

Extracellular Matrix (ECM) and Mechanisms of Cell Communication

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Introduction

- Cells have the ability to bind to each other.
- **Cell adhesion:** The cellular property that mediates the binding
- Cells either
 - Adhere directly to each other: **cell–cell adhesion** or
 - Adhere to extracellular components that provide a structural framework for cell binding.
- These **extracellular components** are collectively referred to as the **extracellular matrix (ECM)**.

Introduction

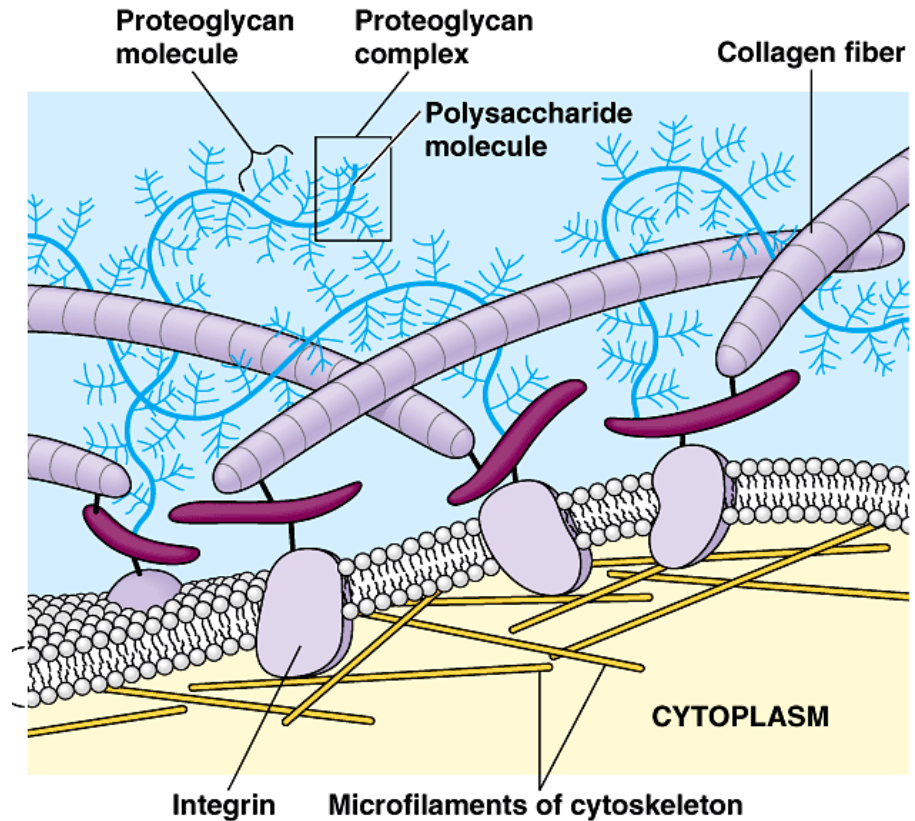
- The extracellular matrix is a dense network of proteins that:
 - lies between cells
 - is made by the cells within the network
- The binding of cells to the ECM is called **cell–matrix adhesion**.

Introduction

- Besides providing structural and adhesive support to cells, the ECM also provides a medium for **cell–cell communication**.
- Cells coordinate their behaviour and the body functions as an integrated whole by **sending** and **receiving** a variety of **chemical signals**.
- A cell's response to a chemical signal takes place in three sequential steps :
 - the signal binds to a receptor protein;
 - signal binding conveys a message to the cell;
 - the cell changes its activity in response to the signal.

Extracellular matrix (ECM)

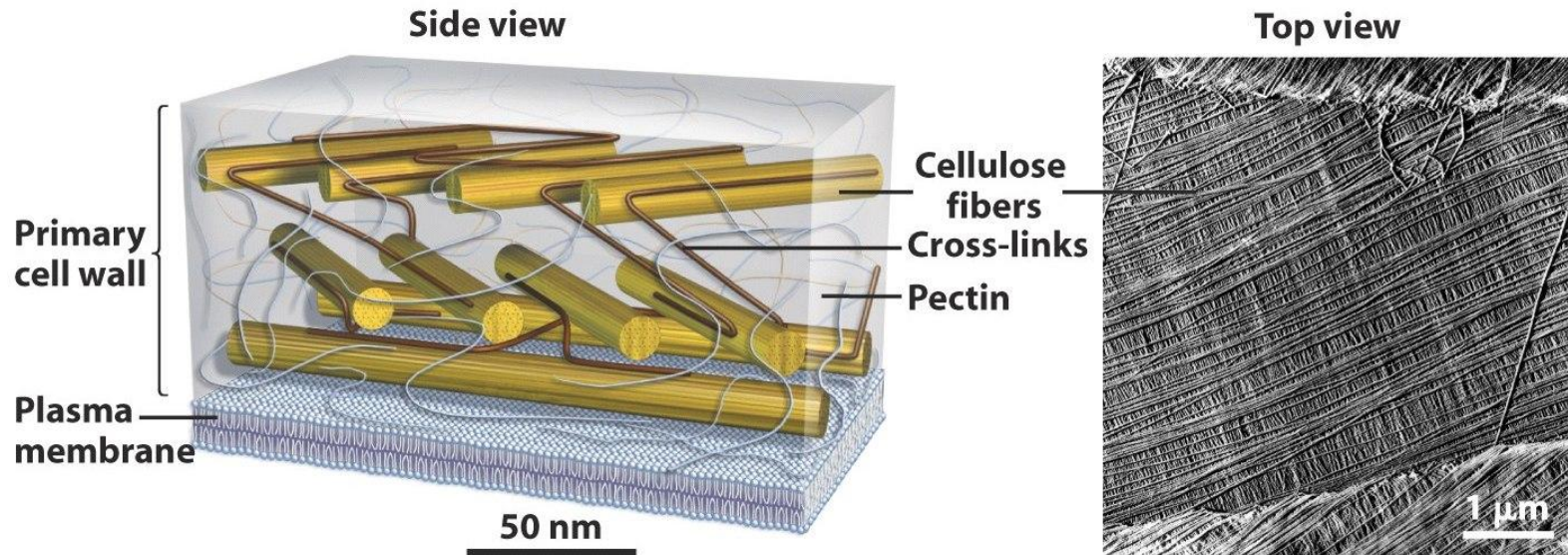
- Surrounds cell
- Provides mechanical support
- Controls the flow of nutrients and signals to the cells
- Consists of
 - Fibrous: collagen, elastin, fibronectin, laminin
 - Non-fibrous: Proteoglycans and polysaccharides



ECM

- All cells in solid tissues are surrounded by extracellular matrix.
- Both plants and animals have ECM.
- The ECM in **plants** is a cross-linked network of **cellulose fibers** and **pectin** (a gel-forming polysaccharide) and surrounds each cell.
- In plants, ECM contributes to the rigidity of the plant.
 - The ability of a tree to grow to a great height and retain its rigidity is partly due to the cellulose ECM of the cell walls together with other biomolecules, including **lignin**.

ECM in plant cells



ECM in animal cells

- In **animals**, the ECM can surround cells as fibrils that contact the cells on all sides, or as a sheet called the basement membrane that cells 'sit on'.
- The ECM in animals functions primarily in
 - cell and body protection and support
 - also affects cell division, motility, embryonic development, and wound healing.
- The ECM in animals is a complex mixture of **glycoproteins** (mainly **collagen**) and **gel-forming polysaccharides** secreted by the cells themselves.

Collagen

- Collagen : most abundant protein found in the human body. About $1/3^{\text{rd}}$ of the total proteins.
- Found abundantly in tendon, cartilage, bone and skin
- Functions:
 - cell movement
 - cell adhesion
 - tissue repair

Collagen provides structural support to tissues

- The principal function of collagens is to provide structural support to tissues.
- Collagens are a family of over 20 different extracellular matrix proteins.
 - Together they are the most abundant proteins in the animal kingdom.
- Mutations of collagen genes can lead to a wide range of diseases, from mild wrinkling to brittle bones.

Fibronectins connect cells to collagenous matrices

- The principal function of the extracellular matrix protein fibronectin is to connect cells to matrices that contain fibrillar collagen.
- At least 20 different forms of fibronectin have been identified.
 - All of them arise from alternative splicing of a single fibronectin gene.

Elastic fibers impart flexibility to tissues

- The principal function of elastin is to impart elasticity to tissues.
- Elastin monomers (known as tropoelastin subunits) are organized into fibers.
 - The fibers are so strong and stable they can last a lifetime.

