G0-1

English (Official)

The theoretical examination lasts 240 minutes and is worth 30 points. There are two problems in theoretical examination.

Before the exam

- Do not open the envelopes with the tasks.
- The start and end of the exam will be marked by an audible signal. The audible signal will sound every hour, as well as 15 minutes and 5 minutes before the end of the exam and at the end of the exam.

During the exam

- The envelope you will receive will contain the tasks (sheets marked Q), special answer sheets (marked A), and working sheets (marked W). You may only write on one side of the sheet, as indicated. If you have written something that you do not think needs to be checked, cross it out with an "X."
- Try to use as little text as possible in your answers. Use equations, logical operators, diagrams, and graphs to explain your solution.
- Please note that most of the tasks do not depend on the solutions to previous ones. The tasks do not have to be solved in sequence.
- There are various signs in your booth; raise them if you have any problems:
  - WC when you need to use the toilet;
  - WATER, when you need a bottle of drinking water;
  - EXTRA SHEETS, when you need additional sheets of paper (new printed sheets are marked with a Z). You may request no more than 5 additional sheets at a time, but there is no limit to the number of requests;
  - HELP in all other cases.

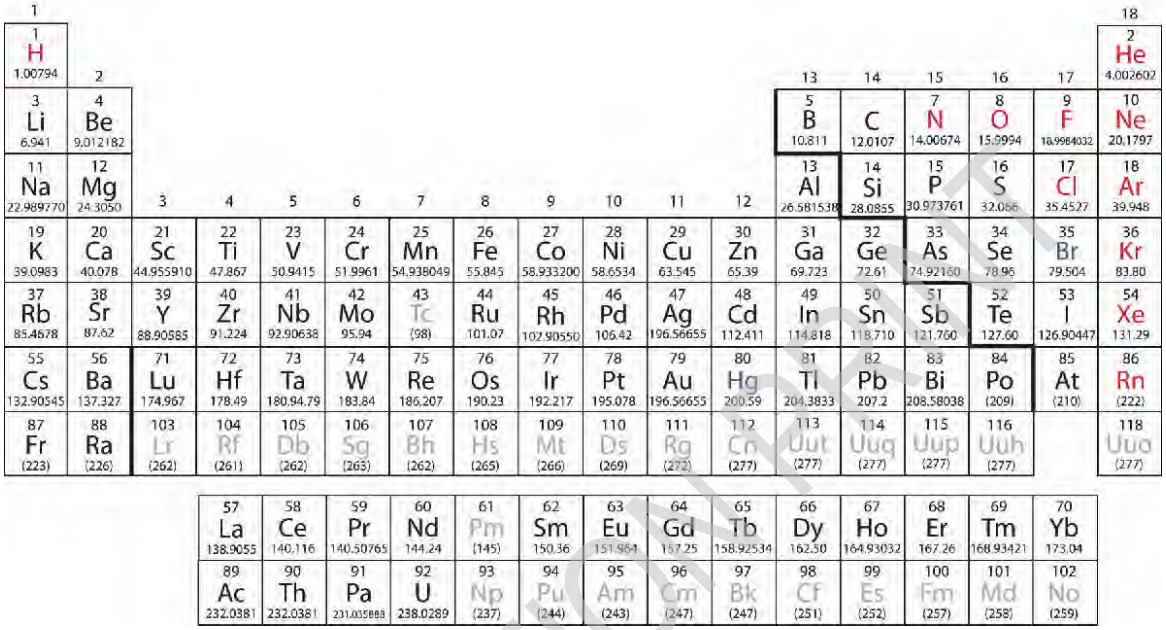
At the end of the exam

- The end of the exam is signaled by an audible signal.
- When you hear the signal, you must stop writing immediately. Put your writing materials aside and hand them to the assistant when he approaches. If you are seen writing after the signal, you will be disqualified.
- Each question is collected to a separate Marking Envelope. Collect the answer sheets (A) for Question 1 in the correct order, then place the working sheets (W) for the same Question and, if necessary, any additional sheets (Z) for the same Question. Place these sheets in the Marking Envelope for Question 1. Repeat the procedure for Question 2.
- Collect the remaining sheets of paper, including the tasks and instructions, and place them in the original envelope in which you received the tasks.
- Place all envelopes in a large kraft envelope.
- Wait in your cubicle until the kraft envelope is collected.
- Wait in your cubicle until your supervisor comes to collect you. He will escort you out of the competition area. You are not allowed to take anything out of the booth or the competition area.

G0-2

English (Official)

Periodic system of elements



Tabulated values and fundamental constants

Quantity	Value
Water density	$\rho = 1000$ kg/m^3
Elementary charge	$e = 1.6 \cdot 10^{-19}$ C
Avogadro's constant	$N_A = 6.02 \cdot 10^{23}$ mol^{-1}
Universal gas constant	$R = 8.314$ J/(mol·K)
Planck's constant	$h = 6.63 \cdot 10^{-34}$ J·s
Speed of light in vacuum	$c = 3.00 \cdot 10^{8}$ m/s

Vision

In this problem, we'll discuss some aspects of the most informative sense organ — vision. In Part A, we'll examine geometric optics and vision correction; in Part B, we'll study the properties of human rhodopsins; and in Part C, we'll learn about microbial rhodopsins. **In your answers please explicitly specify final formula and numerical answer.**

Part A. Geometrical Optics and vision correction

Binocular vision and distance measurement

Humans have binocular vision. Having two eyes separated by $s = 60$ mm results in each eye forming its own image, slightly different from the image in the other eye. This difference allows us to consciously make quantitative estimates of distances to objects.

Measurement procedure:

1. We put our thumb at arm's length and look with one eye at the object to which we want to measure the distance.
2. We close the first eye, open the second, and look at the distance Δx the thumb has moved along the object. For example, we're looking at a car, and the thumb has moved halfway across the car (Fig. 1). We know that the characteristic size of the car is $L = 4$ m, so $\Delta x = 2$ m.
3. Next, we calculate the distance r from the thumb to the object:

$$r = k\Delta x.$$

Fig. 1. Measurement pocedure.

A.1	Determine the coefficient k. The distance between the thumb and the eye is $l = 60$ cm.	0.5pt

A.2	Determine the distance r to the car from the example above.	0.2pt

Focal length of the crystalline lens

A.3	A person observes a tree with a height of $h = 3.0$ m at a distance of $d = 100$ m. It turns out that the size of the tree's image on the retina is $l = 0.6$ mm. Using this data, determine the focal length F of the crystalline lens. The optical system of the eye can be considered to consist of a single thin converging lens (the crystalline lens) and a screen (the retina) on which the image is formed.	0.8pt

Farsightedness and nearsightedness

A.4	Choose which lenses (Fig. 2) are suitable for glasses to correct farsightedness. Farsightedness is a condition where distant objects are seen clearly but near objects appear blurred. Lenses are made of glass with a refractive index greater than that of air.	0.4pt

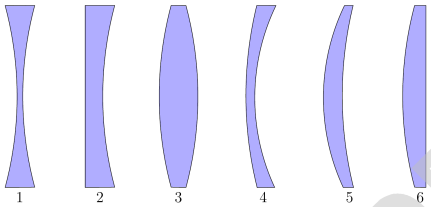


Fig. 2. Lenses.

A.5	A very nearsighted person's eye lacks accommodation, meaning this person's eye can only clearly see objects at a distance of $x = 25$ cm. Determine the focal length of glasses would be needed so that this person could clearly see very distant objects. Here we neglect the distance between the lens of the eye and the lens of the glasses. What lens shape (Fig. 2) would be suitable for such glasses?	1.1pt

Refractive surgery

Modern ophthalmology allows for modification of the optical system itself — the cornea. In the procedure the argon-fluoride excimer laser precisely "evaporate" tissue layers. A laser (Light Amplification by Stimulated Emission of Radiation) generates coherent radiation by stimulated photon emission in a medium with a population inversion, where the number of particles in the excited state exceeds their number in the ground state. Ophthalmology utilizes gas lasers with the active medium consists of short-lived diatomic molecules known as **argon-fluoride excimers, which exist only in the excited state**. When they decay, they emit light.

