General Biophysics (211 بف)

Lecture 2

Prepared by:

Dr. Abdo A. Elfiky

Topics

- Topics of Biophysics:
  - **Molecular and subcellular Biophysics:**
    - The structure and conformation of Biological Molecules.
    - Structure Function Relationships.
    - Conformational Transitions.
    - Ligand Binding and Intermolecular Binding.
    - Diffusion and Molecular Transport.
    - Membrane Biophysics.
    - DNA and Nucleic Acid Biophysics.
    - Protein Biophysics.
    - Bioenergetics.
    - Thermodynamics.
    - Molecular Machines.

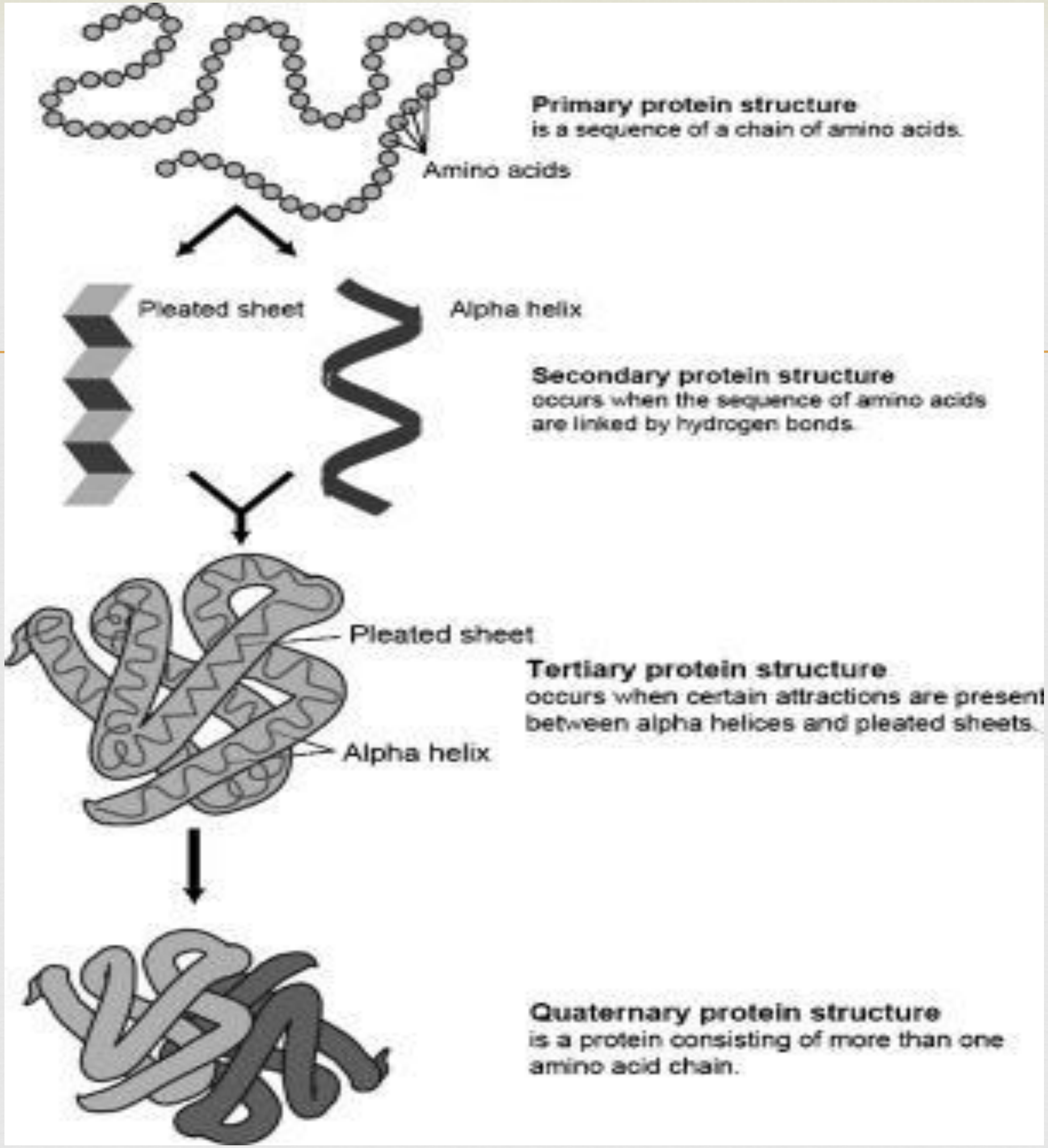
Molecular and Subcellular Biophysics

The structure and conformation of Biological Molecules

- This branch of biophysics deals with determining the structure, size, and shape of biological molecules.
- Many biological molecules are polymers. A *polymer* is a large molecule made by connecting together many smaller molecules. Each of the smaller molecules is called a *residue*.
- The residues making up a polymer may be identical, like links in a typical chain where the links are all ovals. The residues may also be a set of related but not identical molecules—imagine a chain where the links are various shapes: circles, triangles, squares, and rectangles.

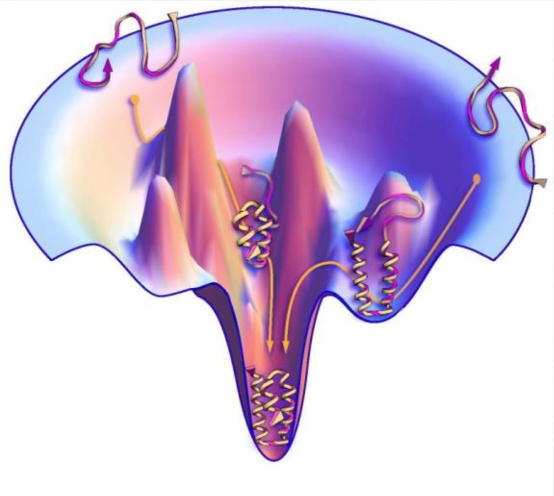
The structure and conformation of Biological Molecules (Continued)

- There are *four levels of structure* in biological molecules: primary, secondary, tertiary, and quaternary.
- *Primary structure* specifies the atoms or groups of atoms making up a molecule and the order in which they are connected to one another.
