Introduction to Molecular Biophysics - Part I

Cell biology and the molecules of life

Overview

Biophysics and biology

The cell

Molecular forces

pH, pK_a, acids and bases

An introduction to the molecules of life

Carbohydrates

Lipids and membranes

XVII century
bioluminescence (A. Kircher)
electricity in biology (Isaac Newton)

XVIII-XIX century
Electric batteries from frog legs experiments and electrophysiology (L. Galvani, A. Volta)
Reaction in solution, diffusion , osmotic pressure (physical chemistry) (Abbe' Nollet, R.J. Duthrochet, J. Van't Hoff)
Thermal motion of particle in solution, fluorescence (brownian motion) (Robert Brown, G.G. Stokes, A. Fick)
Discovery of X-rays: 1895 W. Conrad Rontgen

XX century
Interest in macromolecules—discrete entities (T. Svedberg, 1925, analytical centrifuge)
1910 application of X-rays to atomic crystallography (P. Ewald, M. von Laue, W.H. and W.L. Bragg)
1943 Schrödinger gave a few lectures at Trinity College, Dublin, on

"What is life: the physical aspects of the living cell"

Biophysics: the beginning?

In 1943 Schrödinger gave a few lectures at Trinity College, Dublin, on

"What is life: the physical aspects of the living cell"

These lectures generated an enormous interest for biology between physicists and chemical physicists, which led to the discovery of DNA and protein structure and the development of molecular biology.

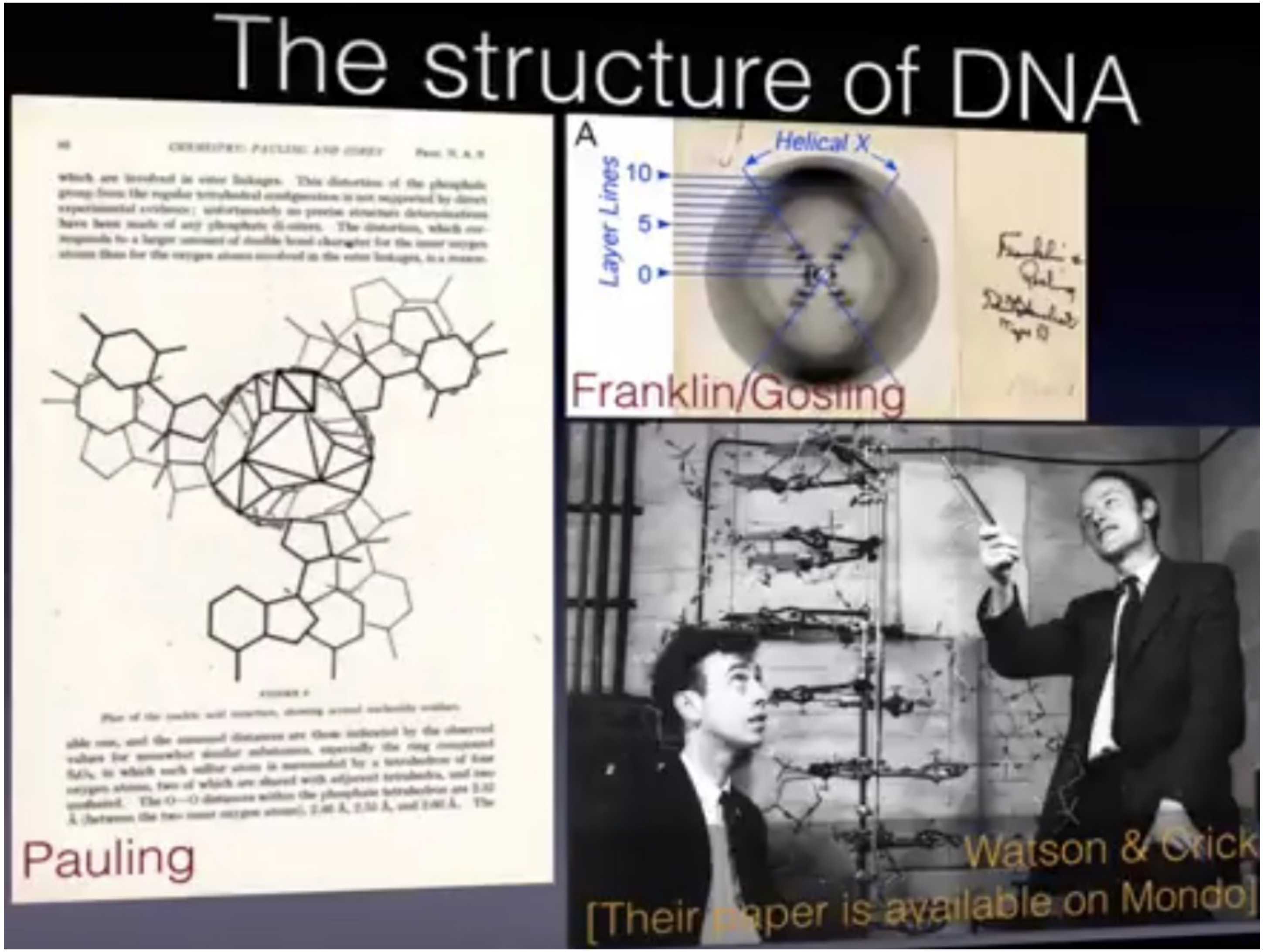
The major successes of modern biology (XX century) have been:

- a molecular explanation of the mechanisms of inheritance
- a molecular explanation of the mechanisms of action of enzymes

Both are due to the application of X-ray diffraction to determine the 3D structure of biological molecules - molecular biology has taken a strong structural emphasis.

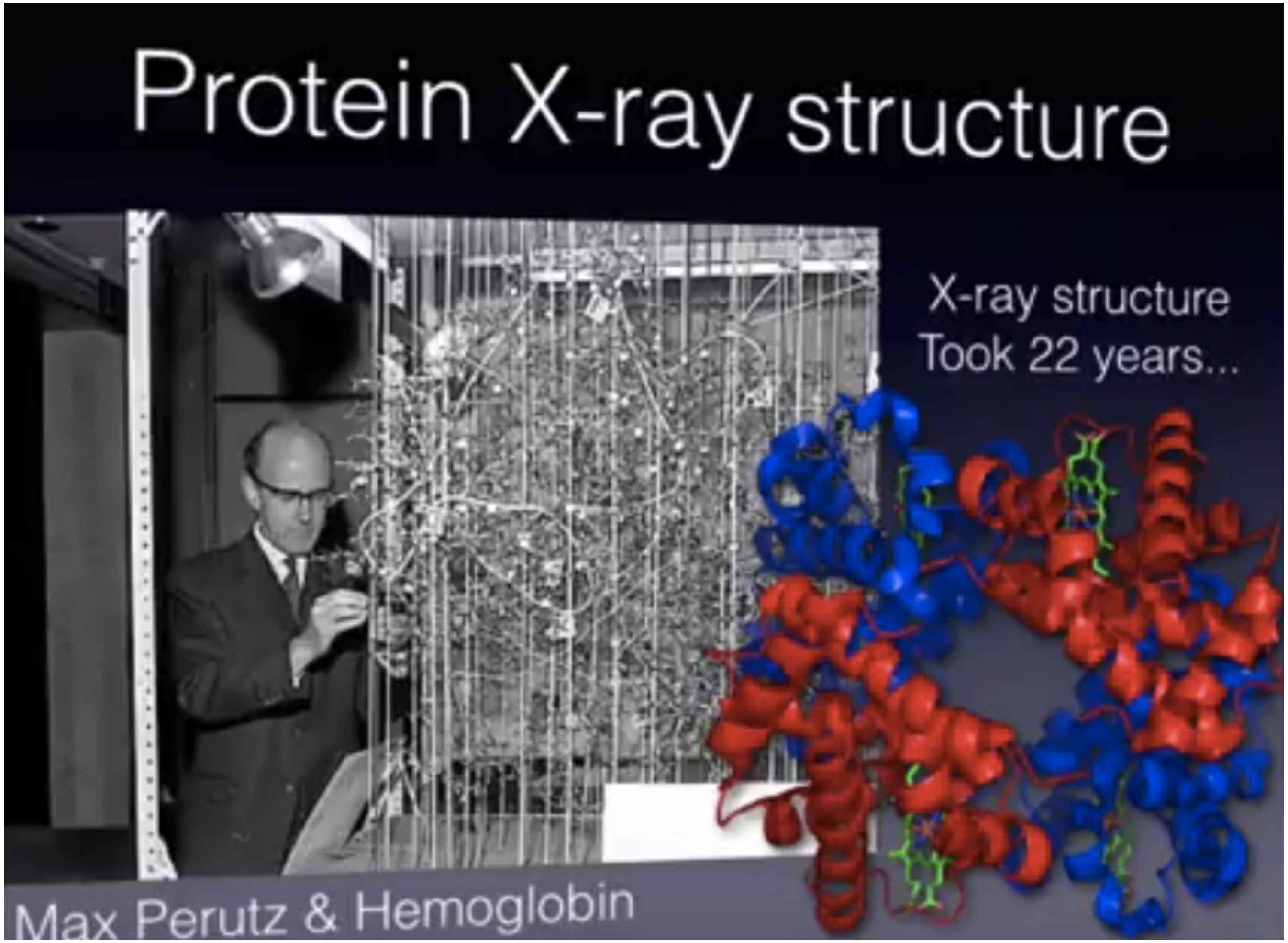
Hystory of (Molecular) Biophysics:

Breakthrough is DNA double-helix model obtained by J.D. Watson(ornithologist) and F.H.C. Crick (physicist) following Rosalind Franklin, R.G. Gosling, M.H.F. Wilkins, A.R. Stokes, H. R. Wilson fibre diffraction/biochemical studies published on Nature in 1953



Higher resolution needed!

The first protein crystal was obtained in 1930, the first X-ray structure by M. Perutz and J. Kendrew in 1957 (myoglobin). Complex problem, needed complementarybiochemical and thermodynamical tools to be solved. Application of physical concepts and methods to biology --- biophysics!



What is life?

What is special about living organisms?

For a long time it was thought that the laws of chemistry and physics did not apply to living organisms, which were subjected to a special ‘vital force’

Only in 1827 the dutch chemist F. Wohler synthesised urea (an organic compound) showing that there was no need of a ‘vital force’ to carry out reactions that were normally occurring in biological entities.

We know now that the distinction between life and non-life is not due to the molecules or the chemistry involved, but it is due to the way these molecules are organised in a complex system and are able to display a complex behaviour.

Evolution

Life is the result of a historical process

Central theory in biology $\mapsto$ Darwin's theory of evolution
(1859 'The origin of the species')

EVOLUTION = RANDOM MUTATION + NATURAL SELECTION

- random mutation causes a variety of traits in a population
- 'favourable traits' $\mapsto$ generation of more offspring
- increased frequency of favourable traits in the population
- because of differences in the environment different traits will be selected in different times and different places.

Gradual, step-by-step transformation driving towards complexity.

The blind watchmaker - R. Dawkins

What are the characteristics of life?

All living organisms:

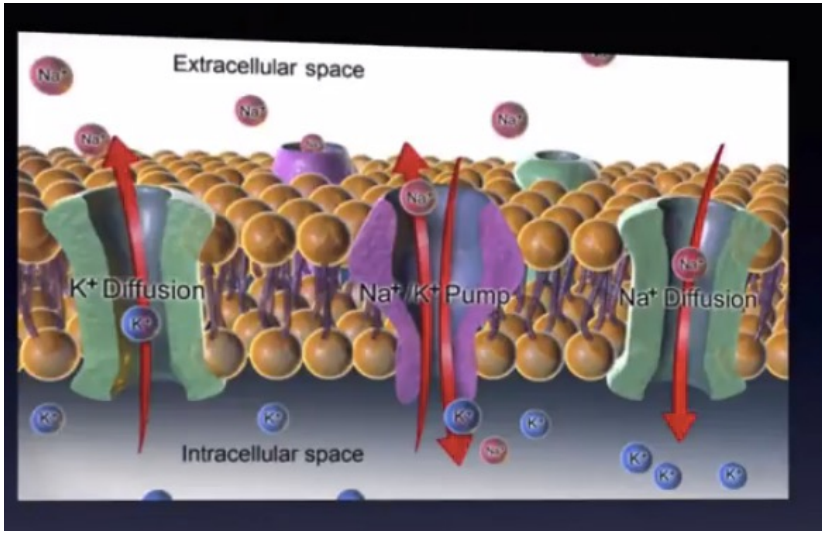
- are made of highly organised and orderly structures
- have the ability to respond to stimuli
- are characterised by growth, development and reproduction
- have regulatory mechanisms that control and coordinates life functions

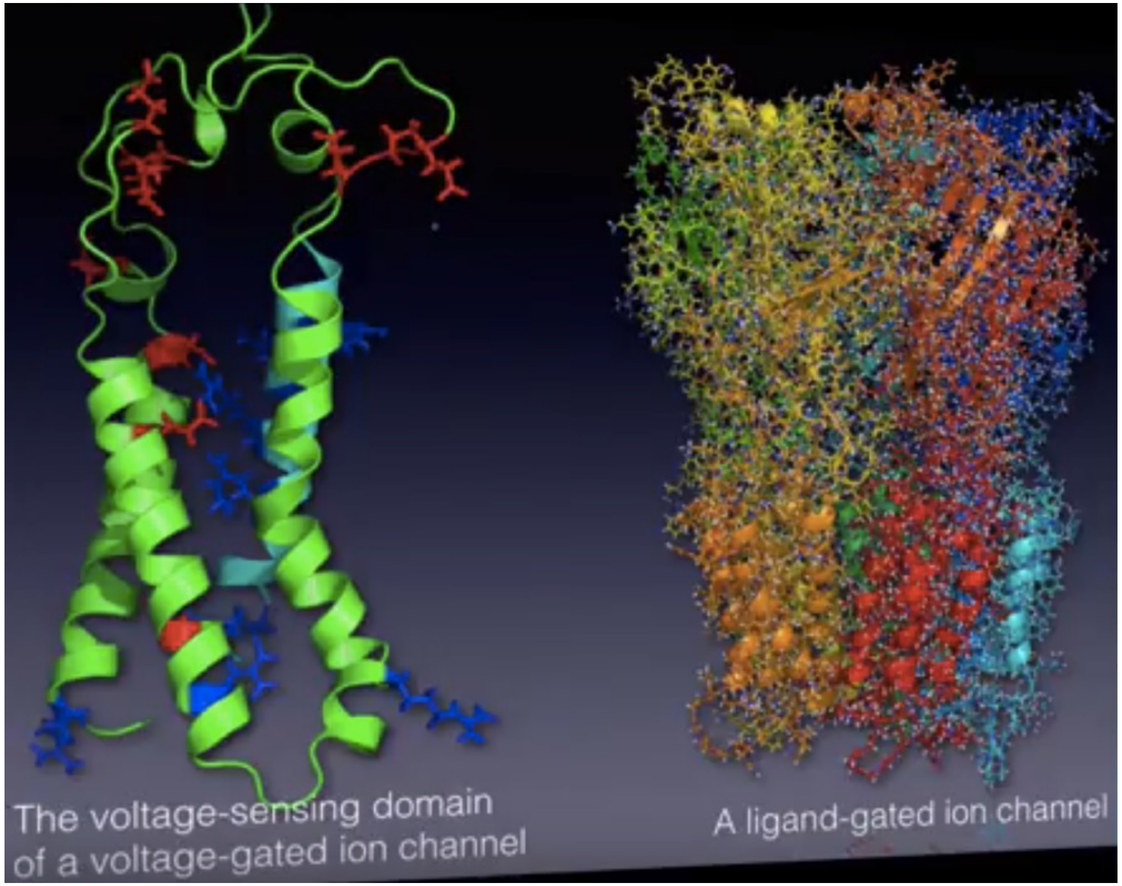
All living organisms are made of cells.

If cell is a highly organized and orderly structure, it doen not obey the second law of thermodynamics.

In reality the cell is not an isolated system: takes in energy from the environment and uses this energy to generate order through chemical reaction. From chemical reactions, heat is generated towards the environment inducing disorder outside (thermal motion). The "controlled burning" of food molecules generates biological order.

Membranes are regulating as timer for such control.

