Water, macromolecules

Miklós Kellermayer

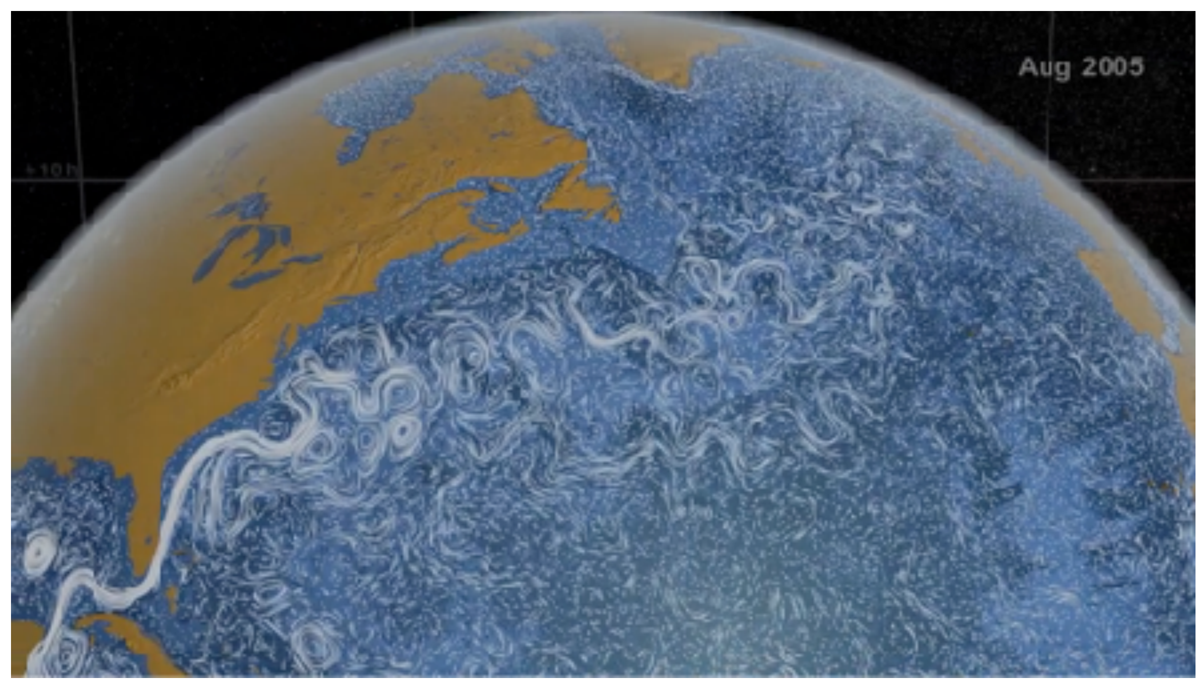
Water

- Source of *inspiration* (music, paintings).
- Thales (580, B.C.): "...water is *source of all things*..."
- Henry Cavendish (1783): water is H_2O.
- Only chemical that naturally exists in *all three states* (solid, liquid, gas).
- 71% of the Earth's surface is covered with water ("blue planet").
- Water is of utmost importance for *life*:
  98% of jellyfish
  94% of three-month human fetus
  72% of newborn
  60% of adult
- Average daily water intake: 2.4 liters.

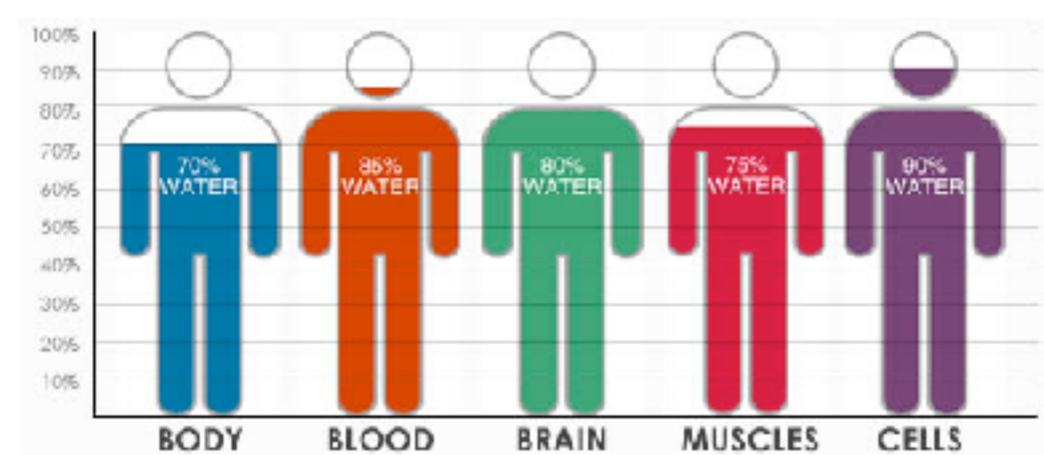
Georg Friedrich **Händel** (1685-1759): ***"Water music"***.

Georg Friedrich Händel *(center)* and King George I (*right*) on the Thames River, 17 July 1717.

Hokusai (1760-1849): Great wave off Kanagawa

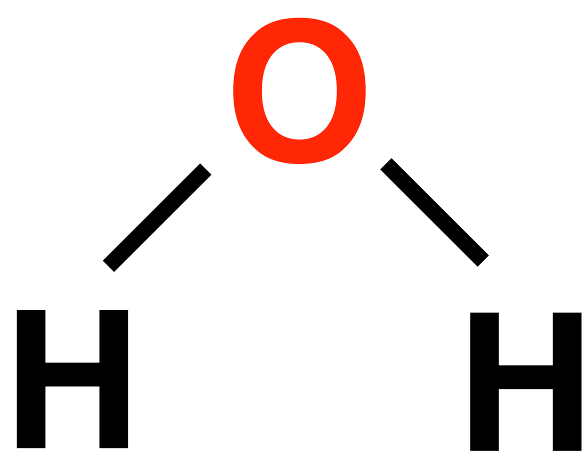


Perpetual motion of oceans on Earth's surface.

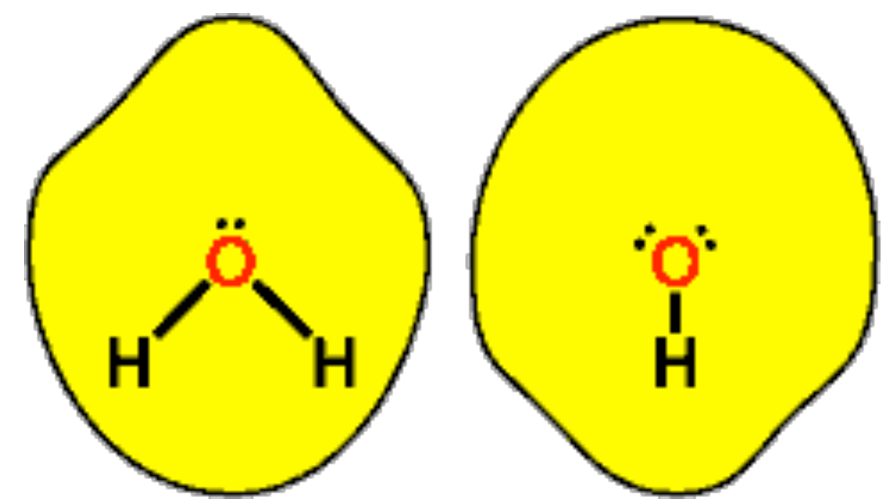


Structure of the water molecule

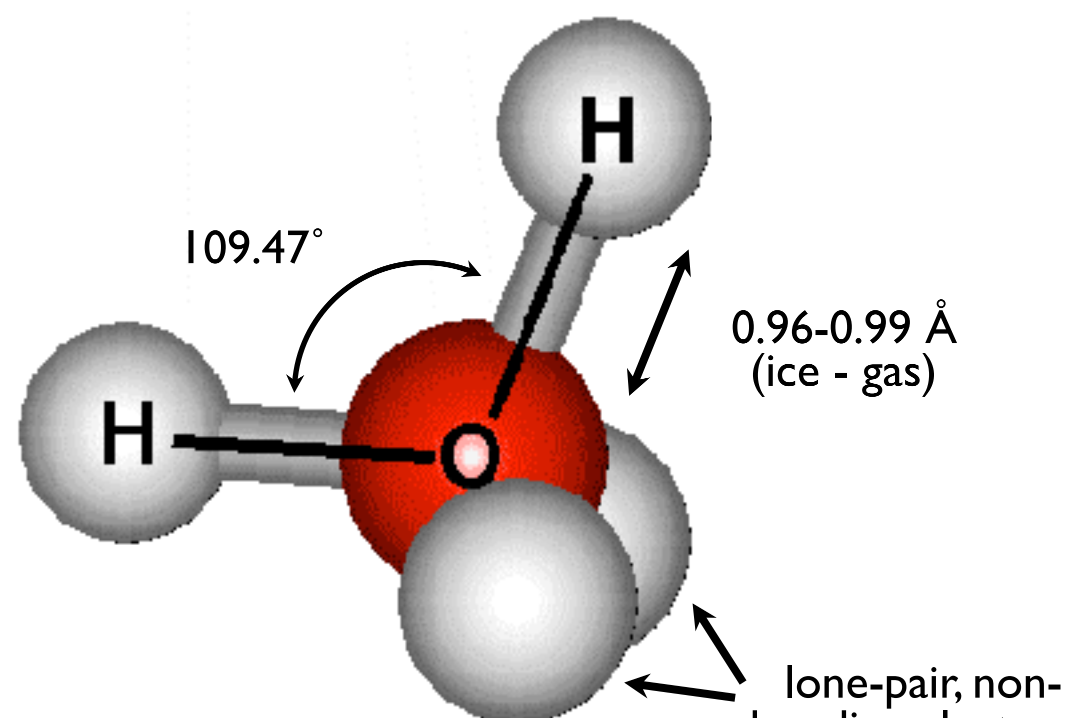
One of the smallest molecules
Barely larger than an atom



van der Waals radius: ~ 3.2 Å
Its shape is not spherical

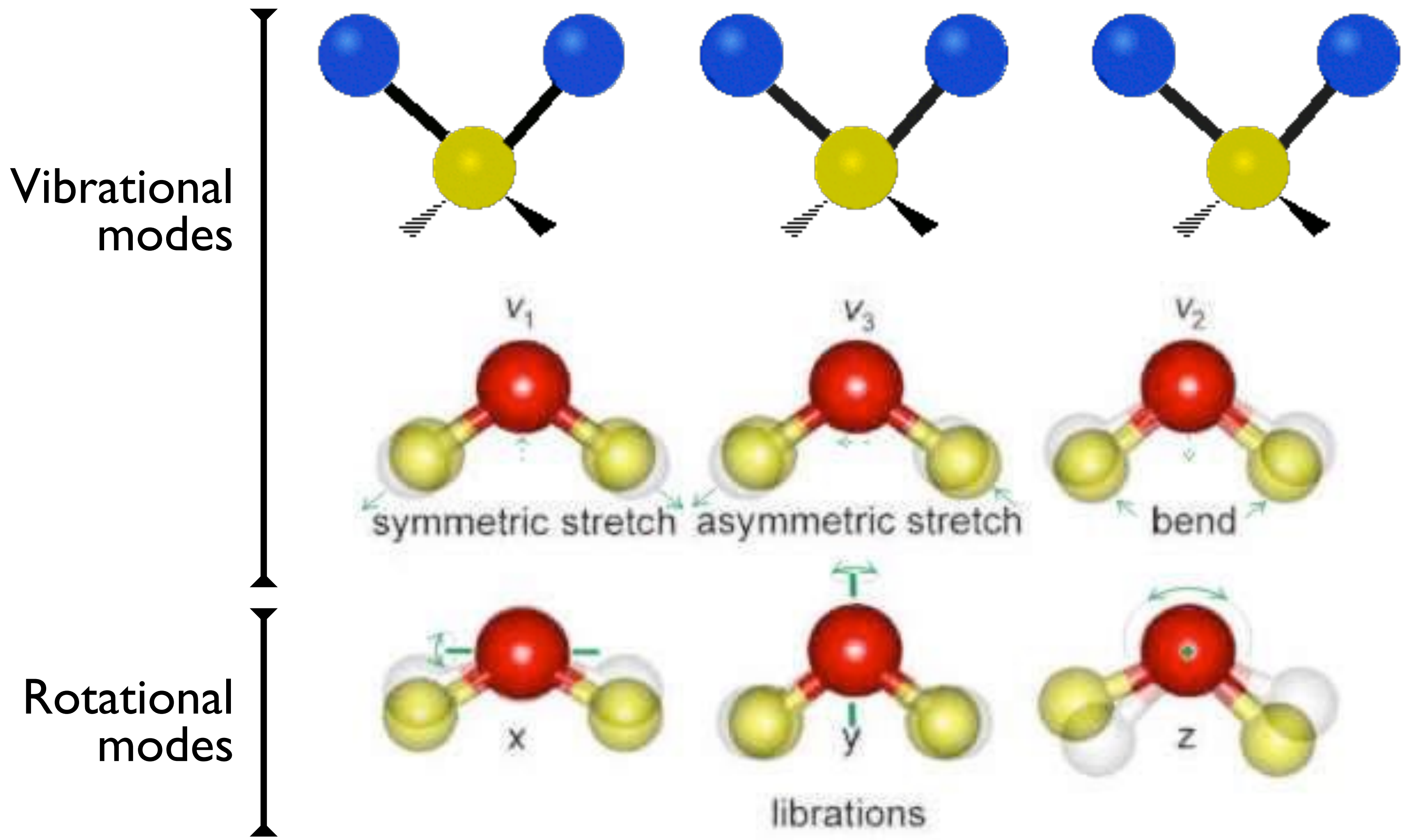


Tetrahedral structure:



Dynamics of the water molecule

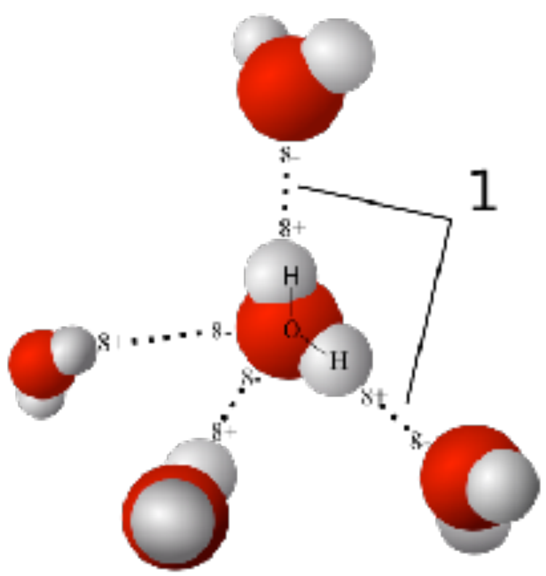
Rotational and vibrational motion

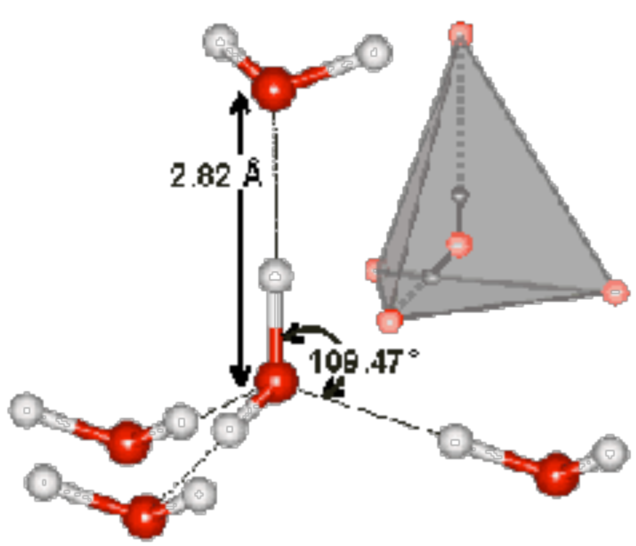


Absorption in the infrared and red spectral region ➛ "blue" color of natural waters: *blue planet*

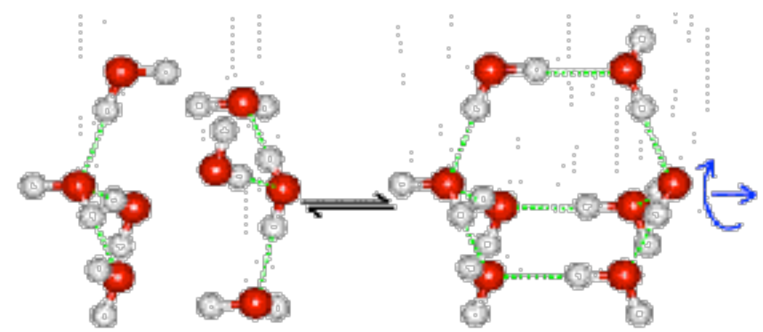
Structure of liquid water

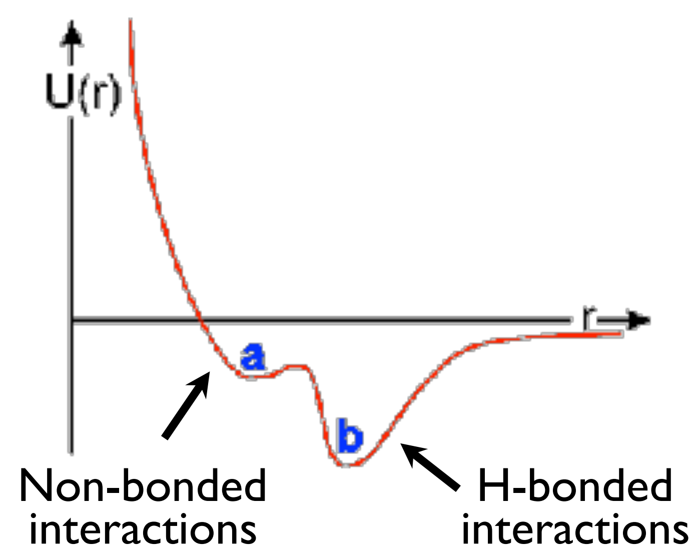
Hydrogen bonds in the vicinity of a water molecule: formation of the water pentamer





