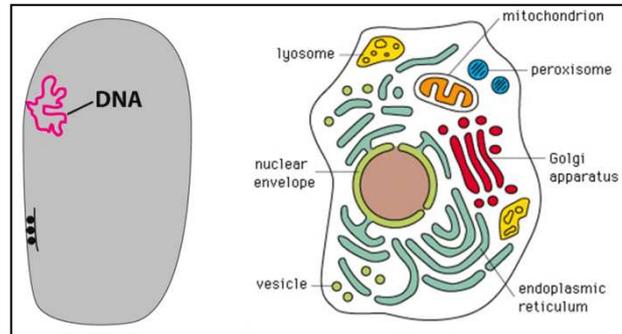


1st lecture: **CELLS: STRUCTURE AND FUNCTIONS**

According to the Cell Theory, all living things are composed of one or more cells. Cells fall into prokaryotic and eukaryotic types. Prokaryotic cells are smaller (as a general rule) and lack much of the internal compartmentalization and complexity of eukaryotic cells. No matter which type of cell we are considering, all cells have certain features in common: DNA, cell membrane, cytoplasm, and ribosomes.

**Cell Size and Shape**

The shapes of cells are quite varied with some, such as neurons, being longer than they are wide and others, such as parenchyma (a common type of plant cell) and erythrocytes (red blood cells) being equidimensional. Some cells are encased in a rigid wall, which constrains their shape, while others have a flexible cell membrane (and no rigid cell wall).

The size of cells is also related to their functions. Eggs (or to use the latin word, ova) are very large, often being the largest cells an organism produces. The large size of many eggs is related to the process of development that occurs after the egg is fertilized, when the contents of the egg (now termed a zygote) are used in a rapid series of cellular divisions, each requiring tremendous amounts of energy that is available in the zygote cells. Later in life the energy must be acquired, but at first a sort of inheritance/trust fund of energy is used.

DNA

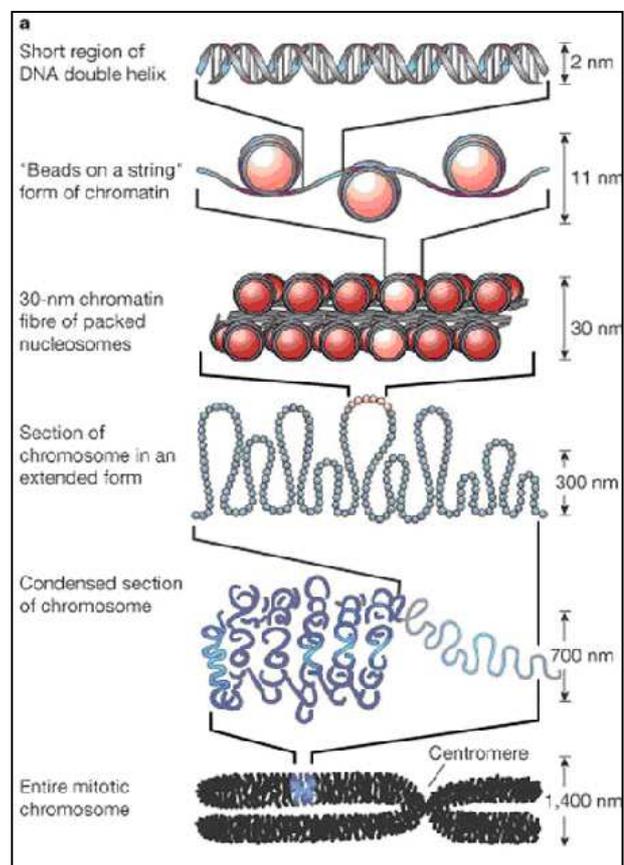
Most bacterial chromosomes contain a circular DNA molecule - there are no free ends to the DNA. Free ends would otherwise create significant challenges to cells with respect to DNA replication and stability.

In eukaryotes the DNA forms linear chromosomes with complex quaternary structure.

Primary structure consists of a linear sequence of nucleotides that are linked together by phosphodiester bonds.

The secondary structure is the set of interactions between bases, i.e., parts of which is strands are bound to each other. In DNA double helix, the two strands of DNA are held together by hydrogen bonds.

The quaternary structure of nucleic acids refers to interactions of the nucleic acids with other molecules. The most commonly seen form is seen in the form of chromatin which leads to its interactions with the small proteins histones.