A.6	The argon-fluorine excimer laser generates ultraviolet radiation with a wavelength of $\lambda = 193$ nm. Calculate the energy of one photon of this radiation.	0.3pt

A.7	The "evaporation" of microscopic tissue layers using a controlled laser beam occurs due to several processes, one of which is bond cleavage. Compare the obtained laser photon energy with the energies of chemical bonds in corneal biomolecules. Mark the bonds for which the excimer laser photon energy suffices for cleavage. $E_{(\mathrm{C-C})} = 348$ kJ/mol $E_{(\mathrm{C-N})} = 305$ kJ/mol $E_{(\mathrm{N-H})} = 391$ kJ/mol $E_{(\mathrm{C-H})} = 413$ kJ/mol $E_{(\mathrm{C-O})} = 360$ kJ/mol $E_{(\mathrm{O-H})} = 463$ kJ/mol	0.4pt

Part B. Rhodopsins, color vision and color blindness

Molar mass of rhodopsin

Rhodopsin (visual purple, UniProtID P08100) is a light-sensitive protein responsible for colorless night vision and is located in rods (a type of retinal cell). The functional form of the protein contains not only amino acids but also an additional cofactor molecule: retinal. The form of this protein without the cofactor is called opsin (the apo form).

Entry (amino acid sequence) P08100 from the UniProt database:

```
MNGTEGPNFYVPFSNATGVVRSPFEYPQYYLAEPWQFSMLAAYMFLLIVLGFPINFLTLY
VTVQHKKLRTPLNYILLNLAVADLFMVLGGFTSTLYTSLHGYFVFGPTGCNLEGFFATLG
GEIALWSLVVLAIERYVVVCKPMSNFRFGENHAIMGVAFTWVMALACAAPPLAGWSRYIP
EGLQCSCGIDYYTLKPEVNNESFVIYMFVVHFTIPMIIIFFCYGQLVFTVKEAAAQQQES
ATTQKAEKEVTRMVIIMVIAFLICWVPYASVAFYIFTHQGSNFGPIFMTIPAFFAKSAAI
YNPVIYIMMNKQFRNCMLTTICCGKNPLGDDEASATVSKTETSQVAPA
```

B.1	Calculate the molar mass of the opsin P08100. Round your answer to the nearest whole number. Ignore any post-translational modifications. **The molar masses of amino acids are provided in the answer sheets.**	0.7pt

Absorption spectrum

The absorption spectrum of proteins in the UV and visible range (wavelengths 250–780 nm) is determined by the amino acids that make up the protein and additional molecules (cofactors) that may also be part of the protein. Only aromatic amino acids (phenylalanine, tyrosine, and tryptophan), which are found in many proteins, absorb in this range, with an absorption maximum around 280 nm. Cofactors typically have absorption maxima significantly different from 280 nm.

B.2	The figure shows two absorption spectra (Fig. 3). Determine which form of the protein (opsin or rhodopsin) these spectra correspond to.	0.2pt

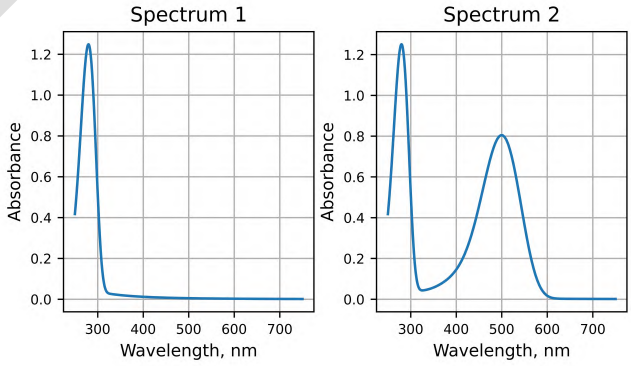


Fig. 3. Absorbance spectra 1 and 2.

Rhodopsin extinction coefficient

The extinction coefficient ε_λ^X is a value that characterizes the absorption of light by a molecule X at a spe-

cific wavelength λ. This value is often used in everyday laboratory practice to quickly and conveniently determine the concentration of molecules in a solution. Absorbance A_λ is related to the extinction coefficient and concentration as follows:

$$A_\lambda = \varepsilon_\lambda c l,$$

where c is the molar concentration of the substance and l is the optical path length. It's possible to determine the unknown extinction coefficient for rhodopsin by conducting a chemical reaction that produces a substance with a known extinction coefficient. Adding excess hydroxylamine NH_2OH and exposing it to light causes the following chemical reaction where the transition of rhodopsin to retinaloxime happens according to a 1:1 ratio:

$$\text{Rhodopsin} + NH_2OH \rightarrow \text{Opsin} + \text{Retinaloxime}$$

The extinction coefficient of retinal oxime $\varepsilon_{365}^{\text{RO}} = 33600$ $M^{-1}{\cdot}cm^{-1}$. In the laboratory, the absorption spectra of the sample were measured before and after the reaction with excess hydroxylamine (Fig. 4). The spectra were measured in the same cuvette.

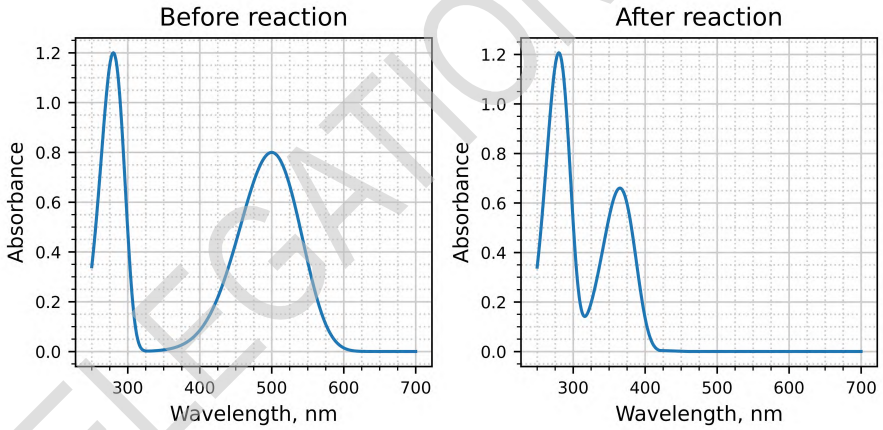


Fig. 4. Absorbance spectra of samples before and after reaction.

B.3	Determine the concentration of retinaloxime in the solution at the end of the experiment if the optical path was $l = 10$ mm.	0.6pt

B.4	Determine the extinction coefficient of rhodopsin $\varepsilon_{500}^{Rhodo}$ based on the experimental data.	0.5pt

B.5	Determine the number of rhodopsin molecules in the solution if the volume of the solution $V = 2$ ml, the optical path $l = 10$ mm.	0.4pt

Color vision

Humans possess color vision because the retina contains light-sensitive receptor cells (cones) of three colors. Each type of cone has a maximum sensitivity near one of the three primary colors: blue, green,

and red, because it expresses one of three opsin genes: OPN1SW, OPN1MW, and OPN1LW. The sensitivity (response magnitude to light with fixed intensity) of these color receptors is shown in Fig. 5. If the ratio of responses of receptors for one light signal is equal to the ratio of responses of receptors for another light signal, such light signals produce indistinguishable colors. For example, a mixture of red and green can be selected so that they are indistinguishable from yellow.

