BIO-212 - Lecture 1
Intro to the Course and Basic Concepts

Aleksandar Antanasijević, Asst. Prof.
Laboratory of Virology and Structural Immunology
Global Health Institute, School of Life Sciences
École Polytechnique Fédérale de Lausanne

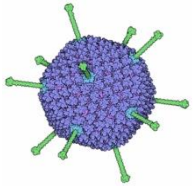
Slides adapted from: Matteo Dal Peraro and Bruno Correia

10th of September 2025

École
polytechnique
fédérale
de Lausanne

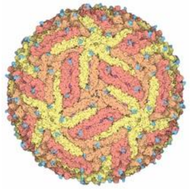
About me …

- **Structural Biologist** with a keen interest in Viruses



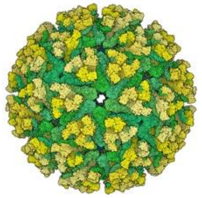
- Background in **Physical Chemistry**
  (University of Belgrade; 2011)

- PhD in **Biochemistry and Molecular Genetics**
  (University of Illinois at Chicago; 2016)



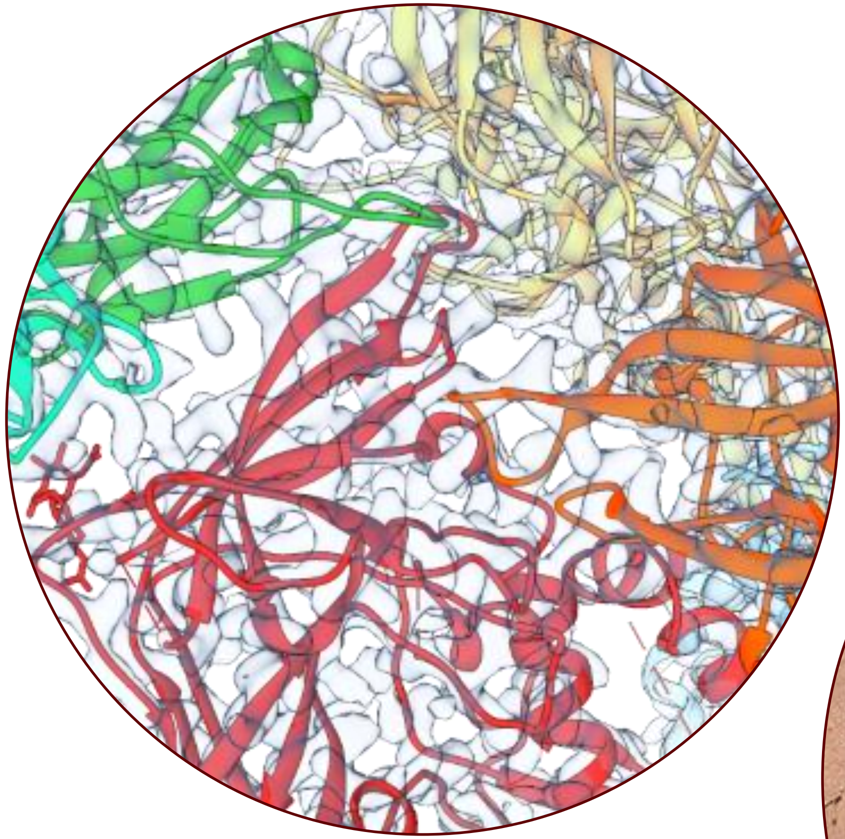
- Postdoc in **Vaccine Design and Evaluation**
  (The Scripps Research Institute; 2022)

- Assistant Professor at the **Global Health Institute**
  (EPFL; 2022)



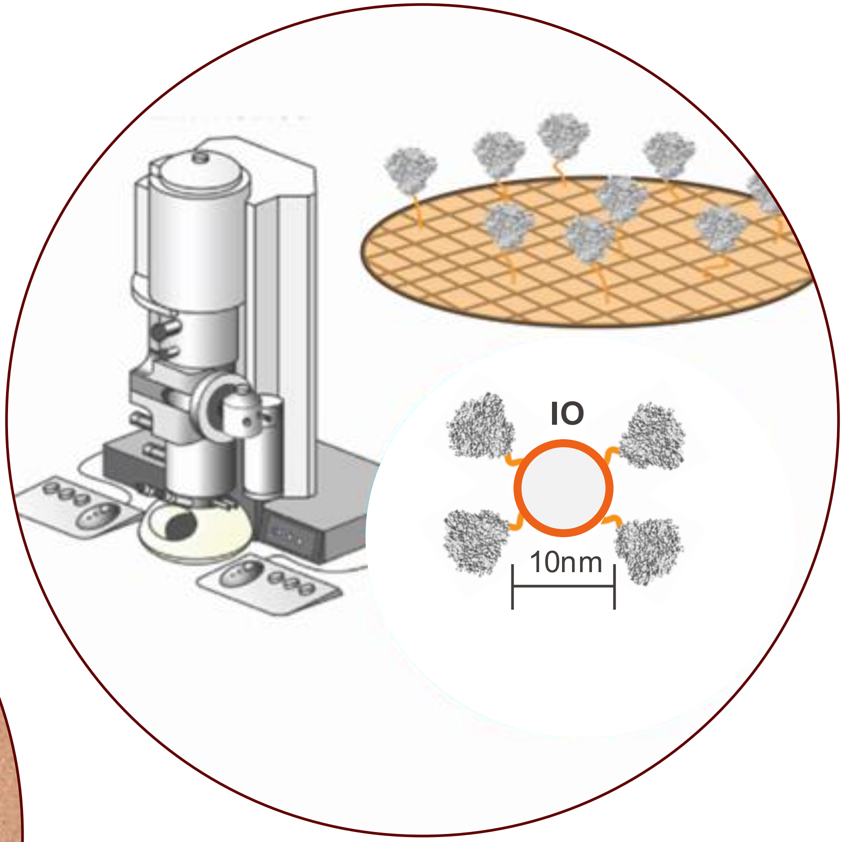
- Contact:
  Office: **SV 3531**
  Email: **aleksandar.antanasijevic@epfl.ch**

About my lab …



Structural Antivenomics

- Venom – antivenom interactions
- Novel antivenom strategies



Viruses and Antibodies

- Structural analyses of antibodies
- Immunogen design and evaluation

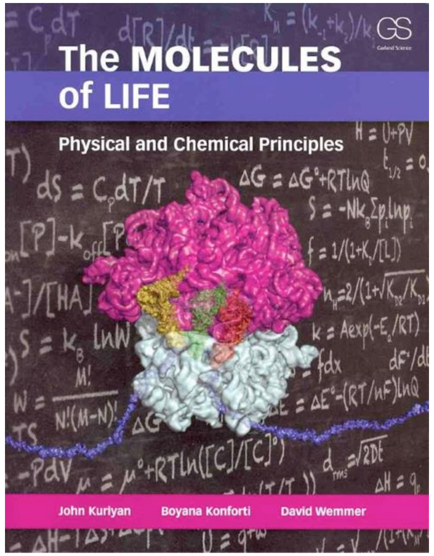
Technology development

- Custom EM grids and nanobeads
- Predictive algorithms

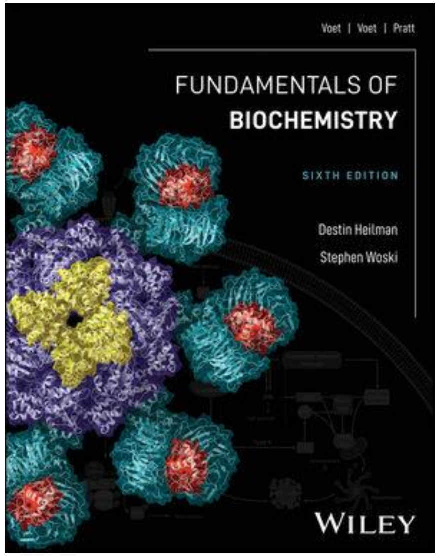
Course Organization

- Primary Learning Resources
  - Lecture slides
  - Exercises
  - Textbooks
- Organization of Exercises:
  - Thursday, 8-10AM at PO01
  - TA Team of 7 members
  - Mix of written exercises and workshops
- Questions and Discussions:
  - Moodle Forum (for general course questions)
  - ED Forum (for exercise or content questions)
  - Ask the Prof in breaks or after class
- Exam:
  - Written exam (3 hours total)
  - Questions will be provided in both English and French and you may answer in either language.
  - Mix of multiple-choice questions and open exercises

Main textbook:
The Molecules of Life



Additional textbook:
Fundamentals of Biochemistry



If a topic is covered on the lecture slides or exercises, it can be on the exam.

Course Organization - Exercise Sessions

Weekend — Wednesday — Thursday

Weekly Material Released | **Lecture** | **Exercises**

Corrections Released

- Exercise Sessions
  - 2h exercise session (8-10AM Thursdays morning, PO01)
  - 7 TAs to help with exercise sessions and exam
  - Give a look ahead of time if you can
  - Pair up with classmates and discuss
  - Discuss with the TAs - do not be shy, they are there to help
  - Work on series before checking the solutions

BIO-212 TA team


Edoardo


Kiruthika


Arthur


Alissa


Mubarak


Shiro

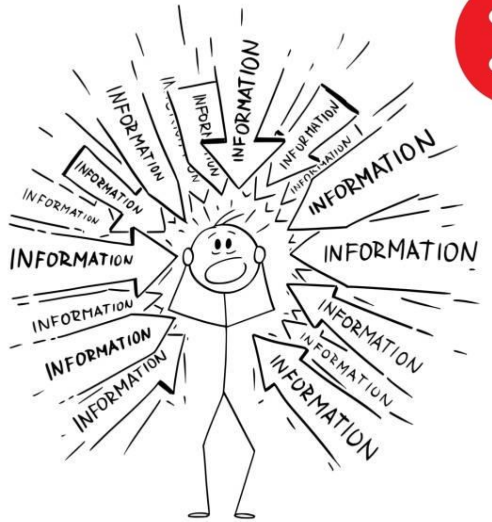

Ekaterina


Nikolas

Please be respectful to the teaching staff!

Learning goals - Biochemistry for Engineers

- Build knowledge of biological systems on the molecular level
- Understanding of the physical and energetic principles that govern molecular interactions in biomolecules
- Learn about the main experimental and computational methods to produce, analyze and engineer biomolecules
- Understand the applicability of concepts taught in this class to bioengineering



Some (hopefully) useful advice

- You are encouraged to ask questions - Approach the Prof and TAs
- Take notes - This is the main learning resource
- Read the book if you can - Expand what we discuss in class
- Attend lectures and exercises regularly
- Provide early feedback - week 4/5 feedback questionnaire

Date	Lecturer	Topic
Week 1 - 10/09	AA	Intro - Atoms, biomolecules and interactions
Week 2 - 17/09	AA	Carbohydrates
Week 3 - 24/09	AA	Lipids
Week 4 - 01/10	MDP	Nucleic Acids
Week 5 - 08/10	MDP	Proteins
Week 6 - 15/10	MDP	Thermodynamics in Biomolecular Systems
		Fall Semester Break
Week 7 - 29/10	MDP	Biomolecular Interactions and Binding
Week 8 - 05/11	AA	Production and Purification of Biomolecules
Week 9 - 12/11	AA	Biophysical Methods for Biomolecule Characterization
Week 10 - 19/11	AA	Measuring Biomolecular Interactions
Week 11 - 26/11	AA	Introduction to Structural Biology
Week 12 - 03/12	AA	Protein Structure Prediction and Engineering
Week 13 - 10/12	AA	Kinetics and Catalysis
Week 14 - 17/12	AA	Course Recap

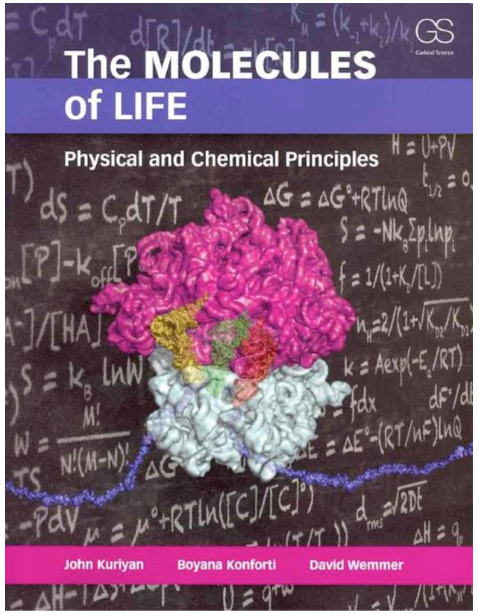
Lecture 1 - Outline

Today:

- The primary biomolecules in living systems
- Energetic principles of atomic and molecular interactions
- From atoms to the building blocks:

Reading suggestions:

- The Molecules of Life (Chapter 1)

