Neurohumoral contour regulation of arterial pressure

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Abstract. The article is devoted to the contour regulation of human arterial blood pressure, as well as other interrelated parameters. A system of algebro-differential equations is proposed for contour modeling. The system of equations has an odd symmetry group which leads to self-regulation and maintaining the contour parameters within a normal values. To calculate the dynamics of the system, original author software was used to solve structural equations. The finite difference scheme of two states was used to bring the equation system to a structural form. As a result, the calculated graphs of the contour parameters dynamics of blood pressure regulation are given. The innovation of the work is in the numerical solution and modeling of the mechanism of blood pressure regulation on the basis of a new approach to solving basic structural equations. Also novelty in the new software is the solver of basic structural equations, including nonlinear or differential equations, tested on this model.

Keywords: blood pressure, structural equations, differential equations

1. Introduction

To feed the tissues and cell structures of human organs it is necessary local oxygen delivery. The capture and delivery of oxygen by hemoglobin proteins is carried out from air vesicle by red blood cells to the human body organs. Muscle contractions of heart for blood pumping in small and large circulation are used for f circular blood flow implementation in human body. At the same time, the blood pressure in the human arterial system experiences jumps in the result of muscular contractions. Neurohumoral feedback factor is used to maintain blood pressure regulation.

The purpose of this work is to build a differential model of the regulation dynamics of human blood pressure and its confirmation as a result of numerical calculation. Since the parameters of such system had an integration factorial form that such equations system is only approximate model for the academic explanation of contour regulation and the mechanism for maintaining blood pressure.

The objectives of this study are as follows:

– to form a differential model of the contour of blood pressure regulation on the basis of theoretical biophysical parameters;

– to bring the differential system of equations to a finite difference structural model of blood pressure regulation contour;

– conduct a numerical calculation of parameters dynamics of equations system and interpret the model adequacy to explain the mechanism for maintaining normal blood pressure.

The theoretical parameters of the arterial pressure regulation circuit were various macro and micro parameters characterizing the human arterial system sections. For the numerical calculation of differential equations model it is proposed to use the original author's mathematical software for solving structural equations. This software has the ability to model the structural equations of two, three and more simultaneous states. When the various states of the system correspond to time intervals but not the objects then the structural models are a finite difference generalization of continuous differential and integral equations.

As a result, it is possible to determine the residuals of structural model equations for each state after estimating the values of hidden variables structural equations corresponding to the parameters of normal blood pressure regulation circuit.

The theory of structural equations is well represented in the theory of simultaneous econometric equations systems [1]. Structural equations can adequately describe the dependencies between the measured and latent variables of the object under study. This method was formed in the 1970s in the works of K. Joreskog, D. Serb [2], O. Duncan [3], G. Blalock [4], A. Goldberger [5] and P. Bentler [6]. A system of interrelated identities and regression equations in which variables can simultaneously act as a resulting in some equations, and as explaining in others, it is commonly called a system of simultaneous (econometric) equations. Identities refer to the functional connection of variables and follow from the pregnant meaning of these variables. The technique for estimating the parameters of econometric equations system has its own characteristics. This is due to the fact that in the regression equations the systems of independent variables and random errors are correlated with each other. The statistical properties and the estimating systems questions of linear equations are well studied.

2. Theory of structural models

The following types of matrices are used in the theory of structural equations:

matrix $\underset{m\times n}{Z} \leftrightarrow z_{ij}$ − matrix of measured variable values for studied objects or states of a dimensional object $m \times n$ where m is the number of measured parameters and n is the number of objects or object states (sample size),

matrix $\underset{g\times n}{P} \leftrightarrow p_{ij}$ − matrix of values of hidden variables dimension objects $g \times n$, where g is the number of hidden parameters,

matrix $\underset{k\times s}{A} \leftrightarrow a_{ij}$ − matrix of parameters of structural dimension equations $k \times s$, where k is number of describing model structural equations and s is the number of parameters in the structural equations.