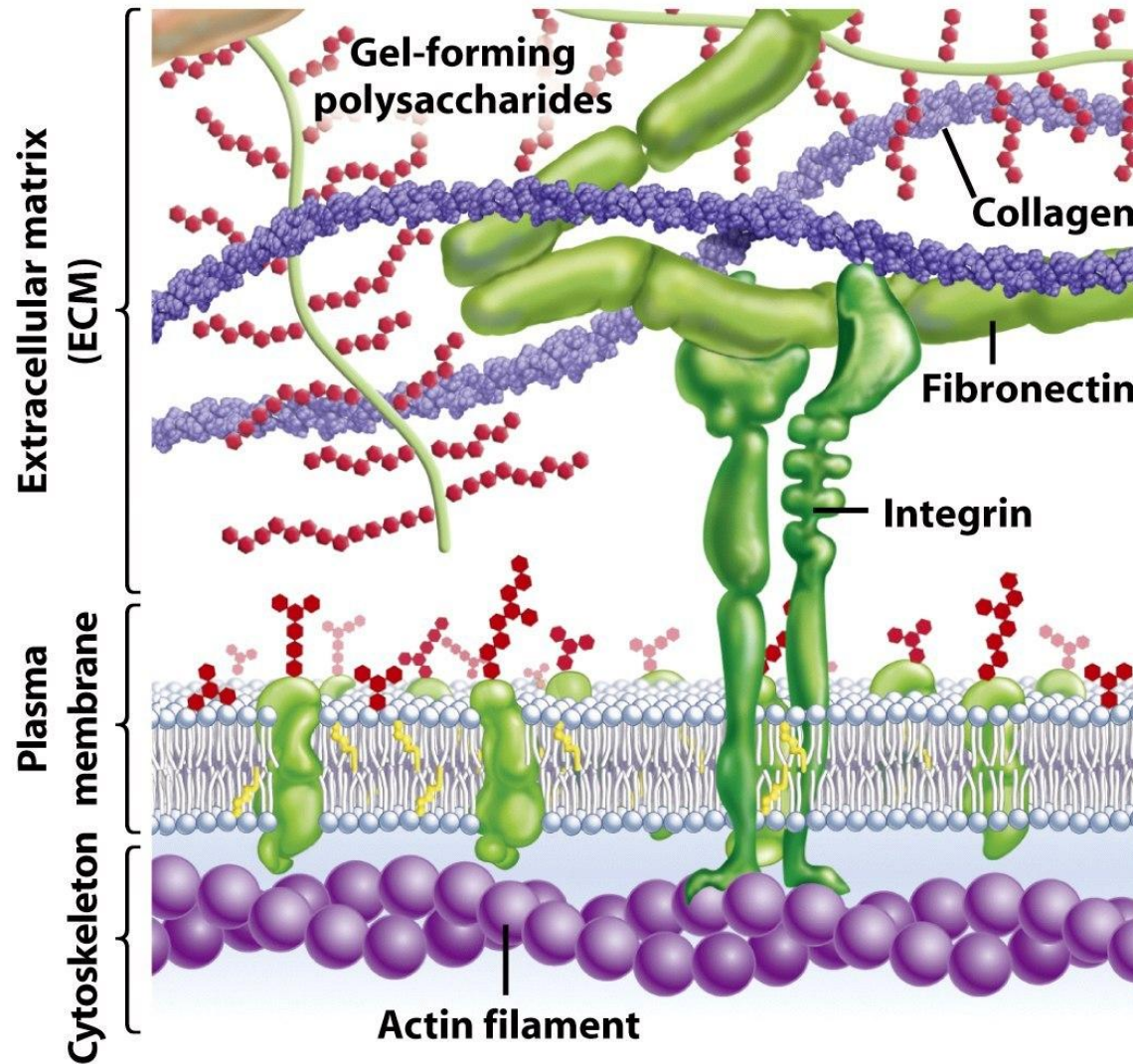
Laminins provide an adhesive substrate for cells

- Laminins are a family of extracellular matrix proteins.
 - They are found in virtually all tissues of vertebrate and invertebrate animals.
- The principal functions of laminins are:
 - to provide an adhesive substrate for cells
 - to resist tensile forces in tissues

Proteoglycans provide hydration to tissues

- Proteoglycans consist of a central protein “core” to which long, linear chains of disaccharides, called glycosaminoglycans (GAGs), are attached.
- GAG chains on proteoglycans are negatively charged.
 - This gives the proteoglycans a rodlike shape due to charge repulsion.
- Proteoglycans attract water to form gels that:
 - keep cells hydrated
 - cushion tissues against hydrostatic pressure
- Proteoglycans can bind to a variety of extracellular matrix components, including:
 - growth factors
 - structural proteins
 - cell surface receptors

ECM

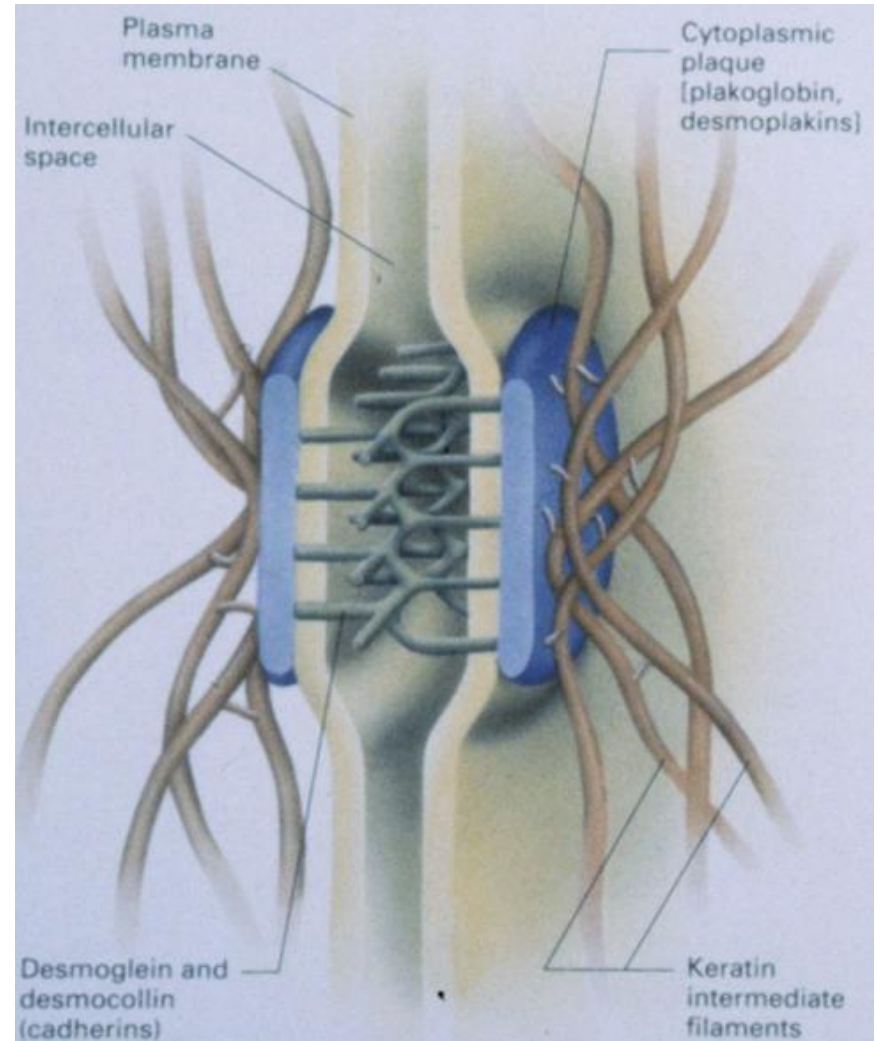


Cell Junctions

- Cell junctions are composed of specialized protein complexes that allow neighboring cells to:
 - adhere to one another
 - communicate with one another
- The proteins in the extracellular matrix and cell junctions control:
 - the three-dimensional organization of cells in tissues
 - the growth, movement, shape, and differentiation of these cells

Desmosomes are intermediate filament-based cell adhesion complexes

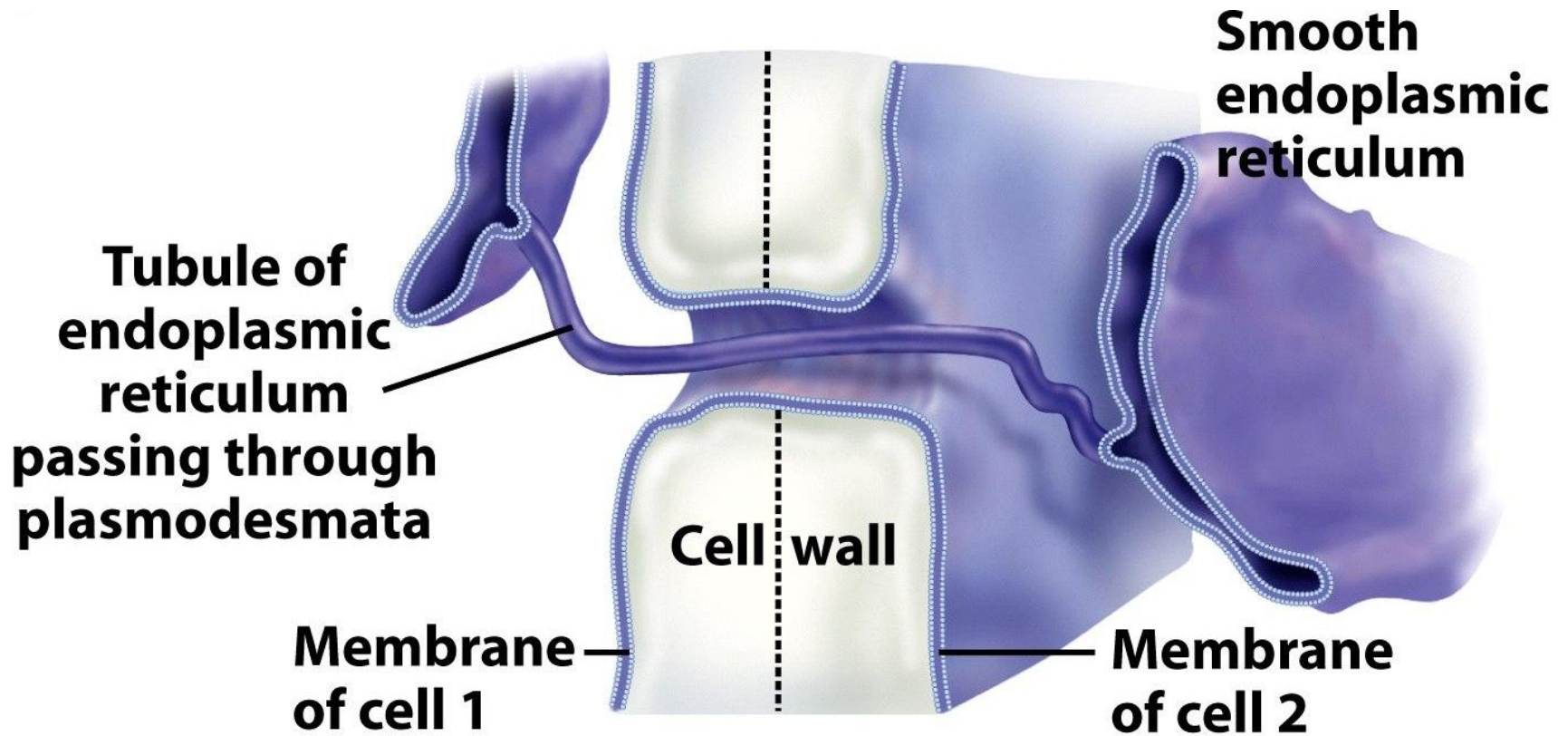
- Desmosomes are components of the junctional complex.
- Desmosomes function as both:
 - adhesive structures
 - signal transducing complexes



