## TOPIC 4.A. Thermodynamics of Biological Processes

Thermodynamic studies the thermal energy and its transformation through the state functions (Entropy, Enthalpy, Gibbs Free Energy, etc..). The living organisms are an open system that exchange with the environment matter and energy. The production of heat in most organisms is done during cellular respiration, but can be also influenced by external sources, such as sun radiation. The transport of heat in human body is done by the circulation of blood through the body, and in order to maintain the temperature constant we can lose, or even gain, heat by convection, conduction and radiation.

**Exercise 4.1a.** Write down the second law of thermodynamics for biological systems:

$$dS = \qquad (4.1a)$$

$d_eS$ is____________________________________________________________

$d_iS$ is____________________________________________________________

*The rate of change in entropy* of an open system (Prigogine equation) is:

$$\frac{dS}{dt} = \frac{d_eS}{dt} + \frac{d_iS}{dt} \qquad (4.2a)$$

It is always valid that rate $d_iS / dt$ >A 0; rates $dS / dt$ and $d_eS / dt$ can be both negative and positive. There are three cases:

1) $dS / dt > 0$ if $d_eS / dt > 0$ or if $d_eS / dt < 0$ $|d_eS/ dt| < d_iS / dt$ is____________________ state;

2) $dS / dt < 0$ if $d_eS / dt < 0$ and $|d_eS/ dt| > d_iS / dt$ is ______________________________state;

3) $dS / dt = 0$ if $d_eS / dt < 0$ and $|d_eS/ dt| = d_iS / dt$ is ______________________________state.

**Problem 4.2a.** The entropy in biological system during irreversible internal processes changed on $d_iS = 3.4\ J \cdot K^{-1}$, and due to interaction with the environment it changed on $d_eS = -3.9\ J \cdot K^{-1}$. Calculate the total change in entropy. Which system state does it correspond (stationary, pathological, or growth)?

| ***Data:*** | ***Solution:*** |
| --- | --- |
| | |

***Answer***: ______________________________________________________________________

## The Main Forms of Energy in Biological Systems

In biological object the primary source of energy is chemical energy that released by the oxidation of nutrients. During the process of cell oxidation, the chemical energy is converted into energy of energy-rich bonds of adenosine triphosphate (ATP). ATP diffuses into the appropriate cell formation, where its transformation into other forms of energy occurs.

**Exercise 4.3a.** Fill in the scheme with kinds of work which are performed in our body:

**Kinds of work**

**Chemical work** is

**Osmotic work** is

**Electric work** is

**Exercise 4.4a.** Fill in the table with the values that correspond to the biological system transition from state 1 to state 2 due to the particular conversion of the chemical energy of ATP into osmotic, electrical and chemical work:

*Table 4.1a.*

| forms of work | Energy per: | |
|---|---|---|
| | **1 molecule** | **1 mol** |
| Electric ($W_{el}$) (4.3a) | | |
| Osmotic ($W_{osm}$) (4.4a) | | |
| Chemical ($W_{chem}$) (4.5a) | | |

where: *e* is electron elementary charge; *F* is the charge of a mole of monovalent ions (Faraday`s number); $N_a$ is Avogadro's number (number of molecules in a mole of substance); *Z* is the integer charge of ion; *R* is universal gas constant; *T* is absolute temperature; *C* is molar concentration; *k* is Boltzmann constant; $\varphi$ is electric potential, $\mu$ is chemical potential.

To quantify the conversion of energy (work carried out in the system) used to use the thermodynamic potential called the Gibbs free energy:

$$\Delta G = \nu \cdot \Delta\bar{\mu} = \nu(W_{chem} + W_{osm} + W_{el}) = \nu(\mu_{02} - \mu_{01}) + \nu RT \ln\frac{C_2}{C_1} + \nu ZF(\phi_2 - \phi_1) . \qquad (4.6a)$$

***Example of problem solution.***

The osmotic work $W_{osm}$ done during the transport of 0.5 mol of sodium from the cell outwards is 2.97 kJ at the temperature t = 37 °C. Find the concentration of sodium ions outside the cell $C_o$ if the intracellular one is $C_i$ = 0.050 mol/L.