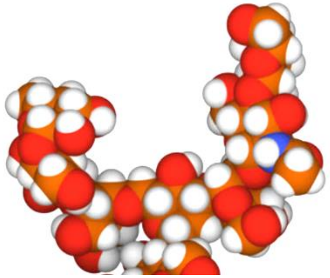


Biomolecule diversity, composition and scales

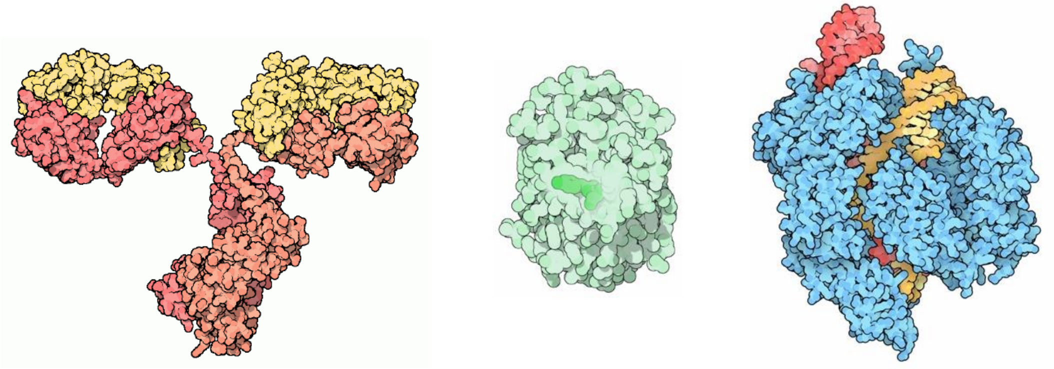
The main types of biomolecules

- Examples of different biomolecules and their functions

Lipids
- Building membranes
- Energy storage
- Cell signaling



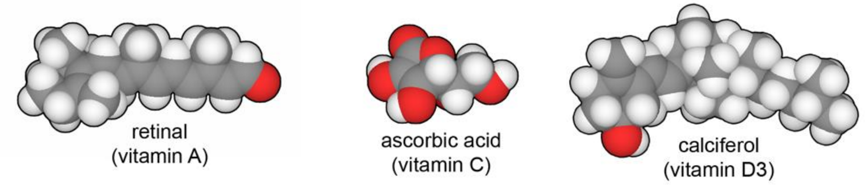
Carbohydrates
- Energy storage
- Nucleic acid component
- Cell signaling



"the workhorses of the cell"

Proteins
- Enzymes
- Membrane transport
- Metabolite cariers
- Immune defense
- Structural support
- Cell motility
- Gene regulation
- Cell signaling

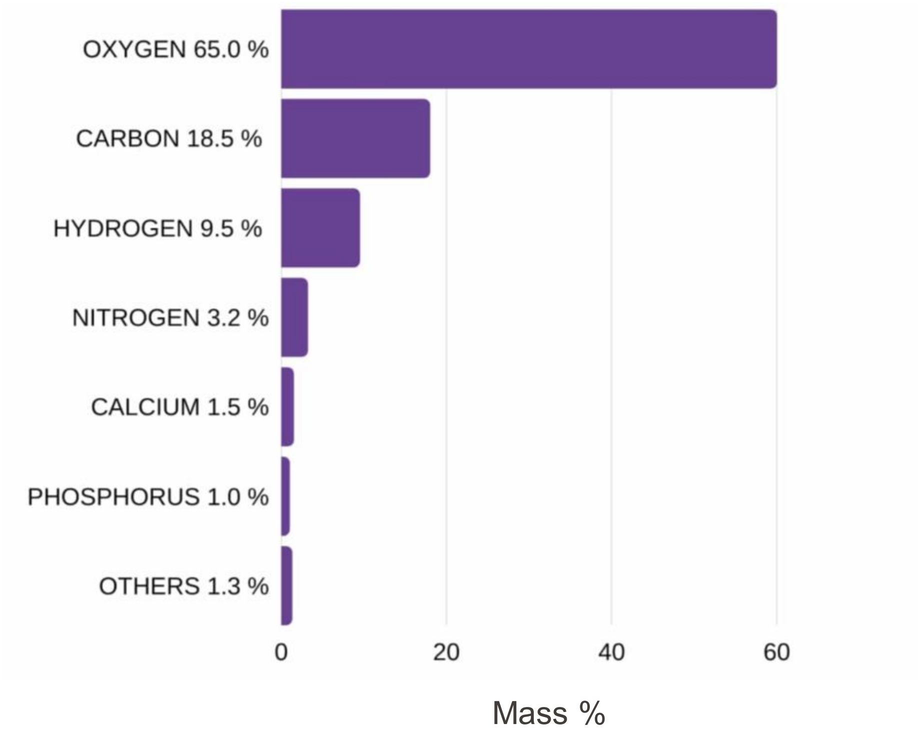
Nucleic acids
- Carrier of genetic information
- Enzyme components



Other biomolecules
- Vitamins, metabolytes, enzyme co-factors, inorganic biomolecules, biological pigments...

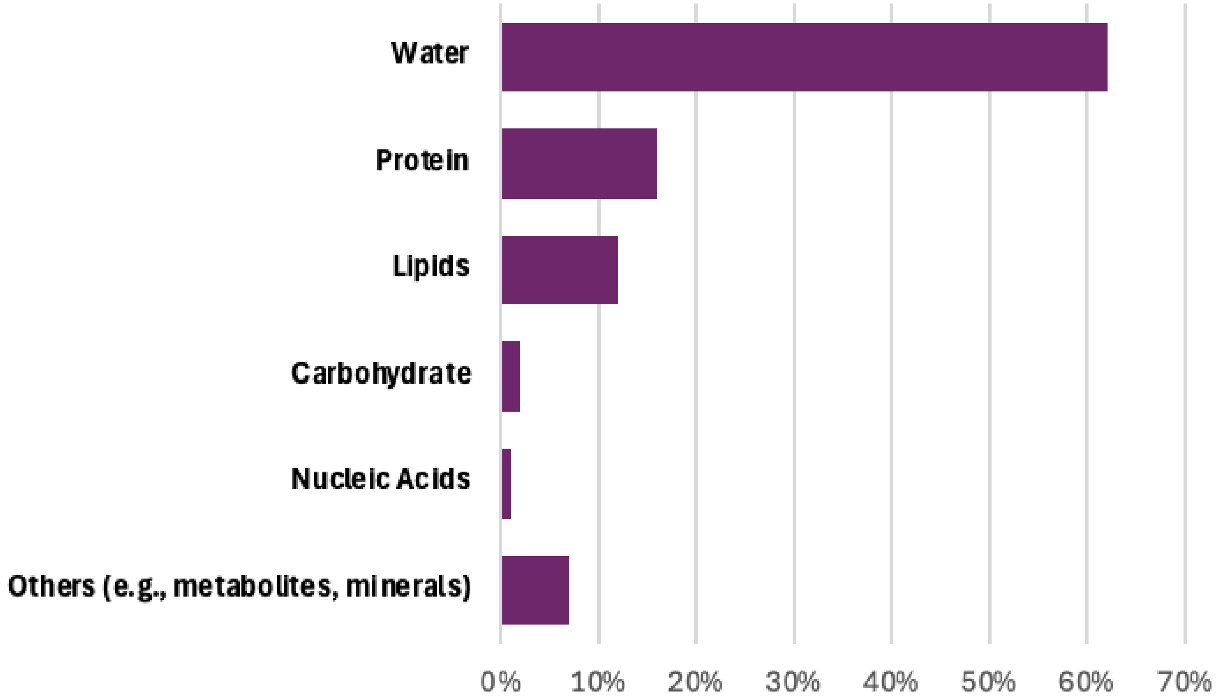
Molecular composition of biological systems

- Atomic composition of human bodies by mass:



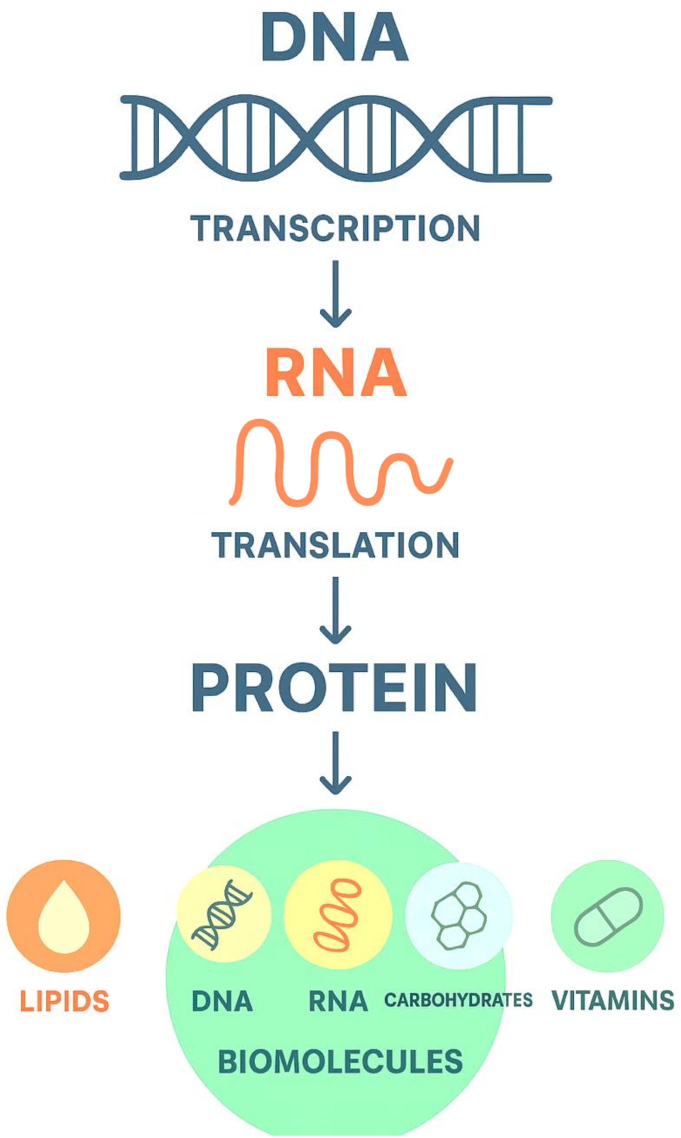
What is the most abundant atom by molarity?

- Molecular composition of human bodies by mass:



Cell and tissue variation (e.g., bone, adipose cells)

Proteins regulate the production of other molecules



- Genetic information is used to build molecules:

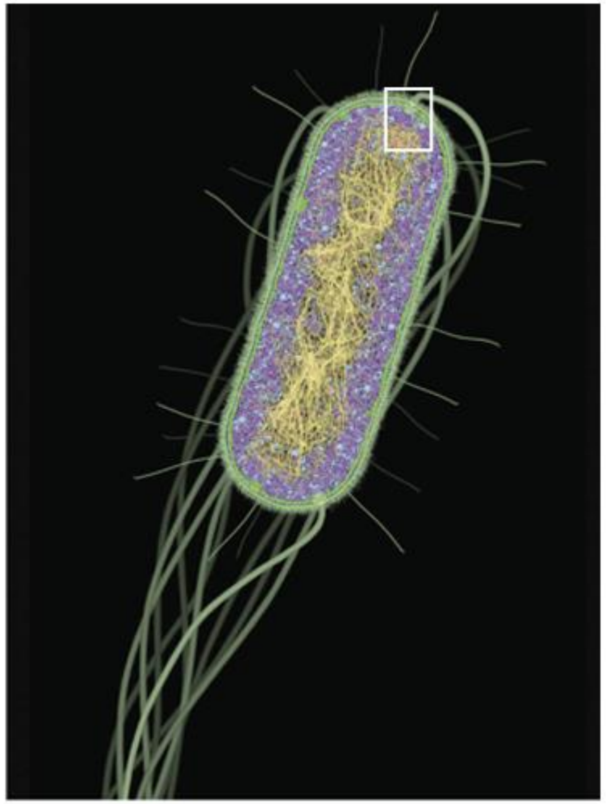
  DNA makes **RNA** makes **Protein**

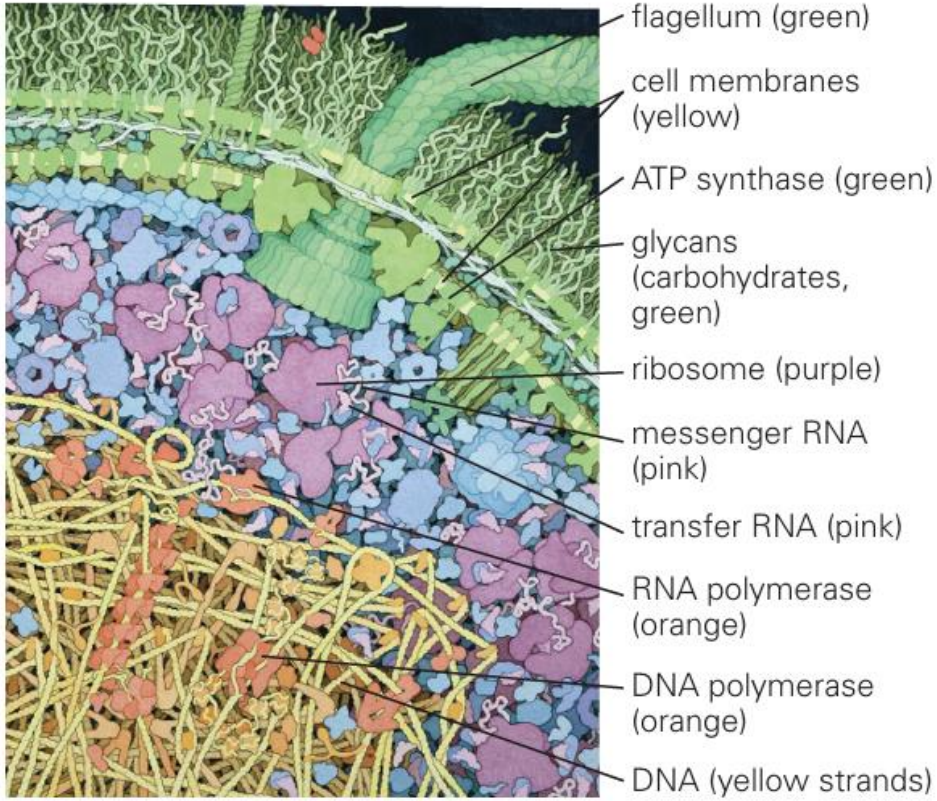
- Proteins regulate this process as well as the synthesis and trafficking of all other biomolecules