Cell Junctions

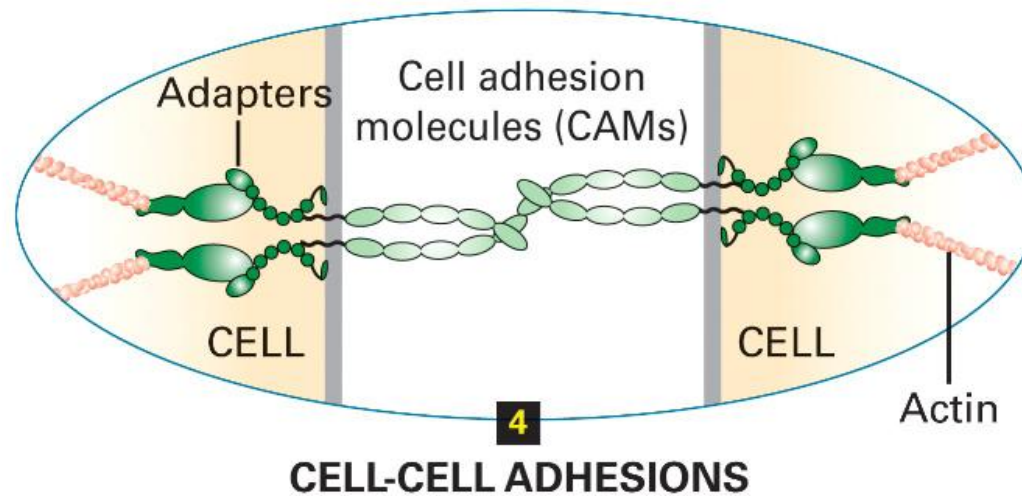
- The cell walls of **plant cells** are perforated by tiny channels, the **plasmodesmata**.
- They function as intercellular cytoplasmic bridges to facilitate **communication** & **transport** of nutrients between plant cells.
- Most plasmodesmata also contain a narrow tube-like structure derived from the smooth ER of the connected cells.
- Plasmodesmata allow ions & small molecules to move directly from one cell to another through the connecting cytoplasm.
- Macromolecules move through some plasmodesmata using energy-dependent processes.

Cell Junctions



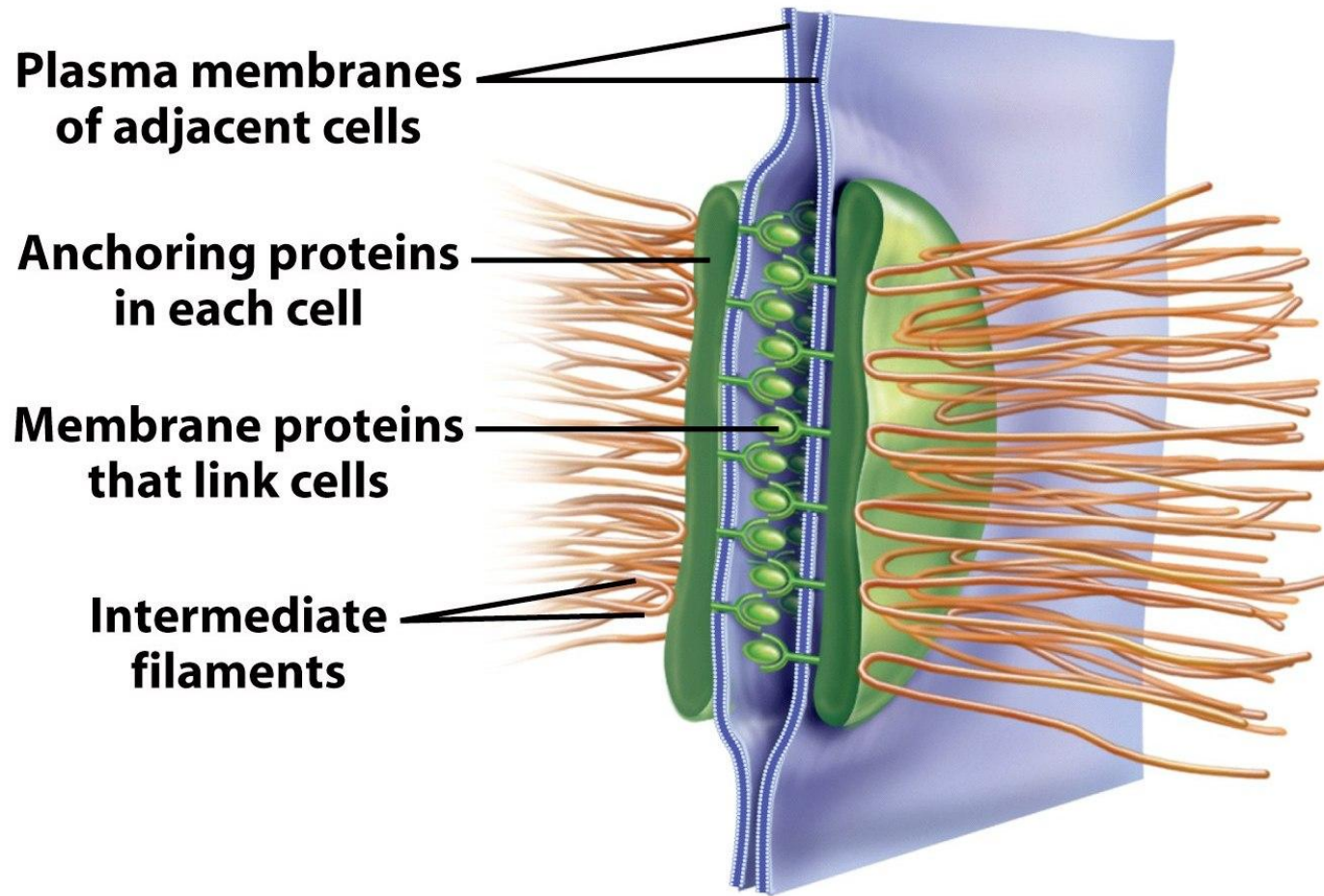
Cell Junctions

- Cells in animals are also linked directly to each other by **cell adhesion molecules (CAMs)**, which are glycoproteins embedded in the plasma membrane.



- They bind to specific molecules on other cells, organising and holding together cells of the same type in body tissues.
- Cell–cell adhesions are strengthened by a number of junctions, namely **anchoring junctions**, **tight junctions**, and **gap junctions**.

Cell Junctions



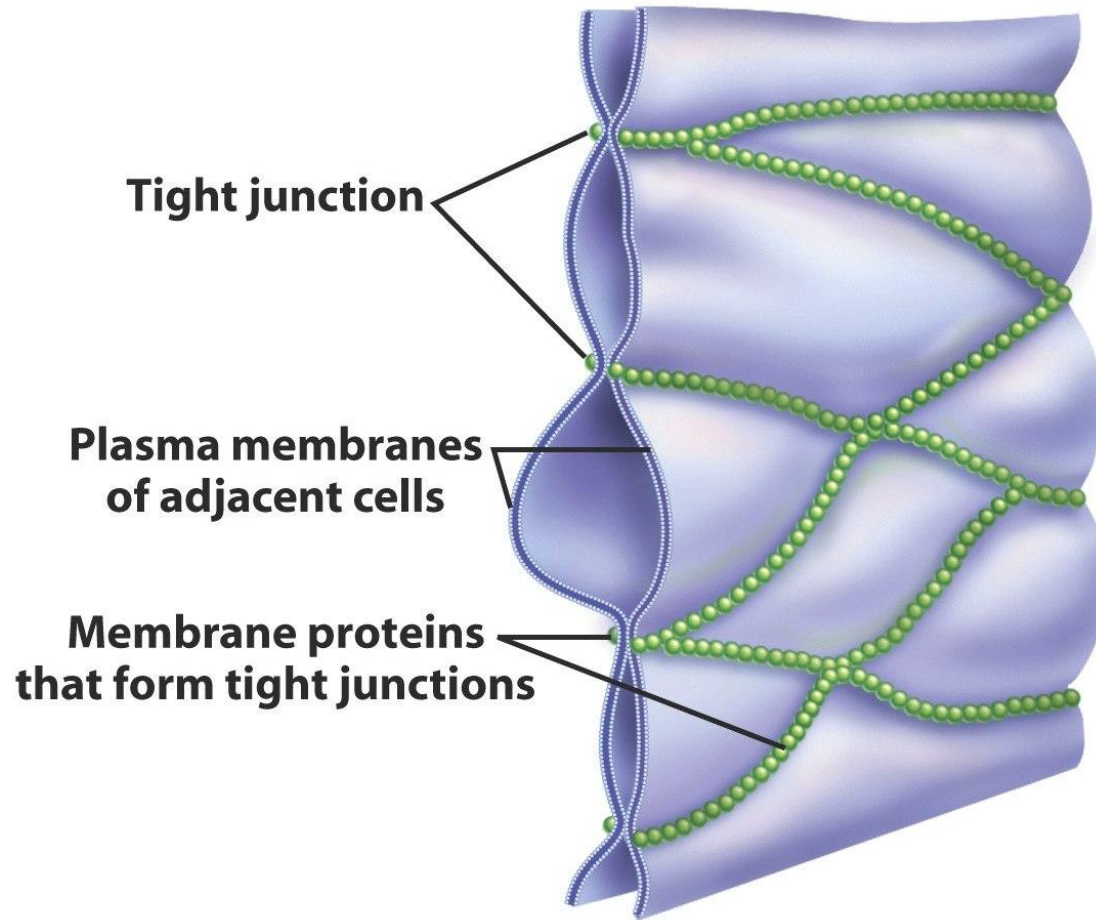
Cell Junctions

- **Anchoring junctions** strengthen the cell-to-cell connections made by CAMs
- **Tight junctions** seal the spaces between cells
- **Gap junctions** create direct channels of communication between animal cells.

