

# Essential Cell Biology Third Edition

# Membrane Structure and Membrane Transport

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Sel hidup adalah suatu sistem yang dapat memperbanyak diri dan berada di dalam suatu "container". "Container" tsb adalah membran plasma. Tanpa membran plasma tidak ada sel → tidak ada kehidupan



## Membran sel bersifat "selective barriers". (A) prokariot; (B) Eukariot



Figure 11-2 Essential Cell Biology (© Garland Science 2010)



Figure 11-3 Essential Cell Biology (© Garland Science 2010)

## Function of cellular membranes:

#### 1. Boundary

Continuous, encloses the cell, nucleus, organelles

#### 2. Selective permeable barrier

Prevent exchange of molecules from one side to the other side. Prevent certain molecules from entering the cytoplasm

#### 3. Movement of soluble molecules

Makes possible the movement of certain substances from outside the cell into the cytoplasm

#### 4. Response to extracellular stimuli

receptor + ligand  $\rightarrow$  signal Transduction  $\rightarrow$ cell response Different types of cells have different receptor molecules

#### 5. Inter-celullar interaction

Plasma membrane mediates cell interaction in multicellular organism  $\rightarrow$  cell communication

#### 6. Place for biochemical activities

#### 7. Energy transduction

Involved in the process of energy transformation

# **STRUKTUR MEMBRAN PLASMA:**

- LIPID BILAYER
- PROTEIN MEMBRAN



Figure 11-4 Essential Cell Biology (© Garland Science 2010)

# Structure of plasma membrane



# Fluid mosaic model (Jonathan Singer & Garth Nicolson, 1960)

# **The Lipid Bilayer**

Amphipathic molecules  $\rightarrow$  spontaneously forms bilayer

- hydrophilic/ polar end & hydrophobic/ non polar end

 most abundant membrane lipids → phospholipids: polar head group & 2 hydrophobic hydrocarbon tails



(B)

(C)

#### 4 types of phospholipids in the mammalian plasma membranes



Figure 10-12. Molecular Biology of the Cell, 4th Edition.

Figure 10-2 part 3 of 3. Molecular Biology of the

Four major phospholipids in mammalian plasma membrane

(different head group). All lipid molecules are derived from glycerol, except sphingomyelin, which is derived from serine

## Table 10–1 Approximate Lipid Compositions of Different Cell Membranes

	PERCENTAGE OF TOTAL LIPID BY WEIGHT					
LIPID	LIVER CELL PLASMA MEMBRANE	RED BLOOD Cell Plasma Membrane	MYELIN	MITOCHONDRION (INNER AND OUTER MEMBRANES)	ENDOPLASMIC RETICULUM	E. COLI BACTERIUM
Cholesterol	17	23	22	3	6	0
Phosphatidylethanolamine	7	18	15	28	17	70
Phosphatidylserine	4	7	9	2	5	trace
Phosphatidylcholine	24	17	10	44	40	0
Sphingomyelin	19	18	8	0	5	0
Glycolipids	7	3	28	trace	trace	0
Others	22	13	8	23	27	30

Table 10-1 Molecular Biology of the Cell 5/e (© Garland Science 2008)







Packaging arrangement of lipid molecules in an aqueous environment: wedge-shaped molecules  $\rightarrow$  form micelles; cylindershaped phospholipid molecules  $\rightarrow$  form bilayers



The spontaneous closure of a phospholipid bilayer to form a sealed compartment. The closed structure is stable because it avoids the exposure of the hydrophobic hydrocarbon tails to water, which would be energetically unfavorable

# Lipid membrane

## Lipid and membrane fluidity

- Fluidity  $\rightarrow$  viscosity
- Mobility → structure
- interaction  $\rightarrow$  intercellular junction.
- Formation in certain structure: cell division, movement, endocytosis, secretion

Singer dan Garth Nicolson :

lipid bilayer  $\rightarrow$  lateral movement inside the membrane  $\rightarrow$  dynamic structure  $\rightarrow$  rapid interaction or semipermanent interaction

Flip flop  $\rightarrow$  flippase enzyme

 $\rightarrow$  passive transmembrane movement



Figure 4.27 The possible movements of phospholipids in a membrane. The types of movements in which membrane phospholipids can engage and the approximate time scales over which they occur. Whereas phospholipids move from one leaflet to another (called flip-flop) at a very slow rate, phospholipids diffuse laterally within a leaflet rapidly.