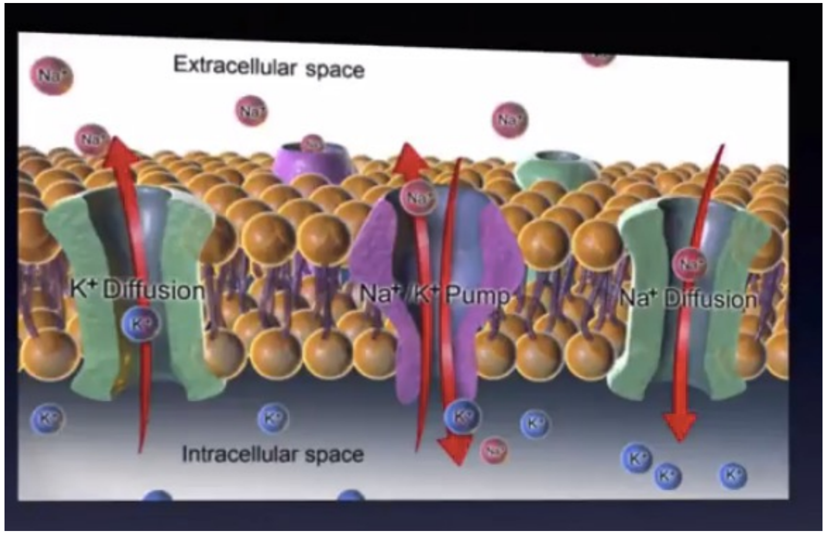


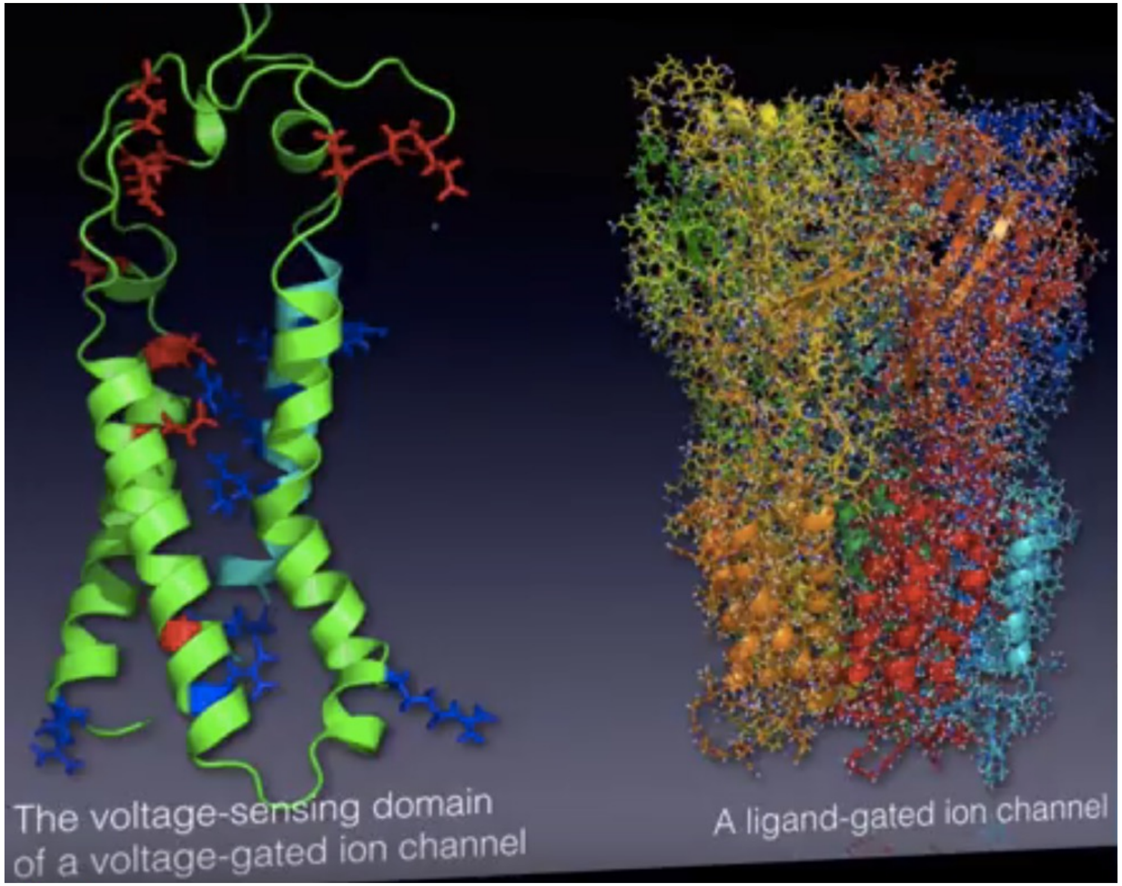


Biology is about distribute/generate/consume energy.

Ion channels are the voltage-sensing domains of a voltage-gated access (heart beats, nerve impulse), which make the cell working as a battery (selective opening of the channel).
Pumps are enzymes in the membrane which move ions in counter direction (ATPase).

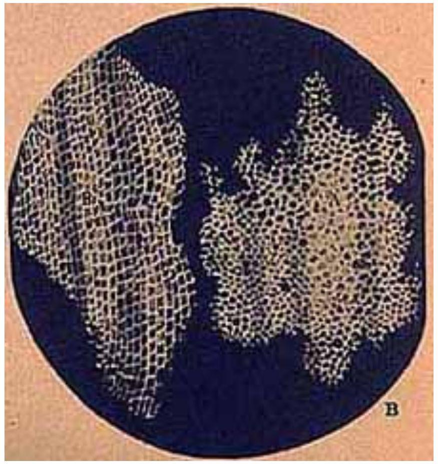
Ligand-gated channels are part of the nerve system (receiving side of the synapsis) and are amazingly specific! One mistake every billion (disease!)



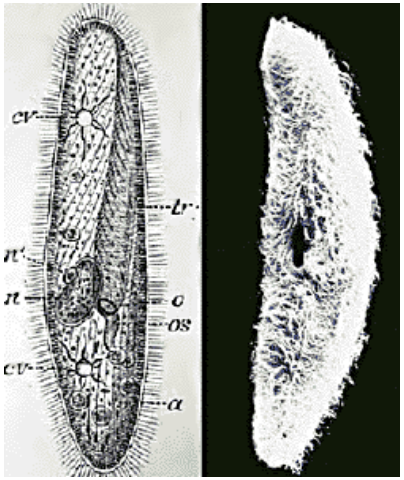


The cell: a bit of history...

Cells were first seen in the 17th century, thanks to the advances of optic and microscopy (first contribution of physics to biology!):



Robert Hook coined the term “cells” for the little structures seen in cork.



Antony van Leeuwenhoek discovered bacteria, free-living and parasitic microscopic protists, sperm cells, blood cells, microscopic nematodes and rotifers, and much more...

But only in the 19th century it was realised the central importance of cell in biology:

➡ The Cell Theory (Schleiden & Schwann, 1839)

“each animal appears as the sum of vital units, each of which bears in itself the complete characteristic of life”

Cells, molecules and life

All living organisms are made of cells.

Some consist of single cells (unicellular), other of many cells (multicellular).

Organisms grow by the growth and division of their cells.

Cells can be taken out of an organisms and can live in the absence of the rest of the organism -> cells are truly alive.

Cells are made of molecules which obey the laws of chemistry and physics, but are organised in complex systems, and are able to display complex behaviour.

Biochemistry: study the organisms as chemical systems.

Molecular/cellular biology and biophysics: underline the organisation of cell And function of macromolecules from simple principles. Explain complex processes from atoms: macromolecular structure; fluctuactions. Make Models: simplify as much as possible, never more!

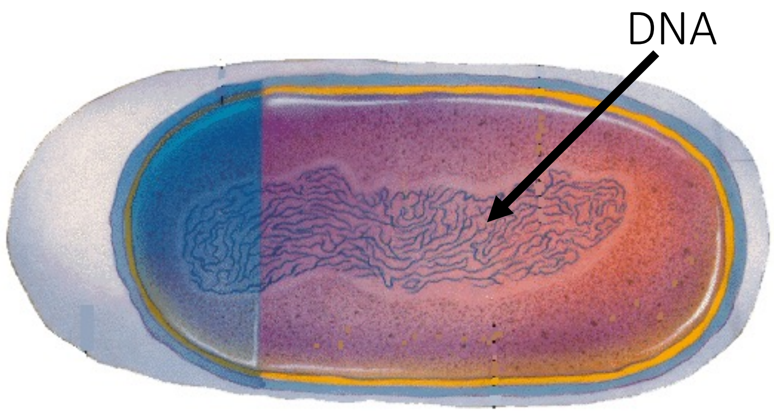
The organisation of the cell

A cell membrane separates the outside from the inside of the cell; the inside is called cytoplasm and contains a high concentration of proteins, small molecules and nucleic acids (DNA and RNA).

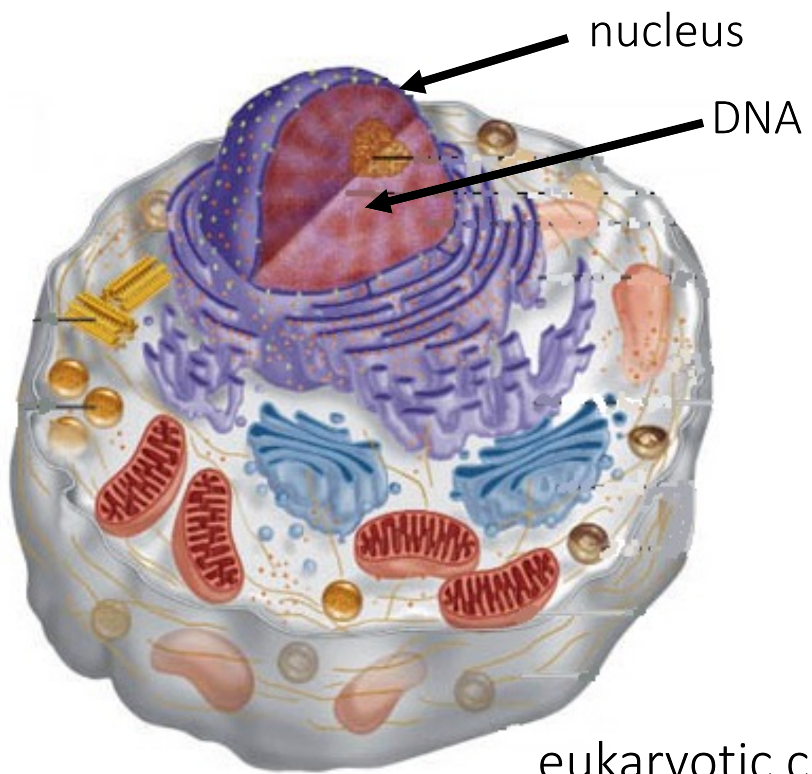
In some cells the DNA is simply spread inside the cell, in others it is enclosed in an organelle called the nucleus.

This divides cells into two classes:

- prokaryotic cells (without nucleus)
- eukaryotic cells (with nucleus)



prokaryotic cell



eukaryotic cell

Classification of living organisms

Prokaryotes

(no nucleus, unicellular)

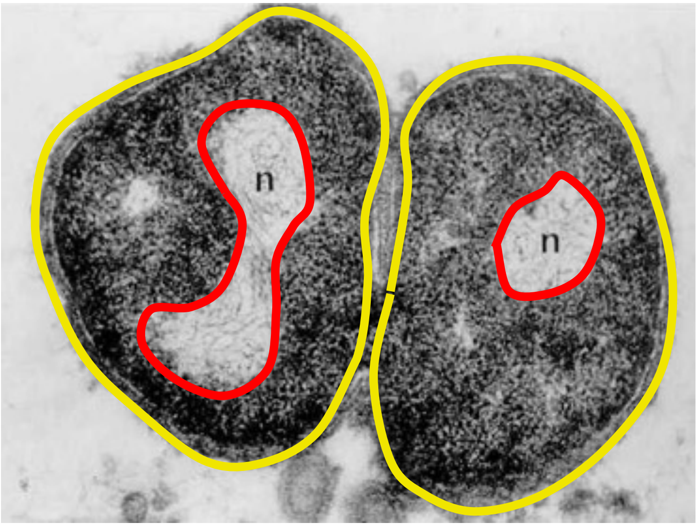
- Archaea
- Bacteria — aerobic, anaerobic, photosynthetic, etc...

Eukaryotes

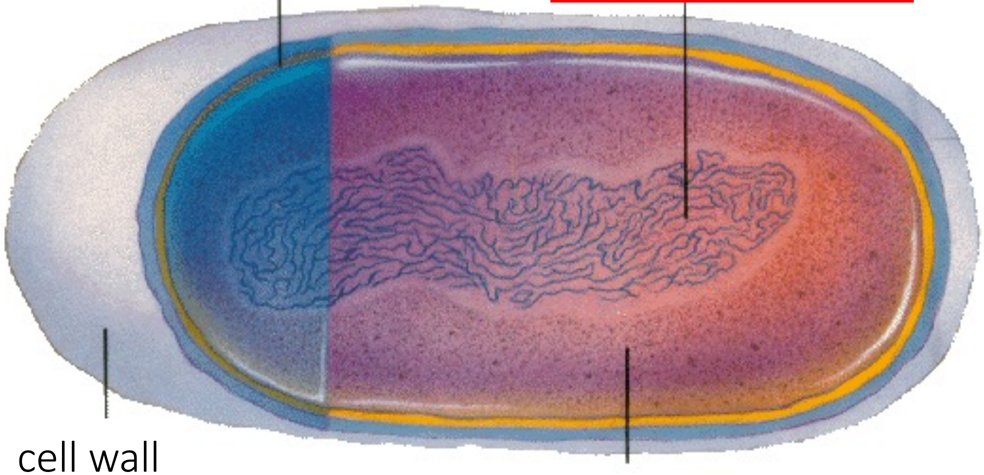
(nucleus)

- Fungi — unicellular/multicellular
- Animals — multicellular
- Plants — multicellular and able to carry out photosynthesis

BACTERIA



An electron micrograph
of two bacteria.

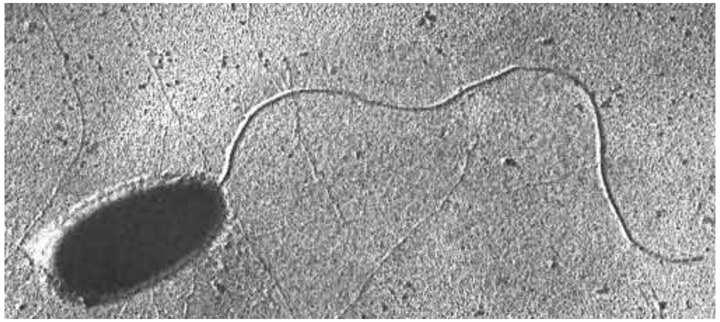


A schematic diagram of a bacterium.

Bacteria are single-cell prokaryotic organisms, ranging in size between 1-5 μm.

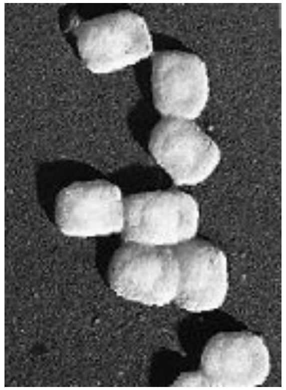
The DNA co-localises in a compact structure called the nucleoid, but there is no physical separation (i.e. no nuclear membrane) between the DNA and the rest of the cell.

Bacteria display a wide variety of shapes:



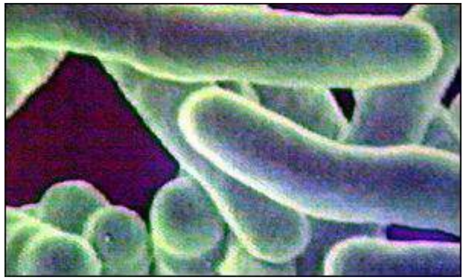
Flagellatae

Spirochete

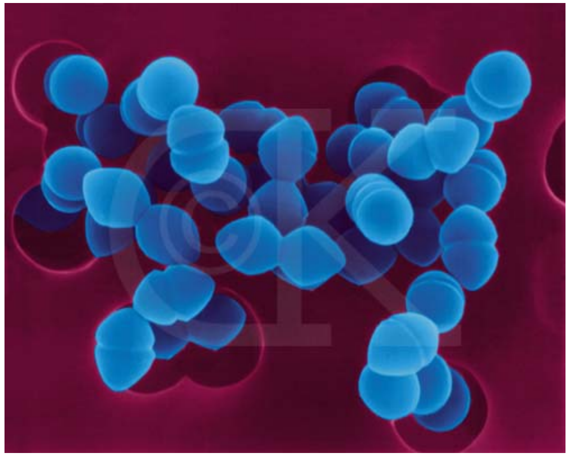


Plague bacteria

Antrax bacteria

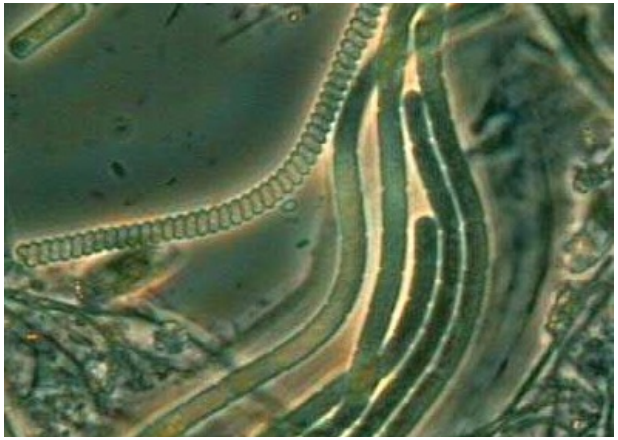


TB bacteria



Enterococcus

Escherichia coli



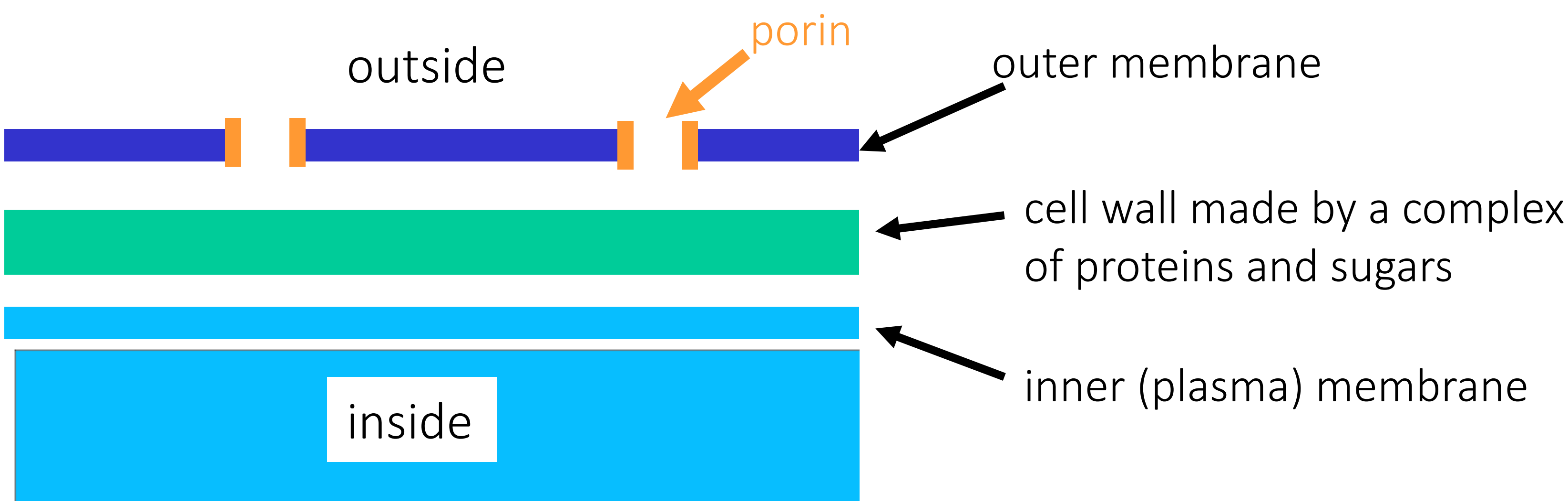
Cyanobacteria

Bacterial cell membrane

Gram positive bacteria $\mapsto$ have only one membrane impermeable to chemicals, surrounded by a cell wall made of a complex of proteins and carbohydrates

