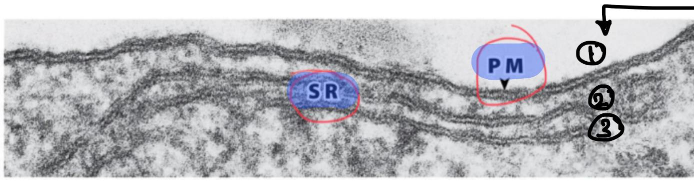
Chapter 8

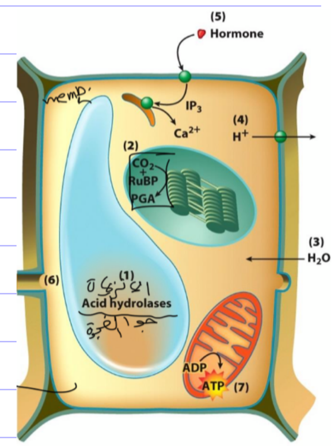
① Plasma membrane: 5–10 nm thick (can't be observed by LM)
the 2 hydrophilic heads are dark in EM.
⟶ all membranes (plasma, cytoplasmic, nuclear) in plants, animals or microorganisms are same ultrastructure!! (same structure & function)



The trilaminar appearance of memb. as plasma and sarcoplasmic memb.

* An overview of membrane functions:

① Compartmentalization: memb. form cont. sheets that enclose intracellular compartments. (acid hydrolases within vesicles)



② scaffold for biochemical activities: memb. provides a framework that organizes enzymes of effective activities. (carbon fixation)

③ Selectively permeable barriers: regulates exchang of substances btw comp. (H_2O) { تنظيم الدخول والخروج }

④ Transporting solutes: memb. proteins facilitate the movement of substances. (H^+) { عندها بروتينات بتحمل وبتنقل المواد }

⑤ responding to external signals: memb. receptors sense the signals from outside to specific ligands. (Hormones)

⑥ intracellular interaction: memb. mediate recognition and interaction between adjacent cells. (plasmodesmata)

⑦ Energy transduction: (تحول الطاقة من شكل لآخر) memb. trasduce photosynthetic energy from chemical ⟶ ATP and store it.

⟶ A brief history of study on plasma membrane:
membs. were found to be lipids because of their dissolving power was matched to that of oil.
the lipid bilayer accounted for the 2:1 ratio of lipids to cell surface. (bi: ثنائي، طبقتين من الليبيدات)
⟶ the most favored orientation was that hydrophilic must face the aqueous solutions.

⇒ evidences that it's not just lipids?

1) Lipid Solubility: was not the sole to a sub. to pentrate it.

2) Surface tension: was calculated much lower than pure lipids; explained by the presence of proteins.

* proteins in lipid bilayer → individual / complexes

* the plasma memb is dynamic; 'cuz of its fluidity.

→ the memb. is lipid–protein held together by non-covalent bonds

the lipid bilayer is a structural backbone and barrier to prevent random movement of sub.

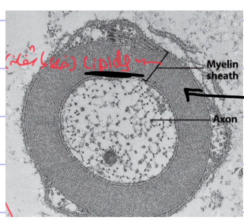
→ The ratio of lipid to protein varies depending on the type of:

a) cellular membrane. b) the organism. c) the cell.

∴ ratio of lipids to cell surface = 2:1 / Lipids to protein: varies

The myelin sheath has a low protein–lipid ratio. [lipid ↑]

inner mitochondrial memb. has a high protein–lipid ratio [protein ↑]



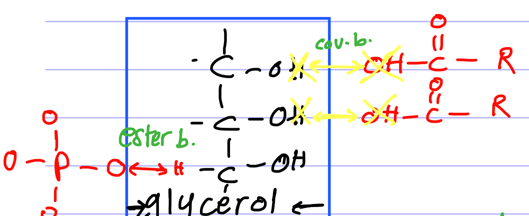
Cause: acts as electrical insulation ([illegible]) to the nerve cell. by a thick layer of lipids ([illegible])

Cause: contains the protein carriers of ETC.

