Ministry of Higher Education and Scientific Research

Al- Mamoun University

Department of BioMedical Engineering

مدخل إلى هندسة الطب الحياتي Introduction to BioMedical Engineering

قسم هندسة الطب الحياتي

المرحلة الأولى للعام الدراسي 2023-2024

الفصل الدراسي الأول

تدريسي المادة :

م. د. ريم شولك الصباغ

Lecture One:

Introduction

The practice of medicine has changed dramatically since you were born. Consider a few of these changes, some of which have undoubtedly affected your own life: Couples can test for pregnancy in their homes, a new vaccine is available for chicken pox, inexpensive contact lenses provide clear vision, artificial hips allow recipients to walk and run, ultrasound imaging follows the progress of pregnancy, and small reliable pumps administer insulin continuously for diabetics. People are living longer because they are not dying in situations that were previously fatal, such as childbirth and bacterial infections. The growth of biomedical engineering is a major factor in this extension of life and improvement of health. Biomedical engineers have contributed to every field of medicine, from radiology to obstetrics to cancer treatment.

Accidents and trauma are major causes of death and disability around the world, victims often have internal injuries, which are life threatening but not easy to diagnose by visual observation. Emergency room treatment has improved enormously over the past few decades, chiefly due to advances in the technology for looking inside of people quickly and accurately. Ultrasound imaging, which can provide pictures of internal bleeding within seconds, has replaced exploratory surgery and other slower, more invasive approaches for localization of internal injuries. Old ultrasound imaging machines weighed hundreds of pounds, but new instruments are smaller and lighter, some weighing only a few pounds, making it possible to get them to the patient faster. Other imaging technologies have also improved: Helical computed tomography (CT) scanners produce rapid three-dimensional internal images of the whole body, and new magnetic resonance imaging (MRI) techniques can reveal the chemistry, not just the shape, of internal structures. As a result of faster and better diagnosis of internal injuries, more accident victims are saved today.

What is biomedical engineering?

Biomedical Engineering (BME): is the use of engineering rules in medicine and biology for healthcare aims

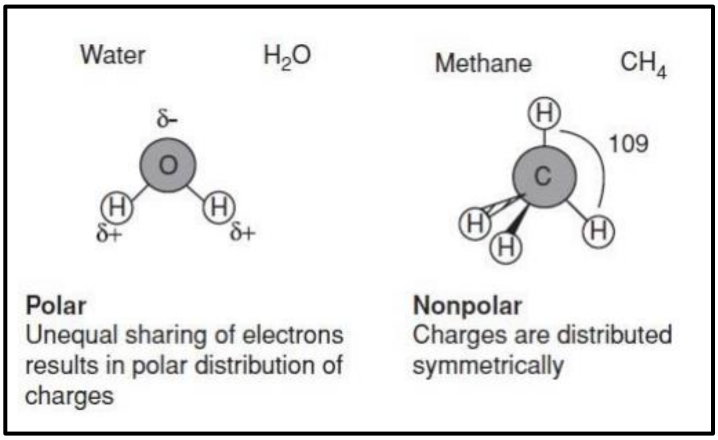
what are the fields of Biomedical Engineering?

- Static limbs
- place maker
- stem cells
- kidney dialysis
- Insulin pumps
- eye lenses
- ultrasound imaging
- artificial heart valves and other more

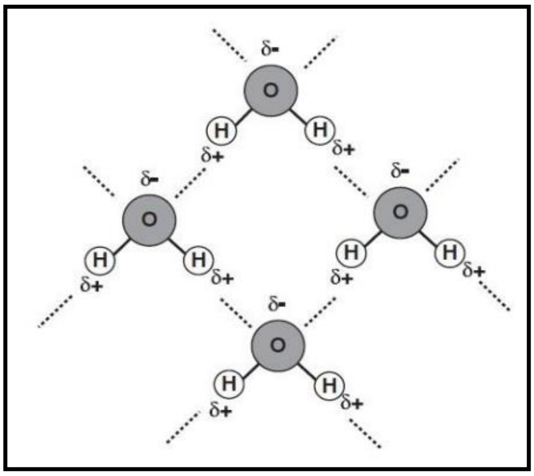
Subspecialty	Examples
Systems biology and Bioinformatics	Modeling of cellular networks DNA sequence analysis Microarray technology
Physiological modeling	Physiology of excitable cells Dynamics of the microcirculation Models of cellular mechanics Pharmacokinetic models of chemotherapy drugs
Biomechanics	Gait analysis Prosthetic joints and limbs Cellular mechanics
Biomedical instrumentation and Biomedical sensors	Electrocardiogram Cardiac pacemaker Glucose sensor O_2 sensor pH sensor
Biomedical imaging	Radiographic imaging Ultrasound imaging Magnetic resonance imaging Optical imaging
Biomolecular engineering and Biotechnology	Drug-delivery systems Artificial skin (tissue engineering) Protein engineering Chromatography and other separation methods Vaccines

Bonding between atoms and molecules

- All basic life processes that allow us to digest food, move, and grow involve chemical reactions: reactions that yield energy, build new molecules, or break down unneeded molecules. The molecules in our body are involved in thousands of chemical reactions.
- Atomic bonding :
  - Ionic bonds: (Na+Cl−)
  - Covalent bonds: (H2)
    - polar or nonpolar



- Molecular bonding
  - Hydrogen bonding



  - Van der Waals interactions

Water: The medium of life

The chemical reactions that drive life occur predominantly in aqueous or water rich environments, for this reason, water is often called "the source of life". Three atoms, two hydrogens and one oxygen are held together by covalent bonds to form water .Water can be a product or a reactant in other chemical reactions. Because the human body is approximately 70% water, it is the ideal environment for these reactions .

The extensive hydrogen bonding network that can form between water molecules gives rise to its unique properties. These properties include high melting and boiling temperatures, high surface tension, and a higher density than ice .

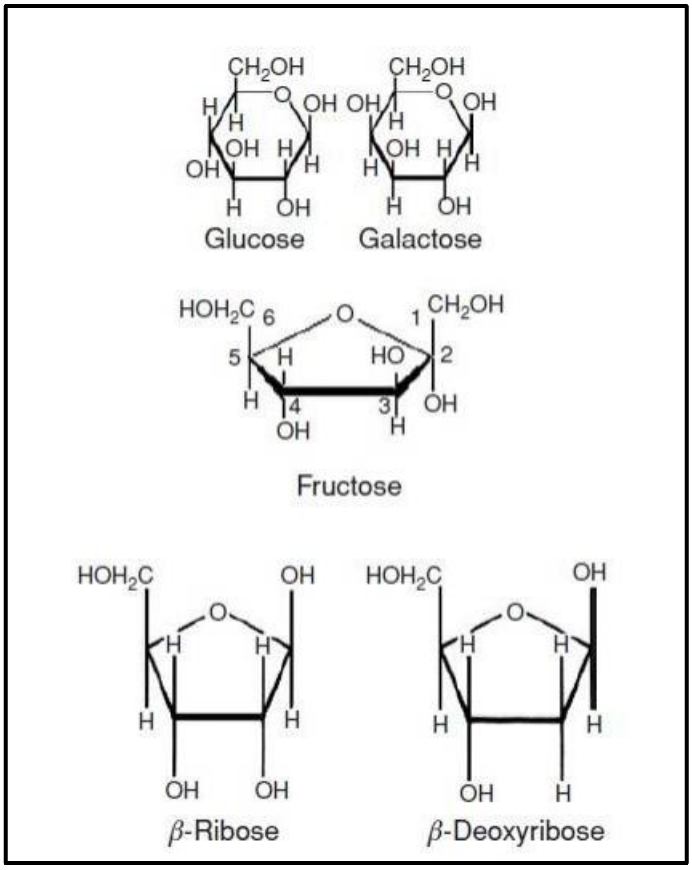
The ability to form hydrogen bonds also makes water an excellent solvent. Water can easily dissolve ions or other polar molecules that are capable of forming hydrogen bonds. These water-soluble molecules are referred to as hydrophilic Nonpolar molecules are not easily dissolved in water and are called hydrophobic .Molecules that contain both hydrophilic and hydrophobic groups are called amphiphilic, for example, phospholipids are amphiphilic molecules that form the plasma membrane surrounding cell.

Carbohydrates

Carbohydrates are abundant in nature and a major source of energy in the human diet.

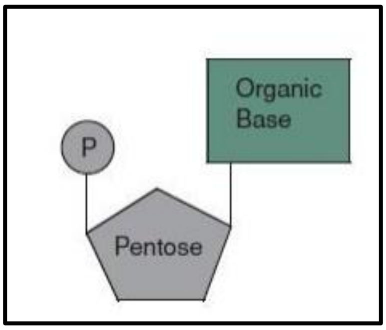
Carbohydrates are divided into groups according to their size, such as monosaccharides, disaccharides (created by coupling together two monosaccharides), and polysaccharides (formed by linking together many monosaccharides).

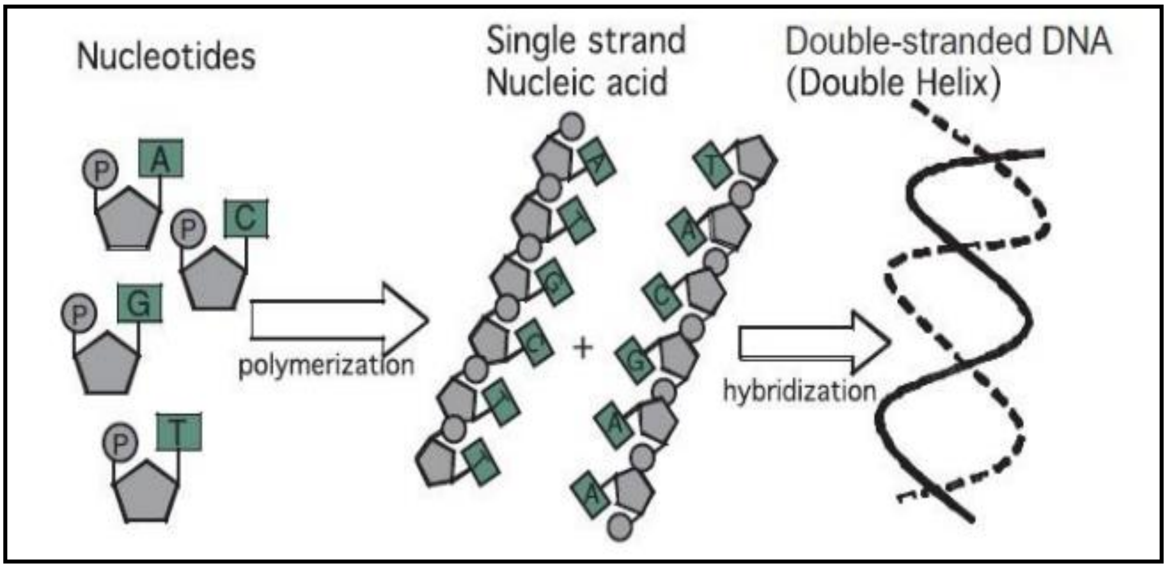
Carbohydrates are usually described by the formula $(CH_2O)_n$, where n is the number of carbon atoms in the molecule. Among the most common monosaccharides are the five-carbon sugars ribose and deoxyribose (which are a part of the structure of nucleotides) and the six-carbon sugars glucose, fructose, and galactose.



