Introduction to Human Physiology and Cellular Physiology

Human Anatomy and Physiology (BME246)

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Lecture Outline

Intro to human physiology

- What is physiology?
- Levels of organization
- Overview of homeostasis
- Body fluids

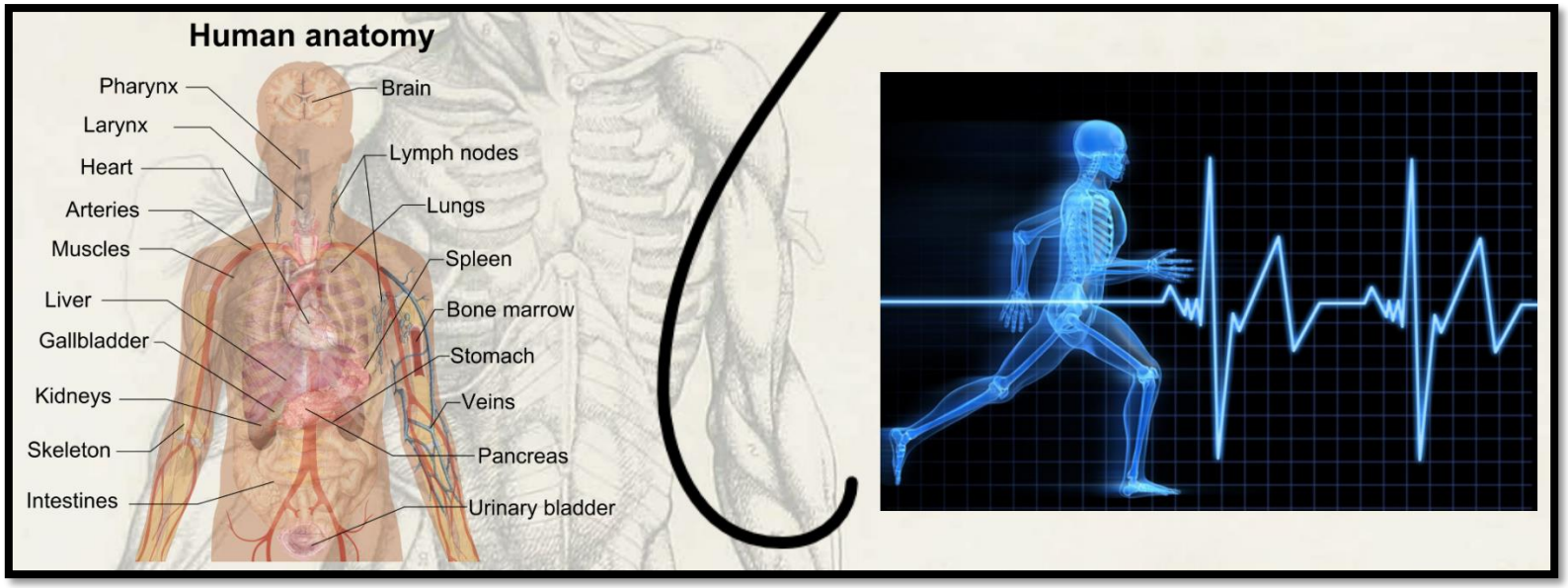
Intro to cellular physiology

- Structure and function of biological membranes
- Transport of molecules accross membranes
- Organelles
  - Nucleus
    - Flow of genetic information and Protein synthesis
  - ER
  - Golgi
  - …
- Cytoskeleton
- Cellular Communication

Introduction to Human Physiology

- **Anatomy** is the science of body **structures** and the relationship among them.
- **Physiology** is the science of body **function and the mechanisms.**

  i.e. How the body parts work?

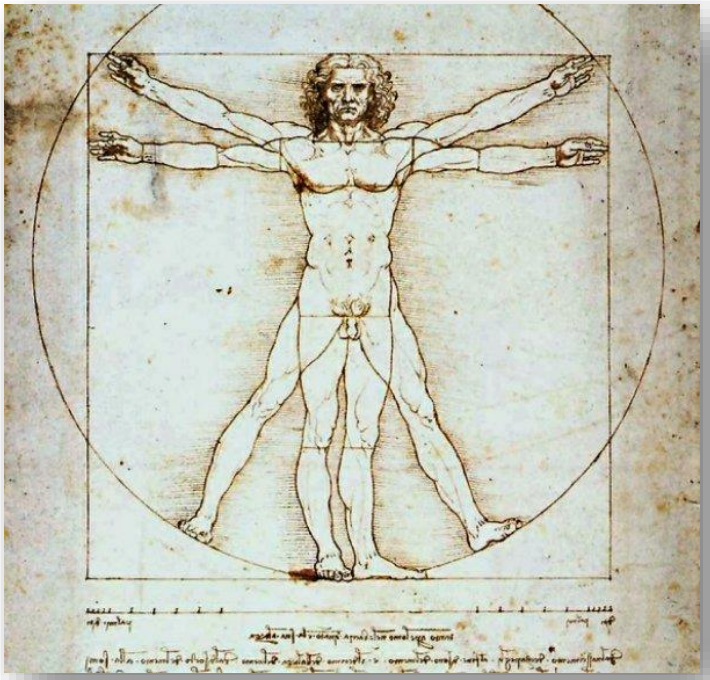


https://edu.glogster.com/glog/anatomy-vs-physiology/1wpsn9lvooo

What is Physiology ?