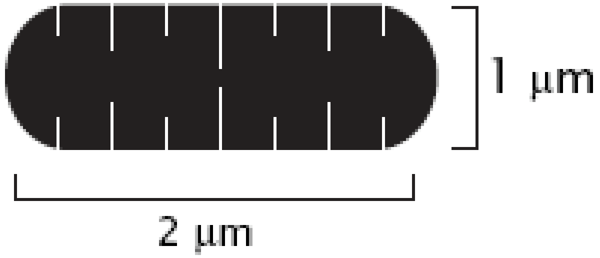
- **Proteins are the most abundant biomolecule** type comprising ~40% of dry mass of the cell

- **Proteins and lipids are chemically the most diverse** species inside the cell (~10^4-10^6 chemically unique molecules in each biomolecule class)

Cells: the minimal unit of life







$V_{E.coli}$ ~ µm^3 = fL

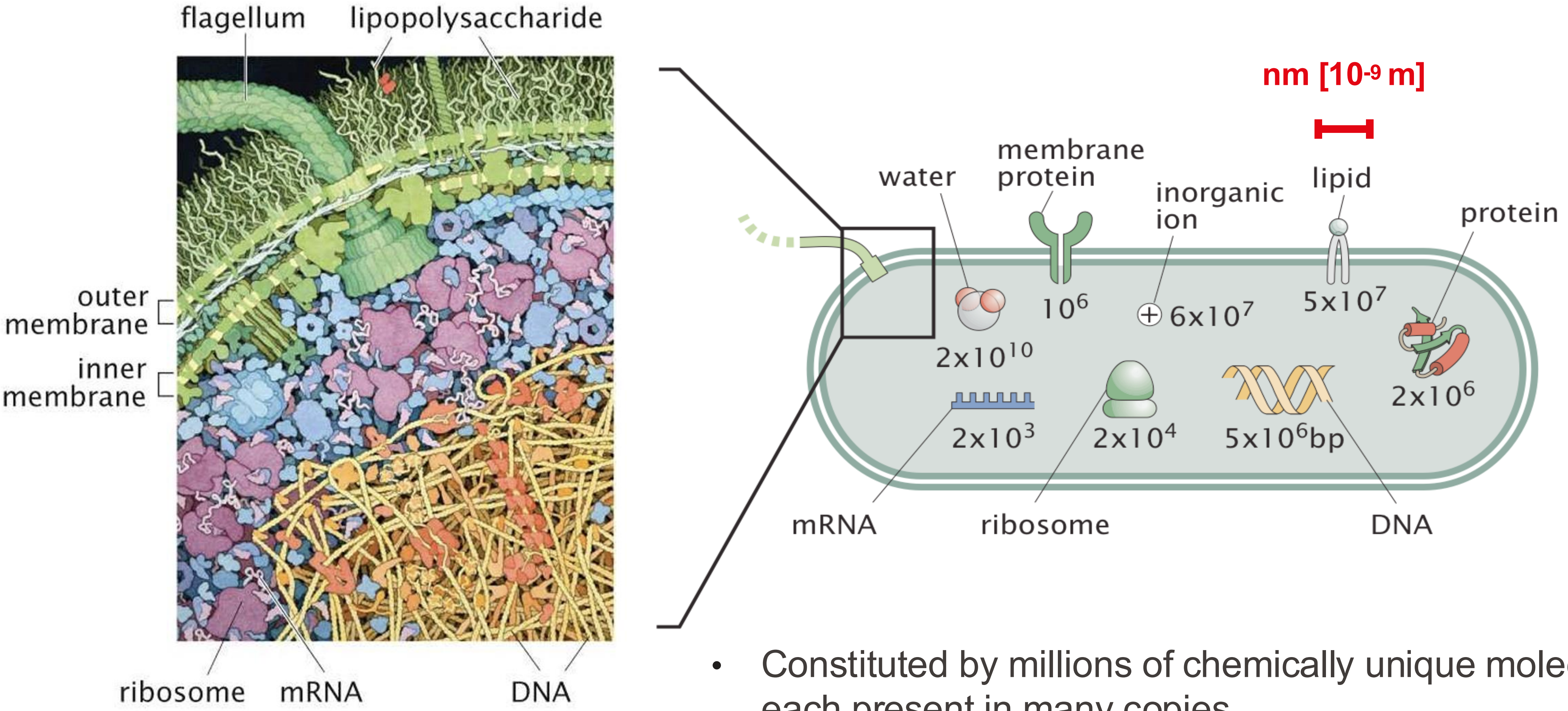
~ $10^{10\text{-}11}$ molecules

$V_{mammalian\ cells}$ ~ $10^{2\text{-}3}$ µm^3 = pL

~ $10^{14\text{-}15}$ molecules

- Cells are small, complex and crowded systems
- Molecular factories that are largely self-sustained in the presence of optimal environment.

Biomolecules per one *E. coli* cell



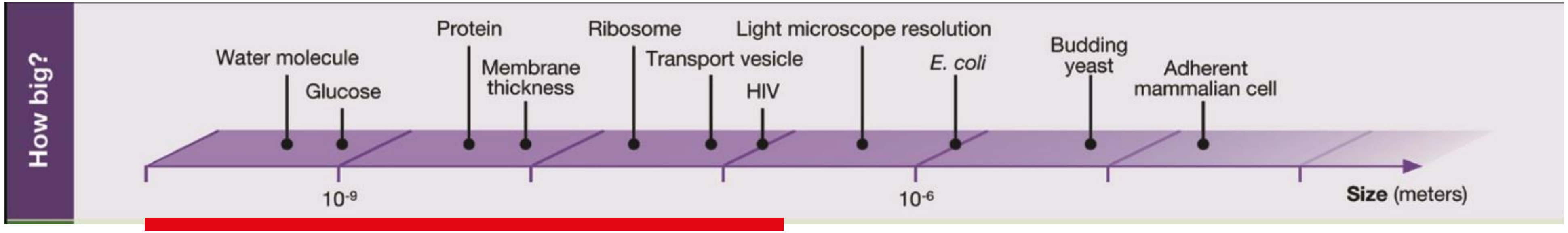
- Constituted by millions of chemically unique molecules each present in many copies
- Their assembly and behavior are governed by physical forces and thermodynamics

from *Physical Biology of the Cell*

What scales are we observing?

The most relevant range

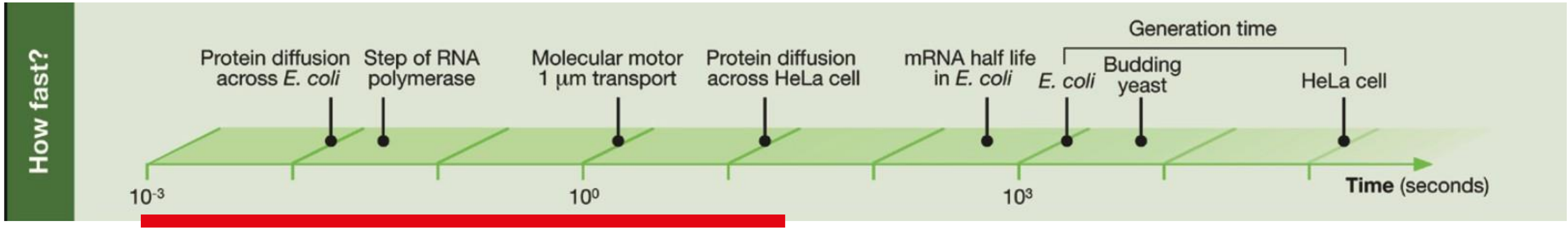
Size



0.1nm — 100nm

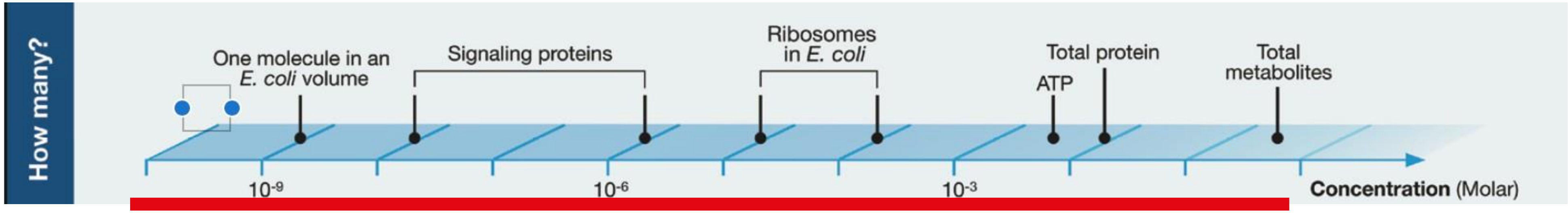
1Å= 0.1nm

Time



ns — s

Quantity



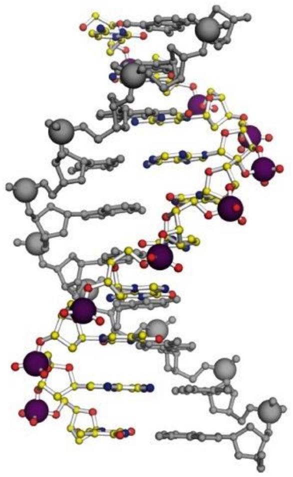
nM — M

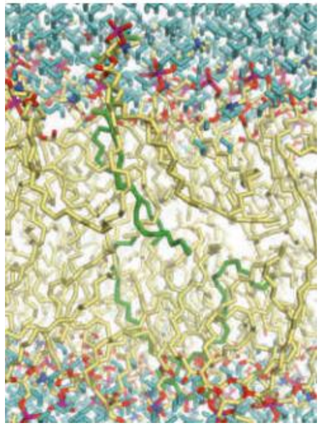
Essential covalent and non-covalent interactions

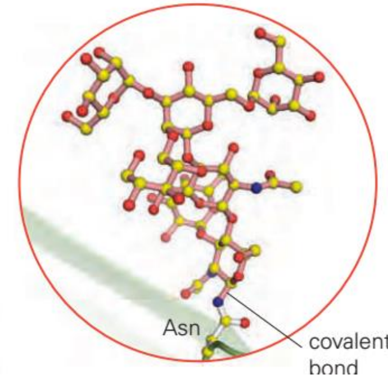
Atoms -> Building Blocks -> Macromolecules

