

# BIOHYSICS OF WATER

KELLERMAYER MIKLÓS





# 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).
- Numerous anomalous properties.
- 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.



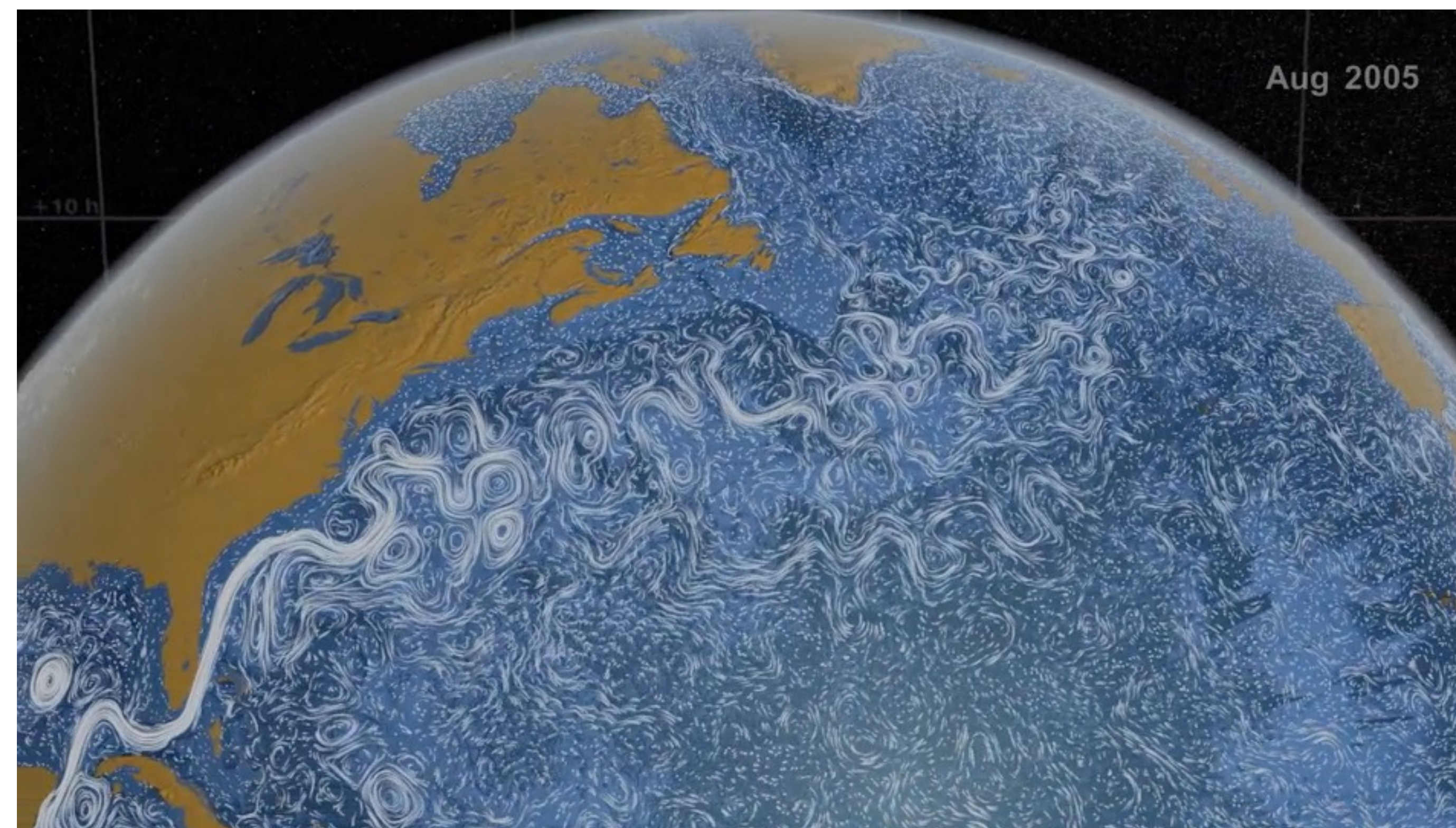
Georg Friedrich **Händel** (1685-1759): “**Water music**”.



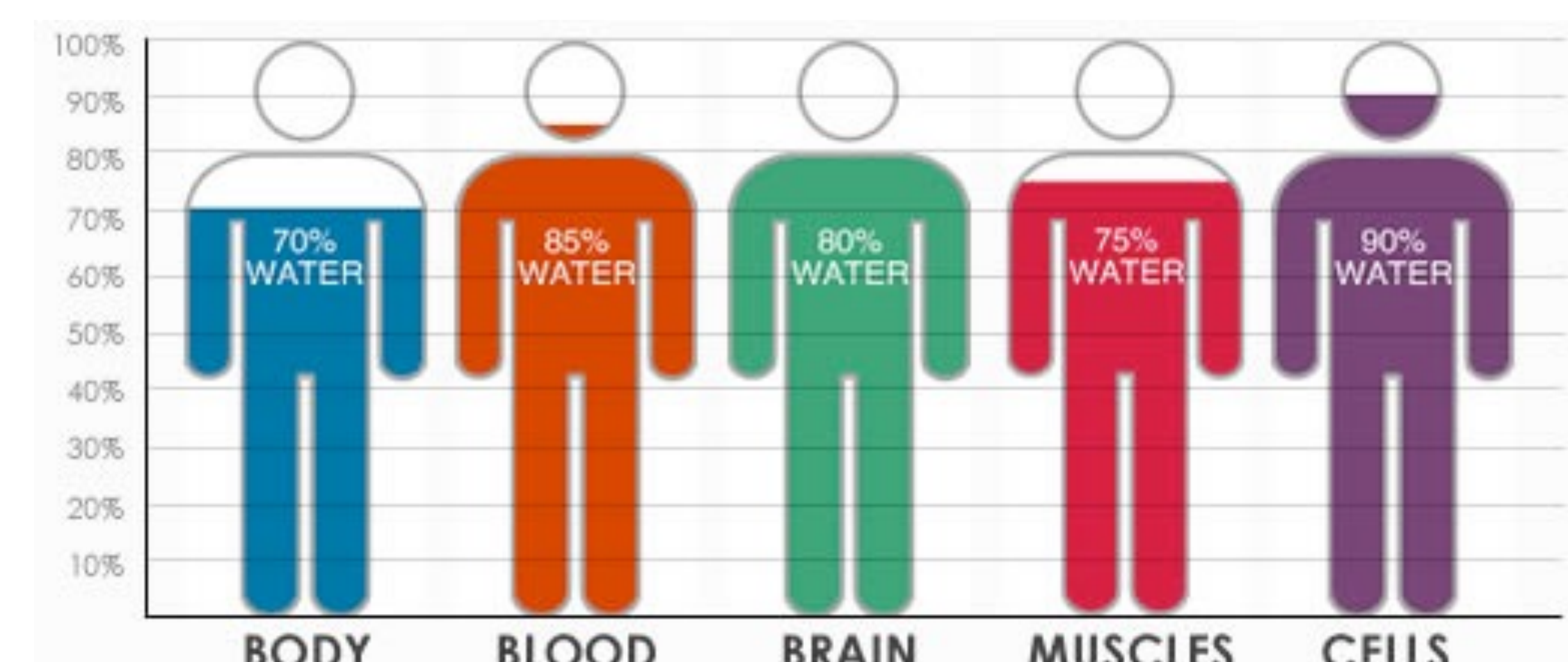
Georg Friedrich Händel (center) and King George I (right) on the Thames River, 17 July 1717.



Hokusai (1760-1849): Great wave off Kanagawa



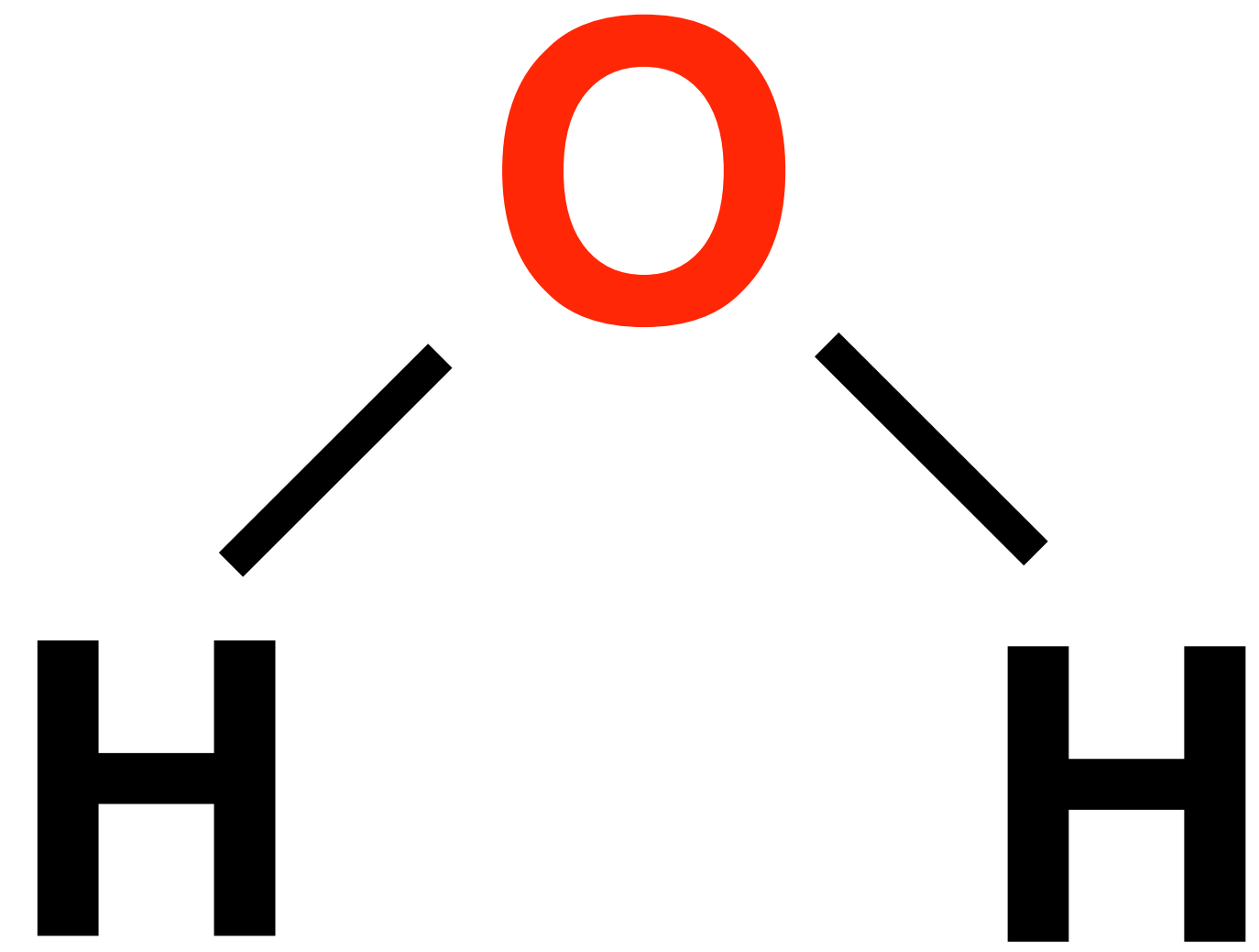
Perpetual motion of oceans on Earth’s surface.



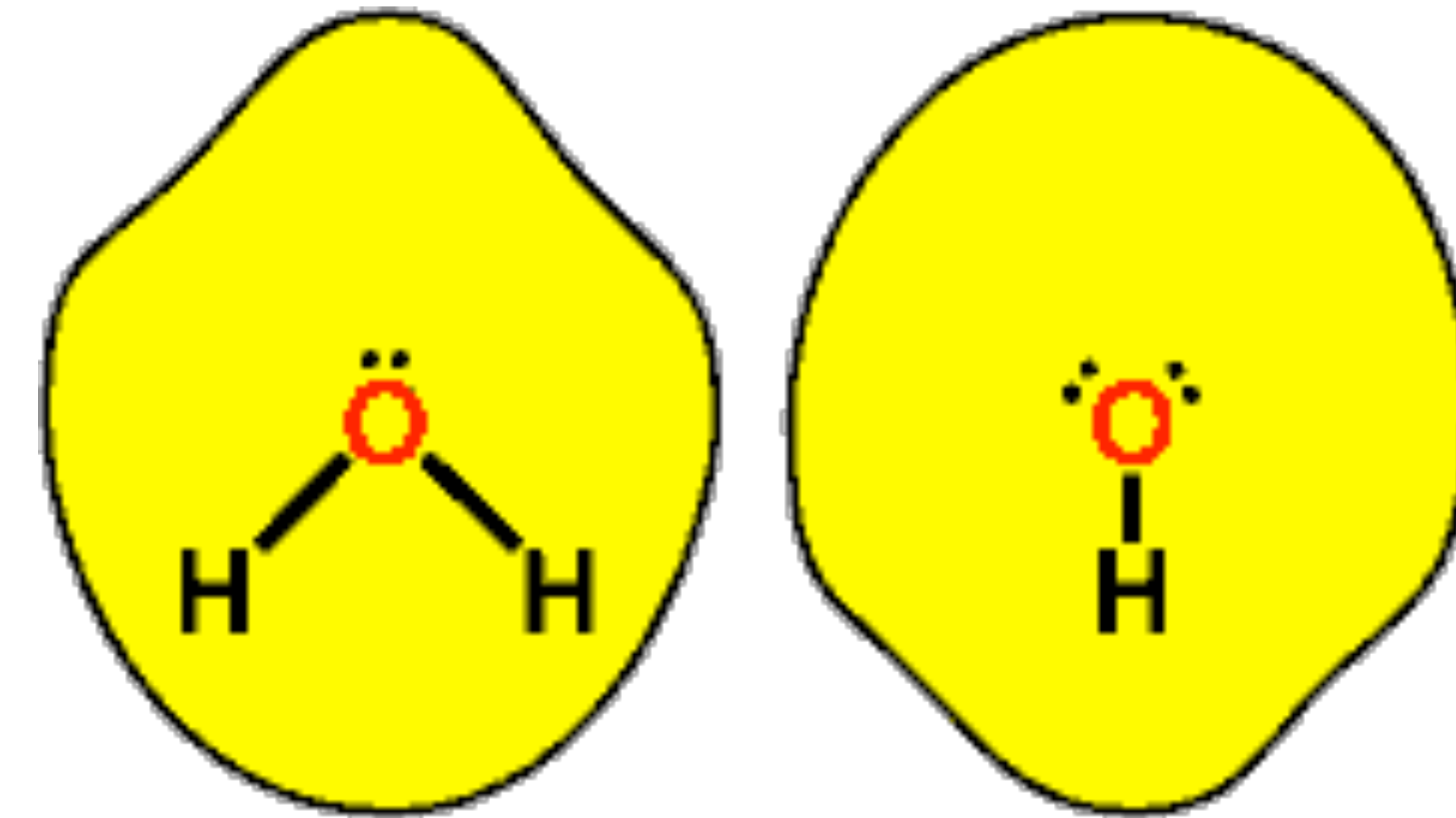


# Structure of the water molecule

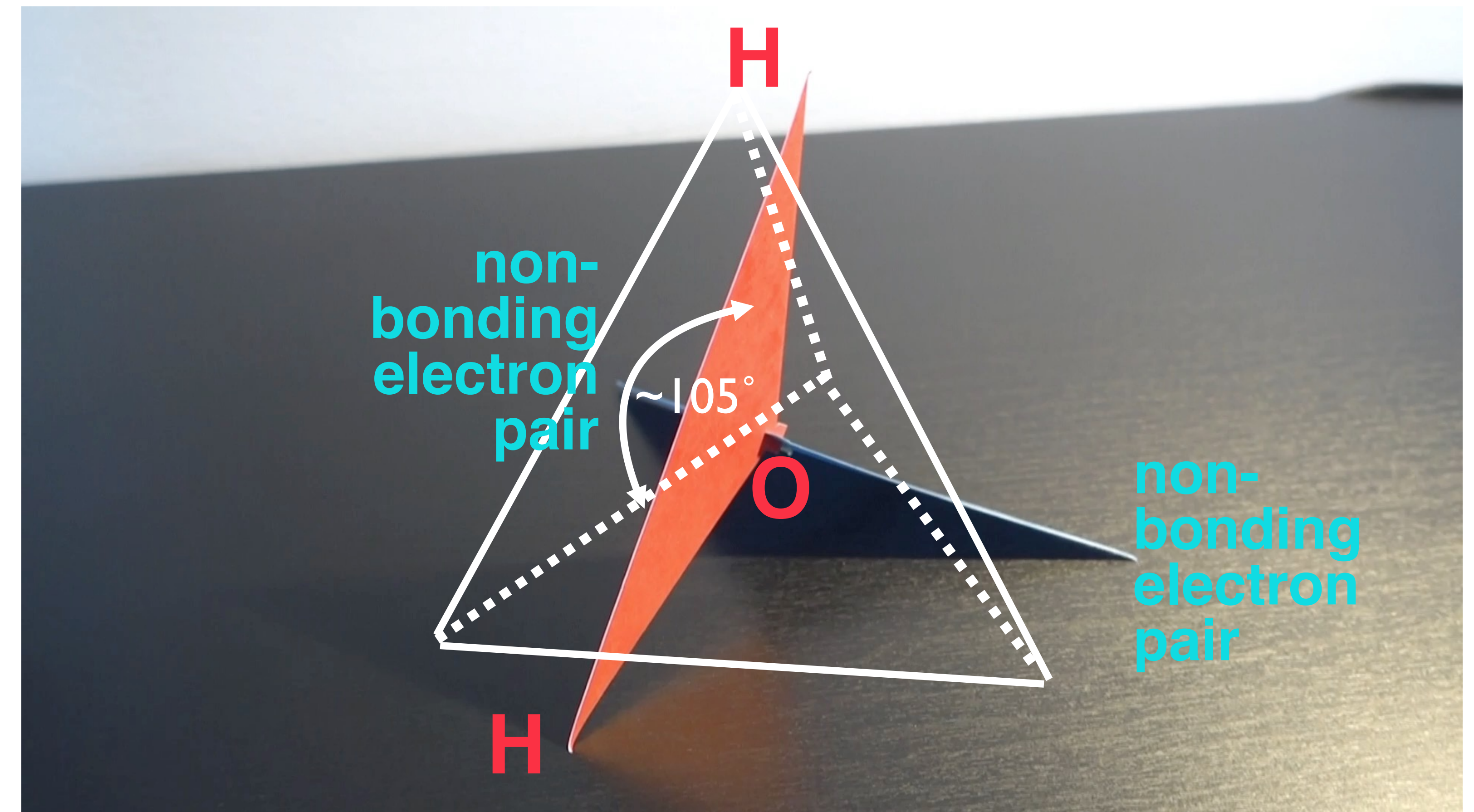
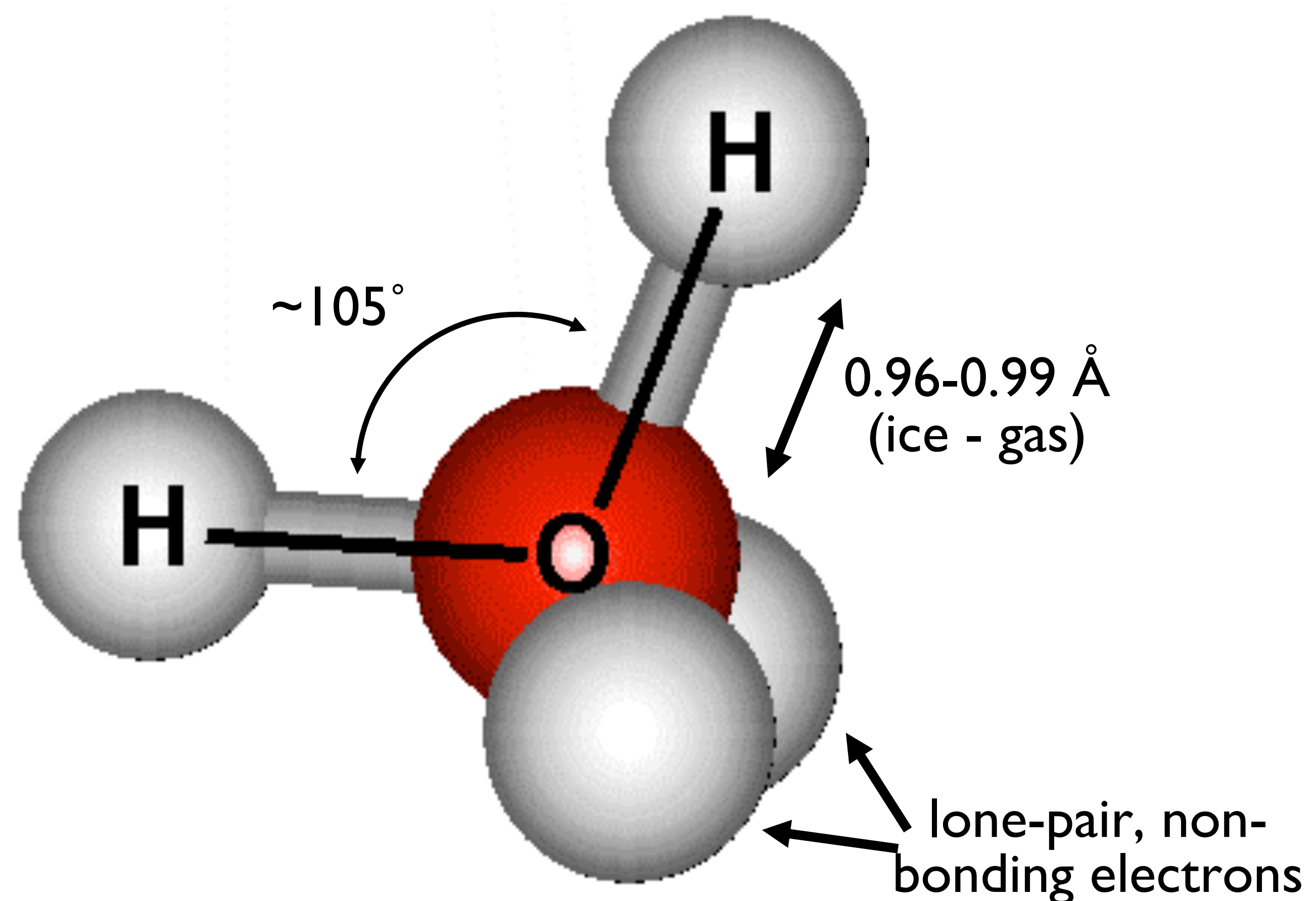
One of the smallest molecules  
Barely larger than an atom



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

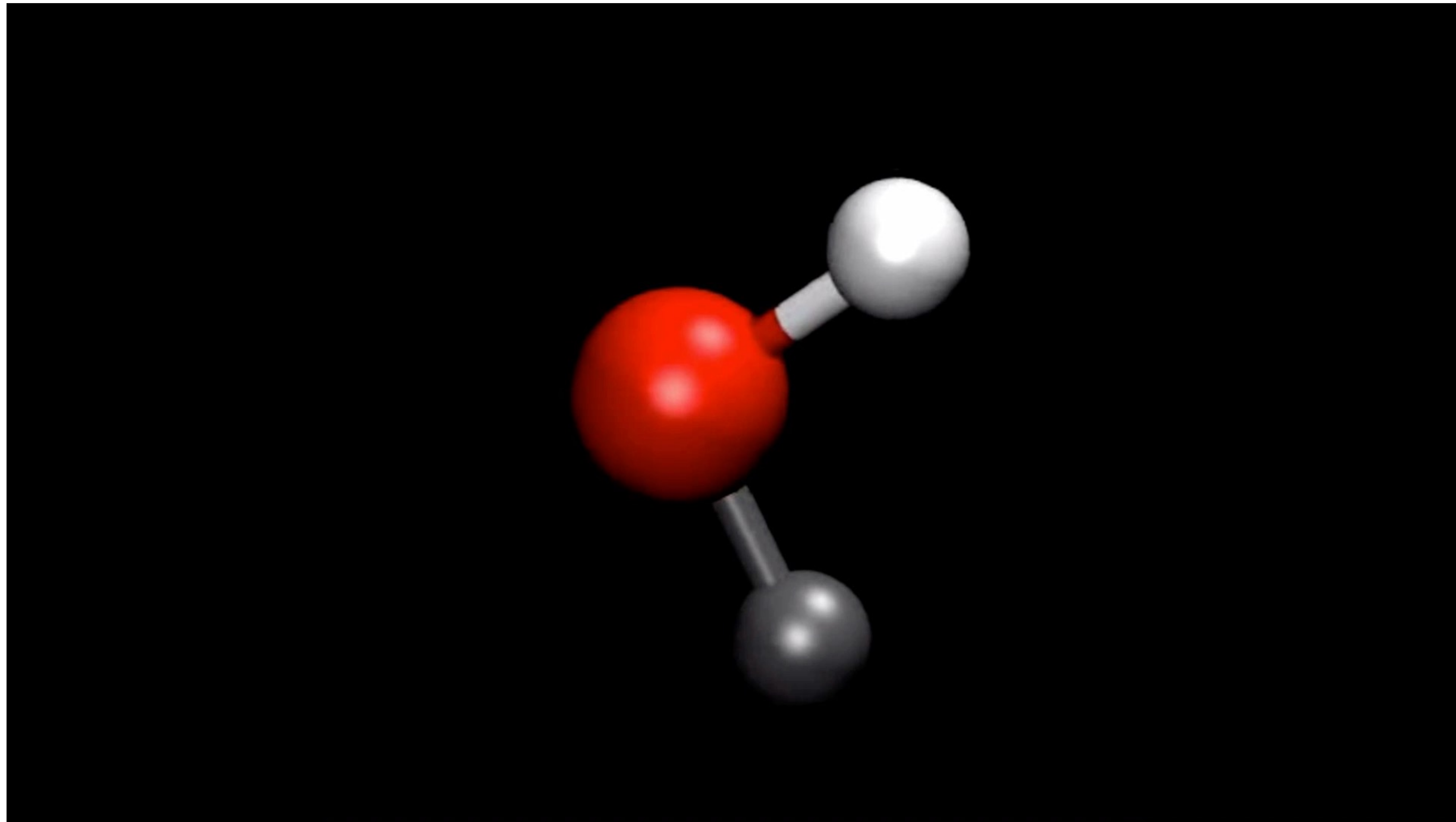


Tetrahedral  
structure:



# Dynamics of the water molecule

Rotational and vibrational motion

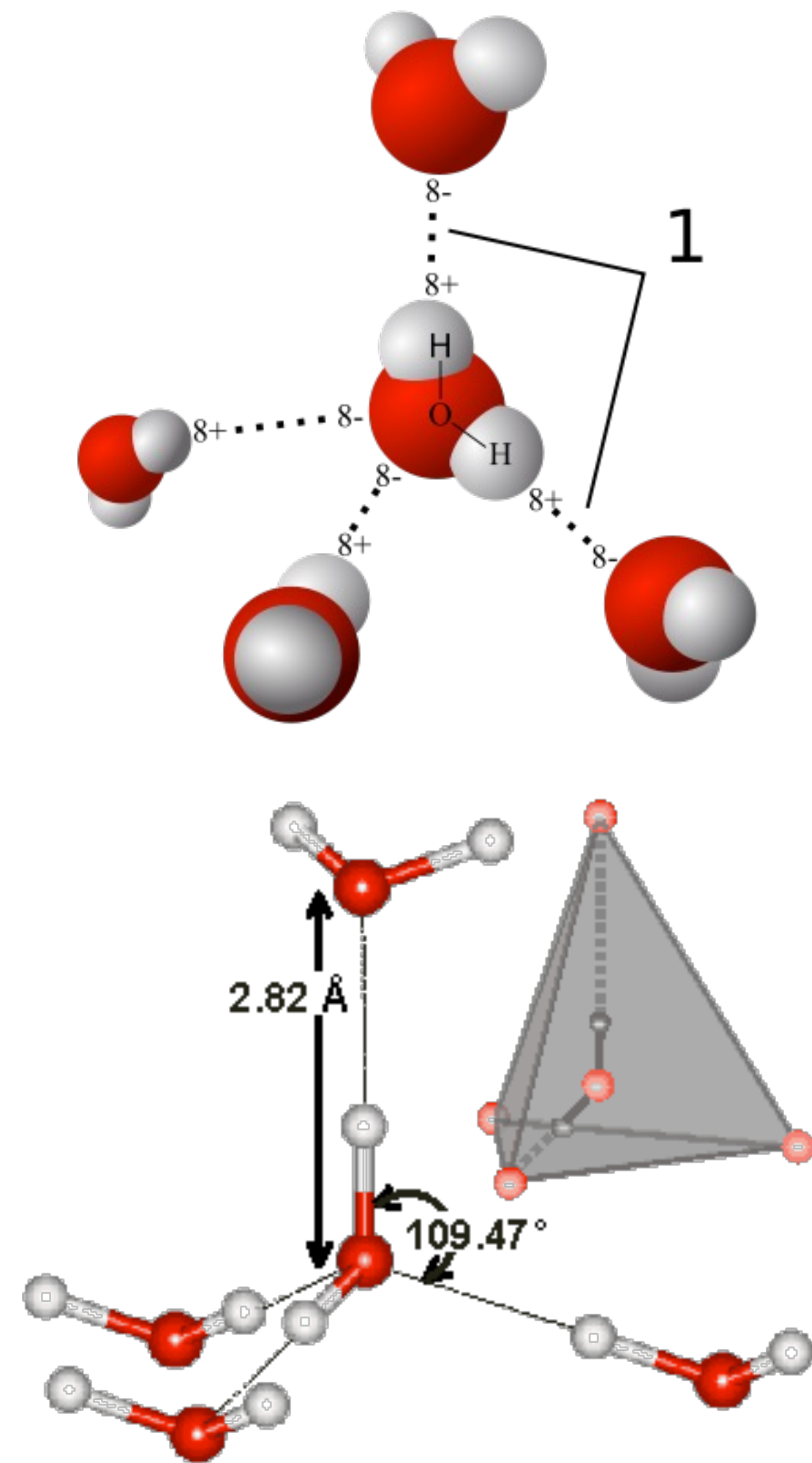


Absorption in the infrared and red spectral region →  
“blue” color of natural waters: *blue planet*

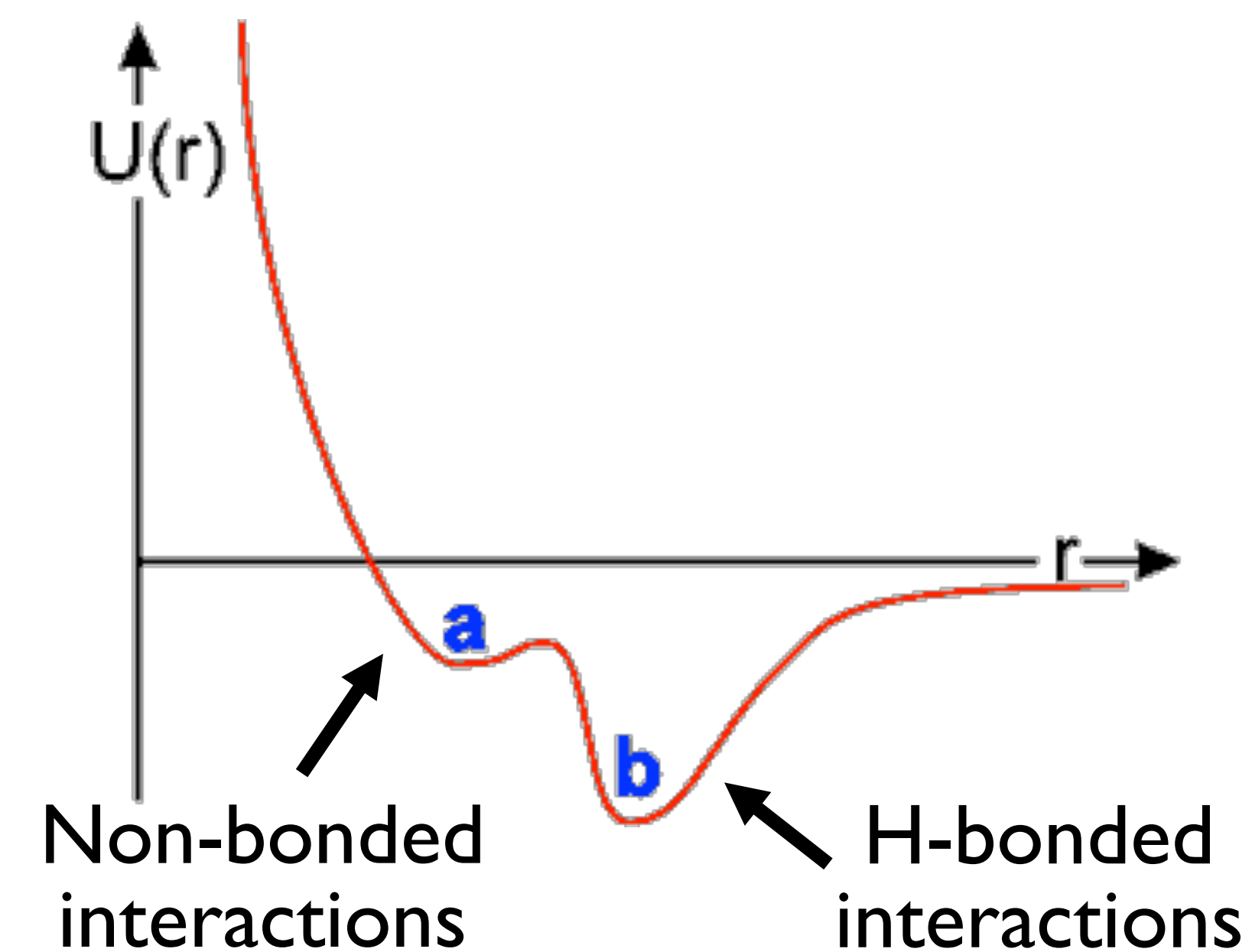
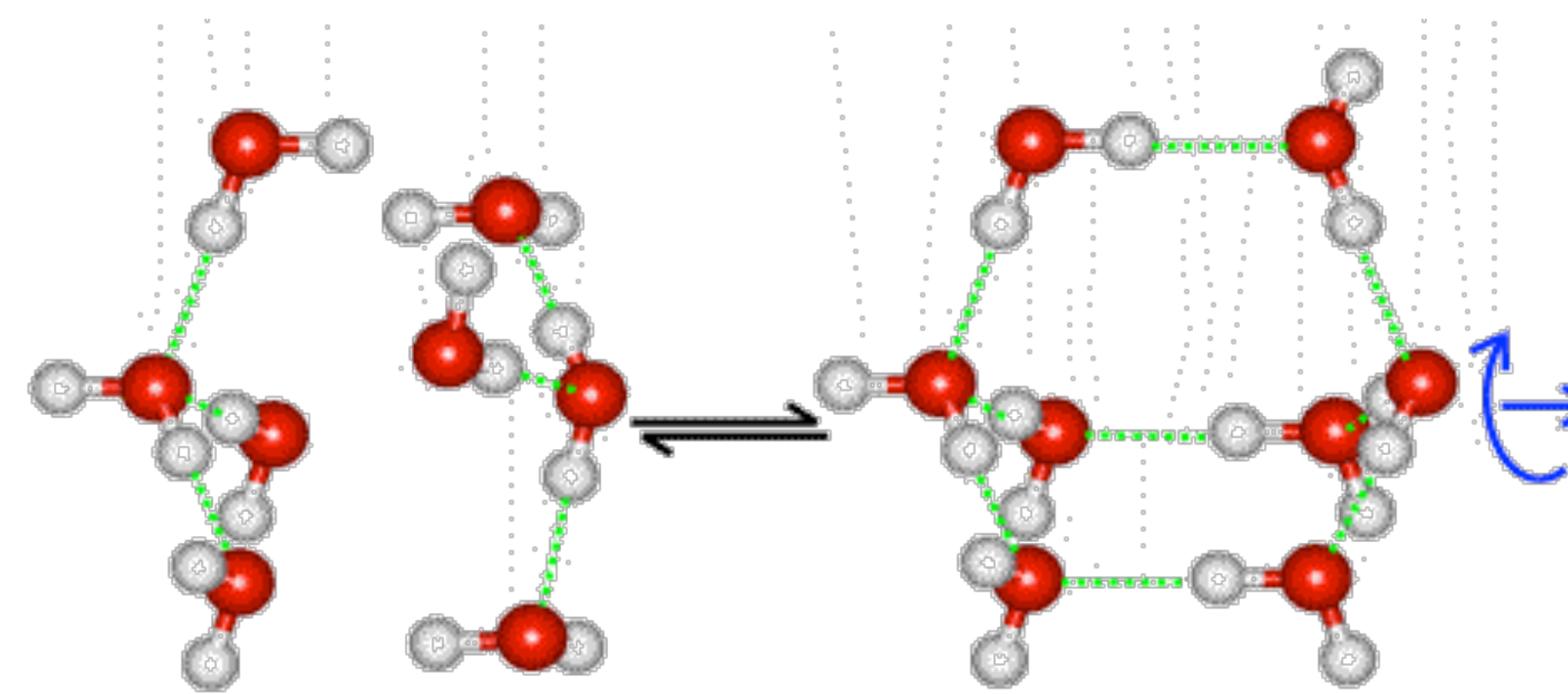


# Structure of liquid water

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

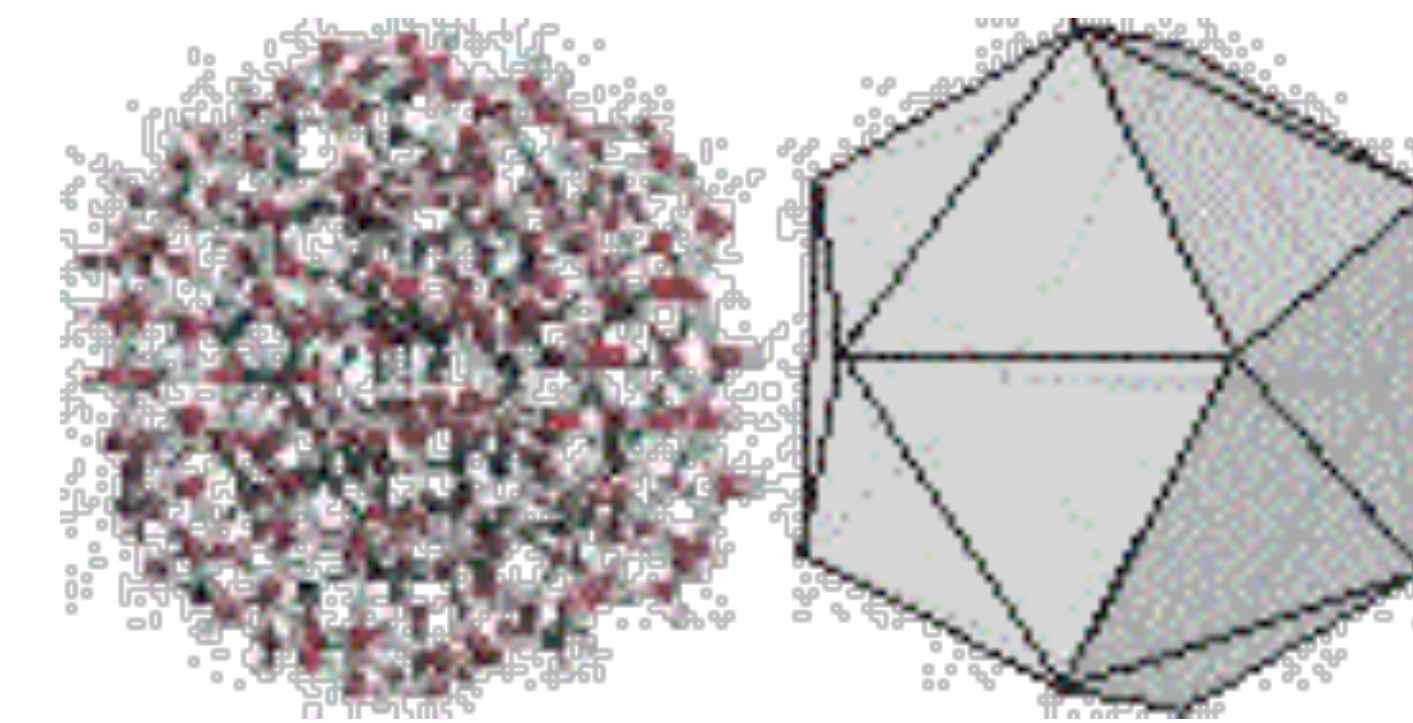


H-bridge: cohesion + repulsion  
Cluster formation: bicyclo-octamer



From clusters to networks:  
280 molecules form  
icosahedral structure

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

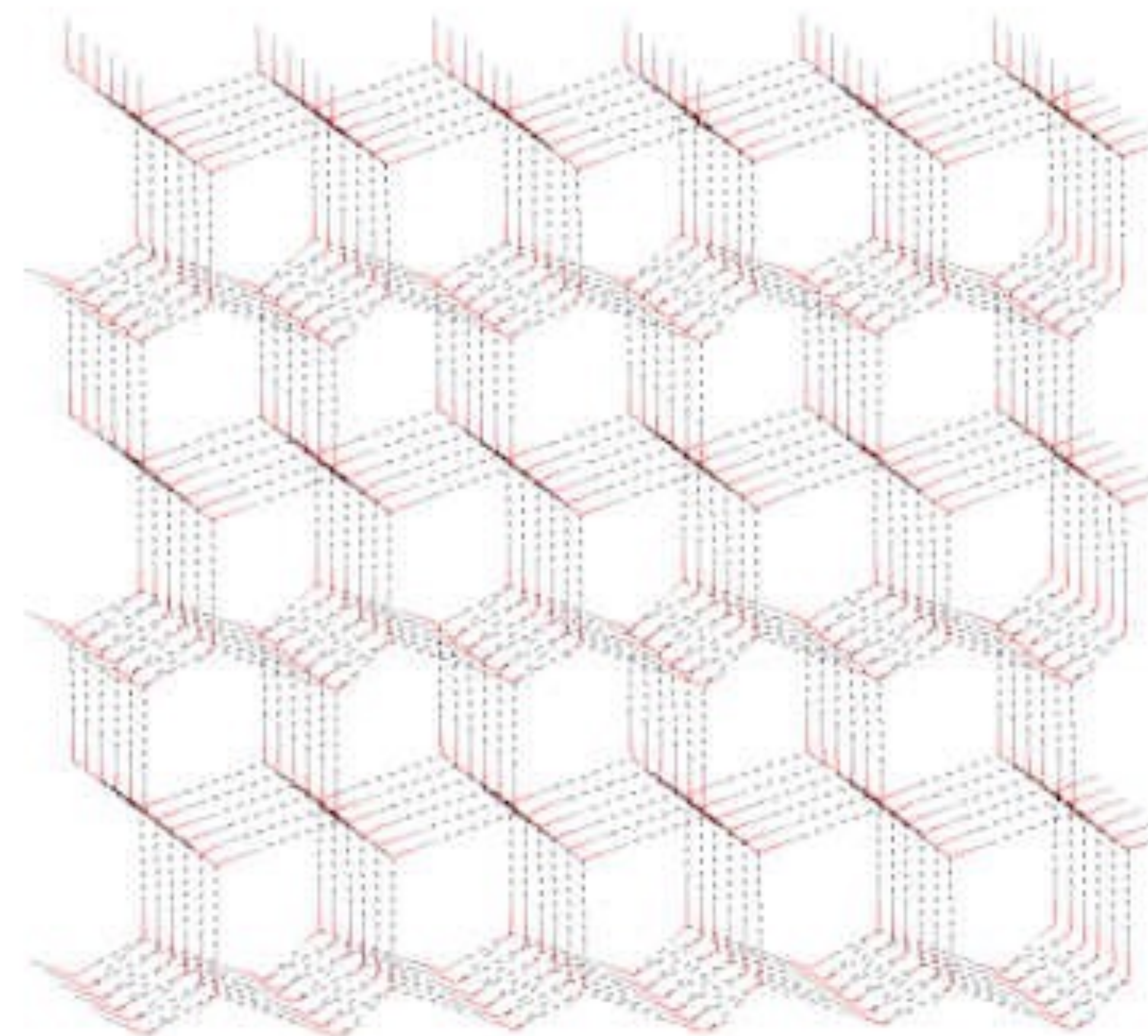
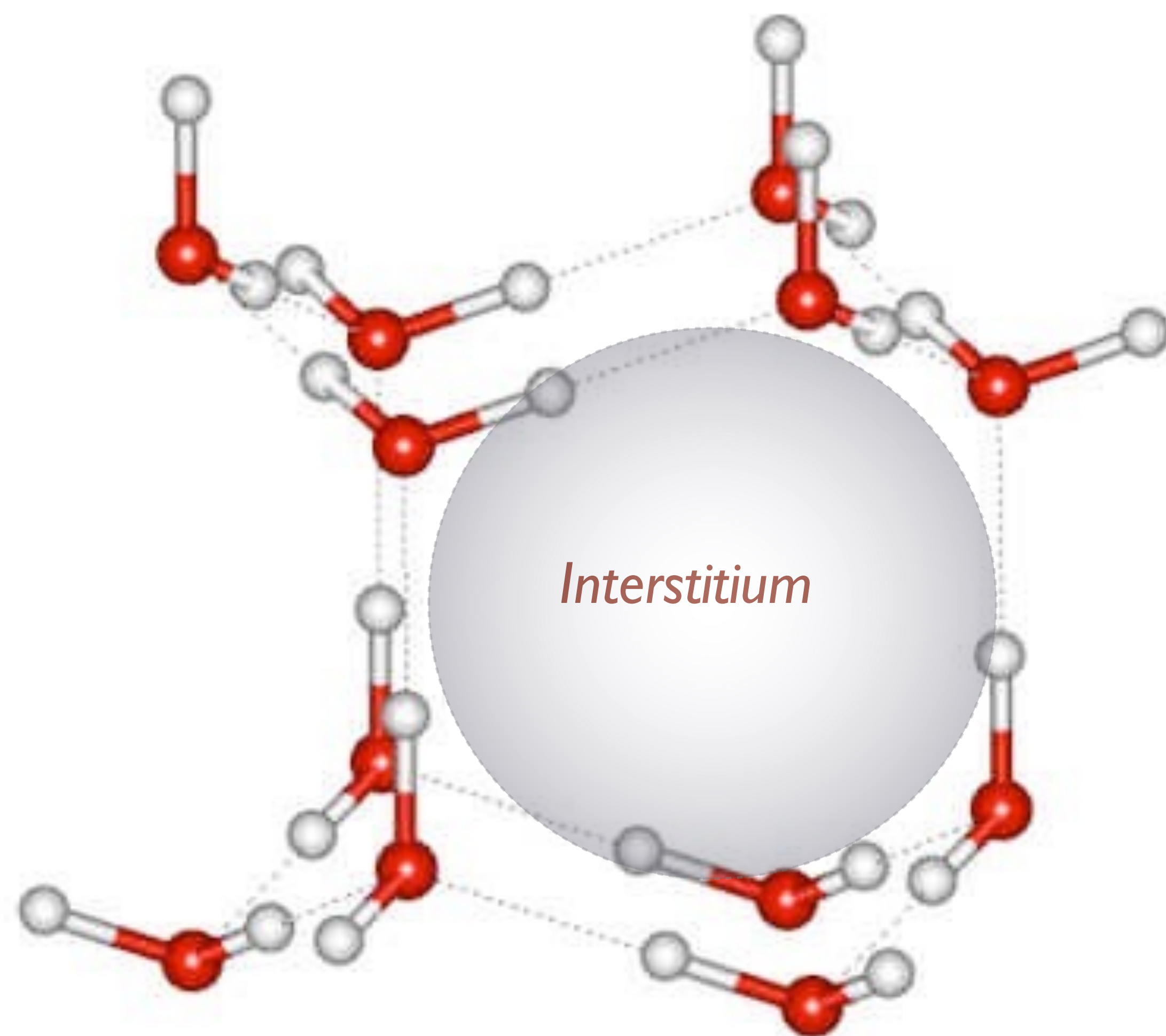


Spatial networks:  
May explain anomalous  
properties of water



# Structure of ice

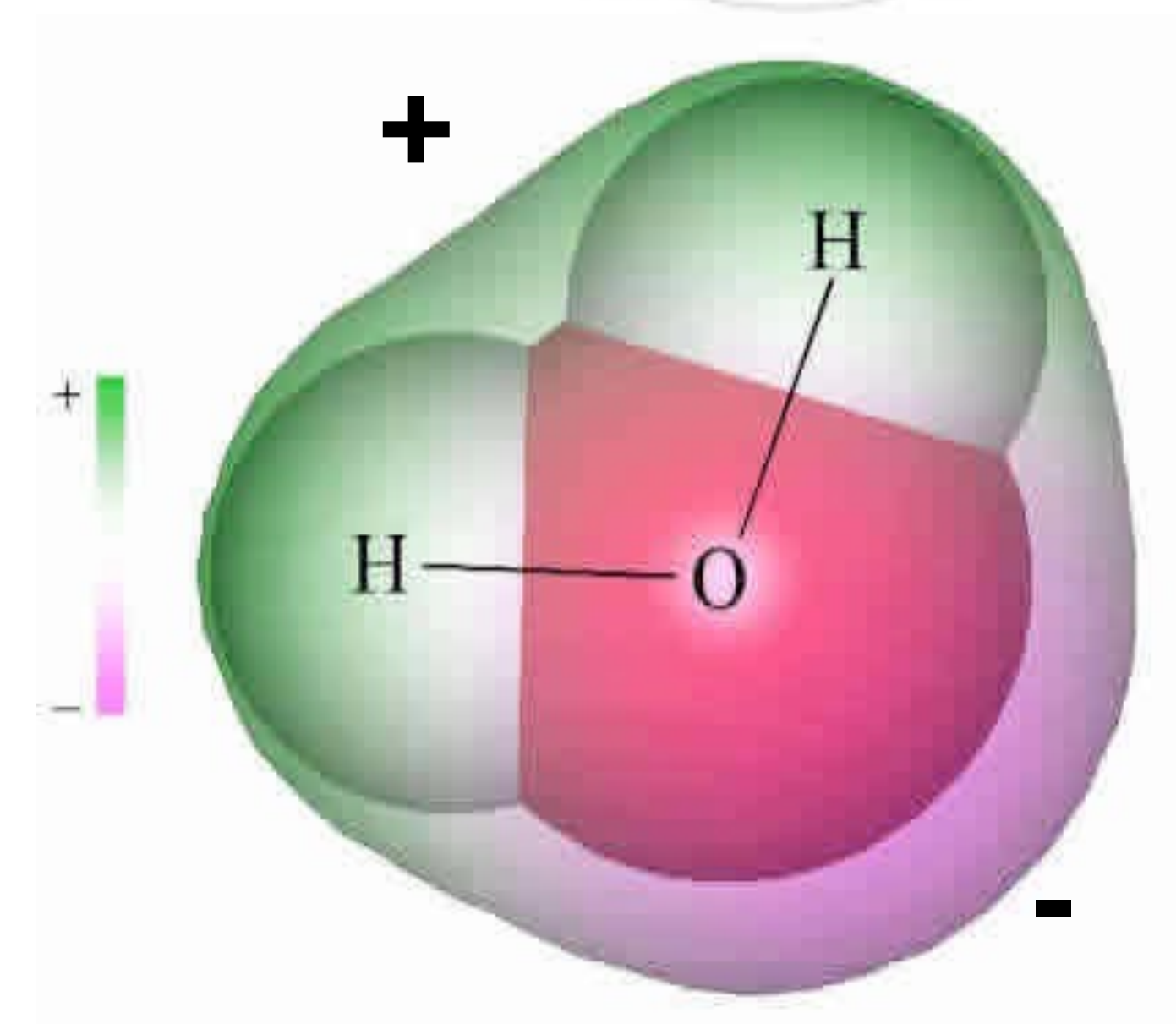
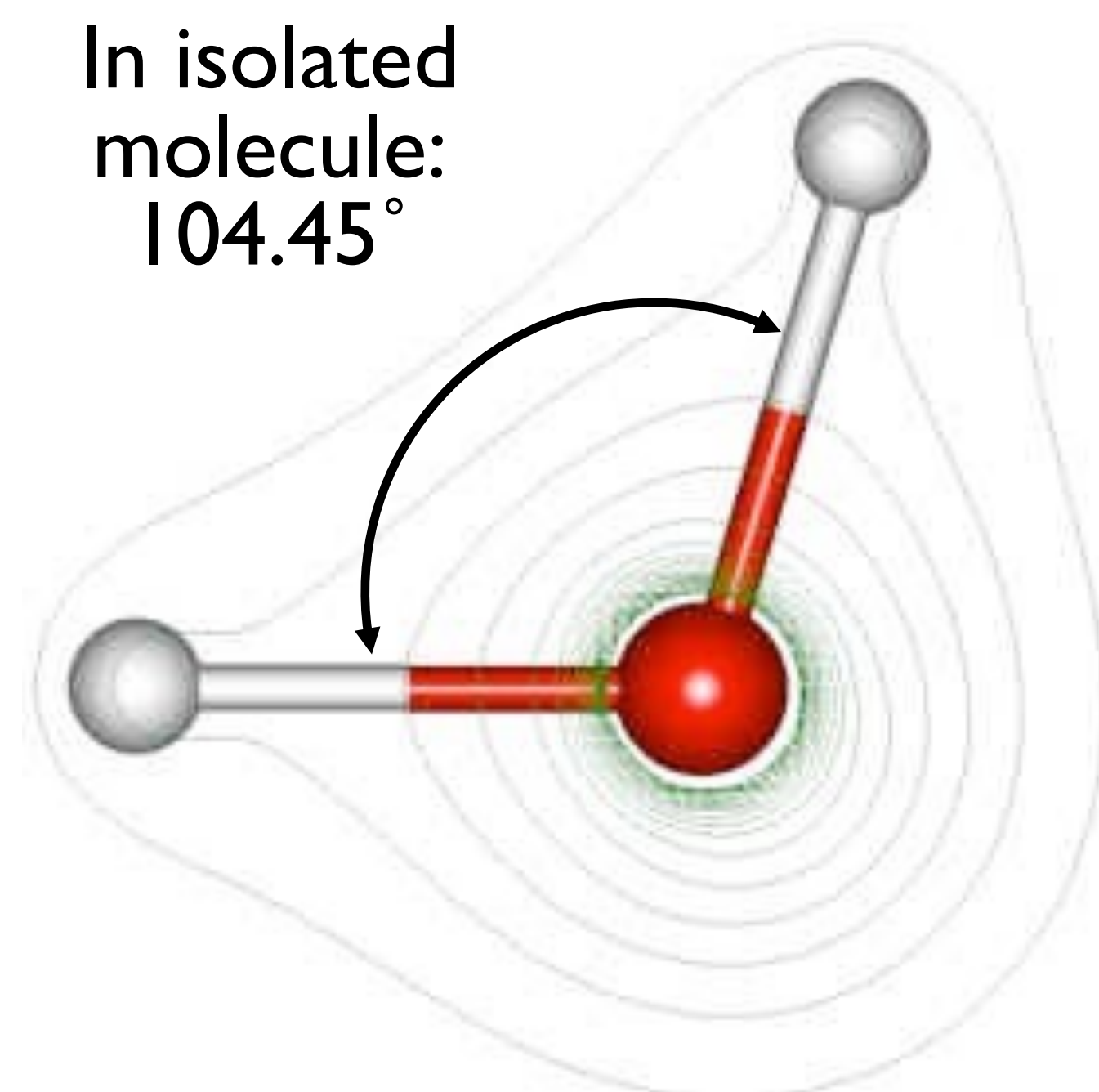
- 9 different forms
- Conventional ice: hexagonal structure
- Coordination number: 4 (each molecule coordinates another four) Interstitium: could incorporate a water molecule - important in the diffusion of gases





# Physical properties of water I.

Large permanent dipole moment  $\longrightarrow$  Good solvent



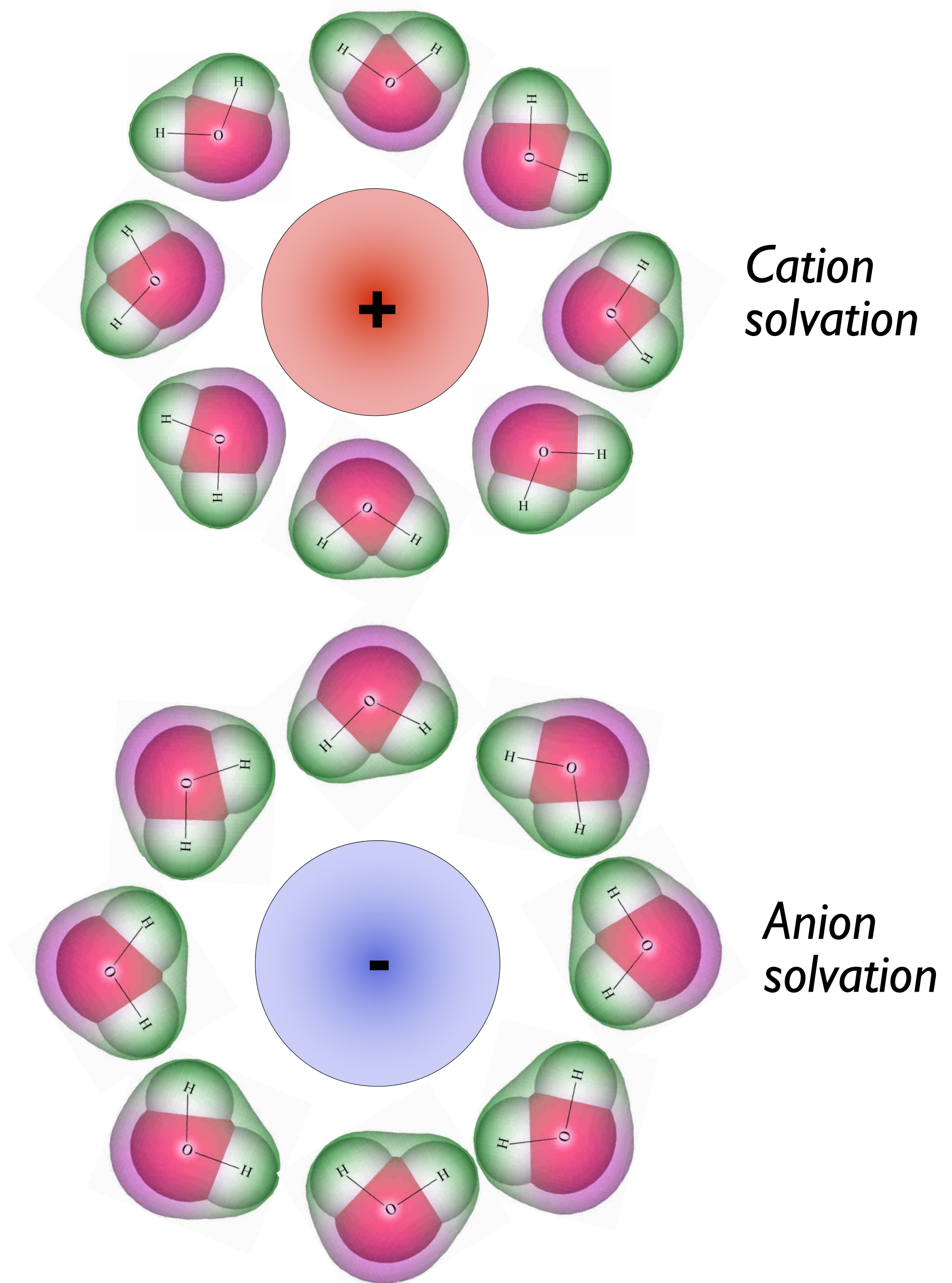
*Dipole moment:* amount of electrical energy stored in the material by an applied voltage, relative to vacuum. It shows how good an electrical insulator the material is. Consequence: water is good solvent.

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

Water stream bends in response to Coulombic forces



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.



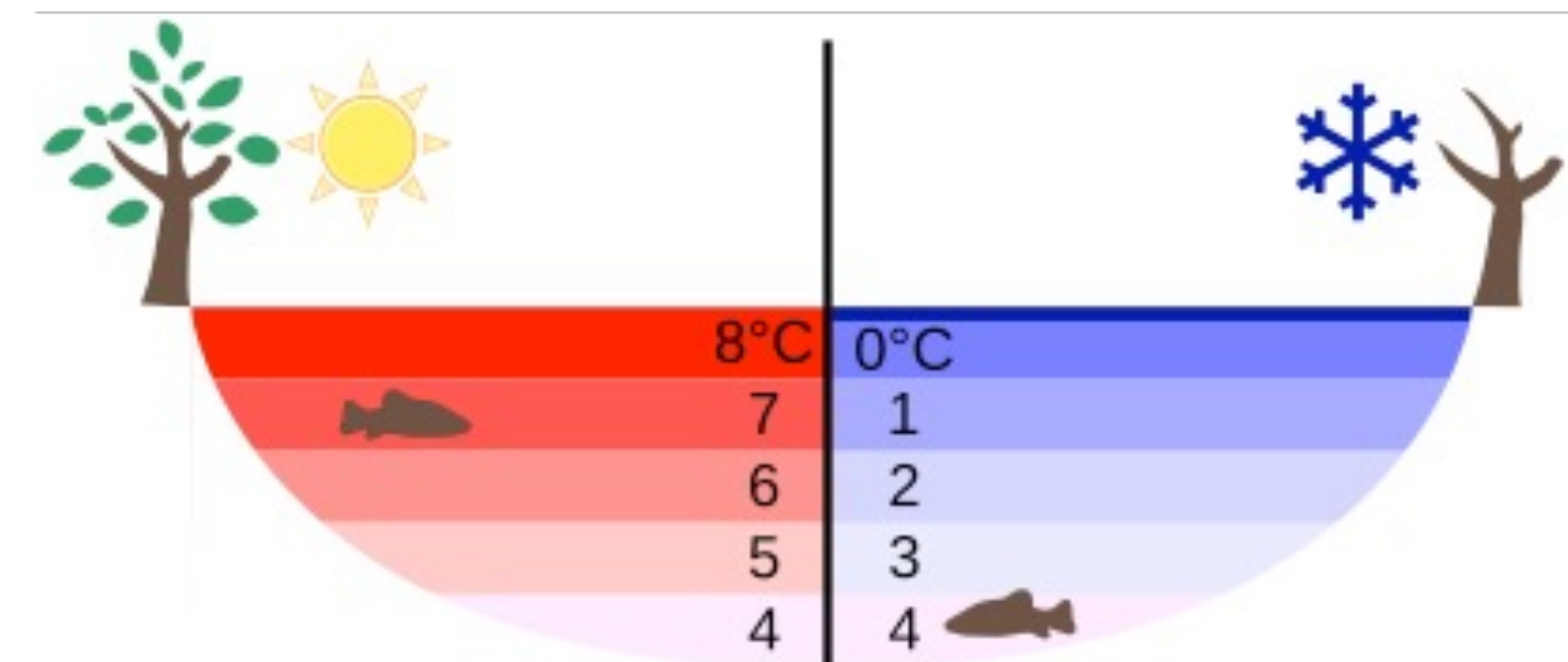
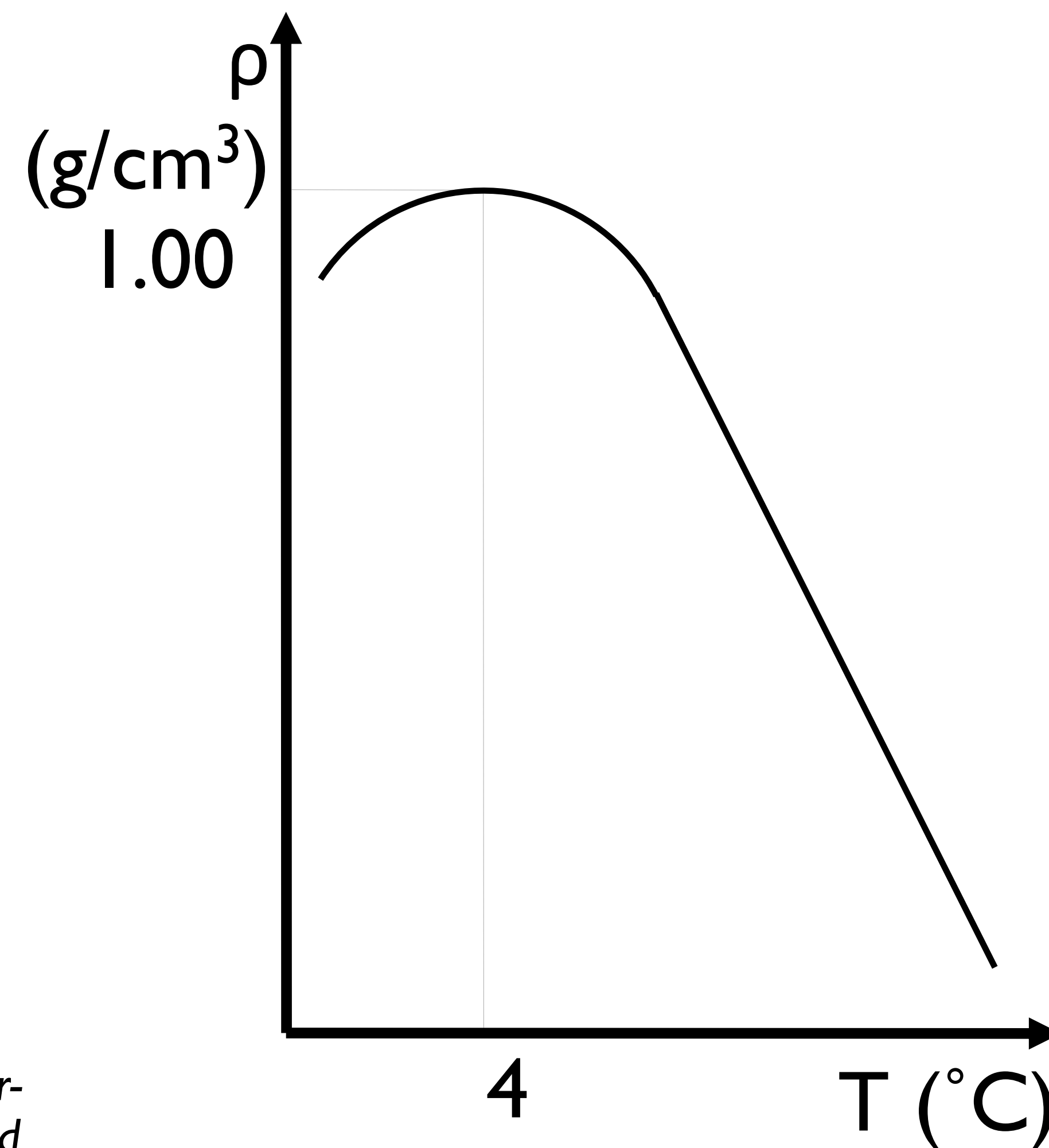
# Physical properties of water II.