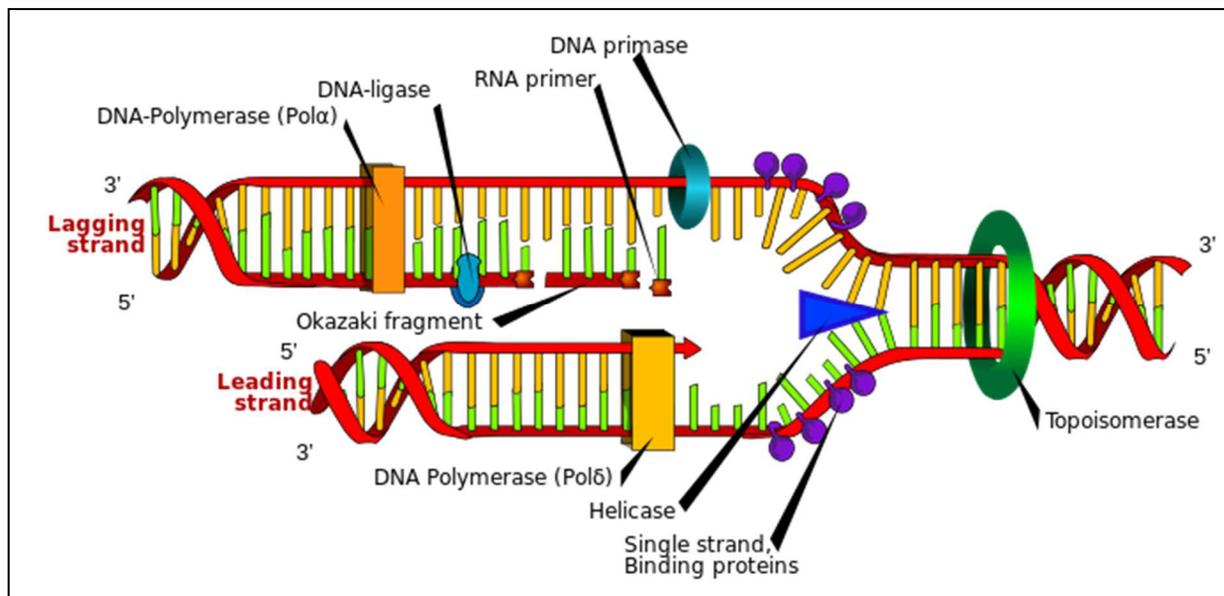


Functions and operation of DNA

- Transcription from DNA to DNA (replication)
- Transcription from DNA to mRNA: the first step of protein biosynthesis (transcription)
- Transcription from DNA to other RNA (ribosomal RNA, transfer RNA) base sequence of these is stored here, their synthesis is direct transcription.

DNA replication is the process of producing two identical copies from one original DNA molecule. This biological process occurs in all living organisms and is the basis for biological inheritance. DNA is composed of two strands and each strand of the original DNA molecule serves as template for the production of the complementary strand, a process referred to as semiconservative replication.

Scheme of the replication fork:



Many enzymes are involved in the DNA replication fork.

The replication fork is a structure that forms during DNA replication. It is created by helicases, which break the hydrogen bonds holding the two DNA strands together. The resulting structure has two branching "prongs", each one made up of a single strand of DNA. These two strands serve as the template for the leading and lagging strands, which will be created as DNA polymerase matches complementary nucleotides to the templates; the templates may be properly referred to as the leading strand template and the lagging strand templates.

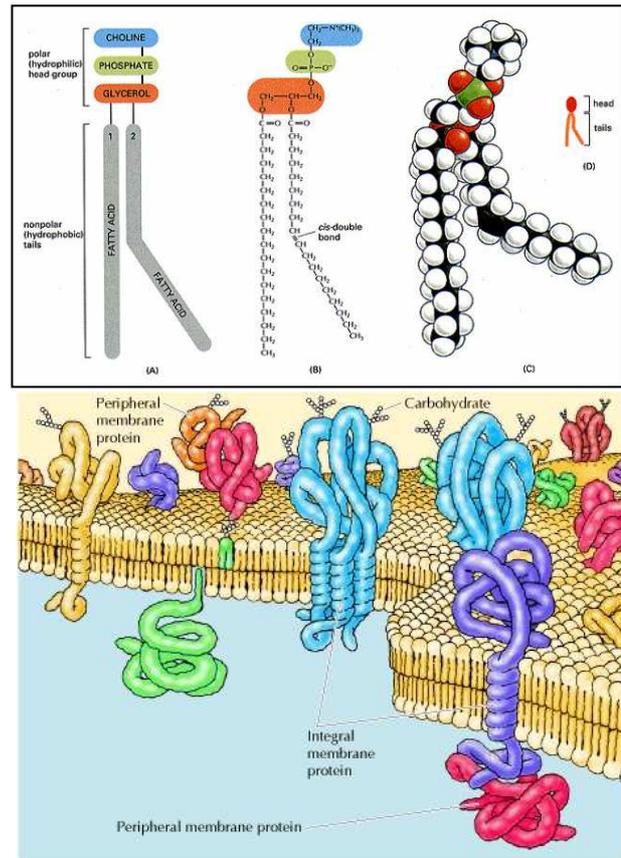
DNA is always synthesized in the 5' to 3' direction. Since the leading and lagging strand templates are oriented in opposite directions at the replication fork, a major issue is how to achieve synthesis of nascent (new) lagging strand DNA, whose direction of synthesis is opposite to the direction of the growing replication fork.

The *leading strand* is the strand of nascent DNA which is being synthesized in the same direction as the growing replication fork. A polymerase "reads" the leading strand *template* and adds complementary nucleotides to the nascent leading strand on a continuous basis.

The *lagging strand* is the strand of nascent DNA whose direction of synthesis is opposite to the direction of the growing replication fork. Because of its orientation, replication of the lagging strand is more complicated than that of the leading strand. The lagging strand is synthesized in short, separated segments. A DNA polymerase extends the segments, forming Okazaki fragments. The fragments of DNA are joined together by DNA ligase.

