VIVEKANANDA COLLEGE
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NAAC ACCREDITED 'A' GRADE

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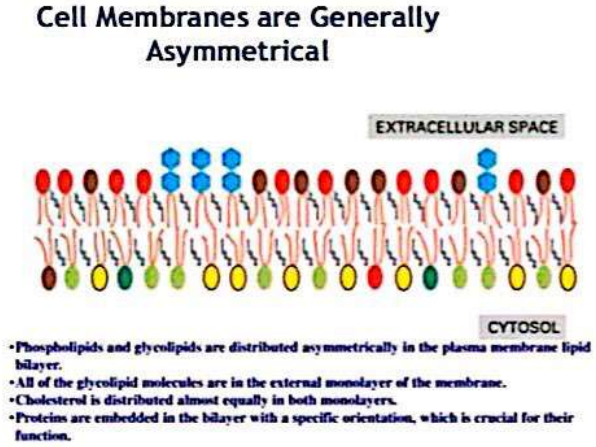
MEMBRANE ASYMMETRY

The cell membrane tends to have different composition on one side of the membrane than on the other side of the membrane. The differences can be caused by the different ratios or types of amphipathic lipid-based molecules, the different positioning of the proteins (facing in or facing out), or the fixed orientations of proteins spanning the membrane. Additionally, there are different enzymatic activities in the outer and inner membrane surfaces.

The reason the cell membrane is asymmetric is because when the proteins are synthesised by the preexisting membranes, they are inserted into the membrane in an asymmetric manner. The asymmetry of the cell membrane allows the membrane to be rigid and allows the cell to have a different intracellular environment from the existing extracellular environment. Additionally, the cell membrane's phospholipids are distributed asymmetrically across the lipid bilayer, in a phenomenon called membrane phospholipid asymmetry. There are three mechanisms for transmembrane movement of phospholipids: 1) spontaneous diffusion, 2) facilitated diffusion, 3) ATP-dependent active translocation.



Integral Proteins and Glycolipids Bind Asymmetrically to the Lipid Bilayer

The spaces inside and outside the closed compartments formed by cellular membranes usually have very different compositions. Such asymmetry is an essential aspect of the structure and function of biological membranes, and is reflected in the asymmetric structure of all integral membrane proteins. That is, each type of integral membrane protein has a single, specific orientation with respect to the cytosolic and exoplasmic faces of a cellular membrane, and all molecules of any particular integral membrane protein share this orientation.This absolute asymmetry in protein orientation confers different properties on the two membrane faces. Proteins have never been observed to flip-flop across a membrane; such movement, involving a transient movement of hydrophilic amino acid and sugar residues through the hydrophobic interior of the membrane, would be energetically unfavorable. Accordingly, the asymmetry of a membrane protein, which is established during its biosynthesis and insertion into a membrane, is maintained throughout the protein's lifetime.

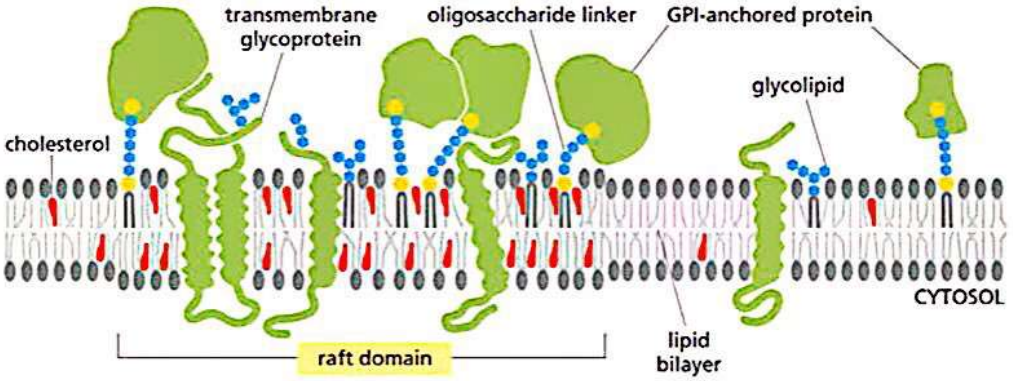
Both glycoproteins and glycolipids are especially abundant in the plasma membrane of eukaryotic cells but are absent from the inner mitochondrial membrane, the chloroplast lamellae, and several other intracellular membranes. Almost invariably, attached carbohydrates are localized to the exoplasmic membrane face. Glycolipids are always found

in the exoplasmic leaflet of membranes and are situated mainly, but not exclusively, on the surface membrane of cells. As with glycoproteins, their polar carbohydrate chains face outward toward the environment and away from the cell.

