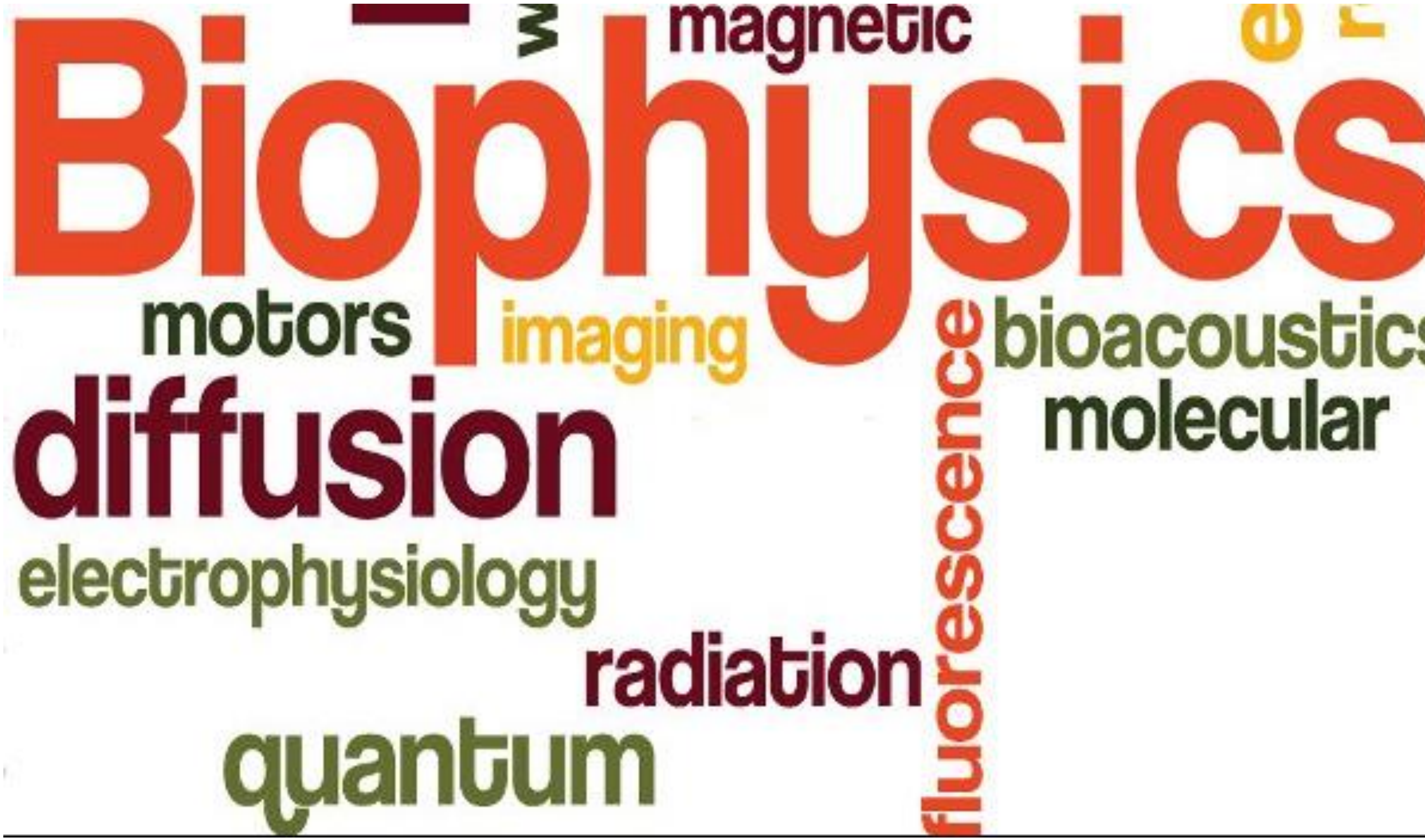
Introduction to Biophysics

Asst. Prof. Phan Anh Tuan


magnetic
Biophysics
motors
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diffusion
fluorescence
electrophysiology
radiation
quantum

What is Biophysics?

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

(Mathematics + Physics + Chemistry + Biology)

Biophysics has been critical to understanding the mechanics of how the molecules of life are made, how different parts of a cell move and function, and how complex systems in our bodies—the brain, circulation, immune system, and others— work.

Biophysics is a vibrant scientific field where scientists from many fields including **math**, **chemistry**, **physics**, **engineering**, **pharmacology**, **and materials** sciences, use their skills to explore and develop new tools for understanding how biology—all life—works.

Biophysics is considered a bridge between Physics and Biology

Application of physics to biology

To use physics to answer questions in biology

INTRODUCTION

Life and nonlife are composed of the same matter and energy.

Life and nonlife differ by how matter and energy are arranged.

Life is characterized by exceptionally complex arrangements of atoms (molecular and supramolecular structures).

These arrangements form dynamically, and over time they undergo changes in conformation and in complex interactions.

Understanding life on a molecular level involves understanding the arrangements of these complex molecular structures, their conformational changes, and how their interactions are regulated and controlled.

Study of these processes gives insights into the fundamental structure and function of life's building blocks and allows us to study diseases that occur when these carefully calibrated equilibria fail (when regulation and control no longer function).

Biochemical and biophysical methods and instrumentation can help provide this understanding and help us investigate these biological processes by using tools from chemistry and physics.

Matter and Energy

1. Atomic nature of matter: atoms and molecules in motion create heat, pressure, diffusion. Measurement of these parameters provides information on molecular number, size, mass and shape.

2. Atoms and molecules have mass and charge: they will move in response to an external gravitational/centrifugal or electric field. Rates of their movement in response to such fields provide information on molecular mass, charge, size and shape.

3. Electromagnetic radiation: speed, amplitude, frequency (energy), phase, polarization, absorbance and emission (frequency or wavelength); constructive and destructive interference.

Matter and Energy

4. Interaction between electromagnetic radiation and matter: elastic and inelastic scattering, absorption and emission (wavelength), resonance (relationship to electronic or nuclear structure), refraction, diffraction, reflection.

5. Interrogation of biological matter with electromagnetic radiation or thermal energy provides information on the structure (positions and types of atoms and their chemical bonding) and dynamics (movements of the atoms), and their interactions and distances from each other.

Matter and Energy

6. Frequencies of absorbed or emitted radiation are determined by electronic and nuclear structure and the local environment around an atom or molecule. Spectroscopic methods therefore provide information on the composition, chemical environment & bound state of an atom.

7. The spontaneous loss of absorbed radiation results either in heat or emitted light (fluorescence or phosphorescence), which can be used to probe distances by resonance transfer.

Matter and Energy

8.Instrumentation is used to generate the thermal/electromagnetic radiation or centrifugal/electric fields that are used to interrogate biological material and to extend the sensitivity, reliability, precision and resolution with which radiation is measured, as well as to allow detection of radiation that is otherwise invisible to human senses.

9.Equations and algorithms describe quantitatively how a change in a measurable parameter (amplitude, frequency, position, phase, radiation or thermal energy scattered/emitted/absorbed by matter) is related to otherwise undetectable atomic features of the matter.

A classification of biosystems according to physics

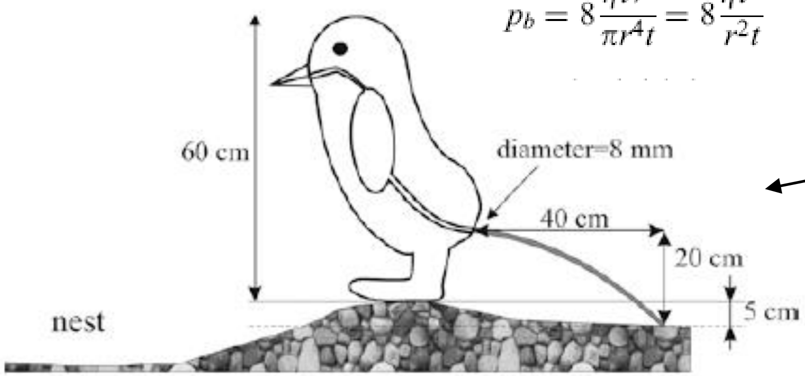
SIZE	FUNCTION
Macroscopic scale (> 1 mm)	Energy transport (e.g. motor proteins)
Microscopic scale (1 mm > size > 100 nm)	Energy conversion (ATP)
Molecular scale (100 nm > size)	Energy storage (glucose)

Other classification schemes are possible!

Biophysics on the macro-scale

Penguins know how to do such experiments!

$$p_b = 8\frac{\eta l V}{\pi r^4 t} = 8\frac{\eta l^2}{r^2 t}$$



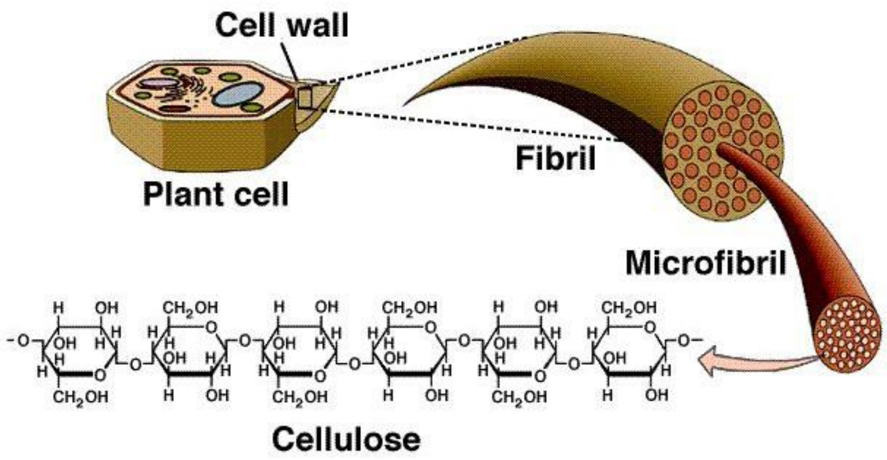
Very high pressure (several times that of humans) allows the penguins to avoid shitting in their own nests and at the same time avoid energetically unfavorable (and painful) turbulent flow; Polar Biology, p. 56, Vol.27 (2003)

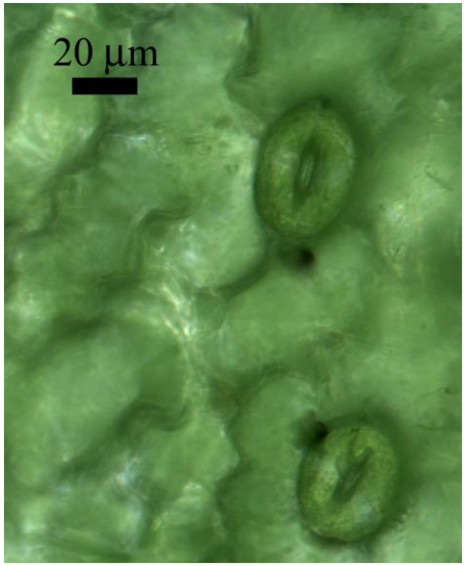
Biophysics on the micro-scale

<u>Examples:</u>

- Study the physical properties of cell membranes (stiffness, porousity, etc) through measurements and simulations.

- Study how water flows into plants and biological systems.





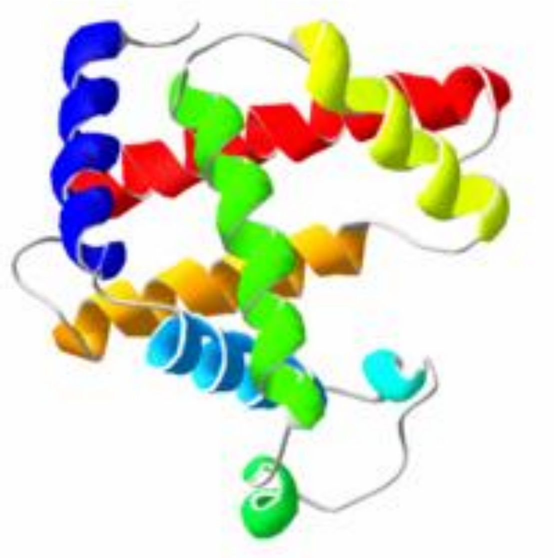
Plant cells

Biophysics on the molecular scale

Examples:

- Study the structure and function of DNA and proteins.

- Study the how proteins transport ions (sodium, potassium) through the cell membrane (important for nerve conduction)



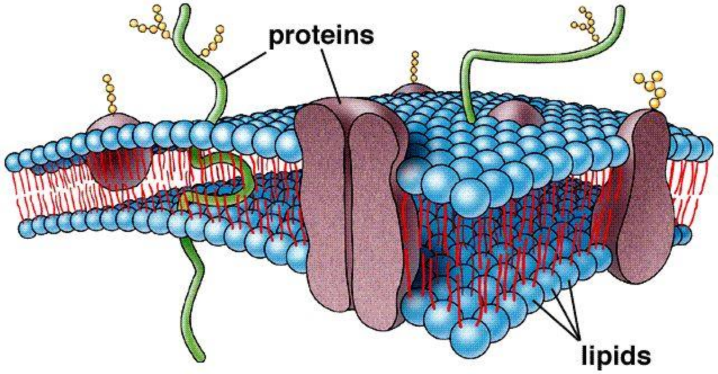
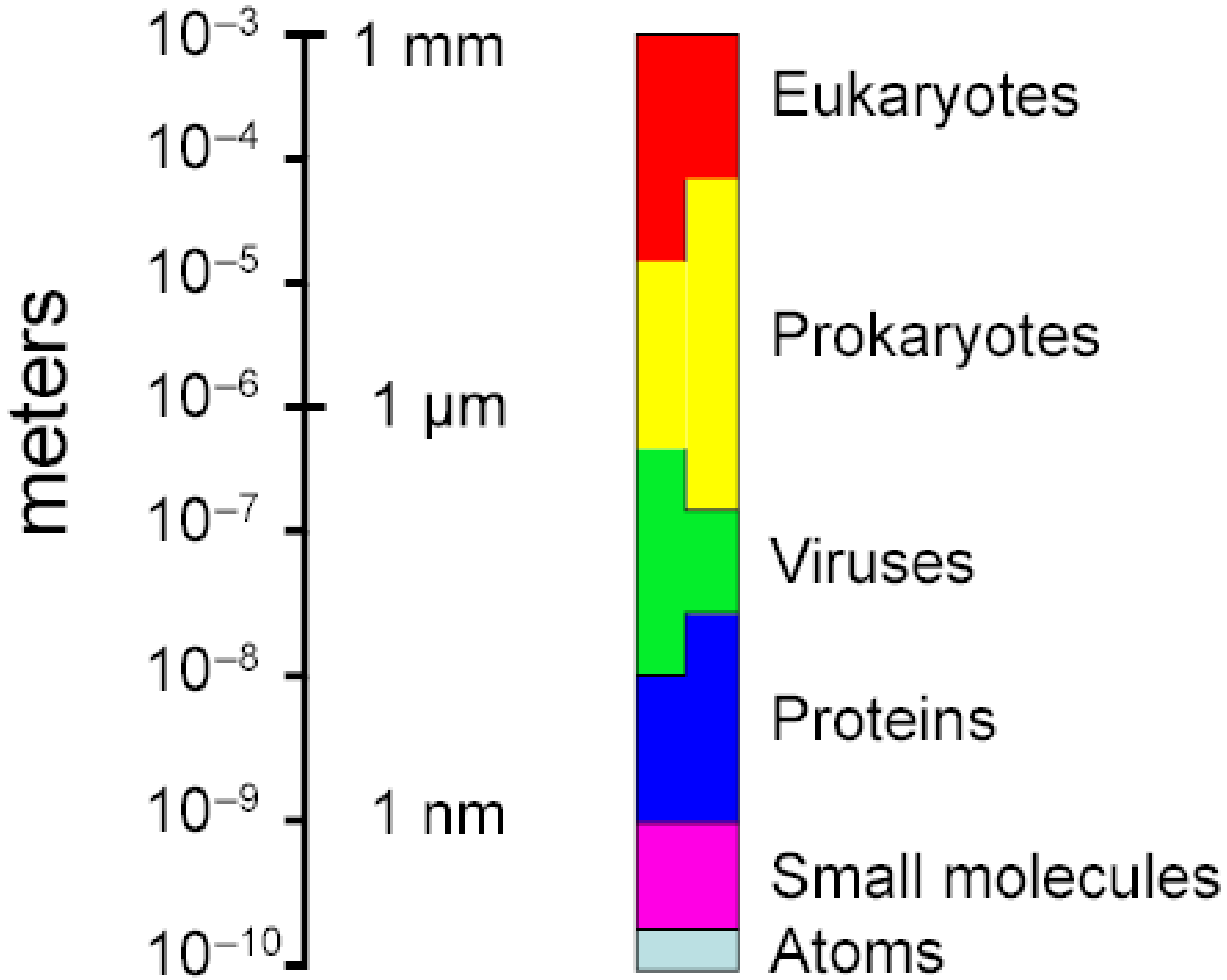