The Cell Membrane

The cell membrane functions as a semi-permeable barrier, allowing a very few molecules across it while fencing the majority of organically produced chemicals inside the cell. Electron microscopic examinations of cell membranes have led to the development of the lipid bilayer model (also referred to as the fluid-mosaic model). The most common molecule in the model is the phospholipid, which has a polar (hydrophilic) head and two nonpolar (hydrophobic) tails. These phospholipids are aligned tail to tail so the nonpolar areas form a hydrophobic region between the hydrophilic heads on the inner and outer surfaces of the membrane. This layering is termed a bilayer since an electron microscopic technique known as freeze-fracturing is able to split the bilayer. Cholesterol is another important component of cell membranes embedded in the hydrophobic areas of the inner (tail-tail) region. Most bacterial cell membranes do not contain cholesterol. Proteins are suspended in the inner layer, although the more hydrophilic areas of these proteins "stick out" into the cells interior and outside of the cell. These proteins function as gateways that will, in exchange for a price, allow certain molecules to cross into and out of the cell. These integral proteins are sometimes known as gateway proteins. The outer surface of the membrane will tend to be rich in glycolipids, which have their hydrophobic tails embedded in the hydrophobic region of the membrane and their heads exposed outside the cell. These, along with carbohydrates attached to the integral proteins, are thought to function in the recognition of self.



The functions of membranes

Separate and connect the two spaces.

- Diffusion barrier – osmotic barrier
- Selective transports:

Passive transport is a movement of biochemicals and other atomic or molecular substances across membranes. Unlike active transport, it does not require an input of chemical energy, being driven by the growth of entropy of the system. The rate of passive transport depends on the (semi-)permeability of the cell membrane, which, in turn, depends on the organization and characteristics of the membrane lipids and proteins. The four main kinds of passive transport are diffusion, facilitated diffusion, filtration and osmosis.

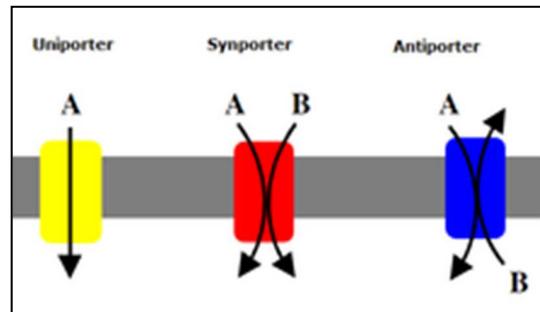
Active transport is the movement of all types of molecules across a cell membrane against its concentration gradient (from low to high concentration). In all cells, this is usually concerned with accumulating high concentrations of molecules that the cell needs, such as ions, glucose and amino acids. The process uses chemical energy, such as from ATP. Active transport uses

cellular energy, unlike passive transport, which does not use cellular energy. Examples of active transport include the uptake of glucose in the intestines in humans.

Symport and antiport

Symport uses the downhill movement of one solute species from high to low concentration to move another molecule uphill from low concentration to high concentration (against its electrochemical gradient).

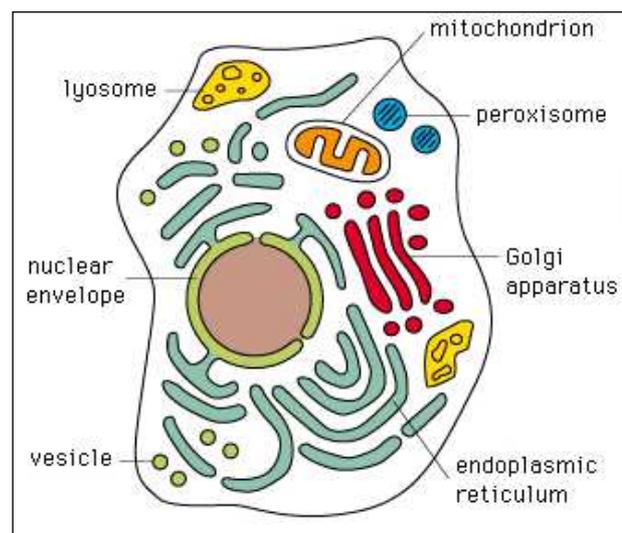
An example is the glucose symporter SGLT1, which co-transporters one glucose (or galactose) molecule into the cell for every two sodium ions it imports into the cell. This symporter is located in the small intestines, trachea, heart, brain, testis, prostate and in the proximal tubule in each nephron in the kidneys.



In an **antiport** two species of ion or other solutes are pumped in opposite directions across a membrane. One of these species is allowed to flow from high to low concentration which yields the entropic energy to drive the transport of the other solute from a low concentration region to a high one.

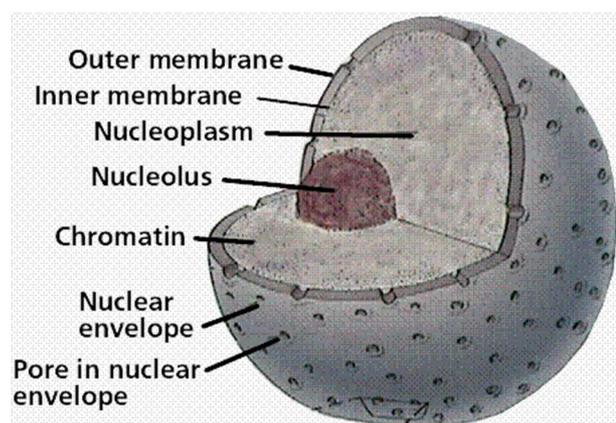
Biological membranes in cells

- Cytoplasmic/cell membrane
- Nuclear membrane
- Other membranes:
 - Mitochondrion
 - Endoplasmic reticulum
 - Golgi complex
 - Chloroplast
 - Vesicles
 - Special (retina, neuron)

