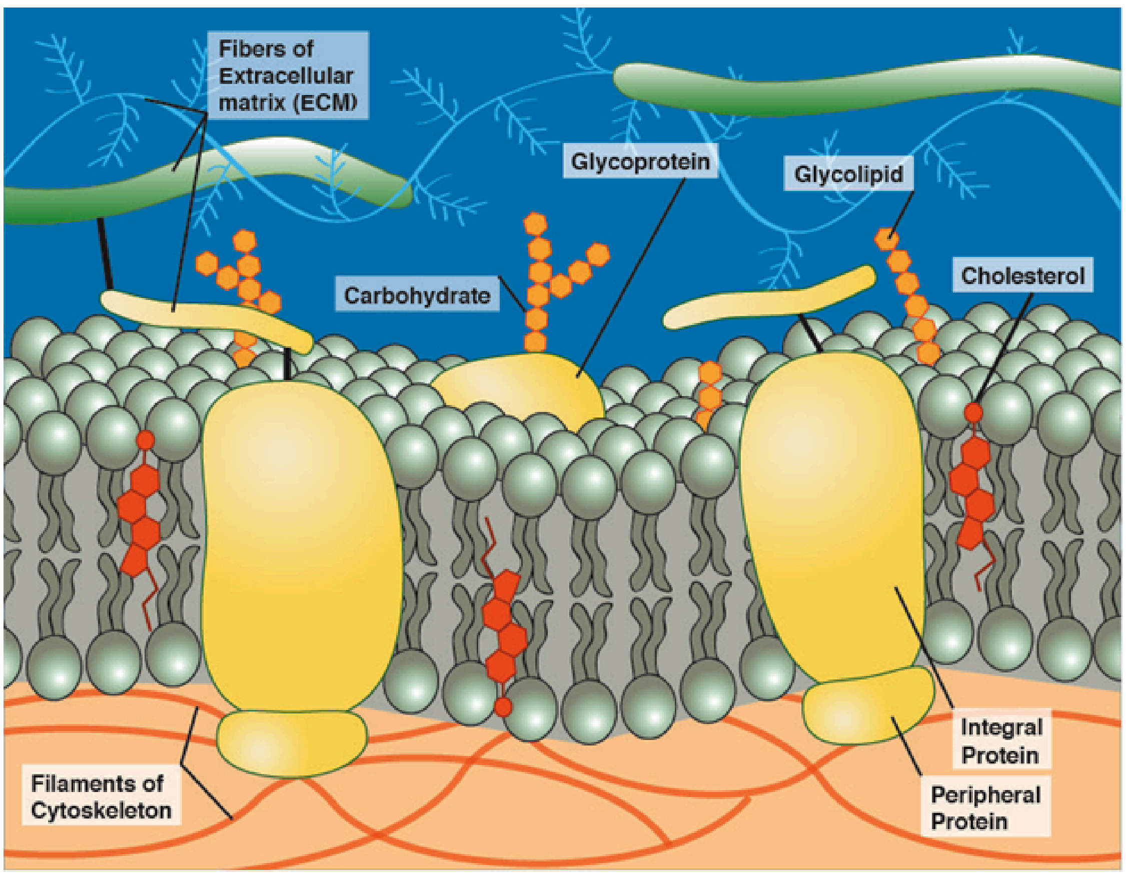
5.1.3

Membrane Proteins

Making up about another 50% of the membrane are the membrane proteins. The figure below demonstrates the relationship of the membrane proteins with the phospholipid bilayer. Note that some of the proteins are found only on the inner or outer surface of the membrane. These are called **peripheral or extrinsic proteins** because they do not extend through the membrane. One function of the peripheral proteins is to attach the membrane to the cytoskeletal proteins inside the cell or to proteins of the extracellular matrix. For example, the cells lining the blood vessels utilize peripheral proteins to attach to the tissues outside the vessel, thus holding the cells in place.

