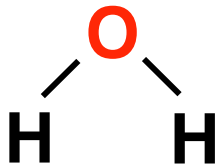


WATER, MACROMOLECULES

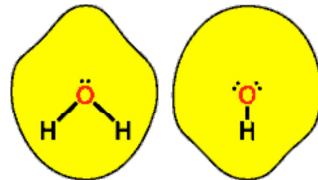
MIKLÓS KELLERMAYER

Structure of the water molecule

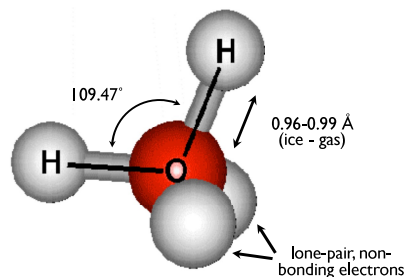
One of the smallest molecules
Barely larger than an atom



van der Waals radius: $\sim 3.2 \text{ \AA}$
Its shape is not spherical



Tetrahedral structure:



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.



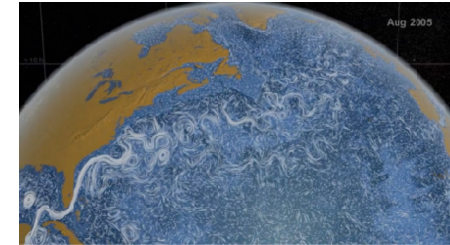
Georg Friedrich Händel (1685-1759): "**Water music**".



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



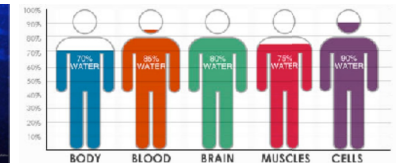
Hokusai (1760-1849): Great wave off Kanagawa



Perpetual motion of oceans on Earth's surface.

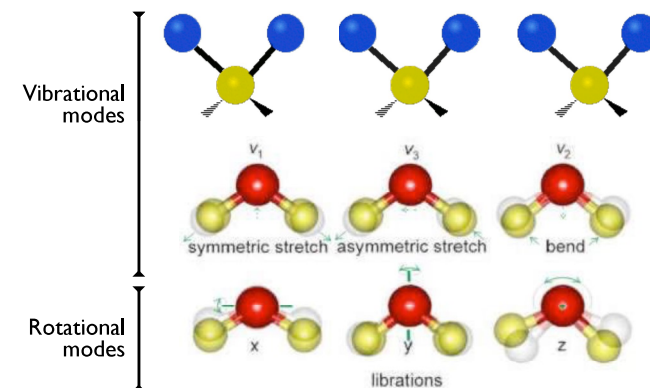


Jellyfish



Dynamics of the water molecule

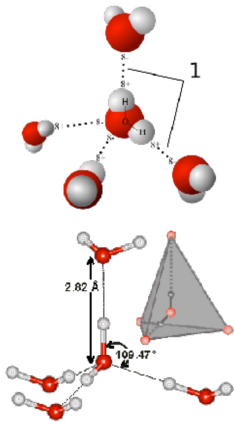
Rotational and vibrational motion



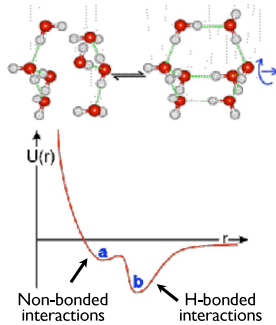
Absorption in the infrared and red spectral region →
"blue" color of natural waters: *blue planet*

Structure of liquid water

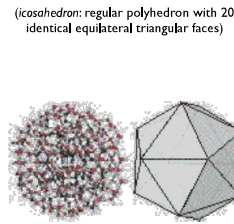
Hydrogen bonds in the vicinity of a water molecule: formation of the water pentamer



