école normale supérieure paris—saclay

Master Monabiphot

BioMolecules of Life

Brahim HEDDI

LBPA

Team « Structure et Interactions des Acides Nucléiques »

école normale supérieure paris-saclay

BRAHIM HEDDI

LABORATOIRE DE BIOLOGIE ET PHARMACOLOGIE APPLIQUÉE (LBPA)

(HTTP://LBPA.ENS-PARIS-SACLAY.FR/VERSION-ANGLAISE/)

CNRS RESEARCHER

TEAM « STRUCTURE ET INTERACTIONS DES ACIDES NUCLÉIQUES »

BRAHIM.HEDDI@ENS-CACHAN.FR

01 81 87 52 07

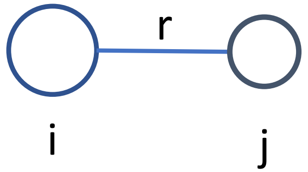
OFFICE NUMBER 3S14

Course outline

- **Molecular bonds and forces**
- Nucleic Acids structure and function
- Proteins structure
- Carbohydrates
- Lipids

INTRODUCTION

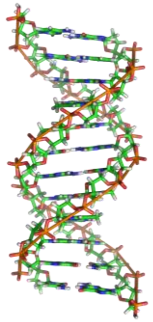
Atom



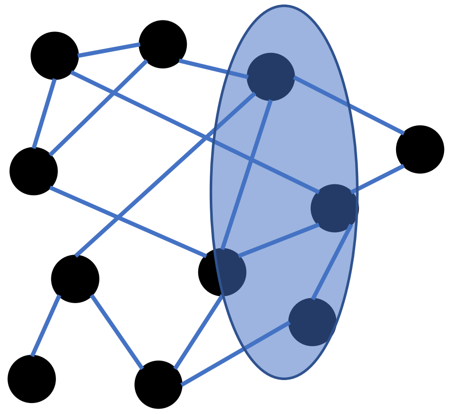
$$U_{bonds} = \sum_{bonds} K_b(r - r_0)$$

Biomolecules:

Nucleic acids
Proteins
Carbohydrates
Lipids



Network



MOLECULAR 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 (non-bonding potentials)
   - Hydrogen bonds
   - Van der Waals forces

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

PERIODIC TABLE OF ELEMENTS

	I A	II A	III B	IVB	V B	VIB	VIIB	VIII B			IB	IIB	III A	IV A	V A	VI A	VIIA	VIIIA
1	H																	He
2	Li	Be											B	C	N	O	F	Ne
3	Na	Mg											Al	Si	P	S	Cl	Ar
4	K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
5	Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
6	Cs	Ba	Ls	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
7	Fr	Ra	Ac															

Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

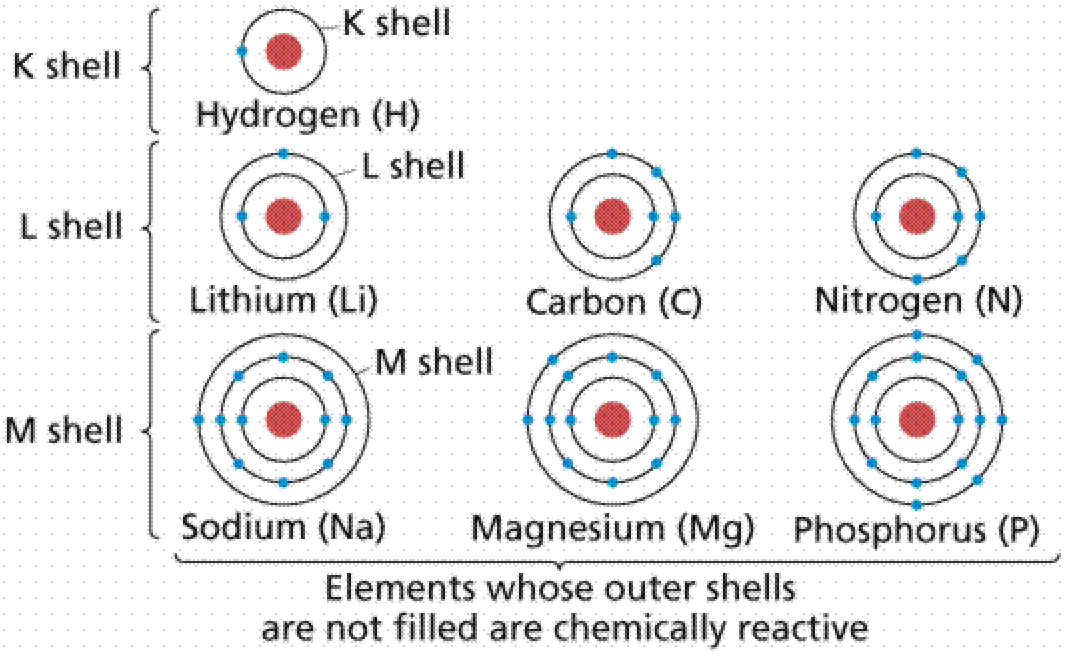
http://www.webelements.com/

WHICH ATOMS ARE CHEMICALLY ACTIVE?

1s

2s,2p

3s,3p,3d



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

AT WHAT TEMPERATURE CAN ATOMS FORM BONDS (GAS→LIQUID)?

The bond energy must be larger than the thermal energy k_BT

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

T=temperature (in Kelvin)

$k_BT=(1.38\times10^{-23}\ \mathrm{J/K})\times(300\ \mathrm{K})=4.14\times10^{-21}\ \mathrm{J}=0.026\ \mathrm{eV}$

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

$$1\ \mathrm{eV} = 1.6\times10^{-19}\ \mathrm{C}\times 1\mathrm{V} = 1.6\times10^{-19}\ \mathrm{J}$$

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

Complete electron transfer from one atom to another

The main contribution to the energy of interaction of two ions with charges q_1 and q_2 is the Coulomb potential, separate by a distance r is :

$$Uc = \frac{q_1 q_2}{4\pi\varepsilon\varepsilon_0 r}$$

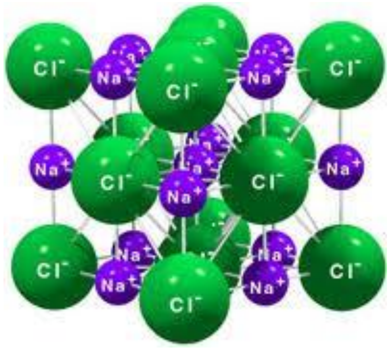
ε dielectric constant of the medium
ε_0 is the permittivity of free space

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***.

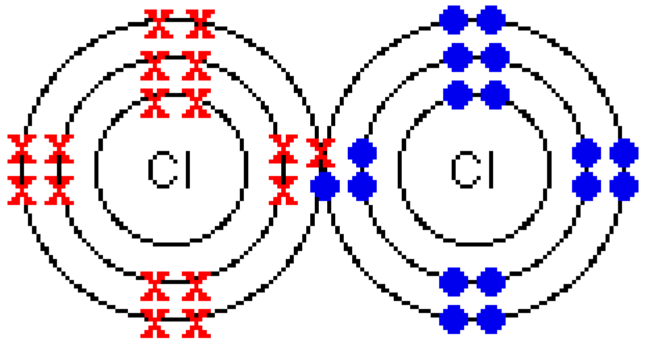


Melting point = 801ºC !

COVALENT BONDS

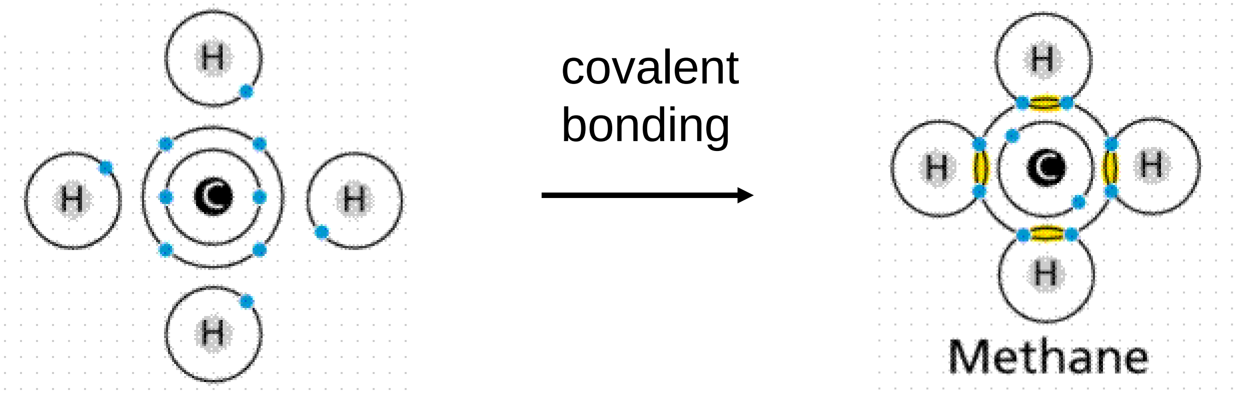
- Atoms can reach stable structures by ***sharing electrons*** to give ***covalent bonds***.