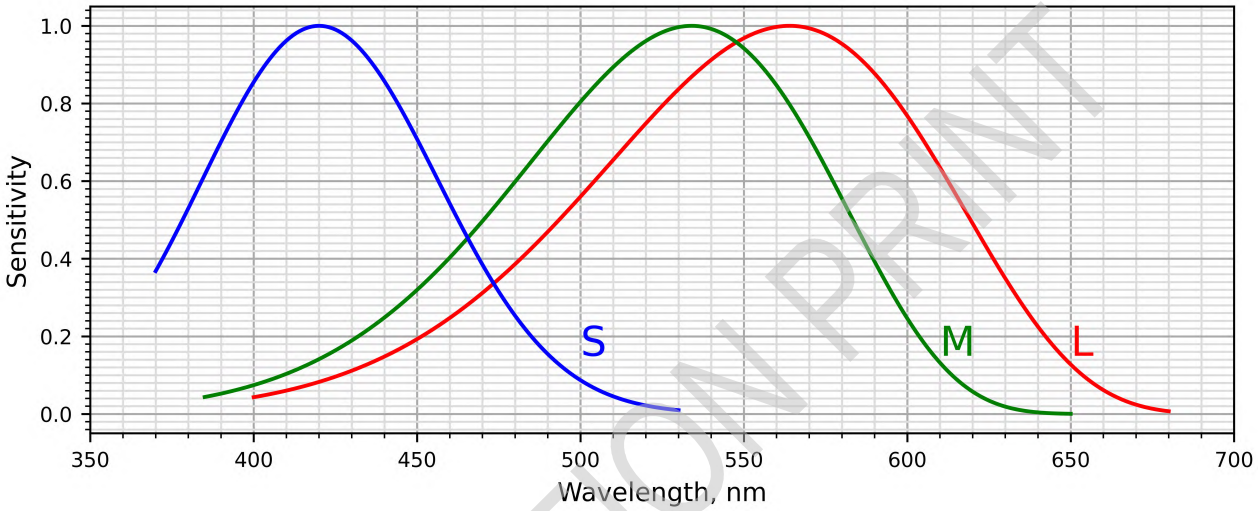


Fig. 5. Receptor sensitivity.

B.6	Determine the ratio r of the sensetivities of the long-wavelength L and medium-wavelength M cones to excitation by monochromatic yellow light (580 nm).	0.4pt
B.7	Determine the intensity ratio x of a mixture of red (630 nm) and green (530 nm) light so that this light is perceived as yellow from the previous question.	0.9pt
B.8	The light now contains a mixture of three colors: red (650 nm), green (547 nm), and violet (420 nm). What intensity ratio (y: red/violet, z: green/violet) must be taken to produce a color identical to the monochromatic color corresponding to a wavelength of 500 nm (blue)? Is it possible to obtain the desired monochromatic color by mixing three selected colors?	1.1pt

Genetics of color blindness

Color blindness is a reduced or absent ability to distinguish all or some colors. It is most often an inherited disorder associated with damage to one of the three genes listed above. The gene locations are shown in the table below; the damaged gene variants OPN1MW and OPN1LW are inherited X-linked recessive while OPN1SW is an autosomal dominant genetic dissorder. Consider that the OPN1MW and OPN1LW genes are completely linked and always inherited together without recombination.

Disordered gene	Color	Disorder name	Gene location (chromosome)	Notation for dominant / recessive
OPN1SW	Blue	Tritanopia	7	A / a
OPN1MW	Green	Deuteranopia	X	$\mathrm{X^D}$ / $\mathrm{X^d}$
OPN1LW	Red	Protanopia	X	$\mathrm{X^P}$ / $\mathrm{X^p}$

B.9 A **father** and **son** have **protanopia**, but the **mother** has **normal color vision**. From whom (mother/father/unable to determine) did the son inherit his protanopia? 0.5pt

B.10 A **man** with **deuteranopia** and **protanopia** married a **woman** with **normal vision**. They had a **son with deuteranopia (without protanopia)** and a **daughter with protanopia (without deuteranopia)**. What is the probability of this marriage having a healthy child? What is the probability of having a child with both anomalies? 1.0pt

B.11 A **man** with **protanopia and tritanopia** married a **woman** with **normal vision**. They had a **son** with **tritanopia (without protanopia)** and a **daughter** with **protanopia (without tritanopia)**. What is the probability of having a healthy child from this marriage? What is the probability of having a child with both anomalies? 1.1pt

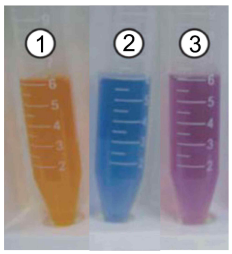
Part C. Microbial rhodopsins

Microbial rhodopsins are light-sensitive transmembrane proteins. Like animal rhodopsins, microbial rhodopsins contain retinal. Microbial rhodopsins are found in bacteria, archaea, protozoan eukaryotes, and viruses.

Absorption spectrum 2

Till date, more than 10,000 genes encoding various microbial rhodopsins have been identified. While similar in structure and homology, different microbial rhodopsins contain different amino acids, which determine their function and spectral properties. The figure (Fig. 6) shows photographs of solutions of different microbial rhodopsins and their possible absorption spectra (in no particular order).

C.1 Specify the maximum absorption spectra of the samples (with an accuracy of ± 10 nm). 0.7pt



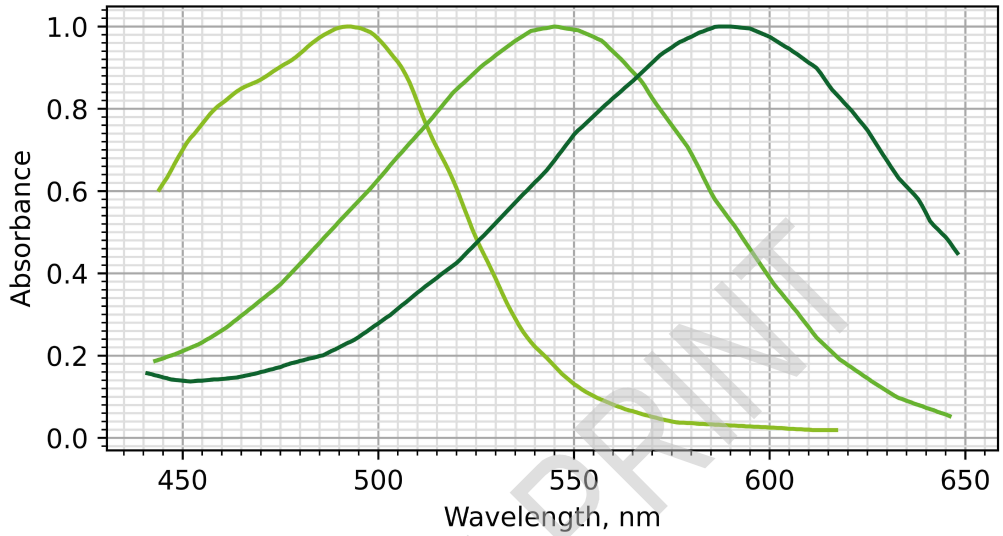


Fig. 6. Left: photograph of microbial rhodopsin samples (1 – orange, 2 – blue, 3 – purple). Right: their absorption spectra (in random order). Photographs and data from https://pubs.acs.org/doi/10.1021/cr4003769.

Proton transfer

Many microbial rhodopsins are proton (H^+) pumps, meaning they actively pump protons through themselves when exposed to light, thereby transferring a proton from one side of the cell membrane to the other. A simple experiment to determine whether microbial rhodopsins are proton pumps is designed as follows. Microbial rhodopsins are heterologously expressed in the cell membrane of *E. coli*. A suspension of *E. coli* cells is placed in a stirred vessel (test tube, volume $V = 3$ ml) containing an aqueous NaCl solution. A pH meter electrode is inserted into the vessel (Fig. 7). When the vessel is illuminated, the microbial rhodopsins absorb light, transferring a proton across the membrane. The pumping rate of rhodopsins is constant.

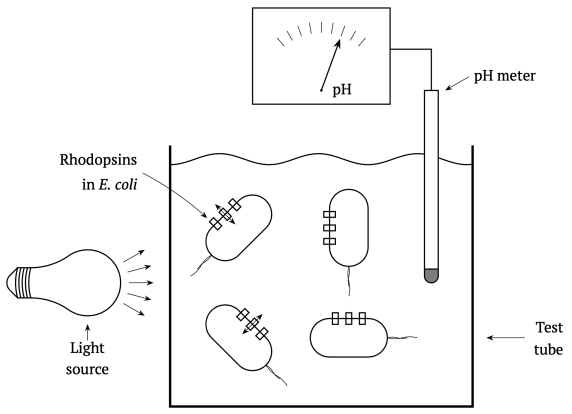


Fig. 7. Experiment scheme. Objects are not shown to scale.