TABLE 1.1

Approximate Values of Some Measured Lengths

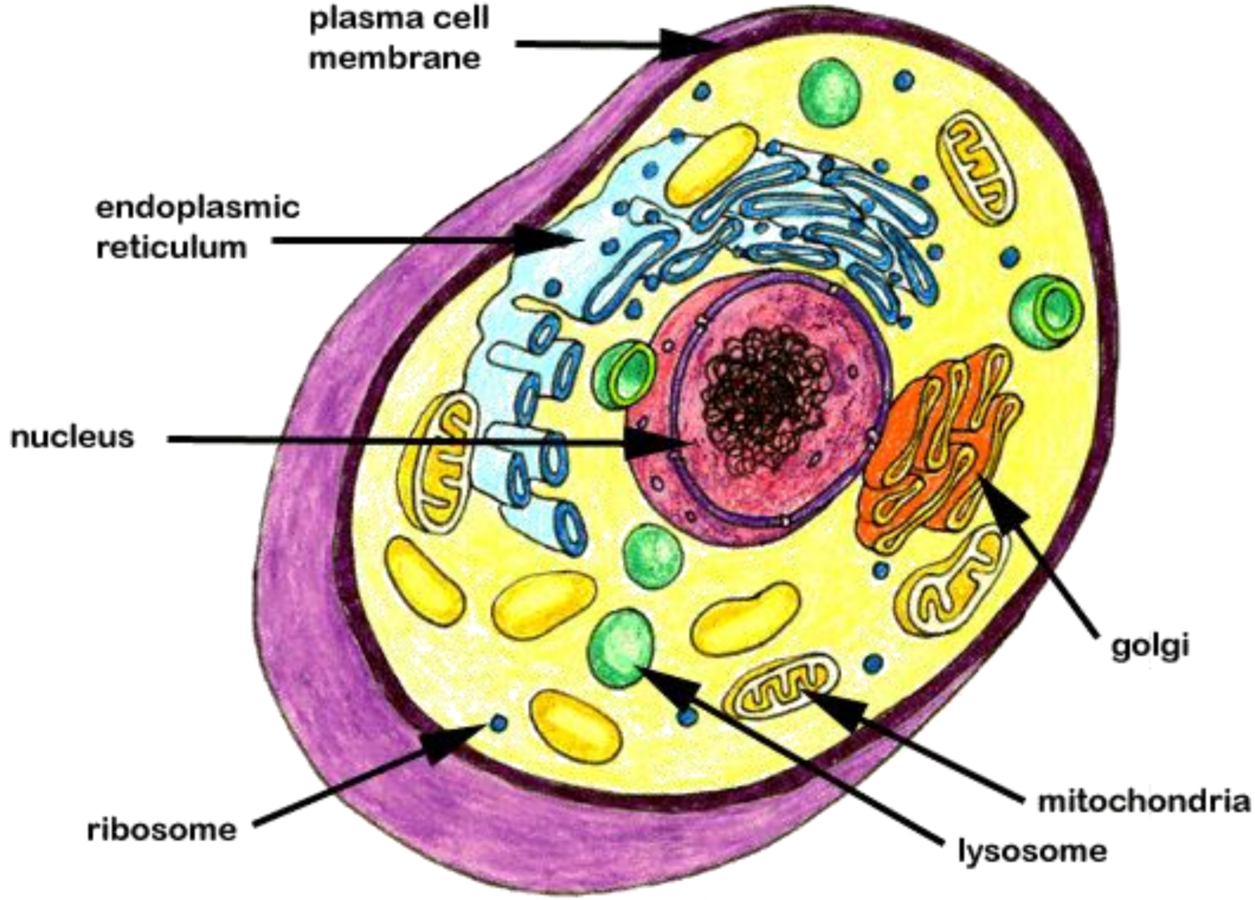
	Length (m)
Distance from Earth to most remote known quasar	1×10^{26}
Distance from Earth to most remote known normal galaxies	4×10^{25}
Distance from Earth to nearest large galaxy (M31, the Andromeda galaxy)	2×10^{22}
Distance from Earth to nearest star (Proxima Centauri)	4×10^{16}
One light year	9×10^{15}
Mean orbit radius of Earth about Sun	2×10^{11}
Mean distance from Earth to Moon	4×10^{8}
Mean radius of Earth	6×10^{6}
Typical altitude of satellite orbiting Earth	2×10^{5}
Length of football field	9×10^{1}
Length of housefly	5×10^{-3}
Size of smallest dust particles	1×10^{-4}
Size of cells in most living organisms	1×10^{-5}
Diameter of hydrogen atom	1×10^{-10}
Diameter of atomic nucleus	1×10^{-14}
Diameter of proton	1×10^{-15}

Range of sizes for bio-objects

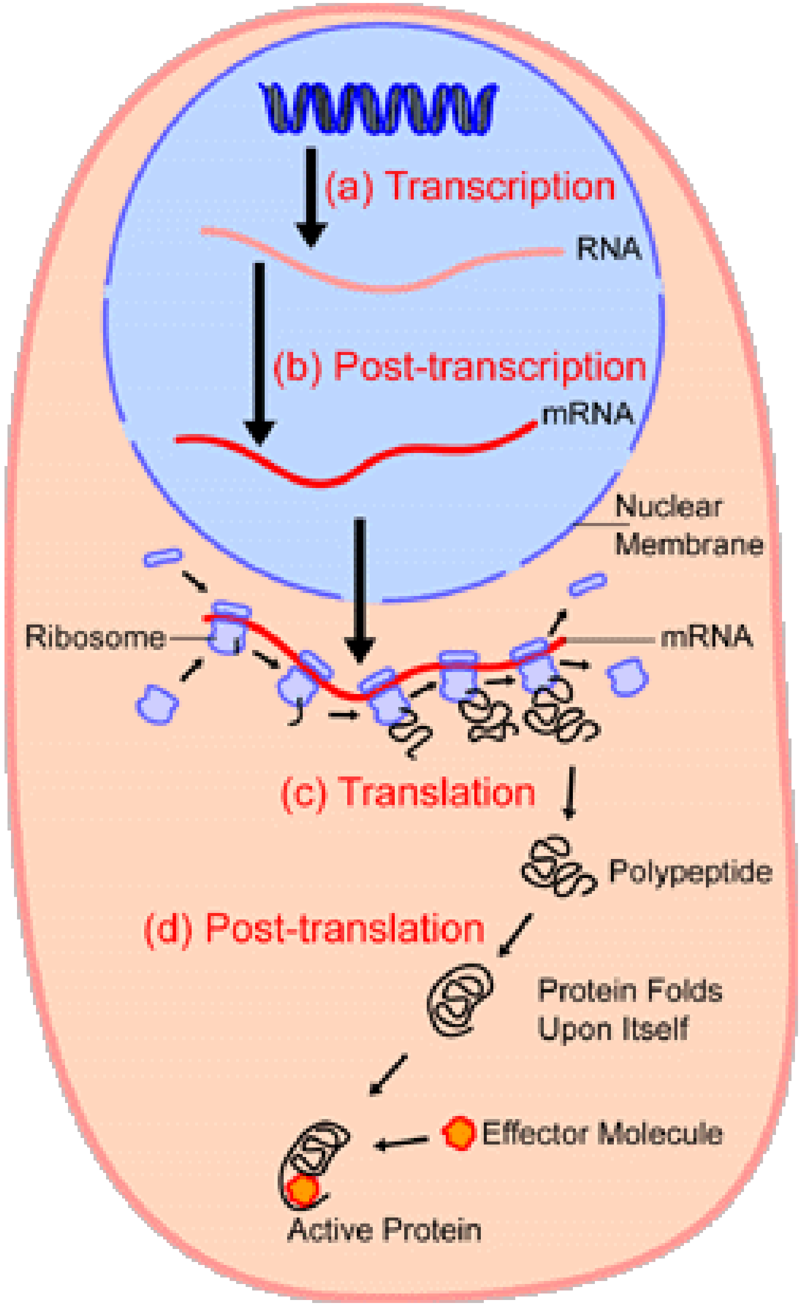


http://en.wikipedia.org/wiki/Virus

A cell

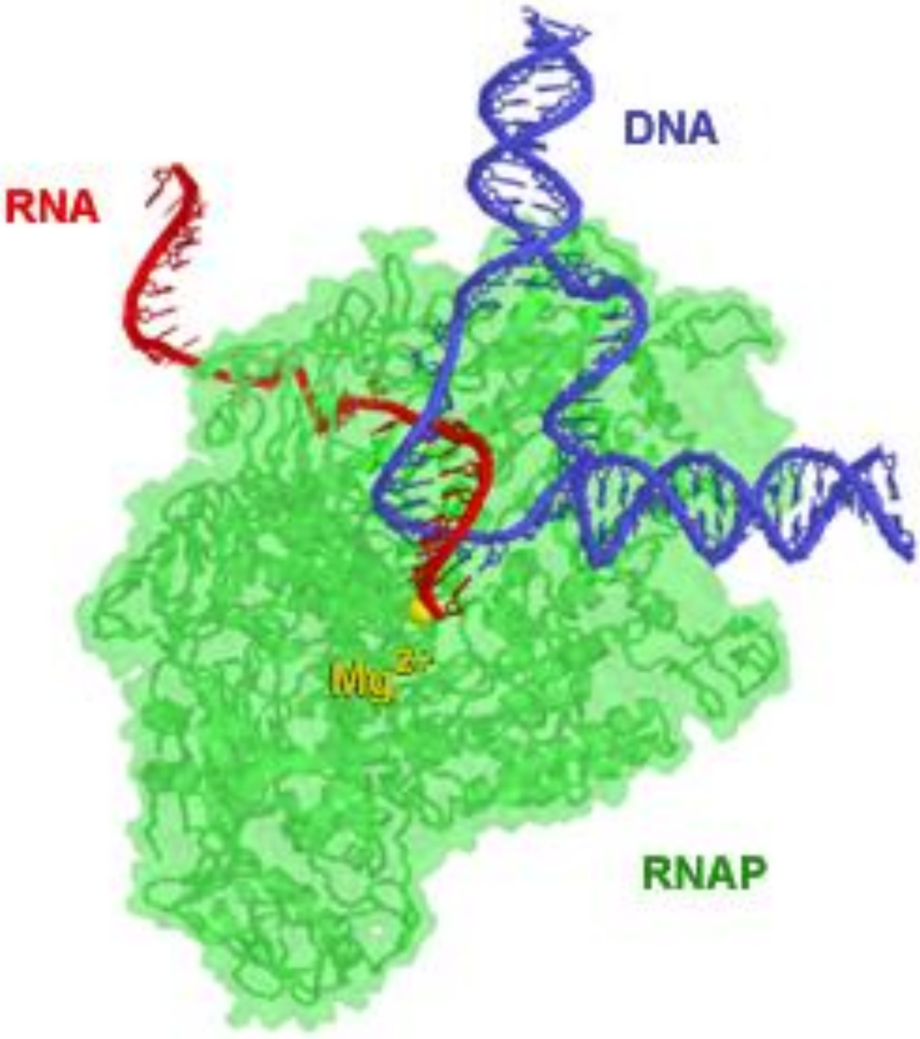


http://web.jjay.cuny.edu/~acarpi/NSC/13-cells.htm

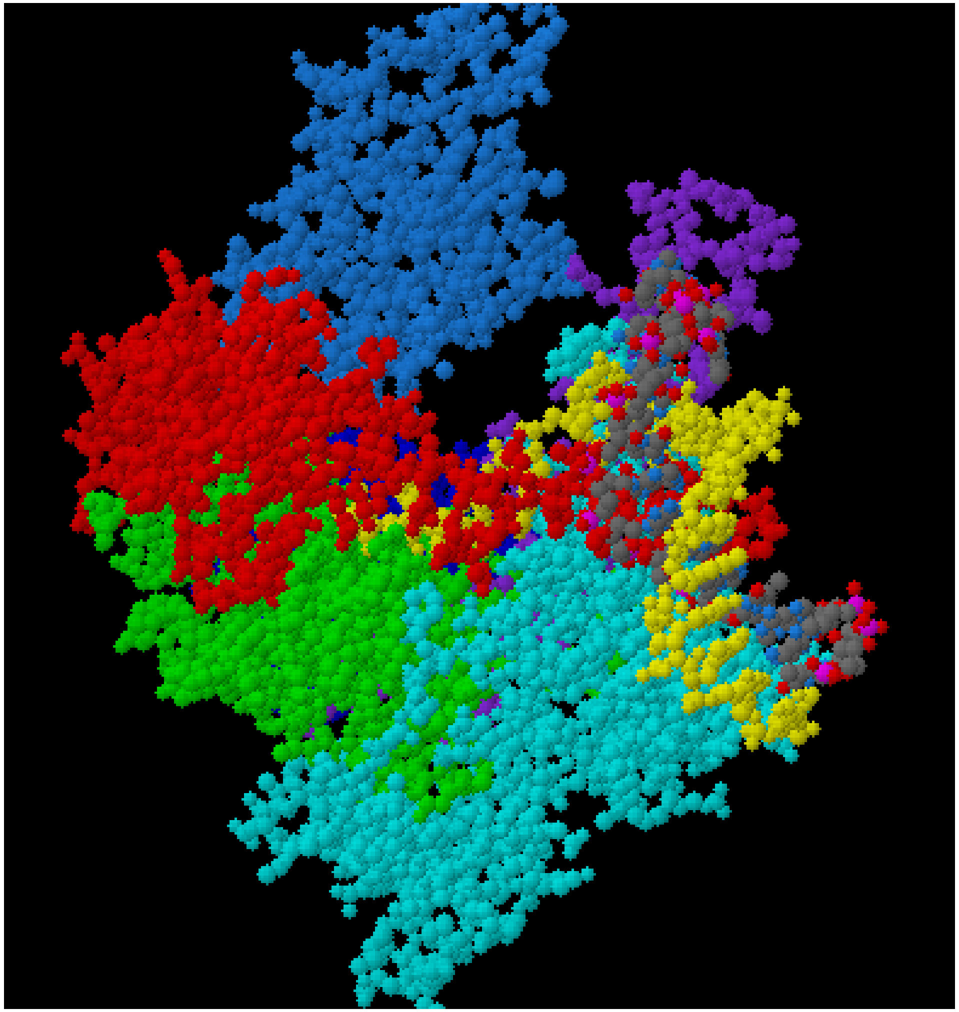


http://en.wikipedia.org/wiki/Cell_(biology)