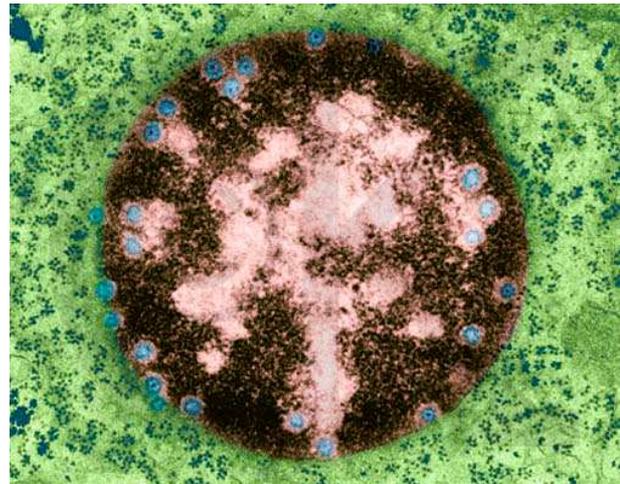


The nucleus

The nucleus occurs only in eukaryotic cells, and is the location of the majority of different types of nucleic acids. Deoxyribonucleic acid, DNA, is the physical carrier of inheritance and with the exception of plastid DNA (cpDNA and mDNA, see below) all DNA is restricted to the nucleus. Ribonucleic acid, RNA, is formed in the nucleus by coding off of the DNA bases. RNA moves out into the cytoplasm.



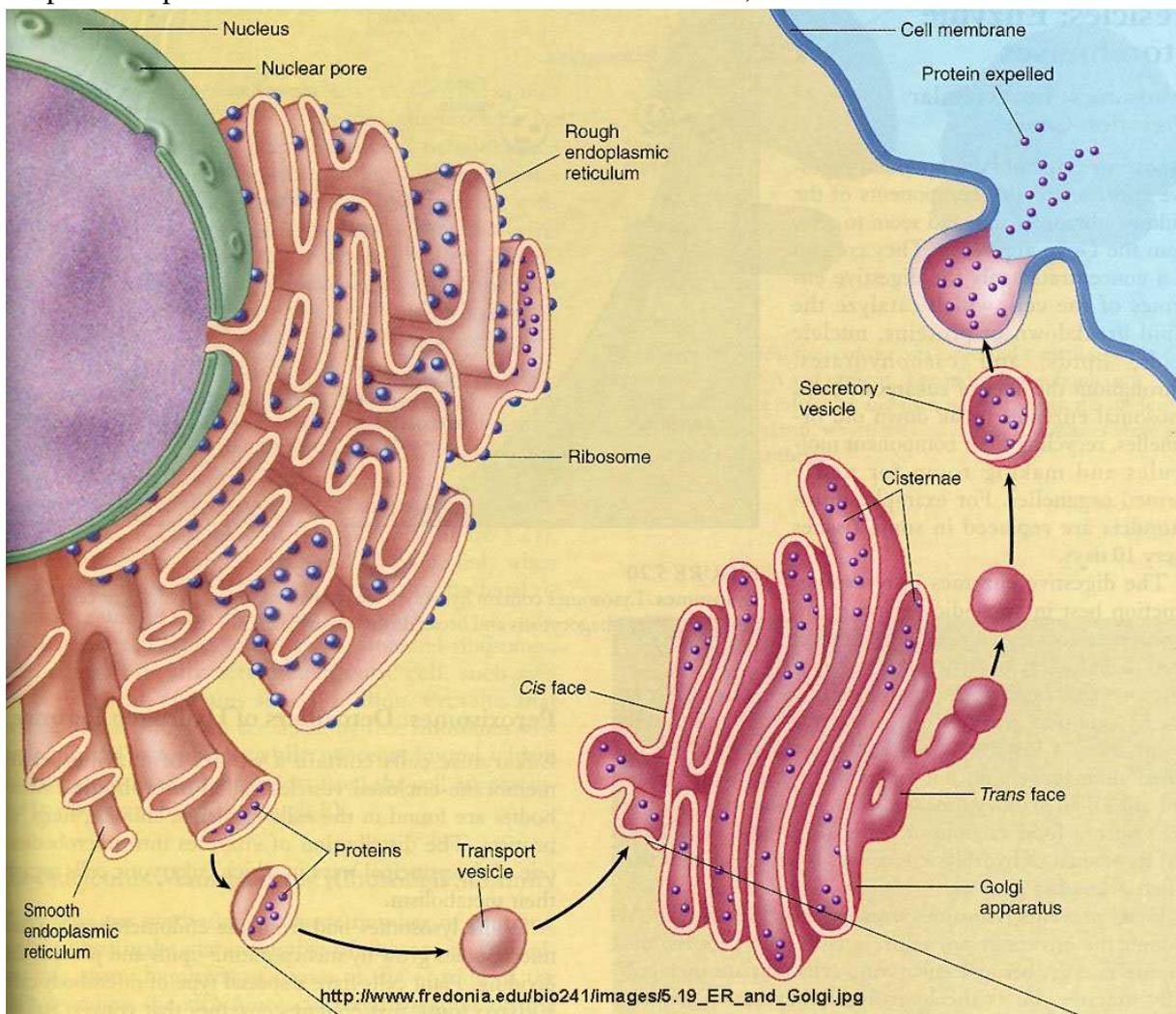
The nucleolus is an area of the nucleus (usually 2 nucleoli per nucleus) where ribosomes are constructed. Note the chromatin, uncoiled DNA that occupies the space within the nuclear envelope.