- The goal of **physiology** is to explain the physical and chemical factors that are responsible for the origin, development, and progression of life.

- **Human physiology** attempts to explain the specific characteristics and mechanisms of the human body that make it a living being.



https://en.wikipedia.org/wiki/Vitruvian_Man

Levels of Structural Organization

Six levels of organization

- ✓ Chemical
- ✓ Celular
- ✓ Tissue
- ✓ Organ
- ✓ System
- ✓ Organismal

Chemical level

Atoms are the smallest unit of matter

Essential atoms for life: C, H, O, N, P, Ca, S, Mg, etc.

Molecules: Two or more atoms joined together

H_2O, CO_2

Carbohydrates

Lipids

Proteins

Nucleic acids…

Cellular level

Basic structural and functional units of an organism

~200 different kinds of cells

Tissue level

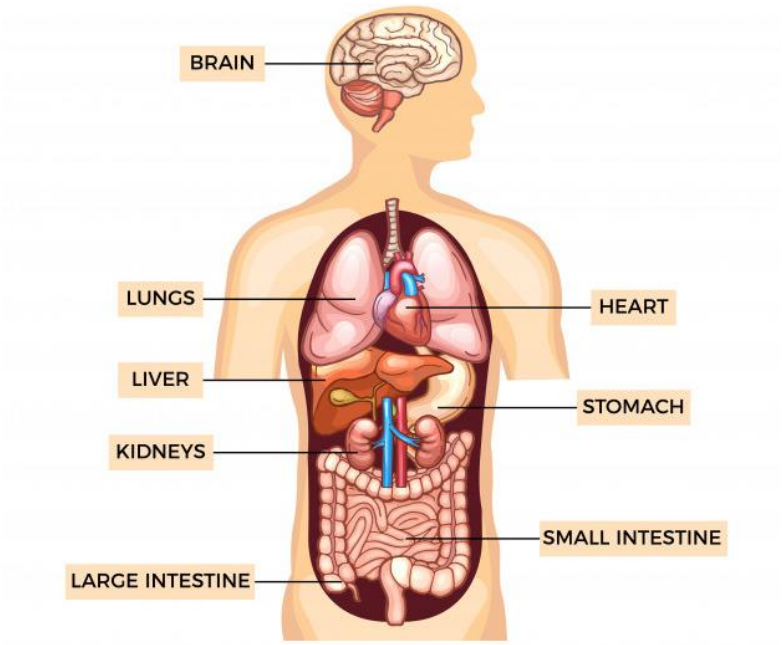
Tissues are groups of cells and material surrounding them

- Epithelial
- Connective
- Muscular
- Nervous

Organ level

Tissues are joined together to form organs

They have specific function and shape



https://www.freepik.com/premium-vector/human-body-organs-systems_4937610.htm

System level

A system consists of related organs with a common function

Major Functional Systems

- The Blood Circulation System
- Respiratory System
- Digestive System
- Musculoskeletal System
- Urinary System (Renal System)
- Reproductive system

Regulation of Body Functions

- Nervous System
- Endocrine System (Hormones)

Body Fluids

- The chemical reactions of life take place in aqueous solutions.
- Human beings are **mostly water**, ranging from about 75% of body mass in infants to about 50–60% in adult men and women.
- «**Polar**» molecule
  - H atoms have partial positive; O atom has partial negative charge
- Beucause of its polar nature water molecules can
  - form hydrogen bonds with each other and **with other polar molecules**
  - interact with **positively or negativeley charged ions**.

Body Fluids

- In a 70-kg adult man, the total body water is about

  60% **~ 42 liters**

- This percentage depends on age, gender, and degree of obesity.

Decreased body water (~40%)	Increased body water (~80%)
Elderly people	Premature and new born babies
Women	People with edema
Obese people	

The total body fluid is distributed mainly between two compartments

1- Intracellular fluid (inside the cell)
40 % body weight
=28 liters

2- Extracellular fluid (outside the cell)
20 % body weight
= 14 liters

a) **Interstitial fluid** (Intercellular)
15 % body weight = 10.5 liters

b) **Intravascular fluid** (Blood Plasma)
5 % body weight = 3.5 liters

c) **Transcellular fluid** (synovial, peritoneal, pericardial, CSF, intraocular spaces)

TOTAL BODY FLUID

60 % = 42 liters

In the extracellular fluid are the **ions and nutrients** needed by the cells to maintain cell life.

For this reason, the extracellular fluid is also called the "***internal environment of the body***"*(the milieu intérieur).*

Homeostasis

- The term "*homeostasis*" is used by physiologists to explain **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.

