Plasma Membranes

Introduction

In this module on General Physiology and Excitable Cells, we're basically going to rely on the plasma membrane to run everything. Concentration gradients, electrical gradients, selective permeability, even the transmission of electrical impulses will depend on the nature of the cell membrane. We start off with something easy, a bit of a warmup—the general nature of cell membranes and their amphipathic nature, discuss fluidity, then finish with how the cell membrane's makeup allows for endocytosis.

Cell Membranes and Fluidity

The cell membrane is composed primarily of phospholipids (more detail in Biochemistry: Metabolism). A phospholipid is a 3-carbon glycerol backbone with a long carbon fatty acid chain on the first and second carbons and a polar head group on the third. The length, shape, and type of fatty acid carbon chains can vary. Some fatty acids are better than others for membrane fluidity. The polar head groups can vary from something as simple as a phosphate to something as complex as sphingolipids.

These phospholipids are **amphipathic** molecules, consisting of both water soluble (**hydrophilic**) and water insoluble (**hydrophobic**) portions. The charged, polar head groups are hydrophilic, and so are happy being next to water, while the fatty acid carbon chains are hydrophobic so do not like being near water. Things that are hydrophobic are lipophilic—they like lipids and each other. So the fatty acids like being near each other. If dropped into some water, these molecules would end up with their hydrophilic regions in contact with water and their lipophilic tails in contact with the lipophilic tails of the other. This means a little sandwich is made—hydrophilic polar heads on either side with the fatty acids in the middle. This creates a **lipid bilayer**, emphasis on "bi." Two layers, each layer consisting of a polar group in contact with water and a hydrophobic fatty acid chain in contact with the fatty acid chains of the next layer.

Membrane fluidity enables the cell to perform important functions like endo- and exocytosis. The membrane can invaginate inwards, evaginate outwards, and can even bud off to form a vesicle. This fluidity is maintained, in part, by the concept of the **lipid raft**: the groupings of proteins that can move around within the lipid bilayer. The fluidity of the membrane is dependent on how well the molecules of the layer can pack together. **Cholesterol** is one of the small molecules that comprise the lipid raft, being small enough to fit between the carbon chains. Thus, when not in excess, cholesterol is not just good, it's vital to cell function. Unsaturated fatty acids, especially those that are processed into the trans configuration, are bad for our cell membranes. They take up a lot of space so the fatty acid chains can't line up, and the membranes become stiff (more details in Biochemistry).

The plasma membrane is impermeable to most molecules. The membrane's impermeability allows the cell to create an internal environment it can control (cytoplasm) separate from an external environment it can't (extracellular matrix). The whole point is to ensure a defensive perimeter, to erect a gate that most substances can't get through. This is how the cell membranes maintain **homeostasis**. Hydrophilic heads readily dissolve small ionic atoms or molecules, but those charged molecules cannot get past the hydrophobic core. Large molecules are denied simply because of their size. Only **small, nonpolar, unionized compounds can pass through** without help. Everything else needs a channel or endocytosis to get into the cell. We will discuss endocytosis at the end of this lesson and will talk more about channels, diffusion, and permeability in the next.

Cell Membrane Proteins

The cell membrane needs proteins in everything it does. Proteins come in various forms. Proteins can serve as conduits for fluid or ionic charge, act as a channel to move otherwise impassable molecules across the cell membrane, activate receptors and translate that message to the cytoplasm, and much more.

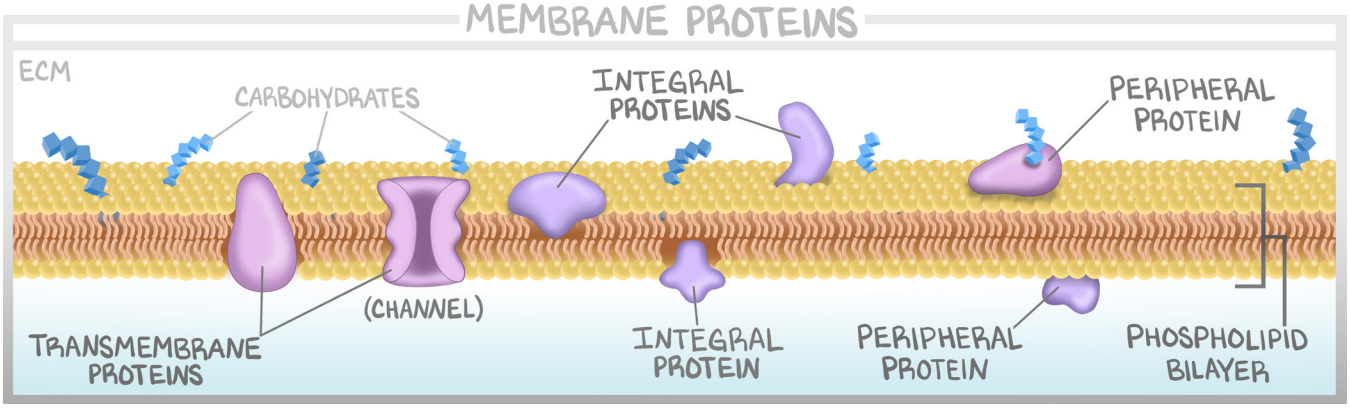


Figure 1.1: The Lipid Bilayer and Membrane Proteins
The lipid bilayer consists of polar heads on either side of the membrane, in contact with the cytoplasm on one side and the extracellular matrix (ECM) on the other side. Transmembrane proteins span the entire membrane. Integral proteins are embedded in the membrane, though they do not necessarily make contact with both sides. Peripheral proteins associate with the membrane on either side but are free to exit into the cytoplasm or the ECM.