RNA polymerase

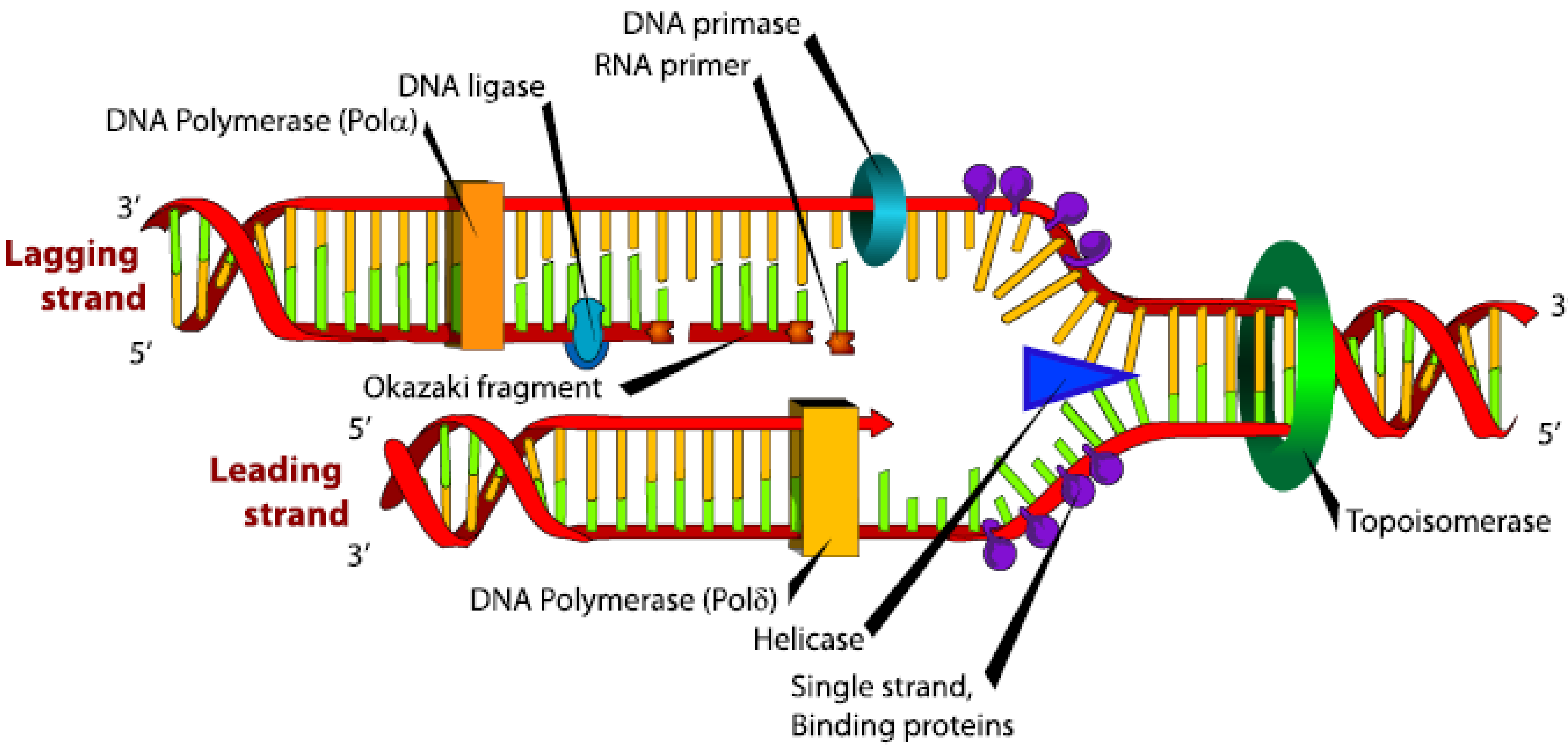


http://en.wikipedia.org/wiki/RNA_polymerase



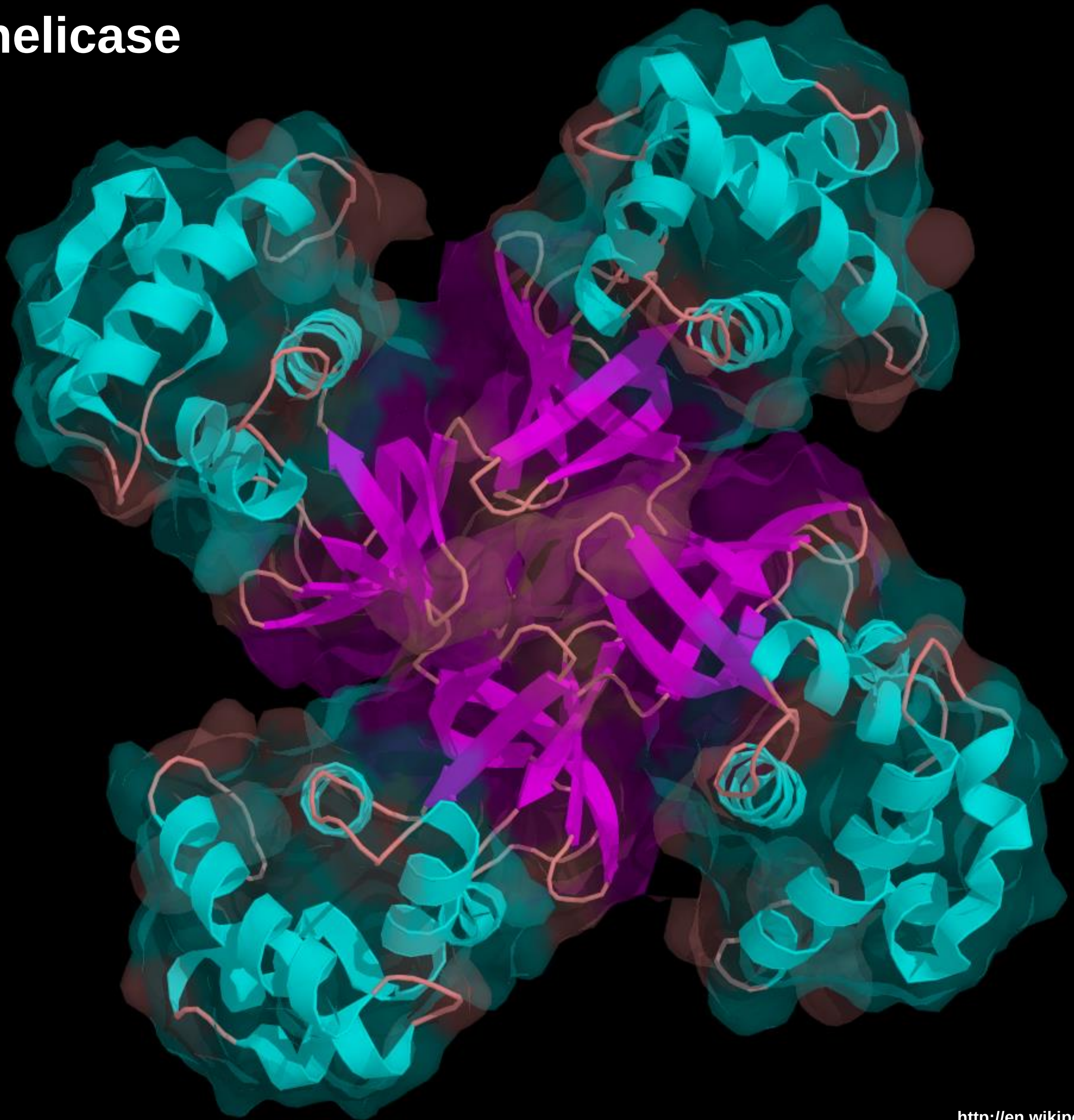
http://dwb.unl.edu/Teacher/NSF/C08/C08Links/www.acsu.buffalo.edu/~jbarnard/RnaPSpin-web.GIF

DNA replication



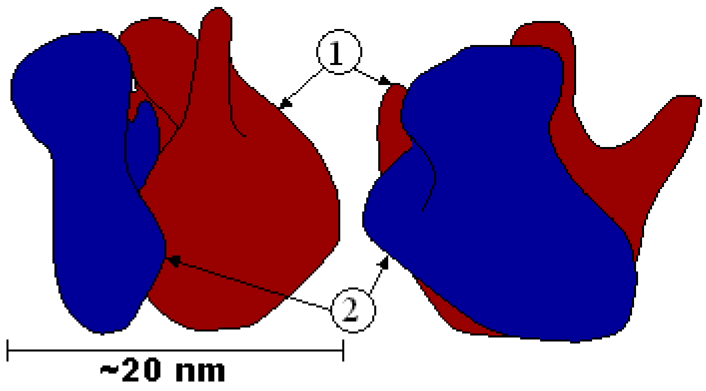
http://en.wikipedia.org/wiki/DNA_polymerase

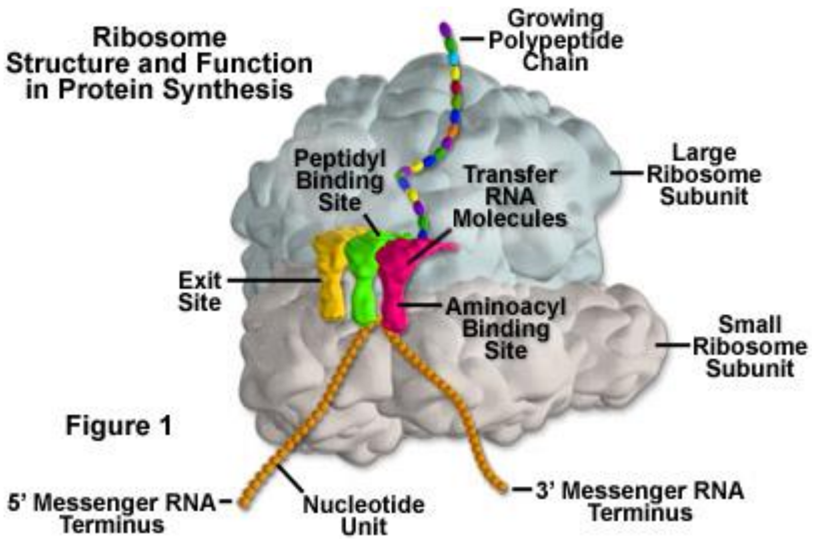
Yeast helicase



http://en.wikipedia.org/wiki/Helicase

Ribosome

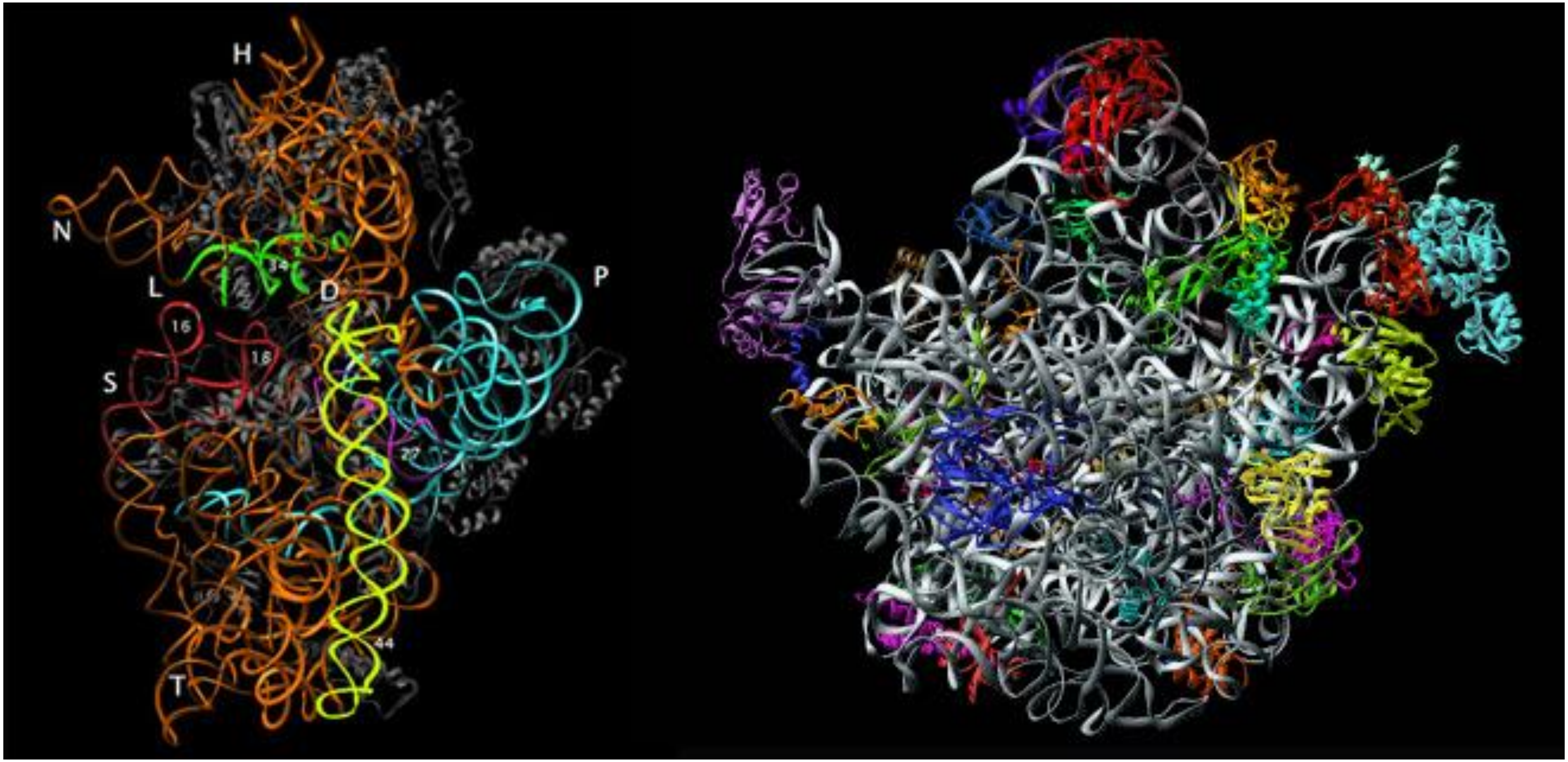




http://en.wikipedia.org/wiki/Ribosome

http://www.molecularexpressions.com/cells/ribosomes/images/ribosomesfigure1.jpg

Ribosome

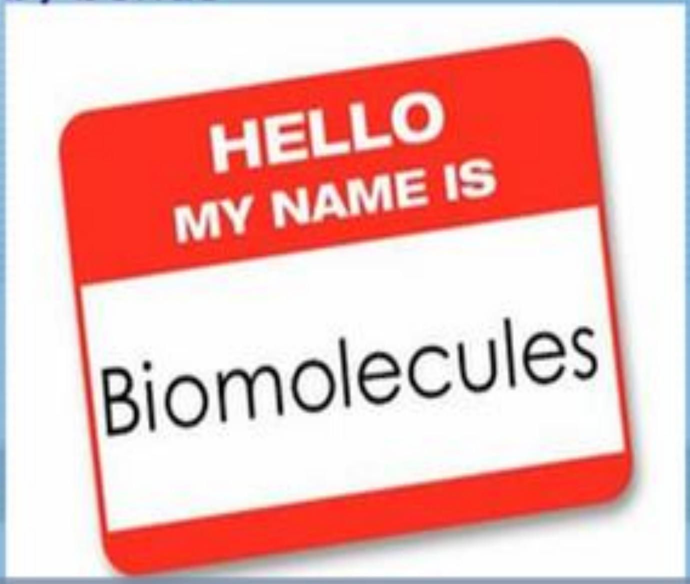


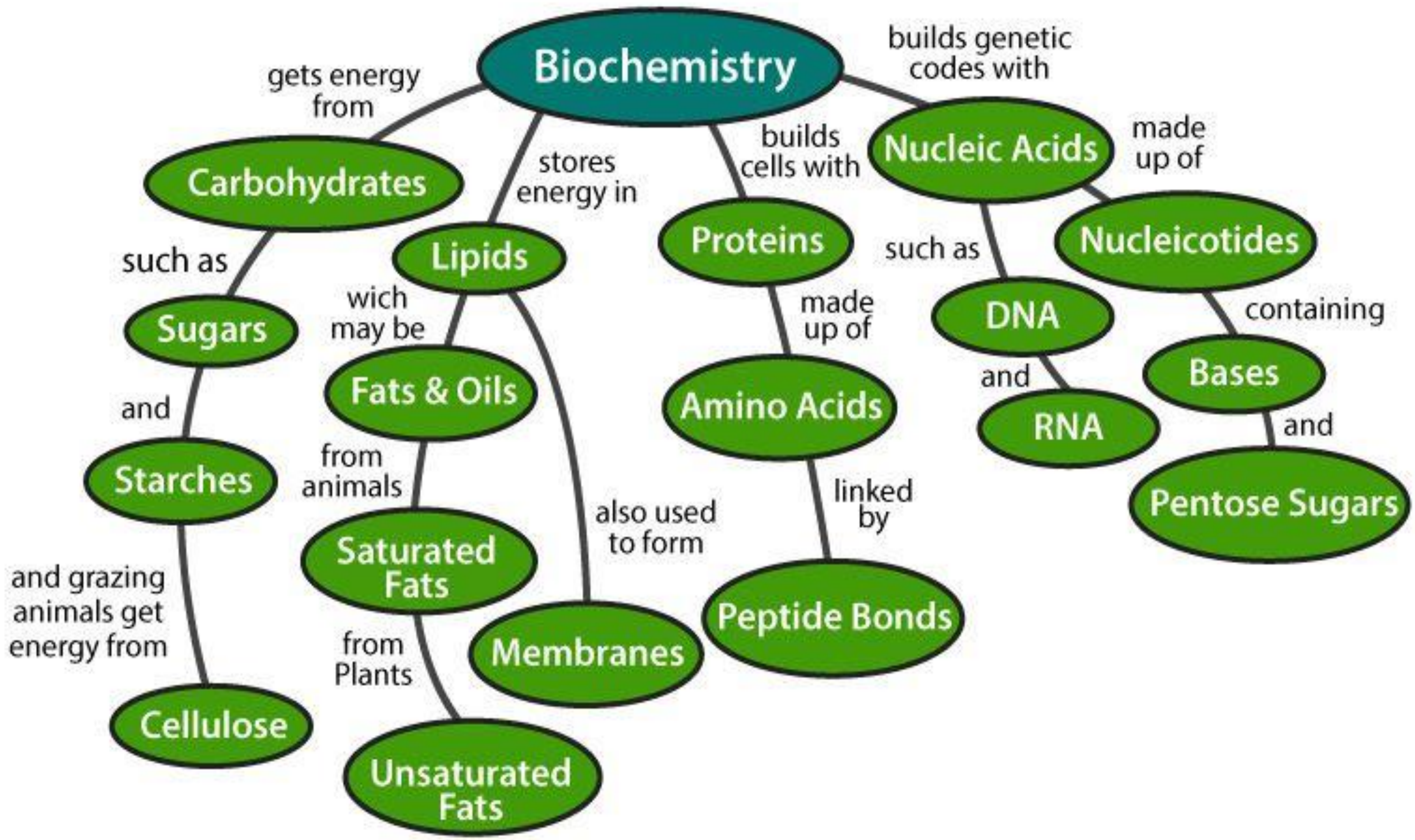
http://www.molgen.mpg.de/~ag_ribo/ag_franceschi/

The understanding of biophysics starts with biomolecules!!

What are biomolecules?