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

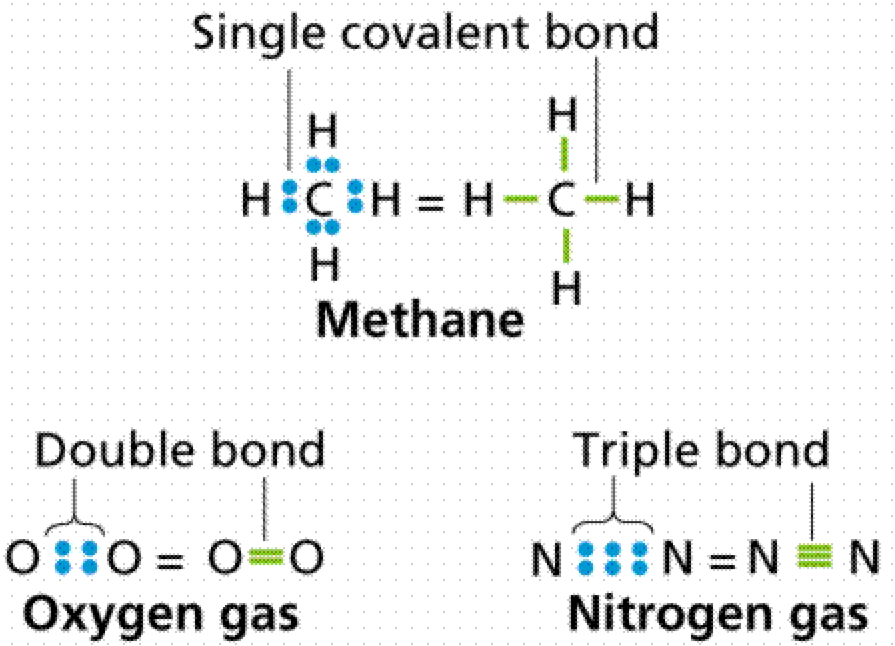


Covalent bonds: methane

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 1.47 Å
N=N 1.24 Å
N≡N 1.10 Å

1Å=10^{-10} m

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

VAN DER WAALS FORCES

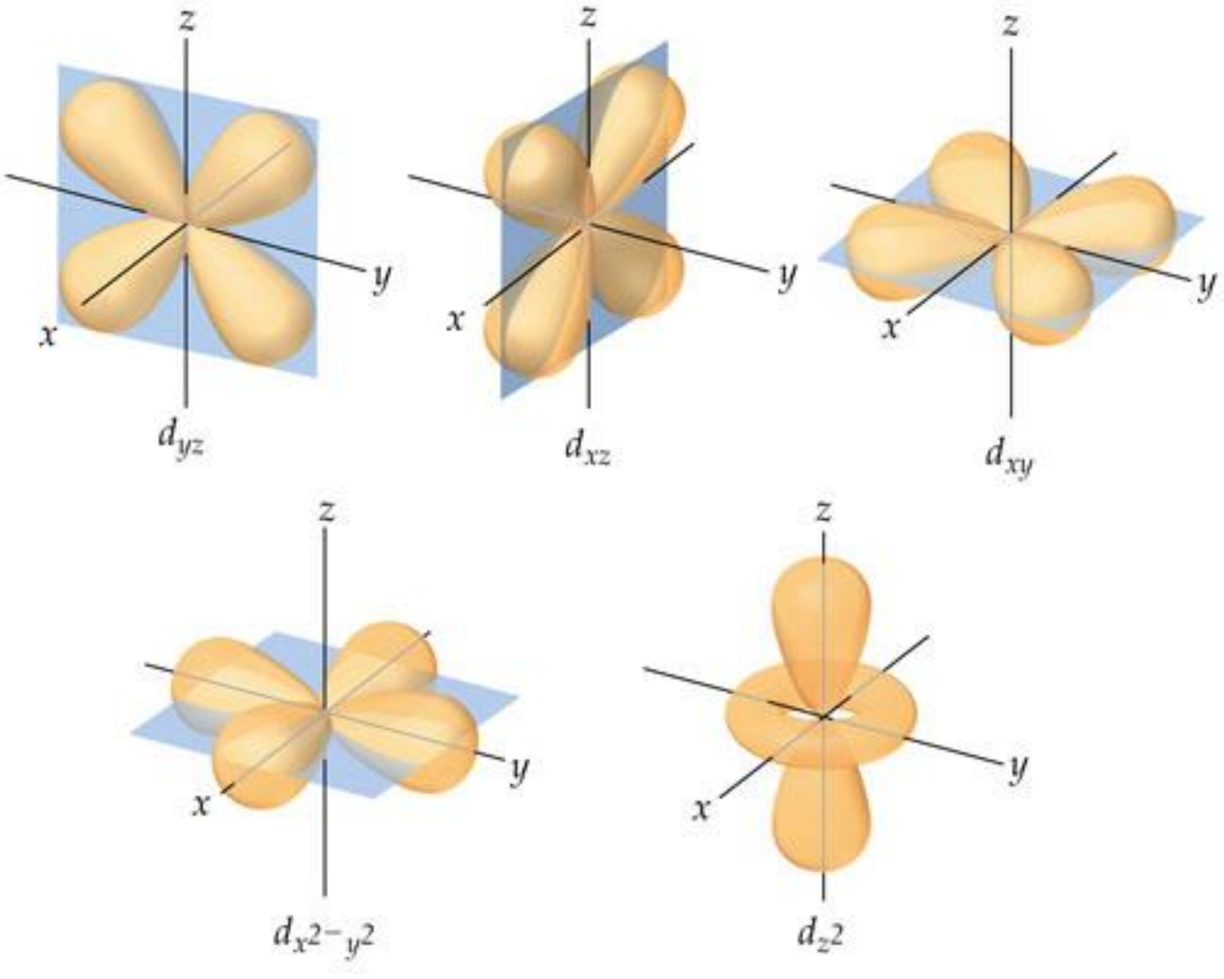
Definition: The attractive or repulsive **forces** between molecules other than
those due to bond formation or to the electrostatic interaction of ions or of ionic groups with one another or with neutral molecules. The term includes: dipole-dipole, dipole-induced dipole and London (instantaneous induced 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

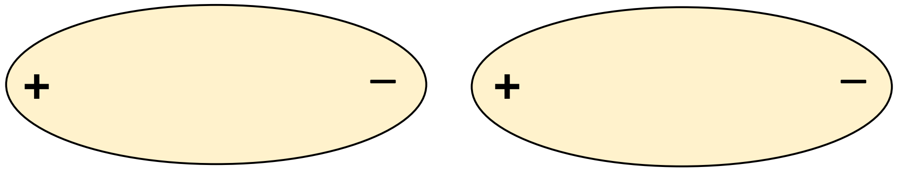
A molecule with an non-spherical electron cloud



Van Der Waals forces: temporary dipoles

A molecule with an non-spherical electron cloud may spontaneously develop an electric dipole (for a fraction of a nanosecond)

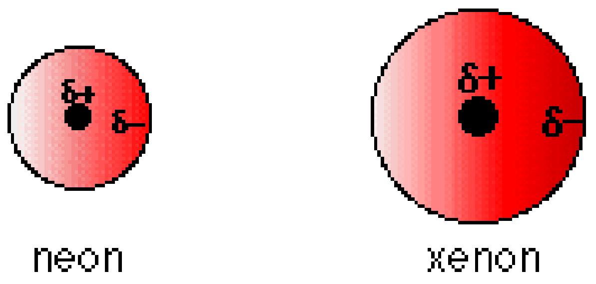
The temporary dipole may interact with other dipoles



VAN DER WAALS FORCES IN NOBLE GASES

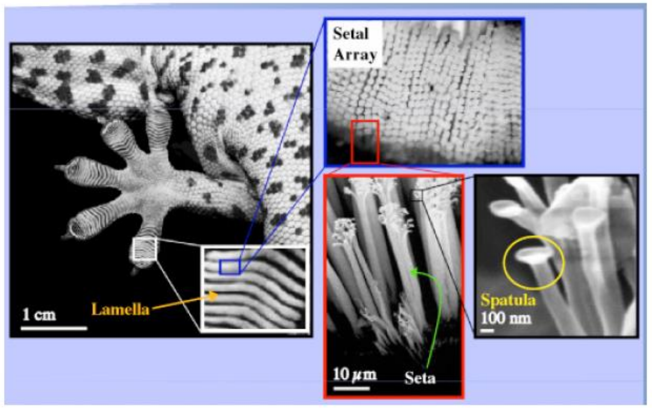
• The larger the noble gas, the more electrons (and bigger electron cloud) you have, and the larger the electrons can move thus giving a bigger temporary dipole.

• 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 bond strength ?

O—H···:N   N—H···:N

O—H···:O   N—H···:O

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.

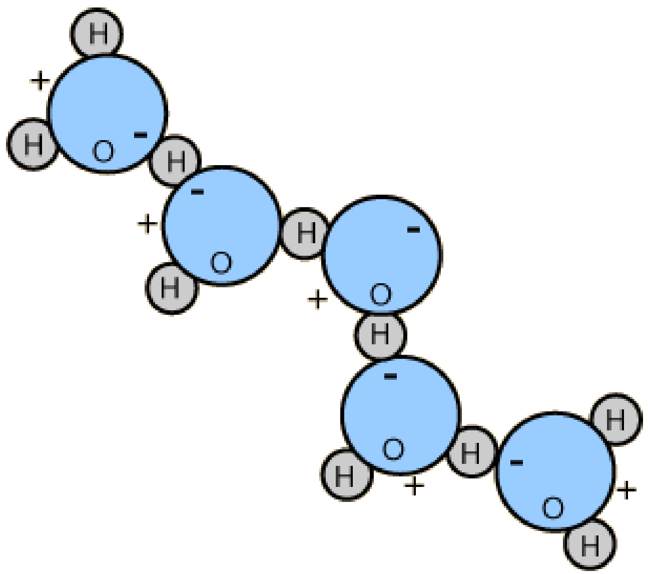
- When hydrogen atoms are joined in a polar covalent bond with a small atom of high electronegativity such as O, F or N, the partial positive charge on the hydrogen is highly concentrated because of its small size. If the hydrogen is close to another oxygen, fluorine or nitrogen in another molecule, 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.

$$\overset{\delta+}{H}—\overset{\delta-}{F} \qquad \overset{\delta+}{H}—\overset{\delta-}{F} \cdots\cdots \overset{\delta+}{H}—\overset{\delta-}{F}$$