The graph (Fig. 8) shows the pH value as a function of time after the light is turned on. Before the light

was turned on, the system was at equilibrium. Consider that the microbial rhodopsins are located in the inner membrane of *E. coli*, while the outer membrane allows protons to pass freely.

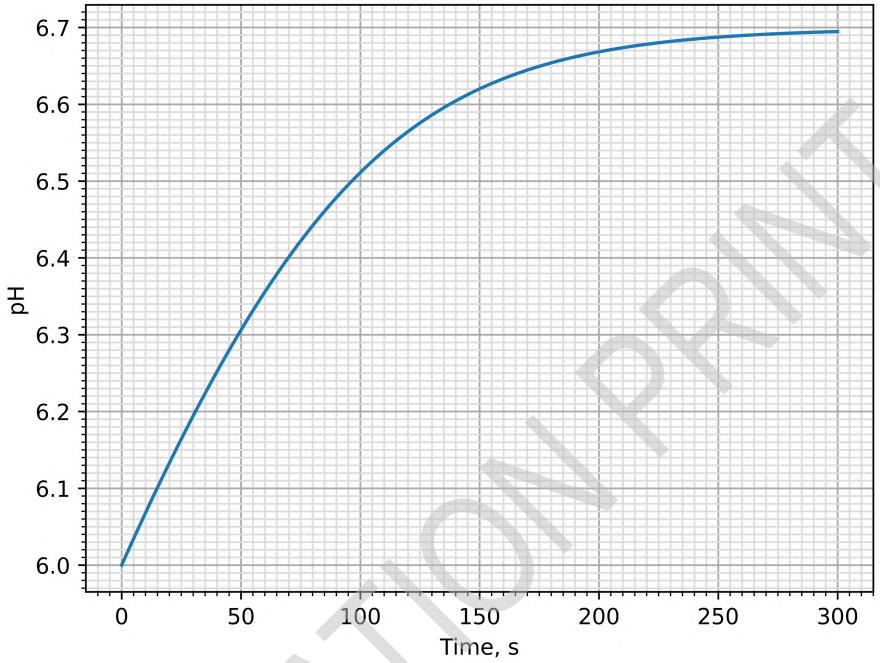


Fig. 8. pH versus time during the experiment. Illumination starts at 0 s.

C.2	Determine which direction (outward or inward) the proton is pumped in this experiment?	0.3pt
C.3	Estimate the initial pumping rate q. The pumping rate equals to the number of protons pumped per unit of time by microbial rhodopsins **through all the cells** of this experimental system.	0.7pt
C.4	Estimate the surface area of one *E. coli* cell using electron microscopy image (Fig. 9).	0.7pt

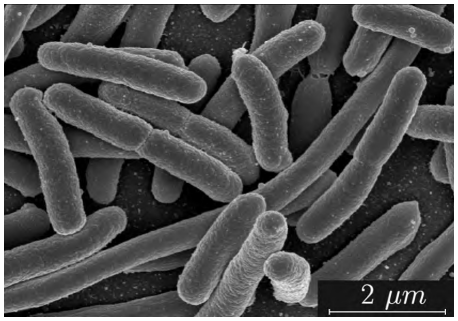


Fig. 9. An electron microscope image of cells.

C.5	Estimate the pumping rate q_1 through one molecule of microbial rhodopsin. The cell concentration in the vessel is $n_{cells} = 6.4 \cdot 10^9$ ml^{-1}. Electron microscopy analysis of the membrane surface revealed that the concentration of microbial rhodopsin molecules on the membrane surface is $\sigma = 5 \cdot 10^3 \mu m^{-2}$.	0.5pt

Cell membrane permeability

It's clear that with prolonged illumination, the pH doesn't increase infinitely, but rather settles at a new value. This can be explained by the fact that the cell membrane is actually permeable to protons, and proton leakage occurs. The flux j (the number of protons passing through a unit membrane area per unit time) is linearly dependent on the difference in proton concentrations n_1 and n_2 on either side of the membrane:

$$j = \alpha(n_1 - n_2),$$

here α is the membrane's proton permeability. Here, the concentration is expressed in units per unit volume.

C.6	Based on the results of the experiment, determine α. Indicate the units of measurement for α.	1.0pt

Part B. Rhodopsins, color vision and color blindness

B.1 (0.7pt)
The molar mass of water is 18.0 Da.

Amino acid	One letter code	AA molar mass, Da	N in protein	Total AA molar mass, Da
Alanine	A	89.1		
Arginine	R	174.2	7	1219.4
Asparagine	N	132.1	16	2113.6
Aspartate	D	133.1	4	532.4
Cysteine	C	121.2	10	1212.0
Glutamate	E	147.1	16	2353.6
Glutamine	Q	146.1	12	1753.2
Glycine	G	75.1	22	1652.2
Histidine	H	155.2	5	776.0
Isoleucine	I	131.2	24	3148.8
Leucine	L	131.2	29	3804.8
Lysine	K	146.2	11	1608.2
Methionine	M	149.2	15	2238.0
Phenylalanine	F	165.2	30	4956.0
Proline	P	115.1	20	2302.0
Serine	S	105.1	17	1786.7
Threonine	T	119.1	24	2858.4
Tryptophan	W	204.2	5	1021.0
Tyrosine	Y	181.2	19	3442.8
Valine	V	117.1	30	3513.0

$M =$

Bloodstream

Part A. Viscosity

The study of the motion of viscous fluids in tubes is an important part of hydrodynamics, necessary both in engineering (oil and water pipelines) and in biology (blood circulation). One of the key characteristics of such flow is the **hydrodynamic resistance** — the quantity that shows what pressure difference is required to provide a given flow rate. For steady laminar flow in a cylindrical tube, the pressure difference is related to the flow rate in the same way that voltage is related to current in electricity:

- The **voltage** U in an electrical circuit corresponds to the **pressure difference** ΔP in a hydrodynamic system: $\Delta P = P_1 - P_2$
- The **electric current** I corresponds to the **volumetric flow rate** of the fluid Q: $Q = \frac{\Delta V}{\Delta t}$
- The **electrical resistance** corresponds to the **hydrodynamic resistance** Z.

Thus, the **"Ohm's law for hydrodynamics"** has the following form:

$$\Delta P = Q \cdot Z.$$

This analogy makes it possible to transfer well-developed methods for calculating complex electrical circuits to the analysis of hydrodynamic systems. While in electricity charge transfer is determined by the properties of the conductor material, in a fluid the motion is defined by internal friction — viscosity.

Divide the fluid into many thin layers of equal thickness Δr, which move relative to each other with different velocities. An internal friction force arises between adjacent layers:

$$F_{fr} = \eta \frac{\Delta v}{\Delta r} S,$$

where η is the viscosity coefficient of the fluid, Δv is the velocity difference between the layers, and S is the contact area between the layers.

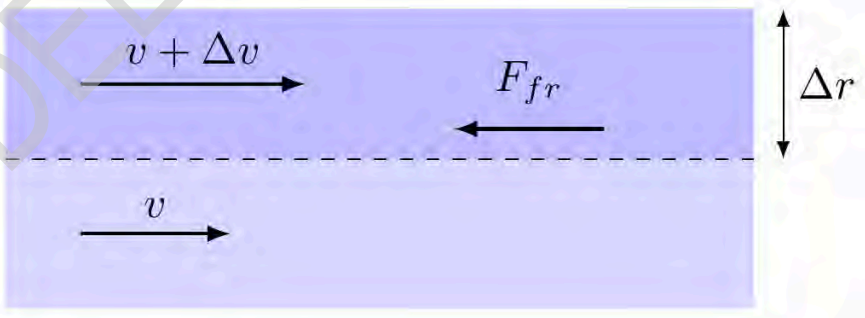


Fig. 1. A schematic illustration of the interaction between two fluid layers: the lower layer moves with velocity v, and the upper layer with velocity $v + \Delta v$. A viscous friction force F_{fr} arises between the layers.