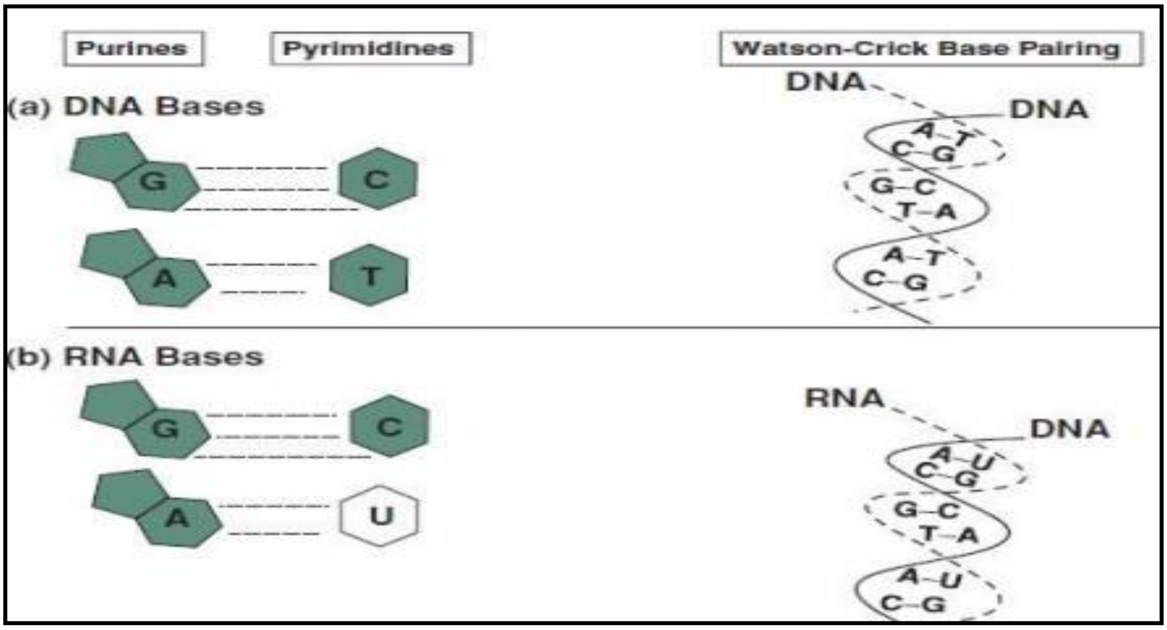
Nucleic acids:

- Nucleic acids are polymers of nucleotides that provide a mechanism for storage of genetic information
- The monomer for nucleic acid polymers is called a nucleotide.
- Nucleotides are composed of three different segments: a five-carbon sugar molecule (or pentose), a phosphate group, and an organic unit (nitrogenous bases), that are covalently coupled together into a single molecule
- There are five nitrogenous bases important in nucleic acids: adenine A, guanine G, cytosine C, thymine T, and uracil U



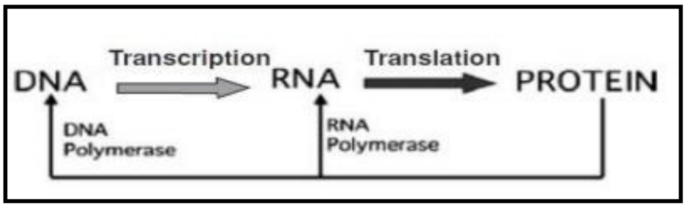


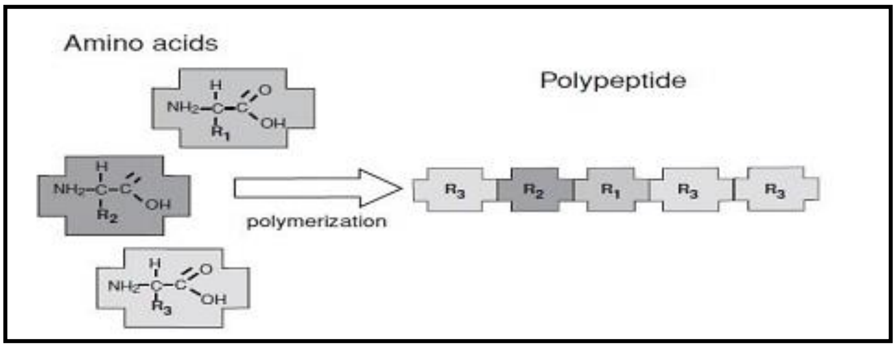
the organic bases that occur (DNA) and (RNA), two are double-ring structures (purines G, A) and three are single-ring structures (pyrimidines C, U, T). Each base pair is composed of a purine and a pyrimidine capable of forming hydrogen bonds with each other. The G and C can form three hydrogen bonds, whereas A and T or U can only form two hydrogen bonds.

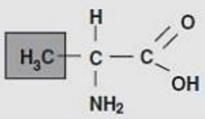
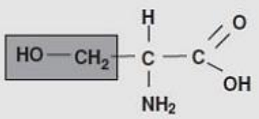
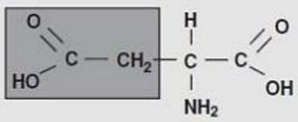
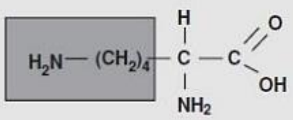


Proteins

- produced by chemical reactions directed by **DNA** (transcription and translation)
- Proteins are made up of one or more polypeptide chains (polymers of amino acids)
- Each amino acid has three functional groups, an amine (NH2), a carboxylic acid (COOH), and a side group (R), There are 20 amino acids, which can be grouped into categories: nonpolar, polar, acidic, and basic.



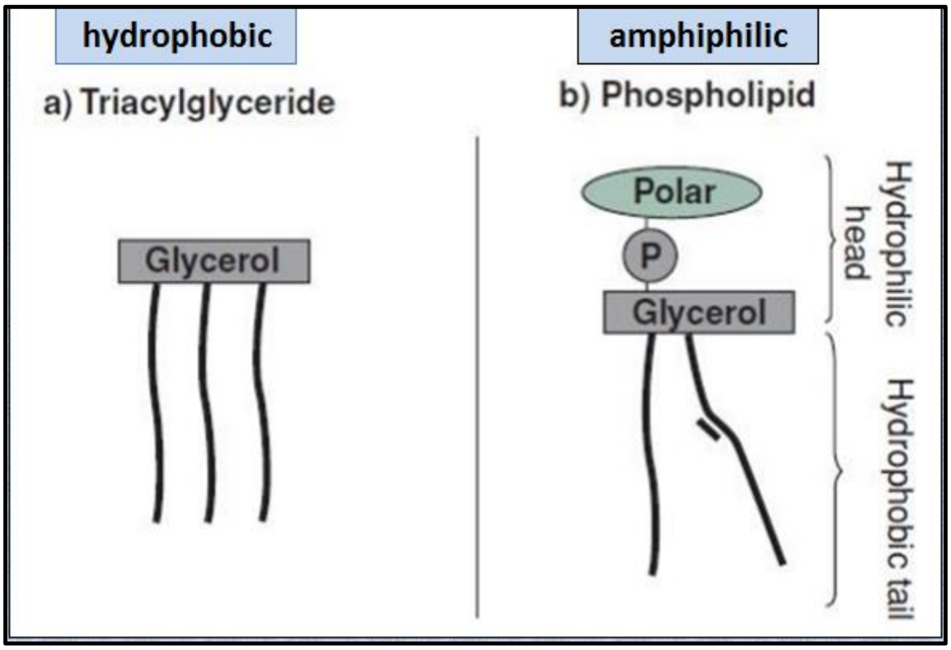


Group	Example	Chemical structure
Nonpolar	Alanine	
Polar	Serine	
Acidic	Aspartic acid	
Basic	Lysine	

Biomedical engineers have converted proteins into devices that perform useful work to improve health : home pregnancy test kits, in which proteins that are immobilized on test strips are used to detect a change in the properties of urine that occur only in pregnancy.

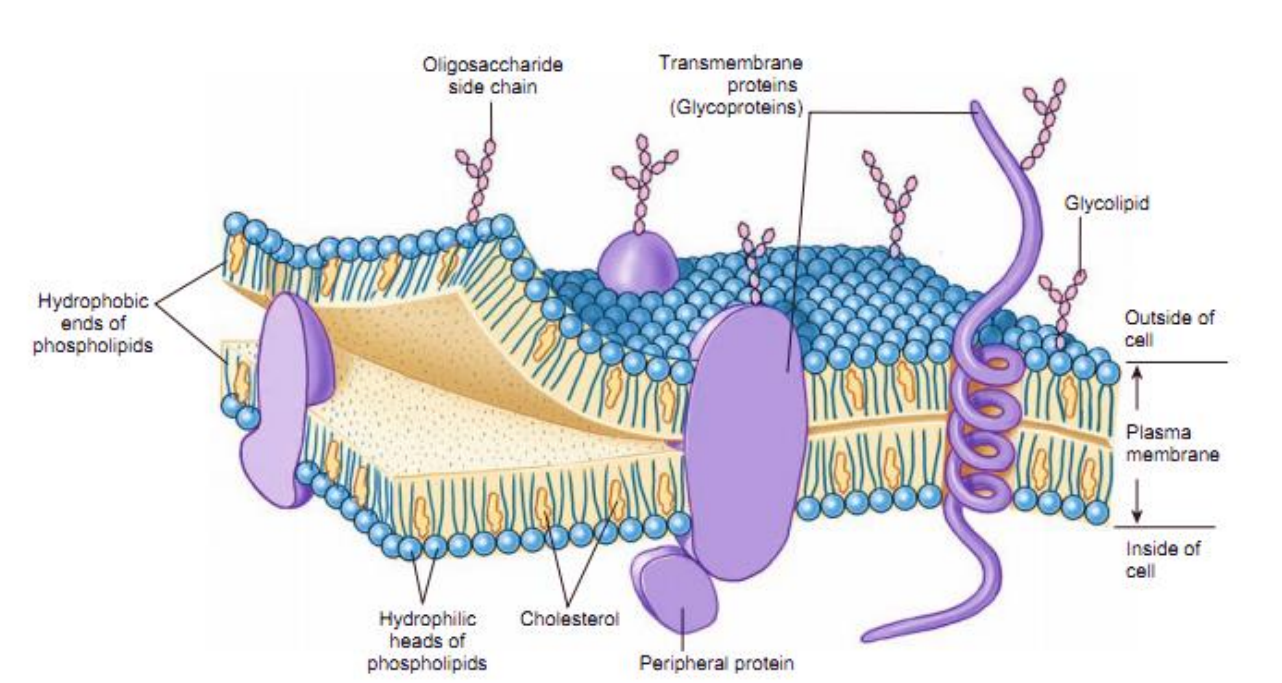
Lipids

- not polymers, they are large molecules
- triglycerides, phospholipids and Steroids (cell communication)
- Triglycerides are composed of three fatty acid chains and a glycerol molecule
- Fatty acid = $CH_3(CH_2)_nCOOH$ (saturated or unsaturated)
- Phospholipids are composed of two fatty acid chains, a glycerol molecule, a phosphate, and a polar group attached via the phosphate , phospholipids are amphiphilic (a polar head group and a nonpolar tail)



Structure of the cell membrane

The main structure of the cell membrane is a lipid bilayer formed of phospholipids. The thickness of the lipid bilayer is approximately 3 nm. In addition to phospholipids, the cell membrane contains proteins. The external surface of the plasma membrane also carries a carbohydrate rich coat called the glycocalyx. On average, the plasma membrane of human cells contains 50% protein, 45% lipid, and 5% carbohydrate.