- There are 4 biomolecules
    - Proteins
    - Carbohydrates
    - Lipids
    - Nucleic Acids
- The 4 biomolecules are large molecules that are necessary for life
    - Bio = Life
    - Molecule = a group of atoms held together by bonds
- Nicknames
    - Organic molecules
        - Organic = living matter
    - Macromolecules
        - Macro = large





Biochemistry
gets energy from
Carbohydrates
such as
Sugars
and
Starches
and grazing animals get energy from
Cellulose
stores energy in
Lipids
wich may be
Fats & Oils
from animals
Saturated Fats
from Plants
Unsaturated Fats
also used to form
Membranes
builds cells with
Proteins
made up of
Amino Acids
linked by
Peptide Bonds
builds genetic codes with
Nucleic Acids
such as
DNA
and
RNA
made up of
Nucleicotides
containing
Bases
and
Pentose Sugars

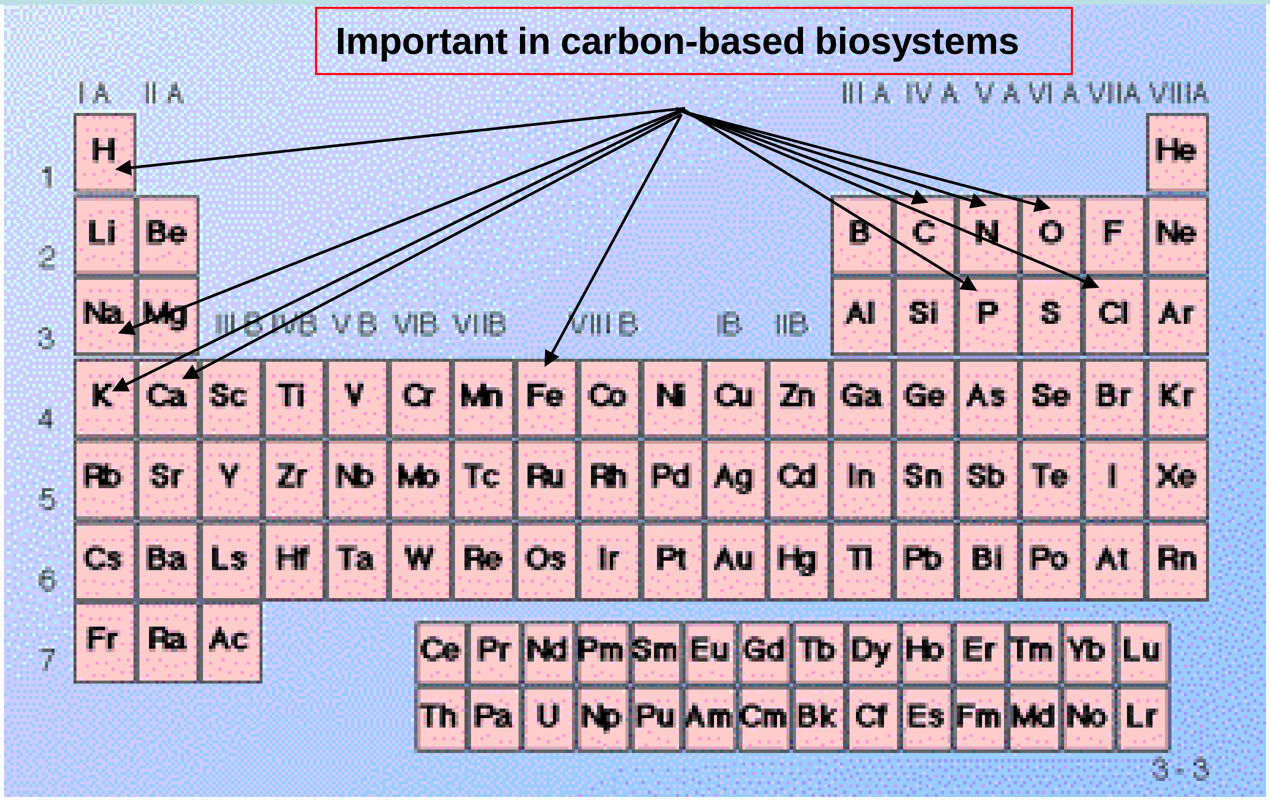
Biomolecular bonds and forces

1. Atoms form strong bonds and create molecules (bonding potentials)
    - Ionic bonds
    - Covalent bonds

2. Molecules interact without forming strong permanent bonds (nonbonding potentials):
    - Hydrogen bonds
    - van der Waals forces

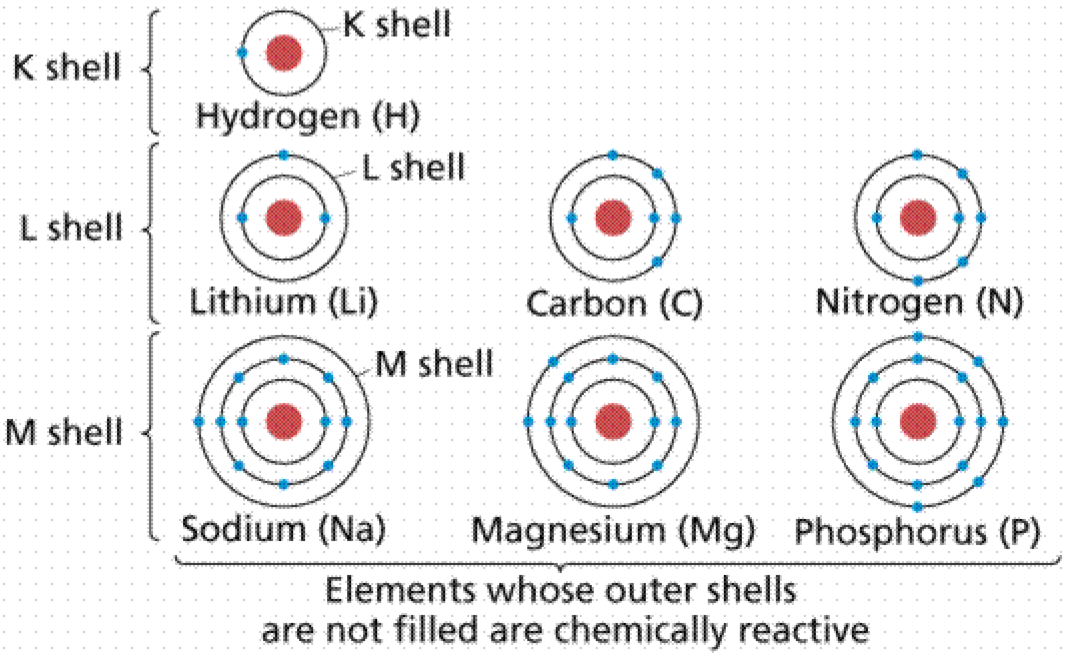
http://www.chemguide.co.uk/atoms/bondingmenu.html#top

Periodic table



http://www.webelements.com/

Which atoms are chemically active?



At what temperature can atoms form bonds (gas→liquid)?

The bond energy must be larger than the thermal energy $k_B T$

$k_B = 1.38 \times 10^{-23}$ J/K (Boltzmann's constant)

T=temperature (in Kelvin)

(remember the ideal gas law $PV = N k_B T$)

$k_B T = (1.38 \times 10^{-23}$ J/K$) \times (300$ K$) = 4.14 \times 10^{-21}$ J$= 0.026$ eV

1 eV is the energy given to an electron by accelerating it through 1 volt of electric potential difference

$$1 \text{ eV} = 1.6 \times 10^{-19} \text{ C} \times 1\text{V} = 1.6 \times 10^{-19} \text{ J}$$

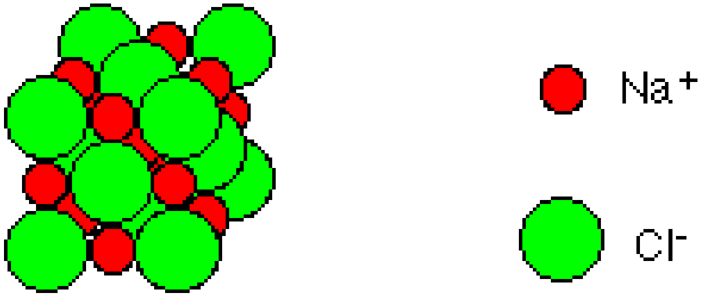
Type	Energy (eV)
Thermal energy of molecule at room temperature	0.03 eV
Visible light (photons)	1.5 – 3.0 eV
Electron striking a TV screen	20000 eV

Ionic bonds

• Sodium (2,8,1) has 1 electron more than a stable noble gas structure (2,8). If it gave away that electron it would become more stable.

• Chlorine (2,8,7) has 1 electron short of a stable noble gas structure (2,8,8). If it could gain an electron from somewhere it too would become more stable.

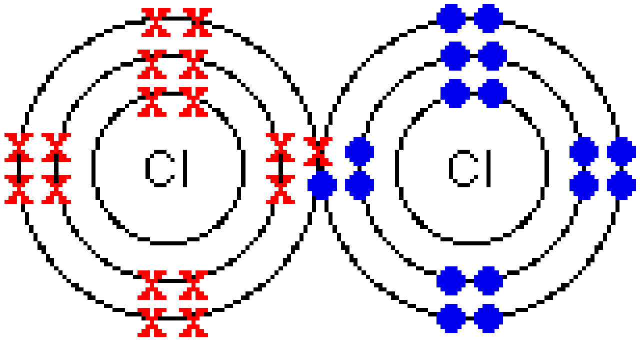
• In order to minimize energy the sodium gives an electron to chlorine and form a hexagonally packed structure as seen below. This is a typical ***ionic bond***.



Covalent bonds

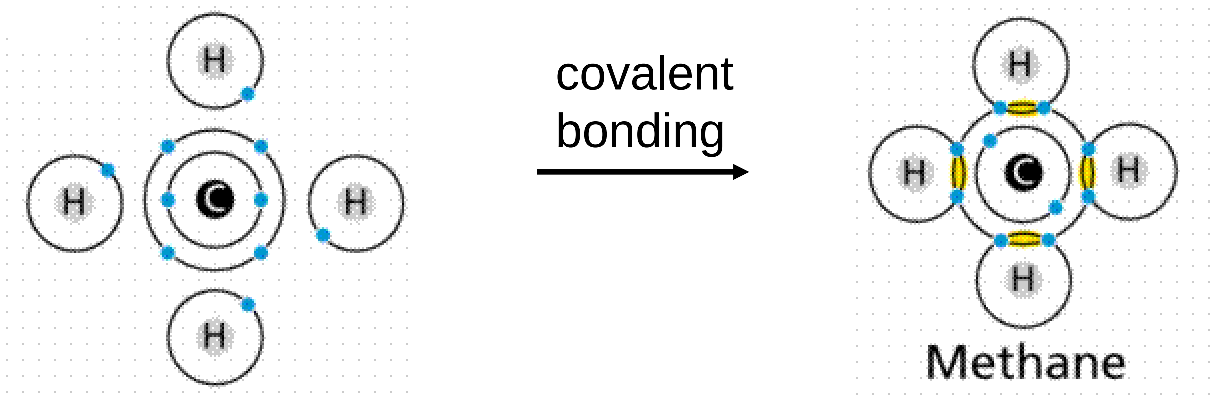
• Atoms can reach stable structures by ***sharing electrons*** to give ***covalent bonds***.

• For example, two chlorine atoms could both achieve stable structures by sharing their single unpaired electron as in the simplified diagram seen below.

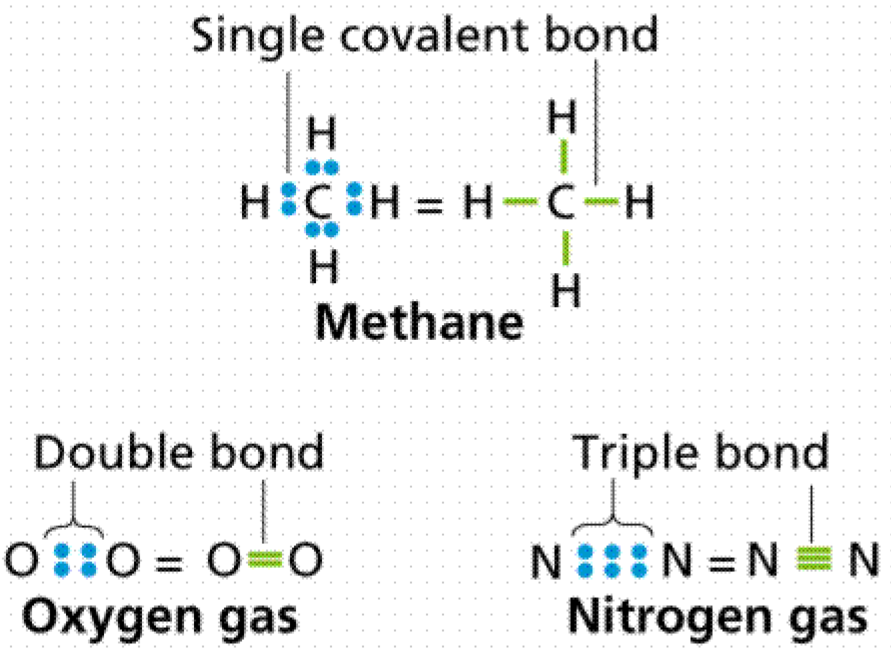


Covalent bonds: methane

Carbon (C) is in Group IVa, meaning it has 4 electrons in its outer shell. Thus to become a "happy atom", Carbon can either gain or lose four electrons. By sharing the electrons with other atoms, Carbon can become a happy atom.



Covalent bonds



N-N 1.47Å
N=N 1.24Å
N≡N 1.10Å

1Å=10^{-10} m

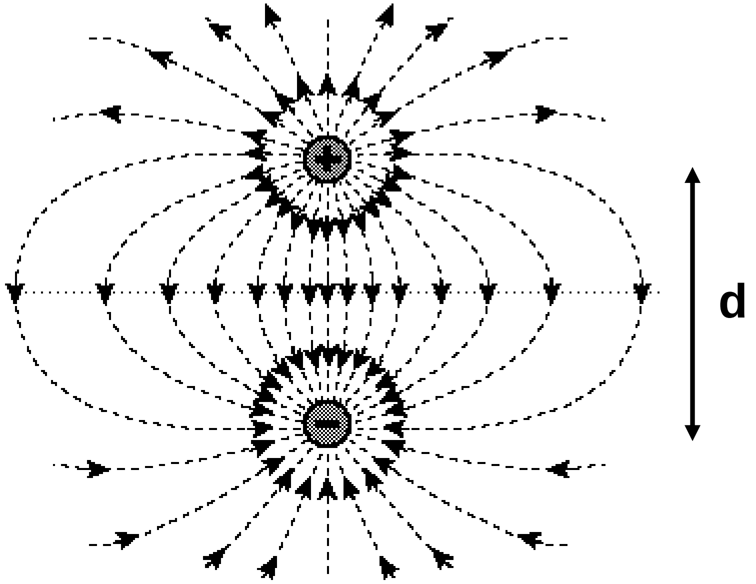
The distance between atoms decreases as the number of sheared electron pairs increases

The electric dipole

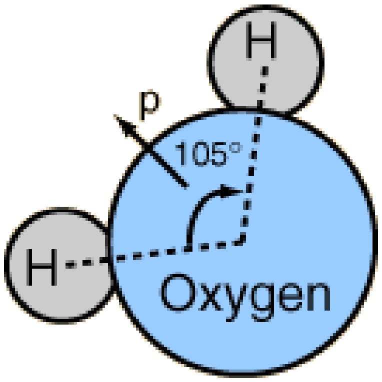
- **Many molecules either have or can develop a electric dipole moment**
- **Two electric charges q and –q are separated by a distance d. Their electric dipole moment (unit Cm) is:**

$$\vec{p} = q\vec{d}$$

- **The electric field is as shown in the figure**



Water as a dipole



Hydrogen and Oxygen form a ***polar covalent*** bond.

• The asymmetry of the water molecule leads to a dipole moment in the symmetry plane pointed toward the more positive hydrogen atoms. The measured magnitude of this dipole moment is $p=6x10^{-30}$ Cm.

• Treating this system like a negative charge of 10 electrons and a positive charge of 10e, the effective separation of the negative and positive charge centers is $d=6x10^{-30}$ Cm/10e=$3.9x10^{-12}$ m.

van der Waals forces

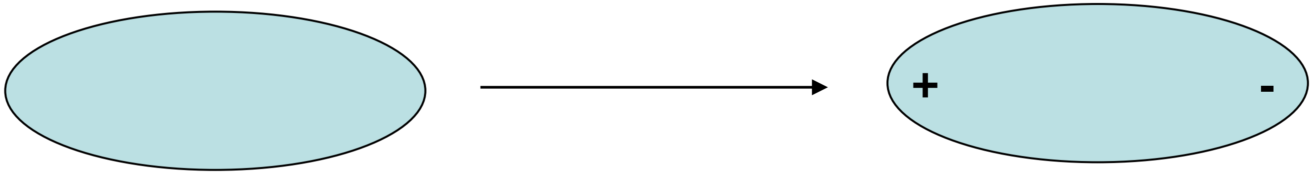
Definition: The attractive or repulsive **forces** between molecules other than those due to bond formation or to the electrostatic interaction of ions or of ionic groups with one another or with neutral molecules. The term includes: dipole-dipole, dipole-induced dipole and London (instantaneous induced dipole–induced Dipole) forces. The term is often used loosely for the totality of nonspecific attractive or repulsive forces.