The system of structural equations is given in the form:

$$\begin{cases} f_1\left(a_{11}, a_{12}, \ldots, a_{1s}; p_{1t}, p_{2t}, \ldots, p_{gt}; z_{1t}, z_{2t}, \ldots, z_{mt}\right) + \varepsilon_{1t} = 0, \\ f_2\left(a_{21}, a_{22}, \ldots, a_{2s}; p_{1t}, p_{2t}, \ldots, p_{gt}; z_{1t}, z_{2t}, \ldots, z_{mt}\right) + \varepsilon_{2t} = 0, \\ \vdots \\ f_k\left(a_{k1}, a_{k2}, \ldots, a_{ks}; p_{1t}, p_{2t}, \ldots, p_{gt}; z_{1t}, z_{2t}, \ldots, z_{mt}\right) + \varepsilon_{kt} = 0. \end{cases}$$

where $f_1, f_2, \ldots, f_k$ − nonlinear functions of their variables, $\varepsilon_{1t}, \varepsilon_{2t}, \ldots, \varepsilon_{kt}$ − in general are the model remnants for the *t*-th object or pressure control stages.

A little change in the distribution of model residues after physiotherapy implies the normalization lack of blood pressure regulation in hypertension without improving the functional relationship of body systems.

Additional conditions in the form of equalities and inequalities can be imposed on the parameters values and hidden variables values. The optimal values of parameters and hidden variables are those values that minimize the absolute values of model residuals and satisfy all additional conditions.

It is assumed that the optimization of the rotation criterion as a function of independent variables of the rotation matrix with constraints is performed by the method of penalty functions [7]. The configuration method was chosen as the method of unconditional optimization of penalty function method [8].

The structural equations of the model can contain simultaneously parameters related to different time States. Thus it is possible to model and solve differential and integral equations. Calculations of this method are carried out with the least error, as it is the result of optimization and minimization of residuals (errors) of equations. The error of the method is minimal, and the method itself is stable, since errors are minimized. As well as other methods of solving equations for the stability of the solution of poorly defined equations may require regularization in the form of the introduction of additional terms in the equation. This method is analogous to the known solvers of Maple, MATLAB, Excel equations. An analogue in particular to the Monte Carlo method in the case of using random search for unconditional minimization of equation errors [1].

3. Theory of arterial pressure regulation

The neurohumoral contour of blood pressure regulation includes primarily the sensory system of baroreceptors covering the arterial system. The processing of information from the sensors is processed by the center carrying out the program to maintain human life. After processing the sensory information, the resulting feedback actions for the muscular activity of the arterial system are taken. Compensating tonus of the capillary system, as well as heartbeats, are performed.

Besides the baroreceptors, one of the factors of the muscular activity of arterial system is the oxygen demand of the tissues and organs. In order to increase the oxygen flow to the tissues, cardiac contractions of the heart are increased for a larger minute blood volume passing through the system of the small and large circles of blood circulation.

If the body is at rest and is not subjected to muscle loads, that the oxygen demand of human muscle tissue decreases and the number of heartbeats per minute decreases too.

Cardiac output is determined, in turn, by heart rate and stroke volume of the heart, i.e. the blood volume discarded by the heart in one contraction.

Changing the frequency of contractions or stroke volume (or both at the same time), the body can increase the blood supply to organs and tissues or reduce it depending on the need.

In order to prepare for great muscular activity in stressful situations, adrenaline is released into the human blood and the back reaction to it in the form of increased cardiac myocardial activity.

The skeletal muscles work, peripheral venous pressure and the chest work during the breathing also increase venous return. The increase of veins and venules resistance during the blood passage reduces venous return and increases the total peripheral resistance of blood vessels which is also determined by the resistance of arteries and arterioles. During the physical work, the decrease in venous return leads to the decrease in cardiac output and circulating blood volume.

After stimuli removal that encourage the activation of sympathetic nervous system, the parasympathetic one reduces the dynamics of the cardiovascular system. It normalizes the frequency and strength of heart contractions and a number of other parameters [9].

4. Structural model of arterial regulation contour

The circulatory system can be in qualitatively different states (phases). There are two main phases: ventricular contraction and blood exile (systole), passive and active ventricular relaxation and filling them with blood (diastole). The mathematical idealization of such object is a dynamic system of differential equations class when the object is described by different systems of equations in different phases.