The nuclear envelope is a double-membrane structure. Numerous pores occur in the envelope, allowing RNA and other chemicals to pass, but the DNA not to pass. Structure of the nuclear envelope and nuclear pores.

Endoplasmic reticulum and Golgi Apparatus

Endoplasmic reticulum is a mesh of interconnected membrane sacks that serve a function involving protein synthesis and transport. Rough endoplasmic reticulum (Rough ER) is so-named because of its rough appearance due to the numerous ribosomes that occur along the ER. Rough ER connects to the nuclear envelope through which the messenger RNA (mRNA) that is the blueprint for proteins travels to the ribosomes. Smooth ER; lacks the ribosomes characteristic

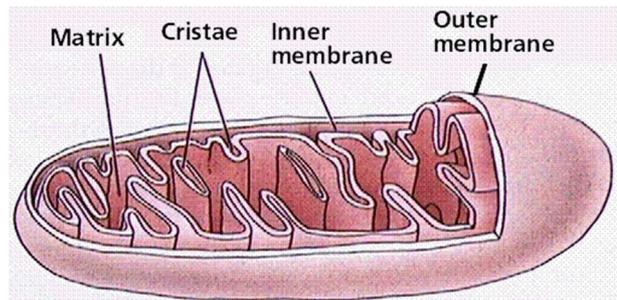


of Rough ER and is thought to be involved in transport and a variety of other functions. Inside the lumen the glycosylation of newly formed protein molecules is going on. Golgi Complexes are flattened stacks of membrane-bound sacs. They function as a modifying and packaging of proteins.

Proteins are moving in transport vesicles from the Rough ER to Golgi and out from Golgi. Another role of the Golgi is to form different vesicles like lysosomes, peroxysomes and storing vesicles.

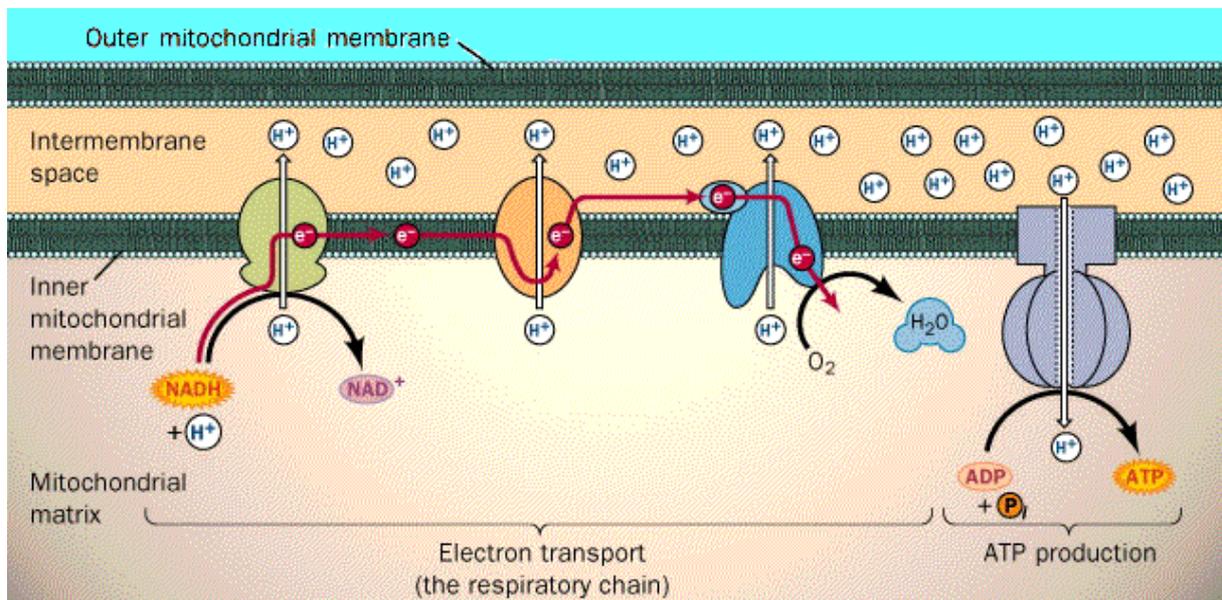
Mitochondria

Mitochondria contain their own DNA (termed mDNA) and are thought to represent bacteria-like organisms incorporated into eukaryotic cells over 700 million years ago (perhaps even as far back as 1.5 billion years ago). They function as the sites of energy release (following glycolysis in the cytoplasm) and ATP formation (by chemiosmosis). The mitochondrion has been termed the powerhouse of the cell. Mitochondria are bounded by two membranes. The inner membrane folds into a series of cristae, which are the surfaces on which ATP is generated.



