

1 | Biology

Biology is the science of life, living organisms and their behaviour.

Living organisms are different from inanimate matter in the ability to breed and create other organisms having the same basic characteristics controlled by a genetic program. The functional basic unit of every living organisms is the cell, which consists of a protoplasm enclosed by a plasma membrane.

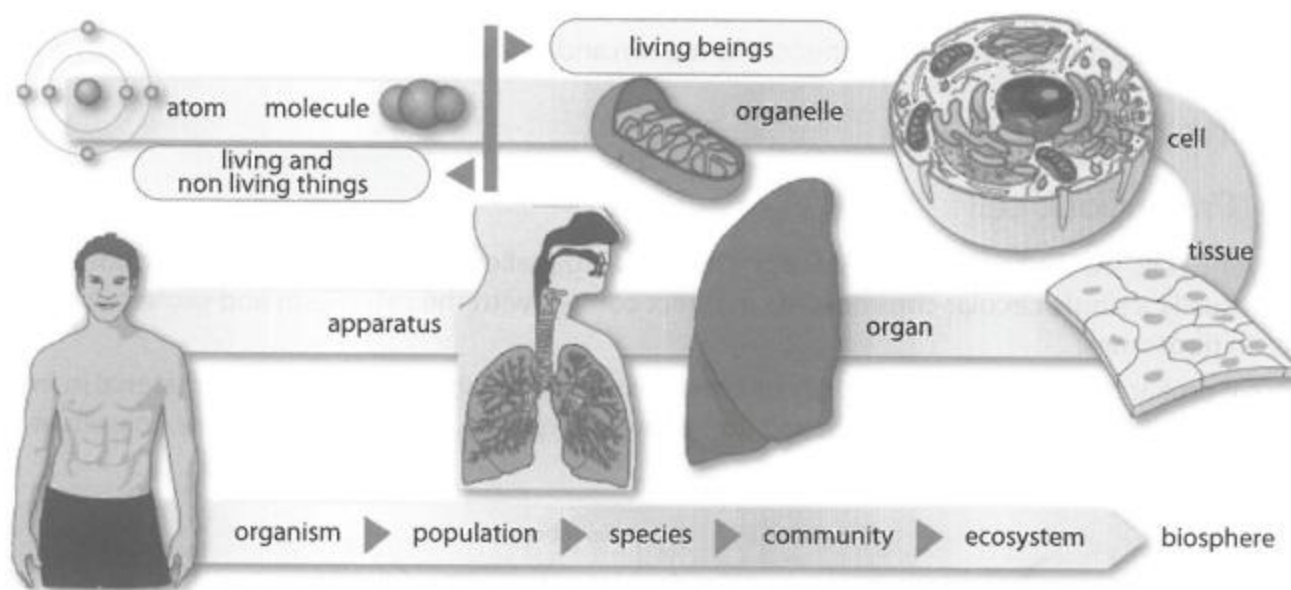
Depending on the presence of a nucleus and organelles, cells can be classified in prokaryotic or eukaryotic.

While unicellular organisms consist of a single cell, multicellular contain a huge number of cells, usually organized in specialized tissues (groups of similar cells) and organs (ordered structure of many different tissues) to carry out specific functions.

The cell is the basic structural and physiological unit of all known living organisms as it can replicate independently. Every single cell contains all the information needed to self-regulate its functions and to transmit such information to the next generation of cells.

All known types of organisms are capable of growth and development, reproduction, response to stimuli, and regulation of their own metabolism. They carry genetic information that can be inherited by the offspring. Populations of living organisms undergo evolution over time.

A key-feature of being alive is the conservation of an organized state, a task that costs energy.



1.1 | Bioelements

The four most important chemical elements for quantity are carbon, nitrogen, oxygen and hydrogen.

Others essential elements like phosphorus, calcium, chlorine, potassium, sodium, magnesium, iodine and iron are present at low concentration.

The most relevant compounds from a biological standpoint are the so-called “biomolecules”: carbohydrates, proteins, lipids and nucleic acids.

1.1.1 | Carbohydrates

Carbohydrates are ternary compounds containing carbon, oxygen and hydrogen. According to their molecular structure they can be classified as monosaccharides, disaccharides and polysaccharides.

Monosaccharides are the principal source of energy for the cell; the most important is glucose, used as input for glycolysis and cellular respiration pathways.

Polysaccharides can be a way to store energy, as starch in plants and glycogen in animals, or provide structural support as cellulose and chitin.

1.1.2 | Proteins

Proteins consist of linear polymers of L- α -amino acids linked by peptide bonds.

They accomplish a wide range of functions, including mechanical support and catalysis of metabolic reactions.

Four different aspects of protein structure are usually taken into account: the primary structure, which is defined by the amino acid sequence, the secondary consisting of their arrangement in space, the tertiary structure which is the three-dimensional shape of a whole protein molecule, and the quaternary structure resulting from the docking of several protein subunits.

Among the 20 most common amino acids, 9 are called “essential” because they cannot be synthesized by the organism and must be supplied with the diet.

1.1.3 | Lipids

Lipids can be defined as hydrophobic small molecules. The most common are triglycerides and phospholipids, used for energy storage and as structural components of cell membranes, respectively.

Sterols (steroid alcohols) are another important class of lipids, which include hormones like estrogens and corticosteroids.

1.1.4 | Nucleotides and nucleic acids

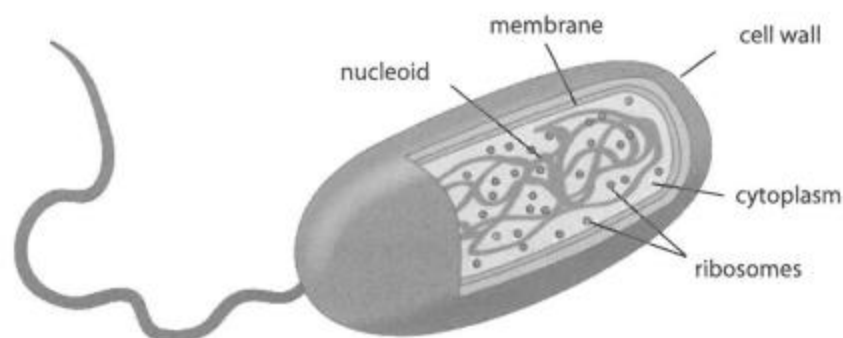
The nucleic acids DNA (deoxyribonucleic acid) and RNA (ribonucleic acid) are linear polymers of nucleotides. They are the physical carrier of genetic information and take part in its transmission and expression.

1.2 | The cell

1.2.1 | Prokaryotic cell

Prokaryotic cells are the simplest kind of cells. They lack organelles like nucleus and mitochondria. Their DNA is usually a single circular chromosome in direct contact with the cytoplasm and protein synthesis occurs in ribosomes.

Although prokaryotes reproduce asexually by binary fission, they can exchange genetic material in many ways, like transformation, transduction, and conjugation. Typically, prokaryotic cells are unicellular organisms.



1.2.2 | Eukaryotic cell

Eukaryotic cells possess a nucleus separated from the rest of the cell by a double layer nuclear membrane with pores to allow the exchange of molecules with the cytoplasm. Within the nucleus, the genetic material is organized in rod-shaped chromosomes. In addition, eukaryotic cells contain organelles and a variety of internal membranes and structures.

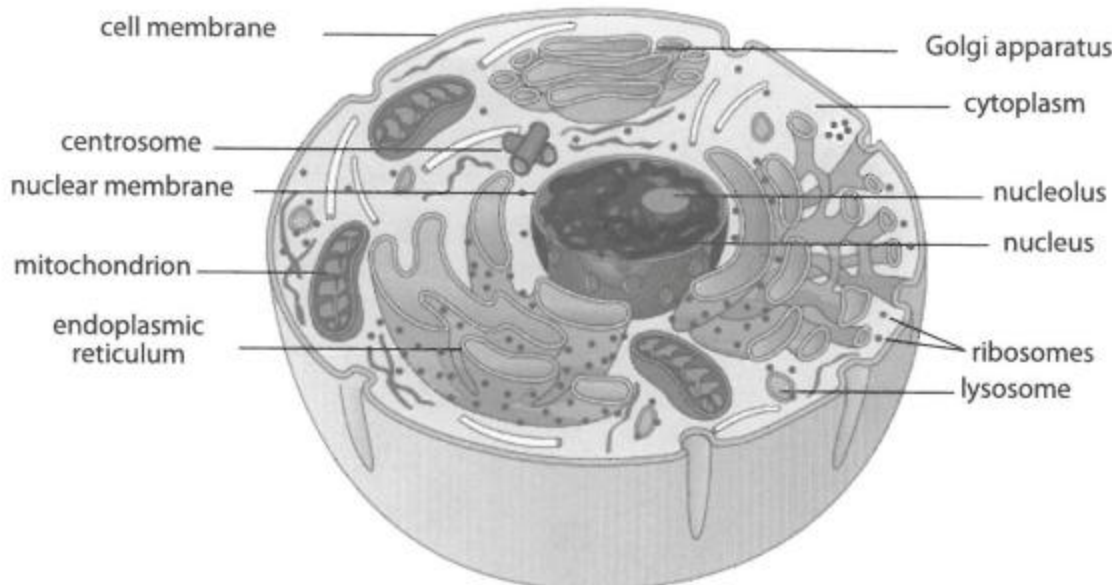
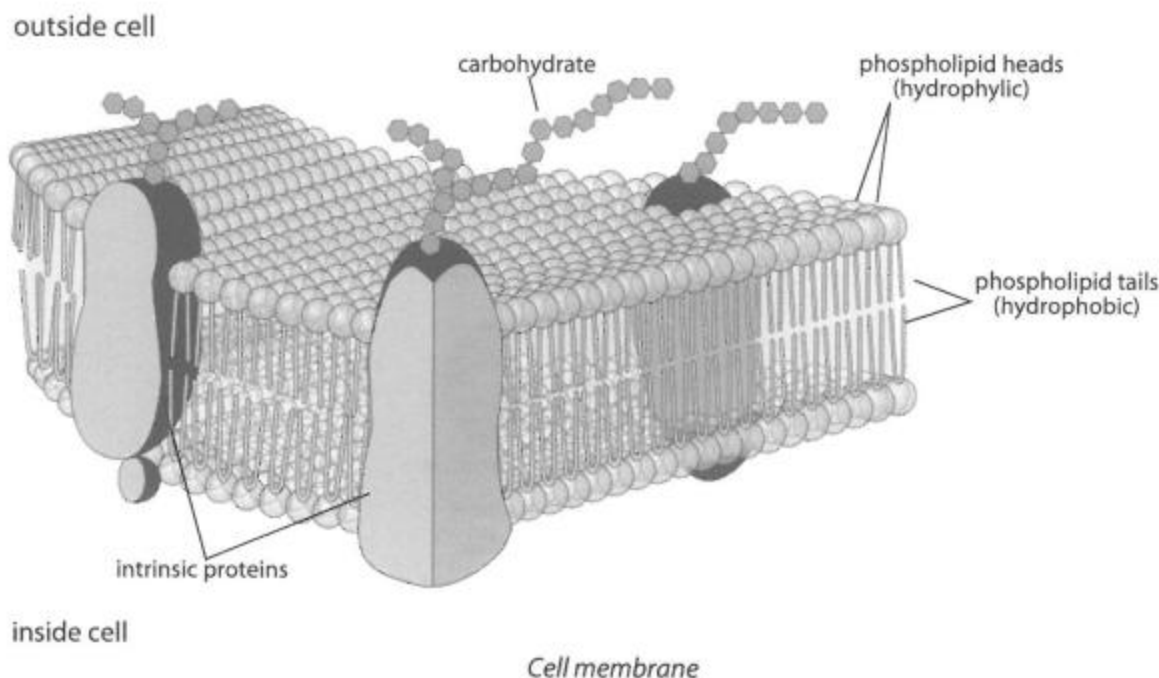


Figure depicts the structures of a typical eukaryotic animal cell

1.2.3 | Cell membrane

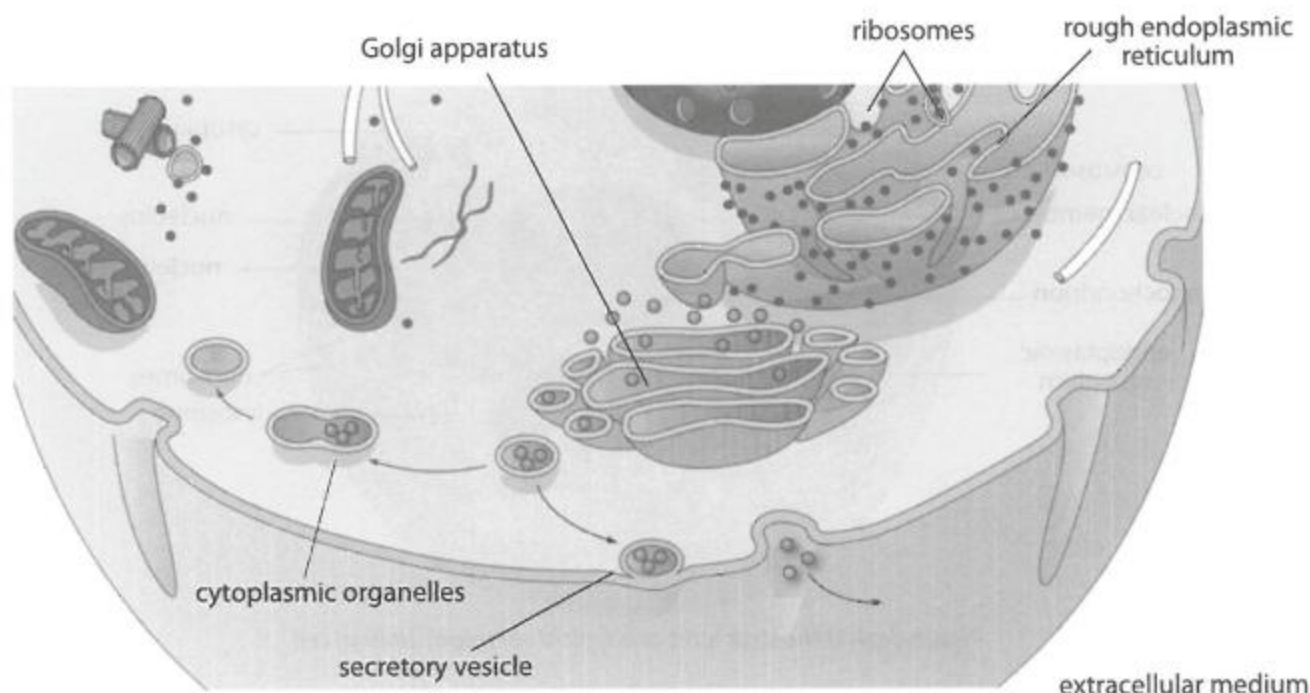
In order to keep the protoplasm separated from the extracellular environment the membrane, a phospholipid bilayer with proteins immersed in, surrounds cells.

The *phospholipid bilayer* consists of two layers of phospholipids. The hydrophobic tails of the two layers associate to form the inner part of the membrane, while the polar hydrophilic heads are in contact the fluid inside and outside of the cell. The cell membrane is selectively permeable and controls the passage of water, ions and organic molecules. It provides a support to the cell shape as well.



Ribosomes are the structures in which protein synthesis happens. They can be free or attached to the rough endoplasmic reticulum (ER), a network of tubular and flattened extensions of the nuclear membrane and is involved in protein transport. ER can be rough or smooth depending on the presence of ribosomes on its surface.

Golgi is the organelle composed of stacks of membrane-bound structures called cisternae. Its function is modifying, sorting and packaging proteins.

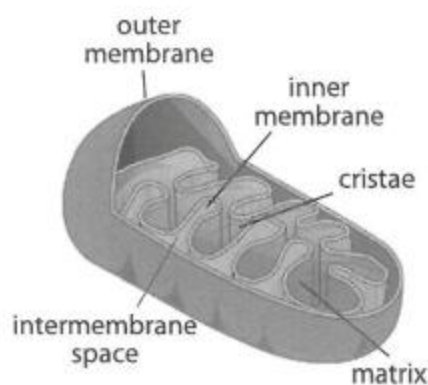


Proteins synthesized in the endoplasmic reticulum are modified and sorted in the Golgi apparatus

Lysosomes are vesicles containing a variety of hydrolytic enzymes in which macromolecules are digested thanks to an acidic environment.

Microsomes are small vesicles similar to lysosomes, carrying out different tasks; the most important are peroxisomes, where oxidation reactions take place.

Mitochondria are double membrane organelles possessing their own ribosomes and DNA. In mitochondria cellular respiration, a set of the metabolic reactions and processes, takes place. This biochemical pathway transforms organic substances and oxygen in CO_2 and H_2O , releasing the energy required for ATP synthesis. For this reason, they can be considered as the "energy factories" of a cell.



Structure of a mitochondrion

Cytoskeleton is a three-dimensional network of protein filaments of three different kinds: microfilaments, intermediate filament and microtubules. It provides mechanical support and helps the cell to maintain its shape. Cell division, chromosome movement and vesicles transport within the cell are controlled by the cytoskeleton.

1.2.4 | Exchange of materials between inside and outside of cells.

Molecules can cross the membrane in different ways. Passive transport happens according to the concentration gradient, namely the difference of concentration between inside and outside the cell. Molecules move from higher concentration zones to lower concentration zones without consuming energy. Active transport occurs against the concentrations gradient by using energy usually provided by ATP hydrolysis.

If the moving molecule is an ion, the distribution of charges on the two sides of the membrane has to be taken into account, since charged molecules move according to electrochemical gradient, the sum of chemical concentration and electric potential.

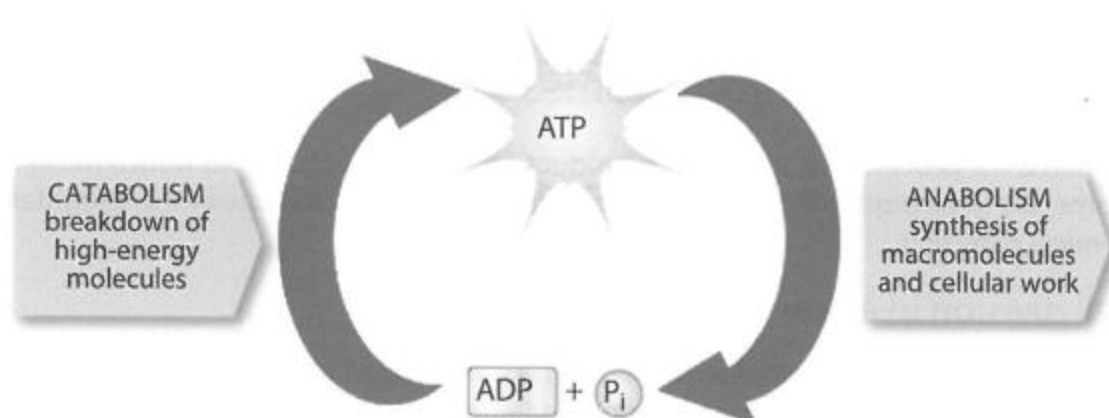
Normally, charges are unevenly distributed at the two sides of the membrane, producing an electric potential of about -70 mV called transmembrane potential.

The charge asymmetry is due to sodium (Na^+) and potassium (K^+) ions, which are 10-fold, more concentrated outside and 30-fold more concentrated inside, respectively.

A specific membrane protein called sodium-potassium pump or " Na^+/K^+ -ATPase", which uses the energy provided by ATP to transfer the two ions across the membrane, creates their concentration gradient.

1.2.5 | Cell metabolism

Metabolism is the term used to define all the chemical reactions taking place inside a cell. All the reactions that transform molecules in smaller components are called altogether "catabolism", while the synthetic reactions that produce cellular macromolecules are called "anabolism".



The molecule of adenosine triphosphate (ATP) is used as a carrier of energy or "energetic currency" to feed all the reactions requiring energy. It consists in three phosphate groups bound to a nucleotide, the adenosine.

The bond between the first and the second phosphate and between the second and the third one are "high-energy bounds": when they are broken down, a large amount of energy is released. ATP is produced by cellular respiration and fermentation.

Catabolism of glucose

In general, cells obtain energy from oxidation of organic substances. The main source of energy is glucose break down. The first step is *glycolysis*, a series of reactions producing pyruvate, CO_2 plus 2 molecules of ATP and two of NADH.

When oxygen is present the second step is *cellular respiration*, which further oxidizes pyruvate to CO_2 and H_2O . Cellular respiration can be outlined in three stages. First, the oxidative decarboxylation of pyruvate release a CO_2 molecule, an acetyl-CoA unit and reduce a molecule of NADH. Second, a group of cyclic reactions called Krebs cycle produces one ATP and reduces three NADH molecules and one of FADH_2 by releasing a CO_2 molecule. The NADH and FADH_2 reduced in the first two stages are used in the third stage, the oxidative phosphorylation.

In this last step, the electrons are transferred from NADH and FADH_2 through the *electron transport chains* to O_2 as a final acceptor with production of H_2O .

The electron transport chain is a group of integral membrane proteins that behave alternatively as *electron acceptors* or *electron donors*, gaining electrons from the former protein of the chain and donating conveying them to the following one. The net result is an electron flow along the transport chain, which drives the transport of H^+ ions across the inner membrane of mitochondria through a "chemiosmotic coupling".

The H^+ ions transport results in an electrochemical potential which is used by *ATP-synthase* enzyme to produce ATP from ADP and phosphate.

The overall balance of oxidative breakdown of glucose can be summarized with:



The released energy is used to produce ATP: the oxidation of a single glucose molecule yields 38 ATP molecules, of which just 2 are resulting from glycolysis.

Autotrophs and heterotrophs

Organisms are classified into autotrophs and heterotrophs according to the way they obtain the energy they need.

Autotrophs organisms are able to synthesize organic molecules from inorganic compounds, as CO_2 e H_2O , using an external energy source. Plants, for example, are photoautotrophic since they use sunlight as an input, while chemoautotrophs use the energy released from redox reactions, instead.

Heterotrophs are those organisms unable to synthesize organic molecules from inorganic ones and therefore need to acquire them from feeding on autotrophs (herbivores), on other heterotrophs (carnivores), on waste products (saprophytes) or obtaining organic matter directly from living organisms (parasites).

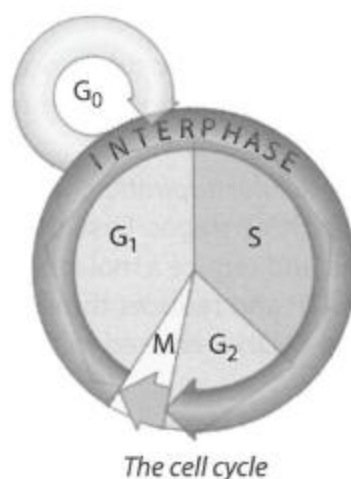
1.3 | Cell division and chromosomes

The cell division is the process that leads to the production of two daughter cells from a mother cell. The whole genome has to be duplicated before each cell division, so that each one of the daughter cells can have an identical copy of it.

1.3.1 | Cell division in eukaryotes

The life cycle of a eukaryotic cell, called *cell cycle*, can be schematized into four distinct phases: G_1 , S, G_2 , and M. The first three stages taken together are called *interphase*, while the cell division occurs in the fourth stage, called *mitosis*. If a cell gets temporary or permanently stuck in G_1 phase, this takes the name of *G_0 phase*. This is the case of neurons, for instance, that lose the ability to divide once they reach maturity, getting permanently stuck in G_0 .

The G_1 (G = gap) is the first phase of the cycle and it's a moment of intense biosynthetic activity and growth. The cell doubles its size and produces new organelles, as well as enzymes required for DNA replication of the subsequent S phase in which DNA replication takes place (S = synthesis).



During the G_2 phase the cell keeps growing and form new organelles as well, in order to get ready for the subsequent division.

