UNIT 1
Introduction.
The Basis of Biochemistry.
1.1. Introduction to Biochemistry.
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   Biomolecules are carbon compounds
   Functional groups of the biomolecules

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   Physical and chemical properties of water
   Water role in the biological processes
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   Chemical equilibrium and exergonic/endergonic reactions
   ATP coupled reactions
   Phosphoryl group transfer potential
   Biological redox reactions
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1. INTRODUCTION TO BIOCHEMISTRY

**Biochemistry Definitions**

- Science related to the chemistry of the living systems.
- Discipline focused on the study of the living systems molecules and how they interact.
- Science that combines Chemistry and Biology.
- Science that uses the Chemistry’s language to explain Biology at molecular level.
- Biochemistry is a science whose boundaries now encompass all aspects of biology, from molecules to cells, to organisms, to ecology and to all aspects of health care.
1. INTRODUCTION TO BIOCHEMISTRY

Biochemistry interacts with several disciplines: Cellular Biology, Genetics, Immunology, Microbiology, Pharmacology and Physiology.

**Biochemistry main goals**

1. What kinds of molecules are biomolecules?
2. What are the structure and chemistry of the biomolecules?
3. How do the biomolecules interact with each other?
4. How does the cell synthesise the biomolecules?
5. How is the energy store and use by the cell?
6. How do cells organise the biomolecules and coordinate their activities?
7. How are the mechanisms that allow the information transferred?
1. INTRODUCTION TO BIOCHEMISTRY

Chemical composition of living systems

H, O, N y C constitute more than 99 % of the atoms of the cells

<table>
<thead>
<tr>
<th>ELEMENT</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen</td>
<td>63</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>25.2</td>
</tr>
<tr>
<td>Carbon</td>
<td>9.5</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>1.4</td>
</tr>
</tbody>
</table>

H, O, N y C, are among the lightest elements capable of forming one, two, three or four covalent bonds, respectively
## Essential elements for the animals

Orange: main elements (structural components of the cells and tissues): diet requirement: \( g/\text{day} \)

Yellow: oligoelements (trace elements): diet requirement: \( \text{mg/day} \) (Fe, Cu y Zn) or even less.

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1. INTRODUCTION TO BIOCHEMISTRY
1. INTRODUCTION TO BIOCHEMISTRY

Biomolecules are carbon compounds

Carbon versatility in forming stable covalent bonds though electron-pair sharing (one, two or three covalent bonds)

Only carbon can form such a variety of molecules (linear, branched and cyclic compound)
1. INTRODUCTION TO BIOCHEMISTRY

Functional groups of the biomolecules:

- Methyl: $\text{R} - \text{C} - \text{H}$
- Ethyl: $\text{R} - \text{C} - \text{C} - \text{H}$
- Phenyl: $\text{R} - \text{C} = \text{C} - \text{C} - \text{H}$
- Amino: $\text{R} - \text{N} - \text{H}$
- Guanidino: $\text{R} - \text{N} - \text{C} - \text{N} - \text{H}$
- Amido: $\text{R} - \text{C} - \text{N} - \text{H}$
- Imidazole: $\text{R} - \text{C} = \text{CH}$
- Carbonyl (aldehyde): $\text{R} - \text{C} = \text{O}$
- Ether: $\text{R}^1 - \text{O} - \text{R}^2$
- Carboxyl (ketone): $\text{R}^1 - \text{C} - \text{O} - \text{R}^2$
- Ester: $\text{R}^1 - \text{C} - \text{O} - \text{R}^2$
- Carboxyl (alcohol): $\text{R} - \text{C} = \text{O} - \text{H}$
- Anhydride (two carboxylic acids): $\text{R}^1 - \text{C} - \text{O} - \text{C} - \text{O} - \text{C} - \text{R}^2$
1. INTRODUCTION TO BIOCHEMISTRY

**Sulfhydryl**

\[ R-S-H \]

**Disulfide**

\[ R^1-S-S-R^2 \]

**Thioester**

\[ R^1-C-S-R^2 \]

- **Phosphoryl**

\[ R-O-P-OH \]

- **Phosphoanhydride**

\[ R^1-O-P-O-P-O-R^2 \]

- **Mixed anhydride** (carboxylic acid and phosphoric acid; also called acyl phosphate)

\[ R-C-O-P-OH \]
# 1. INTRODUCTION TO BIOCHEMISTRY

## Table 3-5

<table>
<thead>
<tr>
<th>Molecular Components of an <em>E. coli</em> Cell</th>
<th>Percentage of total weight of cell</th>
<th>Approximate number of different molecular species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>70</td>
<td>1</td>
</tr>
<tr>
<td>Proteins</td>
<td>15</td>
<td>3,000</td>
</tr>
<tr>
<td>Nucleic acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DNA</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>RNA</td>
<td>6</td>
<td>&gt;3,000</td>
</tr>
<tr>
<td>Polysaccharides</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Lipids</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Monomeric subunits and intermediates</td>
<td>2</td>
<td>500</td>
</tr>
<tr>
<td>Inorganic ions</td>
<td>1</td>
<td>20</td>
</tr>
</tbody>
</table>
2. WATER AS A SUSTAINING LIFE MEDIUM

Water provides conditions for the origin, evolution and flourishing of life
2. WATER AS A SUSTAINING LIFE MEDIUM

WHAT DO YOU HAVE TO KNOW?