Tight junctions form selectively permeable barriers between cells

- Tight junctions are part of the junctional complex that forms between adjacent epithelial cells or endothelial cells.
- Tight junctions regulate transport of particles between epithelial cells.

Cell Junctions



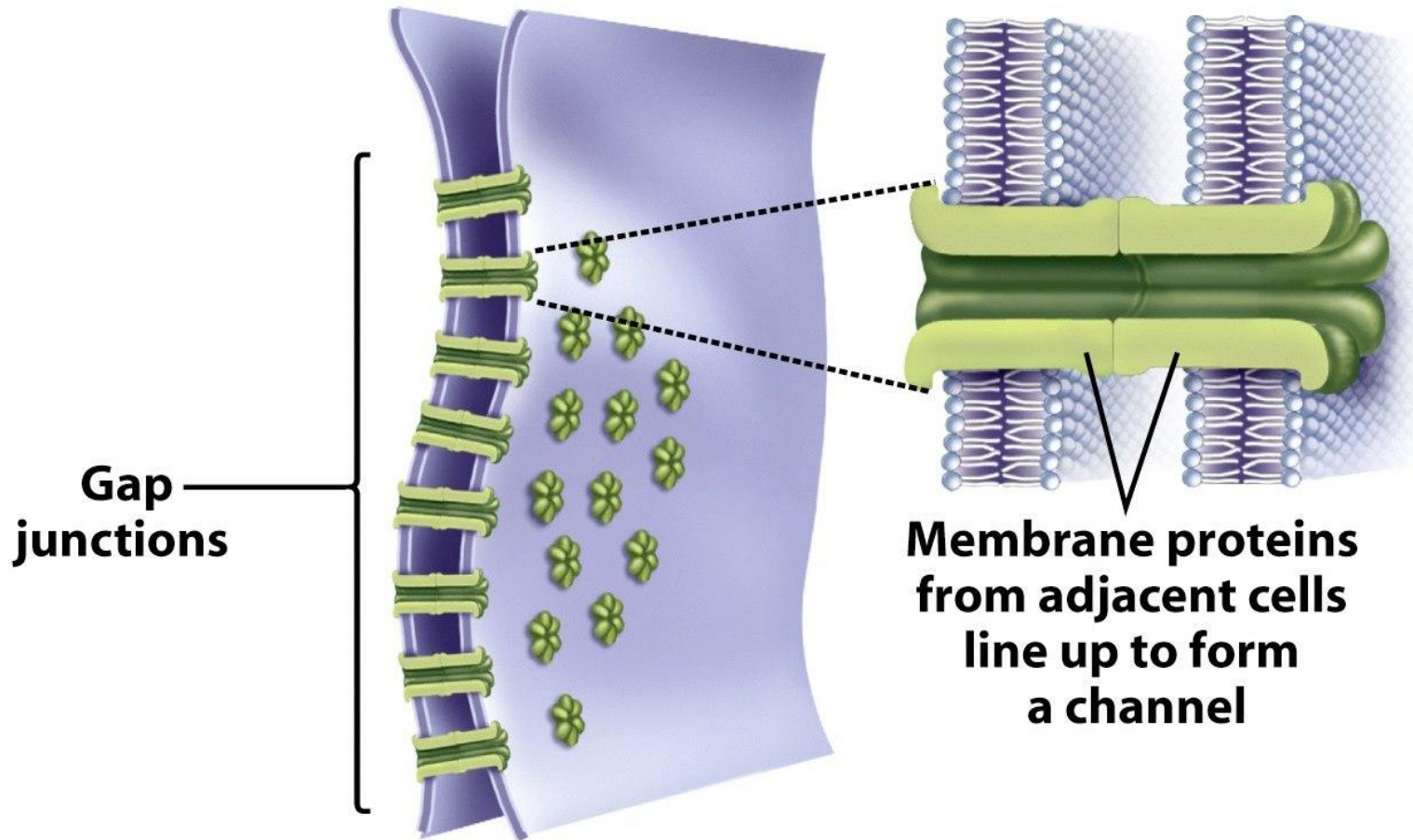
Gap junctions allow direct transfer of molecules between adjacent cells

- Gap junctions are protein structures that facilitate direct transfer of small molecules between adjacent cells.
- They are found in most animal cells.
- The gap junction channels consist of two halves, called connexons or hemichannels.
 - Each consists of six protein subunits called connexins.

Gap junctions allow direct transfer of molecules between adjacent cells

- Gap junction permeability is regulated by opening and closing of the gap junction channels, a process called **“gating.”**
- Gating is controlled by changes in
 - intracellular pH
 - calcium ion flux
 - direct phosphorylation of connexin subunits
- Gap junctions:
 - allow for free diffusion of molecules 1200 daltons in size
 - exclude passage of molecules 2000 daltons

Cell Junctions



Cell Communication

- Cell communication is essential to organise the activities of cells in multicellular organisms.
- For example, the ability of cells to communicate with one another in a regulated way is responsible for:
 - the controlled growth and development of an animal;
 - the integrated activities of its tissues and organs.
- Cell communication also takes place among single-celled organisms.
- The principles of cell communication are similar in unicellular and multicellular organisms, and some components are shared between them.

Cell Communication

- The physical environment is full of signals.
- For example, plants respond to light as a signal by growing toward the source of light.
- However, a cell deep inside a large multicellular organism is far away from the exterior environment.
- Its signals come from neighboring cells and the surrounding extracellular fluids.
- In such organisms, chemical signals are often made in one part of the body and arrive at target cells by local diffusion or by circulation in the blood or the plant vascular system.

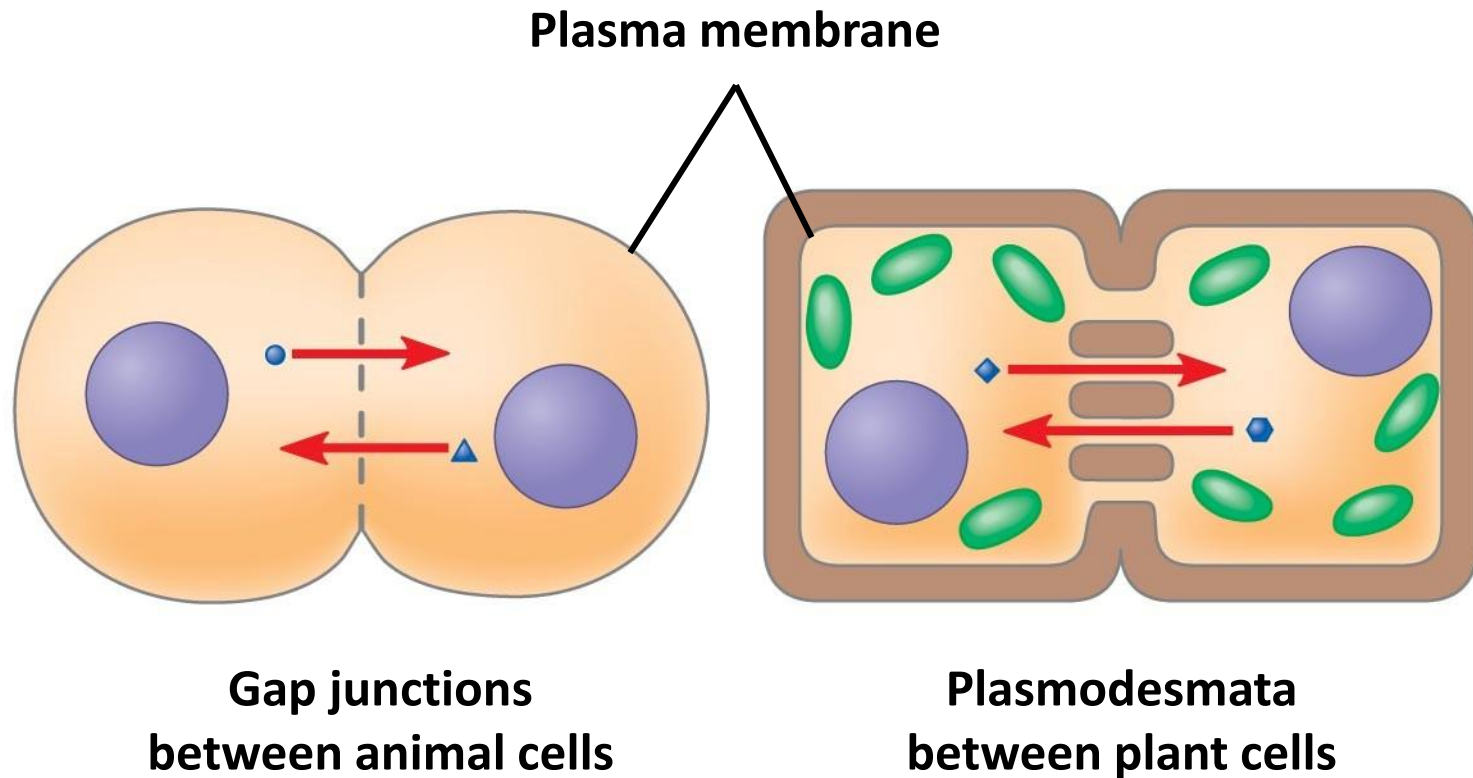
Cell Communication

- Cells communicate with each other in three ways:
 - by **direct contact**;
 - by **local signalling**;
 - by **long-distance signalling**.
- In long-distance signalling, a controlling cell releases a signal molecule that causes a response of target cells.
- Target cells process the signal in three steps:
 - **reception**;
 - **transduction**;
 - **response**.
- This process is called **signal transduction**.

Communication by Direct Contact

- In communication by direct contact, adjacent cells have direct channels linking their cytoplasms.
- In this rapid way of communication, ions and small molecules exchange directly between the two cytoplasms.
- The direct channels of communication are **gap junctions** in animal cells and **plasmodesmata** in plant cells.
- For example, **gap junctions** play a key role in spreading electrical signals from one cell to the next in cardiac muscle.
- **Plasmodesmata** play a key role in distributing plant hormones (which regulate growth) to other cells.

Communication by Direct Contact

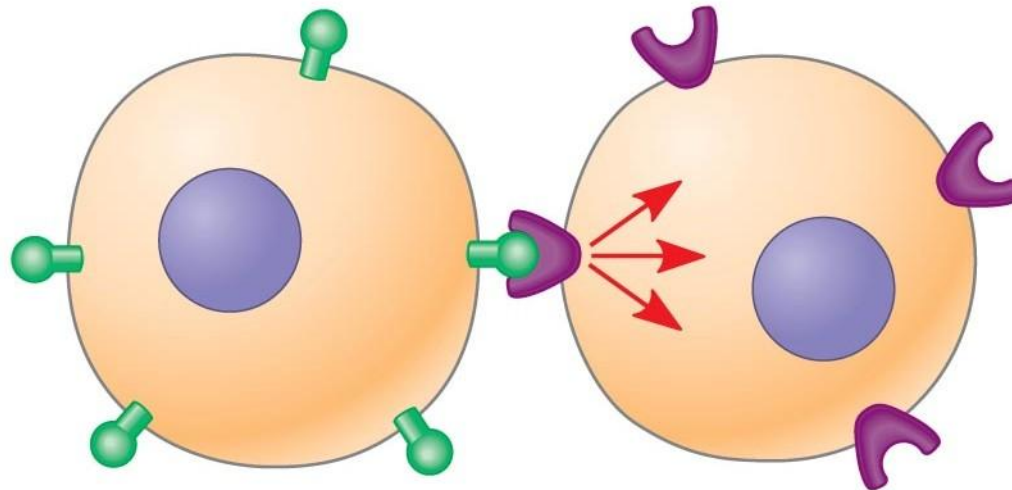


Cell junctions

Communication by Direct Contact

- Cells can also communicate through a process called **cell–cell recognition**.
- In this process, animal cells with particular cell-surface molecules dock with one another, initiating communication between the cells.
- Most of the cell-surface molecules that mediate cell–cell recognition are proteins from the **immunoglobulin (Ig) superfamily**.
- For example, cell–cell recognition of this kind activates particular cells in a mammal's immune system in order to organise and begin an immune response.

Communication by Direct Contact

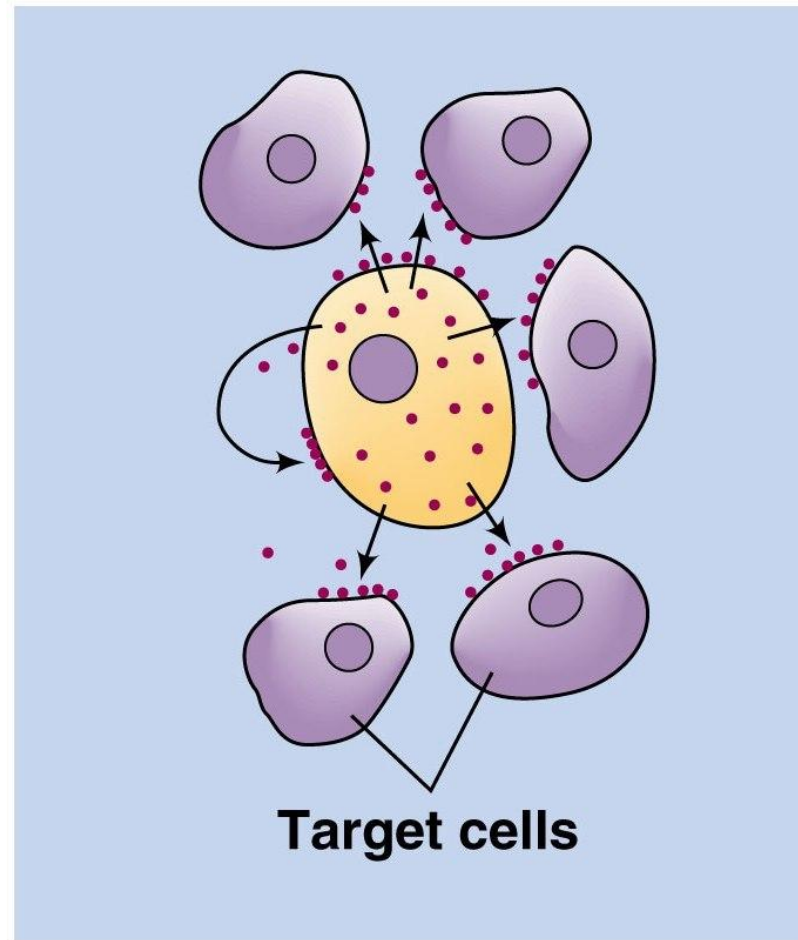


Cell-cell recognition

Communication by Local Signalling

- In local signalling, a cell releases a signal molecule that diffuses through the extracellular fluid and causes a response in nearby target cells.
- The effect of cell signalling is local, so the signal molecule is referred to as a **local regulator** (e.g., a growth factor).
- The process is termed **paracrine regulation** (from the Greek *para*, beside).
- In some cases the local regulator acts on the same cell that produces it.
- This is called **autocrine regulation** (from the Greek *auto*, self).