- *Secondary structure* refers to the initial, simple, three-dimensional structure of a molecule. For example, a molecule, or part of a molecule, may take the shape of a helix or a shape similar to a pleated sheet.
- *Tertiary structure* refers to the fact that a secondary structure, such as a helix or pleated sheet, can fold back on itself.
- *Quaternary structure* refers to the case where two or more tertiary shapes attach to one another to form an even larger molecule or complex


Primary protein structure
is a sequence of a chain of amino acids.
Amino acids
Pleated sheet
Alpha helix
Secondary protein structure
occurs when the sequence of amino acids
are linked by hydrogen bonds.
Pleated sheet
Tertiary protein structure
occurs when certain attractions are present
between alpha helices and pleated sheets.
Alpha helix
Quaternary protein structure
is a protein consisting of more than one
amino acid chain.

The structure and conformation of Biological Molecules (Continued)

- The structure and conformation of biological molecules, as a branch of biophysics, also includes analyzing the forces and energy required for a molecule to maintain a particular shape. With this information, biophysicists develop geometric and mathematical models to predict the secondary and tertiary structure of a molecule, given its primary structure.

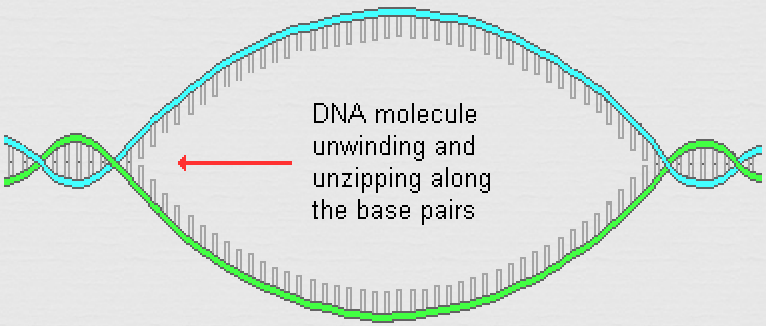


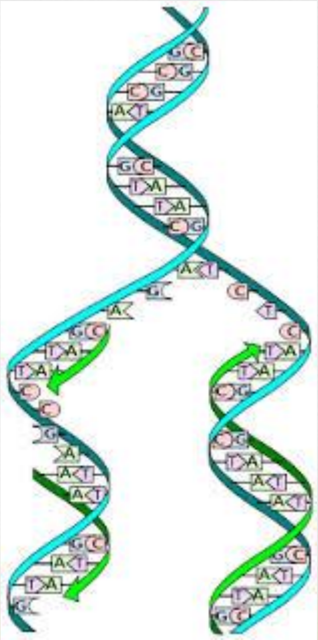
Structure Function Relationships

- Closely related to determining the structure and shape of biomolecules is determining which parts of a molecule are involved in its biological function; called *Active site*, and determining how changes to its structure or shape affect its biological function.

