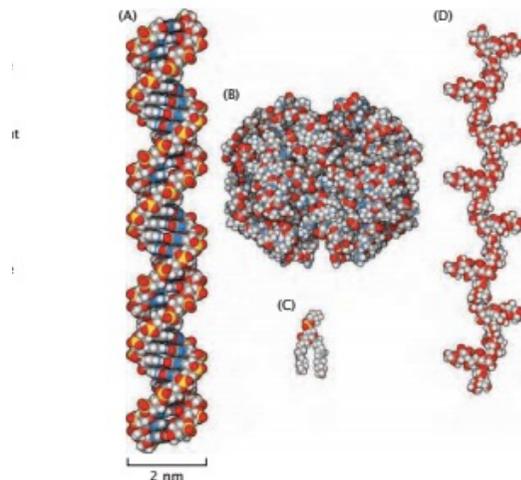


Corso di Biofisica Sperimentale

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The course will be largely devoted to explore the diversity present in biological systems and its **complexity** by analyzing the **function** and **physical properties** associated to the organization of complex (macro)molecular systems .

The large-scale goal being of understanding how the special properties of life may emerge from **fundamental physical and chemical interactions**.



- (A) Atomic structure of a small fragment of the **nucleic acid** DNA in the B form
- (B) atomic structure of the oxygen-carrying **protein** hemoglobin (PDB 1hho)
- (C) phosphatidylcholine **lipid** molecule from a cell membrane
- (D) branched complex **carbohydrate**

What is biophysics?

- Physics provides the laws that govern energy, forces, and interactions.
- Biology brings complex living systems that exhibit self-organization, adaptability, and life processes.
- Biophysics merges these, aiming to explain biological phenomena in terms of physical principles.

Biophysics is the field that applies the theories and methods of physics to understand how biological systems work, i.e. the mechanisms of:

- how the **molecules of life** are made
- how **different parts of a cell** move and function
- how **complex systems in our bodies**—the brain, circulation, immune system, and others— work. (ref. Biophysical Society)

Great scientific challenge not only to understand how its pieces work but also **how the whole is organized internally to achieve specific functional advantages.**

What is biophysics?

Biophysics is the field that applies the theories and methods of physics to understand how biological systems work

Our quest to understand biology using physical laws and engineering principles is greatly aided by the rapid development of sophisticated experimental techniques that physics and technology has supplied for the use by biologists.

Biophysics Exp. techniques

- Light microscope (resolution: 400–600 nm) with various modern upgrades such as confocal, phase contrast, or cryomicroscopy.
- Electron microscope (10–100 nm)
- Neutron scattering (1–10 Å)
- X-ray crystallography (1 Å)
- Patch clamp electrophysiology
- STM, AFM, TEM
- NMR, MRI, fMRI
- Fluorescence spectroscopy
- Microwave absorption
- Laser light scattering
- Synchrotron radiation scattering
- Laser tweezers, etc.

Biophysics core fields

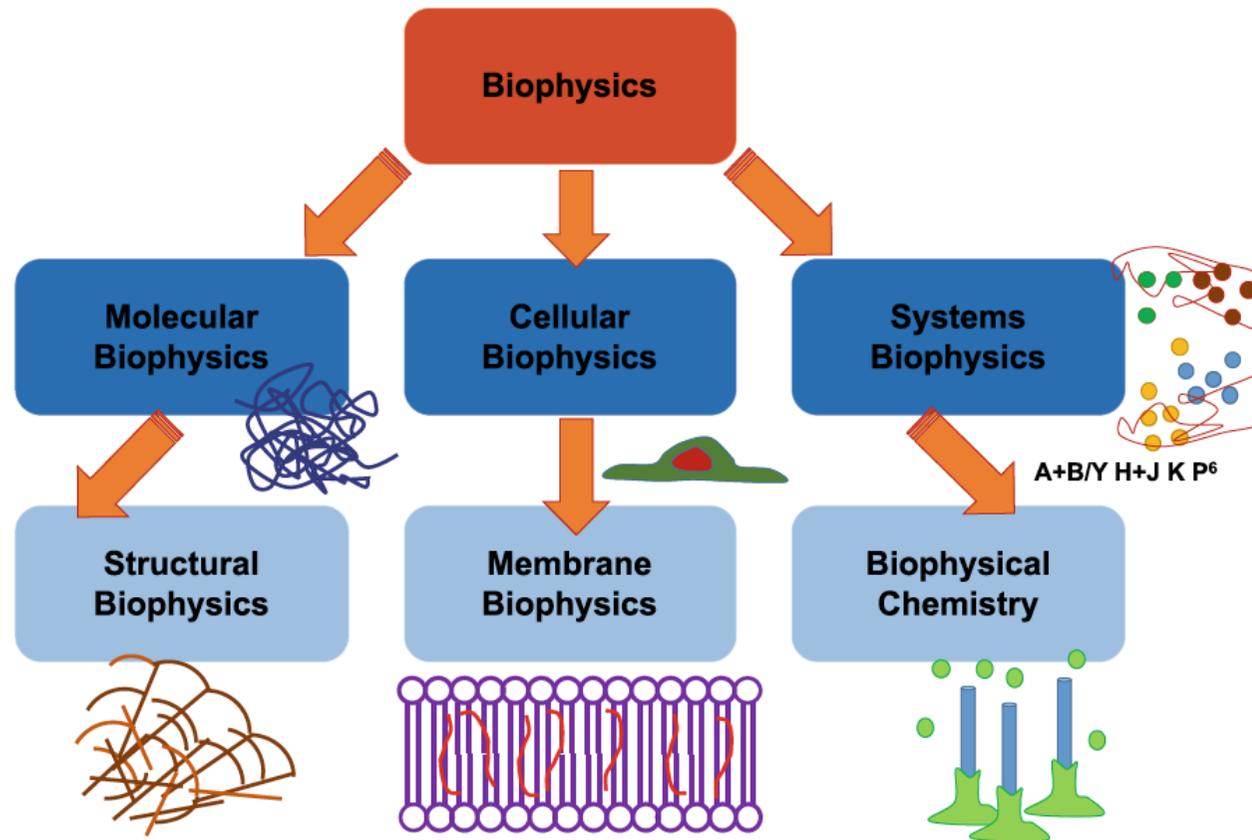


Fig. 1.5 Biophysics or biological physics is divided into at least these three main parts. These subdisciplines may be highly related and partly intertwined

Biophysics core fields

Deutsche Gesellschaft für Biophysik e.V.

Section I

Molecular Biophysics



Section II

Membrane Biophysics



Section III

Cellular Biophysics



DGfB - Conferences

Molecular Biophysics Meeting 2024

[Read more](#)

News

16th Annual Symposium
Physics of Cancer Leipzig,

Job advertisements

Doctoral & Postdoctoral Positions in
Computational Membrane Biophysics in
Erlangen

Biophysics core fields

a. Molecular Biophysics (YES)

- Focus: Study of biological molecules like proteins, nucleic acids (DNA, RNA), and how they interact.
- Methods: Techniques like X-ray crystallography, NMR (Nuclear Magnetic Resonance), and cryo-electron microscopy are used to visualize molecular structures.
- Importance: Understanding how molecular machines, such as enzymes or ion channels, work inside cells.

b. Cellular Biophysics (YES)

- Focus: Understanding the physical principles behind cellular processes like membrane dynamics, energy production, and signaling.
- Methods: fluorescence microscopy, calcium imaging, AFM, cryoEM, optical tweezers, electrophysiology, etc..
- Example: The study of how the cytoskeleton provides mechanical support or the role of cell membrane in cell trafficking, or how cellular respiration occurs within mitochondria.

Section II - Membranes, Cells, and Networks

Membrane Biophysics

Biological membranes are the ubiquitous envelopes of cells and organelles and thus host the communication between cells and within networks.



They are composed of a complex mixture of lipids, embedded integral or peripheral membrane proteins, and carbohydrates. The elucidation of the structure and organization of biological membranes is a still growing research field and new techniques and methodologies have been developed to understand membrane structure and function. Because of the complexity of biological membranes, artificial model membranes are frequently applied for simplification. They include vesicular lipid bilayers, lipid nanodiscs, freestanding and supported planar lipid bilayers, lipid monolayers, and computational lipid bilayers.

The DGfB section “Membrane Biophysics” supports the strong German community contributing research on biological membranes and artificial membrane models in all levels of complexity and covering a wealth of methods and techniques. Our biannual international meetings have an open and informal character. They attract German and European biophysicists and researchers from related disciplines and help us to train, involve and integrate young academics.

The next meeting will be held in 2024 from May 06 to 08 at the Drübeck monastery close to the Harz Mountains. It will be entitled “From Model to Cellular Membranes”. Registration starts October 02, 2023.

[More Information](#)

Biophysics core fields

c. Systems Biophysics (NO)

- Focus: Examines how biological systems work as a whole, including neural networks, muscle contractions, and the immune system's behavior.
- Techniques: Mathematical modeling and computational simulations help describe complex biological networks.

d. Medical Biophysics

Focus: Application of biophysics to understand disease mechanisms and develop medical technologies.

- Examples: Magnetic Resonance Imaging (MRI) uses physics-based principles to image the body's internal structures non-invasively.

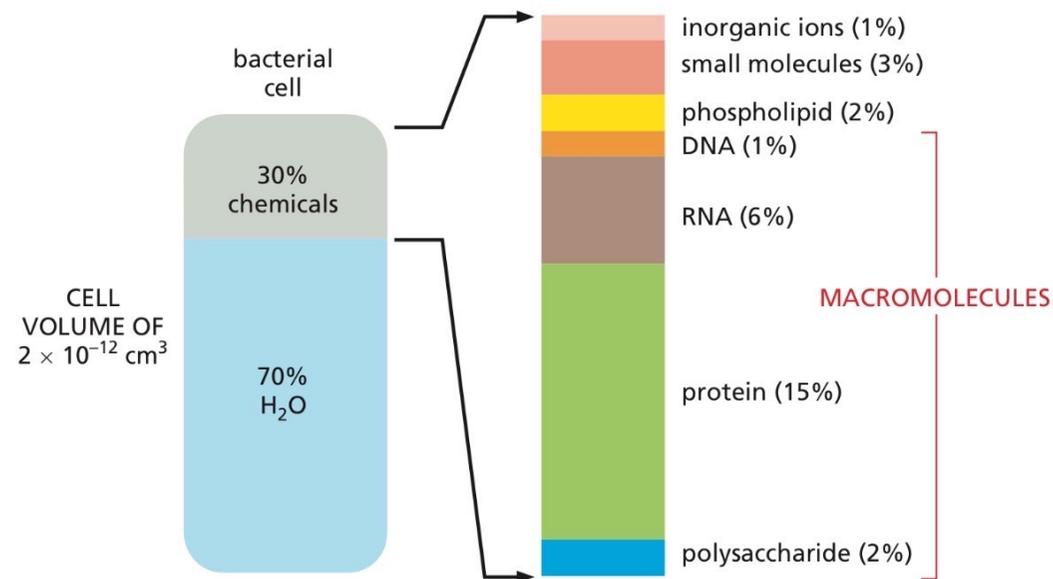
Il Premio Fermi 2024 (SIF) alla microscopia ottica in biologia



Il Premio Enrico Fermi della Società Italiana di Fisica per l'anno 2024 è stato assegnato congiuntamente ad Alberto Diaspro e a Francesco Saverio Pavone per le loro ricerche sperimentali nel campo della fisica applicata a sistemi biologici.

Inside the cell: macromolecules

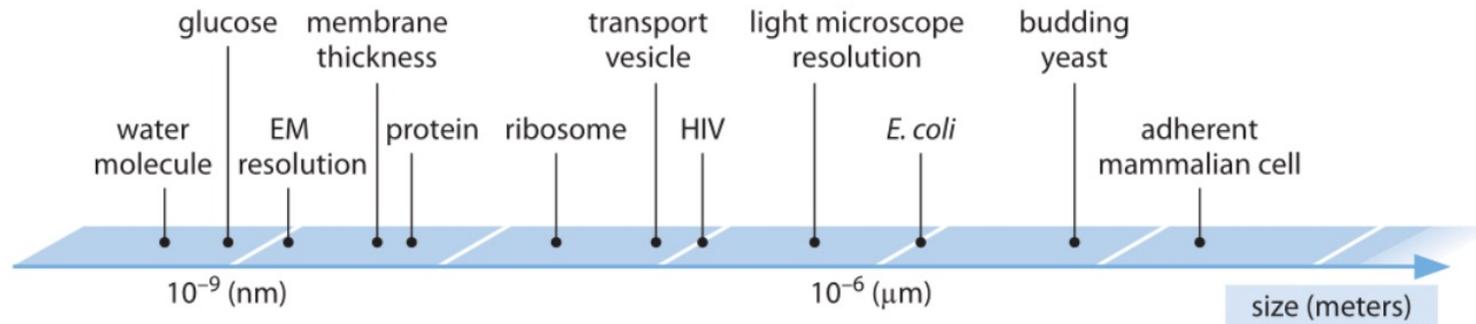
Many of the molecules that make up living organisms tend to be relatively large and structurally complex, and are hence called **macromolecules**. Living organisms also contain a large number of small, simple molecules that are critical to their function, ranging from water and metal ions to sugars such as glucose.



amount of total protein in some mammalian cells : one nanogram

Inside the cell: macromolecules

Many of the molecules that make up living organisms tend to be relatively large and structurally complex, and are hence called **macromolecules**. Living organisms also contain a large number of small, simple molecules that are critical to their function, ranging from water and metal ions to sugars such as glucose.



Biology spans 15 order of magnitude in length scale!

Central Dogma

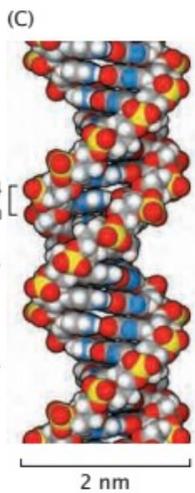
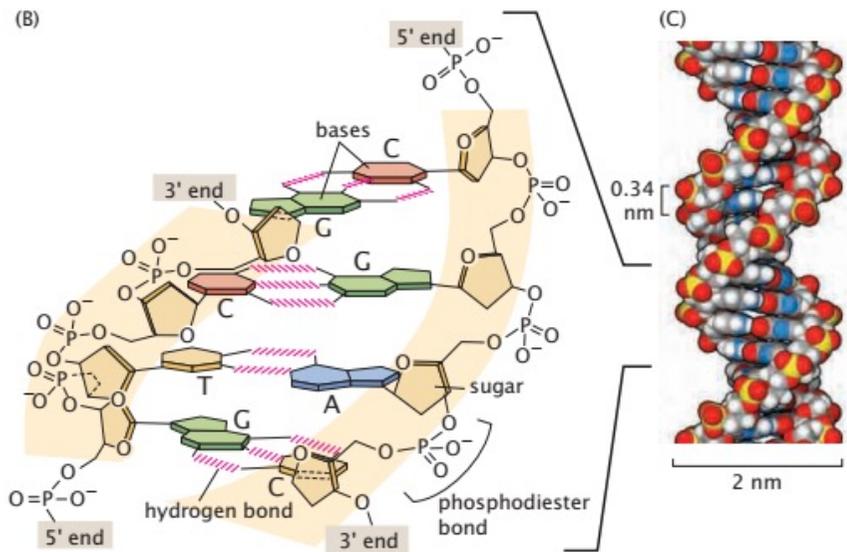
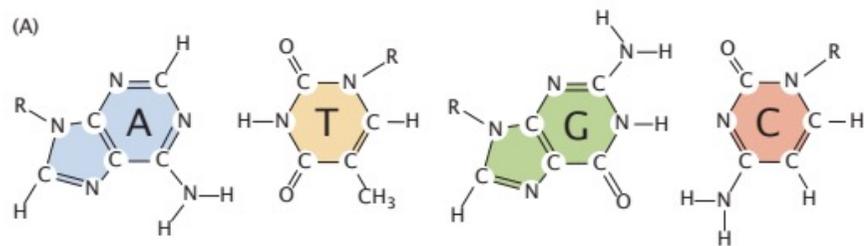
CENTRAL DOGMA OF STRUCTURAL BIOLOGY

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

Also the big variety of sizes and structures in the biological world, responds to the function! The central dogma can be applied to other length scales.

Biophysics: underline macromolecules/cells structure/function/structural transition from simple principles. Explain complex processes
macromolecular structure; cell adaptation; fluctuations.

Make Models: simplify as much as possible, never more!



Biological Stuff Can Be Idealized Using Many Different Physical Models: DNA

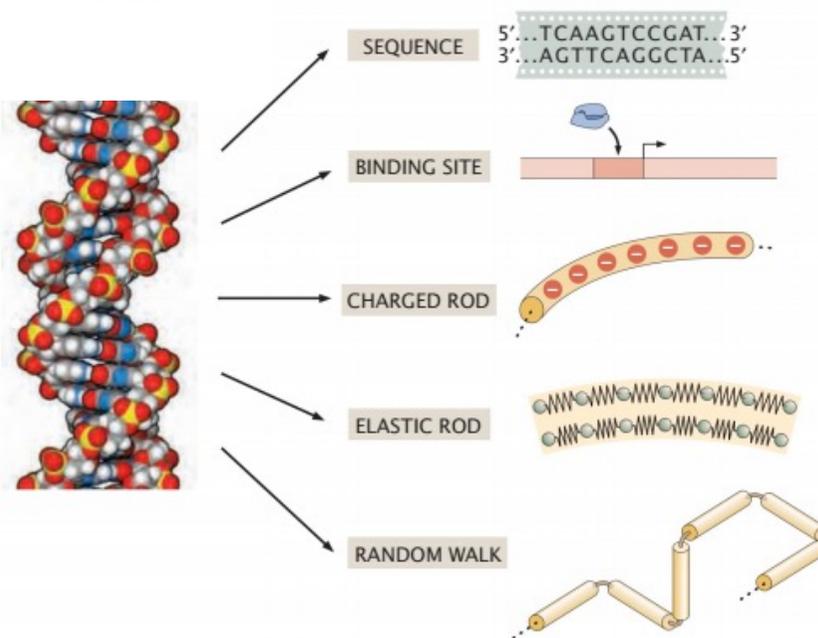


Figure 1.5: Idealizations of DNA. DNA can be thought of as a sequence of base pairs, as a series of binding sites, as a charged rod, as an elastic rod, or as a freely jointed polymer arranged in a random walk, depending upon the problem of interest.

