

CELL JUNCTIONS

Desmosomes • Gap Junctions • Tight Junctions

1. Introduction

Cell junctions are specialised protein complexes that connect adjacent animal cells or link a cell to the extracellular matrix. They are most abundant in epithelial tissue, where they seal, anchor, and electrically/metabolically couple neighbouring cells. Cell junctions are classically grouped into three functional categories:

- **Occluding (sealing) junctions** – e.g. **tight junctions**; block the free passage of substances through the space between cells.
- **Anchoring junctions** – e.g. **desmosomes**, adherens junctions, hemidesmosomes; mechanically attach cells to each other or to the basement membrane.
- **Communicating junctions** – e.g. **gap junctions**; allow direct exchange of ions and small molecules between cell cytoplasms.

Junctional Complex Along the Lateral Membrane of Epithelial Cells

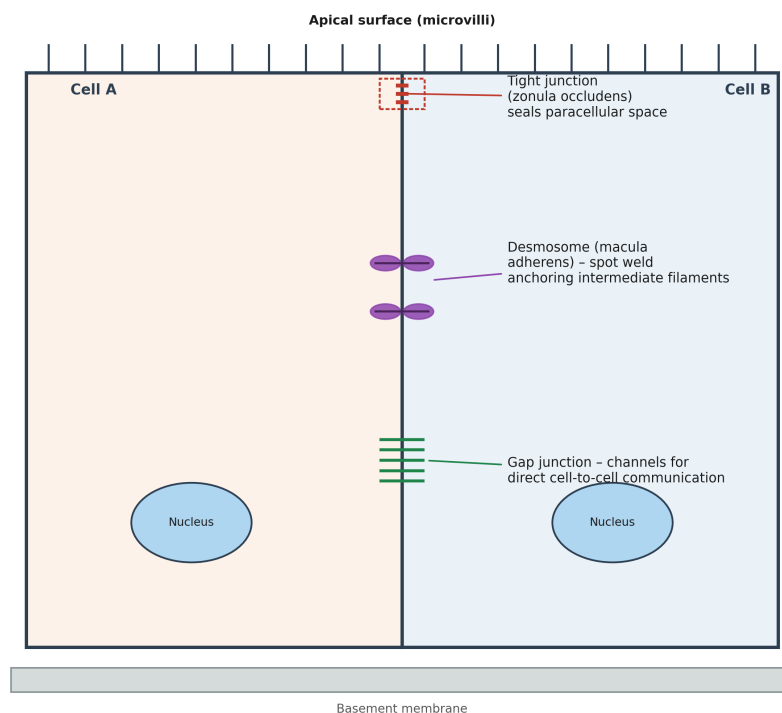


Fig. 1: The three principal junction types arranged along the lateral membrane of adjacent epithelial cells, from apex to base.

Quick comparison Tight junction: **seals** | Desmosome: **anchors** (mechanical strength) | Gap junction: **communicates** (ions/small molecules)

2. TIGHT JUNCTION (Zonula Occludens)

Tight junctions form a continuous, belt-like seal around the **apical-most** region of adjacent epithelial cells, fusing the outer leaflets of neighbouring plasma membranes at discrete “kissing points” and obliterating the intercellular space at those points.

Molecular composition

- **Claudins** – the principal sealing proteins; determine the tightness and ion selectivity of the junction (different claudin combinations create paracellular pores of varying selectivity in different tissues).
- **Occludin** – a four-pass transmembrane protein that stabilises the junction.
- **Junctional adhesion molecules (JAMs)** – immunoglobulin-superfamily proteins aiding assembly and leukocyte transmigration.
- **ZO-1, ZO-2, ZO-3** – cytoplasmic scaffold (plaque) proteins that anchor the strands to the underlying actin cytoskeleton.

Functions

- **Barrier (gate) function** – selectively restricts paracellular movement of ions, water, and solutes across the epithelial sheet (e.g. gut lining, blood–brain barrier).
- **Fence function** – prevents lateral diffusion of membrane lipids/proteins between the apical and basolateral domains, maintaining epithelial cell polarity.