***Data:***

*Na* +

ν = 0.5 mol

$W_\nu = 2.97 kJ = 2.97 \times 10^3 J$

$C_i$ = 0.050 mol/L = $0.05 \cdot 10^3$ mol/m$^3$

***Solution:***

Using Table 4.1a we can see that the osmotic work per one mole should be:

$C_o$ =?

$$W_\nu = RT \ln \frac{C_2}{C_1}$$

Since ions are transported out of the cell, the $C_i = C_1$ and $C_2 = C_o$. One can rewrite the final formula and substitute the numerical values:

$$C_o = C_i \exp \frac{W_\nu}{RT} = C_i \exp \frac{W}{\nu RT} = 50 \exp \frac{2966}{0.5 \cdot 8.31 \cdot 310} =$$

500 mol/m$^3$.

***Answer***: The concentration of sodium ions outside the cell is 500 mol/m$^3$.

**Problem 4.5a.** Calculate the change in the electrochemical potential during the transfer of chloride ions into the frog`s muscle fibers from the extracellular environment, if it is known that the concentration of ions outside the cell is 64 times higher than inside one, and the inner side of the membrane has the potential –88 mV (outer side membranes potential is accepted to be zero). The temperature is 27 °C.

| ***Data:*** | ***Solution:*** |
|---|---|
| | |

***Answer***: ________________________________________

**Problem 4.6a.** The osmotic work done during the transport $\nu$ = 5 moles of chlorine ions into motor cats neuron at $t$ = 38 °C is $W_{osm\,\nu}$ = -34 kJ. Find the ratio of the concentrations of chloride ions outside and inside the cell.

| ***Data:*** | ***Solution:*** |
|---|---|
| | |

***Answer***: ________________________________________

## The Rate of Increase of Entropy and the Dissipative Function

Thermodynamics of irreversible processes considering the thermodynamic parameters that are time-variable.

**Exercise 4.7a.** Define the following terms and write down the formulas:

*Dissipative function* $\beta$ is: $\beta =$ (4.7a)

Write down Prigogine theorem ( the criterion of evolution of an open system)

.............................. (4.8a)

*Conjugation* is ________________________________________________

________________________________________________

*Conjugated (coupled) processes* are ________________________________________________

________________________________________________

Write down Onsager equations:

$J_1 =$ (4.9a)

$J_2 =$

L is________________________________________________

X is________________________________________________

**Problem 4.8a.** As a result of irreversible processes inside a cell at 37 °C the entropy change was 5.8 $J \cdot K^{-1}$ in 15 sec. Calculate the dissipative function.

| ***Data:*** | ***Solution:*** |
| --- | --- |
| | |

***Answer***: ________________________________________________

**Problem 4.9a.** The change in the free energy during transport of two electrons from reduced nicotinamide adenine dinucleotide (NAD) to a molecule of oxygen is $\Delta G^0 = -220$ kJ/mol. This process is conjugated with the synthesis of three molecules of ATP ($\Delta G^0_{ATP} = -30.5$ kJ/mol). Calculate the efficiency η of the conjugation.

| ***Data:*** | ***Solution:*** |
| --- | --- |
| | |

***Answer***: ________________________________________________

*Control questions*

1. What is the difference between a stationary state of the system and the state of thermodynamic equilibrium?
2. What is the statistical nature of entropy? Give its unit of measurement.
3. What does the synergetics study?
4. List the types of "useful" work in the body.
5. What kind of thermodynamic systems are living organisms?