The model is described by a system of algebro-differential equations which is reduced to two systems of six differential equations for each phase (systole and diastole) [9]:

$$\begin{cases} \dfrac{dx_1^1}{dt} = X_1^1\left(x^1, A\right), \\ \dfrac{dx_2^1}{dt} = X_2^1\left(x^1, A\right), \\ \dfrac{dx_3^1}{dt} = X_3^1\left(x^1, A\right), \\ \dfrac{dx_4^1}{dt} = X_4^1\left(x^1, A\right), \\ \dfrac{dx_5^1}{dt} = X_5^1\left(x^1, A\right), \\ \dfrac{dx_6^1}{dt} = 0. \end{cases} \qquad \begin{cases} \dfrac{dx_1^2}{dt} = X_1^2\left(x^2, A\right), \\ \dfrac{dx_2^2}{dt} = X_2^2\left(x^2, A\right), \\ \dfrac{dx_3^2}{dt} = X_3^2\left(x^2, A\right), \\ \dfrac{dx_4^2}{dt} = X_4^2\left(x^2, A\right), \\ \dfrac{dx_5^2}{dt} = X_5^2\left(x^2, A\right), \\ \dfrac{dx_6^2}{dt} = 0. \end{cases}$$

Where measured variables are: time – t; hidden variables: neurohumoral factor – x_1, oxygen content in venous blood – x_2, oxygen liability – x_3, ventricular volume – x_4, artery volume – x_5, systolic intraventricular pressure – x_6; calculated variables: arterial pressure – $\varphi_1(x,A)$, venous pressure – $\varphi_2(x,A)$, diastolic intraventricular pressure – $\varphi_3(x,A)$.

$$X_1^1(x,A)=\frac{A_{12}A_{13}}{x_5}(A_{16}+A_4x_3+A_3x_1)(\varphi_1(x,A)-\varphi_2(x,A))-A_{12}A_{14}(\varphi_1(x,A)-A_{28})-A_{12}x_1;$$
$$X_2^1(x,A)=A_1(A_{22}-x_2)(A_{16}+A_3x_1+A_4x_3)(\varphi_1(x,A)-\varphi_2(x,A))-A_1A_{15};$$
$$X_3^1(x,A)=-\frac{A_2}{A_1}X_2^1(x,A);$$
$$X_4^1(x,A)=-A_{17}(\varphi_1(x,A)-x_6);$$
$$X_5^1(x,A)=A_{17}(x_6-\varphi_1(x,A))-(A_{16}+A_3x_1+A_4x_3)(\varphi_1(x,A)-\varphi_2(x,A)).$$
$$X_1^2(x,A)=X_1^1(x,A);$$
$$X_2^2(x,A)=X_2^1(x,A);$$
$$X_3^2(x,A)=-X_3^1(x,A);$$
$$X_4^2(x,A)=(A_{18}+A_7A_{15}+A_{10}A_{28}+A_6\varphi_2(x,A))(\varphi_2(x,A)-\varphi_3(x,A));$$
$$X_5^2(x,A)=-(A_{16}+A_3x_1+A_4x_3)(\varphi_1(x,A)-\varphi_2(x,A)).$$
$$\varphi_1(x,A)=A_{20}x_5-(A_8A_{20}+A_9A_{19})x_1+A_9x_1x_5-A_8A_9x_2-A_{19}A_{20};$$
$$\varphi_2(x,A)=(A_{11}A_{23}-A_{11}A_{30})x_1-A_{11}x_1x_4-A_{11}x_1x_5-A_4x_4-A_4x_5+A_{21}(A_{23}-A_{30});$$
$$\varphi_3(x,A)=A_{29}(A_{24}(x_4-A_{26})+A_{25}(x_4-A_{26})).$$

The conditions for the transition from the description by system 1 (systole) to the description by system 2 (diastole) are: $x_4-(1-k_1)x_8-k_2=0$, k_1,k_2 – heart inotropic factors, A_1-A_{30} – parameters characterizing some individual property for each person and can be measured.

The condition for the transition from description by system 2 (diastole) to description by system 1 (systole) is: $t-t_{21}-\dfrac{1}{x_1(t_{21})}=0$, t_{21} – the moment of the previous transition 2-1.

5. Software

As a program for solving this system of equations and determining the unknown functions of time, the author's implementation program was used. SEM program for solving and modeling structural equations. The program can enter equations and restrictions in the form of scripts in the Java language. The program performs a dynamic compilation of the input software class which leads to the highest calculation speed. The program solver is an optimization module implemented in Java language based on the method of penalty functions of conditional optimization and coordinate wise descent of unconditional optimization. You can purchase the program at http://svlaboratory.org/blog/blog-single/articleid/36 .

6. Numerical experiment

The numerical experiment of this scientific research consisted in testing the SEM program for solving structural equations using the example of a system of differential equations describing the neurohumoral contour of blood pressure regulation.