Membrane Lipids (→ phospholipids) are amphipathic with 3 main types:

1 phosphoglycerids: diacylglycerides (2 of fatty acids attached to glycerol) attached to phosphate group by ester bond.

∴ they're phospholipids built on a glycerol backbone.



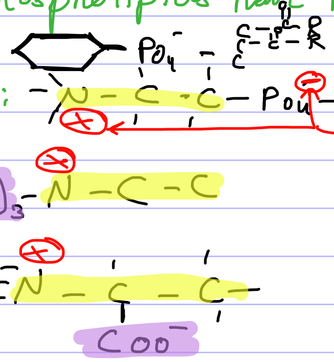
→ most phospholipids have hydrophilic groups attached to PO_4^-

→ inositol:

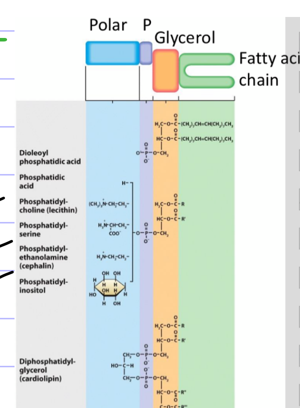
→ ethanolamine:

→ choline: $(CH_3)_3$

→ serine:



hydrophilic head ✓



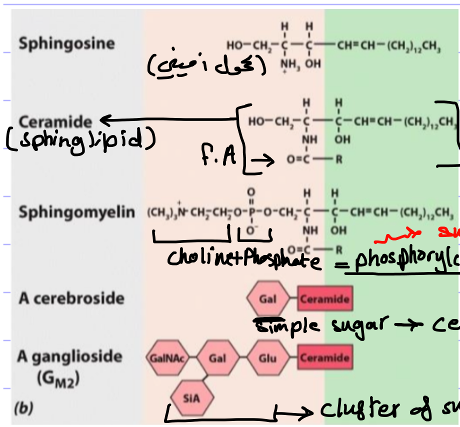
Phosphoglyceride

fatty acyl chains are hydrophopic, unbrancheel hydrocarbons (16 to 22 c.), it may be saturated, monounsaturated, polyunsaturated.
، unsat. وموجودة sat. موجودة بكثرة لمّا ←

*Sphingolipids: are ceramides formed by (Sphingosin to fatty acids)
what is sphingosin ?? it's an amino alchohol containe a long hydrocarbon chain.

∴ Sphingolipids consist of sphingosine linked to fatty acids by its amino group, called a ceramide.

* glycolipids play a role in infectious diseases like toxins that cause cholira, botulisme and influenza virus, that they target the cell by binding to cell surface gangliosides. (SIA)



Ceramide ← (sphing lipid)

F.A →

substitution

choline+Phosphate = phosphorylcholine + ceramide = sphingomyelin

Simple sugar → cerebroside (glycolipid) = galactocerbroside. → nervous sys. موجود بكثرة في

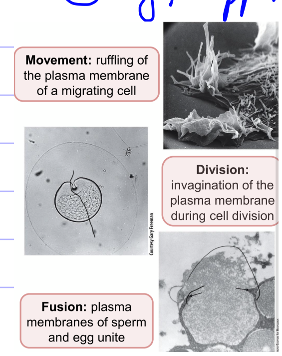
cluster of sugars has SIA ⇒ ganglioside (glycolipid)

⇒ Cholesterol: Smaller and Less amphipathic lipid that fond in ANIMALS only.
* 50% of animal membrane Lipids = Sterols
* it has OH⁻ group is oriented toward memb. surface. (external)
* its carbon rings are flat and rigid that prevent the movement of phospholipid bilayer fatty acid tails.