A cross-sectional view of black membrane, a synthetic lipid bilayer

The influence of cis-double bonds in hydrocarbon chains. Double bonds make it more difficult to pack the chain together, thereby making the lipid bilayer difficult to freeze. Unsaturated fatty acid chain is thinner



lipid bilayer of endoplasmic reticulum (ER)



NEW PHOSPHOLIPIDS ADDED TO CYTOSOLIC HALF OF THE BILAYER



FLIPPASE TRANSFERS PHOSPHOLIPIDS TO OTHER HALF OF BILAYER



symmetric growth of both halves of bilayer



# The fluidity of a lipid bilayer

Depends on:

- -Composition
- -Temperature

The lipid bilayer is not composed exclusively of phospholipids, also contains: cholesterol & glycolipids



as a space-filling model in (C).

# The asymmetry of the lipid bilayer



**Figure 10-11.** The asymmetrical distribution of phospholipids and glycolipids in the lipid bilayer of human red blood cells. The symbols used for the phospholipids are those introduced in <u>Figure 10-10</u>. In addition, glycolipids are drawn with hexagonal polar head groups (*blue*). Cholesterol (not shown) is thought to be distributed about equally in both monolayers.

Lipid asymmetry is functionally important  $\rightarrow$  many cytosolic proteins bind to specific lipid head groups found in the cytosolic monolayer of the lipid bilayer:

- protein kinase C (PKC): is activated in response to various extracellular signals; it binds to cytosolic face where phosphatidylserine is concentrated and requires this negatively charged phospholipid for its activity
- Phosphatidylinositol : PI-3-kinase (lipid kinase)
- Phospholipase C (PLC)



Some functions of membrane phospholipids in cell signaling:

A.Extracellular signals can activate PI 3-kinase, which phosphorylates inositol phospholipids in the plasma membrane. Various intracellular signaling molecules then bind to these phosphorylated lipids and are thus recruited to the membrane where they can interact and help relay the signal into the cell

B.Other extacellular signals activate phospholipases that cleave phospholipid. The lipid fragments then act as signaling molecules to relay the signal into the cell



Membrane proteins can be associated with the lipid bilayer in various ways: Transmembrane:

1. Trans-membrane proteins are thought to extend across the bilayer as a single  $\alpha$  helix

- 2. As multiple  $\alpha$  helices
- 3. As a rolled-up  $\beta$  sheet ( a  $\beta$  barrel)
- **Monolayer associated:** anchored to the cytosolic surface by an amphipatic  $\alpha$  helix that partitions into the cytosolic monolayer of the lipid bilayer through the hydrophobic face of the helix
- Lipid-linked: attached to the bilayer solely by a covalently attached lipid chain (fatty acid / prenyl group) in the cytosolic monolayer
- **Protein-attached:** via an oligosaccharide linker to phosphatidylinositol in noncytosolic monolayer & attached to the membrane by noncovalent interactions with other proteins

#### **Function of Membrane Protein** :



Cell surface identity marker



Enzyme



Cell adhesion



Cell surface receptor



Attachment to the cytoskeleton

#### TABLE 11-1 SOME EXAMPLES OF PLASMA MEMBRANE PROTEINS AND THEIR FUNCTIONS

FUNCTIONAL CLASS	PROTEIN EXAMPLE	SPECIFIC FUNCTION
Transporters	Na⁺ pump	actively pumps Na <sup>+</sup> out of cells and K <sup>+</sup> in (as described in Chapter 12)
Anchors	integrins	link intracellular actin filaments to extracellular matrix proteins (as discussed in Chapter 20)
Receptors	platelet-derived growth factor (PDGF) receptor	binds extracellular PDGF and, as a consequence, generates intracellular signals that cause the cell to grow and divide (as discussed in Chapter 18)
Enzymes	adenylyl cyclase	catalyzes the production of intracellular signaling molecule cyclic AMP in response to extracellular signals (as detailed in Chapter 16)







Figure 11-27 Essential Cell Biology (© Garland Science 2010)



Structure of membrane protein: Bacteriorhodopsin yang berperan sebagai pompa proton. Retinal (purple) and probable pathway taken by protons during the lightactivated pumping cycle. Polar amino acid chains involved in th H+ transfer process (red, yellow and blue)



Figure 11-31 Essential Cell Biology (© Garland Science 2010)

### Protein membran bersifat dinamis, dapat bergerak



Figure 11-32 Essential Cell Biology (© Garland Science 2010)



Figure 11-36 Essential Cell Biology (© Garland Science 2010)



#### 4 ways of restricting the lateral mobility of specific plasma membrane proteins:

The protein can self assemble into large aggregates  $\rightarrow$  can be tethered by interaction with assemblies of macromolecules: Outside the cell (B) Inside the cell (A) Interact with the proteins on the surface of another cell (C)

Cells can confine proteins and lipids to specific domains within a membrane. Asymmetric distribution of membrane proteins is often
essential for the function of epithelium: some are confined to the apical surface of the cells; others are confined to the basal and lateral surface. The plasma membrane is found to consist of at least 3 distinct domains.





