USING BAROREFLECTIVE REGULATION OF BLOOD PRESSURE FOR THE CARDIOVASCULAR SYSTEM

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Abstract. In this article given about using baroreflective regulation of blood pressure for the cardiovascular system of mathematical model A. S. Karavaev and other scientists . ome of the medical parameters in the proposed model are used and projected. Baroreflector arc is a complex system consisting of several links and is used in this model.

Key words: baroreflective regulation of blood, cardiovascular system, mathematical modeling, self-regulation, effect on the upper and working heart, medical parameters.

Аннотация. В данной статье приведено об использовании барорефлекторной регуляции артериального давления для сердечно-сосудистой системы математического моделирования А. С. Караваев и других учённых. Некоторые медицинские параметры в предлагаемой модели используются и прогнозируются. В данной модели используется барорефлекторная дуга, представляющая собой сложную систему, состоящую из нескольких звенов.

Ключевые слова: барорефлекторная регуляция крови, сердечно-сосудистая система, математическое моделирование, саморегуляция, воздействие на верхнее и работающее сердце, медицинские параметры.

Annotatsiya. Ushbu maqolada matematik model sifatida A. S. Karavaev va boshqa olimlarning yurak-qon tomir tizimi uchun qon bosimining barorefleks regulyatsiyasidan foydalanish tasvirlangan. Taklif etilayotgan modeldagi ba'zi tibbiy ko'rsatkichlar qo'llaniladi va bashorat qilinadi. Ushbu modelda bir nechta bo'g'inlardan iborat murakkab tizim bo'lgan barorefleks yoyi qo'llaniladi.

Kalit so'zlar: qonning barorefleks regulyatsiyasi, yurak-qon tomir tizimi, matematik modellashtirish, o'z-o'zini tartibga solish, yurakning yuqori va ish qismiga ta'siri, tibbiy ko'rsatkichlar.

Introduction. Currently, several models are used in the modeling of hemodynamics, differing in the degree of detail of the description of the system. The simplest (and characterized by a "rough" approximation of a real three-dimensional cardiovascular system model) are models with concentrated parameters (or "zero-dimensional" (0D) models).

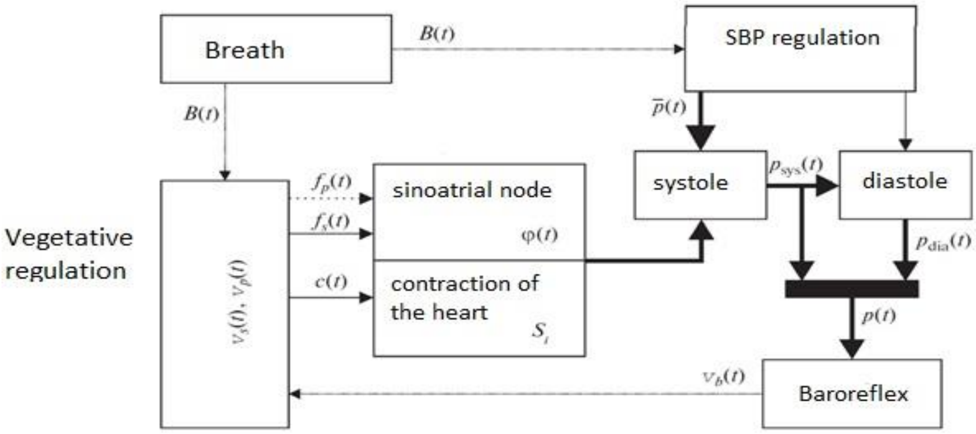
Their main feature is the comparison of the circulatory system of electrical circuits. With this approach, the analogs of pressure and volumetric blood flow are voltage and electric current, and the analogs of vessels are the resistances of individual segments of the electrical circuit. This leads to large computational costs, so multidimensional models are not used in practice for a global description of the arterial system, but are used only for a detailed description of blood flow in local areas of interest to the researcher. One of the important tasks is the modeling of the cardiovascular system (CVS) of a person. In particular, the system of baroreflective regulation of arterial pressure (BRAP) in all these works is modeled by a linear differential equation of the first order with a delay. Such models of blood pressure regulation (BP) are not able to demonstrate stable self-oscillations. In them, only modes of forced self-oscillations are possible under the influence of noise and due to the influence of other elements of the system acting on them [5].