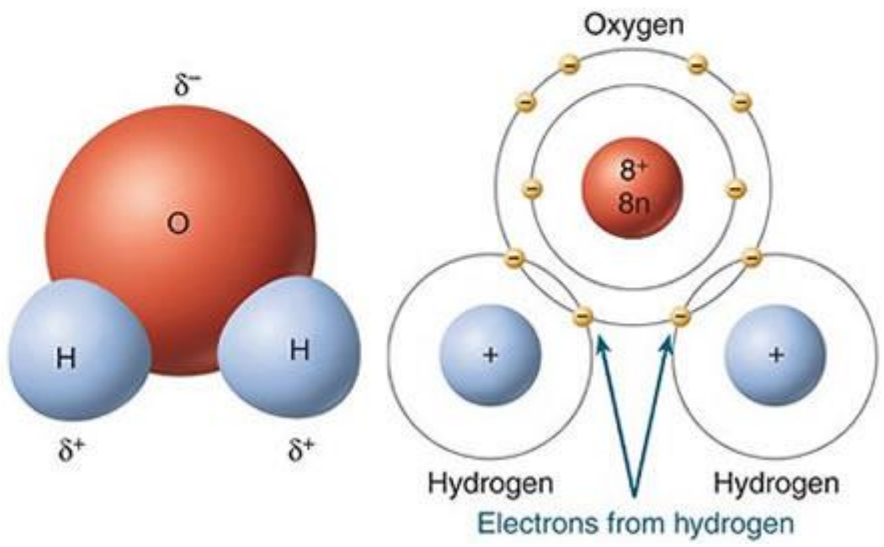
Hydrogen bond strength O—H···:N > O—H···:O > N—H···:N > N—H···:O

HYDROGEN BONDS

- Hydrogen bonds in water
- Each molecule can form up to 4 bonds
→ large boiling point of water



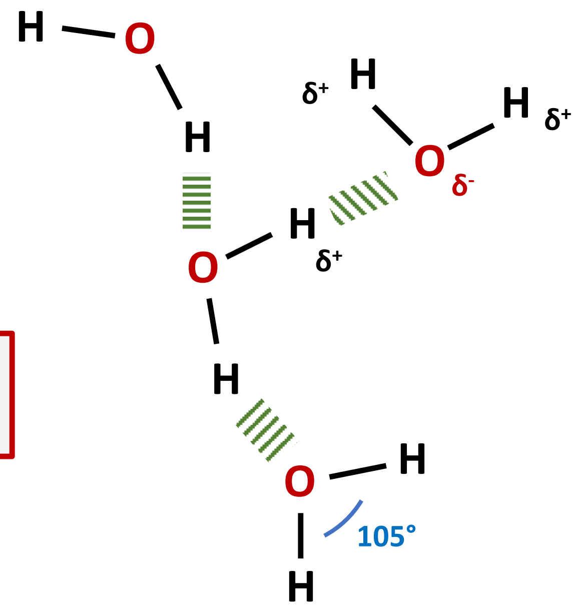
HYDROGEN BONDS:
THE WATER MOLECULE

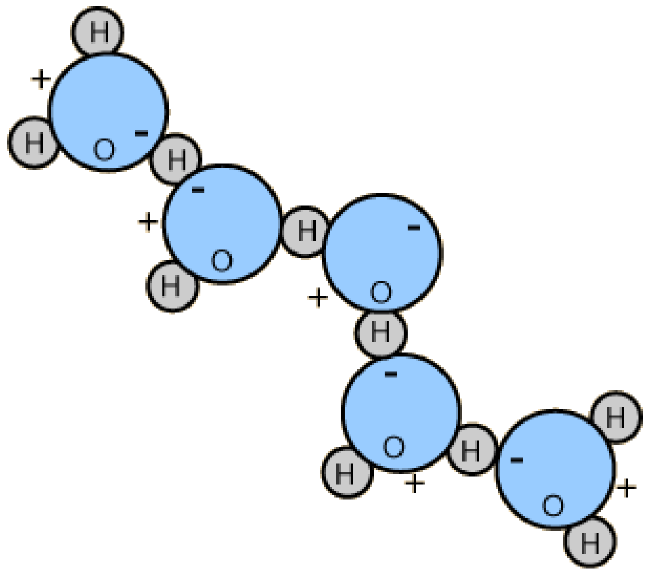


Water is a dipole

HYDROGEN BONDS

- **Hydrogen bonds**





Central role of water in cell
structure and **function**

- **Solvent**

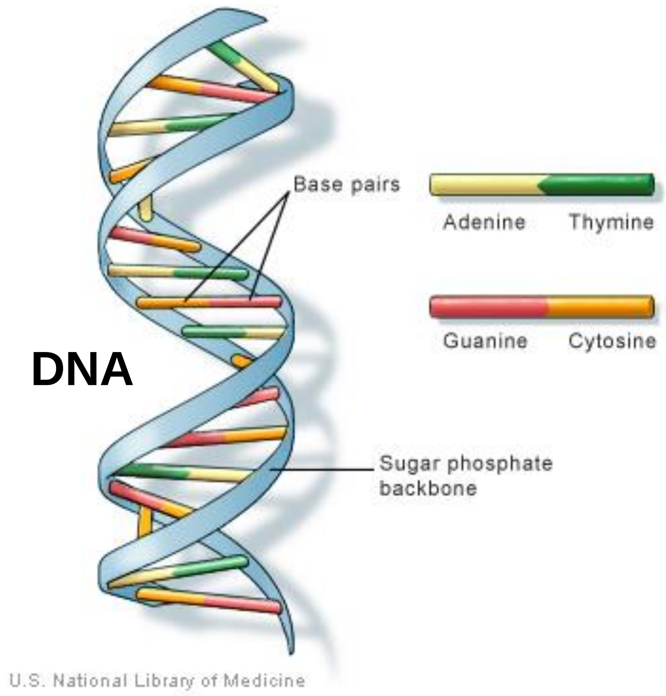
- **Reagent**

	Acid-base equilibrium	H_3O^+/H_2O ; H_2O /HO^-
	Nucleophilic	**Hydrolysis**

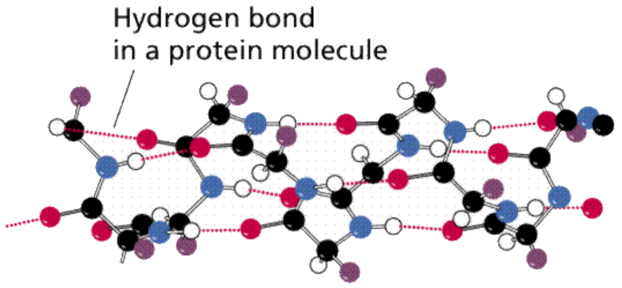
HYDROGEN BONDS IN BIOMOLECULES

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

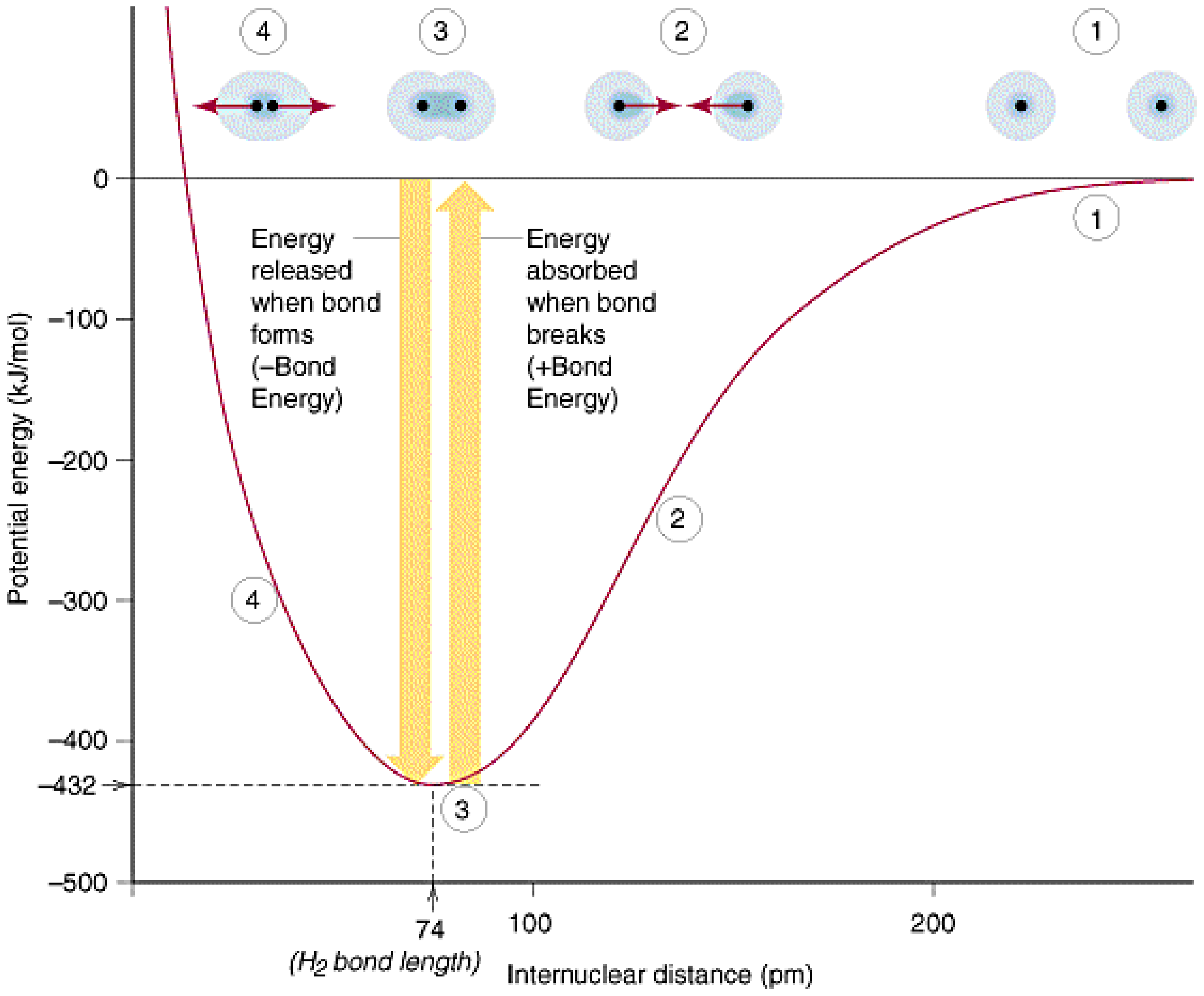
• Very important in ***proteins*** (between backbone oxygen and hydrogen in amino acids), ***DNA*** (between base pairs) and other biomolecules



