Al-Mustaqbal University College

Pharmacy Department / Second Stage

PHYSIOLOGY

L1 : Introduction to Physiology

Dr. Abdulhusein Mizhir Almaamuri

Physiology from Ancient Greek *(physis)* 'nature, origin', and *(-logia)* 'study of') is the scientific study of functions and mechanisms in a living system.As a sub-discipline of biology, physiology focuses on how organisms, organ systems, individual organs, cells, and biomolecules carry out the chemical and physical functions in a living system. According to the classes of organisms, the field can be divided into medical physiology, animal physiology, plant physiology, cell physiology, and comparative physiology

The Cell and Its Functions:

Any Life: Origin → Development → Progression

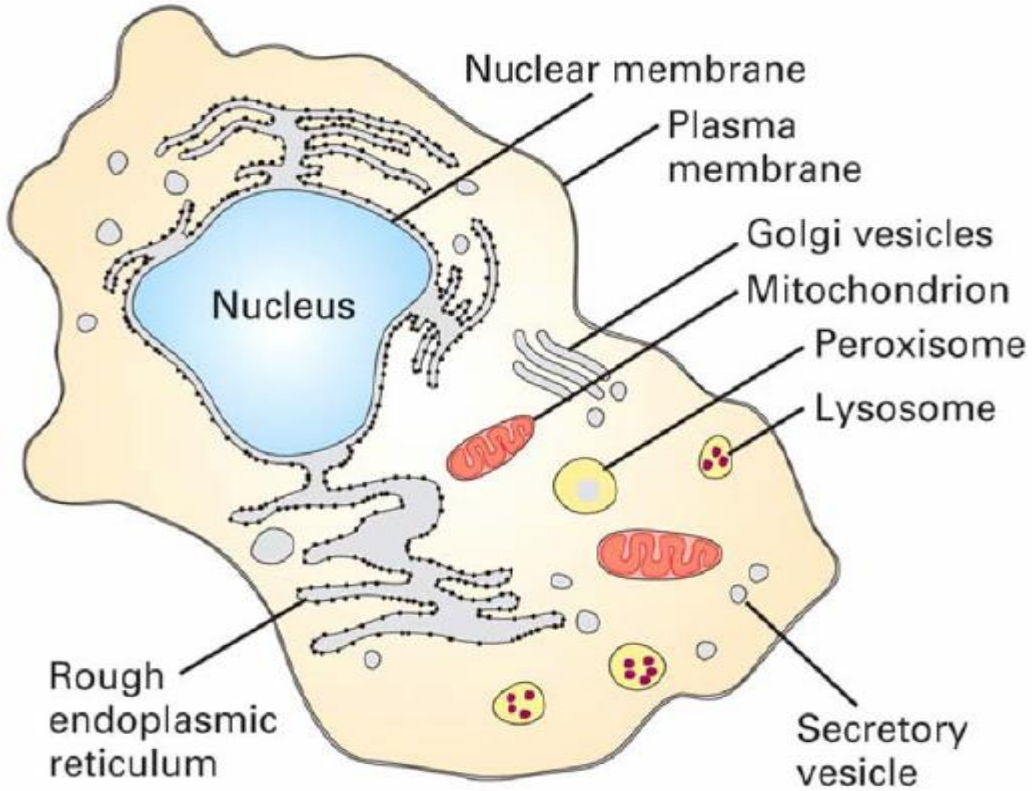
Each of these requires physical and chemical factors.

The goal of physiology is to explain these factors.

Any type of life (simple virus, largest tree, human being) has its own ***functional*** characteristics.

The vast field of physiology can be divided into: Viral, bacterial, cellular, plant and human physiology (and many more subdivisions).

- The basic living unit of the body is the cell. Each organ is an aggregate of many different cells held together by intercellular supporting structures.
- Each type of cell is specially adapted to perform one or a few particular functions.
- Although the many cells of the body often differ markedly from one another, all of them have certain basic characteristics that are alike.



GENERAL PRINCIPLES

Organization of the Body:

The cells that make up the bodies of all but the simplest multicellular animals, both aquatic and terrestrial, exist in an "internal sea" of **extracellular fluid (ECF)** enclosed within the integument of the animal. From this fluid, the cells take up O_2 and nutrients. In animals with a closed vascular system, the ECF is divided into two components: the **interstitial fluid** and the circulating **blood plasma.** The plasma and the cellular elements of the blood, principally red blood cells, fill the vascular system.