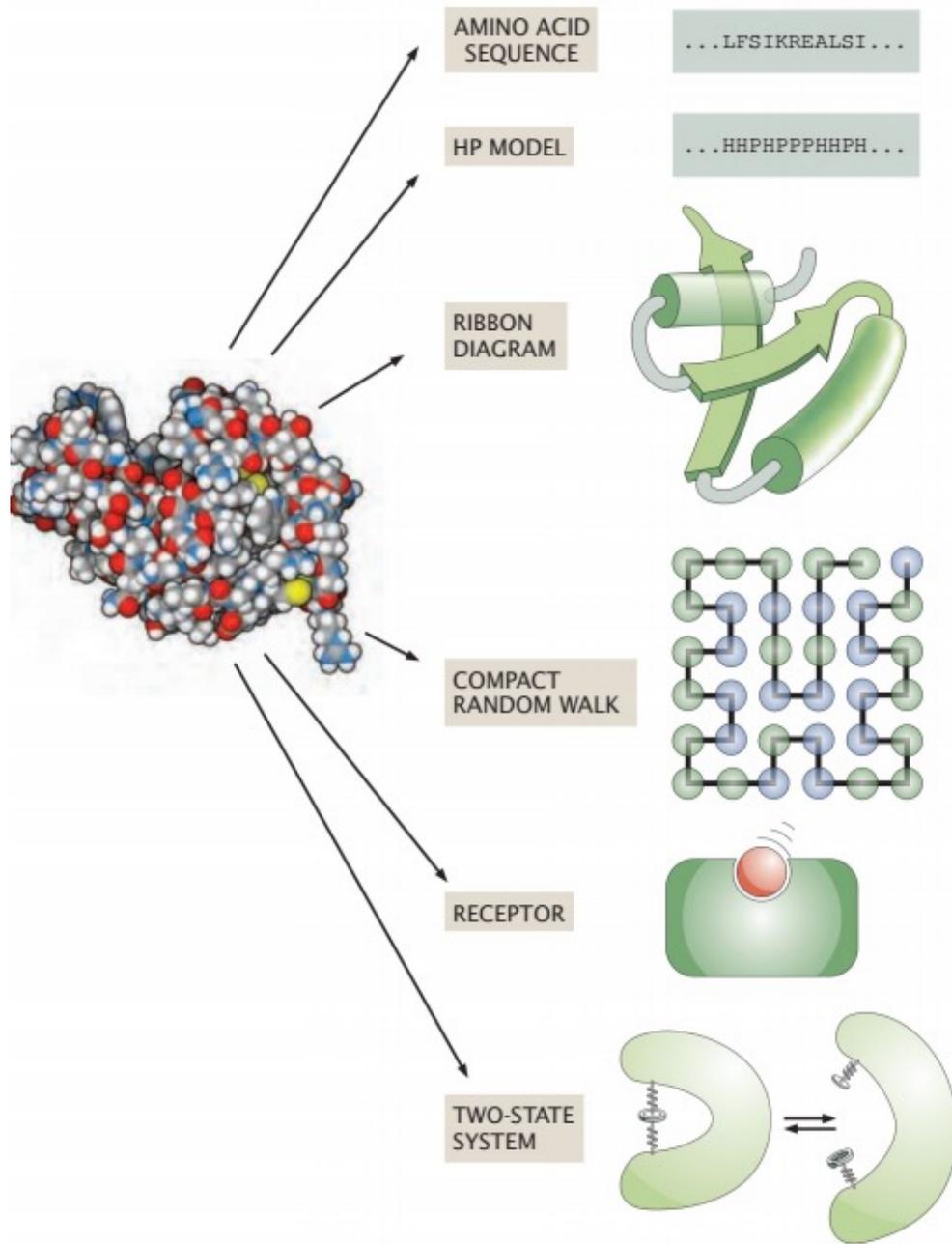
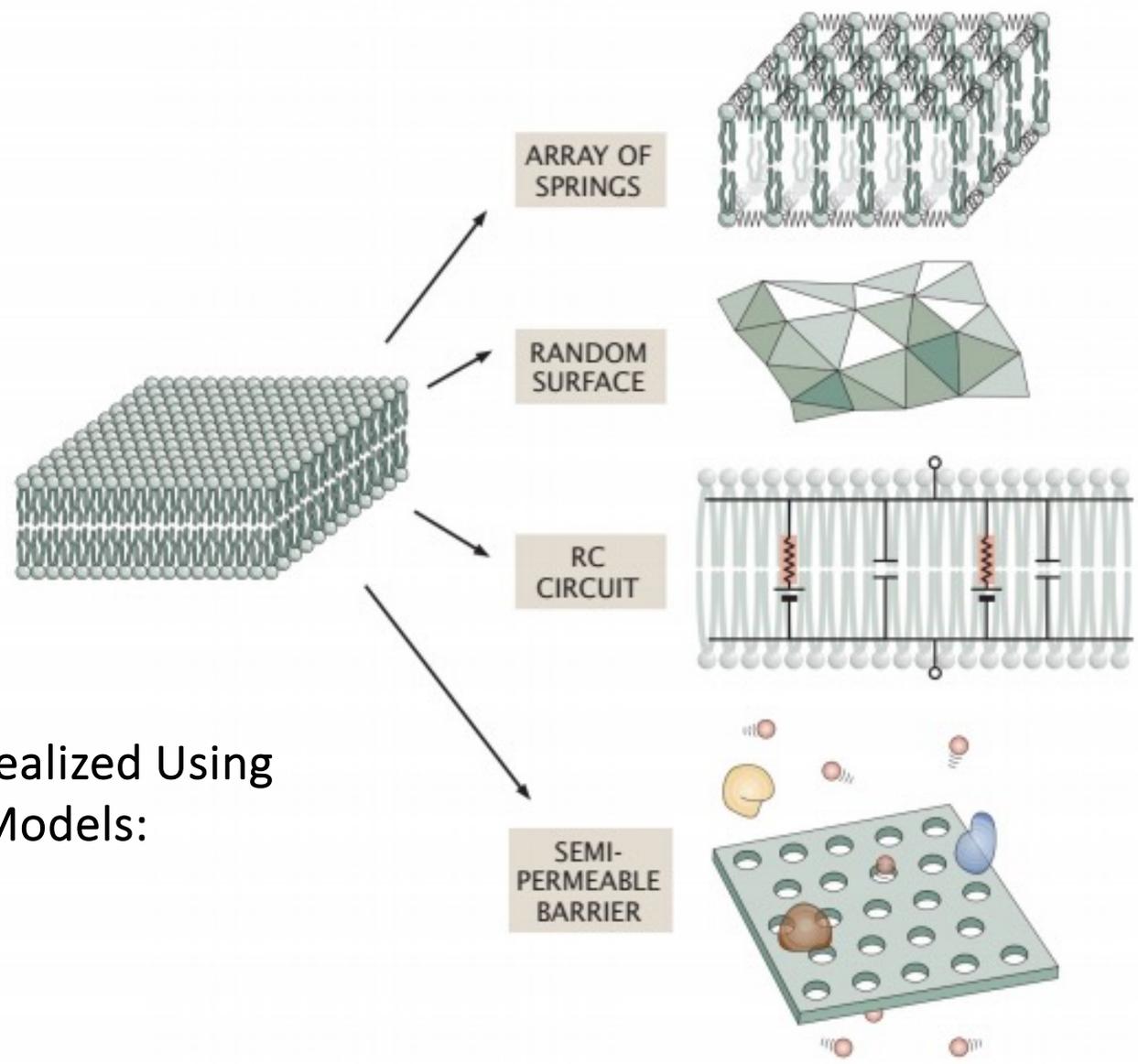


Figure 1.6: Idealizations of protein. Proteins can be thought of as a particular sequence of amino acids, as a simplified sequence reporting only the hydrophobic (H, oil-like) or polar (P, water-like) chemical character of the amino acids, as a collection of connected ribbons and cylinders, as a compact polymer on a lattice, as a binding platform for ligands, or as a two-state system capable of interconverting between different functional forms.

Biological Stuff Can Be Idealized Using Many Different Physical Models: proteins

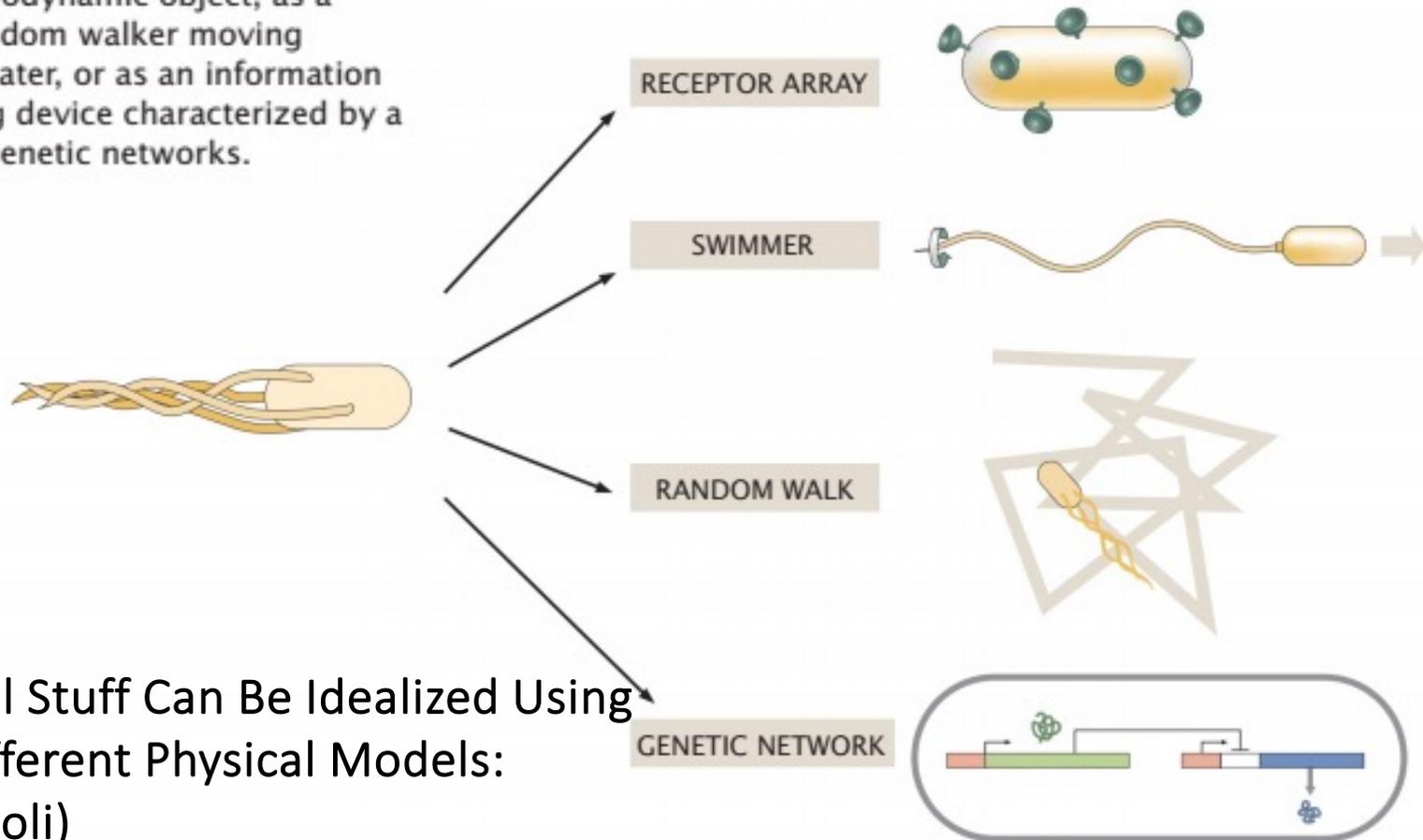
The global conformation of a protein can be seen as a black box, without worrying about the internal machinations

Figure 1.7: Idealization of membranes. A membrane can be modeled as an elastic object that deforms in response to force, as a random surface fluctuating as a result of collisions with the molecules in the surrounding medium, as an electrical circuit element, or as a barrier with selective permeability.



Biological Stuff Can Be Idealized Using Many Different Physical Models:
Lipid membranes

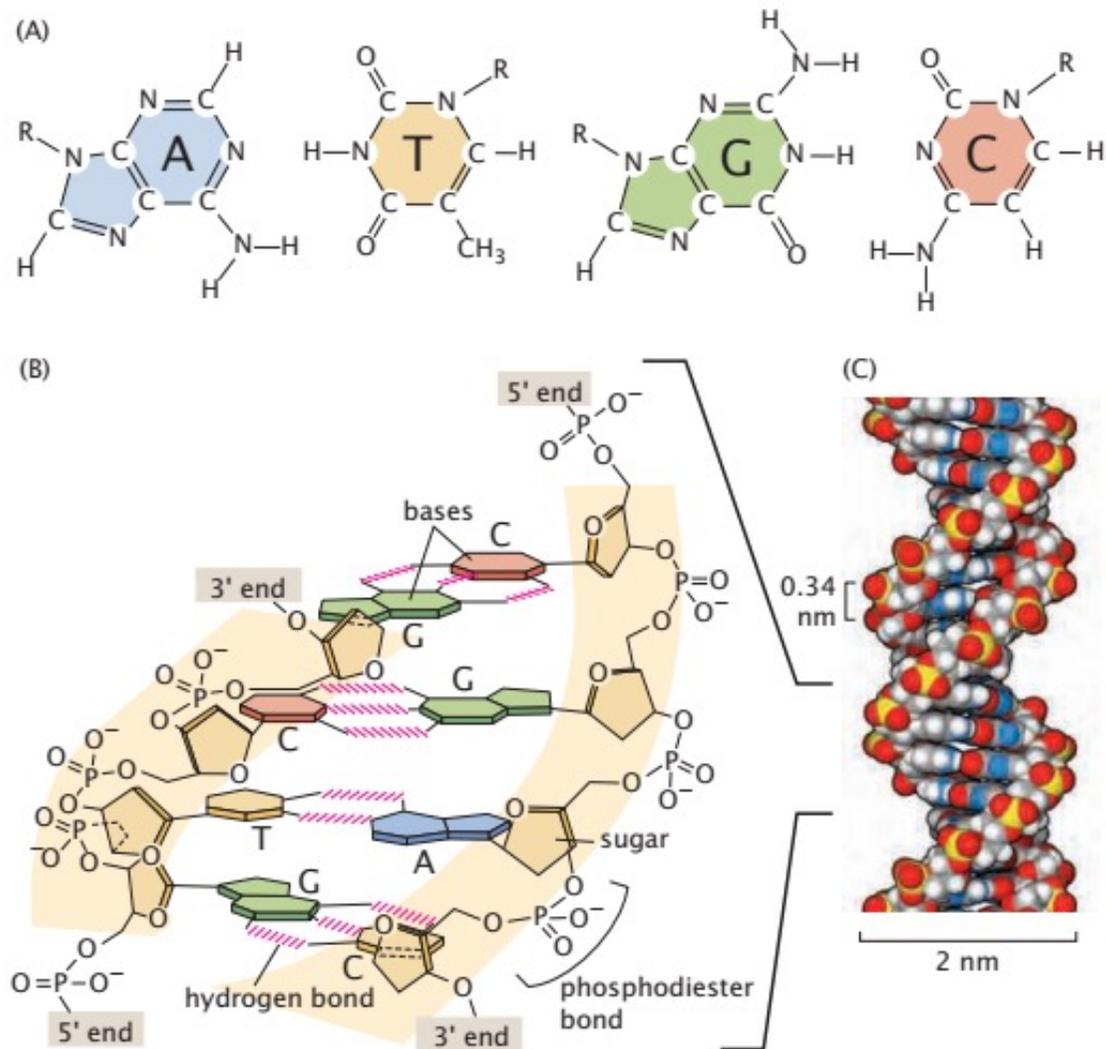
Figure 1.8: *E. coli* idealization. The cell can be modeled as an array of receptors for a ligand of interest, as an elasto-hydrodynamic object, as a biased random walker moving through water, or as an information processing device characterized by a series of genetic networks.



Biological Stuff Can Be Idealized Using Many Different Physical Models: Cells (E-coli)

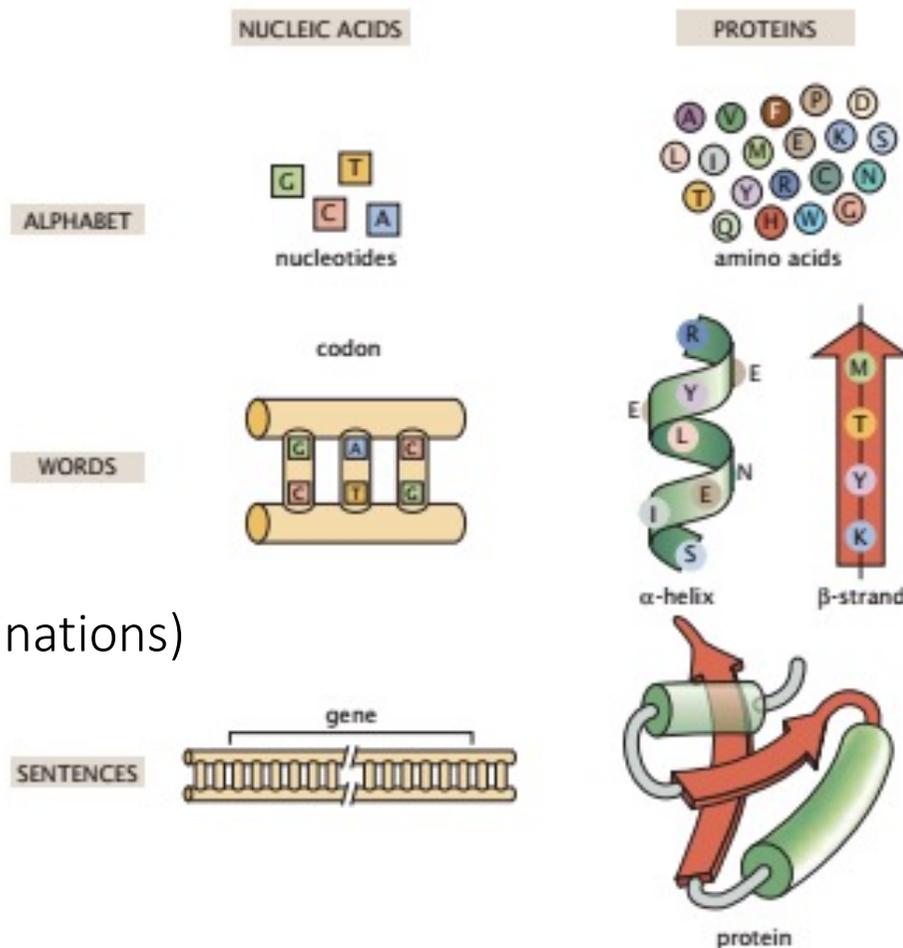
DNA: alphabet with 4 letters

Proteins: alphabet with 20 letters



How can just four nucleotide bases be translated into protein sequences containing 20 different amino acids?

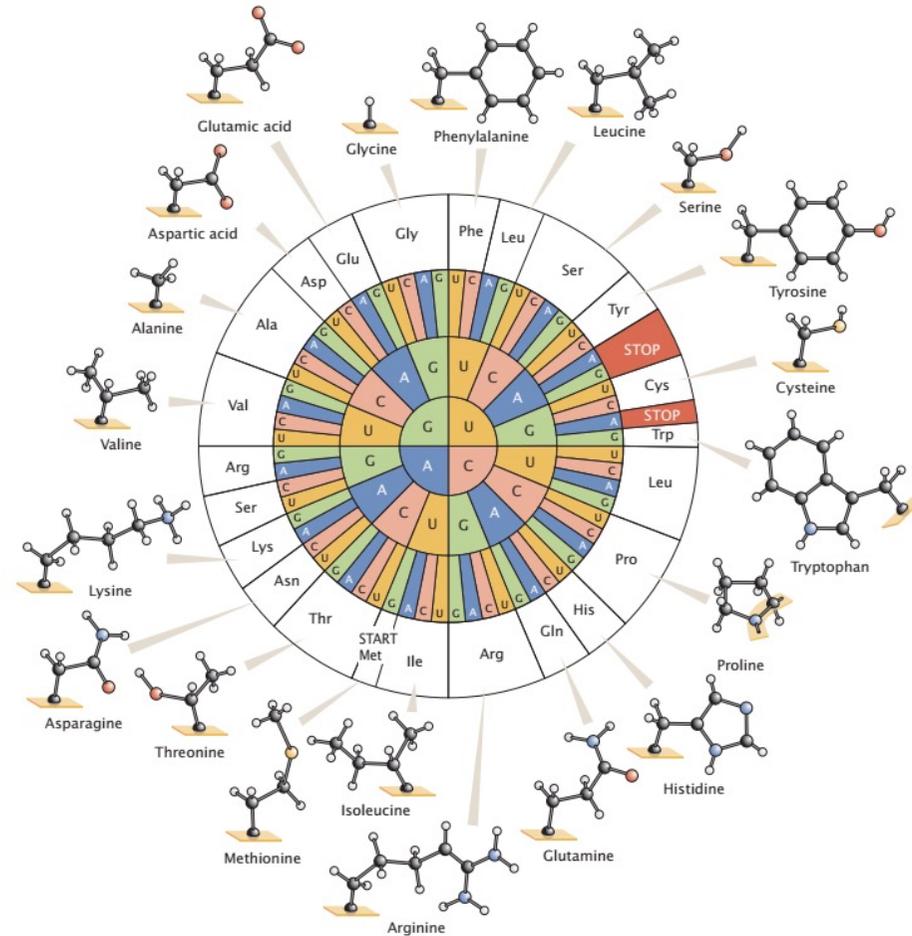
Figure 1.2: Illustration of Crick's "two great polymer languages." The left-hand column shows how nucleic acids can be thought of in terms of letters (nucleotides), words (codons), and sentences (genes). The right-hand column illustrates a similar idea for proteins, where the letters correspond to amino acids, the words to elements of secondary structure such as α helices and β strands, and the sentences to fully folded functional proteins.



64 different codons (4^3 combinations)
 For 20 aminoacids!!

The sequences associated with nucleic acids and proteins are linked mechanistically (**Genetic Code**) through the ribosome which takes nucleic acid sequences (in the form of messenger RNA (mRNA)) and converts them into amino acid sequences (in the form of proteins).

How can just four nucleotide bases be translated into protein sequences containing 20 different amino acids?



The sequences associated with nucleic acids and proteins are linked mechanistically (**Genetic Code**) through the ribosome which takes nucleic acid sequences (in the form of messenger RNA (mRNA)) and converts them into amino acid sequences (in the form of proteins).

History of Biophysics:

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.

High resolution needed!

History of (Molecular) Biophysics:

Breakthrough is DNA double-helix model obtained by J.D.

