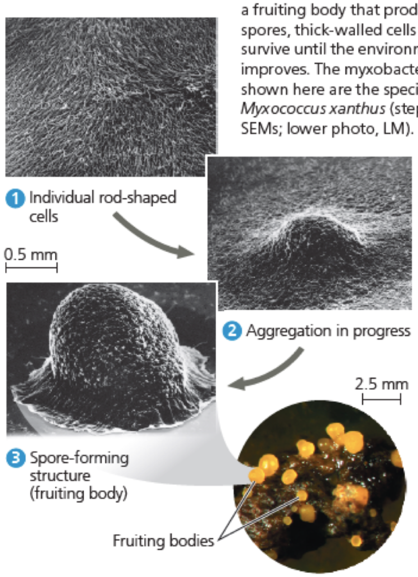
Stanična signalizacija

How does cell signaling fuel the desperate flight of an impala?

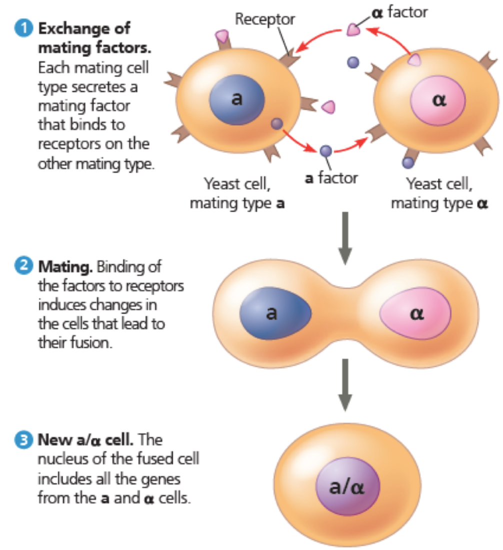


Stanična signalizacija kod jednostaničnih organizama

▼ **Figure 9.2 Communication among bacteria.** Soil-dwelling bacteria called myxobacteria ("slime bacteria") use chemical signals to share information about nutrient availability. When food is scarce, starving cells secrete a signaling molecule that stimulates neighboring cells to aggregate. The cells form a structure called a fruiting body that produces spores, thick-walled cells that can survive until the environment improves. The myxobacteria shown here are the species *Myxococcus xanthus* (steps 1–3, SEMs; lower photo, LM).

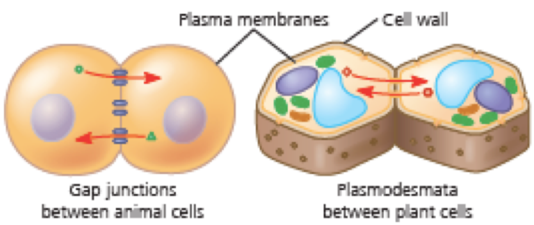


▼ **Figure 9.3 Communication between mating yeast cells.** *Saccharomyces cerevisiae* cells use chemical signaling to identify cells of the opposite mating type and initiate the mating process. The two mating types and their corresponding chemical signaling molecules, or mating factors, are called **a** and **α**.

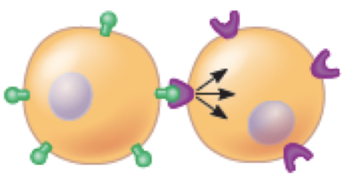


Vrste stanične signalizacije

▼ **Figure 9.4 Communication requiring contact between cells.**



(a) Cell junctions. Both animals and plants have cell junctions that allow molecules, including signaling molecules, to pass readily between adjacent cells without crossing plasma membranes.

