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MATHEMATICAL MODELING OF HYPOMETABOLISM PROCESS TO IDENTIFY PECULIARITIES OF HUMAN ORGANISM DURING THE WORK UNDER CONDITION OF HIGHLANDS

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Предложена математическая модель динамики напряжений респираторных газов с учетом гипометаболизма, который развивается в организме человека на высокогорье. Анализ вычислительных экспериментов позволил сделать выводы о характере изменений режимов функционирования организма при переходных процессах и в стационарных состояниях, влиянии систем внешнего дыхания и кровообращения на формирование уровней управляющих параметров, а также о роли гипометаболизма при воздействии на организм возмущений внутренней и внешней сред.

Ключевые слова: математическая модель, системы дыхания и кровообращения, напряжение газов, гипоксия, гипометоболизм, возбуждающие воздействия, вычислительные эксперименты.

Запропоновано математичну модель динаміки напружень респіраторних газів з урахуванням гіпометаболізму, який розвивається в організмі людини на високогір'ї. Аналіз обчислювальних експериментів дозволив зробити висновки щодо характеру змін режимів функціонування організму при перехідних процесах і в стаціонарних станах, впливу систем зовнішнього дихання та кровообігу на формування рівнів керуючих параметрів, а також ролі гіпометаболізму при впливі на організм збурень внутрішнього і зовнішнього середовищ.

Ключові слова: математична модель, система дихання і кровообігу, напруга газів, гіпоксія, гіпометаболізм, збурюючі впливи, обчислювальні експерименти.

INTRODUCTION

Hypometabolic and hypoxic states are in the focus of attention of researchers since organism is often impacted by hypoxic factors, particularly under conditions of highlands, as well as during significant physical loads or some severe pathologic process.

Hypoxic or exogenous hypoxia is developed during decreasing of partial pressure of oxygen in inhaled air. During hypoxic hypoxia the oxygen tension in arterial blood, the saturation of hemoglobin with oxygen and its total content in the blood are being decreased. Negative impact can be caused also by hypocapnia, developed as a result of compensatory hyperventilation of lungs. Extreme hypocapnia causes worsening of blood supply to brain and heart (vasoconstriction) and respiratory alkalosis. In this connection, it is interesting to investigate the energy reserves of organism and the ways of its strengthening under hypoxic conditions.

THE RELEVANCE OF THE TOPIC

Investigation of the processes of human organism breathing system self-regulation represents particular scientific area that is being widely developed last years as a result of success in mathematical modeling. However the regulation mechanisms of functional state of human organism under conditions of highland hypoxia are not sufficiently studied yet. Impossibility of such investigations was related with the difficulties of experimental determination of the several most important parameters and with the absence of adequate mathematical models for dynamics of these processes.

PROBLEM DEFINITION

Mechanisms of formation of hypometabolic state of human being under conditions of highlands are considered. Mathematical model of functional systems of breathing and blood circulation has been used to analyze this phenomenon on system level.

The purpose of this work is development and investigation of mathematical model of hypometabolism, and development of software for execution of computing experiments with the model.

RESULTS

1. Developed complex of mathematical model of the gas mass carry process in organism and software is applied for assessment of the dynamics of functional state of human being on conditions of work at highlands.
2. Implemented numerical analysis of the models of respiratory exchange control enables to:

- follow dynamics of the main physiological parameters of the model during transient processes and in stationary states;
- forecast and quantitatively assess regulatory reactions of the organism under given disturbances;
- carry out individualization of model developments on condition of availability of array of data on anatomic-physiological peculiarities of specific human being.

Obtained results are well correlated with the physiological experimental data.

Mathematical model of tension dynamics of respiratory gas is developed using ideas of compartmental modeling [1, 2], i.e. describes the mass carry process of respiratory gases among functionally connected but relatively autonomous compartments.

Model represents the system of ordinary nonlinear differential equation whose number depends on the degree of detailing of structural scheme of the object (number of tissue regions, portions of blood washing the tissue etc.), describing the dynamics of oxygen tension p (hereinafter the first index at variable — (1)), carbon dioxide (2) and nitrogen (3) in structural compartments of the system — respiratory tract (second index at variable — (rw)), alveolar space (A), blood of pulmonary capillaries (LC), arterial blood (a), blood of tissue capillaries (ct_i), tissue

reservoirs (t_i) and mixed venous blood ($\bar{v}$).

As distinct from existing models of gas mass transfer in the organism this model presents dynamics of gas partial pressures in alveolar space during the breathing cycle including phases of inhalation, exhalation and pause; process of gas diffusion through air-blood barrier, as well as through capillary-tissue membranes taking into account their structural and functional peculiarities have been considered [3]. In addition tissue reservoirs are differentiated and peculiarities of energy exchange of tissues of brain, heart muscle, liver, kidneys, skeletal muscles, skin and other organism's tissues have been considered. Presented below equations of mathematical model of object have been obtained on the basis of continuity and material balance principles (conservation of mass) using known empiric physiological dependencies among variables. Model equations are described as follows.

Let p_1, p_2, p_3 — partial pressures of oxygen, carbon dioxide and nitrogen in inhaled air and $p_1 + p_2 + p_3 = B$, where B — total barometric pressure.