## Anomalous density-temperature function

Temperature (°C)      Density (kg/m<sup>3</sup>)

+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
<b>+4</b>	<b>999.9720</b>
0	999.8395
-10	998.117
-20	993.547
-30	983.854

Super-cooled water



*Consequences:*

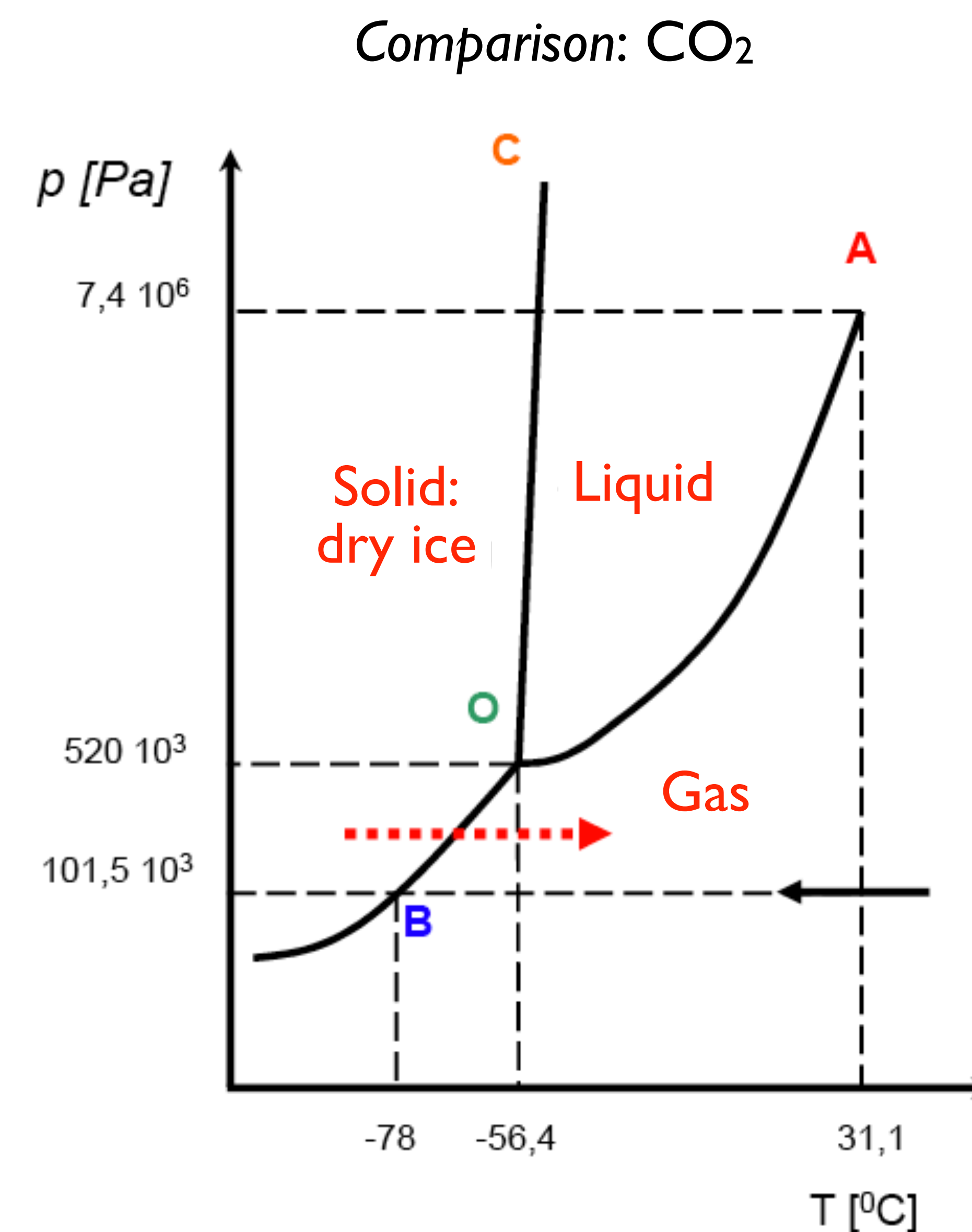
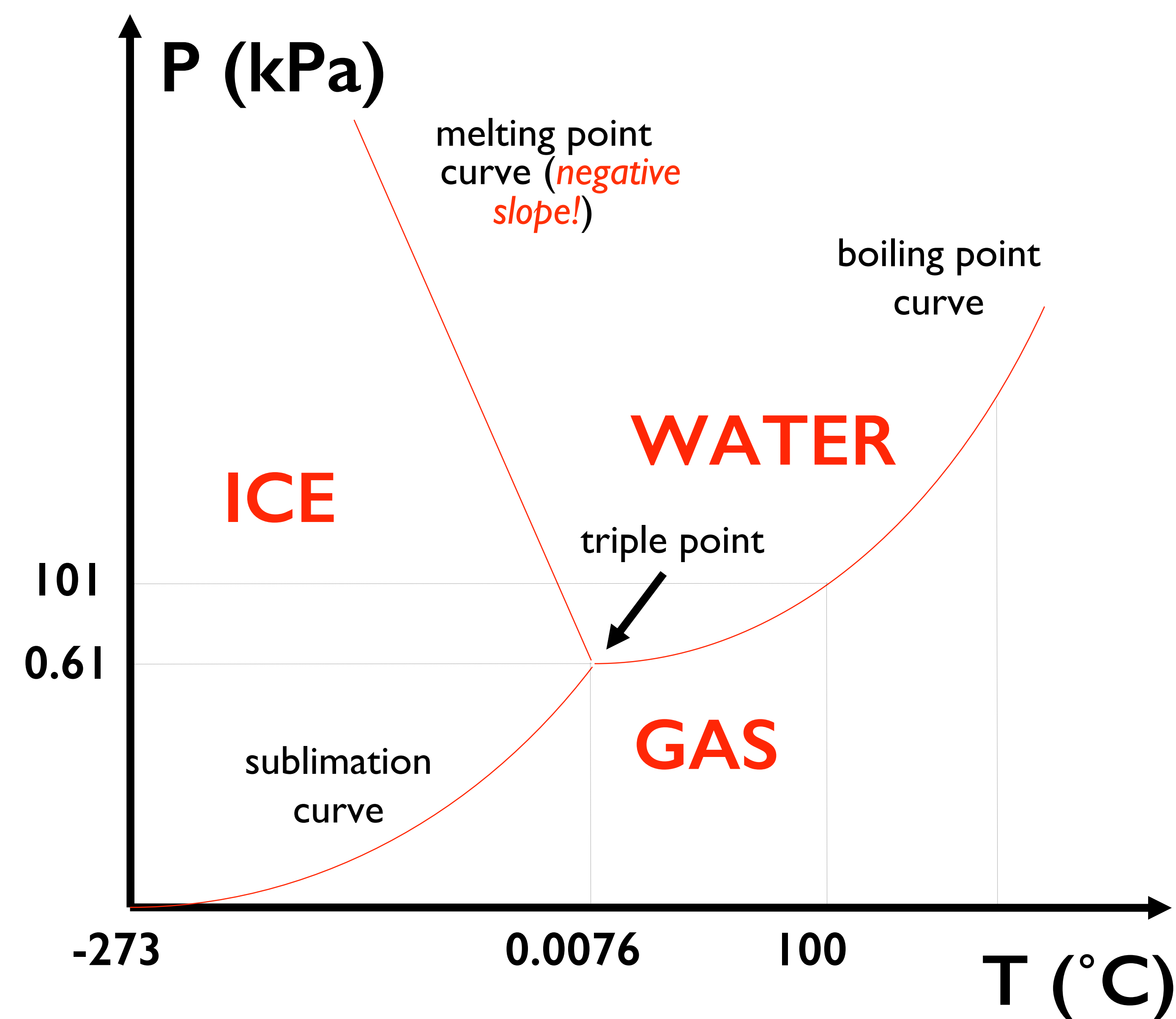
- 4 °C water is always at the bottom of the lake.
- Life persists under frozen lake.
- Creek runs under ice.



# Physical properties of water II.

## 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



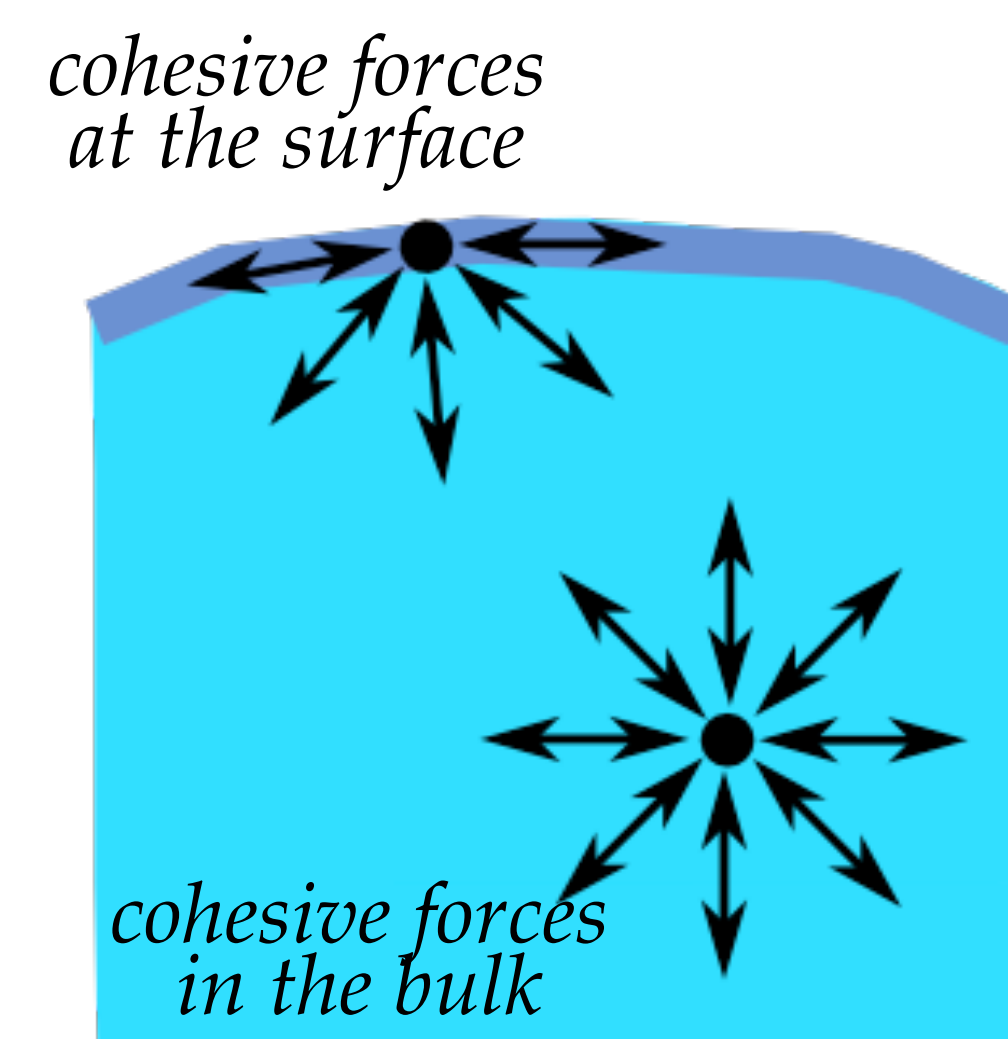


# Physical properties of water IV.

## 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
<b>Water</b>	72.9

### Consequences on **hydrophobic** surface



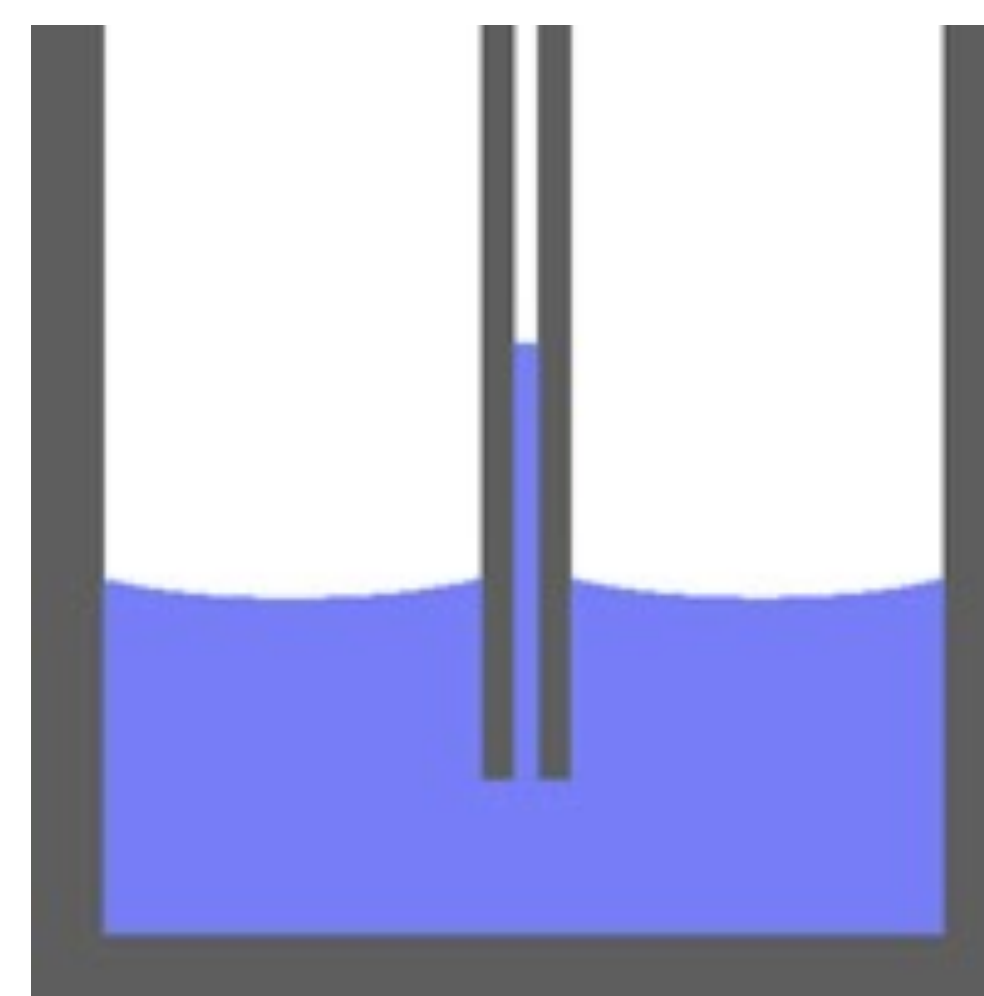
Persisting droplet on a superhydrophobic surface

### Consequences in macroscopic living systems

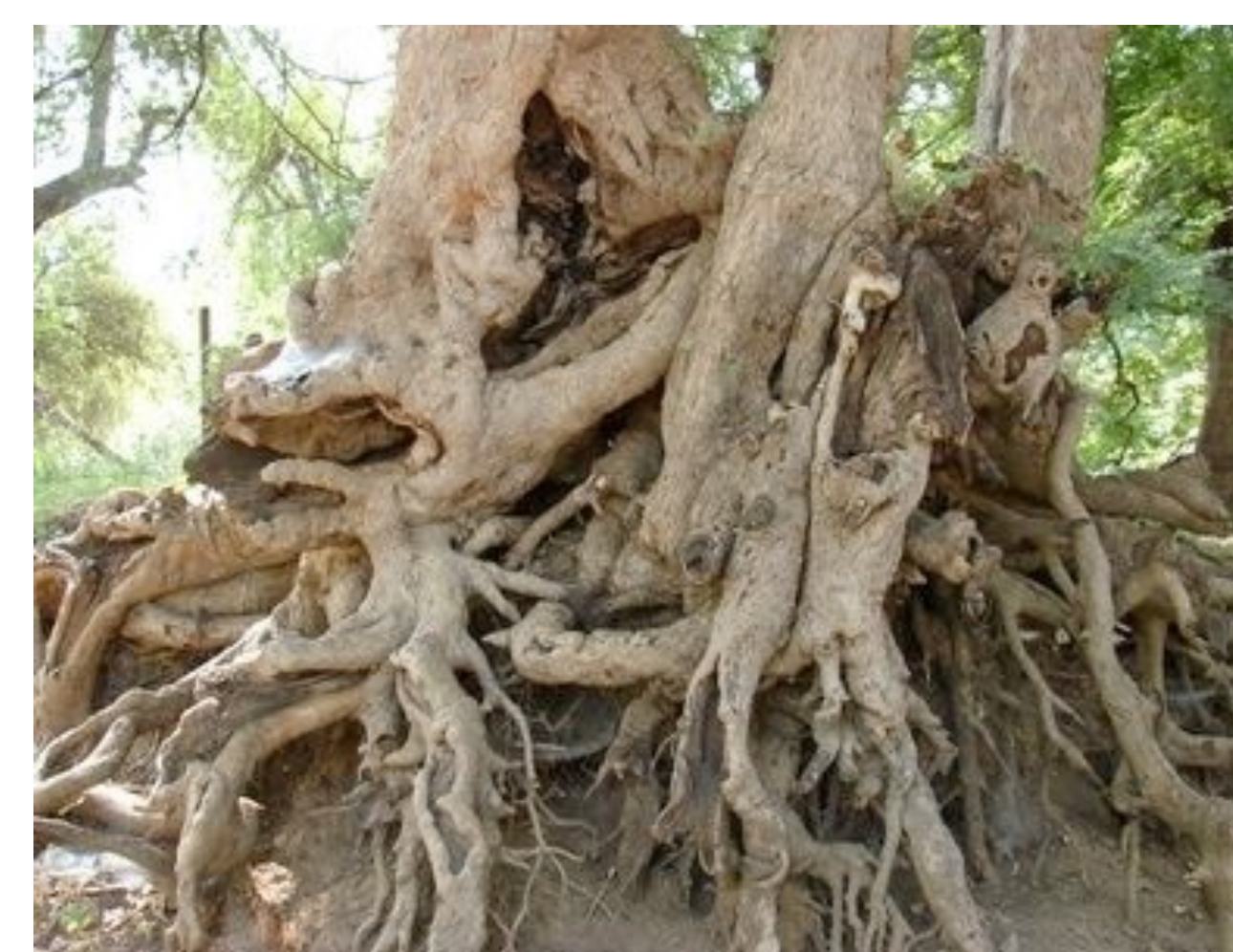


Water striders

### 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	$\sim 0.4 \text{ nm}$

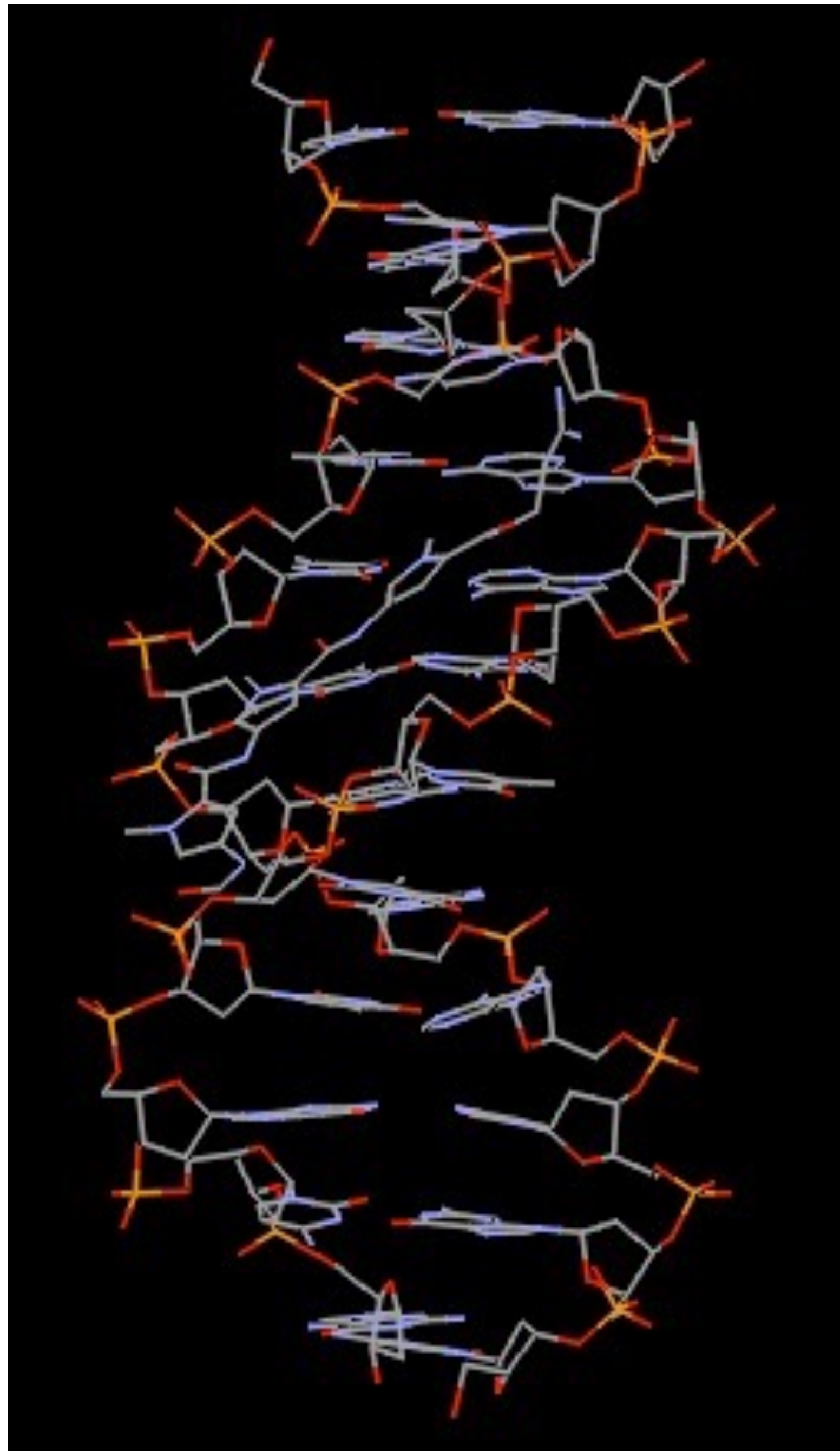


# BIOHYSICS OF BIOLOGICAL MACROMOLECULES

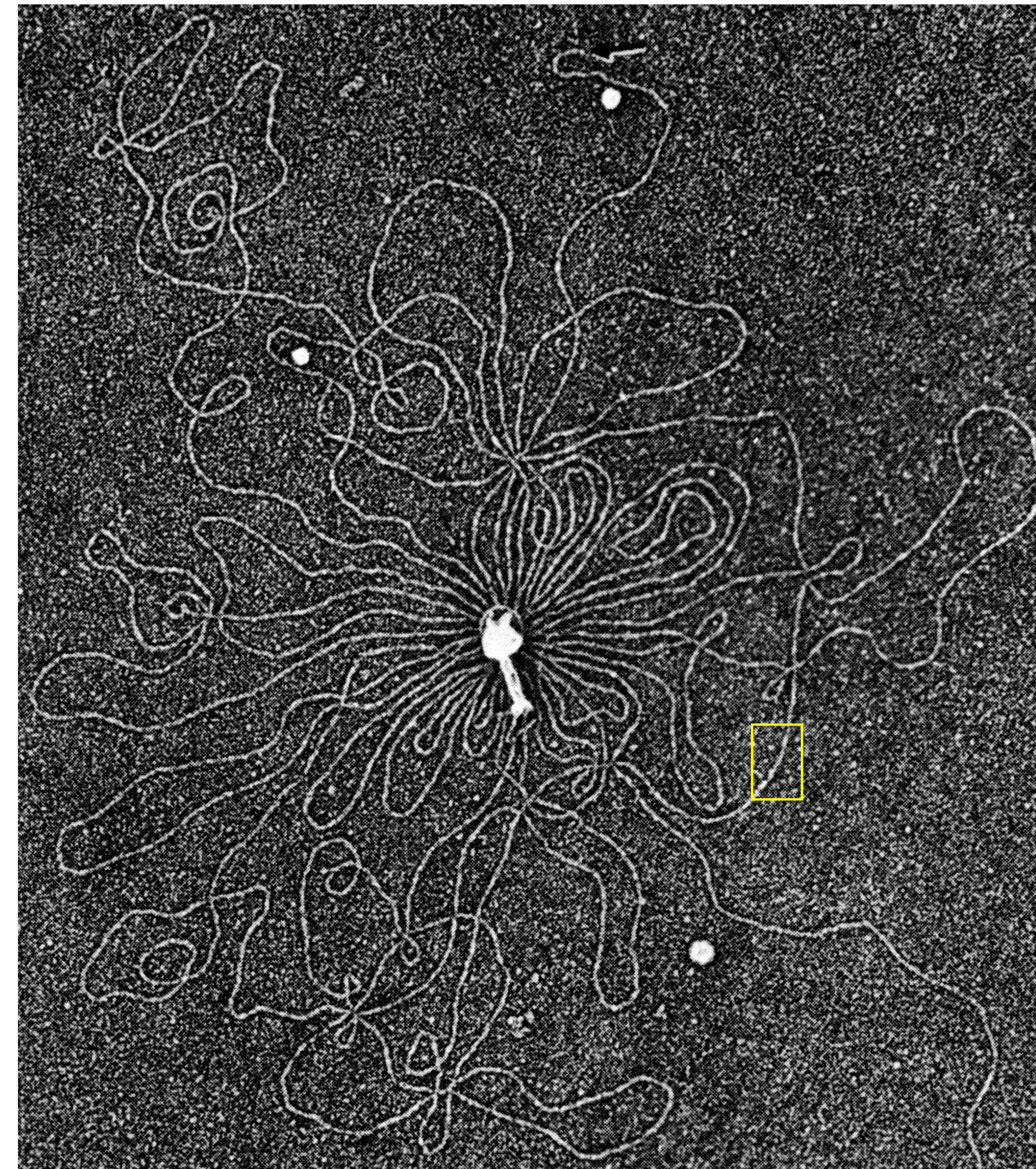
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# Biological macromolecules are **GIANT** molecules



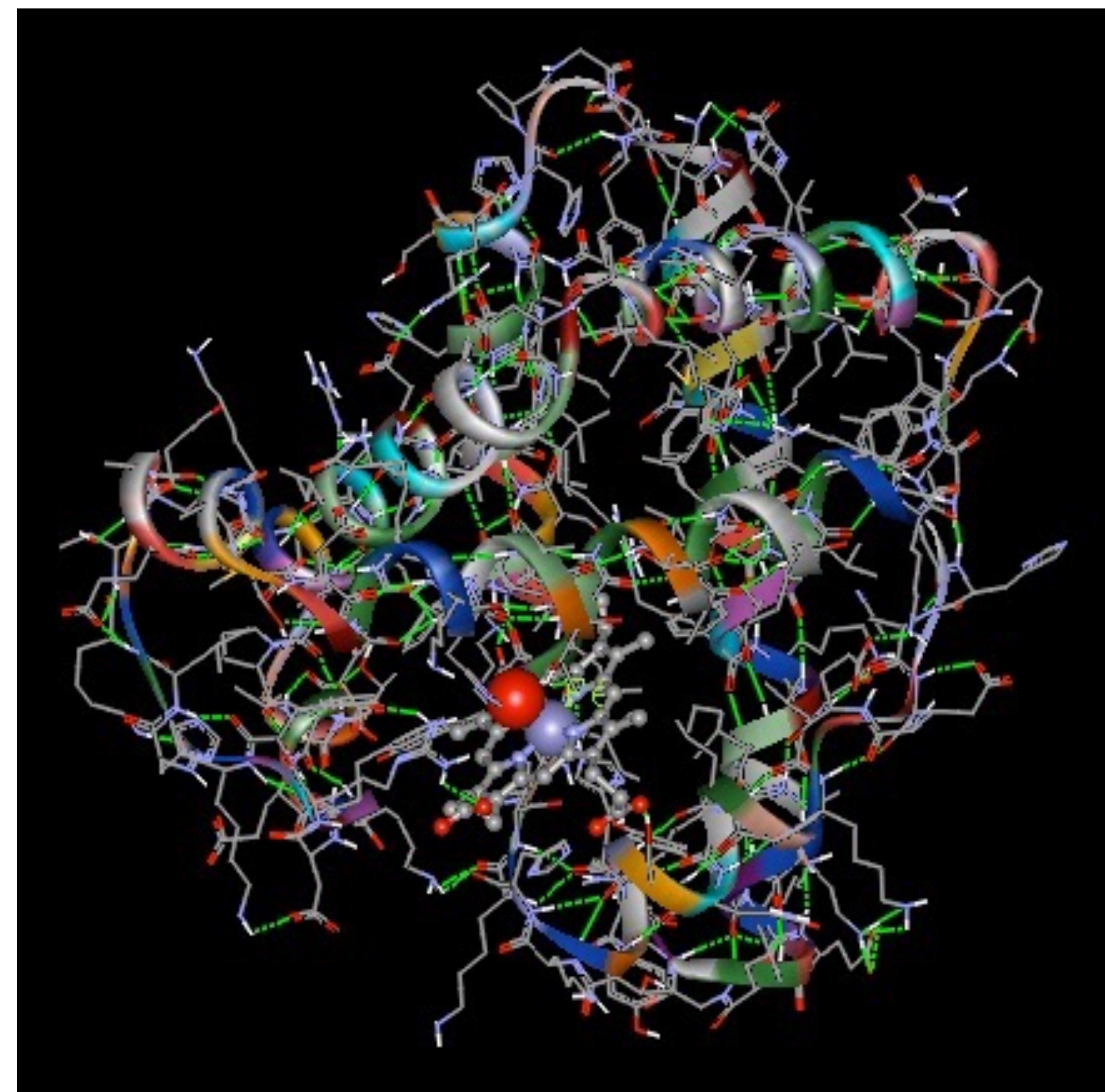
DNS double helix



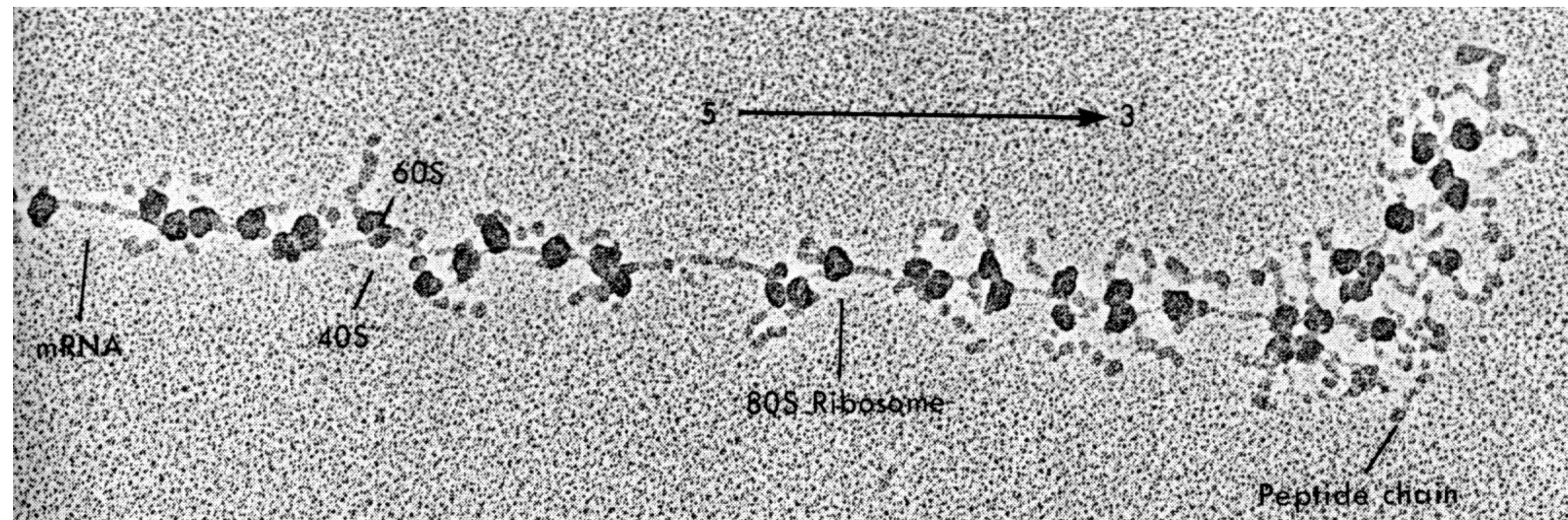
DNA released from bacteriophage head



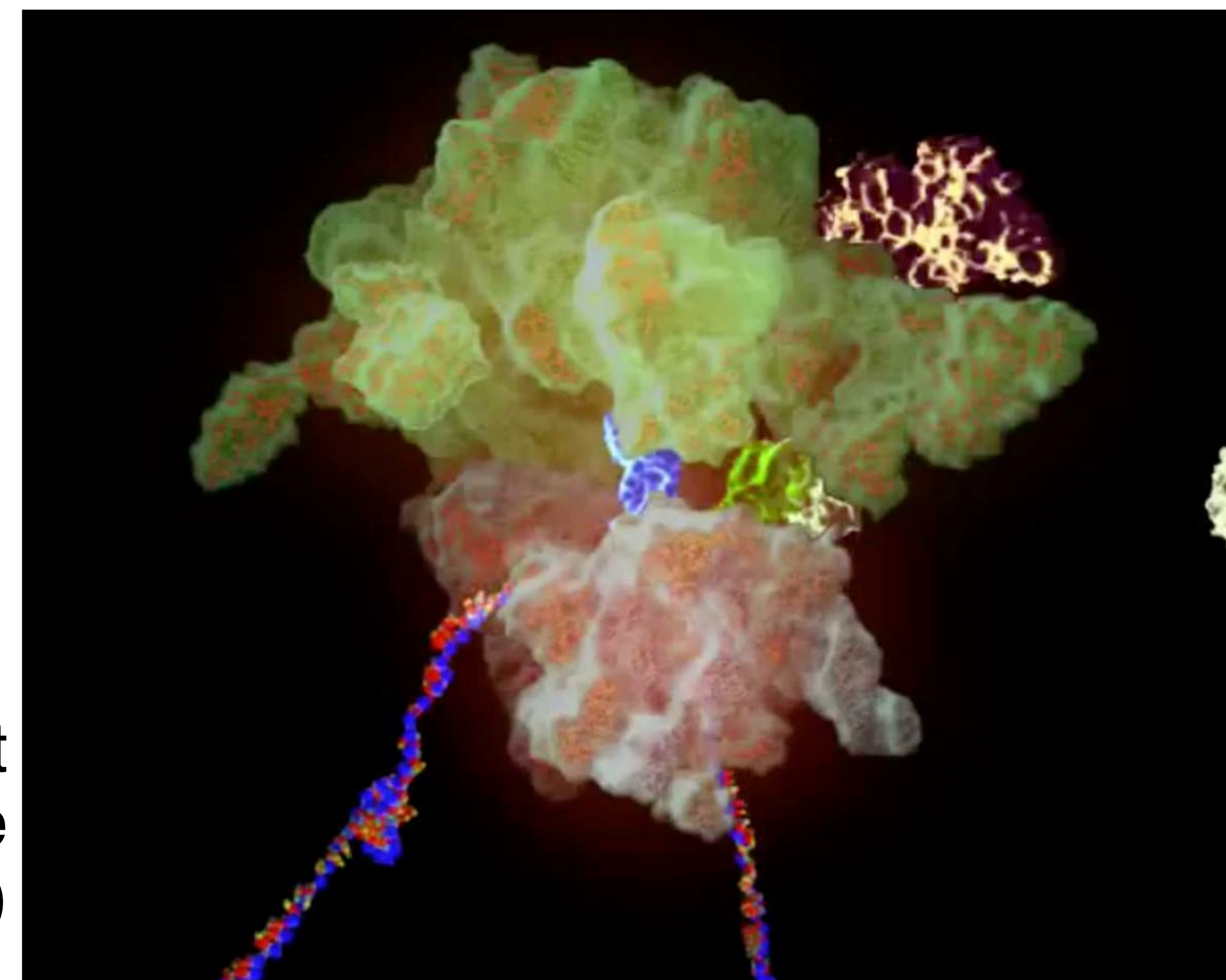
# Biological macromolecules are **EXCITING** molecules