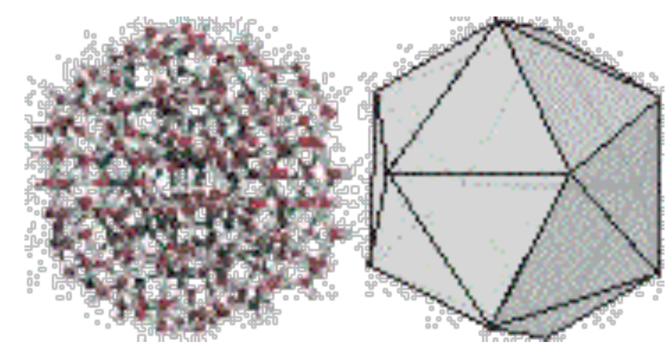
H-bridge: cohesion + repulsion
Cluster formation: bicyclo-octamer





From clusters to networks: 280 molecules form icosahedral structure

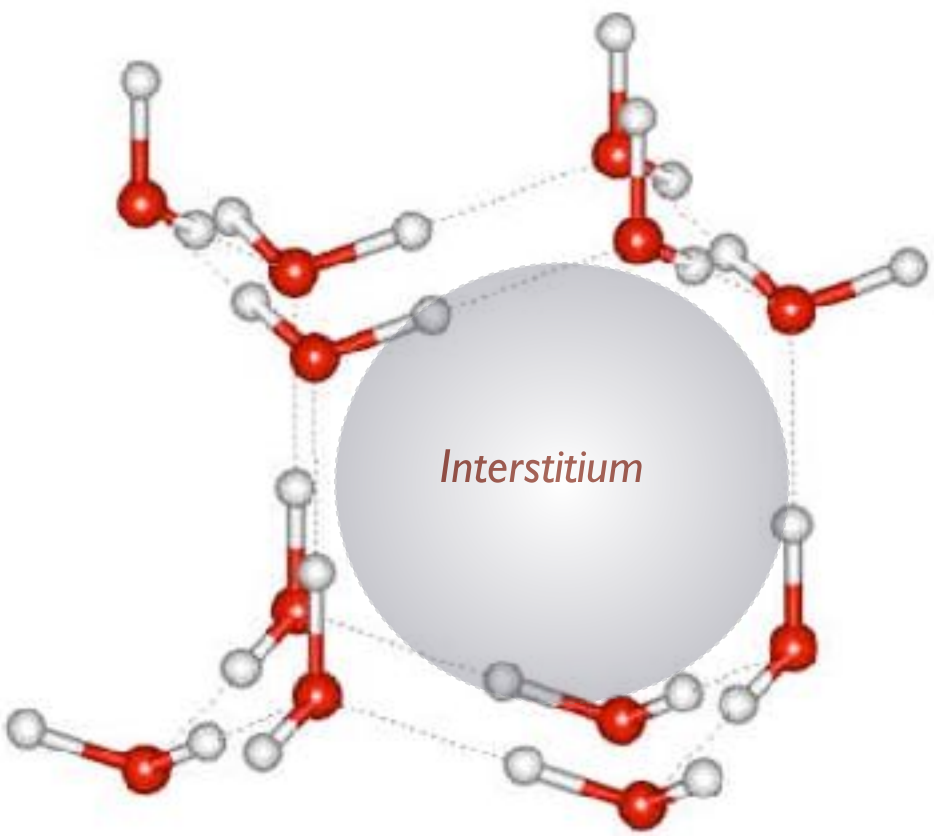
(*icosahedron*: regular polyhedron with 20 identical equilateral triangular faces)

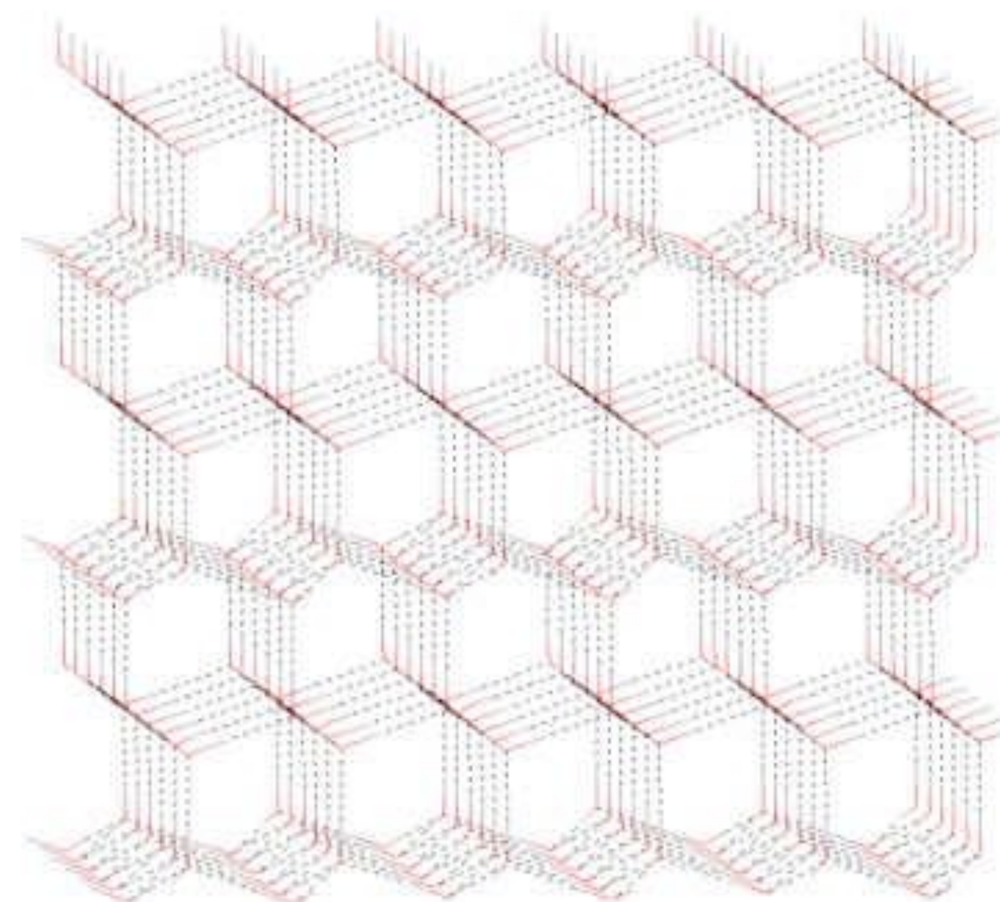


Spatial networks:
May explain anomalous properties of water

Structure of ice

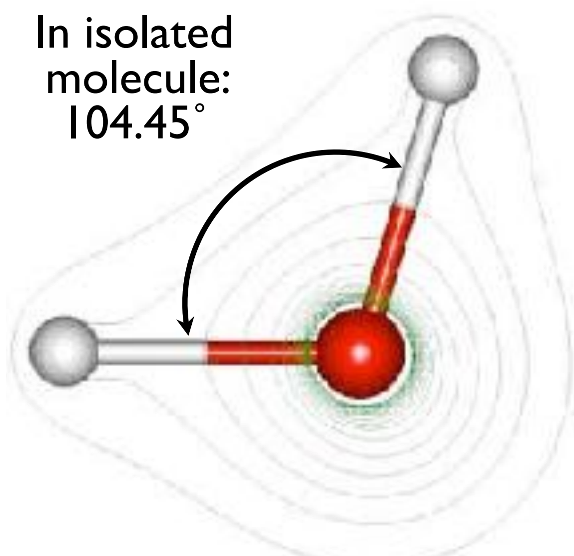
- 9 different forms
- Conventional ice: hexagonal structure
- Coordination number: 4 (each molecule coordinates another four) Interstitium: could incorporate a water molecule - important in the diffusion of gases

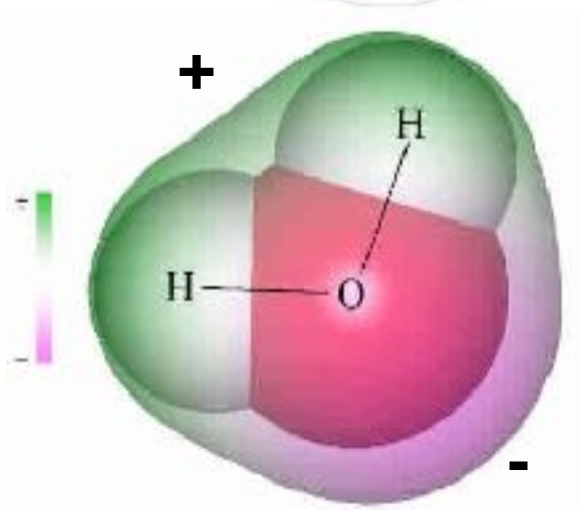




Physical properties of water I.

Large permanent dipole moment → Good solvent

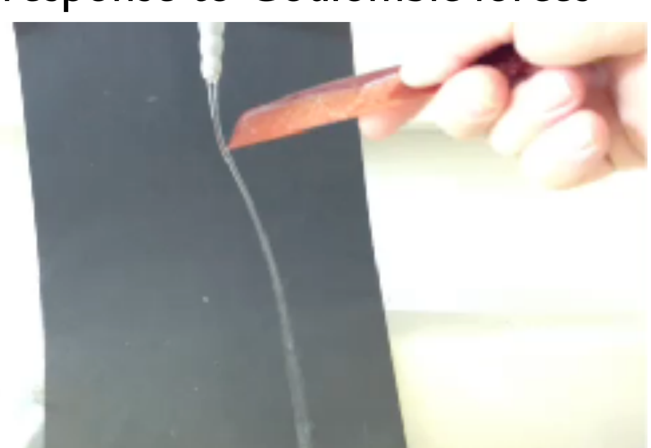




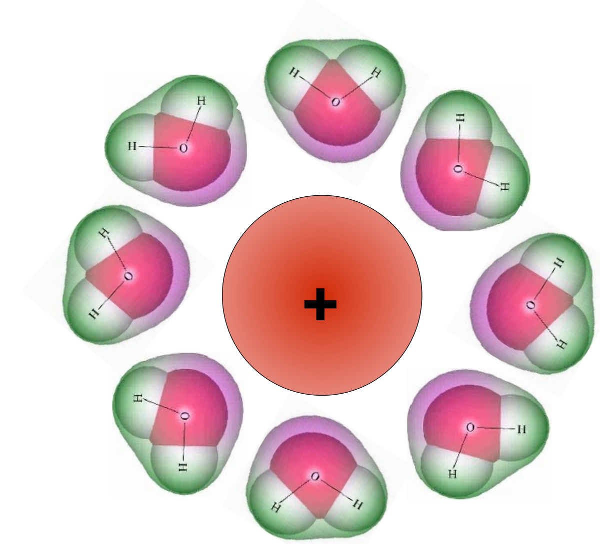
Dipole moment: amount of electrical energy stored in the material by an applied voltage, relative to vacuum. It shows how good an electrical insulator the material is. Consequence: water is good solvent.

Chemical	Dipole moment
Polyethylene	2.25
Methanol	30
Ethylene glycol	37
Glycerol	47
Water	**80**
Titanium dioxide	86-173

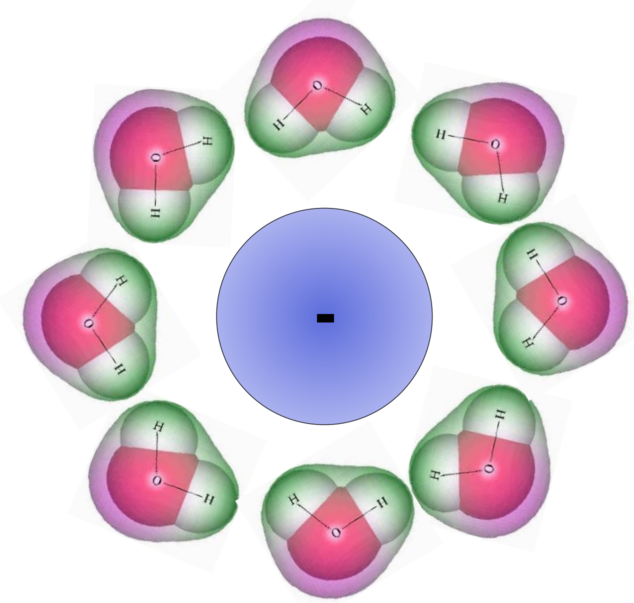
Water stream bends in response to Coulombic forces



Courtesy of Prof. Miklós Zrínyi



Cation solvation



Anion solvation

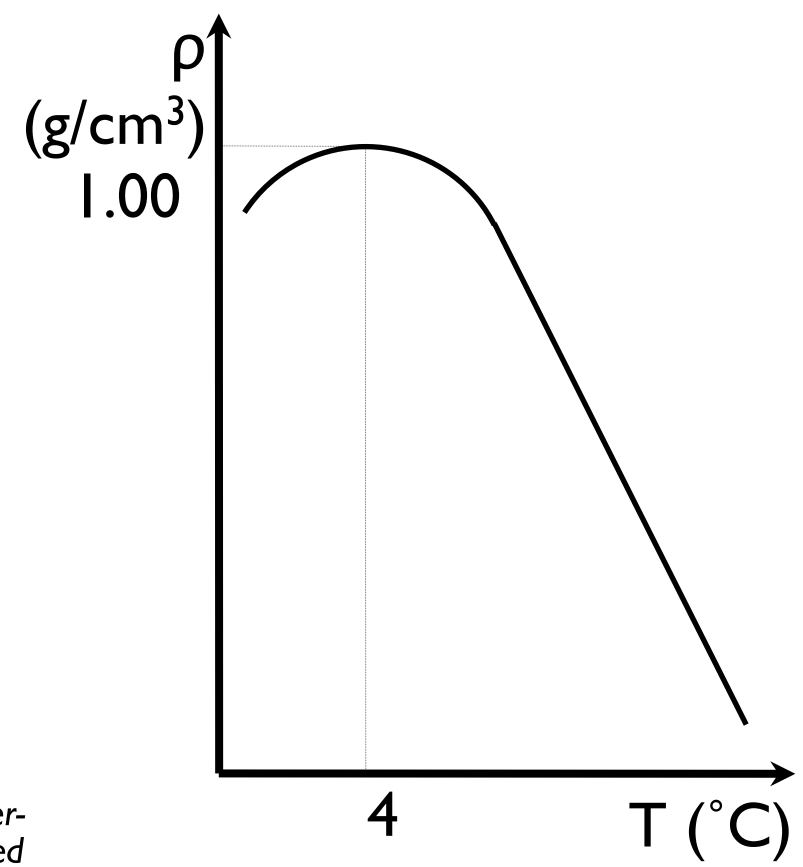
In the *microwave oven*: dipoles rotate according to the oscillating electromagnetic field. Water molecules acquire kinetic energy, which dissipates into the surroundings.

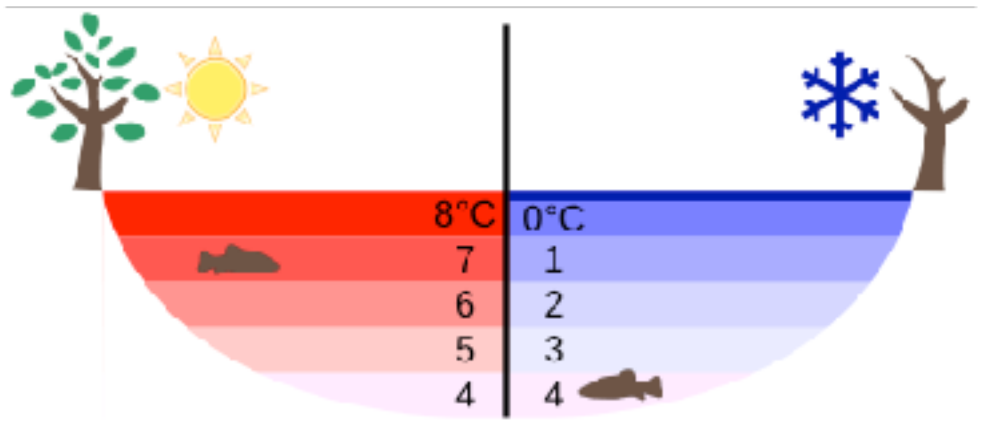
Physical properties of water II.

Anomalous density-temperature function

Temperature (˚C)	Density (kg/m³)
+100	958.4
+80	971.8
+60	983.2
+40	992.2
+30	995.6502
+25	997.0479
+22	997.7735
+20	998.2071
+15	999.1026
+10	999.7026
+4	**999.9720**
0	999.8395
−10	998.117
−20	993.547
−30	983.854

Super-cooled water (applies to the rows from −10 to −30)





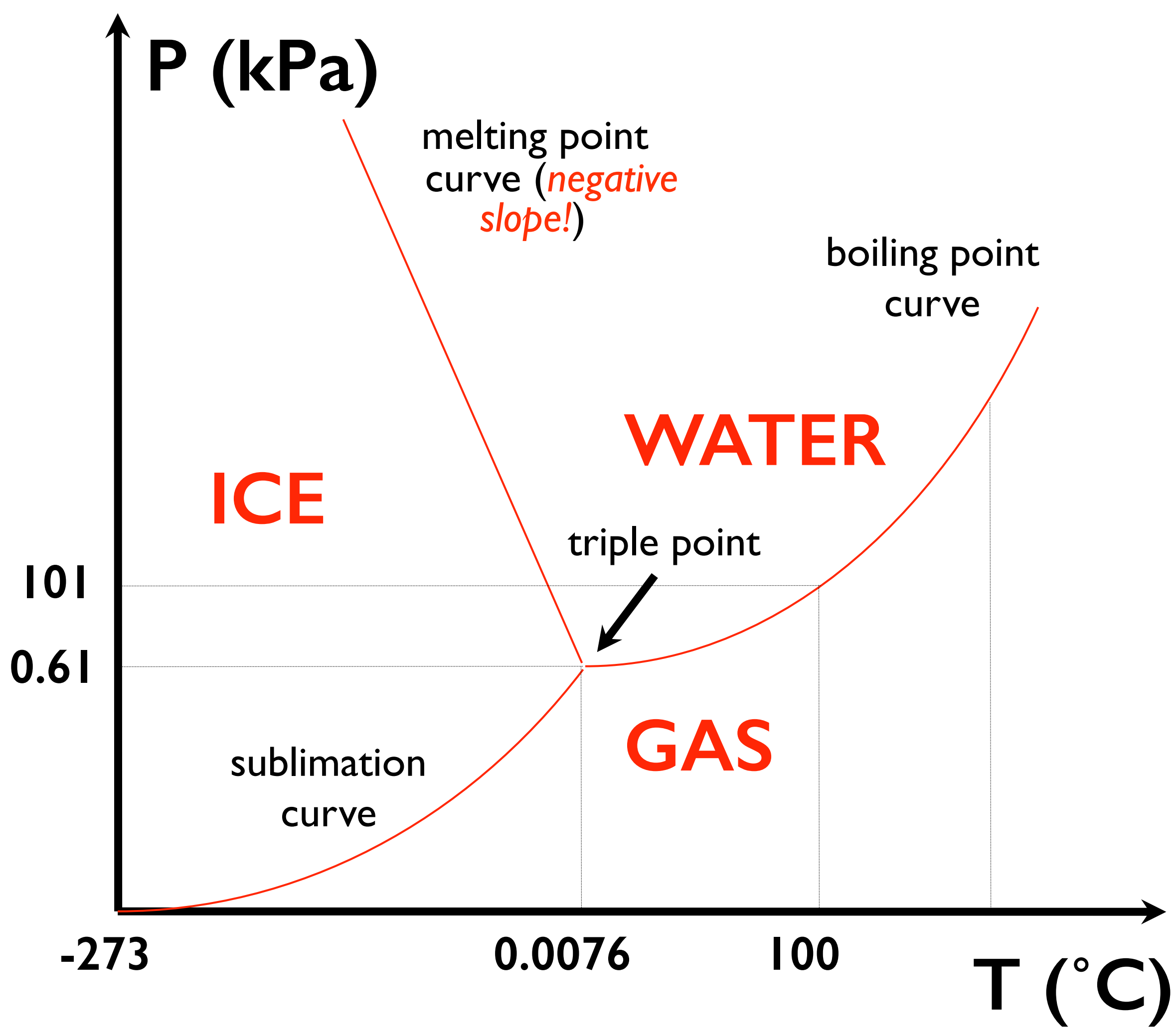
Consequences:

- 4 ˚C water is always at the botötm of the lake.
- Life persists under frozen lake.
- Creek runs under ice.

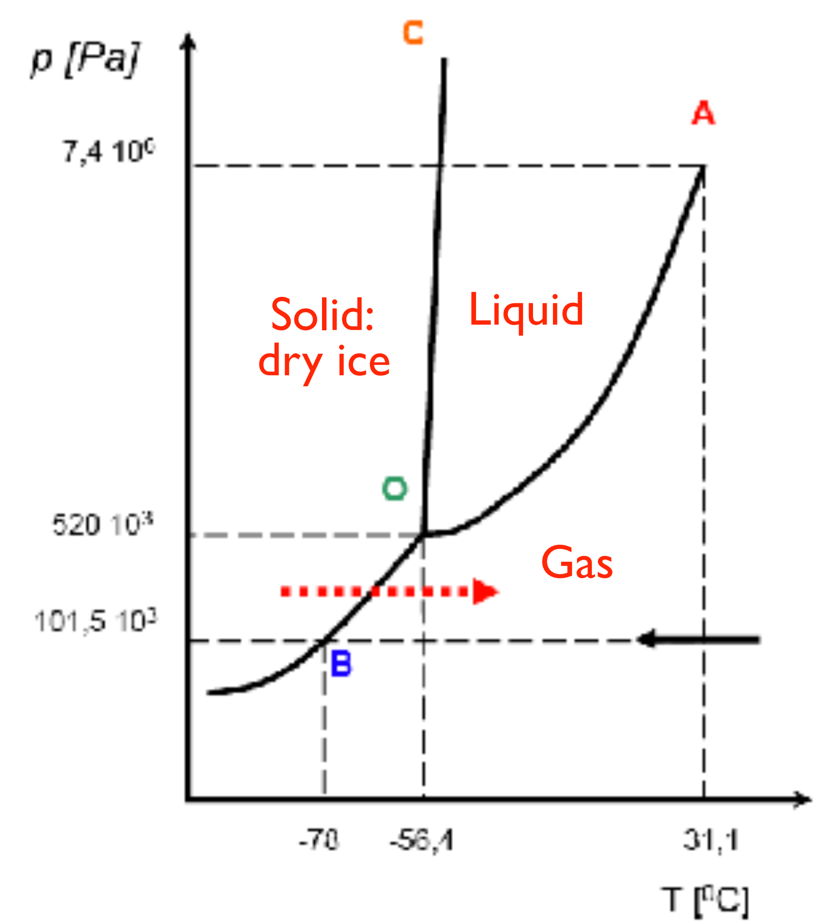
Physical properties of water III.

Anomalous phase diagram

- Phase curve: two phases are in equilibrium
- Area between phase curves: a single phase is present
- Intersection of phase curves: triple point



Comparison: CO_2

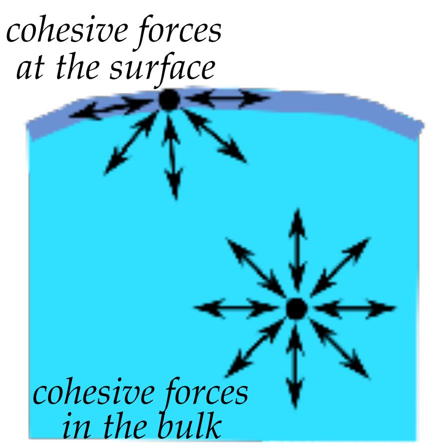


Physical properties of water IV.

Large surface tension

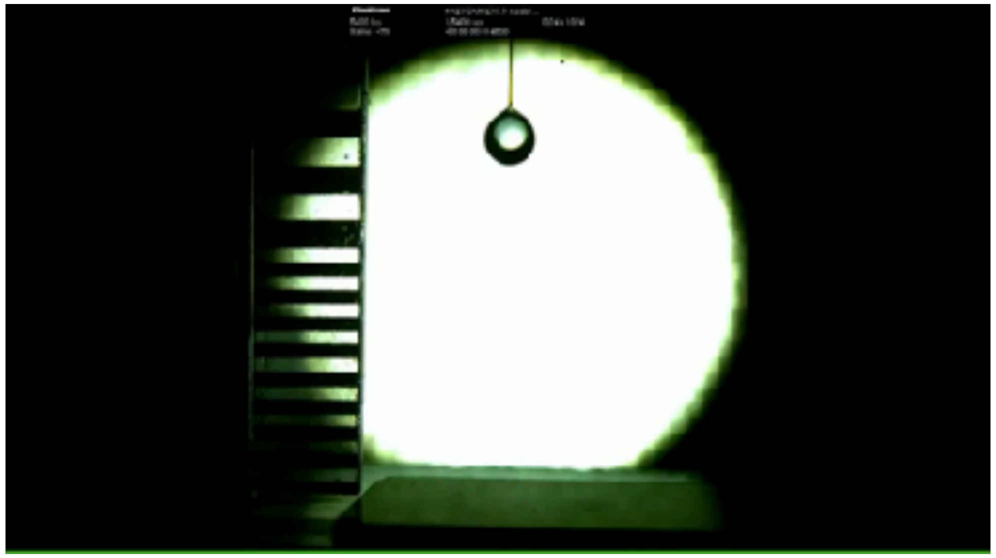
Surface tension: contractive tendency of the liquid that resists external force.

Imbalance of cohesive forces in the ***bulk*** versus the ***surface*** of the liquid.



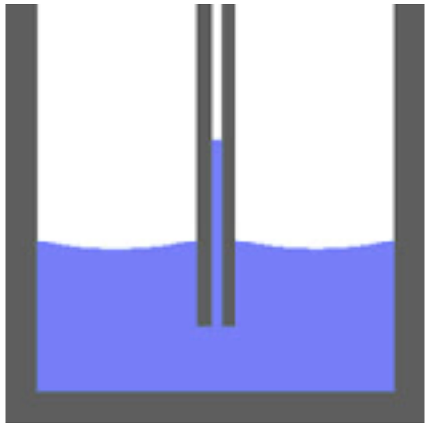
Chemical	Surface tension (mN/m)
Ethanol	24.4
Methanol	22.7
Acetone	23.7
Chloroform	27.1
Benzene	28.5
Water	72.9

Consequences on ***hydrophobic*** surface



Persisting droplet on a superhydrophobic surface

Consequences on ***hydrophilic*** surface



Capillary action (model)

Capillary action aiding plant root function

Consequences in macroscopic living systems

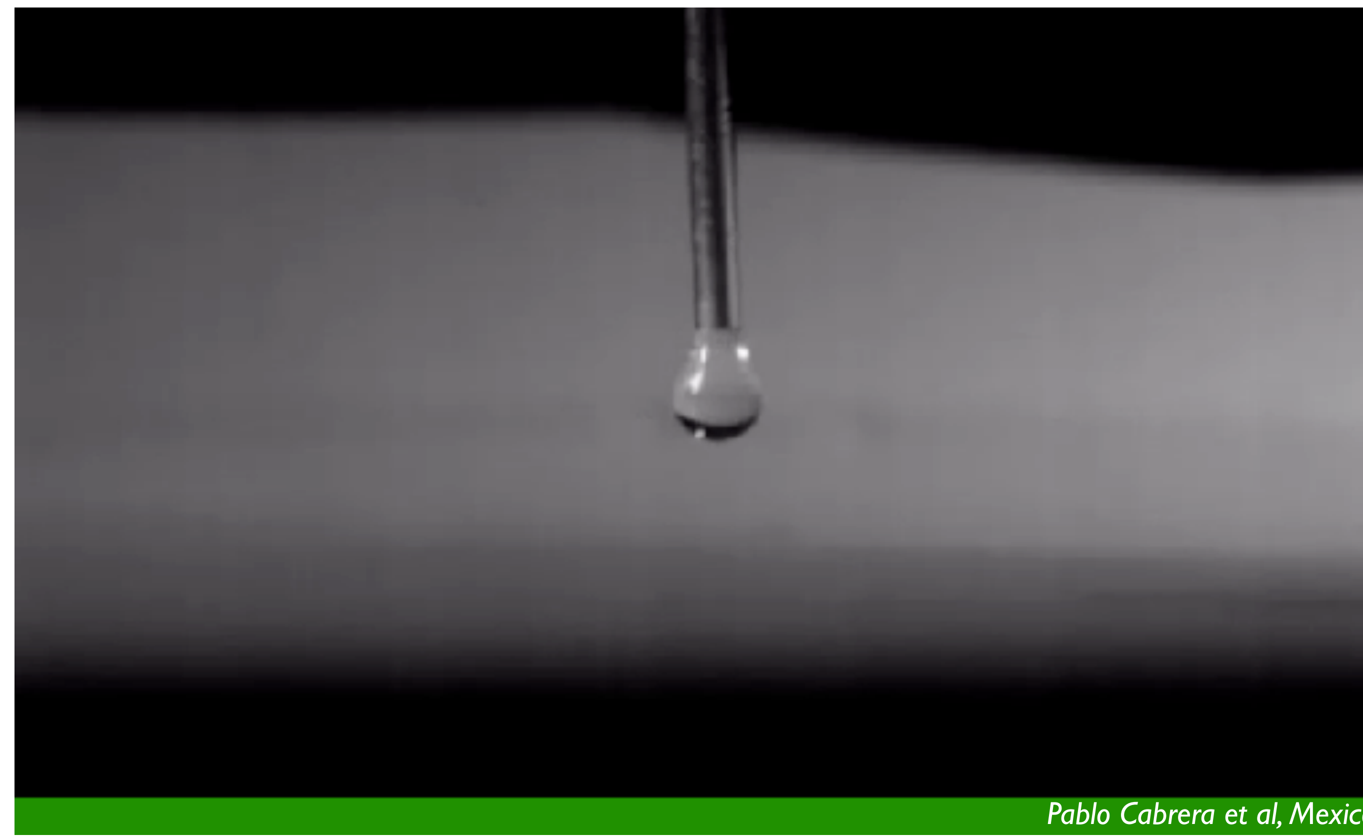
Water striders

"Jesus Christ lizard" (basilisk)

