MODELLING OF CARDIOVASCULAR SYSTEM REGULATION

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Abstract

The article deals with principles of cardiovascular system regulation. The work describes physiological basis of selected regulation mechanisms such as autoregulation and baroregulation. An overview of cardiovascular system models is presented. The paper contains description of linear regulation models and also models containing nonlinear phenomenon. The article describes implementation of heart rate and vascular resistance regulation to existing model of arterial system based on the principle of electromechanical analogy. The implemented regulation model is based on baroreceptor regulation application. There are analysed characteristic properties of baroreceptor regulation such as saturation, hysteresis or step change in baroreceptor impulse rate.

Keywords

Baroreceptor, cardiovascular system, heart rate, modelling, regulation, vascular resistance

INTRODUCTION

The regulatory mechanisms play important role in an operation of a whole living organism. They influence its single parts allowing its adaptation to changes of external and internal conditions.

When we focus on cardiovascular system regulation, we can start with autoregulation and finish with baroreceptor regulation. The both types of regulation cover short time changes of single parameters of vascular system. Impact of humoral regulation exerts later if comparing to the previously types.

The modelling of biological functions can be useful in more cases. We want to model certain physiological system because we want to prepare a model for educational purposes or we want to study certain system more deeply and we want to compare it to a physical equivalent. By modelling of the cardiovascular system we can obtain valuable information about its function and about changing its parameters. By comparing simulated and measured signal it is possible to evaluate the function of really living system.

We can observe appearing of the first models of cardiovascular system or models of this system regulation at the beginning of the 20th century. The interesting work can be mentioned which deals with laws of arterial flow and arterial branching [1], [2] or the works focused on cardiovascular regulation [3], [4], [5], [6].

CARDIOVASCULAR REGULATION

There are many publications pursuing to describe cardiovascular regulation mechanisms, though they can be addressed to different groups of readers. When we need to implement principles and dependencies of cardiovascular regulation to specific system using technical tools, we need appropriate information source for inspiring or comparing of given problem solutions which dispose of bright and relative simply explanation of given phenomenon and also of appropriate mathematical apparatus, e.g. [7]. In this article we first of all focus on two types of cardiovascular system regulation such as autoregulation which involves vascular resistance control and baroregulation adherent to heart rate control and also to vascular resistance regulation [7], [8] and [9].

A. Autoregulation

It is local mechanism which modulates blood flow through tissue based on oxygen (metabolic) demands. This mechanism controls peripheral vascular resistance by biochemical changes corresponding to metabolic activity of tissue (e.g. muscle work) in which concentration of H^+, CO_2, O_2 or lactacid are monitored [7], [8], and [9].

B. Baroregulation

Baroreceptor regulation is global feedback mechanism of nervous system control which keeps the heart rate, vascular resistance and venous pressure in order to arterial pressure remains on demanded level. Baroreceptors divide to low- and high-pressure receptors placed in atrial heart walls and aortic arch or carotids [7], [8], and [9]. In this work we used for our implementation and analysis the high-pressure baroreceptors.

REGULATION MODELS

There are many authors who deal with the modelling of cardiovascular system (CVS) and its regulation. It is needed good knowledge of human physiology for creation of CVS mathematical model. Many works try to extend existingmodels of CVS by implementing of regulatory mechanism and by that way it can be created complex model of CVS which should response to internal and external environment changes.

C. Linear models

We can express oxygen consumption and blood flow by the next equations [7]:

$$M = Q([\mathrm{O}_2]_\mathrm{a} - [\mathrm{O}_2]_\mathrm{v}), \tag{1}$$

$$P_\mathrm{a} - P_\mathrm{v} = R\,Q, \tag{2}$$

where $[O_2]_a$ and $[O_2]_v$ are arterial and venous partial pressures of oxygen in blood, M is metabolic activity (oxygen consumption per unit time), P_a and P_v are arterial and venous pressures, Q is blood flow through vessel segment with resistance R.

Vessel resistance can be expressed as follows:

$$R = R_0\left(1 + A\left[\mathrm{O}_2\right]_\mathrm{v}\right), \tag{3}$$

where $A > 0$. Parameter A represents resistance change sensitivity to oxygen concentration. If $A = 0$, then vessel resistance is unregulated [7].

By the similar way we can write equation for sympathetic activity which is related to baroreceptor regulation:

$$S = S^* + \beta\left(P_{sa}^* - P_{sa}\right), \tag{4}$$

where S^* and P_{sa}^* are normal values of sympathetic activity and mean arterial pressure, β expresses sensitivity of sympathetic activity to changes of mean arterial pressure [7].