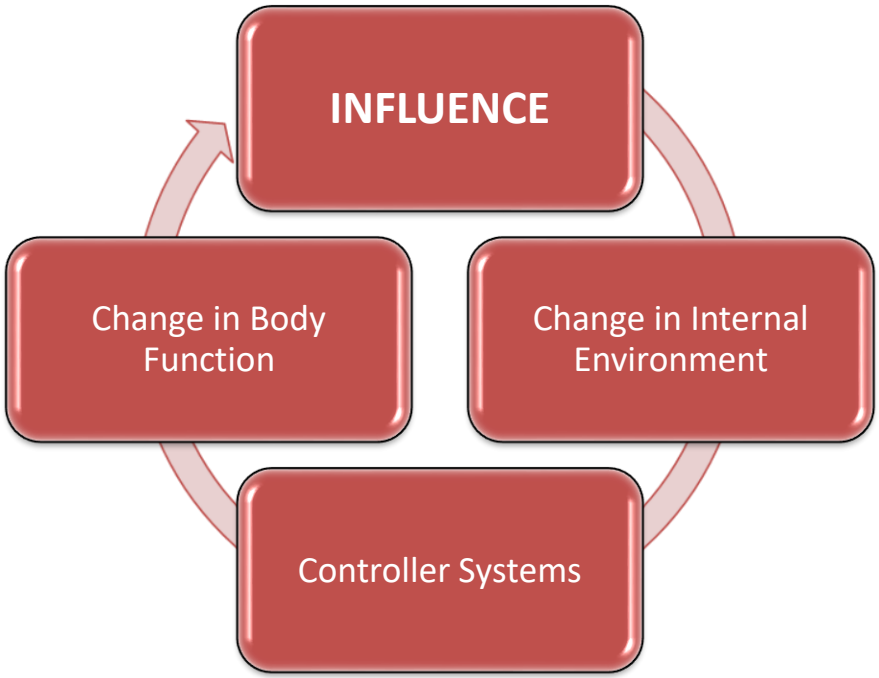
Characteristics of Control Systems

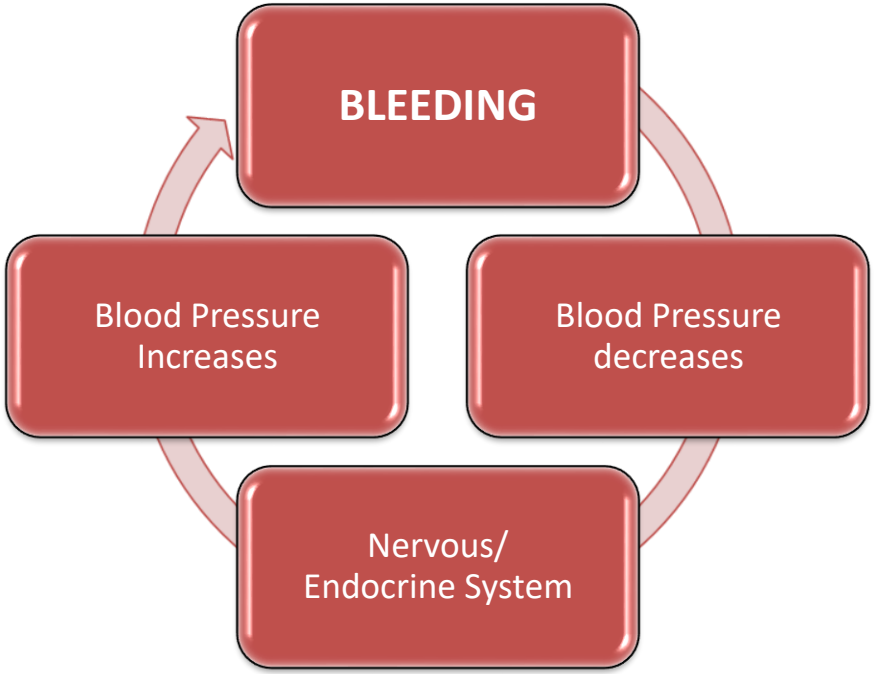
- Most control systems of the body act by ***negative feedback***.

- If some factor becomes excessive or deficient, a control system initiates *negative feedback,* which consists of a series of changes that **return the factor toward a certain mean value**, thus maintaining homeostasis.

Negative Feedback

- Example: Regulation of Arterial Blood Pressure





“Gain” of a control system

- **Gain of a control system is the degree of effectiveness.**

- Transfusion without baroreceptor pressure control system: 100 >>175
- Transfusion with baroreceptor pressure control system: 100 >>125

- Thus, the feedback control system has caused a “correction” of –50 mm Hg—that is, from175 mm Hg to 125 mm Hg.

- There remains an increase in pressure of +25 mm Hg, called the “error,” which means that the control system is not 100 per cent effective in preventing change. The gain of the system is then calculated by the following formula:

$$\text{Gain} = \frac{\text{Correction}}{\text{Error}}$$

- The gain of the person’s baroreceptor system for control of arterial pressure is –2.

- The gains of some other physiologic control systems are much greater than that of the baroreceptor system. For instance, the gain of the system controlling internal body temperature when a person is exposed to moderately cold weather is about –33. Therefore, one can see that the temperature control system is much more effective than the baroreceptor pressure control system.

Positive Feedback

- *Positive feedback* is a kind of vicious cycle and can't be used as control mechanism.

- Positive feedback can sometimes be useful:
  - Delivery
  - Blood clotting
  - Generation of nerve signals

Feed-forward Control

- Some adaptive responses of the body occur so rapidly that **there is not enough time** for changing the internal environment.

- Feed forward control, **increases the "net gain" of the control system**

- Example: Sweating and breathing speeds up even before the start of exercise

Reflex Arc

- Homeostatic control mechanisms can be formulated as reflex arcs.