Transmembrane proteins are proteins that span the entire length of the plasma membrane. These proteins often act as a receptor on the extracellular side, and as a cascade interaction area on the cytosolic side, or they are themselves a channel for a substrate. **Integral proteins** are proteins that are embedded either within or through the plasma membrane. Transmembrane proteins are also integral, but some integral proteins may be only cytoplasmic or only extracellular. **Peripheral proteins** are proteins that are associated loosely with the plasma membrane, often interacting with integral proteins. These act as second messengers or targets of intracellular messages from transmembrane proteins.

Other substances help make up the cell membrane, including glycoproteins, sphingolipids, etc. Don't focus on those until you need to, and then only in Biochemistry.

Endocytosis, Pinocytosis, Phagocytosis

We've said that cells have an impermeable lipid bilayer because they want to prevent most substances from getting into the cytoplasm. But there are many useful things that exist outside the cell. In order to get these things into the cell while still preventing their exposure to the cytoplasm, the cell membrane must create a shield, which we call a vesicle.

If what they want is fluid, ions, or electrolytes that just happen to be around, the cell can undergo a process called **pinocytosis**. The plasma membrane **invaginates** to form a **vesicle**. The vesicle is a membrane-bound droplet with the "outside" material still contained within the vesicle. Eventually that vesicle will fuse, or the cell will find some other way to use what it just gobbled. This is **spontaneous**, requires **no protein mediators**, and **is not regulated**. This is only good for fluid, ions, and electrolytes, and is more likely to be simply a byproduct of membrane fluidity. Constantly changing, recycling the plasma membrane, always in flux. The idea is to keep the membrane always moving a little, so that when it needs to do something big, the processes are all in place.

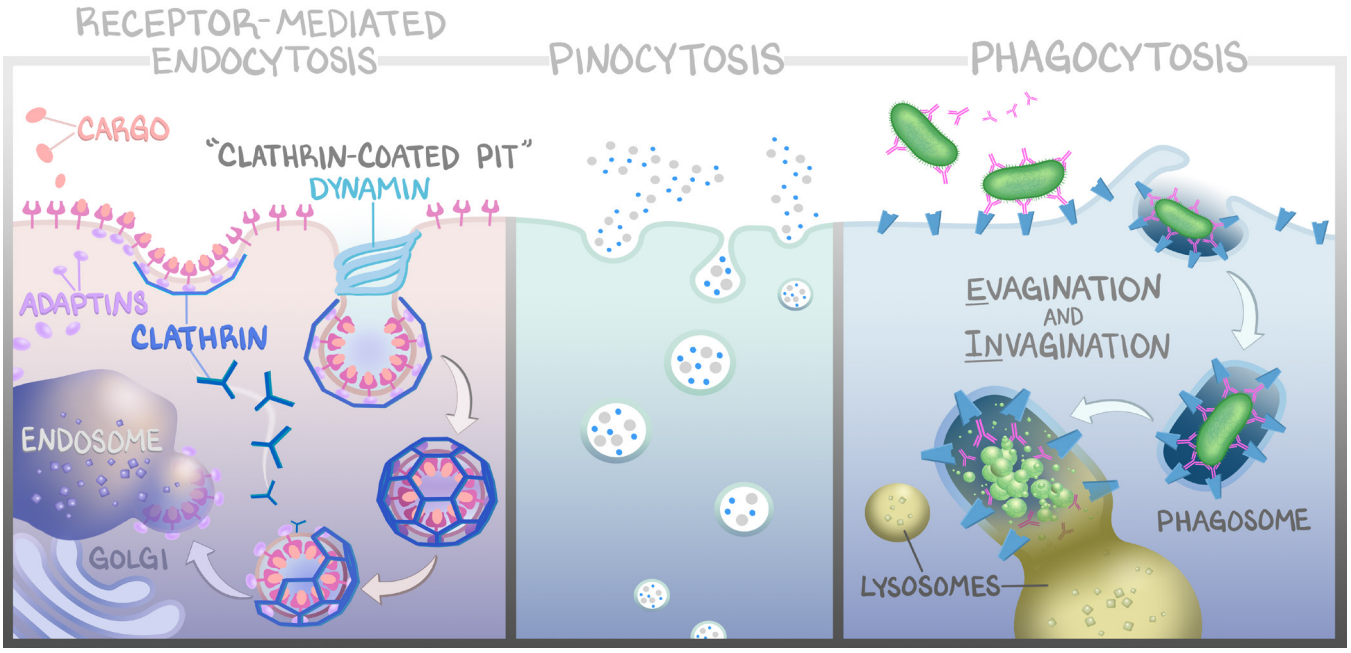
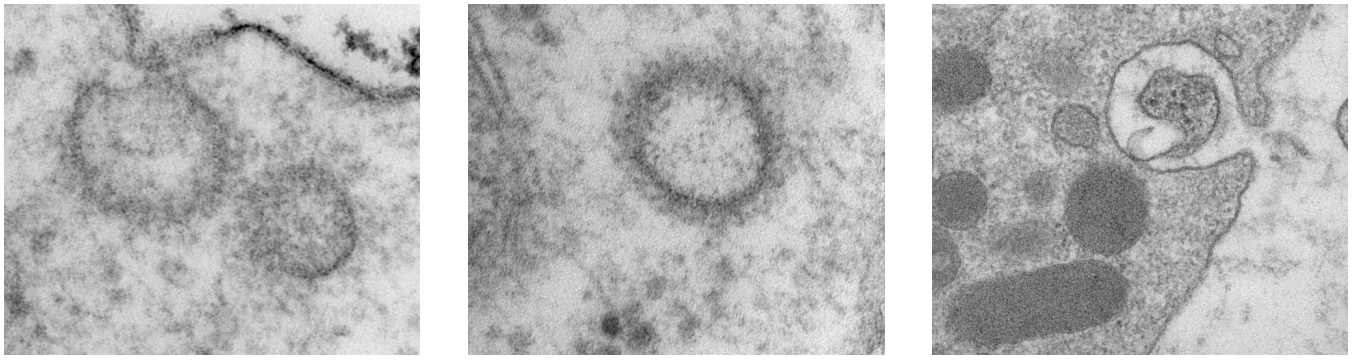