The time derivatives of unknown functions for equations system were replaced by the two-step difference form:

$$\frac{dx}{dt} \approx \frac{x(t_{i+1}) - x(t_i)}{t_{i+1} - t_i}$$

After entering and solving the equations system by the SEM program, the following results were obtained:

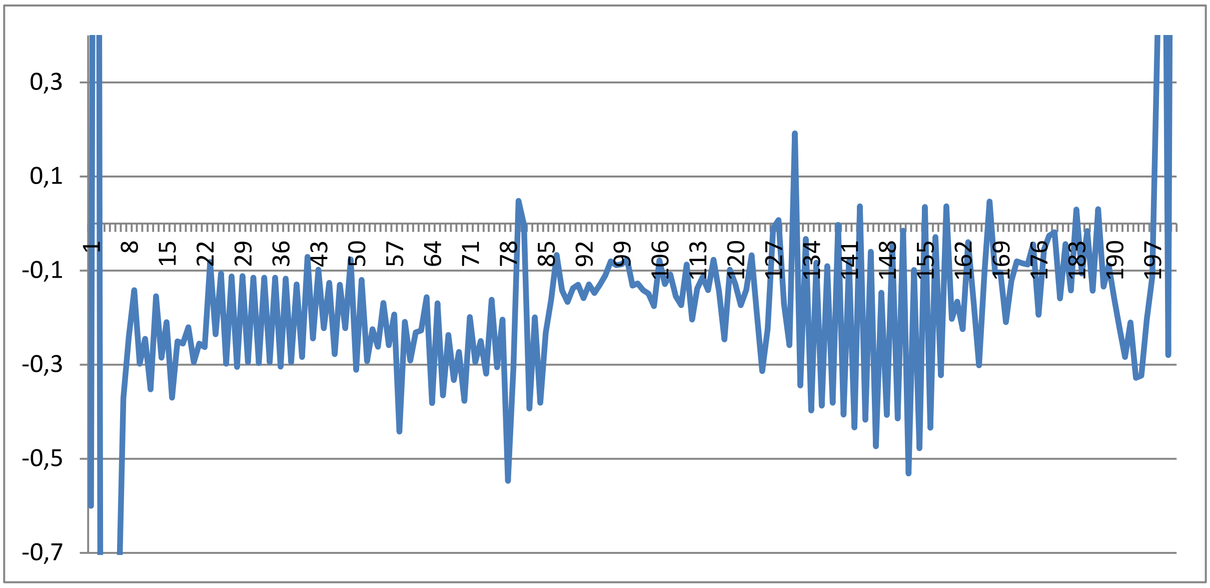

Figure 1. Calculation of the neurohumoral factor.

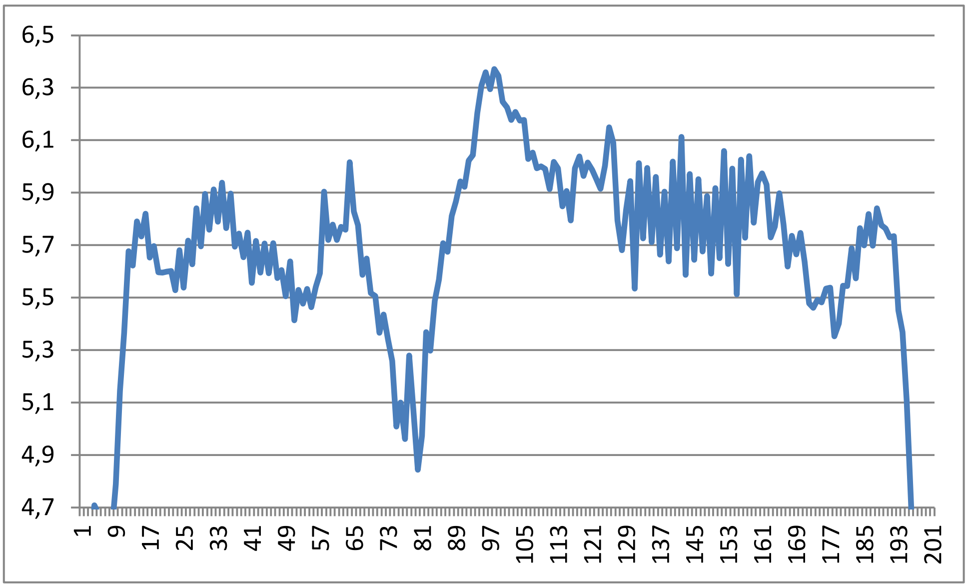

Figure 2. Oxygen content in venous blood.