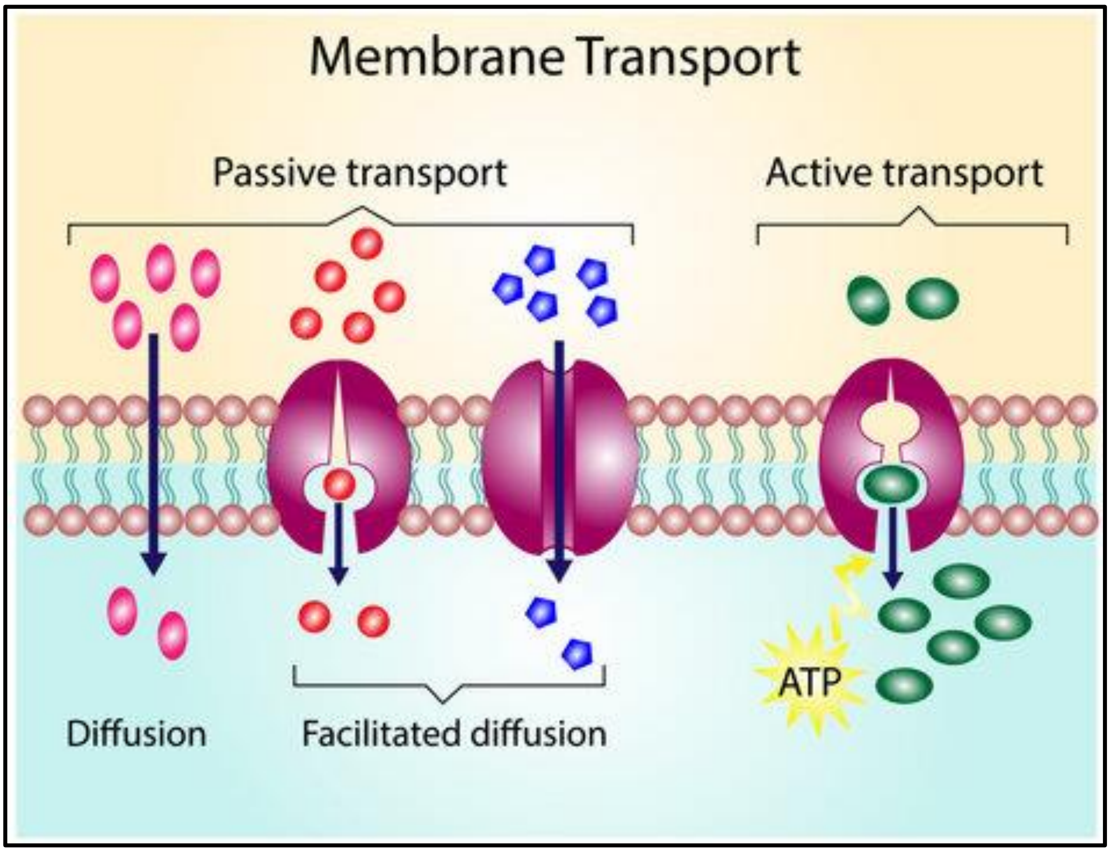


Transport across the cell membrane

- three major modes of transport: passive diffusion, facilitated diffusion, and active transport
- Diffusion : movement of particles from an area of high concentration to an area of low concentration of the membrane , don't require energy
- Passive diffusion : is the process by which water and small uncharged molecules: oxygen (O_2) and carbon dioxide (CO_2) pass through the membrane. For the special case of water, the diffusion of water down its concentration gradient is called osmosis.

- facilitated diffusion : it is done through protein embedded on the membrane, facilitate the diffusion of charged and big molecules (ions, glucose) .

- Active transport : moving a molecule from low concentration on one side of the membrane to an area of high concentration on the other. Active transport requires energy supplied by ATP.



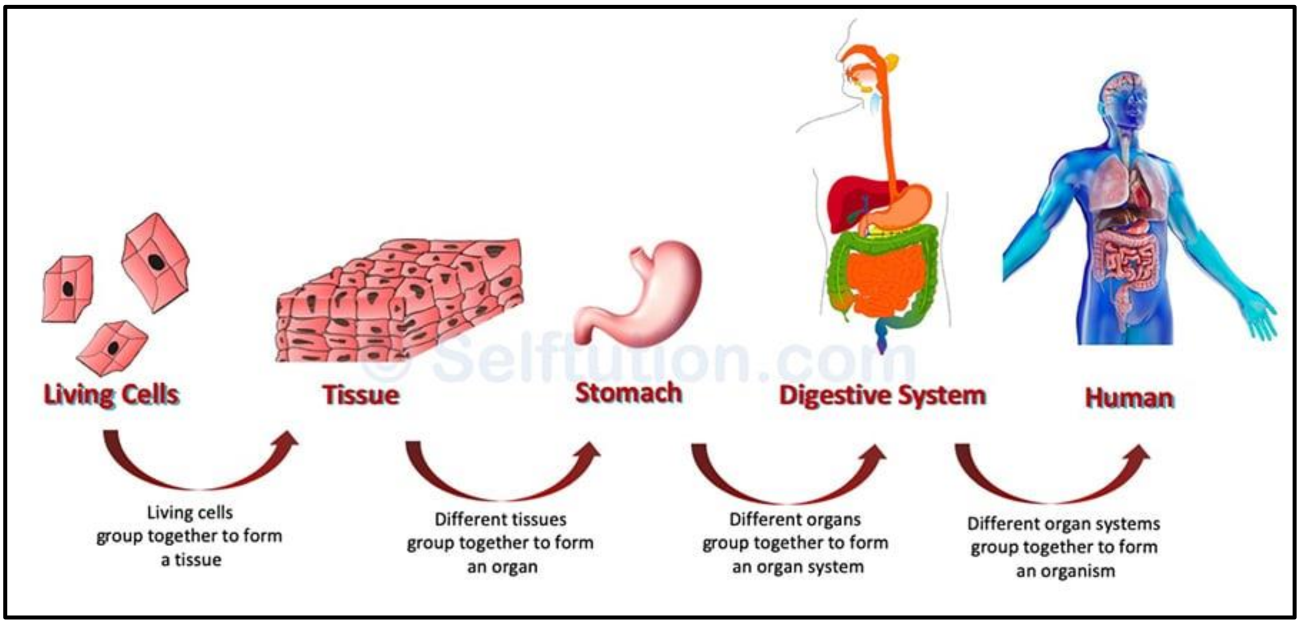
Lecture Two

Cell structure and function

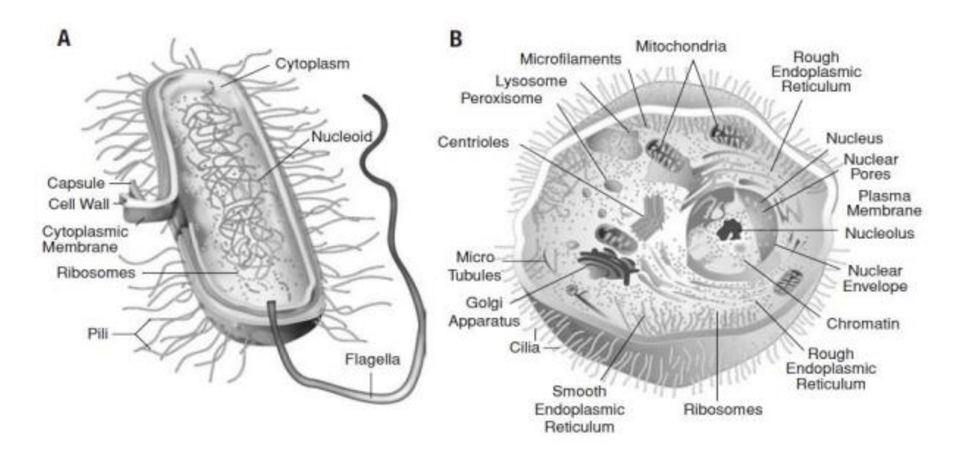
- The cell is the basic functional unit in the body.

- The human body is composed of more than 200 different types of cells (genetically the same) but (different in size, shape, and constituent molecules) and (different properties : liver cells have abundant enzymes for detoxification of chemicals whereas red blood cells instead have abundant hemoglobin for oxygen transport).

- Cells can be divided into two main classes: (prokaryotic بدائيات النوى : bacteria) and (eukaryotic حقيقيات النوى: fungi, algae, plants, animals).
- Human cells are eukaryotic cells, collection of cells of a similar type is called a tissue.
- four general types of tissues: (muscle عضلي), (nervous عصبي), (epithelial ظهاري مغلفة), and (connective رابطة) tissues.
- An organ is a collection of two or more tissues, which are organized into a functional unit.
- Some organs contain all four tissue types; for example, the stomach.



What are the difference between Prokaryote and Eukaryote cells?



Characteristic	Prokaryote	Eukaryote
Nucleus	Absent	Present
Diameter of a typical cell	1 μm	10–100 μm
Cytoskeleton	Absent	Present
Cytoplasmic organelles	Absent	Present
DNA content (base pairs)	1×10^6 to 5×10^6	1.5×10^7 to 5×10^9
Chromosomes	Single circular DNA molecule	Multiple linear DNA molecules

Functions of the major organelles of eukaryotic cells

Organelle	Function
Nucleus	Control center for cell metabolism and reproduction; stores genetic information
Ribosomes	Synthesize proteins
Endoplasmic reticulum (rough and smooth)	Transports proteins and lipids
Golgi apparatus	Packages and processes proteins
Lysosomes	Digests food particles, old organelles, invaders
Cell (plasma) membrane	Controls what comes into and out of the cell, regulates cellular homeostasis
Mitochondria	Performs respiration for all eukaryotic cells—takes glucose and oxygen and converts it to adenosine-5′-triphosphate (ATP) energy; has role in maintaining cell life and death

Cell differentiation and stem cells

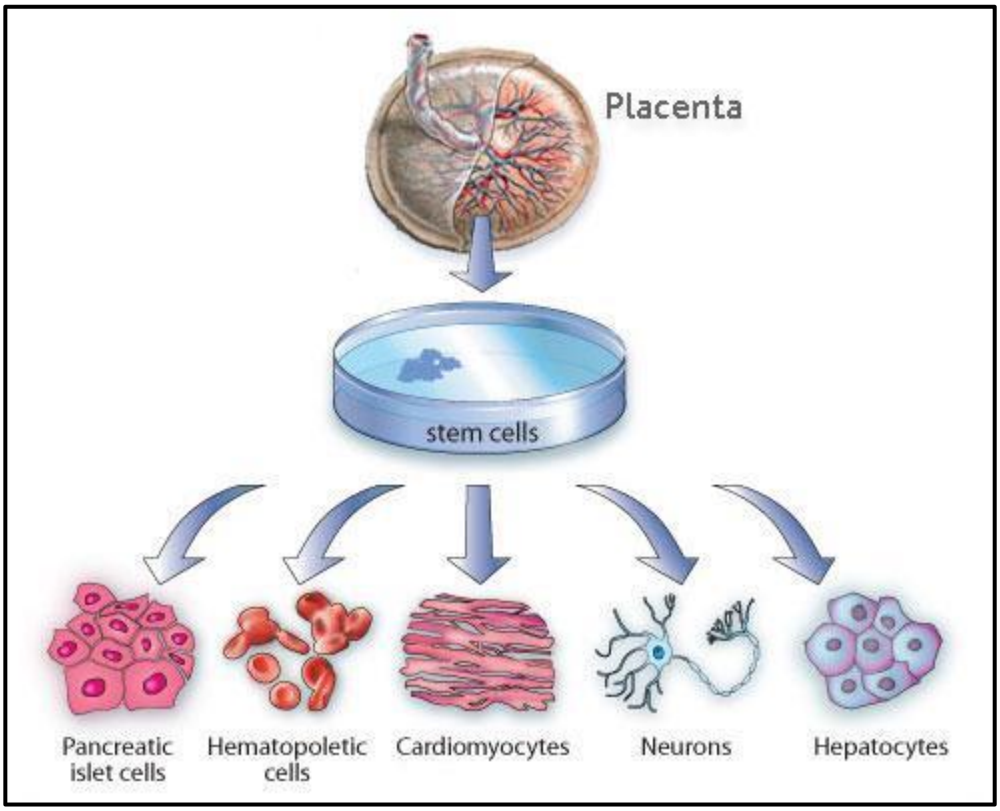
- Cells begin to specialize in function through a process called differentiation.
- Stem cells are unspecialized cells that are capable of changing into more specialized cell types.
- isolated from embryos and are called embryonic stem cells.
- Adult stem cells are isolated from peripheral blood , bone marrow, nervous system , muscle , liver , intestine , skin, and other tissues of adult organisms.
- Stem cells are a potential cell source for cell replacement therapy for diseases as well as seed cells for engineered tissues.

Cell death

- two types of cell death : (necrosis التنخر), (apoptosis موت الخلية المبرمج)
- (necrosis) : tissue damage, the cells swell and burst, releasing their contents (triggering an inflammatory response).
- (apoptosis) : sequence of steps in which chromatin condenses تكثف الكروماتين , cell shrinks تنكمش الخلية , and membrane pinches off الغشاء الخلوي يتقطع to form apoptotic bodies and engulfed by macrophages (immune system specialized cells).
- In apoptosis: no inflammatory effects on neighboring cells because the cellular contents remain membrane-bound during apoptosis, apoptosis is known as cell suicide.