DNA



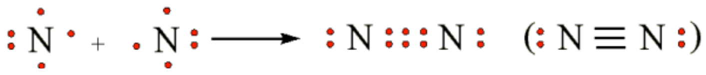
THE MOLECULAR POTENTIAL: HYDROGEN

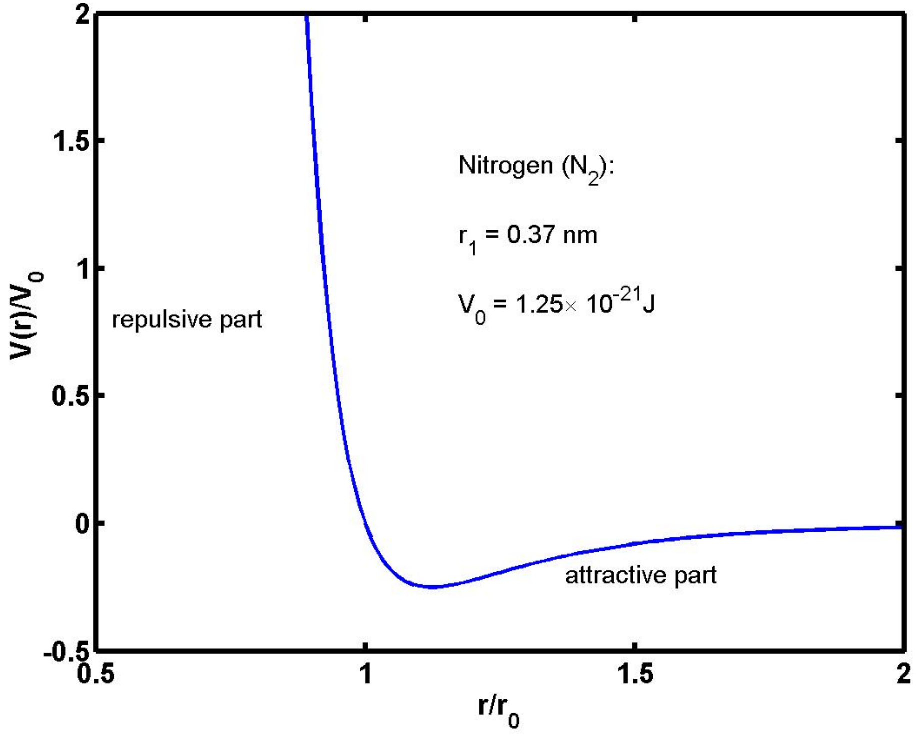


The molecular potential

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

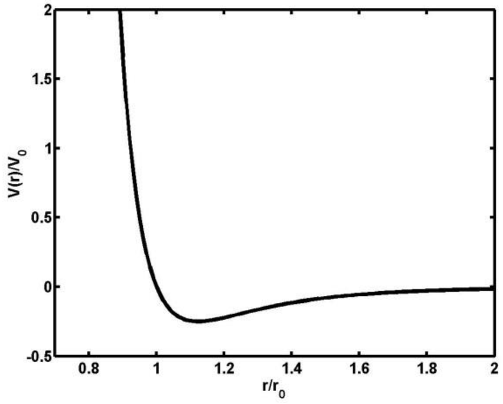
$$V(r) = V_0\left[\left(\frac{r_1}{r}\right)^{12} - \left(\frac{r_1}{r}\right)^{6}\right]$$





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.

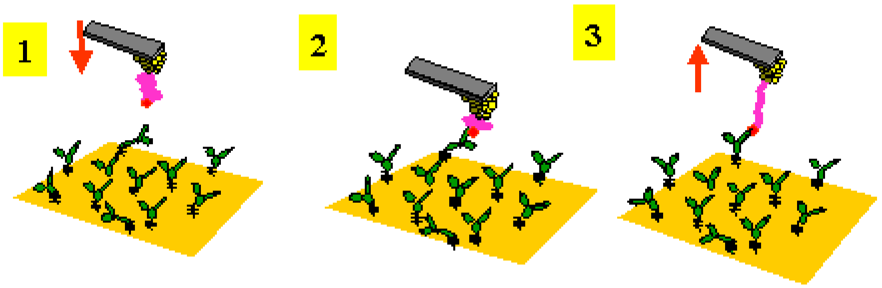
• The term ***1/r¹²***, dominating at short distance, models the repulsion between atoms when they are brought very close to each other.

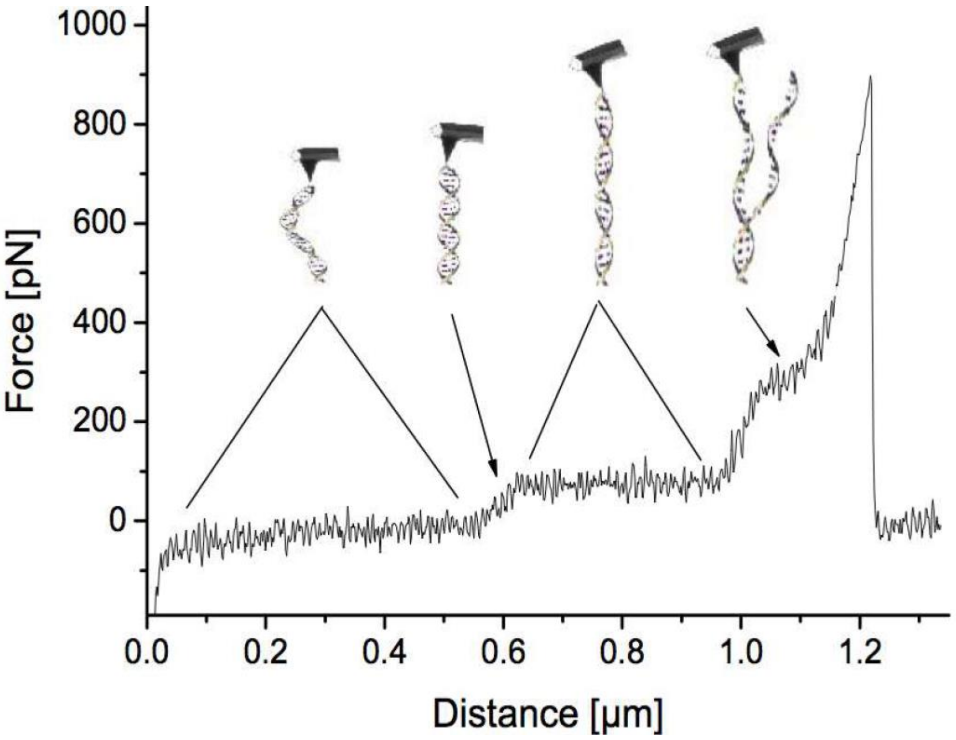
• The term ***1/r⁶***, dominating at large distance, constitute the attractive part. This is the term which gives cohesion to the system.

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 forc	~ 20 kJ/mol
Hydrogen bond	No simple expression	~ 10 kJ/mol
Van der Waals	$\propto \frac{1}{r^6}$ (dipole force)	< 5 kJ/mol

STRETCHING FORCES IN DNA MEASURED BY AFM





The force increases with distance until the DNA double strand breaks at about 70 pN

The hydrogen bonds between base pairs break

EXAMPLE 1

Two atoms in a biological molecule are found to interact in a manner that can be described by a Lennard-Jones potential

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

where $V_0=10^{-21}$ J and $r_1=0.1$ nm. At which separation distance will the atoms be in equilibrium?

ANSWER

The system is in equilibrium at separation distance where the force is zero:

$$\text{Force} = \frac{\text{Change in energy}}{\text{Change in position}} = -\frac{dV(r)}{dr} = -V_0\left[-12\frac{r_1^{12}}{r^{13}} + 6\frac{r_1^6}{r^7}\right] = \frac{6V_0}{r}\left[2\left(\frac{r_1}{r}\right)^{12} - \left(\frac{r_1}{r}\right)^6\right]$$

$$\text{Force} = 0 \quad \text{when } r = 2^{1/6} r_1 = \underline{\underline{0.11\,\text{nm}}}$$

Example 2

The technique known as "optical tweezers" permits measurement of the forces applied to single biological molecules. Calculate the maximum tensile (stretching) force that a polypeptide chain can withstand, assuming that the covalent bonds which hold the backbone together can be described by the Lennard-Jones potential function:

$$V(r) = V_0\left[\left(\frac{r_0}{r}\right)^{12} - \left(\frac{r_0}{r}\right)^{6}\right]$$

in which the values of V_0 and r_0 for carbon-carbon bonds are respectively 0.56×10^{-18} J and 0.152×10^{-9} m, while the corresponding values for carbon-nitrogen bonds are respectively 0.51×10^{-18} J and 0.149×10^{-9} m.