Why is water a polar molecule?
What is a hydrogen bond?
How are water biomolecules linked by hydrogen bonds?
How is the structure of water (liquid and ice)?
Why does ice float in water?
2. WATER AS A SUSTAINING LIFE MEDIUM

WHAT DO YOU HAVE TO KNOW?

Physical and chemical properties of water

- Maximum density at 4 °C
- High boiling point
- High specific heat
- Heat of vaporisation
- Thermal conductivity
- Dielectric constant
- Capacity to form hydration shells surrounding ions
- Solvent of amphipathic molecules
- Solvent of polar and non ionic compounds
- High surface tension
- Transparency
Water’s role as the medium of life:

- **Structural component** of the macromolecules

- **Universal solvent.** Most biological reactions take place within water

- **Substrate or product** in several enzymatic reactions

- Effective **temperature regulations** in living organisms
Acid-Base equilibrium

WHAT DO YOU HAVE TO KNOW?
Can pure water ionise?
Which are the products of the water ionisation?
What is the pH of the pure water? Why?
What is an acid? What is a base?
Which are the relations between pK and the tendency to leave protons?
Which are the relations between pH and pK?
How is pH controlled in the biological fluids?
What are the properties of a buffer?
How is a buffer prepared (phosphate buffer 0.1 M, pH 7.2?)
Cells are open systems that exchange **matter** (nutrients and waste products) and **energy** (heat from metabolism...) with their surroundings.
3. BIOENERGETICS

Enthalpy, entropy and Gibbs free energy

WHAT DO YOU HAVE TO KNOW?

- Meaning of the enthalpy, entropy, free energy and their relations.

- How a concrete reactions is affected by changes in the disorder and randomness

- Definition of the standard-state (including biochemist standard-state)
The order of the biomolecules is thermodynamically possible, if the cells cause an increase of the surroundings entropy.

3. BIOENERGETICS

Enthalpy, entropy and Gibbs free energy

3.25 Producción de orden biológico. El dibujo superior muestra los componentes bioquímicos sencillos, como por ejemplo nucleótidos o azúcares, en una célula esquemática. La biosíntesis más compleja y altamente ordenada de macromoléculas, como por ejemplo el DNA o los polisacáridos, puede ceder espontáneamente calor al entorno. [PI]
3. BIOENERGETICS

Chemical equilibrium and exergonic/endergonic reactions

The point equilibrium for a reaction in solution is a function of the free energy for the process.

\[ \Delta G^o' = - RT \ln K'_{eq} \]

- Free energy changes within the cell depends on the temperature and the concentration of the reactants and products (they could be different to those of the standard conditions)

\[ \Delta G = \Delta G^o' + RT \ln ([C][D]/[A][B]) \]

Mass-action ratio \((Q) = ([C][D]/[A][B])\)
ATP coupled reactions

• Some chemical reactions do not spontaneously process ($\Delta G > 0$): endergonic reactions

• Cells can carried out endergonic reactions coupling them to an exergonic reaction (negative $\Delta G$ value)

• Endergonic reactions usually are coupled to ATP hydrolysis

• The useful free energy from an ATP molecules is store in the two pyrophosphoryl (phosphoric acid anhydride linkages)
3. BIOENERGETICS

Biochemical reactions are coupled

(b) Chemical example

**Reaction 1:**
Glucose + P\textsubscript{i} → glucose 6-phosphate

**Reaction 2:**
ATP → ADP + P\textsubscript{i}

**Reaction 3:**
Glucose + ATP → glucose 6-phosphate + ADP

\[ \Delta G_3 = \Delta G_1 + \Delta G_2 \]
3. BIOENERGETICS

ATP

\[
\Delta G^\circ = -30.5 \text{ kJ/mol (~7.3 kcal/mol)}
\]

\[\text{ATP} + \text{H}_2\text{O} \rightarrow \text{ADP} + \text{P}_i\]

\[
\Delta G^\circ = -32.2 \text{ kJ/mol (~7.7 kcal/mol)}
\]

\[\text{ATP} + \text{H}_2\text{O} \rightarrow \text{AMP} + \text{PP}_i\]

\[
\Delta G^\circ = -33.5 \text{ kJ/mol (~8 kcal/mol)}
\]

\[\text{PP}_i + \text{H}_2\text{O} \rightarrow 2\text{P}_i\]
3. BIOENERGETICS

ATP

• It is an intermediate energy shuttle molecule (connect catabolism and anabolism)

• It is involved in several processes:
  • Biomolecules synthesis
  • Active transport through the membranes
  • Mechanic work (i.e. muscular contraction)

• It transfers phosphoryl groups from high energy compounds to less energetic compounds.