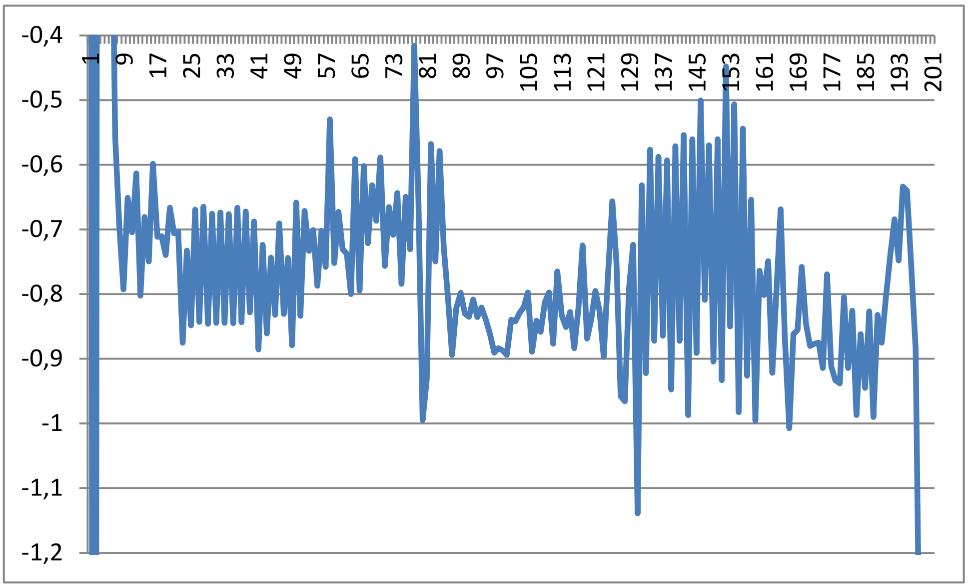

Figure 3. Oxygen liability.

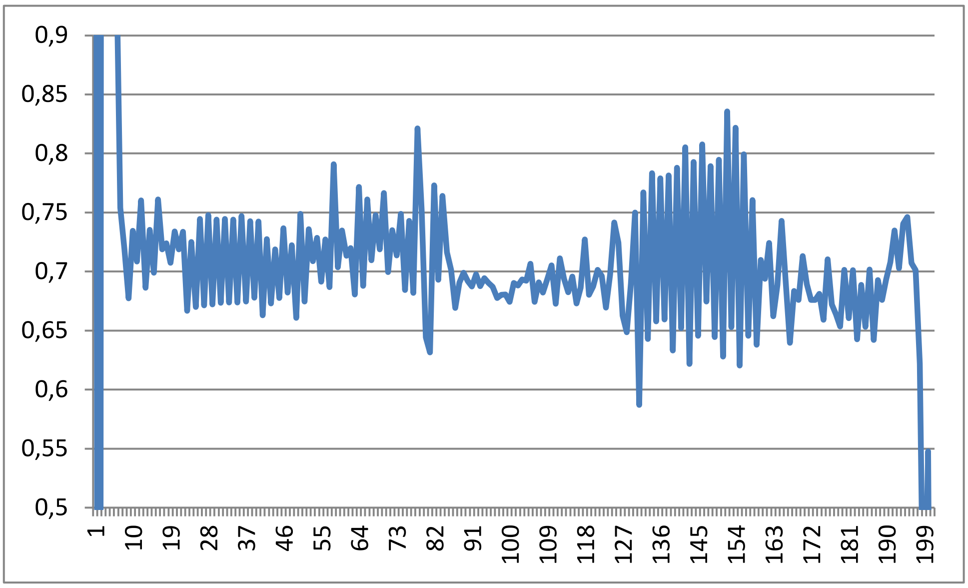

Figure 4. Ventricular volume.