The cardiovascular system of vertebrates responds to hyperopia with vasoconstriction, hypertension, bradycardia, and a decrease in cardiac output. These physiological processes have been known for a long time and are considered in the literature as adaptive reactions independent of each other aimed at limiting the intake of excess (toxic) oxygen into the body by reducing blood circulation. We assume that the vasoconstriction observed in hyperopia, an increase in blood pressure, a slowdown in heart rate, and a decrease in cardiac output are connected in a single mechanism of activation of arterial baroreflex.

Baroreflex plays an important role in the regulation of blood pressure (BP). The baroreflector arc is a complex system consisting of several links. The defeat of one of its elements can lead to violations of baroreflective regulation. The cause may be both congenital conditions (Groll - Hirschowitz syndrome) and acquired organic changes. Violations of baroreflective regulation are often found in patients suffering from arterial hypertension for a long time, who have suffered a myocardial infarction, have signs of atherosclerosis and symptoms of heart failure. In this article, we will use the following medical terms in a mathematical model: baroreflective regulation of blood pressure, self-oscillations under the influence of noise, autonomic regulation, systole, diastole, regulation of systolic blood pressure, self-oscillatory nature of the system, resistance of peripheral vessels.

Methods and models. Authors A. S. Karavaev, Yu. M. Ishbulatov, A. R. Kiselev, V. I. Ponomarenko, M. D. Prokhorov, S. A. Mironov, V. A. Shvarts, V. I. Gridnev, P. Bezruchko in the journal “Human Physiology” in the article “Model of the human cardiovascular system with an autonomous circuit for regulating mean arterial pressure” 2017, vol. 43, no. 1, p. 70–80 studied nonlinearities and the introduction of an autonomous mean arterial pressure regulation circuit in the form of a self-oscillating system with delay makes it possible to qualitatively and quantitatively approximate the statistical and spectral properties of the model signals to the properties of experimental data. The proposed model also makes it possible to reproduce the experimentally observed effect of synchronization by forced breathing of the mean arterial pressure regulation circuit, which has its own oscillation period of about 10 s. This paper presents in vivo and in vitro experimental data, reproduces several observations of plaque growth in mice, and uses in vivo and in vitro experimental data.

Authors A. S. Karavaev, Yu. M. Ishbulatov, A. R. Kiselev, V. I. Ponomarenko, M. D. Prokhorov, S. A. Mironov, V. A. Shvarts, V. I. Gridnev, P. Bezruchko suggests the very beginning of the work of the scientist J.V. Ringwood and S.C. Malpas [15], based on the results of in vitro studies on animals, proposed an autonomous mathematical model of the system of baroreflex regulation of blood pressure in mammals in the form of a first-order nonlinear differential equation with retarded feedback.



Pic. 1. Block diagram of the proposed model. The influence of the vagus is marked by a dotted line, sympathetic activity by a solid line, BP by a thick line, and other influences by a dotted line.

Experimental data, as well as implementations of the well-known model proposed by *K. Kotani* et al. [4], which differs in the most detailed consideration of the features of the dynamics of CVS regulation systems. The proposed dynamic model includes four first-order differential equations, some of which have a delay model of the autonomic regulation of the cardiovascular system.

In the work, a model of the human cardiovascular system was proposed. Its capabilities and limits of applicability were compared with the results of the analysis of experimental signals and temporal implementations of the model proposed earlier in the work of *K. Kotani* et al. [four]. At the same time, two sets of parameters were used for their model. The first was proposed in the original paper [4]. Model parameters K. *Kotani* et al. [4], modified from the original work.

