



NATIONAL UNIVERSITY OF PHARMACY
Department of Educational and Information Technologies

BIOPHYSICS, PHYSICAL METHODS OF ANALYSIS

Lecture 3

**Thermodynamics of biological
processes. Molecular Biophysics.**

Plan of the Lecture

- 1. Energy Transformation.**
- 2. Metabolism.**
- 3. Hess's Law.**
- 4. Entropy.**
- 5. Gibbs Free Energy.**
- 6. Electrochemical Thermodynamics.**

Purpose of the lecture is

- ▶ **to master the basic provisions of the thermodynamics of biological processes and explore physical structure of biologically important molecules.**

Biological thermodynamics

Biological thermodynamics may be defined as the quantitative study of the energy transformations that occur in and between living organisms, structures, and cells and of the nature and function of the chemical processes underlying these transformations.

The field of biological thermodynamics is focused on principles of general thermodynamics in biology and biochemistry. Principles covered include the first law of thermodynamics, the second law of thermodynamics, Gibbs free energy, statistical thermodynamics, reaction kinetics, and on hypotheses of the origin of life.

Presently, biological thermodynamics concerns itself with the study of internal biochemical dynamics as: ATP hydrolysis, protein stability, DNA binding, membrane diffusion, enzyme kinetics, and other such essential energy controlled pathways.

The Laws of Energy Transformation

- **Thermodynamics** is the study of energy transformations in macroscopic systems
- A isolated system, such as that approximated by liquid in a thermos, is isolated from its surroundings
- In an open system, energy and matter can be transferred between the system and its surroundings
- Organisms are open systems

Forms of Energy

Energy is the capacity to cause change. Energy can be converted from one form to another. Energy exists in various forms, some of which can perform work. **Work (thermodynamics), the energy transferred from one system to another by macroscopic forces measurable in the surroundings**

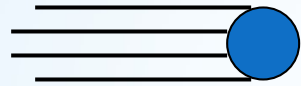
- **Kinetic energy** is energy associated with motion
- **Heat (thermal energy)** is kinetic energy associated with random movement of atoms or molecules
- **Potential energy** is energy that matter possesses because of its location or structure
- **Chemical energy** is potential energy available for release in a chemical reaction

Energy

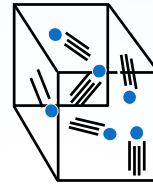
You know that energy cannot be created nor destroyed.

- Many Different Forms

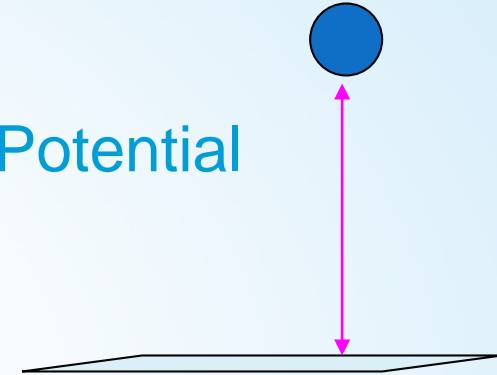
Kinetic



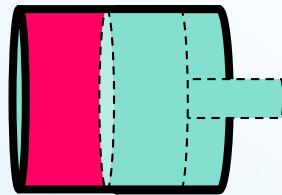
Internal



Potential



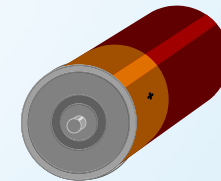
Mechanical



Chemical



Electrical



Energy continuously flows through the biological world in one direction, with new energy from the SUN continuously entering the system to replace the energy dissipated as heat.

Metabolism

- An organism's metabolism transforms matter and energy, subject to the laws of thermodynamics
- **Metabolism** is the totality of an organism's chemical reactions
- Metabolism is an emergent property of life that arises from interactions between molecules within the cell
- A metabolic pathway begins with a specific molecule and ends with a product
- Each step is catalyzed by a specific enzyme. Enzymes are the catalysts used by cells to perform particular reactions
- Catabolic pathways release energy by breaking down complex molecules into simpler compounds
- Anabolic pathways consume energy to build complex molecules from simpler ones

Metabolic Pathways Cooperate To:

1. Obtain Chemical Energy by:
 - a. Capturing Solar Energy, *or*
 - b. Oxidizing Energy Rich Chemicals from the Environment.
2. Convert Nutrient Molecules to *metabolic intermediates*, then monomers or waste products.
3. Polymerize monomers to polymers (proteins, carbohydrates, nucleic acids, lipids).
4. Synthesize and Degrade (turnover) biomolecules.