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



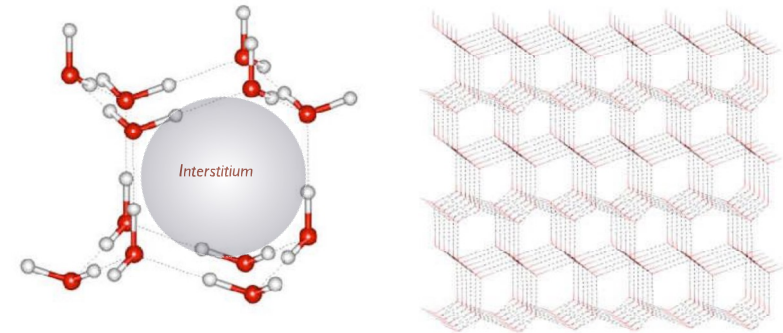
From clusters to networks:
280 molecules form icosahedral structure



Spatial networks:
May explain anomalous properties of water

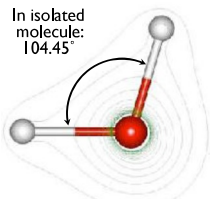
Structure of ice

- 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



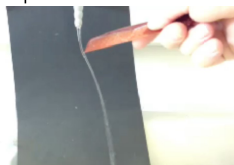
Physical properties of water I.

Large permanent dipole moment → Good solvent



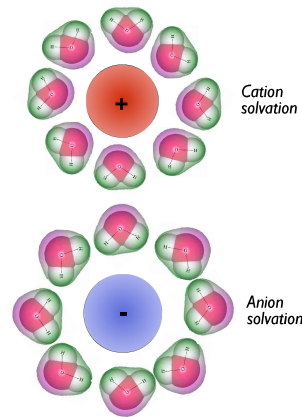
Chemical	Dipole moment
Polyethylene	2.25
Methanol	30
Ethylene glycol	37
Glycerol	47
Water	80
Titanium dioxide	86-173

Water stream bends in response to Coulombic forces



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.

Courtesy of Prof. Miklós Zrínyi

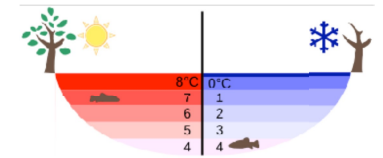
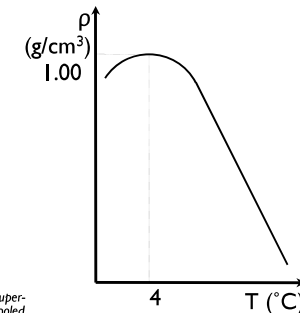


In the microwave oven: dipoles rotate according to the oscillating electromagnetic field. Water molecules acquire kinetic energy, which dissipates into the surroundings.

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



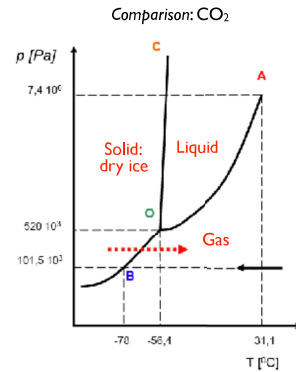
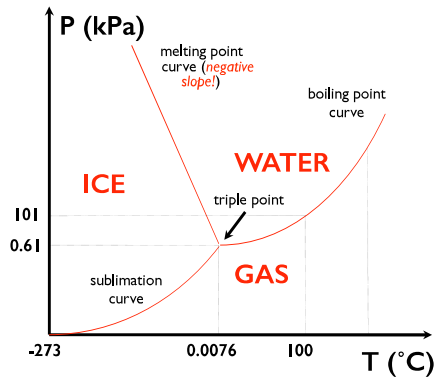
Consequences:

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

Physical properties of water III.

Anomalous phase diagram

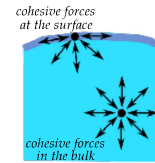
- Phase curve: two phases are in equilibrium
- Area between phase curves: a single phase is present
- Intersection of phase curves: triple point



Physical properties of water IV.