Cell culture technology

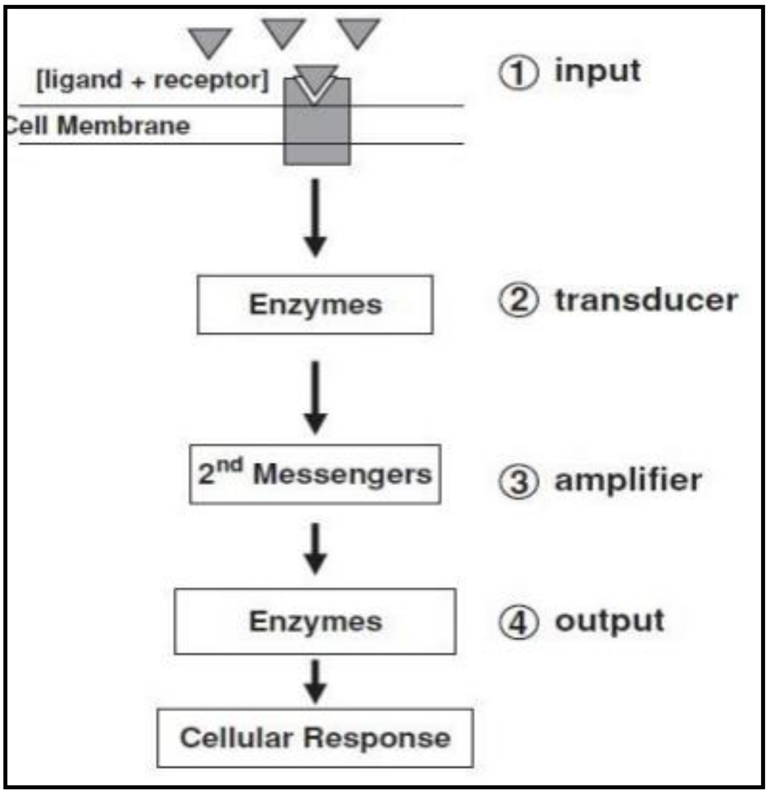
- Human and animal cells can be grown outside of an organism, to produce biological materials: Culture techniques can be used to produce many more cells or to produce cell-related products such as proteins, DNA, or viruses.
- The biotechnology industry is based on cell culture
- Mammalian cell cultures are obtained from the tissues of an animal, usually by one of two general methods: 1) plantation or 2) enzymatic degradation.
- Most mammalian cells have complex medium requirements: A variety of different vitamins, essential amino acids, glucose, and salts must be present in the liquid culture medium for cells to survive and proliferate.



Communication Systems in the Body

- Signaling molecules (ligands) bind to receptors. Enzymes inside the cell convert the binding event into other types of signals (such as turning on an enzyme). Often, the signals are amplified using molecules called second messengers. These second messengers in turn relay the signal by activating enzymes, which produce a response
- Mechanism for signal transduction in a cell is

[ligand + receptor] → transducer → amplifier → response



Biomedical and the signal transition concept

- Biomedical engineers have used short fragments of ligands or receptors to achieve a desired function

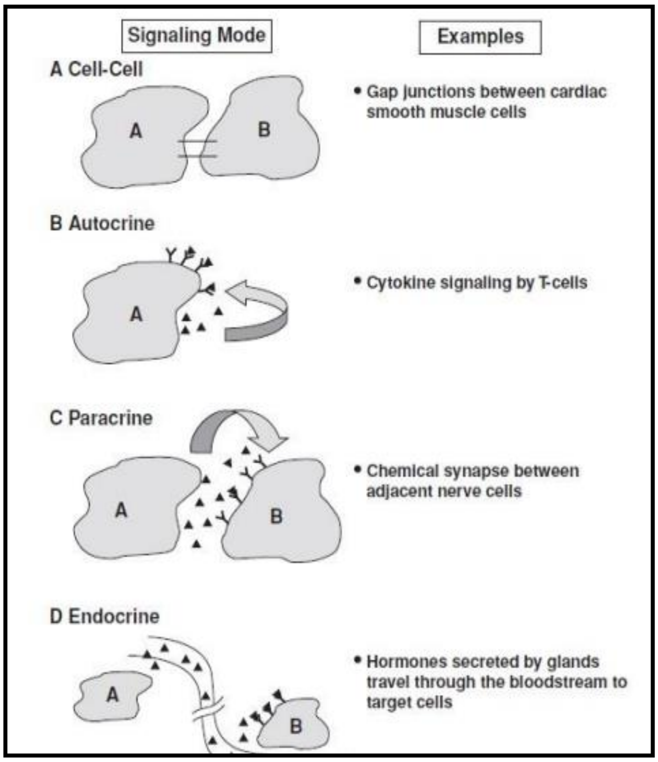
– Ligands مركبات رابطة can be attached to drug-delivery devices to target the drug to a receptor that is found only on the surface of a particular type of cell

– These same ligands can be used to deliver contrast agents to aid in imaging tumor cells

– Receptors themselves can be used in the design of biosensors

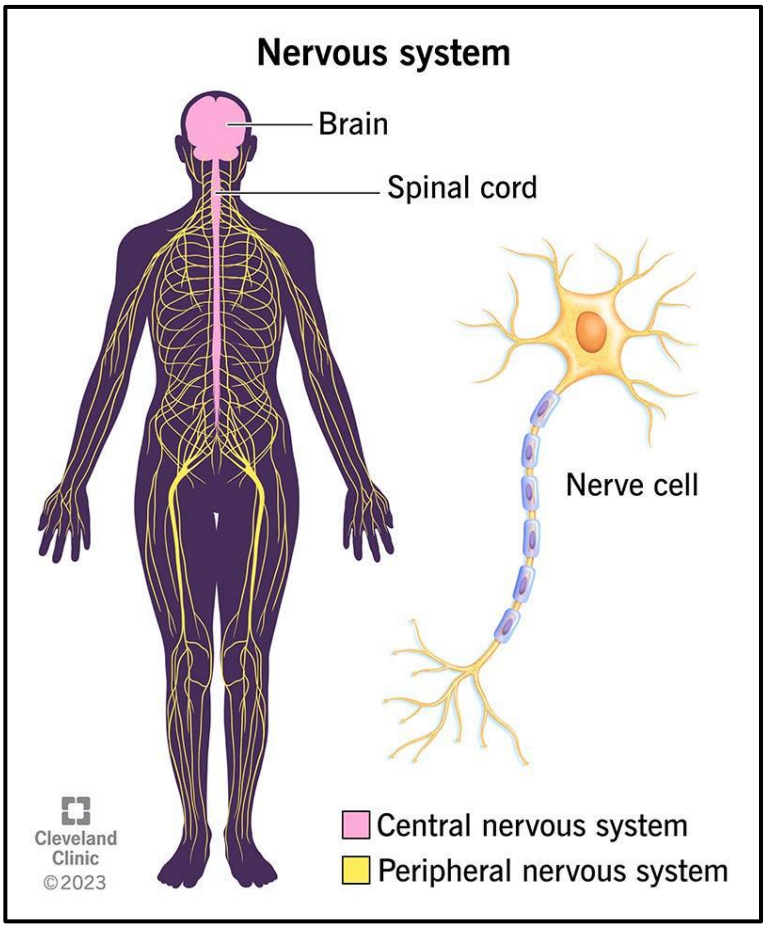
Signaling fundamentals

- Modes of cell signaling. Cells can communicate to each other via :
- direct cell–cell contact through gap junctions or cell surface receptors A.
- Cells also can send signals by secreting signaling molecules (triangles). These molecules or ligands can bind to receptors (Y)
- located on the cell's own surface (B), Or located on a nearby cell (C), or in a distant Cell (D).



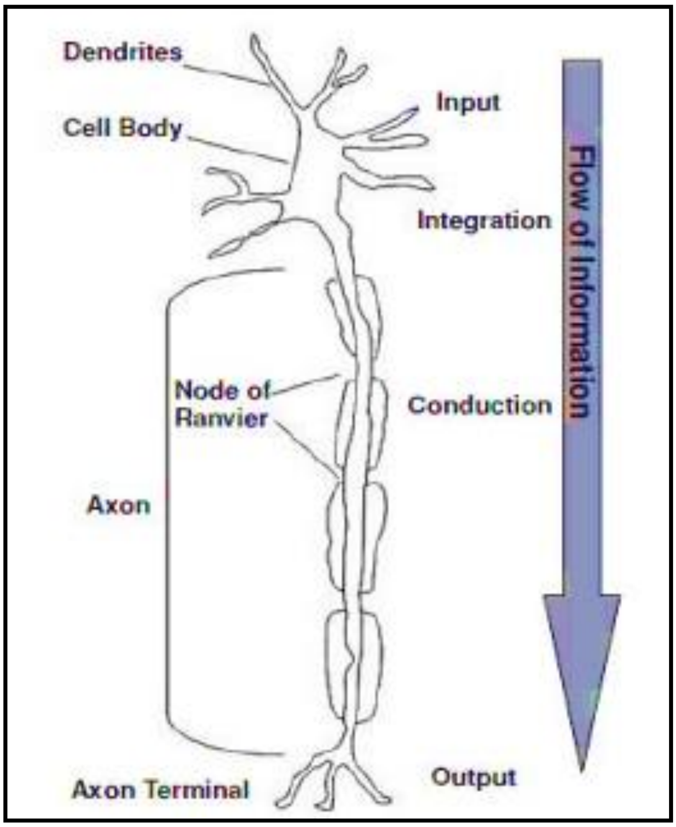
The nervous system

- The nervous system is transmitting signals to and from different parts of body
- consists of two main parts, the central nervous system (CNS) and the peripheral nervous system (PNS)
- The CNS consists of the brain and spinal cord
- The PNS consists mainly of nerves, which are enclosed bundles of the long fibers or axons that connect the CNS to every other part of the body
- Nerves that transmit signals from the brain are called motor nerves, while those nerves that transmit information from the body to the CNS are called sensory .



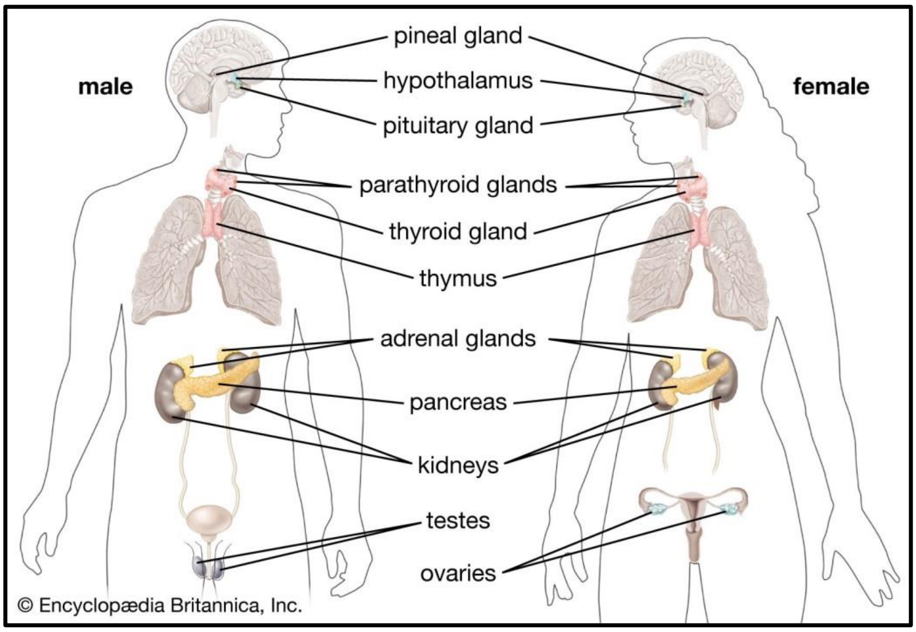
Neuron: is consists of:

- Dendrites الزوائد الشجيرية are extensions that act to receive input signals from other cells (usually other neurons)
- The axon محور عصبي conducts the integrated signal
- The axon terminals نهايات عصبية carry the output signal When an action potential reaches the axon terminal, it is transmitted to the dendrite of a neighboring neuron
- Neurons use a specialized junctions, called synapses الوصلات أو مشابك عصبية العصبية, to accomplish signal transfer



The endocrine system

- The endocrine system works with the nervous system to maintain homeostasis in the body.
- Hormones are chemical messengers that control growth , differentiation, and metabolic activities of cells and tissues.
- Secreted hormones bind to receptors located on the surface of cells of their target tissues, which may be located up to 2 meters from the secretion site. In response to a specific demand, an endocrine gland secretes hormones into the blood for distribution throughout the body to stimulate a response in a target organ.