Structure of hemoglobin subunit



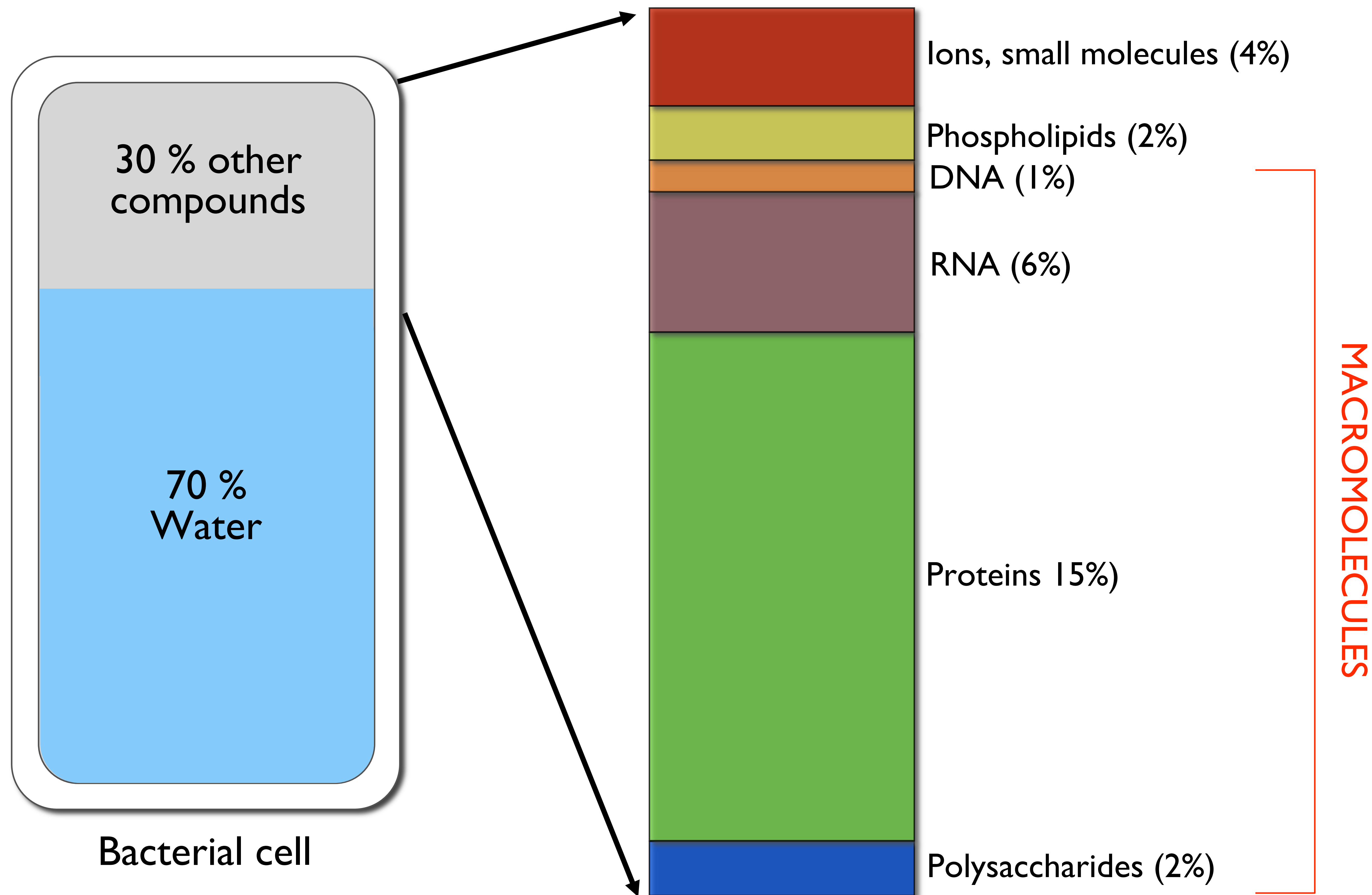
Newly synthesized protein (silk fibroin)



Folding of nascent protein (on the ribosome)



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





# Biological macromolecules: biopolymers

Polymers:  
chains built up from monomers

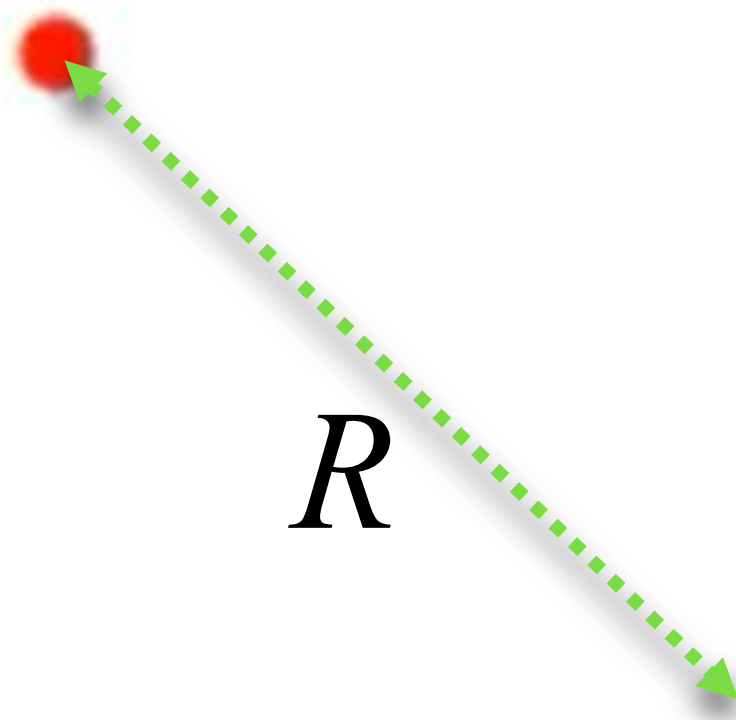
Number of monomers:  $N \gg 1$ ;  
Typically,  $N \sim 10^2 - 10^4$ ,  
but, in DNA, e.g.:  $N \sim 10^9 - 10^{10}$

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., $\alpha$ -glycosidic)
Protein polymer (e.g., microtubule)	Protein (e.g., tubulin)	Secondary

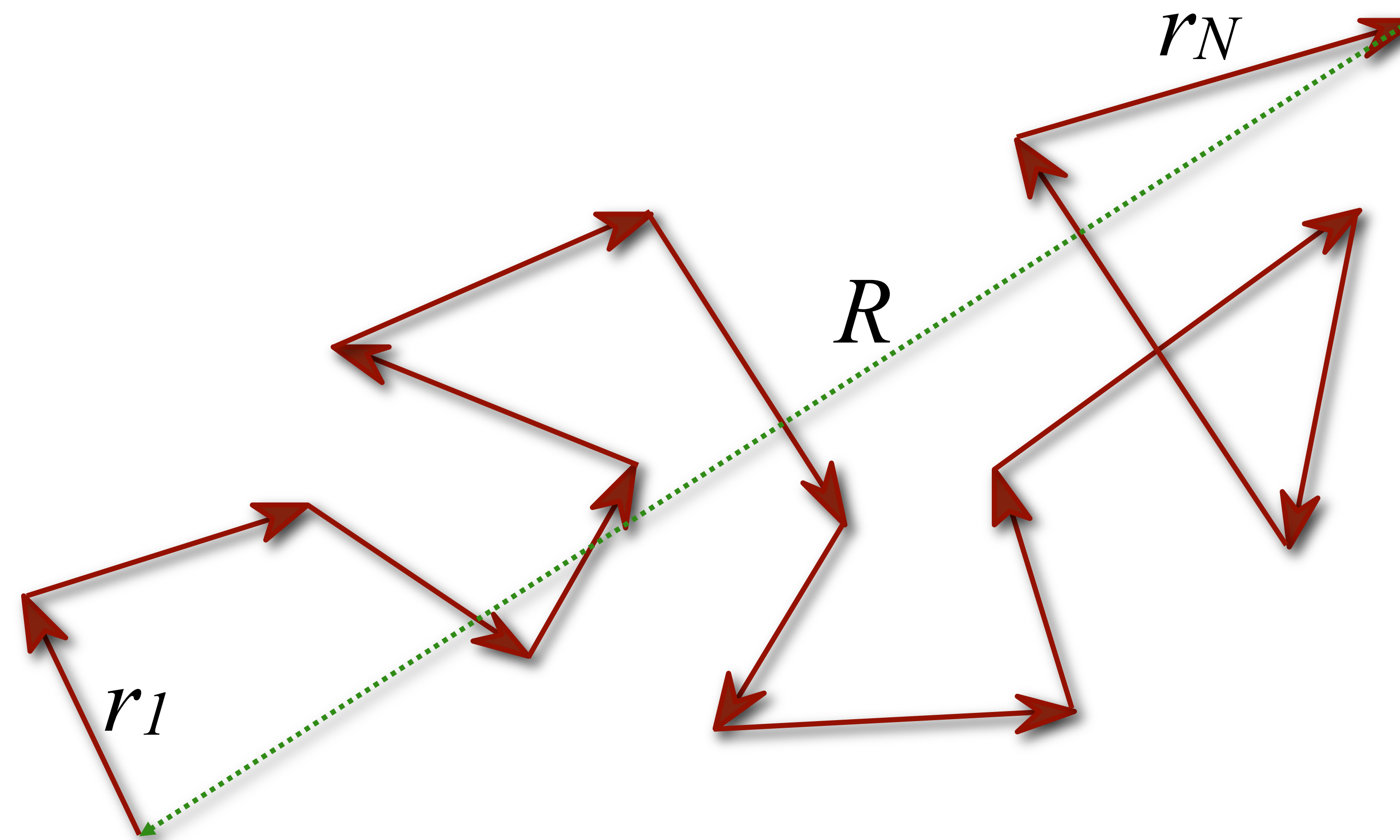


# Shape of the polymer chain resembles random walk

Brownian motion:  
“random walk”



Shape of polymer:  
“random chain”



“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**.

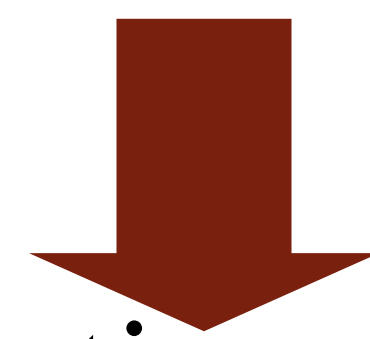
In case of Brownian-movement  $R$  = displacement,  $N$  = number of elementary steps,  $L$  = total path length, and  $l$  = mean free path length.



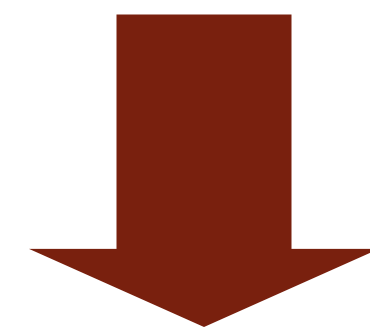
# Biopolymer elasticity

## Entropic (thermal) elasticity

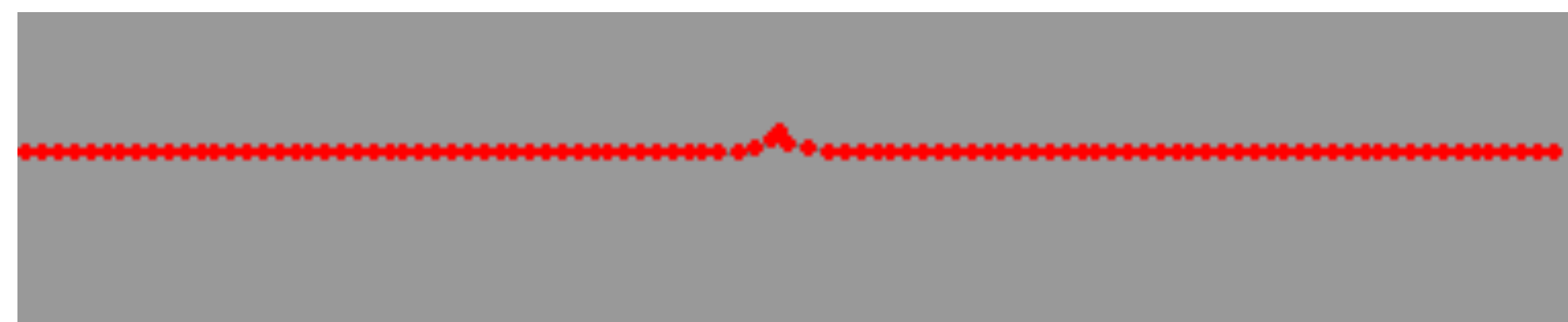
Polymer chain goes through thermal fluctuations of shape.



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).

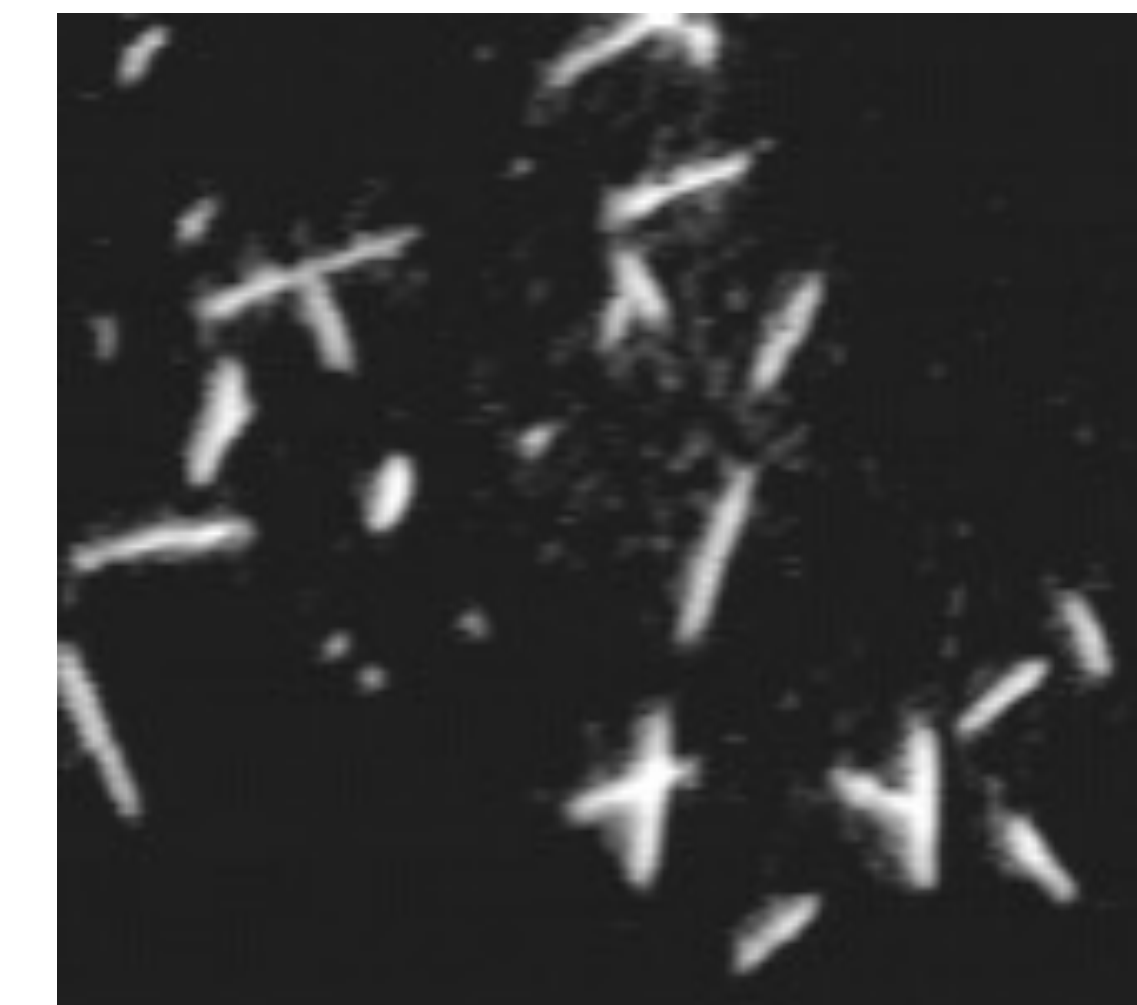


## Relationship between persistence length ( $l$ ) and contour length ( $L$ ) in biopolymers

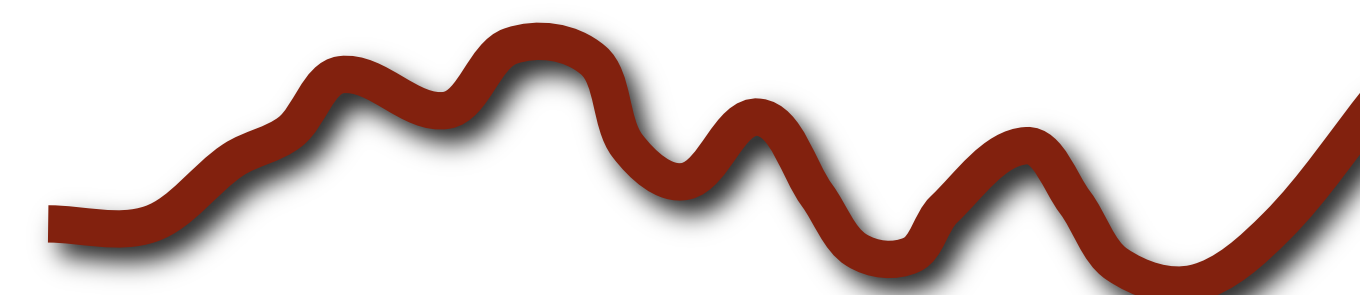
Rigid chain:  $l \gg L$



Microtubule



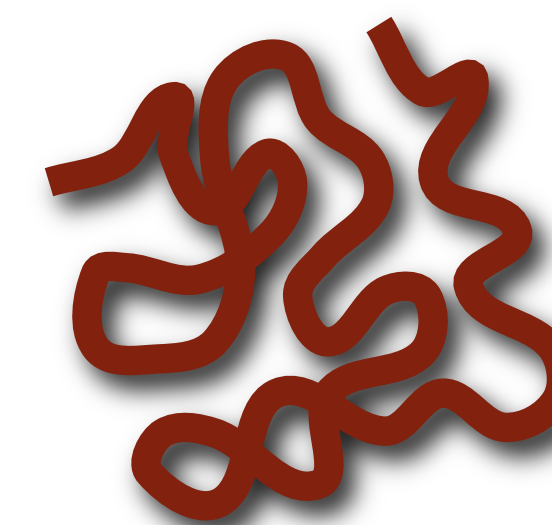
Semiflexible chain:  $l \sim L$



Actin filament



Flexible chain:  $l \ll L$



DNA molecule

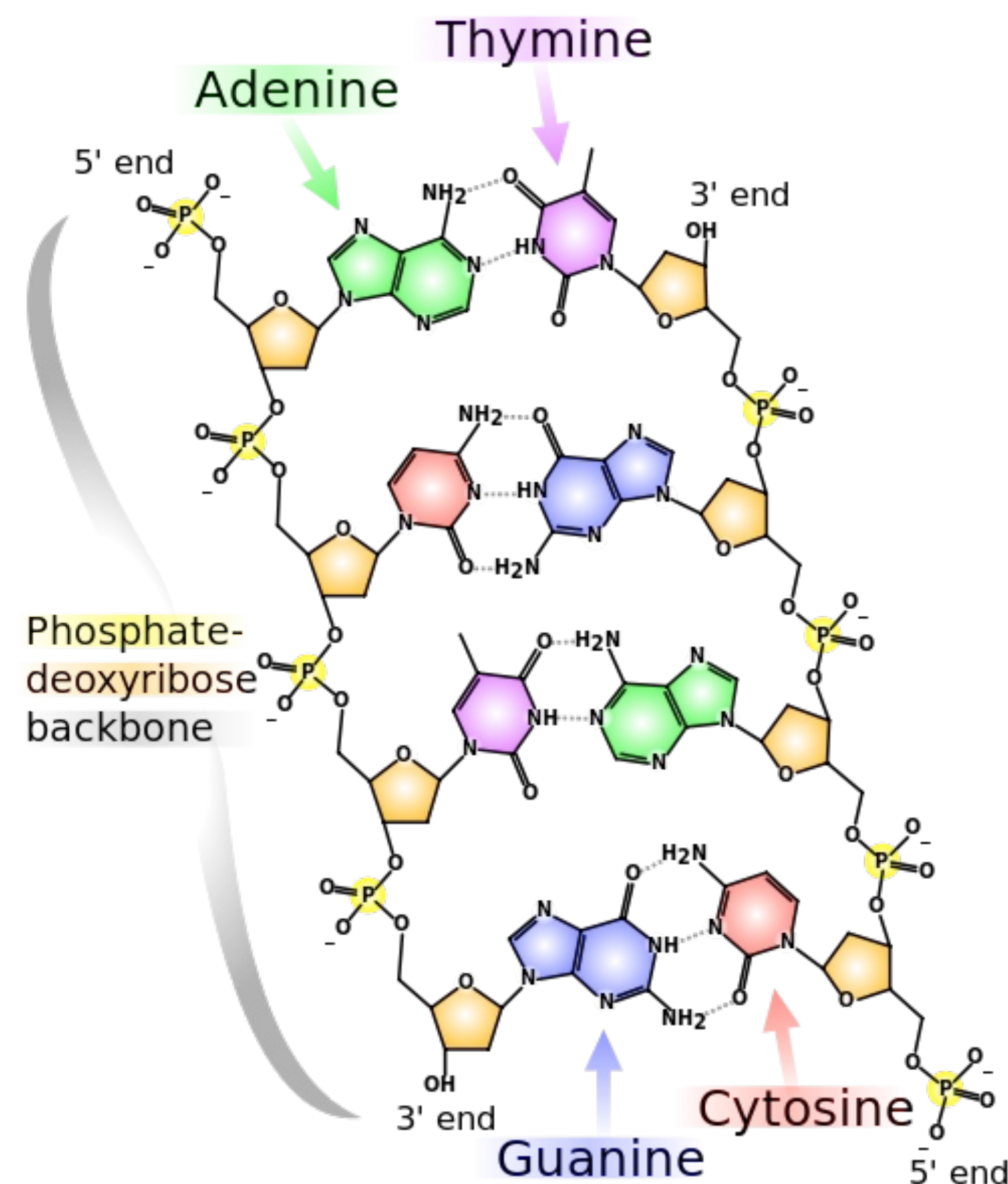




# I. DNA: deoxyribonucleic acid

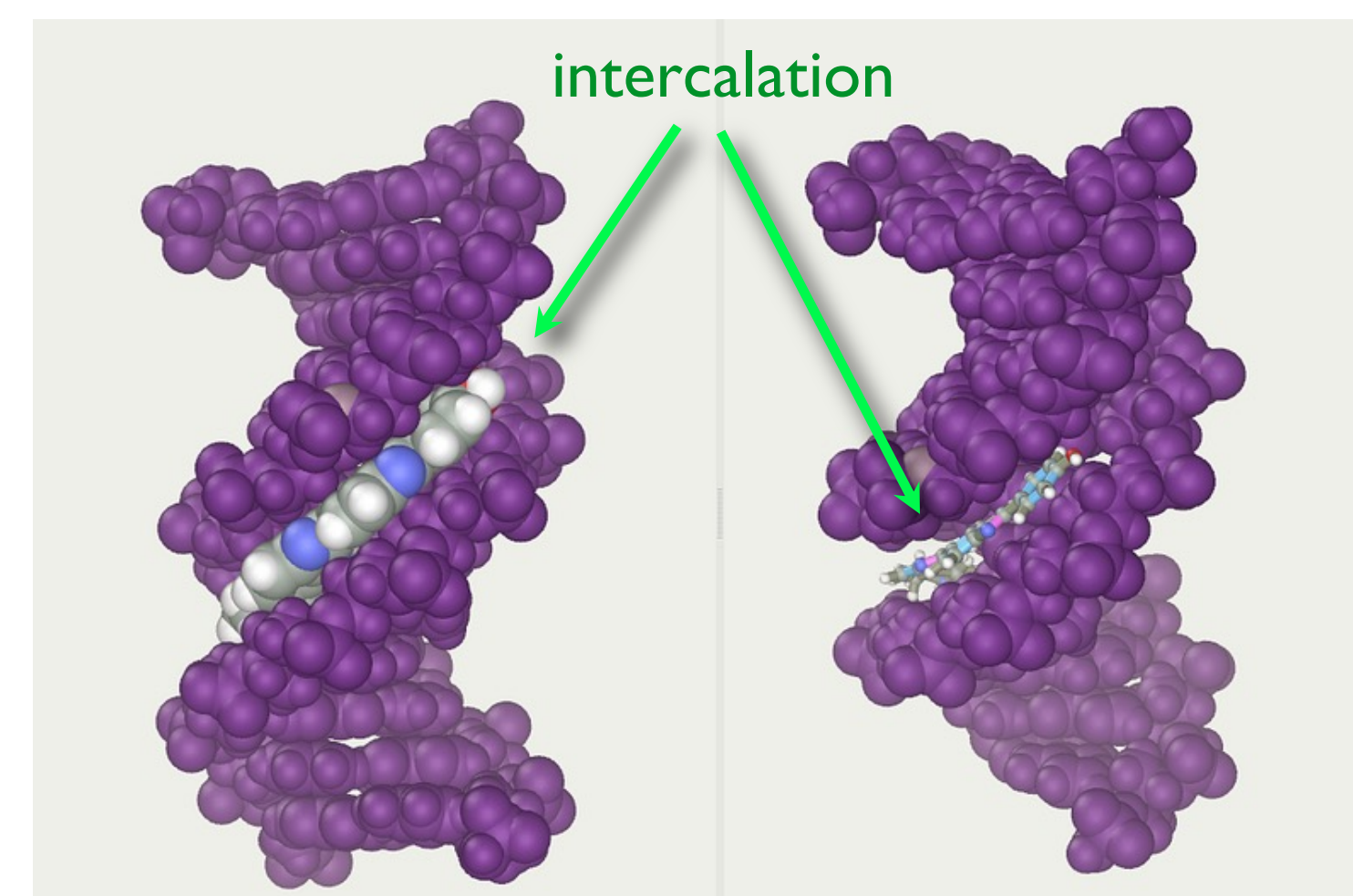
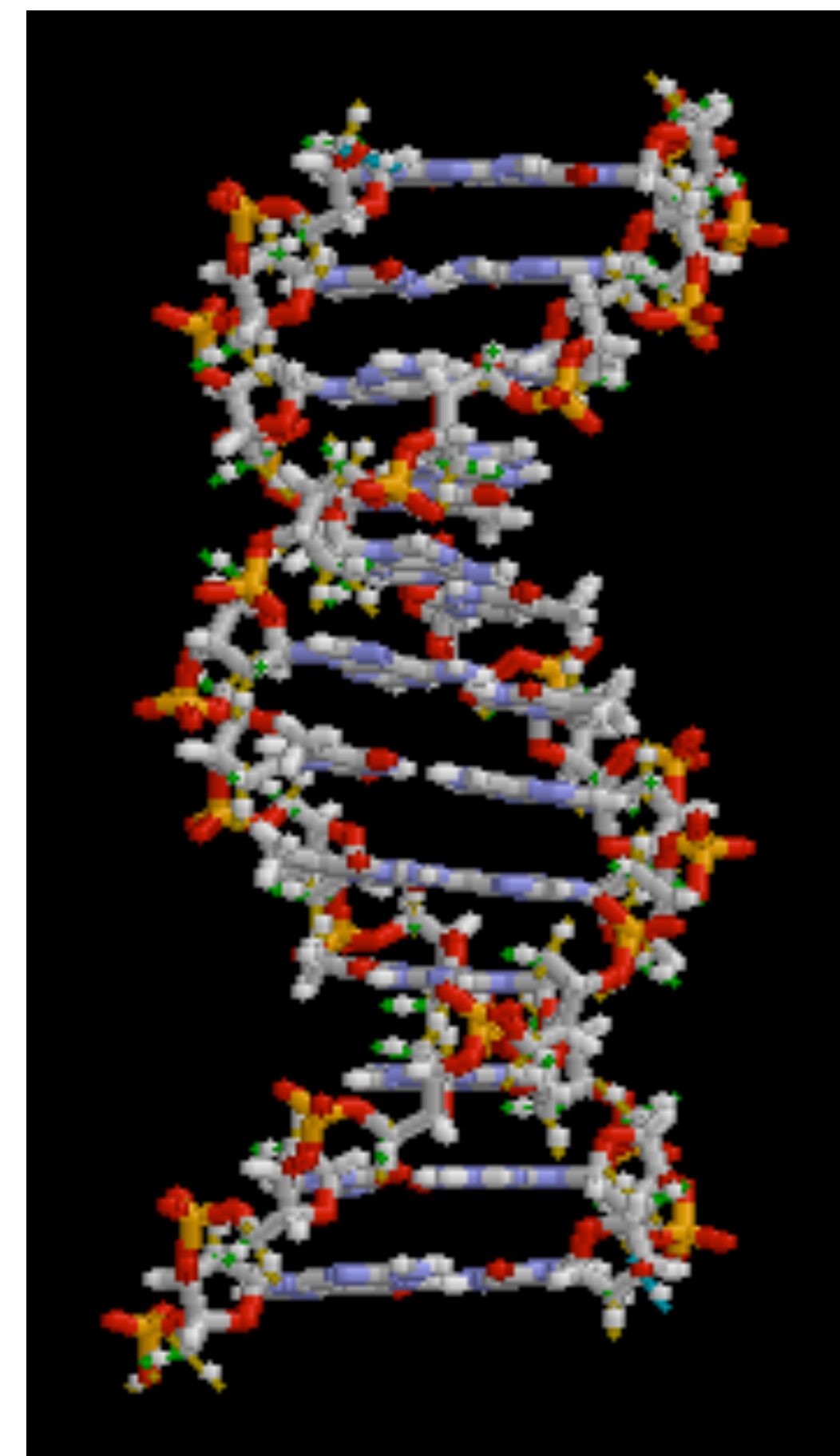
**Function:** molecule of biological information storage