Then dynamics of partial pressures of gases in respiratory tract during breathing cycle can be presented as follows:

$$\frac{dp_{1_{rw}}}{d\tau} = \frac{\dot{V}}{n_1 V_{rw}}[\tilde{p}_1 - \tilde{p}_{1_{rw}}], \tag{1}$$

$$\frac{dp_{2_{rw}}}{d\tau} = \frac{\dot{V}}{n_2 V_{rw}}[\tilde{p}_2 - \tilde{p}_{2_{rw}}], \tag{2}$$

$$\frac{dp_{3_{rw}}}{d\tau} = \frac{\dot{V}}{n_3 V_{rw}}[\tilde{p}_3 - \tilde{p}_{3_{rw}}], \tag{3}$$

where V_{rw} — volume of respiratory tract (generalized reservoir), $\dot{V}$ — ventilation depending of values of respiratory volume and duration of breathing cycle; n_1, n_2, n_3 — conversion factors for respiratory gases and nitrogen respectively, and

$$\tilde{p}_j = \begin{cases} p_j, & (\dot{V} > O), \\ p_{j_{rw}}, & (\dot{V} \le O), \end{cases} \qquad j = \overline{1,3}, \tag{4}$$

$$\tilde{p}_{j_{rw}} = \begin{cases} p_{j_{rw}}, & (\dot{V} > O), \\ p_{j_A}, & (\dot{V} \le O), \end{cases} \qquad j = \overline{1,3}.$$

During modeling of partial pressures of gases in alveolar space with volume V_L it is necessary to take into account gas flow through air-blood barrier

$$G_{j_{LC}} = D_j S_{LC}(p_{j_A} - p_{j_{LC}}), \tag{5}$$

where D_j — coefficients characterizing permeability of gases through air-blood barrier, S_{LC} — area of gas mass transfer surface.

Then

$$\frac{dp_{1_A}}{d\tau} = \frac{1}{n_1(V_L - V_{rw})}[n_1 \dot{V} \tilde{p}_{1_{rw}} - G_{1_{LC}} - n_1 p_{1_A} \frac{dV_L}{d\tau}], \tag{6}$$

$$\frac{dp_{2_A}}{d\tau} = \frac{1}{n_2(V_L - V_{rw})}[n_2 \dot{V} \tilde{p}_{2_{rw}} - G_{2_{LC}} - n_2 p_{2_A} \frac{dV_L}{d\tau}], \tag{7}$$

$$\frac{dp_{3_A}}{d\tau} = \frac{1}{n_3(V_L - V_{rw})}[n_3 \dot{V} \tilde{p}_{3_{rw}} - G_{3_{LC}} - n_3 p_{3_A} \frac{dV_L}{d\tau}]. \tag{8}$$

It is assumed that lung volume during breathing cycle is changed according to

$$V_L = \begin{cases} V_L(\tau_0) + \frac{D}{2}(1 - \cos\frac{\tau - \tau_0}{t_c} 2\pi), at\ inhale\ and\ exhale \\ V_L(\tau_0), at\ pause \end{cases} \tag{9}$$

where D — respiratory volume of lungs, τ_0 — start of breathing cycle, t_c — its duration.

It is also assumed that

$$\dot{V} = \frac{dV_L}{d\tau} \tag{10}$$

($\dot{V} = 0$ during pause).

As it can be seen from the equations (1)–(8), gas diffusion from respiratory tract to alveolar space during pause is not considered.

Equations of blood gas tension dynamics are developed taking into account biophysical and chemical properties of blood. It is known that oxygen and carbon dioxide can be transported with blood flow both physically dissolved in blood plasma, and attached to hemoglobin (and CO_2 is bound also with buffer bases), while nitrogen is transported only in dissolved form.

Changes of blood gas tension in pulmonary capillaries can be influenced by gas flows from alveolar space $G_{j_{LC}}$ (5), from mixed venous blood and gas flow passing with circulating blood into arterial channel. In addition model takes into account presence of pulmonary shunt having volumetric speed of blood flow Q_s. Equations of dynamics of blood gas tension in pulmonary capillaries in connection with above mentioned are as follows:

$$\frac{dp_{1_{LC}}}{d\tau} = \frac{1}{V_{LC}(\alpha_1 + \gamma Hb \frac{\partial \eta_{LC}}{\partial p_{1_{LC}}})}[\alpha_1(Q - Q_s)(p_{1_v^-} - p_{1_{LC}}) + \\ + G_{1_{LC}} + \gamma Hb(Q - Q_s)(\eta_v^- - \eta_{LC})], \tag{11}$$

$$\frac{dp_{2_{LC}}}{d\tau} = \frac{1}{V_{LC}(\alpha_2 + \gamma_{BH} BH \frac{\partial z_{LC}}{\partial p_{2_{LC}}})}[(((1-\eta_{\bar{v}})z_{\bar{v}} - (1-\eta_{LC})z_{LC})\gamma Hb +$$
$$+\gamma_{BH} BH(z_{\bar{v}} - z_{LC}))(Q - Q_S) + \tag{12}$$
$$+(p_{2_{\bar{v}}} - p_{2_{LC}})\alpha_2(Q - Q_S) + G_{2_{LC}} + \gamma Hb V_{LC}\frac{d\eta_{LC}}{d\tau}],$$

$$\frac{dp_{3_{LC}}}{d\tau} = \frac{1}{\alpha_3 V_{LC}}[\alpha_3 p_{3_{\bar{v}}}(Q - Q_s) + G_{3_{LC}} - \alpha_3 p_{3_{LC}}(Q - Q_s)]. \tag{13}$$