A.1	Write down the units of the fluid viscosity coefficient η. Express the answer in the base SI units (kg, m, s).	0.1pt

In many hydrodynamic problems, it is convenient to consider the ratio G of the pressure difference to the tube length:

$$G = \frac{\Delta P}{L},$$

where ΔP is the pressure difference over a tube segment of length L. Then the volumetric flow rate Q for laminar flow in a cylindrical tube depends on the radius R, the viscosity η and G as follows:

$$Q = C\, R^a\, G^b\, \eta^c,$$

where C is a dimensionless constant, and a, b, c are integer powers.

A.2	Using dimensional analysis, find a, b and c.	0.9pt

Part B. Poiseuille's Law

Consider steady flow of an incompressible viscous fluid through a horizontal cylindrical tube of radius R and length L. A pressure difference ΔP is the same across the entire cross-sectional area at the ends of the tube. The fluid velocity $v(r)$ depends on the distance r from the tube axis: the velocity is maximal at the center, and at the wall $r = R$ it is equal to zero.

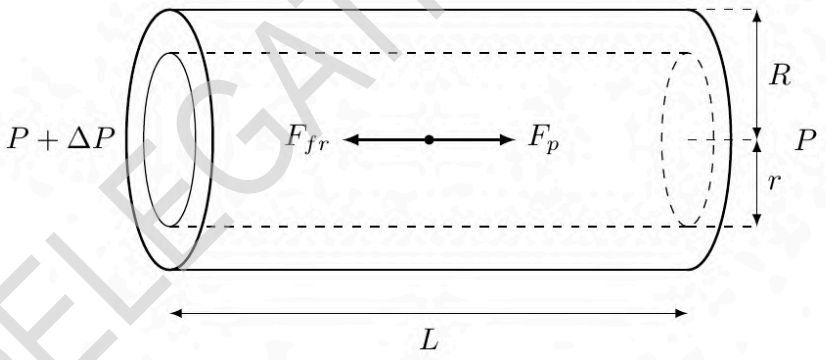


Fig. 2. A selected cylindrical fluid element of radius r and length L inside a tube of radius R. A pressure force F_p acts on its end face, and a viscous friction force F_{fr} acts on its lateral surface.

B.1	Find the pressure force acting on a cylindrical element of fluid with radius r and length L (see Fig. 2). Express your answer in terms of $\Delta P, r$.	0.2pt
B.2	Write down the stationarity condition for flow and find the dependence of $g = \frac{\Delta v}{\Delta r}$ on the radius r. Express the answer in terms of $\Delta P, R, r, \eta, L$. Sketch a graph of the dependence $g(r)$.	0.85pt
B.3	Find the dependence of the velocity $v(r)$ on the radius r. Express the answer in terms of $\Delta P, R, r, \eta, L$.	0.6pt

B.4	Find the maximum velocity in the center of the tube v_{max}. Express your answer in terms of $\Delta P, R, \eta, L$.	0.2pt

B.5	Sketch a graph of the dependence of fluid velocity v on squared radius r^2.	0.15pt

To calculate the volumetric flow rate ΔQ of fluid through a thin cylindrical layer between radii r and $r+\Delta r$ (see Fig. 3), we can note that the area of the end face of this layer is equal to $2\pi r\,\Delta r$. Multiplying it by the velocity v, we obtain:

$$\Delta Q = 2\pi r\,\Delta r \cdot v.$$

This formula can be rewritten as

$$\Delta Q = \pi v\,\Delta(r^2),$$

where the value $v\Delta(r^2)$ is proportional to the area beneath the graph $v(r^2)$.

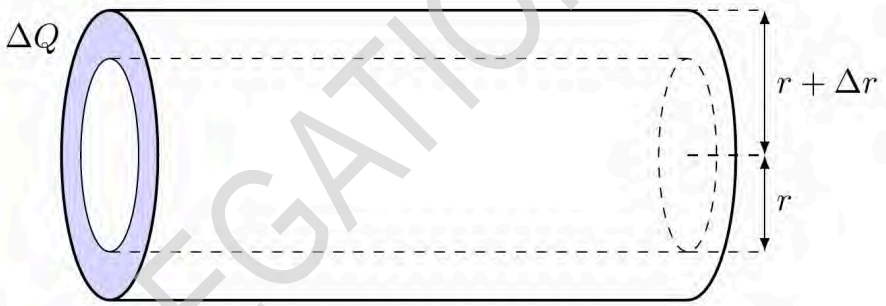


Fig. 3. Fluid flow through a thin cylindrical layer between radii r and $r + \Delta r$.

B.6	Find the total volumetric flow rate Q through a tube with radius R. Express your answer in terms of $\Delta P, R, \eta, L$.	0.4pt

The obtained expression is called Poiseuille's law.

B.7	Find the expression for the hydrodynamic resistance Z of this tube. Express your answer in terms of R, η, L.	0.1pt

Part C. Multiple tubes

A viscous liquid flows with a volumetric flow rate Q through a tube with radius R and length L. This tube splits into N identical parallel narrow tubes, each of them with length βL and radius αR.

C.1	What is the fluid flow rate in each of the narrow tubes? Express your answer in terms of Q and N.	0.2pt

C.2	Find by what factor the pressure difference on a wide tube with radius R differs from the pressure difference on one of the parallel narrow tubes. Express your answer in terms of α, β, N.	0.2pt

Part D. Hydrodynamics of the circulatory system

In the task **B6**, you obtained Poiseuille's law for laminar flow of a viscous incompressible fluid in a cylindrical tube. These ideas can be applied to a real biological system — human blood circulation.

Note: if you have not managed to calculate the dimensionless coefficient C, you can assume it to be equal to 1 (this is an incorrect value) in order to continue solving the problem.

Blood circulation can be conveniently viewed as a hydrodynamic system: the heart creates a pressure gradient, blood flows through a network of vessels, and the total flow rate is the same at all levels — from the aorta to the venous return. In this task, we examine a systemic circulation in a simplified model that is sufficient for quantitative estimates:

- at a fixed temperature, blood is considered a fluid with a constant viscosity coefficient equal to $\eta = 4.00 \cdot 10^{-3}$ Pa·s;
- the volumetric flow rate of blood at rest is equal to $Q_0 = 5.00$ L/min;
- flow is stationary, laminar;
- the walls of the vessels are rigid;
- all vessels of the same level are connected in parallel, and the levels follow in series.

This model does not describe the pulsatility and elasticity of blood vessels, but it clearly shows where resistance is concentrated, how velocity changes at different levels, and how blood properties affect heart function.

Simplified levels of the vessels of the systemic circulation:

Level	Radius R, mm	Length L, cm	Number of vessels n
Aorta	$1.25 \cdot 10^{1}$	$4.00 \cdot 10^{1}$	1.00
Major arteries	2.00	$2.00 \cdot 10^{1}$	$1.00 \cdot 10^{2}$
Arterioles	$3.00 \cdot 10^{-2}$	$6.00 \cdot 10^{-1}$	$5.00 \cdot 10^{5}$
Capillaries	$3.50 \cdot 10^{-3}$	$2.00 \cdot 10^{-1}$	$1.00 \cdot 10^{10}$

D.1	Calculate the hydrodynamic resistances Z of the levels from the table. Round your answers to three significant digits and fill in the table in the answer sheet.	0.9pt

D.2	Find the pressure difference ΔP at each level for the volumetric flow rate Q_0. Round your answers to three significant digits and fill the table in the answer sheet.	0.8pt

During physical activity, the volumetric flow rate increases to $Q = 4Q_0$. The body achieves this by increasing the frequency and strength of heart contractions, as well as increasing the radius of the arterioles by 20%.

D.3	By what factor does the resistance of arterioles decrease as their radius increases by 20%?	0.2pt

D.4	By what factor does the total pressure difference ΔP increase to reach the volumetric flow rate Q?	0.8pt

D.5	By what factor does the mechanical power developed by the heart to pump blood increase compared to when it is at rest?	0.4pt

Part E. Other aspects of the circulatory system

Gas transfer is one of the most important functions of blood. The circulatory system is an organ system that enables blood to move between the immediate environment of each cell and the tissues, where exchange with the external environment takes place.