The interstitial fluid is that part of the ECF that is outside the vascular system, bathing the cells. About a third of the **total body water (TBW)** is extracellular; the remaining two-thirds are intracellular **(intracellular fluid).**

Body Composition :

In the average young adult male, 18% of the body weight is protein and related substances, 7% is mineral, and 15% is fat. The remaining 60% is water.

- Differences Between ECF and ICF

- The **ECF** contains **large** amounts of ***sodium, chloride,*** and ***bicarbonate ions*** plus **nutrients** for the cells, such as ***oxygen, glucose, fatty acids***, and ***amino acids***. It **also** contains ***carbon dioxide*** that is being **transported** from the cells to the **lungs** to be **excreted**, plus other **cellular waste products** that are being **transported** to the **kidneys** for excretion.
- The **ICF** differs **significantly** from the **ECF**; specifically, it contains **large** amounts of ***potassium, magnesium,*** and ***phosphate ions*** instead of the sodium and chloride ions found in the **ECF**.

	ECF	ICF
% from total body water	1/3	2/3
Cell environment	Outside the cell (Vascular or extravascular)	Inside the cell
Main ion composition	Na^+, Cl^-, and HCO_3^-	K^+, Mg^{2+}, and PO^{2-}
pH	7.4	7.4
Osmolarity	~ 300mOs/L	~ 300mOs/L
Function	Carry nutrients and gases into the cells and out of the cell	A vehicle for making intracellular solution (cytoplasm)

- **ECF Transport and Mixing System - The Blood Circulatory System**
- **ECF** is **transported** through all **parts** of the body in **two stages**:
- The **first** stage is **movement of blood** through the body in the **blood vessels**.
- The **second** is movement of **fluid** between the **blood capillaries** and the ***intercellular spaces*** between the **tissue cells**.
- The **walls** of the **capillaries** are **permeable** to **most molecules** in the **plasma** of the blood, with the **exception** of the **large** plasma protein **molecules**.

- ECF also delivers nutrients for the cells, such as O_2, glucose, fatty acids, and amino acids; and washout cellular waste products such as CO_2 and others.
- The difference in ion composition between ICF and ECF confirms the presence of special mechanisms for transporting these ions through the cell membranes.
- The % of body water in the child is more than in adult and decrease greatly in older ages.

- **“Homeostatic” Mechanisms of the Major Functional Systems**
- **Homeostasis:**
  - The term ***homeostasis*** is used by physiologists to **mean *maintenance of nearly constant conditions in the internal environment*.**
  - Essentially **all organs and tissues** of the body **perform functions** that help **maintain these constant conditions**.

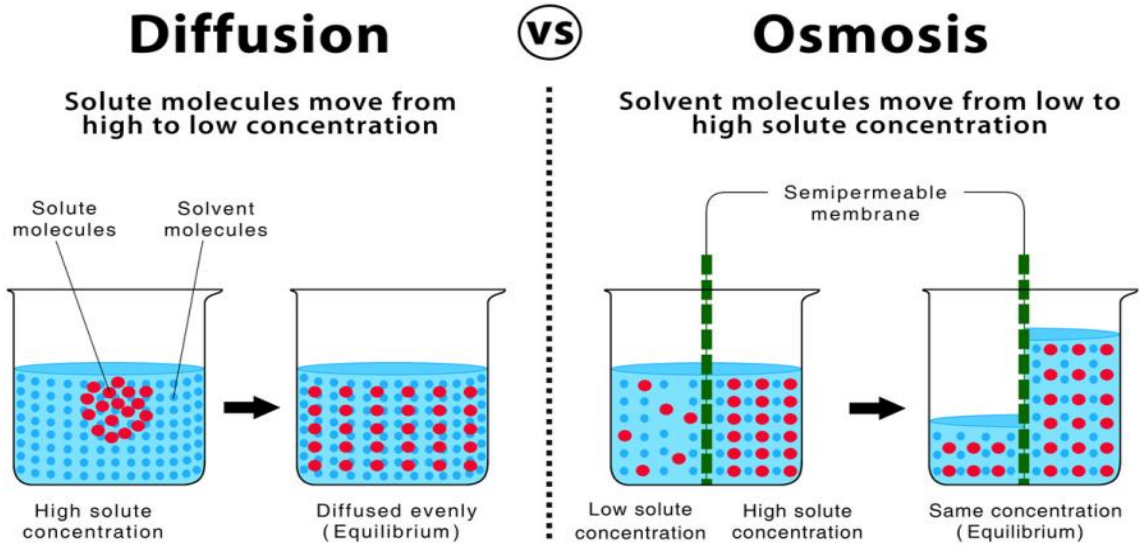
- **DIFFUSION** and **OSMOSIS**

- These are physical phenomena that are very important in physiology.
- Lipid soluble gases and small size unionized solutes cross the biological membranes via diffusion.
- Vascular and cellular volumes are adjusted via osmosis