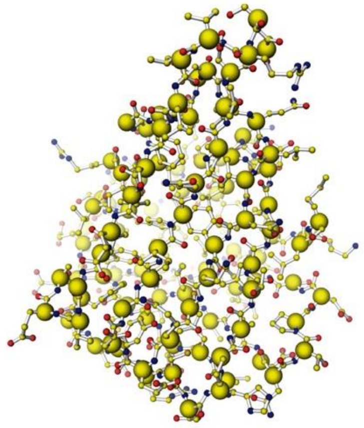
Macromolecular Structure

Nucleic Acids	Lipids	Carbohydrates	Proteins

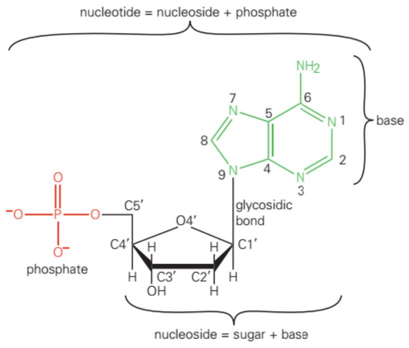


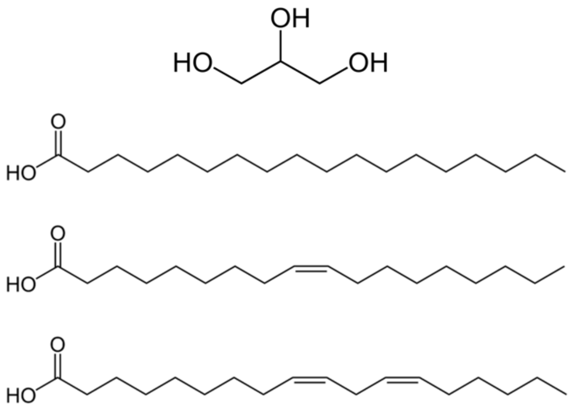


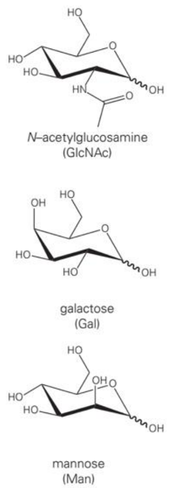


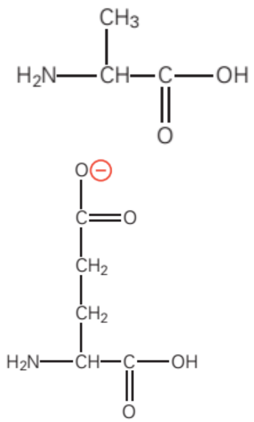


Building Block









Nucleotides	Fatty acids, glycerol	Monosaccharides	Amino acids

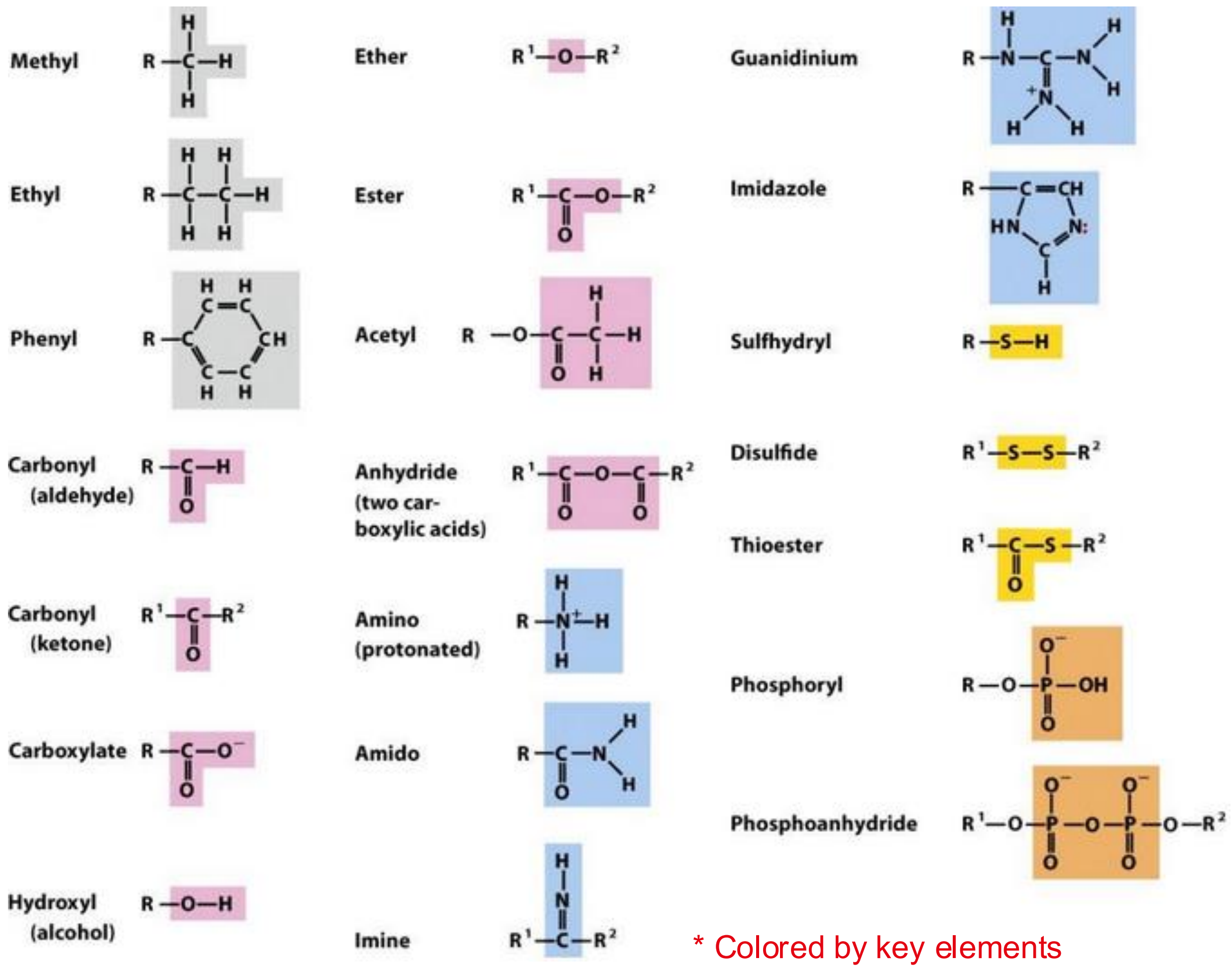
Essential atoms and their properties

	Hydrogen	Oxygen	Nitrogen	Carbon
				
Valent Electrons	H·	·Ö:	·N̈·	·Ċ·
Typical valency (n)	1	2	3	4
Electronegativity	2.1	3.4	3.0	2.6

- **Valency** represents the number of chemical bonds the atom typically forms.
- **Electronegativity** is a chemical property measuring atom’s attraction for electrons in a bond.

Common chemical groups in biomolecules

- Chemical (functional) groups are created through **covalent bonds** between different atoms



* Colored by key elements

- **Methyl** and **ethyl** groups are commonly found in lipids (fatty acid tail)
- **Carbonyl** groups are essential functional group in carbohydrates
- **Carboxylic acid (carboxylate)** is in proteins, lipids and certain carbohydrates.
- **Amino** groups are found in amino acids, nucleotides and some lipids
- **Sulphur-** and **phosphorus**-containing groups comprise amino acids, lipids, nucleotides, vitamins…

Properties of bonds and groups

- Depending on the elements the **resulting bonds and groups can have different properties**

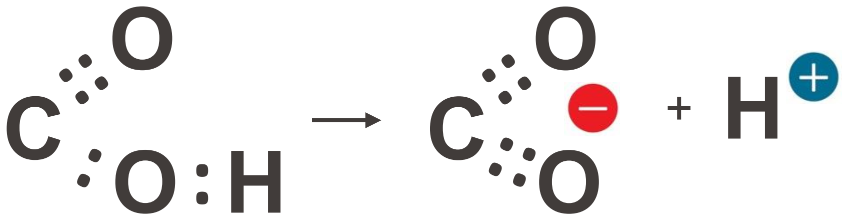
- **C-H** and **C-C** bonds are **non-polar** due to similar/same electronegativity

Comparable attraction of shared electrons

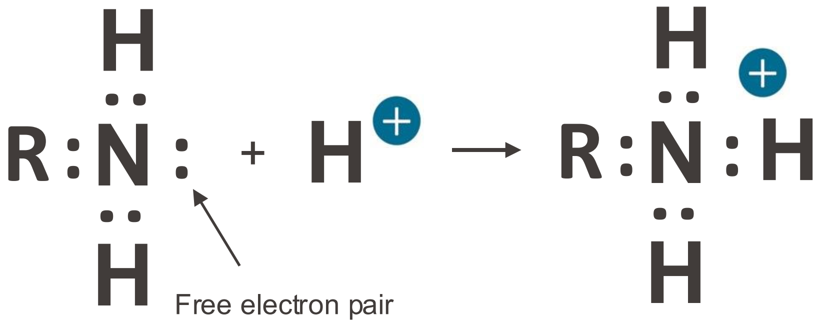
- **O-H**, **N-H, C-N, C-O** and **S-H** bonds are **polar** due to significant difference in electronegativity.

Unequal attraction of shared electrons. Partial oposite potentials in 2 atoms

- **Carboxylate** will release a hydrogen in aqueous solution (pH 7), resulting in **net negative charge**



- **Amino** group will absorb a hydrogen in aqueous solution (pH 7) resulting in **net positive charge**

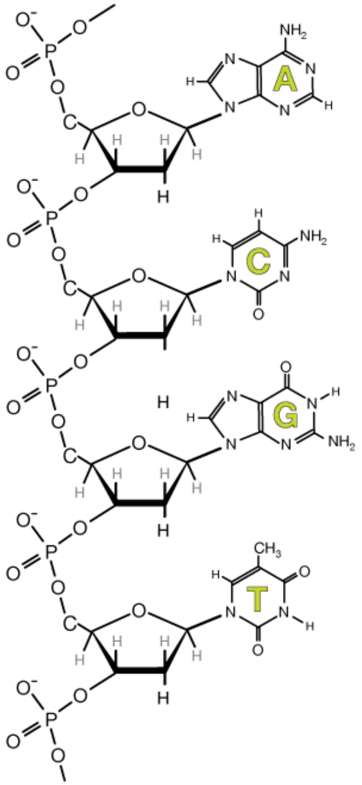


Chemical properties influence molecule assembly

- Atomic composition, polarity and charge of different chemical groups gives rise to non-covalent interactions that play a critical role in 3D assembly of biomolecules

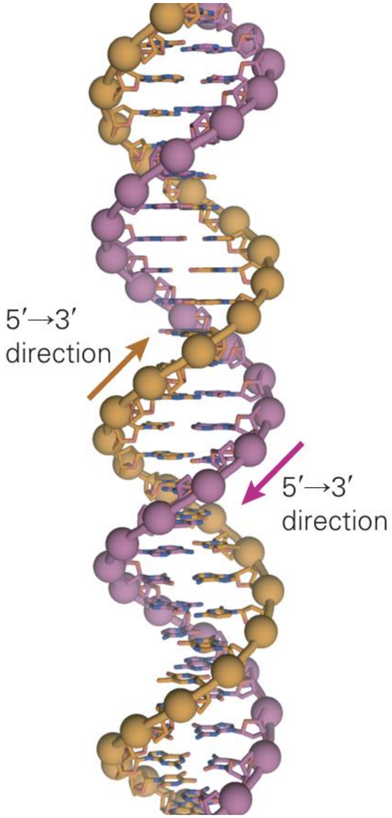
DNA chemically

- Linear polymer
- Length: ~1-2m

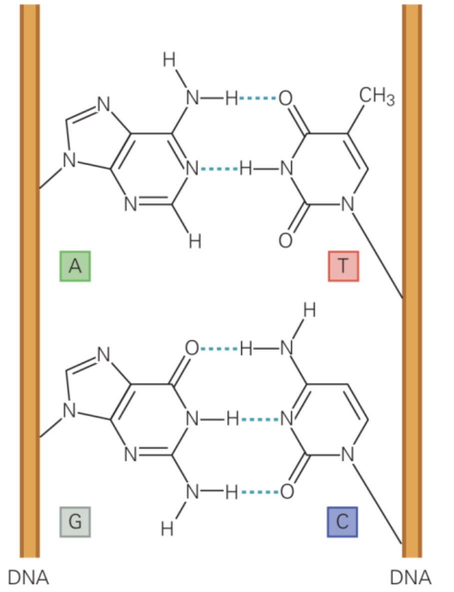


Based on covalent linkages between atoms

DNA in cells



DNA hybridization is driven by non-covalent interactions (hydrogen bonds)



Based on covalent and non-covalent interactions

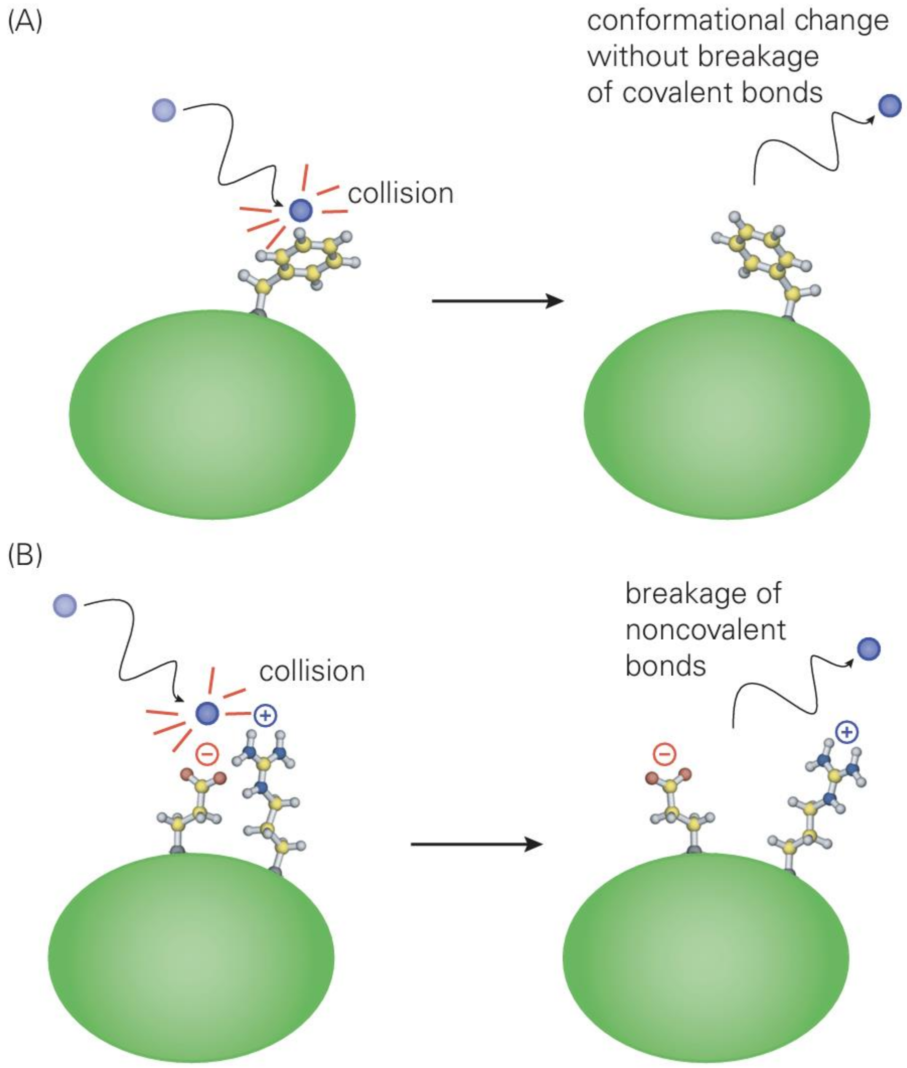
Covalent vs Non-covalent interactions

- **Covalent bonds** involve electron sharing and are very stable (in most cases), requiring **high energy** to break the bond apart.
- Interatomic distances in covalent bonds are well-defined with minimal flexibility.
- **Non-covalent interactions** are based on **transient** attraction or repulsion events and are much weaker than chemical bonds, needing significantly **less energy** to break (dissociate) them.