The second set was proposed by A. S. Karavaev, Yu. M. Ishbulatov, A. R. Kiselev, V. I. Ponomarenko, M. D. Prokhorov, S. A. Mironov, V. A. Shvarts, V. I. Gridnev, B.P. Bezruchko to better match the model with experimental data, and he also used the following table for this model.

Table 1.

Parameters of the proposed model used in the model proposed by Karavaev et al.

$_0$	0.55 c	ε	2.0	k	0.02 1/мм рт. ст.	k_{φ}^{c}	1.6

	35 мм рт. ст.	τ	3. 6 с	k_1	0. 00125 с/мм рт. ст.	$\acute{c}$	2. 0
$_c$	3	k_m^r	2. 5	p_0	50 мм рт. ст	n_c	2. 0
k_S^c	40 мм рт. ст.	f_r	0. 29 1/с	V_S^0	0. 8	k_φ^p	5. 8
k_S^t	10 1/мм рт. ст.	G	1. 65	k_S^b	0. 7	Θ $_p$	0. 5 с
$_{sys}$	0.125 с	r^*	2	k_S^r	0. 025	$\tilde{V}_p$	2. 5
k_p^M	3 мм рт. ст.	α	1	V_p^0	0. 0	n_c, n_p	2. 0
$0C$	1.5 с	β	2	k_p^b	0. 3	τ_c	2. 0
k_v^M	0.015	x^*	0. 5	k_p^r	0. 025	k_c^S	1. 2
$_c$	3.24 с	y^*	0	st $d\xi(t)$	0. 1	Θ $_c$	1. 65 с

Note: T_0 is the contraction period of the denervated heart; n_c - determines the concentration of norepinephrine, the excess of which does not lead to a further increase in the intensity of heart contractions; T_{sys} is the duration of the systolic phase of cardiac contraction; R_0 is the resistance of peripheral vessels at rest; C - elasticity of the aorta; τ_c is the efferent delay in the circuit of peripheral vascular tone regulation; ε – inertial properties of vessels; τ is the total delay in the peripheral vascular tone regulation circuit; *fr* is the respiratory rate; G is the gain of the central nervous system; p_0 is the minimum pressure to which baroreceptors respond; V_S^0– the activity of the sympathetic system at rest; V_p^0 – activity of the parasympathetic system at rest; stdξ(t) – standard deviation of 1/f noise ξ(t); Θ_p is the time delay caused by the finiteness of the rate of change in the concentration of acetylcholine; n_s, n_p - determine the concentrations of norepinephrine and acetylcholine, the excess of which does not lead to a further increase in sympathetic and parasympathetic factors; τ_c – is the characteristic relaxation time of norepinephrine concentration; Θ_c is the time delay caused by the time of development of the heart's response to changes in the concentration of norepinephrine in the muscle wall.

Analysing results of model possibilities. Michael G. Watson, Helen M. Byrne, Charlie Macaskill & Mary R. Myerscough in “Journal of Mathematical Biology volume 81, pages 725–767(2020)” in their article “A multiphase model of growth factor-regulated atherosclerotic cap formation” studied atherosclerosis, which is characterized by the growth of fatty plaques on the inner wall of the artery. In mature plaques, vascular smooth muscle cells (SMC) are recruited from adjacent tissues to deposit a collagen cap over the core of the fatty plaque.

They developed a multi-phase PDE model with non-standard boundary conditions to study the formation of the SMC collagen cap in response to diffusible growth factor signals from the endothelium. The model, parameterized using in vivo and in vitro experimental data, reproduces several observations of plaque growth in mice.