	Diffusion	Osmosis
Definition	It is a net flux of solute particles from areas of high to areas of low concentration across a permeable membrane until equilibrium is achieved	It is the migration of water from areas of low to areas of high solute concentration across a selective permeable membrane (only permeable to water)
Moving object	Solute	water
Driving force	Concentration difference of free particles of a solute or a gas	Concentration difference of free water molecules
Direction of movement	From high to low solute concentration areas	From low to high solute concentration areas
Physical Law	Fick's law of diffusion	van't Hoff
Determinants	• Direct proportionate: Conc. difference of solutes, membrane surface area and temperature * • Inverse proportionate: membrane thickness.	• Inverse proportionate: Conc. difference of osmotically effective solute particles, osmotic pressure**
Transport form	Passive	Passive
* As the temperature increases, the number of randomly moving particles increases and thus diffusion increases; the reverse is true when temperature decreases. ** osmotic pressure: is the extra pressure that must be applied on the solution to stop the migration of solvent through the semi-permeable membrane		

- The ***osmotic pressure*** exerted by molecules or ions, is ***determined*** by the **<u>number of particles</u>** per unit volume of fluid (**not by** the mass or concentration of the particles)
- *The reason for this is that each particle in a solution exerts the same amount of pressure against the membrane.*
- The osmole is used (in place of grams) to express the concentration of a solution in terms of numbers of particles.

- *1 osmole is 1 gram molecular weight of osmotically active solute.*



- *Thus, 180 grams of glucose, which is 1 gram molecular weight of glucose (Wt/Mwt = 180/180), is equal to 1 osmole of glucose because glucose does not dissociate into ions.*

If a solute dissociates into two ions, 1 gram molecular weight of the solute will become 2 osmoles because the number of osmotically active particles is now twice as great as is the case for the non dissociated solute.

- *Therefore, if we put 58.5g NaCl in a 1 Liter this give us 1 gram molecular weight of NaCl [Wt/Mwt =58.5/(23 + 35.5)], if this solute fully dissociated in water this give us 2 osmoles.*

$NaCl \rightarrow 1\ Osm\ Na^{+} + 1\ Osm\ Cl^{-}$

The terms **"Osmolarity"** *vs* "**Osmolality**"

	Osmolarity	Osmolality
Expression	osmoles/L	osmoles/ Kg
Uses for	Determining osmotic pressure for solutions outside the body	Determining osmotic pressure for solutions inside the body
• However, the quantitative differences between osmolarity and osmolality are less than 1%. • Osmolarity (rather than osmolality), is more practical to measure thus it is the usual practice in almost all physiological studies		

The Term "**Tonicity**"

	Tonicity
Expression	Isotonic, hypertonic or hypotonic solution
Uses for	Describe the osmolarity of a solution relative to plasma
Plasma osmolarity	285-300 mOsm/L
Adjusted according to	Freezing point depression of a solution (isotonic fluid has freezing point depression of 0.52°C.

- ICF and interstitial fluid osmolarity are equal to that of plasma.

- Solutions that have the same osmolality as plasma are said to be isotonic; those with greater osmolality are hypertonic; and those with lesser osmolality are hypotonic.
- If solutions are injected or introduced in to eyes and nose, these are to be made isotonic in order to avoid hemolysis of RBC's and to avoid pain and discomfort
- All solutions that are initially isosmotic with plasma remain isotonic unless metabolized or diffuse into the cells.
- 0.9% NaCl (saline) solution remains isotonic since there is no net movement of the osmotically active particles in the solution into cells and the particles are not metabolized.
- 5% glucose solution is isotonic when initially infused intravenously, but glucose is metabolized, so the net effect is that of infusing a hypotonic solution.
- 1% w/v solution of NaCl has freezing point depression of 0.576 °C. Thus, isotonic [NaCl] solution is 0.52/0.576 x 1% = 0.9% w/v.
- Changes in extracellular osmolarity can cause cells, such as the RBCs to shrink or swell as water molecules move across the plasma membrane.

