Plasma membrane

- A human cell, like all cells, is surrounded by an outer border that encloses its cytoplasmic compartments, called the **plasma membrane**, **plasmalemma,** or **cell membrane**.
- **It is a thin semi permeable membrane, composed from lipids (40%), proteins (50%) and carbohydrates (5%) that surrounded cytoplasm of a cell and control the passage of substances into and out of the cell.**
- The integrity and function of the plasma membrane are necessary to the life of the cell.
- Membranes range from 7.5 to 10 nm in thickness so that it's visible only with the transmission electron microscope (TEM).
- **Light microscope (LM):** appears as a very thin limiting border line**.**
- **Electron microscope (EM):** the cell membrane has **a tri-laminar** appearance under TEM after fixation in osmium tetroxide, two electron dense lines (2.5 nm each) separated by an electron lucent intermediate zone (2.5-3 nm).
  Due to the deposition of reduced osmium on the polar heads of the phospholipids, the outer sugar chains, and associated membrane proteins produces the two dark outer lines enclosing the light band of osmium-free fatty acids (Figure1)

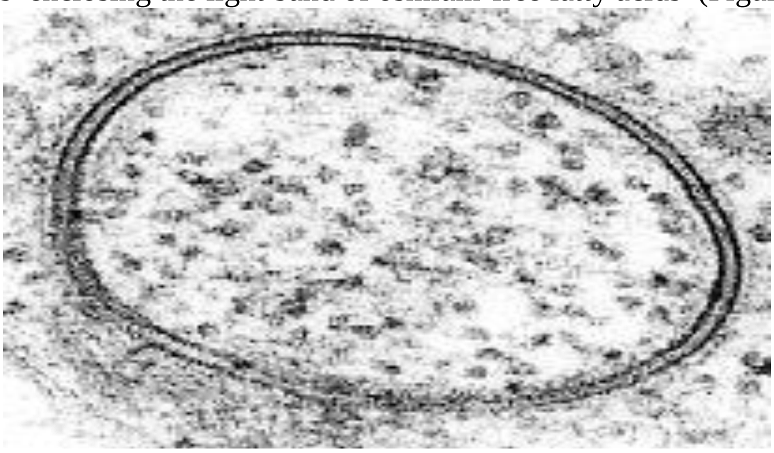

Figure 1: The cell membrane can stain as two dark layers plus one clear layer from the gap between them, similar to two stacked bread sandwiches with space between them.

- ✓ The first widely accepted model of the plasma membrane's structure was proposed in 1935 by Hugh Davson and James Danielli; it was based on the appearance of the plasma membrane in early electron micrographs. They theorized that the structure of the plasma membrane resembles a **sandwich**, with protein being analogous to the bread and lipids being analogous to the filling. In the 1950s, advances in microscopy, notably transmission electron microscopy (TEM), allowed researchers to see that the core of the plasma membrane consisted of a double, rather than a single, layer. A new model that better explains both the microscopic observations and the function of that plasma membrane was proposed by S.J. Singer and Garth L. Nicolson in 1972.
- ✓ The explanation proposed by Singer and Nicolson is called the **fluid mosaic model**. **The fluid mosaic model** describes the structure of the plasma membrane as a mosaic of components including phospholipids, cholesterol, proteins, and carbohydrates that gives the membrane a fluid character (Figure 2).

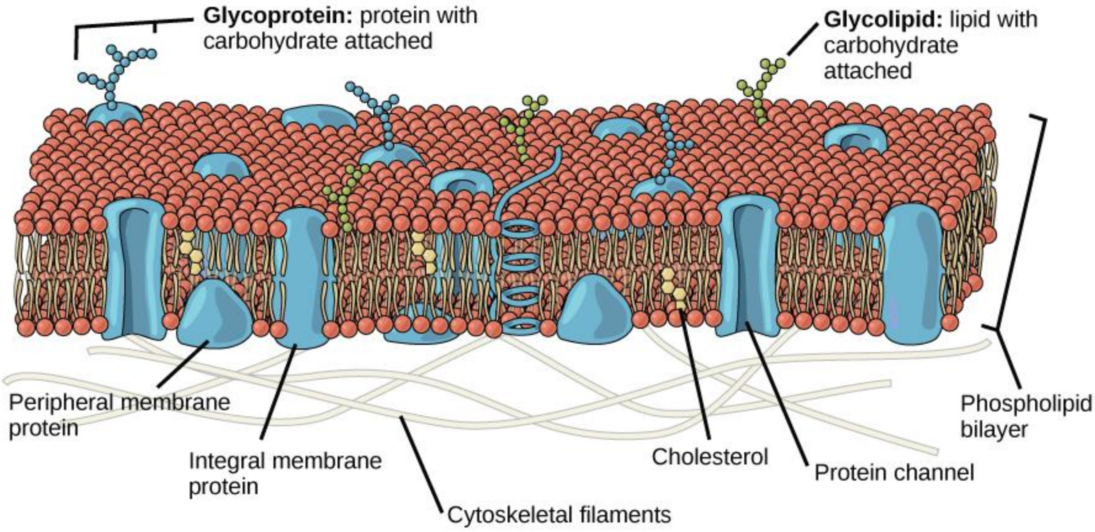

Figure 2: ***The fluid mosaic model of the plasma membrane describes the plasma membrane as a fluid combination of phospholipids, cholesterol, and proteins. Carbohydrates attached to lipids (glycolipids) and proteins (glycoproteins) extend from the outward-facing surface of the membrane.***