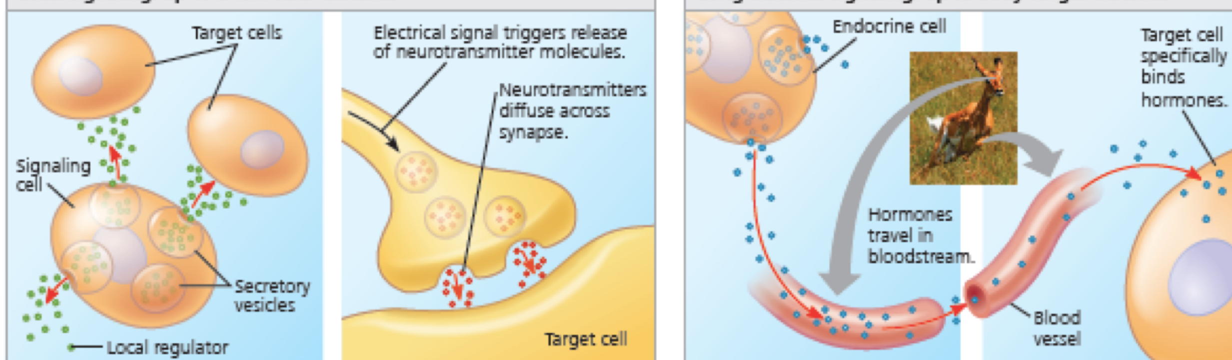


(b) Cell-surface molecules. In many animal cells, cell-surface molecules on adjacent cells interact with each other, resulting in a signal passing between the cells.

▼ **Figure 9.5 Local and long-distance cell signaling by secreted molecules in animals.** In both local and long-distance signaling, only specific target cells that can recognize a given signaling molecule will respond to it.

Local signaling: up to a few cells' distance

Long-distance signaling: up to body-length distance



(a) Paracrine signaling. A signaling cell acts on nearby target cells by secreting molecules of a local regulator (a growth factor, for example).

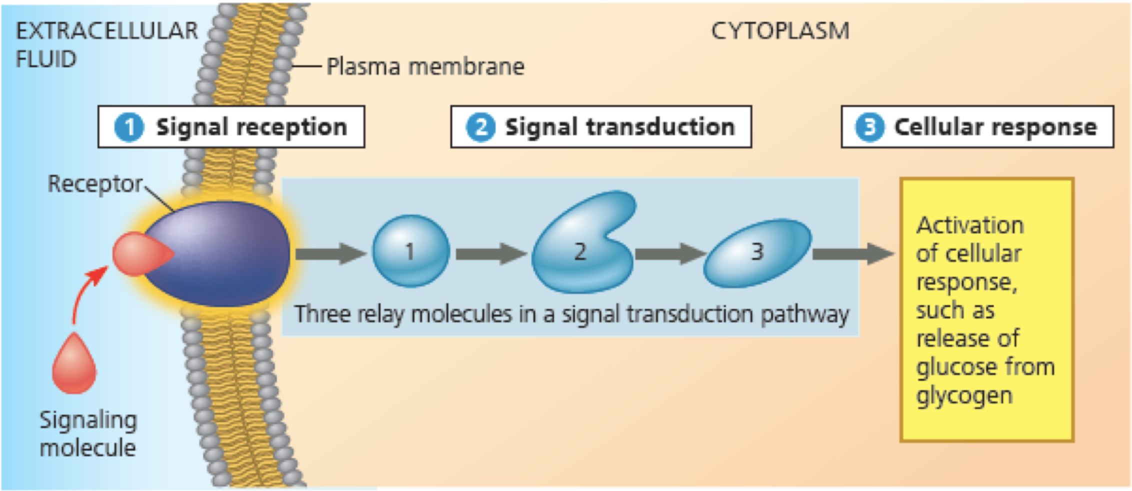
(b) Synaptic signaling. A nerve cell releases neurotransmitter molecules into a synapse, stimulating the target cell, such as a muscle or another nerve cell.

(c) Endocrine (hormonal) signaling. Specialized endocrine cells secrete hormones into body fluids, often blood. Hormones reach most body cells, but are bound by and affect only some cells.