Gram negative bacteria $\mapsto$ have two membranes

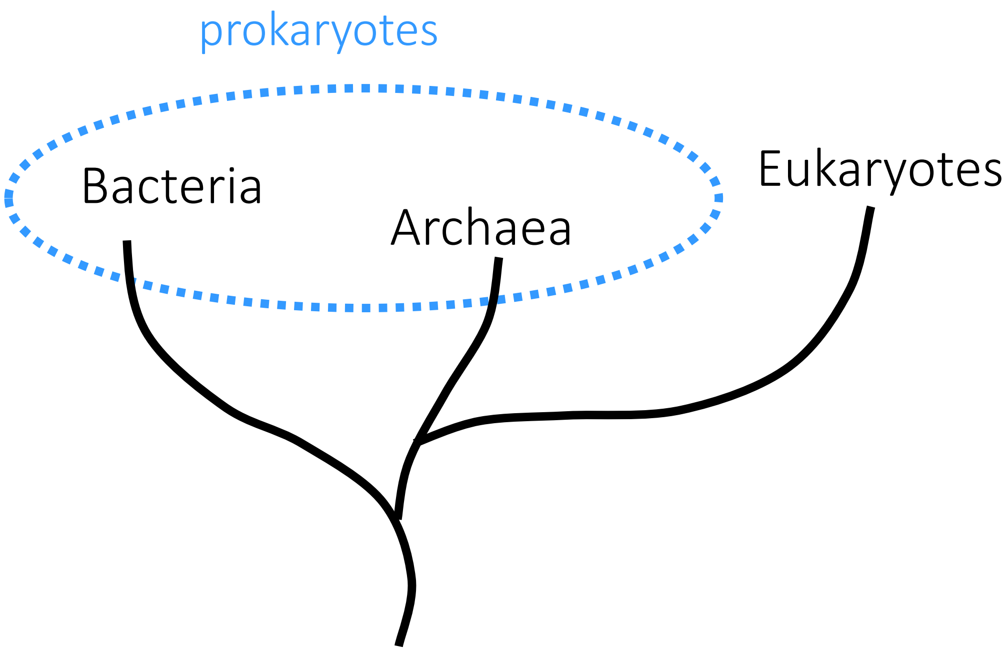
- inner membrane impermeable to chemicals
- outer membrane containing proteins called porins, which make holes into the membrane so that chemicals can go in and out
- a cell wall between the two membranes



ARCHAEA

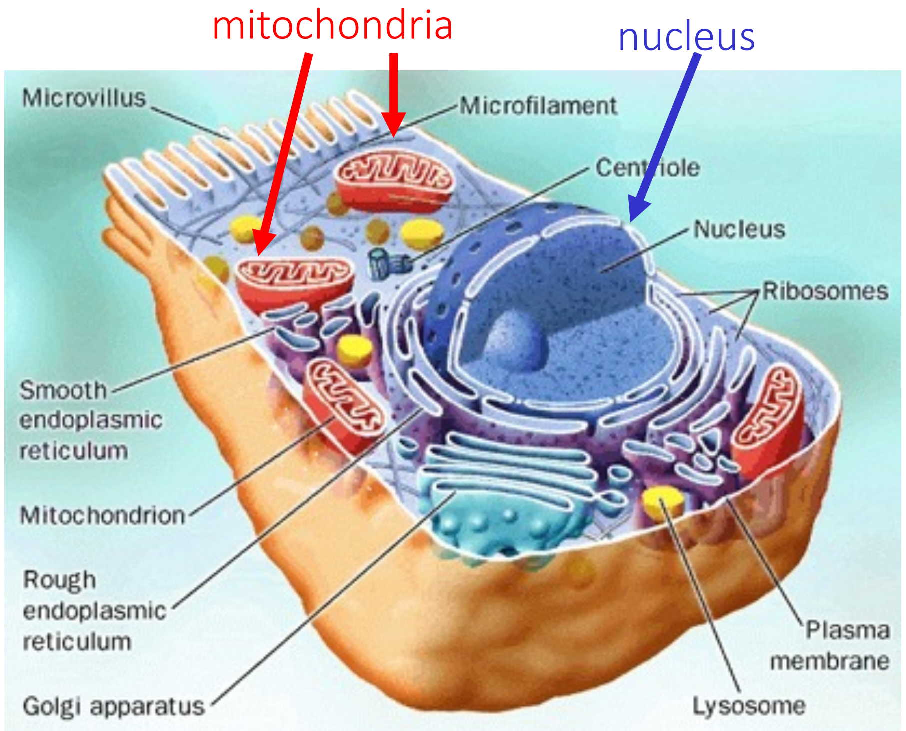
- unicellular organisms
- no nucleus (i.e. prokaryotes)
- live in very unfriendly environments (hot/sulphuric springs, the Dead Sea, deep vents in the oceans...)
- metabolic processes similar to bacteria
- but...processing of genetic information (how they copy, read, use the information written in the DNA) similar to eukaryotes!

Our current picture of the evolution of life:

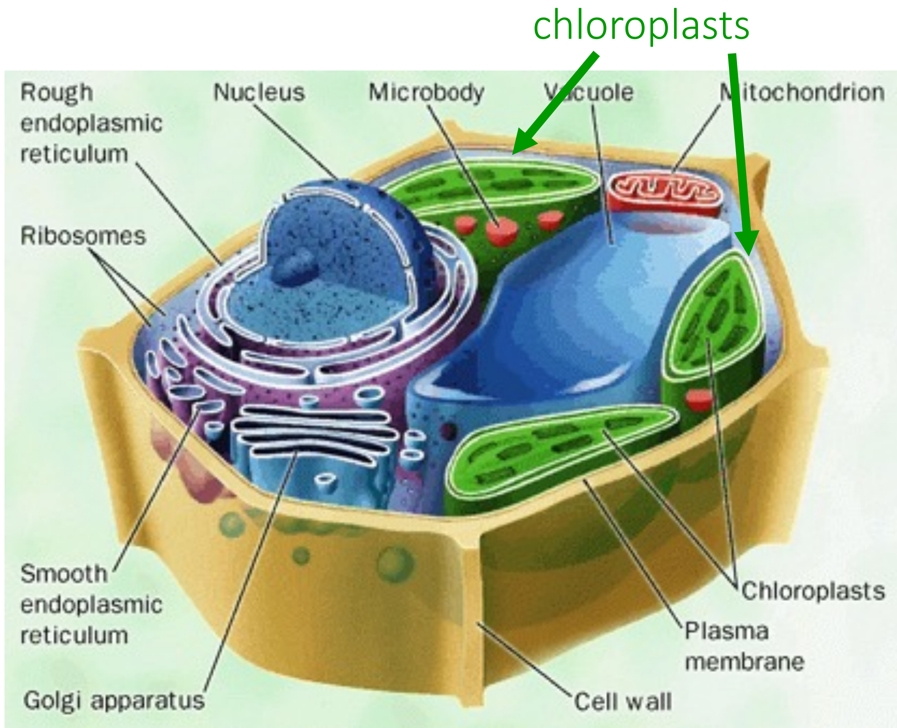


EUKARYOTES

- cell size varies between 5-50 μm
- unicellular organisms (such as yeast and protozoa)
- multicellular organisms such as animals and plants
- complex architecture, containing variety of organelles



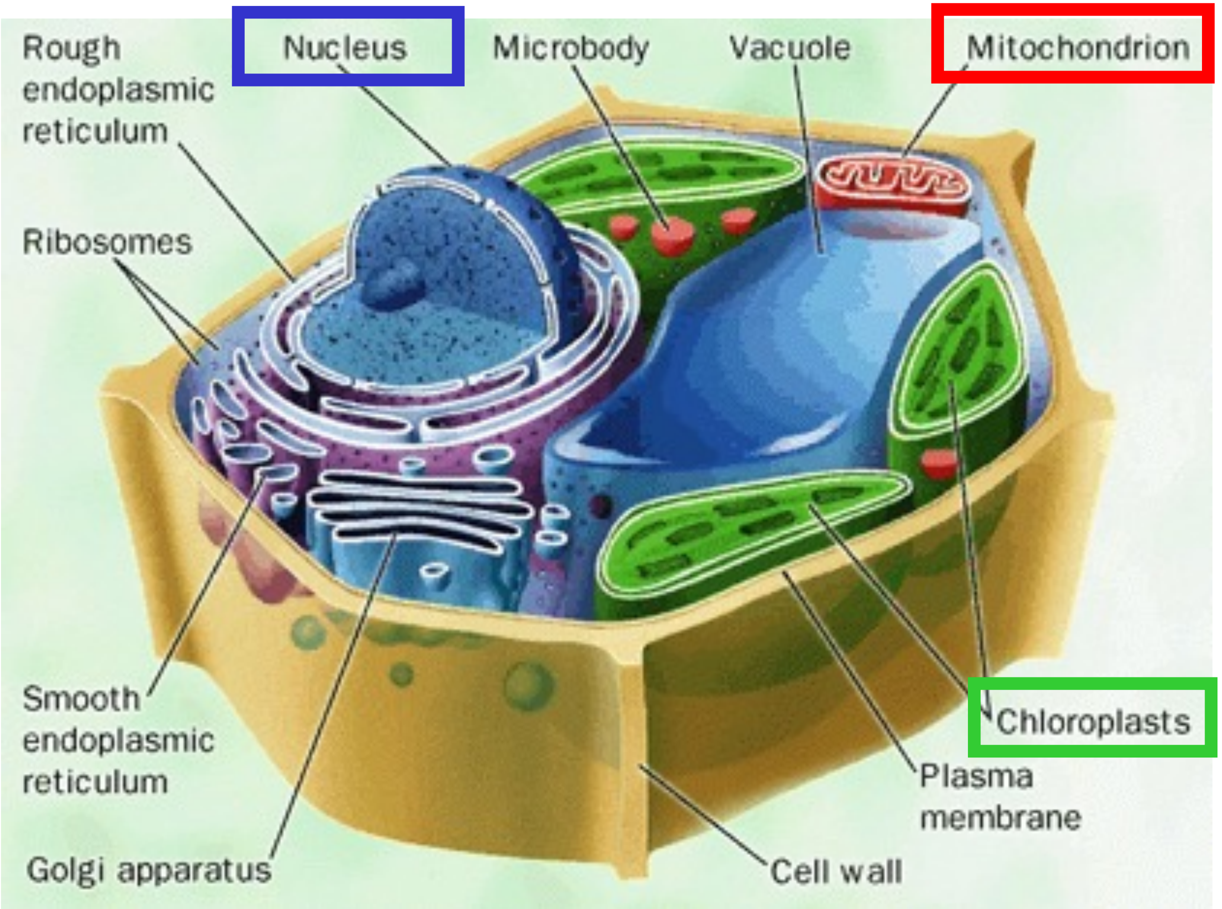
animal cell



plant cell

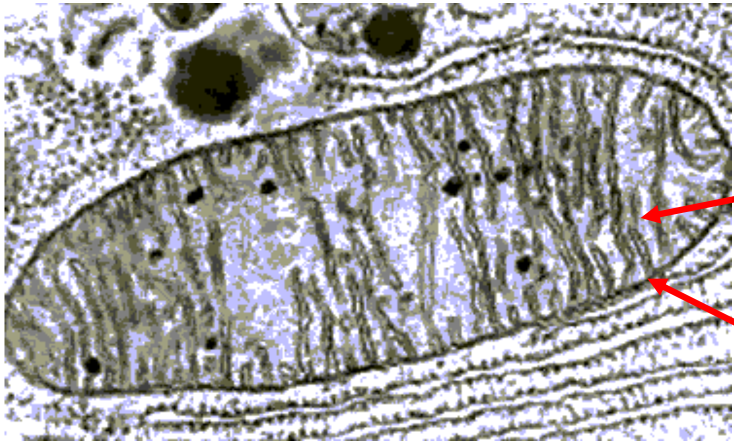
Eukaryotic organelles

- a nucleus (storing DNA)
- mitochondria (produce energy by oxidation of small molecules)
- chloroplasts (carry out photosynthesis; only in plant cells)



plant cell

Mitochondrion

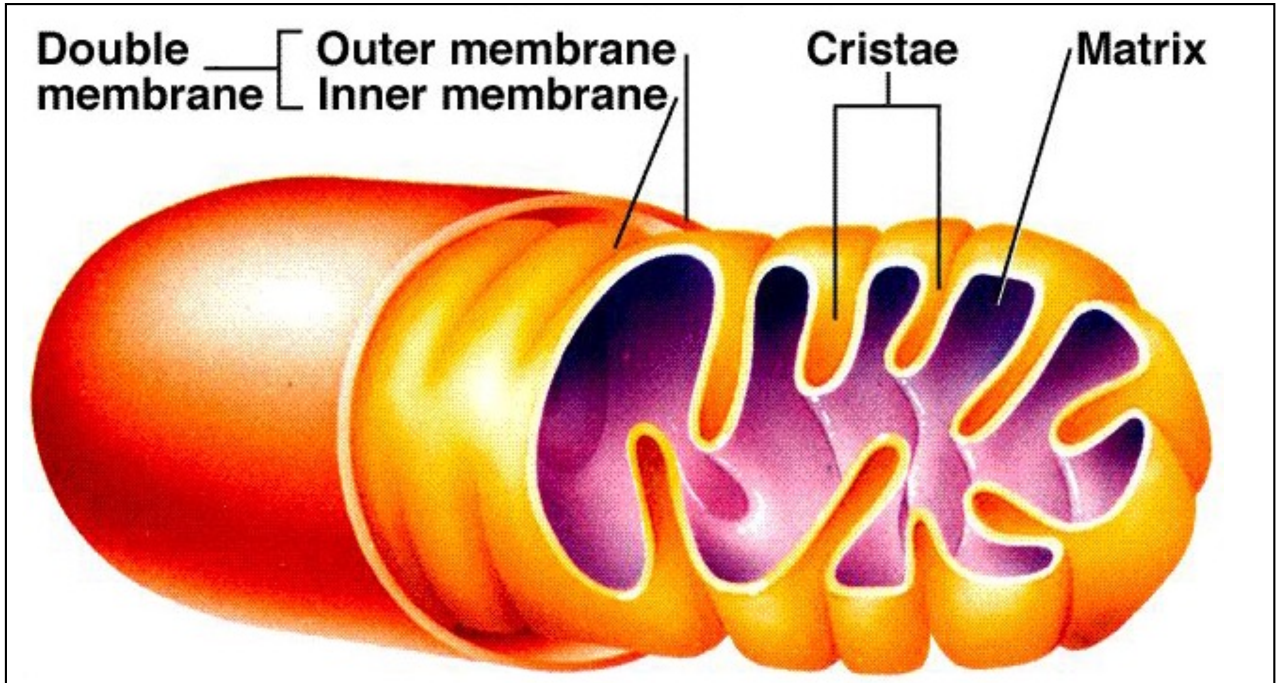


Electron micrograph of a mitochondrion

inner membrane

outer membrane

- one external membrane
- one internal membrane forming many invaginations (cristae)



3D reconstruction

Function of mitochondria:
energy production by oxidation of small molecules (occurring in the mitochondrial matrix)

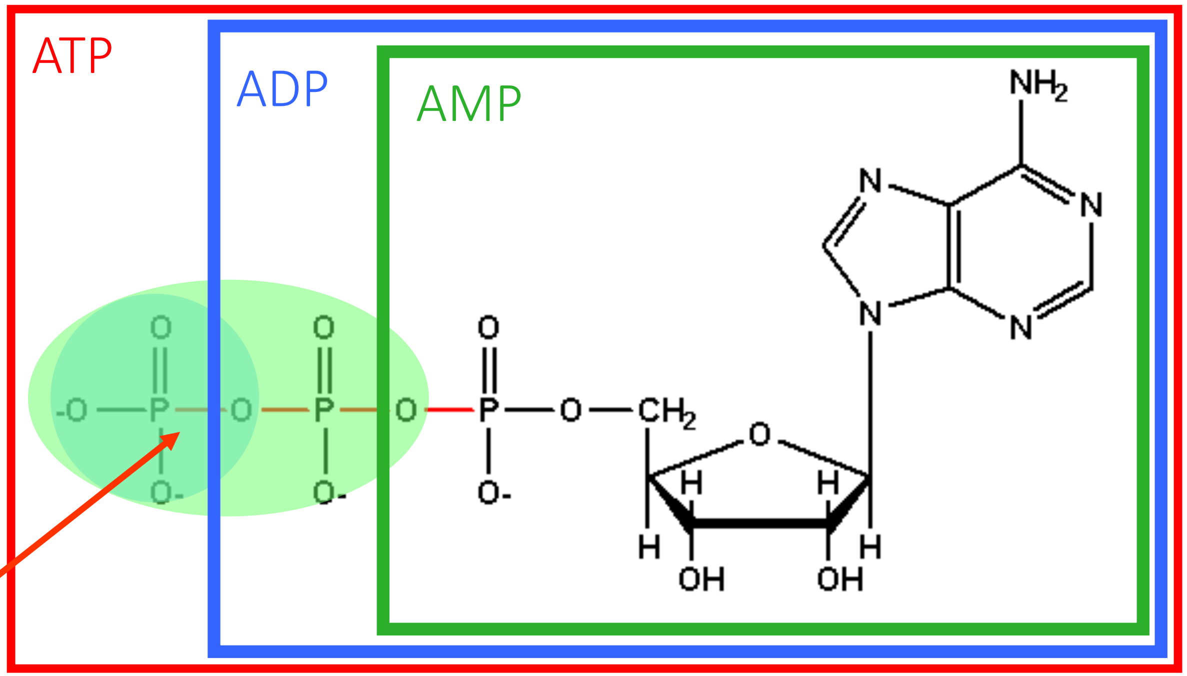
Energy in the cell: ATP

In the cell reactions that require energy are associated with ATP hydrolysis (hydrolysis= breaking down). ATP hydrolysis is an exothermic reaction, and the energy generated can be used to drive a non-spontaneous reaction.

ATP ↦ ADP + P
(ΔH = -30 kJ/mol)

ATP ↦ AMP + PP_i
(ΔH =-30 kJ/mol)

Adenosine Tri/Di/Mono phosphate

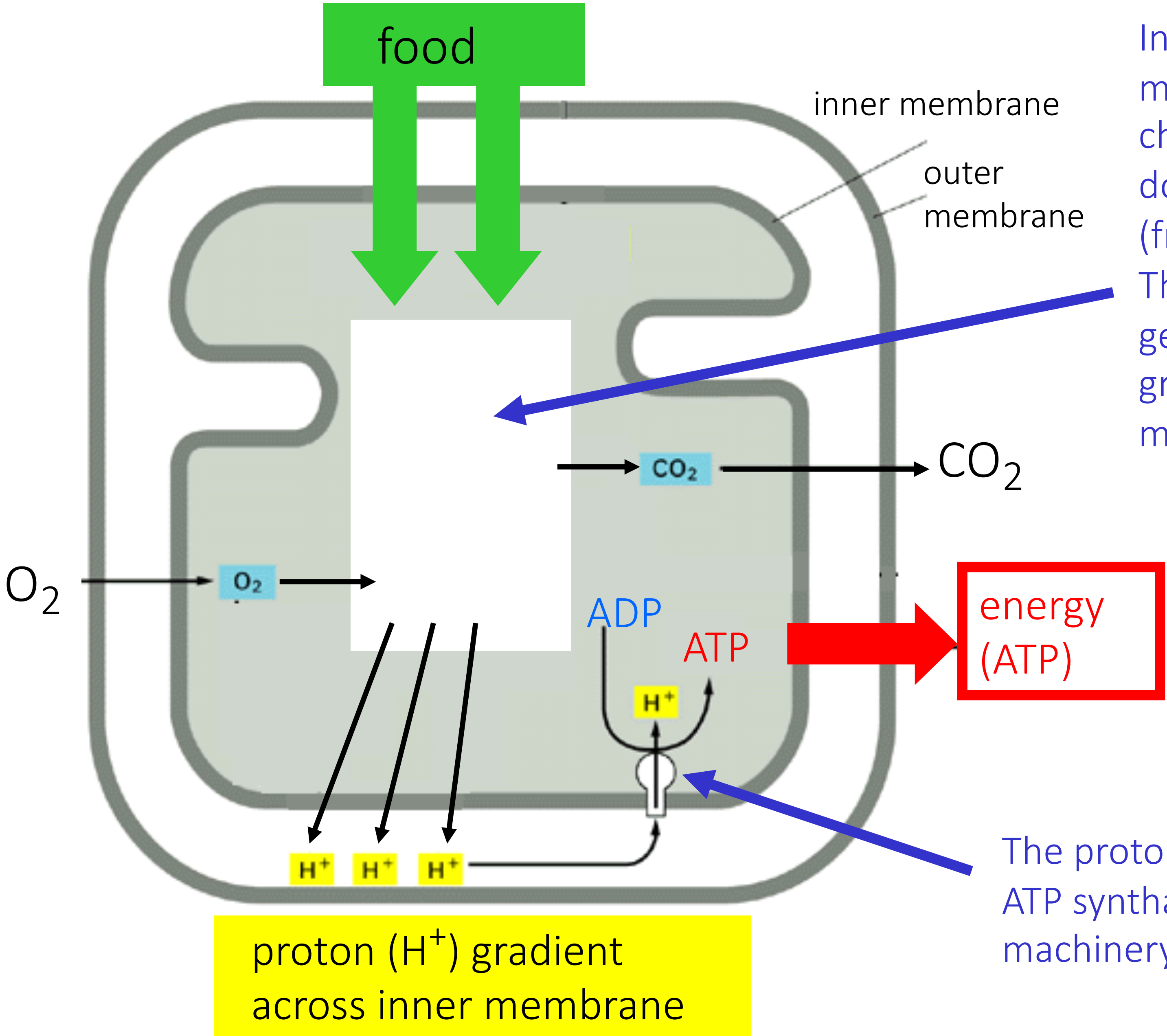


phosphodiester bonds have a large energy of hydrolysis (about 30 kJ/mol)

Energy production: accumulation of ATP

Energy consumption: breaking down (hydrolysis) of ATP ↦ ADP or AMP

What happens in the mitochondrion?

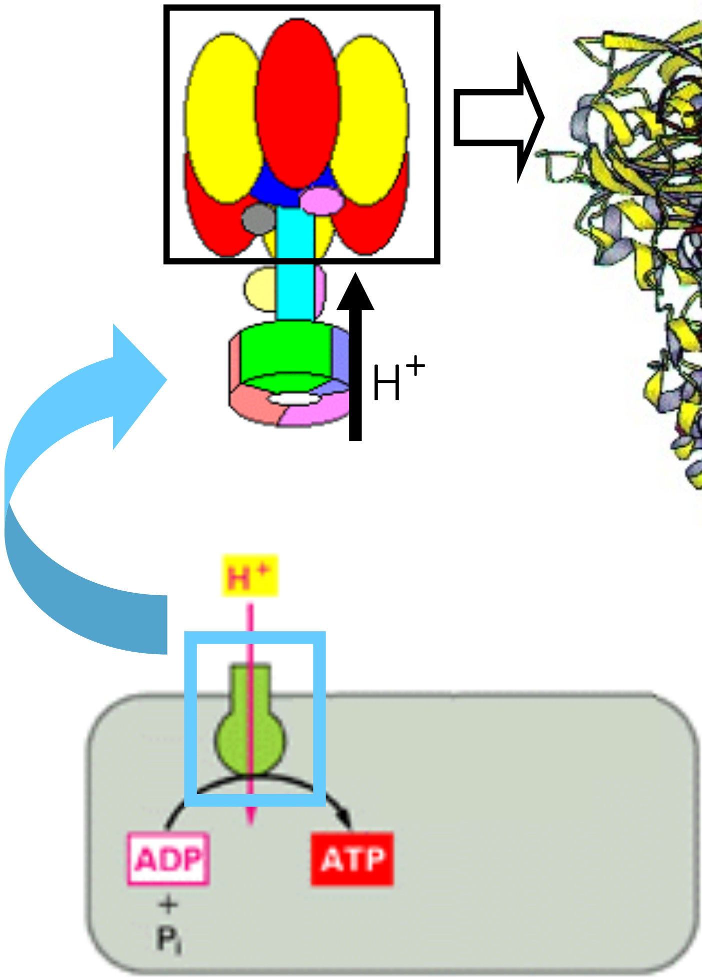


Inside the mitochondrial matrix a complex set of chemical reactions break down small molecules (from food).
This biochemical process generates a proton gradient across the inner membrane

The proton gradient drives the ATP synthase, a complex machinery that makes ATP

ATP production

The complex responsible for ATP production is called ATP synthase



The ATP synthase sits in the mitochondrial inner membrane and uses the H+ gradient to drive ATP synthesis.

John Walker,
Nobel prize 1997

Biological molecules

From a functional point of view biological molecules can be divided into:

small molecules

- made and altered by individual steps of chemical reactions
- used as substrates for making macromolecules
- used to store and distribute energy for cell processes
- broken down to extract chemical energy
- used in signalling

macromolecules

- polymers made by a linear chain of building blocks
- made by linking a defined set of small molecules (monomers) through the repetitive use of a single chemical linkage
  - ↦ proteins: polymers made by a linear chain of amino acids
  - ↦ nucleic acids: polymers made by a linear chain of nucleotides

EVOLUTION of LIFE = EVOLUTION OF MACROMOLECULES

Macromolecules

CENTRAL DOGMA

DNA ------- PROTEIN ------FUNCTION

Biophysics: underline macromolecules function/structural transition of macromolecules from simple principles. Explain complex processes from atoms: macromolecular structure; fluctuactions. Make Models: simplify as much as possible, never more!

Macromolecules

Proteins:

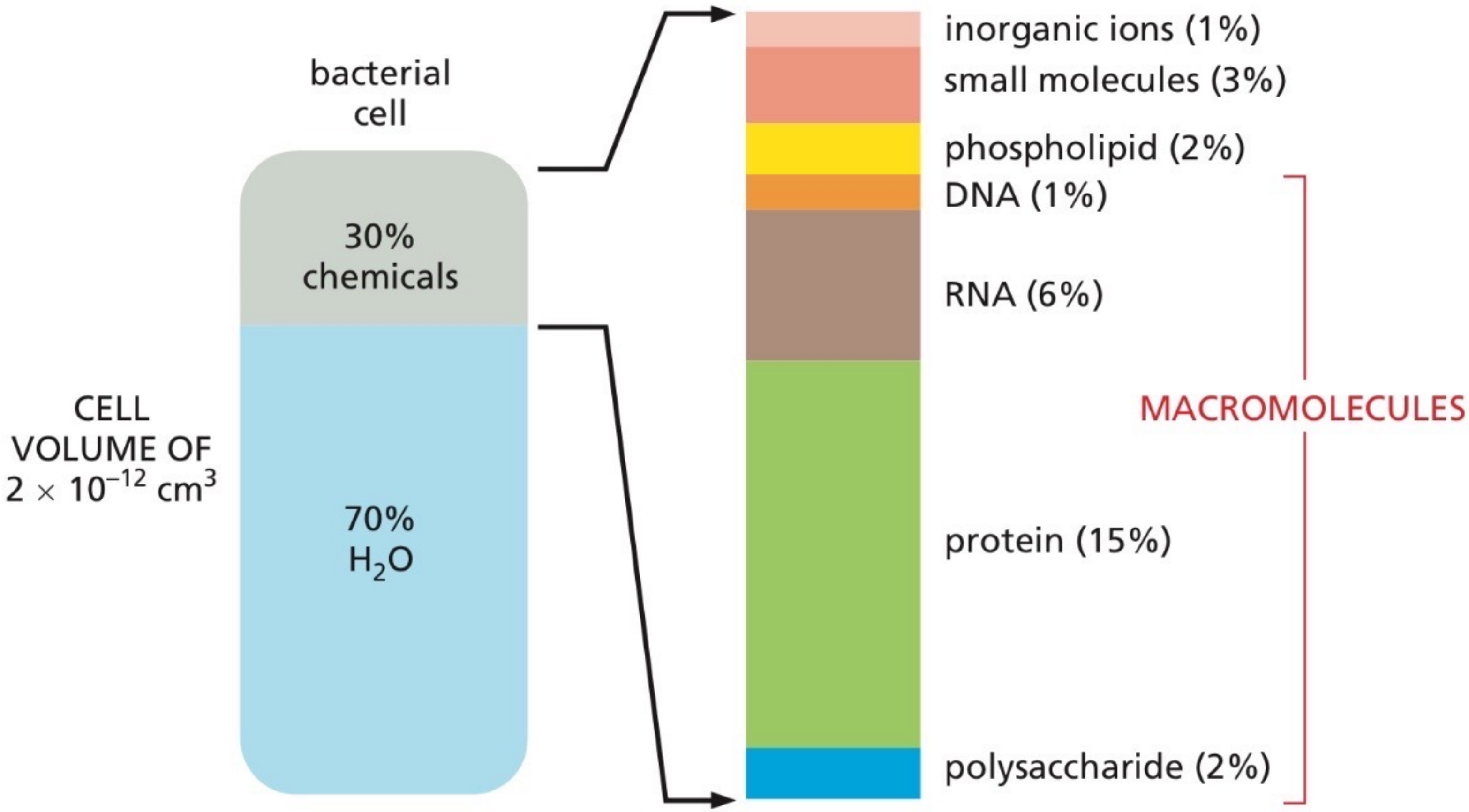
molecular machines, display a wide variety of 3D shapes and of biological functions

- catalyse small molecules synthesis and degradation
- allow cells to move and do work
- maintain cell rigidity
- control genes, switching them on/off
- direct their own synthesis
- move molecules across membranes

Nucleic acids (DNA and RNA):

- contain a coded representation of all proteins of a cell
- contain a coded set of instruction about when proteins have to be made and in which quantities

Macromolecules



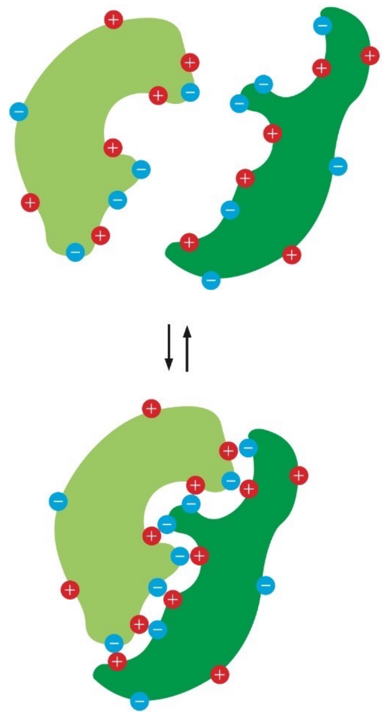
Molecular forces

Covalent bonds:

- strength and direction

Non-covalent interactions:

- multipole interactions
  - ion-ion
  - ion-dipole
  - dipole-dipole ⇨ hydrogen bond
- induction interactions
- dispersion forces



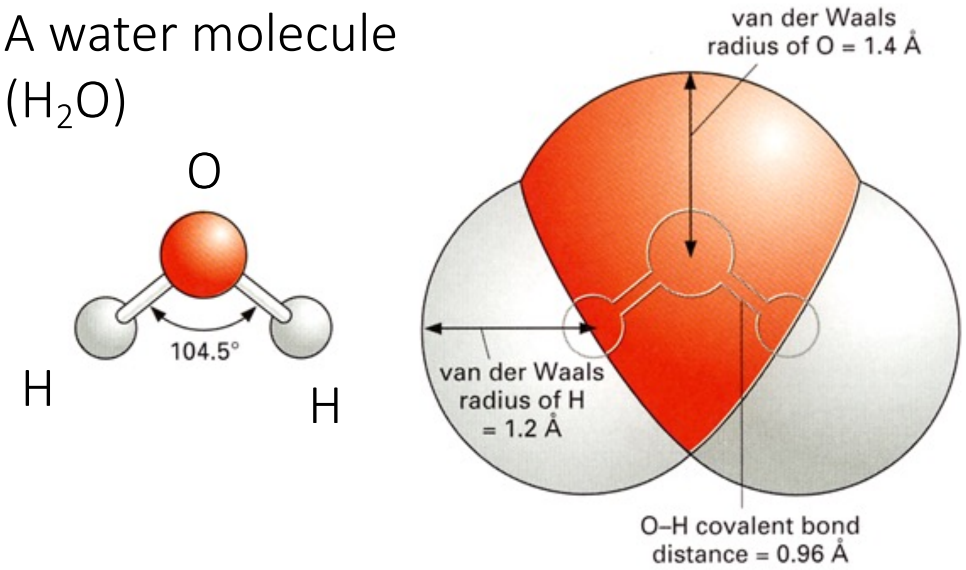
Covalent bonds

Covalent bonds are what hold "molecules" together

- strong (200-800 kJ/mol) ⇨ compare with RT~2.6 kJ/mol at 37º
- have well defined lengths
- have well defined directions

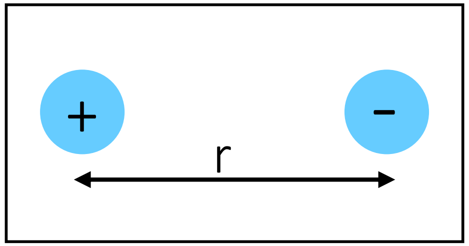
377 kJ/mol—0.15 nm bond length

A water molecule (H_2O)



The Coulomb potential

ion-ion interactions



$$U = \frac{Q_1 Q_2}{4\pi\varepsilon_0\varepsilon_r \mathbf{r}}$$

50-350 kJ/mol

ε_r Characterizes the response of the surrounding medium to an electric field: depends on how easily the molecules are polarized

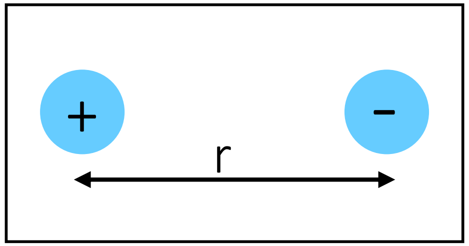
Water has a large value of ε_r (about 80). It counteracts the electric field (water mol. are highly polarizable, easily rotate)

The force between Na^+ and Cl^- at 3 Å distance in water is small, 1.3 kcal/mol ≈ 2RT. Therefore NaCl in water is dissociated and dissolved . Statistical mechanics is used to describe ion distribution in solution

1 kcal/mol = 4.2 kJ/mol = 0.043 eV

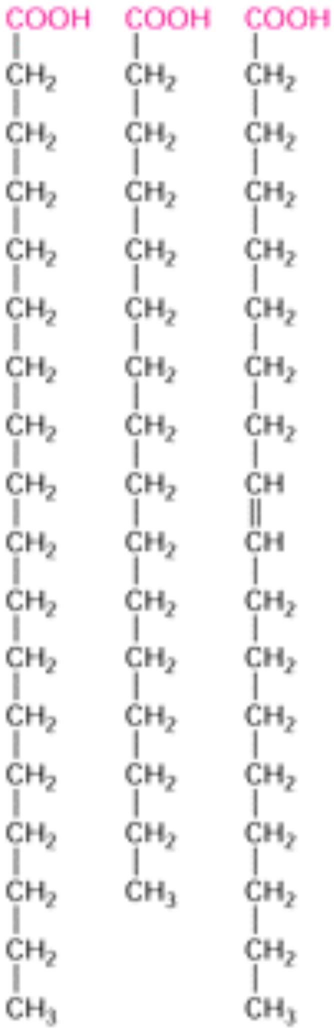
The Coulomb potential

ion-ion
interactions



$$U = \frac{Q_1 Q_2}{4\pi\varepsilon_0\varepsilon_r \mathbf{r}}$$

50-350 kJ/mol



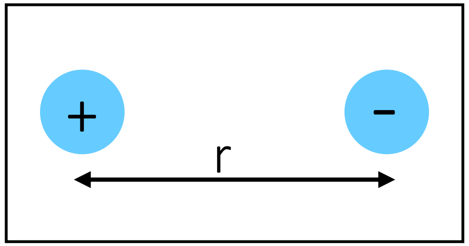
characterizes the response of the surrounding medium to an electric field: depends on how easily the molecules are polarized

Hydrocarbons have ε_r of 2: the hydrophobic core of proteins and membranes experiences strong electrostatic interactions

1 kcal/mol = 4.2 kJ/mol = 0.043 eV

The Coulomb potential

ion-ion interactions



$$U = \frac{Q_1 Q_2}{4\pi\varepsilon_0\varepsilon_r \mathbf{r}}$$

50-350 kJ/mol

The electric potential in a non-homogeneous system should be derived by solving Poisson (or Laplace) equations with the boundary conditions of the specific system. Numerical solutions are often necessary. Too complicated.