- ✓ The plasma membrane is a phospholipid bilayer (fluid at body temperature) with attached or embedded proteins. The proteins are able to change their position by moving laterally; the **fluid-mosaic model** is a working description of membrane structure. It states that the protein molecules form a shifting pattern within the fluid phospholipid bilayer. (Figure 2).
- ✓ The plasma membrane must be very flexible to allow certain cells, such as red blood cells and white blood cells, to change shape as they pass through narrow capillaries.

Chemical structure of plasma membrane

1. **Membrane lipids:** lipid constitutes 40% of the mass of most cell membranes, although this proportion varies depending on the type of cell. Include phospholipids and cholesterol.

i. **Phospholipids**: The fundamental building blocks of all cell membranes, which are amphipathic molecules, consisting of two hydrophobic fatty acid chains linked to a phosphate- containing hydrophilic head group (Figure 3).

   A. The hydrophilic (**polar**) **heads** of the phospholipids molecules face the intracellular and extracellular fluids, consisting of:
      - Phosphoric acid group
      - Glycerol backbone

   B. The hydrophobic (**non polar**) **tail** face each other in the membrane interior, consist of:
      - Saturated fatty acid
      - Unsaturated fatty acid, this double bond introduces a kink in the chain which reduces phospholipid packing (double bond increase fluidity).

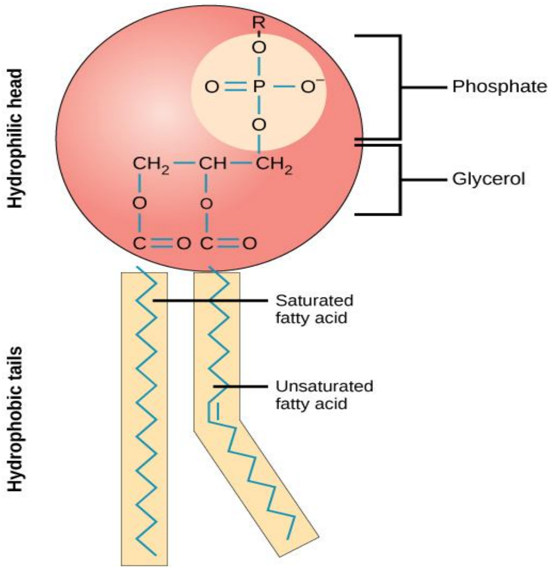

Figure 3: This phospholipid molecule is composed of a hydrophilic head and two hydrophobic tails. The hydrophilic head group consists of a phosphate-containing group attached to a glycerol molecule. The hydrophobic tails, each containing either a saturated or an unsaturated fatty acid, are long hydrocarbon chains.

At body temperature (37C), the phospholipid bilayer of the plasma membrane has the consistency of olive oil. The entire phospholipids molecules can move side away, all these means that the cell is pliable.

ii. Cholesterol: (see the yellow structure in figure 2)

- Cholesterol represent approximately 50% of the total membrane lipids
- Cholesterol is reduces the permeability of the membrane to the most biological molecules.
- Regulate and reduce the fluidity of phospholipids bilayer.
- Have important role in stability of cell membrane and make it more rigid, without cholesterol the membrane easily split apart.

Ratio of phospholipid to cholesterol is 1:1

2. Membrane proteins: (see the blue structure in figure 2)

Proteins constituting approximately 50% of the mass of most cell membranes. Membrane proteins carry out the specific functions of the different membranes of the cell. These proteins are divided into **two** general classes, based on the nature of their association with the membrane:

I. **Integral membrane proteins**: (closely attached protein) are large protein molecules and embedded directly within the lipid bilayer, integral membrane proteins called **transmembrane proteins or called integrins** span the lipid bilayer with proteins exposed on both sides of the membrane proteins linked to both cytoplasmic protein filaments and extracellular matrix(ECM) components. These linkages produce a continuous exchange of influences, in both directions, between the ECM and the cytoplasm. And represent important structures for transportation of various molecules though cell membrane includes protein channels, protein carrier or called transporter, or specific receptors such as G-protein specific receptor. (Will discussed these types in next lecture).

II. **Peripheral membrane proteins**: are small protein molecules and not inserted into the lipid bilayer but are associated with the membrane indirectly (loosely attached), found on the exterior and interior surfaces of membranes, attached either to integral proteins or to phospholipids (head group). Peripheral proteins, along with integral proteins, may serve as enzymes, as structural attachments for the fibers of the cytoskeleton, or as part of the cell's recognition sites. These are sometimes referred to as "cell-specific" proteins.