For more precise description of gas mass carry process in pulmonary capillaries in the section «alveoli — pulmonary capillaries blood» the structure of pulmonary capillaries can be differentiated, considering the elements of pulmonary artery, capillary network itself and pulmonary vein.

In the equations (11)–(13) V_{LC} — volume of blood of pulmonary capillaries, Q — volume velocity of system blood flow, α_1, α_2, α_3 — coefficients of gas solubility in blood; γ, γ_{BH} — physiological constants, determined in Haldane and Verigo-Bohr equations; η — hemoglobin saturation rate (its concentration will be denoted as Hb) with oxygen, determined by empiric dependency

$$\eta_{LC} = 1 - 1{,}75\exp(-0{,}052 m_{LC} p_{1_{LC}}) + 0{,}75\exp(-0{,}12 m_{LC} p_{1_{LC}}). \tag{14}$$

At $m_{LC} = const$ dependency of hemoglobin saturation rate Hb with oxygen has a shape of S-curve, that is approximated by the expression (14). But it is known, that alteration of pH value in blood causes shifting of the curve of oxyhemoglobin dissociation (Bohr effect). Carbon dioxide facilitates displacement of oxygen from oxyhemoglobin, and shape and location of dissociation curve are changed depending on CO_2 tension, namely, with its increasing affinity of hemoglobin with oxygen is decreasing and dissociation curve is shifted to the right, i.e. oxyhemoglobin dissociation is increased. Following equations serve as mathematical interpretation of Bohr effect in the model

$$m_{LC} = 0{,}25(pH_{LC} - 7{,}4) + 1, \tag{15}$$

$$pH_{LC} = 6{,}1 + \lg\frac{BH}{\alpha_2 p_{2_{LC}}}. \tag{16}$$

Dependency (16) is Henderson-Hasselbach equation that is used for determination of correlation among blood acidity (pH), tension of CO_2 in blood and concentration of hydrocarbonates that are buffer bases (BH). Saturation rate of buffer bases of blood with carbon dioxide is expressed by the Michaelis-Menten formula

$$Z_{LC} = \frac{p_{2_{LC}}}{P_{2_{LC}} + 35}. \tag{17}$$

Equations (1)–(17) describe first three links of controlled system — change of partial pressures of gases in respiratory tract, alveoli and blood of pulmonary capillaries.

The blood saturated in pulmonary capillaries is flowing in the arterial channel with volume velocity (Q–Q_s), and, as a result of pulmonary shunt, — mixed venous blood is flowing with volume velocity Q_s, while the arterial blood is flowing out with volume velocity Q. Taking into account conditions of continuity and material balance the following can be written

$$\frac{dp_{1_a}}{d\tau} = \frac{1}{V_a(\alpha_1 + \gamma Hb\ \frac{\partial \eta_a}{\partial p_{1_a}})}[\alpha_1(Q - Q_s)p_{1_{LC}} + \\ + \alpha_1 Q_s p_{1_{\bar{v}}} - \alpha_1 Q p_{1_a} + \\ + \gamma Hb(Q - Q_s)\eta_{LC} + \gamma HbQ_s\eta_{\bar{v}} - \gamma HbQ\ \eta_a], \tag{18}$$

$$\frac{dp_{2_a}}{d\tau} = \frac{1}{V_a(\alpha_2 + \gamma_{BH}\ BH\ \frac{\partial z_a}{\partial p_{2_a}})}[((1 - \eta_{\bar{v}})Q_s z_{\bar{v}} + \\ + (1 - \eta_{LC})(Q - Q_s)z_{LC} - (1 - \eta_a)Q_{z_a})\gamma Hb + (z_{\bar{v}}Q_s + \\ + z_{LC}(Q - Q_s) - z_a Q)\gamma_{BH}\ BH + \alpha_2(Q_s p_{2_{\bar{v}}} + \\ + (Q - Q_s)p_{2_{LC}} - Qp_{2_a}) + \gamma HbV_a\frac{d\eta_a}{d\tau}], \tag{19}$$

$$\frac{dp_{2_a}}{d\tau} = \frac{1}{V_a(\alpha_2 + \gamma_{BH}\ BH\ \frac{\partial z_a}{\partial p_{2_a}})}[((1 - \eta_{\bar{v}})Q_s z_{\bar{v}} + \\ + (1 - \eta_{LC})(Q - Q_s)z_{LC} - (1 - \eta_a)Q_{z_a})\gamma Hb + (z_{\bar{v}}Q_s + \\ + z_{LC}(Q - Q_s) - z_a Q)\gamma_{BH}\ BH + \alpha_2(Q_s p_{2_{\bar{v}}} + \\ + (Q - Q_s)p_{2_{LC}} - Qp_{2_a}) + \gamma HbV_a\frac{d\eta_a}{d\tau}], \tag{20}$$

$$\frac{dp_{3_a}}{d\tau} = \frac{1}{\alpha_3 V_a}[\alpha_3(Q - Q_s)p_{3_{LC}} + \alpha_3 Q_s p_{3_{\bar{v}}} - \alpha_3 Q p_{3_a}].$$