5 Main Classes of Metabolic Reactions

1. Oxidation-Reduction Reactions
2. Reactions that Make or Break Carbon-Carbon Bonds
3. Internal Rearrangements, Isomerizations, Eliminations.
4. Group Transfer Reactions.
5. Free Radical Reactions.

First Law of Thermodynamics

The **first law of thermodynamics** is an expression of the principle of conservation of energy. The law states that energy can be transformed, i.e. changed from one form to another, but cannot be created nor destroyed. It is usually formulated by stating that the change in the internal energy of a system is equal to the amount of heat supplied to the system, minus the amount of work performed by the system on its surroundings.

- Energy is Conserved

$$E = \text{constant}$$

$$(E_{\text{Kinetic}} + E_{\text{Potential}} + E_{\text{Internal}} + E_{\text{Chemical}} + E_{\text{Mechanical}} + E_{\text{Electrical}}) = \text{constant}$$

$$\Delta U = Q - W$$

Energy in chemical reactions:

Free energy (G): It is an amount of energy capable of doing work during a reaction at constant temperature and pressure. When a reaction proceeds with release of free energy, the free energy change ΔG has a negative value and the reaction is called exergonic. Opposite is endergonic reaction in which there is gain of free energy.

Enthalpy (H): Represents the heat content of the reacting systems. When there is release of heat during a reaction it is referred as exothermic reaction and the ΔH is negative. Opposite is endothermic reaction with ΔH positive.

Entropy (S): it is a quantitative expression for the randomness or disorder in the system. There is always an increase in entropy or gain of entropy of the overall system in any reaction.

$$\Delta G = \Delta H - T\Delta S$$

Enthalpy, H

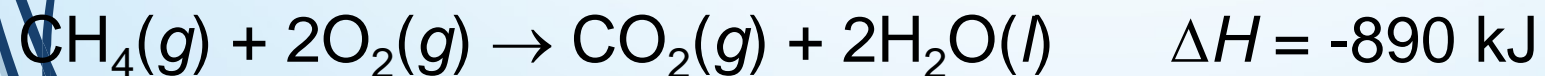
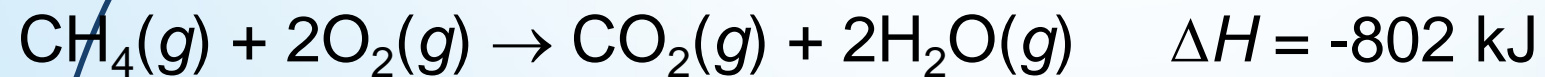
- Closely related to energy: $H = E + PV$
- Therefore changes in H are: $\Delta H = \Delta E + P\Delta V + V\Delta P$
- Most, but not all, biochemical systems have constant V , P : $\Delta H = \Delta E$
- Related to amount of *heat content* in a system

Entropy, S

- Related to disorder: Boltzmann: $S = k \times \ln W$
 $k = \text{Boltzmann constant} = 1.38 \times 10^{-23} \text{ J K}^{-1}$
- Note that $k = R / N_0$
- W is the number of degrees of freedom in the system (number of states)
- Entropy in 1 mole = $N_0 S = R \times \ln W$
- Number of degrees of freedom can be calculated for simple atoms

Hess's Law

- Hess's law: if a reaction is carried out in a number of steps, ΔH for the overall reaction is the sum of change of enthalpy ΔH for each individual step.
- Hess's law states that the change of enthalpy in a chemical reaction (i.e. the heat of reaction at constant pressure) is independent of the pathway between the initial and final states.
- The concepts of Hess's law can be expanded to include changes in entropy and in Gibbs free energy, which are also state functions.
- For example:



Entropy

- Like total energy, E , and enthalpy, H , entropy is a state function.
- Therefore, $\Delta S = S_{\text{final}} - S_{\text{initial}}$
- For a process occurring at constant temperature (an isothermal process):

$$\Delta S = \frac{q_{\text{rev}}}{T}$$

q_{rev} = the heat that is transferred when the process is carried out **reversibly** at a constant temperature.

T = temperature in Kelvin.

An organism is not an isolated system: so S can decrease within an organism

Second Law of Thermodynamics

The second law of thermodynamics: The entropy of the universe does not change for reversible processes and increases for spontaneous processes.