Regulation of Body Functions

- **Nervous System:**
- The nervous system is composed of three major parts:
- 1 - The ***sensory input portion***.
- 2 - The ***central nervous system*** (or ***integrative portion***).
- 3 - The ***motor output portion***.
- **Sensory receptors detect the state of the body or the state of the surroundings**. For instance, **receptors** in the **skin apprise** one whenever an **object touches** the skin at any point.
- The **CNS** is **composed** of the **brain and spinal cord**. The **brain** can **store information, generate thoughts, create ambition**, and **determine reactions** that the **body performs** in **response** to the **sensations**. Appropriate **signals** are then **transmitted** through the **motor output portion** of the nervous system to **carry out one's desires**.
- A **large segment** of the **NS** is called the ***autonomic system***. It **operates** at a **subconscious level** and **controls** many **functions** of the **internal organs**.

Regulation of Body Functions (Continued)

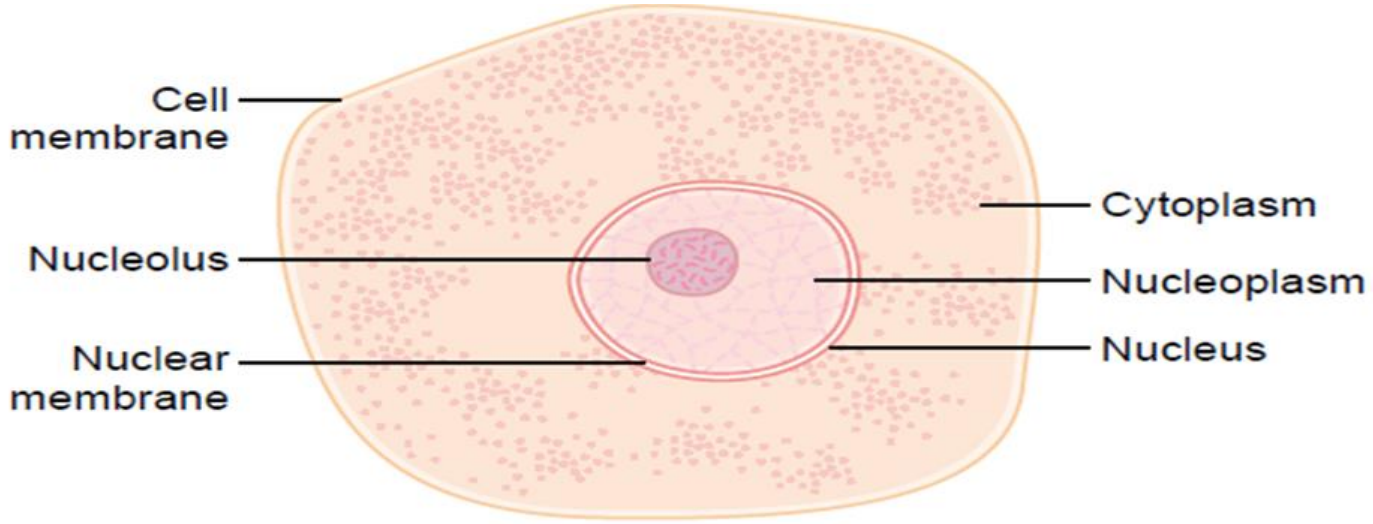
- **Hormonal System of Regulation:**
- There are **eight** major ***endocrine glands*** that **secrete chemical** substances called ***hormones***. Hormones are **transported** in the **ECF** to **all** parts of the **body** to **help regulate** cellular **function**. For instance, **thyroid** hormone **increases the rates** of most **chemical reactions** in all cells, thus helping **to set** the **tempo** of bodily activity. **Insulin controls glucose** metabolism; **adrenocortical** hormones control **sodium ion, potassium ion**, and **protein metabolism;** and **parathyroid** hormone controls **bone calcium and phosphate**.

- Thus, the **hormones** are a **system of regulation** that **complements** the **NS**. The **NS regulates** mainly **muscular and secretory activities** of the body, whereas the **hormonal system regulates** many **metabolic functions**.