Watson (ornithologist) and **F.H.C. Crick**

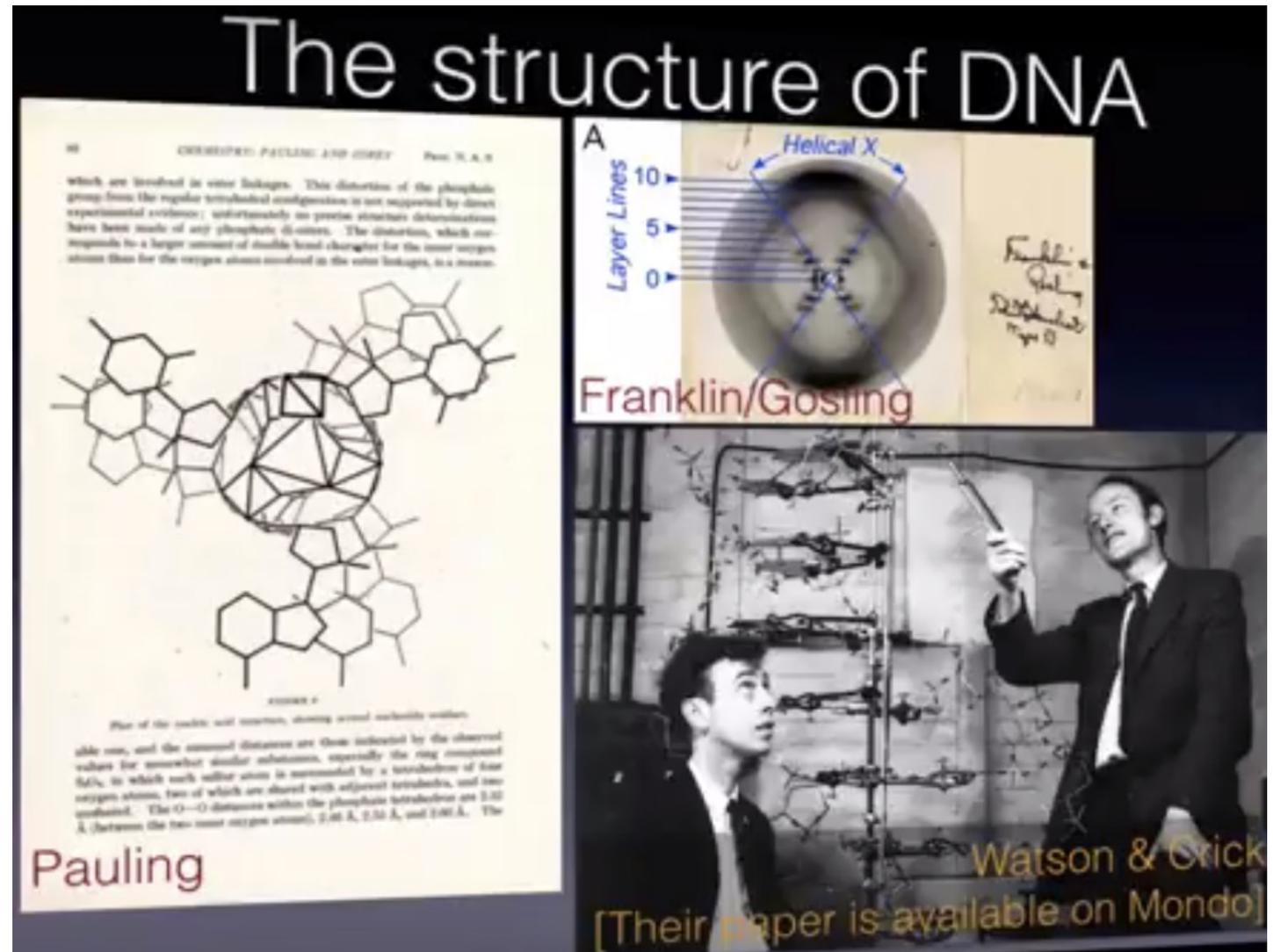
(physicist) following

Rosalind Franklin, **R.G. Gosling**, **M.H.F. Wilkins**,

A.R. Stokes, **H. R.**

Wilson fibre diffraction/biochemical studies

published on Nature in 1953



High resolution needed!

History of (Molecular) Biophysics:

- Feynman's Talk: "There's Plenty of Room at the Bottom" (1959):

In this visionary talk, Feynman laid the foundation for what we now call **nanotechnology** and implied potential applications **for biology and medicine**. He discussed the possibility of manipulating individual atoms and molecules, long before techniques like **cryo-electron microscopy** or **molecular engineering** were available. These ideas have become instrumental in biophysics, where scientists now study biological macromolecules and develop **nanotechnology-based medical devices** and drug delivery systems.

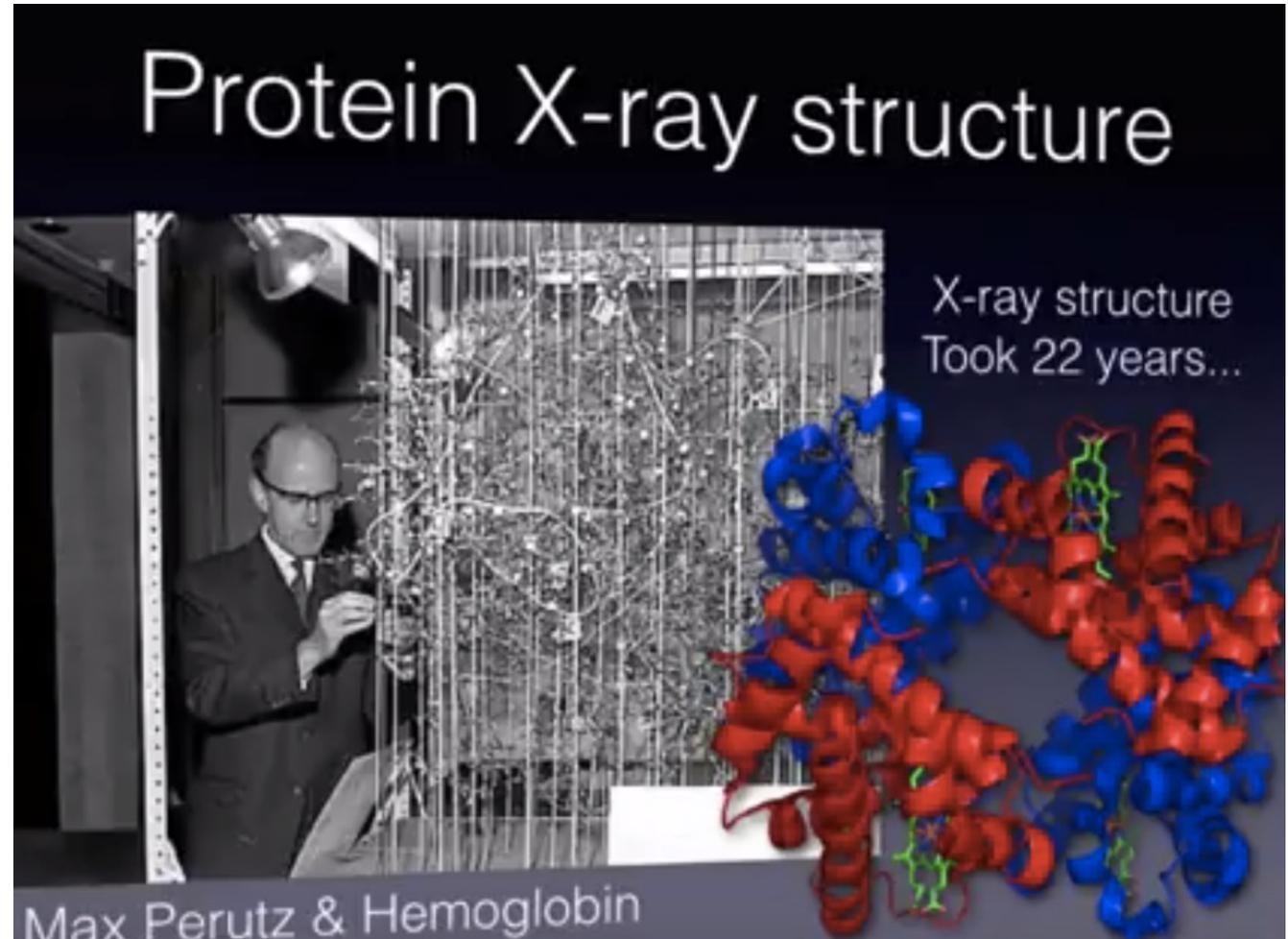
His idea of creating machines at the molecular scale is directly relevant to biophysics, particularly in understanding biological nanomachines like **enzymes**, **motor proteins**, and other molecular structures.



History of (Molecular) Biophysics:

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 complementary biochemical 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**.

Organization is key.

What is life?

Complex systems thinking. Life emerges from the *collective interactions* of molecules — feedback loops, self-replication, adaptation — which are properties of the system, not of any single molecule.

Modern confirmations. Research in **systems biology, synthetic biology, and origin-of-life studies** keeps showing that the transition from chemistry to biology is about *emergence*: when enough molecular complexity and organization is reached, behaviors we call “life” appear.

Life is not just chemistry, but chemistry arranged in a dynamic, self-organizing, complex system.

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?

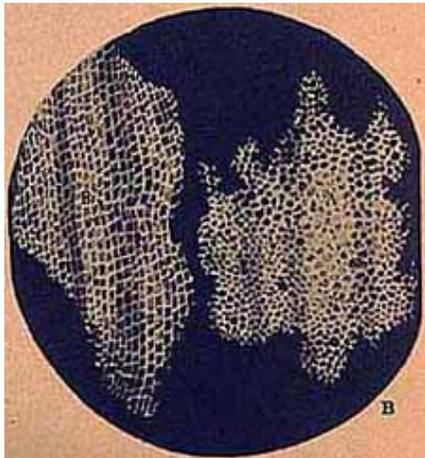
All living organisms:

- 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

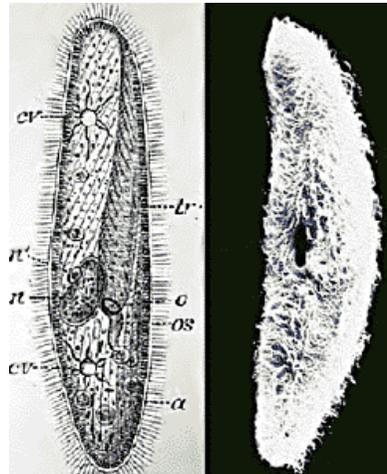
All living organisms are made of cells.

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; fluctuations. Make Models: simplify as much as possible, never more!

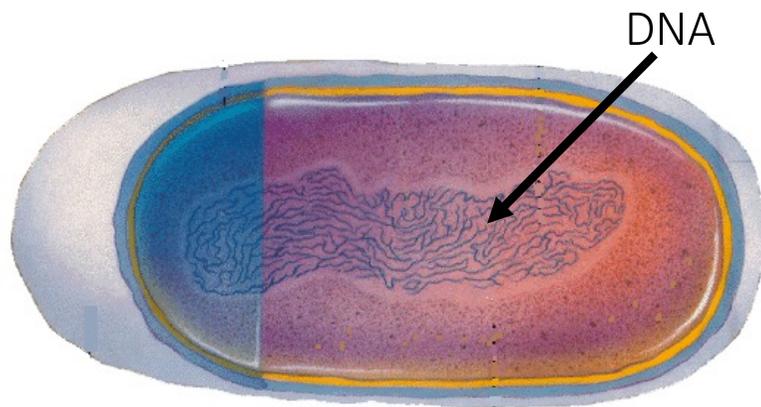
The organisation of the cell

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).

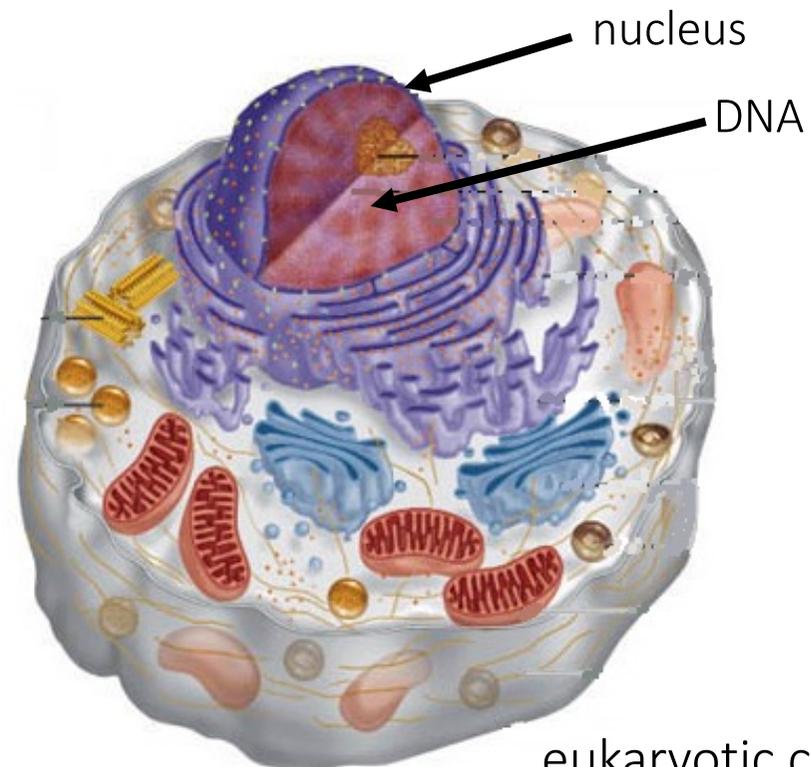
In some cells the DNA is simply spread inside the cell, in others it is enclosed in an organelle called the **nucleus**.

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

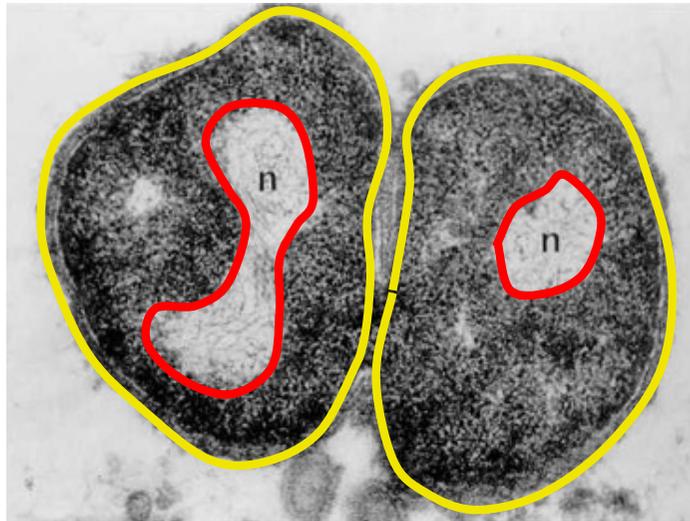
Animals

multicellular

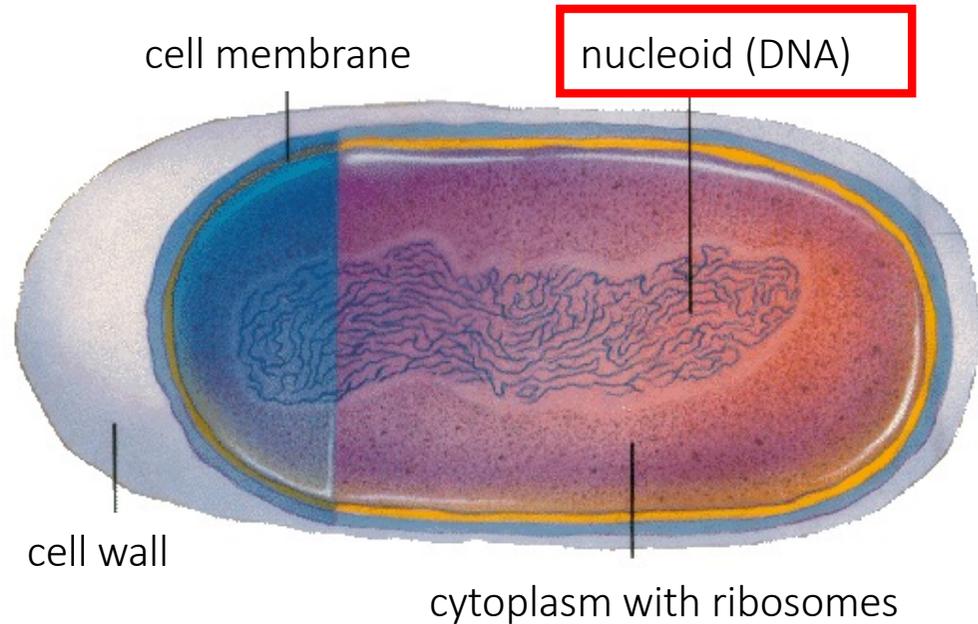
Plants

multicellular and able
to carry out photosynthesis

BACTERIA



An electron micrograph of two bacteria.

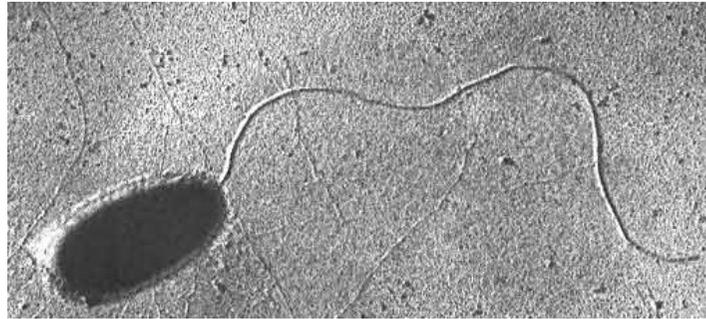


A schematic diagram of a bacterium.

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:



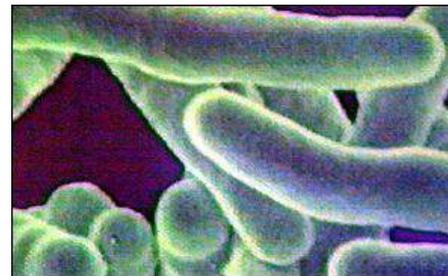
Flagellatae



Spirochete



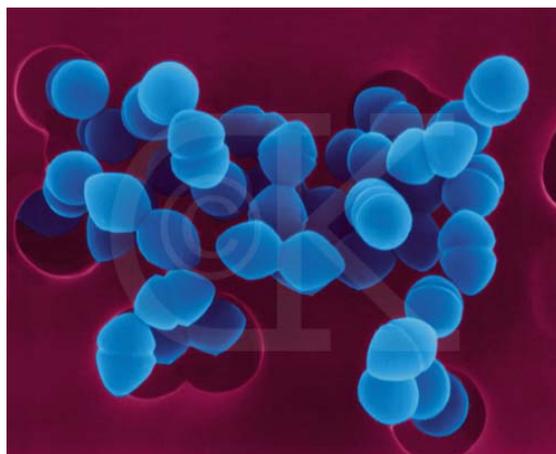
Antrax bacteria



TB bacteria



Plague
bacteria



Enterococcus



Escherichia coli



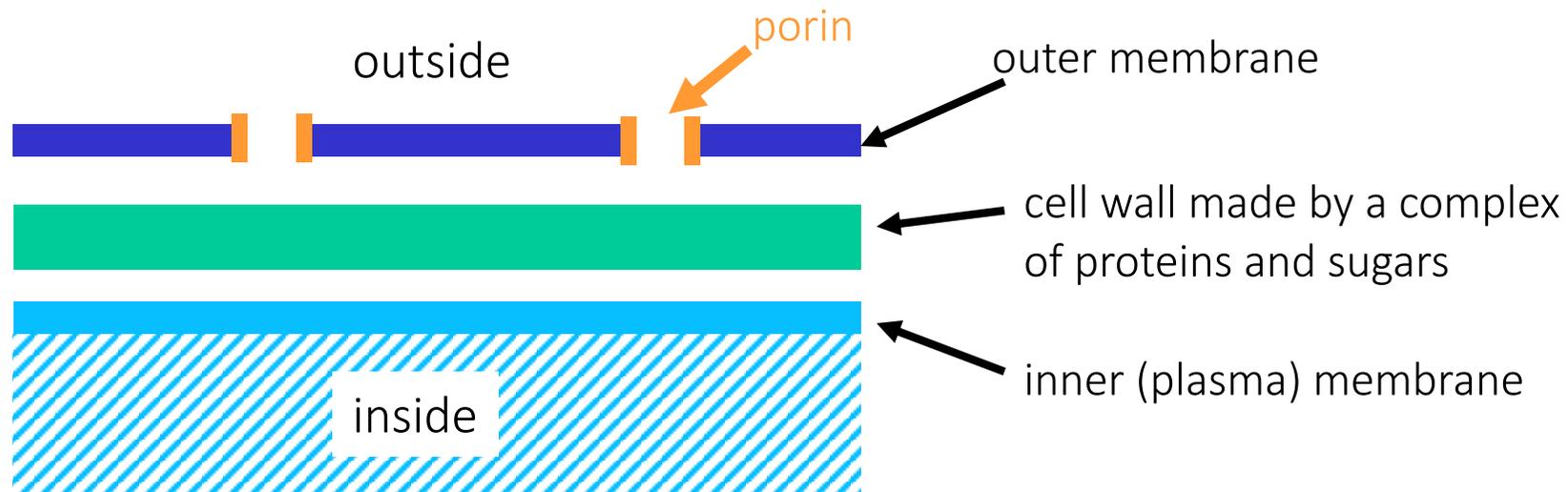
Cyanobacteria

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

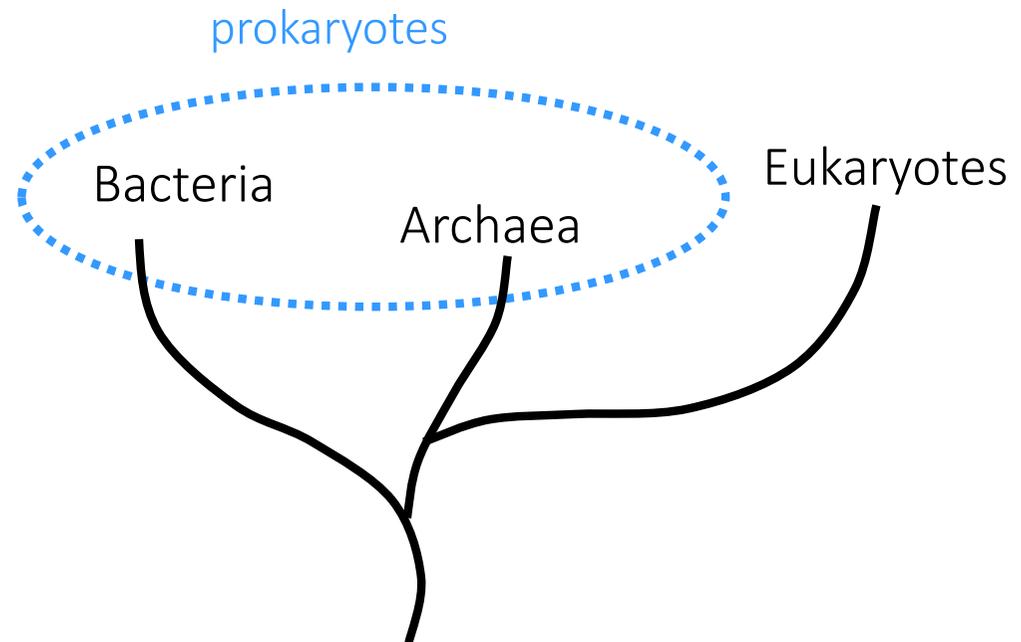
- inner membrane impermeable to chemicals
- outer membrane containing proteins called porins, which make holes into the membrane so that chemicals can go in and out
- a cell wall between the two membranes