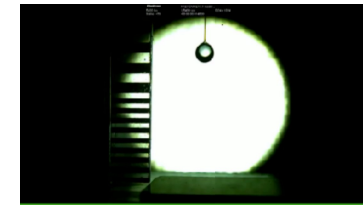
Large surface tension

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



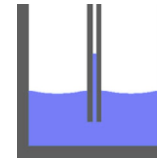
Persisting droplet on a superhydrophobic surface

Consequences in macroscopic living systems



Water striders

Consequences on **hydrophilic** surface



Capillary action (model)



Capillary action aiding plant root function



"Jesus Christ lizard" (basilisk)

Further interesting features of water

Floatig water bridge

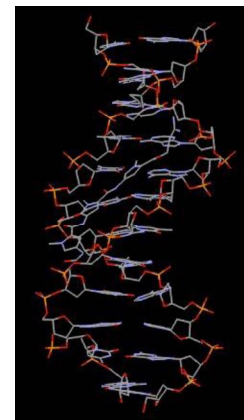


Persisting water droplets on vibrating water surface

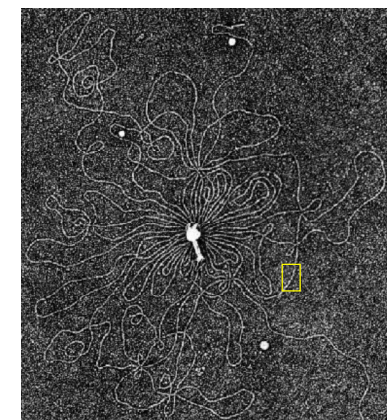


Number of water molecules in the cell	$\sim 1.6 \times 10^{14}$
Distance between water molecules	~ 0.4 nm

Biological macromolecules are **GIANT** molecules

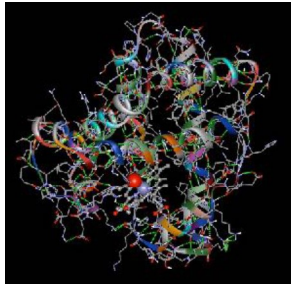


DNS double helix

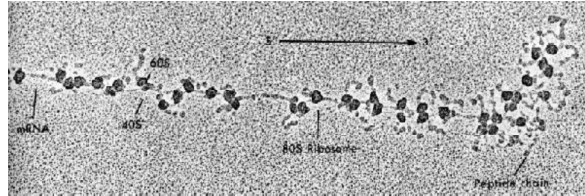


DNA released from bacteriophage head

Biological macromolecules are **EXCITING** molecules

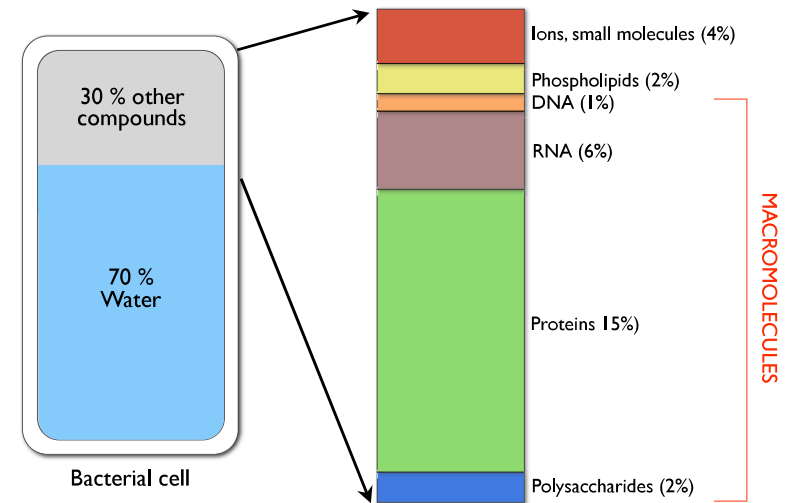


Structure of hemoglobin subunit



Newly synthesized protein (silk fibroin)

Proportion of macromolecules in the cell by mass is **LARGE**



Biological macromolecules: biopolymers

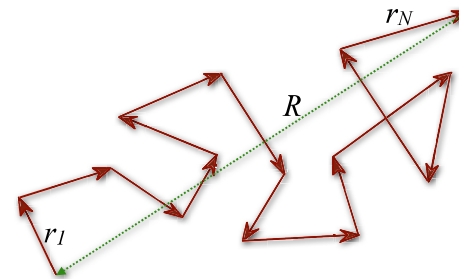
Polymers:
chains built up from monomers

Number of monomers: $N \gg 1$;
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.

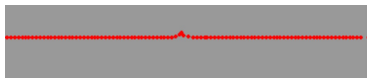
Biopolimer elasticity

Entropic (thermal) elasticity

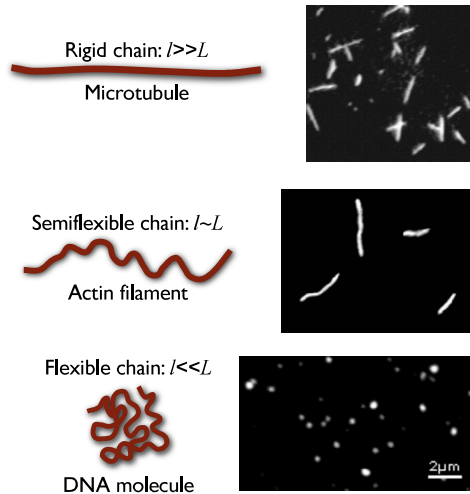
Polymer chain goes through thermal fluctuations of shape.

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).

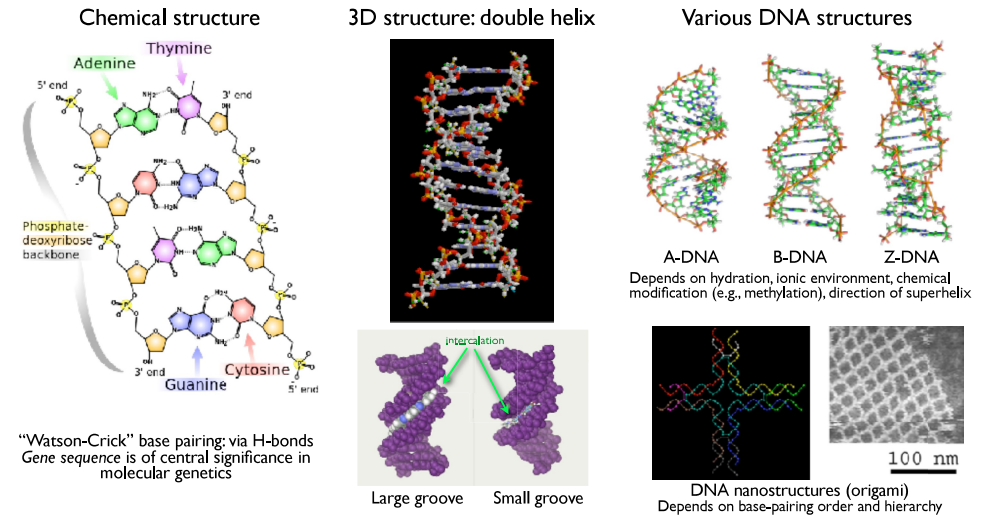


Relationship between persistence length (l) and contour length (L) in biopolymers



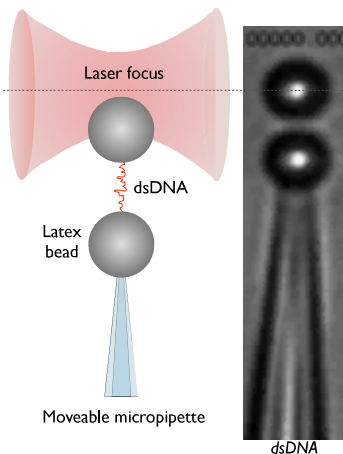
I. DNA: deoxyribonucleic acid

Function: molecule of biological information storage

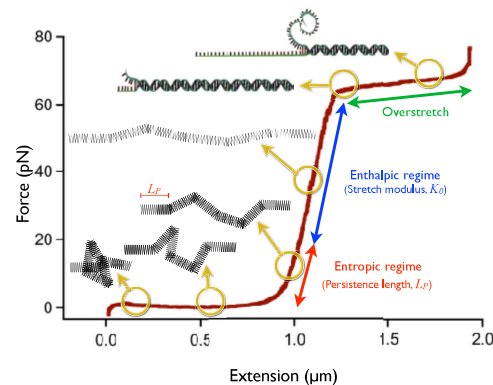


The DNA molecule is elastic!