*Individual assignments*

1. Find osmotic work $W_{osm}$ that was done during the transfer of 6 nmol sodium ions out of the cell when the temperature was 27 °C and the ratio of the concentrations of these ions $C_o / C_i$ (outside to inside the cell) is 5.
2. Calculate the change in electrochemical potential during transport of potassium ions from the motor cat's neuron outside, if it is known that the concentration of ions outside the cell is 27 times lower than inside and internal side of the cell membrane has the potential -70 mV (outer side membranes potential is accepted to be zero). The temperature is 37 °C.
3. Calculate the electrical work done during transfer 3 mmol of potassium ions out of cells if the intracellular potential is -70 mV, and the external one is zero.
4. As a result of irreversible processes inside a cell the entropy change was 8.5 $J \cdot K^{-1}$ in 10 seconds. Calculate the dissipative function. The temperature in the system is 200 K.
5. Find the chemical affinity of the chemical reaction $A \Rightarrow 2B$ if chemical potential of initial compound is $\mu_A^0 = 10\,kJ/mol$ and final one is $\mu_B^0 = 6\,kJ/mol$ (per one molecule).
6. Find the change in electro chemical potential during transport of sodium ions into the cell from the extracellular medium if it is known that the concentration of these ions outside is 10 times greater than inside the cell and the internal side of cytoplasmic membrane has the potential $\varphi_i$ = -70 mV (the outside potential is accepted as usually to be zero). The temperature is is 37 °C.

# TOPIC 4.B. Molecular Biophysics. Water

*Molecular biophysics* studies a structure of biologically important molecules, physical processes underlying their functioning, relationship between the structure and properties of molecules and their biological function. The research objects of molecular biophysics are macromolecules which form all living structures basis.

**Exercise 4.1b.** Define the following terms and answer the questions.

*Macromolecules* are ______________________________________________________________

_____________________________________________________________________________

Macromolecules include_______________________________________________________

*Proteins* are _________________________________________________________________

_____________________________________________________________________________

*Nucleic acids* are _____________________________________________________________

_____________________________________________________________________________

To study macromolecules the following research methods are used:

_____________________________________________________________________________

_____________________________________________________________________________

Bonds stabilizing biological macromolecules can be divided into strong and weak ones.

*Strong* bonds are _____________________________________________________________

*Weak* bonds are ______________________________________________________________

_____________________________________________________________________________

**Exercise 4.2b.** There are formulas which are used to calculate the macromolecules interaction energy in the Table 4.1b. Write interaction type title.

*Table 4.1b*

*Interaction energy formulas in biopolymers*

| № | Interaction Type | Example | Interaction Energy formula |
|---|---|---|---|
| 1 | | Bonds that determine the primary structure | There is no simple dependence |
| 2 | | $COO^-$ \ $Ca^{2+}$ / $COO^-$ | $W_{\text{ion}} = -\frac{q_1 q_2}{4\pi\varepsilon_0 \varepsilon r}$ (4.1b) |
| 3 | | $Na^+(H_2O)n$ | $W_{id} \sim \frac{qp}{r^2}$ (4.2b) |
| 4 | | $SO_2$ $SO_2$ | $W_{\text{dd}} = -\frac{p_1^2 p_2^2}{6\pi\varepsilon_0 \varepsilon k T r^6}$ (4.3b) |
| 5 | | HCl \ $C_6H_6$ / $H_2O$ | $W_{\text{ind}} = -\frac{\alpha p^2}{2\pi\varepsilon_0 \varepsilon r^6}$ (4.4b) |

| | | | |
|---|---|---|---|
| 6 | | Interaction between two hydrogen or helium atoms | $W_{disp} = -\frac{3}{2}\frac{I_1 I_2}{I_1 + I_2}\frac{\alpha_1\alpha_2}{r^6}$ (4.5b) |
| 7 | | -C=O...H-N- | $W_{wat\ bon} \approx W_{int\ mol} + W_{mol}$ (4.6b) |
| 8 | | Formation of lipid bilayer and protein nonpolar regions | There is no simple dependence |

$q_1$, $q_2$ are ______________________________

$\varepsilon_0$ is ______________________________

$\varepsilon$ is ______________________________

$r$ is ______________________________

$p_1$, $p_2$ are ______________________________

$k$ is ______________________________

$T$ is ______________________________

$I_1$, $I_2$ are ______________________________

$\alpha_1$, $\alpha_2$ are ______________________________

**Problem 4.3b.** Two molecules of HCl are placed in water at the distance $r = 4$ Å. The water temperature is equal to 20 °C, the relative permittivity ε = 78.5. Calculate the energy of dipol-dipol interaction, if the molecules dipole moments are equal to $p$=$3.6\times10^{-30}$ C·m?