Connections to biomedical engineering

- Biomedical engineers are beginning to learn how to build instruments that can interface directly with cells and tissues of the nervous system; these new instruments might lead to artificial retinas that can connect directly with visual pathways in the brain or brain–machine interfaces that enable paralyzed people to control robotic arms and computers through their thought processes

- biomedical engineers have been learning how to design artificial organs that secrete or respond to normal hormones (such as insulin and glucagon) for treatment of diabetes.
- The tools of molecular biology engineers can add or subtract key signaling genes in cells and tissues to improve artificial organ function and design cancer diagnostics and therapy
- The immune system is confounding the efforts of biomedical engineers who make implantable electronics, prosthetic joints, imaging contrast agents, artificial organs,… Biomedical engineers are making tremendous progress in control immune system function against these artificial instruments.

Lecture Three

Biomechanics

The use of laws of physics and engineering to describe motion of body, and internal and external forces during moving

- Biomechanics aims to determine the internal forces in muscles, tendons and joints (figure.) . These internal forces are used to explain the relationship between external environments and the internal injuries and tissue stresses.
- Newton’s three laws of motion:

✓ Newton’s First Law: If no force acts on a body, the body’s velocity cannot change

✓ Newton’s Second Law: Mass (m) × Acceleration (a) = Force (F)

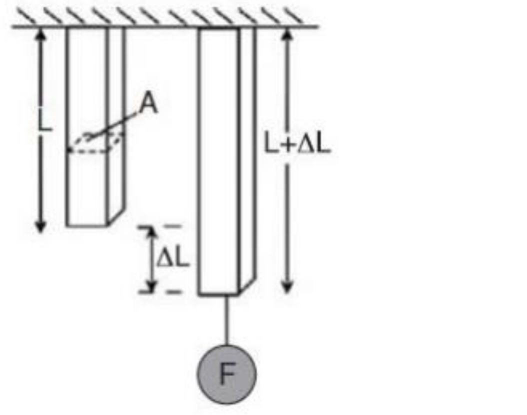
✓ Newton’s Third Law: For every action there is an equal and opposite reaction

- The standard international (SI) unit of force is one Newton (N)

Elastic deformation and Young's modulus

A biological tissue or a synthetic biomaterial that is fixed at one end and suddenly exposed to a constantly load. The material will have changes in the shape or size. The load on the material is defined as stress (σ, is equal to the force divided by the area A (Stress=F/A)). The response is strain, ε, the strain is the fractional increase in length of the material, ΔL/L. Linear elastic deformation is governed by Hooke's law, which states: $\sigma = E\,\varepsilon$

Where σ is the applied stress, E is a material constant called Young's modulus or elastic modulus (Table), and ε is the resulting strain. This equation describes the behavior of many elastic materials, such as springs, which deform linearly upon loading and recover their original shape upon removal of the load.



Deformation in response to applied load.

	E (MPa)
Biological materials	
Bone, long	15,000–30,000
Human compact bone (longitudinal)	17,000
Bone, cancellous	90–500
Bone, vertebrae	100–300
Dentin	13,000–18,000
Enamel	50,000–84,000
Articular cartilage	1–10
Human knee menisci	70–150
Brain tissue, grey matter	0.005
Brain tissue, white matter	0.014
Spinal cord	0.020–0.6
Tendon	1,000–2,000
Tendon, *Tendo achillis*	375
Human small artery	0.1–4
Elastin	0.6
Isolated collagen fibers	1,000
Formalin-fixed myocardium	101
Skin (phase I)	0.1–2
Collagen sponge	0.017–0.028
Polymers	
Poly(ethylene) (high density)	500–1,000
Poly(methyl methacrylate)	2,000–3,000
Polyimides	3,000–5,000
Polyester	1,000–5,000
Polystyrene	2,300–3,300
Poly(tetrafluoroethylene)	400–600
Poly(lactic acid)	1,000–3,000
Rubber (average)	2.8

example: If a force of 1 N is applied to an elastic specimen that has a cross-sectional area of 1 cm^2 and a Young's modulus of 3 GPa, what strain would be observed?

Answer: 3.3×10^{-6} or 3.3×10^{-4} %

Plastic deformation

This type of deformation is irreversible. Plastic deformation ends with the break of the material.

Energy storage with deformation

Strain Energy is added to a material when it is stressed. For an elastic material, the strain energy, U_o, is gived as: $U_o = \sigma\varepsilon$

The ability to store energy is an important property of biological materials. For example, the aorta شريان الوتين is elastic; it stretches when the heart contracts and ejects blood. Because the vessel الوريد is elastic, the energy that is stored by stretching the aorta is recovered during diastole.

Test: If we have three materials: long bone العظم الطويل, dentin عاج السن, and knee meniscus غضروف الركبة, which have Young's module of 30,000, 10,000, and 200 MPa, respectively. What strain energy is required to deform each to a strain of 0.1%? How much strain energy is stored in each, if they are each exposed to a stress of 30 MPa? Which is the most brittle tissue, and which the most compliant?

Answer: Strain energy = 15, 5, and 0.1 kPa, respectively, to deform to 0.1%. Strain energy = 15, 45, and 2,250 kJ/m3, respectively, when exposed to 30 MPa stress. Long bone is the most brittle and knee meniscus the most compliant.

Elasticity, viscosity, and viscoelasticity

Viscoelasticity is the property of materials that have both viscous and elastic properties under deformation. Viscous materials (water) strain linearly with time when a stress is applied. Elastic materials strain when stretched and return to their original state after the stress is removed.

Bone structure and function

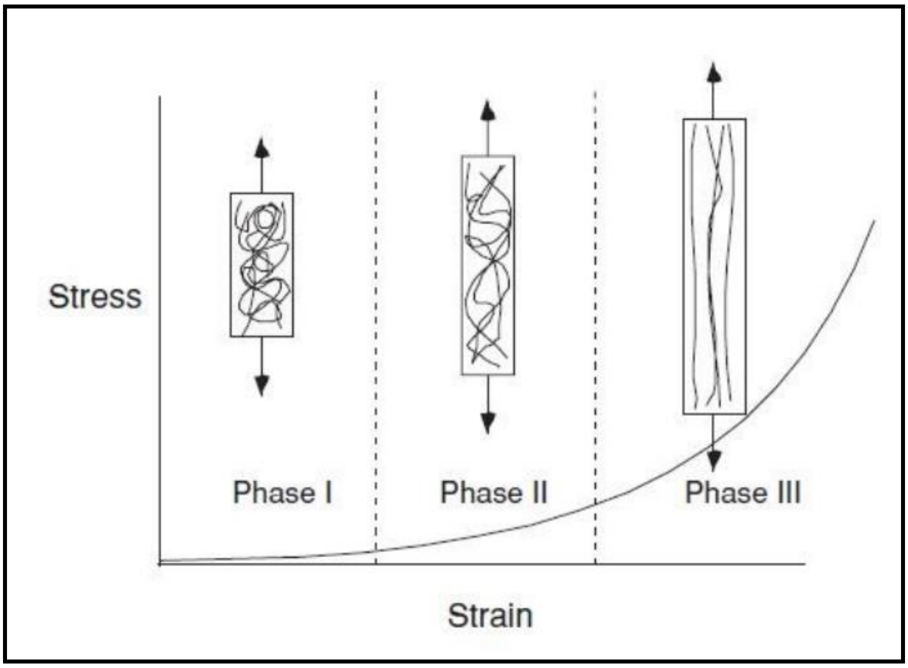
Bone is a hard tissue, which is consists of a mineral phase (60%), an organic collagen-rich matrix (30%), and water (10%). It has some elasticity and it is also strong. Bone has two typical architectures, compact (or cortical) bone and spongy (or cancellous) bone, which differ in their microscopic structure as well as their mechanical properties.

Bones are Anisotropy (mechanical properties depends on the direction of applied loading) , However, metals and many plastics, which display isotropy (similar mechanical properties in all directions).

Structure and function in soft connective tissues

Soft connective tissues surround the organs, protect them from damage such as skin, and blood vessels. In contrast to bone, which is a hard material, soft connective tissues are typically flexible and deformable. It is viscoelastic (protein fibers are embedded in a fluid phase).

The fig. below shows the behavior of skin, With small tensile deformations (Phase I), the tissue behaves as an elastic material; microscopically, collagen fibers within the tissue are <u>deforming</u> <u>without stretching</u>. As the strain increases (Phase II), collagen fibers become deformed, straightening in the direction of the strain and increasing the stiffness of the skin. With increased loads, in deformations that are just less than the ultimate tensile strength (Phase III), the collagen fibers are aligned in the direction of the applied load, and stretched. Ligaments also exhibit these phases of behavior.



<u>Cellular mechanics</u>

Cells have the structure that determines their ability to deform. Red blood cells are slightly larger than the smallest capillaries and, therefore, must deform to move through the circulation. The mechanical properties of cancer cells are an important determinant of cancer advance. Invasion of cancer into normal tissue depends on the ability of cancer cells to create the physical forces that allow them to crawl. Metastasis تفشي one of the lethal elements of cancer, occurs when cells crawl into blood vessels and move through the circulation; the site of deposition of these cells depends on their mechanical properties.

Mechanical properties of the cytoskeleton

The three most important protein fibers of the cytoskeleton are: actin microfilaments, microtubules, and intermediate filaments. These fibers have intrinsic mechanical properties.

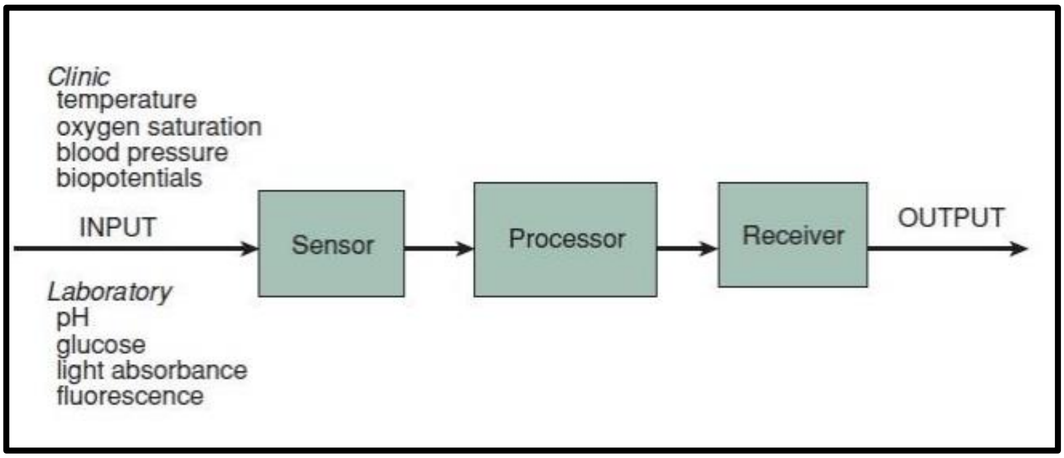
The three main fibers differ greatly in mechanical properties: Actin microfibers are flexible but unable to withstand tensile forces; microtubules are stiffer than actin fibers (but still have poor tensile strength); and intermediate fibers are more flexible than actin and are stronger under tension.

Within the cytoplasm, fibers collect into bundles حزم; bundling greatly enhances the mechanical strength of the system. In addition, when the ability to bundle تحزم and unbundle عدم تحزم fibers is regulated تنظم , the local mechanical properties of the cytoplasm can be controlled via gathering and ungathering of fibers.

Many cytoplasmic constituents participate in the filament-assembly process; actin filaments, for example, are cross-linked by at least four different agents (α-actinin, spectrin, fimbrin, and villin) providing the cell with a variety of tools for dynamically regulating filament assembly. In general, solutions of cytoskeletal fibers are viscoelastic.