Conformational Transitions

- Biomolecules often change their shape as part of their function. For example, the DNA double helix must temporarily unwind in order for the genetic instructions to be read or in order for the DNA to replicate itself for the next generation.





Conformational Transitions (Continued)

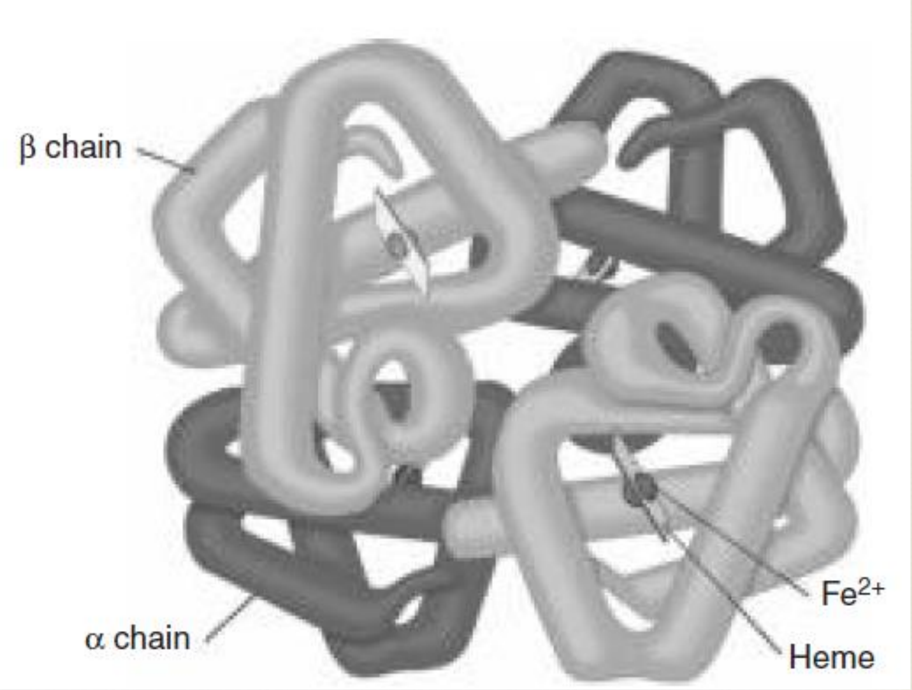
- Biophysicists use a variety of techniques to measure conformational changes in biomolecules, to measure the energy associated with them and to determine the relationship between the various conformations and their biological function.
- Induced conformational transitions can further our understanding of the forces involved and can be used to develop medical treatments and diagnostics.

Ligand Binding and Intermolecular Binding

- A very common theme in subcellular biological function is the binding together of molecules. Sometimes the molecules are roughly equal in size and bind together to form a larger *complex*.
- In other cases of molecular binding, a smaller molecule binds to a larger molecule. In such cases we call the smaller molecule a ligand. A *ligand* is a smaller molecule or atom that binds to a larger molecule. The smaller molecule may be integral to the biological purpose of the larger molecule, or it may simply serve to activate or deactivate the larger molecule in carrying out its purpose.

Ligand Binding and Intermolecular Binding (Continued)

- An example is hemoglobin, a large complex protein that carries oxygen from our lungs, through our blood, to the cells in our body. Hemoglobin is made up of four subunit proteins that bind together.