***Data:*** | ***Solution:***

***Answer:*** ______________________________

## The Structure of Water and Hydrophobic Interactions

**Exercise 4.4b.** Define the following terms and answer the questions.

Water differs from other hydrides by ______________________________

______________________________

______________________________

______________________________

The peak density of water is attained at ______________________________

Most of the special water properties are caused with ______________________________

______________________________

______________________________

*Table 4.2b*

*The special properties of water. Difference from other hydrides*

| Property | Should be according to other hydrides properties | The properties of water |
|---|---|---|
| Melting point | – 95 °C | 0 °C |
| Boiling point | – 80 °C | 100 °C |
| The range between the melting and boiling points | 15 °C | 100 °C |
| permittivity | <10 | 80 |
| The density | Increases with decreasing of the temperature | The peak density it has at 4 °C |

In a water molecule the atoms are located nonlinearly. The angle between O-H bonds is 104.5 degrees. The water electronic structure determines its ability to be simultaneously both donor and acceptor wile forming of a hydrogen bond: two hydrogen atoms of one molecule are linked to the oxygen atoms of a neighboring ones, and the oxygen atom of this molecule is linked to two hydrogen atoms of other molecules (see Fig.4.1b.).

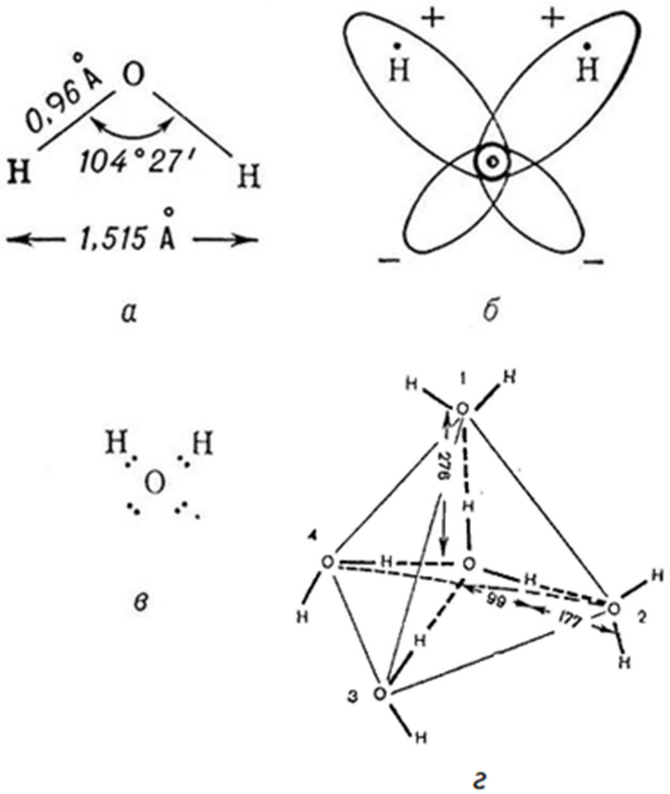



**Fig. 4.1b.** The ordered structure of water.

High heat capacity and specific latent heat of vaporization are provided with________________

________________________________________________________________________

*Flickering clusters model* is ______________________________________________

________________________________________________________________________

The liquid water molecules fluctuation period around the equilibrium position is equals to _____