3. **Membrane glycolipids and glycoprotiens:** Short chains of sugars (oligosaccride) are attached to the outer surface of some protein or lipid molecules. The carbohydrate chains of glycoproteins are serving as the **fingerprints** of the cell. These carbohydrate chains, specific to each cell, help mark the cell as belonging to a particular individual. They account for why people have different blood types, for example.

i. **Glycolipids**:
- Have a structure similar to phospholipids except that the hydrophilic head is a variety of sugars joined to form a straight or branching carbohydrate chain.
- Glycolipids have a protective function.

ii. **Glycoprotein (glycocalyx):**
- The carbohydrate chains of the glycoproteins form a carbohydrate coat that envelops the outer surface of the plasma membrane. On the inside, proteins serve as links to the cytoskeletal filaments and on the outside carbohydrate some serve as links to extracellular matrix.

- Hav**e** an important role in cell recognition, cell to cell attachment or adhesions and act as receptor for chemical messenger or binding sites for different protein hormones**.**
- Cell coat present on special type of cell and don't present on others make some cell effect with virus, bacteria, hormones and drugs.

How Viruses Infect Specific Organs

Specific glycoprotein molecules exposed on the surface of the cell membranes of host cells are exploited by many viruses to infect specific organs. For example, **HIV** is able to penetrate the plasma membranes of specific kinds of white blood cells called T-helper cells and monocytes, as well as some cells of the central nervous system (see figure 4). The **hepatitis virus** attacks only liver cells. These viruses are able to invade these cells because the cells have binding sites on their surfaces that the viruses have exploited with equally specific glycoproteins in their coats. **Also, COVID-19 enters specific cells that have specific receptors.** Human ACE2 (Angiotensin I-Converting Enzyme-2) and TMPRSS2 (TransMembrane Protease Serine 2) are two surface membrane receptors that are involved in **SARS-CoV-2 entry** into host target cells (see figure 5).

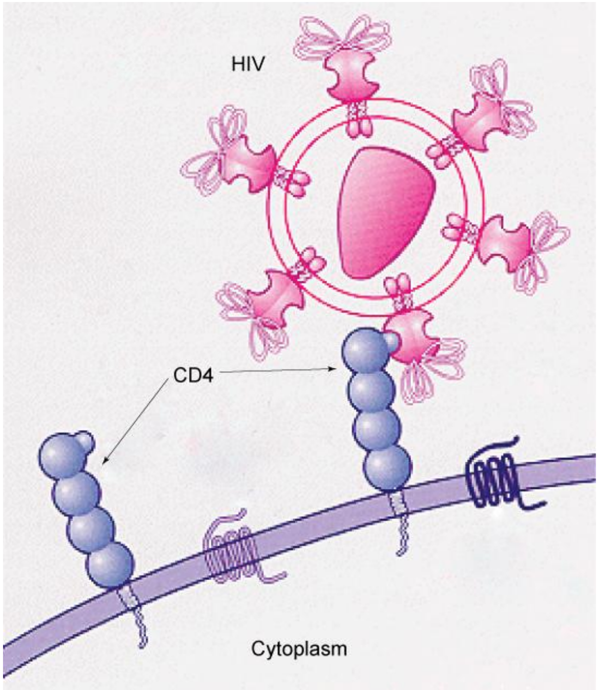

Figure4: HIV docks at and binds to the CD4 receptor, a glycoprotein on the surface of T cells, before entering, or infecting, the cell.

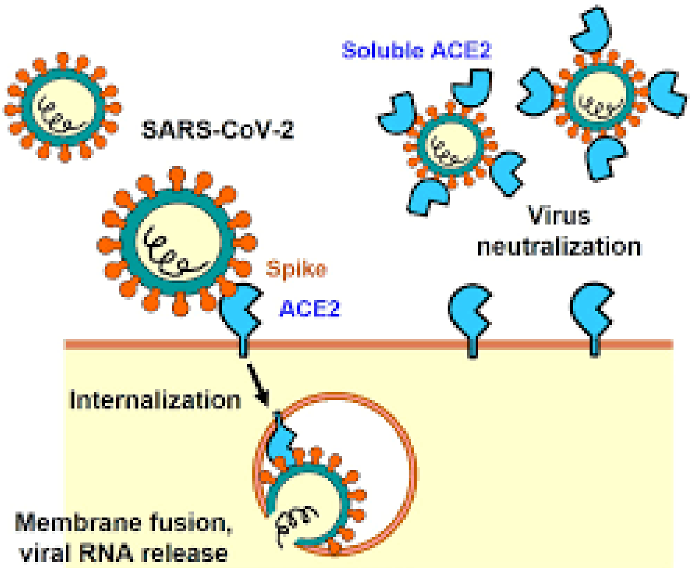

Figure5: ACE2-mediated cell entry of SARS-CoV-2 and inhibition of virus infection by recombinant soluble ACE2 protein.

Functions of Plasma Membrane

1. **Physical barrier:** Establishes a flexible boundary, protects cellular contents, and supports cell structure. Phospholipid bilayer separates substances inside and outside the cell.
2. **Selective permeability:** Regulates entry and exit of ions, nutrients, and waste molecules through the membrane.
3. **Electrochemical gradients:** Establishes and maintains an electrical charge difference across the plasma membrane.
4. **Communication:** Contains receptors that recognize and respond to molecular signals.