ANSWER

$$\text{Force} = \frac{\text{Change in energy}}{\text{Change in position}} = -\frac{dV(r)}{dr} = -V_0\left[-12\frac{r_0^{12}}{r^{13}} + 12\frac{r_0^{6}}{r^{7}}\right] = \frac{12V_0}{r}\left[\left(\frac{r_0}{r}\right)^{12} - \left(\frac{r_0}{r}\right)^{6}\right] \quad \textbf{(*)}$$

At maximum force: $\frac{dF(r)}{dr} = 12V_0\left[-13\frac{r_0^{12}}{r^{14}} + 7\frac{r_0^{6}}{r^{8}}\right] = 0$ **=>** $\frac{7}{13} = \frac{r_0^6}{r^6}$

=> $\mathbf{r \approx 1.10868\ r_0}$

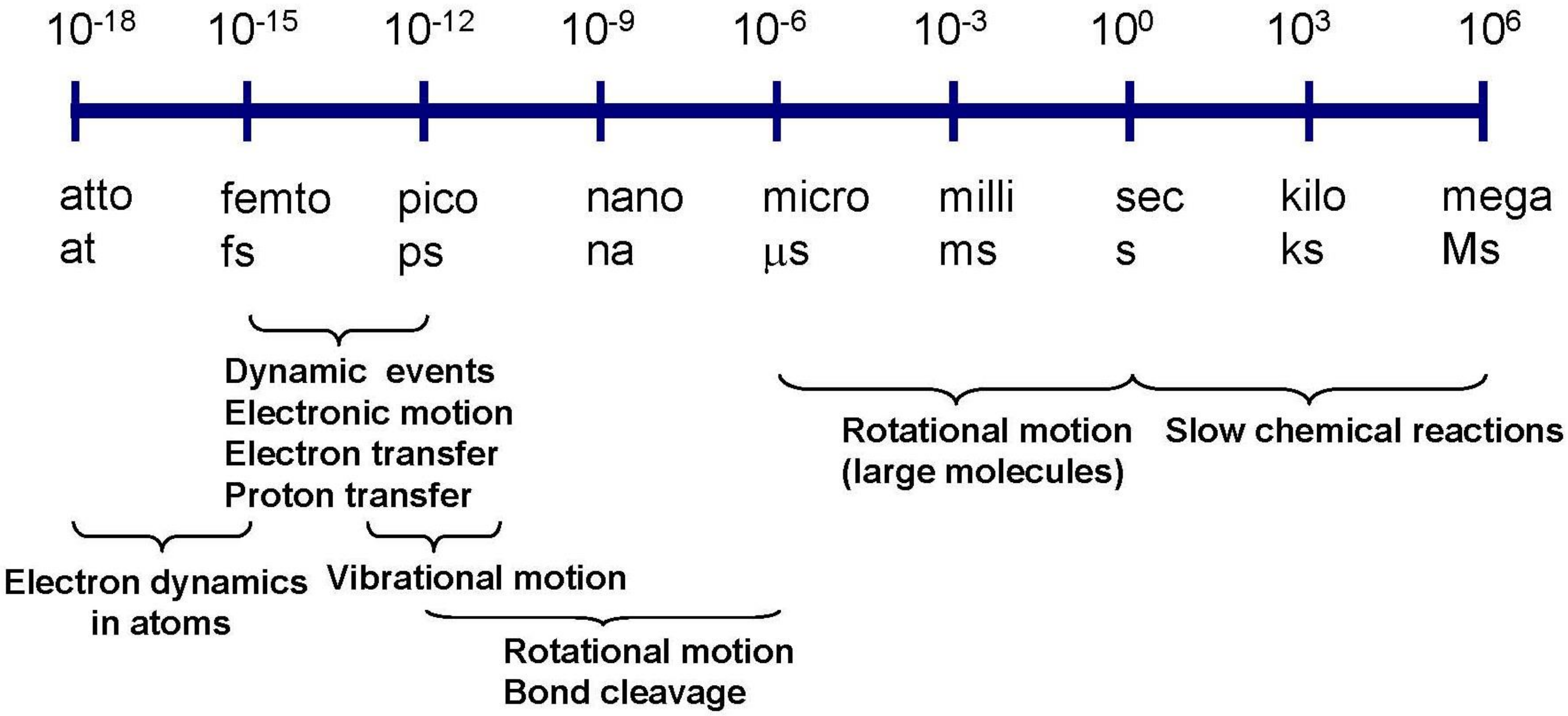
Plugging parameters in equations (*):

For N-C bond, maximum force is: **F ≈ 0.92 nN**

For C-C bond, maximum force is: **F ≈ 0.99 nN**

The maximum force the peptide chain can withstand is 0.92 nN

TIME SCALES AND MOLECULES

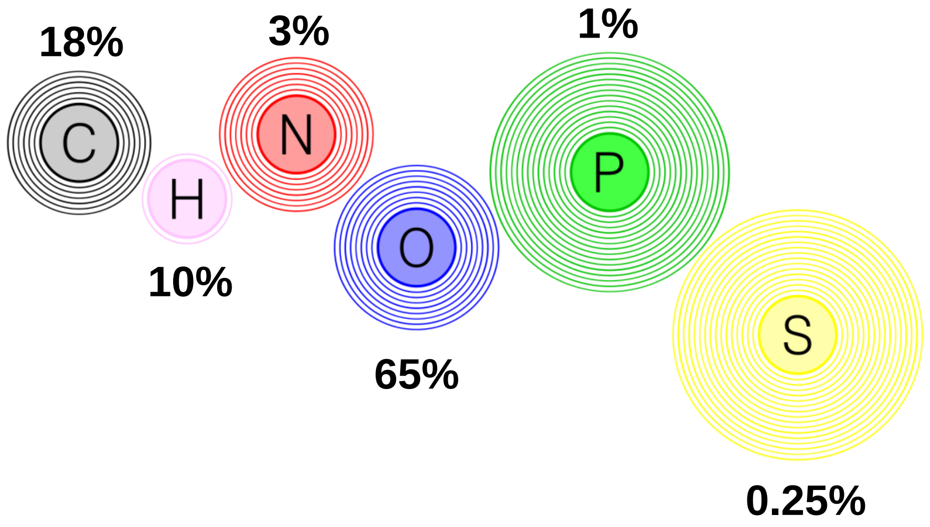


By Gurzadyan

INTRODUCTION TO BIOLOGICAL MATTER

INTRODUCTION TO BIOLOGICAL MATTER

Chemical species	% of cellular mass
Water	70
Ions	1
Small organic molecules	5 to 8
Organic macromolecules	22 to 25



+ Ca 1,5%
+ trace elements

A CLASSIFICATION OF BIOSYSTEMS

SIZE
Microscopic scale (1 mm > size > 100 nm)
Molecular scale (100 nm > size)

Other classification schemes are possible!

TABLE 1.1

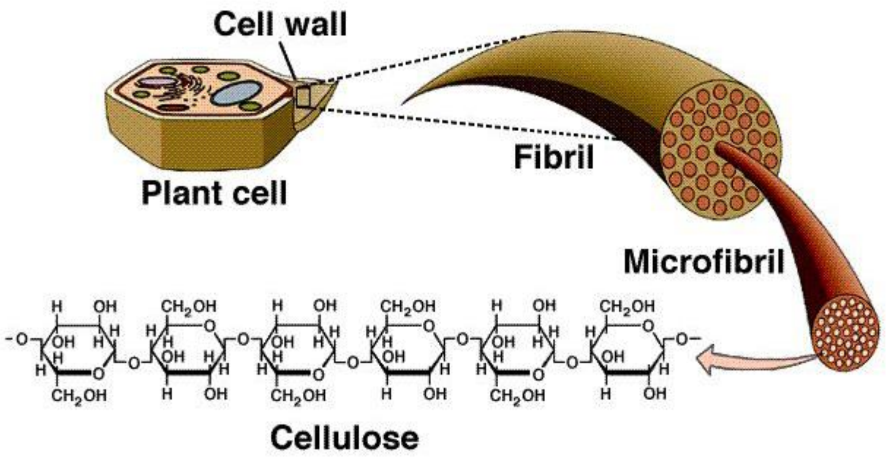
Approximate Values of Some Measured Lengths	
	Length (m)
Distance from Earth to most remote known quasar	1×10^{26}
Distance from Earth to most remote known normal galaxies	4×10^{25}
Distance from Earth to nearest large galaxy (M31, the Andromeda galaxy)	2×10^{22}
Distance from Earth to nearest star (Proxima 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}

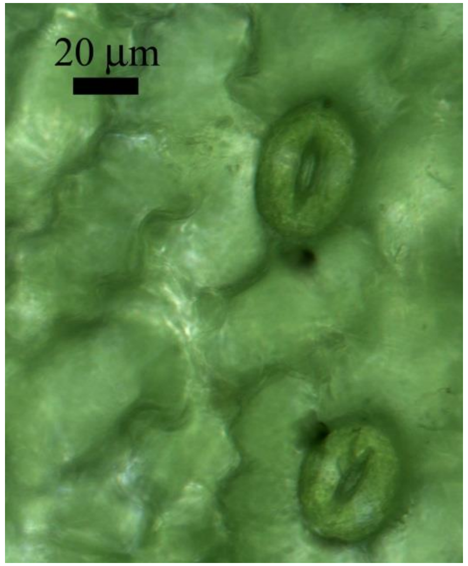
BIOPHYSICS ON THE MICRO-SCALE

Examples:

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

- Study how water flows into plants and biological systems.