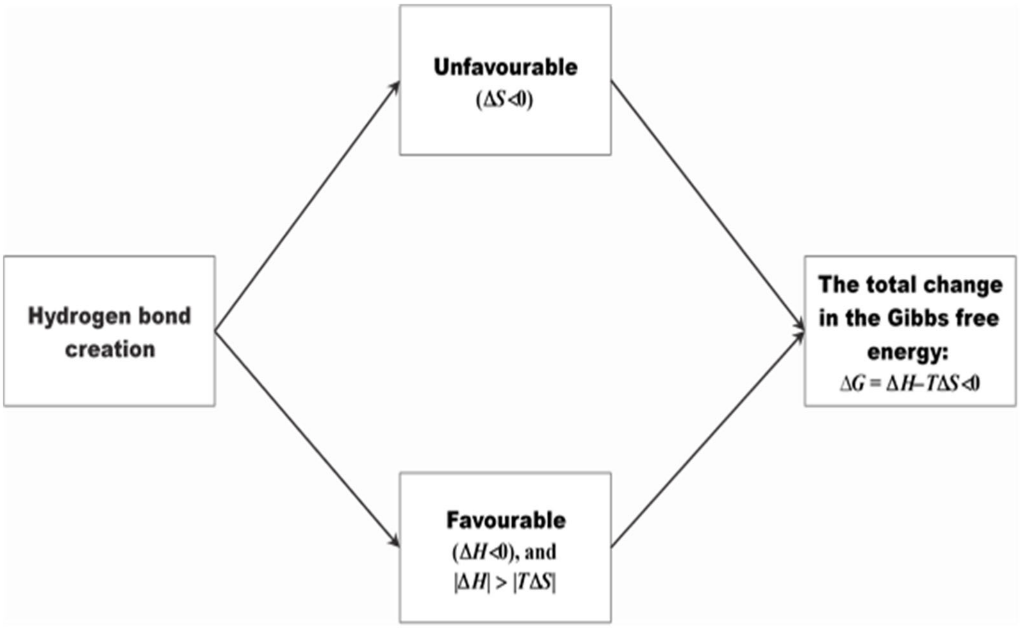



**Fig. 4.2b.** Thermodynamical background of hydrogen bonds creation.

**Exercise 4.5b.** Define the following terms:

*Hydration shell* is ____________________________________________

*Hydrophilic compounds* are ____________________________________________

*Hydrophobic compounds* are ____________________________________________

## The Structure and Properties of Biopolymers

**Exercise 4.6b.** Define the following terms and fill in the Table 4.3b.

*The primary structure is* ____________________________________________

*Chirality* is ____________________________________________

*Stereoisomers* are ____________________________________________

*Left-hand* stereoisomers are ____________________________________________

*Right-hand* stereoisomers are ____________________________________________

*Configurations of* compounds are ____________________________________________

*Conformations of* compounds are ________________________________________________

________________________________________________________________________

*Trans-conformation* is ________________________________________________

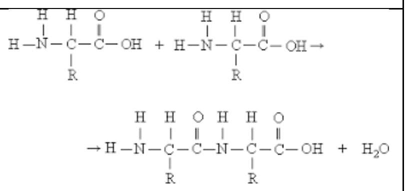
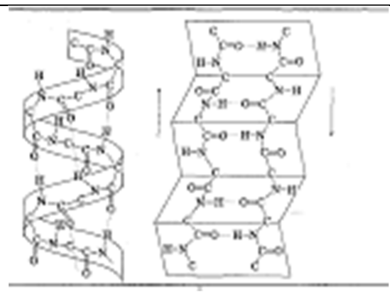
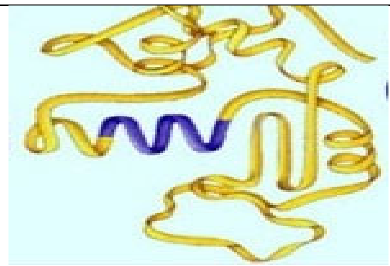
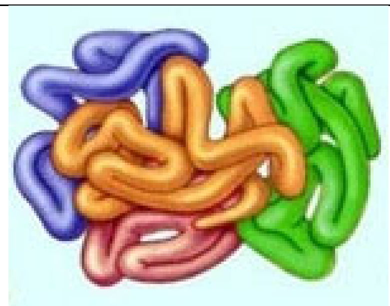
________________________________________________________________________

