

RELATIONSHIP BETWEEN THE ATHLETE'S PRE-START STATE PARAMETERS AND PHYSIOLOGICAL RESPONSE TO STANDARDIZED LOAD

Chikov AE^{1,2}✉, Kutsalo AL¹, Kiselev AD¹, Vladimirov VV¹, Krylova MV¹, Medvedev DS³, Kaplun DI⁴, Shpakovskaya II⁴

¹ Research Institute of Hygiene, Occupational Pathology and Human Ecology of the Federal Medical Biological Agency, Saint Petersburg, Russia

² Almazov National Medical Research Centre, Saint Petersburg, Russia

³ Saint Petersburg Institute of Bioregulation and Gerontology, Saint Petersburg, Russia

⁴ Saint Petersburg Electrotechnical University "LETI", Saint Petersburg, Russia

Intense physical work is characterized by activity of physiological mechanisms as interrelated components joint for physical exertion. Definition of a set of individual and typological patterns of the physiological mechanisms' activity answers the questions related to improvement of the athlete's potential realization efficiency, definition of the limiting components and body's reserve capacity, training load management. The study was aimed to assess the relationship between the responses of physiological mechanisms associated with standardized physical exertion and the pre-start state parameters. The athlete was through the step incremental test with the treadmill involving recording of the gas exchange parameters and heart rate to study physiological patterns. The physiological response parameters were calculated relative to the key phases of the exercise test: pre-start state, aerobic and anaerobic thresholds, peak exertion, rapid and slow recovery phases. The mathematical model "Horseshoe of Rest" characterizing the athlete's pre-start state before performing the test was constructed using the T-SNE dimensionality reduction algorithms. The model enables estimation of the release of non-metabolic CO₂ throughout the testing period (MIC — 0.29) and the exertion period (MIC — 0.35).

Keywords: athlete, physical activity, pre-start state, modeling of energy supply, threshold of anaerobic metabolism, physiological response, standardized load

Author contribution: Chikov AE — analysis of the results; Kiselev AD, Vladimirov VV — manuscript writing, literature review; Kutsalo AL, Medvedev DS — discussion of the results, manuscript writing; Krylova MV — data preparation for analysis; Kaplun DI, Shpakovskaya II — data processing, constructing the pre-start state model.

Compliance with the ethical standards: the study was approved by the Ethics Committee of the Research Institute of Hygiene, Occupational Pathology and Human Ecology of FMBA of Russia (protocol № 2 of 1 March 2021).

✉ **Correspondence should be addressed:** Alexander E. Chikov
Zavodskaja, zd. 6/2, korp. 93, gp. Kuzmolovskij, 188663, Russia; chikov.alexandr@yandex.ru

Received: 21.08.2023 **Accepted:** 17.09.2023 **Published online:** 30.09.2023

DOI: 10.47183/mes.2023.037

ВЗАИМОСВЯЗЬ ПОКАЗАТЕЛЕЙ «ПРЕДСТАРТОВОГО» СОСТОЯНИЯ СПОРТСМЕНА С ФИЗИОЛОГИЧЕСКОЙ РЕАКЦИЕЙ НА СТАНДАРТИЗИРОВАННУЮ НАГРУЗКУ

А. Е. Чиков^{1,2}✉, А. Л. Куцало¹, А. Д. Киселев¹, В. В. Владимиров¹, М. В. Крылова¹, Д. С. Медведев³, Д. И. Каплун⁴, И. И. Шпаковская⁴

¹ Научно-исследовательский институт гигиены, профпатологии и экологии человека ФМБА России, Санкт-Петербург, Россия

² Национальный медицинский исследовательский центр имени В. А. Алмазова Минздрава России, Санкт-Петербург, Россия

³ Санкт-Петербургский Институт биорегуляции и геронтологии, Санкт-Петербург, Россия

⁴ Санкт-Петербургский государственный электротехнический университет «ЛЭТИ» имени В. И. Ульянова (Ленина), Санкт-Петербург, Россия