Sounds boring:

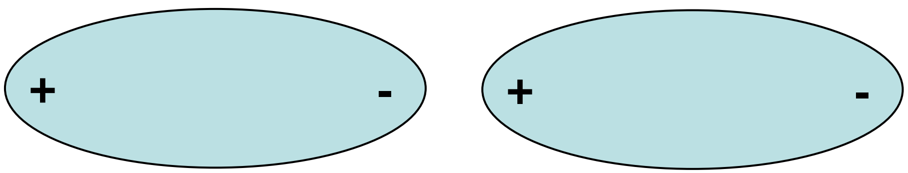
But is extremely important in biological systems

van der Waals forces: temporary dipoles

1) A molecule with an nonspherical electron cloud may spontaneously develop an electric dipole (for a fraction of a nanosecond)



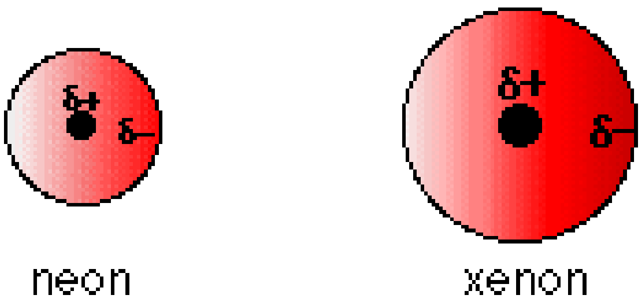
2) The temporary dipole may interact with other dipoles



van der Waals forces in noble gases

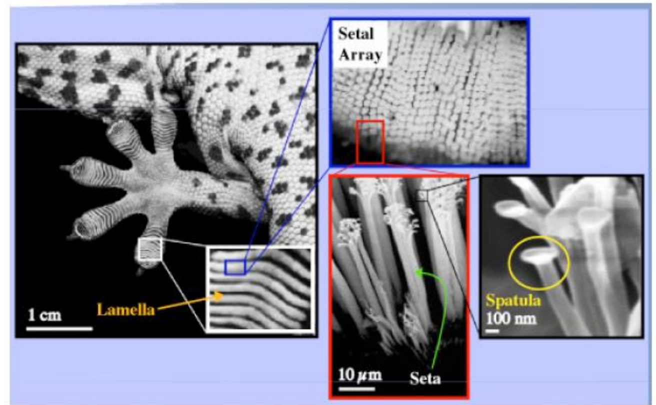
• The larger the noble gas, the more electrons (and bigger electron cloud) you have, and the larger the electrons can move thus giving a bigger temporary dipole.

• Because of the greater temporary dipoles, xenon molecules are "stickier" than neon molecules. Neon molecules will break away from each other at much lower temperatures than xenon molecules - hence neon has the lower boiling point.



Noble gas	**Boiling point**
neon	-246°C
argon	-186°C
krypton	-152°C
xenon	-108°C
radon	-62°C

van der Waals forces: Gecko foot



To learn more about Geckos and Van der Waals interactions you may want to look at:

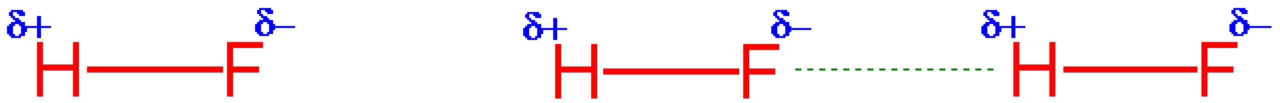
Autumn, Sitti, Liang et al. *Evidence for van der Waals adhesion in gecko setae* PNAS, **99**, pp. 12252-12256 (2002)

- Geckos get their ability to stick to and climb walls using van der Waals forces.
- The trick is to get enough area of the gecko foot and wall close enough so that van der Waals interactions become effective. Since the van der Waals force falls of as $1/r^6$, this means close to within 1 nm.
- The gecko has superfine, flexible bristles under its feet that press very tiny protrusions (called spatula) onto surfaces. This allows close contact.
- Not all the spatula fully stick at the same time. It has been calculated that if the spatula make full contact, the van der Waals forces would be strong enough to support a gecko weighing 90 kg !!!

Hydrogen bonds

• Hydrogen bonding differs from other uses of the word "bond" since it is a force of attraction between a hydrogen atom in one molecule and a small atom of high electro negativity in another molecule.

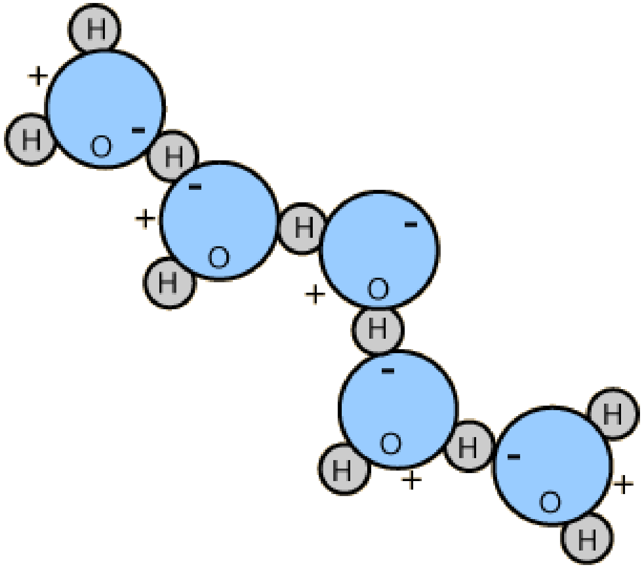
• When hydrogen atoms are joined in a polar covalent bond with a small atom of high electronegativity such as O, F or N, the partial positive charge on the hydrogen is highly concentrated because of its small size. If the hydrogen is close to another oxygen, fluorine or nitrogen in another molecule, then there is a force of attraction termed a dipole-dipole interaction. This attraction or "hydrogen bond" can have about 5% to 10% of the strength of a covalent bond.



Hydrogen bonds

- **Hydrogen bonds in water**
- **Each molecule can form up to 4 bonds**

→ large boiling point of water



Hydrogen bond strength

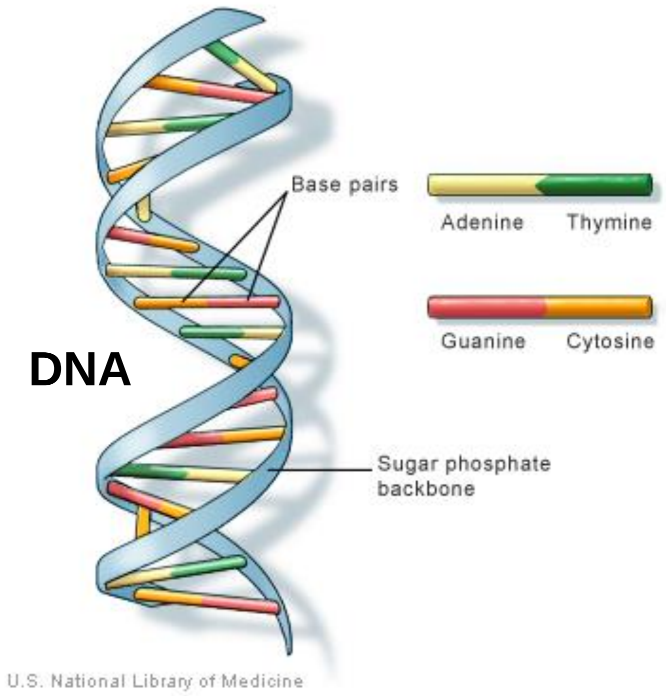
O—H...:N > O—H...:O > N—H...:N > N—H...:O

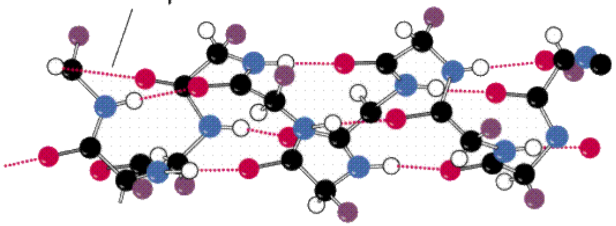
Hydrogen bonds in biomolecules

• Usually stronger than van der Waals forces, but much weaker than ionic and covalent bonds

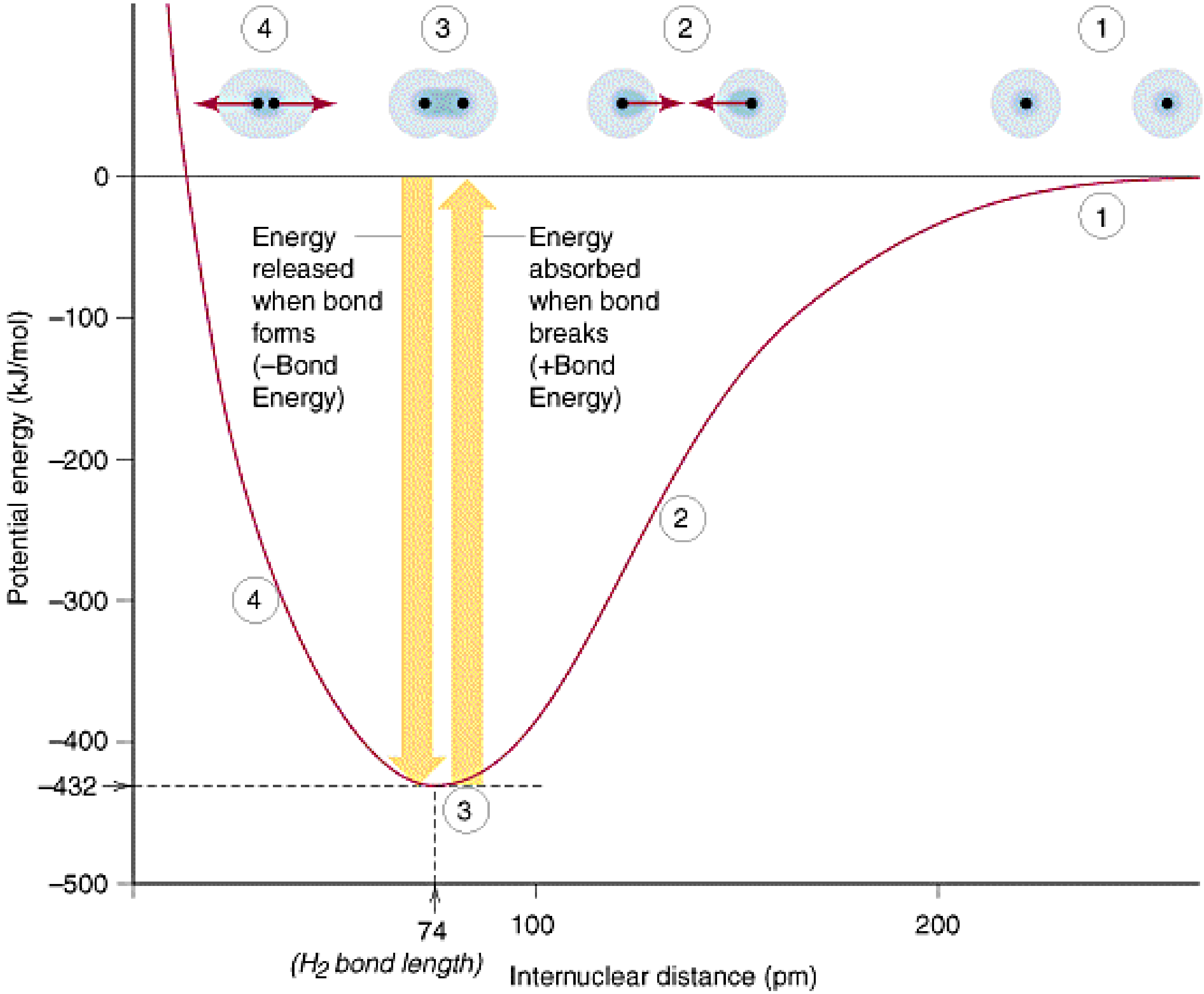
• Very important in ***proteins*** (between backbone oxygen and hydrogen in amino acids), ***DNA*** (between base pairs) and other biomolecules

DNA





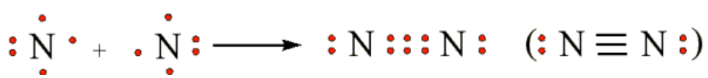
The molecular potential: Hydrogen

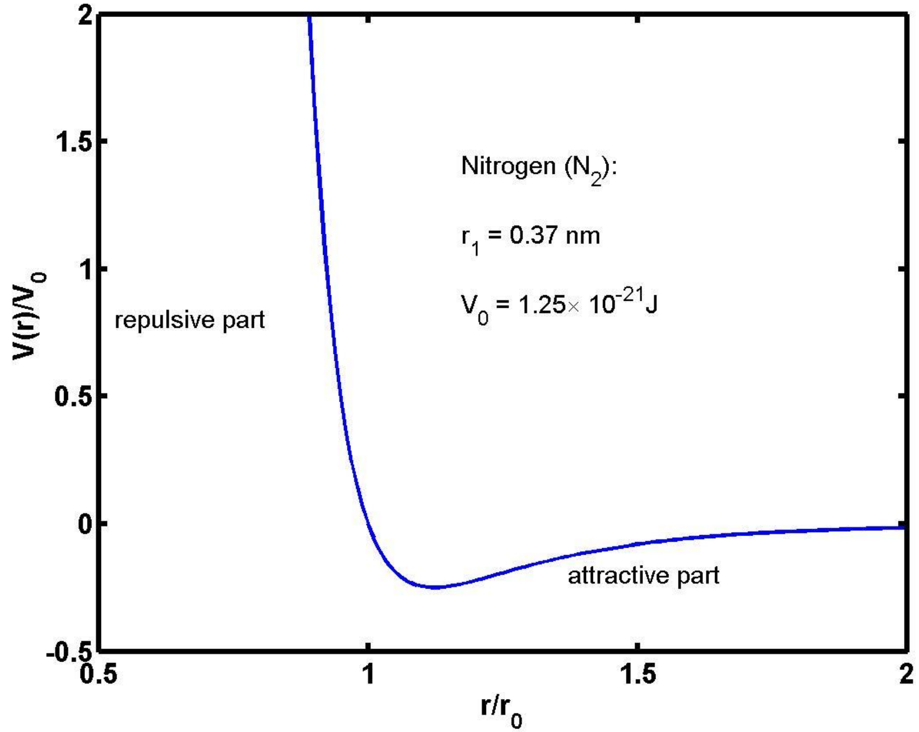


The molecular potential

Molecules often exhibit a potential energy that can be approximated by the Lennard-Jones potential which goes to zero when $r = r_1$

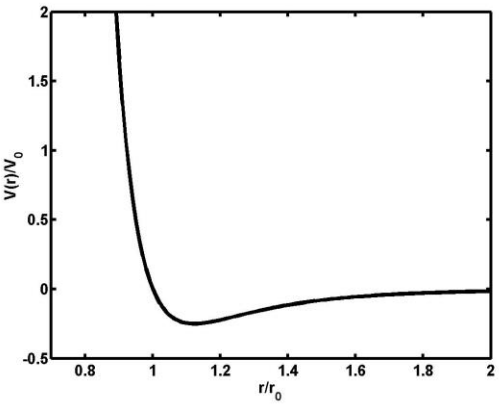
$$V(r) = V_0\left[\left(\frac{r_1}{r}\right)^{12} - \left(\frac{r_1}{r}\right)^{6}\right]$$





The Lennard-Jones potential

$$V(r) = V_0\left[\left(\frac{r_1}{r}\right)^{12} - \left(\frac{r_1}{r}\right)^{6}\right]$$



• Named after John Lennard-Jones who found it in 1931.

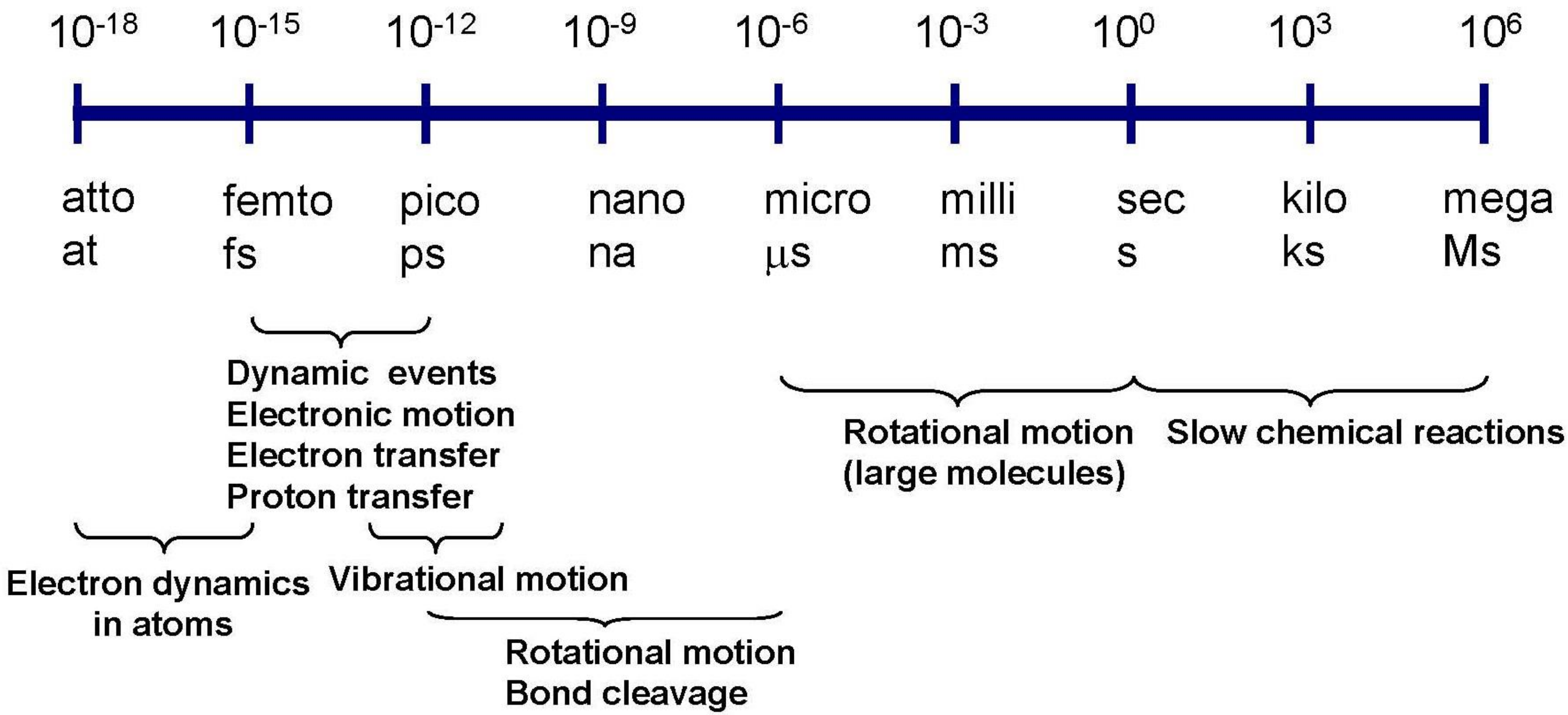
• The term ***$1/r^{12}$***, dominating at short distance, models the repulsion between atoms when they are brought very close to each other.