ARCHAEA

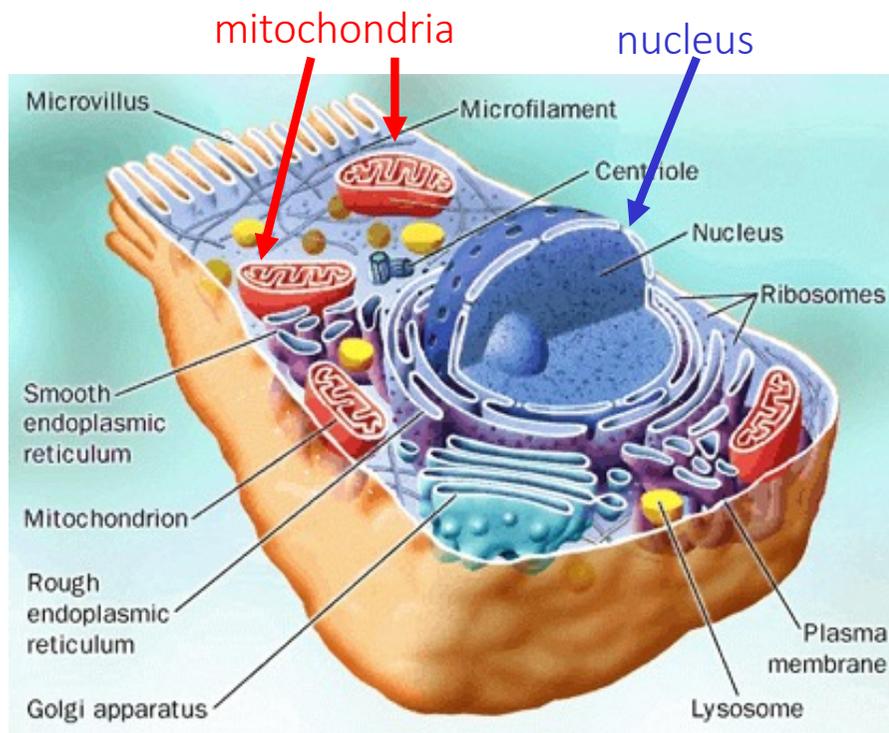
- unicellular organisms
- no nucleus (i.e. prokaryotes)
- live in very unfriendly environments (hot/sulphuric springs, the Dead Sea, deep vents in the oceans...)
- metabolic processes similar to bacteria
- but...processing of genetic information (how they copy, read, use the information written in the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

Our current picture of the evolution of life:

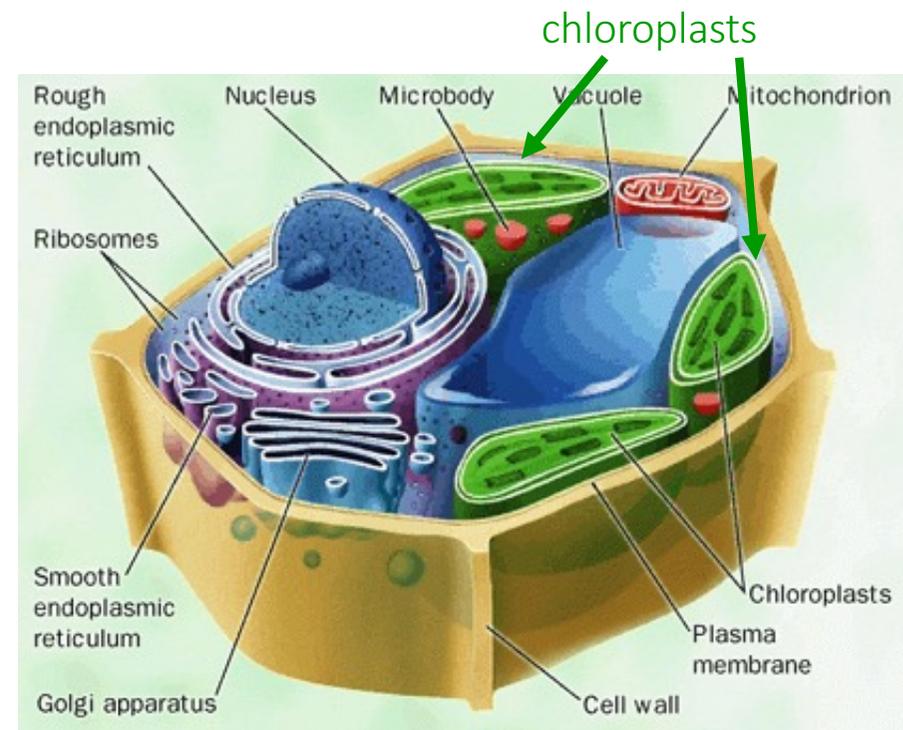


EUKARYOTES

- 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



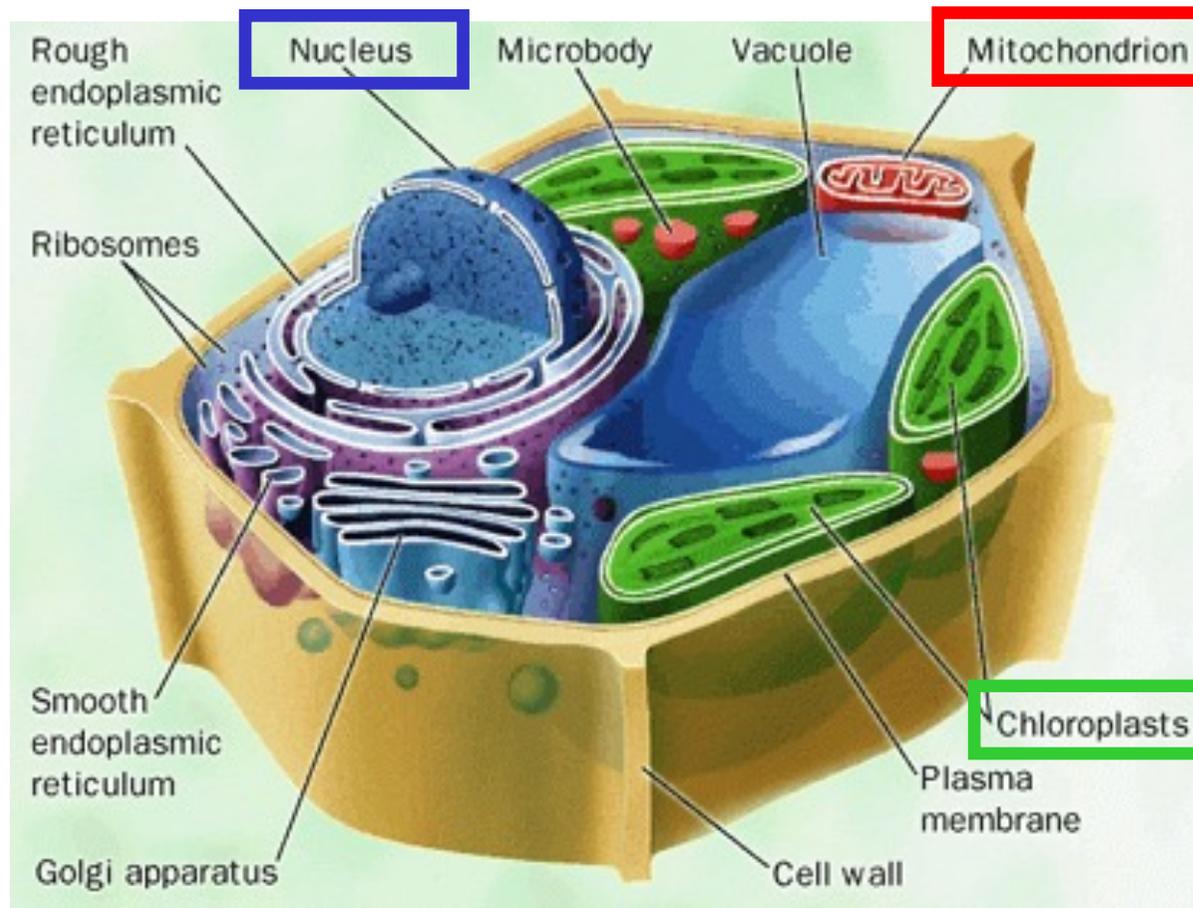
animal cell



plant cell

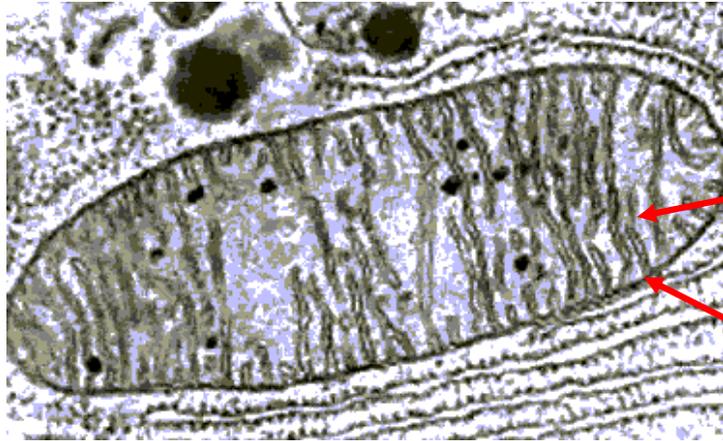
Eukaryotic organelles

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



plant cell

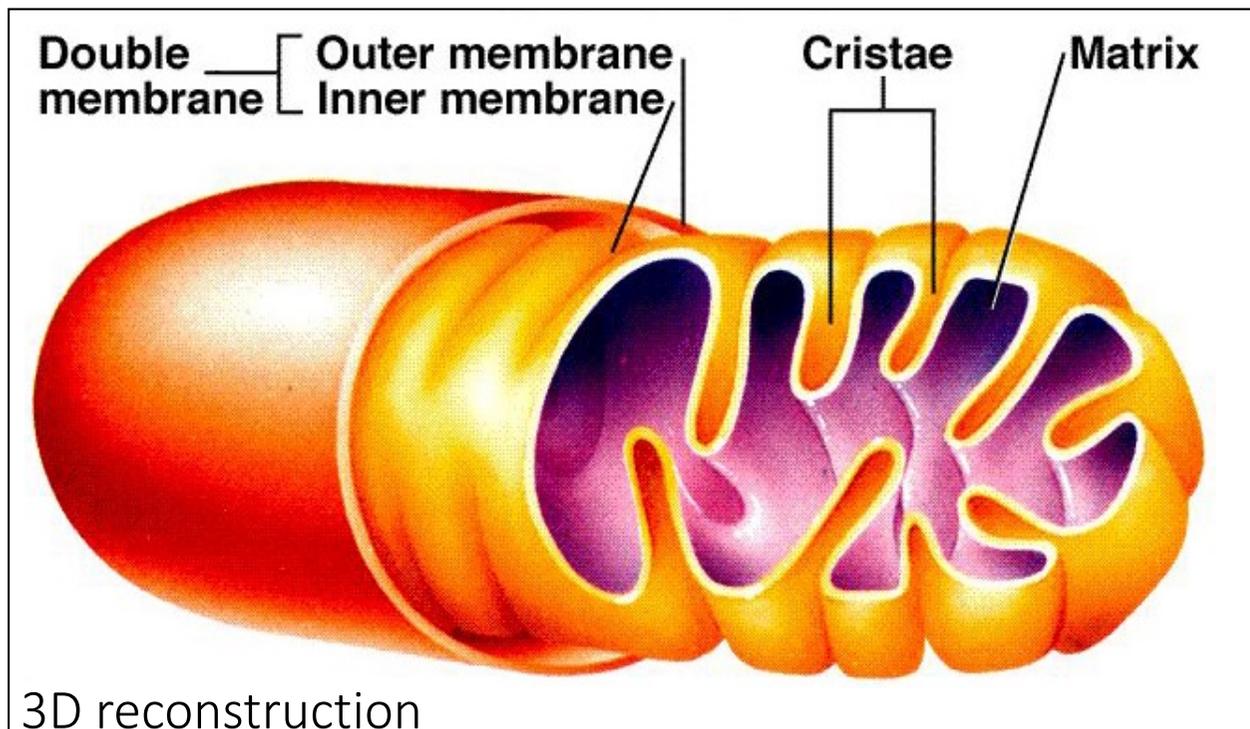
Mitochondrion



Electron micrograph of a mitochondrion

inner membrane
outer membrane

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



3D reconstruction

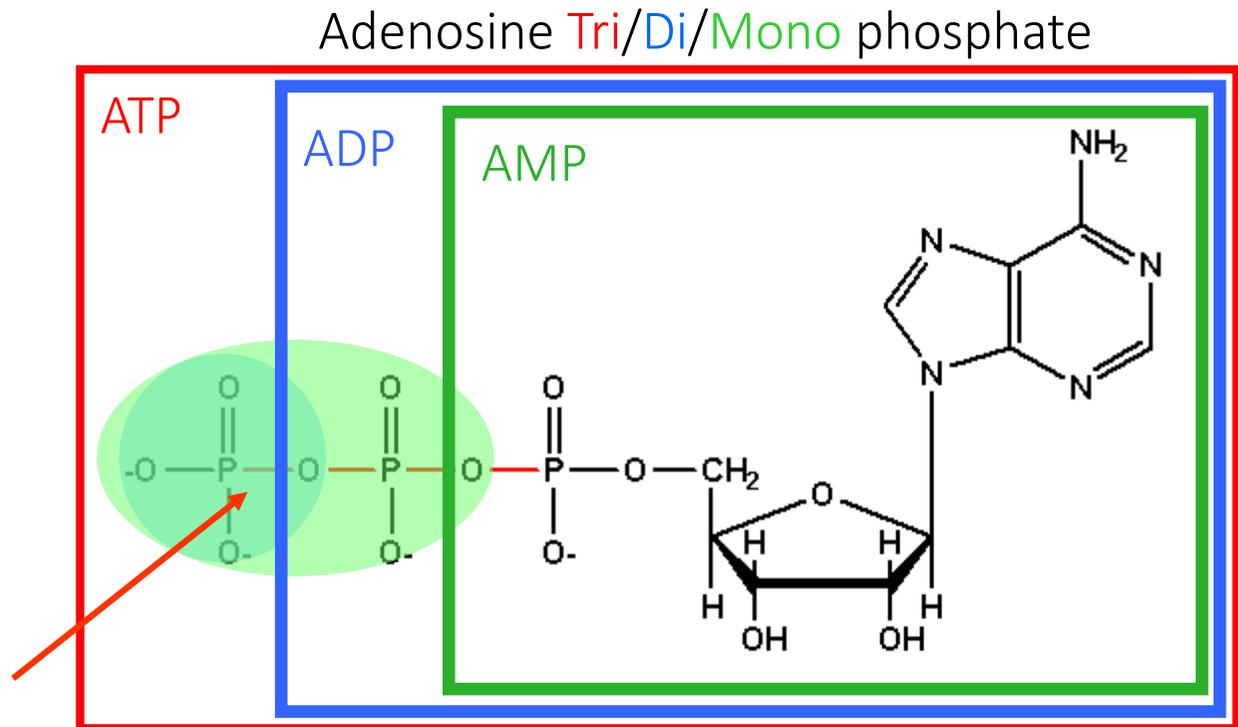
Function of mitochondria:
energy production by oxidation of small molecules (occurring in the mitochondrial matrix)

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.



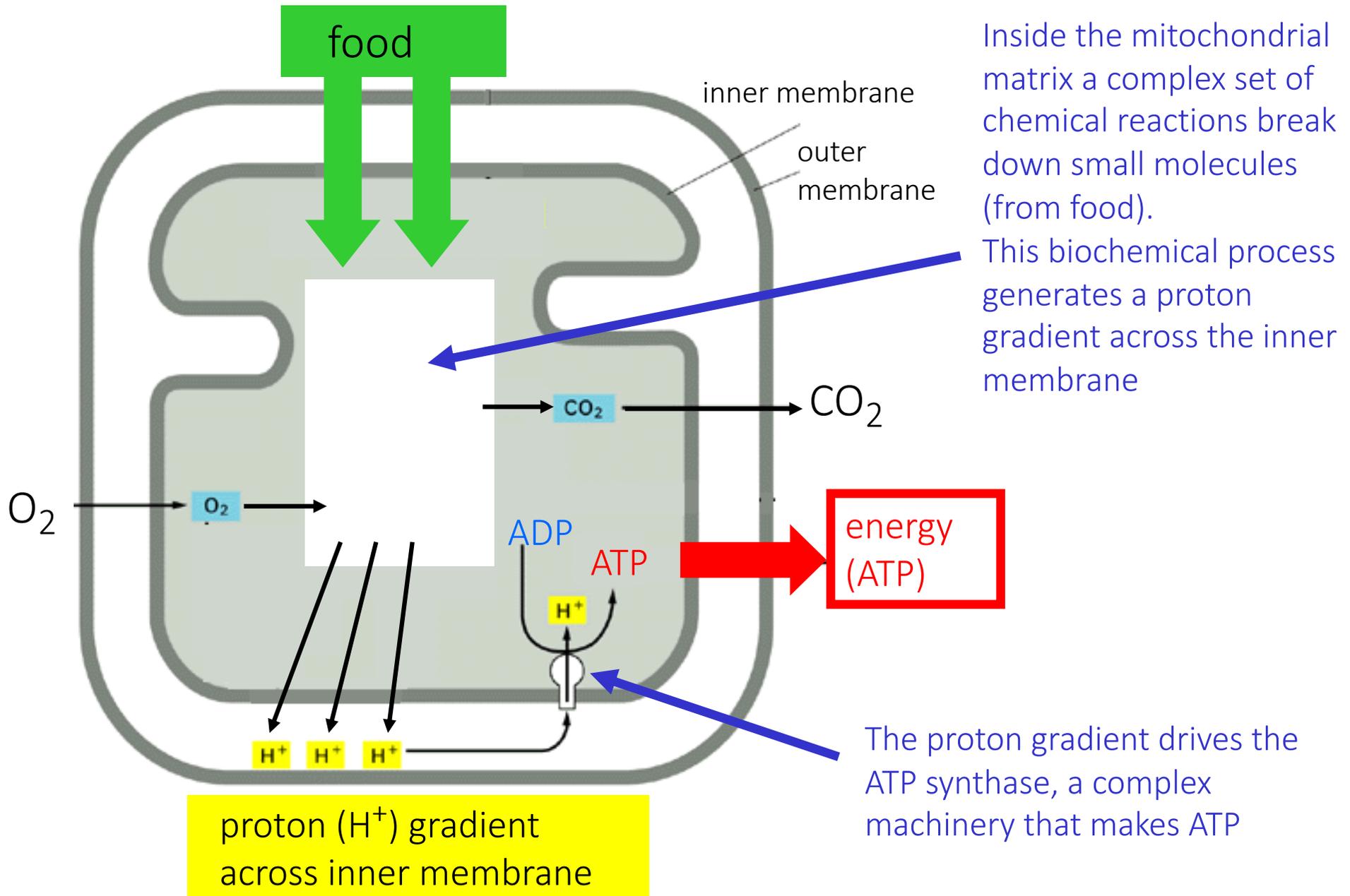
phosphodiester
bonds have a large
energy of hydrolysis
(about 30 kJ/mol)