*Cis-conformation* is ________________________________________________

________________________________________________________________________

*Table 4.3b*

*The proteins levels of structural organization*

| **The level of structural organization of proteins** | **Structure** | **Bonds** | **Scheme** |
|---|---|---|---|
| The primary structure | | |  |
| Secondary structure | | |  |
| Tertiary structure | | |  |
| The quaternary structure (not for all proteins) | | |  |

The energy dependence of ethane and other molecules, containing axial symmetry $C_3$, on the angle of rotation $\varphi$ is determined in the following way:

$$U = \frac{1}{2}U_0(1 - \cos 3\varphi), \qquad (4.7b)$$

where $U_0$ is the height of the potential barrier between two trans-conformations.

*Bonds orientation effect* is ______________________________________________________________

______________________________________________________________________________

The interaction energy depends on__________________________________________________

**Problem 4.7b.** Calculate the potential energy value of ethane molecules ($\nu = 5\ mol$), if it is known, that the angle of $CH_3$ group rotation φ for them is relative to another one and equals to 30 degrees (the height of the potential barrier is $U$=12200 J·mol$^{-1}$).

| ***Data:*** | ***Solution:*** |
|---|---|
| | |

***Answer:***______________________________________________________________

The total energy of Van der Waals interactions can be written as:

$$U(r) = \frac{A}{r^{12}} - \frac{B}{r^6}, \qquad (4.8b)$$

where *U(r)* is *Lennard-Johns* potential, *A* and *B* are empirical constants.
The system exists in equilibrium, so as the energy is minimal at a distance:

$$r_0 = \sqrt[6]{\frac{2A}{B}}, \qquad (4.9b)$$

then the minimum energy is:

$$U_{\min} = -\frac{B^2}{4A}. \qquad (4.10b)$$

**Problem 4.8b.** Effective radius $r_0$ of Van der Waals interaction of two oxygen atoms is equal to 0.32 nm. Calculate the minimum energy of their interaction if the constant of the Lennard-Jones potential is equal to $A = 609\times10^{-9}$ kJ·nm$^{12}$·mol$^{-1}$.

| ***Data:*** | ***Solution:*** |
|---|---|
| | |

***Answer:***______________________________________________________________

**Problem 4.9b.** Calculate the Van der Waals interaction effective radius $r_0$ of carbon and nitrogen atoms. The Lennard-Jones potential empirical constants are equal to $A = 907.2\times10^{-9}$ kJ·nm$^{12}$·mol$^{-1}$; $B = 1537.2\times10^{-6}$ kJ·nm$^{6}$·mol$^{-1}$.

| ***Data:*** | ***Solution:*** |
| --- | --- |
| | |

***Answer:***________________________________________________________

Protein molecules tend to be in a state with minimal internal energy. This state is achieved by stabilizing the chemical groups in the space with hydrogen bonds. Thus, the ordered system, called the *secondary structure* of the protein, is formed.

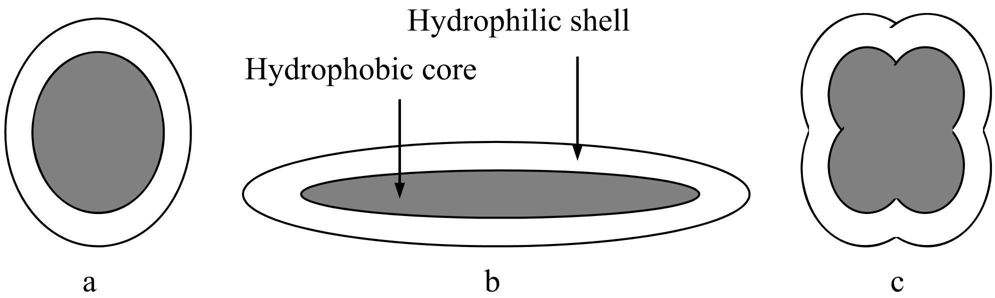



**Fig. 4.3b.** Various forms of a protein globule: *a* – sphere ($b = b_s$); *b* – ellipsoid ($b > b_s$); *c* – permolecular structures ($b < b_s$)