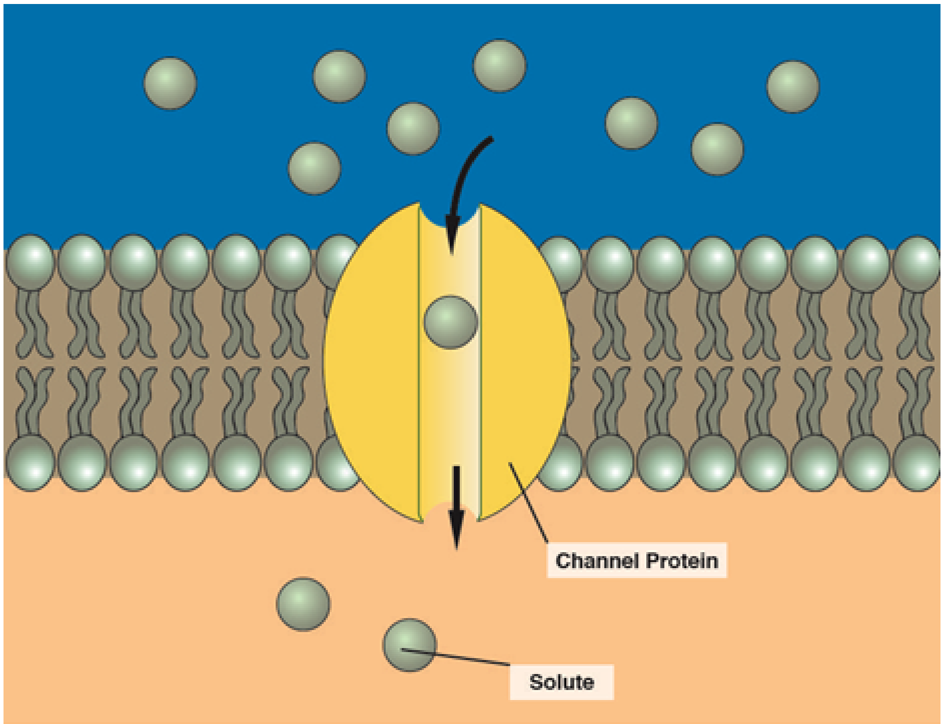


Cell Membrane Model: Relationship of Lipids, Proteins & Carbohydrates. *Image created by BYU student, Hannah Crowder 2013*

Other proteins pass all the way through the membrane. These proteins are called **integral or intrinsic proteins** and have segments that associate with the hydrophobic region of the membrane. These integral proteins perform a number of important functions in the cell. Based on their functions, these integral proteins can be grouped into the following categories:

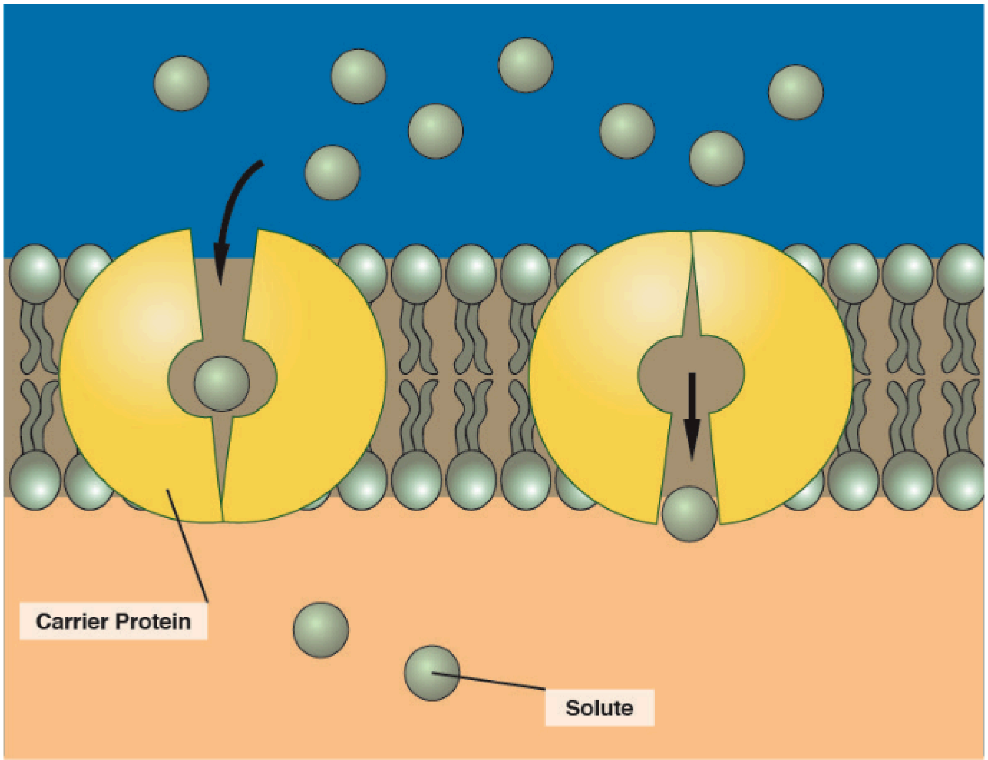
Transport Proteins

Integral proteins can act as transporters that facilitate the movement of compounds across the membrane. One type of transport protein, called **channels**, form a 'tunnel' for hydrophilic materials, such as ions and even water to cross the membrane. These channel proteins are usually gated; like a door, they allow substances to cross only when they are open. We will have more to say about channel gating later.



Channel proteins allow solutes, such as ions, to move across the membrane. *Image created by BYU student, Hannah Crowder 2013*

Carrier proteins are another type of transport protein. Carriers have sites that bind to specific solutes. For example, one type of carrier binds with glucose, while another carrier binds to urea. Once the solute binds, the carrier protein changes shape, allowing the solute to move across the membrane. Imagine a revolving door. As these doors turn (change shape), they are open to either the inside of the building or to the outside but never to both at the same time. You can enter a revolving door from the outside of a room and move the door until it is open to the inside of the room. At no time in this process was the door open to both sides at the same time. This is how carrier proteins work. Carrier proteins bind to solutes and then move them across the membrane by changing shape.



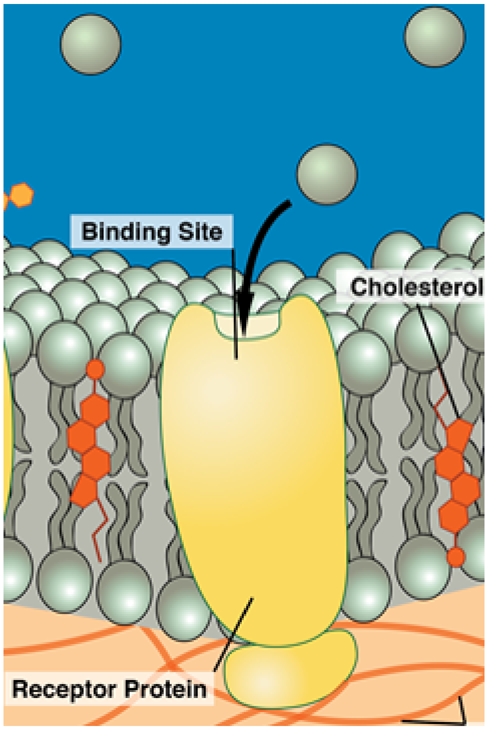
Carrier Proteins. *Image created by BYU student, Hannah Crowder 2013*

Enzymes

Integral membrane proteins can function as enzymes, catalyzing important chemical reactions. The enzyme, lactase, which digests the disaccharide lactose in the small intestine is an integral membrane protein in the cells that line the lumen of the duodenum. The discomfort associated with lactose intolerance is caused by having insufficient amounts of this enzyme in the body.

Receptor Proteins

Integral proteins may act as receptor proteins and allow the cell to respond to extracellular chemical messengers which regulate the activity of the cell. When a chemical signal (also known as a ligand) binds to its specific receptor protein, it transmits a signal to the inside of the cell through a shape change in its transmembrane protein structure. This shape change will then activate or inhibit intracellular events that result in altered cell function. For example, epinephrine (adrenaline) is a ligand that binds to receptors on specialized cardiac cells causing intracellular changes that make your heart beat faster when you are frightened or experiencing an 'adrenaline rush.' There are many types of receptor proteins expressed in our bodies, but we will look at one of the most abundant and well-studied: G-protein coupled receptors.