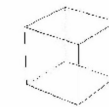
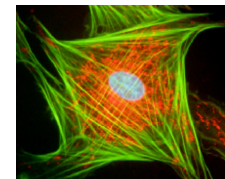
Force measurement: with optical tweezers



Force versus extension curve of a single dsDNA molecule



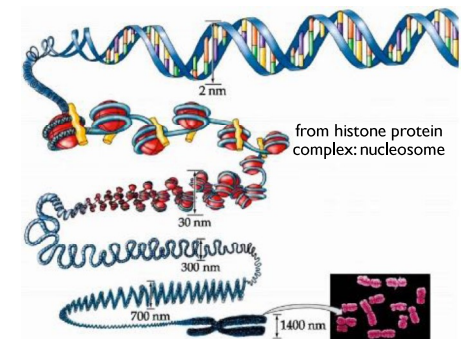
How much DNA is in a cell?



Simplified cell model: cube

Solution: DNA needs to be packed

Chromosome condensation

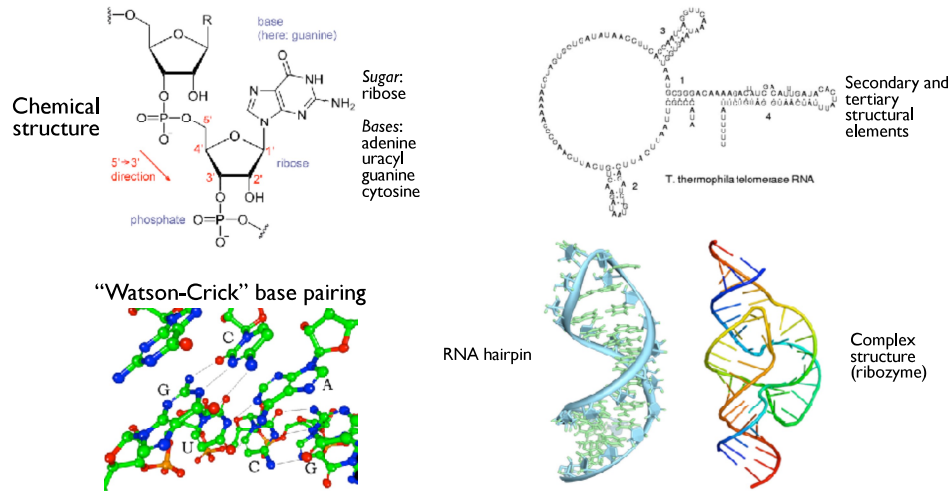


	Cell: 20 μm edge cube	Analog - Lecture hall: 20 m edge cube
DNA thickness	2 nm	2 mm
Full length of human DNA	~2 m	~2000 km (!!!) (Perimeter of Hungary: ~2200 km)
Persistence length of dsDNA	~50 nm	~50 cm
End-to-end distance (R)	~350 μm (!)	~350 m (!)
Volume of fully compacted DNA	~2 × 2 × 2 μm ³	~2 ×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

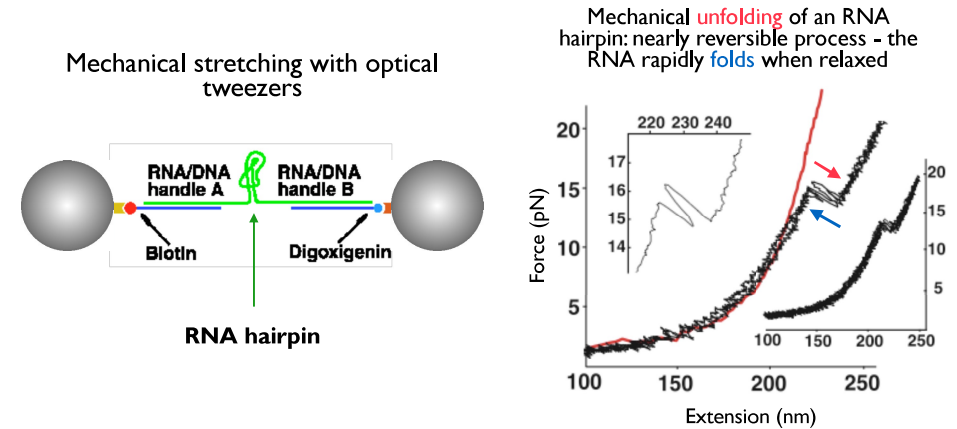
- **Condensins** play a role in high-order DNA packaging
- DNA chain: complex linear path with roadblocks!