- A reflex arc has five components:

STIMULUS	**An increase in blood pressure**
1. Receptor	Baroreceptors
2. Afferent Pathway	N. Vagus
3. Integration Center	Brain Stem (Circulation Center)
4. Efferent Pathway	N.Vagus
5. Effector Organ	Heart
RESPONSE	**Cadiac contractility and heart rate is decreased**

Introduction to Cellular Physiology

Cells are the structural & functional units of all living organism

- Smallest units that perform all vital physiological functions
- Each cell maintains homeostasis at cellular level
- Homeostasis at tissue, organ, organ system, and organism level due to coordinated action of many cells

Biological Membranes

- The structure and functions of the cells are highly dependent on the membranes.
  - The cell membrane (aka. the **plasma membrane**) is a biological membrane that separates the interior of the cell (cytosol) from the outside environment (the extracellular space).
  - Create internal compartments and surround various organelles (e.g. Nucleus, ER, Golgi, …): **organellar membranes**
- They are impermeable barrier for most water-soluble molecules: **Semi-permiable**

Structure of Biological Membranes: Fluid-mosaic model

- ˜5 nm in thickness
- It consists of lipid bilayer with embedded proteins.
- Is not a solid structure: It is a dynamic and fluid structure, all molecules move along the membrane plane
- Components of the biological membranes:
  1. Phospholipids
  2. Proteins
     a) Integral proteins
     b) Peripheral proteins
  3. Carbohydrates

Structure of Biological Membranes: Fluid-mosaic model

✓ Lipid bilayer

- **Phospholipids** are amphipathic molecules (i.e. have both polar and nonpolar ends) which causes the formation of lipid bilayer.

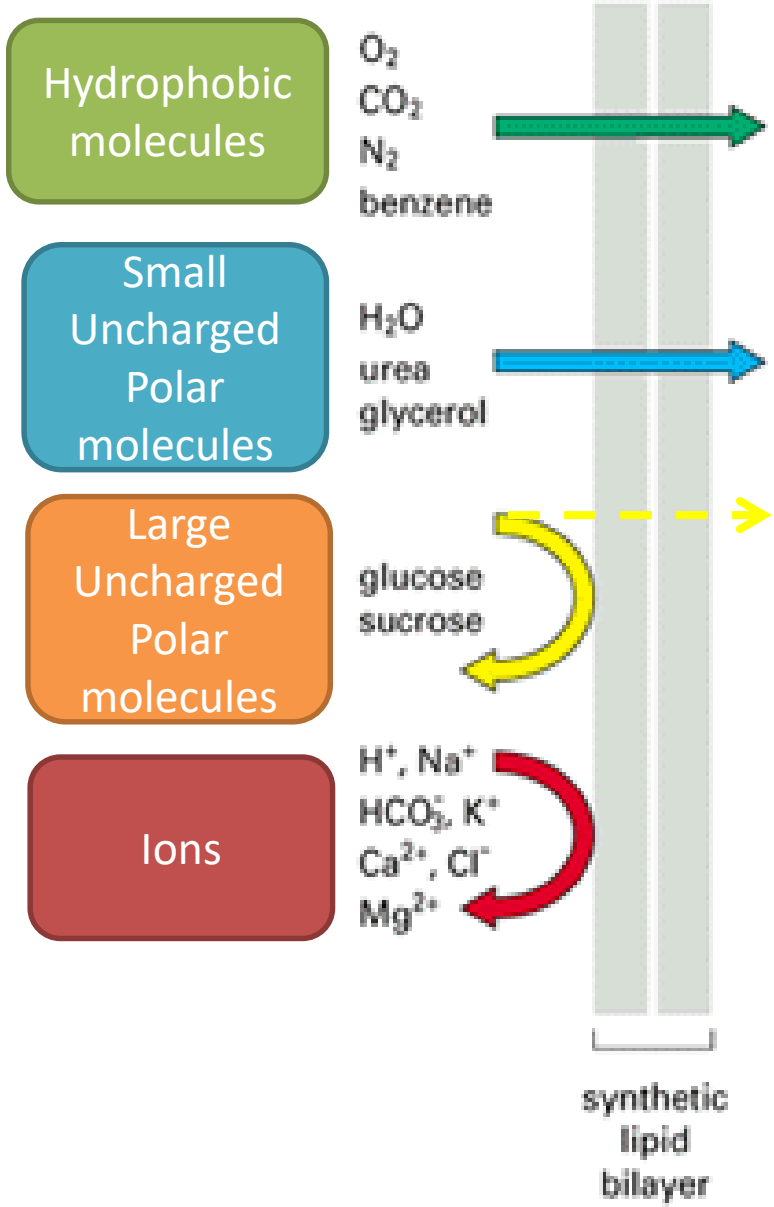
✓ Proteins

- Receptors for external stmuli
- Transportation of molecules accross membranes
- Electron transport and oxidative phosphorylation
- Cell-cell, Cell-ECM interactions
- Generation of concentration gradients for ions
- Cellular communication and intracellular signaling
- Enzymatic activity
- Antigen

Transport accross cell membranes

Because of their hydrophobic internal parts, lipid bilayer:

- is **permeable** to
  - Small, uncharged, polar molecules
  - Hydrophobic molecules
  - Gases
- is **impermeable** to
  - Charged molecules (e.g. Na^+, Cl^-, K^+, Ca^{2+})
  - Large water soluble molecules (e.g. Proteins, nucleic acids, sugars, nucleotides etc.)