Further interesting features of water

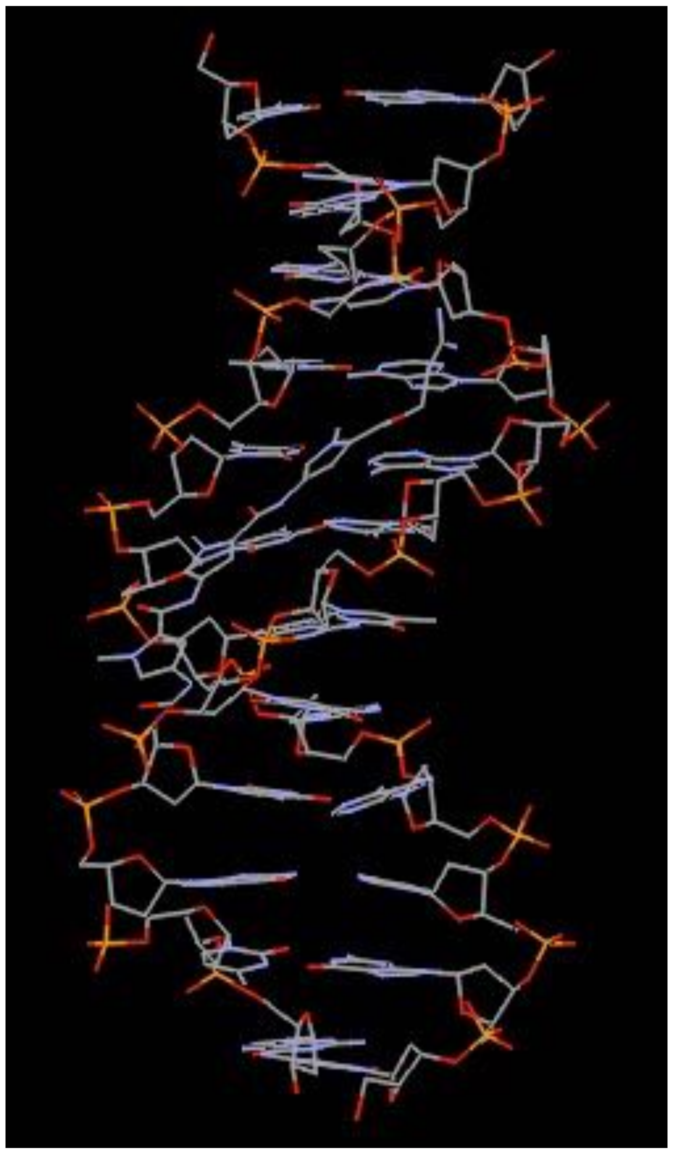
Floatig water bridge

Persisting water droplets on vibrating water surface

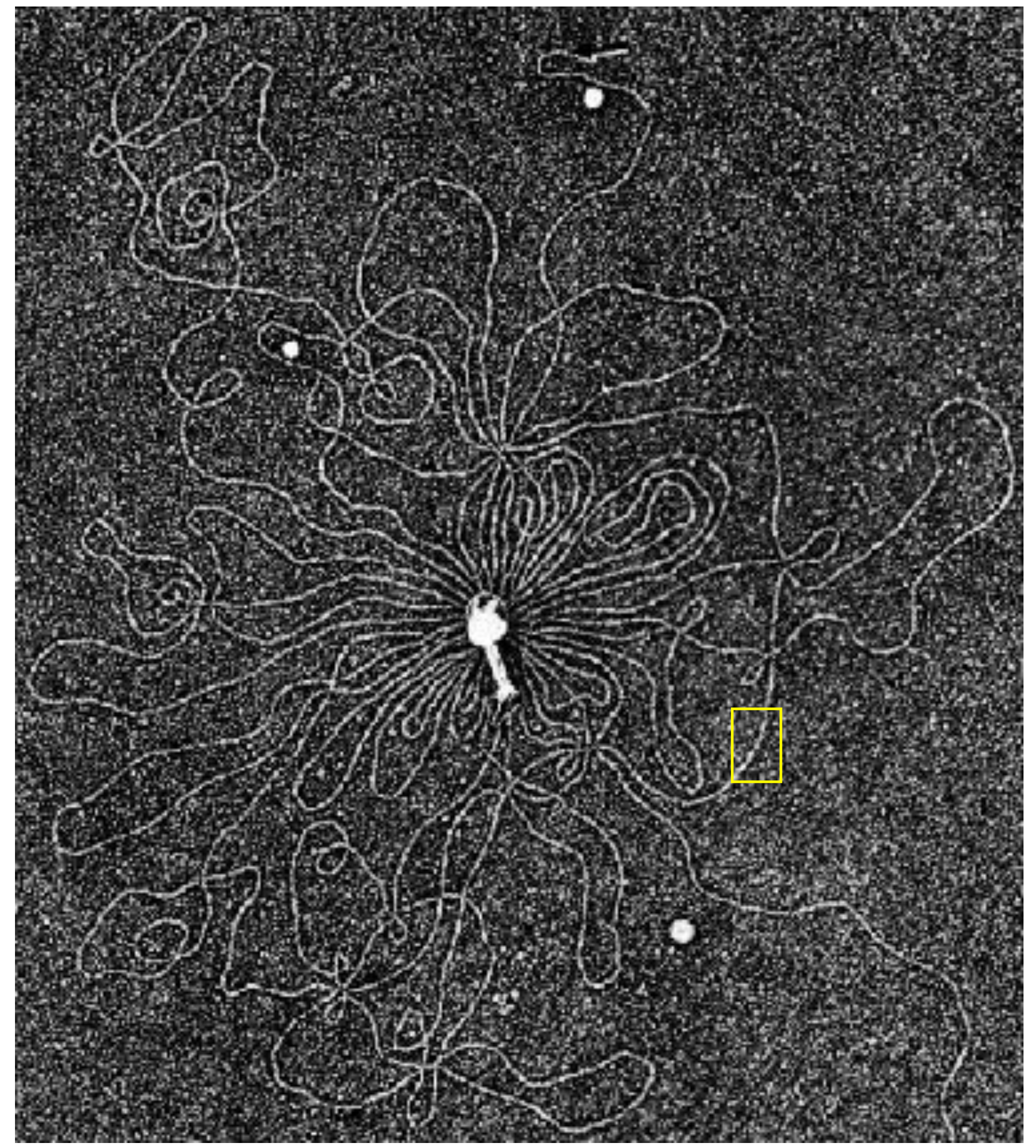


Number of water molecules in the cell	~1.6×10^{14}
Distance between water molecules	~0.4 nm

Biological macromolecules are GIANT molecules

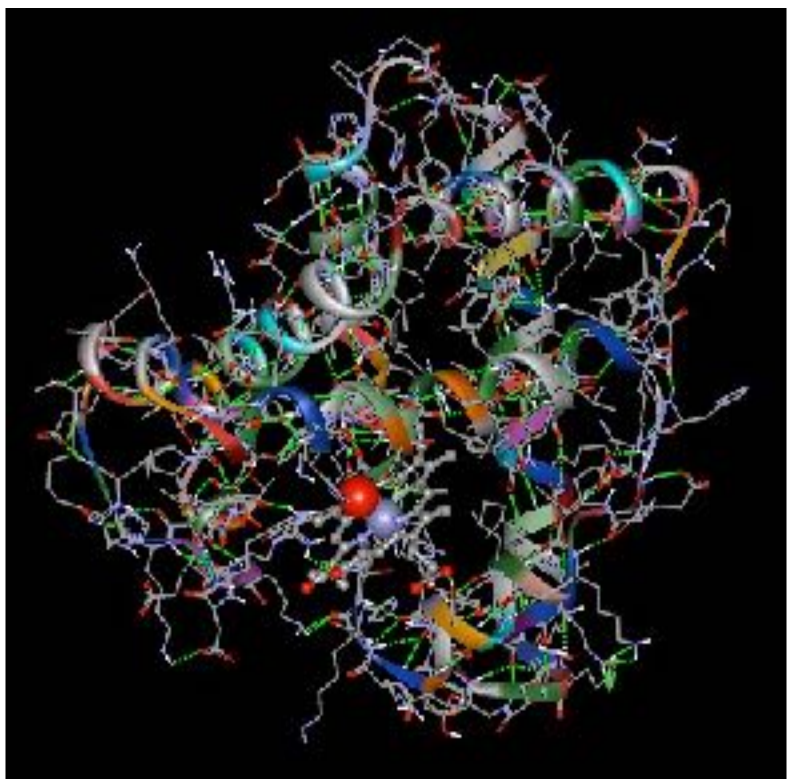


DNS double helix

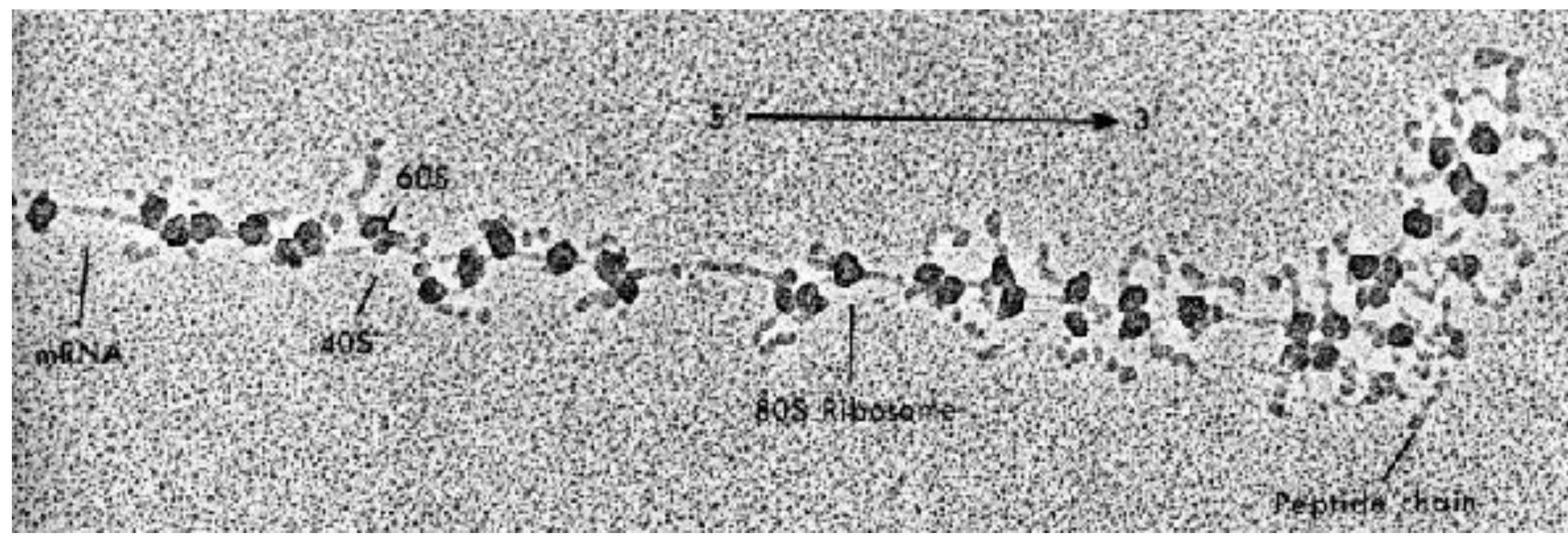


DNA released from bacteriophage head

Biological macromolecules are EXCITING molecules

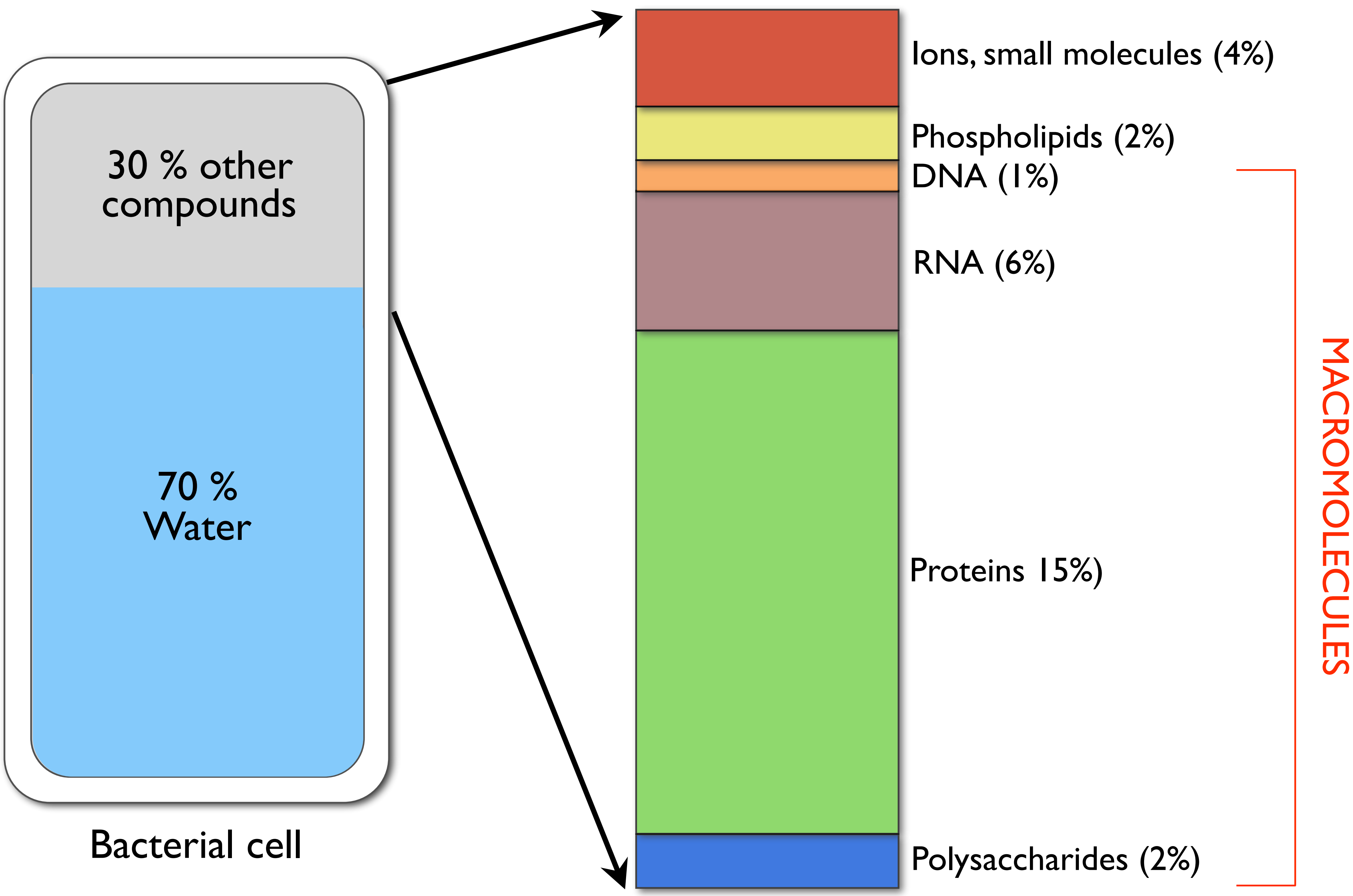


Structure of hemoglobin subunit



Newly synthesized protein (silk fibroin)

Proportion of macromolecules in the cell by mass is LARGE



Biological macromolecules: biopolyers

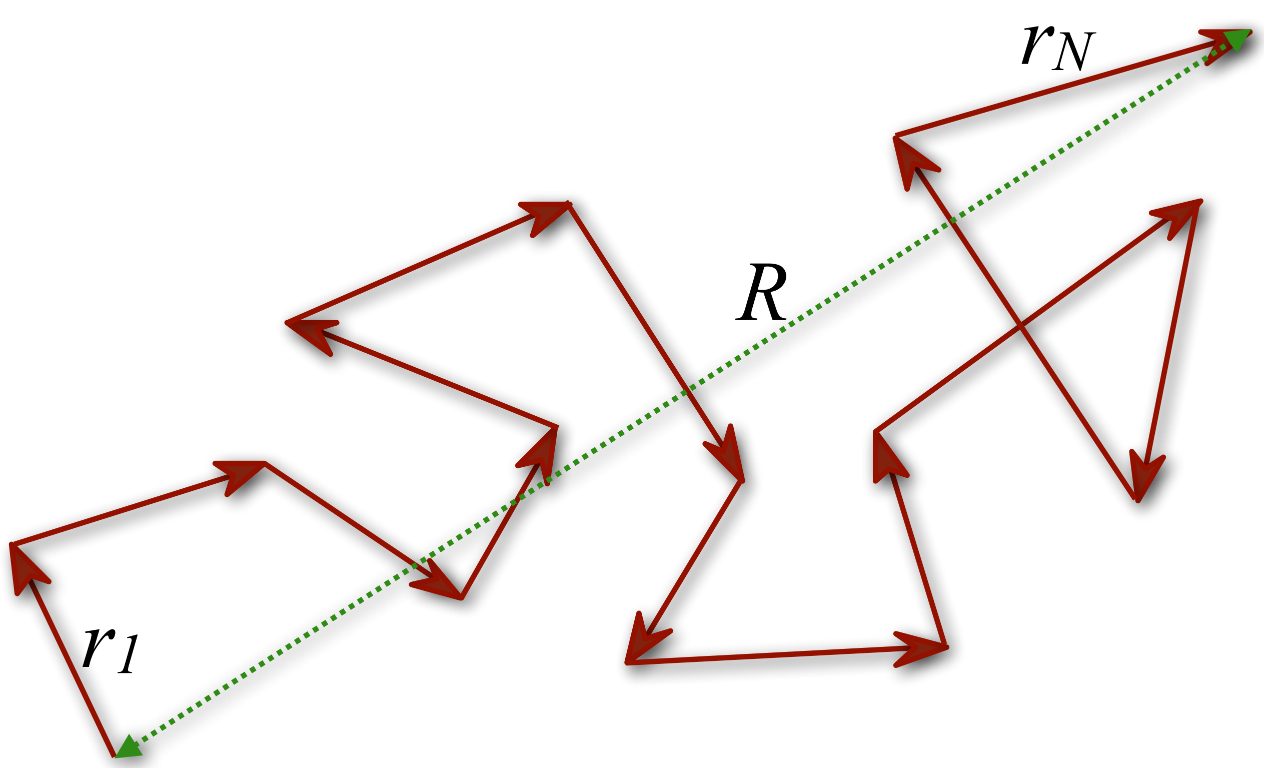
Polymers:
chains built up from monomers

Number of monomers: N>>1;
Typically, $N \sim 10^2 - 10^4$,
but, in DNA, e.g.: $N \sim 10^9 - 10^{10}$

Biopolymer	**Monomer**	**Bond**
Protein	Amino acid	Covalent (peptide bond)
Nucleic acid (RNA, DNA)	Nucleotide (CTUGA)	Covalent (phosphodiester)
Polysaccharide (e.g., glycogen)	Sugar (e.g., glucose)	Covalent (e.g., α-glycosidic)
Protein polymer (e.g., microtubule)	Protein (e.g., tubulin)	Secondary

Shape of the polymer chain resembles random walk

Brownian-movement - "random walk"



"Square-root law":

$$\langle R^2 \rangle = Nl^2 = Ll$$

R = end-to-end distance

N = number of elementary vectors

$l = |\vec{r}_i| =$ correlation length

r_i = elementary vector

$Nl = L$ = contour length

l is related to **bending rigidity**.

In case of Brownian-movement R = displacement, N = number of elementary steps, L = total path length, and l = mean free path length.

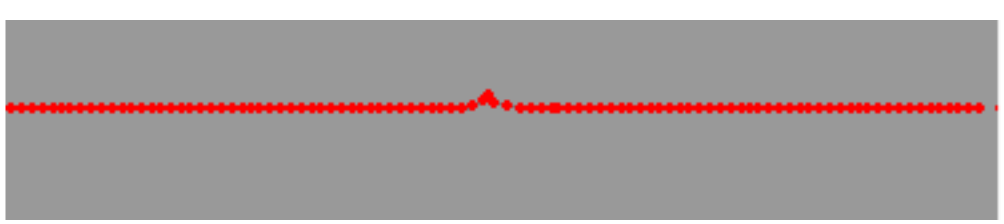
Biopolimer elasticity

Entropic (thermal) elasticity

Polymer chain goes through thermal fluctuations of shape.