• The term ***$1/r^{6}$***, dominating at large distance, constitute the attractive part. This is the term which gives cohesion to the system.

Bonds and forces: summary

Bond/force	Distance dependence	Approximate bond energy (kJ/mol)
Covalent bond	No simple expression	200 kJ/mol
Ionic bond	$\propto \frac{1}{r^2}$ (Coulomb force)	< 20 kJ/mol
Hydrogen bond	No simple expression	< 10 kJ/mol
Van der Waals	$\propto \frac{1}{r^6}$ (dipole force)	< 5 kJ/mol

Time scales and molecules



By Gurzadyan

Biomolecular structure and function

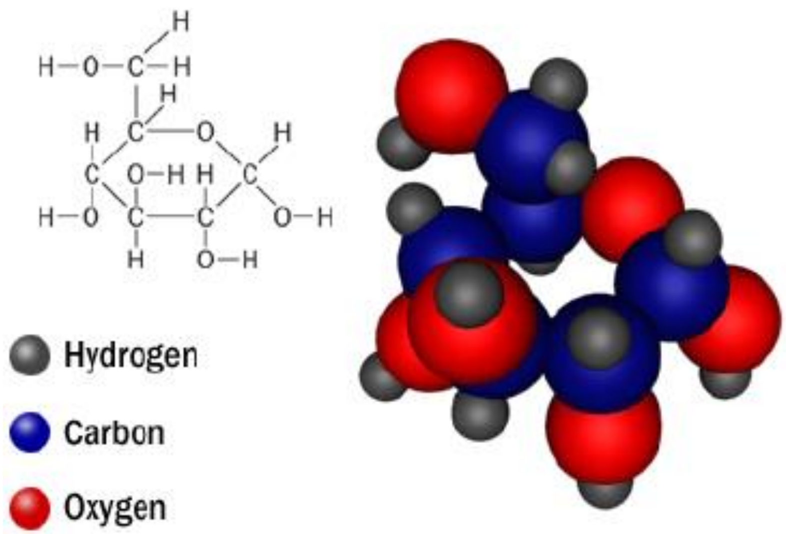
Now that we know something about bonds and forces, we can try to understand the structure and function of more complex biomolecules.

Two important molecules involved in energy transport and conversion:

-Glucose

-Adenosine Triphosphate (ATP)

Glucose



Numerous covalent bonds:

-carbon-carbon

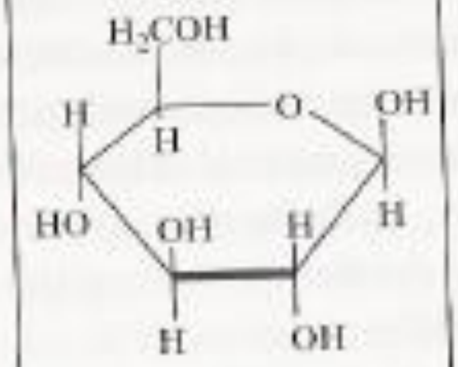
-carbon-oxygen

-carbon-hydrogen

-oxygen-hydrogen

- **Carbohydrates are the human body's key source of energy, through aerobic respiration.**
- **Glucose is broken down in mitochondria (singular: mitochondrion) of every cell during the respiration process**
- **How much energy is released in this reaction??**

Glucose



Number	Type	Energy (aJ)
5	C–C	2.90
7	C–O	4.06
7	C–H	4.83
5	O–H	3.85
Total	=	15.64

1 aJ = 10^{-18} J

What kind of energy is released when glucose reacts with oxygen? A calculation based on bond energies gives:

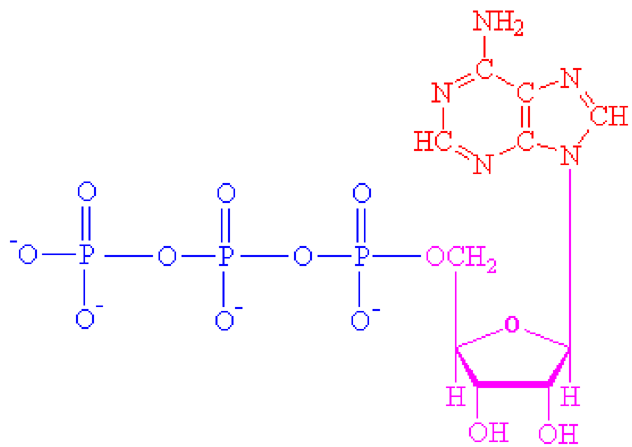
$$\underset{-15.64\,aJ}{C_6H_{12}O_6} + \underset{-4.92\,aJ}{6O_2} \rightarrow \underset{-14.76\,aJ}{6CO_2} + \underset{-9.24\,aJ}{6H_2O} + 3.44\,aJ$$

Since glucose has an molecular weight of 180 g/mol, this gives about 10 kJ energy per gram of glucose:

$$\left(\frac{1}{180g/mol}\right)\times\left(6.02\times10^{23}\,molecules/mol\right)\times\left(3.4\times10^{-18}\,J\right)\approx10^{4}\,J$$

ATP

Adenosine 5'-triphosphate (ATP) is a nucleotide often called the "molecular currency" of intracellular energy transfer.



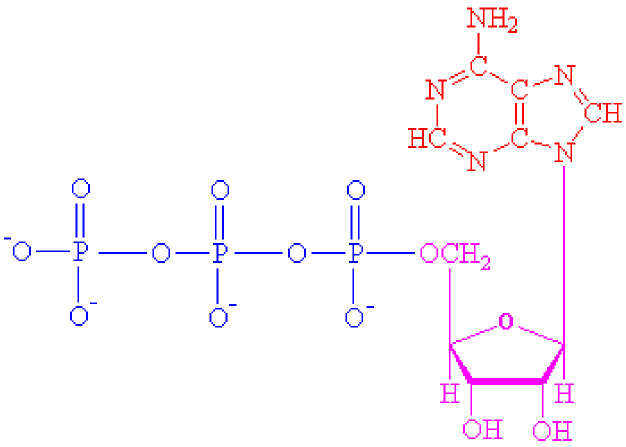
A nucleotide consists of:

1) Phosphate group

2) Organic (cyclic) base

3) Sugar group

ATP

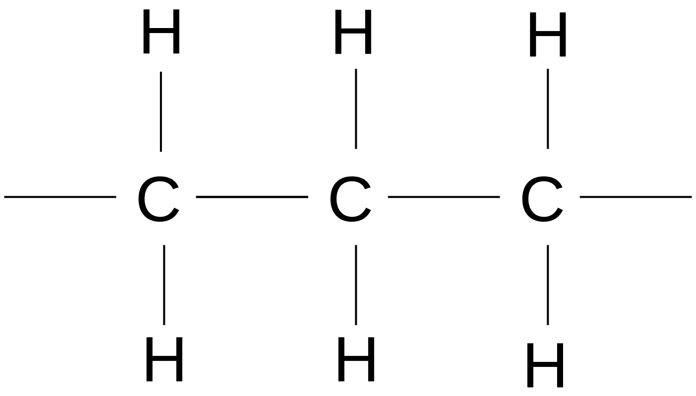


The reaction between ATP and water (often called ATP hydrolysis) is shown below. ATP hydrolysis generates energy of typically 0.09 aJ (or about **$20k_BT$**, where k_B is Boltzmann's constant and T=309 K is physiological temperature).

$$ATP + H_2O \longrightarrow ADP + HPO_4$$

The electrostatic repulsion between the negatively charged phosphate groups is the reason why energy is released in ATP hydrolysis.

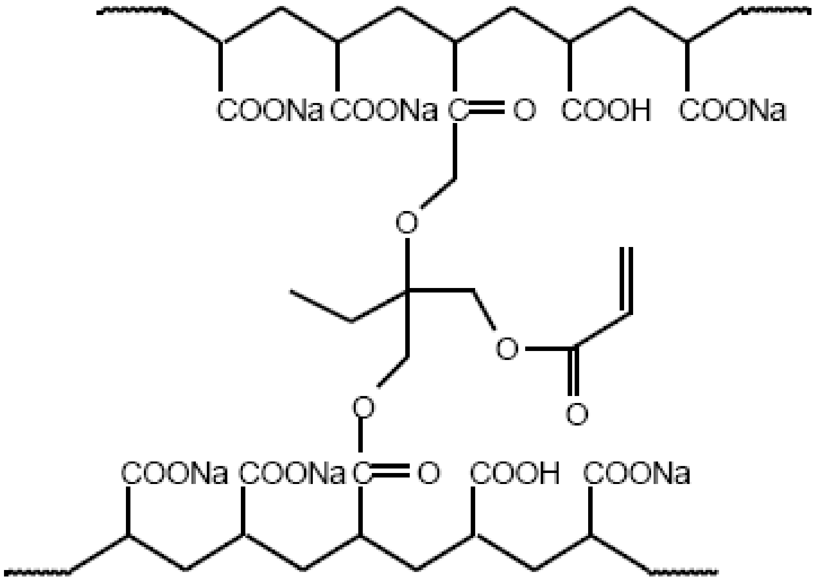
POLYMERS



A polymer is a long chain of molecules. It consists of repeating units called monomers

Polyethylene is a simple polymer; $(CH_2)_n$ found in plastic bags, etc

Polymers for adsorbing water



Sodium Polyacrylate; *CH_2-CH(CO_2Na)-*

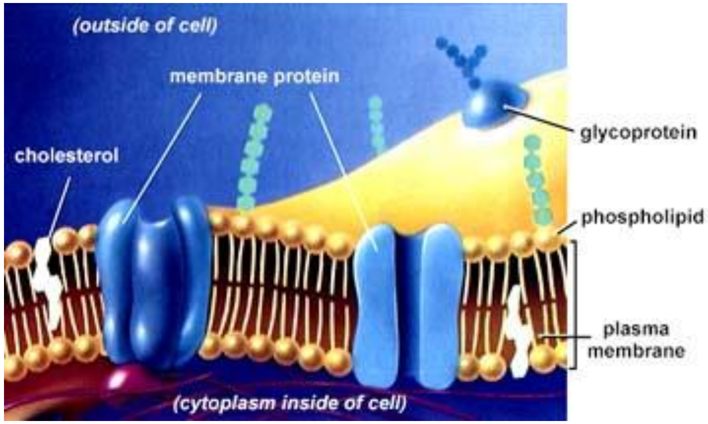
Can take up to ***800 times*** its own weight in water, and is found in diapers, etc

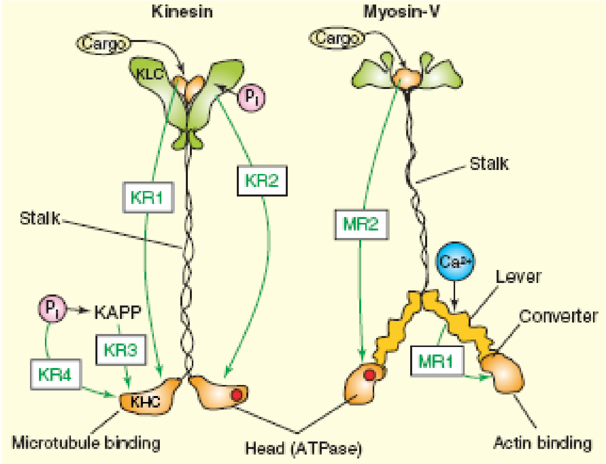
WHAT ARE BIOPOLYMERS?

- Proteins
- Ribonucleic acid (RNA)
- Deoxyribonucleic acid (DNA)

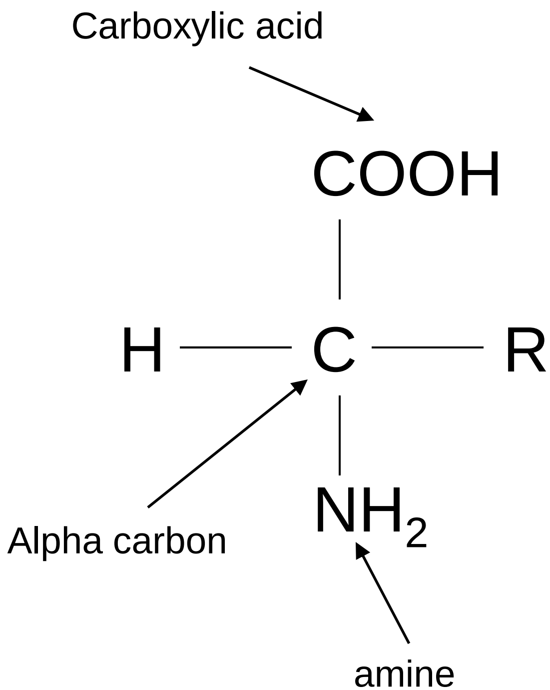
Proteins

- name comes from greek ('prota'=primary importance)
- vital to our metabolism
- catalyze biochemical reactions (enzymes=proteins)
- Important in cell signaling (membrane proteins)
- Important for transport of molecules (motor proteins)

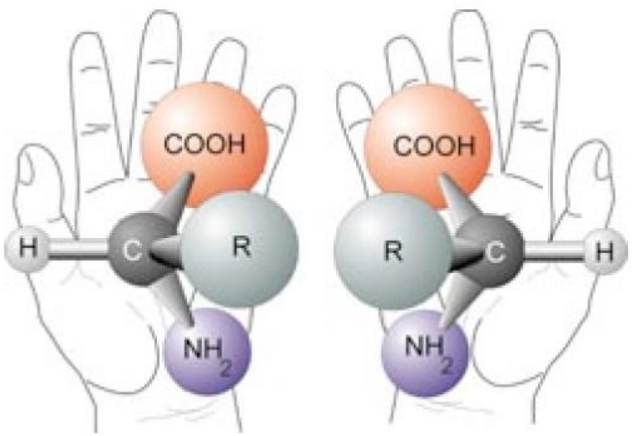




Amino acids



Two steric forms: L and D



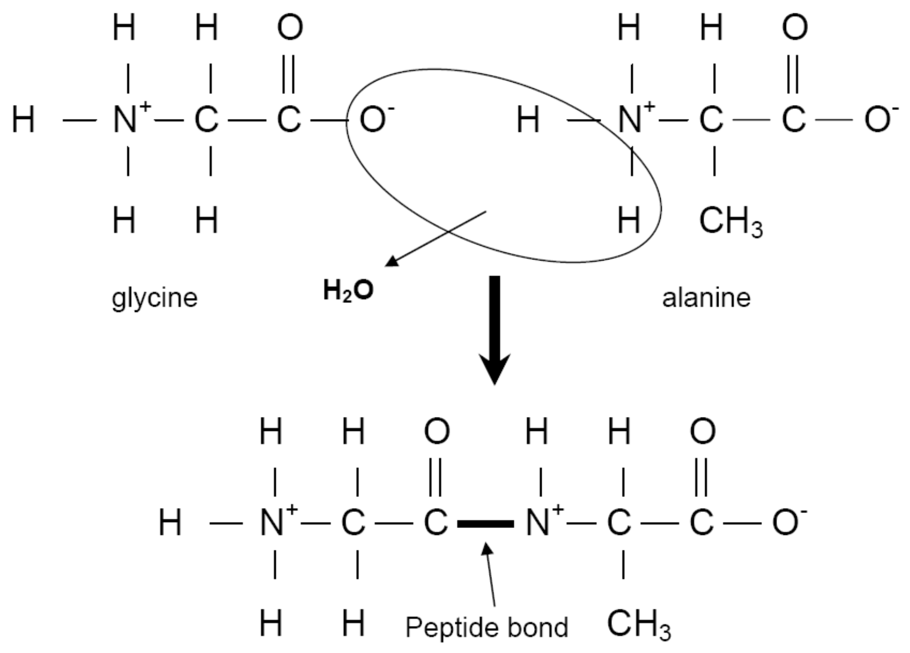
Amino acids are the building blocks of proteins and are extremely important in biology!

Amino acids

20 standard amino acids. Some essential amino acids cannot be synthesized by the human body from other compounds through chemical reactions, and must be obtained from food.

Isoleucine	Alanine
Leucine	Asparagine
Lysine	Aspartate
Methionine	Cysteine
Phenylalanine	Glutamate
Threonine	Glutamine
Tryptophan	Glycine
Valine	Proline
Arginine*	Serine
Histidine*	Tyrosine

Two amino acids can form a complex via ***peptide*** bonds!