Energy production: accumulation of ATP

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

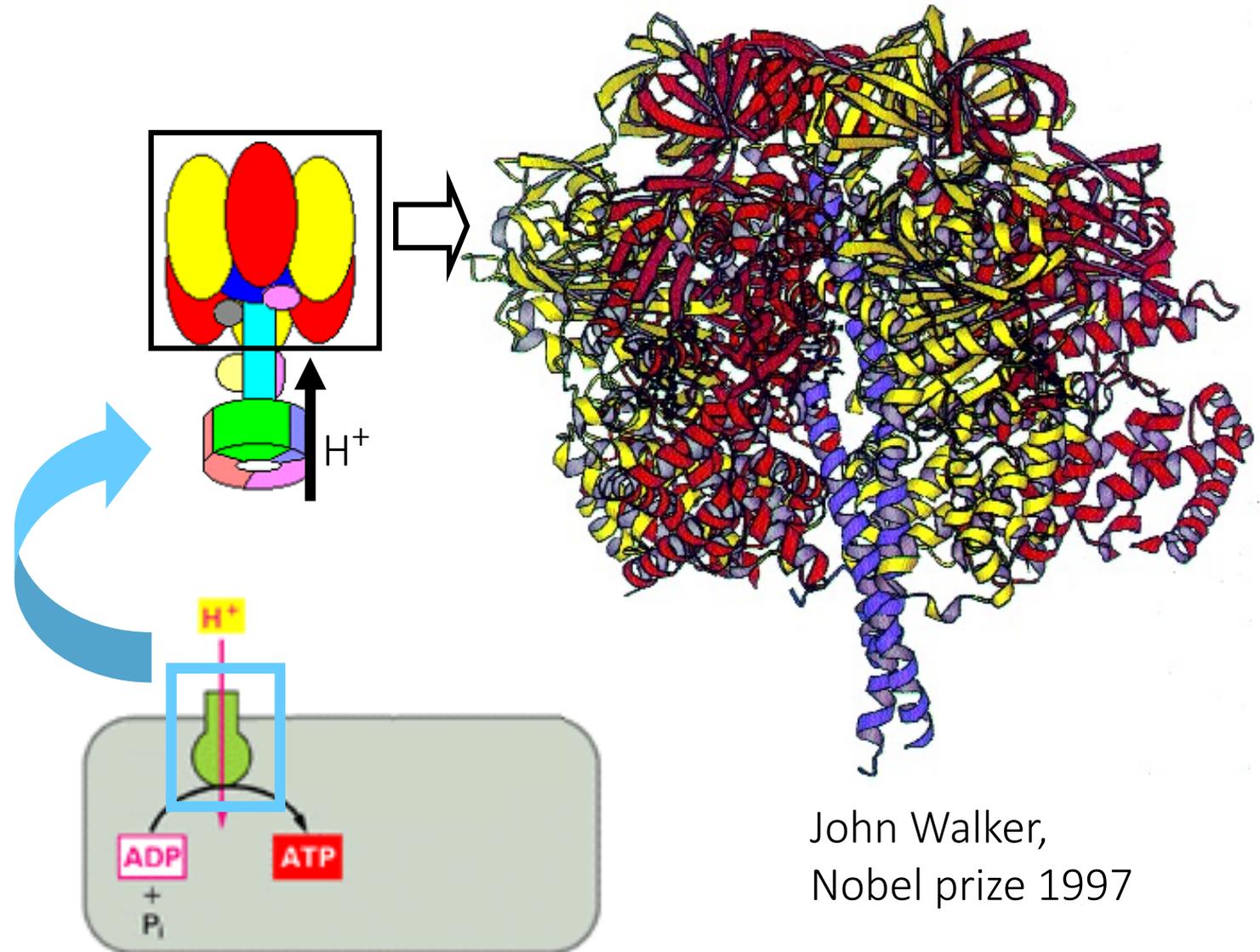
What happens in the mitochondrion?



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

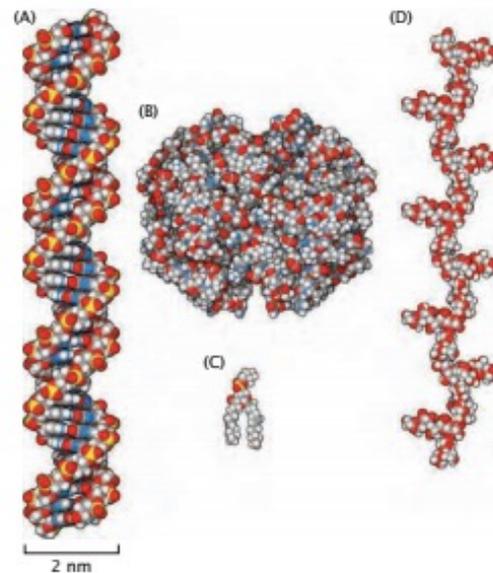
- polymers made by a linear chain of building blocks
- made by linking a defined set of small molecules (monomers) through the repetitive use of a single chemical linkage
 - ↳ **proteins**: polymers made by a linear chain of amino acids
 - ↳ **nucleic acids**: polymers made by a linear chain of nucleotides

EVOLUTION of LIFE = EVOLUTION OF MACROMOLECULES

Macromolecules

Macromolecules can be assembled by the cell from a **small number of simpler subunit** or precursor molecules. It is the combinatorial assembly of these simple subunits that gives rise to their tremendous structural diversity.

A cell needs only a few chemical reactions to be able to synthesize these sets of subunits from the food in its environment.



Atoms: O, C, N, H, sometime S, P

- (A) Atomic structure of a small fragment of the nucleic acid DNA in the B form
- (B) atomic structure of the oxygen-carrying protein hemoglobin (PDB 1hho)
- (C) phosphatidylcholine lipid molecule from a cell membrane
- (D) branched complex carbohydrate

Macromolecules

Proteins:

Structural elements that catalyze reactions fundamental to life
(TENS OF THOUSANDS OF DIFFERENT PROTEINS IN A SINGLE ORGANISM!!)

Carbohydrates:

Energy storage, surface properties on cell membranes, cell walls

Lipids:

Cell membranes, separate organelles in cells (HUNDREDS OF DIFFERENT LIPIDS EXIST)

Nucleic Acids:

Memory, operating instructions, constitute the operation mechanism to generate 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; fluctuations. Make Models: simplify as much as possible, never more!

Macromolecules

Proteins:

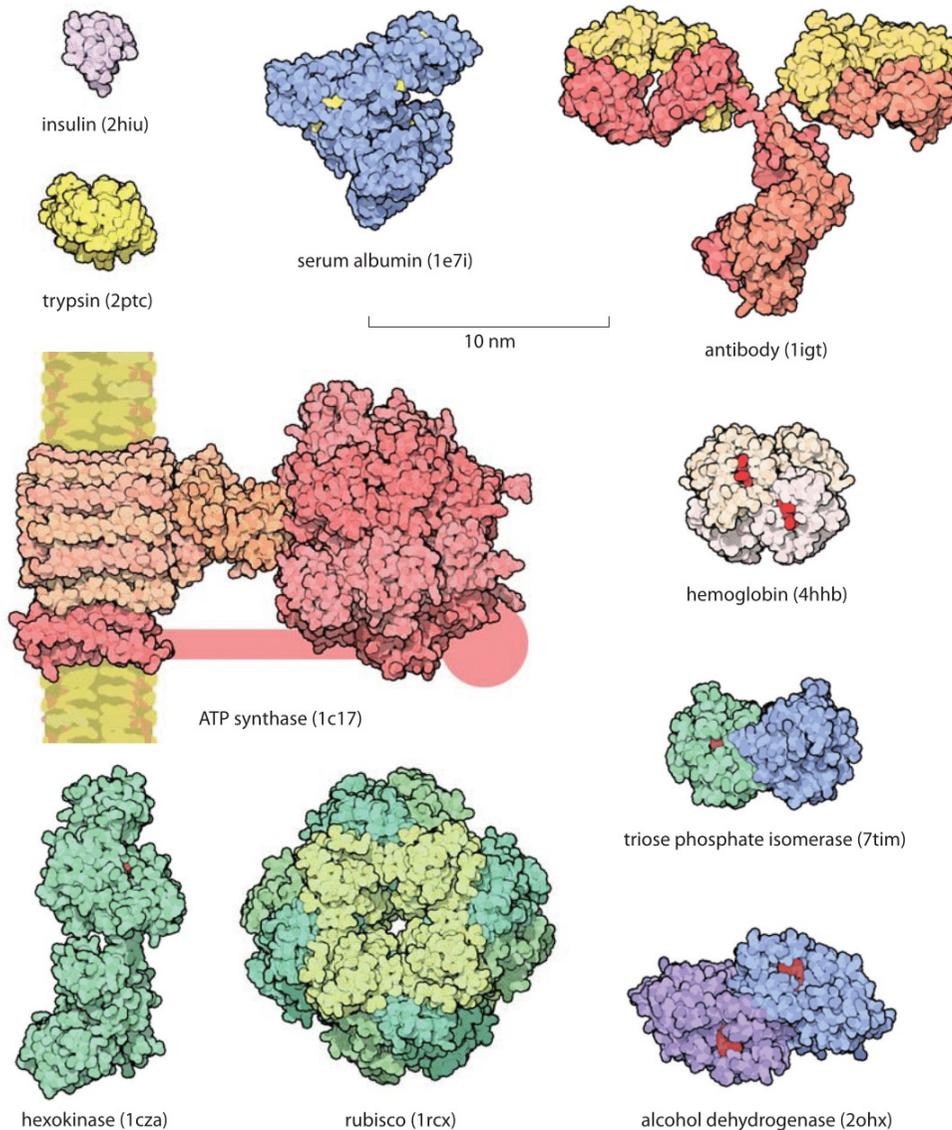
molecular machines, display a wide variety of 3D shapes and of biological functions

- 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

Proteins

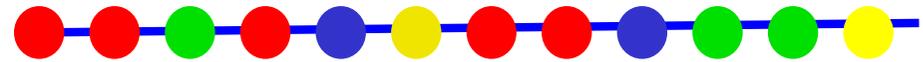


organism	median protein length (amino acids)
<i>H. sapiens</i>	375
<i>D. melanogaster</i>	373
<i>C. elegans</i>	344
<i>S. cerevisiae</i>	379
<i>A. thaliana</i>	356
5 eukaryotes (above)	361
67 bacteria	267
15 archaea	247

Nucleic Acids

Nucleic acids

Nucleic acids are linear chains of nucleotides.

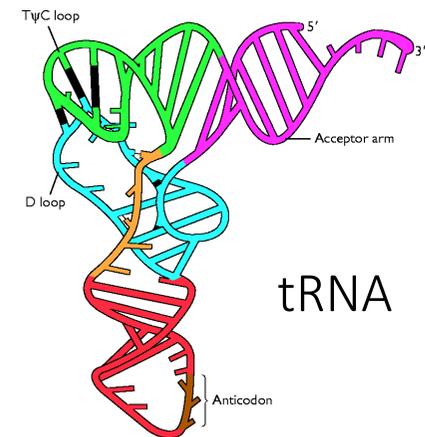


There are 5 different types of nucleotides, but either type of nucleic acid (DNA or RNA) contains only 4.

DNA	●	●	●	●	●
	A	C	G	T	
RNA	●	●	●	●	●
	A	C	G	U	

These chains fold in 3D due to the hydrogen bonds between pairs of nucleotides (A=T / A=U; C=G):

- in DNA two chains wraps around each other forming a double helix
- RNA can assume a variety of shapes



Overview of nucleic acid architecture

1) structure and chemistry of nucleotides:



- 2) how nucleotides are linked together through phosphodiester bonds to form a nucleic acid chain
- 3) base pairing and the 3D structure of DNA and RNA

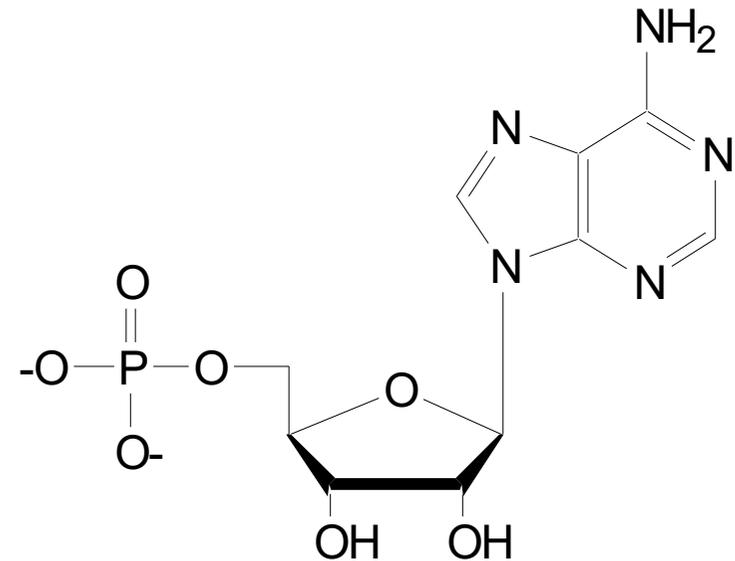
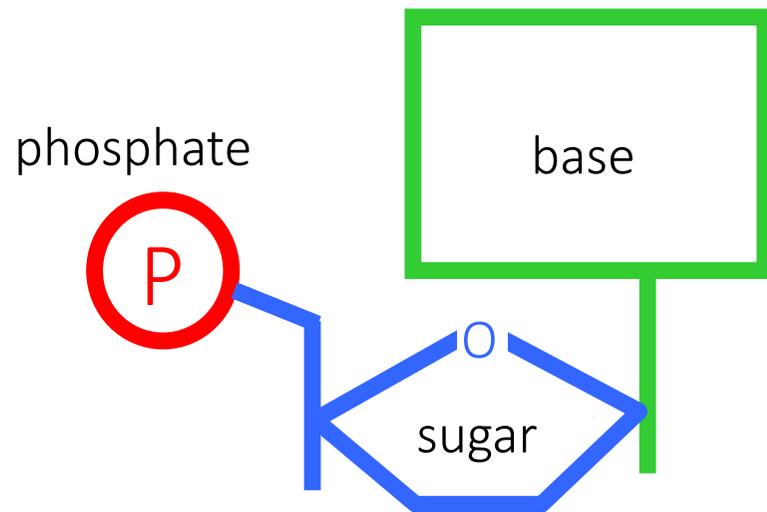
Structure of nucleotides

A nucleotide has 3 parts:

a sugar

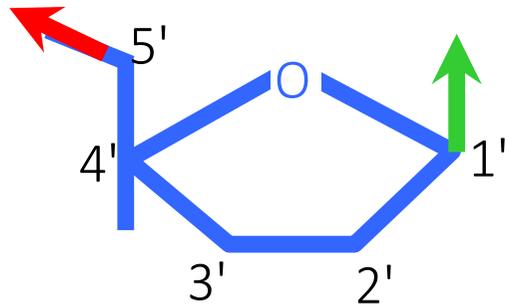
a phosphate

a base



example: Adenosine MonoPhosphate
(AMP)

Sugars: ribose or deoxyribose

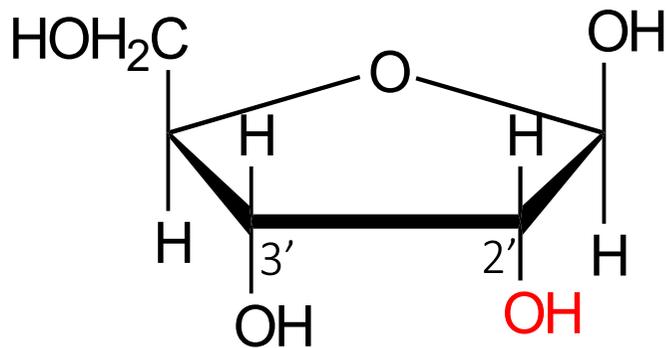


The sugar in nucleic acids is a pentose (5 C atoms numbered from 1' to 5'):

- the 1' C is linked to the **base**
- the 5' C is linked to the **phosphate**

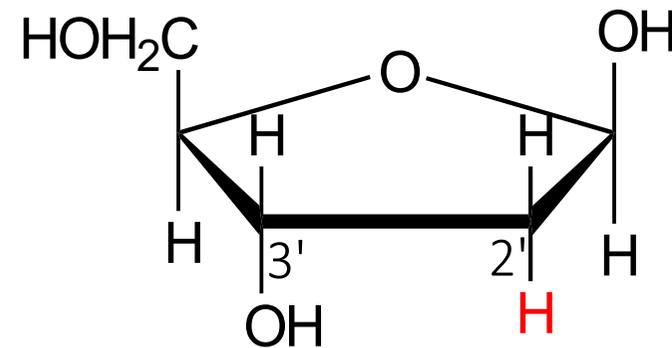
There are two sugars used in nucleic acids:

ribose, in RNA



ribose has a OH group both on the 2' and 3' C

2'-deoxyribose, in DNA

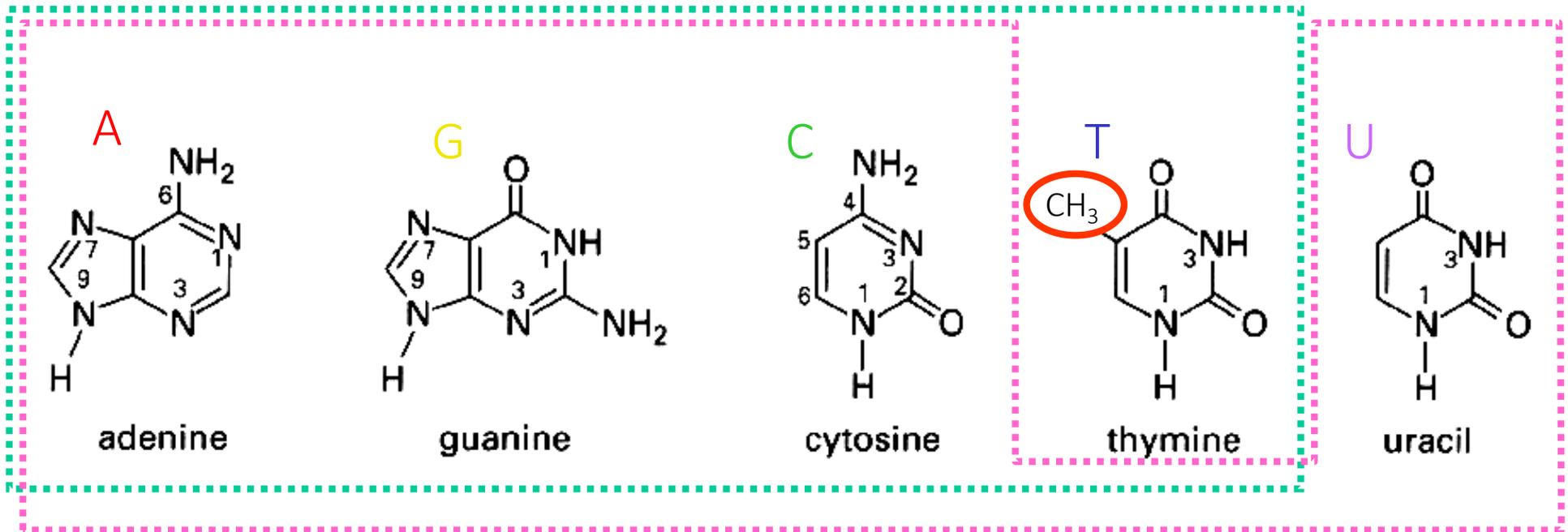


in **2'-deoxyribose** the OH at 2' is substituted by an H

Bases: A, T, C, G, U

PURINES: two fused rings

PYRIMIDINES: 1 ring only



DNA contains A, T, C, G

RNA contains A, U, C, G

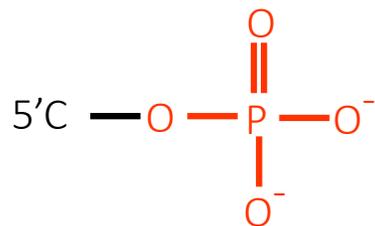
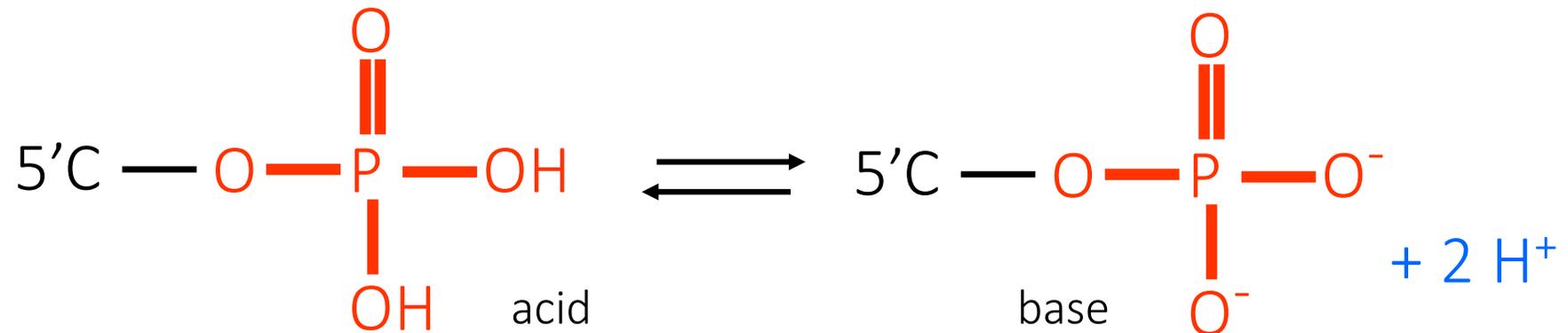
in RNA T is substituted by U
(lacks CH₃ in position 5)

'Bases' is a misleading name: none of them is protonated at neutral pH

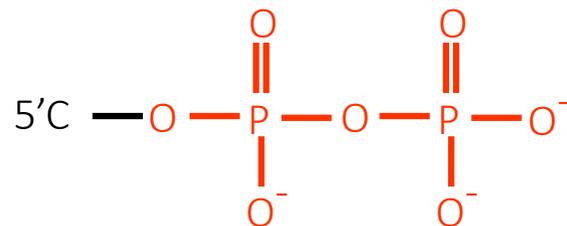
The phosphate group

Why 'nucleic acid'?