Communication by Local Signalling

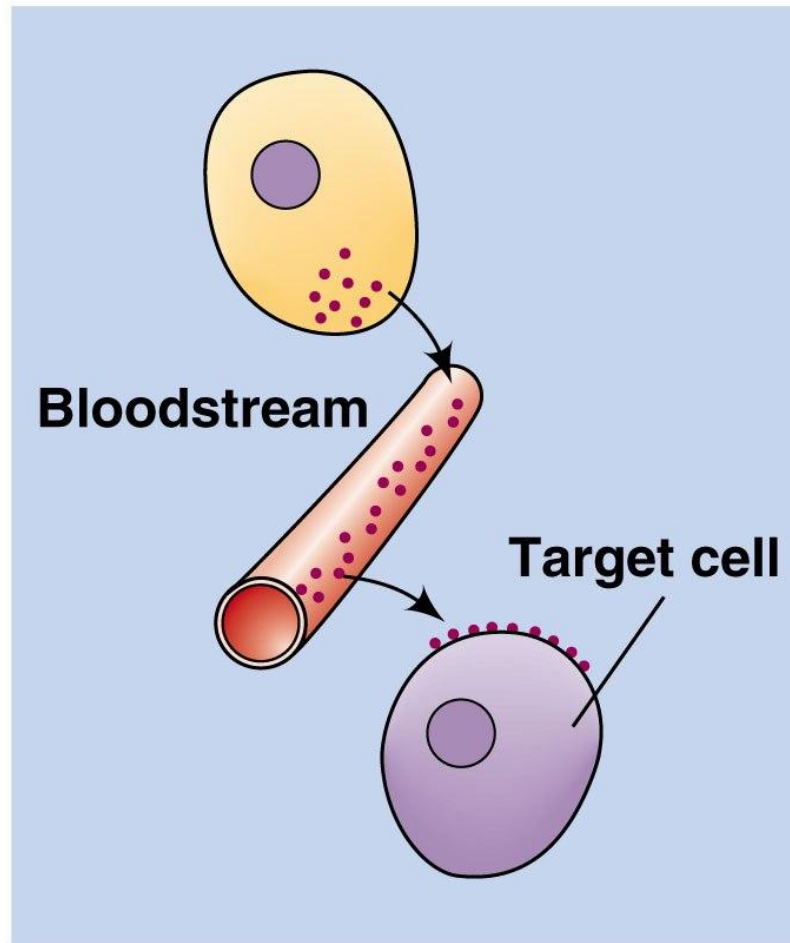


Local regulators

Communication by Long-Distance Signalling

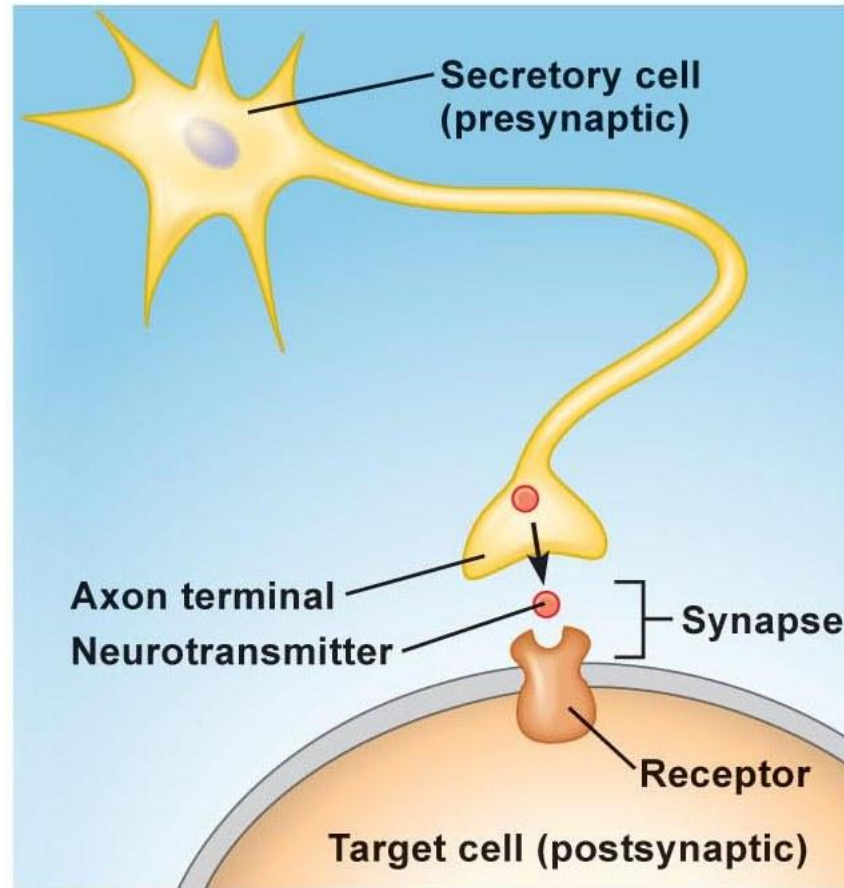
- In this form of communication, a controlling cell secretes a long-distance signalling molecule called a **hormone**.
- Hormones produce a response in target cells that may be far from the controlling cell.
- The process is called **endocrine regulation** (from the Greek *endo*, within).
- For example, in response to stress, cells of a mammal's adrenal glands secrete the hormone **epinephrine** (also known as **adrenaline**) into the bloodstream.
 - Epinephrine acts on target cells to increase the amount of glucose in the blood.

Communication by Long-Distance Signalling



Hormones

Synaptic Signalling: Local or Long-Distance?



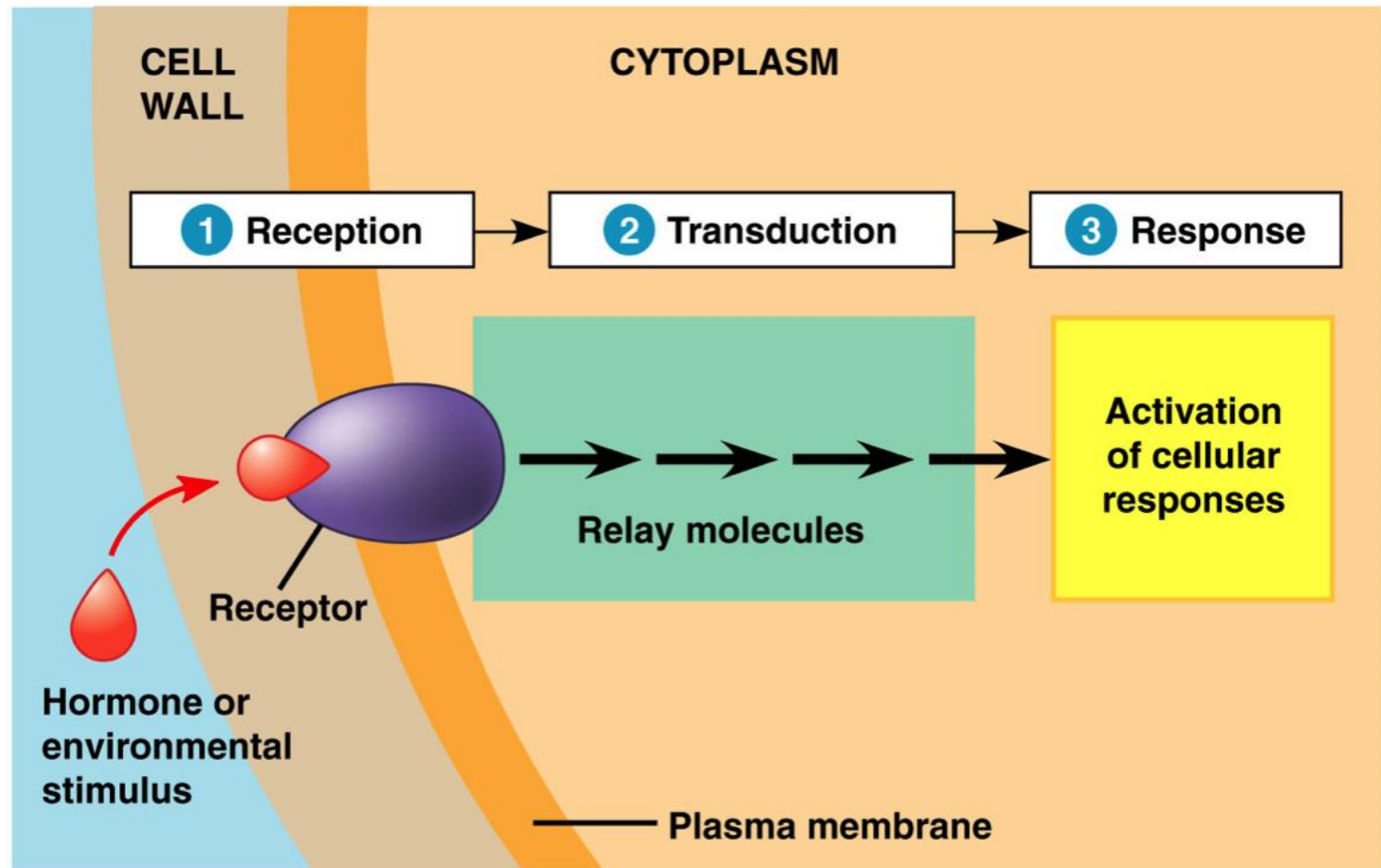
Neurotransmitters

**Target cells process the signal in
three steps**

The Three Stages of Signal Transduction

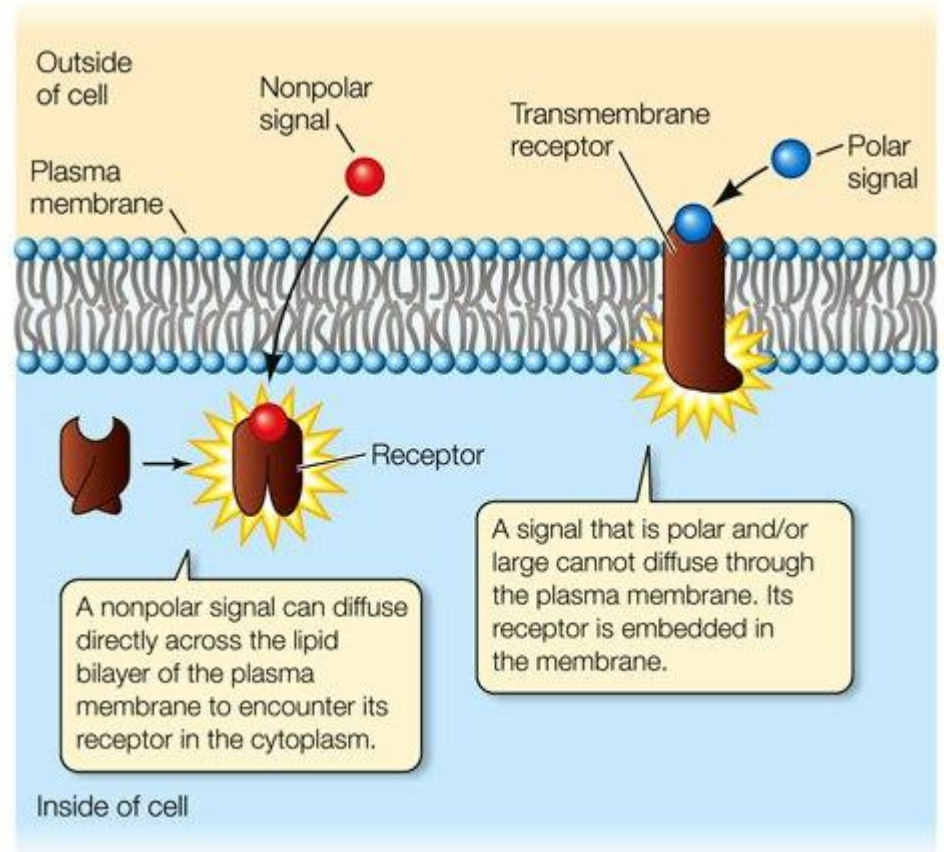
- The three stages of signal transduction are reception, transduction, and response.
- **Reception** is the target cell's detection of a chemical signal coming from outside the cell. (This is the job of **receptors**.)
- In a mammal, all cells may be exposed to a chemical signal that is circulated in the blood, such as epinephrine.
- However, most body cells are not capable of responding to this signal.
 - Only cells with the appropriate receptors can respond!

The Three Stages of Signal Transduction



Receptors: Cell-Surface vs Intracellular

- Depending on the nature of its signal, a receptor may be located in the plasma membrane or in the cytoplasm of the target cell.
- Peptide hormones and neurotransmitters are polar signals recognised by cell-surface receptors in animals.
- Steroid hormones are relatively small, non-polar signals recognised by intracellular receptors in animals.