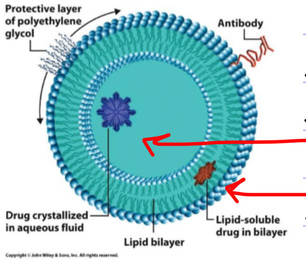
The nature and importance of lipid bilayer :-
* cell membranes have unique (distinct) composition of lipids, differing in Lipid type, head groups and fatty acyl chains.
* Lipid composition determines → Physical State of memb. (L, solid)
→ influence memb. protein activity.

(precursor) Lipids —influence→ messengers that regulate cellular functions.

↝ The entire lipid bilayer is 6 nm thick. (60 Å) $60 * 10^{-10}$ m = $6 * 10^{-9}$ m
it's always cont. and unbroken sheets, forming extensive interconnected networks within the cell. (Mitochondria, chloroplast and Golgi apparatus) are double memb. bounded organells.
* lipid bilayer is flexible ; as these 3 :→
it helps to maintain the internal cell composition and seperate the electric charge across the plasma memb.



memb. ل, أهمل لدراسة



Liposomes: synthetic vesicles

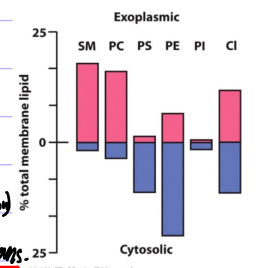
→ the lipid bilayer can self-assemble early in vitro.
→ phospholipids assemble walls that is fluid-filled spheral vesicles (liposomes)
→ can deliver drugs or DNA within the body; they can be linked to its wall or in its lumen.
→ They are specific to a target cell, contain a specific proteins on its surface specific binding to it.
* how not to classify it strange (no phagocytosis)?
by protective layer that protect it from immune destruction.

Cealyx, a stealth liposome containing doxorubicin "therapy to breast cancer".

⇒ The assymetry of lipid bilayer :-

consist of 2 distinct leaflets that have a distinctly different lipid comp
← كل layer كأنك لـ تركيب الخاص بالليبيدات فتختلف خصائصه الكيميائية والفيزيائية
منها (independent, semi-stable).

→ outer leaflet : higher PC + SM
→ inner leaflet : higher PI + PS + PE
→ CI (cholesterol) [outer] = [inner]

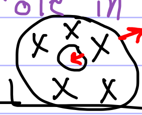


* PE (inner) provides memb. dynamics, curvature it for division. (fusion)
* PI (inner) can be phosphorylated to phosphoinositid for signal trans.
* PS → (outer) : on aging lymphocytes marks for destruction by macrophages.
  → (inner) : PS⁻ bind to lysine and arginine on adjacent proteins (!!موجبة)

SM: sphingomyelin
PC: phosphatidylcholine
PS: phosphatidylserine
PE: phosphatidylethanolamine
PI: phosphatidylinositol
CI: cholesterol

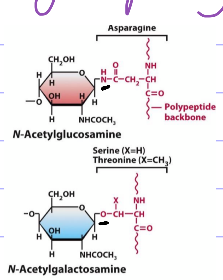
Membrane Carbohydrates:

→ plasma membrane have (2-10)% by weight with 90% glycoproteins and 10% glycolipids. it play a role in mediating the interaction of a cell and sorting protein to diff. cellular compartments.
→ carboh. don't like cytosol



Glycoproteins (90%)

have short, branched hydrophilic oligosaccaride (<15 sugars); which can be attached to amino group by N-linkage or O-linkage.

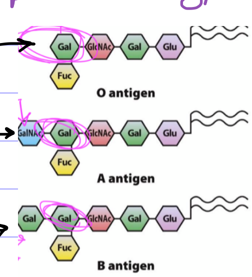


Two types of linkages that join sugars to a polypeptide chain

Glycolipids (10%)

of RBCs plasma memb determine person's B type.

O : مش مرتبط بأشي
A : N-acytelgalactosamine ← مرتبط ب
B : Galactose ← مرتبط ب
AB ← مرتبط ب Both



Blood-group antigens
(gangliosids)

* **Membrane Proteins:-** it attaches to the bilayer asymmetrically. giving a sidedness of the membrane.

