Dual-contoured model of cardiovascular system regulation

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Abstract. The purpose of the study is to create a model of the cardiovascular system that gives an adequate description of the processes of hemodynamic regulation for the needs of intensive care. An overview of the most recent significant blood circulation models that take the regulation processes into account is proposed, the peculiarities and limitations of such models are identified. The methods of computational hemodynamics and mathematical modeling are used. A zero-dimensional dynamic mathematical model of cardiovascular system with two regulatory contours suggested by its authors is described. The results of the study are of interest to intensive care doctors in selecting a treatment strategy.

1. Introduction
Cardiovascular diseases are the diseases of heart and blood vessels, which are one of the leading causes of mortality worldwide. This determines the relevance of using the latest technologies in the diagnostics and treatment of cardiovascular diseases.

The modern trend of medical diagnostics is the application of mathematical methods to analyze the patient's condition and support the decision system. Such an approach became feasible due to the development of the mathematical cardiology – scientific discipline at the boundary between cardiology, medicine and mathematics. Through the simulation modeling technique capabilities of mathematical cardiology have enabled to identify the major reasons of cardiovascular diseases [1]. Today, the medical community has become aware that the usage of mathematical modelling of blood circulation processes in order to predict the treatment results of cardiovascular deceases and to help in making medical decisions is a priority area in the diagnosis [2-4].

There are enough articles in which the human blood circulation models are structured and systematized. The study [5] describes a model with lumped Windkessel parameters, which is the basis for a whole family of zero-dimensional models. Despite the simplicity of such models, they are often used in clinical practice to evaluate various hemodynamic parameters [6]. In studies [7, 8], it is noted that zero-dimensional models, due to lower computational expenditure, will allow to simulate the arterial system completely, which is very important for the study of hemodynamics of blood circulation.

Many models of blood circulation describing the heart and vessels without regulation have been worked out in detail. For instance, the Department of Biomedical Engineering at Tambov State Technical University offers a detailed 16-chamber model of the cardiovascular system with a pulsating heart, consisting of four elastic chambers that are connected in series: left and right heart, systemic and pulmonary circulation. The model is focused on intensive care units [9].

However, in [1] it was shown that the use of only blood circulation models without taking regulation into account is insufficient to support medical decision-making. Attempts are being made to create multi-scale models [10]. According to the results of studies [11, 12], the development trend of
mathematical modeling in the field of medicine and visualization will significantly improve the quality of prediction of therapeutic effects. According to recent research, real-time control of the regulation of heart and blood vessels will allow to ensure the treatment of the cardiovascular system diseases without external invasive effects, taking into account the individual characteristics of the patient [1].

The experience acquired in the analysis of patients with acute circulatory disorders helped to establish the importance of the processes of regulation, reflex and humoral regulation, central management and organization of autonomous functional systems in the pathogenesis of acute circulatory disorders [1]. It becomes evident that the regulatory reactions of the organism arising in response to pathology and therapeutic measures should be taken into account while choosing the therapeutic effect [1].

When examining and normalizing the processes of regulation, it should be considered that they can be compensating, stabilizing and protective. These parameters deviate the parameters of the cardiovascular system from the normal pattern, however, they can be useful [1]. This should be reflected in the creation of a blood circulation model in order to select the right strategy of therapeutic modalities.

A team of scientists [13] has developed a model for solving the problems of simulation modeling of the parameters of autonomic regulation of heart rate and mean arterial pressure. Their studies showed that the work of the heart and blood vessels is controlled by various mechanisms that are independent of each other: the heart is regulated through the release of blood and heart contractions, and the vessels through the mechanisms of the nervous system.

The regulatory processes are largely unexplored and are characterized by complex mechanisms of action. Many authors propose various hypotheses for the regulation of the cardiovascular system.

Researchers [14] propose a circulatory model that makes the evaluation of vegetative regulatory mechanisms possible. The model [15] of the human cardiovascular system with a loop of vegetative regulation describes the rhythm of the heart, regulation of the heart and blood vessels function by the vegetative nervous system, baroreflex and the formation of blood pressure. In [16], a regulation model based on an electromechanical analogy is proposed.

Researcher Burkhoff [17] has developed a software simulator of blood circulation, which allows to study the hemodynamic principles of the functioning of the cardiovascular system in details. The developed model predicts the patient's condition under the influence of the effects of hardware and surgical treatment. The work [18] demonstrates the scenario of using the model using the developed simulator to optimize the choice of treatment strategy for acute coronary syndrome.

In the Laboratory of Numerical / Hybrid Modeling of the Cardiovascular System of the Institute of Clinical Physiology (Rome), a software simulator of the human cardiovascular and respiratory system was created [19]. It has a modular structure and describes peripheral, systemic and pulmonary circulation. The lumped parameter model, which is the basis of the software simulator, allows to simulate various states of the circulatory system based on the Starling law and the time-varying elasticity of blood vessels.

One of the most complete and well-developed models is the model of V A Lischuk [1]. In contrast to the classical ideas about the cardiovascular system, in which the model is divided into an uncontrollable part (the object of regulation) and regulation, V A Lischuk developed a multi-linked self-regulation of functional systems of the body, consisting of autonomous subsystems of self-regulation.

The model considers the regulation of three functional circulatory systems – cardiac output, tissue blood flow and blood pressure. The cardiovascular system is presented in the form of four reservoirs: bulbar center, heart, arterial and venous reservoir and generalized capillary tissue system. The disadvantage of the presented regulation model [1] is that it uses a simplified hemodynamic model that describes the static modes of the circulatory process.

To date, many models of the cardiovascular system have been created and described but it is impossible to distinguish a model that fully meets all the requirements of a diagnostician and researcher. Consequently, it is relevant to create a holistic model that adequately describes the patient's circulatory system for the needs of intensive care units. The aim of the study is the creation and software implementation of a model of the cardiovascular system that includes the circuits of blood circulation.
regulation and focuses on the use of intensive care in the wards, fulfilling the requirements: computational speed, individualization and completeness of the considered parameters, simplicity and intuitiveness of the presented results.

2. Materials and research methods
The Department of Biomedical Engineering at Tambov State Technical University has developed a six-chamber zero-dimensional dynamic mathematical model of the cardiovascular system, taking into account the processes of regulation (figure 1), which is based on a model [9]. Methods of computational hemodynamics and mathematical modeling were used while creating the model. In this work, a zero-dimensional model of blood circulation is proposed for the first time, in which a multi-level concept of regulation of the cardiovascular system is implemented.

![Blood circulation model with regulation.](image)

The constructed model contains two levels of regulation – lower and upper (central) levels. For the figure 1 the following designations have been introduced: PC – blood vessels of the pulmonary circulation, RH – right heart, LH – left heart, B – venous system, A – arterial system, MLC – microvessels of the large circulation circle, EF – effector elements (elements that transmit a disturbing
signal to organs and tissues), LR – local regulator, \( H_i \) – laws of local regulation, \( k_i \) – regulation coefficient, \( d_{BLH}, d_{LH} \) – ventricular contraction coefficients, \( T \) – period of heart contractions, \( y_i \) – control signals in regulation subsystems, \( y_i^L \) – control signals of central regulation, \( U_B \) – unstressed volume of veins, \( Z \) – central level of regulation. In figure 1, the lower figure describes the central level of regulation, the inputs and outputs of which are connected with the upper figure that describes the lower level of regulation.

At the initial stage, the pressure for all chambers of the system is calculated. Moreover, let us make the calculation of blood flow from the aorta into the right atrium, from the arteries of the head into the capillaries of the head, from the arteries of the body into the capillaries of the body, from the capillaries of the body into the veins of the body, from the capillaries of the head into the veins of the head, from the veins of the head into the right atrium, from the veins of the body into the right atrium, from the pulmonary arteries into the pulmonary veins, from the pulmonary capillaries into the pulmonary veins, from the pulmonary veins into the left atrium.

Blood flows from the aorta to the arteries of the systemic circulation of blood are calculated separately, taking into consideration the inertial properties of blood, as well as flows for the valves are calculated. When there is a pressure difference towards the opening side, the valve opens. Valve closure occurs when a pressure difference is opposite to the normal blood flow. The main regulatory functions adopted in the model are homeostasis of blood pressure, regulation of peripheral blood flow, central venous pressure and pumping properties of the heart.

The contours of peripheral blood flow regulation (index \( \rho \)), arterial (index A) and venous pressure (index B), regulation of left and right heart loads (contours LH, RH, T) were chosen as subsystems (local regulators) of the regulation system. Each subsystem is modeled by an automatic integral regulator, which input can receive a signal about the value of the controlled value \( x_i \) that are the circulatory functions \( q_{A,B}, P_A, P_B, N_{LH}, N_{PH}, N \) in the model (1):

\[
x_i \in \{ x_\rho, x_A, x_B, x_{LH}, x_T \} = \{ q_{A,B}, P_A, P_B, N_{LH}, N_{PH}, N \},
\]

where \( N_{LH} \) and \( N_{PH} \) are the capacities of the left and right heart, \( N \) is the total capacity of the heart.