Reversible (ideal):

$$\Delta S_{univ} = \Delta S_{system} + \Delta S_{surroundings} = 0$$

Irreversible (real, spontaneous):

$$\Delta S_{univ} = \Delta S_{system} + \Delta S_{surroundings} > 0$$

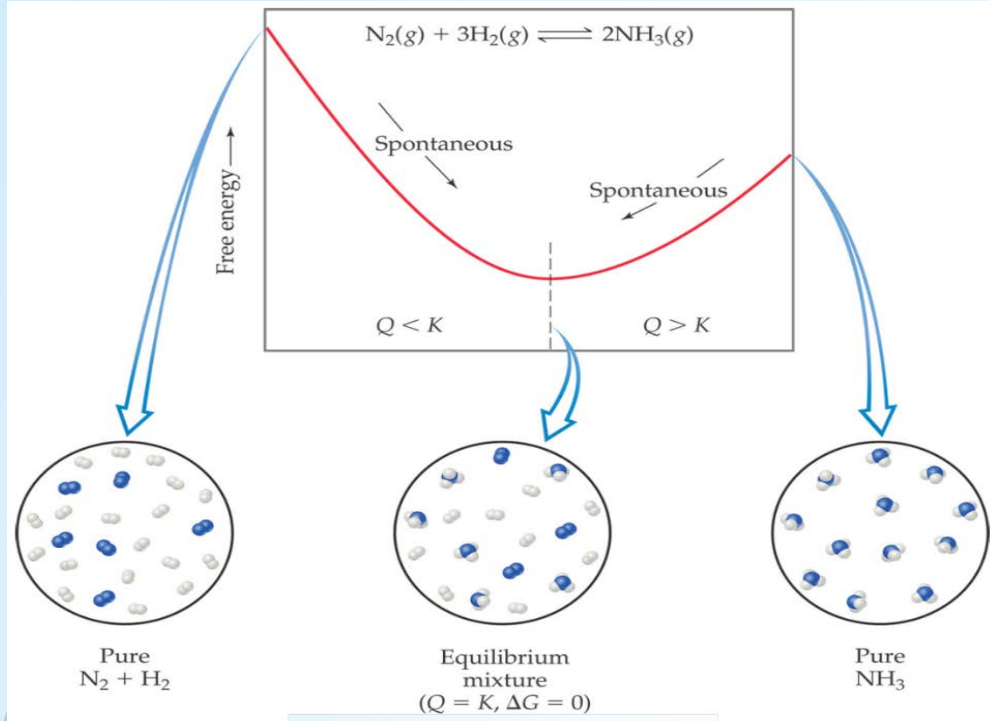
The entropy of the universe increases (real, spontaneous processes).

But, entropy can decrease for individual (living) systems.

$-T \Delta S_{universe}$ is defined as the Gibbs free energy, ΔG .

For spontaneous processes: $\Delta S_{universe} > 0$ And therefore: $\Delta G < 0$

Gibbs Free Energy



1. If ΔG is negative, the forward reaction is spontaneous.
2. If ΔG is 0, the system is at **equilibrium**.
3. If ΔG is positive, the reaction is spontaneous in the reverse direction.

- Free energy is the energy available to do work in any system.
- Free energy is important to cells (organisms) and cells store and release free energy using the ATP molecule.
- The chemical reactions inside of cells can be explained using the Laws of Thermodynamics.
- The chemical reactions (inside and outside of cells) can be predicted based on free energy changes.

Standard Free Energy Changes

Standard free energies of formation, ΔG_f° are analogous to standard enthalpies of formation, ΔH_f° .

$$\Delta G_f^\circ = \sum \Delta G_{reactants}^\circ - \sum \Delta G_{products}^\circ$$

ΔG° can be looked up in tables, or calculated from S° and ΔH° .

Free Energy Changes

Very key equation:

$$\Delta G = \Delta H_{sys}^\circ - T\Delta S_{system}$$

This equation shows how ΔG° changes with temperature.

(We assume S° & ΔH° are independent of T.)

Dependence on Concentration

- Actual ΔG of a reaction is related to the concentrations / activities of products and reactants:

$$\Delta G = \Delta G^\circ + RT \ln [\text{products}]/[\text{reactants}]$$

- If all products and reactants are at 1mol, then the second term drops away; that's why we describe ΔG° as the *standard* free energy

The starting molecules of a chemical reaction are called the reactants or, substrates.

The molecules at the end of a reaction are called the products.