Chemical structure



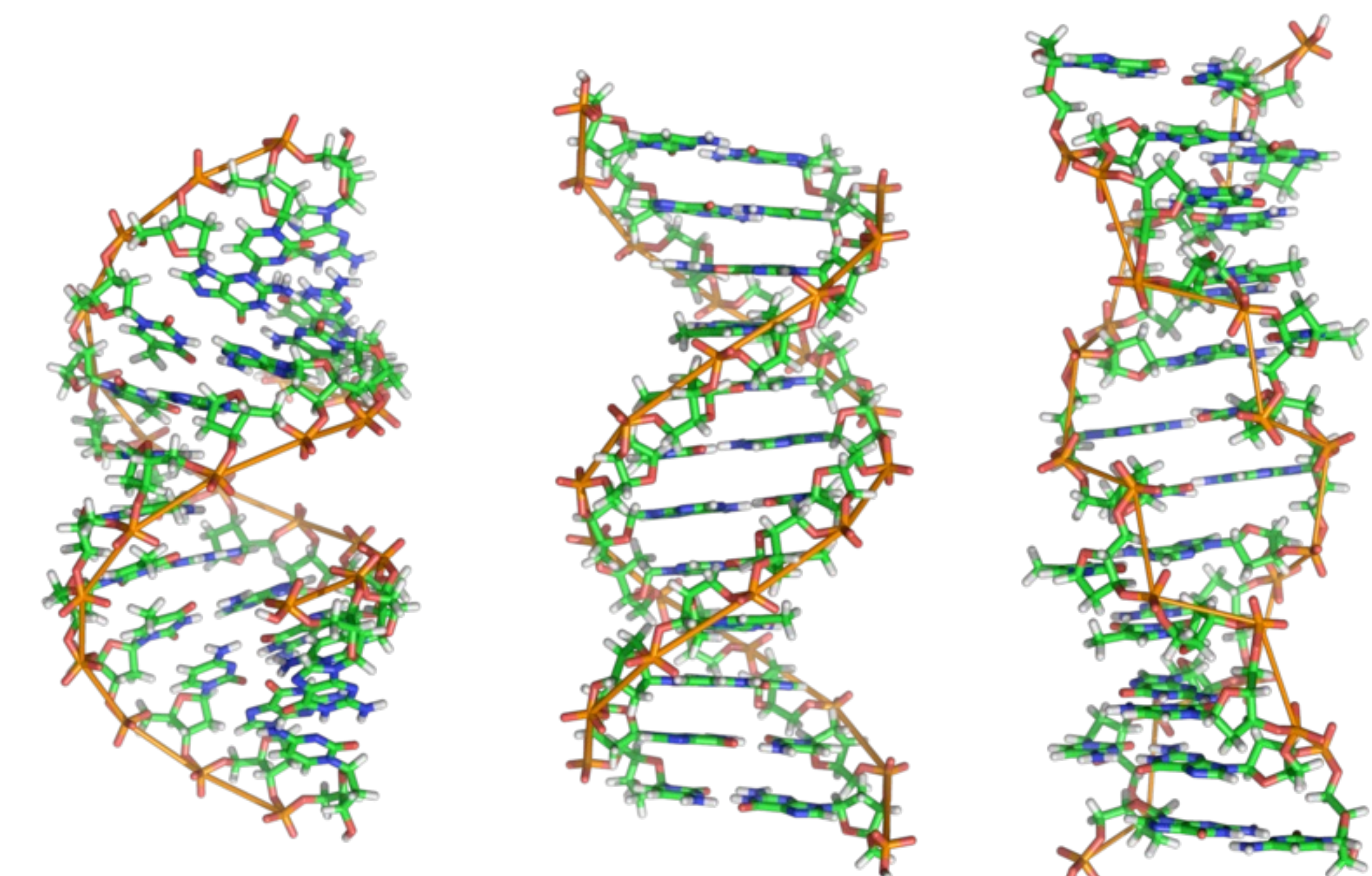
“Watson-Crick” base pairing: via H-bonds  
Gene sequence is of central significance in molecular genetics

3D structure: double helix



Large groove Small groove

Various DNA structures

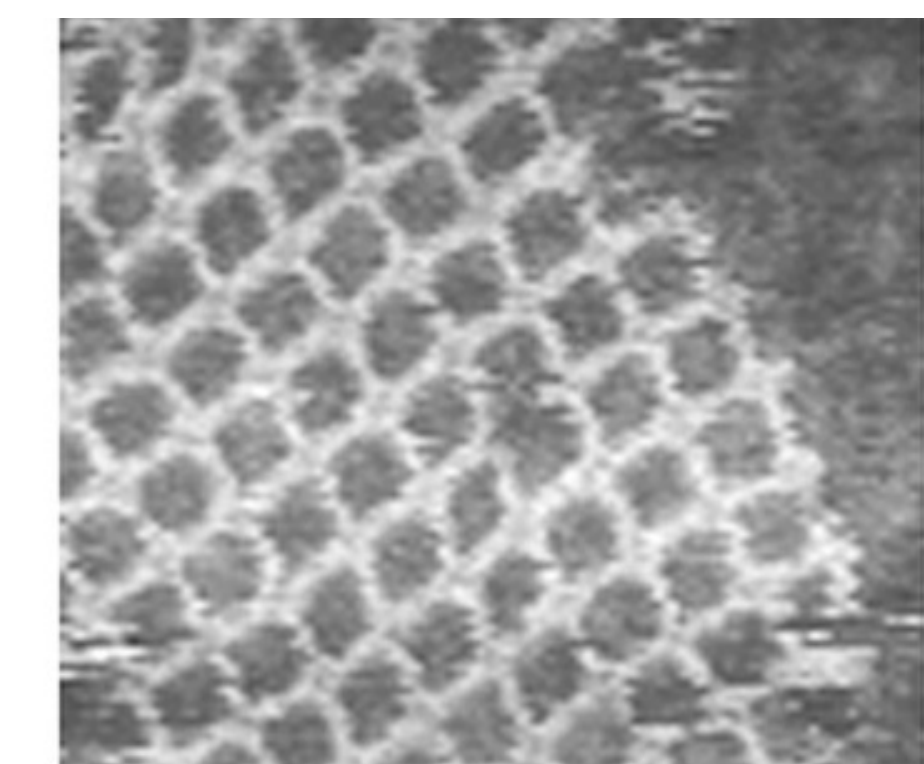
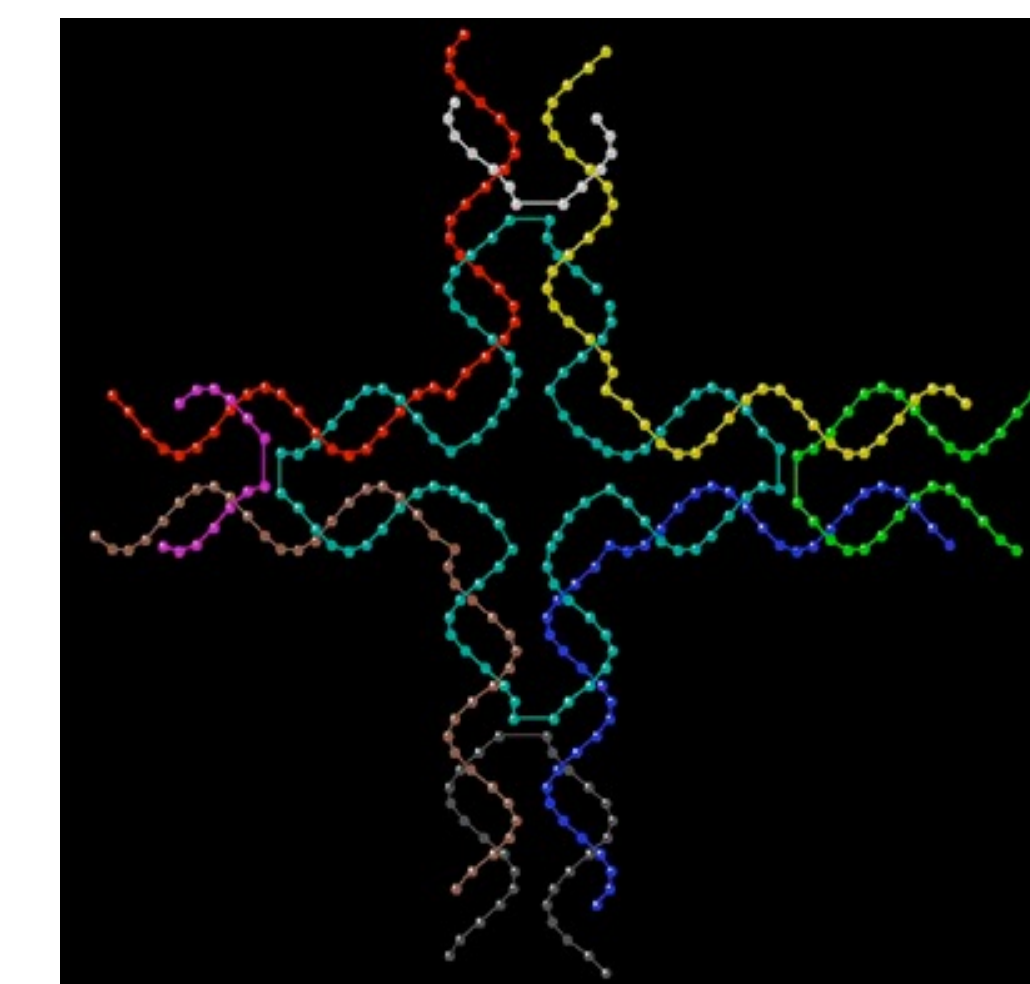


A-DNA

B-DNA

Z-DNA

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

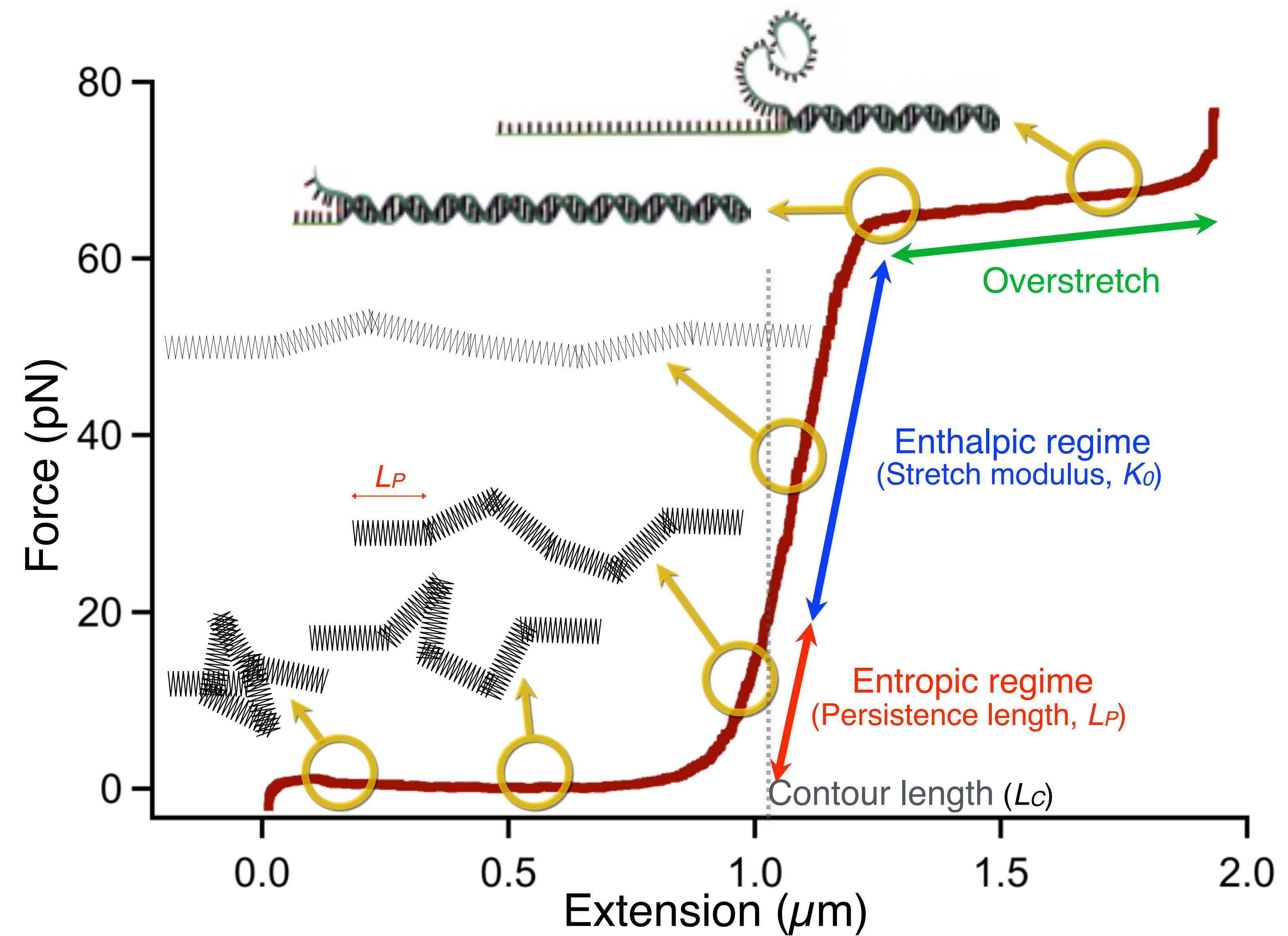
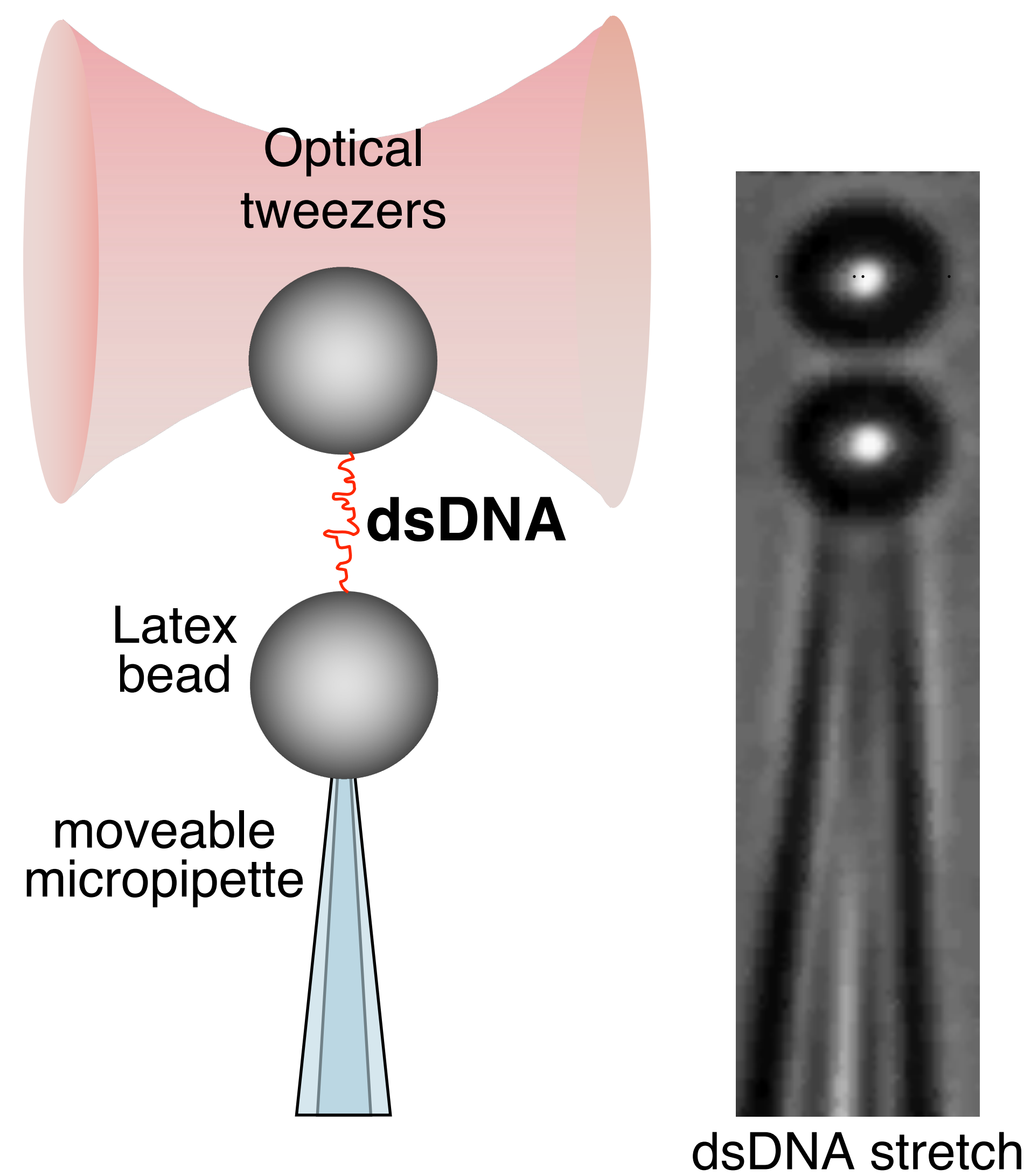


100 nm

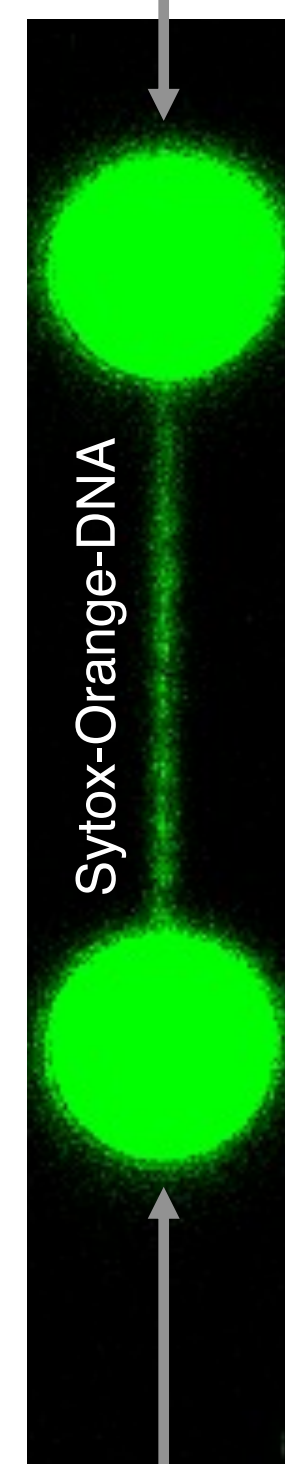
DNA nanostructures (origami)  
Depends on base-pairing order and hierarchy



# The DNA molecule is elastic!

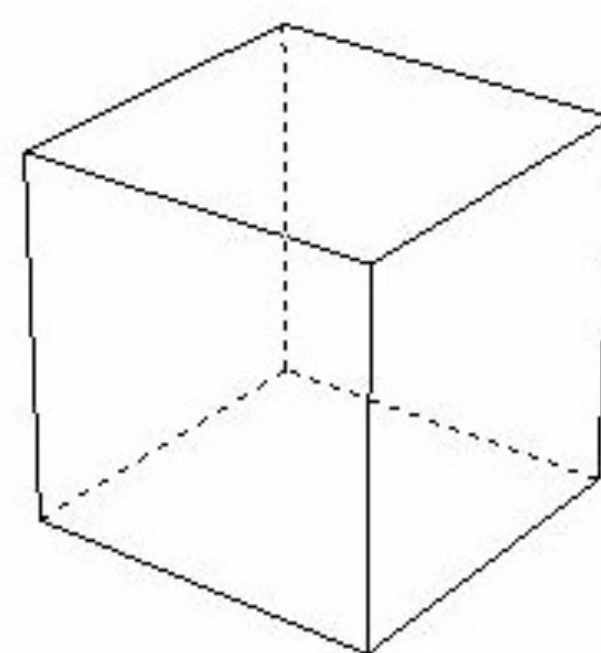
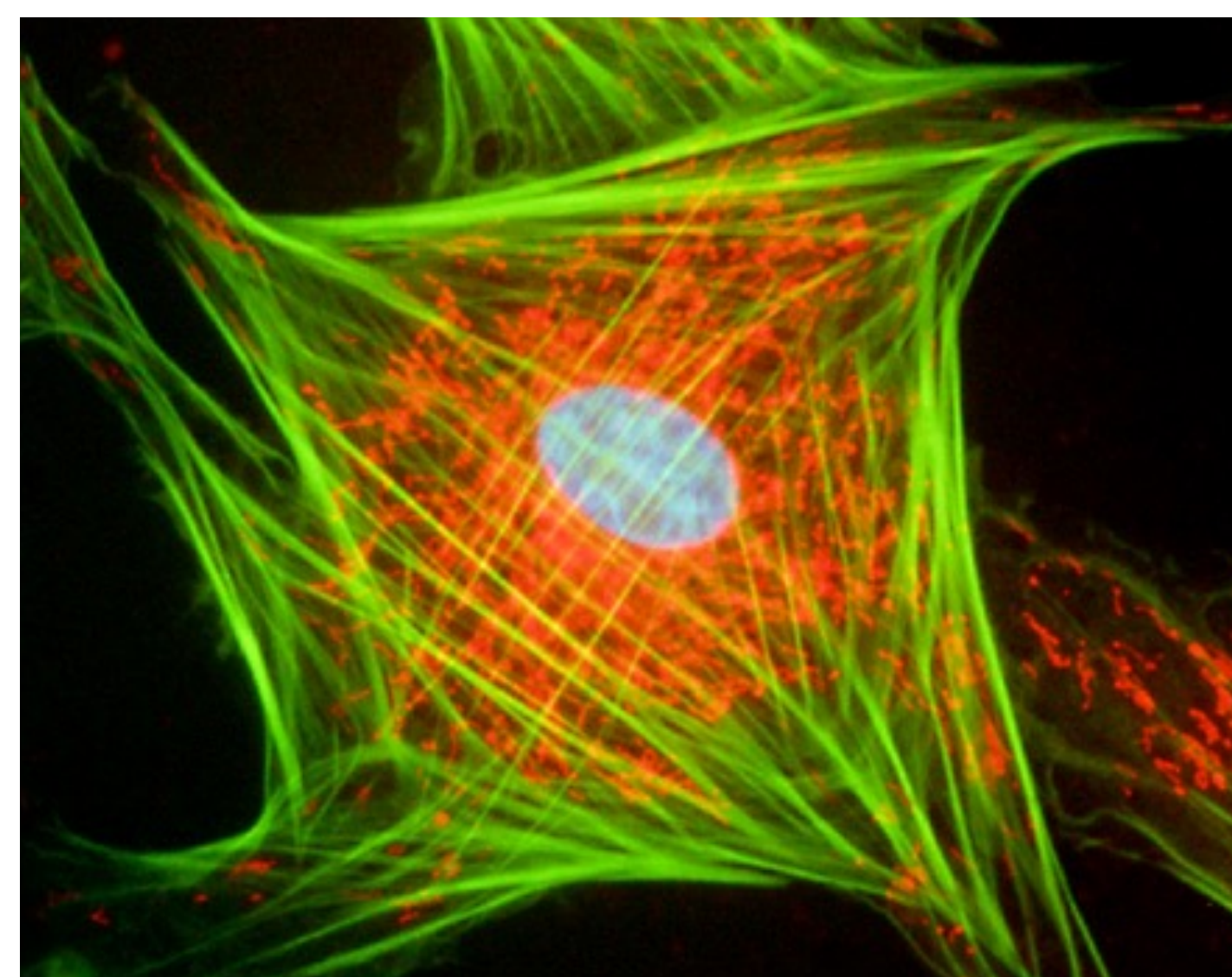


Optical trap





# How much DNA is in a cell?

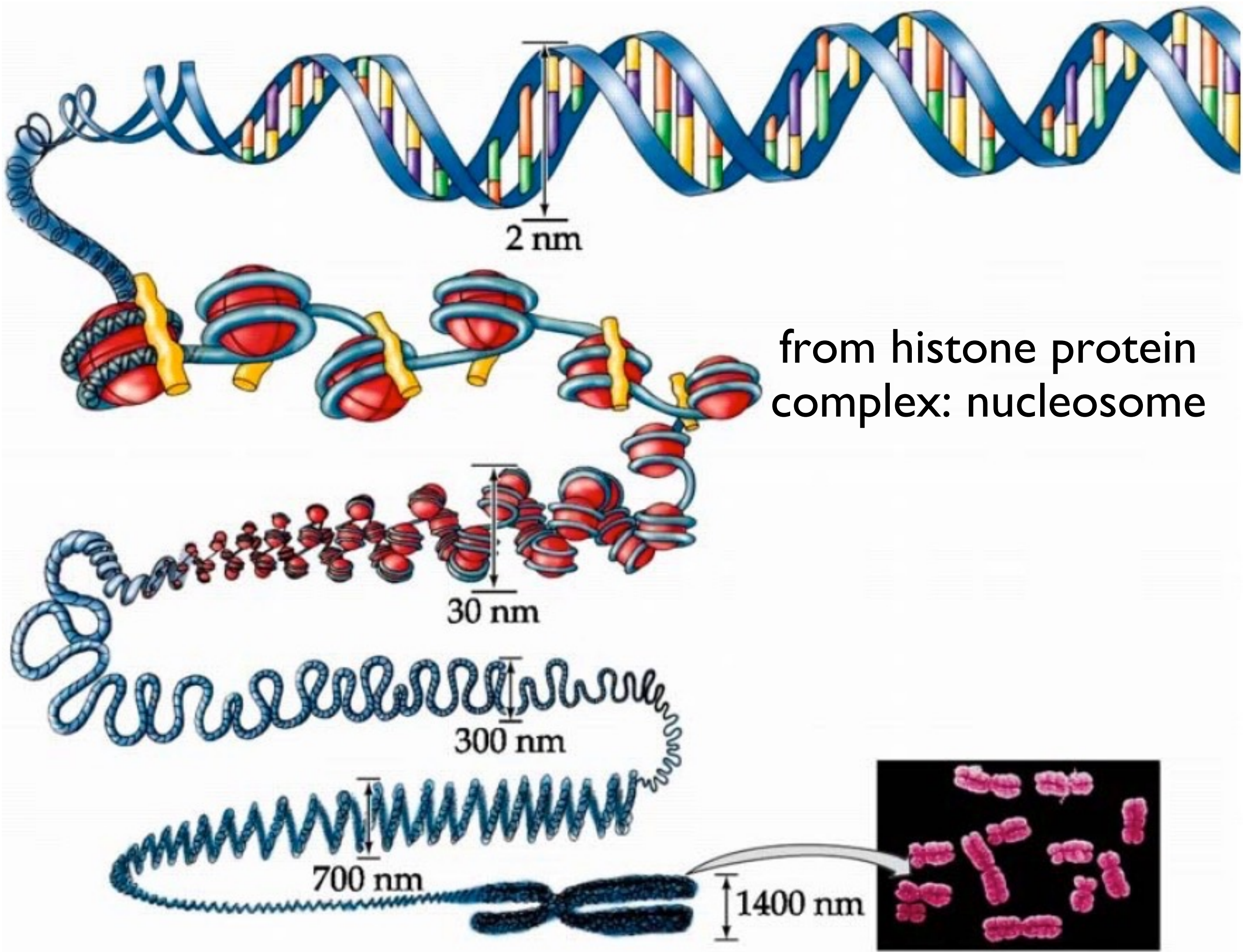


Simplified cell  
model: cube

	<b>Cell:</b> 20 $\mu\text{m}$ edge cube	Analog - <b>Lecture hall:</b> 20 m edge cube
DNA thickness	2 nm	2 mm
Full length of human DNA	$\sim 2$ m	$\sim 2000$ km (!!!) (Perimeter of Hungary: $\sim 2200$ km)
Persistence length of dsDNA	$\sim 50$ nm	$\sim 50$ cm
End-to-end distance (R)	$\sim 350$ $\mu\text{m}$ (!)	$\sim 350$ m (!)
Volume of fully compacted DNA	$\sim 2 \times 2 \times 2$ $\mu\text{m}^3$	$\sim 2 \times 2 \times 2$ $\text{m}^3$ (= 8 $\text{m}^3$ )

**Solution:** DNA needs to be packed

Chromosome condensation

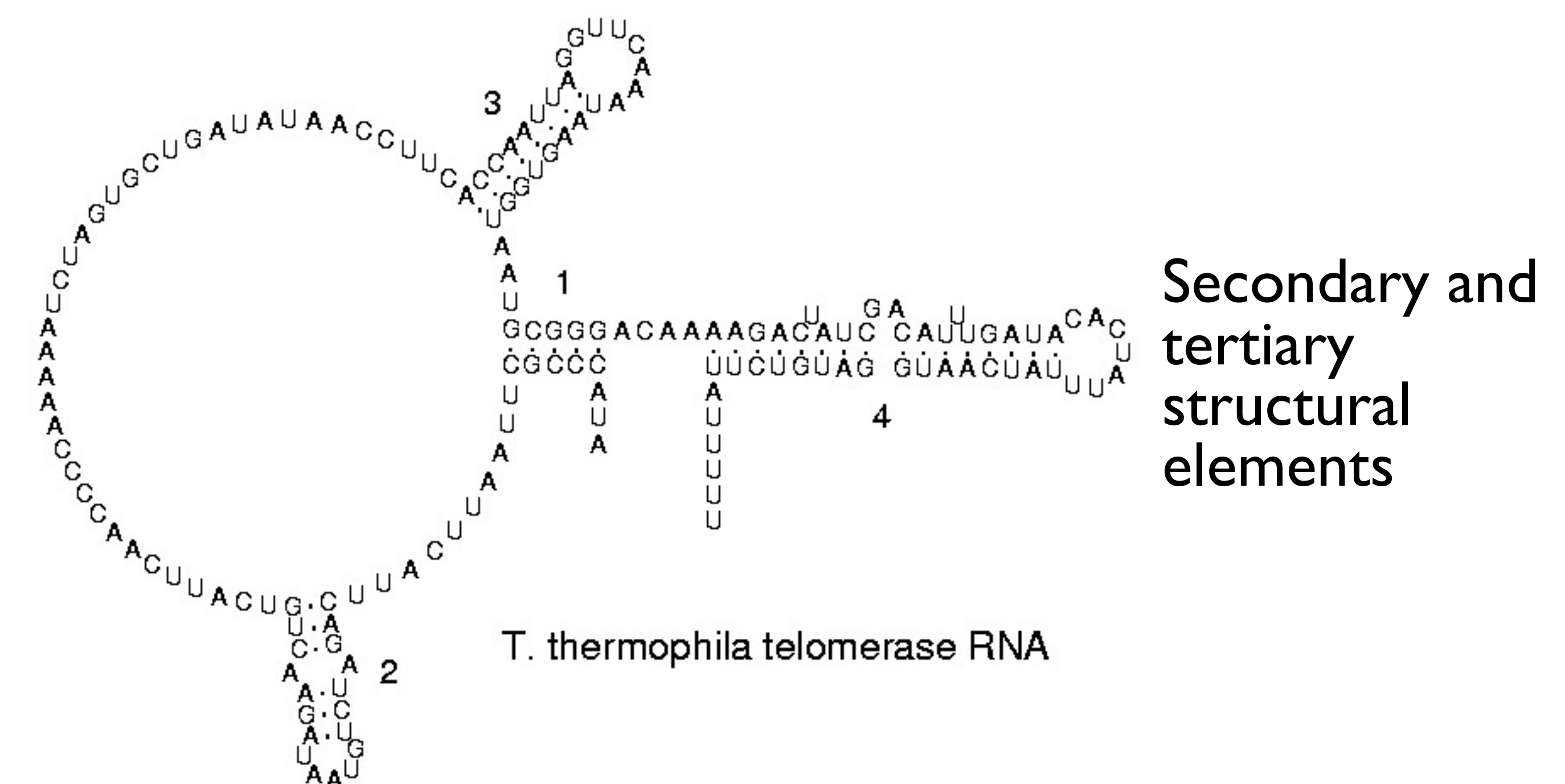
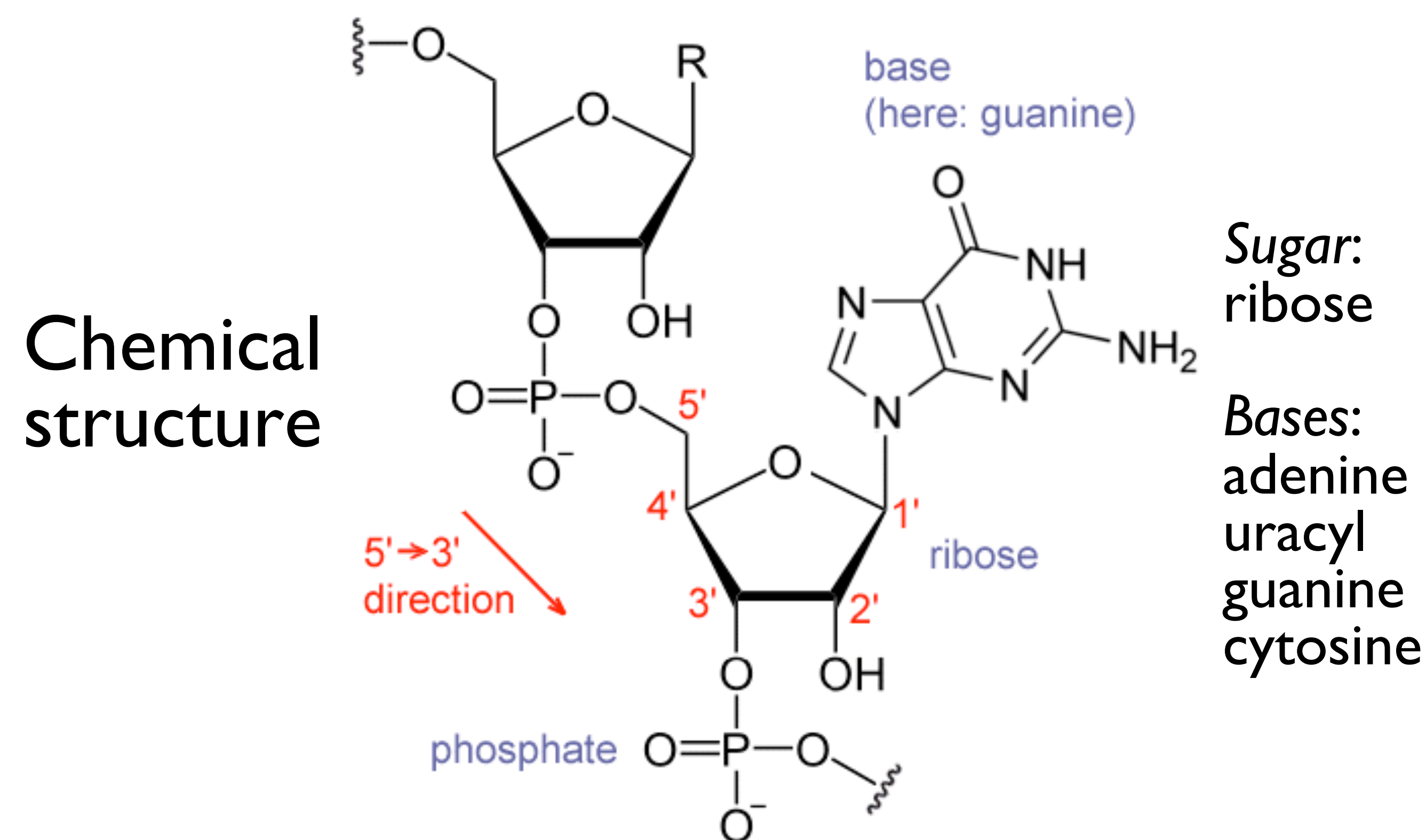


- **Condensins** play a role in high-order DNA packaging
- DNA chain: complex linear path with roadblocks!