Termodynamically speaking, electrostatic interactions including H-bonds, are usually considered as enthalpic terms of the system energy, while hydrophobic interactions the entropic one.
When examined better, it appears that the Coulomb potential energy in water is an entropy driven force

1 kcal/mol = 4.2 kJ/mol = 0.043 eV

Electrostatic self-energy

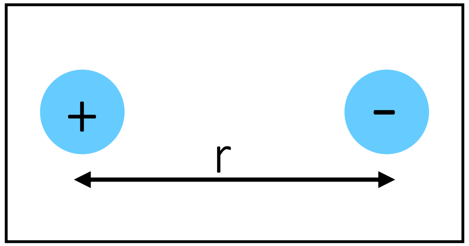
$$G = \frac{1}{\varepsilon_r r}\int_0^q q'dq' = q2/2\varepsilon_r r$$

Is the self-energy of a charge, or the energy of placing an ion in a dielectric medium (calculated from the work done to bring an increment dq’ on the surface of a sphere with radius r and charge q’)

For water, it is the **hydration energy**.
To transfer a Na^+ ion with r = 0.95 Å from water to an hydrocarbon medium (ε goes from 80 to 2), the work necessary is of 85 kcal/mol.
In fact inorganic ions are generally insoluble in organic solvents.
It is difficult to move an ion inside a protein of a lipid bilayer!
Ions are always attracted towards the region with higher ε

Multipole interactions

ion-ion interactions



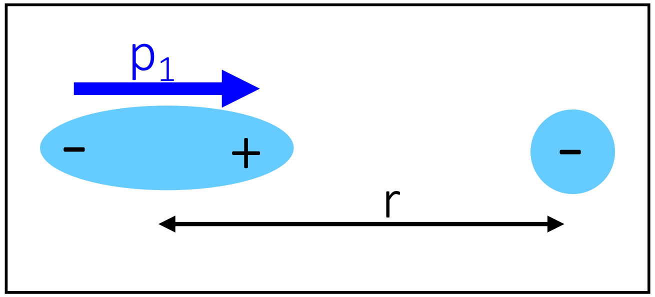
$$\frac{Q_1 Q_2}{4\pi\varepsilon_0\varepsilon_r \mathbf{r}}$$

50-350 kJ/mol

Even in neutral molecules, dipoles result from the unequal distribution of e^- due to differences in electronegativity between atoms.

335 kJ/mol—0.25 nm bond length
Becomes 12.6 kJ/mol in water!!

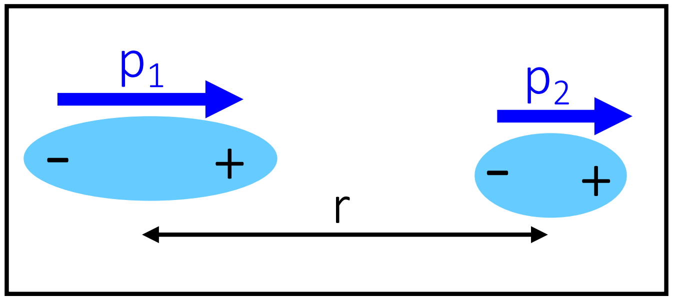
ion-dipole interactions



$$\frac{Q_1 p_1}{4\pi\varepsilon_0\varepsilon_r \mathbf{r}^2}$$

1-50 kJ/mol

dipole-dipole interactions



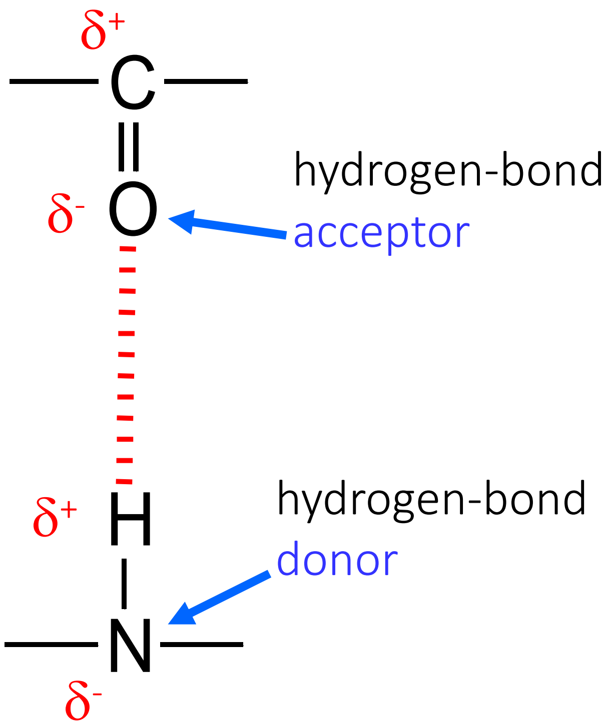
$$\frac{p_1 p_2}{4\pi\varepsilon_0\varepsilon_r \mathbf{r}^3}$$

0.1-10 kJ/mol

Hydrogen bond

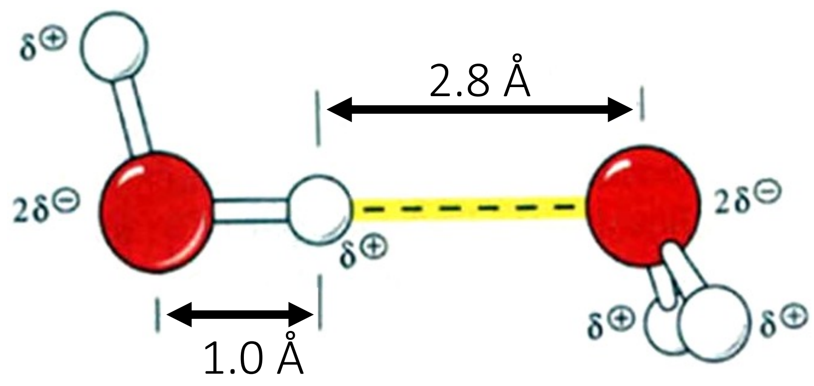
Hydrogen bonds are a particular case of a dipole-dipole interaction, unusually strong because the small size of the H atom allows the dipoles to come close to each other (~15-30 kJ/mol)

17 kJ/mol—**0.30 nm** bond length
Becomes 4.2 kJ/mol in water!!



Donors and acceptors must be electronegative atoms (O, N)

Hydrogen bonding in water:

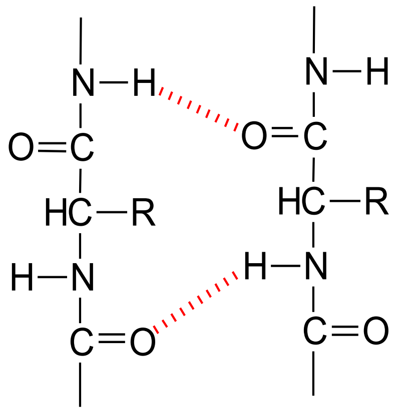


Hydrogen bonds have a defined lenght and orientation

Hydrogen bonds in biology

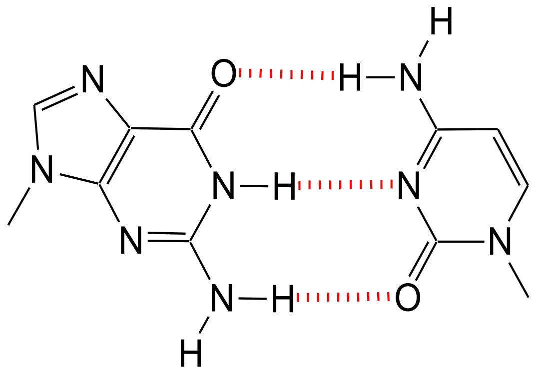
Hydrogen bonding interactions play a fundamental role in determining both the conformation of biological macromolecules and their interactions with other molecules.

The 3D structures of proteins are stabilized by hydrogen bonds between main-chain amide groups:



protein secondary structure: a β-sheet

The pairing of the bases in DNA is mediated by H-bonds:



Guanine-Cytosine base pair

Induction forces

Ions and dipoles can polarise the electron cloud of an adjacent molecule. This causes an attractive force between the ion/permanent dipole and the induced dipole.

Interaction proportional to
- r^{-4} for ion-induced dipole
- r^{-6} for permanent dipole/induced dipole interactions

Dispersion forces

Random fluctuations of the electron clouds cause temporary dipoles even in uncharged molecules; these temporary dipoles will induce dipoles in the adjacent molecules causing a weak attractive force (He liquefies at 4K).

Van der Waals attractive forces!

0.4 kJ/mol—0.35 nm bond length
Does not change in water!!

Dispersion forces

Fluctuactions of transient dipole moments can be attractive or repulsive. The attractive configurations have a lower potential E than the repulsive ones, meaning have larger weights in Boltzmann average and therefore a net attraction.

The fluctuactions in the electronic structure responsible for the transient dipole moments are much faster than molecular rotation in liquids. Therefore such forces are not dependent on the specific medium.

Hydrophobic forces

Hydrophobic forces are very relevant in biology. They are primarily driven by an energy cost of creating hydrocarbon-water contact.
There is a reduction of entropy of water close of a hydrophobic surface: water becomes structured, even ice-like. It restricts the possible orientations close to the surface and decrease entropy.

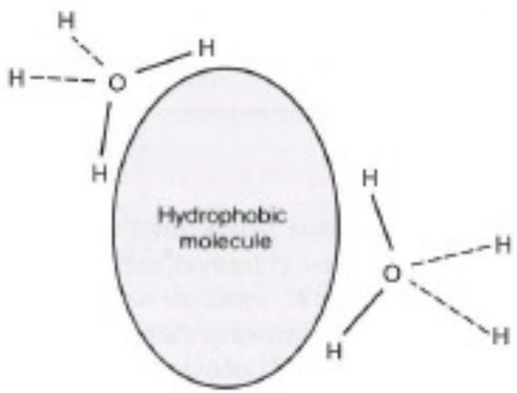


Fig 2.7 Water molecules adjacent to a hydrophobic molecule suffer restrictions in orientation as they form hydrogen bonds with other water molecules.

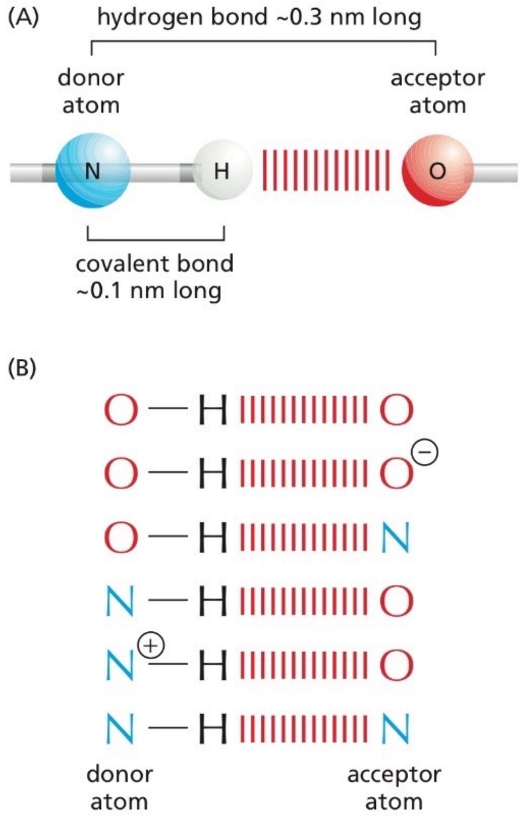


Figure 2–4 Hydrogen bonds. (A) Ball-and-stick model of a typical hydrogen bond. The distance between the hydrogen and the oxygen atom here is less than the sum of their van der Waals radii, indicating a partial sharing of electrons. (B) The most common hydrogen bonds in cells.

TABLE 2–1 Covalent and Noncovalent Chemical Bonds

Bond type		Length (nm)	Strength kJ/mole**	
			in vacuum	in water
Covalent		0.15	377 (90)	377 (90)
Noncovalent	ionic*	0.25	335 (80)	12.6 (3)
	hydrogen	0.30	16.7 (4)	4.2 (1)
	van der Waals attraction (per atom)	0.35	0.4 (0.1)	0.4 (0.1)

*An ionic bond is an electrostatic attraction between two fully charged atoms. **Values in parentheses are kcal/mole. 1 kJ = 0.239 kcal and 1 kcal = 4.18 kJ.

Classes of biological molecules

From a chemical point of view biological molecules can be divided into four classes:

- carbohydrates
- lipids
- amino acids (building blocks of proteins)
- nucleotides (building blocks of nucleic acids,
  i.e. DNA and RNA)

Protein architecture

Secondary structure

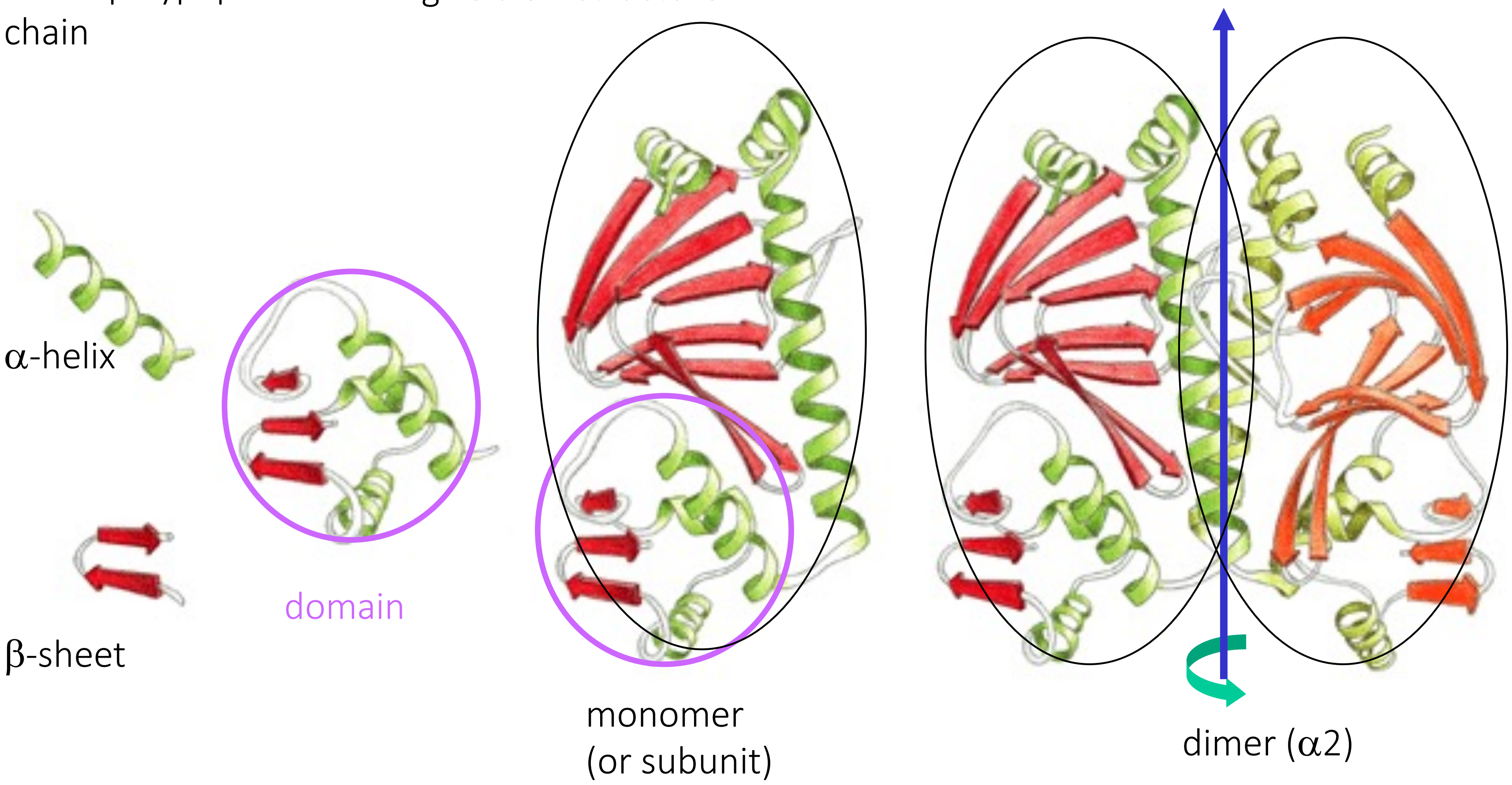
local organisation of the polypeptide chain

Tertiary structure

how the secondary structure elements pack together to give a 3D structure

Quaternary structure

the number and relative position of the subunits in a multimeric protein



Carbohydrates in biology

- Carbohydrates serve as energy stores
- Carbohydrates have a structural role
- Carbohydrates can be linked to proteins and lipids
- Ribose and deoxyribose sugars form part of RNA and DNA (will see this when we study nucleic acids)

3 classes of carbohydrates:

monosaccharides – simple sugars such as glucose

oligosaccharides – often disaccharides such as sucrose

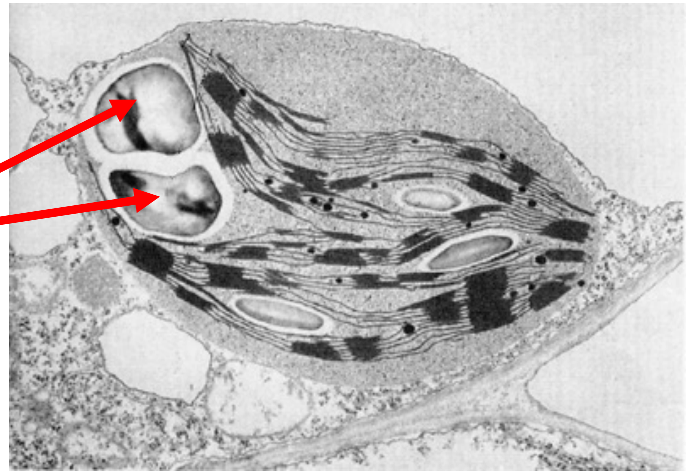
polysaccharides – cellulose, glycogen, starch.

The word saccharide from Greek sakcharon (σάκχαρο) meaning sugar.

Carbohydrates are used as energy stores

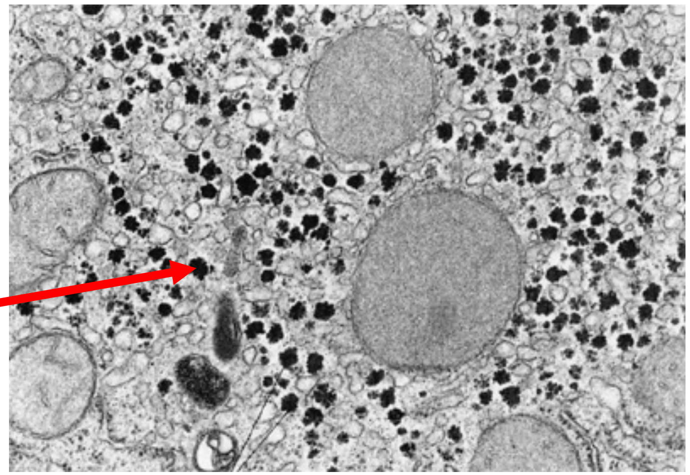
Plants store glucose in the form of starch.
Starch is a polymer of glucose subunits.

starch granules
in plant cell



Animals store glucose in muscle and the liver as glycogen – a polymer of glucose – but with more branches than starch.

glycogen granules
in liver cell (black spots)



Carbohydrates have a structural role

Cellulose – structural polysaccharide of plants – extremely abundant. Unbranched polymer of glucose – linkage between glucose subunits differs from that of starch.

Animals such as cattle and insects such as termites do not produce a cellulase to break down cellulose and instead rely on a symbiotic relationship with bacteria or protozoa.

Chitin – structural polysaccharide in the exoskeletons of insects and shellfish. Similar to cellulose – but glucose moieties are slightly modified.

Carbohydrates and sugars

Carbohydrates – literally "hydrates of carbon":

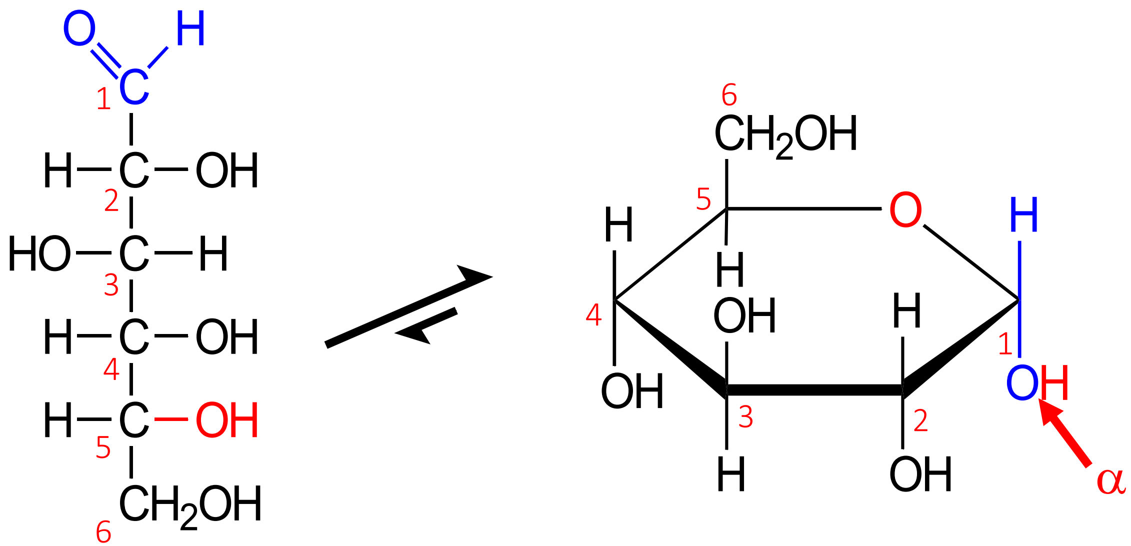
can be written as $C_n(H_2O)_n$ or $(CH_2O)_n$

Glucose is $(CH_2O)_6$

Carbon compounds with multiple hydroxyl groups:
most commons are n=5 (pentoses) and n=6 (hexoses)

When n≥5 the linear form of the sugar can close up forming a ring structure

Glucose solution < 1% in open chain form



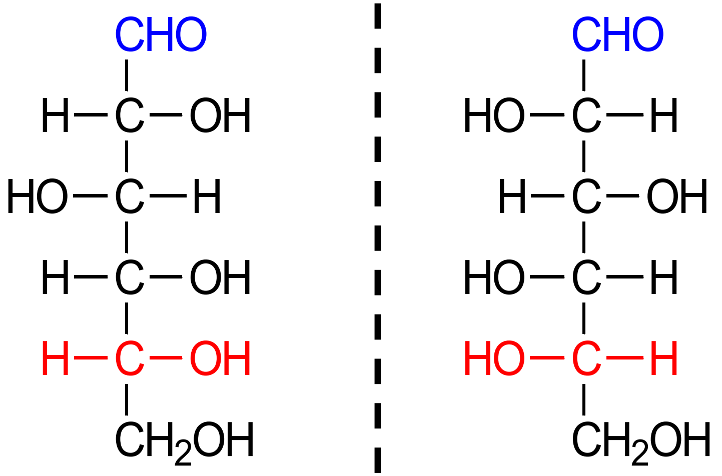
D-Glucose

α-D-Glucopyranose

D- and L-sugars

When one molecule is exactly the mirror image of another molecules, we have two different “enantiomers” of the same sugar (called D- and L-)

- have the same chemistry
- rotate polarised light in opposite directions
- may have different biological properties



D-Glucose L-Glucose

D-Glucose and L-Glucose are mirror images of each other - enantiomers.

Most of the common monosaccharides in biology are D-sugars

Almost each carbon is asymmetric:

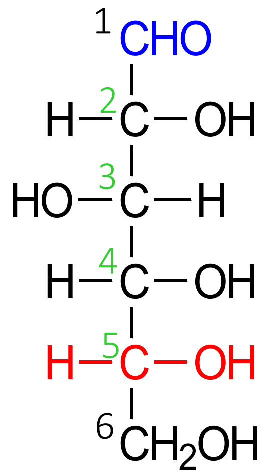
Isomers of D-glucose:

D-aldoses with 6 carbons (hexoses)

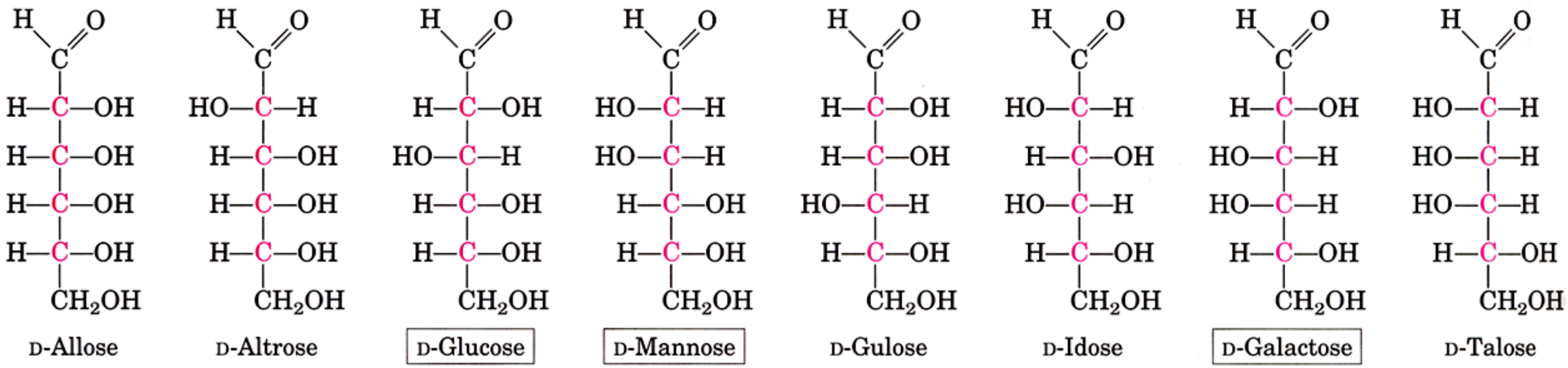
4 asymmetric carbon atoms (2, 3, 4, 5)

2^4 = 16 possible isomers

8 D/L pairs – 8 different names

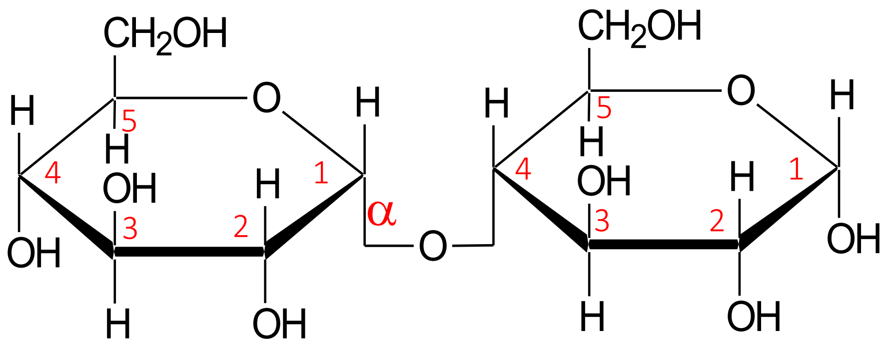


Each different configuration (isomer) is a different sugar:



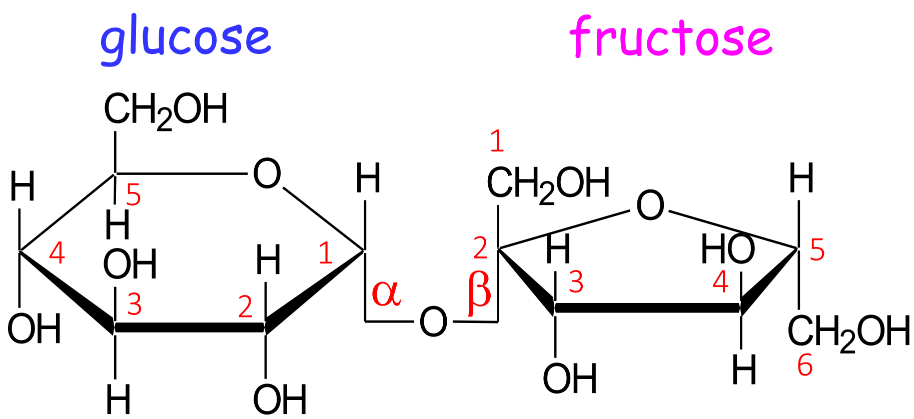
Disaccharides

Maltose consists of 2 glucose units joined by an O-glycosidic bond:



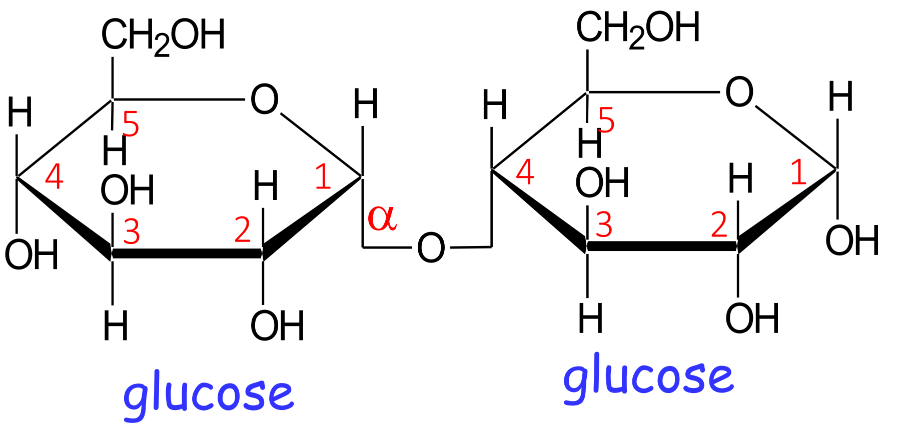
linkage α(1→4)α

Sucrose is a disaccharide containing glucose and fructose subunits:



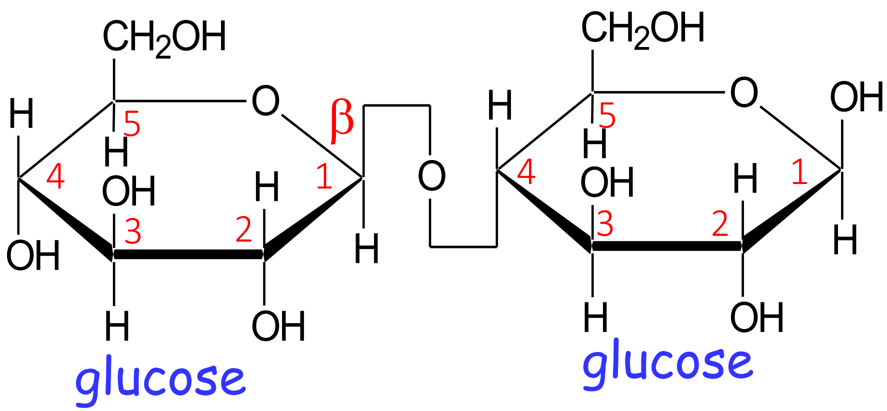
linkage α(1→2)β

Polysaccharides: starch and cellulose



Starch contains α-1,4 linkages

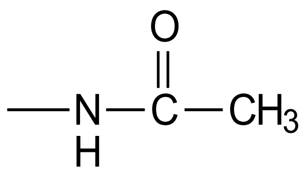
(only two units shown – actually 1000s)



Cellulose contains β-1,4 linkages

Cotton is almost pure cellulose

In chitin the 2'-OH is replaced by:



Proteins and sugars

Glycoproteins are proteins with oligosaccharides covalently linked to the protein side chains. Proteins that are secreted from the cell often have sugars attached to them.

Proteoglycans are macromolecules of the cell surface and extracellular matrix which contain some protein and large amounts of carbohydrate (cartilage).

Carbohydrates are attached to glycoproteins and lipids on the surface of red blood cells. Different blood groups (A,B and O) result from different glycosylation patterns.

Bacterial cell walls contain a network of short peptides and sugar moieties.