Free energy and equilibrium

- Gibbs: $\Delta G^{\circ} = -RT \ln K_{\text{eq}}$
- Rewrite: $K_{\text{eq}} = \exp(-\Delta G^{\circ}/RT)$
- K_{eq} is equilibrium constant; formula depends on reaction type
- For $aA + bB \rightarrow cC + dD$,
 $K_{\text{eq}} = ([C]^c[D]^d)/([A]^a[B]^b)$
- Thus if reaction is just spontaneous, i.e. $\Delta G^{\circ} = 0$, then $K_{\text{eq}} = 1$
- If $\Delta G^{\circ} < 0$, then $K_{\text{eq}} > 1$: *Exergic*
- If $\Delta G^{\circ} > 0$, then $K_{\text{eq}} < 1$: *Endergic*
- Reactions in a closed system eventually reach equilibrium and then do no work
- Cells are not in equilibrium; they are open systems experiencing a constant flow of materials
- A defining feature of life is that metabolism is never at equilibrium
- A catabolic pathway in a cell releases free energy in a series of reactions
- Closed and open hydroelectric systems can serve as analogies

Thermodynamics and Kinetics

- We distinguish between *thermodynamics* and *kinetics*:
- *Thermodynamics* characterizes the energy associated with equilibrium conditions in reactions
- *Kinetics* describes the *rate* at which a reaction moves toward equilibrium
- *Free energy* is directly related to the equilibrium of a reaction
- It doesn't tell us how fast the system will come to equilibrium
- Kinetics, and the way that enzymes influence kinetics, tell us about *rates*
- Today we'll focus on equilibrium energetics; we'll call that *thermodynamics*

Gibbs Free Energy

The free energy function is the key to assessing the way in which a chemical system will spontaneously evolve.

$$dG = -SdT + VdP + \sum \mu_i dn_i + \gamma dA + f dl$$

constant T

constant P

don't change
shape

don't stretch it

$$dG = \sum \mu_i dn_i$$

Electrochemical Thermodynamics

Every substance has a unique tendency to contribute to a system's energy. We call this property **Chemical Potential**. μ

When the substance is a charged particle (such as an electron or an ion) we must include the response of the particle to an electrical field in addition to its Chemical Potential. We call this **Electrochemical Potential**.

$$\mu = \mu + z F \phi$$

These are perhaps the most fundamental measures of thermodynamics.

ATP powers cellular work by coupling exergonic reactions to endergonic reactions

- A cell does three main kinds of work
 - Chemical
 - Transport
 - Mechanical
- To do work, cells manage energy resources by **energy coupling**, the use of an exergonic process to drive an endergonic one
- Most energy coupling in cells is mediated by ATP
- ATP (adenosine triphosphate) is the cell's energy shuttle
- ATP is composed of ribose (a sugar), adenine (a nitrogenous base), and three phosphate groups

Dissipative Function

The rate of entropy production in open system under constant temperature and pressure is given by product of reaction rate and the work done by the system.

Now we introduce expression for the rate of entropy production in unit volume:

$$\Theta = 1/V (dS/dt)$$

and function Ψ : $\Psi = T \Theta$

The function Ψ is proportional to the rate of entropy in unit volume and is called dissipative function

Ψ depends on the rate of flux and driving force of the process, which are time-dependent parameters, therefore Ψ is also a function of time

Heat of Dissipation

In agreement with II. law of thermodynamics any irreversible process is accompanied by heat of dissipation. In open system it is possible that this heat leaves the system and the total entropy of the system stays constant, or even decreases.

We can write for the rate of entropy production in non-linear systems:

$$dS/dt = d_i S_n/dt + d_i S_d/dt$$

where

$d_i S_n/dt$ part of entropy production bound in the system

$d_i S_d/dt$ part of entropy production crossing the boundaries of the system

How the Hydrolysis of ATP Performs Work

- The three types of cellular work (mechanical, transport, and chemical) are powered by the hydrolysis of ATP
- In the cell, the energy from the exergonic reaction of ATP hydrolysis can be used to drive an endergonic reaction
- Overall, the coupled reactions are exergonic

The Regeneration of ATP

- ATP is a renewable resource that is regenerated by addition of a phosphate group to adenosine diphosphate (ADP)
- The energy to phosphorylate ADP comes from catabolic reactions in the cell
- The ATP cycle is a revolving door through which energy passes during its transfer from catabolic to anabolic pathways