Previous equations and their combination offer model of regulation mechanisms. Their advantage is relative simplicity but on the other hand their disadvantage is that they did not represent real function of regulation mechanism and can be used only in the limited range of input parameters.

D. Overview of nonlinear baroregulation models

The description of relation blood pressure to baroreceptor activity can be found in work [4]. The author presents differential equation which expresses baroreceptor activity n:

$$n = k_1\left(p - p_0\right) + k_2\,\frac{\mathrm{d}p}{\mathrm{d}t} + N, \tag{5}$$

where p is arterial pressure, k_1 and k_2 are constant parameters, p_0 is threshold value of arterial pressure at which baroreceptor activity changes and N characterizes threshold value of baroreceptor activity [4].

Another approach can be found in [5]:

$$\Delta n = \Delta p\left(a_1 e^{-\frac{t}{\tau_1}} + a_2 e^{-\frac{t}{\tau_2}} + a_3 e^{-\frac{t}{\tau_3}}\right)\sin^{\frac{1}{2}}\left(\frac{n}{m}\pi\right), \tag{6}$$

where Δn is baroreceptor activity change which respond to change of pressure Δp. Parameters a_1, a_2 a a_3 are coefficients representing adaptation speed, m is value of saturation activity of baroreceptors and τ_1, τ_2, τ_3 are time constants which characterizes successive decrease of baroreceptor activity. Equation 6 can be denoted as unified baroreflex model.

An attempt to create one complex model of cardiovascular system and its regulation is the attempt of Guyton et al. [3]. In this work it is introduced schematic diagram consisting of single blocks which represent mathematical operation between physiological variables [10]. The work [10] is inspired by Guyton's model and implements this design in SIMULINK simulation environment.

CARDIOVASCULAR SYSTEM MODEL BASED ON ELECTROMECHANICAL ANALOGY

A human cardiovascular system and its properties represent a dynamic system which can be transformed using appropriate electromechanical analogies to system consisting of discrete electrical elements such as resistor, inductor or capacitor. A blood pressure is equivalent to electrical voltage and a blood flow can be modeled as electrical current. The properties of the vascular system are expressed by single electrical elements. Magnetic field energy is interconnected with kinetic energy of blood flow by inductivity which represents blood density. On the other hand electric field energy is interconnected with elastic deformation of tube by capacity which represents compliance of blood vessel and resistive components correspond to blood viscosity. Then the whole arterial tree can be built by connection of vessel segments consisting of single elements (see Fig. 1) [11], [12], [13], [14], [15].

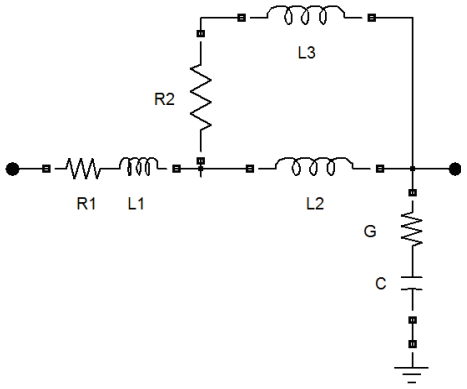

Fig. 1: The vessel segment model

IMPLEMENTATION OF BARORECEPTOR REGULATION MECHANISMS

Baroreceptors are connected to short time regulation loop of several CVS parts such as vascular resistance and heart rate. These two parameters are included in equation for calculation of mean arterial pressure p_{cs} (assumption that mean arterial pressure in aortic arch is equal to mean arterial pressure in carotids):

$$p_{cs} = R_a \, SV \, H \tag{7}$$

Parameter SV represents heart stroke volume, H is heart rate and R_a is peripheral vascular resistance.

For modelling the baroreceptor regulation we can use modified form of equation (6) [6]:

$$n = N + \int_{-\infty}^{t} \left(\frac{\mathrm{d}p_{cs}}{\mathrm{d}t} \left(a_1 e^{-\frac{t-s}{\tau_1}} + a_2 e^{-\frac{t-s}{\tau_2}} + a_3 e^{-\frac{t-s}{\tau_3}} \right) \left[\frac{n(m-n)}{\left(\frac{m}{2}\right)^2} \right] \right) \mathrm{d}s \tag{8}$$

Then the baroreceptor activity can be divided to four parts [6]:

$$n = \Delta n_1 + \Delta n_2 + \Delta n_3 + N\,, \tag{9}$$

where N represents basal impulse frequency of baroreceptors. Δn_1, Δn_2, Δn_3 parameters are related to impulse frequency sensitivity to changes of arterial pressure.