The Cell and Its Functions

Organization of the Cell

A typical cell, as seen by the light microscope has two major parts, the **nucleus** and the **cytoplasm**. The nucleus is separated from the cytoplasm by a **nuclear membrane,** and the cytoplasm is separated from the surrounding fluids by a **cell membrane**, also called the **plasma membrane.**



The different substances that make up the cell are collectively called ***protoplasm.*** Protoplasm is composed mainly of five basic substances: water, electrolytes, proteins, lipids, and carbohydrates.

Physical Structure of the Cell

The cell is not only contain fluid, enzymes, and chemicals; it also contains highly organized physical structures, called ***intracellular organelles***. The physical nature of each organelle is as important as the cell's chemical constituents for cell function. For instance, without one of the organelles, the **mitochondria**, more than 95 per cent of the cell's energy release from nutrients would cease immediately.

Membranous Structures of the Cell

Most **organelles** of the cell are covered by membranes composed primarily of **lipids** and **proteins**. These membranes include the *cell membrane*, *nuclear membrane*, *membrane of the endoplasmic reticulum*, and *membranes of the mitochondria*, *lysosomes, and Golgi apparatus*. The membrane that surrounds the cell is:

Made up of ***lipids*** and ***proteins***. **Semipermeable** (allowing some substances to pass through it and excluding others). Generally referred to as the **plasma membrane**.

Membrane Lipids

- The major lipids are phospholipids The shape of the phospholipid molecule (**amphipathic molecule**) reflects its solubility properties: the "**head**" end of the molecule contains the **phosphate portion** and is relatively **soluble in water** (**polar**, **hydrophilic**) and the "**tail**" ends are relatively **insoluble** (**nonpolar**, **hydrophobic**).
  - *In the membrane, the **hydrophilic ends** of the molecules are exposed to the **aqueous environment** that bathes the exterior of the cells and the aqueous cytoplasm.*
  - *The **hydrophobic ends** meet in the water-poor **interior of the membrane**.*

- The lipids of the membranes provide a barrier that impedes the movement of water and water-soluble substances from one cell compartment to another because water is not soluble in lipids.

Membrane Proteins

- The protein molecules in the membrane often do penetrate all the way through the membrane, thus providing specialized pathways, often organized into ***actual pores***, for passage of specific substances through the membrane.

- Many different proteins are embedded in the membrane. They exist as:

✓ ***Integral proteins****: separate globular units that many pass through or are embedded in one leaflet of the membrane.*

✓ ***Peripheral proteins****: associated with the inside or outside of the membrane.*

- The amount of protein varies significantly with the function of the membrane but makes up on average 50% of the mass of the membrane.

- The proteins in the membrane carry out many functions:

- ***Cell adhesion molecules*** *(CAMs) that anchor cells to their neighbors or to basal laminas.*
- ***Pumps****, actively transporting ions across the membrane.*
- ***Carriers****, transporting substances down electrochemical gradients by facilitated diffusion.*
- ***Ion channels****, which, when activated, permit the passage of ions into or out of the cell.*
- ***Receptors*** *that bind ligands or messenger molecules, initiating physiologic changes inside the cell.*
- ***Enzymes****, catalyzing reactions at the surfaces of the membrane*.