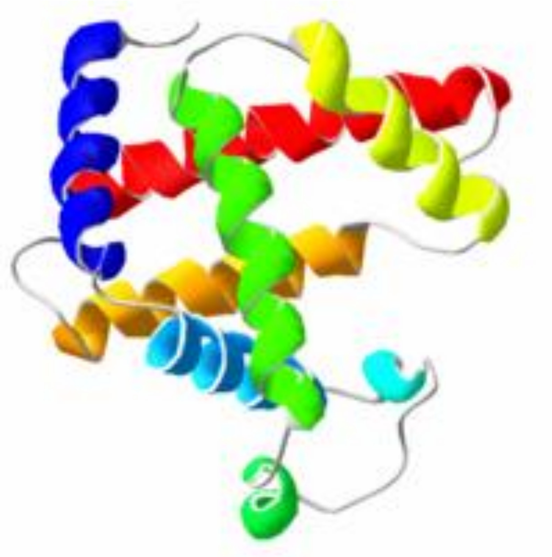
Plant cells

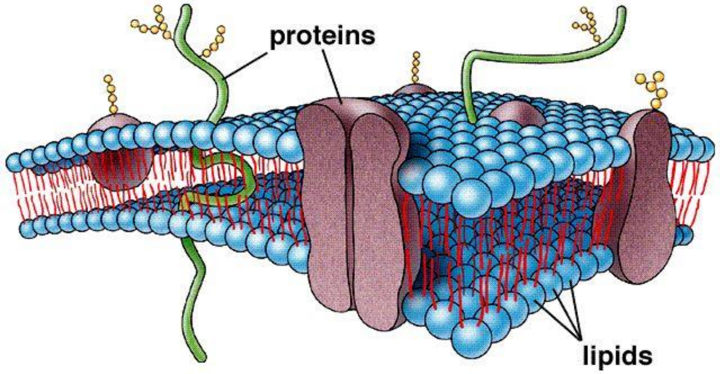
BIOPHYSICS ON THE MOLECULAR SCALE

<u>Examples:</u>

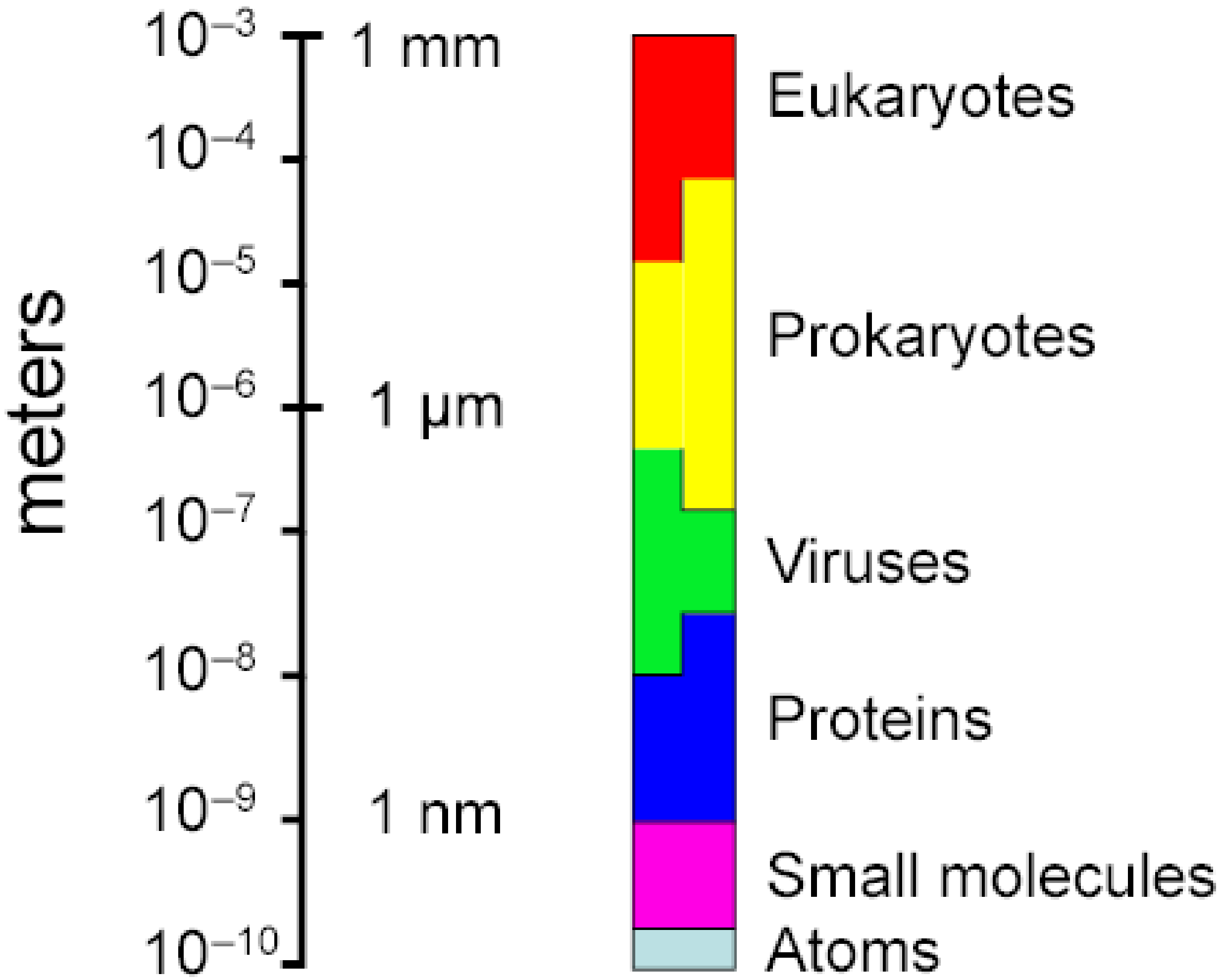
- Study the structure and function of DNA and proteins.