Интенсивная физическая работа характеризуется активностью физиологических механизмов как взаимосвязанных компонентов, объединенных для выполнения физической нагрузки. Определение набора индивидуально-типологических паттернов активности физиологических механизмов отвечает на вопросы, связанные с повышением эффективности реализации потенциала спортсмена, определением лимитирующих звеньев и резервных возможностей организма, управлением тренировочной нагрузкой. Целью работы было изучение взаимосвязи реакции физиологических механизмов при выполнении стандартизированной физической нагрузки с показателями «предстартового» состояния. Для исследования физиологических закономерностей спортсменов выполнял ступенчато-возрастающий тест на беговой дорожке с фиксацией показателей газообмена, частоты сердечных сокращений. Расчет показателей физиологических реакций производили относительно ключевых фаз нагрузочного тестирования: «предстартового» состояния, аэробного и анаэробного порогов, пика нагрузки, фаз быстрого и медленного восстановления. С использованием алгоритмов понижения размерности T-SNE была разработана математическая модель «Подкова_покоя», характеризующая «предстартовое» состояние спортсмена перед выполнением теста. Модель позволяет оценить уровень выделения неметаболического CO₂ за весь период тестирования (MIC — 0,29) и за период нагрузки (MIC — 0,35).

Ключевые слова: спортсмен, физическая нагрузка, «предстартовое» состояние, моделирование энергообеспечения, порог анаэробного обмена, физиологическая реакция, стандартизированная нагрузка

Вклад авторов: А. Е. Чиков — анализ результатов исследования; А.Д. Киселёв, В. В. Владимиров — подготовка текста статьи, анализ литературных источников; А. Л. Куцало, Д. С. Медведев — обсуждение результатов исследования, подготовка текста статьи; М. В. Крылова — подготовка данных к анализу; Д. И. Каплун, И. И. Шпаковская — обработка данных, разработка модели предстартового состояния.

Соблюдение этических стандартов: исследование одобрено этическим комитетом ФГУП «НИИ ГПЭЧ» ФМБА России (протокол № 2 от 01 марта 2021 г.).

✉ **Для корреспонденции:** Александр Евгеньевич Чиков
ул. Заводская, зд. 6/2, кorp. 93, гп. Кузьмолловский, 188663, Россия; chikov.alexandr@yandex.ru

Статья получена: 21.08.2023 **Статья принята к печати:** 17.09.2023 **Опубликована онлайн:** 30.09.2023

DOI: 10.47183/mes.2023.037

Regular muscle work of considerable volume and intensity is ensured by the coordinated activity of various physiological mechanisms reflecting the systemic nature of the response to exertion [1–3]. In this context physiological mechanisms and appropriate responses mean the set of interrelated components and their responses to the standardized incremental exercise to failure. Each physiological mechanism has a common architecture and is distinguished by the characteristics of its components, to which, in our opinion, it is appropriate to attribute the sources of energy supply (aerobic, lactic and alactic ATP resynthesis pathways) and the factors of their realization characterizing the dynamic and processual aspects of energy supply (performance, capacity, rate of deployment and switching between various ATP resynthesis pathways). These physiological mechanisms provide the leading functional system (LFS) that is responsible for the goal-directed activity realization at the whole-body level [4, 5]. Performing the activity requires an adequate (depending on the exercise characteristics) level of body's physiological reserves. Energy generation is ensured by the coordinated activity of the cardiovascular, respiratory, muscular, nervous, hemic systems, etc. [6]. The required physical performance intensity can be ensured by the adequate energy generation level only [7, 8]. Definition of a set of individual and typological patterns of the physiological mechanisms' activity answers a number of questions related to improvement of the athlete's potential realization efficiency, definition of the limiting components and body's reserve capacity, training load management aimed at ensuring health preservation and professional longevity [9–11]. Due to complex organization of physiological patterns associated with muscle work, assessing such patterns using mathematical modeling and machine learning algorithms seems to be promising [12–15]. For example, there are a number of successful solutions for prediction of lactate threshold in amateur runners using recurrent neural networks [12, 16].

It should be noted that the functional system development involving cortical influences begins even before the start of intense physical exertion (competitions or exercise testing to failure) (pre-start state). We believe that the correlation of pre-start state with physiological response to physical exertion is important, since it will make it possible to predict in advance the responses of body's systems.

The study was aimed to assess the relationship between the responses of physiological mechanisms associated with standardized physical exertion and the athlete's pre-start state.

METHODS

The study involved athletes aged 24.7 ± 4.0 , who specialized in complex-coordination and cyclic sports and were first-class sportsmen or candidates for master of sport. The athletes were tested in the preparatory period of the annual training cycle. Assessment results of 1495 athletes were used to build the

models. The subjects were through standardized exercise testing in the form of the treadmill incremental exercise. The exercise testing protocol was as follows: first stage — 5 km/h, stage duration — 2 min, speed increment at each stage — 1.5 km/h. The following primary parameters were recorded within 3 min before testing (pre-start state), during testing and during the recovery period (15 min) using the Oxycon Pro ergospirometry system (Erich Jaeger; Germany): heart rate (HR, bpm), minute ventilation (VE, L/min), oxygen uptake (VO_2 , L/min) and carbon dioxide production (VCO_2 , L/min), respiratory exchange ratio (RER), oxygen pulse (O_2HR , mL/beat), respiratory oxygen equivalent (EqO_2) and carbon dioxide equivalent (EqCO_2). The criterion for stopping was the athlete's failure or reaching a maximum estimated HR (heart rate) calculated according to the following formula:

$$\text{HR}_{\max} = 220 - \text{age}.$$

Failure when doing exercises was reported in 1358 athletes, 137 athletes were stopped after reaching the maximum HR.

When assessing physiological responses, parameters in the following phases of exercise testing were taken into account:

- 1) pre-start state;
- 2) aerobic threshold;
- 3) anaerobic threshold;
- 4) rapid recovery phase.

Phases two, three, and four were set using the AT_Inter tool [16] using a recommender system to determine the aerobic and anaerobic thresholds and the rapid recovery phase by conventional methods and machine learning methods (cluster analysis) [8]. More than 100 indicators characterizing the body's physiological responses to the standardized physical exertion were calculated based on primary parameters.

Data processing was performed using Python 3 and scikit-learn libraries (open-source machine learning libraries). The Maximal Information Coefficient (MIC) was used to estimate nonlinear relationships between the parameters [17]. The indicator's range is 0–1, where 0 corresponds to statistical

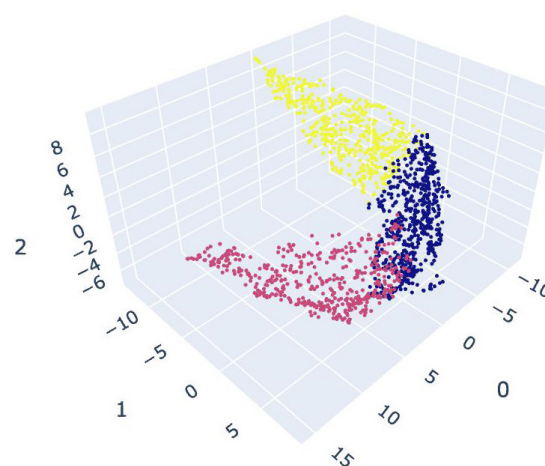


Fig. The "Horsechoe of Rest" model of pre-start state

Table 1. Values of the assessed athletes' pre-start state primary parameters

Parameter	Mean	Error of the mean
HR	86.1	12.9
VE	15.7	3
VO_2	519.1	98.6
VCO_2	417.6	86.3
O_2HR	6.1	1.3
EqO_2	27.1	3.4
EqCO_2	33.6	3.5

Table 2. Correlation between non-metabolic CO₂ and characteristic 2 of the “Horsehoe of Rest” model

Parameter	Coordinate 2
CO ₂ _non_physiol_total	0.29
CO ₂ _non_physiol_L	0.35

independence and 1 corresponds to dependencies between parameters. The critically significant level of the relationship used in the study is 0.2 at $p < 0.05$.

RESULTS

The athlete's body state in the first phase of exercise testing is characterized by changes in the function of body's physiological systems, such as cardiovascular and respiratory systems, resulting from cortical influences associated with the upcoming intense physical exertion (Table 1).

The correlation analysis revealed no significant correlations between the pre-start state primary parameters and the indicators of body's physiological response to the standardized physical exertion ($p > 0.05$). That is why we decided to use the dimensionality reduction t-SNE algorithm for reduction to three-dimensional map in order to build a “Horsehoe of Rest” model characterizing the pre-start state (Figure). The t-SNE algorithm (t-distributed Stochastic Neighbor Embedding) is a nonlinear dimension reduction technique [18, 19]. The main idea of the method is the search for the multidimensional feature space projection onto a plane, from n-dimensional space to three-dimensional, i.e. the search is performed for new data representation, with which the neighborhood observations are preserved [20]. Primary parameters of the pre-start state were input to the described algorithm. The new synthetic characteristics 0, 1 and 2, which accumulated information from original characteristics but had no clear interpretation, were the output. Each point of the “Horsehoe of Rest” model corresponded to one observation having characteristics 0, 1 and 2 (Figure). All observations formed a horseshoe indicating that there was a pattern inherent to the athletes' pre-start state.

The MIC value was calculated to evaluate the non-linear relationship between the parameters obtained during the major phases of testing and the interpretation of new synthetic characteristics 0, 1 and 2. The findings showed that coordinates 0 and 1 showed no significant correlations (the maximum correlation values did not reach the critically significant level, MIC = 0.2) with the exercise testing results. The characteristic 2 showed a significant correlation with the non-metabolic carbon dioxide emission: 1) over the period of testing (CO₂_non_physiol_total); 2) over the period of exertion (CO₂_non_physiol_L). MIC was 0.29 and 0.35, respectively (Table 2). Non-metabolic CO₂ was calculated for the period of exertion and the recovery period as the amount of carbon dioxide emitted that exceeded the level at RER 0 > 1.

DISCUSSION

The non-metabolic CO₂ associated with intense physical exertion is generated due to activity of anaerobic lactic mechanism and neutralization of its metabolites by buffer systems, specifically by plasma bicarbonate. Thus, the pre-start state parameters allow one to judge the activity of this mechanism and the systems maintaining homeostasis via CO₂ removal from the lungs, neutralization of increased acidity by buffer systems of blood, primarily by bicarbonate and hemoglobin systems, involving carbonic anhydrase [21]. CO₂ removal also depends on individual perfusion characteristics of the lung alveoli [22, 23].

The literature provides very little data on the role and significance of CO₂ emission for assessment of physical performance [24]. The majority of researchers pay attention to the maximum oxygen uptake and uptake at the aerobic threshold level when evaluating physical performance. However, the athlete's body capacity depends not only on the consumed amount of O₂ as an equivalent of energy production, but also on the parameters limiting physical performance, specifically on CO₂ emission as an integral indicator of the anaerobic mechanism activity [25]. It is well-known that the increase in CO₂ levels and the decrease in pH to the known values resulting from the anaerobic lactate mechanism activity stimulate the LFS, and the values moving out of the optimal range inhibit the system due to inhibition of the enzyme systems' activity, reduced nerve impulse transmission speed, muscle contractility, etc. [26–28].

CONCLUSIONS

The relationship between the new synthetic characteristic 2 and the values of non-metabolic carbon dioxide emission associated with the standardized physical exertion has been revealed based on the “Horsehoe of Rest” model developed. The non-metabolic CO₂ value is an integrated parameter of the anaerobic lactate mechanism activity and the mechanisms underlying utilization of its metabolites having a significant impact on the LFS [27]. In subsequent papers we are going to show the value of non-metabolic CO₂ for the duration of doing incremental exercises to failure and introduce the study results into the already constructed model [16] in order to determine individual and typological patterns of the physiological mechanisms' activity associated with the standardized physical exertion.

References

- Ozhgibesova MA, Ganeeva ER, Kurilyak MM. Key mechanisms of muscle growth. Scientific Journal Scientific Review. Pedagogical sciences. 2019; 4: 31–4. Russian.
- Piuccoa T, Diefenthaeler F, Prossera A, Binic R. Validity of different EMG analysis methods to identify aerobic and anaerobic thresholds in speed skaters. Journal of Electromyography and Kinesiology. 2020; 52.
- Zignoli A, Fornasiero A, Stella F, Pellegrini B, Schena F, Biral F, et al. Expert-level classification of ventilatory thresholds from cardiopulmonary exercising test data with recurrent neural networks. European Journal of Sport Science. 2019; 19 (9): 1221–9.
- Anokhin PK. Printsipial'nye voprosy obshchey teorii funktsional'nykh sistem. Printsipy sistemnoy organizatsii funktsiy. M.: Nauka; 1973. 120 s. Russian.
- Bykov EV, Balberova OV, Kolomiets OI, Chipyshev AVCh. Correlation of functional testing data and results of competitive activities of athletes with different directions of physical activity. Scientific notes of the University. P.F. Lesgaft. 2018; 8: 32–8.

- Russian.
6. Ham J-H, Park H-Y, Kim Y-H, Bae S-K, Ko B-H, Nam S-S. Development of an anaerobic threshold (HRLT, HRVT) estimation equation using the heart rate threshold (HRT) during the treadmill incremental exercise. *J Exerc Nutrition Biochem*. 2017; 21 (3): 43–9.
 7. Kiselev AD. Modeling of elements of sports activities for the assessment and development of special performance. *Physical education and sports training*. 2021; 35: 72–80. Russian.
 8. Wasserman K, Hansen JE, Sue DY, Stringer W, Sietsema K, X-G Sun, et al. *Principles of Exercise Testing and Interpretation*. 3rd ed. Lipincott Williams & Wilkins, 1999; p. 551.
 9. Korzeniewski B. Regulation of ATP supply in mammalian skeletal muscle during resting state intensive work transition. *Biophysical Chemistry*. 2000; 83 (1): 19–34.
 10. Sales MM, Sousa CV, Alves PM. Response to "A comprehensive integrative perspective of the anaerobic threshold engine": the driver is not a part of an engine. *Physiology & Behavior*. 2019; 15.
 11. Giovanelli N, Scaini S, Billat V, Lazzer S. A new field test to estimate the aerobic and anaerobic thresholds and maximum parameters. *European Journal of Sport Science*. 2020; 20 (4): 437–43.
 12. Etxegaraia U, Portillo E, Irazusta J, Arriandiaga A, Cabanes I, et al. Estimation of lactate threshold with machine learning techniques in recreational runners. *Applied Soft Computing*. 2018; 63: 181–96.
 13. Moxnes JF, Sandbakk Ø. Mathematical modelling of the oxygen uptake kinetics during whole-body endurance exercise and recovery. *Mathematical and Computer Modelling of Dynamical Systems*. 2018; 24 (1): 76–86.
 14. Morton RH, Billat V. Modelling decremental ramps using 2- and 3-parameter "critical power" models. *Journal of Sports Sciences*. 2013; 31 (7): 731–5.
 15. Lin C-W, Huang C-F, Wang J, Fu L-L, Mao T-Y. Detection of ventilatory thresholds using near-infrared spectroscopy with a polynomial regression model. *Saudi Journal of Biological Sciences*. 2020; 27 (6): 1637–42.
 16. Chikov A, Egorov N, Medvedev D, Chikova S, Pavlov E, Drobintsev P, et al. Determination of the athletes' anaerobic threshold using machine learning methods. *Biomedical Signal Processing and Control*. 2022; 73: 47–53.
 17. Reshef DN, Reshef YA, Finucane HK, Grossman SR, McVean G, Turnbaugh PJ, et al. Detecting novel associations in large data sets. *Science*. 2011; 334 (6062): 1518–24.
 18. Van der Maaten L, Hinton G. Visualizing data using t-SNE. *Journal of machine learning research*. 2008; 9: 11.
 19. James G, Witten D, Hastie T, Tibshirani R. *An Introduction to Statistical Learning: with Applications in R / 1nd ed*. Statistical Theory and Related Fields. 2021; 6 (1): 440.
 20. McInnes L, Healy J, Melville J. Uniform manifold approximation and projection for dimension reduction. 2018 Feb. Available from: <https://arxiv.org/abs/1802.03426>.
 21. Occhipinti R, Boron WF. Role of carbonic anhydrases and inhibitors in acid-base physiology: insights from mathematical modeling. *International Journal of Molecular Sciences*. 2019; 20 (15): 38–41.
 22. Naumenko ZhK, Chernyak AV, Neklyudova GV, Chuchalin AG. Ventilation-perfusion ratio. *Journal of Practical Pulmonology*. 2018; 4: 86–90. Russian.
 23. Ovsyannikov RYu, Lebedinsky KM. Choice of ultimate expiratory pressure with mechanical respiratory support (review). *General resuscitation*. 2022; 18 (6): 50–8. Russian.
 24. Chesnokova NP, Ponukalina EV, Morrison VV, Bizenkova MN. Lecture 4. Physiology of blood gas transport and tissue oxygen supply. *Scientific review. Medical sciences*. 2017; 2: 40–2. Russian.
 25. Torevsky VI, Litvak AL. The relationship between O₂ consumption and blood supply of contracting muscles when working at different capacities in aerobic endurance trainees. *Theory and practice of physical culture*. 2006; 4: 49–54. Russian.
 26. Anaev EKh. Lactat and lungs: from theory to practice. *Pulmonology*. 2014; 6: 108–14. Russian.
 27. Mikhaylov SS. *Biokhimiya dvigatel'noy deyatel'nosti*. M.: Sport, 2016; 296 s. Russian.
 28. Lazareva EA. Bioenergetic performance criteria for athletes specializing in various distances of athletics running. *Features of the formation of a healthy lifestyle: factors and conditions*. 2015; 179–82. Russian.