Let's express changes in organism gas tensions in tissue capillaries blood (ct_i) and tissues (t_i). Tissue reservoirs are considered on the level of organs and tissues, namely, brain, heart, liver, kidneys, skeletal muscles (sk.m.), skin, adipose and bone tissues (let m — number of tissue reservoirs).

Krogh model has been chosen as a model of tissue reservoir [4, 5], where capillary network of tissues or organs is represented with one generalized cylindrical capillary in the inlet of whose arterial blood is coming. During flowing of blood along the capillary respiratory exchange between capillary blood and tissue is occurring through its wall. Then blood is flowing in the vein.

In the same way as other equations of mathematical model, equations of

dynamics pO_2, pCO_2, pN_2 in blood of tissue capillaries and tissue are compiled on the basis of principles of materiality of balance and flow continuity.

$$\frac{dp_{1_{ct_i}}}{d\tau} = \frac{1}{V_{ct_i}(\alpha_1 + \gamma Hb \frac{\partial \eta_{ct_i}}{\partial p_{1_{ct_i}}})}[\alpha_1 Q_{t_i}(p_{1_a} - p_{1_{ct_i}}) - G_{1_{t_i}} + \gamma Hb Q_{t_i}(\eta_a - \eta_{ct_i})] \tag{21}$$

$$\begin{aligned}\frac{dp_{2_{ct_i}}}{d\tau} &= \frac{1}{V_{ct_i}(\alpha_2 + \gamma_{BH} BH \frac{\partial z_{ct_i}}{\partial p_{2_{ct_i}}})}[\alpha_2 Q_{t_i}(p_{2_a} - p_{2_{ct_i}}) - G_{2_{t_i}} + \\ &+ Q_{t_i} BH \gamma_{BH}(z_a - z_{ct_i}) + \\ &+ (1-\eta_a)\gamma Hb Q_{t_i} z_a - (1-\eta_{ct_i})\gamma Hb Q_{t_i} z_{ct_i} + \gamma Hb V_{ct_i} \frac{d\eta_{ct_i}}{d\tau}],\end{aligned} \tag{22}$$

$$\frac{dp_{3_{ct_i}}}{d\tau} = \frac{1}{\alpha_3 V_{ct_i}}[\alpha_3 p_{3_a} Q_{t_i} - \alpha_3 p_{3_{ct_i}} Q_{t_i} - G_{3_{t_i}}]. \tag{23}$$

Rate of intensity of metabolic process in tissue regions of this model is characterized by the rate of oxygen consumption $q_{1_{t_i}}$ and rate of carbon dioxide evolution $q_{2_{t_i}}$. It is considered, that dependence of oxygen consumption rate $q_{1_{t_i}}$ in tissues of brain, kidneys and heart is determined by equation of Michaelis-Menten: $q_{1_{t_i}}(\tau) = q^0_{1_{t_i}} \frac{p_{1_{t_i}}}{R + p_{1_{t_i}}}$, and in peripheral tissues, including skeletal muscles, by correlation

$$q_{1_{t_i}}(\tau) = q^0_{1_{t_i}} \left(\frac{\eta_{ct_i}(\tau)}{\eta^0_{ct_i}} \right)^2, \tag{24}$$

where $q^0_{1_{t_i}}$ — consumption rate of O_2 at given intensity of load under normal conditions of external environment, R — *const*, $\eta^0_{ct_i}$ — saturation rate of *Hb* in blood with oxygen in these conditions, and $\eta_{ct_i}(\tau)$ — saturation rate of *Hb* in changed conditions of experiment.

In addition, for definiteness it is considered that consumption rate of O_2 in heart muscles is linear function of the value of volume velocity of systemic blood flow

$$q_{1_{sk.m.}} = \alpha Q + \beta,$$

$$q_{2_{t_i}} = n_{t_i} q_{1_{t_i}}, \tag{25}$$

where n_{t_i} — respiratory coefficient.

In this connection dynamics of gas tension in tissue reservoirs in normal physiological organism may be described by the equations

$$\frac{dp_{1_{t_i}}}{d\tau} = \frac{1}{V_{t_i}(\alpha_{1_{t_i}} + \gamma_{Mb_i} Mb_i \frac{\partial \eta_{Mb_i}}{\partial p_{1_{t_i}}})}(G_{1_{t_i}} - q_{1_{t_i}}), \tag{26}$$

$$\frac{dp_{2_{t_i}}}{d\tau} = \frac{1}{V_{t_i}\alpha_{2_{t_i}}}(q_{2_{t_i}} + G_{2_{t_i}}), \tag{27}$$

$$\frac{dp_{3_{t_i}}}{d\tau} = \frac{1}{\alpha_{3_{t_i}} V_{t_i}} G_{3_{t_i}}, \tag{28}$$

where $\eta_{Mb_i} = 1 - \exp(-0{,}12\, p_{1_{t_i}})$ — saturation rate of myoglobin with oxygen, $0 \le \eta_{Mb_i} \le 1$, γ_{Mb_i} — coefficient characterizing maximal amount of O_2, that can be attached with 1 g of myoglobin (Mb_i).