Ligand Binding and Intermolecular Binding (Continued)

Biophysicists studying ligand binding and other intermolecular binding seek to measure and understand:

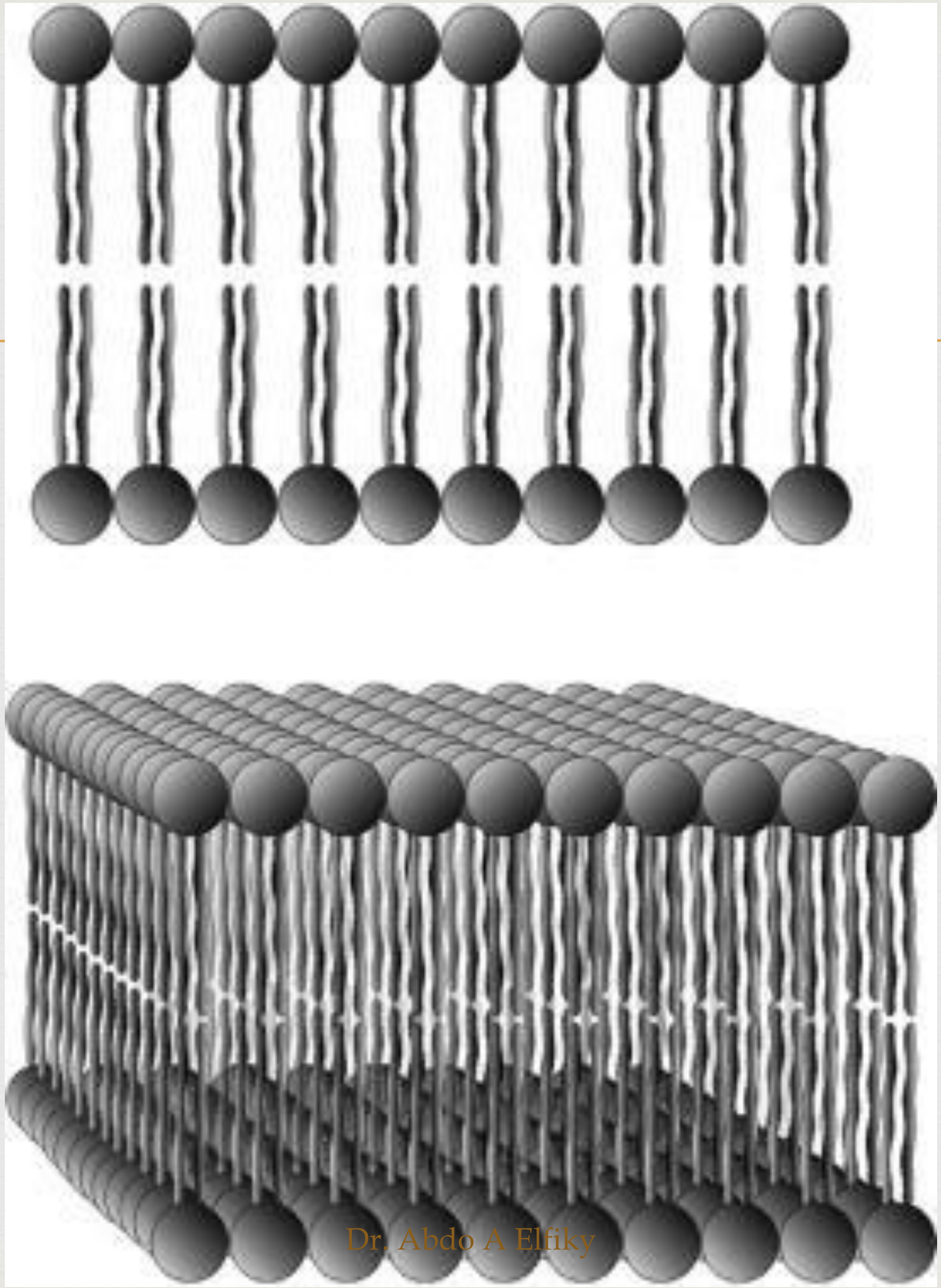
- The forces and energy involved in binding.
- The interaction between multiple binding sites.
- How changes to the molecules affect binding.
- The relationship between binding and conformational transitions.
- The relationship between binding and biological function.
- The competition between different ligands that can bind to the same molecule.
- The rate at which binding occurs and the factors that affect binding rates.

Diffusion and Molecular Transport

- In fluids, molecules are continually moving, randomly colliding, and jostling about. *Diffusion* is the process of molecules spreading out, as a result of this random motion. By spreading out, we mean that the random motion will cause molecules to move from a region of higher concentration to one of lower concentration.
- The physics of diffusion can be described mathematically and can be used to better understand and predict biological activity in cells.