Blood pressure is controlled at the level of central regulation. Each local controller contains a local regulator (LR) that generates a normalized mismatch signal \( w_i \) (2):

\[
w_i = \frac{x_i(n) - \bar{x_i}}{\bar{x_i}},
\]

where

\[
\bar{x_i} = \frac{1}{T(n)} \int_{t(n-1)}^{t(n)} x_i(t) dt,
\]

Local regulations laws \( H_i \) are stated as (3):

\[
y_i(t) = k_i(t) \int_{t_i}^{t} w_i(t) dt,
\]

where \( k_i \) is the regulation coefficient, \( m_i \) is the characterizing time of the regulator.

Dimensionless \( y_i \) signals affect the control properties of the blood circulation model through effector elements. The parameters that have the strongest impact on the blood circulation are chosen as the regulating ones. For the vascular system, this is the general peripheral conductivity \( \rho_{A,B} \) and the unstressed volume of the veins \( U_B \). As for the heart, effector outputs act on ventricular contraction coefficients \( d_{BLH}, d_{PH} \) and heart rate period \( T \). The period of heart contractions varies according to the change in the total capacity of the whole heart.

The central level of regulation balances the stresses arising in the subsystems of local regulation (figure 1 – Z block – central level of regulation). The \( y_i \) signals are selected as the characteristics of intense in the control subsystems. Information about them is supplied to the regulator at the central level, processed and formed into the control signals \( y_i^L \) of local regulators (4):
where $k^i_h$ – the weights of individual local stresses in the assessment of the average intensity.

This signal is compared to each signal from the periphery and the necessary control signals $y'_c$ are generated, delivered separately to the first level (5):

$$y'_c(n) = \hat{A} k^i \left[ y^i(n) - y_c(n) \right], \; j \epsilon \{ \rho, A, B, LH, PH, T \},$$

where $\hat{A}$ is the coefficient, characterizing the overall activity of the second level of regulation, $k^i_c$ – the central regulation coefficient. The signals $y'_c$ control the amplification coefficient $k_j$ in the first level regulation contours (6):

$$k^j(n) = k^j \left[ y'_c(n) \right] = k^j_c + y'_c(n).$$

The purpose of this control is to achieve the absence of misalignments in the central regulator, i.e. $y'_c = 0$.

### 3. Results and discussion

The model is implemented in the MATLAB Simulink software environment. Let us consider the regularities of the circulatory system, which can be observed by examining the proposed model. At the initial stage of the simulation study, the results of the model in established mode are shown.

Figure 2 shows the dynamics of the volumes of the right ventricle and right atrium. In this regard the correlation between changes in blood volumes is visible due to the fact that blood leaves the right atrium and enters the right ventricle.

![Figure 2. Changes in blood volume: 1 – in the right atrium over time, 2 – in the right ventricle over time.](image)

Figure 3 shows the dynamics of changes in blood volume during the passage of blood from the right ventricle to the pulmonary arteries. The interrelation between changes in volumes is observed.
Figure 3. Changes in blood volume: 1 – in the right ventricle over time, 2 – in the pulmonary artery over time.

Figure 4 shows the dynamics of changes in blood volume during the passage of blood from the pulmonary veins to the left atrium.

Figure 4. Changes in blood volume: 1 – changes in the volume of the left atrium over time, 2 – changes in the volume of the pulmonary veins over time.

Figure 5 shows the dynamics of changes in blood volume during the passage of blood from the left atrium to the left ventricle.

The results shown in figures 2-5 demonstrate the adequacy of the model on the example of the relationship between the parameters of the cardiovascular system model. The dynamics of blood volumes in the ventricles and atria, shown in the graphs, and their correct ratio allow us to trace the work of the model while describing systemic and pulmonary circulation.
To date, many models that take the regulation of blood circulation into account have been created and worked out [9, 13-19]. The results obtained using our model correlate with the results of these researchers, which indicates the adequacy of the model. However, unlike the above-mentioned studies, the developed model is based on the innovative concept of multilevel regulation, consisting of two interconnected contours.

Due to the simplicity of the model and the visibility of the results, the model can be used in intensive care units. This is possible due to the speed in calculating the hemodynamic parameters, which meets the requirements of the speed of the medical decision-making support system. To include regulatory contours in the work, it is necessary to formulate the requirements for setting regulation coefficients, which is the subject of further research.

4. Conclusion

A further development of zero-dimensional models of the cardiovascular system is the inclusion of multi-level regulation in the description of processes, which provides an extension of the possibilities of using mathematical methods in medical decision-making support system in the treatment of cardiac patients. Due to this, it will be possible to predict the state of the circulatory system as a result of therapeutic effects and manipulations without harming the patient.

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