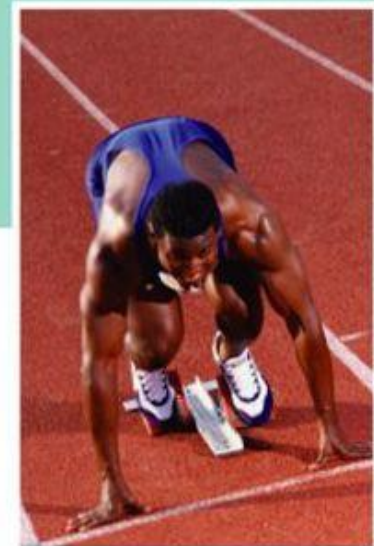
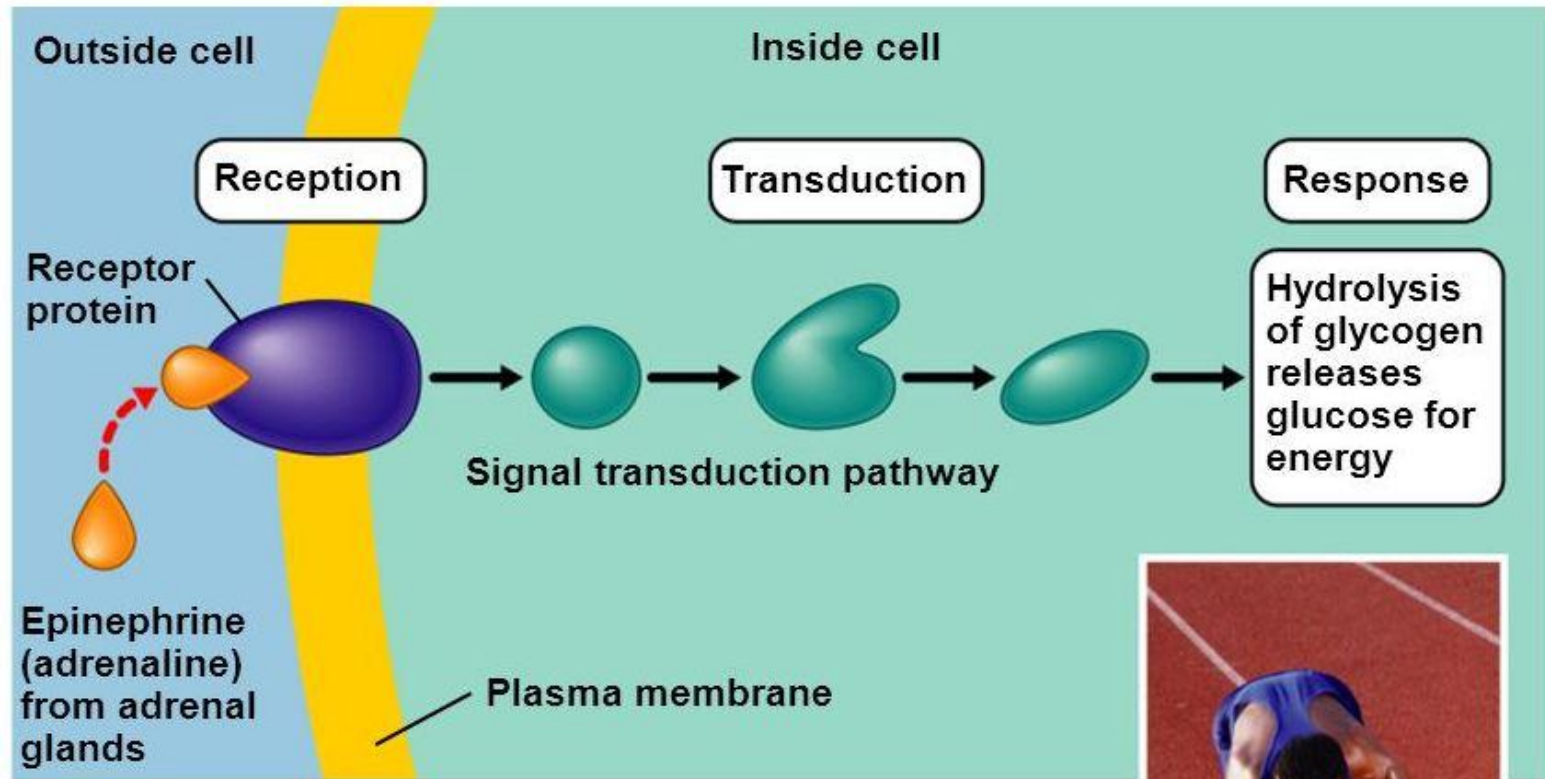
The Three Stages of Signal Transduction

- **Transduction** is the process of changing the signal into the form necessary to cause the cellular response.
- It usually starts with a shape change in the receptor which, in turn, activates the synthesis of **second messengers**.
- Second messengers are small molecules (*e.g.*, cAMP) and ions (*e.g.*, Ca^{2+}) in the cell that **amplify** the signal and transfer it from the receptor to other proteins that carry out the response.
 - For example, each molecule of epinephrine that arrives at the plasma membrane ultimately results in the release of 10^8 molecules of glucose into the blood-stream .
- The chain of reactions that amplifies and distributes the signal on its way to the ultimate cellular response is called a **signalling cascade**.

The Three Stages of Signal Transduction

- In the third and last stage, the transduced signal causes a specific cellular **response**.
- The response depends on the signal and the receptors on the target cell.
- The response can involve any of the following proteins:
 - **ion channels**, which open or close in order to regulate ion flow across the membrane;
 - **enzymes**, which catalyse biochemical reactions;
 - **transcription factors**, which turn the expression of particular genes on and off.

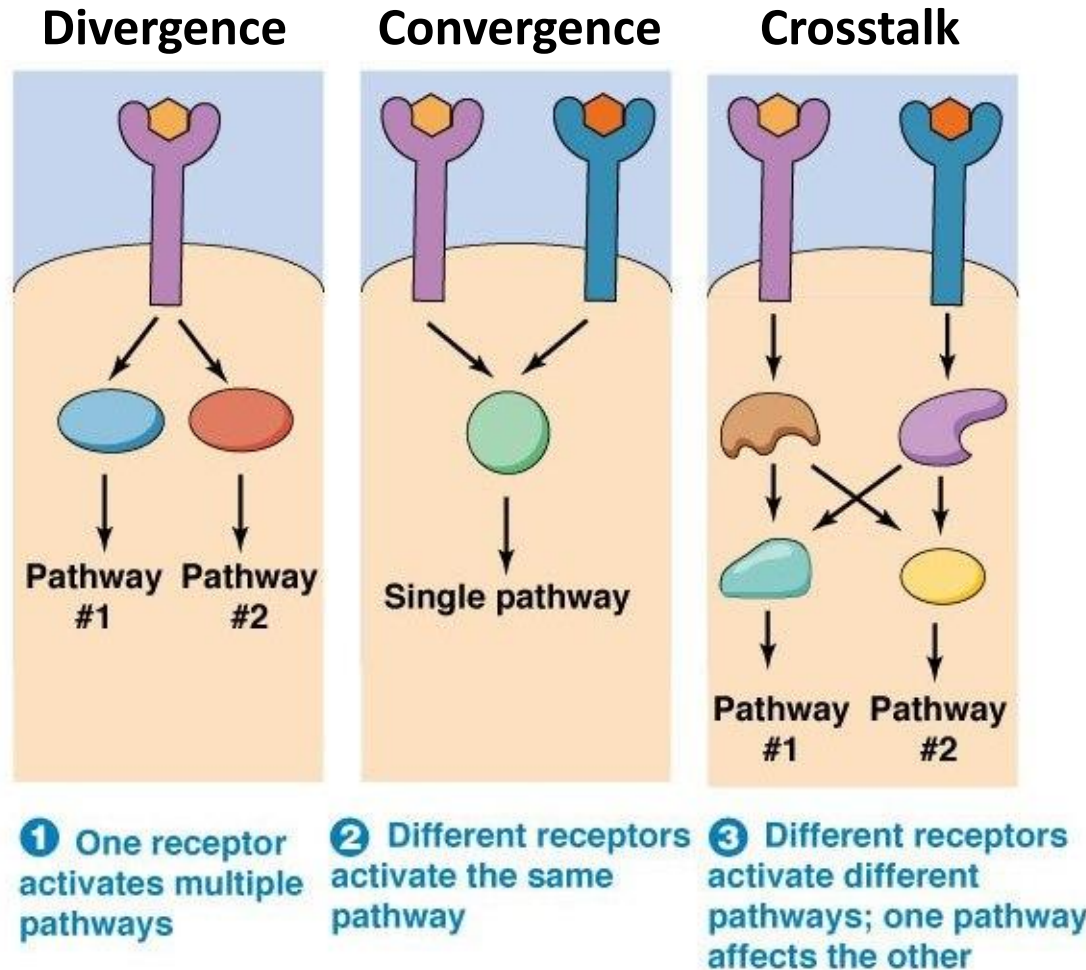
The Three Stages of Signal Transduction



Integration of Multiple Signals

- Each cell receives a complex combination of signals which simultaneously trigger many different signalling pathways.
- Signalling pathways usually have multiple steps and can:
 - **diverge** (*i.e.*, go in different directions);
 - **converge** (*i.e.*, meet at a particular point);
 - **crosstalk** (*i.e.*, interact with each other).
- Divergence causes multiple responses to a single signal.
- Convergence causes signal integration and coordination.
- Crosstalk leads to modifications, or fine-tunings, of the cellular responses controlled by the signalling pathways.