The solution can be expressed by the next differential equations:

$$\frac{\Delta n_k}{\mathrm{d}t} = \frac{\mathrm{d}p_{cs}}{\mathrm{d}t} a_k \left[\frac{n(m-n)}{\left(\frac{m}{2}\right)^2} \right] - \frac{1}{\tau_k} \Delta n_k\,, \quad k = 1, 2, 3\,, \tag{10}$$

where a_k and τ_k are equal to coefficients in equation (6). Expression $\frac{\mathrm{d}p_{cs}}{\mathrm{d}t}$ represents time change of mean arterial pressure.

E. Sympathetic and parasympathetic activity

Heart rate, contractility and vascular resistance increase by increasing of sympathetic activity. On the other hand parasympathetic activity decreases the heart rate and it has small influence to contractility and vascular resistance changes [9]. Relation of sympathetic and parasympathetic activity to pressure in carotids can be characterized by sigmoidal function and expressed by following equations [5], [6]:

$$n_s(n) = \frac{N_s}{1 + \left(\frac{n}{N}\right)^{\upsilon_n}}\,, \tag{11}$$

$$n_p(n) = \frac{N_p}{1 + \left(\frac{n}{N}\right)^{-\upsilon_n}}\,, \tag{12}$$

where p_{cs} mean pressure value in carotids defined as average value of given pressure during one heart cycle. Parameter υ_n represents slope of single curves and N_s, N_p are saturated values of sympathetic and parasympathetic activity.

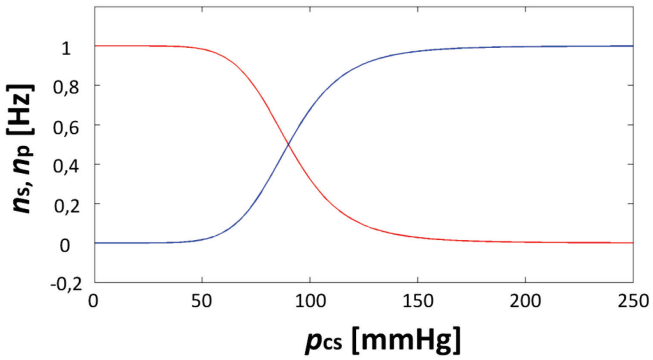

Fig. 3: Dependency of sympathetic (blue curve) and parasympathetic activity (red curve) on mean arterial pressure in carotids.

F. Efferent response

Efferent response of corresponding organs on sympathetic and parasympathetic stimulation can be expressed as their linear combination [6]:

$$\sigma_i(n) = \alpha_i n_s(n) - \beta_i n_p(n) + \gamma_i\,, \tag{13}$$

where coefficients α_i, β_i, a γ_i characterizes strength of sympathetic or parasympathetic stimulation. Index i describes appropriate organ response: $i \in E = \{H, R_{ps}\}$.

E includes also heart rate H and peripheral resistance R_{ps}. Dynamic response is modeled by ordinary differential equations of first order:

$$\frac{\mathrm{d}x_{\mathrm{H}}(t)}{\mathrm{d}t} = \frac{1}{\tau_{\mathrm{H}}}\left(-x_{\mathrm{H}}(t) + \sigma_i(n)\right), \tag{14}$$

$$\frac{\mathrm{d}x_{R_{\mathrm{ps}}}(t)}{\mathrm{d}t} = \frac{1}{\tau_{R_{\mathrm{ps}}}}\left(-x_{R_{\mathrm{ps}}}(t) + \sigma_i(n)\right), \tag{15}$$

The equation (14) represents chronotropic effect which is dynamical heart rate change and the equation (15) characterizes dynamic change of vascular resistance [6], [8] and [9].

G. Numerical implementation

Solution of the equation (6) and its modification (10) are basis for our numerical implementation of regulation mechanisms to existing model of CVS based on electromechanical analogy. We used MATLAB programming environment and its SIMULINK part for performing of simulations. We divided baroreceptor regulation to 4 functional units:

1. *Baroreceptors*
2. *CNS (Central Nerve System)*
3. *Heart rate and vascular resistance*
4. *Controlled signal source of blood pressure*

The Fig. 3 characterizes functional connection of single regulation units.