I. Transport of small molecules and ions

A) Passive transport

- Simple diffusion
- Facilitated diffusion
  - **Pores** (un-gated channels)
  - **Channel proteins** (gated pores)
  - **Carrier proteins** (permeases)

B) Active transport

- ATP dependent
- Dependent on ion gradients

II. Transport of large molecules

A) Endocytosis

- Phagocytosis
- Pinocytosis
- Receptor dependent endocytosis

B) Exocytosis

Transport of Small Molecules

A) Passive Transport: **No energy required**

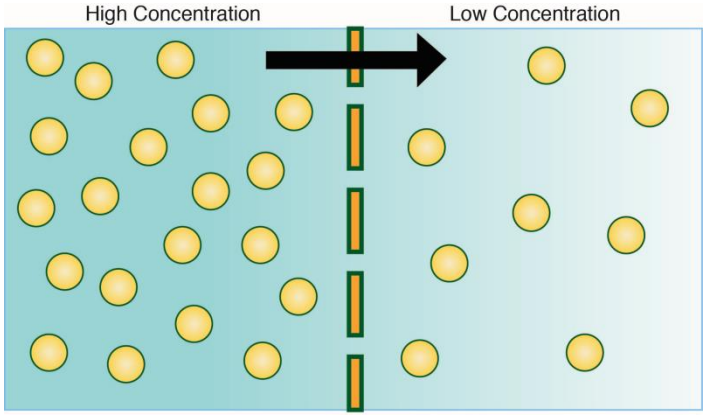
1) Simple diffusion
2) Facilitated diffusion

Direction and driving force of transport

Uncharged molecules
The concentration difference of the molecule on both sides of the membrane:
In the direction of the concentration gradient

Molecules with a net charge
Concentration gradient+
Electrical potential difference=
In the direction of the electrochemical gradient

1) Simple diffusion



Hydrophobic molecules

Small Uncharged Polar molecules

O_2, CO_2, H_2O, alcohol etc.

2) Facilitated diffusion

i. Pores (ungated channels)
ii. Channel proteins (gated pores)
iii. Carrier proteins (transporters, carriers, permeases)

- ✓ They are found in all biological membranes and in very different forms.
- ✓ Each protein carries a specific group of molecules (eg. **sugars, amino acids, ions**).

B) Active Transport: **REQUIRES ENERGY**

- ✓ Transport against electrochemical gradient
- ✓ Require specialized proteins
- ✓ From low conc. to high conc.
    1. ATP hydrolysis (Primary active transport): Na-K ATPase, SERCA
    2. Ion gradient (Secondary active transport): Uptake of glucose in the intestines
    3. Light energy: Channelrhodopsin

	Passive Transport			Active Transport	
	Diffusion	**Facilitated Diffusion**	**Osmosis**	**Primary Active Transport**	**Secondary Active Transport**
Net Flow of Direction	High to low concentration	High to low concentration	High to low concentration	Low to high concentration	Low to high concentration
Membrane Protein Usage	No	Yes	No	Yes	Yes
Selectivity	No	Yes	Diffusion of solvent	Yes	Yes
Energy Usage	No	No	No	Yes (ATP)	Yes (ionic gradient)
Molecules Transported	Nonpolar; O_2, CO_2, lipids	Ions; Na^+, K^+, Ca^{2+} Glucose	Solvent	Ions; Na^+, K^+, Ca^{2+}	Polar: A.acid, glucose, ions

Transport of Large Molecules

Endocytosis

- In endocytosis, the material to be internalized is surrounded by an area of plasma membrane, which then buds off inside the cell to form a vesicle containing the ingested material.
  - If material is in solid form, it is phagocytosis.
  - If material is in liquid form, it is pinocytosis.

Exocytosis

- *Exocytosis* is the process of expelling substances from cells through the fusion of vesicles with the cell membrane.
- It is the opposite of endocytosis.

Cytoplasm vs. Cytosol

- The **cytosol**, aka. intracellular fluid (ICF) or cytoplasmic matrix, is the liquid found inside cells.
- Cytosol + Organelles = **Cytoplasm**

Membrane bound organelles

- ✓ Cells can concentrate and isolate enzymes and reactants in a smaller volume, thereby increasing the rate and efficiency of chemical reactions.
- ✓ Cells can confine potentially harmful proteins and molecules in membrane-bound organelles, protecting the rest of the cells from their harmful effects.