$$\mathbf{E_{covalent\ bonds} \sim 100\text{-}900\ kJ/mol}$$

$$\mathbf{E_{non\text{-}covalent\ interactions} \sim 0.1\text{-}20\ kJ/mol}$$

* Depends on the medium in which the molecules are

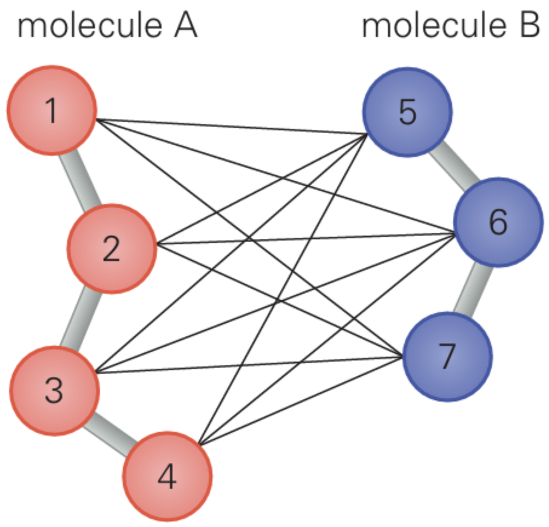


Noncovalent interactions are broken and remade due to thermal fluctuations and collisions with other molecules

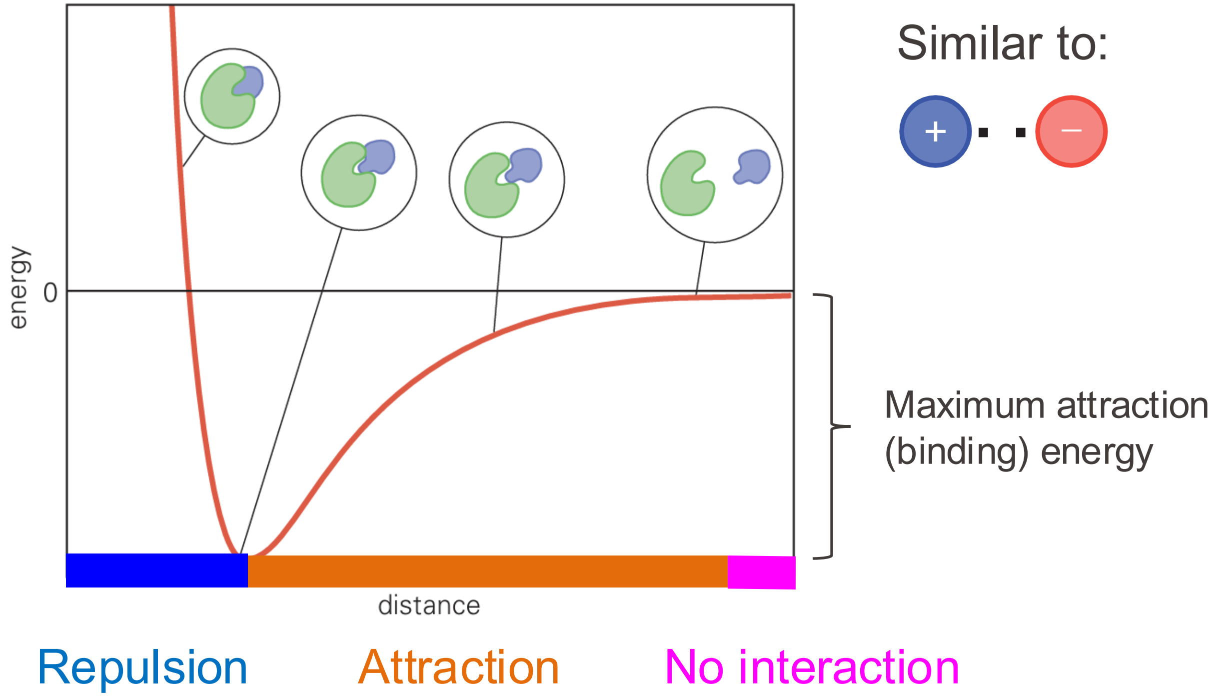
Properties of non-covalent interactions

- The energy of non-covalent interactions is dependent on the **distances** between molecules and local **environment** (i.e., solvent, interacting partners).

- The interactions between molecules can be attractive or repulsive, and their dependence on distance and environment is best expressed through energy potential (U)



$$U(total) = \sum_{i=1}^{n} U(i)$$

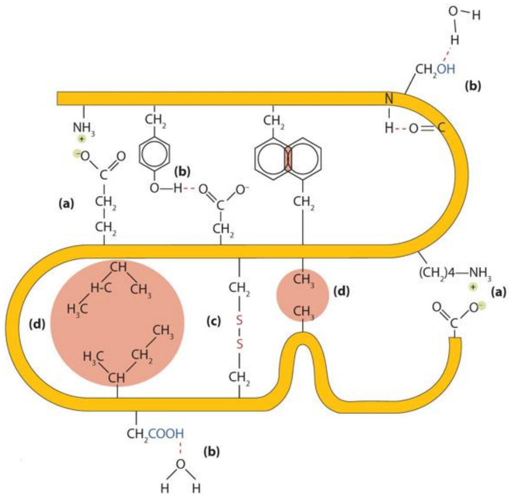


- System energy **reduces with distance indicating attractive interactions**, but starts to **sharply increase** when the distance is so small that **two molecules start to clash** with each other

Thermodynamic view of biomolecular systems

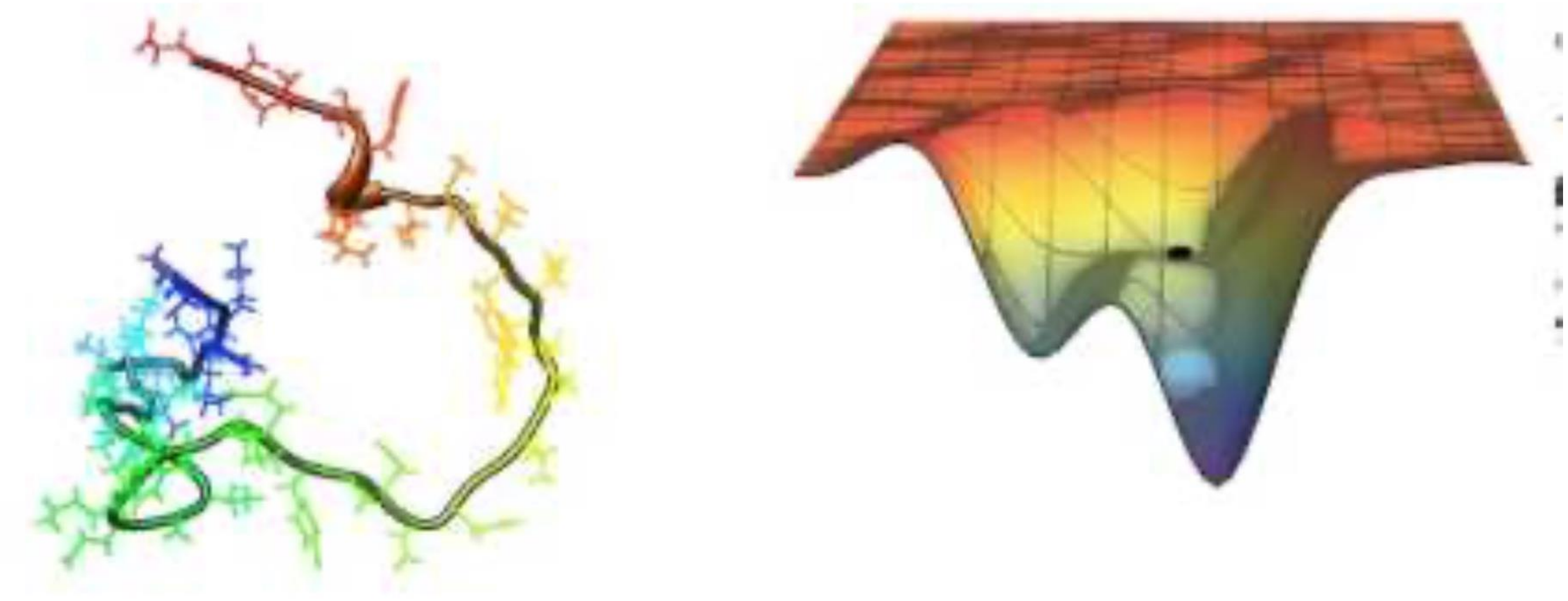
- Biomolecule assembly and function are driven by the tendency to reach the thermodynamically most favored (=lowest energy) state.

Example: Protein folding process



$$U(total) = \sum_{i=1}^{n} U(i)$$

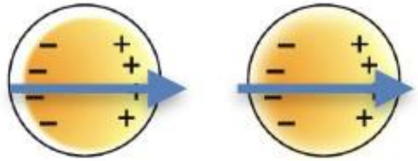
1000s of interactions



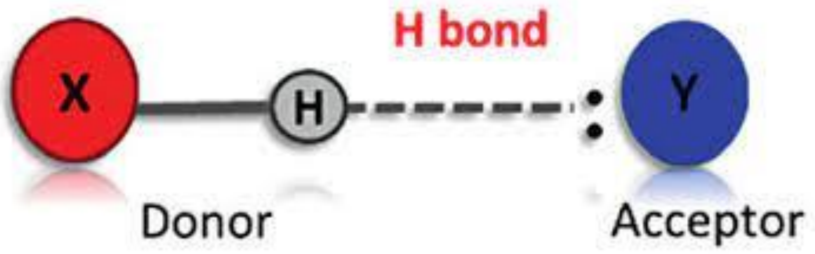
Different types of non-covalent interactions

- Depending on the nature of chemical groups there are several important interactions that take place in biological systems:
  - **Electrostatic (ionic) interactions**
  - **Van der Waals interactions**
  - **Hydrogen bonds**
  - **Hydrophobic effect**