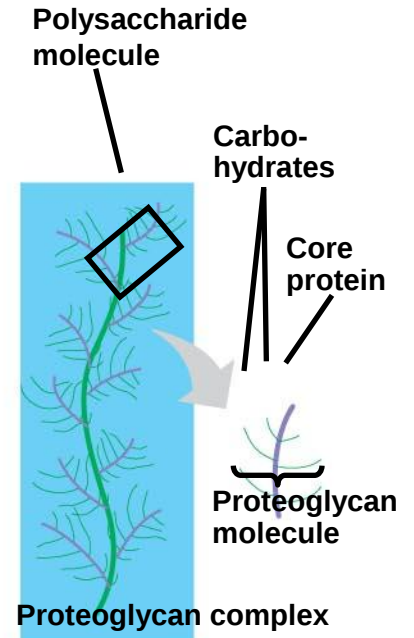
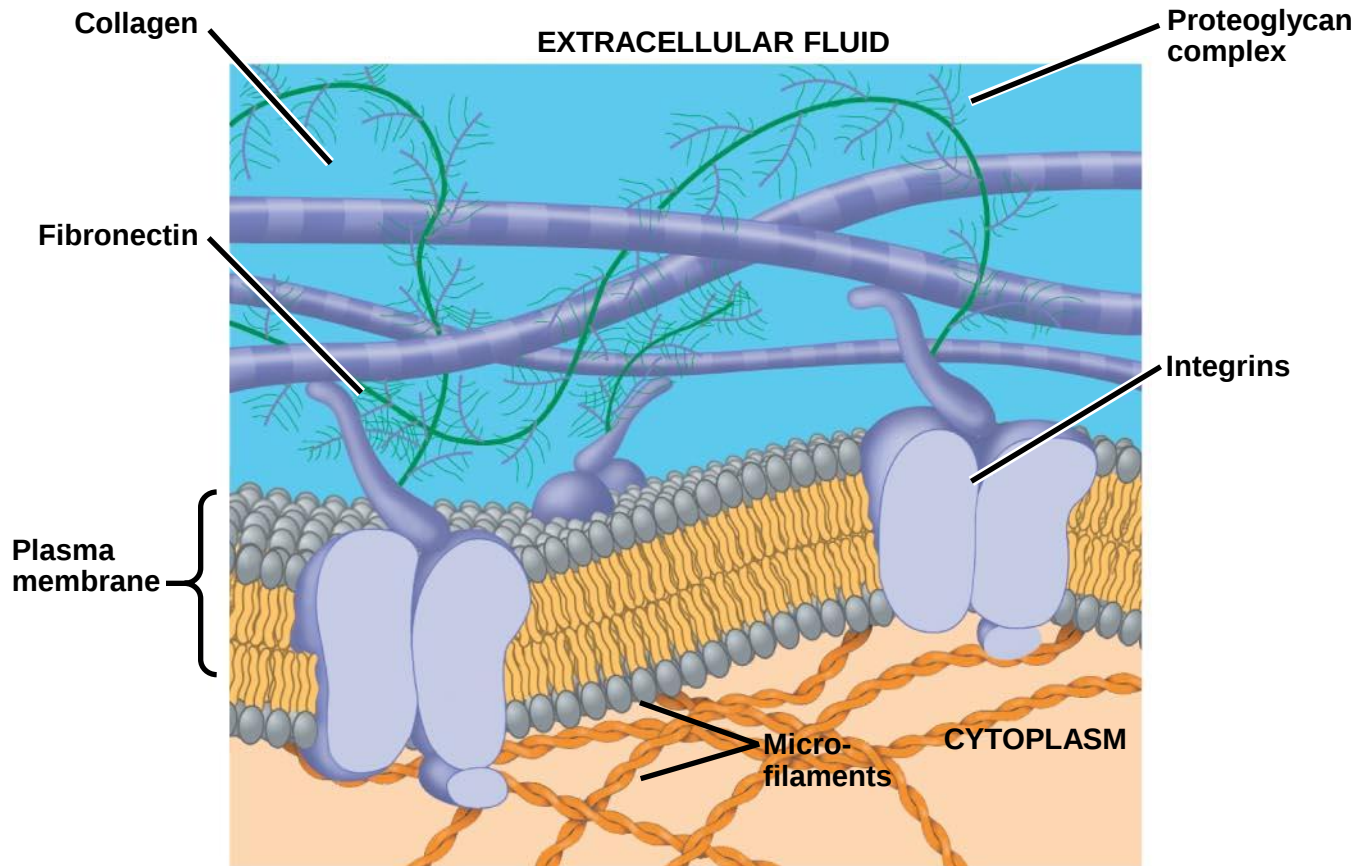
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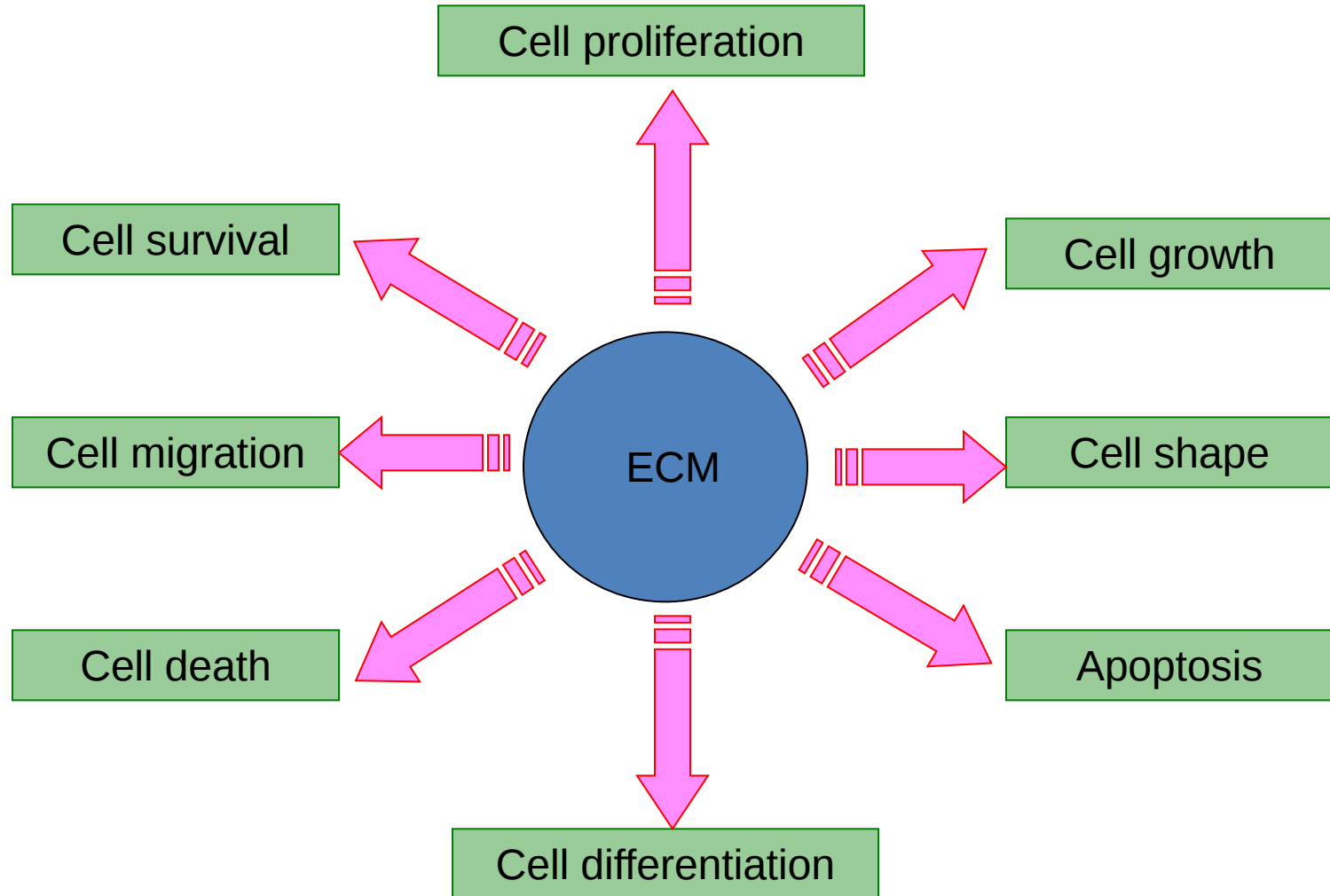
Summary

- Cell junctions are specialised protein complexes that allow neighbouring cells to adhere to and/or communicate with each other.
- The ECM is a dense network of proteins that lies between cells and is made by the cells within the network.
- Cell–cell and cell–ECM adhesions control the 3D organisation of cells in tissues as well as the growth, movement, shape, and differentiation of these cells.
- ECM is composed of:
 - Collagen, proteoglycans, and fibronectin, which the cell secretes.
 - Different from the plant extracellular matrix, which is composed of cellulose.
- Collagen: Most abundant glycoprotein, forms strong fibers outside of the cell.
- Proteoglycans: another class of glycoproteins, collagen fibers are embedded in a network made from proteoglycans.
- Fibronectin: Glycoprotein that attaches the ECM to the cell itself.
- Integrins: Cell surface receptor that connects to fibronectin, which attaches to the ECM
- Cells receive many signals from the physical environment and from other cells.

ECM of an animal cell



ECM plays role in almost each event of cell



Summary

- ✓ Autocrine signals affect the cells that secrete them; paracrine signals diffuse to and affect nearby cells; and hormones are carried through the circulatory systems of animals or the vascular systems of plants.
- ✓ A signal transduction pathway involves the interaction of a signal (often a chemical ligand) with a receptor; the transduction and amplification of the signal via a series of steps within the cell; and a cellular response.

Summary

- ✓ Cells respond to signals only if they have specific receptor proteins that can be activated by those signals. Most receptors are located on the cell surface.
- ✓ A cascade of events, one following another, occurs after a receptor is activated by a signal.
- ✓ Often, a soluble second messenger conveys signaling information from the primary messenger (ligand) at the membrane to downstream signaling molecules in the cytoplasm.
- ✓ Activated enzymes may, in turn, activate other enzymes in a signal transduction pathway, leading to impressive amplification of a signal.
- ✓ The cellular responses to signals may include the opening of ion channels, the alteration of enzyme activities, or changes in gene expression.
- ✓ Signal transduction pathways involve modification of enzymes and transcription factors. A great deal of crosstalk occurs between pathways.

Summary

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Extra Reading:

pp. 881–883

Chapter 19

*Figures are mainly obtained from
Molecular Biology of the Cell, 5th Ed.

Molecular Biology of THE CELL

Fifth Edition



ALBERTS JOHNSON LEWIS RAFF ROBERTS WALTER