2. RNA: Ribonucleic acid

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

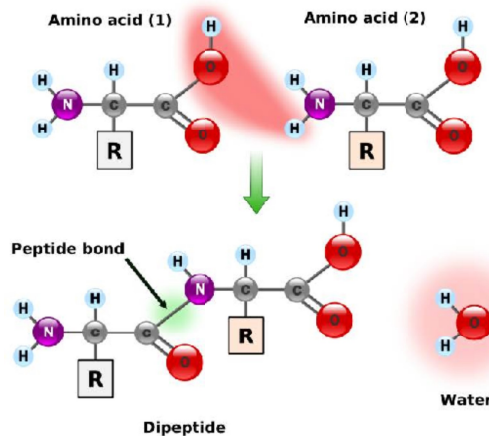


RNA structure can be perturbed with mechanical force



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 release of water

Protein structure

Primary

Amino acid sequence

Determines spatial structure as well.

Secondary

α-helix
β-sheet
β-turn (β-hairpin)



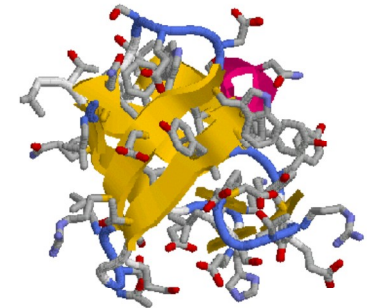
α-helix:
•right handed
•3.4 residue/turn
•H-bridges



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.

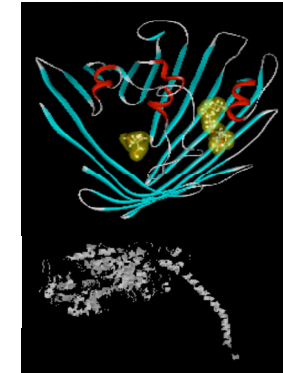
Protein structure classes

1. All alpha



calmodulin

2. All beta



porin

(3. Alpha-beta)

4. Multidomain

Domain:
folding subunit

myosin

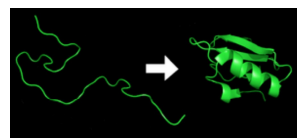
Although there are as many sequences as proteins, the spatial structures are classified into a surprisingly small number of classes!

How is the three-dimensional structure acquired?



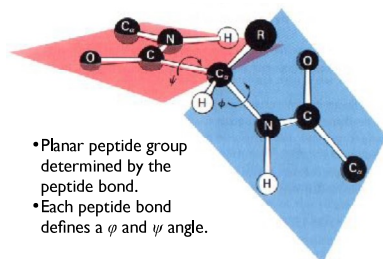
Christian Anfinsen
(1916-1995)

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?

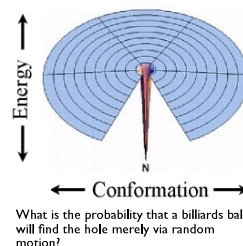


- Planar peptide group determined by the peptide bond.
- Each peptide bond defines a ϕ and ψ angle.

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

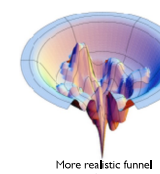
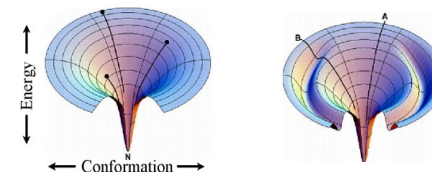
i = number of possible angular positions of a given ϕ or ψ angle
 n = total number of ϕ and ψ angles

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} (!!!)