where *b* is ________________________________________________________

$b_s$ is __________________________________________________________

*The helix-coil transition* in proteins occurs under the equality condition of α-helix ($G_\alpha$) free energy of and the free energy of the created coil ($G_{coil}$):

$$G_\alpha = H_\alpha - T_{\text{melt}}S_\alpha = H_{\text{coil}} - T_{\text{melt}}S_{\text{coil}} = G_{\text{coil}}, \quad \text{or} \quad \Delta G = G_{\text{coil}} - G_\alpha = \Delta H - T_{\text{melt}}\Delta S = 0.$$

It follows that: $$T_{\text{melt}} = \frac{\Delta H}{\Delta S}. \qquad (4.11b)$$

*The melting point of the DNA* double helix depends on__________________________________

______________________________________________________________________

**Problem 4.10b.** The protein helix-coil transition temperature is equal to 330 K. Calculate the change in the entropy of this process if the enthalpy has changed on magnitude 18810 J.

***Data:***

***Solution:***

***Answer:*** ____________________________________________________________

## Enzyme Catalysis

**Exercise 4.11b.** Define the following terms and answer the questions.

*Enzymes* are ____________________________________________________________

________________________________________________________________________

There are the following *types of enzymes*: ________________________________________

________________________________________________________________________

According to the *Arrhenius* equation, the reaction rate constant is equal to:

$$k = A\exp\left(-\frac{E_{act}}{RT}\right), \qquad (4.12b)$$

$A$ is ________________________________________________________________

$E_{act}$ is ______________________________________________________________

The factor $\exp\left(-\frac{E_{act}}{RT}\right)$ determines _______________________________________

*"Lock-and-key" model* is ____________________________________________________

________________________________________________________________________

________________________________________________________________________

The *Michaelis-Menten* equation defines the chemical reaction rate:

$$\upsilon = \frac{\upsilon_{max}[S]}{k_m + [S]}. \qquad (4.13b)$$

So the *Michaelis constant* $k_m$ is numerically equal to the substrate concentration, at which the reaction rate is equal to ½ max one.

***Example of problem solution***

The rate of the chemical reaction increases with increasing temperature. This effect is characterized by a temperature coefficient which is equal to the ratio of rate at temperature ($t$ + 10°) to the rate at temperature $t$. Calculate the reaction activation energy $E_{act}$, for which the temperature coefficient is equal to 2 at temperature $t$ = 27 °C.

***Data:***

$$k_{temp} = \frac{v_{T+10}}{v_T} = 2$$

$$T = 27\ °C$$

***Solution:***

The ratio of reaction rates is equal to the ratio of the constants of these reactions: $\frac{v_{T+10}}{v_T} = \frac{k_{T+10}}{k_T}$.

| $E_{act}$ – ? | According to the Arrhenius equation, the chemical reaction rate is equal to: $k = A\exp\left(-\frac{E_{act}}{RT}\right)$, and the temperature coefficient is: $k_{temp} = \frac{v_{T+10}}{v_T} = 2$, then: |
|---|---|

$$k_{temp} = \frac{v_{T+10}}{v_T} = \frac{A\exp\left(-\frac{E_{act}}{R(T+10)}\right)}{A\exp\left(-\frac{E_{act}}{RT}\right)} = \exp\left(-\frac{E_{act}}{R(T+10)} + \frac{E_{act}}{RT}\right) = \exp\left(\frac{E_{act}(T+10) - E_{act}T}{R(T+10)T}\right) =$$

$$\exp\left(\frac{E_{act}(T+10-T)}{R(T+10)T}\right)$$

So: $k_{temp} = \exp\left(\frac{10E_{act}}{R(T+10)T}\right)$.