Integral (dynamic ↔ laterally movement)

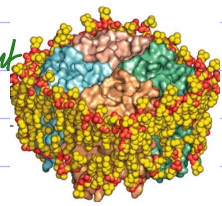
(25−30)% of proteins
60% of current drug targets

→ Channel protein cores are hydrophilic but aquaporines cores are hydrophobic

function: receptors, channels or agents that trasfers ē during photosynthesis or respiration.

* within the lipid bilayers, their fatty acyl chains are attached by van der waals to the integral proteins to form a lipid shell

non-covalent (van der waals)



Peripheral (dynamic ↔ can be released or recruited; weak bond: [illegible])

outside the bilayer "attached non-covalently to it" (lipid-protein)

(fibriller network) – membrane "skeleton" to provide a mechanical support
– anchor for integral proteins.
– enzymes, specialized coats or factors that transmit transmembrane signals.

* peripheral proteins associate with the memb. by weak electrostatic bonds, can be solubilized by extraction with high salt concentration solutions.

Lipid-anchored

found in:

outer leaflet: Glycophosphotadylinositol (GPI) which anchors the lipid bilayer to the protein
can be released by inositol-specific phopholipases.
"GPI-anchored" proteins
– receptors, enzymes and cell adhesion.
– e.g.:- scrapie protein → PrP^c ←

inner leaflet: anchored by long hydrocarbon chain.
e.g.:- Src + Ras that are implicated in transformation of normal cell → malignant cell

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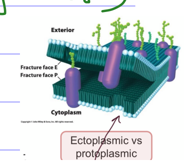
* specific sites of memb. proteins can form important functional interactions with specific lipid molecules.
e.g.: KcsA K^+ channels (tetrameric): 4 subunits ⟷ (with) anionic lipids
it doesn't open normally in a bilayer that lacks a specific lipid molecule.

* usually are globular proteins (to has a core for transfering subs.)
* it was understood by the results of freeze-fracture replication. →



* Membrane fluidity:- (physical state)

1. if the temperature of bilayer is kept relatively warm (37°C), the lipid exists in a relative fluid state → individual lipids can rotate around their axis or move laterally within the plane.

2. **TABLE 4.2** Melting Points of the Common 18-Carbon Fatty Acids

Fatty acid	cis Double bonds	M.p. (°C)
Stearic acid	0	70
Oleic acid	1	13
Linoleic acid	2	−9
Linolenic acid	3	−17
Eicosapentanoic acid (EPA)*	5	−54

The higher degree of unsaturation the lower the melting point.
+ the shorter the fatty acyl the lower the melting point.

→ Cholestrol abolishes the sharp transition temps. and creates a condition of intermediate fluidity; (1) it increases memb. durability ([illegible]) & decreases memb. permeability.
([illegible])

* Internal temperature can fluctuate the temp. so cells respond to it by altering phospholipid composition. if the temp. is lowered, cells can remodel memb. to make them more cold resistant. (How?) كيف أعدل على الغشاء على أنه يصير يقاوم للبرد

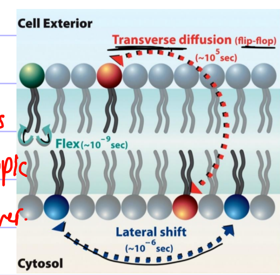
→ Remodeling is accomplished by: ① desaturating single bonds to form = bonds.
② reshuffling (تبديل) chains btw different lipids to form 2 unsaturated fatty acyl chains.

by desaturases

phospholipases (splits the glycerol backbone to fatty acid chain) & acyl-transferases (tranfer F.A. chains between phospholipids)

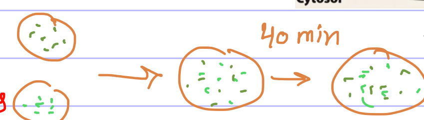
* lipid Rafts: Cl + SM on the outer leaflet, that provide a favorable environment for cell receptors and GPI-anchored proteins.