The recognition of the cell-surface carbohydrate on neutrophils in the first stage of their migration out of the blood at sites of infection: specialized transmembrane protein, lectins, are made by the endothelial cells in the response to the chemical signals emanating from the site of infection. Lectins recognise the particular groups of sugars carried by glycolipids and blood vessel wall

Component	Composition	Function	How It Works	Example
Phospholipi d molecules	Phospholipid bilayer	Provides permeability barrier, matrix for proteins	Excludes water-soluble molecules from nonpolar interior of bilayer	Bilayer of cell is impermeable to water- soluble molecules, like glucose
Transmembrane proteins	Carriers	Transport molecules across membrane against gradient	"Escort" molecules through the membrane in a series of conformational changes	Glycophorin carrier for sugar transport
	Channels	Passively transport molecules across membrane	Create a tunnel that acts as a passage through membrane	Sodium and potassium channels in nerve cells
	Receptors	Transmit information into cell	Signal molecules bind to cell- surface portion of the receptor protein; this alters the portion of the receptor protein within the cell, inducing activity	Specific receptors bind peptide hormones and neurotransmitters
Interior protein network	Spectrins	Determine shape of cell	Form supporting scaffold beneath membrane, anchored to both membrane and cytoskeleton	Red blood cell
	Clathrins	Anchor certain proteins to specific sites, especially on the exterior cell membrane in receptor-mediated endocytosis	Proteins line coated pits and facilitate binding to specific molecules	Localization of low- density lipoprotein receptor within coated pits
Cell surface markers	Glycoproteins	"Self"-recognition	Create a protein/carbohydrate chain shape characteristic of individual	Major histocompatibility complex protein recognized by immune system
	Glycolipid	Tissue recognition	Create a lipid/carbohydrate chain shape characteristic of rissue	A, B, O blood group markers 31

#### Table 6.1 Components of the Cell Memorale

TABLE 12–1 A COMPARISON OF ION CONCENTRATIONS INSIDE AND OUTSIDE A TYPICAL MAMMALIAN CELL					
COMPONENT	INTRACELLULAR CONCENTRATION (mM)	EXTRACELLULAR CONCENTRATION (mM)			
Cations					
Na⁺	5–15	145			
K⁺	140	5			
Mg <sup>2+</sup>	0.5	1–2			
Ca <sup>2+</sup>	10-4	1–2			
H+	7 × 10 <sup>-5</sup> (10 <sup>-7.2</sup> M or pH 7.2)	4 × 10 <sup>-5</sup> (10 <sup>-7.4</sup> M or pH 7.4)			
Anions*					
CI-	5–15	110			

\* The cell must contain equal quantities of positive and negative charges (that is, be electrically neutral). Thus, in addition to Cl<sup>-</sup>, the cell contains many other anions not listed in this table; in fact, most cellular constituents are negatively charged (HCO<sub>3</sub><sup>-</sup>, PO<sub>4</sub><sup>3-</sup>, proteins, nucleic acids, metabolites carrying phosphate and carboxyl groups, etc.). The concentrations of Ca<sup>2+</sup> and Mg<sup>2+</sup> given are for the free ions. There is a total of about 20 mM Mg<sup>2+</sup> and 1–2 mM Ca<sup>2+</sup> in cells, but this is mostly bound to proteins and other substances and, for Ca<sup>2+</sup>, stored within various organelles.

## MEMBRANE TRANSPORT: Relative Permeability of phospholipid bilayer

The rate at which a molecule diffuse across a synthetic lipid bilayer depends on its size and solubility





## Setiap membrane sel memiliki karakteristik transporternya

Figure 12-5 Essential Cell Biology (© Garland Science 2010)

## Movement of substance through the membrane

- 1. Passive (by diffusion) : spontanenous movements from high concentration to the lower concentration
- 2. Active: use the energy



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## Na+ outside the cell is like water behind a high dam





The Na+K+ pump plays a central role in membrane transport in animal cells

Figure 12-9 Essential Cell Biology (© Garland Science 2010)



Figure 12-19a,b Essential Cell Biology (© Garland Science 2010)

#### TABLE 7-1 Mechanisms for Transporting Ions and Small Molecules Across Cell Membranes

Property	Passive Diffusion	Facilitated Diffusion	Active Transport	Cotransport*
Requires specific protein	-	+	+	+
olute transported gainst its gradient	-		+	+
Coupled to ATP hydrolysis	-		+	
Driven by movement of cotransported ion lown its gradient	_		Ξ	+
Examples of molecules ransported	O <sub>2</sub> , CO <sub>2</sub> , steroid hormones, many drugs	Glucose and amino acids (uniporters); ions and water (channels)	Ions, small hydrophilic molecules, lipids (ATP- powered pumps)	Glucose and amino acids (symporters); various ions and sucrose (antiporters

#### Transport Mechanism

\*Also called *secondary active transport*.