Then: $\left(\frac{10E_{act}}{R(T+10)T}\right) = \ln k_{temp}$ .

So: $E_{act} = \frac{R(T+10)T \ln k_{temp}}{10}$.

Substituting problem conditions:

$$E_{act} = \frac{8.31 \times (273 + 27 + 10) \times (273 + 27) \times \ln 2}{10} = 53.6\ kJ \cdot mol^{-1}.$$

Units of measurement check:

$$E_{act} = \frac{J \cdot K \cdot K}{mol \cdot K \cdot K} = J \cdot mol^{-1}.$$

***Answer:*** The energy activation of reaction is equal to 53.6 $kJ \cdot mol^{-1}$.

**Problem 4.12b.** When the substrate is concentrated as [S] = 3 $mmol \cdot L^{-1}$ enzymatic reaction proceeds at rate $\upsilon = 12$ $mmol \cdot s^{-1}$. Michaelis constant is $k_m = 3{,}7$ $mmol \cdot L^{-1}$. Calculate the maximum rate $\upsilon_{max}$ of this reaction. At which substrate concentration the reaction rate is equal to half the maximum?

| ***Data:*** | ***Solution:*** |
|---|---|
| | |

***Answer:***______________________________________________

**Exercise 4.13b.** Define the following terms and answer the questions.

*Inhibitor* is ______________________________________________

______________________________________________

*Competitive inhibitor* is ______________________________________________

______________________________________________

*Non-competitive inhibitor* is ______________________________________________

______________________________________________

The structure and properties of nucleic acids are determined by their function in the organism: the storage and transmission of genetic information. Fill in the Table 4.4b.

*Table 4.4b*

*Differences between DNA and RNA*

| Characteristic | DNA | RNA |
|---|---|---|
| Composition | | |
| Structure | | |
| Form | | |
| Localization | | |
| Function | | |

***Control questions***

1. Triple point of water
2. Describe the mechanism of the biopolymers stabilizing structure forces.
3. Features of nucleic acids spatial organization.
4. "Helix-coil" transition. Thermodynamic transition conditions.
5. The “lock”-and-key model.
6. Physical content of the Arrhenius equation.

***Individual assignments***

1. Two molecules of $H_2SO_4$ are placed in water on the distance $r = 5$ A. The water temperature is 25 °C, relative permittivity is $\varepsilon = 80$. Calculate the energy of dipol-dipol interaction, if the molecules dipole moments are equal to $p = 3.9\times10^{-30}$ C·m?
2. Calculate the entropy change during the protein transition from helix to coil state under the conditions with temperature is 60 °C, if the change in enthalpy is equal to 19110 J.
3. Calculate the Van der Waals interaction effective radius $r_0$ of sulfur and nitrogen atoms. The Lennard-Jones potential empirical constants are equal to $A = 906.4\times10^{-9}$ kJ·nm$^{12}$·mol$^{-1}$; $B = 1334.2\times10^{-6}$ kJ·nm$^{6}$·mol$^{-1}$.
4. Van der Waals interaction effective radius $r_0$ of two oxygen atoms is equal to 0.32 nm. Calculate their interaction minimum energy if the Lennard-Jones potential constant is equal to $A = 609\times10^{-9}$ kJ·nm$^{12}$·mol$^{-1}$.
5. The protein denaturation occurs under the conditions with the temperature 45 °C. During the process enthalpy change is equal to $\Delta H = 175$ kJ·mol$^{-1}$. Calculate the entropy change ΔS.
6. Energy barrier between two cis-conformation of ethane molecules at rotation around the C-C-bond by the angle φ = 120o is equal to U0 = 12.5 kJ·mol-1. Calculate the potential energy of ethane molecules if the angle is equal to φ = 0o, 240o, 360o.