The Phospholipid Composition Differs in Two Membrane Leaflets

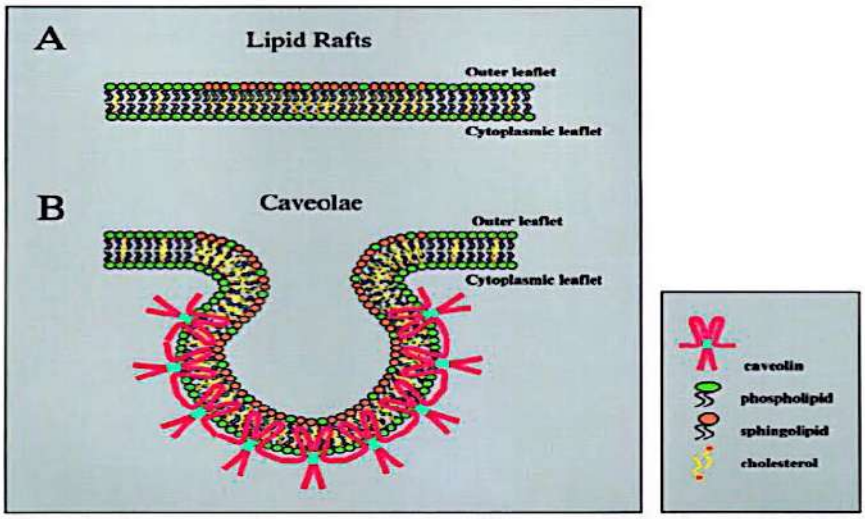
Most kinds of phospholipid, as well as cholesterol, are generally present in both membrane leaflets, although they are often more abundant in one or the other. For instance, in plasma membranes from human erythrocytes and certain canine kidney cells grown in culture, almost all the sphingomyelin and phosphatidylcholine, both of which have a positively charged head group are found in the exoplasmic leaflet. In contrast, lipids with neutral or negative polar head groups (e.g., phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol) are preferentially located in the cytosolic leaflet. Phosphorylated forms of phosphatidylinositol are cleaved as a result of cell stimulation by certain hormones, generating in the cytosol soluble forms of the "head groups" that affect many aspects of cellular metabolism.

The relative abundance of a particular phospholipid in the two leaflets of a plasma membrane can be determined based on its susceptibility to hydrolysis by phospholipases, enzymes that cleave the phosphoester bonds that connect the phospholipid head groups.Phospholipids in the cytosolic leaflet are resistant to hydrolysis by phospholipases added to the external medium, because the enzymes cannot penetrate to the cytosolic face of the plasma membrane. It is not clear how these differences in lipid composition of the two leaflets arise. One possibility is that certain lipids bind to specific protein domains that occur preferentially in one membrane leaflet.



Lipid rafts and caveolae

Lipid rafts are membrane microdomains enriched in cholesterol and sphingolipids. Lipid rafts are also characterized by the presence of glycosylphosphatidylinositol (GPI)-anchored proteins and proteins involved in signal transduction. GPI-anchored proteins are peripheral membrane proteins that associate with the bilayer through a covalent attachment to the glycolipid GPI. The 5–25 nm clusters of sphingolipid, cholesterol, and protein that make up a lipid raft are more tightly packed than the phospholipids of the surrounding bilayer, forming distinct microdomains that can freely



diffuse in the plane of the membrane. Unlike most of the phospholipid bilayer, lipid raft microdomains are resistant to solubilization by detergents. Lipid has always

To understand the fun Caveolae, small pits in the plasma membrane, are the most abundant surface subdomains of many mammalian cells. The cellular functions of caveolae have long remained obscure, but a new molecular understanding of caveola formation has led to insights into their workings. Caveolae are formed by the coordinated action of a number of lipid-interacting proteins to produce a microdomain with a specific structure and lipid composition. Caveolae can bud from the plasma membrane to form an endocytic vesicle or can flatten into the membrane to help cells withstand mechanical stress. The role of caveolae as mechanoprotective and signal transduction elements is reviewed in the context of disease conditions associated with caveola dysfunctionction of caveolae it is necessary to have a clear understanding of its structure within the plasma membrane. On a basic level it is also necessary to recall that the plasma membrane itself is a highly organized structure that provides a barrier for the cell that protects it from the exterior environment. The plasma membrane has hundreds of lipid and protein species. An understanding of how these basic components interact is required to delineate the role of the plasma membrane in the exchange of materials and signals across its bilayer. The fluid mosaic model of the plasma membrane describes the organization of plasma membrane components including the extracellular matrix, lipid bilayer, proteins and cytoskeleton ;however it assumes that the membrane is homogeneous and lacks a consideration of ordered domains. It has long been recognized that lipids are involved in the regulation of signal transduction and one way in which this occurs is through microdomains within the plasma membrane called lipid rafts.It has been relatively difficult to define rafts though it is apparent that they are regions of the plasma membrane that are more ordered than the rest of the membrane. It has also proven a challenge to distinguish between different types of lipid rafts.For example, it is generally accepted that caveolae are lipid rafts, but it is important to recognize that not all lipid rafts are caveolae. Also, while the plasma membrane has distinguishable microdomains within them, intracellular organelles also have microdomains that may not be comparable at a functional level to those found in the plasma membrane. Plasma membrane lipid rafts contain regions that are enriched in sphingolipids which associate laterally with each other through their head groups and rafts are also enriched in cholesterol which is situated between the interacting sphingolipids.The lipids are organized and assemble to form microdomains within the plasma membrane on the exoplasmic leaflet. The lipid composition of lipid rafts provides a degree of insolubility in non-ionic detergents, a property that is often exploited to isolate lipid rafts . In fact, this property is often used as the sole method to identify a membrane domain as a lipid raft. However, these detergent-based methods can alter the molecular composition of lipid rafts, including caveolae, thus non-detergent methods are now often used to isolate caveolae .