The link of breathing system «blood — tissue reservoirs» can be detailed at the account of both differentiation of tissue reservoirs and modeling of transport and exchange functions of blood in arterioles, tissue capillaries and venules.

To conclude the model it is necessary just to present equations representing the dynamics of gas tension in mixed venous blood:

$$\frac{dp_{1_v^-}}{d\tau} = \frac{1}{V_v^-(\alpha_1 + \gamma Hb \frac{\partial \eta_v^-}{\partial p_{1_v^-}})}[\alpha_1(\sum_{i=1}^{m} Q_{t_i} p_{1_{ct_i}} - Q p_{1_v^-}) + \gamma Hb(\sum_{i=1}^{m} Q_{t_i} \eta_{ct_i} - Q\eta_v^-)), \tag{29}$$

$$\begin{aligned}\frac{dp_{2_v^-}}{d\tau} = {} & \frac{1}{V_v^-(\alpha_2 + \gamma_{BH} BH \frac{\partial z_v^-}{\partial p_{2_v^-}})}[\alpha_2(\sum_{i=1}^{m} Q_{t_i} p_{2_{ct_i}} - Q p_{2_v^-}) + \\ & + \gamma Hb(\sum_{i=1}^{m} Q_{t_i}(1-\eta_{ct_i}) z_{ct_i} - (1-\eta_v^-) Q z_v^-) + \\ & + \gamma_{BH} BH(\sum_{i=1}^{m} Q_{t_i} z_{ct_i} - Q z_v^-) + \gamma Hb V_v^- \frac{d\eta_v^-}{d\tau}],\end{aligned} \tag{30}$$

$$\frac{dp_{3_v^-}}{d\tau} = \frac{1}{\alpha_3 V_v^-}(\alpha_3 \sum_{i=1}^{m} p_{3_{ct_i}} Q_{t_i} - \alpha_3 p_{3_v^-} Q). \tag{31}$$

It is obvious that equations (1)–(31) represent dynamics of gas mass transfer in organism in simplified form. However the principle of model development allows the possibility to consider also arteriovenous anastomosis and model gas tension on the walls of vessels — capillary, change of blood volume in tissue capillaries, enabling to solve different tasks of theoretical and applied physiology.

The model is developed for average statistical (reference) person and it uses the known experimental data on diffusion coefficients and gas permeability through the membranes separating the medium, on other parameters characterizing gas transport in the organism and metabolic processes taking place in tissues.

It would be important to clarify the role of these parameters in stabilization of transients occurring during violation of equilibrium state caused by changes of internal or external conditions. Transients caused by changes of composition of inhaled air, transition from steady state to load and vice versa, during pressure difference and process of the control of level of organism's gas homeostasis have been studies. Data obtained in other studies [6, 7] have been accounted during the work with the model.

On the model described above the simulation of functional self-organization of physiological breathing system under conditions of highlands has been carried out.

It was assumed that before experiments the gas mass transfer system in organism was in stationary state, breathing gas normoxic (21 % O_2 and 79 % N_2). Calculations have been executed for normal physiological data of person weighting 75 kg, volume velocity of oxygen consumption under calm conditions q = 4,3 ml/sec, Q = 96 ml/sec, Hb=0,14 g/ml, BH=0,479 g/ml, D=550 ml, t_c = 4 sec. To determine initial status of the system in simulation of arbitrary extreme situation it was necessary to simulate first calm conditions under normal external conditions Q_{t_i}, $p_{1_{t_i}}$, and $p_{2_{t_i}}$ since experimental determination of initial values is complicated. Therefore starting from certain determined approximated state of the system (1)–(31) trajectories $p_{1_{t_i}}$ and $p_{2_{t_i}}$ have been put in steady regime for time T. Calculations have been executed during time interval T = 3000 sec with simulation time-step $\Delta\tau = 0{,}01$.

Air pressure at sea level everywhere on the globe is on average close to one atmosphere. Going up from the see level air pressure is decreasing; respectively its density is also decreasing: air becomes more and more rarefied, i.e. amount of oxygen in inhaled air is decreased. Therefore for simulation of highlands conditions known data of air pressure and oxygen content at different heights have been taken [8].

In present work computer analysis of model at different heights has been carried out: 1 km (Bo = 674 mm Hg), 2 km (Bo = 596 mm Hg), 3 km (Bo = 526 mm Hg), 4 km (Bo = 462 mm Hg) with oxygen content in air respectively 18,5 %, 16,2 %, 14,3 %, 12,6 %. At the time zero values of gas tensions in arterial blood and skeletal muscles were taken at normal state, i.e. in calm conditions at sea level.