- Elongated particles, observable with microscope
- Number: ~10 – 1000 /cell

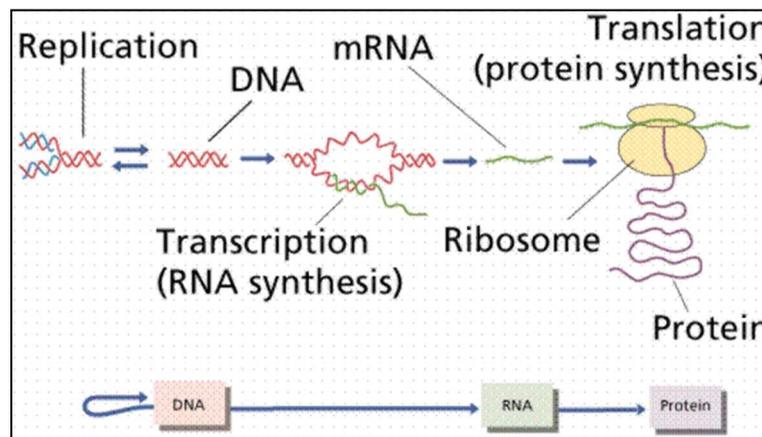
Terminal oxidation: the substrate hydrogens arrive in the form of NADH or FADH. These are oxidized in multiple phases, at last with oxygen. H⁺ ions accumulate in the intermembrane space. This Δc is converted to ATP.



Protein biosynthesis

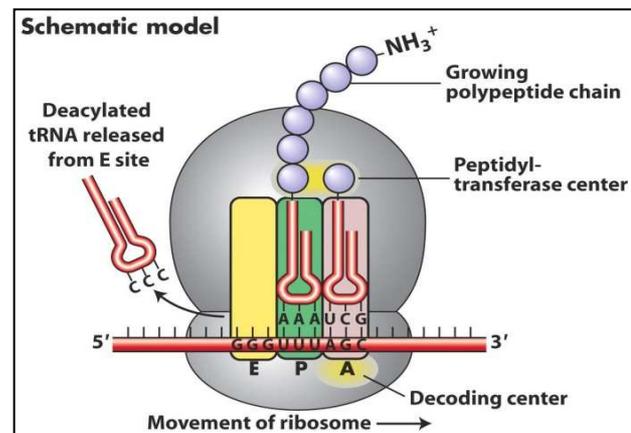
The genetic information (the amino acid sequence of proteins) is stored in DNA. The information flow has two steps:

1. Transcription: is the making of a messenger RNA molecule off a DNA template according to the base pairing rules.
2. Translation: is the construction of an amino acid sequence (polypeptide) from a mRNA molecule.



Ribosomes

Ribosomes are the organelles (in all cells) where proteins are synthesized. They occur in both prokaryotes and eukaryotes. Eukaryotic ribosomes are slightly larger than prokaryotic ones. Structurally the ribosome consists of a small and larger subunit. Biochemically the ribosome consists of ribosomal RNA (rRNA, about two-thirds of all mass) and some 50 structural proteins. The smaller subunit has a binding site for the mRNA. The larger subunit has three binding sites for tRNA.



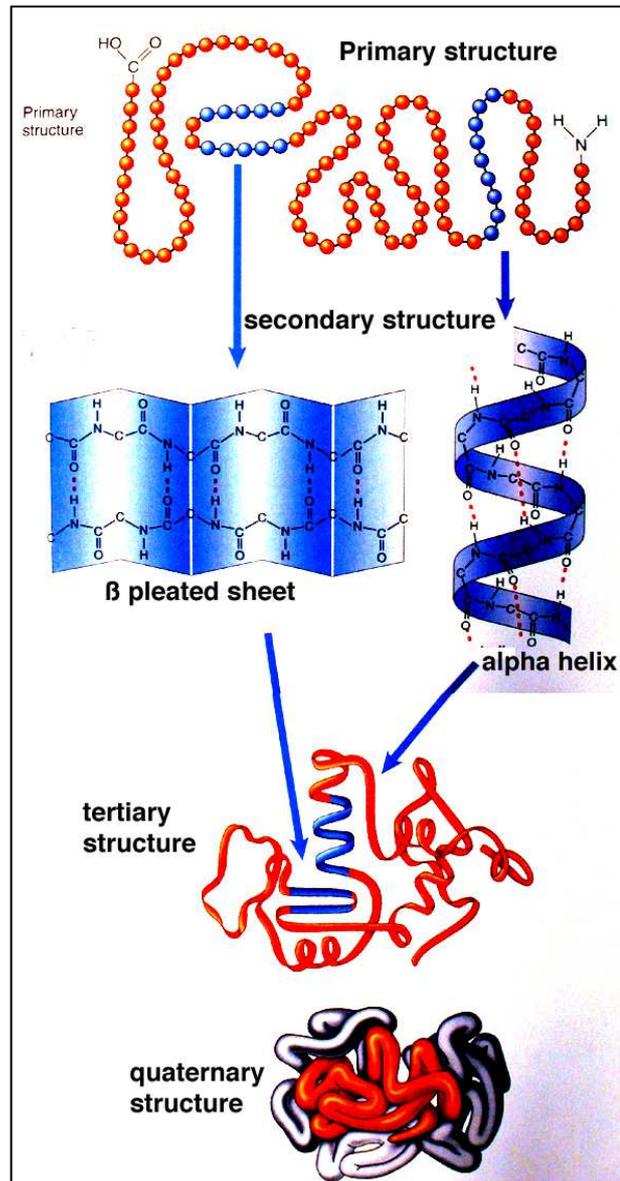
Structure of protein molecules

The **primary structure** of proteins results from linking together various combinations of these 20 amino acids with peptide bonds, which link the carboxyl group of one amino acid to the amino group of another amino acid. Proteins are sometimes referred to as polypeptides because they consist of chains of amino acids. The chains can be just a few amino acids long, or they can consist of chains of a thousand of amino acids or more.