Protein folding is guided by the shape of its conformational space

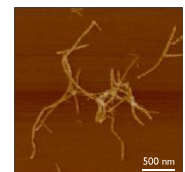
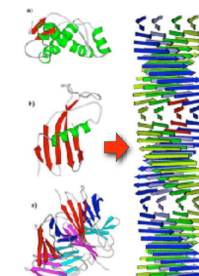
Shape of conformational space:
"Folding funnel"



- 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

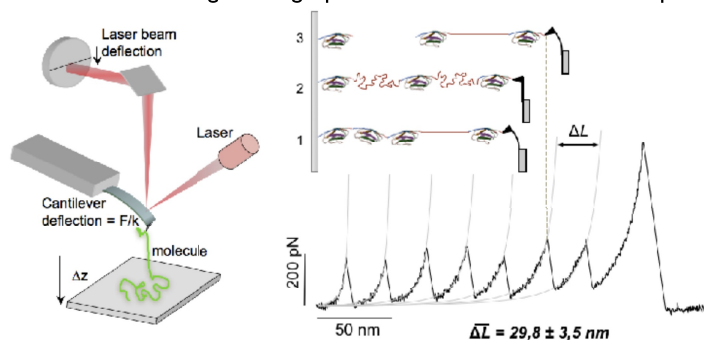


β -fibrils:
undissolved precipitate
cross- β structure

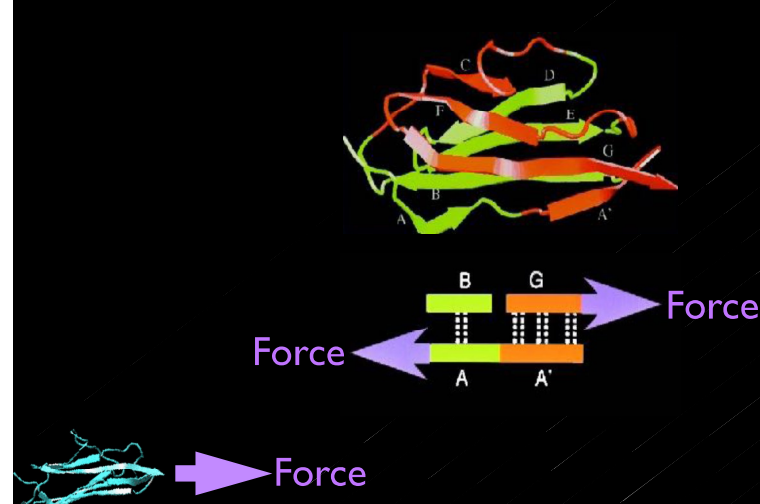
Methods of protein unfolding (denaturation)

- Heat
Break secondary chemical bonds
- Chemical agent
Disrupt secondary and tertiary structure
- Mechanical force

Mechanical unfolding of a single protein with atomic force microscope

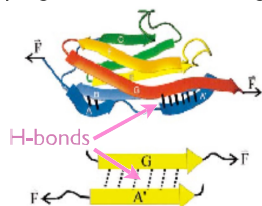


Structural basis of mechanical stability

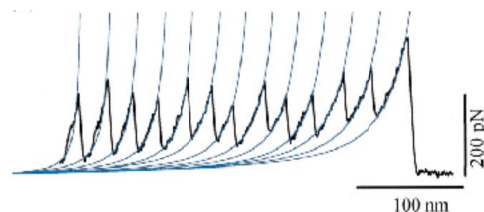


Biological logic of mechanical stability

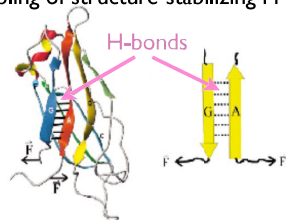
Parallel coupling of structure-stabilizing H-bonds



High unfolding forces



Serial coupling of structure-stabilizing H-bonds



Low unfolding forces