Membrane Biophysics

- The membrane is what defines the boundary between a cell and the outside world.
- Cell membranes are typically made of a double layer of lipid molecules. Lipids are fats or oils.
- Lipid molecules have a string-like shape with a "head" at one end. The shape and physical characteristics of lipid molecules make them associate with each other in the form of a bilayer with the molecule heads on the outside of the bilayer and tails on the inside.



Membrane Biophysics (Continued)

- Membranes limit and control the movement of molecules into and out of the cell and from one region of the cell to another. Membranes are also able to create electrical potential across their surface, by controlling the flow of ions into and out of the cell.
- Understanding the physics of lipids and membranes can help us to better understand and predict how cells will behave under various conditions.

Membrane Biophysics (Continued)

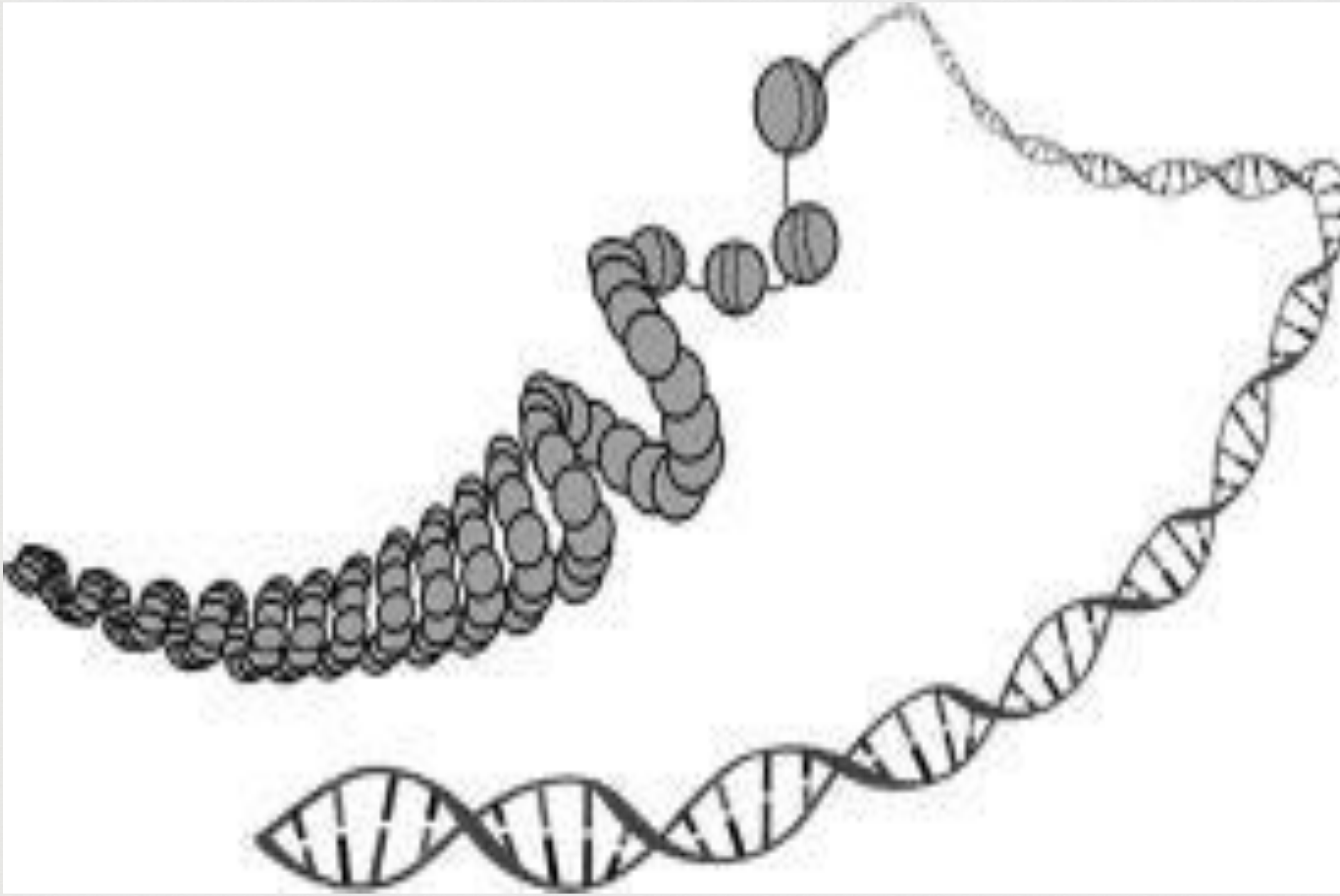
- Membrane biophysicists often use lipid vesicles to study membranes.
- A vesicle is a small hollow sac. Lipid vesicles are small hollow spheres of artificial membrane that can be made from various types of lipids. Thus a lipid vesicle is like a cell with nothing inside it, just the membrane alone. This provides a simple tool to conduct experiments on the behavior of membranes without the complications of other parts of the cell.
- It is possible to also place drugs or chemical agents inside lipid vesicles.