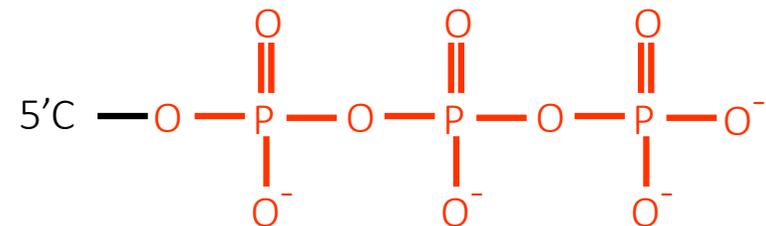
The acidic character is due to the presence of the phosphate group:



NMP=nucleotide
monophosphate



NDP=nucleotide
diphosphate



NTP=nucleotide
triphosphate

where N could be A, C, G, T, U

Overview of nucleic acid architecture

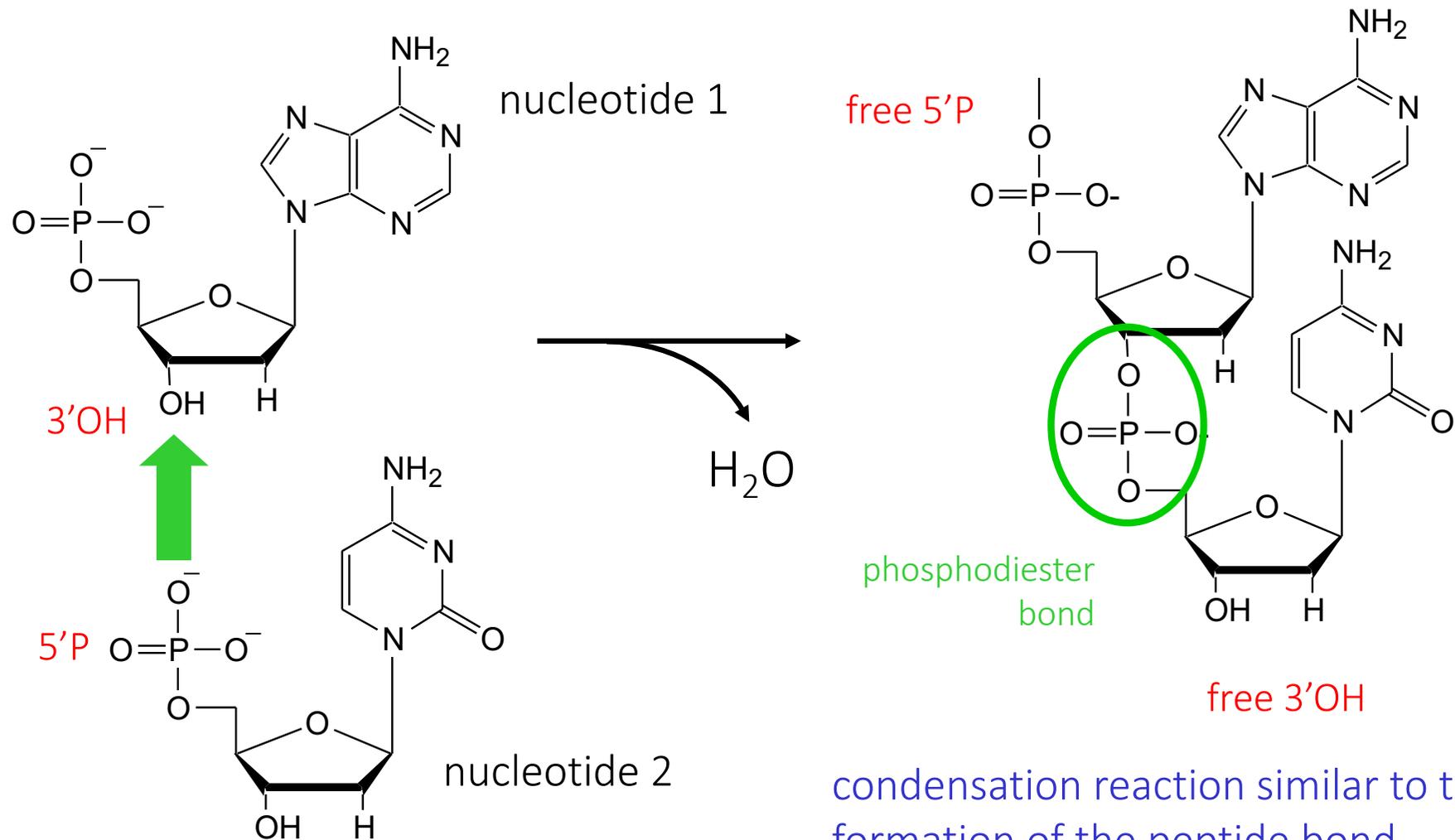
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- 3) base pairing and the 3D structure of DNA and RNA

Polymerisation of nucleotides

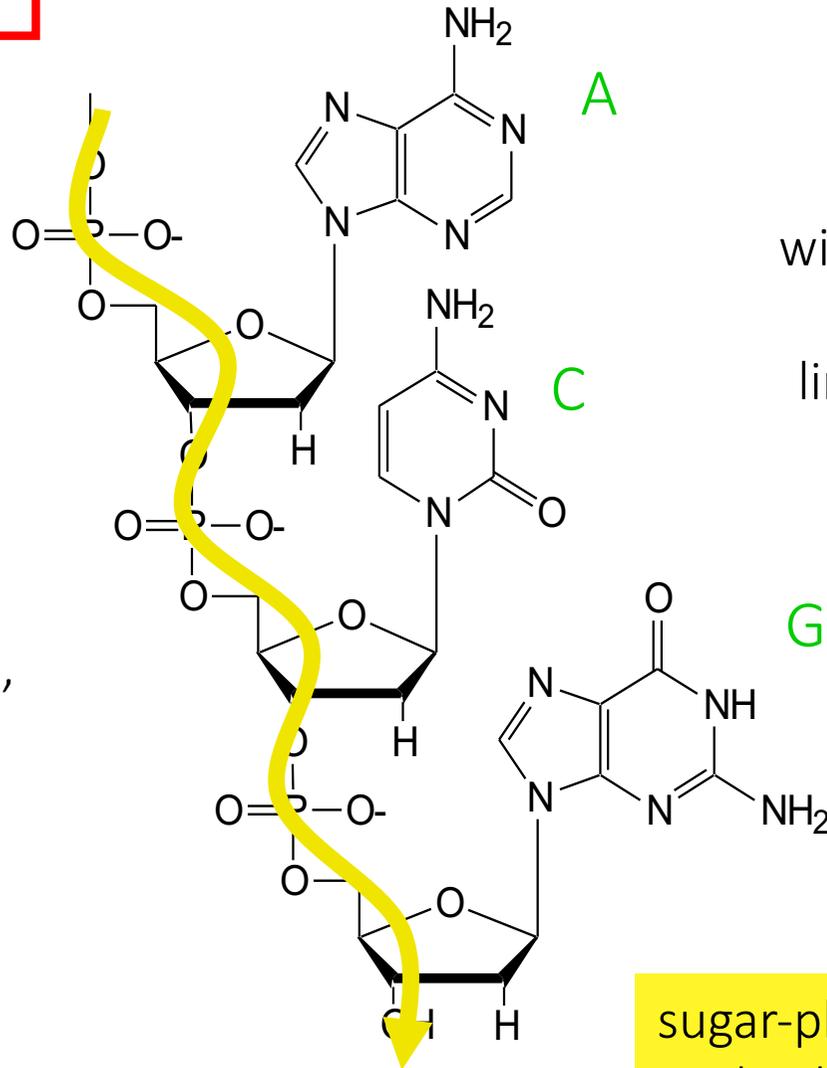
The OH on the 3' of the sugar of one nucleotide forms a bond (**phosphodiester bond**) with the phosphate on the 5' of another nucleotide.



condensation reaction similar to the formation of the peptide bond

Primary sequence

free 5' P



Convention:
nucleotide sequences are read in the 5' \rightarrow 3' direction, so that the first nucleotide has a free 5' P and the last a free 3' OH
Here: **ACG**...

free 3' OH

sugar-phosphate backbone

The primary structure of a nucleotide chain is a sugar-phosphate backbone with all the bases sticking out.

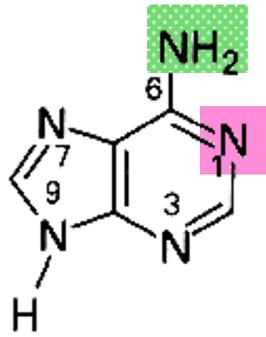
A chain is defined by the linear sequence of the bases.

The chain has a polarity, with one end having a free 5' P and the other end a free 3' OH.

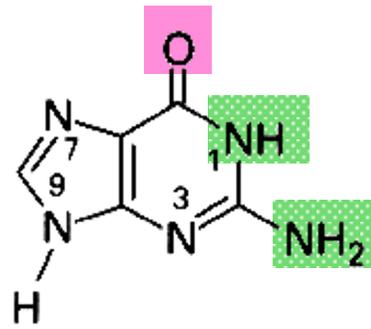
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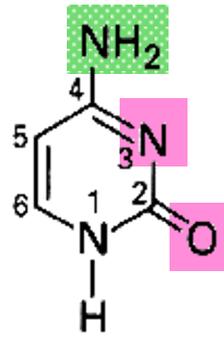
Base pairing



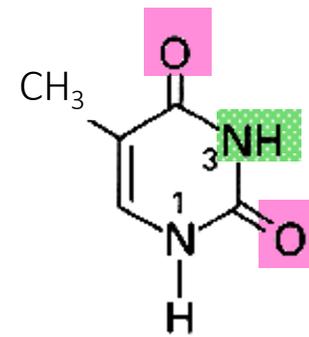
adenine



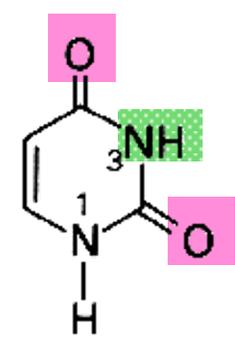
guanine



cytosine



thymine

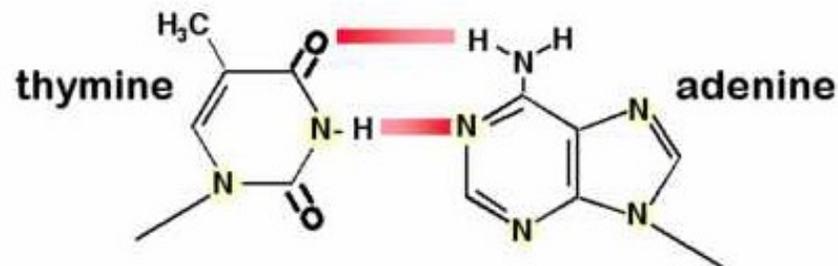


uracil

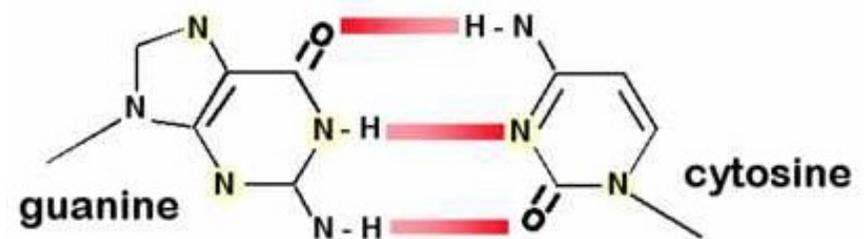
 Hydrogen bond donor

 Hydrogen bond acceptor

Watson-Crick base pairing:



2 hydrogen bonds



3 hydrogen bonds

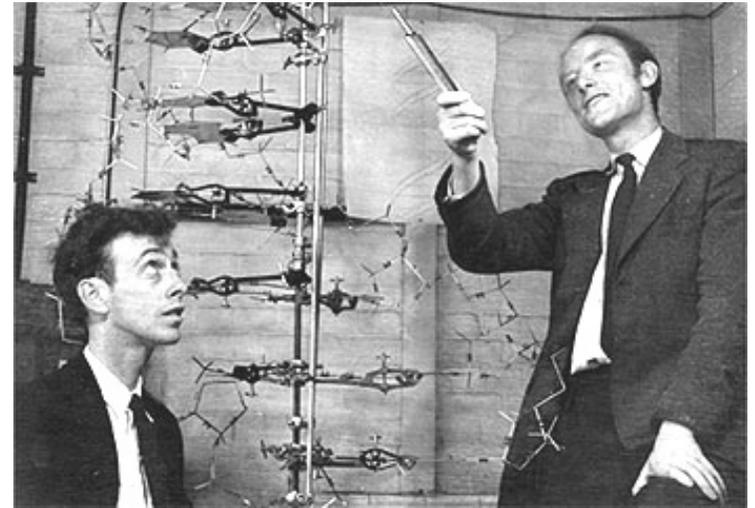
uracil has the same HB properties as thymine and can therefore make the same HB with adenine

Deoxyribonucleic acid (DNA)

DNA is the cellular library storing all the information required to build all proteins. This information is stored in units called **genes**: each gene is a segment of DNA containing a coded representation of a protein.

1944: DNA carries the genetic information
(Avery, MacLeod, McCarthy)

1953: **Double helical structure of DNA unravelled by J. Watson and F. Crick** by careful analysis of the diffraction patterns from DNA fibers collected by R. Franklin and M. Wilkins.

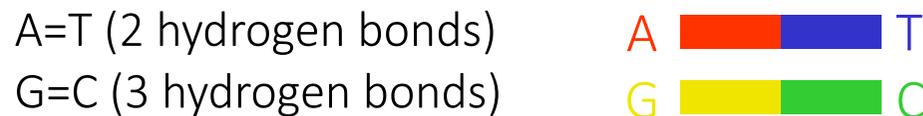


Information available?

- DNA is made by long chains of polynucleotides
- the base composition is such that $[A]=[T]$ and $[C]=[G]$
- fiber diffraction pattern indicated the presence of an helix with 10 units per turn and a characteristic spacing of 3.4 Å.

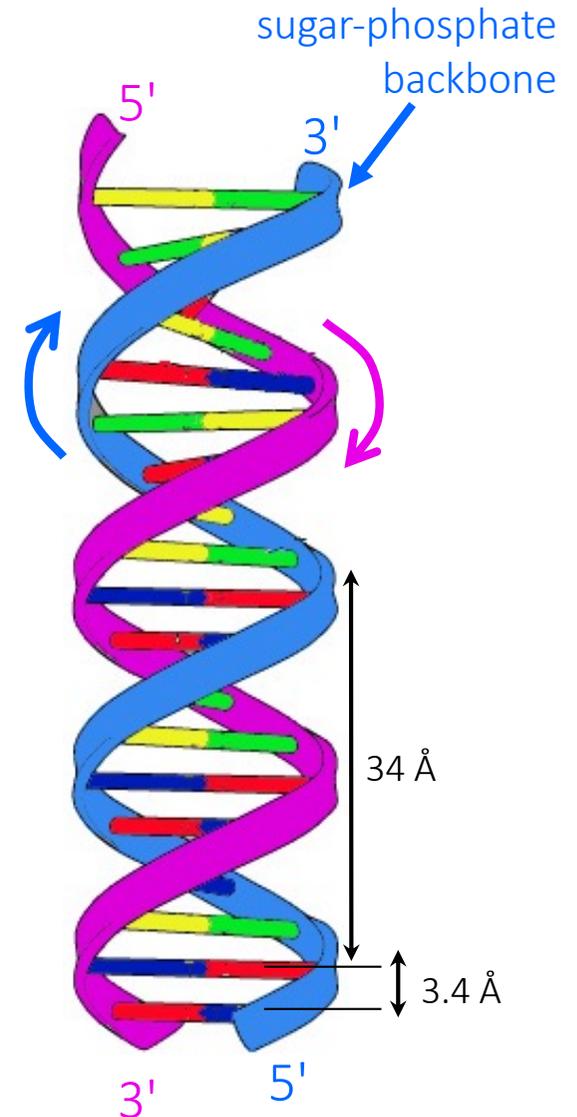
Model of DNA proposed by Watson & Crick

- DNA consists of two polynucleotide chains (strands) winding into a **right-handed double helix**
- the orientation of the two strands is **antiparallel**
- the sugar-phosphate backbone is on the outside
- the bases project into the interior
- the two strands are held together by base-pairing:

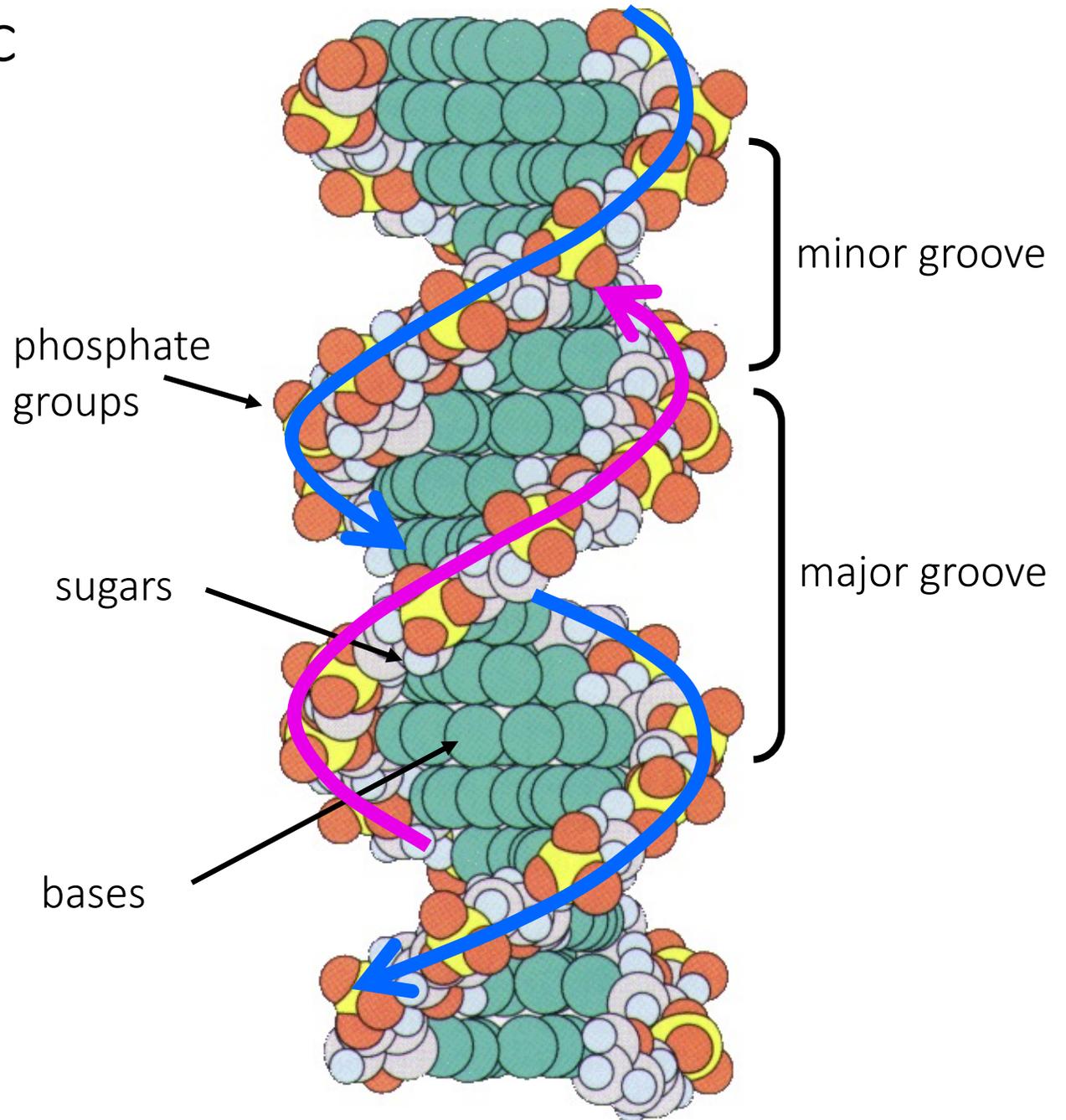


- pairs of bases are stacked on top of each other, 3.4 Å apart along the helical axis
- one helical turn is 34 Å, corresponding to 10 base pairs