For every height set of experiments have been carried out under following conditions:

I. Hypoxia in calm state with compensation — increasing of $Q_{sk.m}$ in 2 times, V_{inhale} in 1,5 times: V_{inhale} = 800 ml; tc = 4,0 sec; t_{inhale} = t_{exhale} = 1,5 sec; Q = 117,1 ml/sec; Q_{brain} = 14,88; Q_{heart} = 6,135; Q *sk.m.* = 38,45; $Q_{other\ tissues}$ = 57,595; q = 4,44 ml/sec; q_{brain} = 0,632; q_{heart} = 0,4725; $q_{sk.m.}$ = 1,488; $q_{other\ tissues}$ = 1,849.

II. Load hypoxia with compensation — increasing of $q_{sk.m.}$ and $Q_{sk.m.}$ in 2 times, V_{inhale} in 1,5 times: V_{inhale} = 800 ml; tc = 4,0 sec; t_{inhale} = t_{exhale} = 1,5 sec; Q = 117,1 ml/sec; Q_{brain} = 14,88; Q_{heart} = 6,135; $Q_{sk.m.}$ = 38,45; $Q_{other\ tissues}$ = 57,595: q = *5,9292 ml/sec*; q_{brain} = 0,6321; q_{heart} = 0,4725; $q_{sk.m.}$ = 2,9756; $q_{other\ tissues}$ = 1,849.

III. Load hypoxia with compensation — increasing of $q_{sk.m.}$ in 2 times, $Q_{sk.m.}$ in 4 times, V_{inhale} up to 1000 ml: V_{inhale} = 1000 ml; tc = 3,0 sec; t_{inhale} = t_{exhale} = 1,5 sec; Q = *159,2 ml/sec*; Q_{brain} = 14,88; Q_{heart} = 9,84; $Q_{sk.m.}$ = 76,90; $Q_{other\ tissues}$ = 57,595; q = *6,2146 ml/sec*; q_{brain} = 0,6321; q_{heart} = 0,7579; $q_{sk.m.}$ = 2,9756; $q_{other\ tissues}$ = 1,8490.

Results of experiments are presented in the table and on figures 1–4.

On figures 1–4:

row 1 — Hypoxia in calm state with compensation — increasing of $Q_{sk.m.}$ in 2 times, V_{inhale} in 1,5 times:

row 2 — Load hypoxia with compensation — increasing of $q_{sk.m.}$ and $Q_{sk.m.}$ in 2 times, V_{inhale} in 1,5 times:

row 3 — Load hypoxia with compensation — increasing of $q_{sk.m.}$ in 2 times, $Q_{sk.m.}$ in 4 times, V_{inhale} up to 1000 ml:

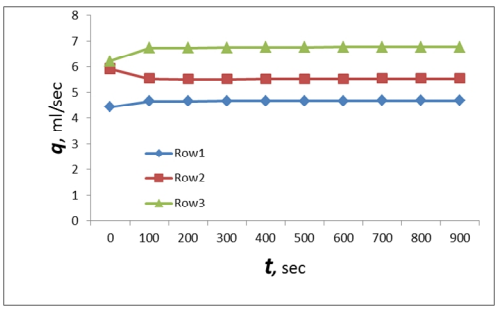

Fig. 1. Oxygen consumption at height 1 km

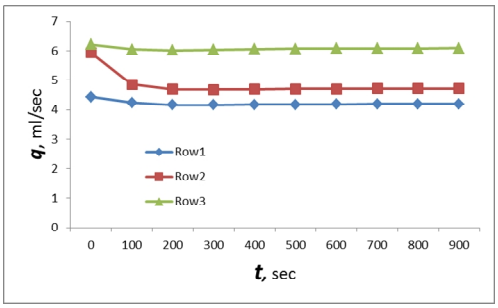

Fig. 2. Oxygen consumption at height 2 km

Comparative analysis of results demonstrates, that with the same values $\dot{V}$ and Q levels of p_aO_2 are below normal, and levels of $p_{sk.m.}O_2$, p_aCO_2, $p_{sk.m.}CO_2$ are higher, but later on significantly decreasing.

To approximate gas tension levels to normal values, $\dot{V}$ and $Q_{sk.m.}$ have to be significantly higher.