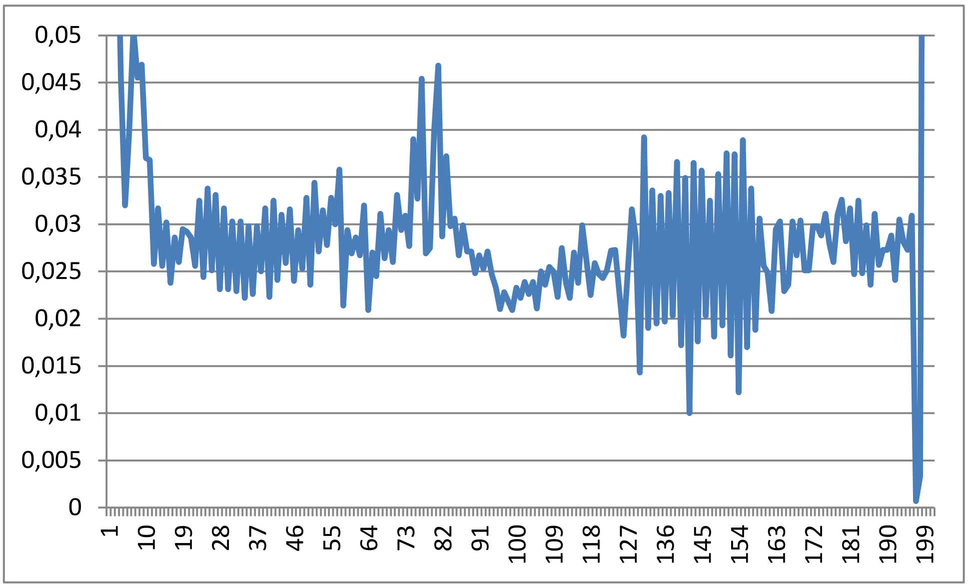

Figure 5. Volume of arteries.

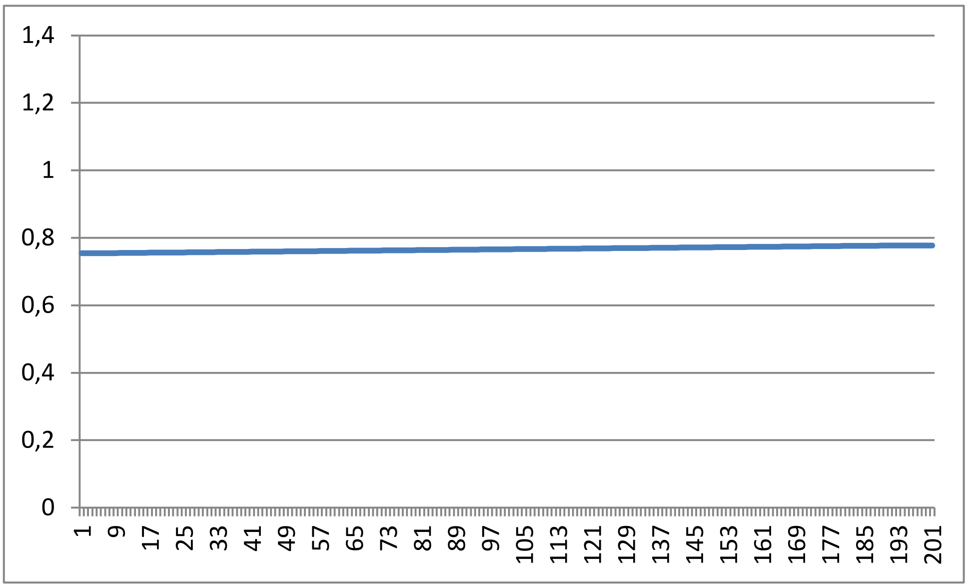

Figure 6. Systolic intraventricular pressure.

The accuracy of the calculations was characterized by $\varepsilon = 0.0001$.The model errors in replacing the derivatives with their first-order difference form, its parameters and function values had a value within 10%. The reliability of the results is proposed to be assessed by interpreting the graphs. The graphs show that during insufficient or fluctuating values of oxygen content in blood, the neurohumoral factor is activated. When the neurohumoral factor is activated the volume of heart ventricles increases to force blood.With increased activity of neurohumoral factor it is occurred the arteries tone changes and their volume slightly increases. At the same time the homeostasis and maintenance of systolic intraventricular pressure is carried out. According to the physiological meaning and interpretation of the results of the graphs, it can be concluded that adequate results were obtained. Testing the SEM program on the example of differential equations of neurohumoral circuit for maintaining blood pressure has a good interpretation which confirms the possibility of using the solver of structural equations for solving differential and integral equations. The proposed method is an analogue of the local variation method for optimizing functionals and is used in this work to solve differential equations, which determines its nove

7. Conclusion

An algebraic differential equations system is formed to describe the neurohumoral contour of blood pressure regulation. Replacing the equations with difference scheme of two simultaneous states leads to the possibility the differential equations system interpreting as structural equations. The solution of the equations system and the unknown functions values calculation showed good interpretational character explaining the mechanism of dynamic regulation and maintenance of arterial pressure.

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