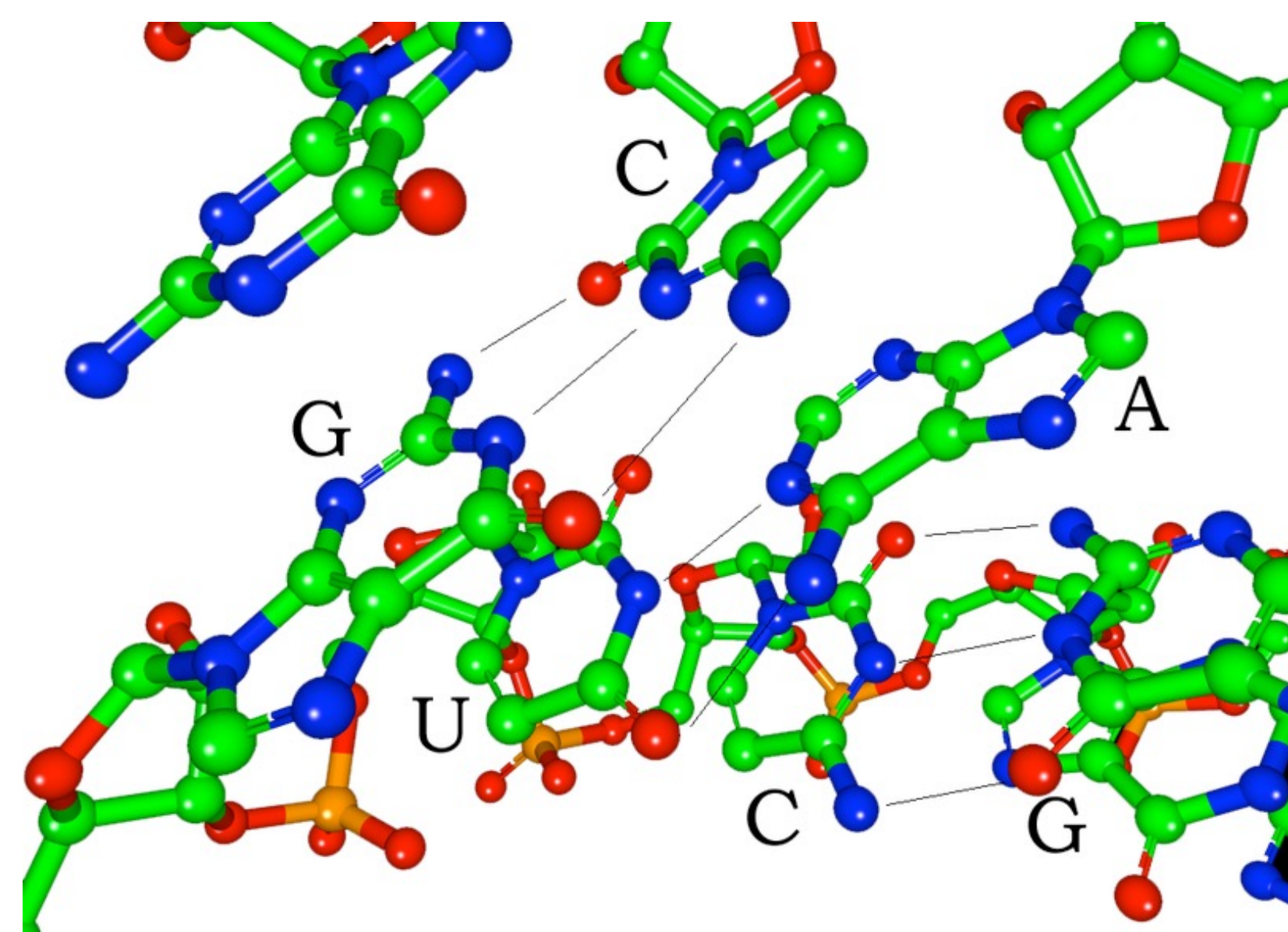


# 2. RNA: Ribonucleic acid

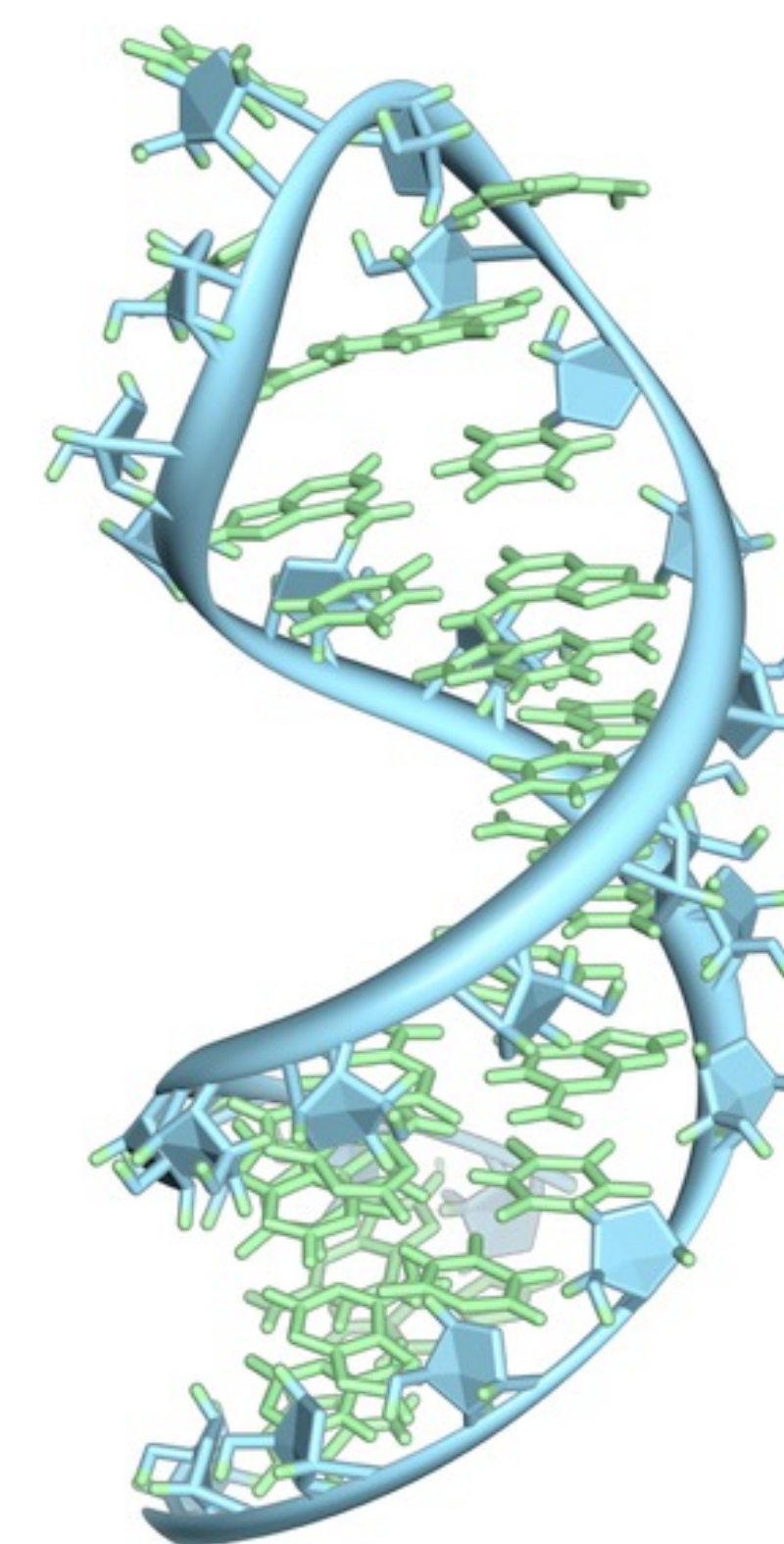
**Function:** information transfer (transcription), structural element (e.g., ribosome), regulation (turning gene expression on and off)



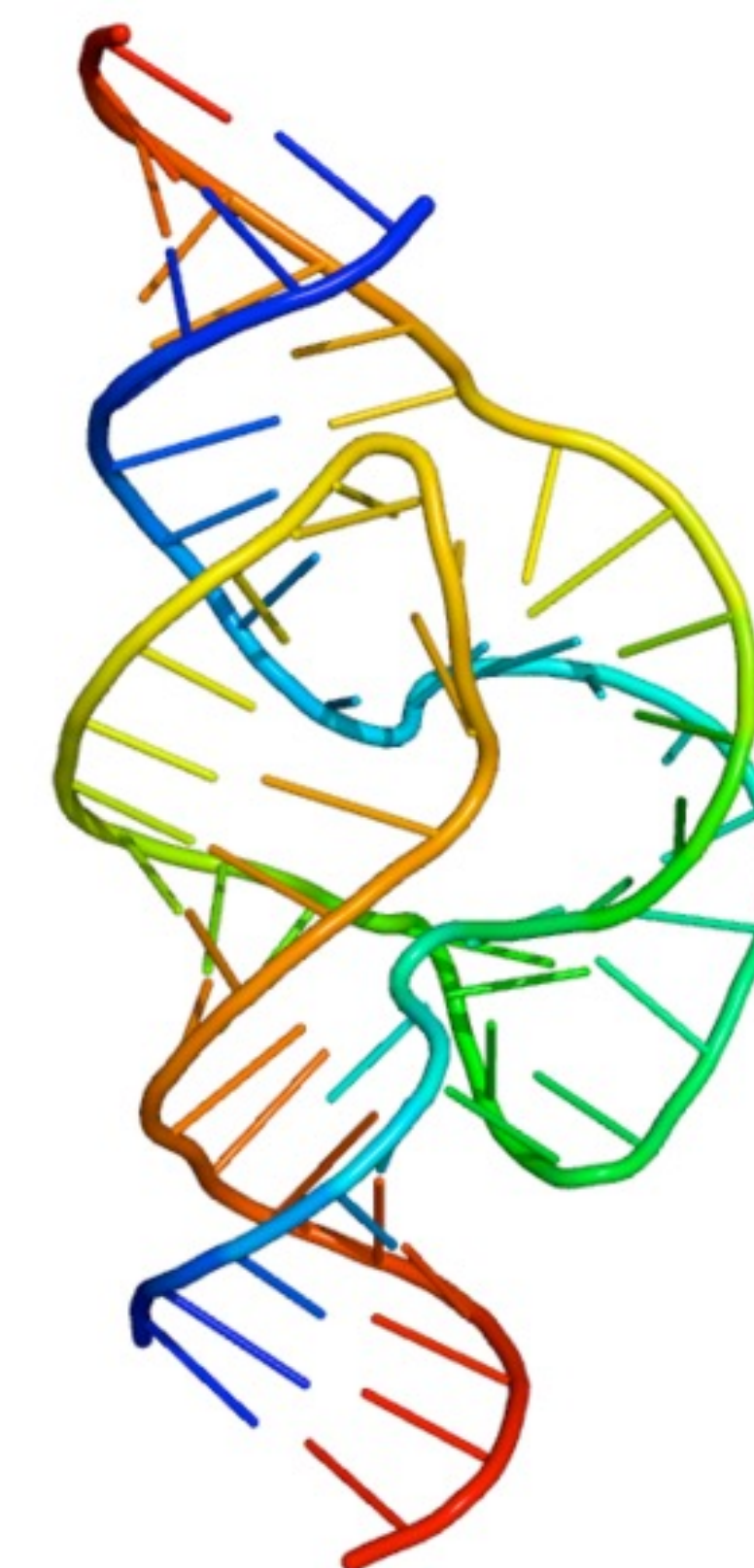
“Watson-Crick” base pairing



RNA hairpin



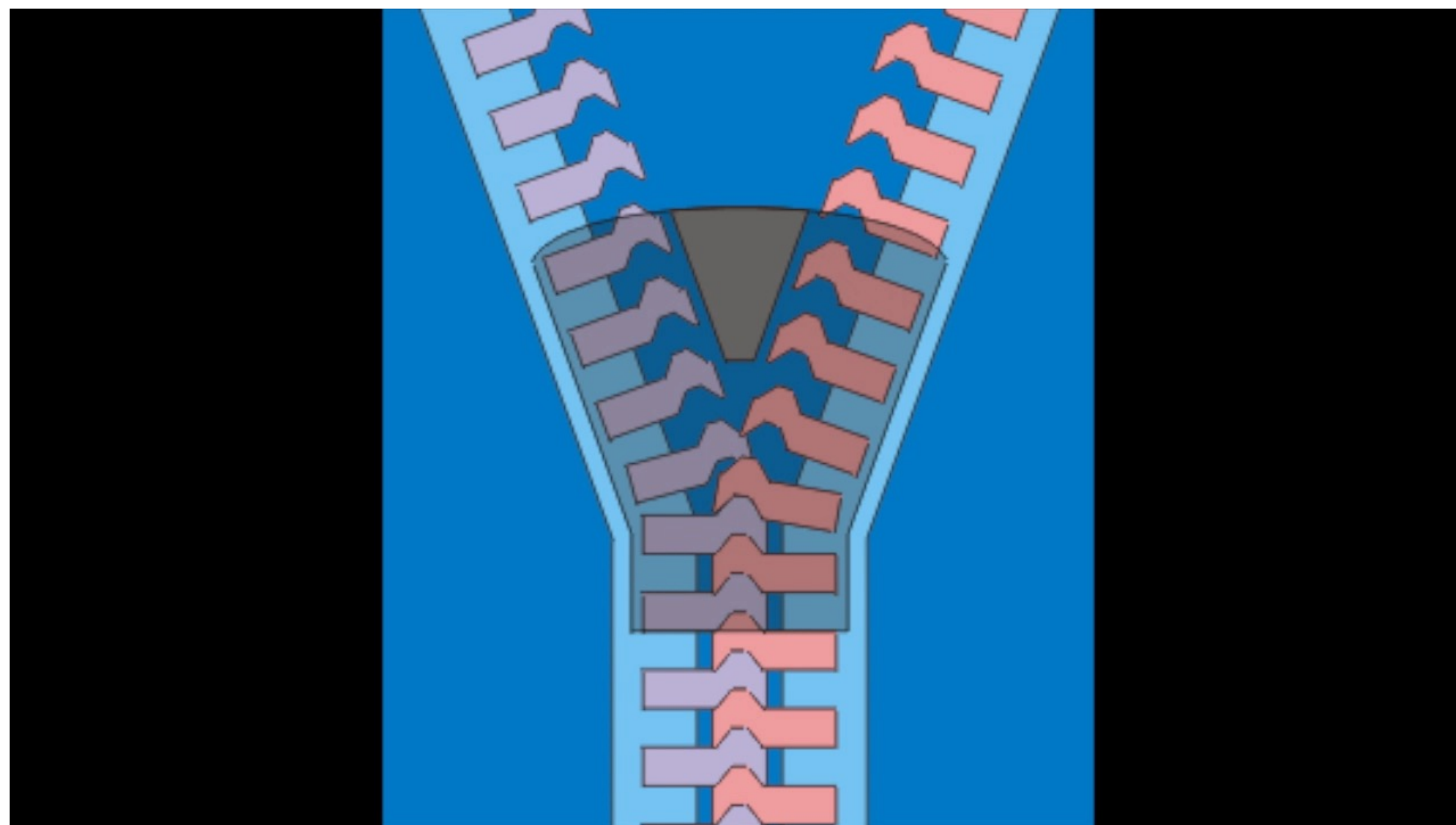
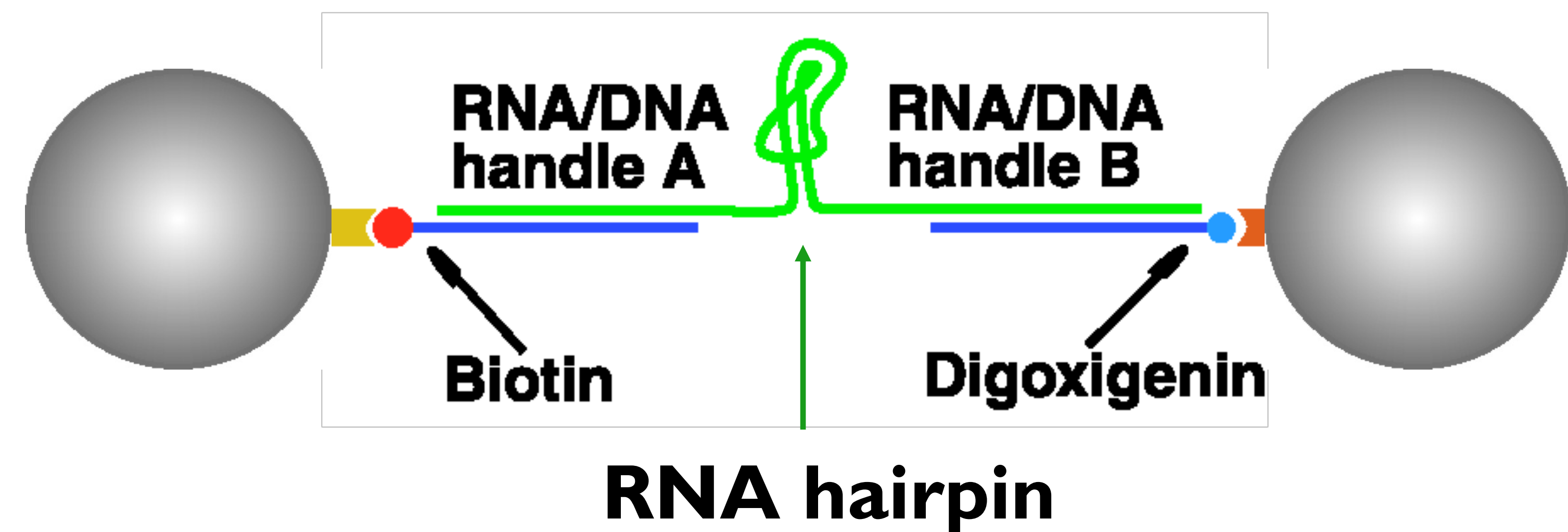
Complex structure (ribozyme)



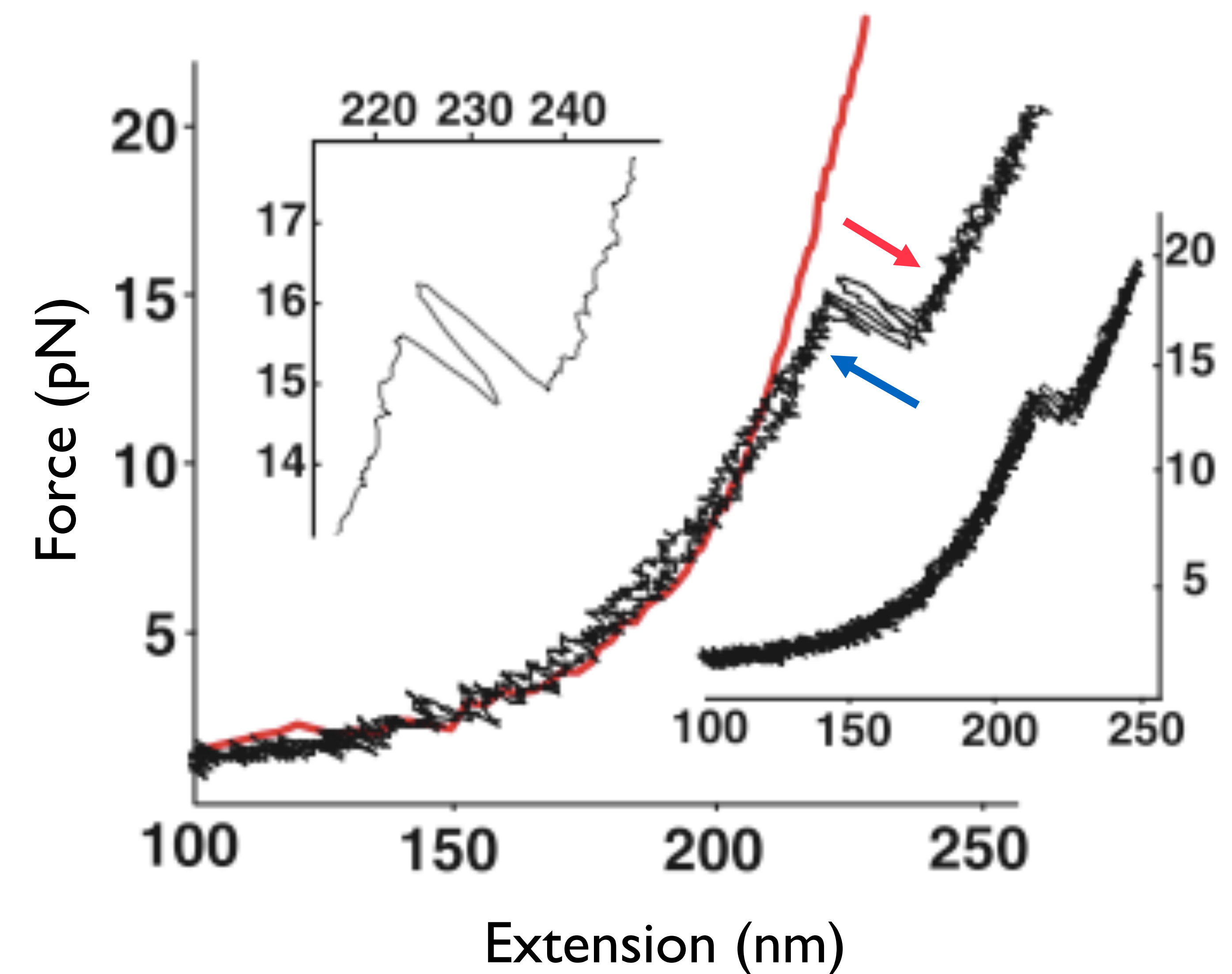


# RNA structure can be perturbed with mechanical force

Mechanical stretching with optical tweezers



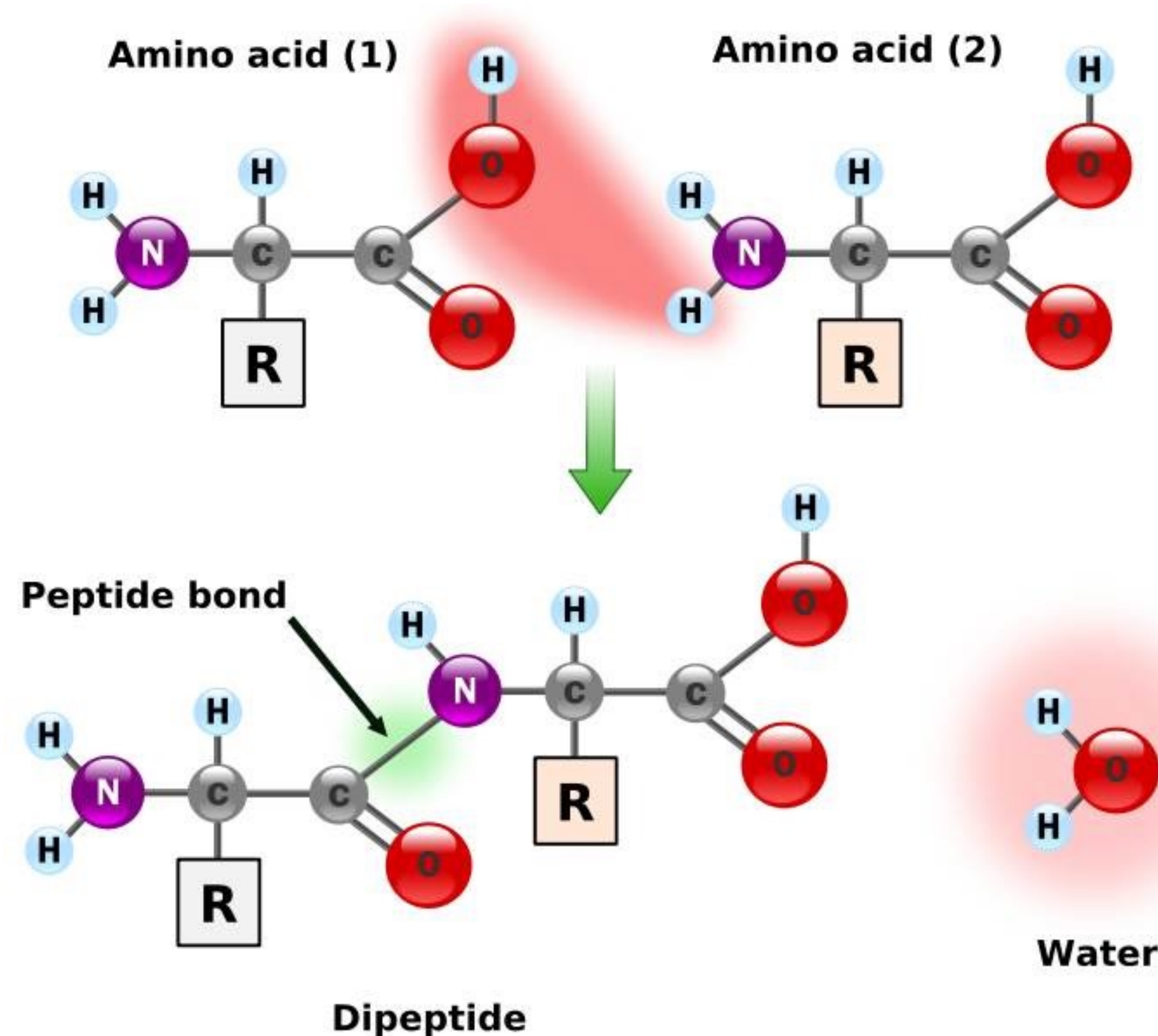
Mechanical **unfolding** of an RNA hairpin: nearly reversible process - the RNA rapidly **folds** when relaxed





# 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 release of water



# Protein structure

## Primary

Amino acid sequence

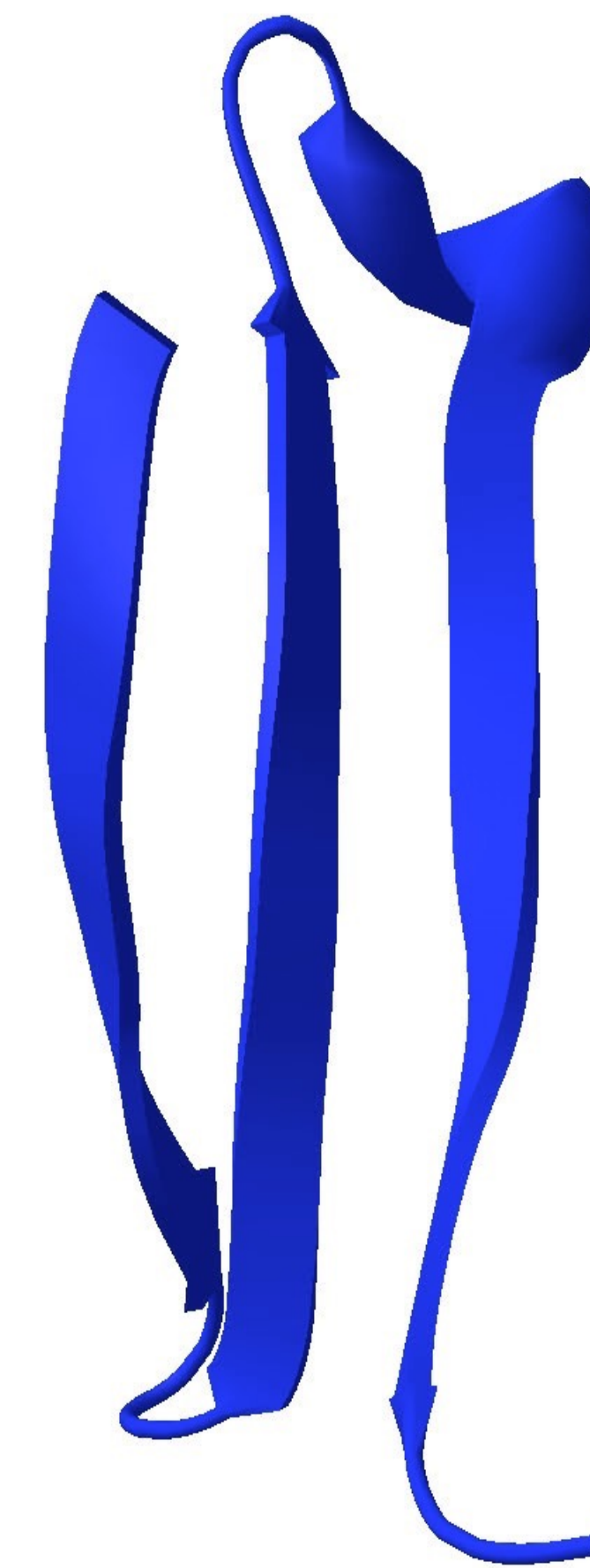
Determines spatial structure as well.