Configurational entropy (orientational disorder of elementary vectors) increases.

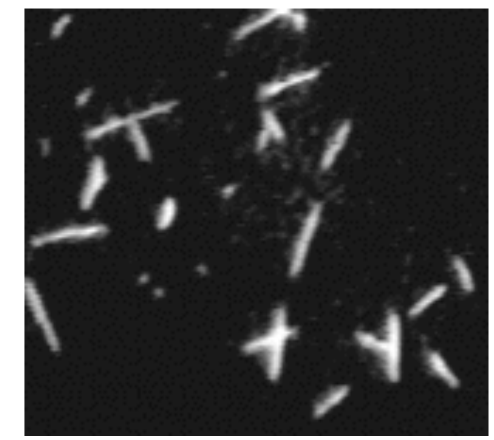
Due to the entropy maximization of the system the chain shortens (end-to-end distance falls below contour length).



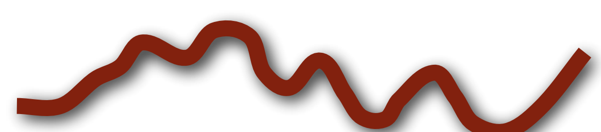
Relationship between persistence length (l) and contour length (L) in biopolymers

Rigid chain: $l \gg L$

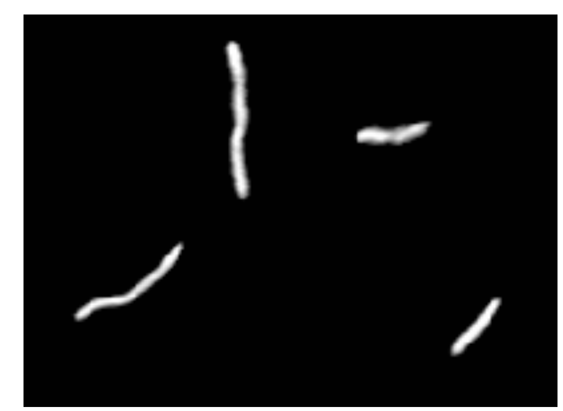
Microtubule



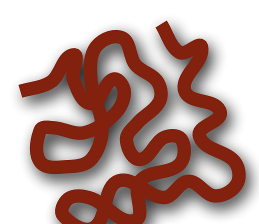
Semiflexible chain: $l \sim L$



Actin filament



Flexible chain: $l \ll L$

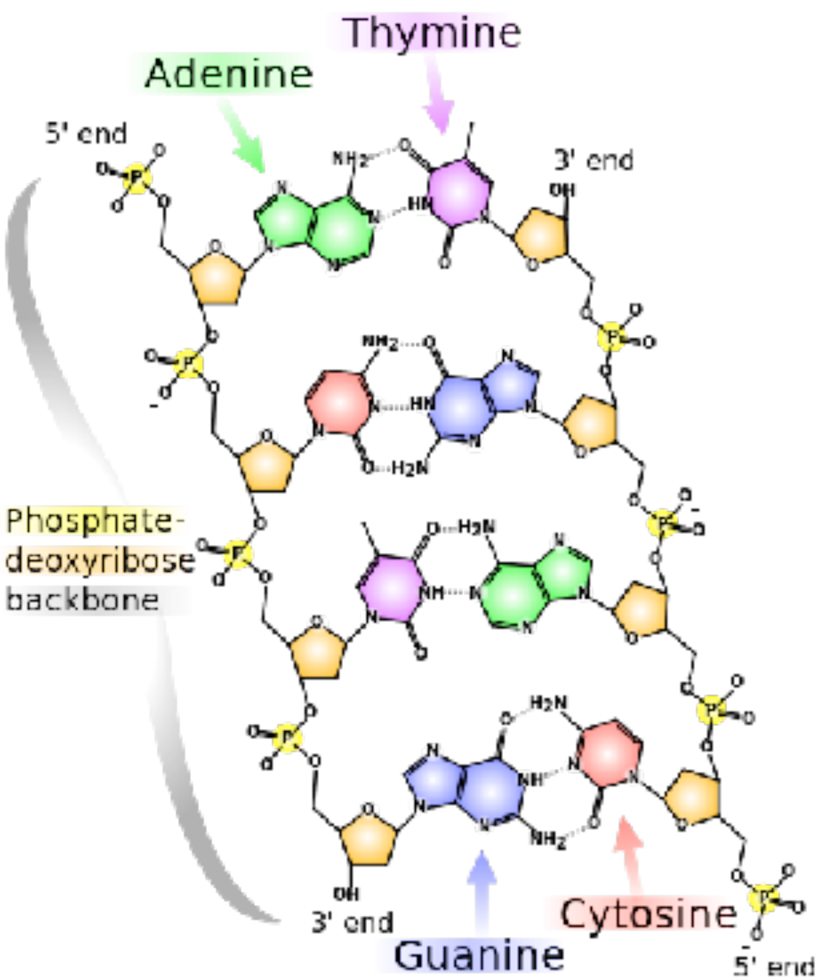


DNA molecule

1. DNA: deoxyribonucleic acid

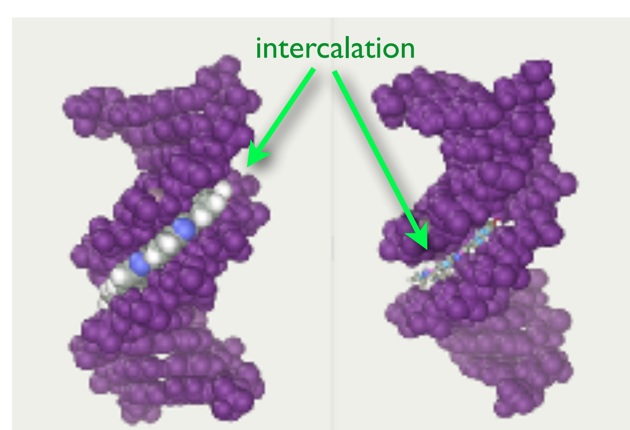
Function: molecule of biological information storage

Chemical structure



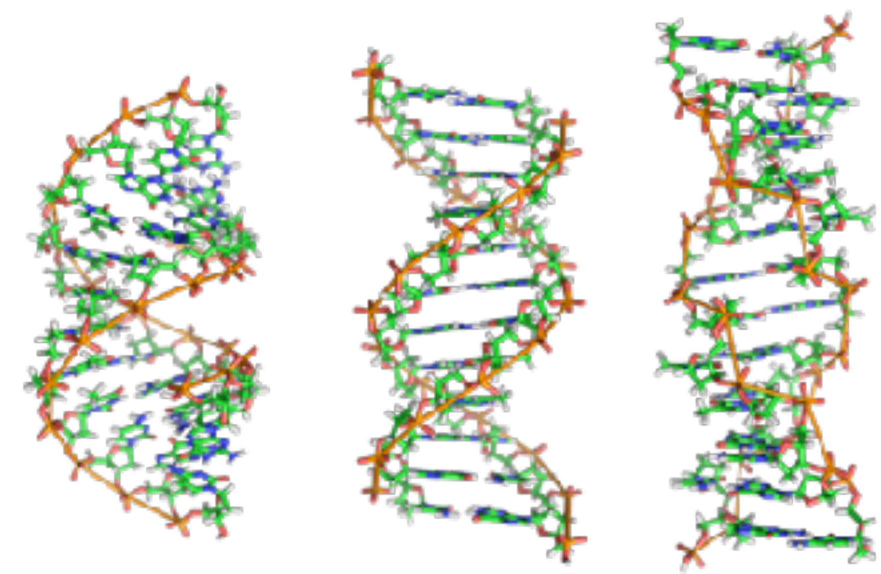
"Watson-Crick" base pairing: via H-bonds
Gene sequence is of central significance in molecular genetics

3D structure: double helix



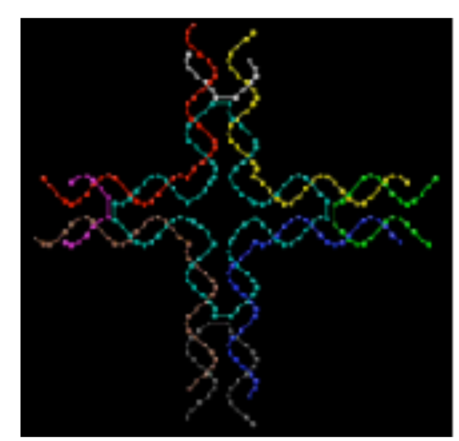
Large groove Small groove

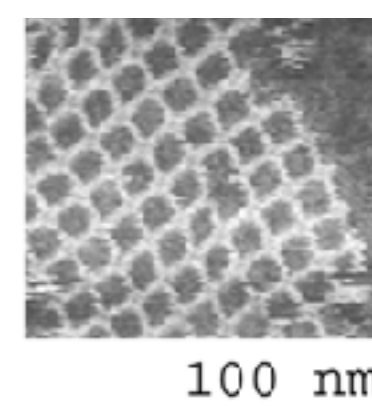
Various DNA structures



A-DNA B-DNA Z-DNA

Depends on hydration, ionic environment, chemical modification (e.g., methylation), direction of superhelix

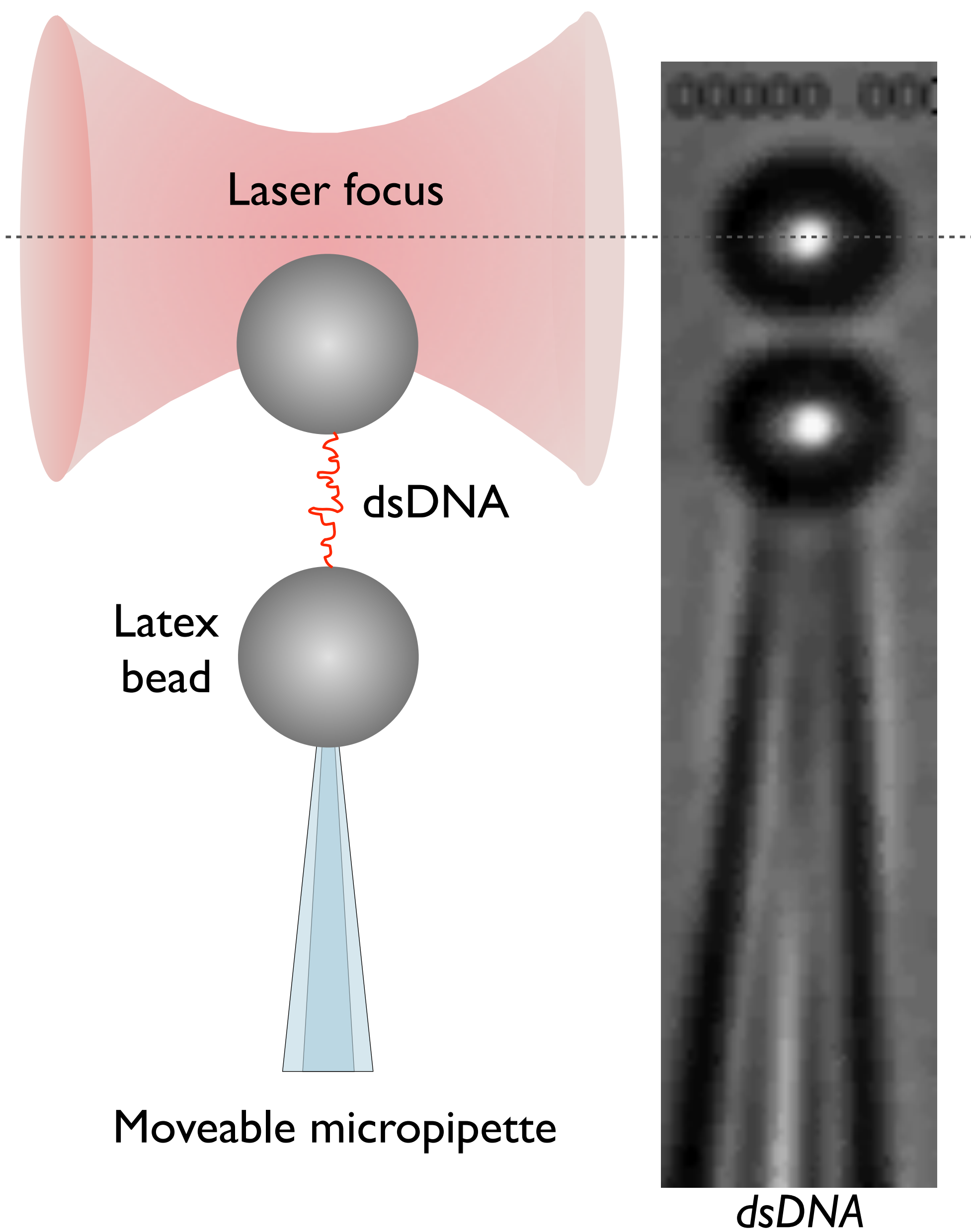




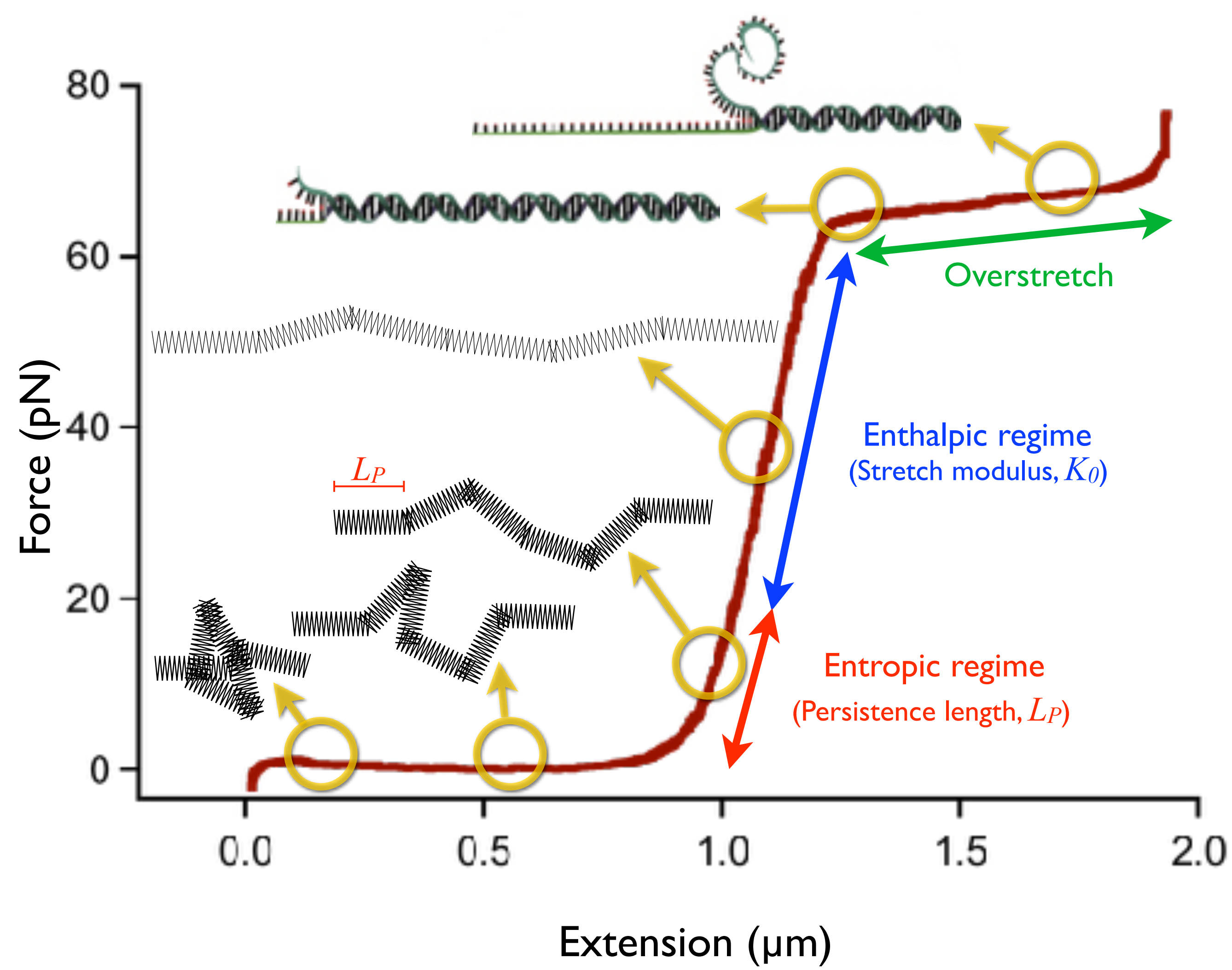
DNA nanostructures (origami)
Depends on base-pairing order and hierarchy

The DNA molecule is elastic!