Nucleus

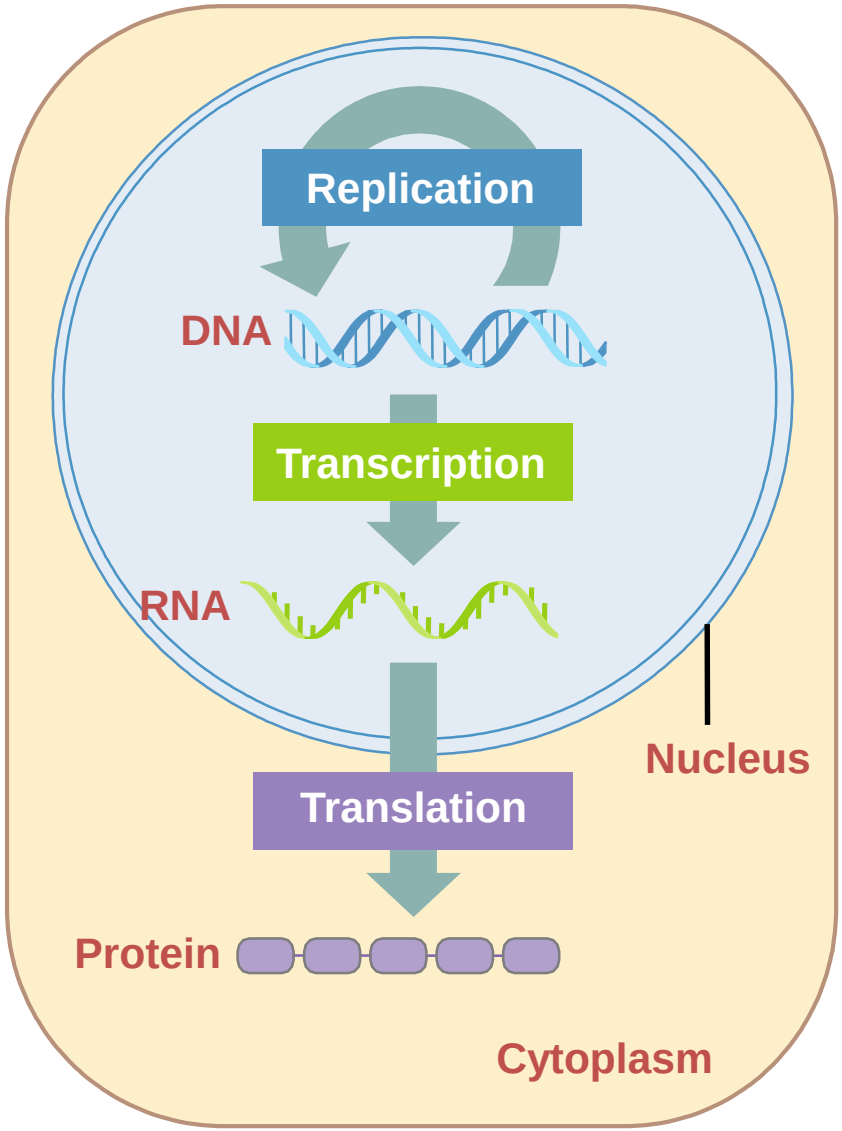
- Contains cell's genetic material, organized as multiple long linear DNA molecules in complex with *histone* proteins
- Enclosed by nuclear envelope: double membrane that isolates nuclear contents from the cellular cytoplasm.
- Because the nuclear membrane is impermeable to large molecules, *nuclear pores* are required to regulate nuclear transport of molecules between nucleus and cytoplasm
- Replication of DNA, transcription and processing of mRNAs take place within the nucleus.
- It plays a central role in cell proliferation.
- It guides all the metabolic activities of the living cell.

Central Dogma

Replication: producing two identical copies of DNA from one original DNA molecule

Transcription: Copying a gene's DNA sequence information to make an RNA molecule (mRNA)

Translation: "Decoding" a messenger RNA (mRNA) and using its information to build a **polypeptide**, or chain of amino acids.



Functions of Proteins

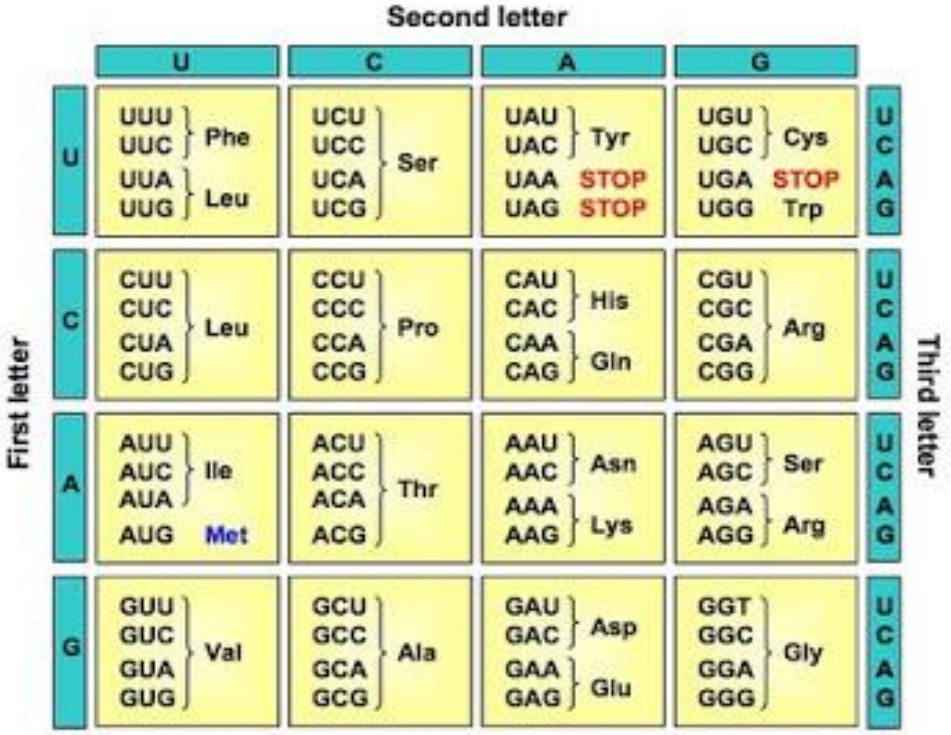
1. Enzyme
2. Structural proteins (collagen, elastin etc.)
3. Transport protein (Albumin etc.)
4. Motor proteins (Actin/myosine etc.)
5. Storage proteins (Ferritin etc.)
6. Signal proteins
7. Receptor proteins
8. Proteins that regulate gene expression
9. Specialized proteins

Proteins

- Proteins consist of one or more long chains of amino acid residues.
- Proteins differ from one another primarily in their sequence of amino acids (*primary structure*), which is dictated by the nucleotide sequence of their genes, and which usually results in protein folding into a specific three-dimensional structure that determines its activity (*secondary and tertiary structure*).
- There are 20 different types of amino acids in the nature. The linkage between two amino acid is called “peptide bond”.