Lecture Four

Bioinstrumentation



- The input is detected by a sensor (converts it into an electrical signal)
- A signal is modified by a processor (amplification , filtering , comparison)
- The output is displayed (as digital signal), stored, communicated by a receiver

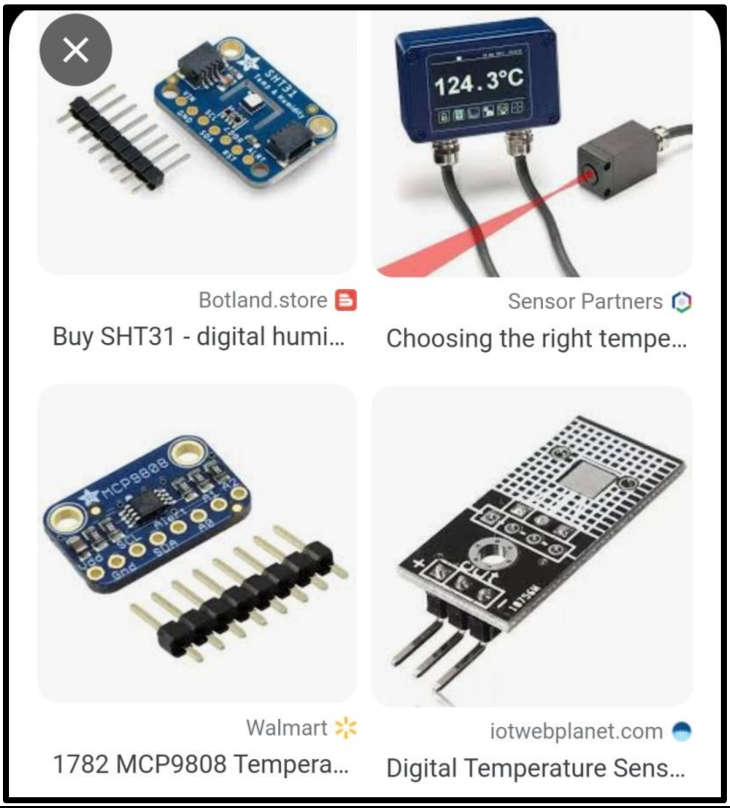
Ohm's law is helpful for understanding basics of instrument design and operation: **V=IR** (I: current through the conductor in units of amperes (A), V : voltage (V), 1 ohm (Ω) is equal to 1 V/A)

Test: A current of 1 micro-A (μA) flows through a device after it is connected to the poles of a 9 V battery. What is the resistance of the device? Answer: $9 \times 10^6\ \Omega$

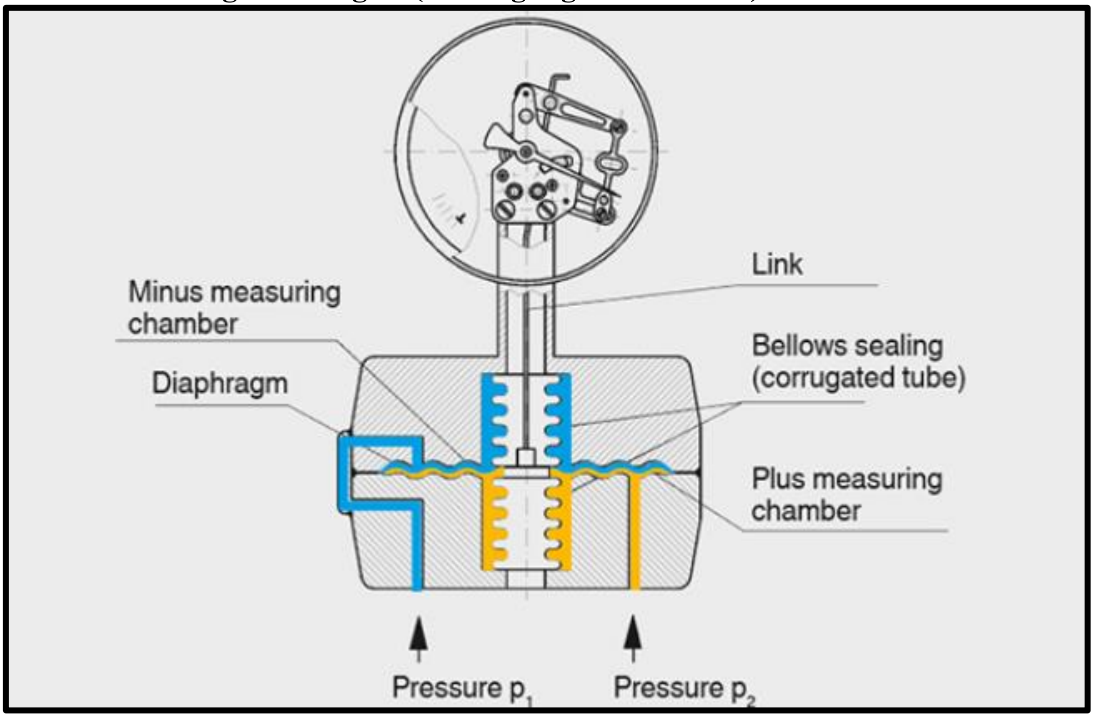
Types of sensors

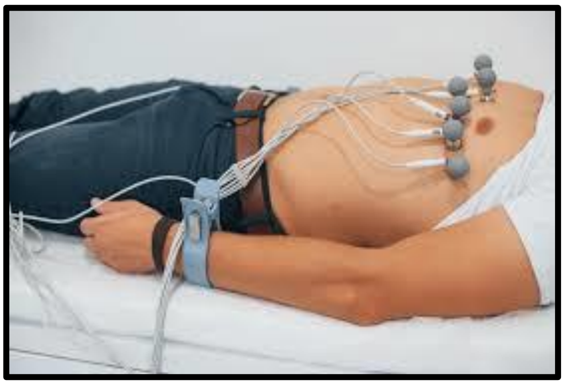
Sensor type	Sensing element	Example
Thermal	Thermocouple, thermistor	Electronic thermometer
Mechanical	Strain gauge, piezoelectric sensor	Pressure transducer
Electrical	Electrode	Electrocardiograph (ECG), electroencephalograph (EEG)
Chemical	Electrode	pH meter
Optical	Photodiode, photomultiplier	Pulse oximeter

Thermal sensors

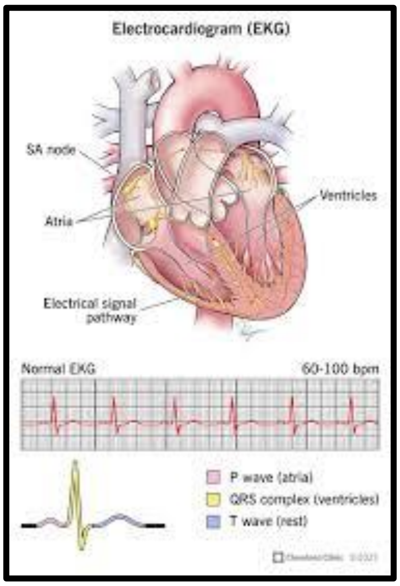


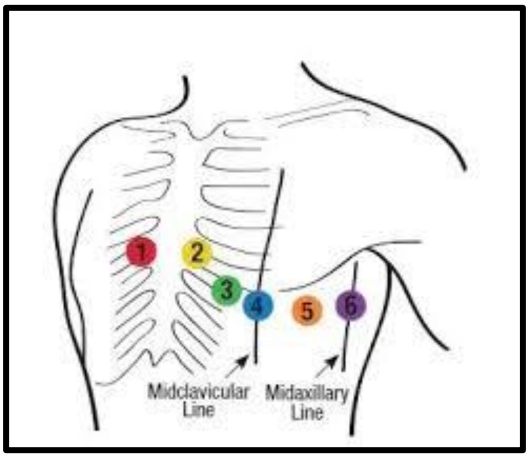
Mechanical sensors: change in length (strain gauge $\varepsilon = \Delta L / L$)



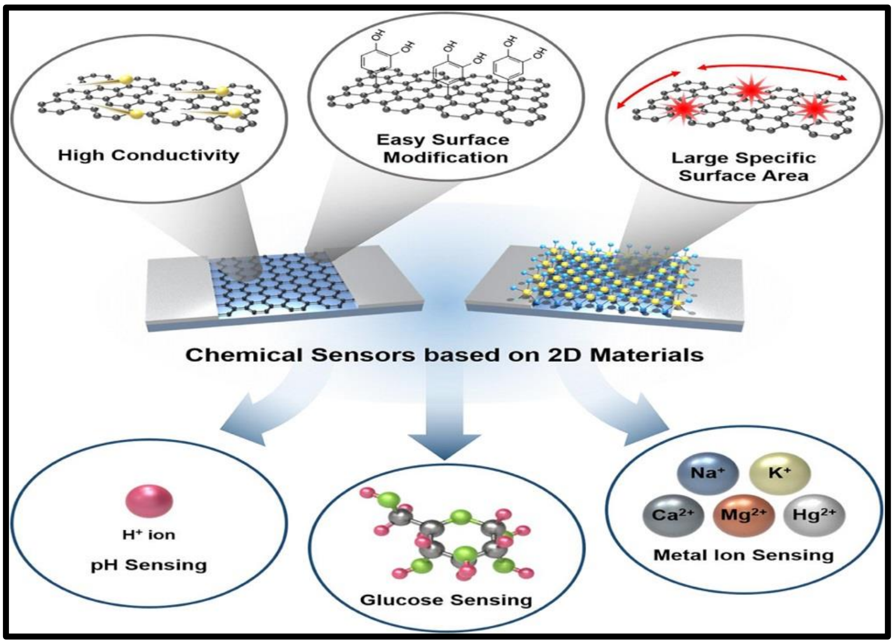


Electrical sensors: electrocardiograph, or ECG

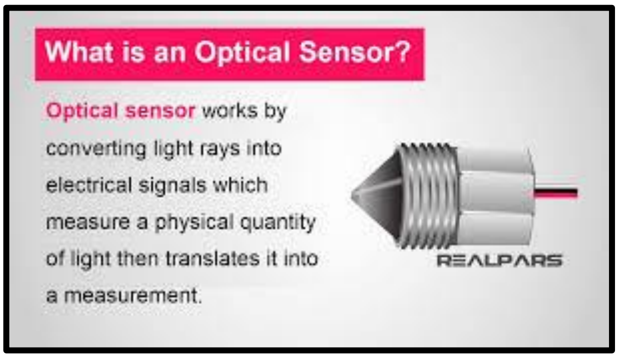


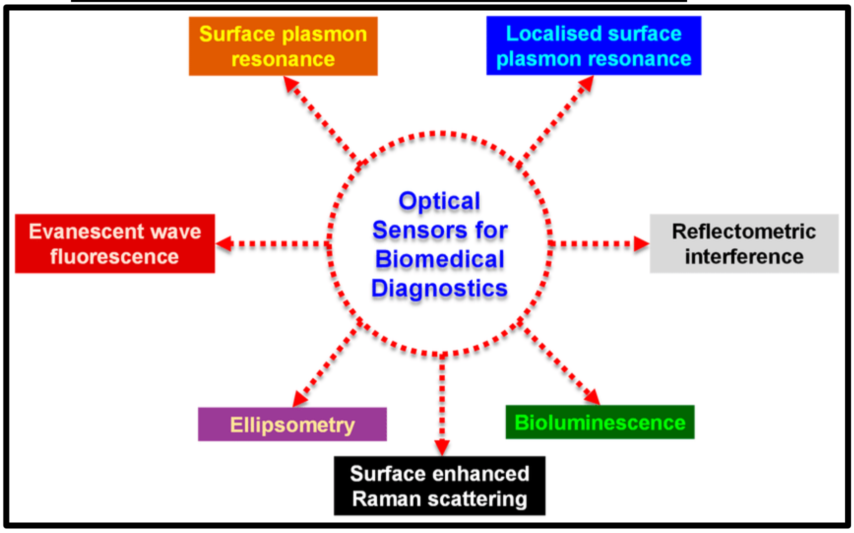


Chemical sensors: uses an ion selective electrode (ISE) to detect ions. Sensors that use a biological molecule is biosensors



Optical sensors





Instruments in medical practice

Input	Instrument	Sensor	Output
Temperature	Oral digital thermometer	Thermistor	Temperature display
Blood pressure	Digital sphygmomanometer	Stethoscope or strain gauge	Pressure
Blood oxygen	Pulse oximeter	Photodiode	Percent oxygen saturation
Biopotentials			
Cardiac biopotentials	Electrocardiograph (ECG)	Skin electrodes	Electrocardiogram
Neural biopotentials	Electroencephalograph (EEG)	Scalp electrodes	Electroencephalogram
Retinal biopotentials	Electroretinograph (ERG)	Contact lens electrodes	Electroretinogram
Muscle biopotential	Electromyograph (EMG)	Needle electrodes	Electromyogram

1- Measurement of body temperature

The normal body temperature is 98.6◦F (or 37◦C). Usually, a temperature above 99.5◦F (or 37.5◦C) is a sign of an infection, Hyperthermia, elevated body temperature, as a result of prolonged exercise or exposure to excessive heat.