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



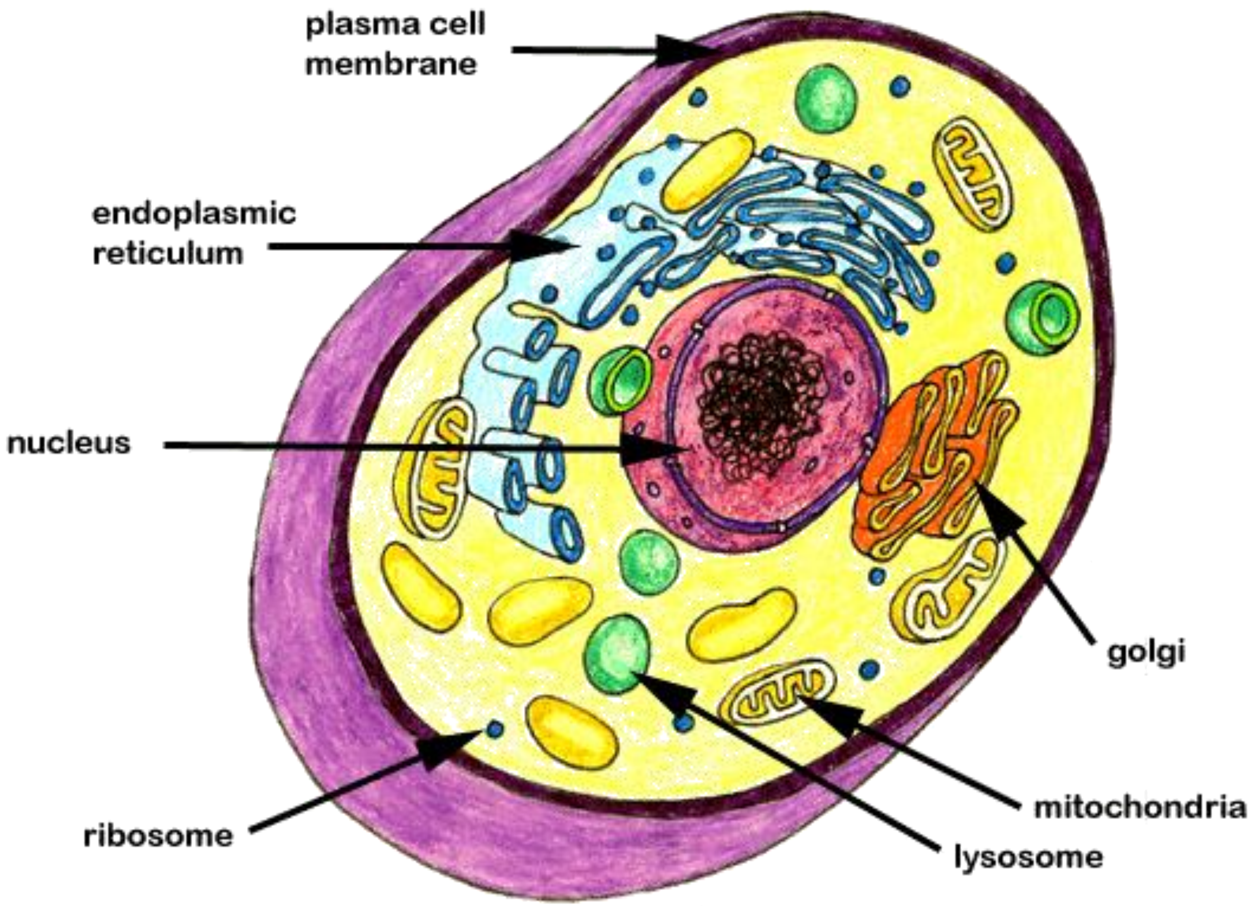


RANGE OF SIZES FOR BIO-OBJECTS



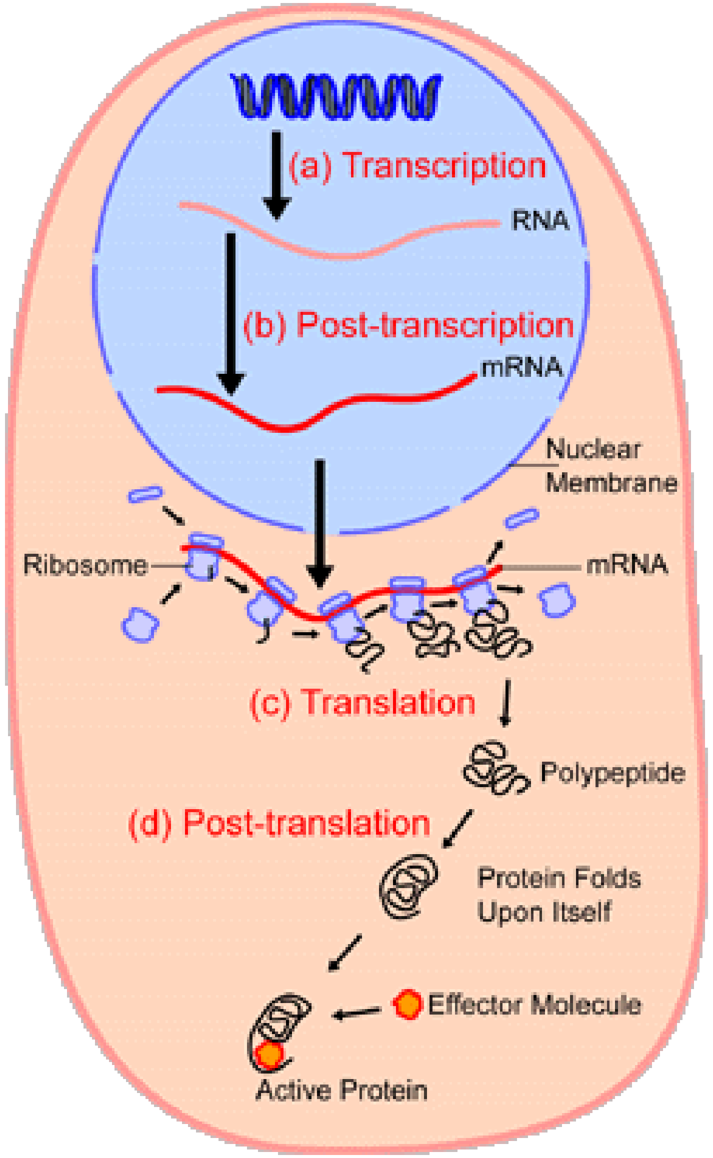
http://en.wikipedia.org/wiki/Virus

A CELL



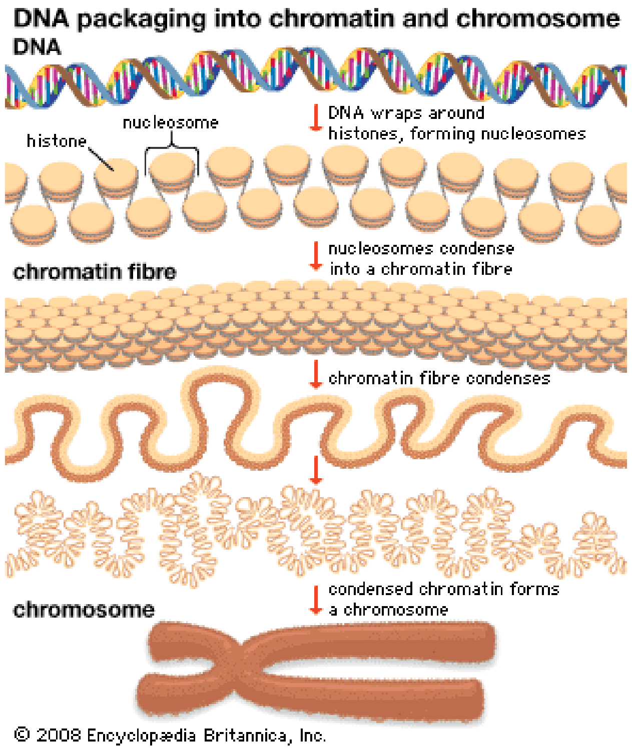
http://web.jjay.cuny.edu/~acarpi/NSC/13-cells.htm

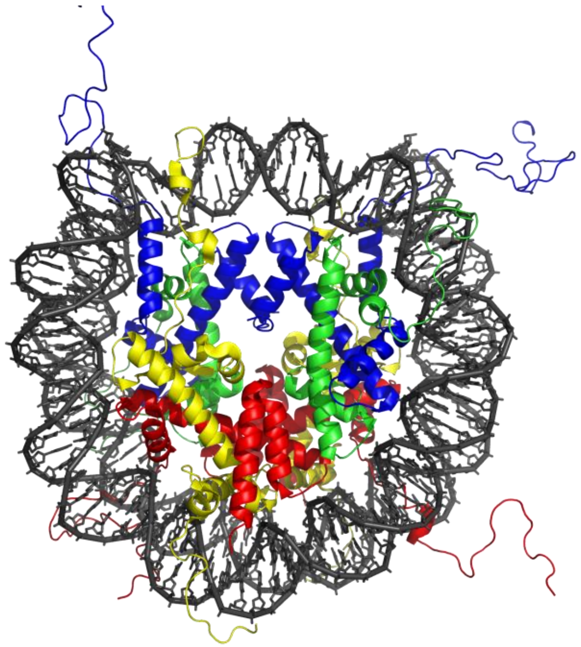
A CELL

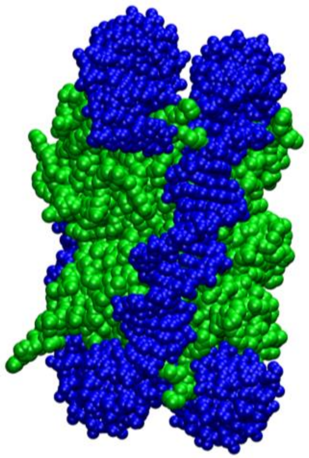


http://en.wikipedia.org/wiki/Cell_(biology)

NUCLEOSOME

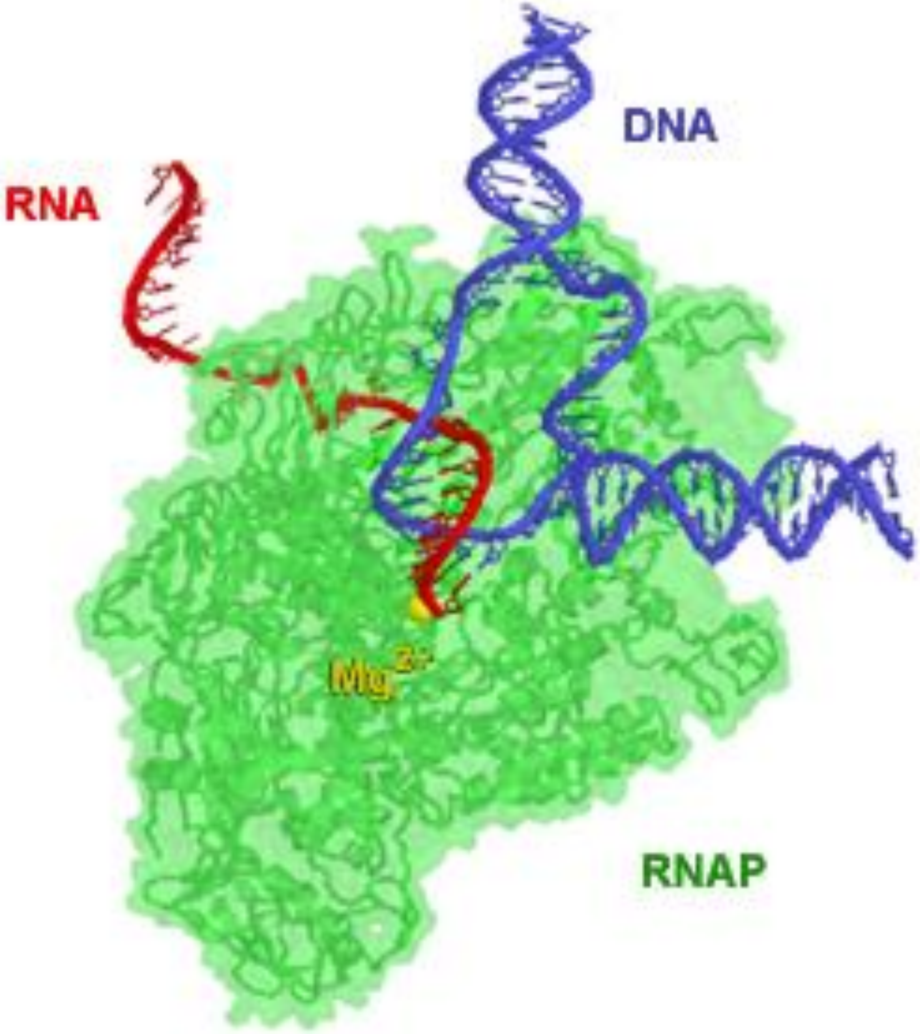






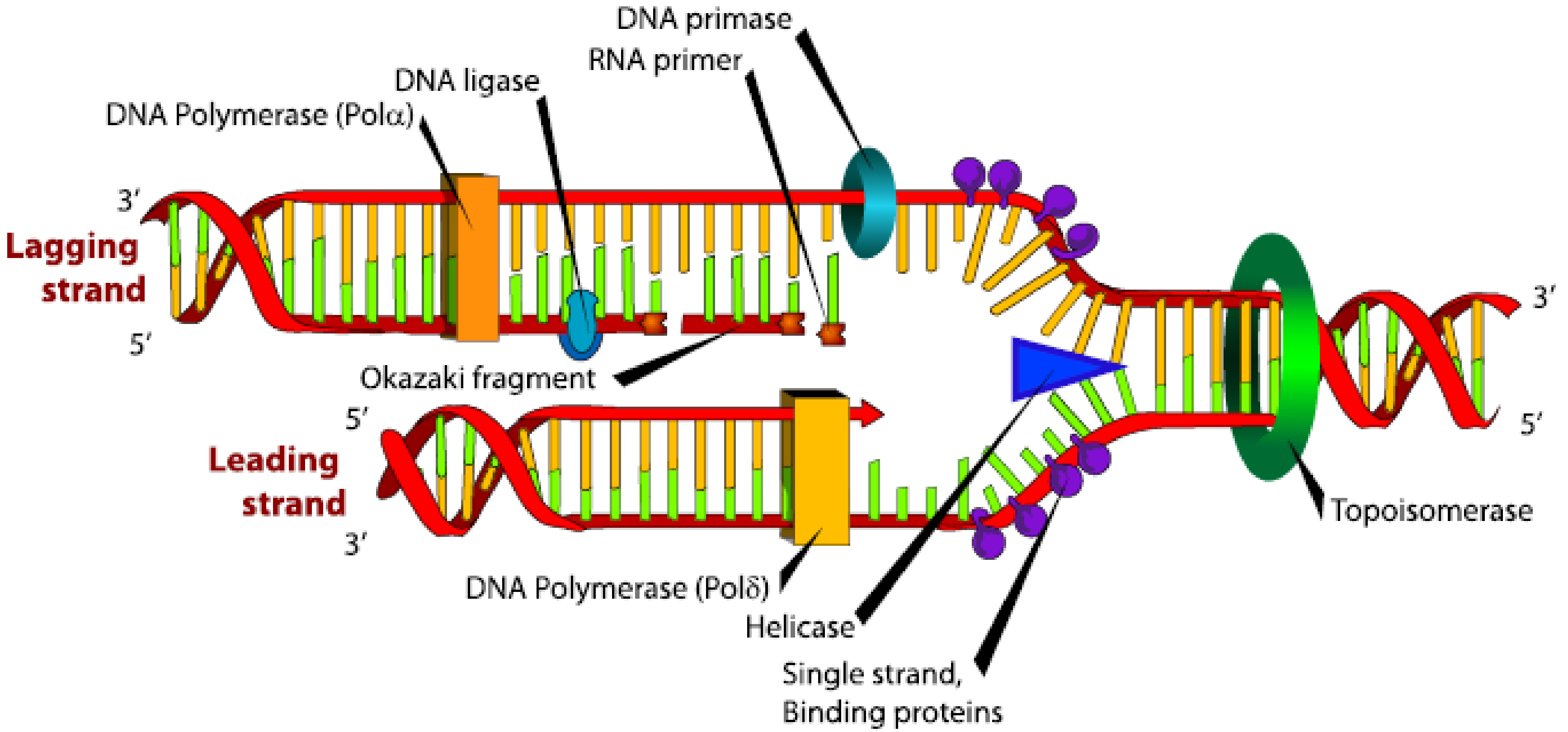
If DNA stretch ~ 2 m
Chromosomes ~ 5.10^{-6} m