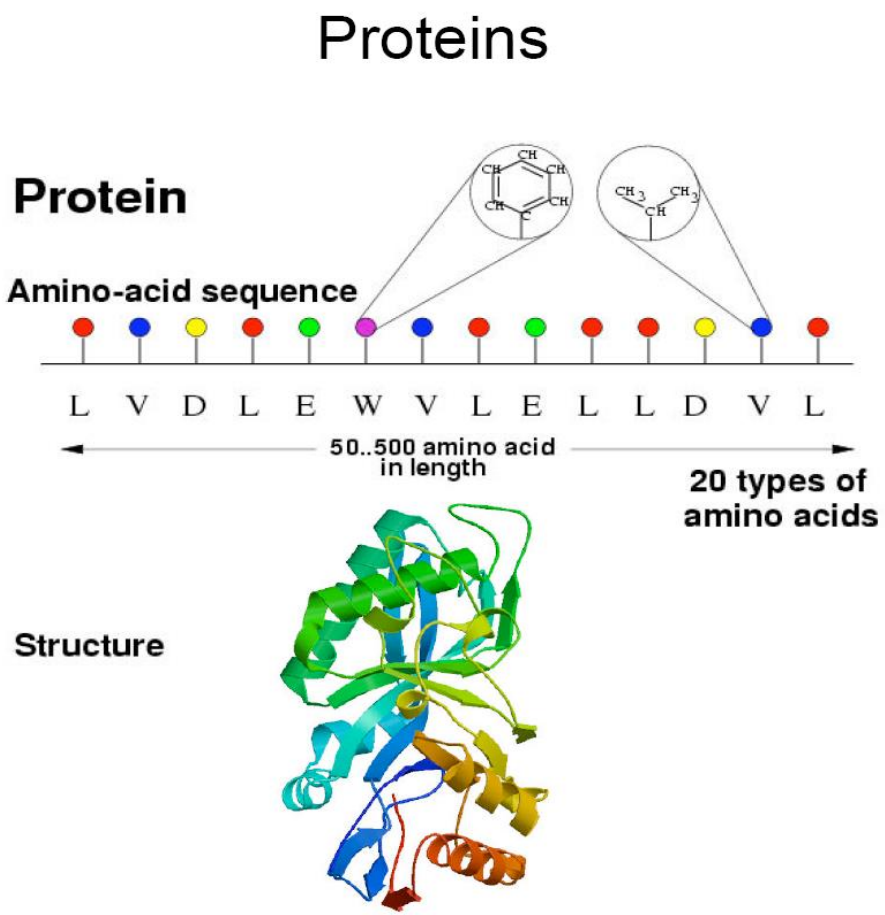
< 50 peptide bonds Polypeptide

> 50 peptide bonds Protein

Biopolymers

(monomer: amino acid)

Proteins are build up of amino acids



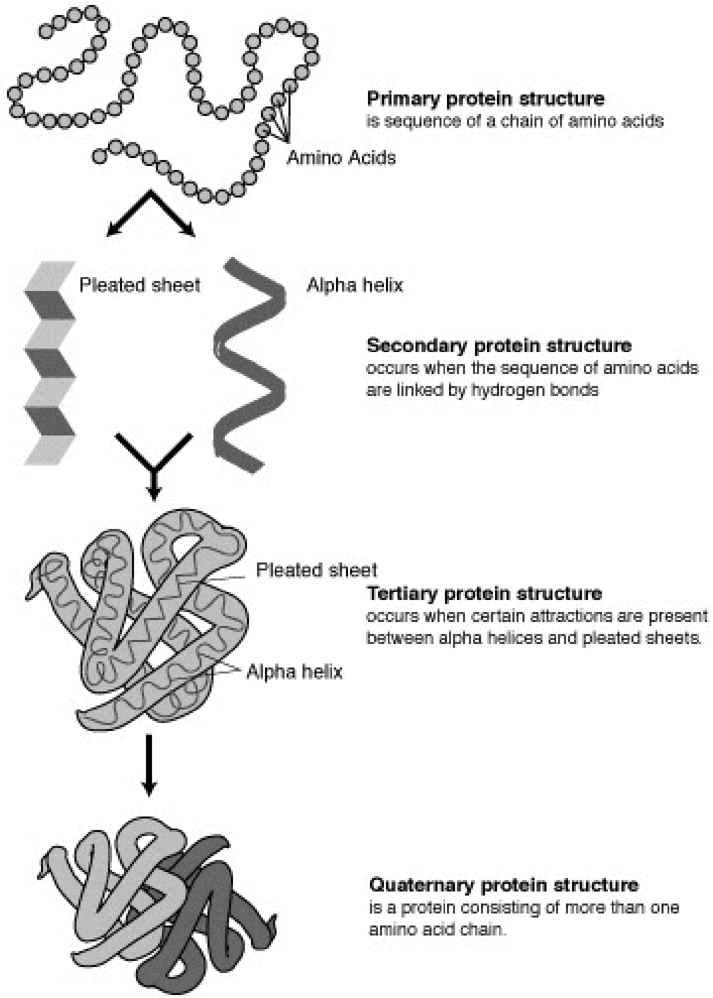
Protein structure

Primary structure: the amino acid sequence

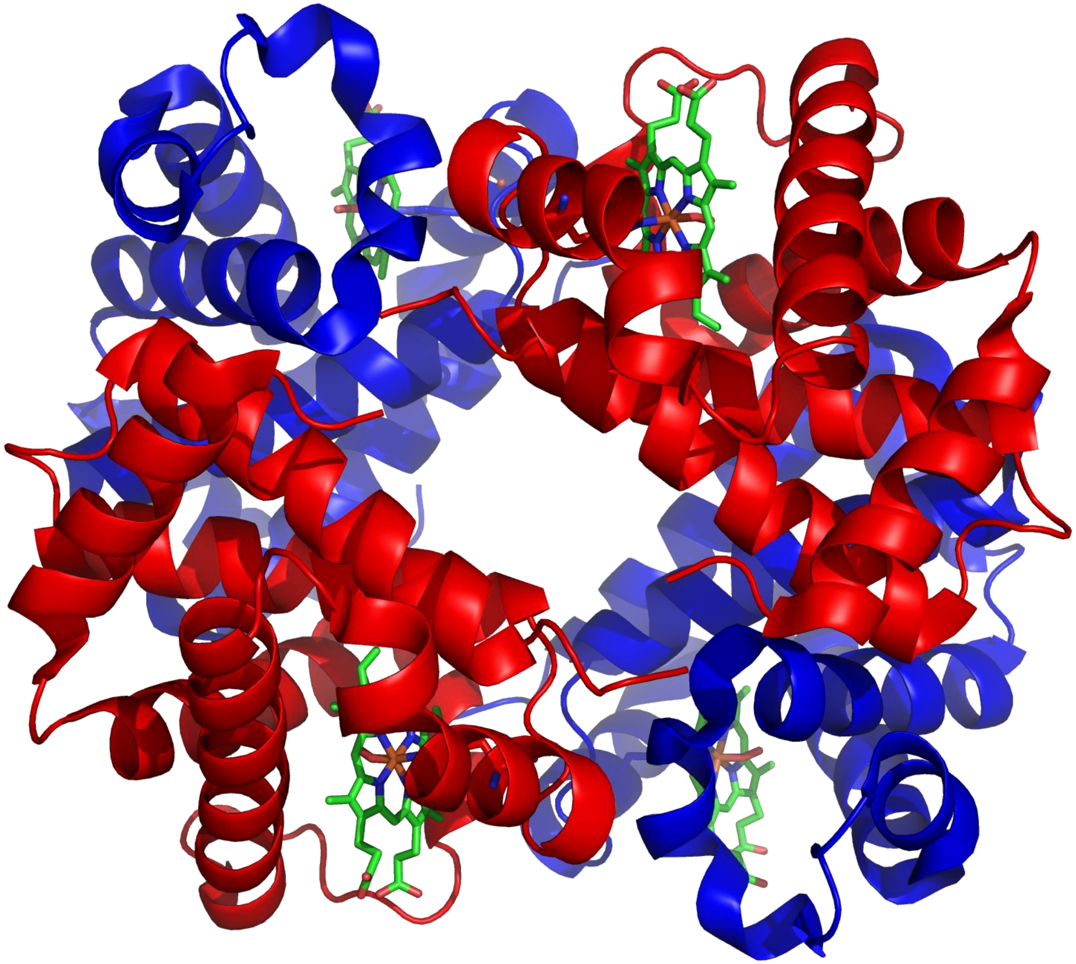
Secondary structure: highly regular sub-structures--alpha helix and strands of beta sheet. Secondary structures are locally defined, meaning that there can be many different secondary motifs present in one single protein molecule

Tertiary structure: Three-dimensional structure of a single protein molecule; a spatial arrangement of the secondary structures

Quaternary structure: complex of several protein molecules or polypeptide chains, usually called *protein subunits* in this context, which function as part of the larger assembly or protein complex.



Quaternary Structure

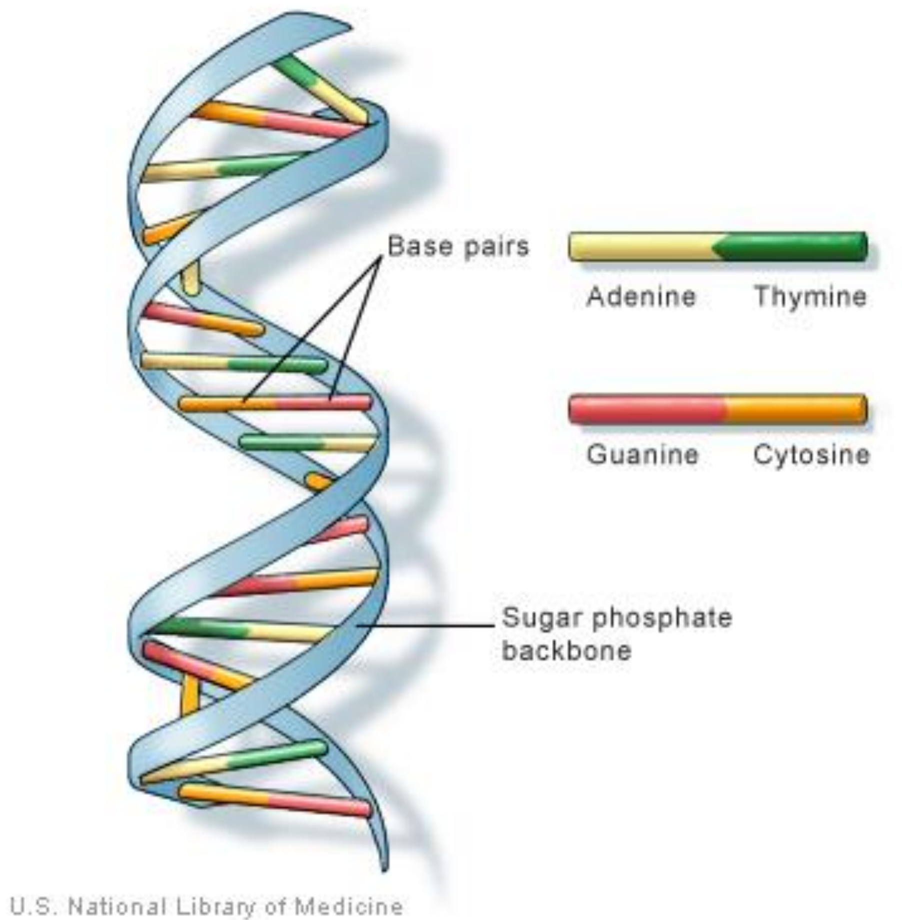


Hemoglobin

http://en.wikipedia.org/wiki/Hemoglobin

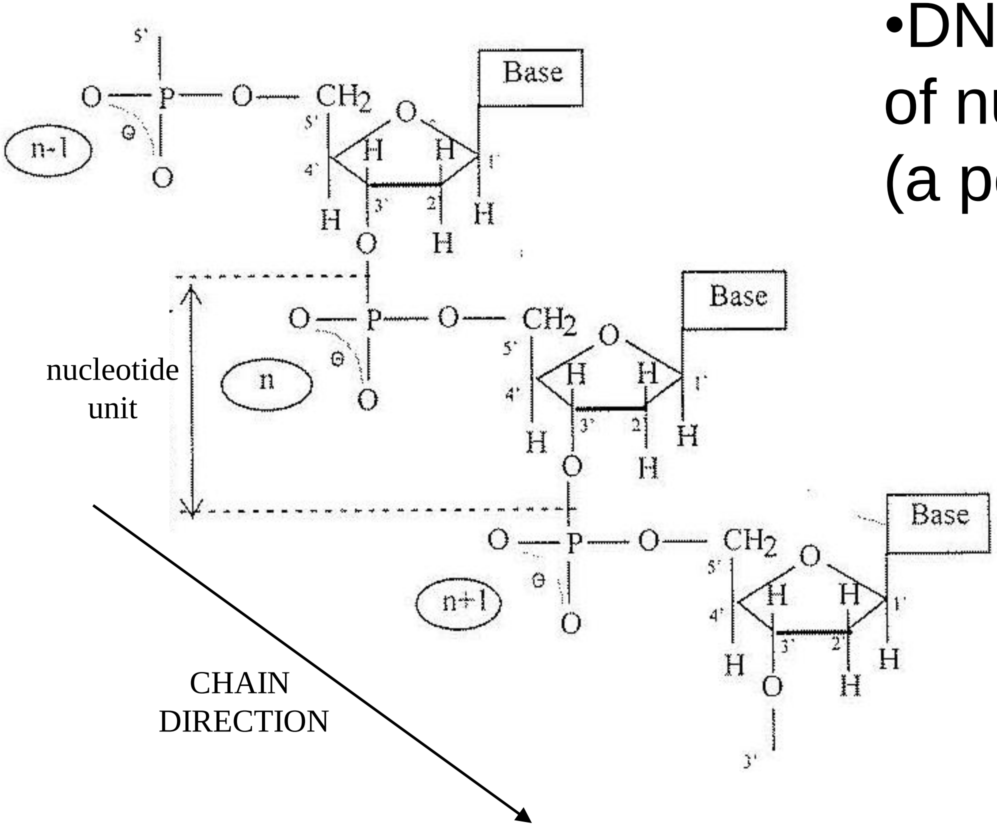
DNA as a biopolymer

Deoxyribonucleic acid (DNA) is a nucleic acid — usually in the form of a double helix - that contains the genetic instructions specifying the code of life.



http://molvis.sdsc.edu/dna/index.htm

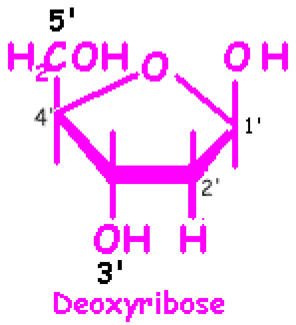
DNA as a biopolymer



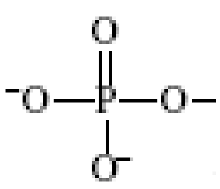
•DNA is a long biopolymer of nucleotide monomers (a polynucleotide).

Building blocks of DNA

1)



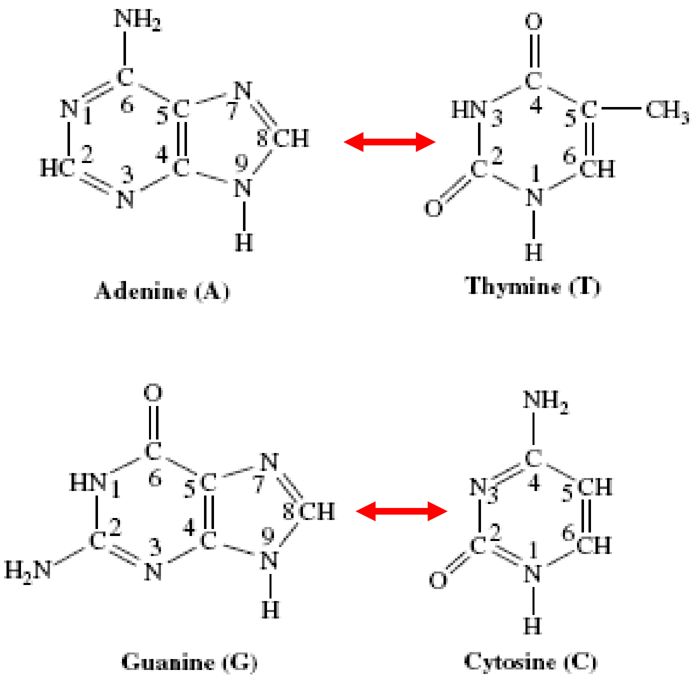
2)



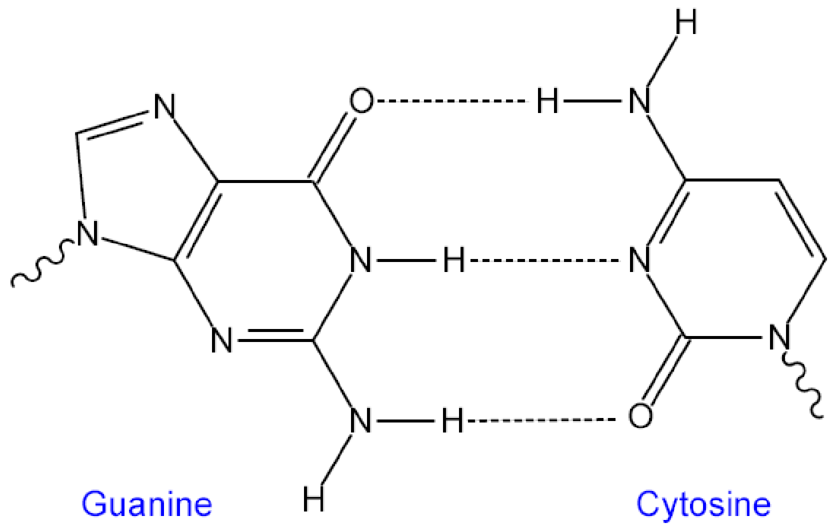
phosphate

3)