Converting a temperature from degrees Fahrenheit to degrees Celsius is simple and can be calculated using the following equation:

$$T\text{deg C} = \frac{5}{9}(T\text{deg F} - 32)$$

Test: Room temperature is usually about 75◦F. Convert this number to ◦C.

Answer: 24◦C

2- Measurement of blood pressure:

The normal average of blood pressure is 120/80 mmHg. Individuals who are hypertension have blood pressure of 140/90 mmHg or higher. Blood pressure can become too low hypotension after trauma or hypothermia.

Blood pressure is often reported as (systolic over diastolic) pressure. Systolic pressure is the maximum pressure on the arterial walls during contraction of the ventricles of heart, whereas diastolic pressure occurs during the relaxation of the ventricles.

3- Measurement of oxygen saturation in the blood

Lung diseases can cause low oxygen levels in the blood, a condition known as hypoxemia, It is measured by pulse oximeter

The pulse oximeter measures the difference in light absorbance at two wavelengths: one in the red portion of the visible region (Red 660 nm) and another in the IR region (910 nm).

These measurements provide information on the ratio of oxyhemoglobin (hemoglobin [Hb] bound to oxygen) to deoxyhemoglobin (Hb without oxygen) in the tissue. Red light is not absorbed well by oxygenated blood, but IR light is absorbed. By using photodiodes to produce small light beams at these two wavelengths, and detectors to measure the fraction of each light beam that passes through the tissue, the device calculates the ratio of red to IR absorbance.

4- Measurement of blood glucose

The self-testing of blood glucose detects higher levels of glucose in blood (diabetics) or lower levels. The test strips are precoated with a glucose sensitive enzymes, which convert Glu. To H_2O_2 that reacts with a dye and produce a blue color. the density of the color is expressed as concentration of glucose in the blood stream.

5- Measurement of cardiac electrical potential by electrocardiogram (ECG)

The electrocardiogram (ECG or EKG) provides a reliable method for screening and earliest diagnosis of heart disease.

6- Devices for electrical stimulation of tissues

Electrically excitable tissues; heart, brain, and muscle can be stimulated by the controlled implanted of currents.

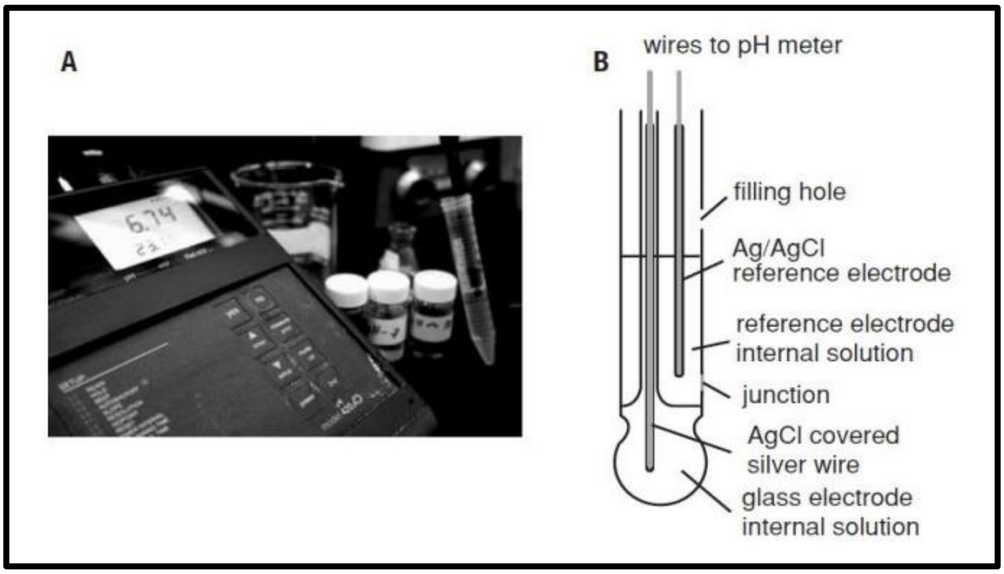
- patient whose heart rate is too slow (a condition called bradycardia), a pacemaker can restore normal cardiac rhythm. A pacemaker is a small, battery-powered device that is implanted in the chest.
- The deep brain stimulator is used to treat patients with Parkinson's disease: electrical signals reduces the severity of the symptoms.

- Similar approaches are useful for treating some kinds of chronic pain and may be useful in other diseases in the future.

Instruments in the research laboratory

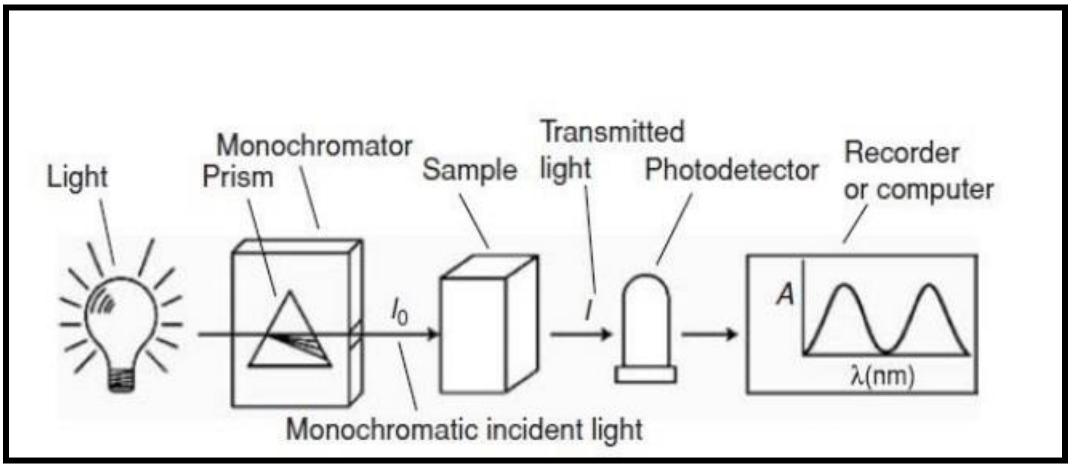
1- Measurement of pH

pH meters consist of a single electrode, which contains both a reference and sensing electrode, and an easy-to-read digital display.



2- Spectrophotometry

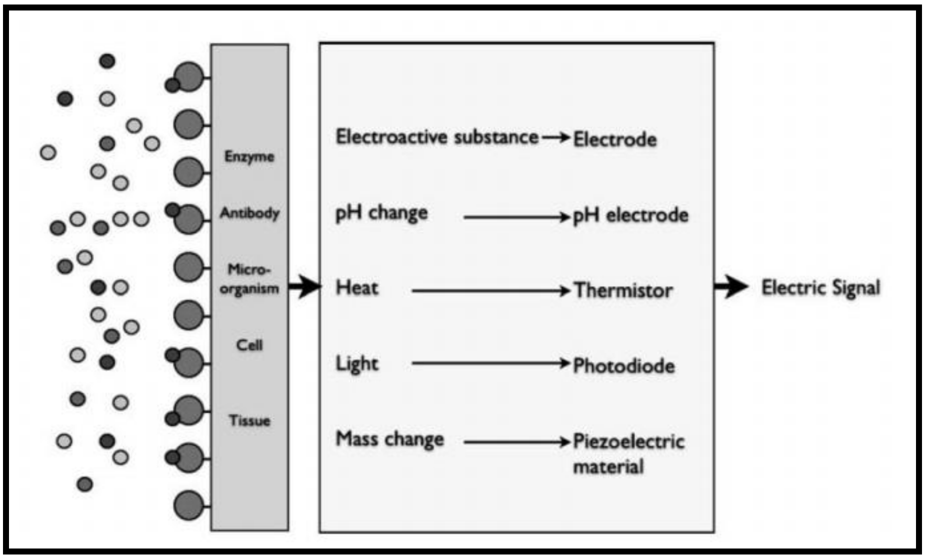
A spectrophotometer is tool used to measure the density of light through a biological sample. Many biological molecules absorb light better at some wavelengths than others: For example, Hb absorbs light throughout the range of wavelengths from 600 to 1000 nm, but it absorbs best near 600 nm.



Biosensors

A biosensor uses a biological sensing element (such as an enzyme or tissue) to create a change that can be converted into an electrical signal.

Often, the biological sensing element is connected to one of the other sensors (such as a thermistor or photodiode)



Lecture Five

Bioimaging

Bioimaging is allowing us to **see inside the body** and to visualize biological structure and function at microscopic levels **digitally**.

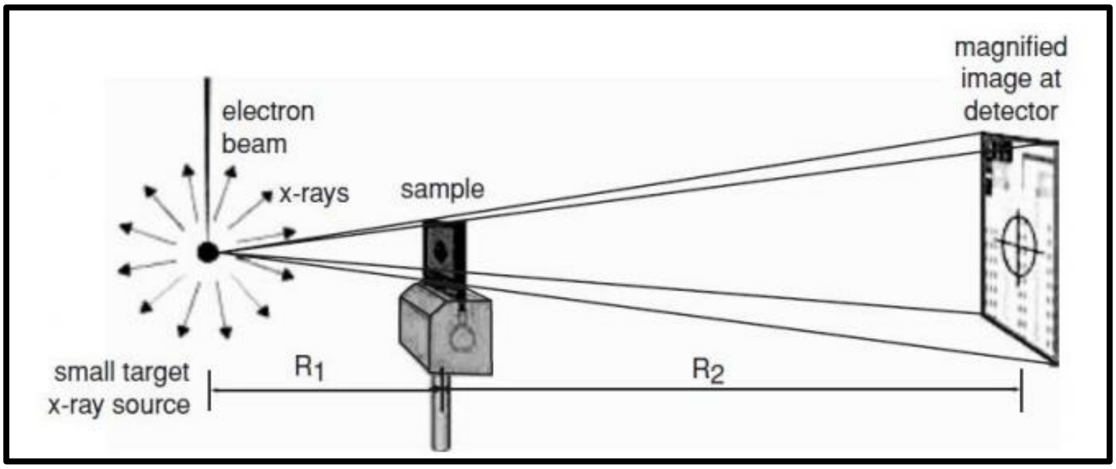
Digital images can be readily processed to improve their quality, make measurements, and extract features of interest.

In general, an energy source interacts with the target (body) and produces a signal. The energy can come from electrons, ultrasound, light, x-rays, or even radio frequency (RF). Transducers are needed to convert the signal into a measurable form, a voltage.

Advanced microscopic techniques were developed, such as **electron microscopy**, which uses electrons instead of visible light to create images of objects. **Gamma camera** imaging (which can create images from radioactive substances injected into the body), **ultrasound imaging**, **positron emission tomography (PET)** imaging, **computed tomography (CT)** to create **three-dimensional** images from x-rays, and **magnetic resonance imaging (MRI)**, which now provides high-resolution images of the inside of the body without the hazards of x-rays or other forms of ionizing radiation.

X-rays

The image is a 3-D map of the object's susceptibility to penetration by the rays.

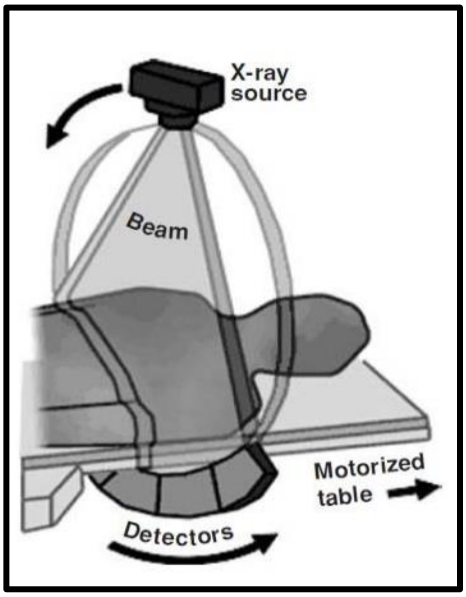


X-rays are electromagnetic radiation with wavelengths 0.1 nanometer. Because the rays have energy to knock electrons out of atoms, x-rays are ionizing radiation. Loss of electrons **turns atoms into ions** or charged particles; if the material is human tissue, and ions are generated within the tissue, these ions can later damage cells.

The film is darker where the body is less dense and lighter where the body is denser (like bone).

Computed tomography (CT)

The idea of CT is to take x-rays at many different angles and use the many images that were thus acquired to recreate a three-dimensional image of the body.



Whereas the contrast of CT is limited in soft tissue, CT is valuable for imaging the head, lungs, abdomen, pelvis, and extremities.