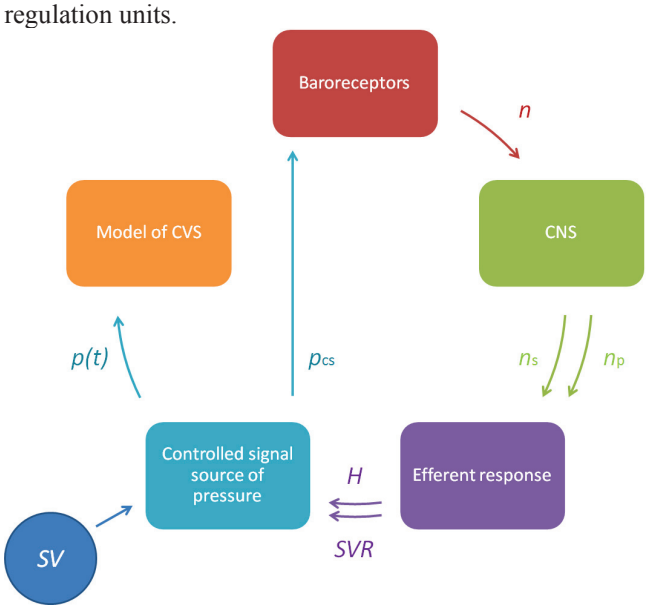

Fig. 3: Functional connection of regulation units

ANALYSIS OF PROPERTIES OF BARORECEPTOR REGULATION

When the arterial pressure in carotids or aortic arch changes, nonlinear phenomena appear and they are related to adaptation of organism on pressure change by using the baroreceptor regulation.

H. Threshold and saturation

A threshold value of pressure exists when the basal baroreceptor activity increases. By successive increasing of baroreceptor activity saturation occurs and impulse frequency of baroreceptors keeps unchanged. We get the same result as in [5] (see Fig. 3).

I. Hysteresis

Baroreceptor response to mean arterial pressure changes can be expressed by sigmoidal function (function with shape of letter "S" – see Fig. 3) [5]. Hysteresis can appear when the arterial pressure is slowly increased and then slowly decreased to starting value (see Fig. 4).

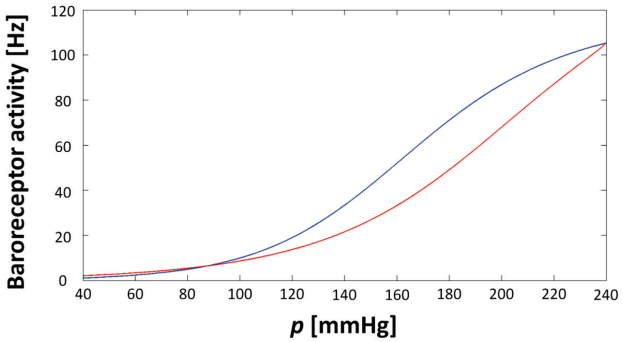

Fig. 4:Hysteresis curve – baroreceptor activity change (the blue curve represents baroreceptors response to blood pressure increasing and the red curve is corresponding to its decreasing).

J. Step change

During short-time blood pressure step change baroreceptor activity also increases corresponding to blood pressure. At long-time blood pressure change baroreceptors adapt and their impulse frequency decreases towards basis threshold value but at keeping increased blood pressure [5]. The simulation output you can see in the Fig 5.

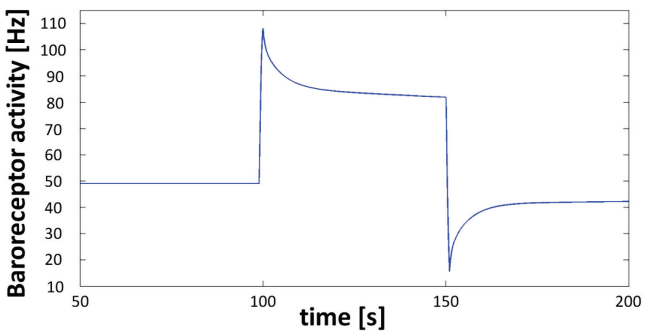

Fig. 5: Step change of baroreceptor activity during blood pressure change from 100 mmHg to 150 mmHg and vice versa.

CONCLUSION

The baroreceptor regulation controls the important parameters of cardiovascular system. Within the work heart rate and vascular resistance regulation were described and implemented to the existing model of cardiovascular system based on electromechanical analogy. The baroreceptor regulation is not linear and its created model was based on differential equations by which analysis in simulation environment several nonlinear phenomena appear such as saturation, hysteresis or step change in baroreceptor impulse rate. Simulation results are comparable to data listed in works [5] and [6]. Our future work will be focused on extending of regulation model, for example by including of further regulation parts of cardiovascular system such as vessel compliance, heart muscle contractility or change of metabolic needs.

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