Authors Diego Sadler, Jeanne M. DeCara, Cardio-Oncology International Collaborative Network in “Cardio-Oncology volume 6, Article number: 28 (2020)” in their article “Perspectives on the COVID-19 pandemic impact on cardio-oncology: results from the COVID-19 International Collaborative Network survey” studied the participation of one thousand four hundred and fifteen providers (43 countries): 986 cardiologists, 306 oncologists and 118 trainees / therapists. 63% (195/306) of oncologists vs. 92% (896/976) of cardiologists reported treatment/elective procedures being discontinued (p = 0.01). 46% (442/970) of cardiologists and 25% (76/303) of oncologists changed the scope of their practice (p = <0.001). Academic physicians (74.5%) felt better provided with personal protective equipment (PPE) compared to non-academic physicians (74.5% vs 67.2%; p = 0.018). Telemedicine was less common in Europe at 81% (74/91) and Latin America at 64% (101/158) than in the US at 88% (950/1097) (p = <0.001). 95% of all groups supported more active leadership from the medical professional communities.

Authors Javid J. Moslehi, Ronald M. Witteles in the Journal of the American College of Cardiology, Volume 77, Issue 4, 2 February 2021, Pages 402-404 studied patients with the risk of cancer therapy-associated cardiac dysfunction (CTRCD), initiation of cardio protective therapy (CPT) is constrained by the low sensitivity of ejection fraction (EF) to minor changes in left ventricular (LV) function. Global longitudinal strain (GLS) is a reliable and sensitive marker of LV dysfunction, but available observational data were insufficient to support a standard GLS-based CPT strategy.

Authors Ikue Tai-Nagara, Yukiko Hasumi, Dai Kusumoto, Hisashi Hasumi, Keisuke Okabe, Tomofumi Ando, Fumio Matsuzaki, Fumiko Itoh, Hideyuki Saya, Chang Liu, Wenling Li, Yoh-Suke Mukouyama, W. Marston Linehan, Xinyi Liu, Masanori Hirashima, Yutaka Suzuki, Shintaro Funasaki, Yorifumi Satou, Mitsuko Furuya, Masaya Baba & Yoshiaki Kubota in “Nature Communications volume 11, Article number: 6314 (2020)” in their paper “Blood and lymphatic systems are segregated by the FLCN tumor suppressor “Studied blood and lymphatic vessels are structurally very similar, but never share a common lumen, thus retaining their distinct functions. Although lymphatic vessels originally arise from embryonic veins, the molecular mechanism that maintains the separation of these two systems has not been elucidated. Here, the authors show that a genetic deficiency in folliculin, a tumor suppressor, leads to misconnection of blood and lymph vessels in mice and humans. The absence of folliculin results in lymphatic venous endothelial cells caused by ectopic expression of Prox1, the main transcription factor for lymphatic specification.

The authors in the journal Niccolò Dal Santo & Andrea Manzoni "Advances in ComputationalMathematics volume 45, pages2463–2501(2019)" in their article "Hyper-reduced order models for parameterized unsteady Navier-Stokes equations on domains with variable shape" studied a new general and efficient from a computational point of view, a way to solve parametrized fluid flows modeled with non-stationary Navier-Stokes equations defined in regions with a variable shape, when using the reduced basis method, flexible boundary parameterization, and generate deformations of the region (and mesh) using a rigid expansion obtained by solutions of harmonic expansion or problems of linear elasticity theory.

The discussion of the results. Creation of mathematical models of systems of biological nature, claiming their qualitative and quantitative description, is an important step in the study of living systems. The presence of such models can provide important fundamental information about the structure of the systems under study and the features of the interaction of their elements, makes it possible to study the behavior of systems over time and when changing control parameters, and predict the effect of physiological samples and medications on the system.

Conclusion. A model of the human cardiovascular system was proposed in the work. Its capabilities and limits of applicability were compared with the results of the analysis of experimental signals and temporal implementations of the model with the help of which was proposed by Karavaev et al. A brief theoretical review of the model and comparison with other scientists is made. The following conclusions can then be drawn.

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