MicroCT imaging has also been developed that allows imaging of very small structures in body.

Ultrasound imaging

Ultrasound imaging is based on the spread of high-frequency sound waves through tissue.

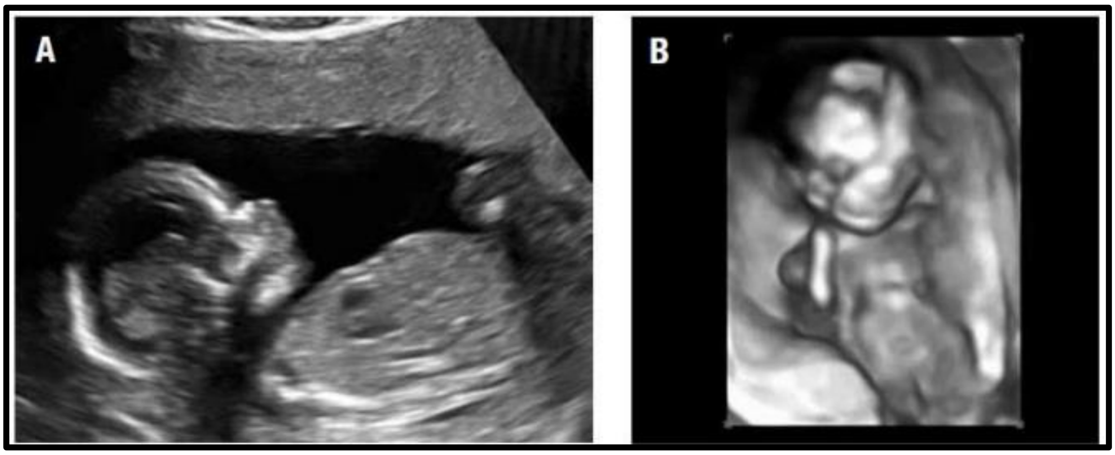
- fast: Structure and dynamic function can be recorded from rapidly moving tissues, such as a beating heart, and visualized at the same speed in which they happen (imaging in real time).
- safe (pregnant women).
- It can be used for therapy, such as for breaking up kidney stones.
- It is excellent for emergency medicine because of its ability to image internal bleeding and localize internal injuries.
- relatively inexpensive.
- One important **limitation**, is that ultrasound imaging is difficult through bone and air (such as in the lungs).

Piezoelectric crystals (كريستال كهروضغطية) are used to generate a pulse of ultrasound in the megahertz range, from or from 2 to 13 MHz (10^6Hz), the echoes, or reflections, return to the transducer, which measures them using the piezoelectric crystal.

The location of each echo is determined by the time (t) between the generation of the pulse and the reception of the echo. In ultrasound, the speed of sound is assumed to be constant in tissue, at about the same speed as sound in water (1540 m/s). The pulse travels at this speed (c), for a distance of 2d, twice the distance from the transducer to the structure. The time is therefore related to the distance by:

$$C = \frac{2d}{t} \quad \text{or} \quad d = \frac{ct}{2}$$

Test: What is the time required to receive an echo from the aorta, assuming that the transducer is abutted to the abdominal wall, and the aorta is 6 cm deep? Answer: t = 0.00008 seconds.



Doppler imaging

It is valuable to measure the velocity of a tissue, such as the rate of blood flow or the rate of wall motion in the heart. Velocity can be measured with ultrasound imaging by exploiting the Doppler effect.

In the case of blood flow, the echo comes from the moving particles (blood cells) in the blood. If the cell is moving toward the transducer, the wavelength will be shorter and the frequency will be higher; if moving away, the opposite will be true. Faster motion produces a larger change in frequency.

Biomolecular engineering: Biotechnology

It is examining the changes in chemical components within a biological system and developing methods for modifying these chemicals or their interactions.

Drug delivery

Controlled drug-delivery systems can take a variety of forms like miniature mechanical pumps, polymer matrices or microparticulates, externally applied transdermal patches, and transplanted, genetically engineered cells. In most cases, the goal of controlled drug delivery is maintenance of plasma or tissue drug levels at a constant level for a prolonged period.

Genetically engineered cells for controlled drug delivery

Future drug-delivery systems will probably use biological components that allow self-regulation of drug release, like enzymes or antibodies, as the signaling element for regulation of release.

Tissue engineering

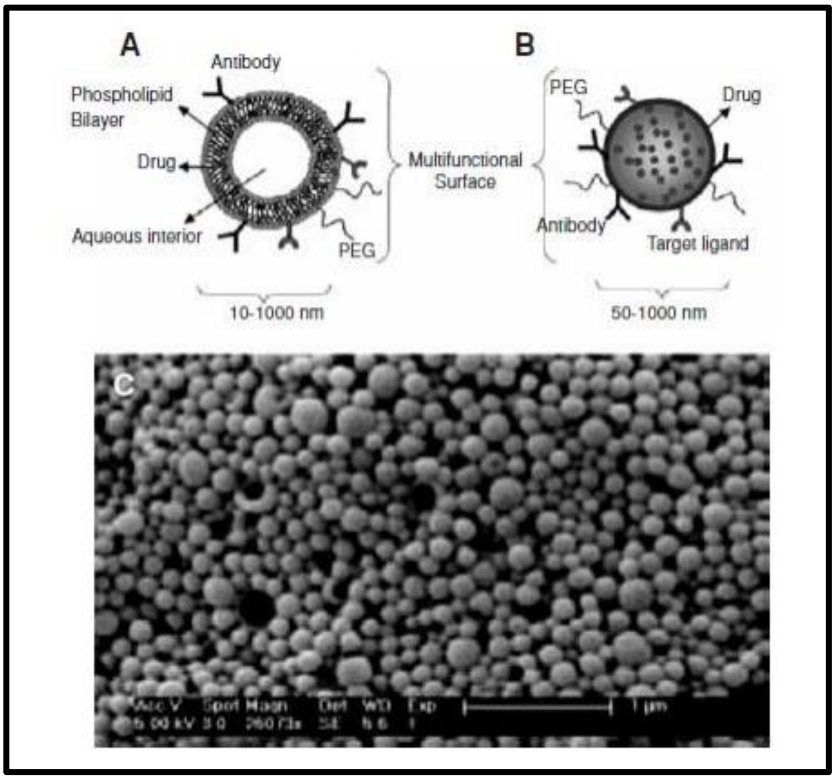
It combines knowledge from the biological sciences with materials science and engineering to accomplish several goals: to quantify structure, function relationships in normal and pathological tissues, to develop new approaches to repair tissues, and to develop replacements for tissues. Tissue engineering utilizes living cells as engineering materials.

Example of tissue engineering: Artificial skin

These systems are designed to serve as substitutes for the main functions of skin. Some systems are acellular (without cells) silicone membranes (to retain fluid).

Another approach is to take a small sample of tissue from the patient, by a surgical procedure called a biopsy, and expand the autologous epidermal cells in vitro. Using optimized cell culture techniques, it is possible to achieve a 10,000-fold amplification in cell number by the end of 3–4 weeks, which is still too slow for many clinical situations. This time delay can be avoided by using allogeneic cells.

Nanobiotechnology



Examples of drug-delivery nanoparticles:

A. Liposomal systems are vesicular with targeting groups, such as Poly ethylene glycol (PEG), attached to the surface lipids.

B. Solid biodegradable nanoparticles are formed from a polymer emulsion with drug dispersed in the polymer matrix and targeting or PEG groups attached to the surface.

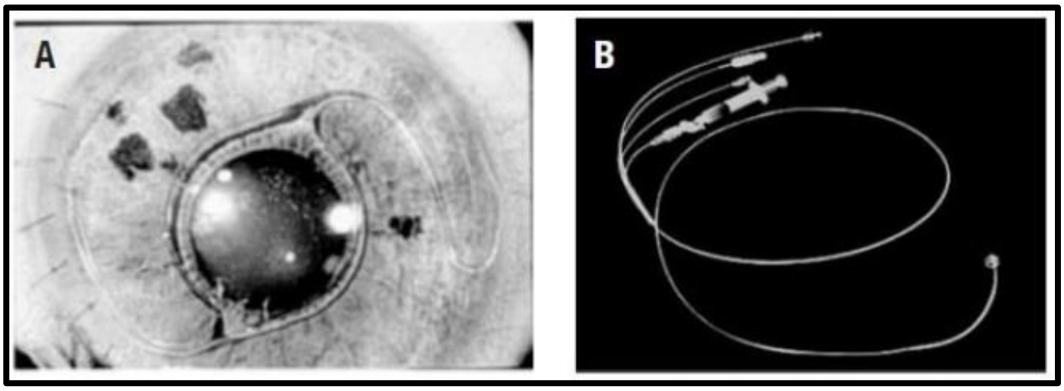
C. Scanning electron micrograph of surface-modified PLGA nanoparticles.

Aspect of biomolecular engineering	Brief definition	Example
Bioprocess engineering	Use of engineering analysis to design large-scale processing of biological materials	Bioreactor design; bioseparations such as chromatography and electrophoresis
Metabolic engineering	Analysis and redirection of the metabolic activity of a cell	Gene therapy to correct metabolic defects
Biomaterials engineering	Design and synthesis of new materials that can be used in biological systems	Materials for prosthetic heart valves
Pharmacological engineering	Analysis of modes of drug administration and the fate of drugs in the human body	Controlled delivery systems for contraceptives; design of dose regimens for chemotherapy drugs
Tissue engineering	Quantifying structure–function relationships in normal and pathological tissues, developing new approaches to repair tissues, and developing replacements for tissues	Tissue-engineered skin; polymer scaffolds for tissue regeneration
Cellular engineering	Use of functional genomic concepts to predict changes in cellular function with gene expression, regulation of cellular function by ligand binding to receptors and intracellular signaling networks	Analysis and manipulation of cell adhesion and motility
Nanobiotechnology	Use of engineering tools to create devices or materials with nanometer scale precision, and the application of these devices in biological systems	Nanoparticles for drug targeting

Biomaterials in current use

Many medical devices involve polymeric biomaterials: catheters and contact lenses.

For materials that contact blood, the most common problem is formation of blood clots, which may be initiated by the material surface. The most common problem for non–blood-contacting applications, such as tissue implants, is the development of a foreign body response (FBR) that isolates the device from the rest of the body.



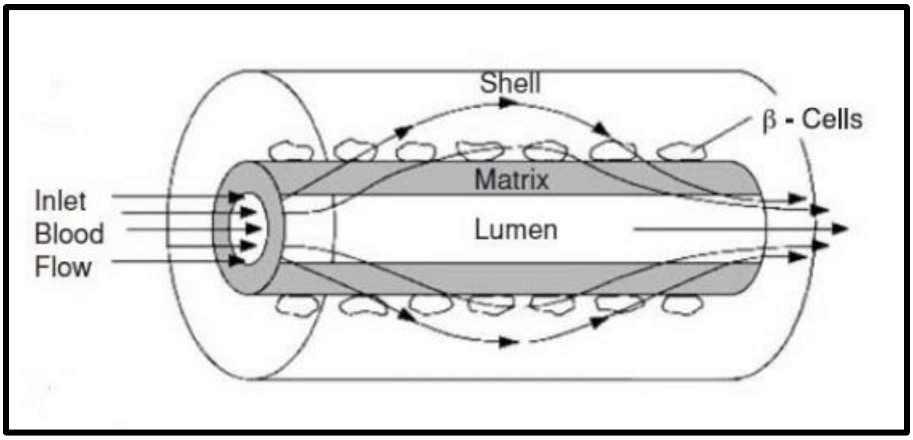
Plastic implantable lenses and catheter. A. Intraocular lens, which is implanted in front of the natural lens in extremely nearsighted patients, to allow normal vision without glasses. The artificial lens is made of polymethyl methacrylate. B. Example of a polymer catheter.

Artificial heart

Pacemakers are complex medical devices that allow for modulation of the electrical stimulation of the heart.

Design of a hollow-fiber biohybrid artificial pancreas

Islets are maintained in the shell of the hollow-fiber device, and blood flows through the lumen of the fibers.



Artificial liver

- Approaches similar to those used to develop an artificial biohybrid pancreas have been used to create artificial livers.
- Hepatocytes are used in a hollow fiber bioreactor, two charcoal columns, a membrane oxygenator, and a pump.