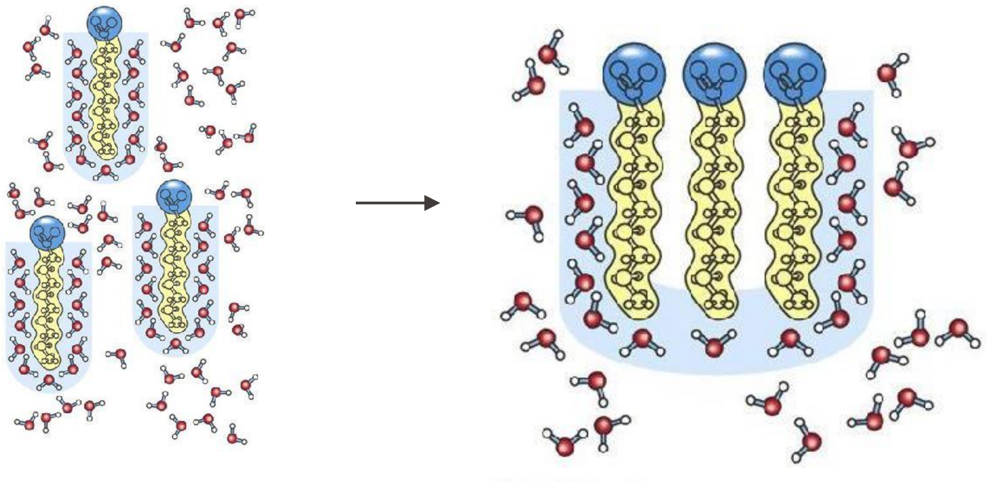
van der Waals interactions



Hydrogen bonds



Hydrophobic effect

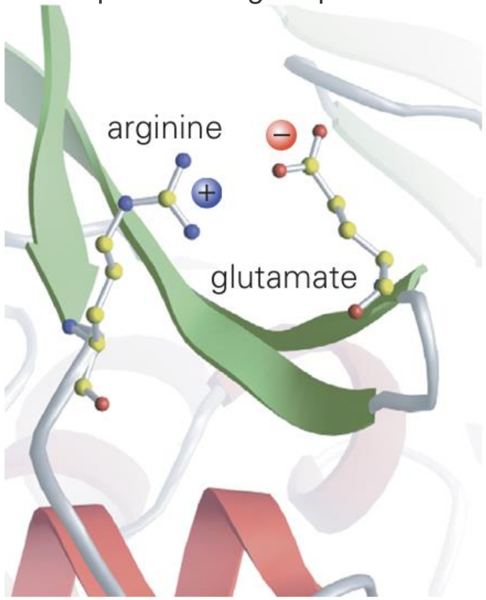


Ionic interactions

Ionic or electrostatic interactions

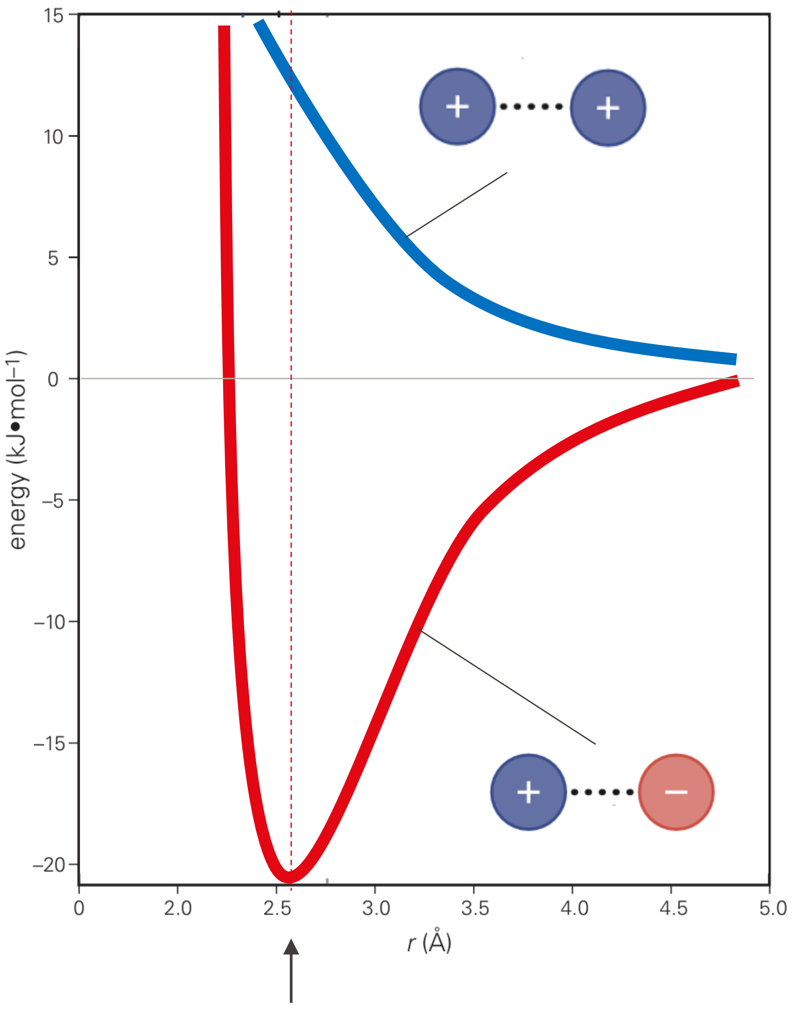
- Simplest kind of interaction between two charged groups and/or ions
- It can be attractive or repulsive. If charges are opposite these interactions are called **salt bridges**

Example salt bridge in proteins



$$U(r) = \frac{1}{4\pi\epsilon_0}\frac{1}{D}\frac{q_1 q_2}{r}$$

ϵ_0 - Permittivity of vacuum = 8.854×10^{-12} $C^2 \cdot N^{-1} \cdot m^{-2}$
D - Dielectric constant of solvent
r - Distance between groups
q_n - Charges of two groups



Most optimal distance for attractive interactions

- Electrostatic potential energy is described by Coulomb's law

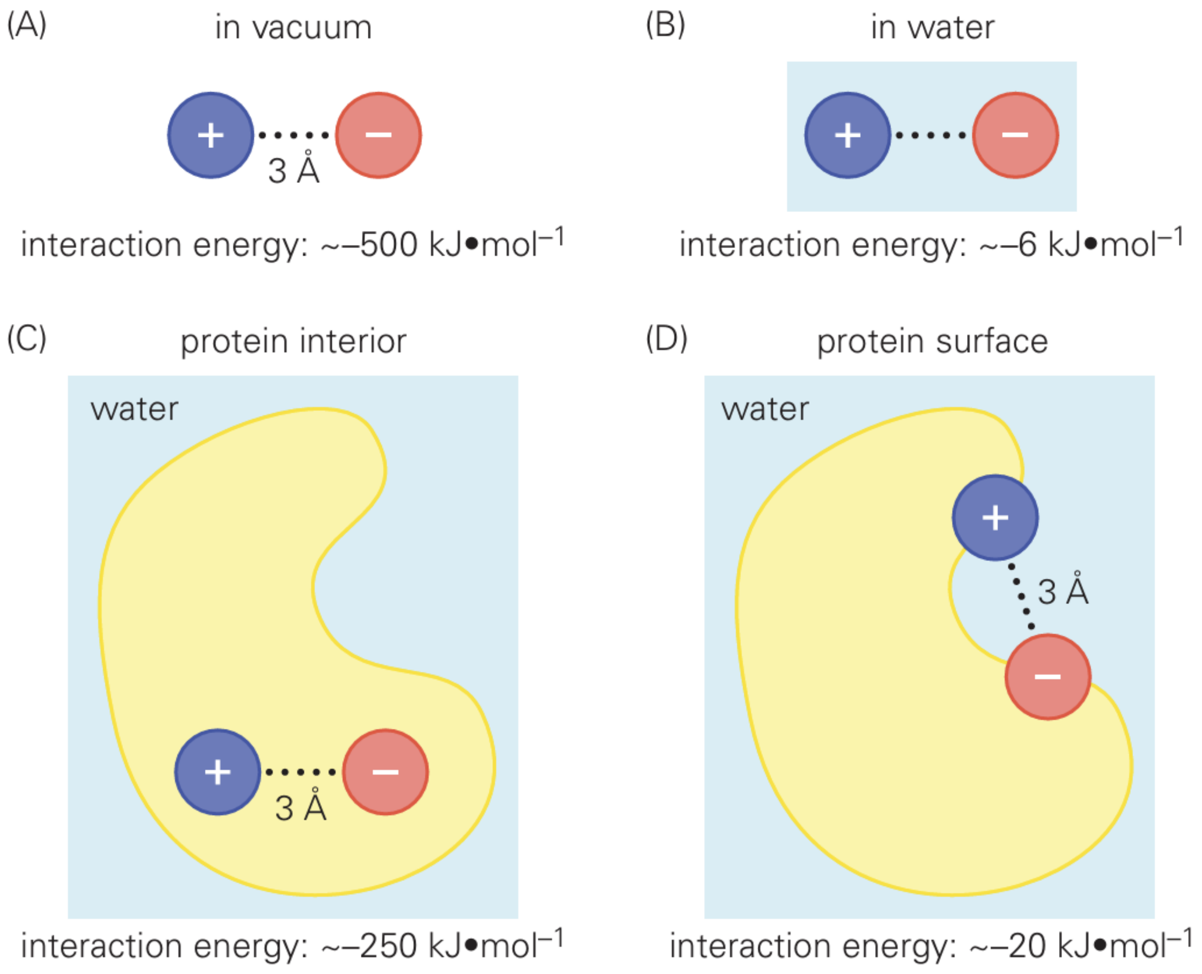
Ionic or electrostatic interactions

- The relative strength of ionic interactions are **influenced by the environment (medium)**
- This is expressed through factor **D** in Coulomb's law equation

$$U(r) = \frac{1}{4\pi\epsilon_0} \frac{1}{D} \frac{q_1 q_2}{r}$$

D_{water} (25˚C) = 78.5
$D_{methanol}$ (25˚C) = 33.0
$D_{heptane}$ (25˚C) = 1.9

- The stabilizing effect of salt bridges is different in biomolecule **interior** (not exposed to water) compared to **exterior** (exposed to water)



van der Waals interactions

- These interactions occur due to attraction of dipoles created by polar bonds or proximity to other polar/charged atoms or groups
- Individual **vdW interactions are very weak** and quickly deteriorate with distance **U(r) ~ 1/r^6**
- The interaction potential does not depend directly on the medium, but different solvents can compete with interacting groups (indirect effect)

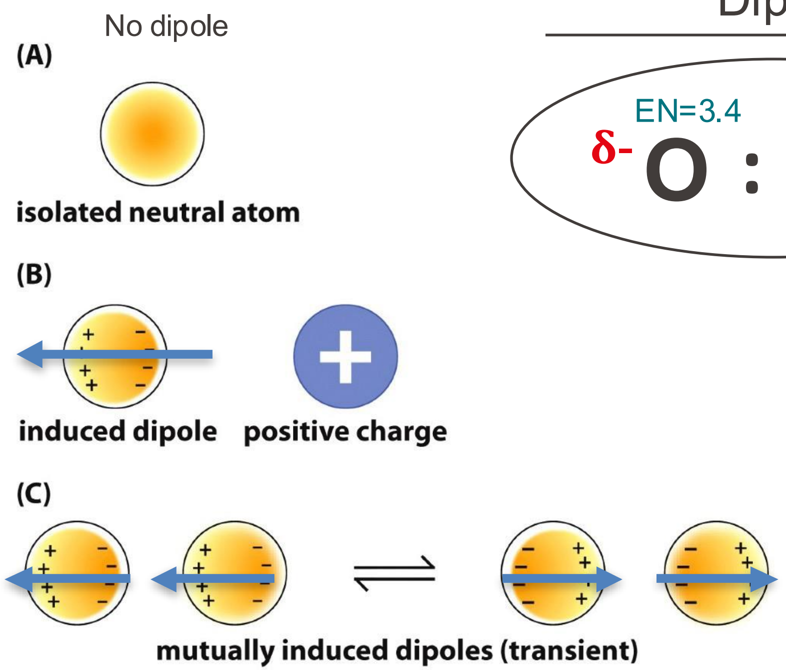
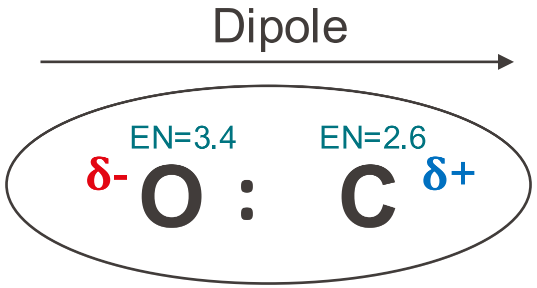
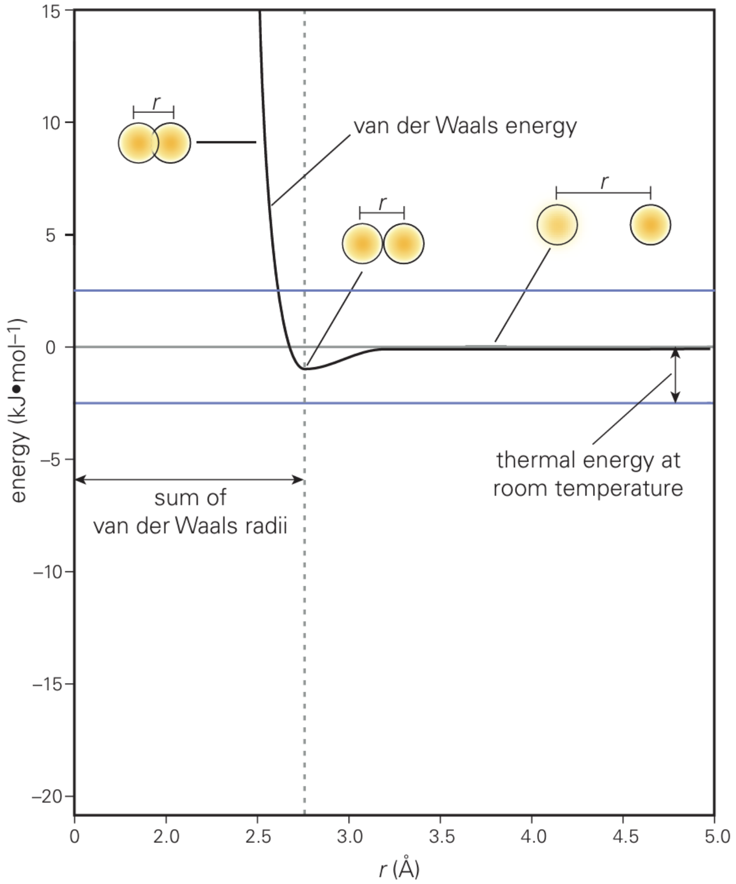


Figure 1.5 The Molecules of Life (© Garland Science 2013)