Литература

1. Ожгибесова М. А., Ганеева Е. Р., Куриляк М. М. Ключевые механизмы мышечного роста. *Научное обозрение. Педагогические науки*. 2019; 4: 31–4.
2. Piuccoa T, Diefenthaler F, Prossera A, Binic R. Validity of different EMG analysis methods to identify aerobic and anaerobic thresholds in speed skaters. *Journal of Electromyography and Kinesiology*. 2020; 52.
3. Zignoli A, Fornasiero A, Stella F, Pellegrini B, Schena F, Biral F, et al. Expert-level classification of ventilatory thresholds from cardiopulmonary exercising test data with recurrent neural networks. *European Journal of Sport Science*. 2019; 19 (9): 1221–9.
4. Анохин П. К. Принципиальные вопросы общей теории функциональных систем. *Принципы системной организации функций*. М.: Наука, 1973; 120 с.
5. Быков Е. В., Балберова О. В., Коломиец О. И., Чипышев А. В. Ч. Взаимосвязь данных функционального тестирования и результатов соревновательной деятельности спортсменов с различной направленностью физических нагрузок. *Ученые записки университета им. П. Ф. Лесгафта*. 2018; 8: 32–8.
6. Ham J-H, Park H-Y, Kim Y-H, Bae S-K, Ko B-H, Nam S-S. Development of an anaerobic threshold (HRLT, HRVT) estimation equation using the heart rate threshold (HRT) during the treadmill incremental exercise. *J Exerc Nutrition Biochem*. 2017; 21 (3): 43–9.
7. Киселев А. Д. Моделирование элементов спортивной деятельности для оценки и развития специальной работоспособности. *Физическое воспитание и спортивная тренировка*. 2021; 35: 72–80.
8. Wasserman K, Hansen JE, Sue DY, Stringer W, Sietsema K, X-G Sun, et al. *Principles of Exercise Testing and Interpretation*. 3rd ed. Lipincott Williams & Wilkins, 1999; p. 551.
9. Korzeniewski B. Regulation of ATP supply in mammalian skeletal muscle during resting state intensive work transition. *Biophysical Chemistry*. 2000; 83 (1): 19–34.
10. Sales MM, Sousa CV, Alves PM. Response to "A comprehensive integrative perspective of the anaerobic threshold engine": the driver is not a part of an engine. *Physiology & Behavior*. 2019; 15.
11. Giovanelli N, Scaini S, Billat V, Lazzer S. A new field test to estimate the aerobic and anaerobic thresholds and maximum parameters. *European Journal of Sport Science*. 2020; 20 (4): 437–43.
12. Etxegaraia U, Portillo E, Irazusta J, Arriandiaga A, Cabanes I, et al. Estimation of lactate threshold with machine learning techniques in recreational runners. *Applied Soft Computing*. 2018; 63: 181–96.
13. Moxnes JF, Sandbakk Ø. Mathematical modelling of the oxygen uptake kinetics during whole-body endurance exercise and recovery. *Mathematical and Computer Modelling of Dynamical Systems*. 2018; 24 (1): 76–86.
14. Morton RH, Billat V. Modelling decremental ramps using 2- and 3-parameter "critical power" models. *Journal of Sports Sciences*. 2013; 31 (7): 731–5.
15. Lin C-W, Huang C-F, Wang J, Fu L-L, Mao T-Y. Detection of ventilatory thresholds using near-infrared spectroscopy with a polynomial regression model. *Saudi Journal of Biological Sciences*. 2020; 27 (6): 1637–42.
16. Chikov A, Egorov N, Medvedev D, Chikova S, Pavlov E, Drobintsev P, et al. Determination of the athletes' anaerobic threshold using machine learning methods. *Biomedical Signal Processing and Control*. 2022; 73: 47–53.
17. Reshef DN, Reshef YA, Finucane HK, Grossman SR, McVean G, Turnbaugh PJ, et al. Detecting novel associations in large data