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# **Diffusion through the membrane**

Non-electrolite substance passively diffuse trough the membrane if:

- Concentration of one compound is higher than the other
- The membrane should be permeable to that compound
  - The compound can pass trough the membrane
  - Can pass trough aqueous pores (aquaporin : water)

#### **Determinant factor for penetration speed of solutes/ compound:**

- Solubility in nonpolar solvent
- Size

#### Diffusion of water trough the membrane $\rightarrow$ osmosis

- Semi-permeable membrane
   Water molecule moves faster trough cell membrane compared to soluble ions or polar compound
- Water moves trough semi-permeable membrane from high concentration to low concentration

# Ion diffusion trough the membrane

- 1. The membrane is very impermeable against charged molecules, including small ion .
- 2. Cell membrane has ion channel that is permeable for a certain ion

Ion channel opens and closes trough:

- voltage-gated channels → depends on the difference in ion charge in both sides of membrane, example: K-ion channel
- 2. ligand-gated channels → change in molecule conformation by the presence of bound molecule to this channel, e.g acetylcholine

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## Facilitated difussion

diffusion of compound from high concentration to low concentration. The compound binds to facilitative transporter

(integral protein)  $\rightarrow$  as a diffusion fasilitator on cell membrane



Figure 11-5 Molecular Biology of the Cell 5/e (© Garland Science 2008)

## Active Transport : against concentration gradient

a) needs energy

b) involve integral protein  $\rightarrow$  pump

- 1. Binds to hydrolize ATP : Na+/K+-ATP-ase (natrium-kalium pump )→ type-P pump
  - Ca2+-ATP-ase Ca transport from ER to extracellular part or inside ER
  - H+/K+-ATP-ase in epithelial cell in digestive system
- 2. Co-transport : bind to ion gradient
  - Transfer of glucosa : Na ion epithelial
  - Sucrosa H+ ion ( in plants )
- $\rightarrow$  simport
- → antiport



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# Animation: Na – K with hydrolised ATPase



**Figure 4.44** Schematic concept of the Na<sup>+</sup>/K<sup>+</sup>-ATPase transport cycle. Sodium ions (1) bind to the protein on the inside of the membrane. ATP is hydrolyzed, and the phosphate is transferred to the protein (2), changing its conformation (3) and allowing sodium ions to be expelled to the external space. Potassium ions then bind to the protein (4), and then the phosphate group is removed (5), which causes the protein to snap back to its original conformation, moving the potassium ions to the inside of the cell (6). Unlike facilitated diffusion, the changes in the shape of the protein are driven by energy from ATP hydrolysis, which allows the transport system to move these ions against their electrochemical gradients. Note that the actual Na<sup>+</sup>/K<sup>+</sup>-ATPase is a tetramer consisting of two different membrane-spanning subunits; a larger  $\alpha$  subunit, which carries out the transport activity, and a smaller  $\beta$  subunit, which functions primarily in the maturation and assembly of the pump within the membrane.

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## **Co-transport : animation**



#### example : Oralit - Pocari



Oralit & pocari contains sugar and Na+ that can avoid the body from dehydration  $\rightarrow$  because always induce water uptake

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# **Oral Rehydration Salts and Ionic Drinks**



- General composition of ionic drinks: water, sugar, Sodium chloride (Na<sup>+</sup> dan Cl<sup>-</sup>), Kalium (K<sup>+</sup>)
- Our body needs ions: (Na<sup>+</sup>), (K<sup>+</sup>), (Ca<sup>2+</sup>), (Mg<sup>2+</sup>), (Cl<sup>-</sup>), (HPO<sub>4</sub><sup>2</sup>-), dan (HCO<sub>3</sub>-)
- Ions cannot be produced by our body 2014 MIT/EGR/RRE/AB,SITH ITB

# Mechanism in membrane Transport: intravenous



http://www.colfir.net/rof/chantal.proulx/images/circulation/aquaporine.jpg

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# **Mechanism HCI Secretion**



 Hydrogen ions are formed from the dissociation of water molecules.