RNA polymerase



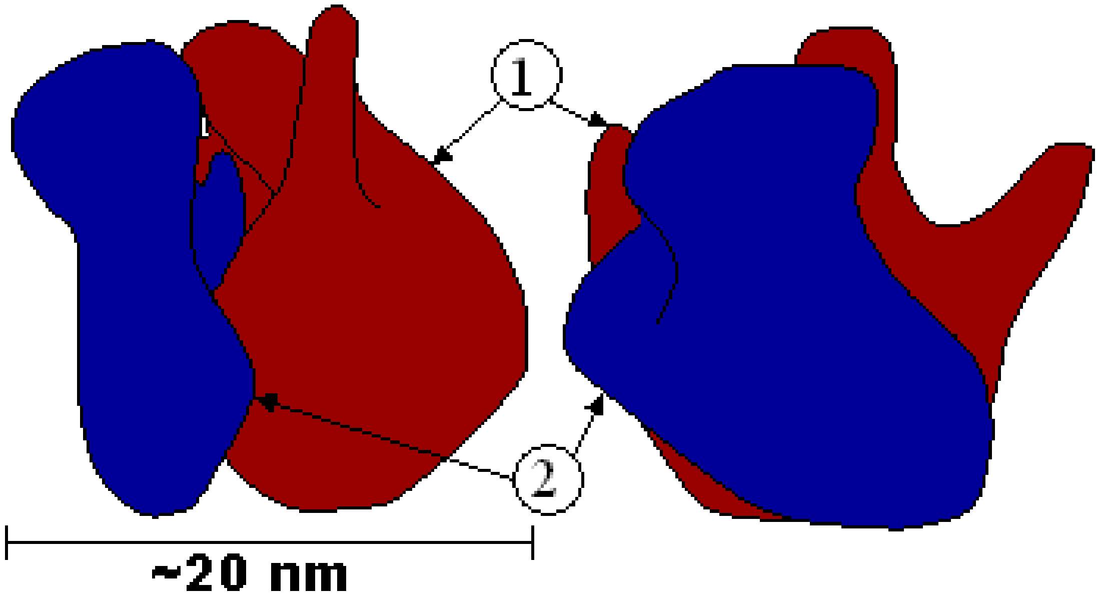
http://en.wikipedia.org/wiki/RNA_polymerase

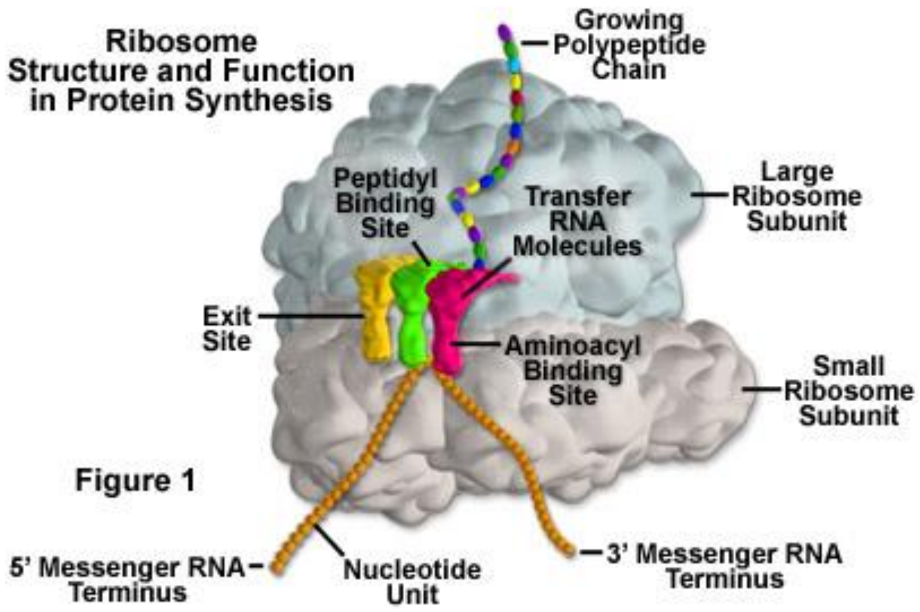
DNA replication



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

RIBOSOME

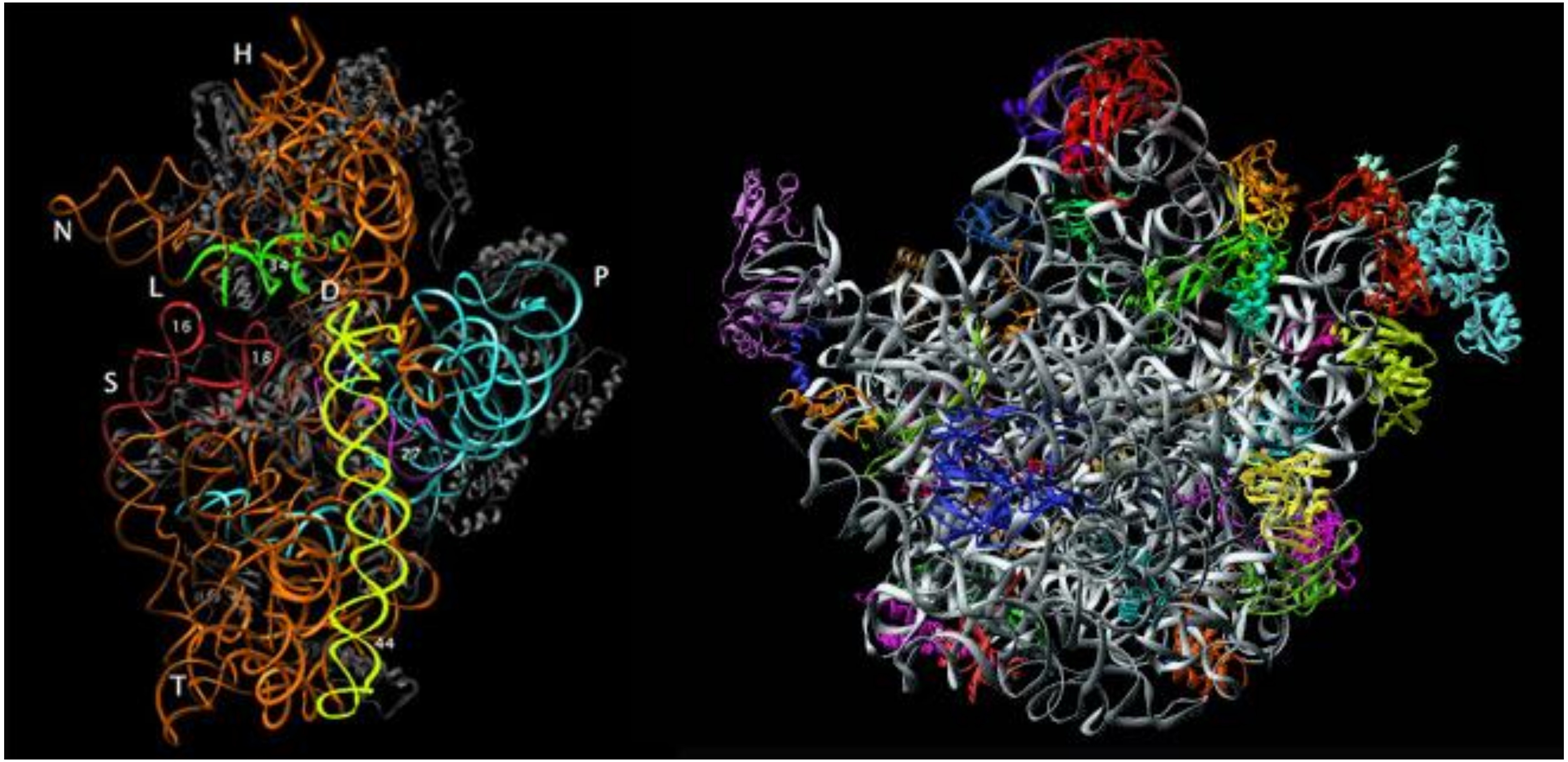




http://en.wikipedia.org/wiki/Ribosome

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

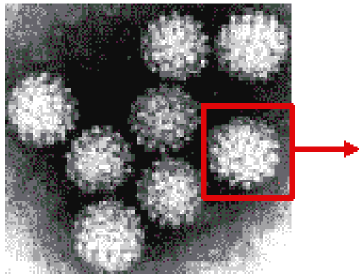
RIBOSOME

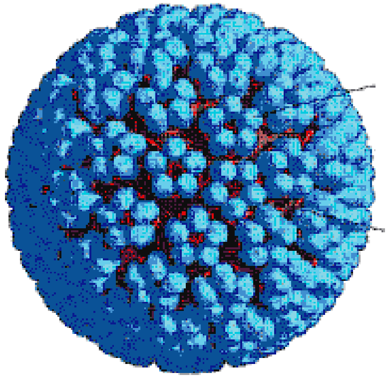


http://www.molgen.mpg.de/~ag_ribo/ag_franceschi/

TRANSCRIPTION FACTOR E2

PAPILLOMAVIRUS





Related to
Cancer
damage to skin …