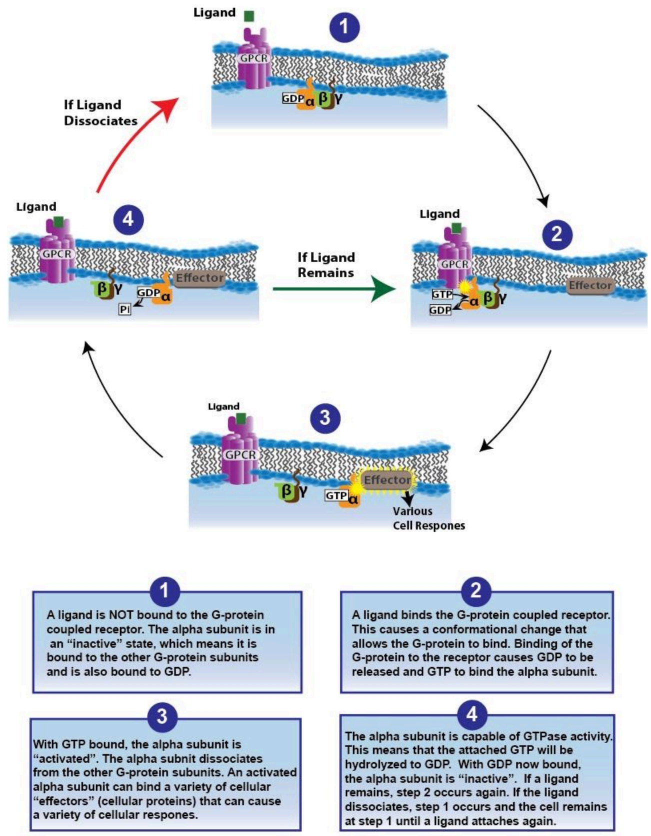


Receptor Protein. *Image created by BYU student, Hannah Crowder 2013*

G protein-Coupled Receptor (GPCR)

The GPCR complex is composed of two units: a receptor protein that binds to the chemical signal (the ligand) and the G protein complex associated with the inner side of the membrane (i.e. a peripheral protein complex). The GPCR has a ligand binding site on the external surface and a G protein binding site on the internal surface. The G protein complex is composed of three subunits: the alpha, beta, and gamma subunits. The alpha subunit has a site that can bind **Guanosine Triphosphate (GTP)** or **Guanosine Diphosphate (GDP)**, hence the name ***G* protein**. In its inactive form, the G-alpha subunit is bound to GDP, and the three subunits (alpha, beta, and gamma) are bound together. When a ligand binds to the receptor on the surface of the cell, the G protein binding site changes shape, allowing the G protein to bind to the intracellular region of the receptor. This binding causes the G protein to then change shape, and the GDP exits the binding site on the alpha subunit and is replaced by a GTP from the cytoplasm. The binding of GTP causes the alpha subunit to separate from the other two subunits (beta/gamma dimer). Once separated, the alpha subunit (and sometimes the beta/gamma dimer) can then bind to and activate other proteins inside the cell. The mechanism of action is typically mediated by one of two enzymes: adenylate cyclase or phospholipase C. These effector proteins will be discussed later in the semester, but for now remember that they create intracellular signaling molecules called 'second messengers' that result in changes in cell function. Cellular responses include activation of metabolic enzymes, opening or closing ion channels, turning on transporters, initiating gene transcription, regulating motility, regulating contractility, stimulating secretion, and even controlling memory. After a short period of time, the G-alpha subunit hydrolyzes the GTP into a GDP and phosphate, allowing it to reunite with the beta/gamma dimer, turning off the signal.

To date, approximately 800 genes for G protein-coupled receptors have been identified. G-proteins are very common in physiology, and it is important to study the details related to these receptors. It would be a good idea to learn and be able to explain the following figure.



Ligand Activation and G-Protein Effect. *Image drawn by JS Fall 2014*

Attachment Proteins

Integral proteins are involved in attaching cells to each other, as well as to the extracellular matrix and to intracellular structural proteins. Often, a peripheral protein functions as a link between the integral proteins and the structural proteins or the extracellular matrix. These attachments can confer tissue strength and shape. The inability to form these connections can result in several pathological conditions, including muscular dystrophy.

Marker Proteins

These proteins allow cells to identify one another. Functions of these marker proteins include the ability of sperm cells to recognize the oocyte during fertilization, as well as the ability of our immune cells to distinguish between our own cells and a foreign cell, such as a bacterial cell, that might be trying to invade our bodies.