Plasma Membrane Structural Components

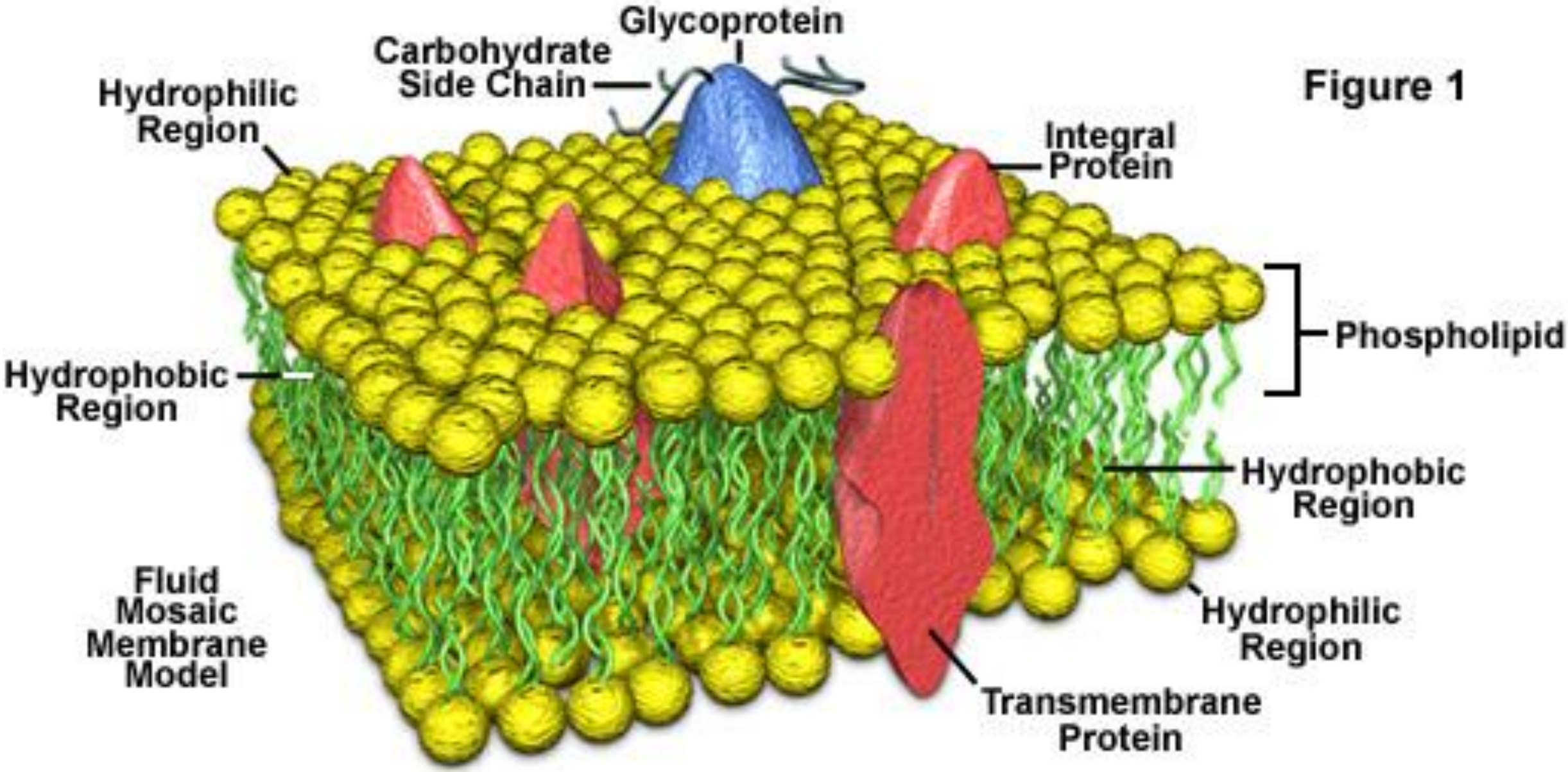


Figure 1

So, Proteins may function as **receptors** that bind neurotransmitters and hormones, initiating physiologic changes inside the cell. Proteins also function as **enzymes,** catalyzing reactions at the surfaces of the membrane. In addition, some glycoproteins function in antibody processing and distinguishing self from non self.

Underlying most cells is a thin, fuzzy layer plus some fibrils that collectively make up the **basement membrane** or, more properly, the **basal lamina.** The basal lamina and, more generally, the extracellular matrix are made up of many proteins that hold cells together, regulate their development, and determine their growth.

Cell Adhesion Molecules

Cells are attached to the basal lamina and to each other by **cell adhesion molecules (CAMs)**. These adhesion proteins have attracted great attention in recent years because they are important in embryonic development and formation of the nervous system and other tissues; in holding tissues together in adults; in inflammation and wound healing; and in the metastasis of tumors. Many pass through the cell membrane and are anchored to the cytoskeleton inside the cell. Some bind to like molecules on other cells (homophilic binding), whereas others bind to other molecules (heterophilic binding). Many bind to **laminins,** a family of large cross-shaped molecules with multiple receptor domains in the extracellular matrix