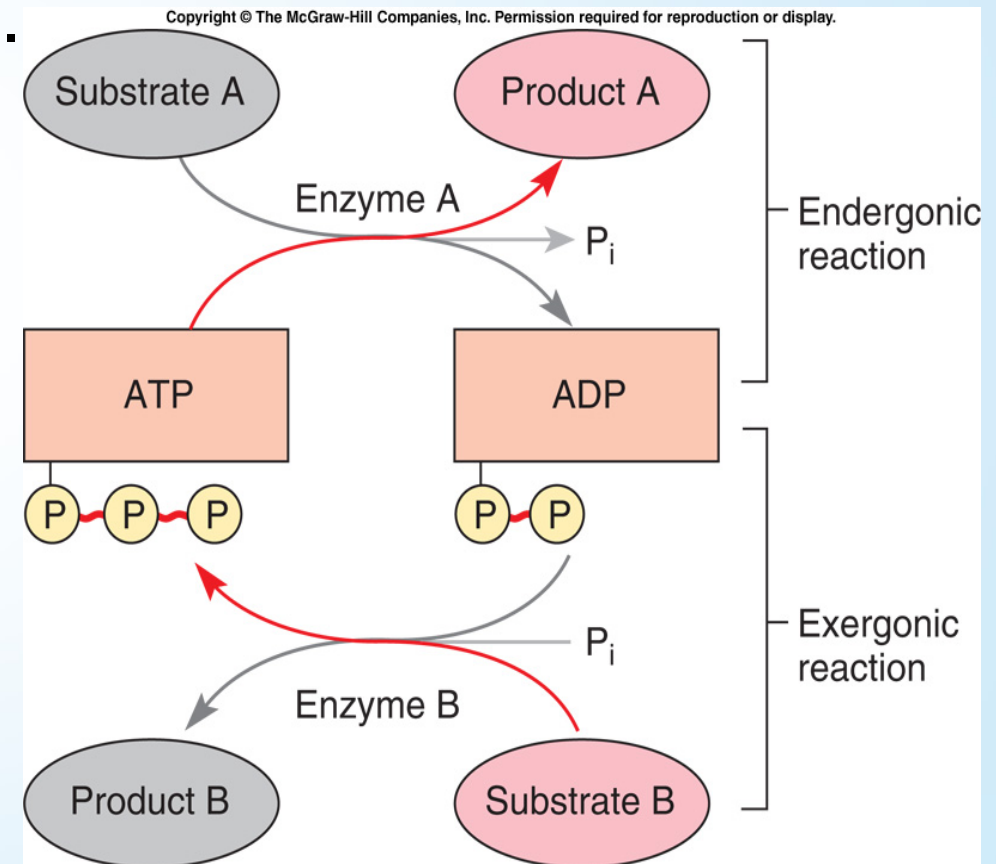
Coupled reactions

- All chemical reactions require an initial input of energy called the **activation energy**.
- The activation energy initiates a chemical reaction by destabilizing existing chemical bonds.

➔ When exergonic reactions are used to pay for the initiation of endergonic reactions.

➔ Usually endergonic reactions are coupled with the breakdown of ATP.

➔ More energy than is needed is released by the breakdown of ATP so heat is given off.



Control Questions

- 1. The laws of thermodynamics in chemistry and biology.**
- 2. Chemical and electrochemical potentials.**
- 3. Dissipative function.**
- 4. The ATP role.**
- 5. Coupled reactions.**

Recommended literature:

Basic:

1. Vladimir Timanyuk, Elena Zhivotova, Igor Storozhenko. Biophysics: Textbook for students of higher schools / Kh.: NUPh, Golden Pages, 2011.- 576p.
2. Vladimir Timaniuk, Marina Kaydash, Ella Romodanova. Physical methods of analysis / Manual for students of higher schools/- Kharkiv: NUPh: Golden Pages, 2012. – 192 p.
3. Philip Nelson. Biological Physics. – W. H. Freeman, 1st Edition, 2007. – 600 p.
4. Biophysics, physical methods of analysis. Workbook: Study guide for the students of higher pharmaceutical educational institutions / Pogorelov S. V., Krasovskiy I. V., Kaydash M. V., Sheykina N. V., Frolova N. O., Timaniuk V. O., Romodanova E.O., Kokodii M.H. – Kharkiv., – 2018. – 130 p.
5. Center for distance learning technologies of NPhaU. Access mode: <http://nuph.edu.ua/centr-distancijnih-tehnologijj-navcha/>

Support:

1. Eduard Lychkovsky. Physical methods of analysis and metrology: tutorial / Eduard Lychkovsky, Zoryana Fedorovych. – Lviv, 2012. – 107 p.
2. Daniel Goldfarb. Biophysics DeMYSTiFied. – McGraw-Hill Professional, 1st Edition, 2010. – 400 p.



Thanks for
your attention