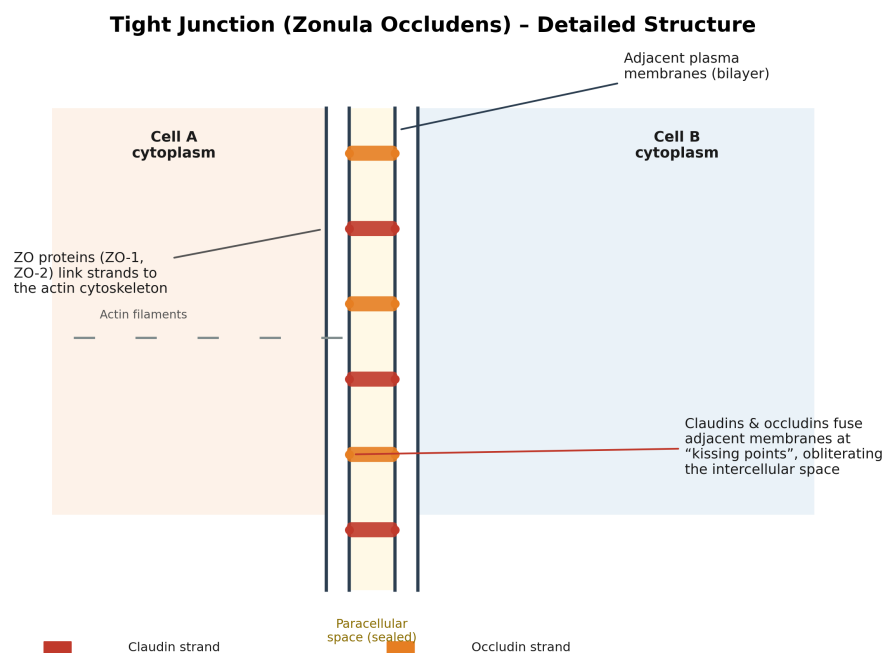


Fig. 2: Claudin and occludin strands fuse adjacent membranes at repeated “kissing points”, sealing the paracellular space.

3. DESMOSOME (Macula Adherens)

Desmosomes are button-like, spot-weld anchoring junctions distributed at intervals along the lateral membrane. They provide strong mechanical adhesion and distribute shearing/tensile stress across a sheet of cells, which is why they are abundant in tissues subject to mechanical stress such as the epidermis and cardiac muscle.

Molecular composition

- **Desmosomal cadherins** – **desmoglein** and **desmocollin**; their extracellular domains interdigitate across the ~30 nm intercellular gap in a Ca^{2+} -dependent manner.
- **Cytoplasmic plaque proteins** – **desmoplakin**, **plakoglobin**, and **plakophilin** form a dense plate on the inner face of the membrane linking cadherins to intermediate filaments.
- **Keratin intermediate filaments (tonofilaments)** – loop into the plaque, distributing mechanical stress throughout the cytoskeleton and across the whole epithelial sheet.

Related junction: **Hemidesmosomes** look structurally similar under the microscope but attach the basal cell surface to the underlying basement membrane, using **integrins** instead of cadherins.

Desmosome (Macula Adherens) - Detailed Structure

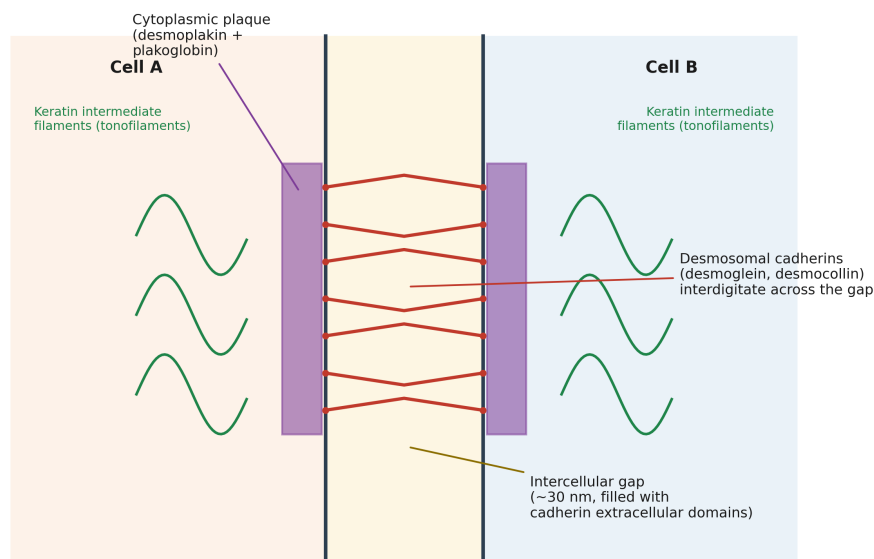


Fig. 3: Desmosomal cadherins interdigitate across the intercellular gap and anchor keratin intermediate filaments via the cytoplasmic plaque.

4. GAP JUNCTION

Gap junctions are clusters of intercellular channels that directly connect the cytoplasms of adjacent cells, allowing electrical and metabolic coupling. A single gap junction plaque may contain hundreds to thousands of individual channels.

Molecular composition

- **Connexin** – the transmembrane protein subunit; six connexins oligomerise to form a **connexon (hemichannel)** in each cell's membrane.
- Two connexons, one donated by each cell, dock end-to-end across the narrow (~2–4 nm) extracellular gap to form a complete, continuous channel.
- In invertebrates the analogous channel proteins are called **innexins**.

Functions

- **Electrical coupling** – allows rapid spread of action potentials, e.g. between cardiac myocytes and smooth muscle cells, synchronising contraction.