## Secondary

$\alpha$ -helix  
 $\beta$ -sheet  
 $\beta$ -turn ( $\beta$ -hairpin)



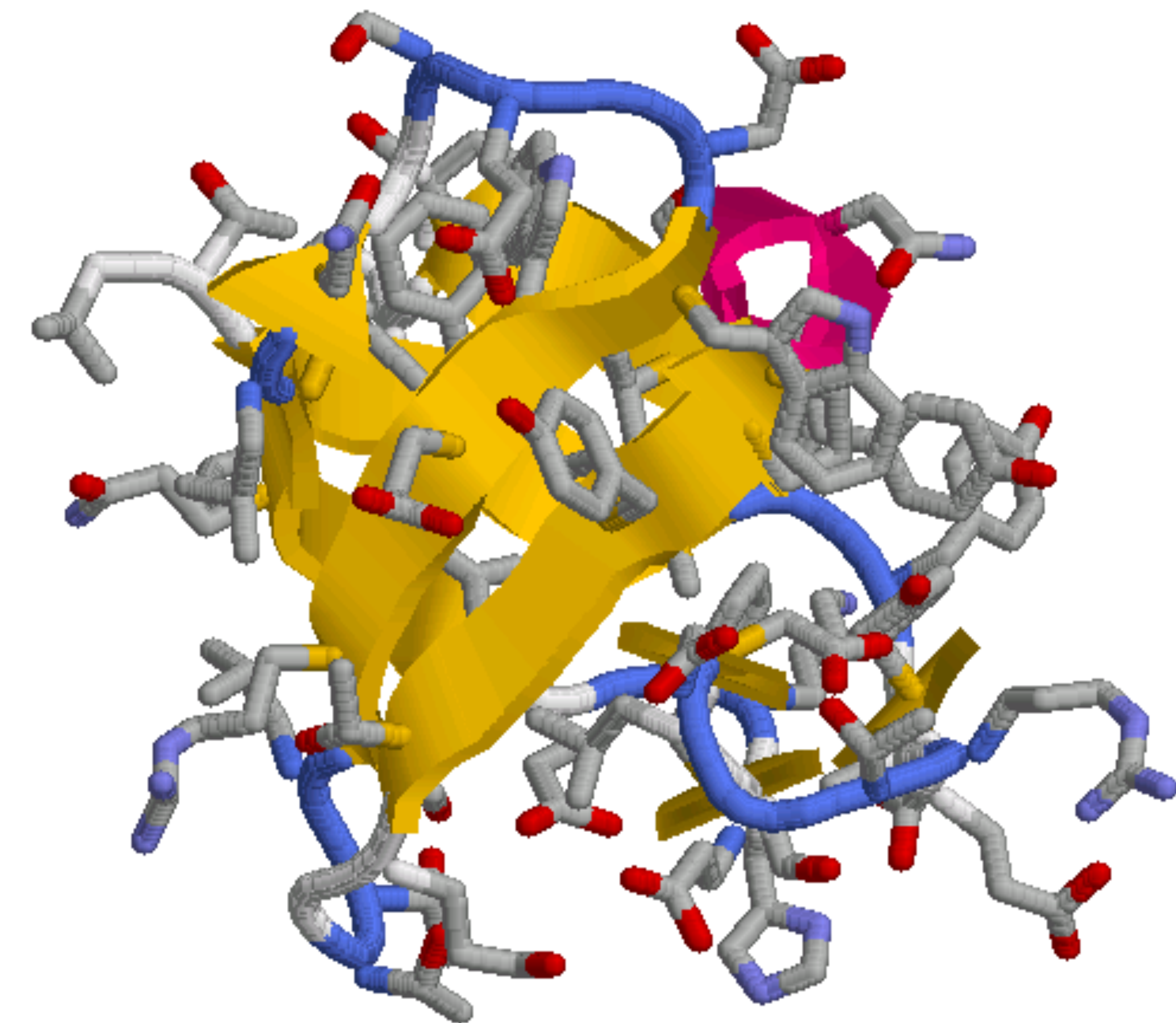
$\alpha$ -helix:  
•right handed  
•3.4 residue/turn  
•H-bridges



$\beta$ -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.



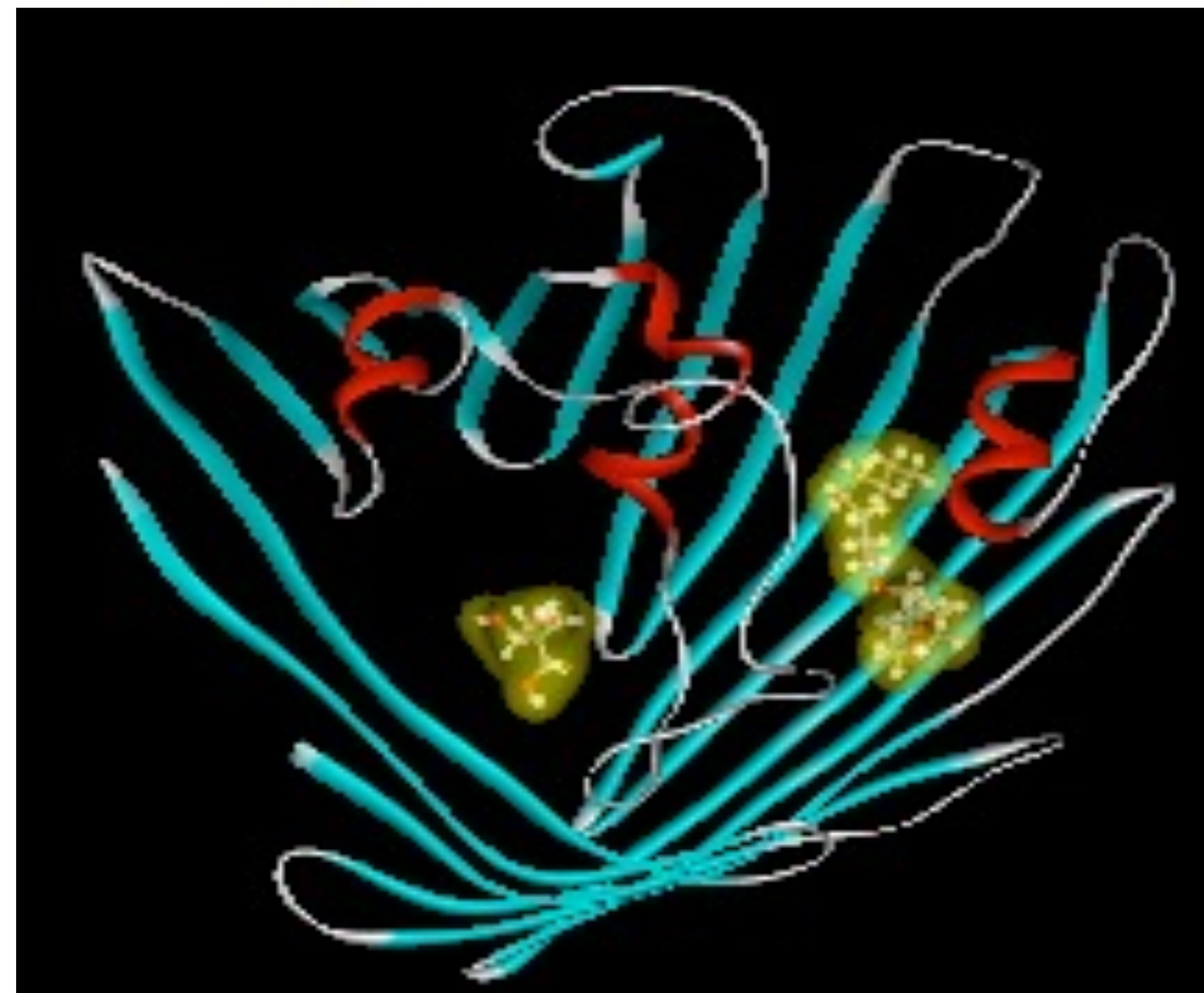
# Protein structure classes

1. All alpha



calmodulin

2. All beta

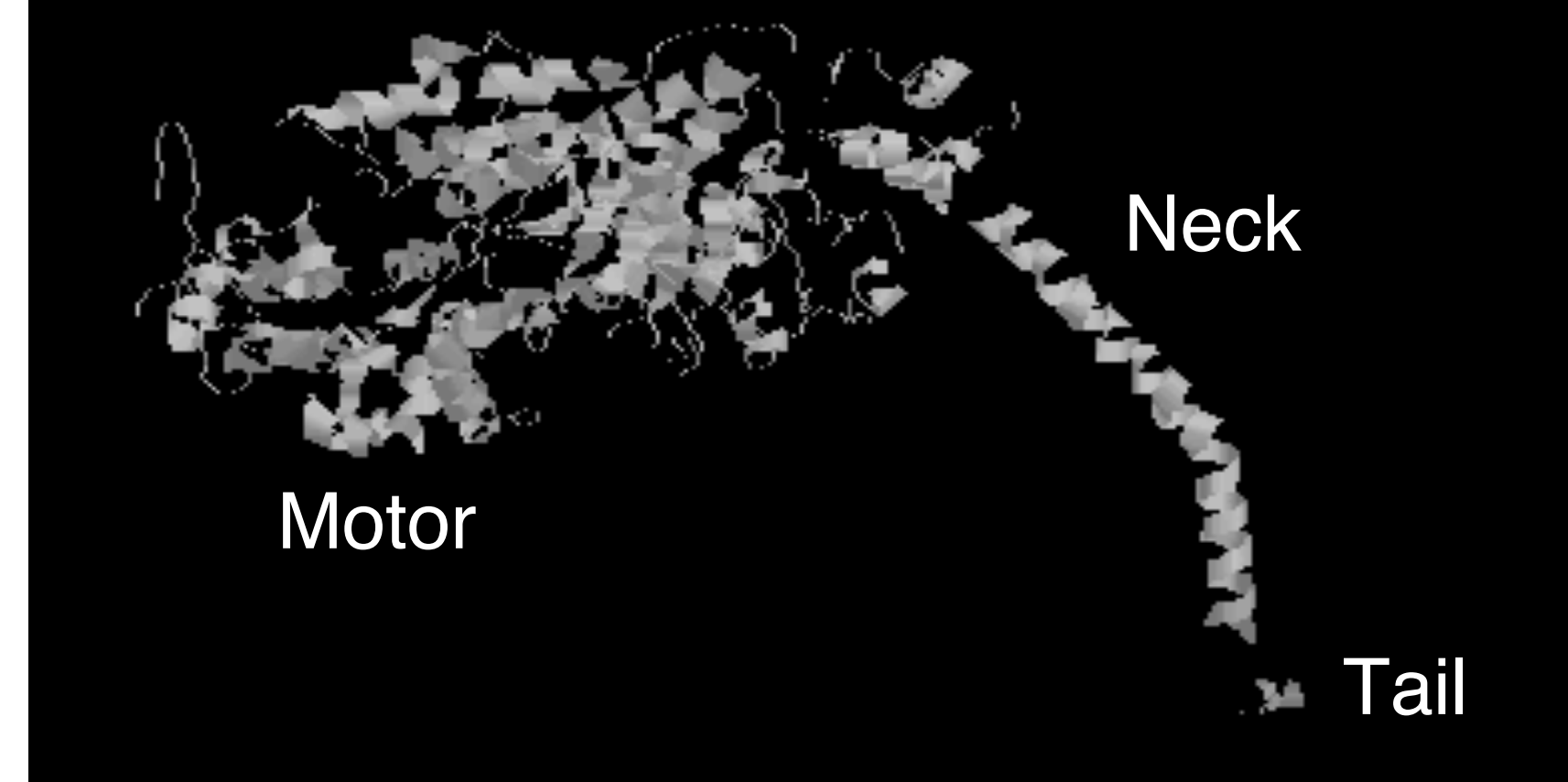


porin

(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!

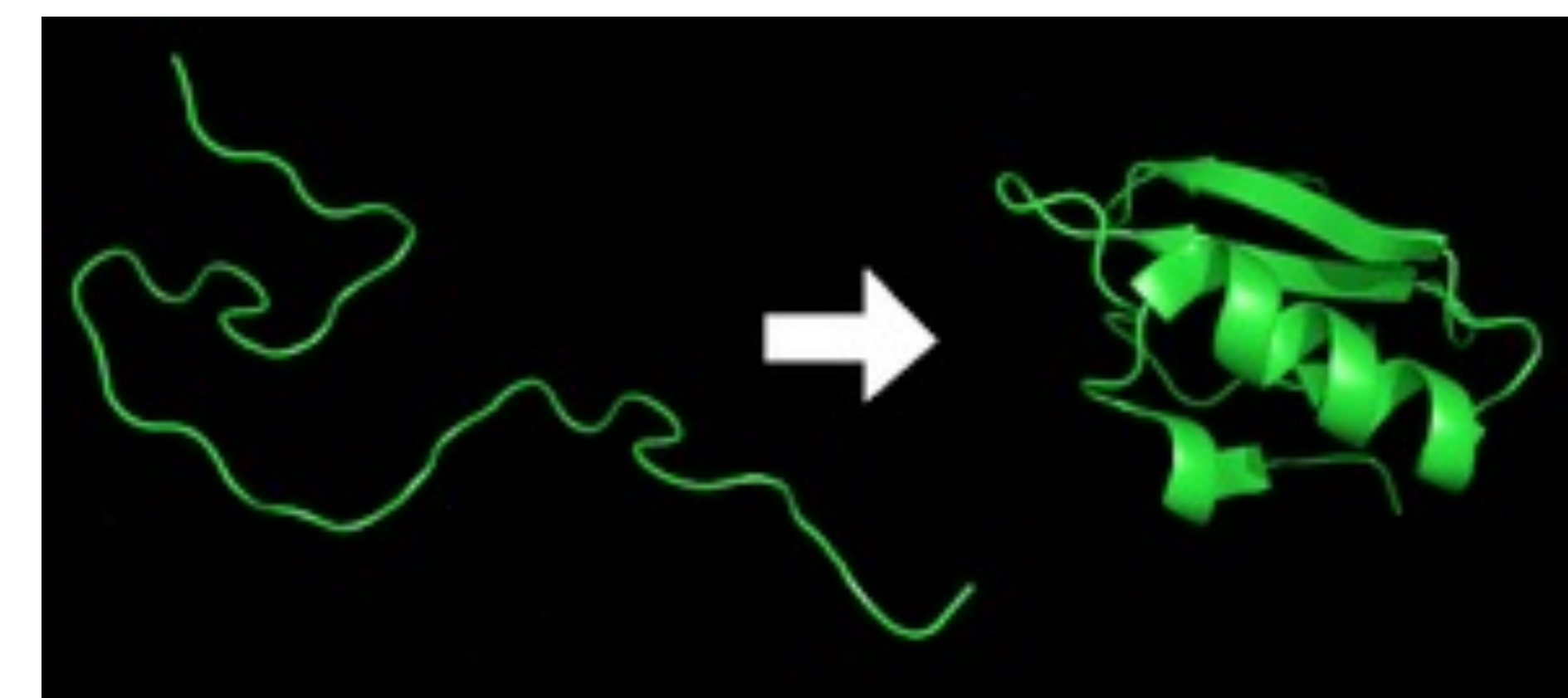


# How is the three-dimensional structure acquired?



Christian Anfinsen  
(1916-1995)

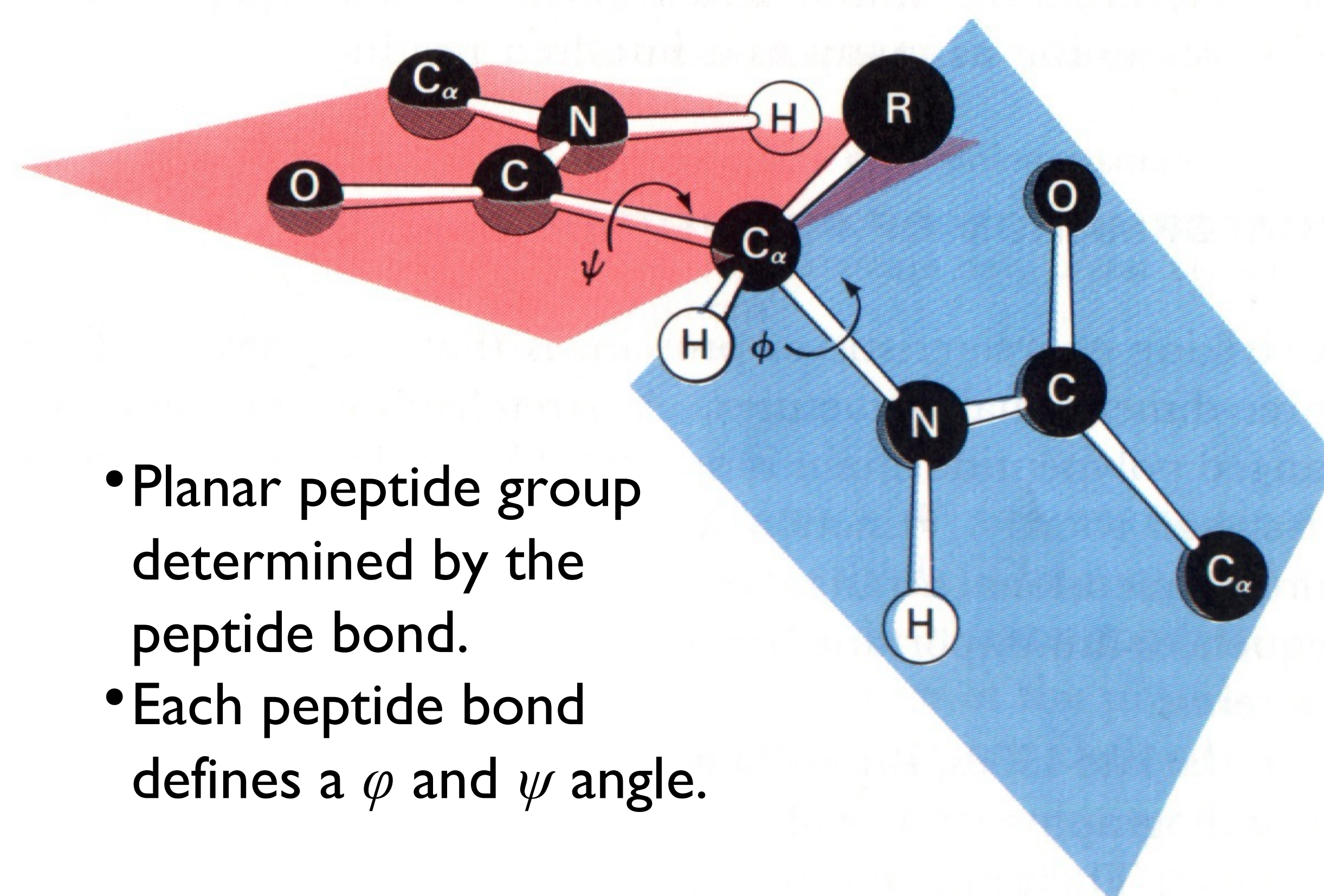
**Anfinsen:** proteins fold spontaneously (sequence determines structure)



Unfolded  
state

Native state (N)  
Lowest energy

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



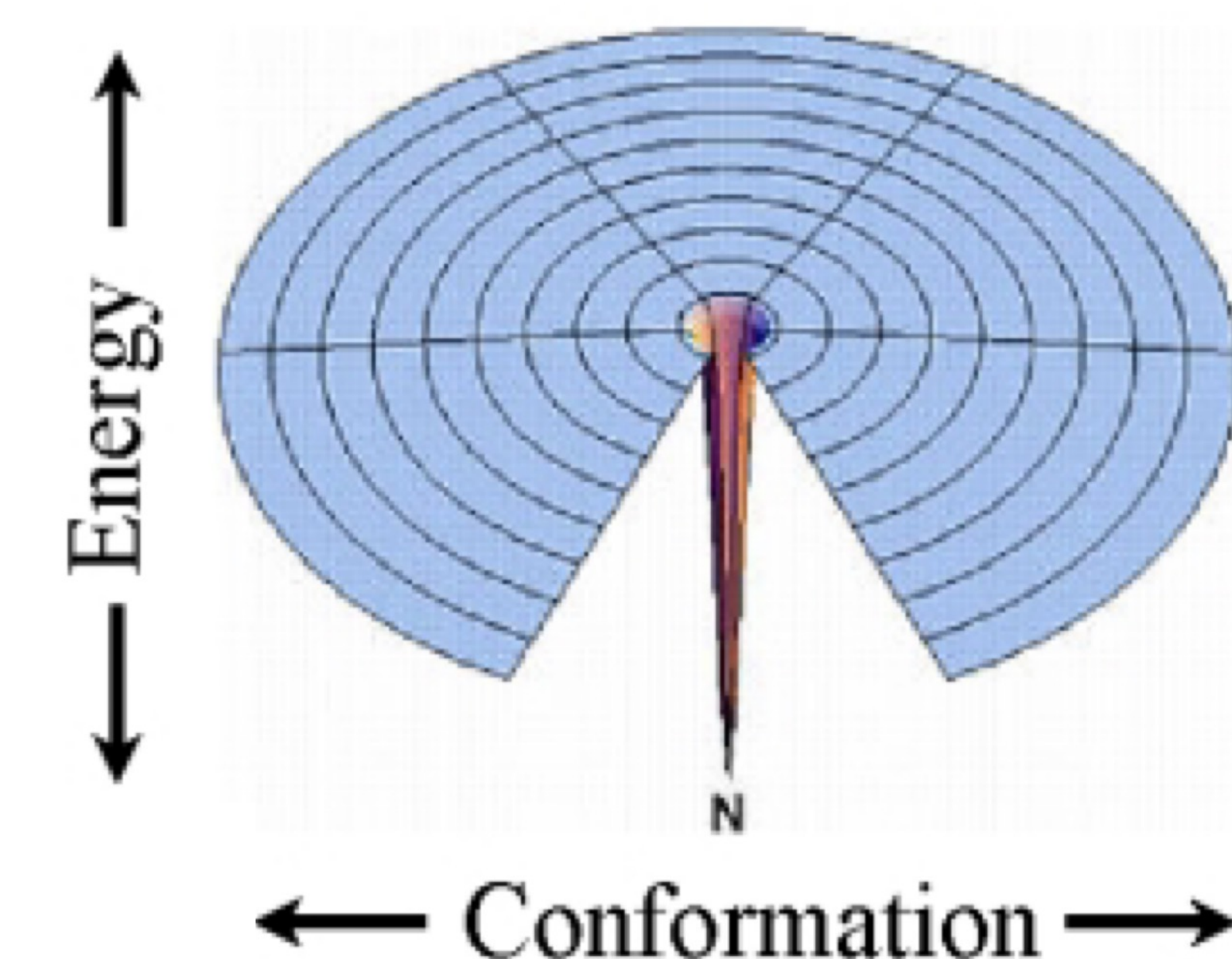
- Planar peptide group determined by the peptide bond.
- Each peptide bond defines a  $\phi$  and  $\psi$  angle.

Number of possible conformations (degrees of freedom):

$$i^n$$

$i$  = number of possible angular positions of a given  $\phi$  or  $\psi$  angle  
 $n$  = total number of  $\phi$  and  $\psi$  angles

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

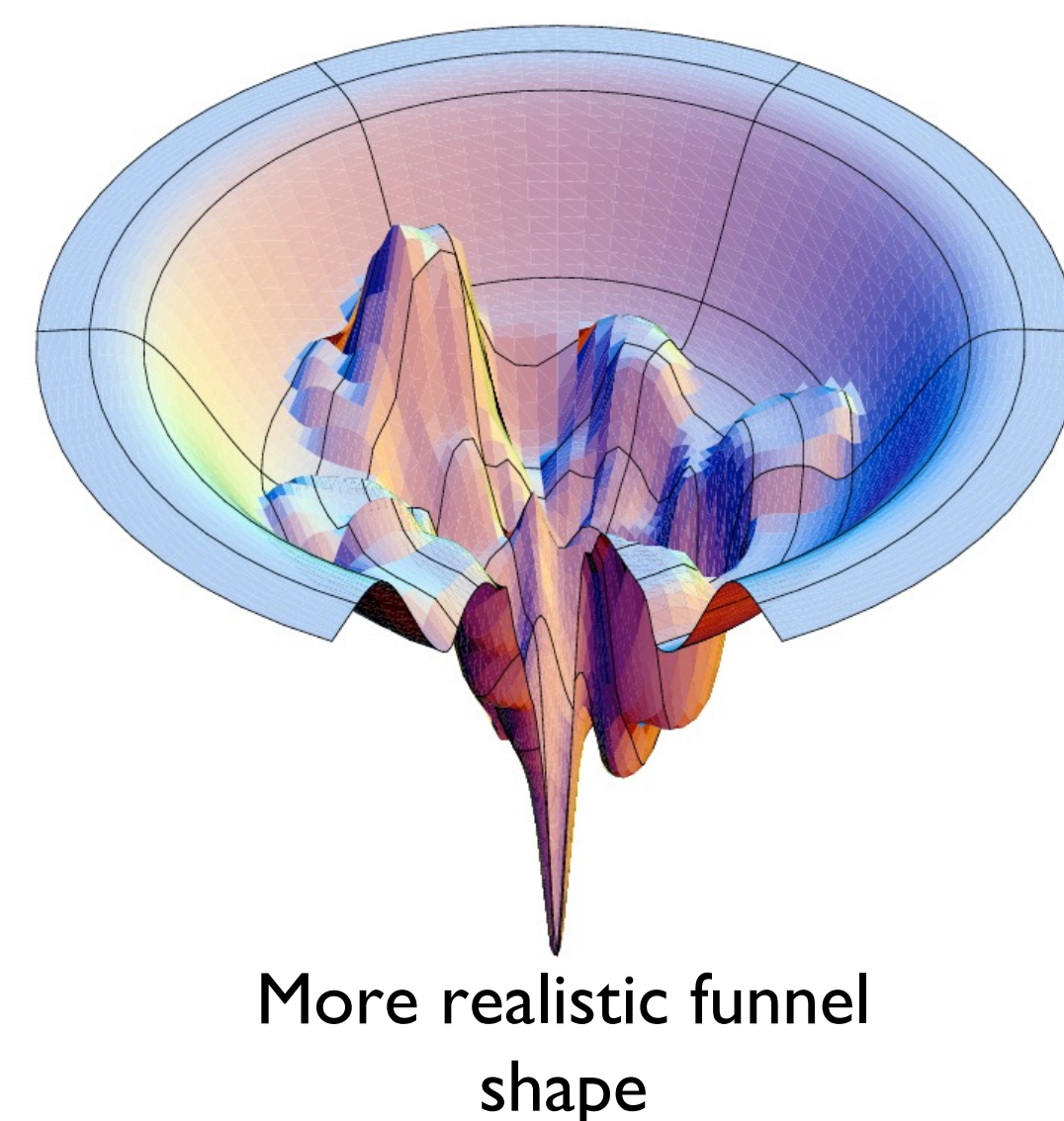
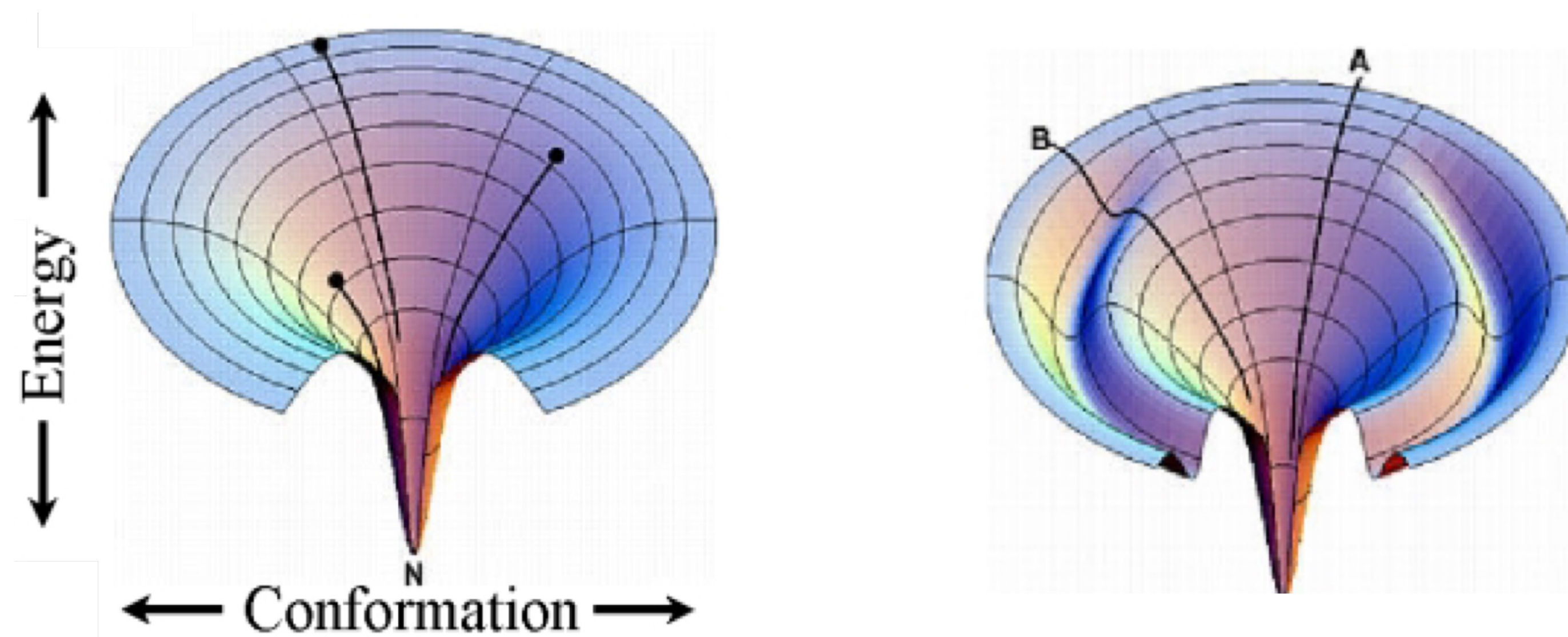


What is the probability that a billiards ball will find the hole merely via random motion?