Membrane Biophysics (Continued)

- Targeting: ways to attach certain molecules to the outer surfaces of such lipid vesicles to help the vesicles bind to specific sites in the body.
- In this way we can create targeted delivery systems to deliver drugs or chemicals to a specific location in the body (for example, to the site of a tumor).
- By understanding the physics of lipid conformational transitions, we can control these conformational transitions, and thus control the ability of the lipid vesicles to contain the drug or chemical inside them.
- Once the drug-filled lipid vesicles are in the bloodstream, we can apply a stimulus like heat or mild radiation to a specific part of the body to cause the lipid vesicles to release the drugs at that place.

DNA and Nucleic Acid Biophysics

- DNA (deoxyribonucleic acid) is the biochemical that makes up our genes and controls our physical heredity. A closely related nucleic acid is RNA (ribonucleic acid), which serves many purposes within the cell.
- DNA biophysics includes studying:
  - Conformational transitions in DNA, including winding, unwinding, bending, stretching, and supercoiling
  - Binding of proteins, RNA, and other molecules to DNA
  - Energy changes associated with conformational transitions and binding and their effect on function



Protein Biophysics

- Proteins are involved in nearly every biological process within the cell. Examples include catalyzing biochemical reactions, regulating biochemical processes, and transporting molecules across cell membranes, from cell to cell and from one part of a cell to another. Proteins are also involved in cell motility.

Protein Biophysics (Continued)

- In order to carry out these functions, proteins typically must fold into very specific shapes, bind with other molecules, or undergo one or more conformational transitions.
- Understanding the physics of protein folding, conformational transitions, and binding is important for understanding and possibly controlling their role in biological processes.

Bioenergetics

- This branch of biophysics studies the physics of energy flow in living systems.
- At the core of bioenergetics is the study of how organisms and cells obtain the energy they need to carry out biological processes. This includes where the energy comes from, how the energy is stored, how the energy is converted into various forms, and where and how excess or unusable energy is released.

Thermodynamics

- The laws of thermodynamics describe how energy behaves in physical systems, biological or otherwise.
- The first law of thermodynamics states that energy cannot be created or destroyed.
- The second law of thermodynamics states that in a closed system the orderliness of the system can never increase, but can only decrease over time.
- Living things are so complex and highly organized and they have the ability to stay organized, So it would appear that living things may somehow violate the laws of thermodynamics, but living things are not closed systems. They interact with their environment.