- **Metabolic/chemical coupling** – permits diffusion of ions, cyclic AMP, IP₃, and other signalling molecules and metabolites smaller than about 1 kDa between cells.
- **Developmental signalling** – coordinates groups of cells during embryonic development and tissue homeostasis.
- Channels can close in response to a fall in cytoplasmic pH or a rise in Ca²⁺, isolating a damaged or dying cell from its healthy neighbours.

Gap Junction - Detailed Structure

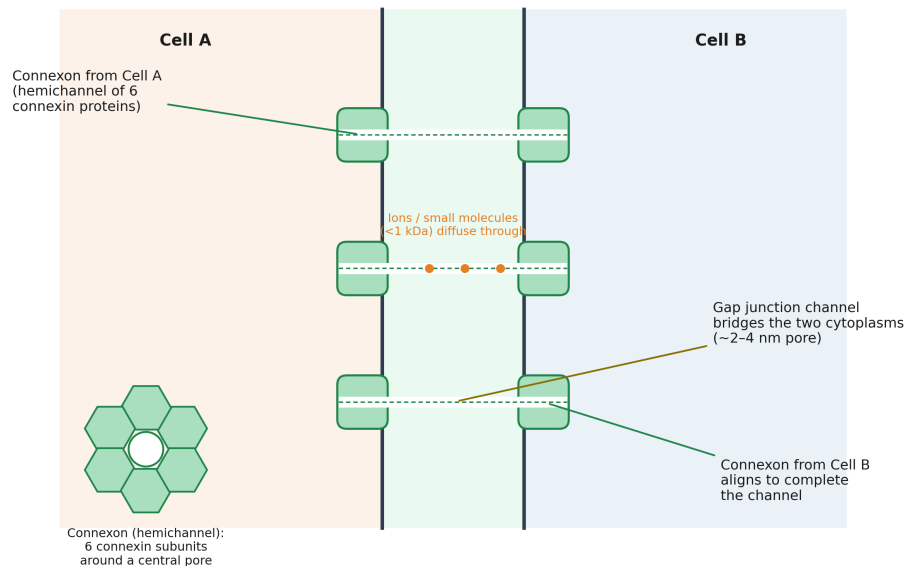


Fig. 4: Aligned connexons from adjacent cells form continuous channels that permit direct cytoplasm-to-cytoplasm exchange of ions and small molecules.

5. Comparison at a Glance

Feature	Tight junction	Desmosome	Gap junction
Category	Occluding	Anchoring	Communicating
Location	Most apical (zonula)	Scattered spots (macula)	Anywhere along membrane
Key proteins	Claudins, occludin, ZO proteins	Desmoglein, desmocollin, desmoplakin	Connexins (connexons)
Cytoskeletal link	Actin filaments	Keratin intermediate filaments	None
Main function	Seals paracellular space; maintains polarity	Mechanical strength / stress distribution	Electrical & metabolic coupling

6. Clinical Significance

Desmosome-related disorders

- **Pemphigus vulgaris** – autoantibodies against **desmoglein 3** disrupt desmosomes in the deep epidermis, causing painful mucocutaneous blistering.
- **Pemphigus foliaceus** – autoantibodies against **desmoglein 1** cause more superficial skin blistering.
- **Staphylococcal scalded skin syndrome** – a bacterial exfoliative toxin cleaves desmoglein 1 directly.
- **Arrhythmogenic right ventricular cardiomyopathy (ARVC)** – mutations in desmosomal plaque proteins weaken cardiac cell adhesion, predisposing to arrhythmia.

Tight junction-related disorders

- Mutations in **claudin-14** cause a form of hereditary deafness; mutations in **claudin-1** cause neonatal ichthyosis–sclerosing cholangitis syndrome.
- The *Vibrio cholerae* zonula occludens toxin (Zot) and *Clostridium perfringens* enterotoxin both transiently open tight junctions, altering epithelial permeability.

Gap junction-related disorders

- Mutations in **connexin 26 (GJB2)** are the single most common cause of hereditary non-syndromic sensorineural deafness.
- Mutations in **connexin 32 (GJB1)**, expressed by Schwann cells, cause the X-linked form of Charcot–Marie–Tooth disease, a peripheral neuropathy.

7. Summary

- **Tight junctions** seal the paracellular space and maintain epithelial polarity (claudins, occludin, ZO proteins; linked to actin).
- **Desmosomes** are spot-weld anchoring junctions giving mechanical strength (desmogleins/desmocollins; linked to keratin intermediate filaments).
- **Gap junctions** are clusters of connexon channels enabling direct electrical and metabolic coupling between cells.
- Each junction type has a distinct disease profile – from blistering skin diseases and deafness to inherited neuropathies and cardiomyopathy.

End of notes – Cell Junctions