# Protein folding is guided by the shape of its conformational space

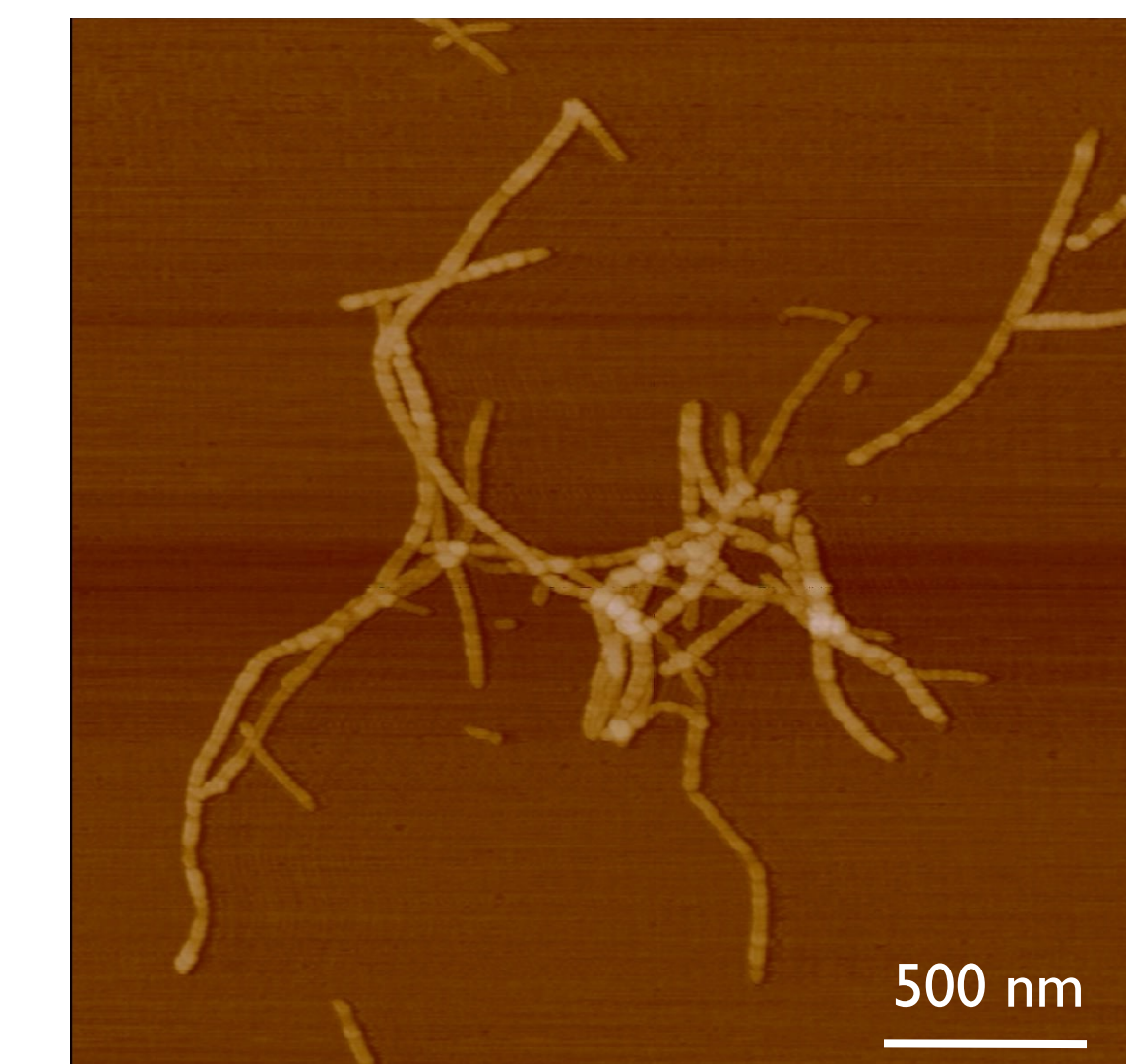
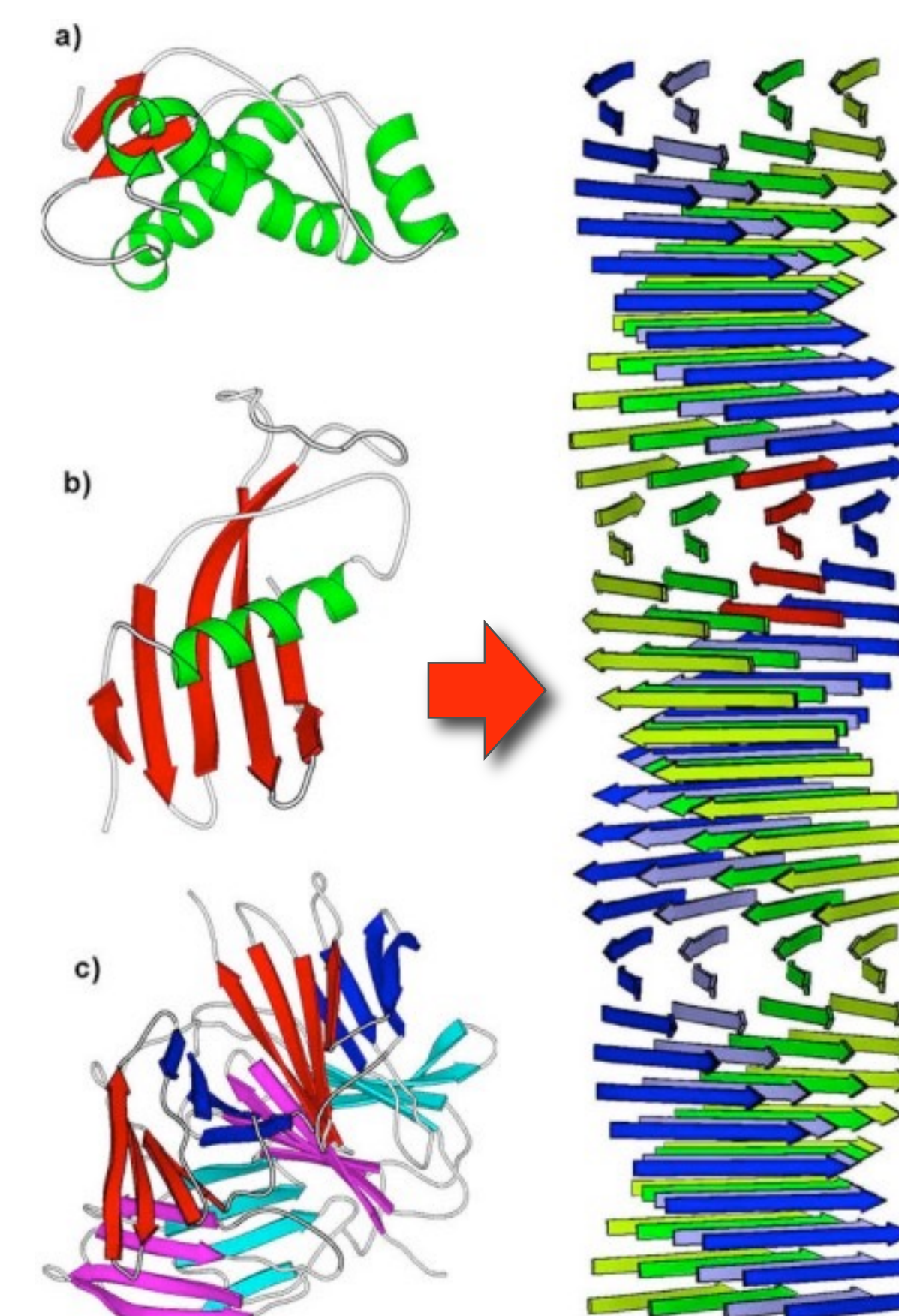
## Shape of conformational space: “Folding funnel”



- 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



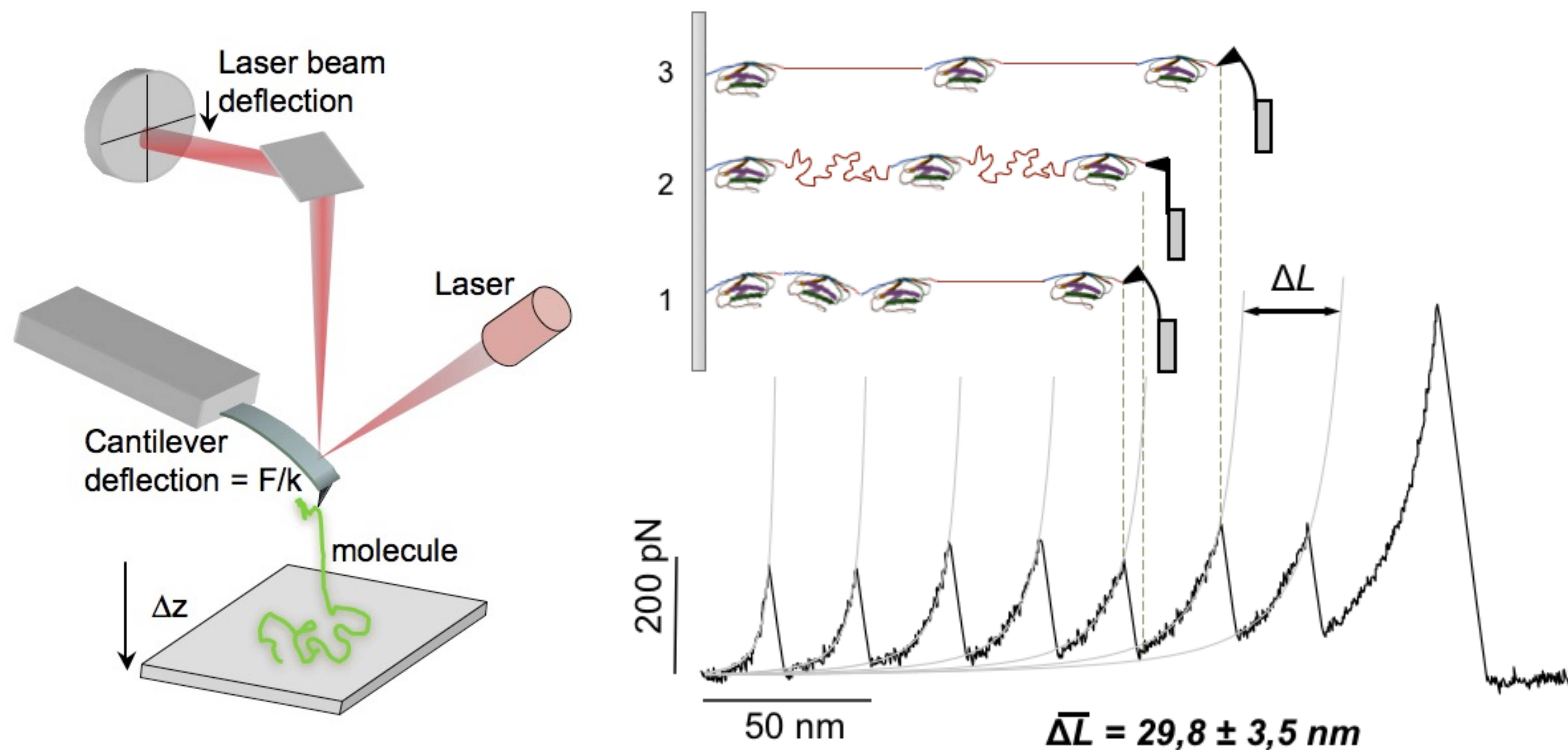
$\beta$ -fibrils:  
undissolved precipitate  
cross- $\beta$  structure



# Methods of protein unfolding (denaturation)

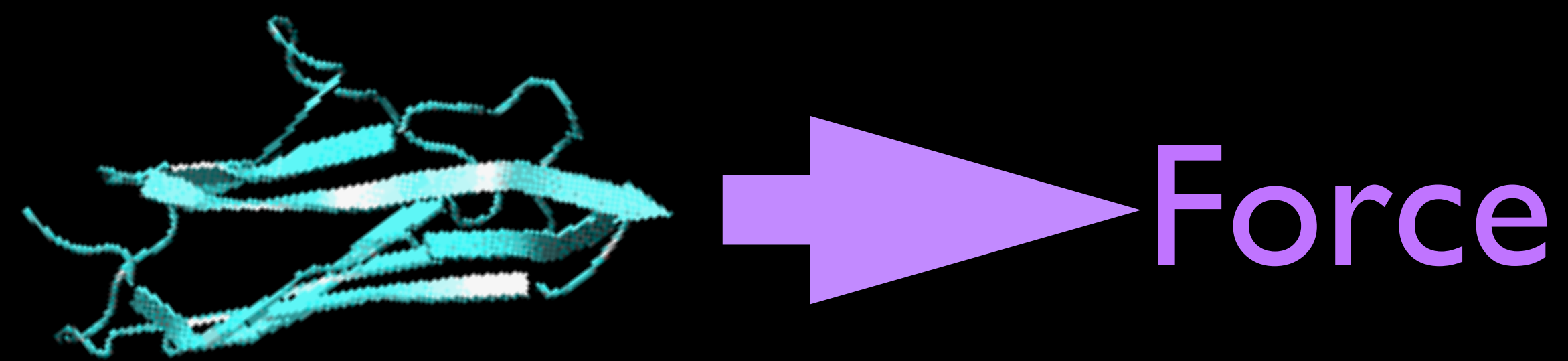
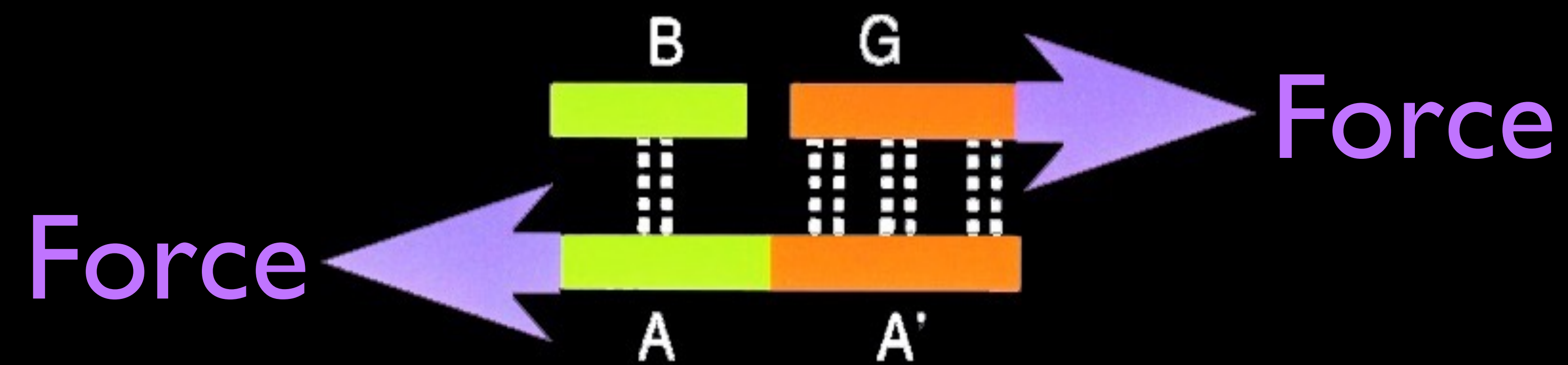
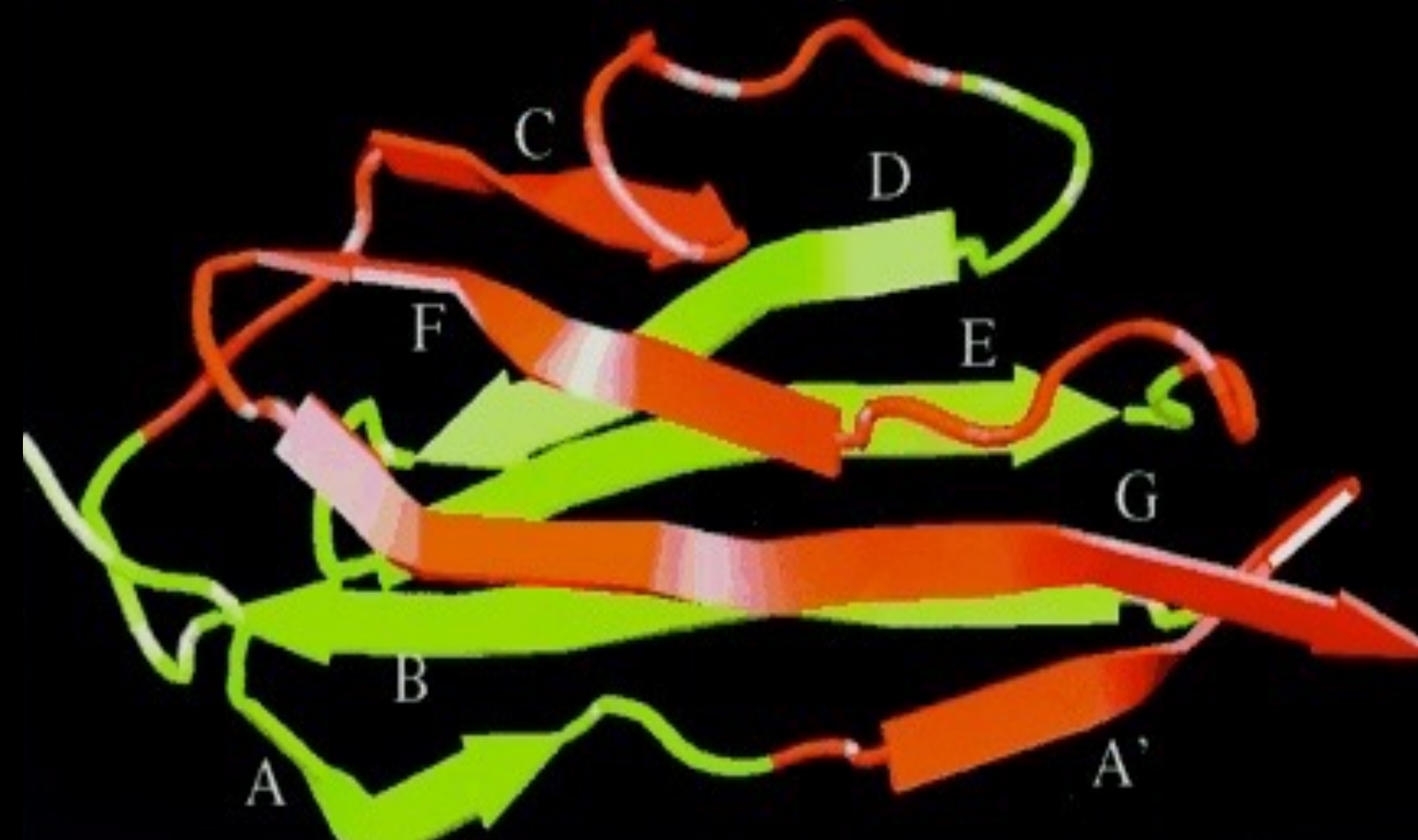
- Heat
  - Chemical agent
  - Mechanical force
- Break secondary chemical bonds  
Disrupt secondary and tertiary structure

Mechanical unfolding of a single protein with atomic force microscope





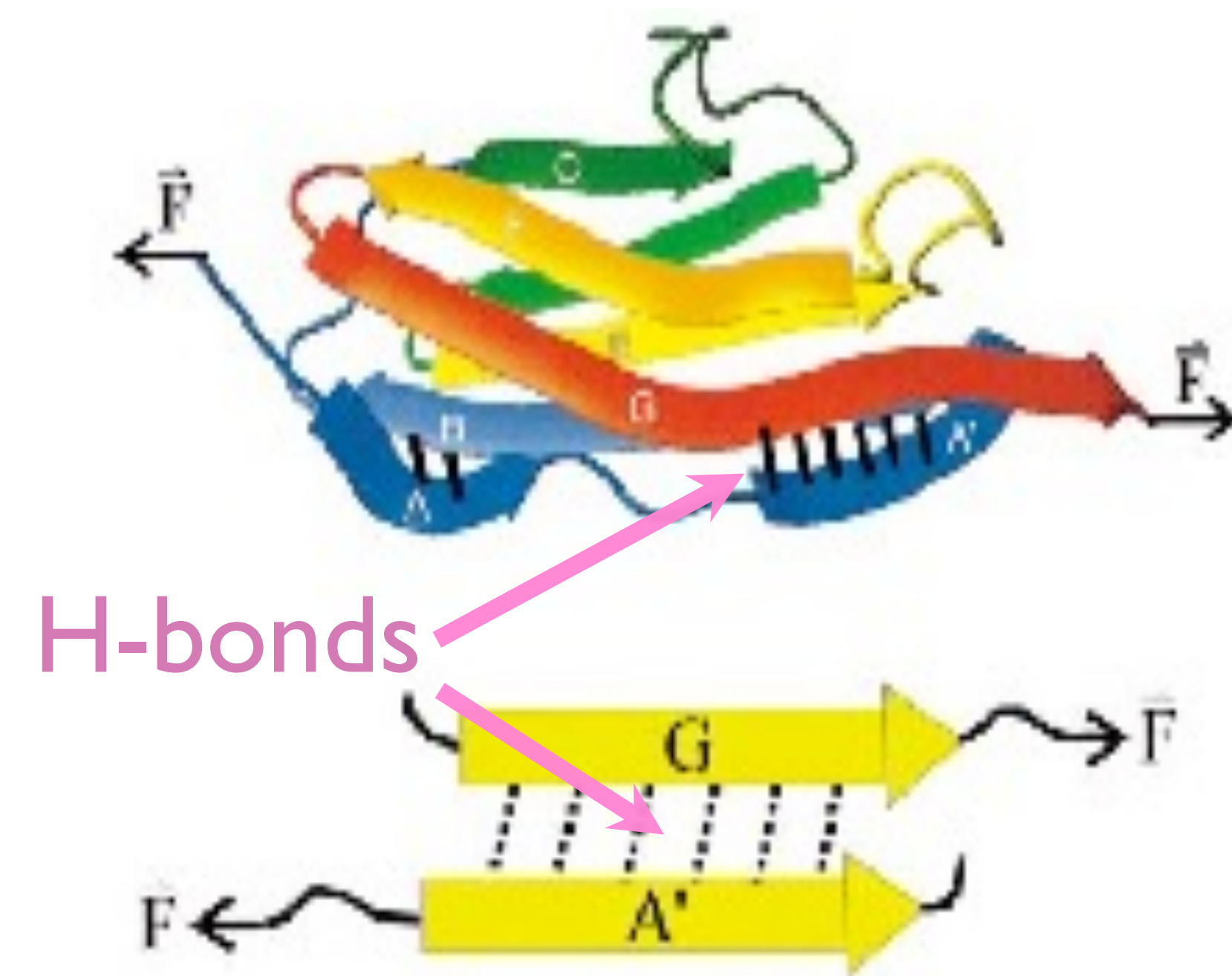
# Structural basis of mechanical stability



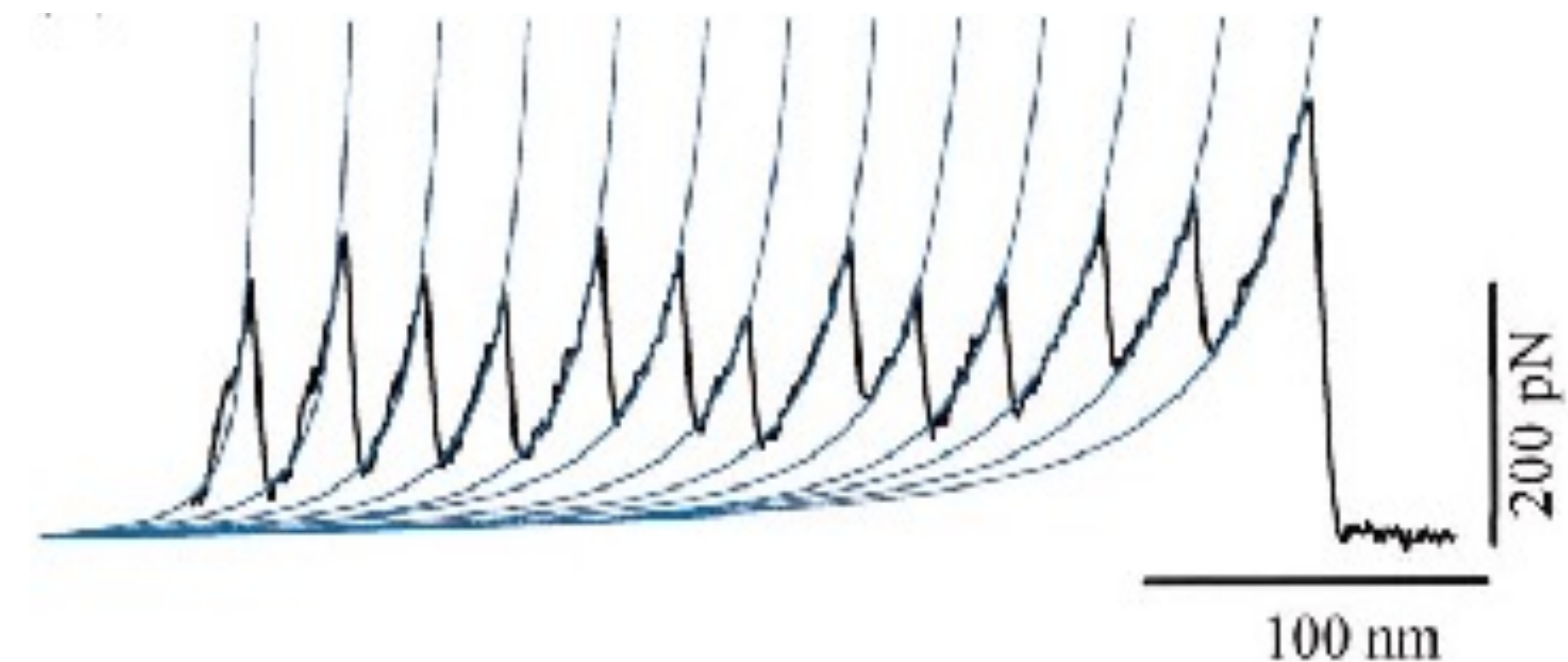


# Biological logic of mechanical stability

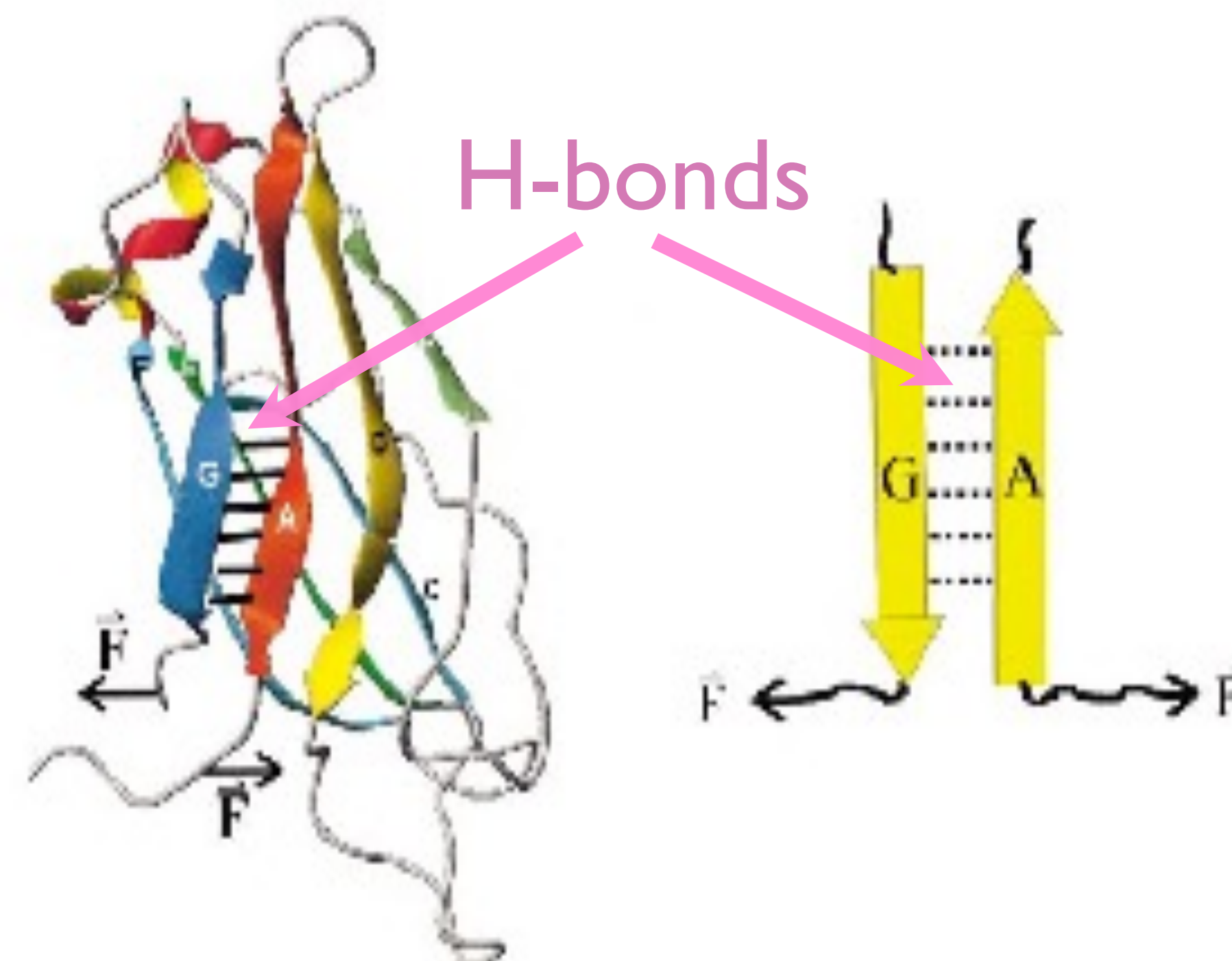
Parallel coupling of structure-stabilizing H-bonds



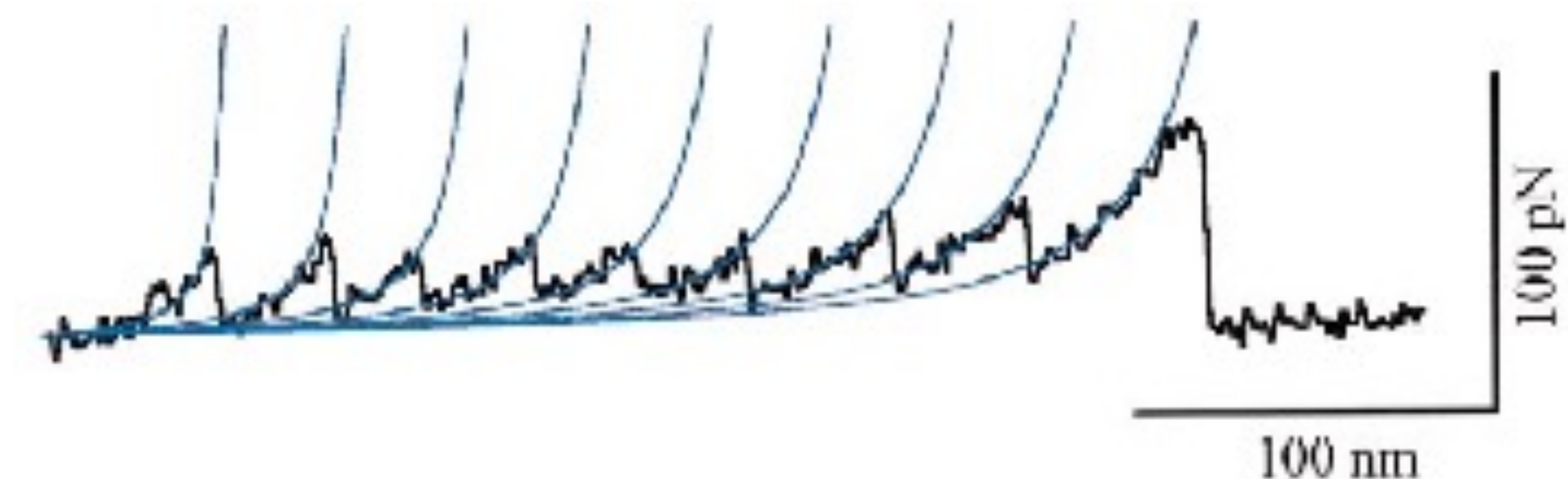
High unfolding forces



Serial coupling of structure-stabilizing H-bonds



Low unfolding forces



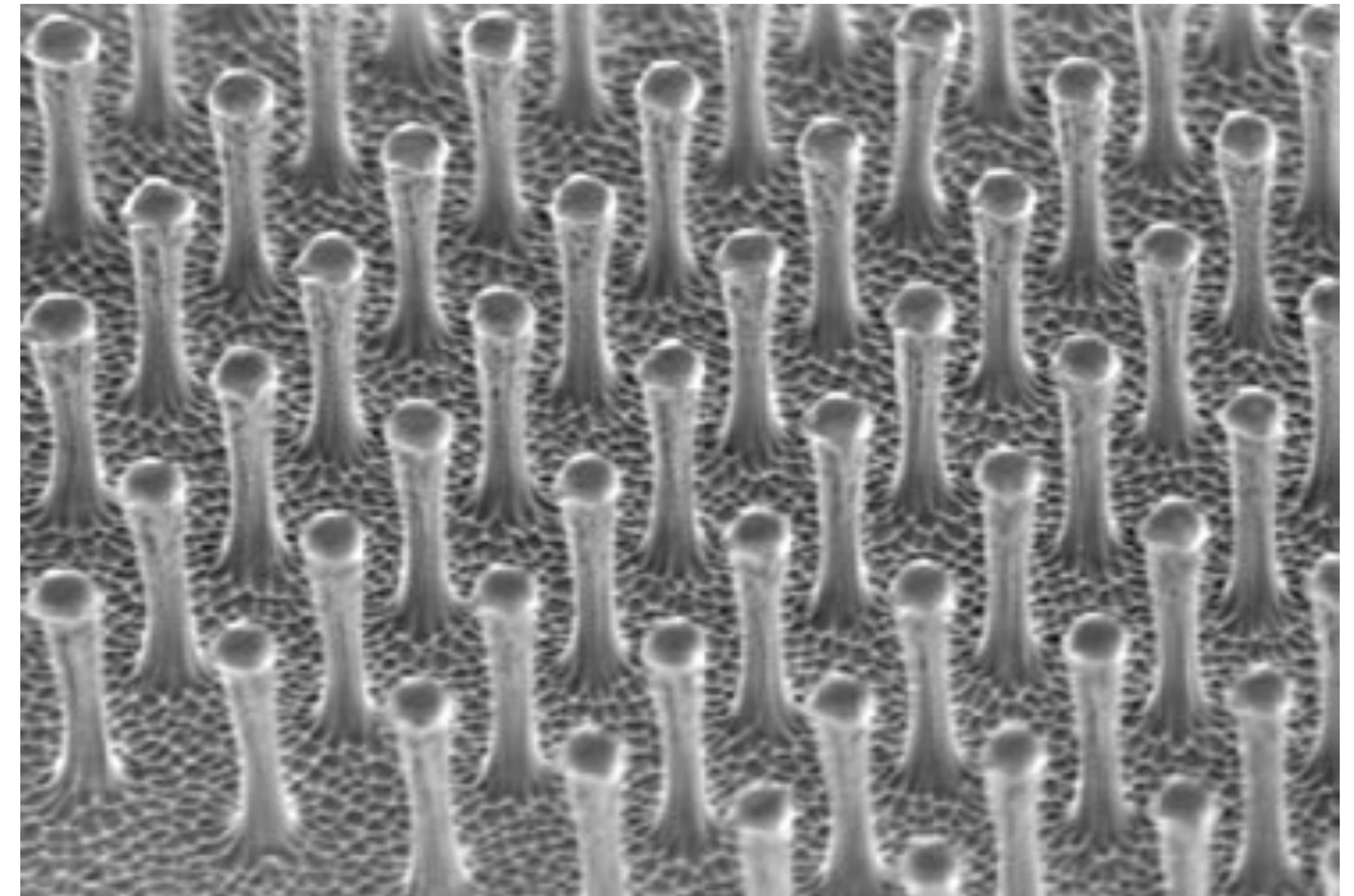


# Macroscopic mechanical stability

Highly efficient glue based on the principle of parallel coupling



Artificial gecko foot  
(prepared with nanotechnology methods)



Surface attachment  
of the gecko foot:  
Numerous Van der  
Waals interactions -  
between bristles  
and surface -  
coupled in parallel



# Feedback



<https://feedback.semmelweis.hu/feedback/index.php?feedback-qc=UQH93G5VJY8XJ437>