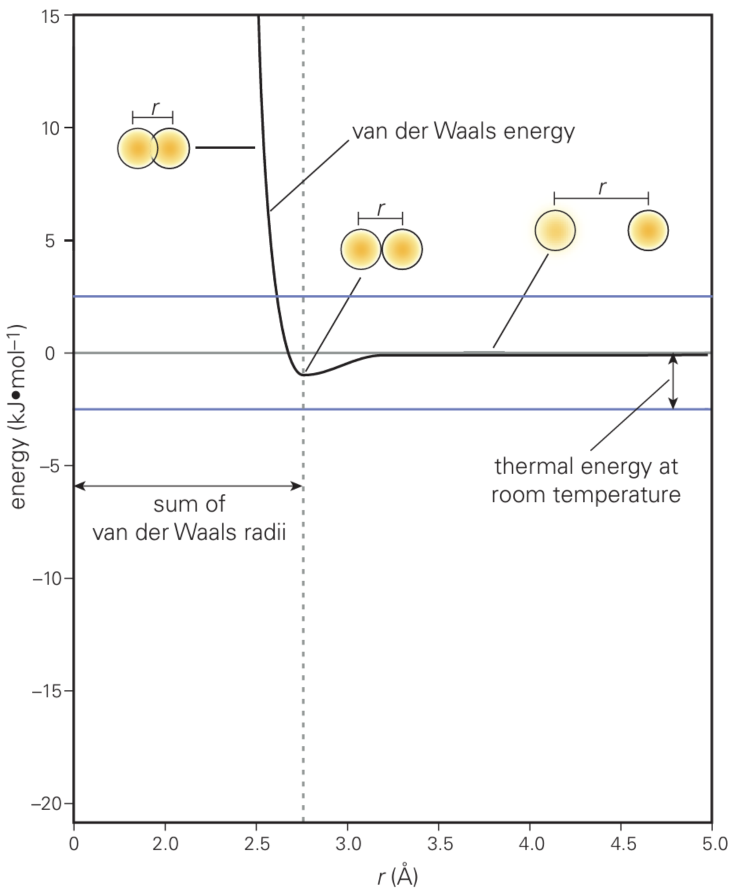


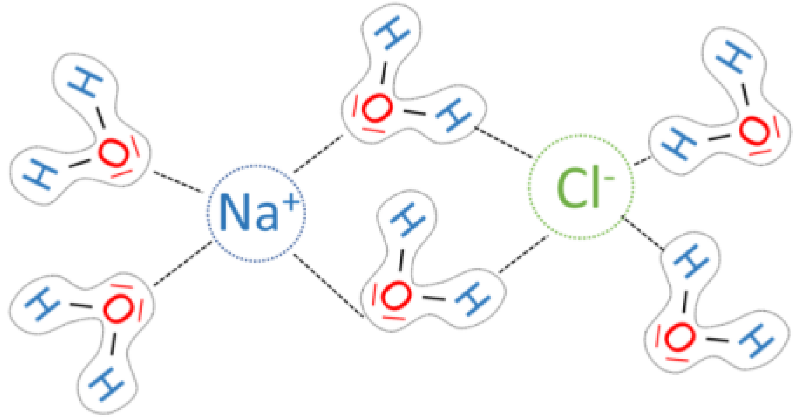


London dispersion forces

van der Waals interactions

- The property of an atom or group to create an electric dipole moment in an electric field is called **polarizability**
- Even non-polar groups and atoms can be polarized and contribute to vdW interactions
- The radius of each atom determines **the distance of minimal energy** (sum of vdW radii).
- Below the distance of minimal energy, the electron orbitals of atoms start to clash causing repulsion



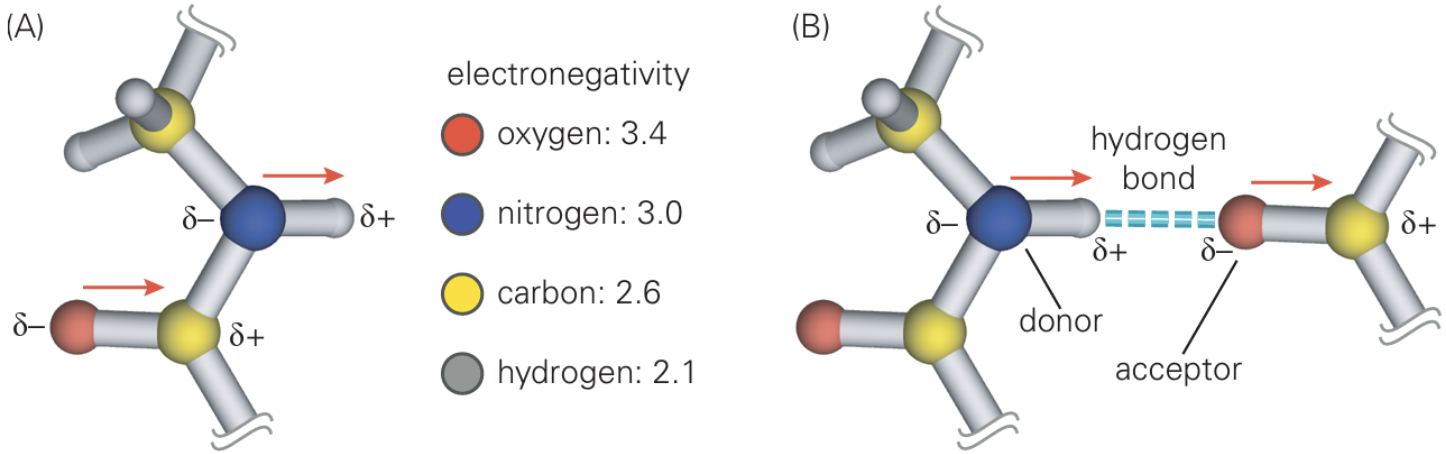


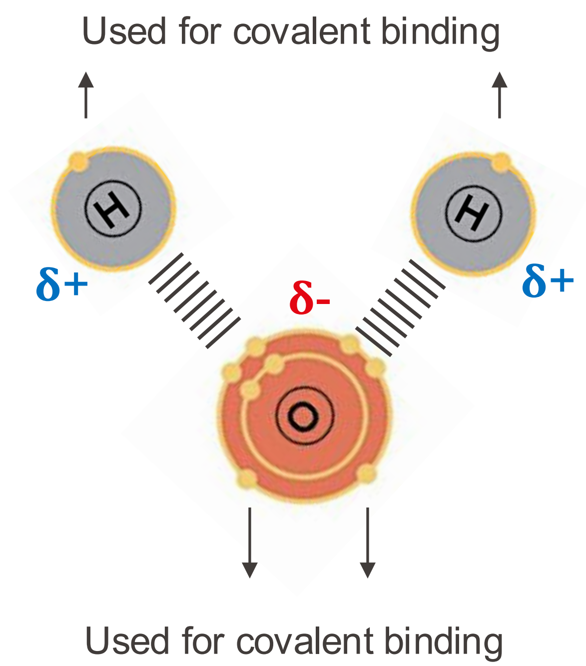
Example of vdW forces between ions and water molecules

EPFL

Hydrogen bonds

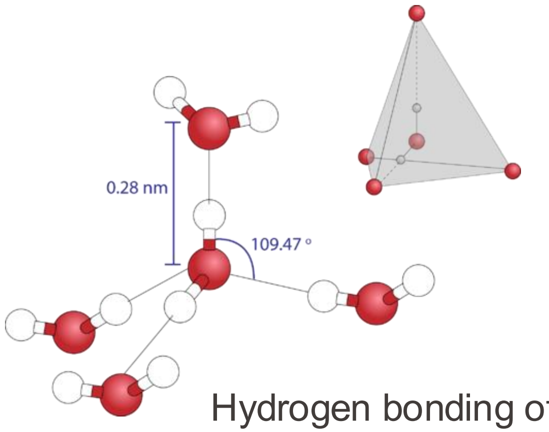
- Interactions between polar groups in which a hydrogen atom with a partial positive charge is close to an atom with a partial negative charge. Can be thought of as a special case of vdW interaction.
- Hydrogen bond **donor group** consists of strongly **electronegative atom** bound to hydrogen (e.g., **N-H, O-H, S-H**). This does not include **C-H bonds** since they are **non-polar**.
- Hydrogen bond **acceptor group** consists of a polarized atom with a free electron pair in the valent level that gives it partial negative charge (e.g., O, N, S). This once again does not include carbon as it does not have a free electron pair in the valent level.



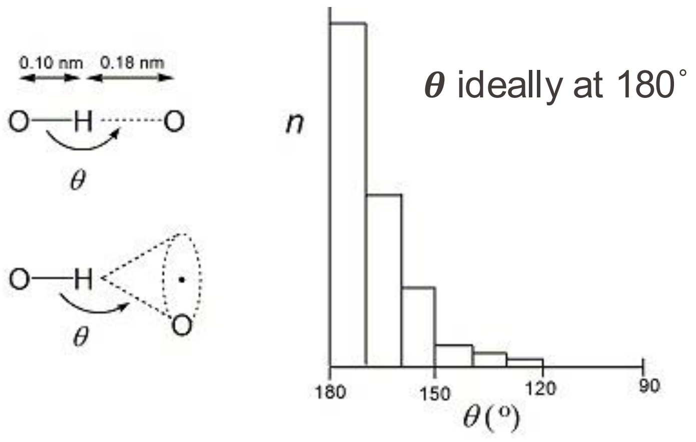


Hydrogen bonds

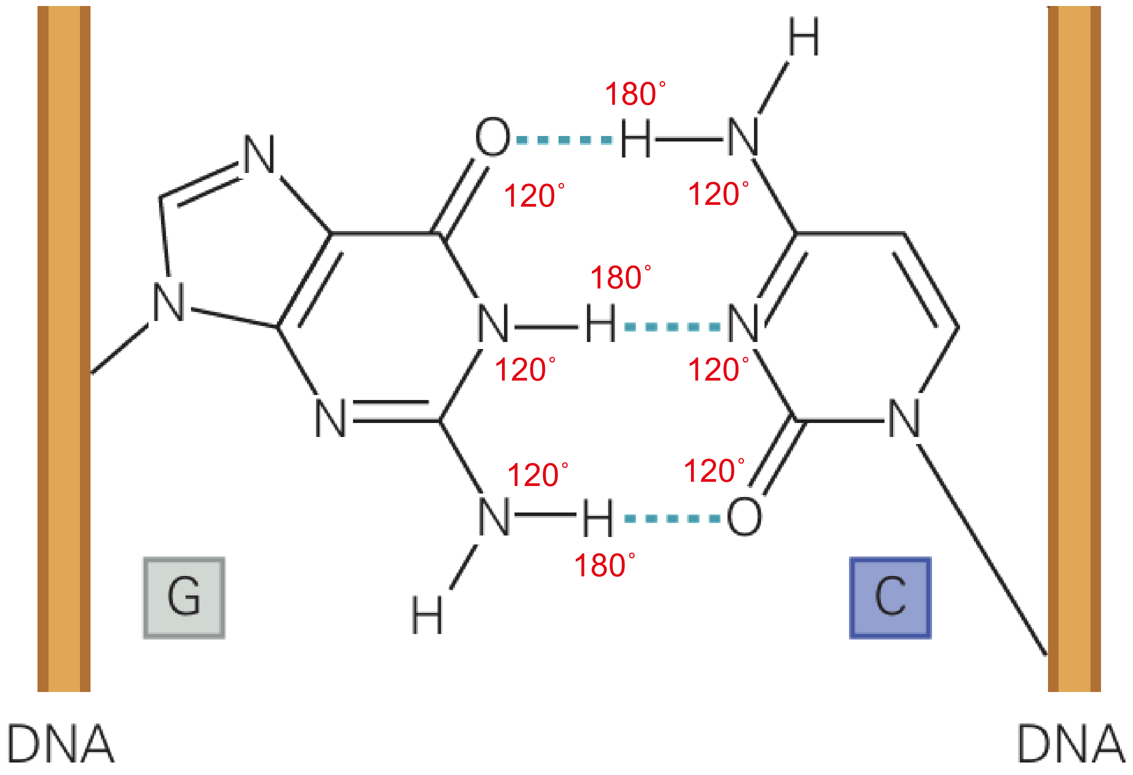
- H-bonds are environment-, distance-, and angle-dependent (position of donor and acceptor atoms)
- Typical distances between 2.4-3.5 Å and their energy decreases with distance ***U(r) ~ 1/r³***