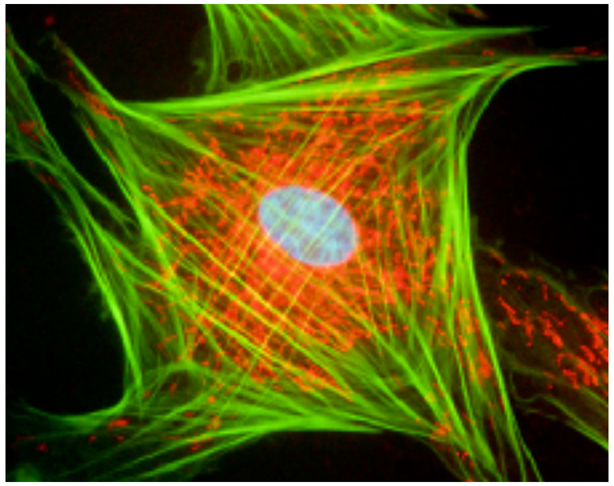
Force measurement: with optical tweezers

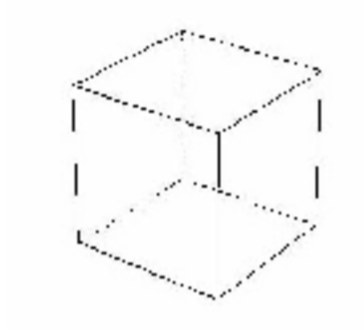


Force *versus* extension curve of a single dsDNA molecule



How much DNA is in a cell?



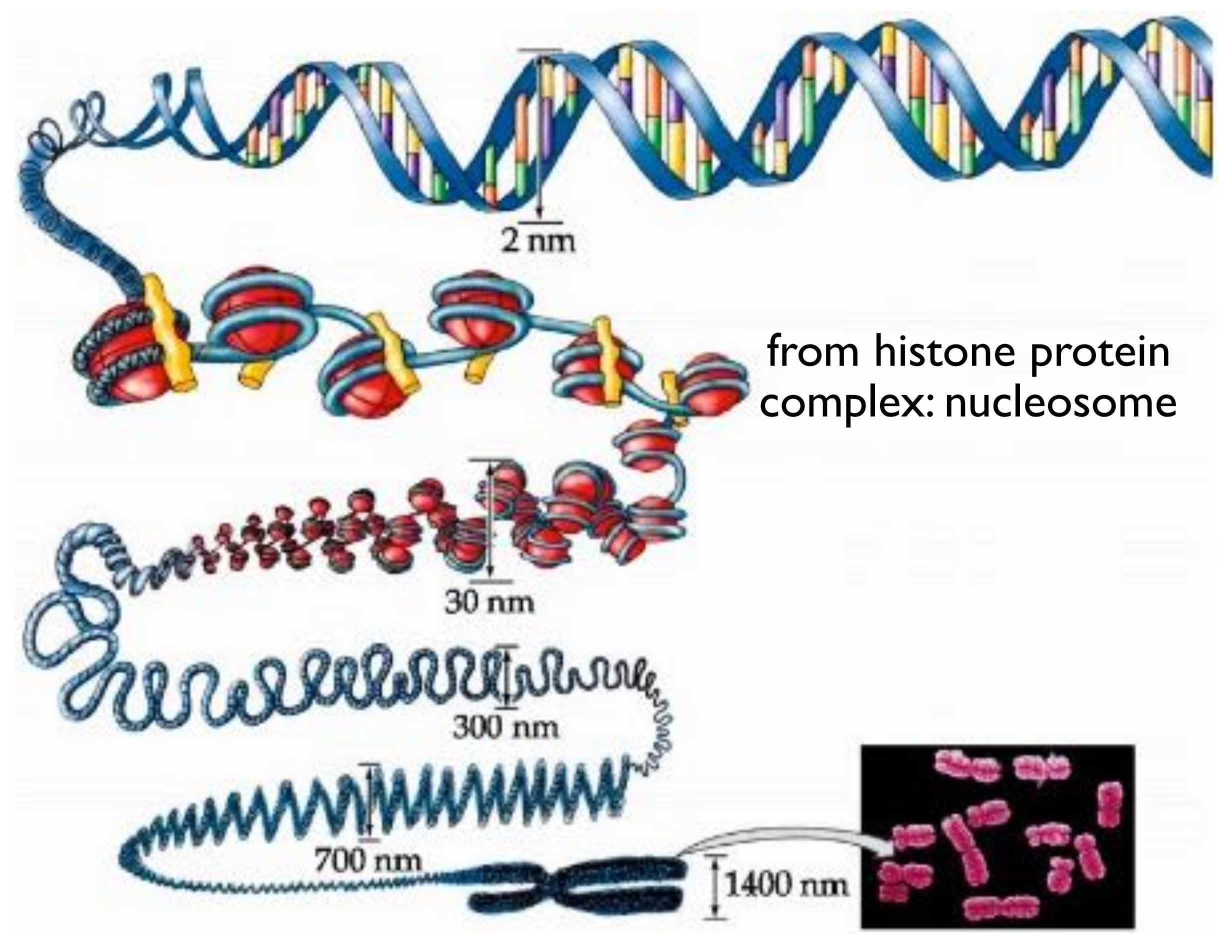


Simplified cell model: cube

	Cell: 20 μm edge cube	Analog - **Lecture hall:** 20 m edge cube
DNA thickness	2 nm	2 mm
Full length of human DNA	~2 m	~2000 km (!!!) (Perimeter of Hungary: ~2200 km)
Persistence length of dsDNA	~50 nm	~50 cm
End-to-end distance (R)	~350 μm (!)	~350 m (!)
Volume of fully compacted DNA	~2 x 2 x 2 μm^3	~2 x 2 x 2 m^3 (= 8 m^3)

Solution: DNA needs to be packed

Chromosome condensation



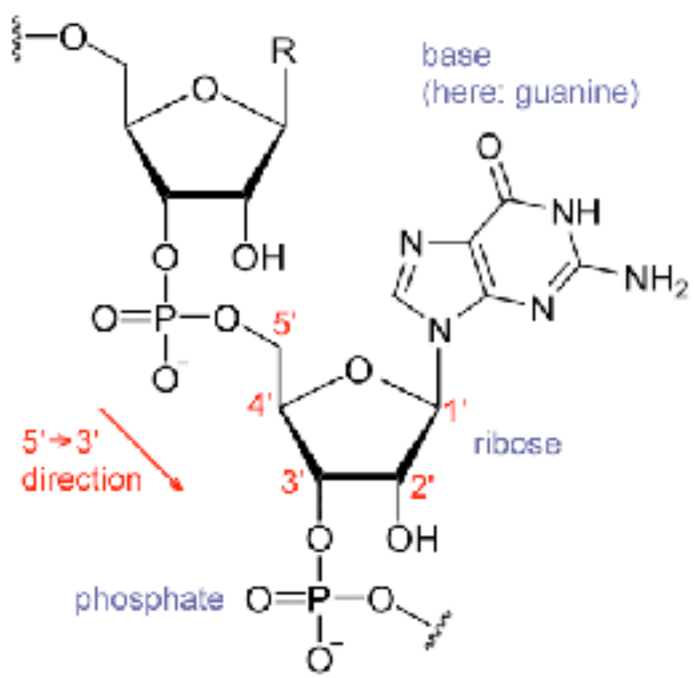
from histone protein complex: nucleosome

- ***Condensins*** play a role in high-order DNA packaging
- DNA chain: complex linear path with roadblocks!

2. RNA: Ribonucleic acid

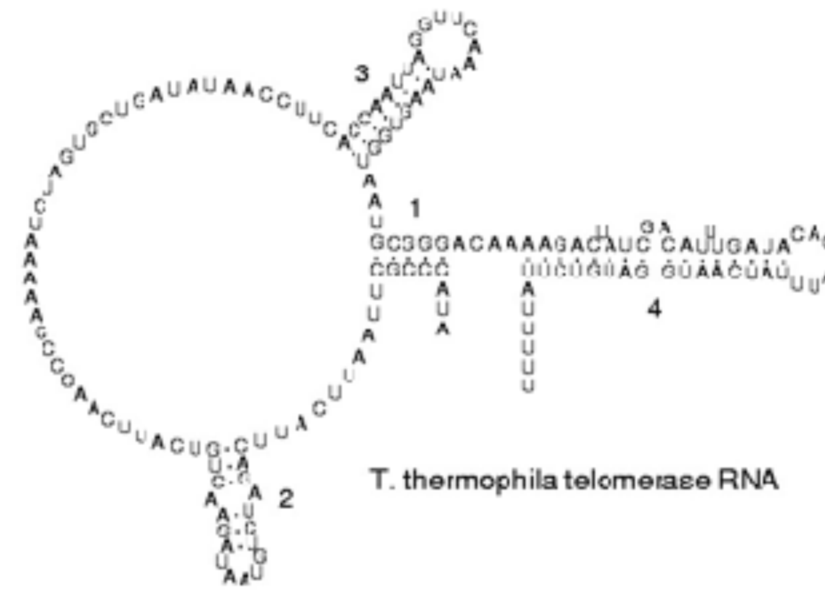
Function: information transfer (transcription), structural element (e.g., ribosome), regulation (turning gene expression on and off)

Chemical structure



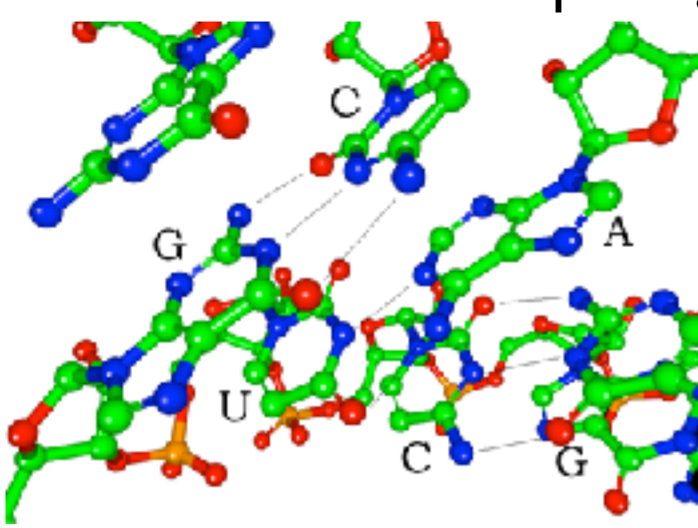
Sugar: ribose

Bases:
adenine
uracyl
guanine
cytosine

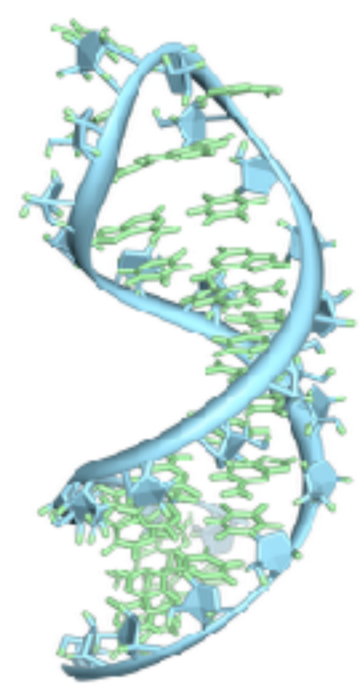


Secondary and tertiary structural elements

"Watson-Crick" base pairing



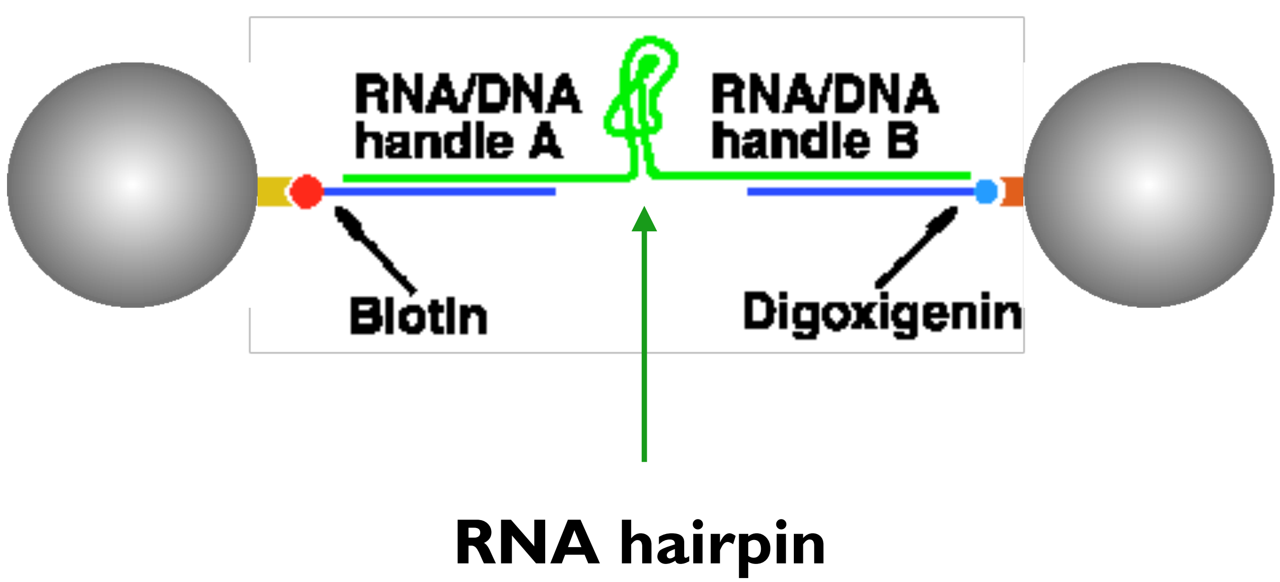
RNA hairpin



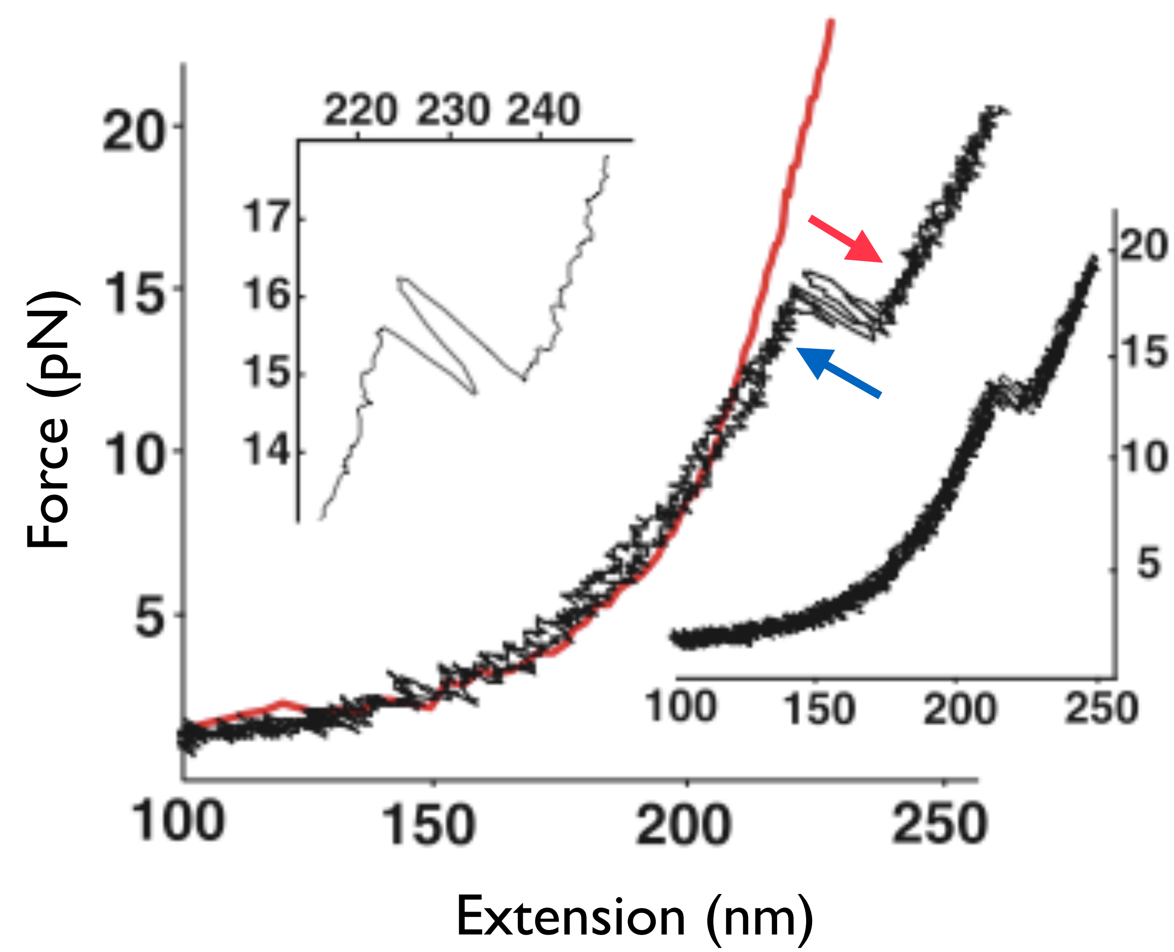
Complex structure (ribozyme)