Protein Synthesis

- The sequence of amino acid is encoded in the genome (DNA). But not all of the genome is participated in protein sythesis:
  - Exon: The part that participates in protein synthesis
  - Intron: Silent part of genome



Levels of Protein Structure

- Primary, Secondary, Tertiary, Quaternary
- Primary structure of the protein dictates;
  - Secondary and tertiary geometry.
  - Hydrophobic/philic properties
  - Charge of protein (negative or positively charged)
  - Different chemical properties

Endoplasmic Reticulum

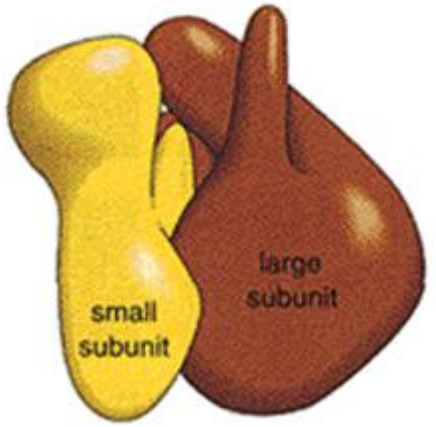
- Reticulum: Network
- ER is a continuous membrane system that forms a series of flattened sacs within the cytoplasm of eukaryotic cells
  - Granular (Smooth) ER: GER
  - Agranular (Rough) ER: AGER
- Serves multiple functions

Endoplasmic Reticulum

- GER: Protein synthesis and sorting (membrane proteins, organellar proteins and secreted proteins)
- AGER: Lipid synthesis (fatty acids and phospholipids)
- Enzymes of AGER in liver cells play a role in detoxification of toxic substances (barbutals, amphetamines, morphins).
- Sarcoplasmic reticulum (Ca^{2+} storage and release)
- ER makes the cell more resistant to mechanical effects.

Ribosome

- The ribosome is a complex molecular machine, found within all living cells, that serves as the site of **protein synthesis**.
- Composed of 2 subunits containing different kinds of proteins and rRNAs
- Ribosomes link amino acids together in the order specified by messenger RNA (mRNA) molecules.



Golgi apparatus

- The Golgi apparatus (aka. *Golgi complex*, *Golgi body*), is closely related to the ER.
- It usually is composed of four or more stacked layers of thin, flat, enclosed vesicles lying near one side of the nucleus.
- This apparatus is prominent in secretory cells, where it is located on the side of the cell from which the secretory substances are extruded.
- Golgi makes terminal modifications of proteins ("packages the proteins").

Lysosome

The lysosomes provide an *intracellular digestive system* that allows the cell to digest

1. damaged cellular structures (otophagy)
2. food particles that have been ingested by the cell
3. unwanted matter such as bacteria

The lysosomes contain hydrolytic enzymes that can break down many kinds of biomolecules and low pH inside (4.5–5.0).

If lysosomal digestive enzymes are released into cytoplasm the cell digests itself. This process called “autolysis”.

Peroxisome

- Peroxisomes, contain oxidases. Several of the oxidases are capable of combining oxygen with hydrogen ions derived from different intracellular chemicals to form hydrogen peroxide (H_2O_2).
- Hydrogen peroxide is a highly oxidizing substance and is used in association with *catalase, another oxidase* enzyme present in large quantities in peroxisomes, to oxidize many substances that might otherwise be poisonous to the cell.
- For instance, about half of the alcohol a person drinks is detoxified by the peroxisomes of the liver cells in this manner.

Mitochondrion

- Mitochondria generate most of the cell's supply of ATP, used as a source of chemical energy via oxidative phosphorylation (=respiration).
- Mitochondria are present in all areas of each cell’s cytoplasm, but the total number per cell varies from less than a hundred up to several thousand, depending on the amount of energy required by the cell.
- Mitochondrion is composed mainly of two lipid bilayer–protein membranes
- Mitochondria are self-replicative, which means that one mitochondrion can form a second one, a third one, and so on, whenever there is a need in the cell for increased amounts of ATP.
- Mitochondria contain DNA similar to that found in the cell nucleus. The DNA of the mitochondrion plays a similar role, controlling replication of the mitochondrion itself.