• Group transfer potential: ATP hydrolysis
The ATP hydrolysis releases energy (which is not able to promote a chemical reaction in an isothermic system)

ATP is involved in many enzymatic reactions (The hydrolysis of ATP adds free energy to the system)

The phophoryl groups are transferred to the reaction reactants or to the aminoacid residues (belonging to an enzyme) Free energy increase
3. BIOENERGETICS

Phosphoryl group transfer potential

**Phosphoryl group transfer potential**: phosphorylated compound capability that implies a phosphoryl group transference.

Due to the magnitude of the group transfer potential, ATP can transfer free energy from high energy phosphate compounds (catabolism products) to lower energy compounds such as glucose.

**SUCH TRANSFER IS CRUCIAL IN LINKING ENERGY-PRODUCING AND ENERGY-UTILISING METABOLIC PATHWAYS IN LIVING CELLS**
3. BIOENERGETICS

Phosphoryl group transfer potential

\[ \Delta G^{\circ} \text{ of hydrolysis (kJ/mol)} \]

-70
-60
-50
-40
-30
-20
-10
0
1,3-Bisphosphoglycerate
Adenine
Rib
P
P
P
ATP
P
P
P
Phosphoenolpyruvate
Creatine
Phosphocreatine
Glucose 6-
P
Glycerol-
P
P
\text{High-energy compounds}
\text{Low-energy compounds}
3. BIOENERGETICS

**Biological redox reactions**

**WHAT DO YOU HAVE TO KNOW?**

When does a molecule become oxidised? Or reduced?

What is the redox potential (oxidation-reduction potential)?

Which is the relation between redox potential and free energy changes?
Reducing equivalents (protons and electrons) derived from oxidations of substrates (cellular oxidation) are transferred to the “Universal electron transporters/carriers”:

NAD\(^+\), NADP\(^+\), FMN y FAD: hydrosoluble coenzymes that can be reduced or oxidised (reversible reaction)

Liposolubles quinones (ubiquinone and plastosequinone), Fe-S proteins and cytochromes
Electron transporters

Nicotinamide coenzymes

- They transport 2 electrons
- They derive from niacin (nicotinic acid) \((\text{B}_3)\) to provide nicotinamide portion
- They transfer hydride \((\text{H}^-)\) to and from the reactants
  - Nicotinamide adenine dinucleotide \((\text{NAD}^+)\)
  - Nicotinamide adenine dinucleotide phosphate \((\text{NADP}^+)\)

- \(\text{NAD}^+\) is mainly involved in oxidative reactions. **Catabolism is oxidative**
- \(\text{NADPH}\) is mainly involved in reductive reactions. **Anabolism is reductive**
3. BIOENERGETICS

Electron transporters

Nicotinamide coenzymes

Nicotinamide

\[
\begin{align*}
&\text{Nicotinamide} \\
&\text{A side} \\
&\text{B side} \\
&\text{NADH (reduced)} \\
&\text{NAD}^+ \text{ (oxidized)}
\end{align*}
\]

In NADP⁺ this hydroxyl group is esterified with phosphate.

(a)
NAD+ accepts a hydride from the reduce substrate AH₂

\[
\begin{align*}
\text{NAD}^+ + 2e^- + 2H^+ \rightarrow \text{NADH} + H^+ \\
\text{AH}_2 \rightarrow A + 2H^+ + 2e^- \\
\text{AH}_2 + \text{NAD}^+ \rightarrow A + \text{NADH} + H^+
\end{align*}
\]

NADPH serves as hydride donor for an oxidise substrate

\[
\begin{align*}
\text{NADPH} + H^+ \rightarrow \text{NADP}^+ + 2e^- + 2H^+ \\
A + 2H^+ + 2e^- \rightarrow \text{AH}_2 \\
A + \text{NADPH} + H^+ \rightarrow \text{AH}_2 + \text{NADP}^+
\end{align*}
\]
During the mitochondrial electron transport, electrons flux from NADH to oxygen. The released free energy is used for ATP synthesis.

Photosynthetic organisms use light to promote electron transport from electrons donors such as water, to electron acceptors (with higher negative redox potential).

\[
\frac{1}{2} \text{O}_2 + \text{NADH} + \text{H}^+ \rightarrow \text{H}_2\text{O} + \text{NAD}^+ \quad \Delta E^0' = 0.82 - (-0.32) = 1.14 \text{ V}
\]
Flavin nucleotides

- They are forms of riboflavin (vit. B2)
- They contain ribitol (alcohol) and a flavin (isoalloxazine ring)
- Two coenzymes: flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD)
- The isoalloxazine ring is reduced by accepting one or two electrons (one or two hydrogen atoms) from a reduced substrate
- Flavin coenzymes are bound either very tightly or covalently to a flavoprotein (flavoenzyme). Ex. Succinate dehydrogenase: catalyze the succinate oxidation to produce fumarate (energy production)
- The redox potential of the isoalloxazine ring depends on the specific flavoprotein
Flavin nucleotides

Flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN)