Lecture: Biological membranes

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Biological membranes

A. In aqueous solution, phosphoglycerides spontaneously form into a lipid bilayer, with a back-to-back arrangement of lipid monolayers.

- Polar head groups (Hydrophilic) are in contact with the aqueous environment, nonpolar tails (Hydrophobic) are buried within the bilayer, the major force driving the formation of lipid bilayers is hydrophobic interaction.

- The arrangement of hydrocarbon tails in the interior (depending on the saturation of the fatty acids) can be:
  1) Rigid → (if rich in saturated fatty acids).
  2) Fluid → (if rich in unsaturated fatty acids).

- Fatty acids types:
  1) Saturated F.As → no double bonds / straight hydrocarbon tail.
  2) Unsaturated F.As → contain one or more double bonds / may occur in Cis (i.e., with angle/kink) or Trans configuration.

B. Liposomes → Lipid bilayer separating an aqueous internal compartment from the bulk aqueous phase, and they are used for drug transport and in gene delivery.

C. Micelles → The form in which lipids are absorbed, they are closed lipid monolayers with a fatty acid core (i.e., hydrophobic tails inside) and polar surface (i.e., hydrophilic heads outside).

  ** Micelles may contain bile salts / cholesterol / complicated lipids (e.g., lecithin) / lipid-soluble vitamins (A, D, E, K).

  ** Once they reach the small intestine, protein are added to the micelles forming chylomicrons which are then distributed to the blood and lymphatic system (i.e., lacteals in small intestine) for fat utilization.
• Lipid Movement in Membranes:
  1) **Lateral diffusion** → **Rapid**
  2) **Transverse diffusion** (i.e., **flip-flop**) → **Slow**.

• The presence of **cholesterol** increases rigidity with **heat**, membranes become more disordered; the transition temperature is higher for more rigid membranes; (Less rigid membranes → Lower transition temperature).

• **Plant** membranes have a **higher** percentage of **unsaturated** fatty acids than animal membranes.

• The presence of **cholesterol** is characteristic of **animal** rather than plant membranes. (cholesterol is originally from animals and it’s impossible to be found in plants)

• **Animal** membranes are **less fluid** (**more rigid**) than plant membranes. (The membranes of prokaryotes → contain no appreciable amounts of steroids, are the most fluid).

• Membranes may be composed of all the following: (**sphingomyelin** / **cerebroside** / **ganglioside** / **phosphoacylglycerol** / **cholesterol** [inside or outside]).

** Recall from the previous lecture → Deficiency in degradation of gangliosides and the demyelination of nerve cells in both the brain and the spinal cord leads to MS (i.e., Multiple Sclerosis التصلب اللويحي).

• In the fluid mosaic structure of the lipid membrane we can notice the red and green markers which symbolize carbohydrates that are essential in the membrane acting as **cell markers** for **cell recognition**.

** Cell recognition helps the cell to identify self-cells from invaders, viruses or even bacteria.

• Carbohydrates added to proteins are called **glycoproteins**.
• Carbohydrates added to lipids are called **glycolipids**.
• Carbohydrates may be:
  1) **Oligosaccharides** → (3-10 monosaccharides).
  2) **Polysaccharides** → (>10 monosaccharides).
**Membrane proteins:**

1. **Integral/Transmembrane protein** → exposed to the aqueous environment on both sides of the membrane and it’s used to transport molecules across the membrane. *(N-terminal)* outside for the attachment of drugs/prostaglandins/hormones and *(C-terminal)* inside anchored to another membrane by *N-myristoylation/S-palmitoylation*

2. **Peripheral protein** → located on the surface of the membrane.

### ((Diffusion))

<table>
<thead>
<tr>
<th>Simple / Passive</th>
<th>Facilitated</th>
<th>Active</th>
<th>Secondary transport</th>
</tr>
</thead>
<tbody>
<tr>
<td>- <em>It doesn't require energy.</em></td>
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<td>- Requires energy.</td>
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<td>- The diffusion of molecules <em>from higher to lower concentrations</em> because of the semipermeable membrane. <em>(with conc. gradient)</em></td>
<td>- A <em>carrier/channel</em> embedded in the membrane is needed to transport molecules such as <em>(glucose, Na+, Cl-)</em>.</td>
<td>- Energy from ATP hydrolysis.</td>
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<td>- Linear (i.e., having only one dimension) in the concentration difference.</td>
<td>- The rate of this diffusion is <em>saturable</em> with respect to the <em>concentration</em> difference between the two phases. <em>(velocity stabilizes)</em></td>
<td>- Against conc. gradient.</td>
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<tr>
<td>- The dependence on temperature is <em>mild.</em></td>
<td>- <em>(with conc. gradient)</em></td>
<td>- Examples: 1. <em>(Ca+ pump)</em> 2. <em>(H+ pump)</em> 3. <em>(Na+/K+ ATPase)</em> <em>(3Na+ outside / 2K+ inside)</em></td>
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<td>- The temperature dependence substantially different due to the presence of an activated binding event.</td>
<td>- The asymmetry of the cell membrane is due to the distribution of carbohydrates, proteins and ions all over its surfaces.</td>
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![Diagram](image)
Asymmetry of the Na+ -K+ transport system in plasma membranes

Energy Transduction by Membrane Proteins

Facilitated diffusion.

LDL receptor (i.e., Low-Density Lipoprotein) is the carrier for bad cholesterol → enters the cell by endocytosis → distributes the cholesterol to the peripheral tissues for (estrogen, progesterone and testosterone) synthesis → ends up with recycling its receptors → back to the cell membrane.

-The plateau in this line represents the saturation effect that is seen whenever a carrier protein is involved in transport.
VITAMINS:

1) → Water-soluble vitamins: “their excess won’t lead to diseases, they are excreted with urine.”

2) → Lipid-soluble vitamins:

- **Retinoids** →
  - A family of molecules that are related to retinol (vitamin A).
  - Are essential for (vision/ reproduction/ growth/ maintenance of epithelial tissues).
  - **Retinoic acid**, derived from oxidation of dietary retinol, mediates most of the actions of the retinoids, except for vision, which depends on retinal, the aldehyde derivative of retinol.

- **Retinol** →
  - A primary alcohol containing a β-ionone ring with an unsaturated side chain.
  - Found in animal tissues as a retinyl ester with long-chain fatty acids.

- **Retinal** →
  - The aldehyde derived from the oxidation of retinol. Retinal and retinol can readily be interconverted.

- **Retinoic acid** →
  - The acid derived from the oxidation of retinal. Retinoic acid cannot be reduced in the body → cannot give rise to either retinal or retinol.

- **β-carotene** →
  - Plant foods (e.g., carrots) contain β-carotene, which can be oxidatively cleaved in the intestine to yield two molecules of retinal.

  **In humans, the conversion is inefficient, and the vitamin A activity of β-carotene is only about one sixth that of retinol.**

  **Vitamin A function** → serves as the site of the primary photochemical reaction in vision.

  **Vitamin A deficiency** causes Nyctalopia (i.e., Night Blindness الخشى الليلي).

  **Remember: the suffix (-ol) → alcohol // (-al) → aldehyde.**

  **Excess fat-soluble vitamins cause toxicity.**

\[\begin{array}{ccc}
\text{Retinol} & \xrightarrow{\text{Oxidation}} & \text{Retinal} \\
\xrightarrow{\text{Reduction}} & & \xrightarrow{\text{Oxidation}} \text{Retinoic acid}
\end{array}\]
Vitamin A

Skeletal formula of retinoic acid

Colored vision
Vitamin D

- **Vitamin D Function**: Regulates calcium (and phosphorus) metabolism.
- **Found in** dairy products.
- **Distribution**:

1. **Diet**: Ergocalciferol (vitamin D2) من الأكل
   - Found in plants and cholecalciferol (vitamin D3).
   - Found in animal tissues, are sources of preformed vitamin D activity.
   - Ergocalciferol and cholecalciferol differ chemically only in the presence of an additional double bond and methyl group in the plant sterol.

2. **Endogenous vitamin precursor**;
   - 7-Dehydrocholesterol, an intermediate in cholesterol synthesis, is converted to cholecalciferol in the dermis and epidermis of humans exposed to sunlight (i.e., UV light) Preformed vitamin D is a dietary requirement only in individuals with limited exposure to sunlight.
   - Exposure to UV light must be (before 10 am and after 4 pm) to form cholecalciferol. The sunlight between (10am-4pm) leads to various skin problems and cancers.