Each chromosome is a single long DNA molecule associated with various proteins in a complex called chromatin. The double helix, negatively charged, is wrapped around histones proteins, positively charged, to pack the DNA in the limited volume of the nucleus. Histones are organized in complexes of 8 molecules, the nucleosomes, which are the basic units of chromatin.

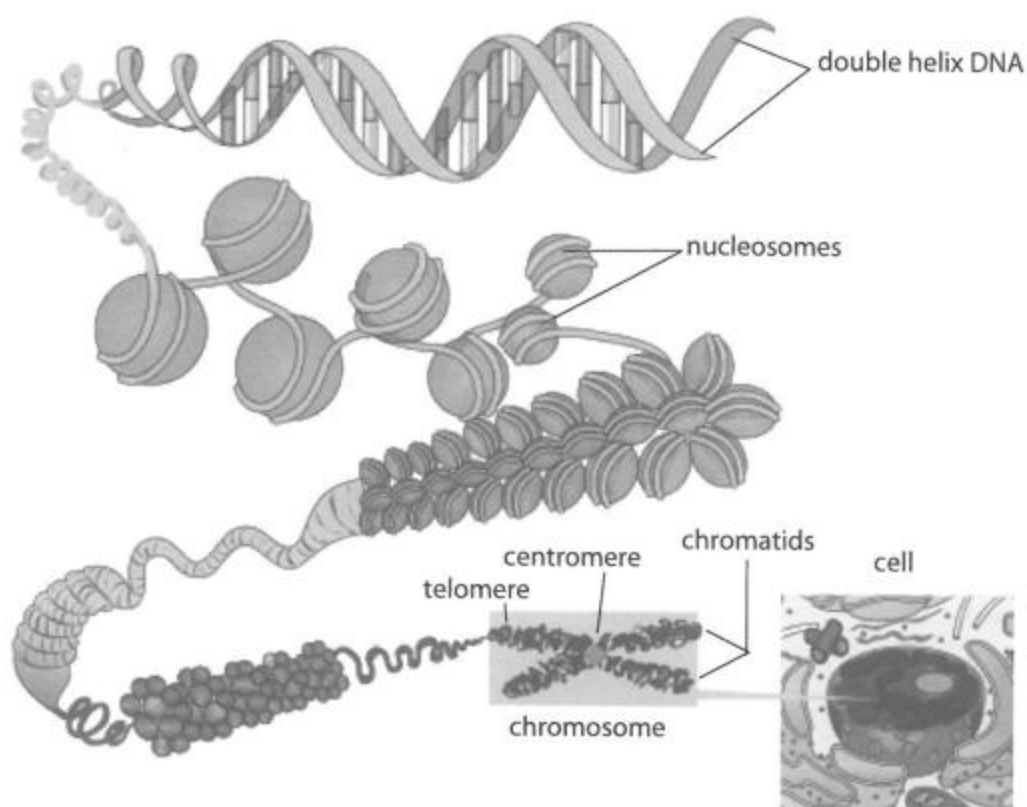
This structure makes the chromatin look like "beads on a string" when observed with an electron microscope.

Two adjacent nucleosomes are connected by an additional histone molecule, resulting in a more compact fiber of 30 nm of diameter.

This, in turn, can be further wrapped around itself to form 300 nm thick fibers, compact enough to fit in the nucleus.

When cell division occurs, chromatin undergoes additional spiralization, so that chromosomes become visible also under optical microscope.

In general, all the proteins bound to DNA are included in the definition of chromatin, even though histones are by far the most abundant.



Mitosis

The process of mitosis results in the duplication of the nucleus of an eukaryotic cell into two genetically identical nuclei, each one with a full set of chromosomes. The division of the cytoplasm, called cytokinesis, follows generally, but not necessarily, the division of the nucleus.

At the beginning of mitosis the chromosomes lose the appearance of undifferentiated mass of chromatin they have during interphase to condense into short and stubby corpuscles.

Given that the DNA is duplicated during the S phase of the cell cycle, when mitosis starts each chromosome consists of two identical strands of DNA, called sister chromatids.

Chromatids are tied together by a region called *centromere*, while the ends of chromosomes are referred to as telomeres.