Proteins are more than just strings of amino acids, however. There are attractive and repulsive forces among the amino acids in the chain that determine the **secondary structure** of the protein. For example, the hydrogen on the amino group of one amino acid can form a weak "*hydrogen bond*" to the oxygen atom in the carboxyl group of another amino acid elsewhere on

the chain. Hydrogen bonding can cause portions of the polypeptide chain to form zig-zag sections called "*beta sheets*" (which are very prominent in the protein fiber in silk, for example), and it can also cause sections of the polypeptide to twist into a cork screw-shaped structure called an "*alpha helix*." Other sections of a polypeptide may be referred to as "random coils" because they fold but do not have a regular structural shape.

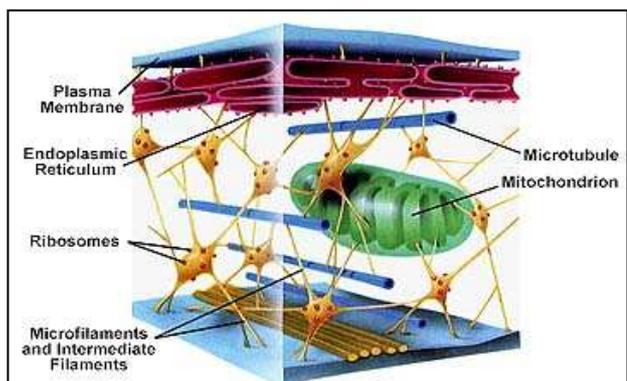
Proteins also have a **tertiary level of structure** as a result of ionic, hydrogen, or covalent bonds between the "-R" groups of the amino acids. As a result, alpha helical segments, beta pleated sheets, and random coils fold upon themselves. Folding and placement in a cell will also be influenced by the polarity of the amino acids. Some amino acids have side chains that are polar and others have non-polar side chains. If some sections of the chain contain mostly non-polar amino acids, while other sections contain mostly polar amino acids, the non-polar sections will self-associate in the interior of the molecule away from water, and the polar sections will be arrayed on the exterior of the molecule.



Finally, **quaternary structure** refers to the association of two or more polypeptide chains or subunits into a larger entity. For example, the hemoglobin molecule (shown in the bottom) consists of two alpha subunits and two beta subunits; each of these four polypeptide chains has a binding site for oxygen. Transport proteins in cell membranes frequently consist of multiple subunits as well.

Cytoplasm

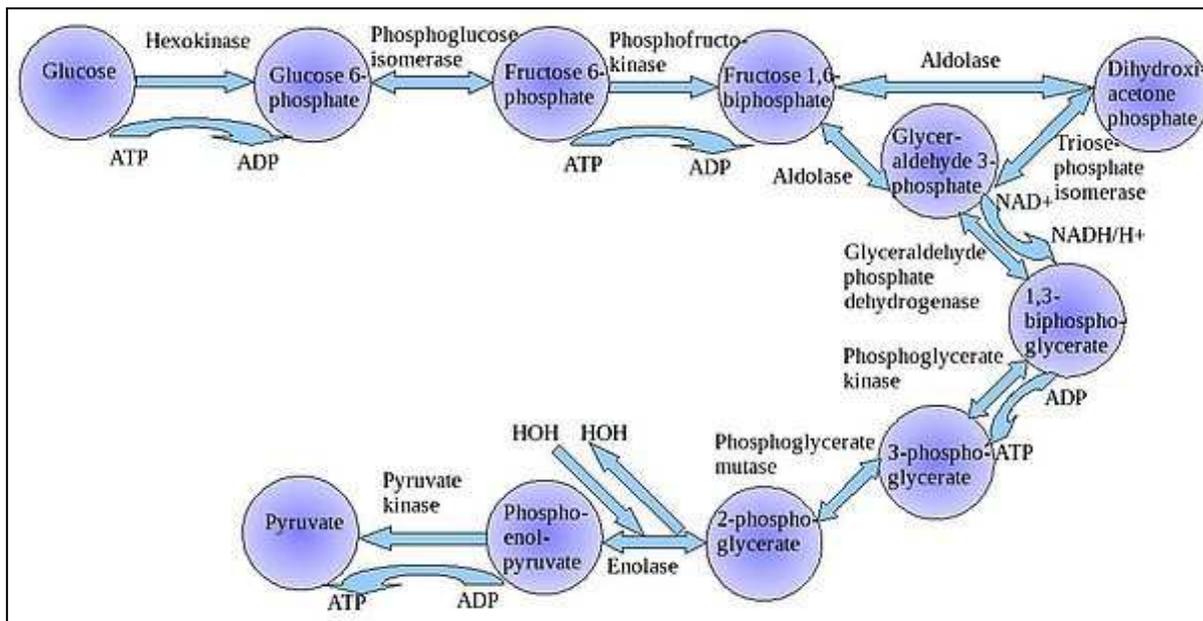
The cytoplasm was defined earlier as the material between the plasma membrane (cell membrane) and the nuclear envelope. Fibrous proteins that occur in the cytoplasm, referred to as the **cytoskeleton** maintain the shape of the cell as well as anchoring organelles, moving the cell and controlling internal movement of structures. Microtubules function in cell division and serve as a "temporary scaf-



folding" for other organelles. Actin filaments are thin threads that function in cell division and cell motility. Intermediate filaments are between the size of the microtubules and the actin filaments. It is not a simple liquid, it has an inner structure, slightly elastic and deformable like *gels*.