RNA structure can be perturbed with mechanical force

Mechanical stretching with optical tweezers

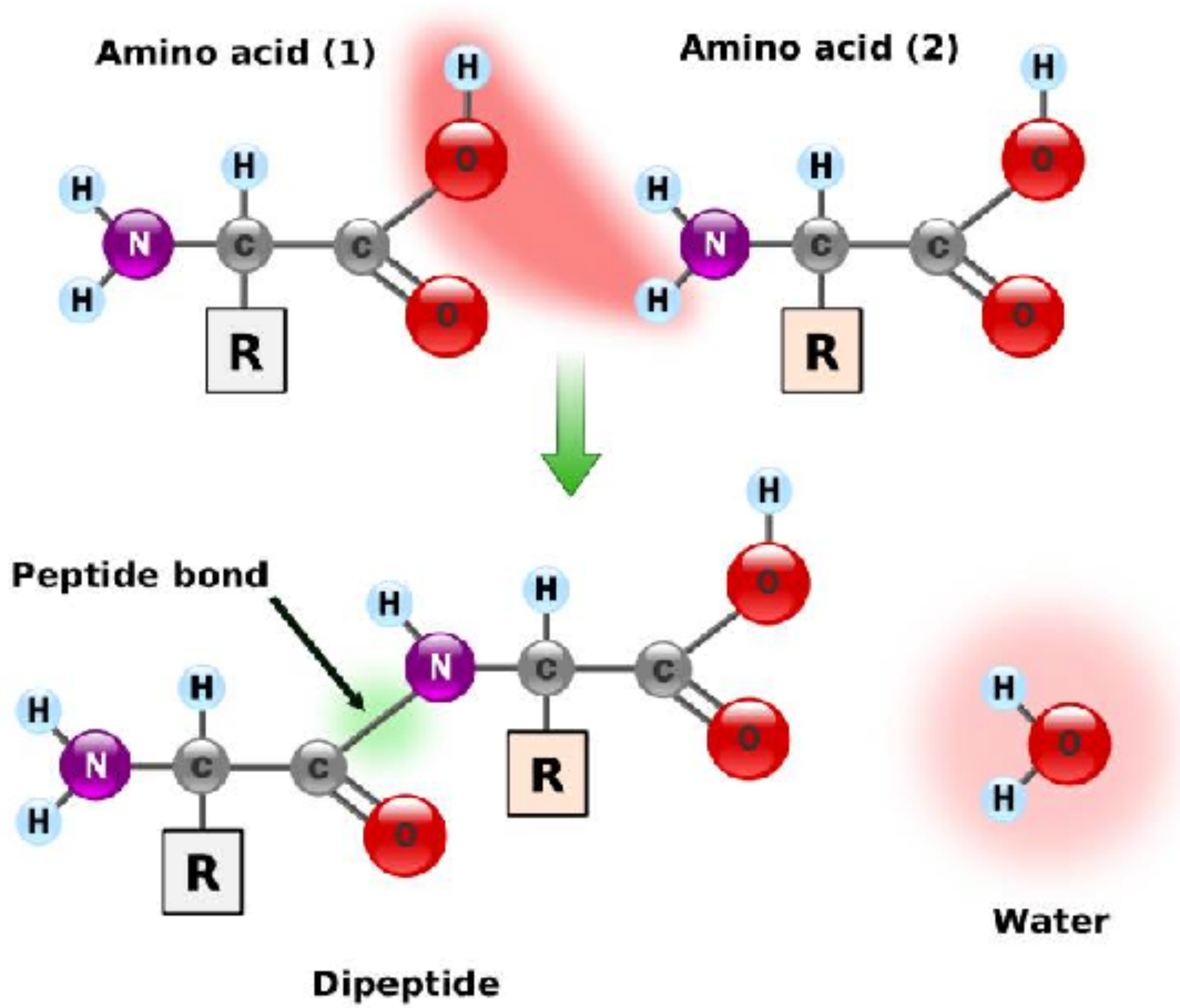


Mechanical unfolding of an RNA hairpin: nearly reversible process - the RNA rapidly folds when relaxed



3. Proteins: polymers connected with peptide bonds

Function: most important molecules of the cell. Highly diverse functions - - structure, chemical catalysis energy transduction, motoric functions, etc.



Formation of the peptide bond: condensation reaction followed by the relase of water

Protein structure

Primary

Amino acid
sequence

Determines
spatial structure
as well.

Secondary

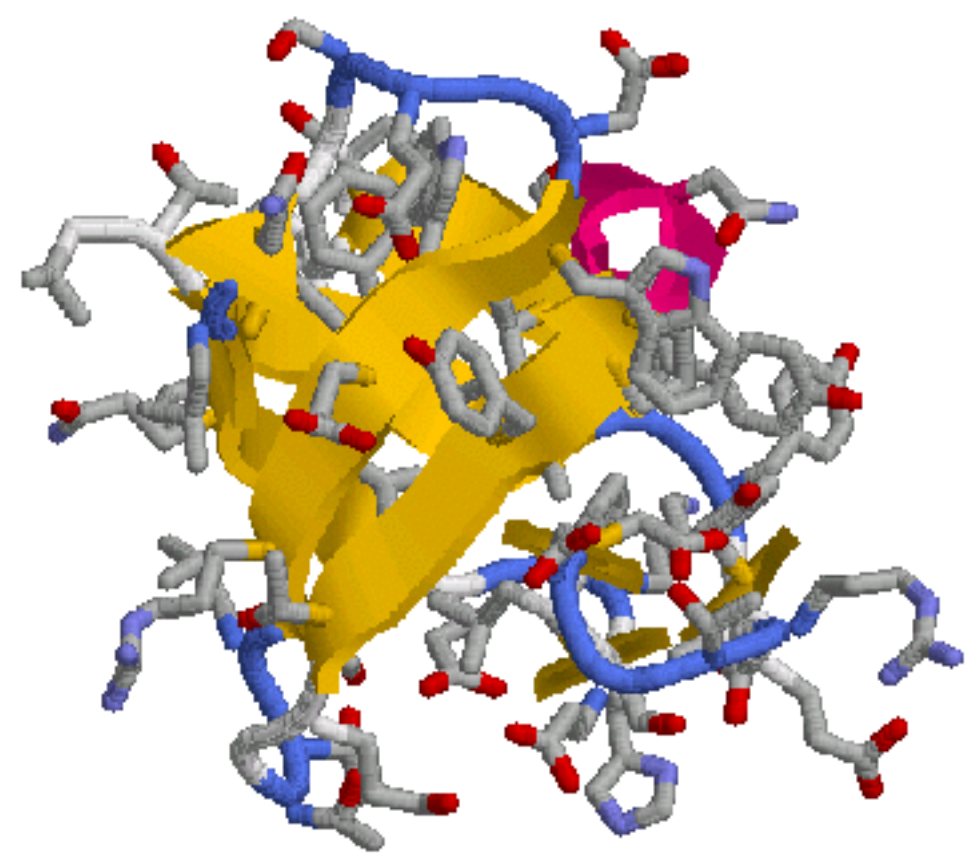
α-helix
β-sheet
β-turn (β-hairpin)

α-helix:
- right handed
- 3.4 residue/turn
- H-bridges

β-sheet:
- parallel or
- antiparallel
- H-bridges between distant residues

Tertiary

3D structure of
single-chain protein



*Quaternary structure: binding of independent subunits into a complex

Bonds holding protein structure together

Weak (secondary) bonds

1. ***Hydrogen bond***: proton sharing between proton-donor side chains.

2. ***Electrostatic interaction*** (salt bridge): between oppositely charged residues.

3. ***van der Waals bond***: weak interaction between atoms (molecules) with closed electron shells.

4. ***Hydrophobe-hydrophobe interaction***: between hydrophobic residues (in the interior of the molecule).

Covalent bond

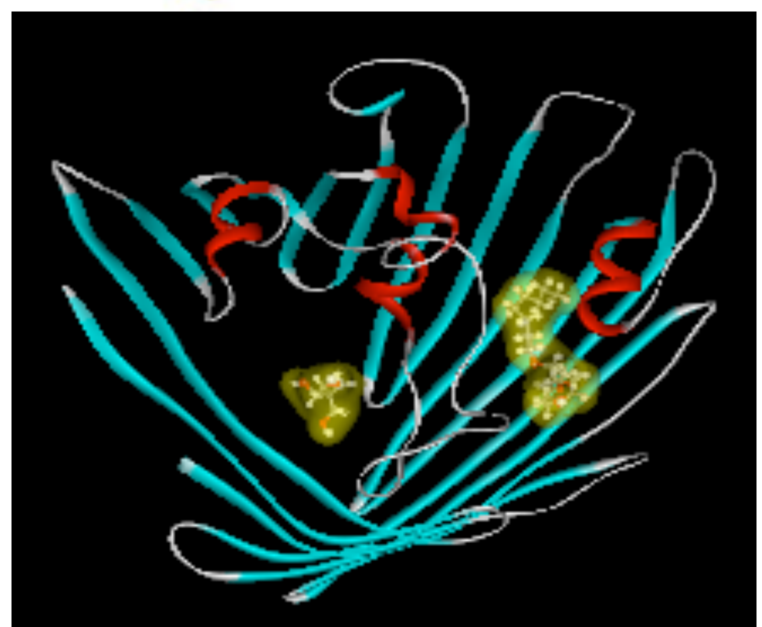
5. ***Disulfide bridge***: between cysteine side chains; connects distant parts of the protein chain.

Protein structure classes

1. All alpha

calmodulin

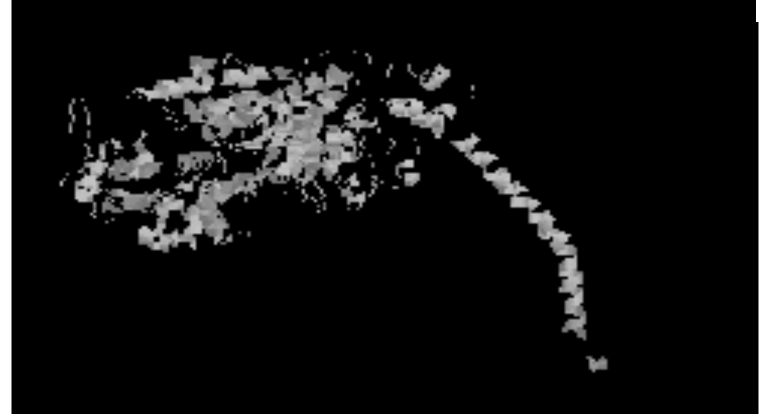
2. All beta



porin

(3. Alpha-beta)

4. Multidomain



myosin

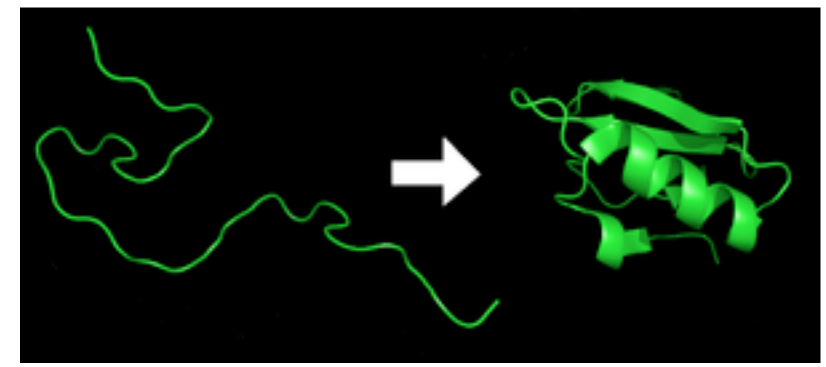
Domain:
folding subunit

Although there are as many sequences as proteins, the spatial structures are classified into a surprisingly small number of classes!

How is the three-dimensional structure acquired?

Christian Anfinsen (1916-1995)

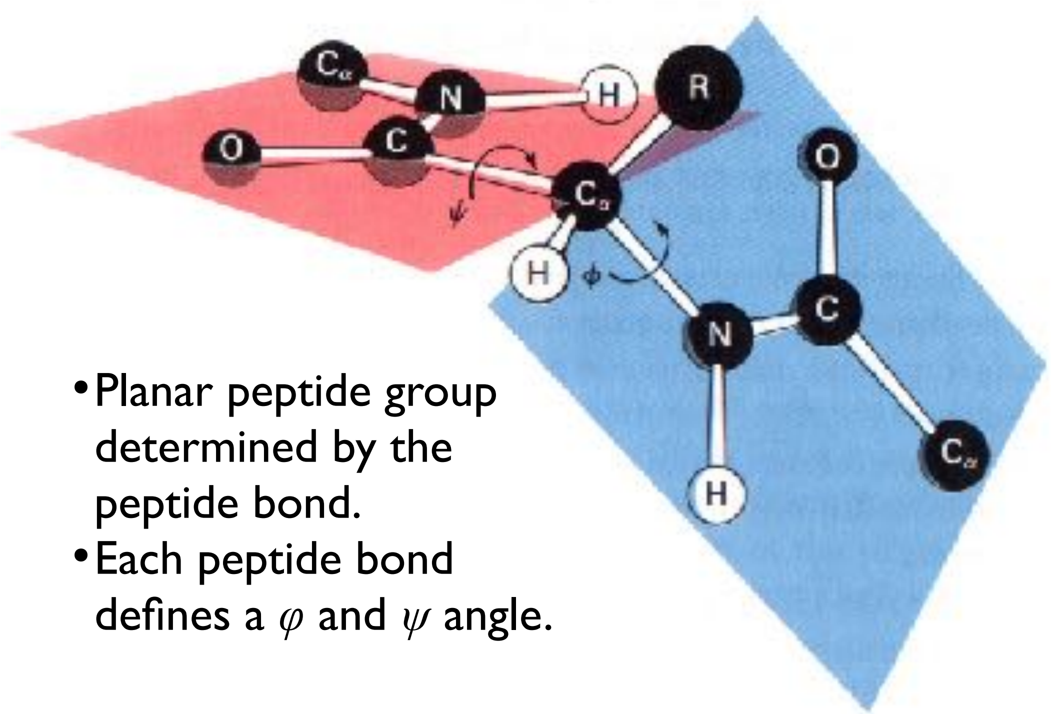
Anfinsen: proteins fold spontaneously (sequence determines structure)



Unfolded state

Native state (N) Lowest energy

Levinthal's paradox (Cyrus Levinthal, 1969)**:**
Are all available conformations explored?

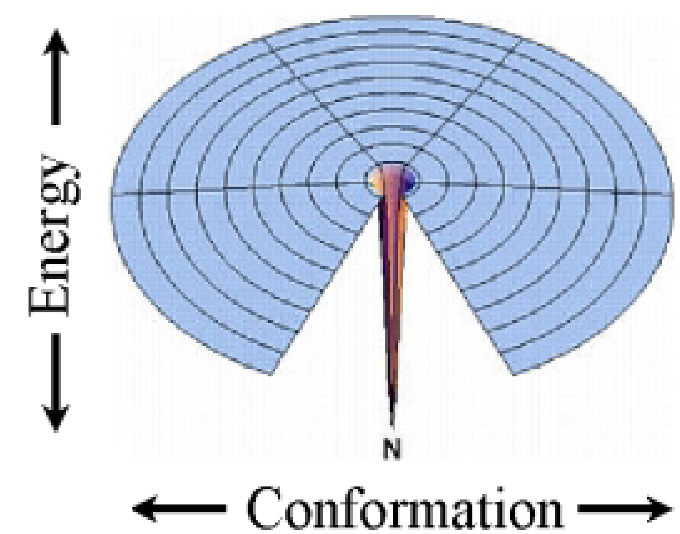


- Planar peptide group determined by the peptide bond.
- Each peptide bond defines a φ and ψ angle.

Number of possible conformations (degrees of freedom): i^n

i = number of possible angular positions of a given φ or ψ angle
n = total number of φ and ψ angles

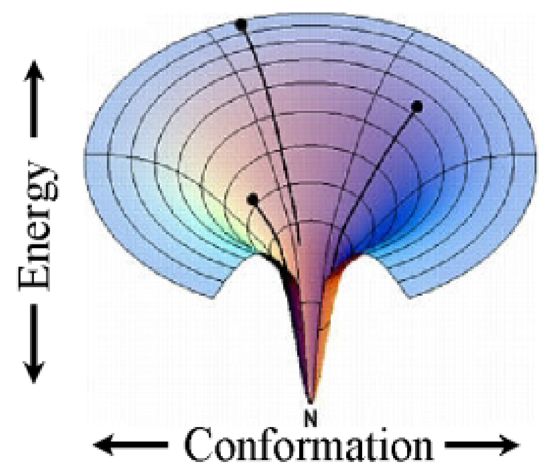
Example: in a peptide composed of 100 residues the number of possible φ or ψ angles is 2. n=198. Number of possible conformations: 2^{198}(!!!)