CYTOSKELETON

Cytoskelton

- Gives the cell its unique Providing mechanical support to the cell
- Cell movement
- Movement of chromosomes into daughter cells during cell division
- Intracellular transport of organelles and vesicles

Basic components of the cytoskeleton

- Actin filaments (microfilaments)
- Intermediate filaments
- Microtubules

Actin Filaments (Microfilaments)

- Diameter: 7nm
- The most abundant cytoskelton protein is actin in most of the cell types
- Actin polymerization→ Actin filaments
- Cellular contraction, migration, widening of the surface area, cytokinesis

Actin Filaments (Microfilaments)

- Cell membrane protrusions and extensions
  - Motion
  - Phagocytosis
  - Absorption
  - Nutrition

Intermediate Filaments

- Diameter: 10 nm
- Structural support
- Intermediate filaments are most extensively developed in regions of cells that are subject to *mechanical stress* (for example, in association with desmosomes)

Type	Protein	Size (kd)	Site of expression
I	Acidic keratins	40–60	Epithelial cells
	(~15 proteins)		
II	Neutral or basic keratins	50–70	Epithelial cells
	(~15 proteins)		
III	Vimentin	54	Fibroblasts, white blood cells, and other cell types
	Desmin	53	Muscle cells
	Glial fibrillary acidic protein	51	Glial cells
	Peripherin	57	Peripheral neurons
IV	Neurofilament proteins		
	NF-L	67	Neurons
	NF-M	150	Neurons
	NF-H	200	Neurons
	α-Internexin	66	Neurons
V	Nuclear lamins	60–75	Nuclear lamina of all cell types
VI	Nestin	200	Stem cells of central nervous system

Microtubules

- Diameter: 25 nm
- Organelle and vesicle transport within the cell
- Seperation of chromosomes during cell division
- Cell movement (cilia and flagella)

CELLULAR COMMUNICATION

While every cell in our body functions as a single life unit, they need to communicate with each other to maintain homeostasis and perform specialized functions.

External signals

- Chemical messengers: Odorants, metabolites, ions, hormones, growth factors, neurotransmitters
- Light, mechanical, thermal stimuli are transduced into chemical messengers
- Most chemical messengers interact with specific cell-surface receptors, triggering a series of intracellular reactions that mediate the cell's response to that stimulus.

Mechanisms of cellular communication

1) Direct cellular communication with cell-cell contact (Juxtacrin)

- Cellular junctions
- Cell to cell recognition
- Nanotubes

2) Indirect cellular communication

- Chemical communication
  - Autocrine
  - Paracrine
  - Neurotransmitters (Synaptic transmission)
  - Endocrin (Hormones)

1. Direct cellular communication requiring physical cell-cell contact (Juxtacrine)

Intercellular junctions

- Cells can be connected directly to each other with specialized structures
- **Desmosomes** are cell structures specialized for cell-to-cell adhesion. Prevents excessive stretching of the tissues
- **Tight junctions** are the areas where two cells are almost stuck together. They form tight barriers that prevent leakage between cells
- **Gap junctions** allows direct communication between two cells. Cytoplasms of the two cells are interconnected by tunnels made up of connexon proteins.

Cell to Cell recognition

- The cell membrane contains surface carbohydrate molecules (glycolipids, glycoproteins) that generate signals for other cells
- Example: Recognition of self and non-self cells in immune system

Nanotubes

- ✓ Filamentous membrane extensions
- ✓ Ions → Organelles
- ✓ Embryonic development, maintenance of homeostasis, spread of infectious agents, drug resistance, etc.

2. Indirect cellular communication that does not require cell-cell contact

Communication via chemical messengers

- ✓ A cell can communicate with another cell locally or at a distance via effective chemical signaling molecules.
- ✓ Chemicals are secreted from one cell and target another cell.
- ✓ It mostly requires ligand-receptor interaction.

- **Ligand:** Extracellular chemicals that act as a signal transduction molecule.
- **Receptor:** Proteins in the target cell membrane that specifically bind ligand.

1. Receptor ligand interaction is highly specific.
2. Only cell A has the appropriate receptor for this chemical messenger and, therefore, it is the only one among the group that is a target cell for the messenger.
3. The amount of receptors can also be modified
   a. Decrement of the receptor: downregulation
   b. Increment of the receptor: upregulation

Chemical Communication

- Local chemical communication
  - Autocrine
  - Paracrine
  - Neurotransmitters (Synaptic transmission)
- Long-distance chemical communication
  - Hormones
  - Neurohormones

Paracrine and Autocrine Communication

- **Paracrine signals:** After secretion, the ligand spreads by diffusion and acts on the target cells in the close vicinity.
- **Autocrine signals:** Ligand affects the cell that secretes its own.

Neurotransmitters (Synaptic transmission)

- Special form of paracrine communication.
- After secreted by neuronal cells, NTs diffuses to the synaptic cleft and binds to their receptor on nearby neuron / gland / muscle cell.

Hormones and Neurohormones

- **Hormones:** Chemical messengers secreted from the endocrine glands. They act on target cells at long distances through blood circulation.
- **Neurohormones:** Chemicals secreted from neuron cells act on target cells at long distances through blood circulation.

Signaling Molecules: Ligands

- ✓ Ligands bind to receptors in target cells act as chemical signals (*first messenger*).
- ✓ *Second messengers* are intracellular signaling molecules released by the cell to trigger physiological changes such as proliferation, differentiation, migration, survival, and apoptosis (cAMP, cGMP, IP_3, DAG, and Ca^{+2}).
- ✓ The cell releases second messenger molecules in response to exposure to extracellular signaling molecules—the first messengers.

Secondary messengers multiply the signal during intracellular signal transduction: Signal amplification

Cellular responses

Activation of receptor may cause;

1. Changes plasma membrane permeability, transport function or electrical status
2. Changes in cellular metabolism
3. Changes cellular secretory activity
4. Changes proliferation and differentiation rate of the cell
5. Cellular contractility
6. Changes in gene expression

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