Figure 1.2: Endocytosis, Pinocytosis, and Phagocytosis
Receptor-mediated endocytosis is mediated by ligands (cargo) binding their receptor, summoning adaptins and creating a clathrin coat. Invagination of the membrane continues as the clathrin coat continues to assemble. Eventually, dynamin releases the vesicle, the clathrin is recycled, and the vesicle is fused with an endosome. Pinocytosis is a product of membrane fluidity, is spontaneous, and carries nothing more than water and ions. Phagocytosis involves an evagination outward around the pathogen to be internalized, followed by fusion with a lysosome for destruction.

Receptor-mediated endocytosis is where we should spend most of our time. Receptor-medicated endocytosis is **clathrin-mediated**. In this process, cargo receptors on the surface of the cell membrane bind their ligand, the "cargo." This causes an intracellular reaction with **adaptins**, and other accessory proteins bind to the intracellular portion of the receptor, creating a scaffolding upon which **clathrin** can then bind. Clathrin forms a hexagonal-shaped coat around the region of activated receptors as the cell membrane **invaginates** at the ligand-binding site . As this happens, clathrin continues to build a spherical structure around the budding vesicle, known as a **clathrin-coated pit**. **Dynamin** then clips the last bit of invaginating plasma membrane from the cell membrane, forming a clathrin-coated vesicle inside the cell. As clathrin detaches for use in the next endocytosis, the vesicle becomes an **early endosome**. The endosome then separates the material into "of-the-cell" and "of-the-cargo." The "of-the-cell" **receptors** and their **cell membrane** are recycled back to the cell membrane for future endocytosis. The "of-the-cargo" ligands are dispatched either to the Golgi apparatus for further processing or to specialized endosomes with lytic enzymes for degradation (**lysosomes**).

An important distinction here is that this does not let the ligands into the cell. They are within the cell's plasma membrane, but they remain separated from the cytoplasm by the vesicle's plasma membrane. The extracellular contents that the ligands were in before endocytosis are the same extracellular contents the ligands are now in the vesicle. This endocytosis is used for foreign material, or material that will need to be processed by organelles that have a plasma membrane themselves, such as lysosomes and the Golgi apparatus.



(a) (b) (c)

Figure 1.3: Endocytosis and Phagocytosis
(a) Electron micrograph of clathrin-coated endocytosis demonstrating a vesicle about to be separated from the cell membrane and another vesicle already freed. (b) Electron micrograph of the vesicle, clearly showing the clathrin coating. (c) Electron microscopy of phagocytosis with a nearly engulfed particulate and closing vesicle membrane.

Phagocytosis is a specialized form of endocytosis that is the process of engulfing large particulate matter. Instead of the cell membrane INvaginating around the object, it **Evaginates**, meaning it reaches out and wraps around the phagocytosed particle. In humans the most common phagocytes are neutrophils and macrophages. The vesicle-enclosed foreign particle is called a phagosome, and it fuses with a lysosome, becoming a phagolysosome. The end result is similar to receptor-mediated endocytosis. Phagocytosis is discussed in detail in Immunology.

Conclusion

This was an introduction to cell membranes. We'll take advantage of this information in the next several lessons. The next is on using those transmembrane proteins as transporters.

Citations

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