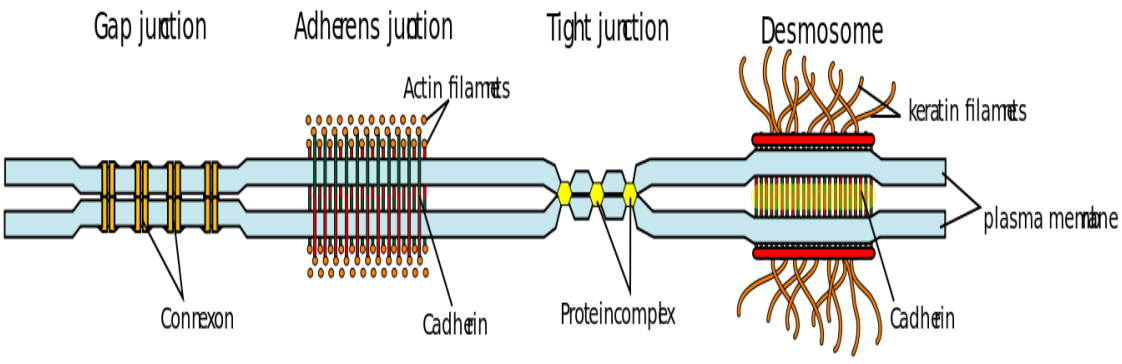
Cell Junctions

Cell junctions (or intercellular bridges) are a class of cellular structures consisting of multiprotein complexes that provide contact or adhesion between neighboring cells or between a cell and the extracellular matrix in animals. They also maintain the paracellular barrier of epithelia and control paracellular transport. Cell junctions are especially abundant in epithelial tissues. Combined with cell adhesion molecules and extracellular matrix, cell junctions help hold animal cells together.

Cell junctions are also especially important in enabling communication between neighboring cells via specialized protein complexes called communicating) junctions. Cell junctions are also important in reducing stress placed upon cells.

In vertebrates, there are three major types of cell junction:

- Adherens junctions, desmosomes and hemidesmosomes (anchoring junctions)
- Gap junctions(communicating junction)
- Tight junctions (occluding junctions)



GAP JUNCTIONS:

Gap junctions are a specialized intercellular connection between a multitude of animal cell-types. They directly connect the cytoplasm of two cells, which allows various molecules, ions and electrical impulses to directly pass through a regulated gate between cells.

One gap junction channel is composed of two connexons (or hemichannels), which connect across the intercellular space. Gap junctions are analogous to the plasmodesmata that join plant cells. Gap junctions occur in virtually all tissues of the body, with the exception of adult fully developed skeletal muscle and mobile cell types such as sperm or erythrocytes. Gap junctions, however, are not found in simpler organisms such as sponges and slime molds.

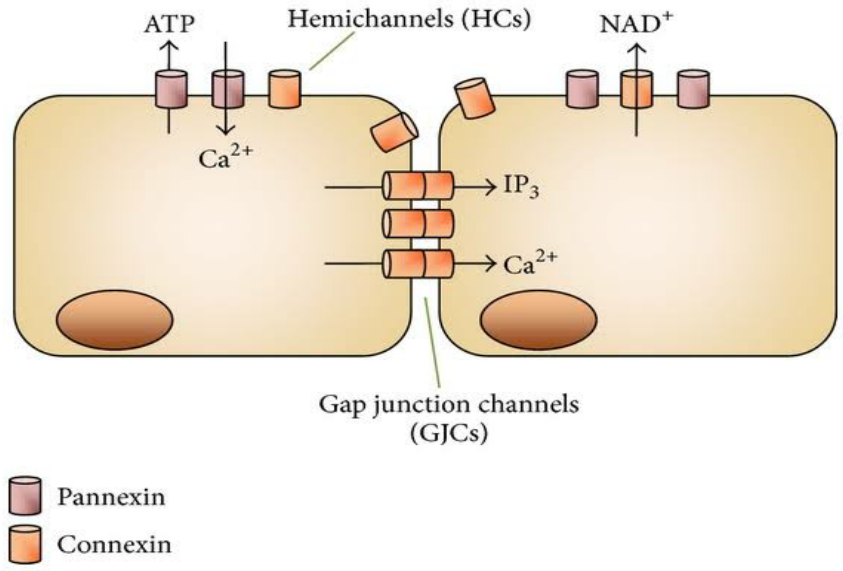


Fig: Gap junction

A gap junction may also be called a nexus or macula communicans. While an ephapse has some similarities to a gap junction, by modern definition the two are different.

In vertebrates, gap junction hemichannels are primarily homo- or hetero-hexamers of connexin proteins. Invertebrate gap junctions comprise proteins from the innexin family. Innexins have no significant sequence homology with connexins. Though differing in sequence to connexins, innexins are similar enough to connexins to state that innexins form gap junctions in vivo in the same way connexins do. The recently characterized pannexin family, which was originally thought to form inter-cellular channels (with an amino acid sequence similar to innexins), in fact functions as a single-membrane channel that communicates with the extracellular environment, and has been shown to pass calcium and ATP.At gap junctions, the intercellular space is between 2 and 4 nm and unit connexons in the membrane of each cell are aligned with one another.

Gap junction channels formed from two identical hemichannels are called homotypic, while those with differing hemichannels are heterotypic. In turn, hemichannels of uniform connexin composition are called homomeric, while those with differing connexins are heteromeric. Channel composition is thought to influence the function of gap junction channels.

Occurances: Gap junctions appear to be in all animal organs and tissues and it will be interesting to find exceptions to this other than cells not normally in contact with neighboring cells. Adult skeletal muscle is a possible exception. It may be argued that if present in skeletal muscle, gap junctions might propagate contractions in an arbitrary way among cells making up the muscle. At least in some cases this may not be the case as shown in other muscle types that do have gap junctions.

Function: Gap junctions may be seen to function at the simplest level as a direct cell to cell pathway for electrical currents, small molecules and ions. The control of this communication allows complex downstream effects on multicellular organisms.

- In the 1980s, more subtle but no less important roles of gap junction communication have been investigated. It was discovered that gap junction communication could be disrupted by adding anti-connexin antibodies into embryonic cells. Embryos with areas of blocked gap junctions failed to develop normally.

- The "**bystander effect**" with its connotations of the innocent bystander being killed is also mediated by gap junctions. When cells are compromised due to disease or injury and start to die messages are transmitted to neighboring cells connected to the dying cell by gap junctions. This can cause the otherwise unaffected healthy bystander cells to also die.

- Death of some cells and their surrounding matrix may be required for a tissue to reach its final configuration and gap junctions also appear essential to this process.

- Gap junctions electrically and chemically couple cells throughout the body of most animals. Electrical coupling can be relatively fast acting. Tissues in this section have well known functions observed to be coordinated by gap junctions with inter-cellular signaling happening in time frames of micro-seconds or less.

- Gap junctions are particularly important in cardiac muscle: the signal to contract is passed efficiently through gap junctions, allowing the heart muscle cells to contract in unison. Gap junctions are expressed in virtually all tissues of the body, with the exception of adult fully developed skeletal muscle and mobile cell types such as sperm or erythrocytes.

- A gap junction located in neurons is often referred to as an electrical synapse.

TIGHT JUNCTIONS:

Tight junctions, also known as occluding junctions or zonulae occludentes (singular, zonula occludens) are multiprotein junctional complexes whose general function is to prevent leakage of transported solutes and wat

er and seals the paracellular pathway. Tight junctions may also serve as leaky pathways by forming selective channels for small cations, anions, or water. Tight junctions are present mostly in vertebrates (with the exeption of Tunicates). The corresponding junctions that occur in invertebrates are septate junctions.

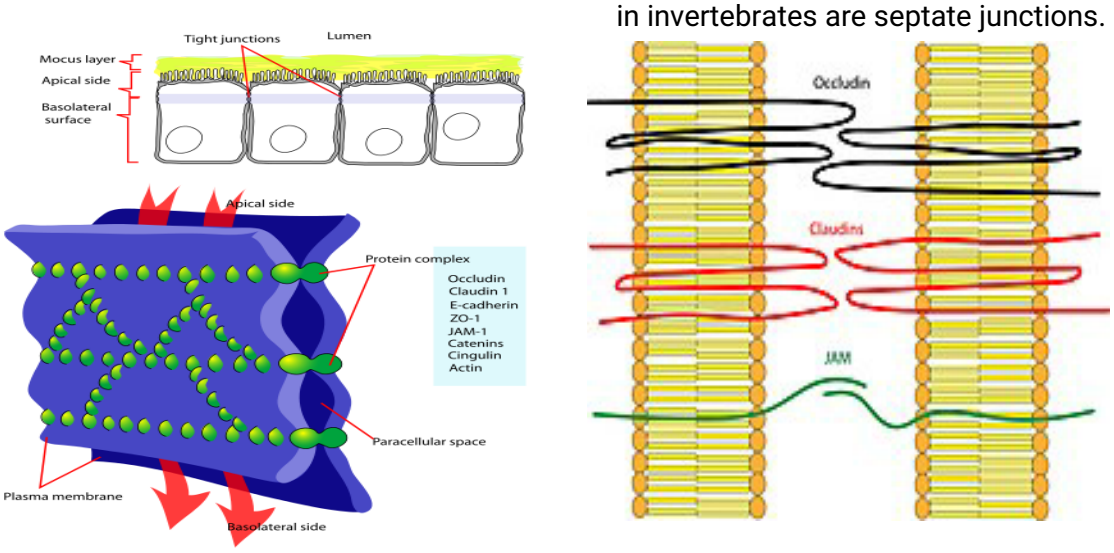


Fig: Tight Junction

Tight junctions are composed of a branching network of sealing strands, each strand acting independently from the others. Therefore, the efficiency of the junction in preventing ion passage increases exponentially with the number of strands. Each strand is formed from a row of transmembrane proteins embedded in both plasma membranes, with extracellular domains joining one another directly. There are at least 40 different proteins composing the tight junctions.[2] These proteins consist of both transmembrane and cytoplasmic proteins. The three major transmembrane proteins are occludin, claudins, and junction adhesion molecule (JAM) proteins. These associate with different peripheral membrane proteins such as ZO-1 located on the intracellular side of plasma membrane, which anchor the strands to the actin component of the cytoskeleton.[3] Thus, tight junctions join together the cytoskeletons of adjacent cells.

Occurances: Tight junctions are located within our body's epithelia.In human physiology there are two main types of epithelia using distinct types of barrier mechanism. Epidermal structures such as skin form a barrier from many layers of keratinized squamous cells. Internal epithelia on the other hand more often rely on tight junctions for their barrier function. This kind of barrier is mostly formed by only one or two layers of cells

Functions: They perform vital functions:

- They hold cells together.
- Barrier function, which can be further subdivided into protective barriers and functional barriers serving purposes such as material transport and maintenance of osmotic balance:
- Tight junctions help to maintain the polarity of cells by preventing the lateral diffusion of integral membrane proteins between the apical and lateral/basal surfaces, allowing the specialized functions of each surface (for example receptor-mediated endocytosis at the apical surface and exocytosis at the basolateral surface) to be preserved. This aims to preserve the transcellular transport.
- Tight junctions prevent the passage of molecules and ions through the space between plasma membranes of adjacent cells, so materials must actually enter the cells (by diffusion or active transport) in order to pass through the tissue.

DESMOSOMES:

A desmosome ("binding body"), also known as a macula adherens (Latin for adhering spot), is a cell structure specialized for cell-to-cell adhesion. A type of junctional complex, they are localized spot-like adhesions randomly arranged on the lateral sides of plasma membranes.

Desmosomes are composed of desmosome-intermediate filament complexes (DIFC), which is a network of cadherin proteins, linker proteins and keratin intermediate filaments. The DIFCs can be broken into three regions: the extracellular core region, or desmoglea, the outer dense plaque, or ODP, and the inner dense plaque, or IDP.

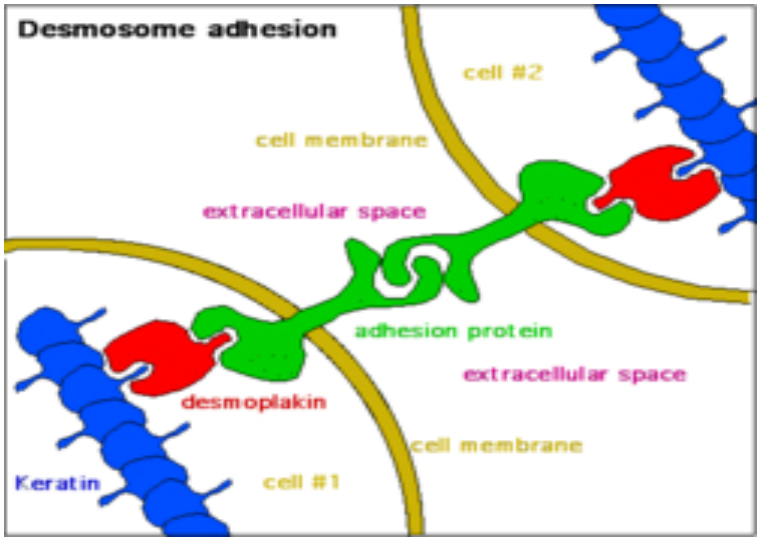


Fig: Desmosome Adhesion

The extracellular core region, approximately 34 nm in length, contains desmoglein and desmocollin, which are in the cadherin family of cell adhesion proteins. Both have five extracellular domains, and have calcium-binding motifs. Extracellular calcium helps form the cadherin adhesion by allowing the cadherin extracellular domain on desmoglein and desmocollin to become rigid. They bind to each other via heterophilic interactions in the extracellular space near their N-termini, in contrast with the homophilic binding characteristic of other cadherins. Desmoglein and desmocollin have a single pass transmembrane region plus an intracellular anchor to secure its position in the cell membrane. Desmogleins and the desmocollin Dsc "a" form contain an intracellular cadherin domain, which binds to plakoglobin.

The outer dense plaque, which is about 15–20 nm in length, contains the intracellular ends of desmocollin and desmoglein, the N-terminus side of desmoplakin, and the armadillo family of mediatory proteins plakoglobin and plakophilin.

The inner dense plaque, also about 15–20 nm in length, contains the C-terminus end of desmoplakin and their attachment to keratin intermediate filaments. Desmoplakin is the most abundant part of the desmosome, as it operates as the mediator between the cadherin proteins in the plasma membrane and the keratin filaments.

Occurances: Desmosomes are one of the stronger cell-to-cell adhesion types and are found in tissue that experience intense mechanical stress, such as cardiac muscle tissue, bladder tissue, gastrointestinal mucosa, and epithelia.

Function: Desmosomes are intercellular junctions that provide strong adhesion between cells. Because they also link intracellularly to the intermediate filament cytoskeleton they form the adhesive bonds in a network that gives mechanical strength to tissues.