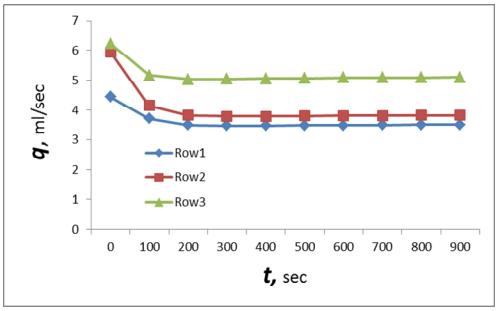

Fig. 3. Oxygen consumption at height 3 km

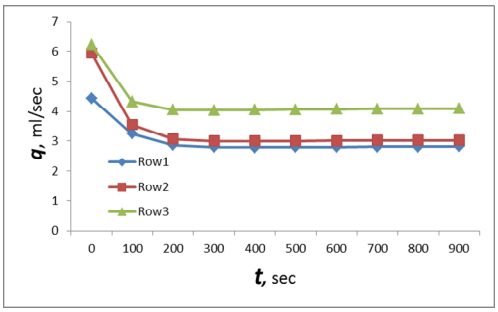

Fig. 4. Oxygen consumption at height 4 km

Table Results of experiments

I	V_{inh}=800 ml, t_c=4 s, $\dot{V}$ =12 l/min, Q=117 ,1 ml/sec, q=4.44 ml/sec											
	H=1 km B_0=674 mm Hg			H=2 km B_0=596 mm Hg			H=3 km B_0=526 mm Hg			H=4 km B_0=462 mm Hg		
t, c	0	100	2800	0	100	2800	0	100	2800	0	100	2800
q, ml/sec	4.4414	4.6629	4.6912	4.4414	4.2340	4.2052	4.4414	3.7204	3.5163	4.4414	3.2325	2.8227
P_aO_2, mm Hg	92.9	70.33	73.76	92.9	46.53	45.25	92.9	34.28	30.35	92.9	26.82	21.58
$P_{sk.m.}O_2$, mm Hg	26.71	35.95	33.46	26.71	30.81	27.71	26.71	25.86	21.41	26.71	21.92	16.33
P_aCO_2, mm Hg	26.17	34.73	18.40	26.17	34.22	16.61	26.17	33.54	13.93	26.17	32.89	11.21
$P_{sk.m.}CO_2$, mm Hg	32.03	47.53	22.07	32.03	47.13	19.69	32.03	46.65	16.30	32.03	46.19	12.94
II	V_{inh}=800 ml, t_c=4 s, $\dot{V}$ =12 l/min, Q=117,1 ml/sec, q=5,93 ml/sec											
	H=1 km B_0=674 mm Hg			H=2 km B_0=596 mm Hg			H=3 km B_0=526 mm Hg			H=4 km B_0=462 mm Hg		
t, c	0	100	2800	0	100	2800	0	100	2800	0	100	2800
q, ml/sec	5.9292	5.5470	5.5540	5.9292	4.8573	4.7243	5.9292	4.1594	3.8328	5.9292	3.5410	3.0263
P_aO_2, mm Hg	92.9	58.16	60.08	92.9	39.28	37.17	92.9	29.41	25.79	92.9	23.17	18.78
$P_{sk.m.}O_2$, mm Hg	26.71	25.66	24.08	26.71	21.96	19.61	26.71	18.68	15.48	26.71	16.03	12.13
P_aCO_2, mm Hg	26.17	36.14	21.81	26.17	35.26	18.66	26.17	34.36	15.18	26.17	33.58	12.01
$P_{sk.m.}CO_2$, mm Hg	32.03	48.92	27.24	32.03	48.29	22.94	32.03	47.65	18.38	32.03	47.09	14.31
III	V_{inh}=1000 ml, t_c=3 s, $\dot{V}$ =20 l/min, Q=159,2 ml/sec, q=6,21 ml/sec											
	H=1 km B_0=674 mm Hg			H=2 km B_0=596 mm Hg			H=3 km B_0=526 mm Hg			H=4 km B_0=462 mm Hg		
t, c	0	100	2800	0	100	2800	0	100	2800	0	100	2800
q, ml/sec	6.2146	6.7337	6.7791	6.2146	6.0453	6.0920	6.2146	5.1688	5.0975	6.2146	4.3299	4.0948
P_aO_2, mm Hg	92.9	67.67	70.52	92.9	43.58	43.83	92.9	31.26	29.45	92.9	23.74	20.91
$P_{sk.m.}O_2$, mm Hg	26.71	35.12	32.75	26.71	29.29	27.05	26.71	23.53	20.74	26.71	19.04	15.72
P_aCO_2, mm Hg	26.17	31.00	16.01	26.17	30.43	14.50	26.17	29.70	12.20	26.17	29.00	9.94
$P_{sk.m.}CO_2$, mm Hg	32.03	40.79	19.13	32.03	39.98	17.09	32.03	38.98	14.13	32.03	38.03	11.20

CONCLUSIONS

Presented results of computer analysis of the model show that hypometabolism is a necessary condition for stabilization of the status of organism during highland hypoxia.

Calculations using mathematical model (1)-(33) with hypometabolism mechanism (24) demonstrates that stabilization of the status of the breathing and blood circulation system require less metabolic cost of regulatory mechanism during the work under conditions of highlands.