Lipids

Water insoluble compounds (soluble in organic solvents)

Biological role:

- energy supply
- energy store
- components of cellular and organelle membranes

Fatty acids and triacyglycerols

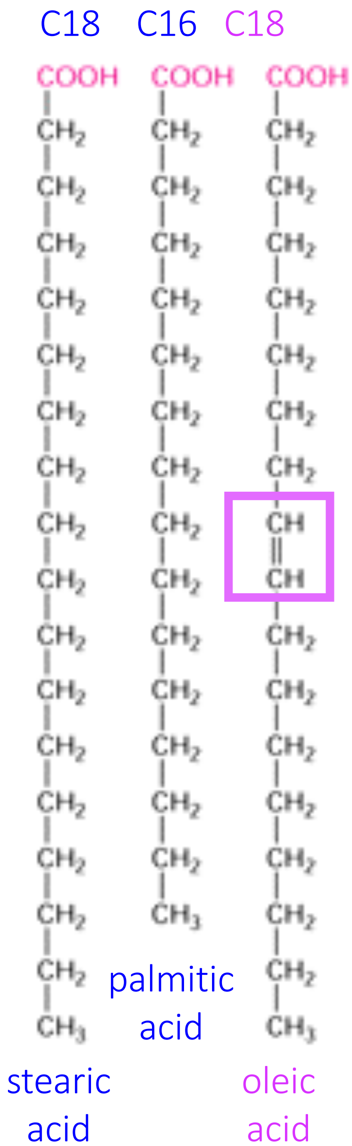
Phospholipids

Steroids and cholesterol

Cell membranes

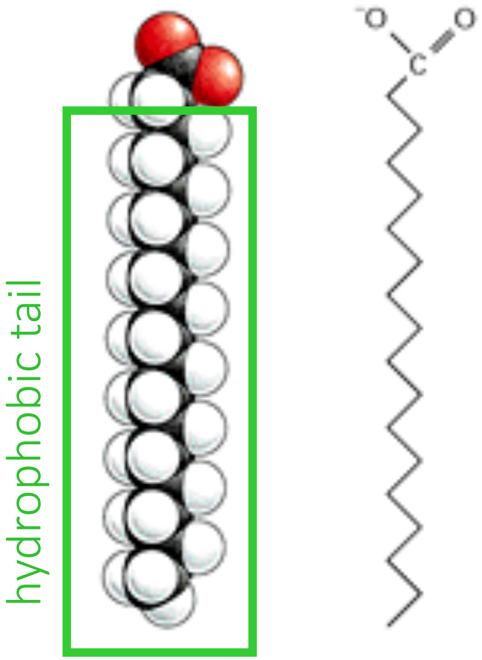
Fatty acids

Carboxylic acids with long hydrocarbon chains (12-24 -CH_2- units)

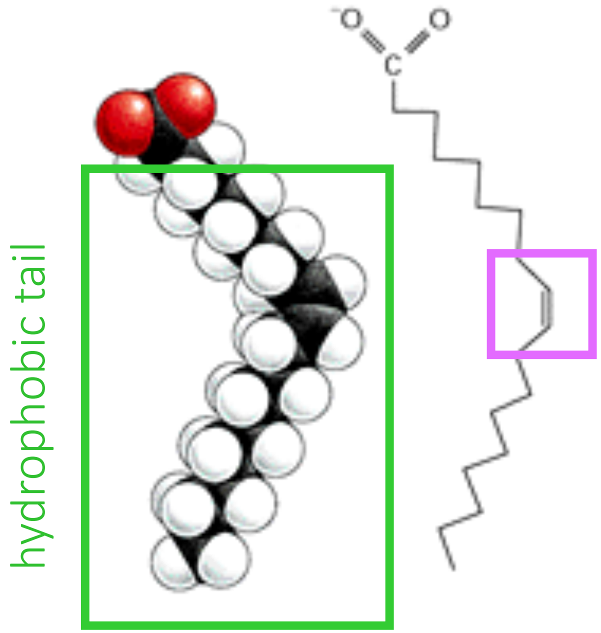


Some have one or more double bonds and are called unsaturated. The double bond is rigid and creates a kink in the chain; the rest of the chain is free to rotate

Stearic acid - saturated



Oleic acid - unsaturated



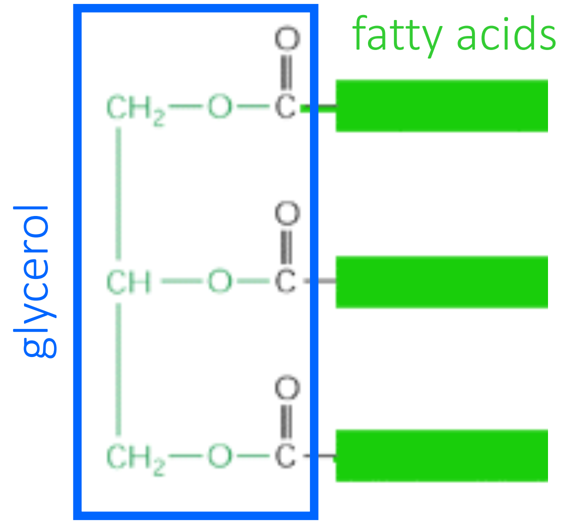
Fatty acids are used as E storage

To ensure a continuous supply of fuel for oxidative metabolism, animal cells store glucose in the form of glycogen and fatty acids in the form of fats.

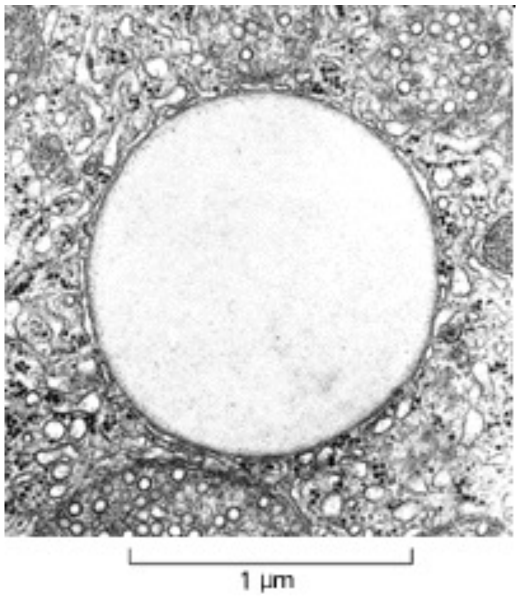
A fat molecule is composed of three molecules of fatty acid linked to glycerol: triacylglycerols (triglycerides).

Fat is a far more important storage form than glycogen, because its oxidation releases more than six times as much energy.

Triglycerides have no charge and are virtually insoluble in water, coalescing into droplets in the cytosol of adipose cells.

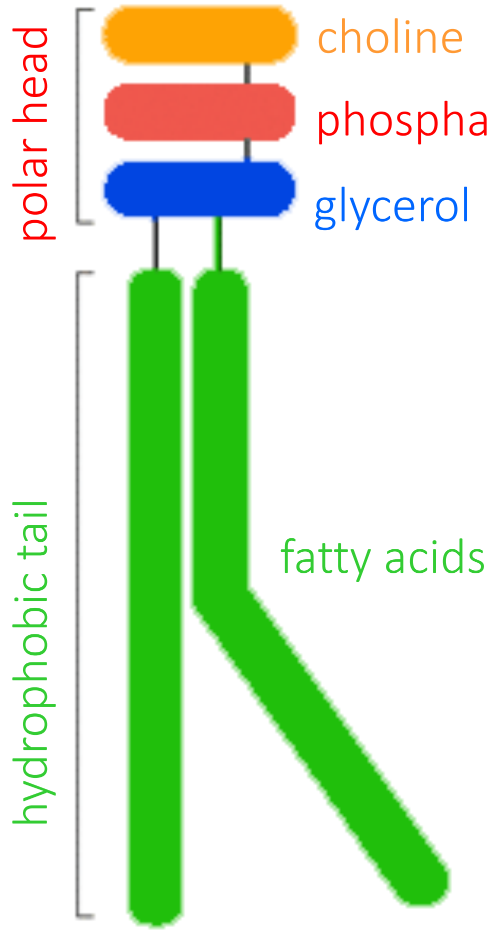


fat droplet

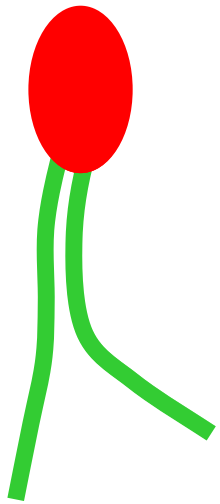


Phospholipids

In phospholipids, two of the OH groups of glycerol are linked to fatty acids, while the third is linked to a phosphate group, which can be further linked to a polar group such as choline, serine, inositol, etc...



Very asymmetric molecule:
- hydrophilic HEAD
- hydrophobic TAIL



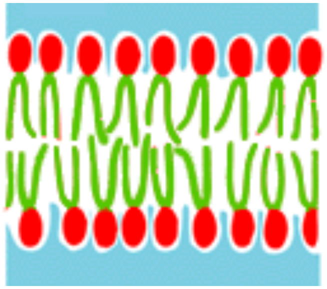
Phospholipids and membranes

Phospholipids are the major constituent of cell membranes.

When in aqueous environment the heads have affinity for the water molecules, while the tails tend to avoid water by sticking together.

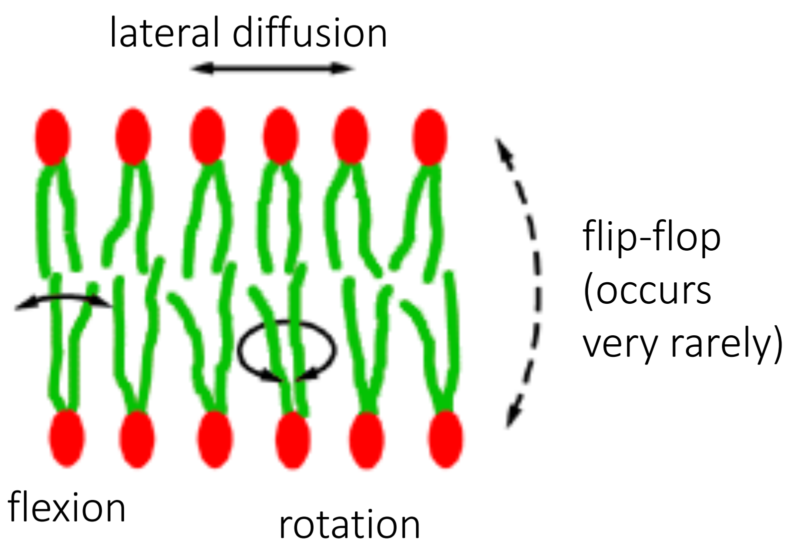
Cellular membranes are essentially made up by phospholipid bilayers.

micelle

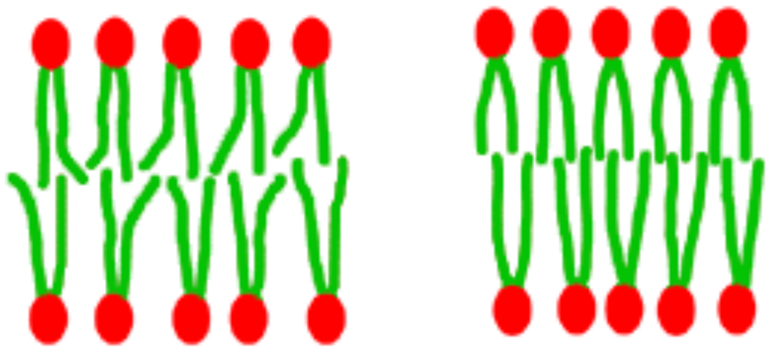


lipid bilayer

Phospholipid mobility



Saturated vs unsaturated lipids

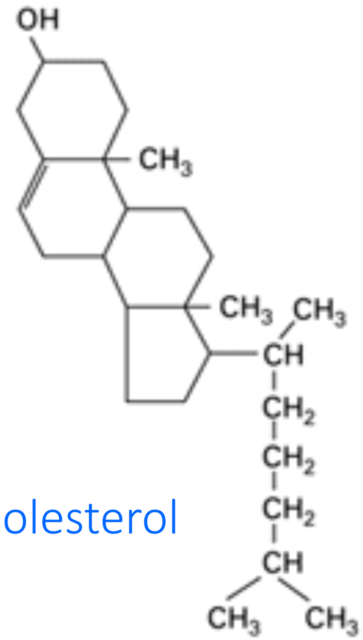


unsaturated, more difficult to pack, more fluid

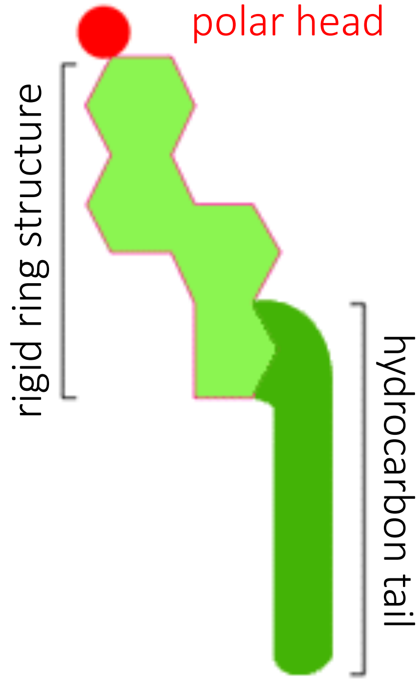
saturated, easier to pack, less fluid

Cholesterol and steroids

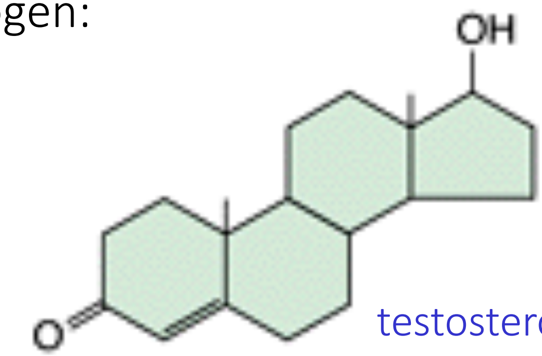
Steroids (such as cholesterol) have a rigid structure made up by 4 rings.



Cholesterol

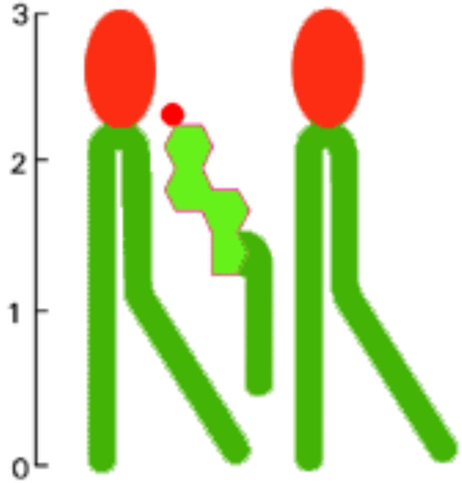


Other important steroid are the sex hormones, such as testosterone and estrogen:



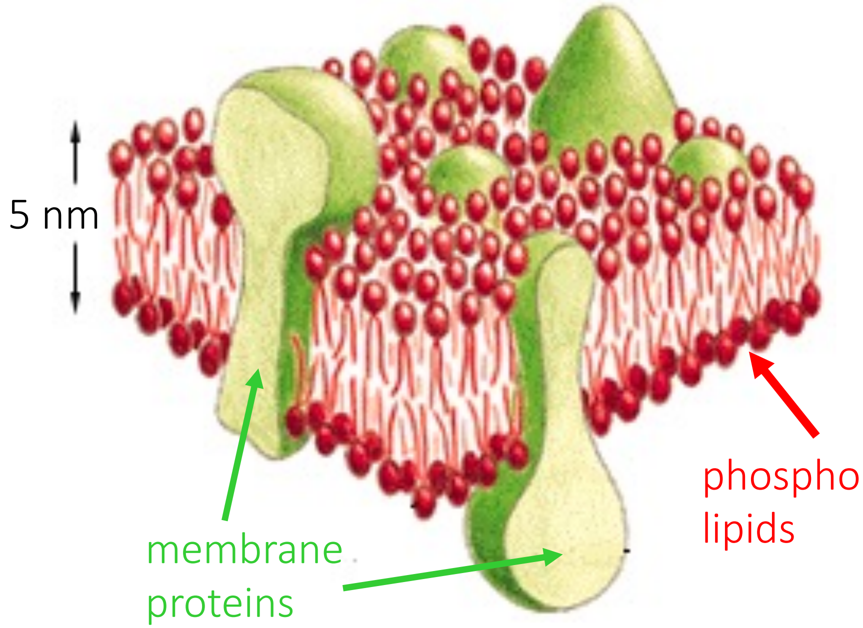
testosterone

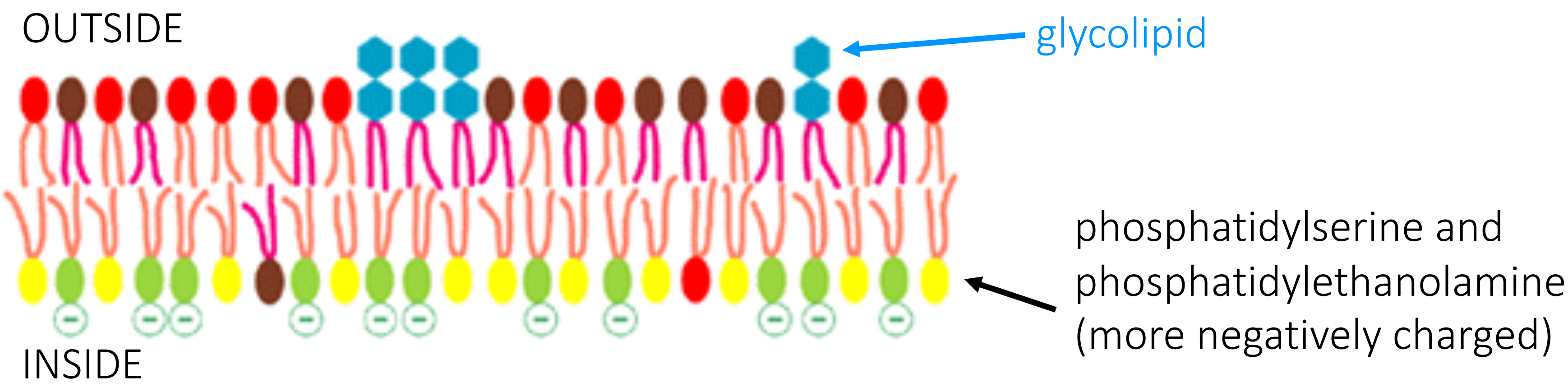
Cholesterol is an important component of the eukaryotic membranes and has a key role in controlling the membrane fluidity.