The two strands are therefore held together by **non covalent interactions** (HB between paired bases, hydrophobic interactions between the stacked bases)



A more realistic model:

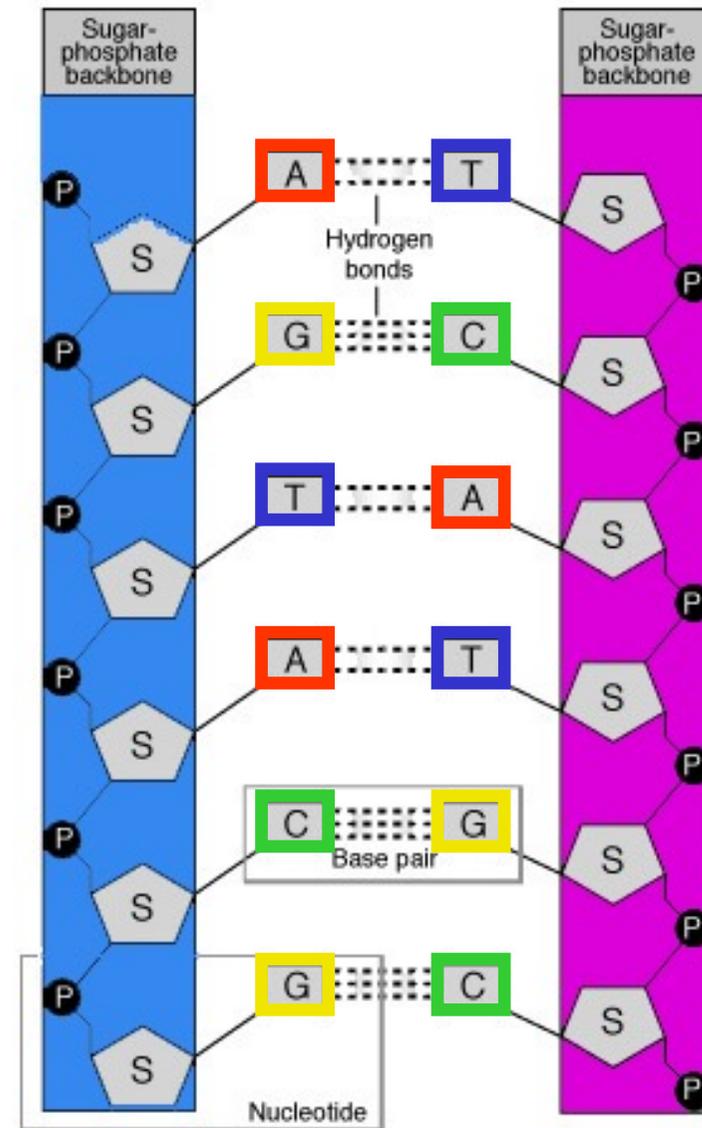


The two strands have complementary sequences

If I know the sequence of one strand I can always find the other:

5' **AATCGAACACCGTACCGT** 3'
|||||
3' **TTAGCTTGTGGCATGGCA** 5'

Strands can be temporarily separated by breaking the hydrogen bonds and hydrophobic interactions holding them together (for example, by increasing the temperature); the two strands can then re-anneal going back to the original structure.



Energy Considerations for Unwinding DNA:

A-T pairs are held by two hydrogen bonds.
G-C pairs are held by three hydrogen bonds.

Base Pair Energetics:

On average, the energy required to break a hydrogen bond in DNA is approximately **1-2 kcal/mol per bond**.

A-T pairs: ~2-4 kcal/mol

G-C pairs: ~3-6 kcal/mol

ATP Hydrolysis:

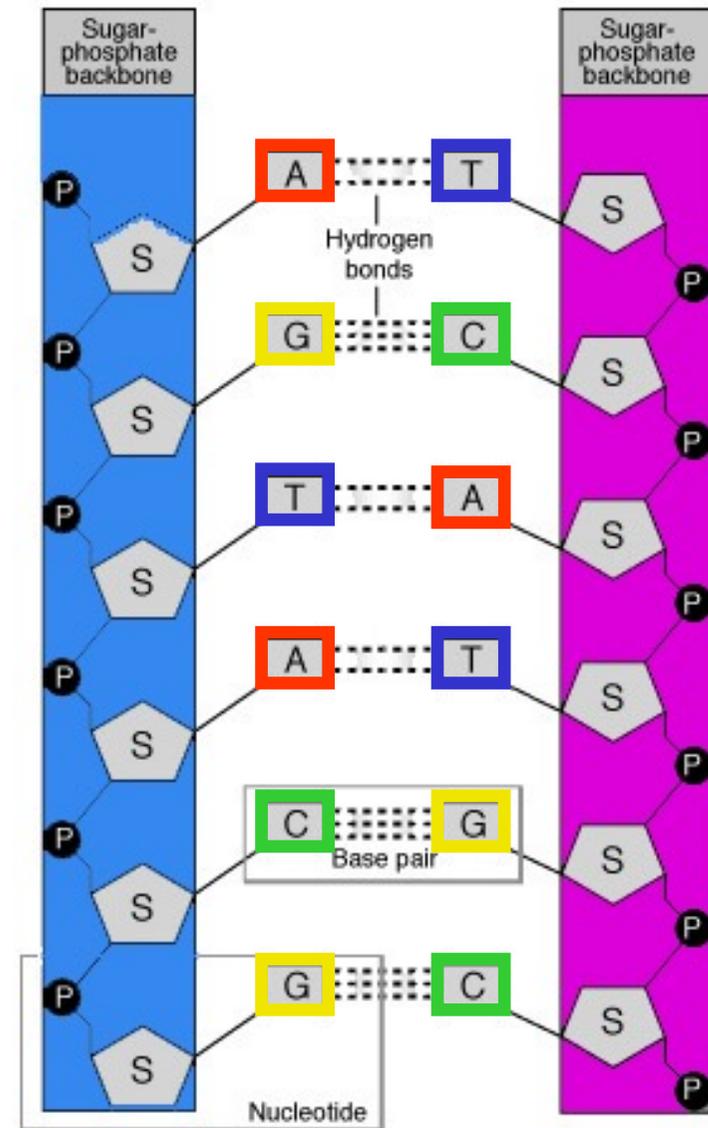
Helicase enzymes unwind the DNA by consuming ATP. **The hydrolysis of one molecule of ATP releases about 7.3 kcal/mol** of energy under physiological conditions.

For each base pair of DNA unwound, a helicase hydrolyzes one molecule of ATP. (at rate of 50 to 1,000 base pairs per second!)

1kcal/mol= 4.184 kJ/mol

1 kcal/mol≈0.043 eV

23 kcal/mol≈1.0 eV



Lipids

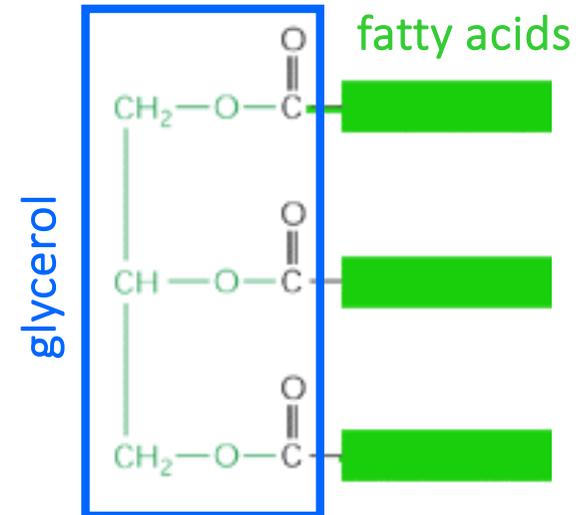
Fatty acids are used as E storage

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**.

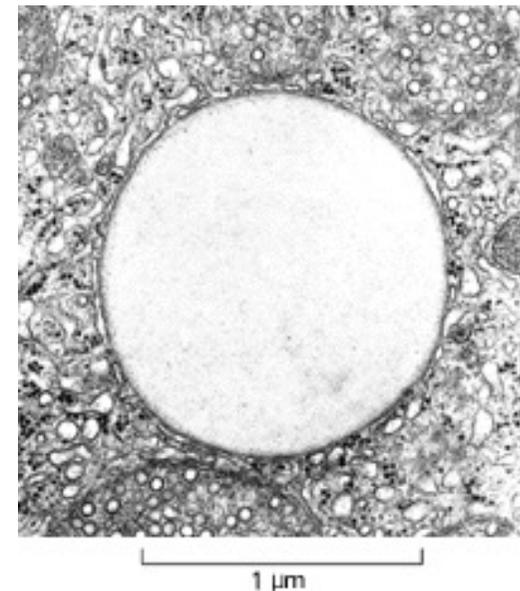
A fat molecule is composed of three molecules of fatty acid linked to glycerol: triacylglycerols (*triglycerides*).

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.



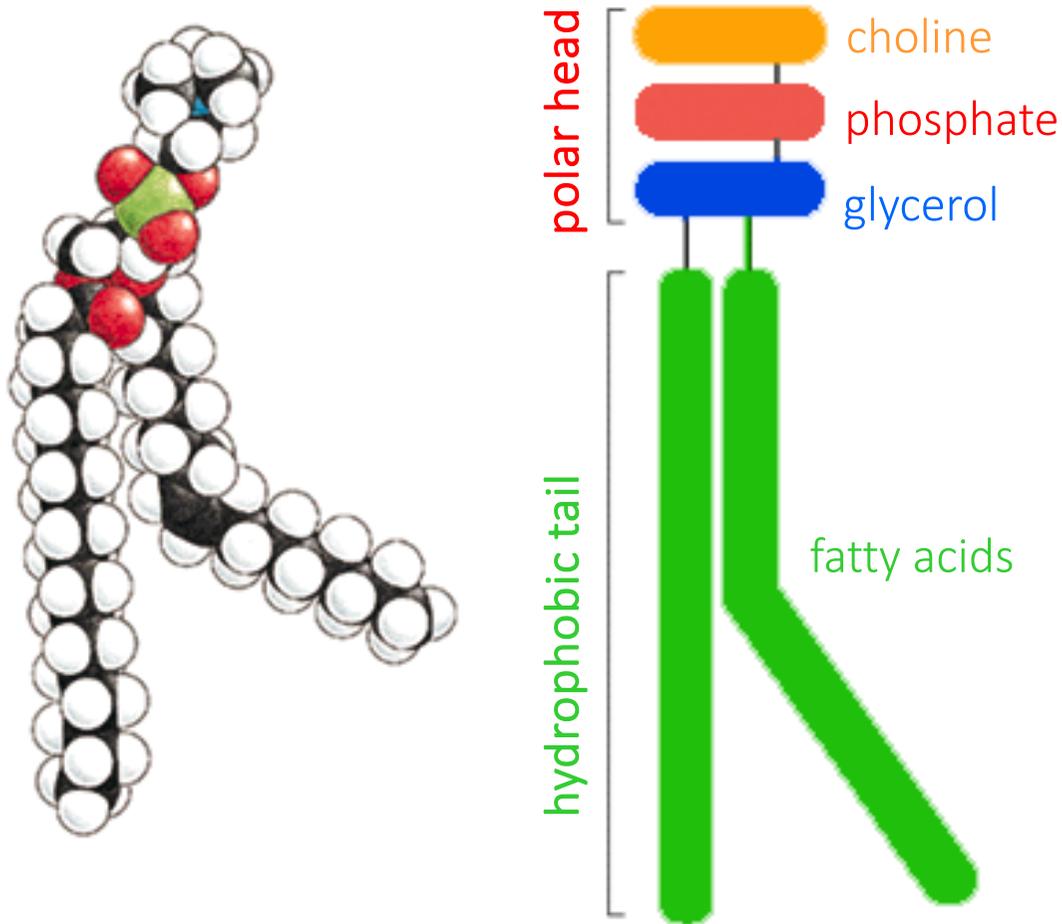
fat droplet



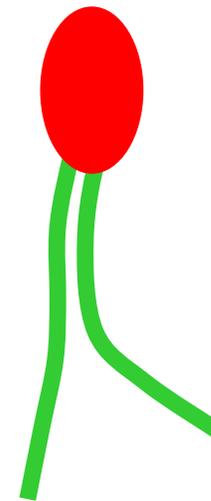
Phospholipids

3

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

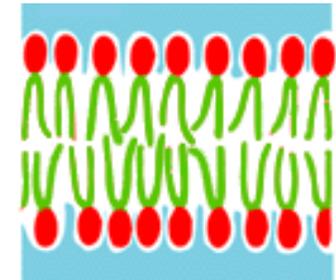
Phospholipids are the major constituent of cell membranes.

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

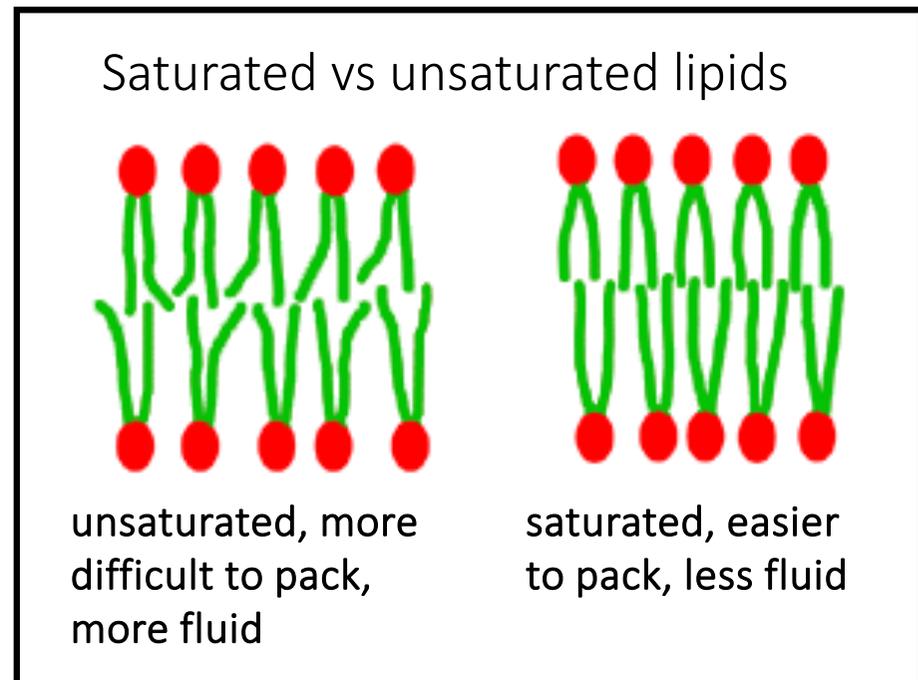
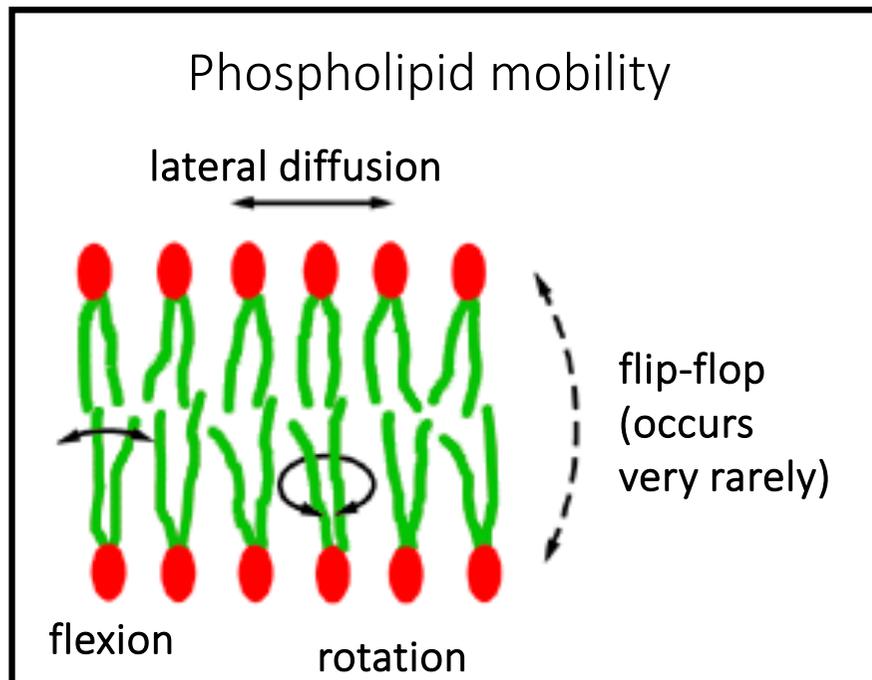
Cellular membranes are essentially made up by phospholipid bilayers.



micelle

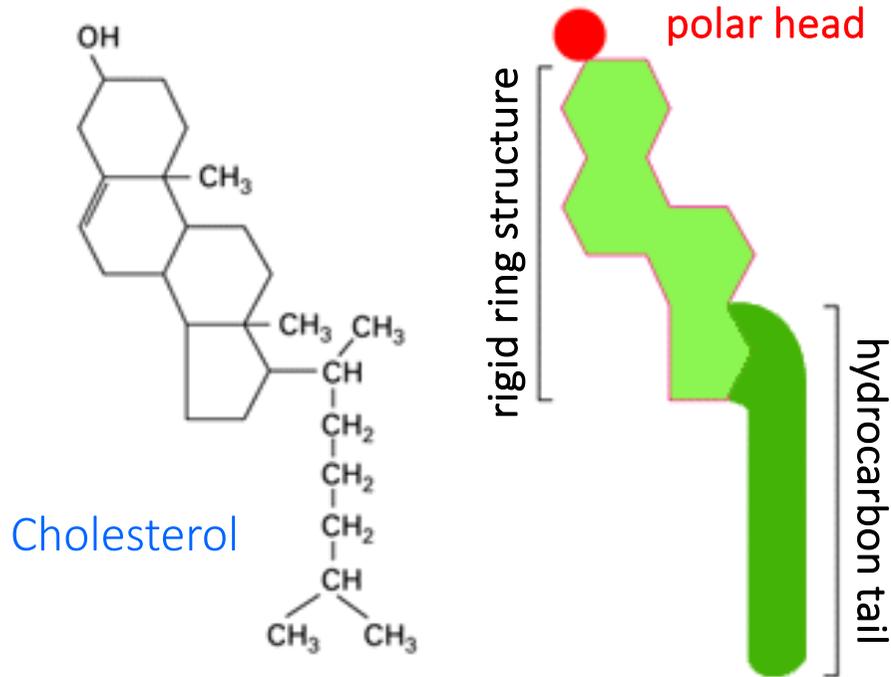


lipid bilayer

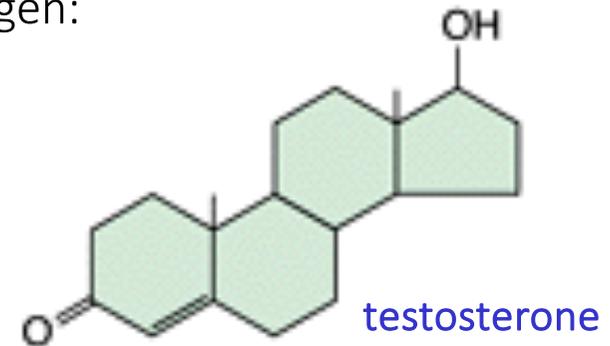


Cholesterol and steroids

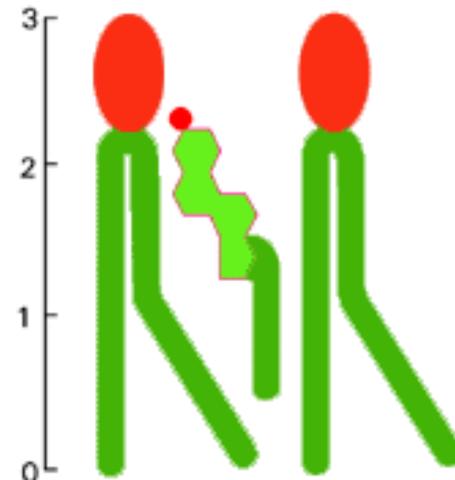
Steroids (such as cholesterol) have a rigid structure made up by 4 rings.