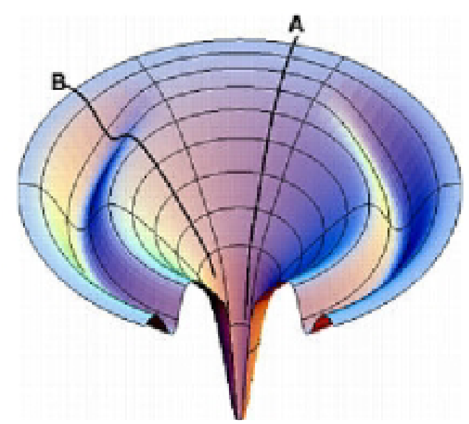


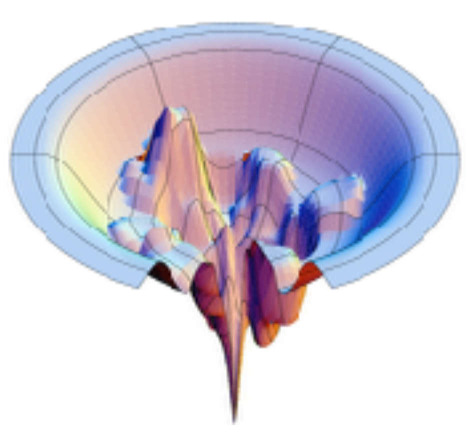
What is the probability that a billiards ball will find the hole merely via random motion?

Protein folding is guided by the shape of its conformational space

Shape of conformational space: "Folding funnel"





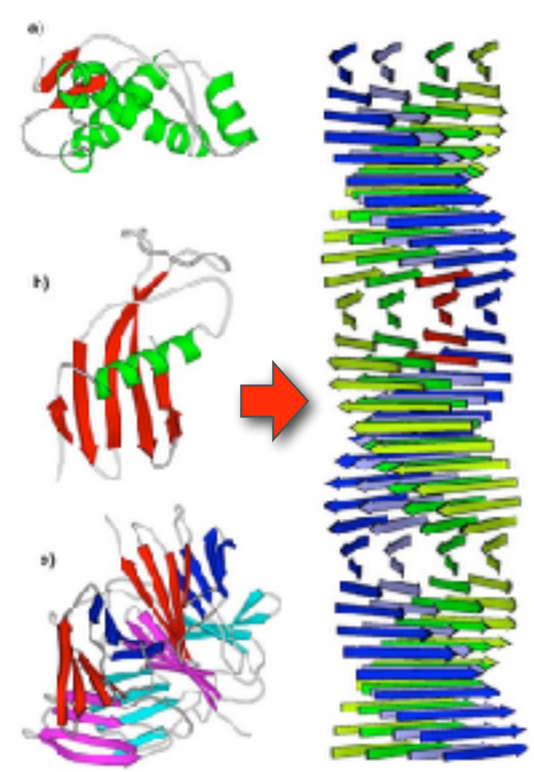


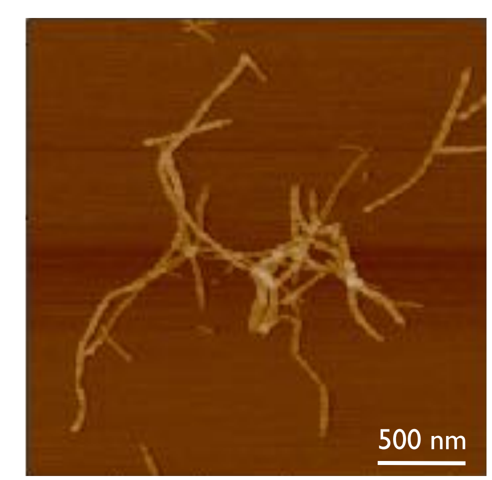
More realistic funnel shape

- Proteins "slide down" the wall of the funnel.
- Folding funnel shape can be complex (determination of the shape is usually very difficult).
- A protein may get stuck at intermediate states (pathology).
- In the living cell chaperones assist folding.

Pathology

- Protein "folding diseases"
- Alzheimer's disease
- Parkinson's disease
- II-type diabetes
- Familial amyloidotic neuropathy





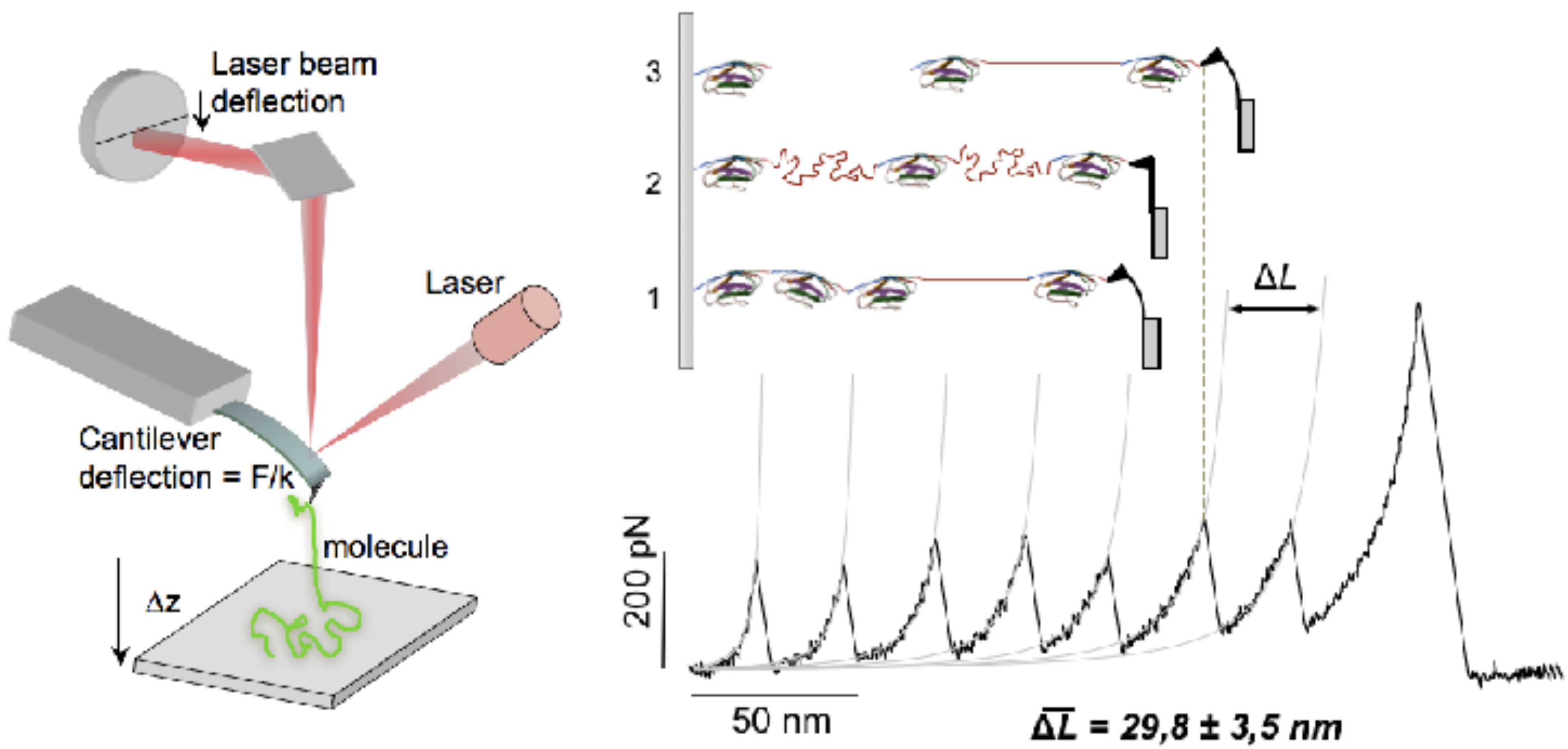
β-fibrils:
undissolved precipitate
cross-β structure

Methods of protein unfolding (denaturation)

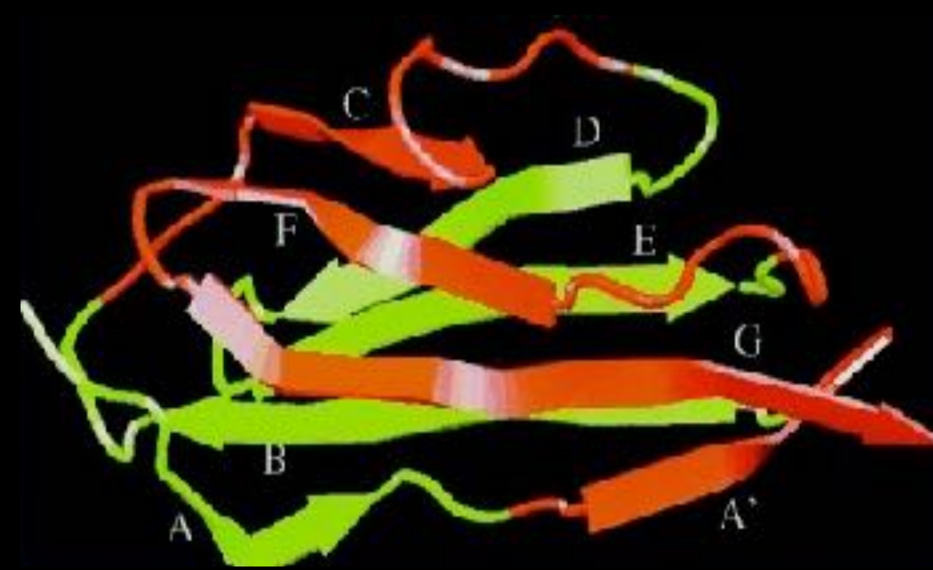
- Heat
- Chemical agent
- Mechanical force

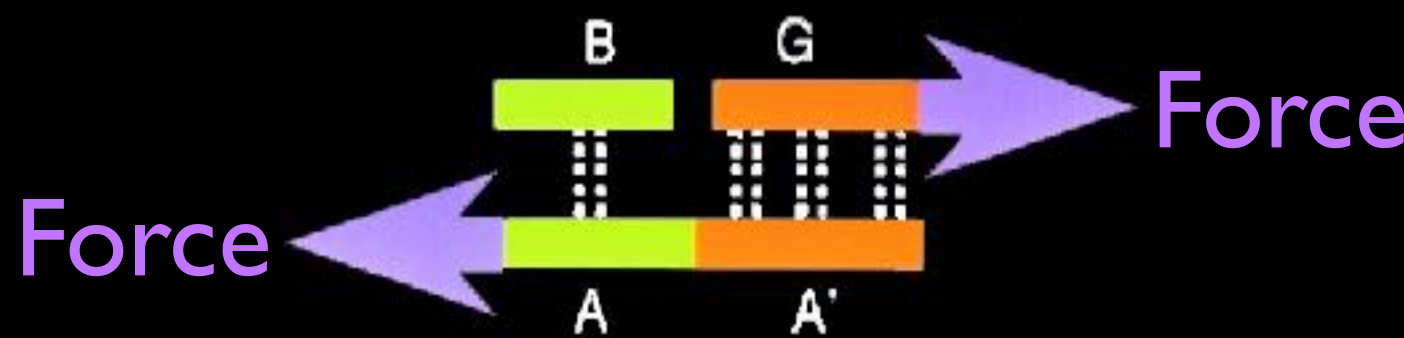
Break secondary chemical bonds
Disrupt secondary and tertiary structure

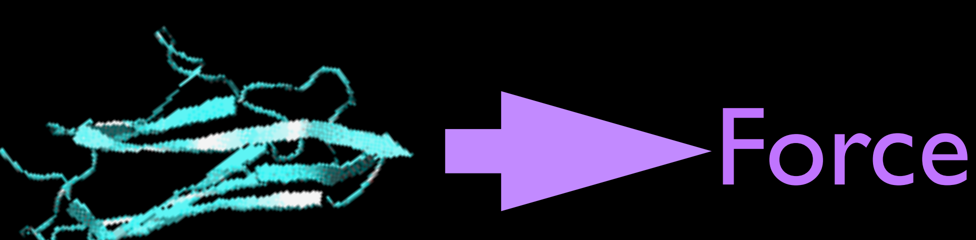
Mechanical unfolding of a single protein with atomic force microscope



Structural basis of mechanical stability

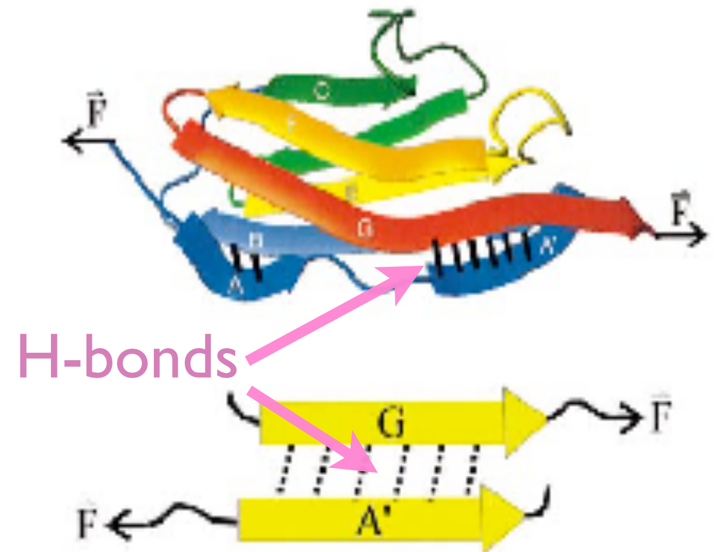




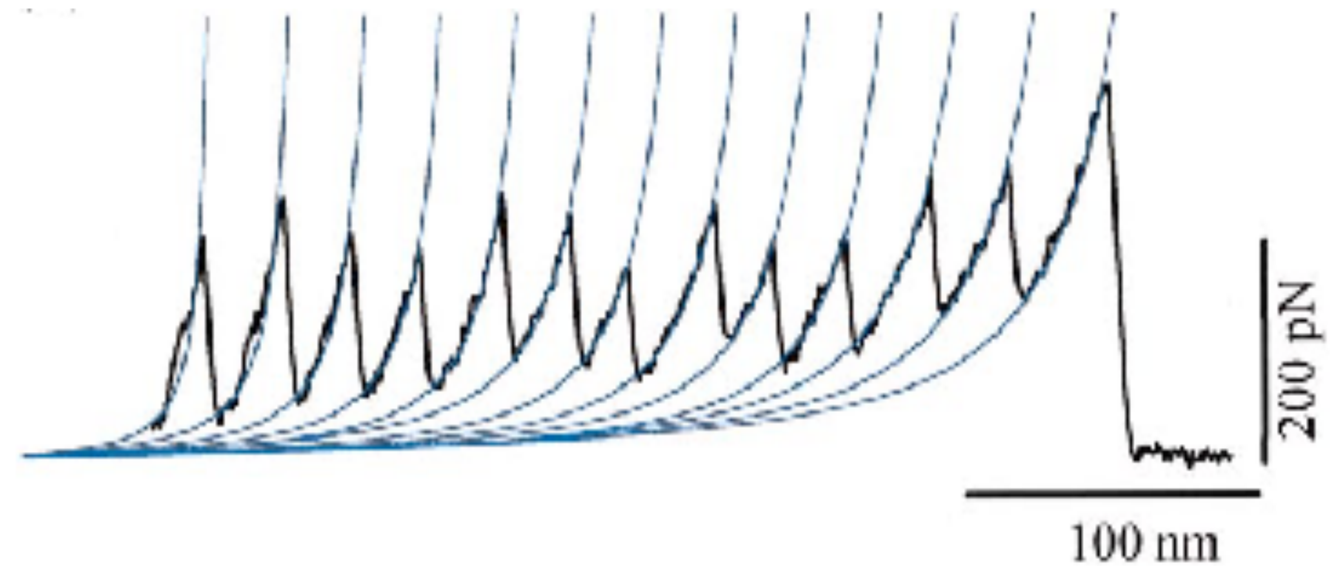


Biological logic of mechanical stability

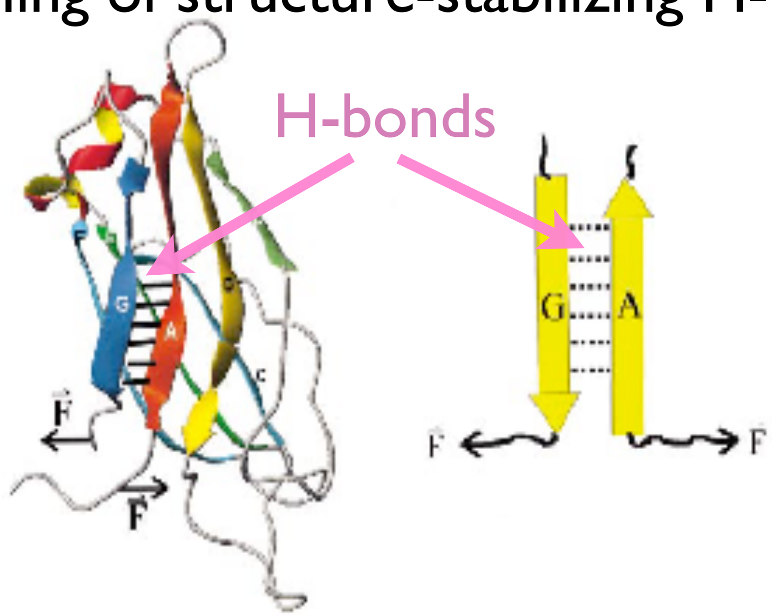
Parallel coupling of structure-stabilizing H-bonds



High unfolding forces



Serial coupling of structure-stabilizing H-bonds



Low unfolding forces