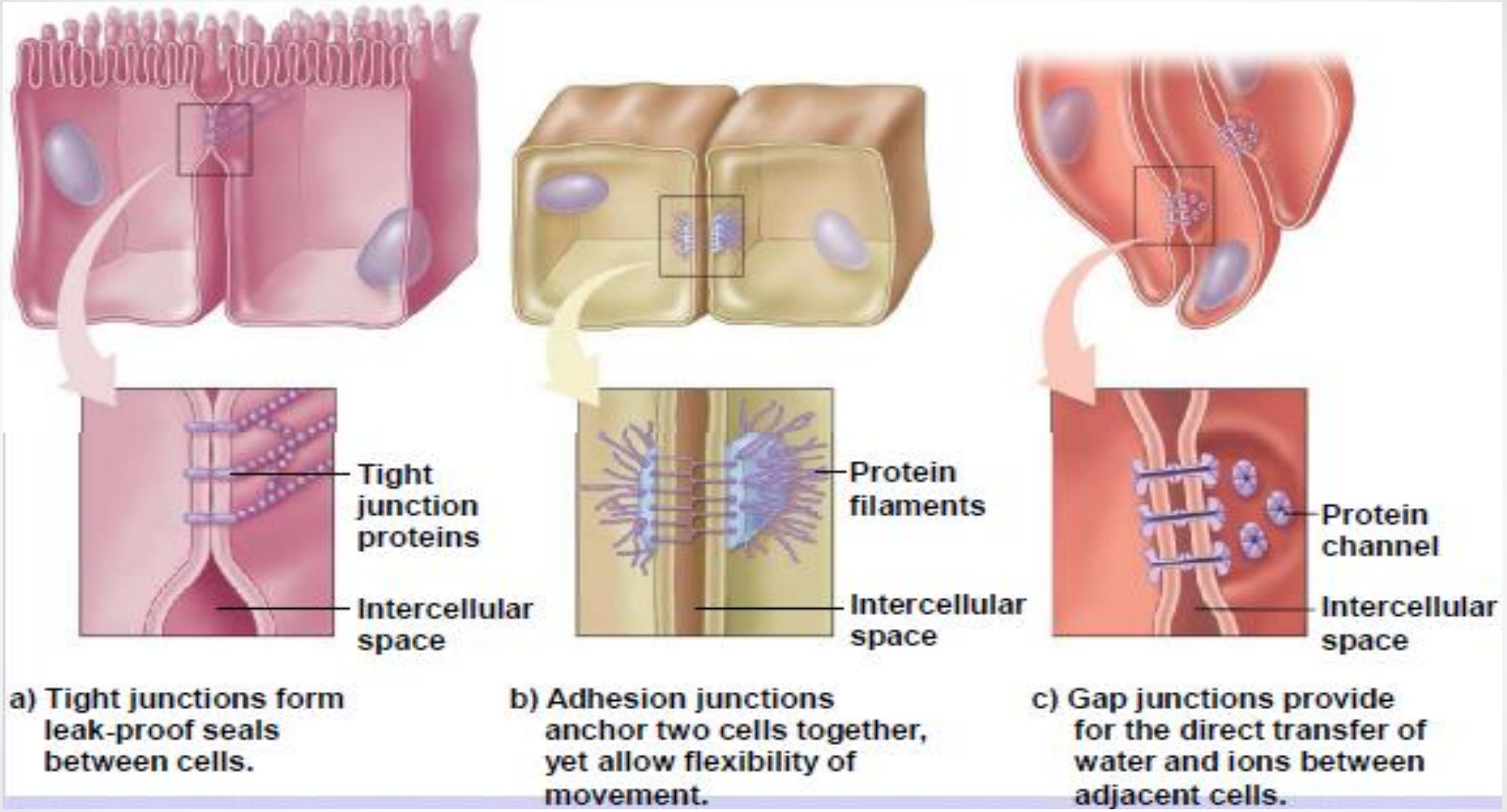
Intercellular Connections

Two types of junctions form between the cells that make up tissues: junctions that fasten the cells to one another and to surrounding tissues, and one type that permit transfer of ions and other molecules from one cell to another. The types of junctions that tie cells together and endow tissues with strength and stability, include the

1- **Tight junction** ،which is also known as the **zonula occludens** ,tight junctions between epithelial cells are also essential for transport of ions across epithelia **.**

2-The **desmosome** and **zonula adherens** (hold cells together, and the **hemidesmosome** attach cells to their basal laminas.

3-Gap Junctions At gap junctions, the intercellular space narrows from 25 nm to 3 in the membrane of each **connexons** nm, and hexagonal arrays of protein units cell are lined up with one another.



a) Tight junctions form leak-proof seals between cells.

b) Adhesion junctions anchor two cells together, yet allow flexibility of movement.

c) Gap junctions provide for the direct transfer of water and ions between adjacent cells.


Thank you.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