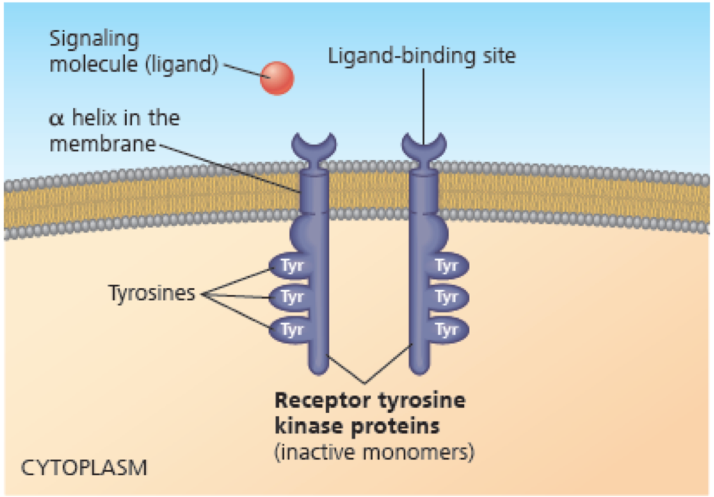
3 faze stanične signalizacije

▶ **Figure 9.6 Overview of cell signaling.** From the perspective of the cell receiving the message, cell signaling can be divided into three stages: signal reception, signal transduction, and cellular response. When reception occurs at the plasma membrane, as shown here, the transduction stage is usually a pathway of several steps (three are shown as an example), with each specific relay molecule in the pathway bringing about a change in the next molecule. The final molecule in the pathway triggers the cell's response.

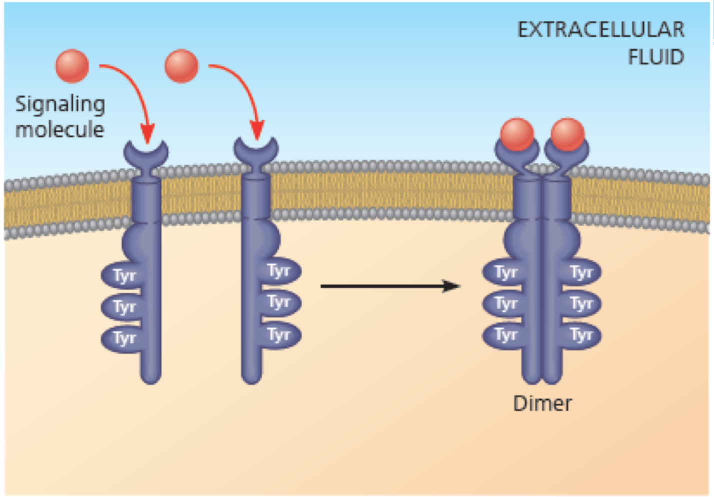
VISUAL SKILLS *Where would the epinephrine in Sutherland's experiment fit into this diagram of cell signaling?*



Primanje signala

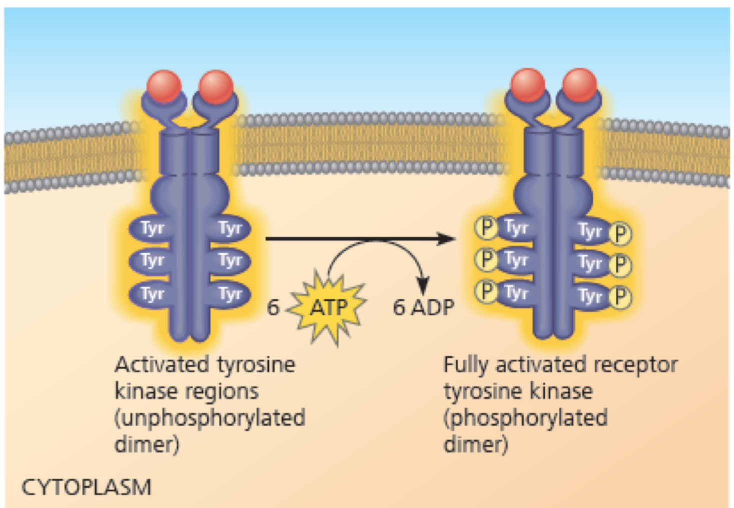


1 Many receptor tyrosine kinases have the structure depicted schematically here. Before the signaling molecule binds, the receptors exist as individual units referred to as monomers. Notice that each monomer has an extracellular ligand-binding site, an α helix spanning the membrane, and an intracellular tail containing multiple tyrosines.