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

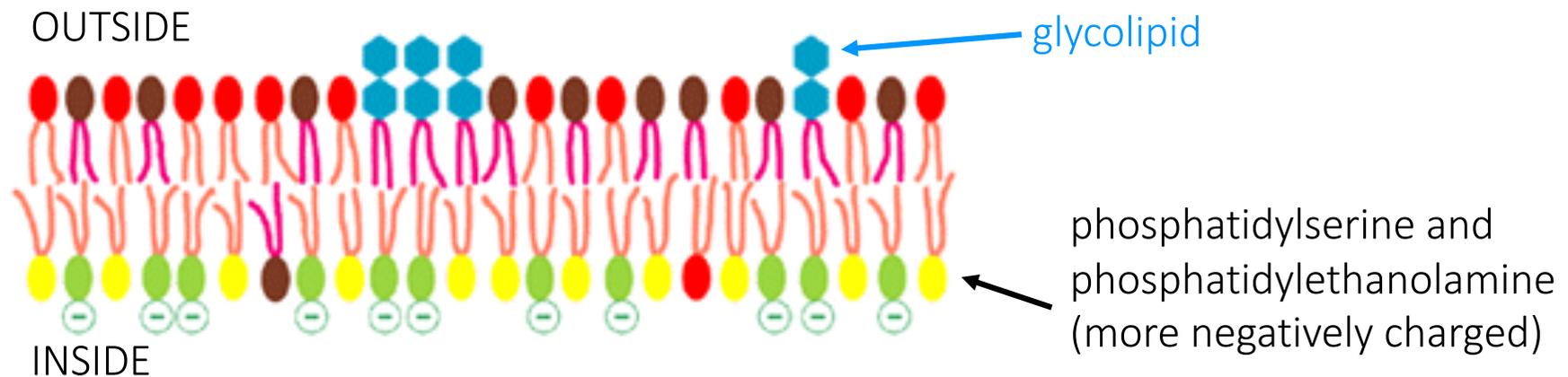
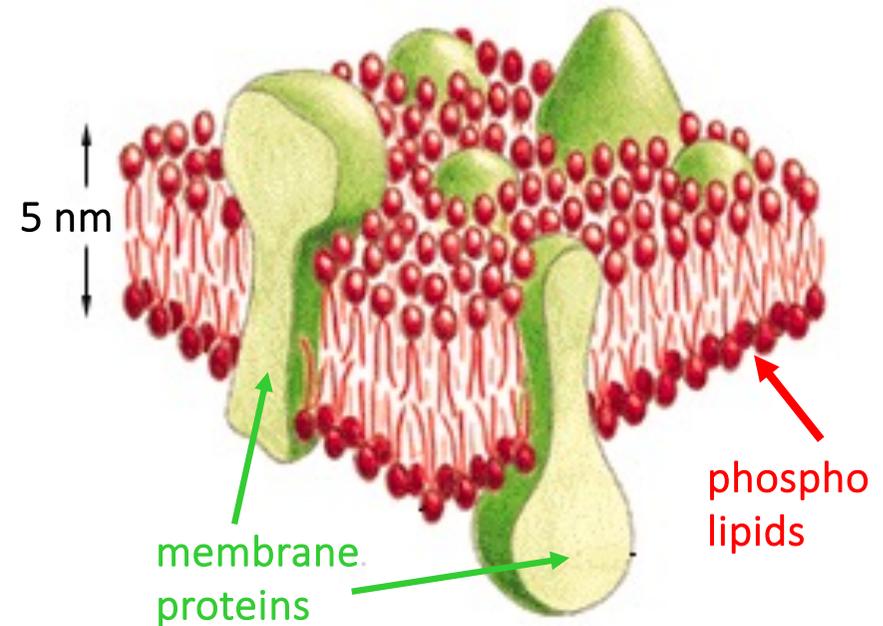


Cholesterol is an important component of the eukaryotic membranes and has a key role in controlling the membrane fluidity.



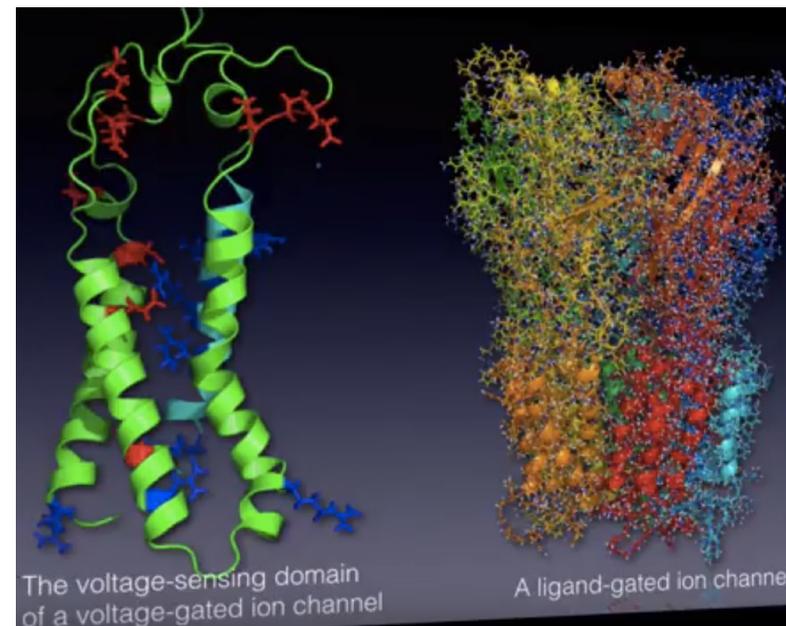
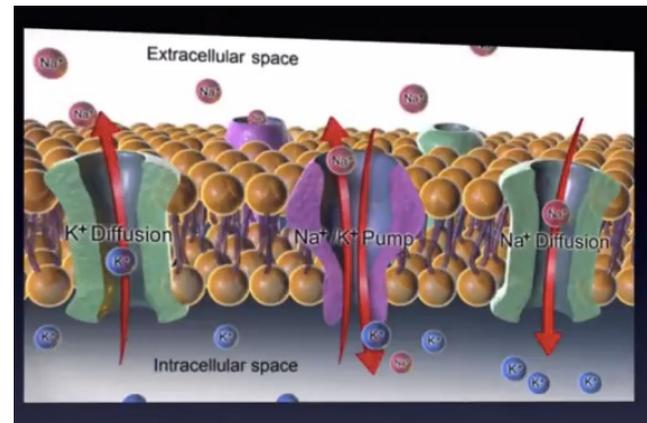
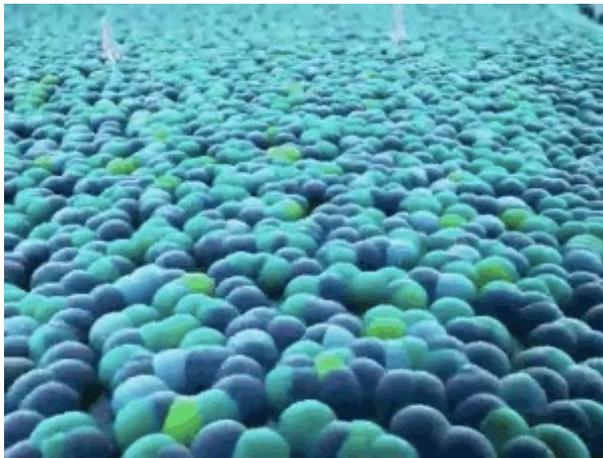
Cell membranes

- 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 (H₂O is actively transported in)
- many proteins are embedded in the membrane
- the membrane is highly asymmetric



Cell membranes

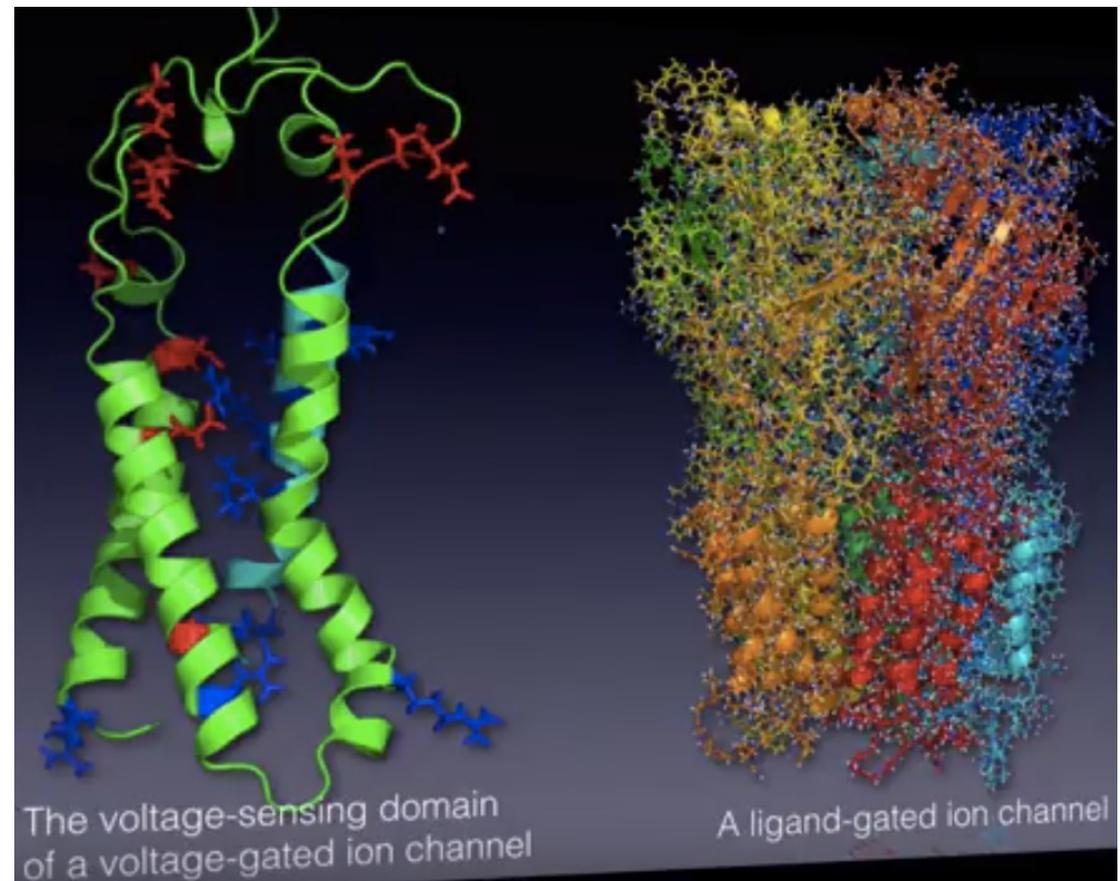
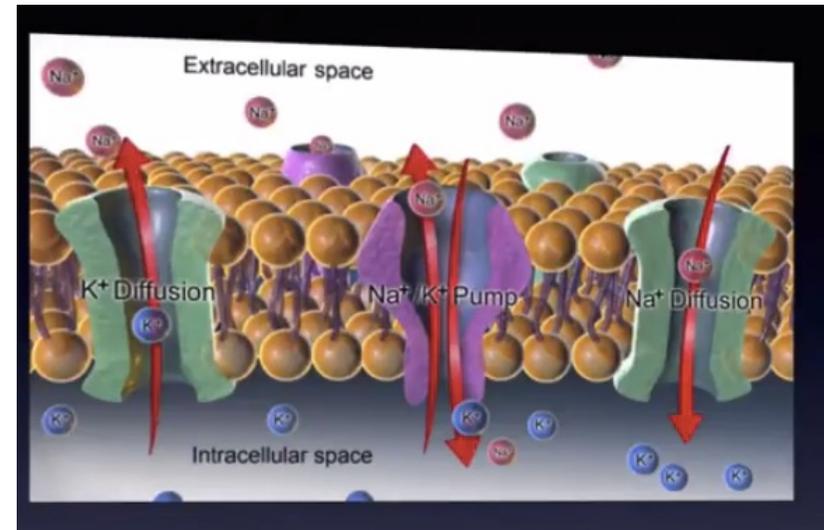
Also, we know that **cell membranes** play a crucial role in cell-cell, cell-environment communication. How much do we know about molecular interactions at the cell membrane?



Cell is a highly organized and orderly structure: does it 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.

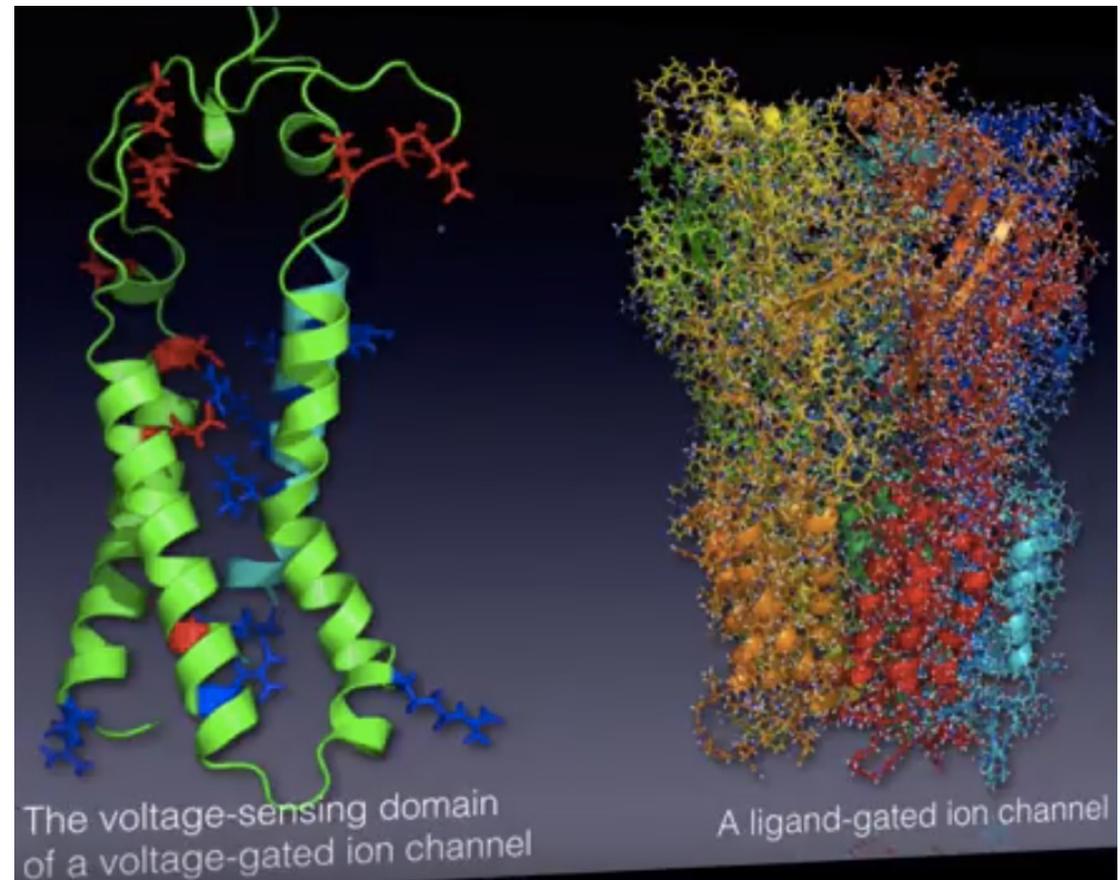
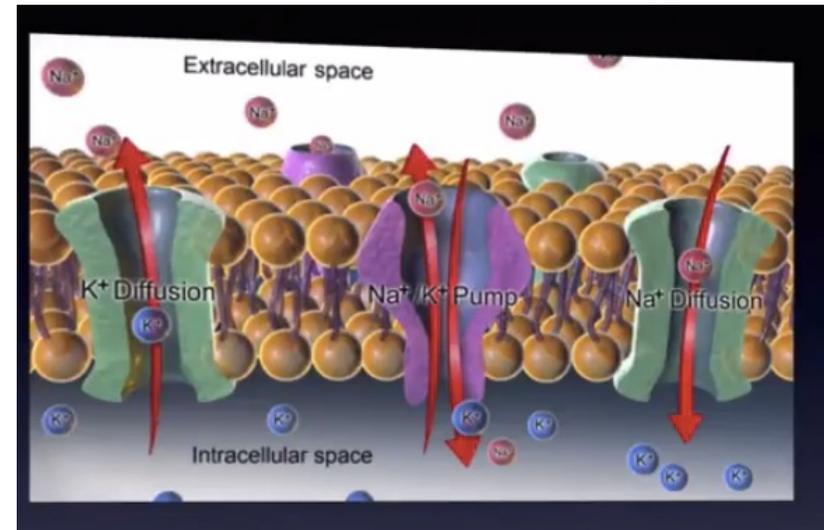


Biology is about
distribute/generate/consume energy.

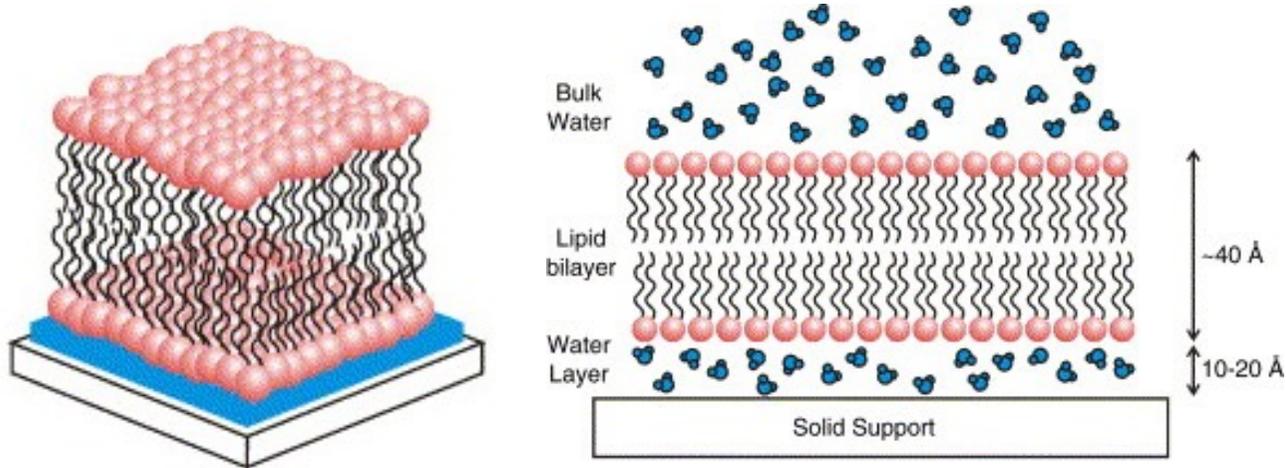
Ion channels are the voltage-sensing domains of a voltage-gated access (heart beats, nerve impulse), which make the cell working as a battery (selective opening of the channel).

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!)

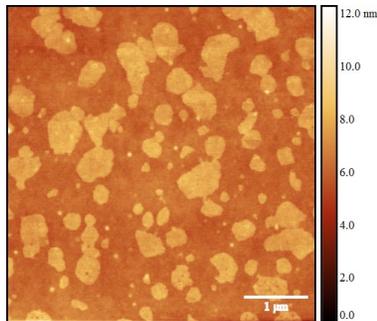


Artificial lipid bilayers

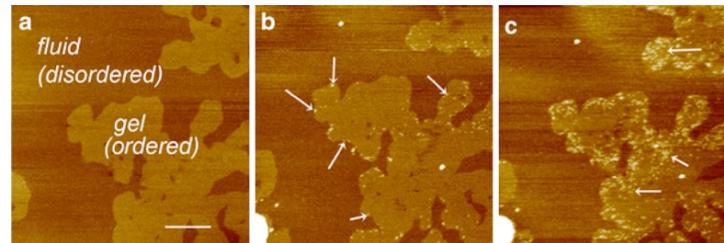


✓ Multicomponent model membranes for mimicking cellular membranes

Lipids behaviour



Protein-lipid interactions



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

Carbon nanotubes interactions