Cell membranes

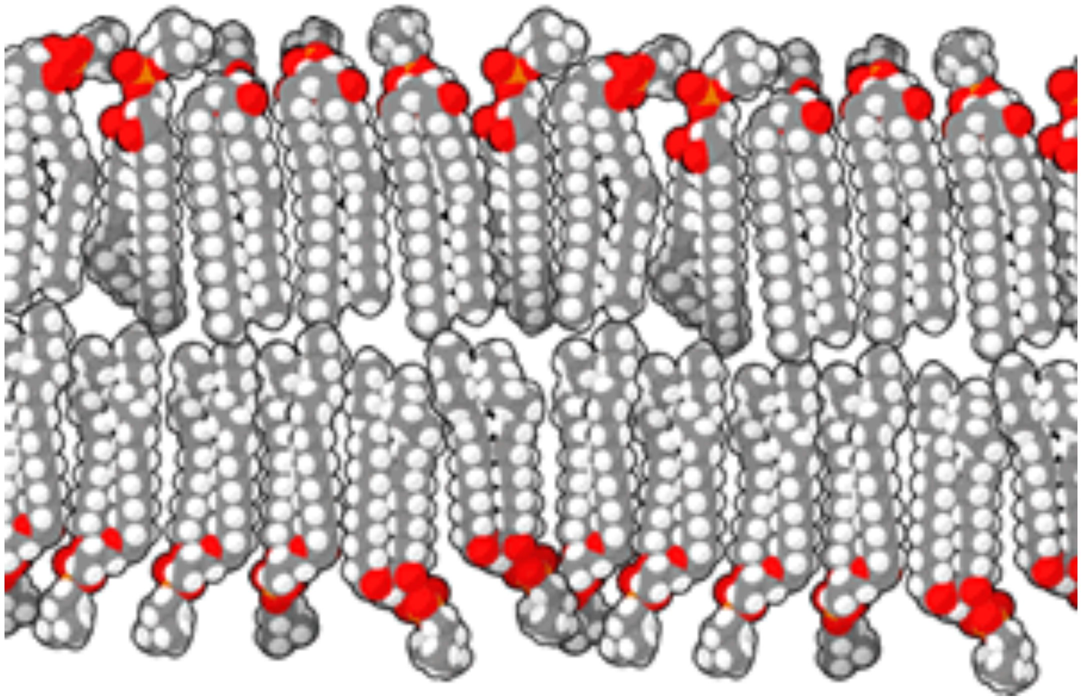
- biological membranes are fluid
- the fluidity is controlled by the % of saturated/unsaturated fatty acid and the % of cholesterol
- membranes are impermeable to ions and most polar molecules (H_2O is actively transported in)
- many proteins are embedded in the membrane
- the membrane is highly asymmetric



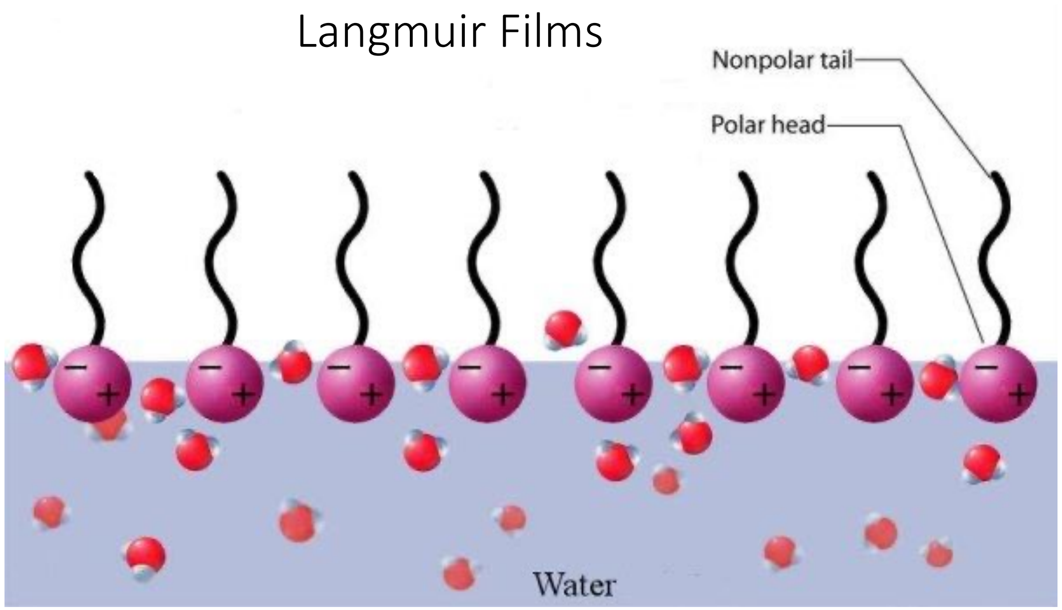


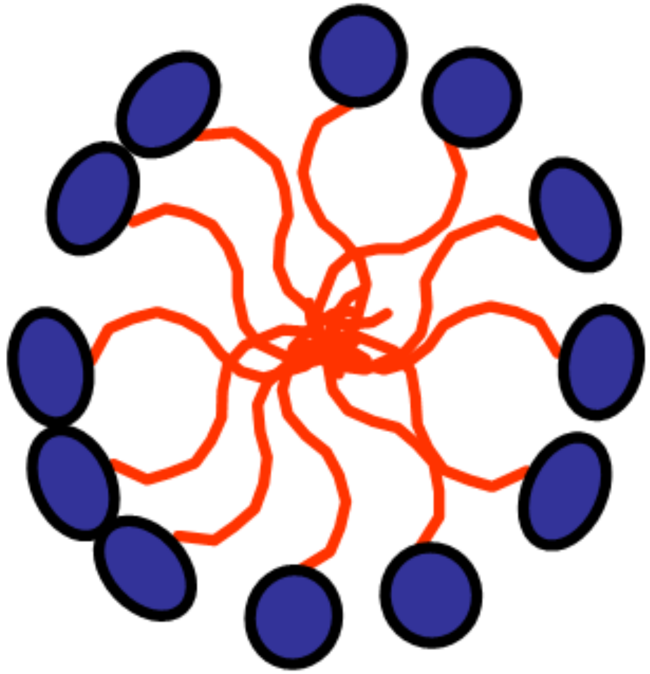
Self-assembly

Membranes are made of strongly anisotropic molecules
Strongly anisotropic molecules like to self-organizing



1-Self-organized monolayers (on liquid surfaces)

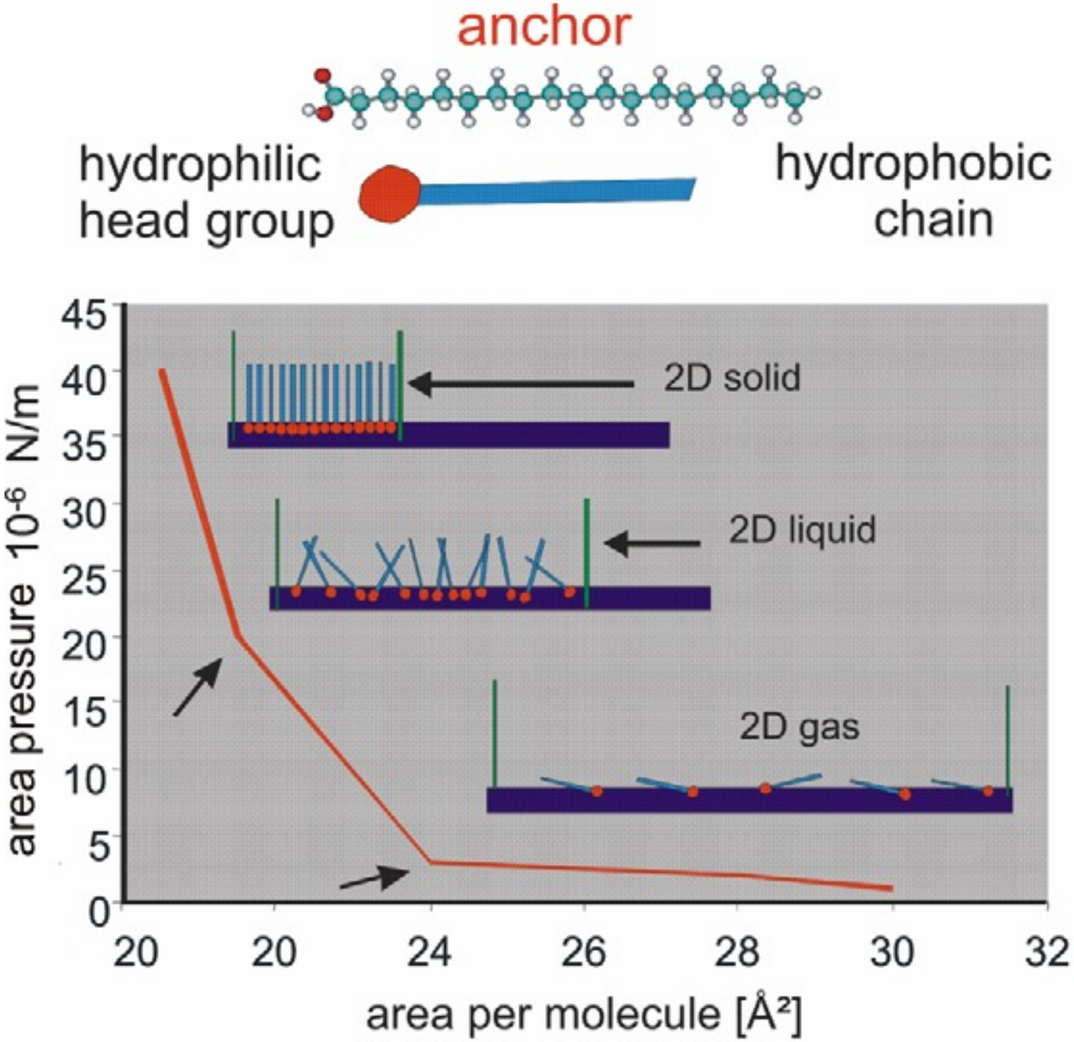


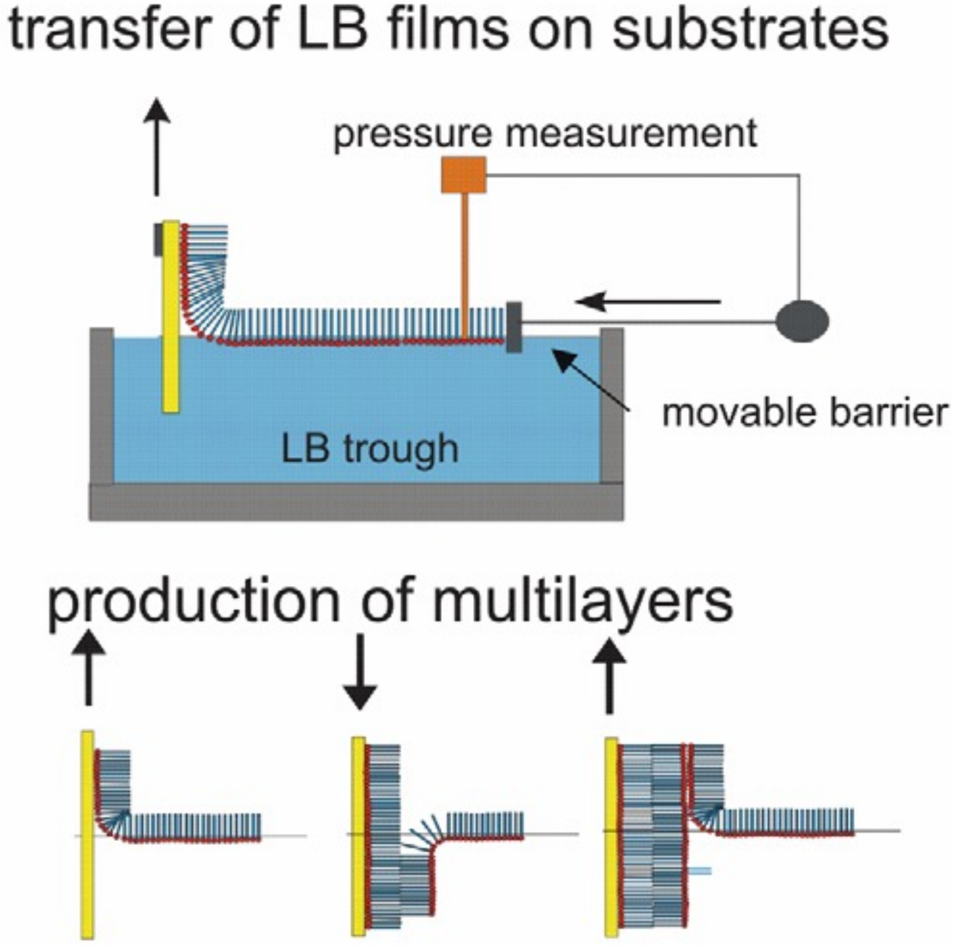


The term ‘‘molecular self-assembly” refers to spontaneous formation of an ordered molecular overlayer on the surface, often proceeding through several consecutive stages where 1D and 2D ordered structures can also exist.

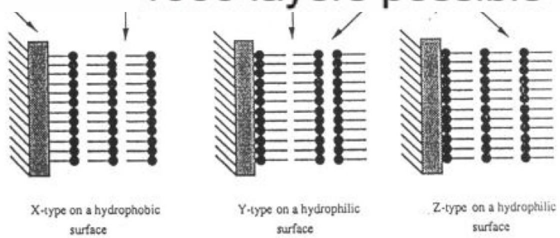
Thermodynamically, molecular self-assembly proceeds toward the state of lower entropy , and must therefore be compensated by a sufficient decrease of enthalpy due to intermolecular and molecule-surface interactions.

2-Self-organized monolayers (on solid surfaces)



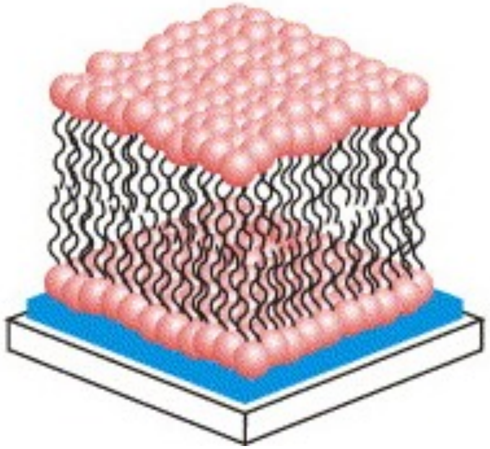


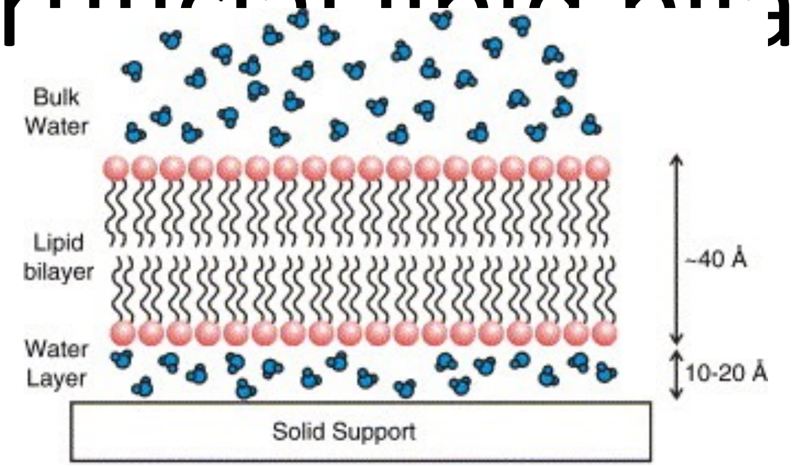
>1000 layers possible



Progress in Surface Science 84 (2009) 230–278

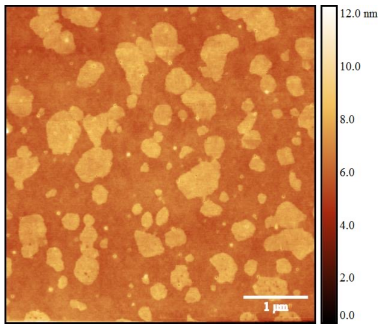
Artificial lipid bilayers



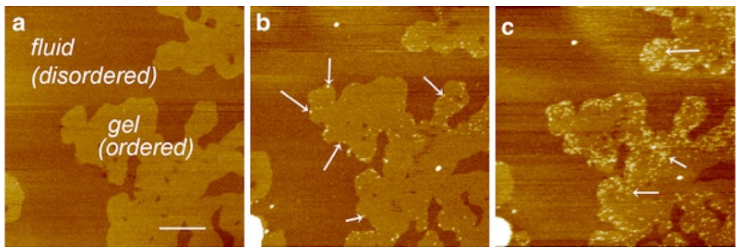


✓ **Multicomponent model membranes for mimicking cellular membranes**

Lipids behaviour

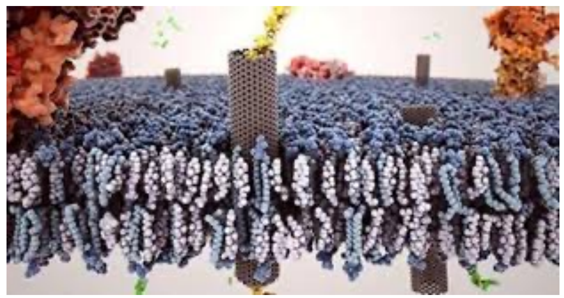


Protein-lipid interactions



Alessandrini, Facci. *J Mol Recognit*. 2011;24(3):387-96.

Carbon nanotubes interactions



Summary

The cell theory - organisation of the cell - prokaryotic and eukaryotic cells.

Gram positive and Gram negative bacteria - archaea and the evolution of life - eukaryotic cells and specialised organelles - the mitochondrion and energy production - the evolution of eukaryotic cells.

Covalent and non-covalent interactions - the hydrogen bond

Acids and bases - dissociation of water - pH

Biological molecules - small molecules - macromolecules - classification

Carbohydrates - biological roles - monosaccharides - D and L sugars - disaccharides - polysaccharides

Lipids - fatty acids and triacylglycerols - phospholipids and membranes - steroids - organisation of cell membranes