- sets. *Science*. 2011; 334 (6062): 1518–24.
18. Van der Maaten L, Hinton G. Visualizing data using t-SNE. *Journal of machine learning research*. 2008; 9: 11.
 19. James G, Witten D, Hastie T, Tibshirani R. *An Introduction to Statistical Learning: with Applications in R / 1st ed.* Statistical Theory and Related Fields. 2021; 6 (1): 440.
 20. McInnes L, Healy J, Melville J. Uniform manifold approximation and projection for dimension reduction. 2018 Feb. Available from: <https://arxiv.org/abs/1802.03426>.
 21. Occhipinti R, Boron WF. Role of carbonic anhydrases and inhibitors in acid-base physiology: insights from mathematical modeling. *International Journal of Molecular Sciences*. 2019; 20 (15): 38–41.
 22. Науменко Ж. К., Черняк А. В., Неклюдова Г. В., Чучалин А. Г. Вентиляционно-перфузионное отношение. *Практическая пульмонология*. 2018; 4: 86–90.
 23. Овсянников Р. Ю., Лебединский К. М. Выбор конечно-экспираторного давления при механической респираторной поддержке (обзор). *Общая реаниматология*. 2022; 18 (6): 50–8.
 24. Чеснокова Н. П., Понукалина Е. В., Моррисон В. В., Бизенкова М. Н. Лекция 4. Физиология транспорта газов кровью и кислородного обеспечения тканей. *Научное обозрение. Медицинские науки*. 2017; 2: 40–2.
 25. Тхоревский В. И., Литвак А. Л. Взаимосвязь между потреблением O₂ и кровоснабжением сокращающихся мышц при работе разной мощности у лиц, тренирующих аэробную выносливость. *Теория и практика физической культуры*. 2006; 4: 49–54.
 26. Анаев Э. Х. Лактат и легкие: от теории к практике. *Пульмонология*. 2014; 6: 108–14.
 27. Михайлов С. С. *Биохимия двигательной деятельности*. М.: Спорт, 2016; 296 с.
 28. Лазарева Э. А. Биоэнергетические критерии работоспособности спортсменов, специализирующихся на различных дистанциях легкоатлетического бега. Особенности формирования здорового образа жизни: факторы и условия. 2015; 179–82.