1. Gray J.S. The multiple factor theory of respiratory regulation. *Science*. 1946. V.103. P.739–744.
2. Grodins F. Mathematical analysis and digital simulation of the respiratory control system. *J. Appl. Physiol*. 1967. Vol. 22, № 2. P.260–276.
3. Bioecomedicine. United information space / edited by V.I. Grytsenko. Kiev: Naukova dumka, 2001. 318 p. (in Russian).
4. Lauer N.V., Kolchinskaya A.Z., Kulikov M.A. Calculation of parameters of organism's oxygen regimes and development of oxygen cascades. *Organism's oxygen regime and its regulation*. - Kiev: Naukova dumka, 1966, p.16–22 (in Russian).
5. Kolchinskaya A.Z., Man'kovskaya I.N., Misiura A.G. *Breathing and oxygen regimes of dolphins' organisms*. — Kiev: Naukova dumka, 1980. 332 p. (in Russian).
6. Biloshyts'kyi P. V., Kliuchko O. M., Onopchuk Yu. M. Study of hypoxia issues by Ukrainian scientists in the area of Elbrus mountain. *Bulletin of NASU*. 2007, no 3–4. P. 44–50 (in Russian).
7. Onopchuk Yu.N., Misiura A.G. Methods of mathematical modeling and control in theoretical research and applied problem solving in sports medicine and physiology. *Sports medicine*. 2008, no 1. P. 181–188 (in Russian).
8. *Table of International Standard Atmosphere.* Available at: http://www.vsetabl.ru/154.htm.

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MATHEMATICAL MODELING OF HYPOMETABOLISM PROCESS TO IDENTIFY PECULIARITIES OF HUMAN ORGANISM DURING THE WORK UNDER CONDITION OF HIGHLANDS

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Introduction: Hypometabolic and hypoxic states are in the focus of attention of researchers since organism is often impacted by hypoxic factors, particularly under conditions of highlands, as well as during significant physical loads or some severe pathologic process.

Hypoxic or exogenous hypoxia is developed during decreasing of partial pressure of oxygen in inhaled air. During hypoxic hypoxia the arterial oxygen tension, the saturation of hemoglobin with oxygen and its total content in the blood are being decreased. Negative impact can be caused also by hypocapnia, developed as a result of compensatory hyperventilation of lungs. Extreme hypocapnia causes worsening of blood supply to brain and heart (vasoconstriction) and respiratory alkalosis. In this connection, it is interesting to investigate the energy reserves of

organism and the ways of its strengthening under hypoxic conditions.

Problem definition: Investigation of the processes of human organism breathing system self-regulation represents particular scientific area that is being widely developed last years as a result of success in mathematical modelling. However the regulation mechanisms of functional state of human organism under conditions of highland hypoxia are not sufficiently studied yet. Infeasibility of such investigations was related with the difficulties of experimental determination of the several most important parameters and with the absence of adequate mathematical models for dynamics of these processes.

The main task of this work consists in investigation of the mechanism of formation of hypometabolic state of human being under conditions of highlands. Mathematical model of functional systems of breathing and blood circulation has been used to analyze this phenomenon on system level.

The purpose of this work is to develop and to investigate the mathematical model of hypometabolism, and to develop the software for execution of computing experiments with the model.

Results:

1. Developed complex of mathematical model of the gas mass carry process in organism and software is applied for assessment of the dynamics of functional state of human being on conditions of work at highlands.

2. Implemented numerical analysis of the models of respiratory exchange control enables to:

- follow dynamics of the main physiological parameters of the model during transient processes and in stationary states;
- forecast and quantitatively assess regulatory reactions of the organism under given disturbances;
- carry out individualization of model developments on condition of availability of array of data on anatomic-physiological peculiarities of specific human being.

Obtained results are well correlated with the physiological experimental data.

Conclusions: Presented results of computer analysis of the model demonstrate that hypometabolism is a pre-requisite for stabilization of organism's state under highland hypoxia.

Calculations on mathematical model of the process of gas mass transfer with hypometabolism mechanism demonstrate that stabilization of breathing and blood circulation system state require less metabolic cost of regulatory mechanisms under highland conditions.

***Keywords*:** mathematical model, breathing and blood circulation system, gas tensions, hypoxia, hypometabolism, disturbing impacts, computing experiments.

1. Gray J.S. The multiple factor theory of respiratory regulation. *Science*. 1946. V.103. P.739–744.
2. Grodins F. Mathematical analysis and digital simulation of the respiratory control system. *J. Appl. Physiol*. 1967. Vol. 22, № 2. P.260–276.
3. *Bioecomedicine. United information space* / edited by V.I. Grytsenko. Kiev: Naukova dumka, 2001. 318 p. (in Russian).

4. Lauer N.V., Kolchinskaya A.Z., Kulikov M.A. Calculation of parameters of organism's oxygen regimes and development of oxygen cascades. *Organism's oxygen regime and its regulation*. - Kiev: Naukova dumka, 1966, p.16–22 (in Russian).
5. Kolchinskaya A.Z., Man'kovskaya I.N., Misiura A.G. *Breathing and oxygen regimes of dolphins' organisms*. — Kiev: Naukova dumka, 1980. 332 p. (in Russian).
6. Biloshyts'kyi P. V., Kliuchko O. M., Onopchuk Yu. M. Study of hypoxia issues by Ukrainian scientists in the area of Elbrus mountain. *Bulletin of NASU*. 2007, no 3–4. P. 44–50 (in Russian).
7. Onopchuk Yu.N., Misiura A.G. Methods of mathematical modeling and control in theoretical research and applied problem solving in sports medicine and physiology. *Sports medicine*. 2008, no 1. P. 181–188 (in Russian).
8. *Table of International Standard Atmosphere.* Available at: http://www.vsetabl.ru/154.htm.

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