The dynamic nature of plasma memb.:-



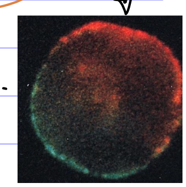
The phospholipid can move: 1- laterally: it takes seconds, in the same leaflet.
2- flip-flops it takes hours to days, it is in 2 leaflets
↳ (why?) the hydrophilic head has to pass through hydrophobic tails. (so?) flippase moves them from one leaflet to another.

The diffusion of proteins after cell fusion:-



Labled proteins have shown that memb. proteins can move btw fused cells.

توزع البروتينات (تحرك)



أحمر وأخضر

* Cell fusion is induced by virus or polyethylen glycol.

restrictions:
* Proteins can be labled and tracked with ① fluroscence recovery after photobleaching (FRAP) & ② single particle tracking (SPT)

الاختلافات بين FRAP & SPT ?

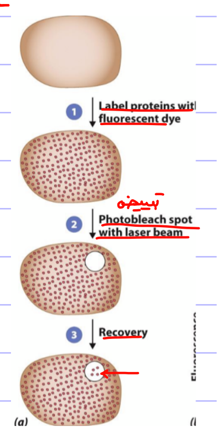
* SPT is applied on individual proteins + it uses TIRF: total internal reflection fluerescent microscope which has a high tracking ability.
* the rate of diffusion by FRAP is different depending on protein's type.
← نتائج: — مش نفس السرعة من البروتينات، حجمه + إذا كان متحرك أسرع lipid bilayer is
صفوفه في الـ plasma memb.

* epithelial cells of intestinal wall or Kidney tubules are highly polarized whose surfaces carry out different functions.

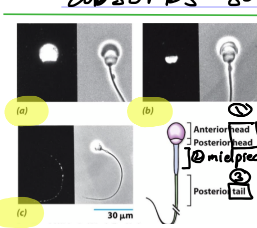
The apical plasma memb. absorbs sub. from lumen

The lateral plama memb. interacts with neighboring epithelial cells.

The basal adheres to an underlying basement memb.



FRAP



sperms may have the most highly differentiated structure
each having its own specialized function
غشاء واحد ← بس بروتينات مختلفة

8.8 on slides : Band 3 is 2 homodimers of glycoproteins that exchanges Cl^- and HCO_3^- across RBC memb.

*Glycophorin A: is a dimer with 16 oligosaccarides chains bearing -ve charge to prevent cells from clumping.

*RBC (erythrocyte) is the most studied memb. → preperation ?? "ghosts" can be prepared by hemolysis (put it in hypotonic soln.) for isolation of intact membs.

*Memb. proteins can be purified by fractionation by SDS-PAGE electrophoresis.
الفصل الكهربائي

*The major component of internal memb. skeleton is spectrin.

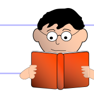
Spectrin ←non. cov.→ Ankyrin ←non. cov.→ Band 3 (memb. surface)
Spectrin ⇄ Actin (cytoplasmic proteins)
→ tropomyosin

*8.9 :-

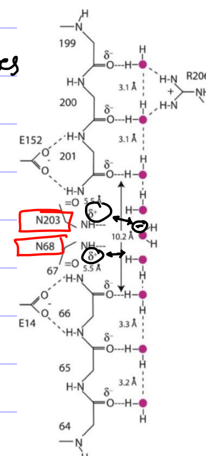
Selective permeability allows for separation and exchange of materials across the plasma membrane

Substances move across membranes by:
1) simple diffusion through the lipid bilayer;
2) simple diffusion through an aqueous, protein-lined channel;
3) diffusion facilitated by a protein transporter;
4) active transport, requires an energy-driven protein "pump" to move substances against a concentration gradient

*8.10 : easy , just read it from slides



A pair of positive charged residues (N203) & (N68) attract the oxygen of each water molecule to prevent H- bonds.



← aquaporin channel (hydrophopic core to pass the water through it)

*8.11 , 8.12 ; 8.13 : on slides