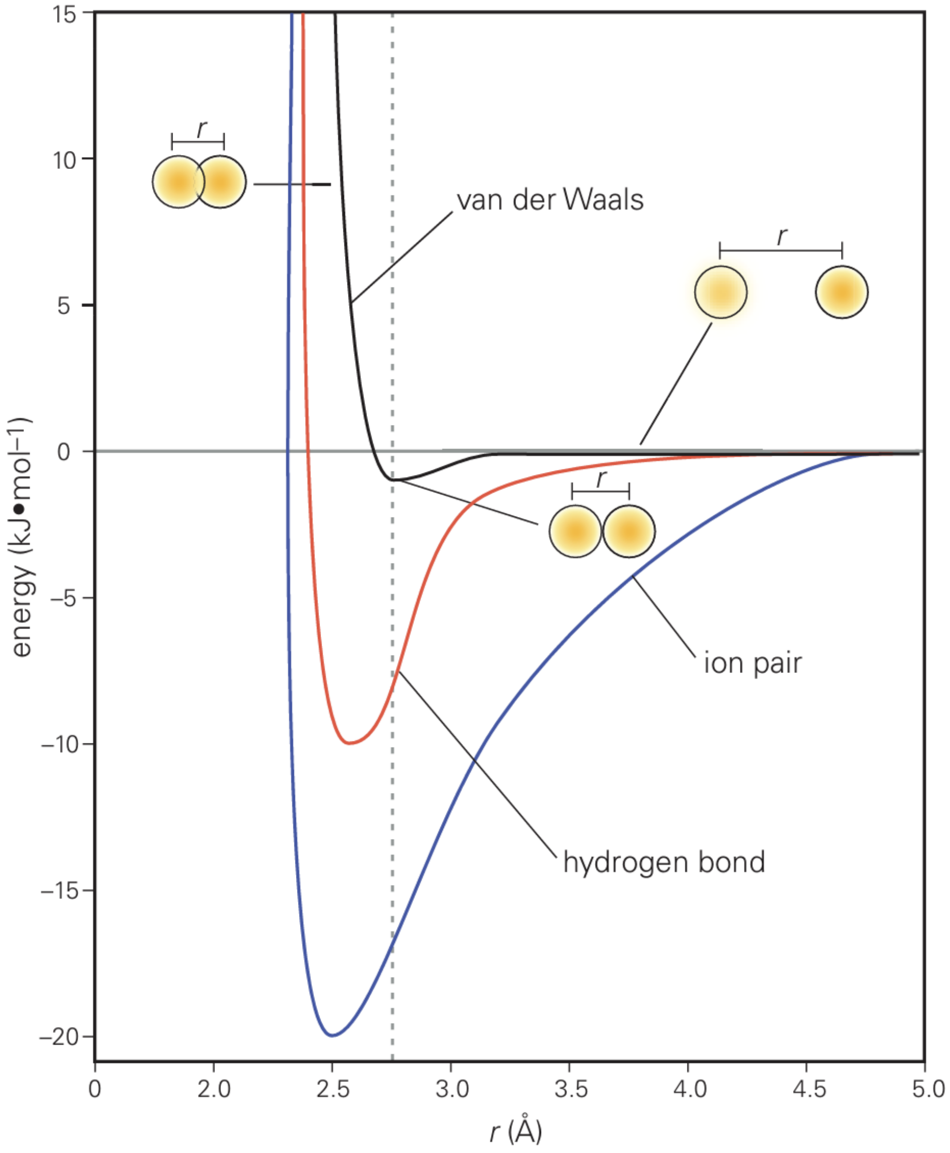
Hydrogen bonding of water



Hydrogen bonding between 2 DNA strands



Comparison of non-covalent interactions

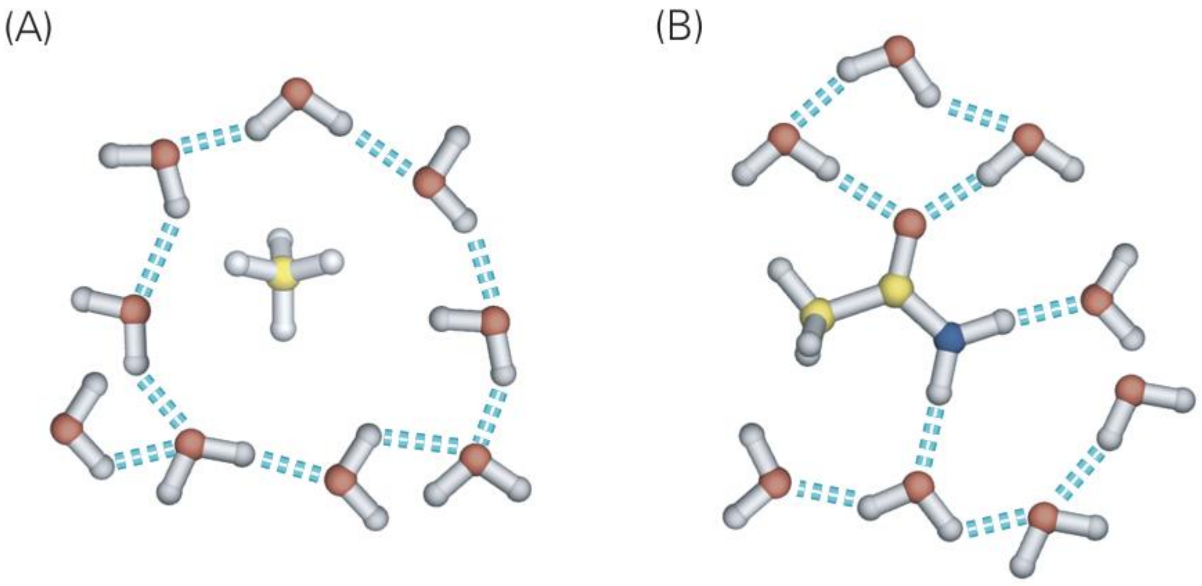


- These primary types of non-covalent interactions differ in their magnitude, with **salt bridges (electrostatic) contributing the most energy per interaction.**
- Hydrogen bonds can have a profound stabilizing effect on the local assembly contributing ~10kJ/mol of energy under optimal geometry.
- While vdW interactions appear to be lower in max energy, they can occur between **any pair of atoms**, while the previous two require special chemical groups
- Therefore, the **total energy contribution of vdW is on the same level as the other two**, when taking into consideration the entire molecule
- **Thermal energy (= k_B*T) of the system** will impact the ability of atoms or groups to form non-covalent interactions, and it should always be considered.

Hydrophobic effect

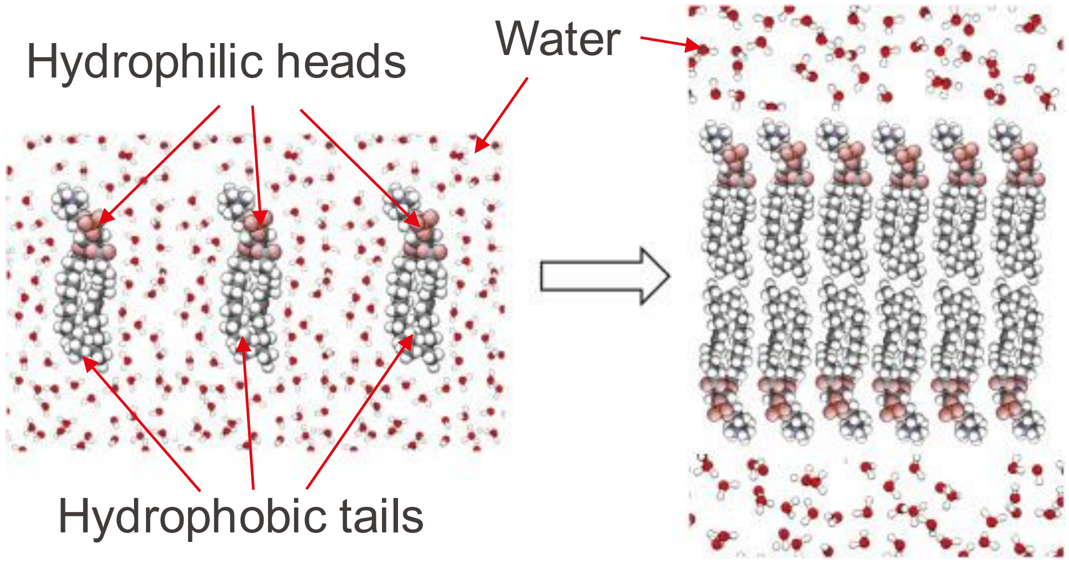
- Hydrophobic groups (e.g., C-C and C-H) are **non-polar** — that is, they do not form hydrogen bonds.
- Hydrophobic groups **prefer to cluster with other hydrophobic groups** rather than interact with water, in part because they cannot form hydrogen bonds with water.

Hydrophobic molecules do not dissolve well in water.



Methane (hydrophobic) **Acetamide** (hydrophilic)

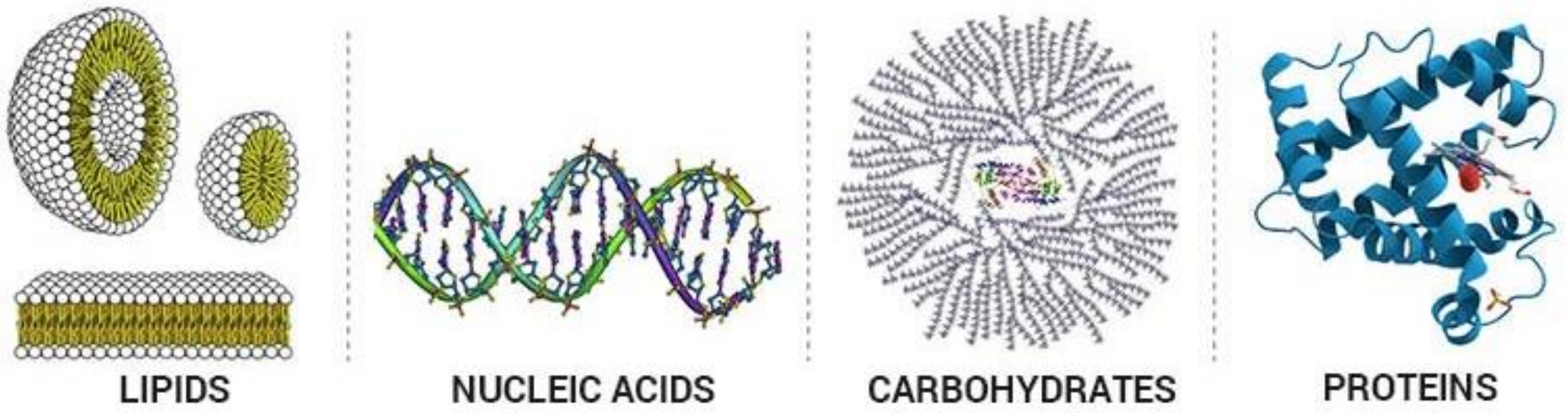
Hydrophobic clustering of fatty acid tails in lipids.



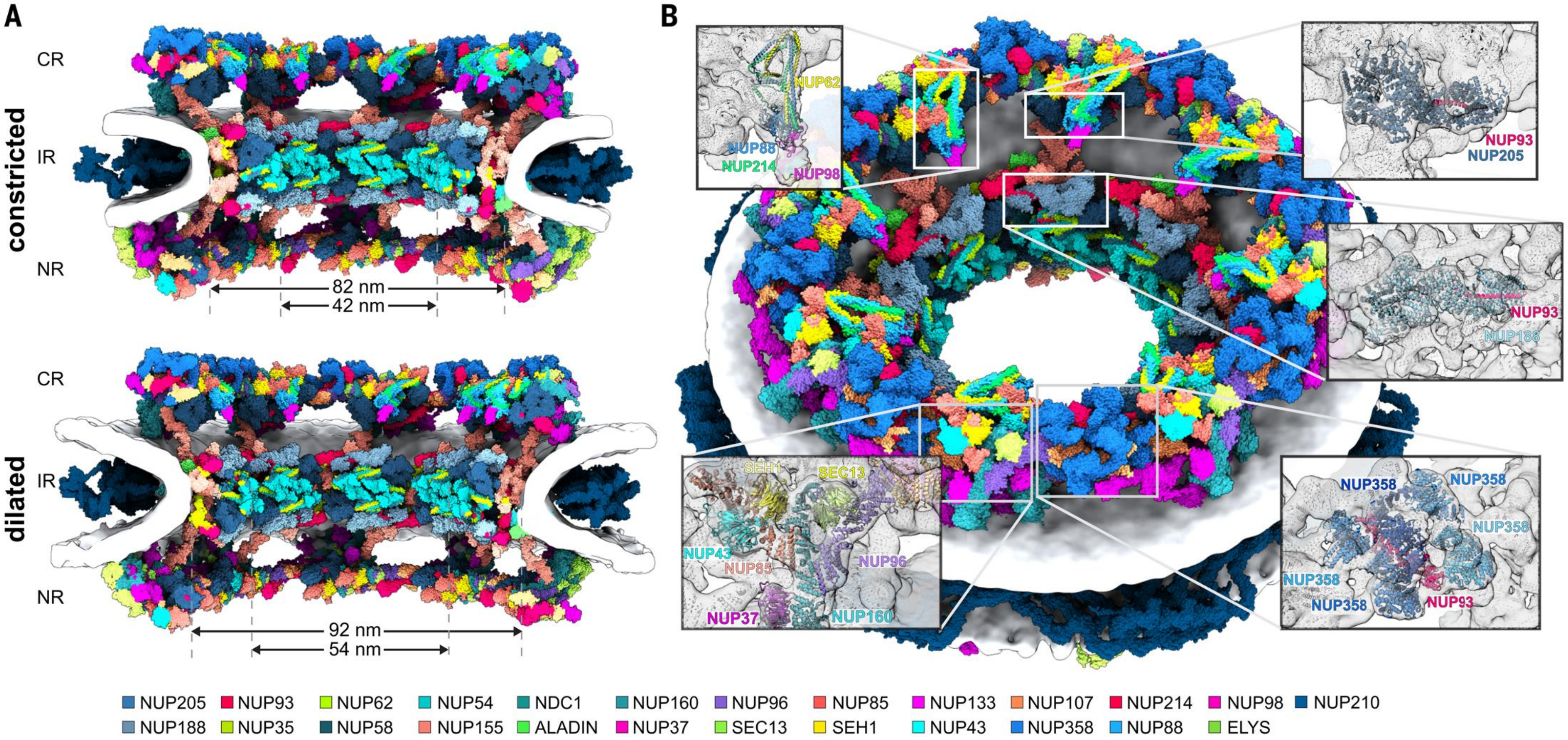
Assembly of cellular and organelle membranes

Tying it all together

- Biological macromolecules can consist of millions of atoms covalently bound into diverse chemical groups with different physicochemical properties.
- The covalent and non-covalent interactions formed between these groups, as well as with the external molecules (e.g., solvent) influence how the molecules assemble in cells.
- The main determining factor is thermodynamic drive towards reaching the lowest energy state
- The 3D assembly (= structure) of biomolecules and their complexes determines the biological function



The nuclear pore complex



~500 proteins + lipid bilayer

(~10^7 atoms working in sync to support the function)

Summary of key concepts

- The most abundant classes of biomolecules are **proteins, lipids, nucleic acids** and **carbohydrates**
- Their composition is largely based on the following elements: **H, N, C, O, P, S.**
- The energy of chemical group interaction within biomolecules and between different biomolecules is determined by **noncovalent interactions.**
- All atoms are polarizable and attract each other at short distances through **van der Waals interactions.**
- **Electrostatic interactions** occur between charged chemical groups. They can be very strong, but are attenuated by water molecules (screening effect).
- **Hydrogen bonds** are very common in biological macromolecules and are a consequence of strong polarization of covalent bonds.
- **Hydrophobic effect** is an essential driving force in biological systems due to the aqueous medium.