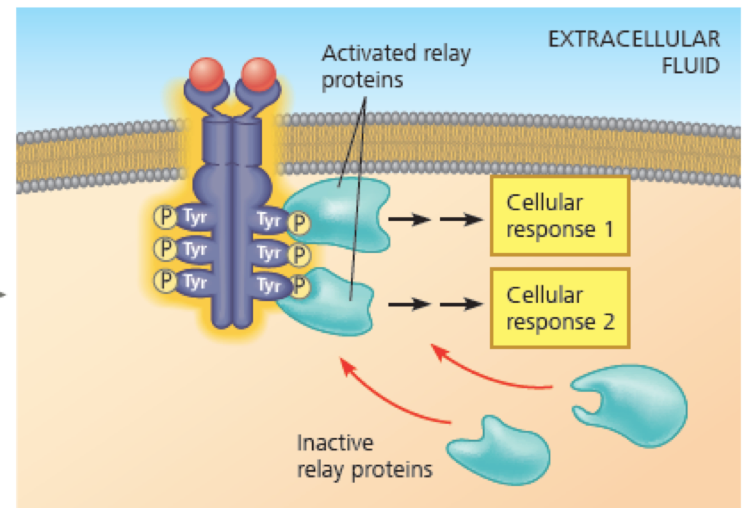


2 The binding of a signaling molecule (such as a growth factor) causes two receptor monomers to associate closely with each other, forming a complex known as a dimer, a process called dimerization. (In some cases, larger clusters form. The details of monomer association are a focus of current research.)

Provođenje signala

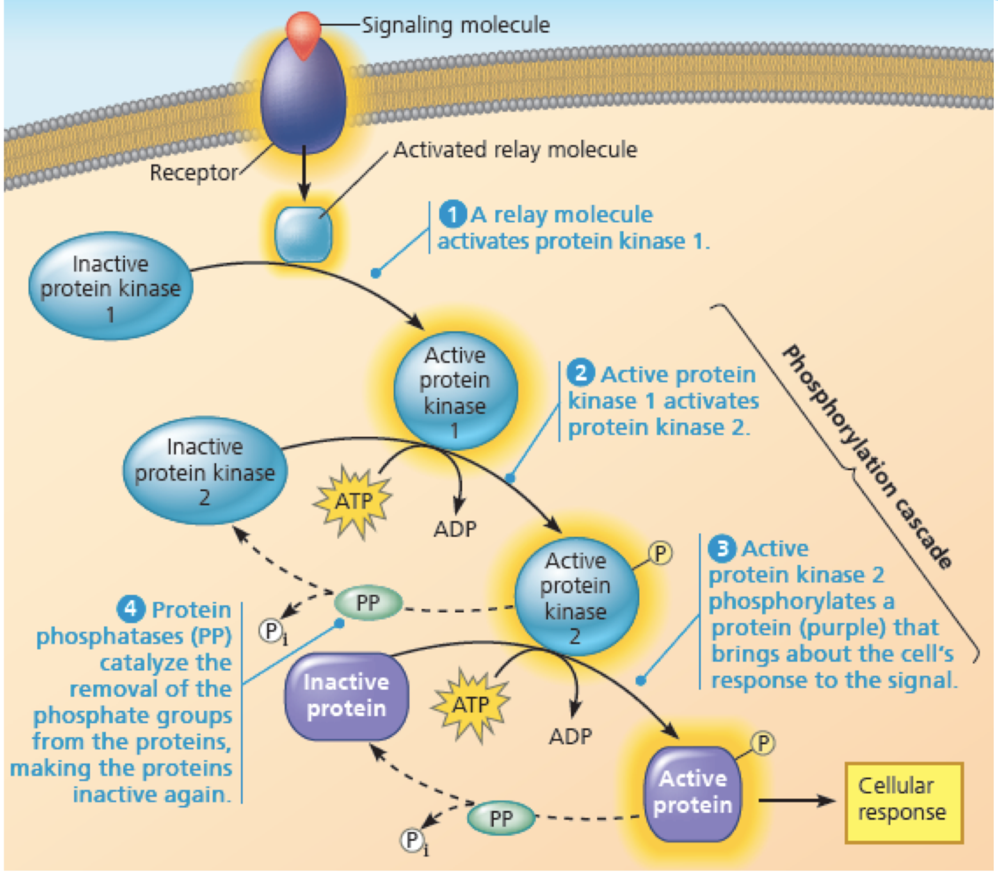


3 Dimerization activates the tyrosine kinase region of each monomer; each tyrosine kinase adds a phosphate from an ATP molecule to a tyrosine that is part of the tail of the other monomer.



4 Now that the receptor is fully activated, it is recognized by specific relay proteins inside the cell. Each such protein binds to a specific phosphorylated tyrosine, undergoing a resulting structural change that activates the bound relay protein. Each activated protein triggers a transduction pathway, leading to a cellular response.

Provođenje signala



Stanični odgovor

* Citoplazmatska aktivnost
* Aktivacija gena u jezgri
* Stanična smrt