Molecular Machines

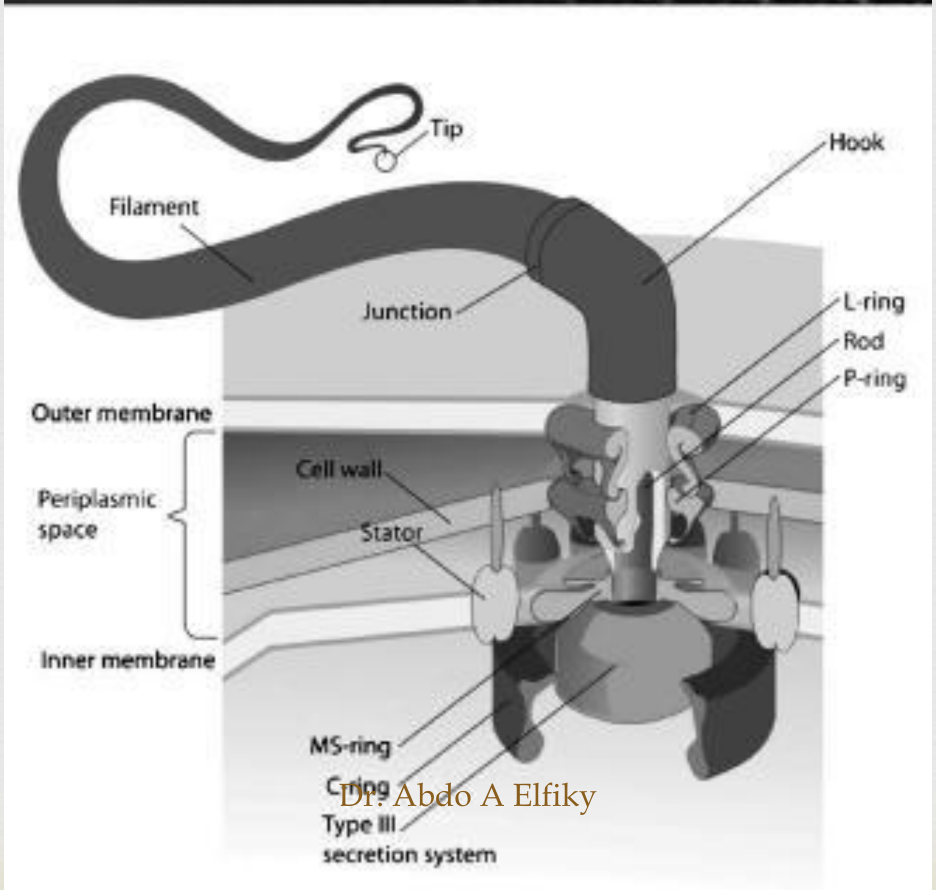
- A machine is a device that can alter the direction and/or size of a force (for example, a pulley, a lever, or an inclined plane).
- A motor is a special type of machine that also has the ability to convert potential energy into mechanical energy, that is, into a mechanical force or motion.
- The difference between an ordinary machine and a motor is that, in the case of a motor, the force being changed does not come from outside the machine, but is generated by the machine (the motor) itself. The motor can continue to generate mechanical force as long as it has a source of potential energy or fuel needed to do so.

Molecular Machines (Continued)

- Living things are full of machines and motors. For example, our muscles use our bones as levers to redirect and in some cases magnify or decrease the forces they apply. Muscles themselves are motors; muscle fibers have the ability to convert chemical potential energy from the food we eat into the mechanical force of muscle contraction.
- Cilia: These are hairlike projections on the surface of some cells that move, allowing the cell to swim. Or in the case of cells that don't swim but have cilia, the motion of cilia can be used to push substances past the cells. For example, cilia on the inner surface cells of the lungs help clean the lungs by moving dust and other particles up and out of the lungs.

Molecular Machines (Continued)

- Flagella: These are longer, whiplike structures that stick out from the body of some cells and move to propel the cell forward.
- Pseudopodia: Some cells move by temporarily pushing out on their membrane at one or more locations, changing the shape of the cell and causing the cell to crawl along.
- Secretions: Cells that manufacture proteins or other substances to be used elsewhere in the body (for example, pancreatic cells that manufacture insulin) must somehow move the manufactured molecules from inside each of the cells where they are made, to the cell's surface, and through the cell membrane into the bloodstream.


Tip
Hook
Filament
Junction
L-ring
Rod
P-ring
Outer membrane
Periplasmic space
Cell wall
Stator
Inner membrane
MS-ring
Type III secretion system

Molecular Machines (Continued)

- Separation of chromosomes (DNA) during cell division: When a cell is getting ready to divide, it first duplicates its chromosomes. The cell then has to somehow move and separate the two copies of the chromosomes off to two opposite sides of the cell so that the two daughter cells each get a single copy of the cell's DNA.
- In all cases where organisms generate motion, the source of that motion always comes from individual molecules acting as motors and machines in order to generate and direct forces. For example, the motion generated by muscle contraction, at the lowest level, results from individual molecules of one protein (myosin) binding to and pushing against the molecules of another protein (actin).

Quiz (p.33)

- Questions:

  1 to 5