- **Vitamin D deficiency** → (In adults → Osteomalacia // (In children → Rickets) إكتئب
- Has a regulatory function in **blood clotting (coagulation)**.
- The principal role of vitamin K is in the **post-translational modification of various blood clotting factors**, in which it serves as a **coenzyme** in the **carboxylation** of certain glutamic acid residues present in these proteins.
- Vitamin K converts **inactive** clotting factors into **modified** clotting factors. (e.g., the conversion of **Thrombin** into **Fibrin** [i.e., blood clots] in the presence of Ca$^+$ by a carboxylation reaction)
- **Vitamin K** exists in several forms:
  1) In **plants** phylloquinone (vitamin K1).
  2) In **intestinal bacterial flora** (vitamin K2) → For **therapy**, a **synthetic** derivative of vitamin K (Menadione).

Vitamin E

- Serves as an **anti-oxidant**; necessary for **reproduction** in rats and maybe in humans.
- Many claims have been made about vitamin E's potential to promote health and prevent and treat disease. The mechanisms by which vitamin E might provide this protection include its function as an **antioxidant** and its roles in **anti-inflammatory processes**, **inhibition of platelet aggregation**, and **immune enhancement**.
- **Antioxidant** nutrients like vitamin E **protect cell constituents from the damaging effects of free radicals** that, if unchecked, might contribute to **cancer development**.
  **Remember:** **Glutathione** / **cysteine** / **glycine** are **anti-oxidants** too.
- **Vitamin E** deficiency → **hemolysis** of RBC's (i.e., **hemolytic anemia**).
- All **canned food** lack vitamin C and contain vitamin E to **avoid oxidation** and **prevent color transfer**.
  **Remember:** **Vitamin C** deficiency → **Scurvy**.
What Are Prostaglandins and Leukotrienes, and What Do They Have to Do with Lipids?

- The unsaturated fatty acid arachidonic acid is the precursor of prostaglandins and leukotrienes, compounds that have a wide range of physiological activities:

1. Stimulation of smooth-muscle contraction.
2. Induction of inflammation are common to both classes of compounds. Elevate body temperature (fever) & causing pain.
3. Prostaglandins are also involved in control of blood pressure.
4. Inhibition of blood-platelet aggregation.

A. Prostaglandins

- Two groups:
  1. PGE for ether-soluble.
  2. PGF for phosphate. (fosfat in Swedish=buffer-soluble).

- Derived from the prostate gland, they were isolated from seminal fluid in 1935 by a Swedish physiologist. Prostaglandins are produced by the seminal vesicles. Many other tissues secrete prostaglandins for various functions.
- Each group contains numerous subtypes, named PGE1, PGE2, and so forth.
Prostaglandins act in many tissues by **regulating the synthesis of the intracellular messenger 3,5-cyclic AMP (cAMP)**. Because cAMP mediates the action of diverse hormones, the prostaglandins affect a wide range of cellular and tissue functions.

- They have a **six-membered ring** containing an ether. They are produced by platelets (i.e., thrombocytes) and act in the formation of blood clots and the reduction of blood flow to the site of a clot.

- The nonsteroidal anti-inflammatory drugs (NSAIDs) — (e.g., aspirin/ibuprofen) → were shown to inhibit the enzyme prostaglandin H2 synthase (i.e., cyclooxygenase or COX), which catalyzes an early step in the pathway from arachidonate to prostaglandins and thromboxanes.

- PTT test → **Partial Thromboplastin Time** to test blood coagulation levels.

**B. Thromboxanes**

- (Also called prostaglandin I2 or PGI2) is a prostaglandin member of the eicosanoid (20 polyunsaturated fatty acids) family of lipid molecules.

- Prostacyclin is produced in the endothelial cells (lining the walls of arteries and veins) from prostaglandin H2 (PGH2) by the action of the enzyme prostacyclin synthase.

- They inhibit platelet activation and are also an effective vasodilator.

**C. Prostacyclins**

- First found in leukocytes (WBC’s) contain three conjugated double bonds.

- Powerful biological signals. For example, leukotriene D4, derived from leukotriene A4, induces contraction of the muscle lining the airways to the lung.

- Overproduction of leukotrienes causes asthmatic attacks, and leukotriene synthesis is one target of antiasthmatic drugs such as prednisone. The strong contraction of the smooth muscles of the lung that occurs during anaphylactic shock is part of the potentially fatal allergic reaction in individuals hypersensitive to (bee stings/penicillin/other agents).

- Bronchial asthma treatment → **Inhaled Corticosteroids**.