E.1	The figure below schematically depicts the circulatory systems of the following vertebrates: 1. Amphibians; 2. Mammals; 3. Fishes; Match the numbers 1-3 in the list with the letters A-C in the diagram. Each letter can be used only once.	0.2pt

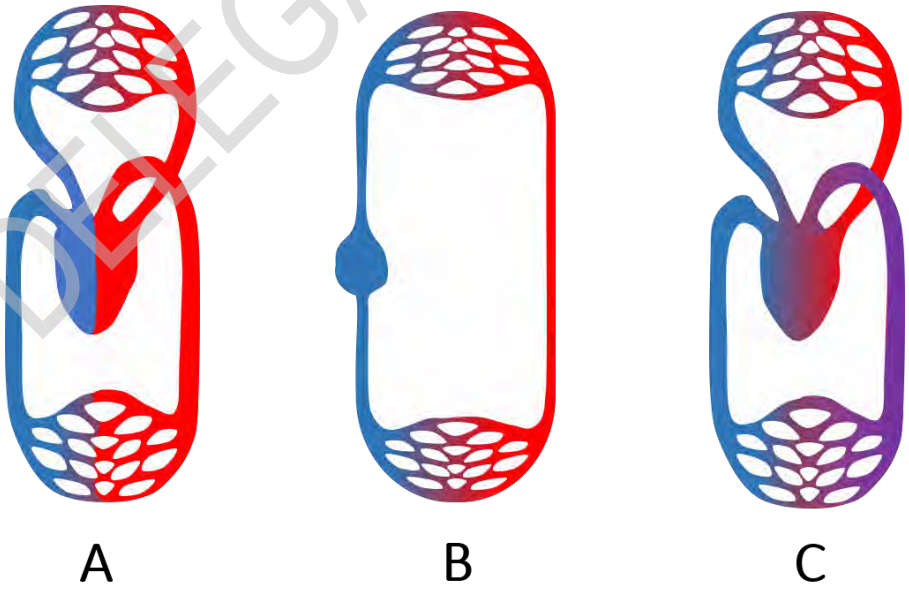


Fig. 4. Types of circulatory systems of vertebrates.

Next, we will consider only the human cardiovascular system.

The partial pressures of oxygen and carbon dioxide change as these gases move through the circulatory system. The figure below shows some parts of the human circulatory system marked with numbers. The partial pressures of gases in these parts are given below with letters A-E.

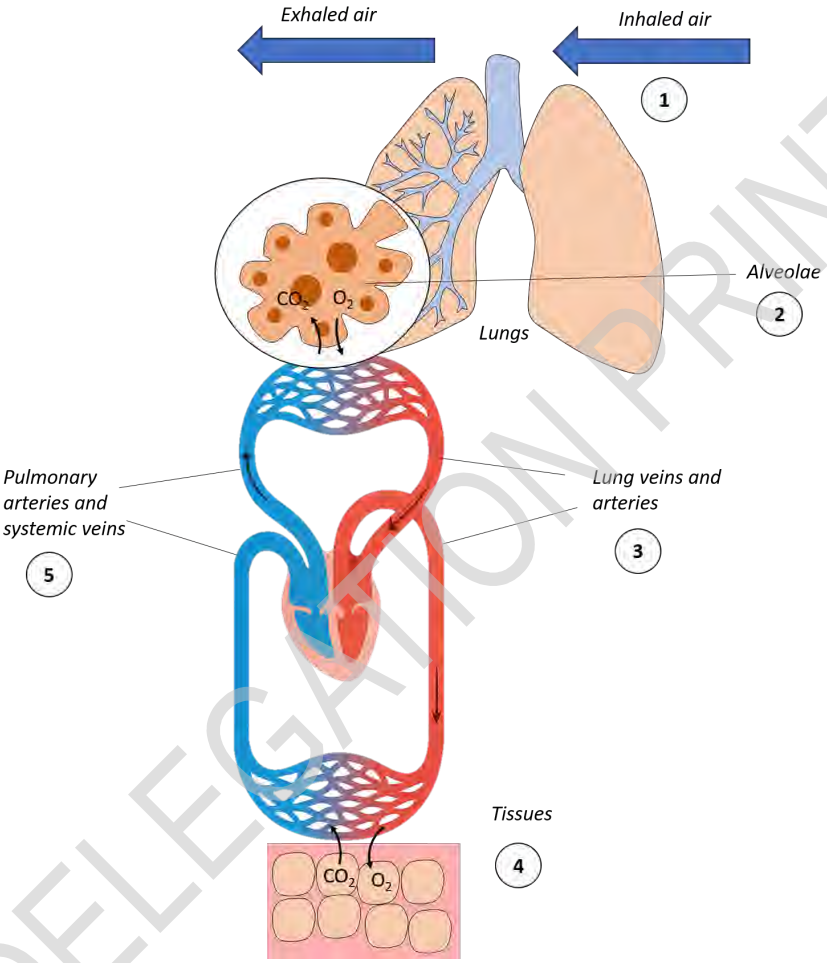


Fig. 5. Parts of the circulatory system.

A. $P(\mathrm{O_2}) = 100$ mm Hg, $P(\mathrm{CO_2}) = 40$ mm Hg;

B. $P(\mathrm{O_2}) < 40$ mm Hg, $P(\mathrm{CO_2}) > 46$ mm Hg;

C. $P(\mathrm{O_2}) = 160$ mm Hg, $P(\mathrm{CO_2}) = 0.3$ mm Hg;

D. $P(\mathrm{O_2}) = 40$ mm Hg, $P(\mathrm{CO_2}) = 46$ mm Hg;

E. $P(\mathrm{O_2}) = 105$ mm Hg, $P(\mathrm{CO_2}) = 40$ mm Hg.

E.2	Match the numbers 1-5 on the diagram with the letters A-E. Each letter should be used only once.	0.3pt

It should be noted that gravity also affects blood flow. When we stand or sit, gravity acts on the blood in our legs, for example, making it difficult for it to flow upward. The table below lists some possible factors that contribute to the return of blood through the veins to the heart.

A. Contraction of the skeletal muscles surrounding the vein.	E. Lower viscosity of venous blood compared to arterial blood.
B. Low wall thickness of veins compared to arteries.	F. Contraction of the walls of certain veins.
C. The functioning of valves inside blood vessels.	G. Low blood oxygen saturation.
D. Negative pressure in the chest during inhalation.	H. Negative pressure in the atria during ventricular systole.

E.3 Mark with an "X" the factors that actually help blood flow through the veins. 0.3pt

Arterial pressure in the body is not constant, but depends on many factors. In particular, certain hormones affect arterial pressure.

E.4 The table in the answer sheet contains a list of human hormones. For each hormone, indicate its chemical nature and the organ responsible for its production in the table: write down an "X" in the appropriate cells. In addition, write down an "X" in the last row corresponding to those hormones that cause an increase in arterial pressure (AP). 0.9pt

The diffusion of oxygen from the air into the blood occurs in the alveoli. Fick's law states that when there is a concentration gradient Δn, the particle flux j (the number of particles per unit time per unit area) is proportional to Δn:

$$j = \frac{\Delta N}{\Delta S \Delta t} = D\frac{\Delta n}{d}.$$

Here, D is the diffusion coefficient, and d is the thickness of the barrier.

Let us assume that one mole of oxygen provides energy $Q = 470$ kJ/mol, and the power generated by a person is $W = 1$ kW. The difference in oxygen concentration between the alveolar air and the capillaries corresponds to a pressure difference of $\Delta p = 8$ kPa, and the body temperature is $T = 37\,^{\circ}$C.

E.5 Estimate the effective surface area of the lungs S. 0.3pt
Use $D = 10^{-11}$ m²/s, $d = 1$ μm.

Part F. Acid-base balance

For regular functioning of the body's cells, a constant pH value of blood and intercellular fluid is required. The hydrogencarbonate buffer solution, consisting of carbonic acid $\mathrm{H_2CO_3}$ and hydrogencarbonate $\mathrm{HCO_3^-}$, plays the most important role in maintaining homeostasis. At a temperature of $37\,^{\circ}$C, for carbonic acid $\mathrm{p}K_{a_1} = 3.57$. Dissociation at the second stage of carbonic acid can be neglected.

To understand how a buffer solution works, let us consider two solutions:

(A) 1 liter of $0.15\ \mathrm{M}\ \mathrm{H_2CO_3}$;

(B) 1 liter of buffer solution obtained by mixing 500 ml of $0.30\ \mathrm{M}\ \mathrm{H_2CO_3}$ and 500 ml of $0.30\ \mathrm{M}\ \mathrm{NaHCO_3}$.

F.1	Determine the pH of the solutions.	0.6pt

Let 0.2 liters of $0.1\ \mathrm{M\ HCl}$ be added to each solution.

F.2	Find the new pH values of the solutions. Calculate the change in pH in each case.	1pt

Carbonic acid is formed in the body as a result of the dissolution (aq) of carbon dioxide in water:

$$\mathrm{CO_{2\,(aq)} + H_2O \rightleftharpoons H_2CO_3}.$$

The equilibrium constant for carbon dioxide hydration is $K_h = 3.0 \cdot 10^{-3}$.

The concentration of carbon dioxide in the blood corresponds to its partial pressure $p(\mathrm{CO_2}) = 5.3$ kPa. The relationship between the partial pressure of gas p and its concentration C in the solution in equilibrium is given by Henry's law:

$$C = kp,$$

where k is Henry's constant. The Henry's constant for the dissolution of carbon dioxide at a temperature of $37\,^\circ$C

is equal to $k = 2.3 \cdot 10^{-4}$ mol/(m$^3\cdot$ Pa).

F.3	Find the molarity of carbon dioxide in blood.	0.2pt

F.4	Determine the molarity of carbonic acid and the molarity of hydrogencarbonate ions in blood at $\mathrm{pH}\ 7.4$.	0.4pt

F.5	Determine the solubility of carbon dioxide in blood, i.e., the total molarity of all forms of $\mathrm{CO_2}$.	0.2pt

Another buffer system in blood is a mixture of protonated and deprotonated hemoglobin. The chemical equilibrium equations for oxyhemoglobin and deoxyhemoglobin are as follows:

$$\mathrm{Hb \cdot O_2 \cdot H^+ \rightleftharpoons Hb \cdot O_2 + H^+}, \quad \mathrm{p}K_a = 8.18;$$

$$\mathrm{Hb \cdot H^+ \rightleftharpoons Hb + H^+}, \quad \mathrm{p}K_a = 6.62.$$

F.6	At $\mathrm{pH}\ 7.4$, find what fraction α of oxyhemoglobin is protonated. Find the analogous fraction of protonated deoxyhemoglobin β.	0.4pt

Part G. Oxygen Transfer

Since oxygen is poorly soluble in water, organisms need special adaptations to transfer it efficiently. Large multicellular organisms have evolved proteins that store and transfer oxygen. However, unlike

some transition metals, the side chains of amino acids cannot reversibly bind oxygen. Therefore, iron is used to transfer gases in the human body. Due to the high reactivity of free iron ions, it is used in a bound form. Heme is a protein-bound compound into which iron is incorporated.

G.1 The gross formula of heme is $\mathrm{C}_a\mathrm{H}_b\mathrm{O}_c\mathrm{N}_d\mathrm{Fe}$, and the mass fractions of the elements in the compound are $w(\mathrm{C}) = 66.24\%$, $w(\mathrm{H}) = 5.23\%$, $w(\mathrm{O}) = 10.38\%$, $w(\mathrm{N}) = 9.09\%$. From this information, determine the numbers a, b, c and d. 0.3pt

There are four levels of protein structural organization: primary, secondary, tertiary, and quaternary.

G.2 Below is a list of chemical bonds that appear in the structures mentioned above. Write down the letters representing the chemical bonds in the appropriate cells of the table below. Note that the same letters may be used in different cells. 0.3pt

A. Disulfid bridges (–S–S–).
B. Ionic bonds.
C. Hydrogen bonds within a molecule.
D. Hydrophobic interactions.
E. Peptide bonds.
F. Intermolecular hydrogen bonds.

Myoglobin is an oxygen-binding protein found in skeletal muscles and heart muscles.

Under normal conditions, in the absence of damage or inflammation of muscle tissue, myoglobin hardly enters the bloodstream.

In turn, hemoglobin transfers gases in the blood and consists of four subunits. Each subunit consists of heme and a polypeptide chain associated with it.

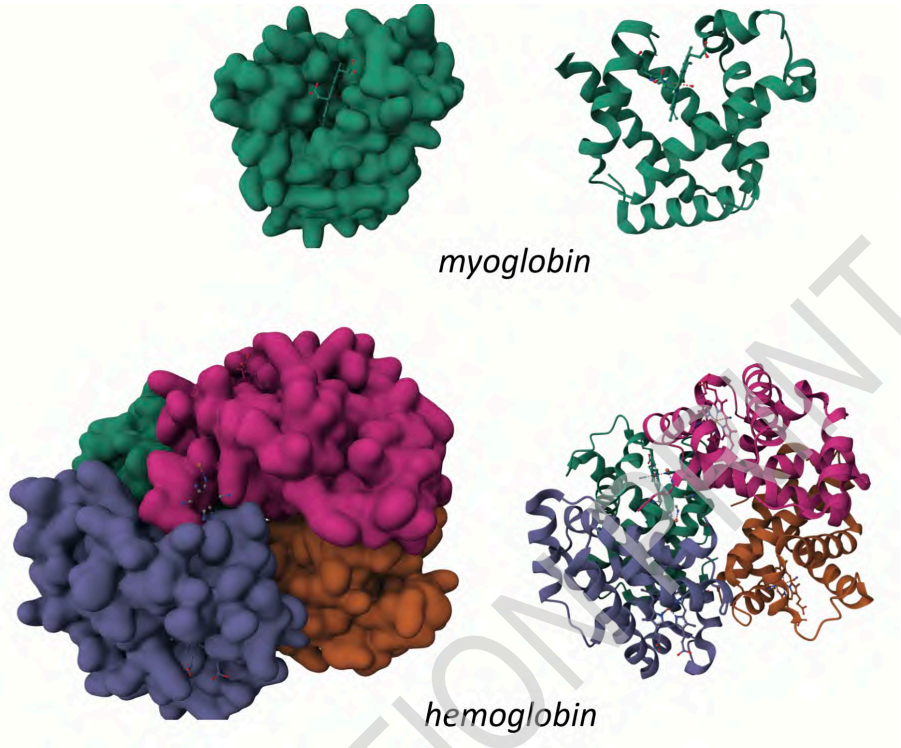


Fig. 6. Myoglobin and hemoglobin.

G.3	The table in the answer sheet lists various proteins found in nature. Indicate which of them, in their functional state, possess a quaternary structure and which only a tertiary structure.	0.35pt

An important feature of many proteins is the reversible binding of other molecules. A molecule that reversibly binds to a protein is called a ligand, and the binding site on the protein molecule is called the binding center. Myoglobin can both bind oxygen molecules and release them, which means that there is an interaction between the protein and the ligand.

Let us consider, in general terms, the equilibrium in solution between protein P, ligand L and complex PL. Ligand binding is described by the reaction

$$\mathrm{P} + \mathrm{L} \rightleftharpoons \mathrm{PL}$$

with an equilibrium constant K_a (a — association reaction). The fraction of occupied ligand binding sites is called the degree of saturation and is denoted by θ:

$$\theta = \frac{[\mathrm{PL}]}{[\mathrm{PL}] + [\mathrm{P}]}.$$

G.4	Find an expression for θ in terms of $[\mathrm{L}]$ and K_a. What is the equilibrium constant K_a if the ligand concentration at which exactly half of the binding sites are occupied is $[\mathrm{L}]_{0.5}$?	0.2pt

For gases, the formulas obtained remain valid, but instead of concentrations, it is necessary to work with partial pressures. For example, the oxygen pressure at which the degree of myoglobin saturation is 50% is equal to $p_{50}(\mathrm{O_2}) = 2$ mm Hg.

Carbon monoxide CO is extremely dangerous to humans. Carbon monoxide can also bind with myoglobin, and the corresponding constant is $p_{50}(\mathrm{CO}) = p_{50}(\mathrm{O_2})/200$.