 Carbonic anhydrase converts CO<sub>2</sub> and water to  $HCO_3^-$  and  $H^+$ . •HCO<sub>3</sub><sup>-</sup> is exchanged for Cl<sup>-</sup> on the basal side of the cell and  $HCO_3^$ diffuses into the blood. K<sup>+</sup> and Cl<sup>-</sup> ions diffuse into the canaliculi. Hydrogen ions are pumped out of the cell into the canaliculi in exchange for K<sup>+</sup>, via the H+/K+ ATPase

## Various Anesthetic Drugs (and its mechanism) **Example:** Cocaine

A stimulant of a central nervous system and appetite suppressant.

This drug binds to dopamine transporter protein  $\rightarrow$  presynaptic neuron can't reuptake the dopamine from postsynaptic neuron  $\rightarrow$  pre-synaptic neuron will in polarization state.



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Figure 15-12s Molecular Biology of the Cell S/s (© Garland Science 2008)

TABLE 12-2 SOME EXA	MPLES OF TRANSPORTERS		
TRANSPORTER	LOCATION	ENERGY SOURCE	FUNCTION
Glucose transporter	plasma membrane of most animal cells	none	passive import of glucose
Na <sup>+</sup> -driven glucose pump	apical plasma membrane of kidney and intestinal cells	Na <sup>+</sup> gradient	active import of glucose
Na <sup>+</sup> -H <sup>+</sup> exchanger	plasma membrane of animal cells	Na <sup>+</sup> gradient	active export of H <sup>+</sup> ions, pH regulation
Na <sup>+</sup> -K <sup>+</sup> pump (Na <sup>+</sup> -K <sup>+</sup> ATPase)	plasma membrane of most animal cells	ATP hydrolysis	active export of Na $^{\scriptscriptstyle +}$ and import of K $^{\scriptscriptstyle +}$
Ca <sup>2+</sup> pump (Ca <sup>2+</sup> ATPase)	plasma membrane of eucaryotic cells	ATP hydrolysis	active export of Ca <sup>2+</sup>
H+ pump (H+ ATPase)	plasma membrane of plant cells, fungi, and some bacteria	ATP hydrolysis	active export of H <sup>+</sup>
H+ pump (H+ ATPase)	membranes of lysosomes in animal cells and of vacuoles in plant and fungal cells	ATP hydrolysis	active export of H <sup>+</sup> from cytosol into vacuole
Bacteriorhodopsin	plasma membrane of some bacteria	light	active export of H <sup>+</sup>







## **TIPE TRANSPOR MEMBRAN APA YANG TERJADI?**

Figure 12-22 Essential Cell Biology (© Garland Science 2010)



#### TIPE TRANSPORT MEMBRAN YANG TERJADI PADA DAUN MIMOSA?

Figure 12-27 Essential Cell Biology (© Garland Science 2010)





The squid Loligo has a nervous system that is set up to allow the animal to respond rapidly to threats in its environment.

Figure 12-32 Essential Cell Biology (© Garland Science 2010)





Figure 12-35 Essential Cell Biology (© Garland Science 2010)



Figure 12-39b Essential Cell Biology (© Garland Science 2010)







influx of Cl<sup>-</sup> tends to keep membrane polarized, decreasing the likelihood of firing an action potential

Figure 12-43 Essentia

TABLE 12-3 SOME EXAMPLES OF ION CHANNELS				
ION CHANNEL	TYPICAL LOCATION	FUNCTION		
K* leak channel	plasma membrane of most animal cells	maintenance of resting membrane potential		
Voltage-gated Na <sup>+</sup> channel	plasma membrane of nerve cell axon	generation of action potentials		
Voltage-gated K <sup>+</sup> channel	plasma membrane of nerve cell axon	return of membrane to resting potential after initiation of an action potential		
Voltage-gated Ca <sup>2+</sup> channel	plasma membrane of nerve terminal	stimulation of neurotransmitter release		
Acetylcholine receptor (acetylcholine- gated Na <sup>+</sup> and Ca <sup>2+</sup> channel)	plasma membrane of muscle cell (at neuromuscular junction)	excitatory synaptic signaling		
Glutamate receptors (glutamate-gated Na <sup>+</sup> and Ca <sup>2+</sup> channels)	plasma membrane of many neurons (at synapses)	excitatory synaptic signaling		
GABA receptor (GABA-gated Cl <sup>-</sup> channel)	plasma membrane of many neurons (at synapses)	inhibitory synaptic signaling		
Glycine receptor (glycine-gated Cl⁻ channel	plasma membrane of many neurons (at synapses)	inhibitory synaptic signaling		
Stress-activated cation channel	auditory hair cell in inner ear	detection of sound vibrations		





Table 12-3 Essenti