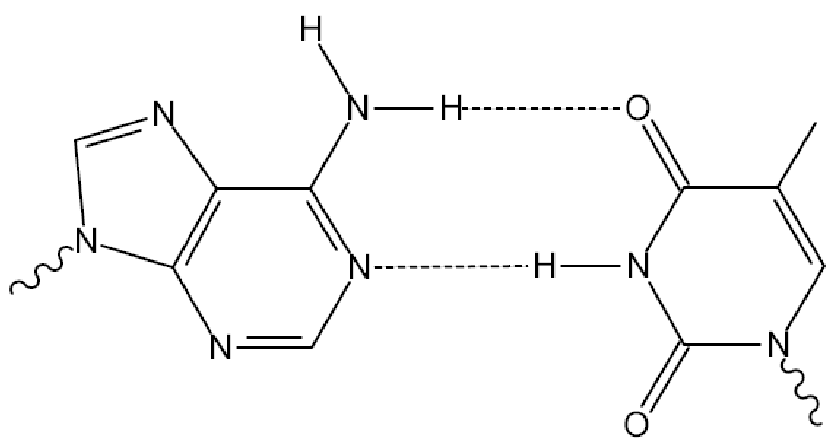
- A can pair with T
- C can pair with G



DNA base pairs

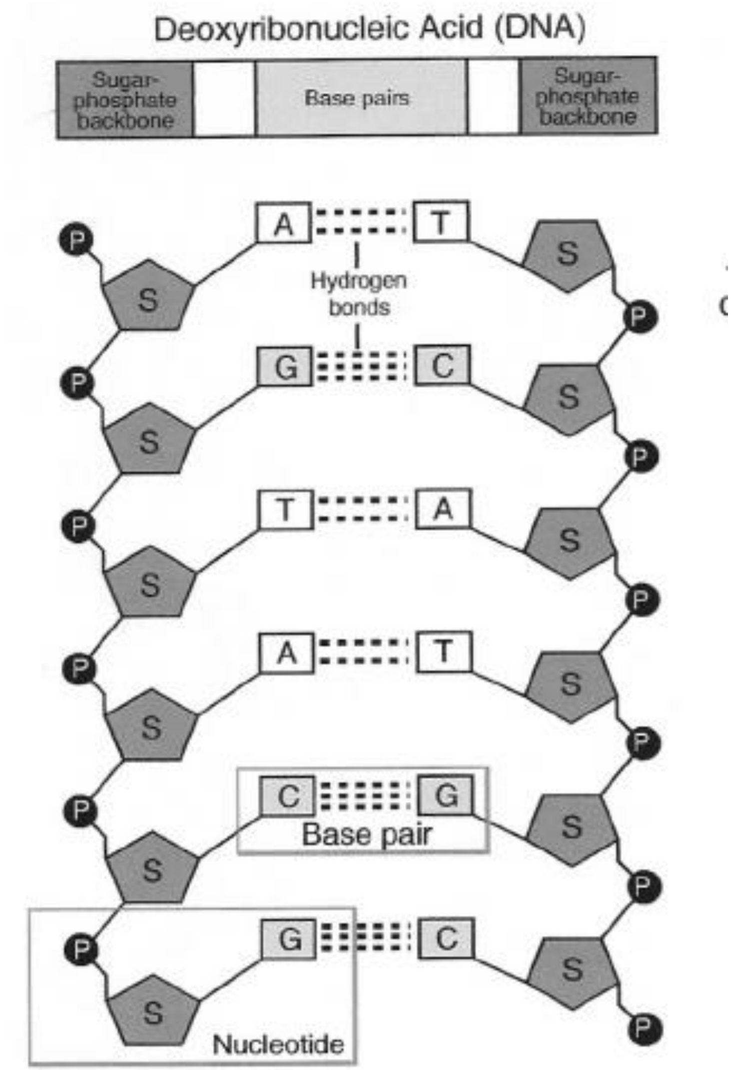


Guanine Cytosine



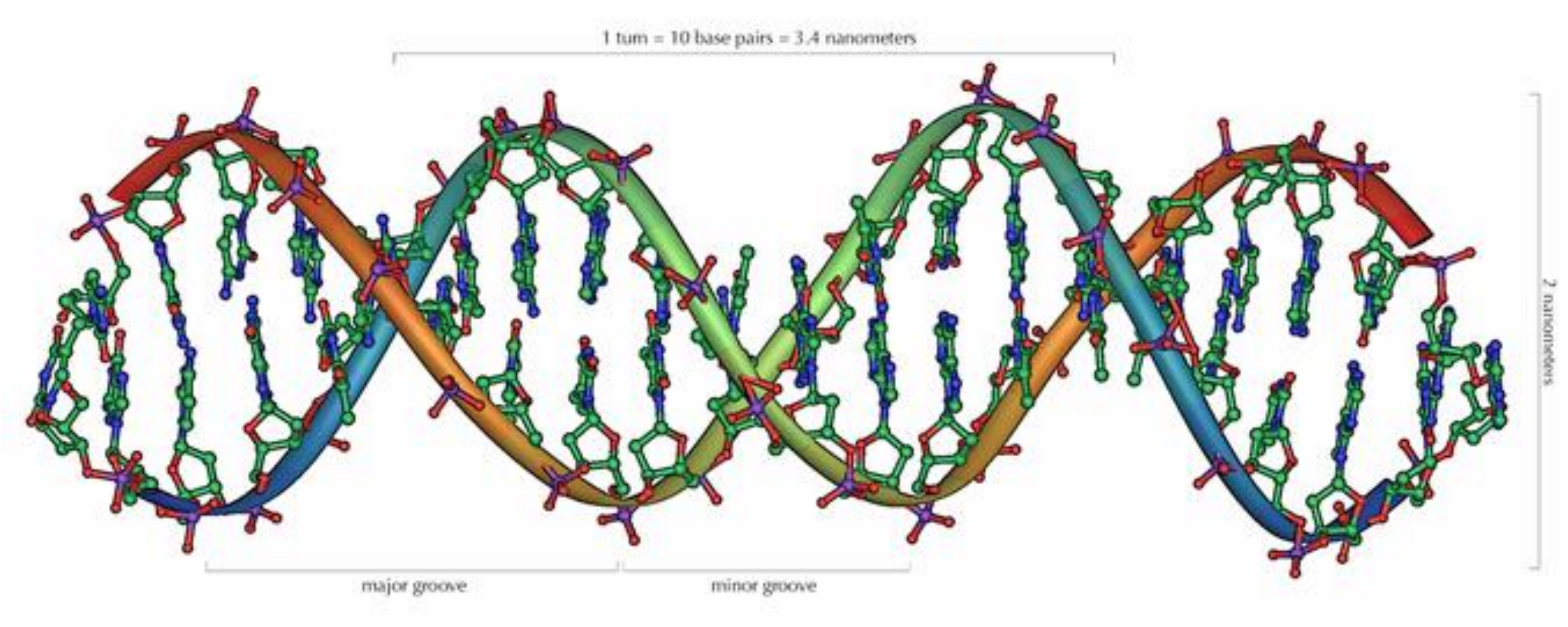
Adenine Thymine

DNA as a biopolymer

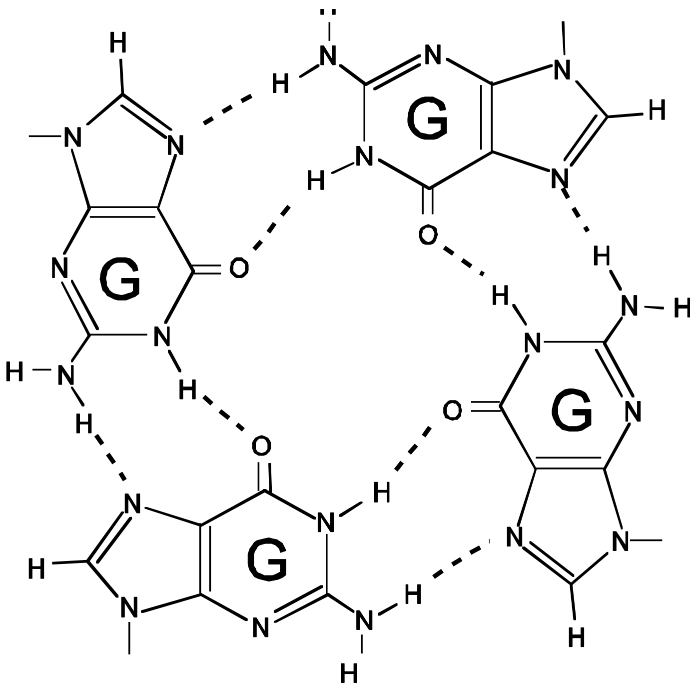


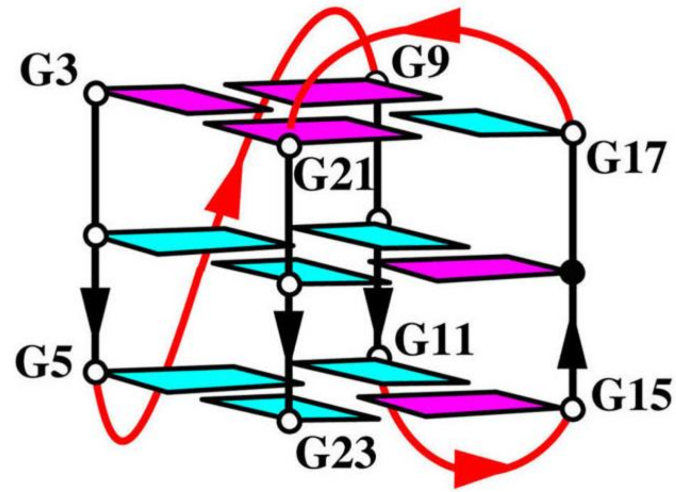
DNA as a biopolymer

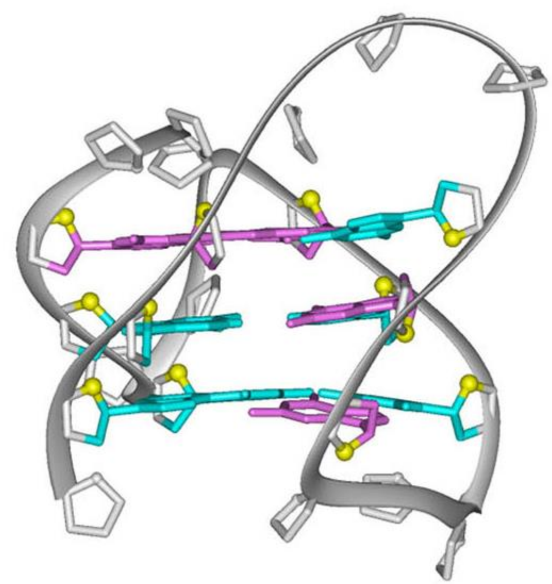
Each turn of the DNA helix has a length 3.4 nm



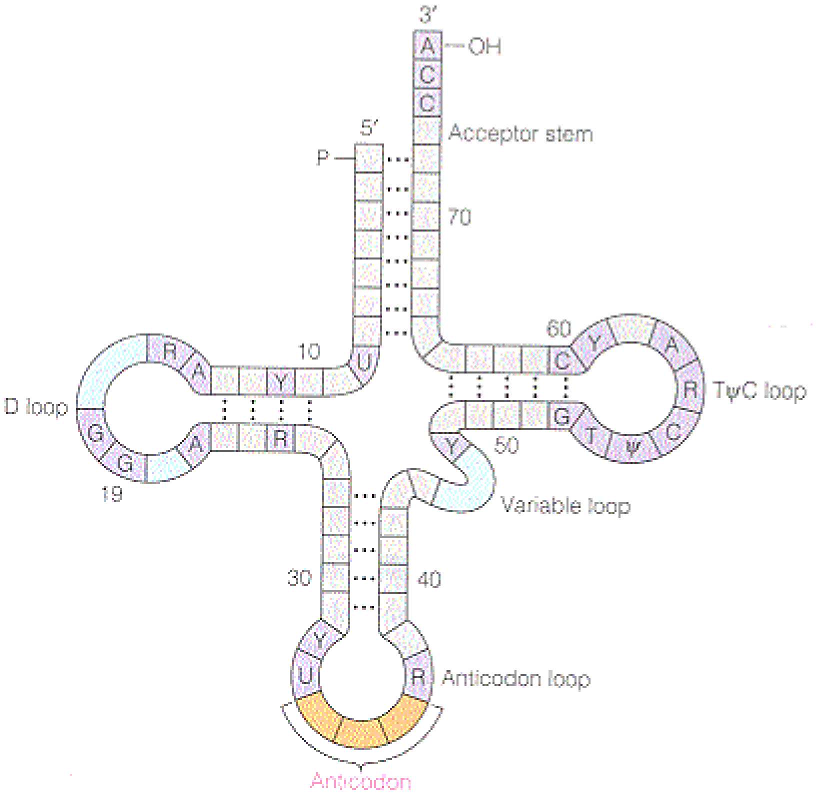
DNA quadruplex







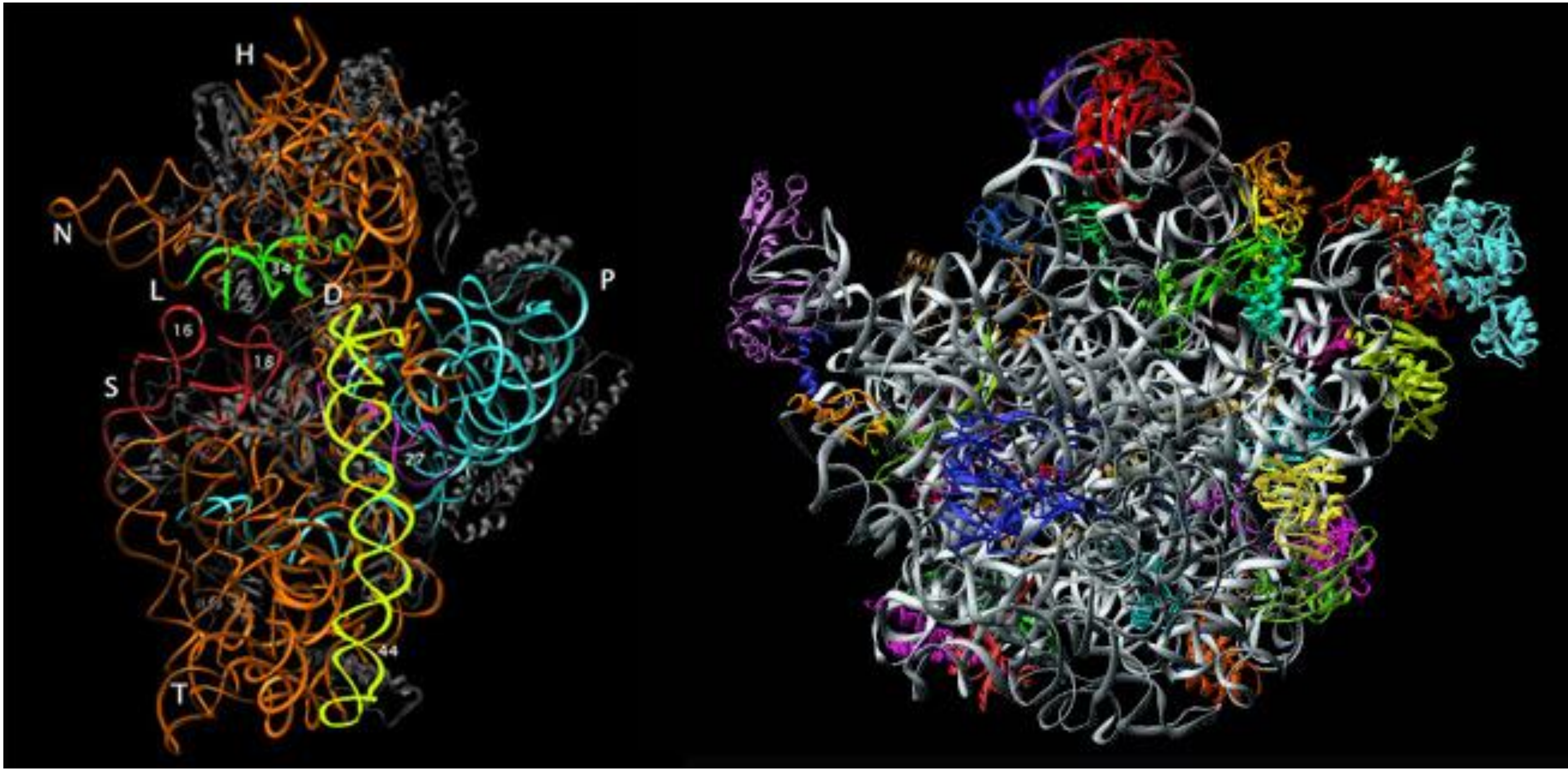
RNA as a biopolymer



tRNA

http://en.wikipedia.org/wiki/Transfer_RNA

Ribosome



http://www.molgen.mpg.de/~ag_ribo/ag_franceschi/

Thank you