G.5 Sketch graphs showing the dependence of the degree of saturation θ on the partial pressure of gases. Indicate which graph corresponds to which gas. 0.25pt

The temperature dependence of the equilibrium constant is described by the Van 't Hoff equation:

$$\frac{\Delta \ln(K_a)}{\Delta T} = \frac{\Delta_r H^\circ}{RT^2},$$

where $\Delta_r H^\circ$ is the standard molar enthalpy of reaction (the index r denotes the change in value during the association reaction). Assuming that $\Delta_r H^\circ$ is almost independent of temperature in the specified range, the equation can be transformed to the form

$$\ln K_a = -\frac{\Delta_r H^\circ}{RT} + \mathrm{const}.$$

The table in the answer sheet shows the experimental values of the association constants at different temperatures in a specific buffer solution.

T,° C	10	20	30	35	40
K_a	3.09	1.38	0.66	0.48	0.33

G.6 From the given data, determine the standard molar enthalpy of reaction $\Delta_r H^\circ$ for oxygen binding. Plot the required graph on graph paper in the answer sheets. 0.9pt

For a protein with n binding sites, it can be approximated that n ligands attach in one stage:

$$\mathrm{P} + n\mathrm{L} \rightleftharpoons \mathrm{PL}_n.$$

A graph in the coordinates $\log_{10}\left(\frac{\theta}{1-\theta}\right)$ versus $\log_{10}([\mathrm{L}])$ is called a Hill graph.

G.7 Find the dependence of $\log_{10}\left(\frac{\theta}{1-\theta}\right)$ on $\log_{10}([\mathrm{L}])$. Express your answer in terms of n, $\log_{10}([\mathrm{L}])$ and the equilibrium constant K_a. 0.2pt

It turns out that there is cooperative interaction between subunits in hemoglobin. When $\mathrm{O_2}$ binds to one of the units, the others slightly change their shape, thereby increasing their affinity for oxygen. Conversely, when all subunits are in a bound state and one subunit releases oxygen, the others also tend to release oxygen. The slope of the Hill graph n_H represents a measure of cooperativity.

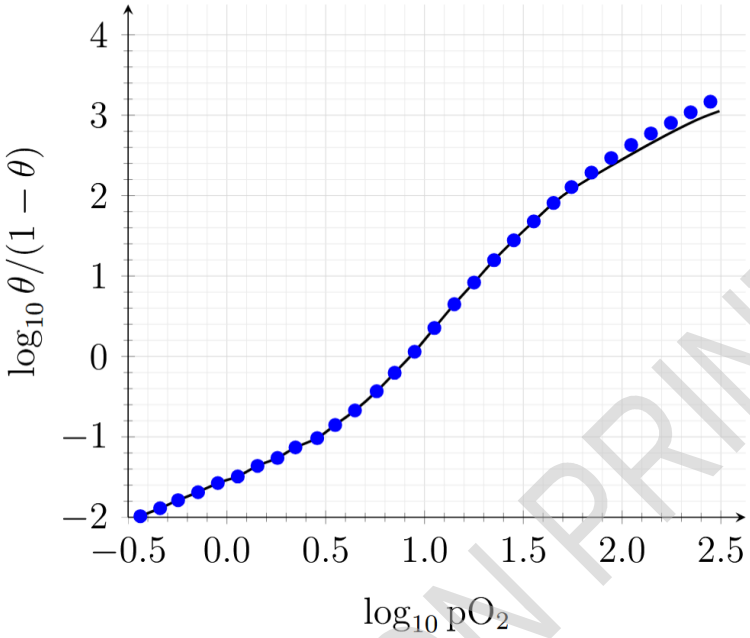


Fig. 7. Hill graph.

G.8	Determine n_H as the slope of the tangent to the graph at $\theta = 0.5$. What is the theoretical maximum possible value of n_H? Let us note that in practice this value is not achieved.	0.2pt

Hemoglobin can be found in two states: R and T. Oxygen has a greater affinity for hemoglobin in the R state, and in the absence of oxygen, the T state is more stable. It is due to the transitions between these states that hemoglobin binds sufficient oxygen in the lungs and releases it in the tissues.

G.9	Give the reason why myoglobin cannot be used as an effective oxygen carrier (efective binding and release of oxygen molecules) from the lungs to the tissues. A. The myoglobin molecule has a hyperbolic oxygen saturation curve. B. The concentration of myoglobin in the blood is significantly lower than the concentration of hemoglobin. C. The myoglobin molecule is lighter, which makes it too mobile. D. The myoglobin molecule is too small, which can cause it to enter other tissues.	0.1pt

In fact, hemoglobin transfers not only oxygen, but also protons $\mathrm{H^+}$. To account for the effect of pH on oxygen binding and release, we can consider the equilibrium equation in the form

$$\mathrm{Hb \cdot H^+ + O_2 \rightleftharpoons Hb \cdot O_2 + H^+},$$

where $\mathrm{Hb \cdot H^+}$ is the protonated form of hemoglobin.

The figure below shows the hemoglobin saturation curves at different pH values. The upper and the lower curves correspond to $\mathrm{pH}\ 7.2$ and $\mathrm{pH}\ 7.6$.

G.10 Choose the correct statement: 0.2pt
1. Curve A corresponds to $\mathrm{pH}\ 7.2$, curve B corresponds to $\mathrm{pH}\ 7.6$.
2. Curve A corresponds to $\mathrm{pH}\ 7.6$, curve B corresponds to $\mathrm{pH}\ 7.2$.

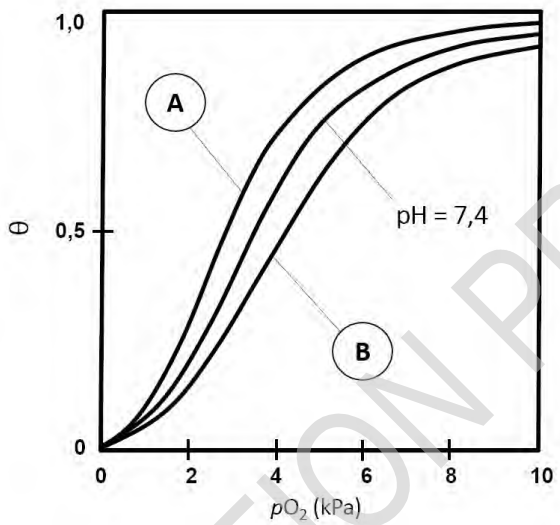


Fig. 8. The influence of pH on the hemoglobin saturation curve.

The observed influence of pH on oxygen binding and release is called the Bohr effect and determines the different degree of saturation of hemoglobin in different parts of the human body.

G.11 Which curve corresponds to hemoglobin in the lungs, and which corresponds to hemoglobin in tissues (mark with an "X" in the table in the answer sheets). 0.1pt

G.12 In certain conditions, increased level of myoglobin in blood could be a result of: 0.1pt
A. State of alcohol intoxication.
B. Myocardial infarction.
C. Use of sleeping pills.
D. Alzheimer's disease.

E.4 (0.9pt)

Chemical nature	Insulin	Adrenalin	Vaso-pressin	Testos-terone	Thyroxine	Cortisol
Amino acids derivatives						
Peptides and proteins						
Fat-soluble steroids						

Organ	Insulin	Adrenalin	Vaso-pressin	Testos-terone	Thyroxine	Cortisol
Posterior pituitary gland						
Adrenal gland						
Islets of Langerhans of the pancreas						
Thyroid gland						
Testicles						

	Insulin	Adrenalin	Vaso-pressin	Testos-terone	Thyroxine	Cortisol
Increases AP						

E.5 (0.3pt)

$S \approx$

F.1 (0.6pt)

$\mathrm{pH}_A =$

$\mathrm{pH}_B =$

G.2 (0.3pt)

Structure	Primary	Secondary	Tertiary	Quaternary
Bonds				

G.3 (0.35pt)

Structure	Tertiary only	Quaternary
Myoglobin		
Hemoglobin		
Pepsin		
Tobacco mosaic virus capsid		
Trypsin		
ATP synthase		
Albumin		

G.4 (0.2pt)

$\theta =$

$K_a =$