(Gels: some macromolecules in solutions – like proteins or carbohydrates – form a crosslinked structure holding the liquid in form. This shows a quasi solid properties – like jelly or jam.)

Glycolysis occurs in the cytosol of the cell. It converts glucose $C_6H_{12}O_6$, into pyruvate, $CH_3COCOO^- + H^+$. The free energy released in this process is used to form the high-energy compounds, ATP and NADH.



Glycolysis is a purely anaerobic reaction. Glycolysis is a determined sequence of ten reactions involving ten intermediate compounds (one of the steps involves two intermediates). The intermediates provide entry points to glycolysis. For example, most monosaccharides, such as fructose, glucose, and galactose, can be converted to one of these intermediates. It occurs, with variations, in nearly all organisms, both aerobic and anaerobic.

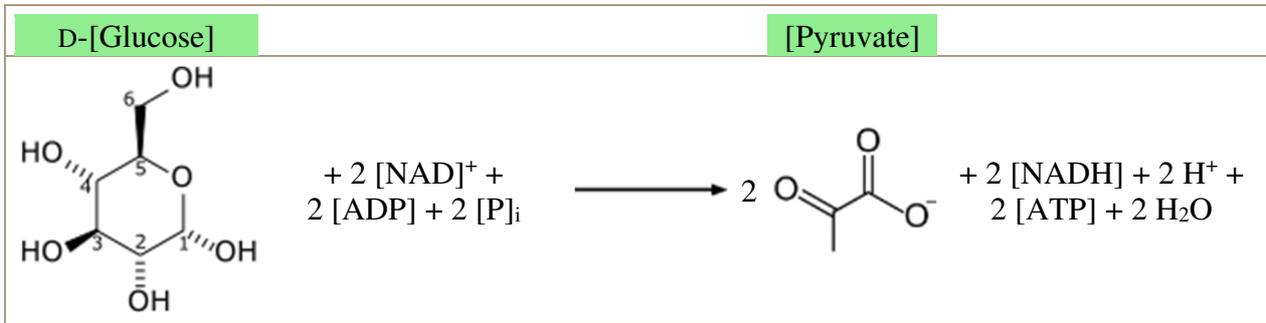
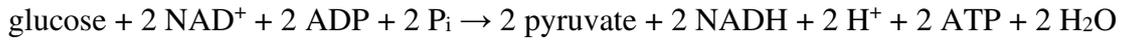
The entire glycolysis pathway can be separated into two phases:

1. The Preparatory Phase – in which ATP is consumed and is hence also known as the investment phase
2. The Pay Off Phase – in which ATP is produced.

For simple fermentations, the metabolism of one molecule of glucose to two molecules of pyruvate has a net yield of two molecules of ATP. Most cells will then carry out further reactions to 'repay' the used NAD⁺ and produce a final product of ethanol or lactic acid.

Cells performing aerobic respiration synthesize much more ATP, but not as part of glycolysis. These further aerobic reactions use pyruvate and NADH + H⁺ from glycolysis. Eukaryotic aerobic respiration produces approximately 34 additional molecules of ATP for each glucose molecule, however most of these are produced by a vastly different mechanism to the substrate-level phosphorylation in glycolysis.

The overall reaction of glycolysis is:

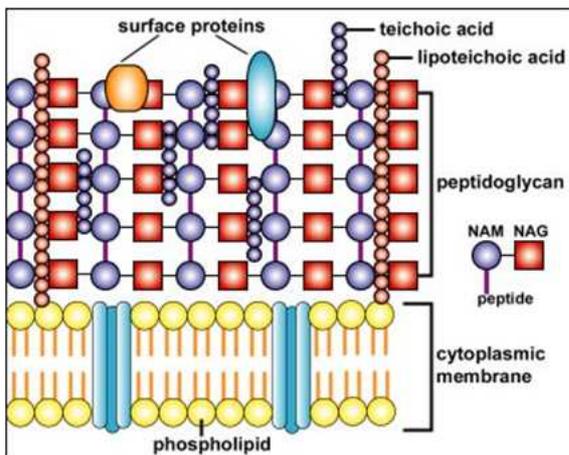


The lower-energy production, per glucose, of anaerobic respiration relative to aerobic respiration, results in greater flux through the pathway under hypoxic (low-oxygen) conditions.

The Cell Wall

Not all living things have cell walls, most notably animals and many of the more animal-like Protists. Bacteria have cell walls containing peptidoglycan. Plant cells have a variety of chemicals incorporated in their cell walls. Cellulose is the most common chemical in the plant primary cell wall. Some plant cells also have lignin and other chemicals embedded in their secondary walls. The cell wall is located outside the plasma membrane. Plasmodesmata are connections through which cells communicate chemically with each other through their thick walls. Fungi and many protists have cell walls although they do not contain cellulose, rather a variety of chemicals (chitin for fungi).

Gram positive



and negative cell wall:

