Chapter 11
Development of Simple Model of the Arterial Baroreflex

Aleksei Anisimov, Alena Tomchuk, and Timofey Sergeev

Abstract It is extremely difficult to develop a full-fledged model of the dynamic operation of the cardiovascular system. This is primarily due to the fact that not only individual organs, but also the activities of the whole body contribute to this complex process. And the temporal scales of cardiovascular system oscillations include fractions of seconds (for pacing, baro- and chemoreceptors, respiratory activity), minutes (for renin-angiotensin system), hours (for renal regulation, ambient temperature influence, blood viscosity) and even a day. Rhythms in each of the above frequency ranges may demonstrate very complex behavior. At the same time, direct measurement of values of parameters characterizing rhythm regulation (which are described in more detail below) may be difficult and sometimes impossible without direct intervention into the cardiovascular system, which is practically unrealizable in standard investigations. That is why mathematical modeling of dynamic behavior of cardiovascular system is sometimes the only possibility to study the processes on qualitative level. Therefore, in this study we attempted to develop a simple model of baroreceptor control based on electrodynamic analogies, which still can provide valuable information for future experiments.

Keywords Model · Arterial baroreflex · Feedback · Arterial blood pressure

11.1 Introduction

Blood pressure (BP) is one of the main indicators of vital functions of the human body, reflecting the work of the entire cardiovascular system in an integral form [1]. Therefore, the construction of models that allow us to trace the interaction of various

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elements involved in the regulation of BP is a very urgent and complex task, which has not been fully solved even with the increased computing power [2, 3].

Currently, a very wide set of methods for processing cardiorhythmograms is used to assess heart rate (HR) fluctuations, which are described in many works. This diversity is largely due to the wide spread and introduction into clinical practice of Holter monitors, which allow recording electrocardiogram (ECG) signals for several days [4–7].

Much less attention is paid to the analysis of BP fluctuations and their relationship with the HR and respiratory rate. This is due to the insufficient number of appropriate tools (the existing systems of long-term BP registration work on the basis of cuff measurement methods which excludes the registration of a continuous curve BP), and considerable difficulties encountered in the attempts of theoretical model of the interaction of all the elements involved in the regulation and maintenance of optimal BP.

In addition to the average (static), the dynamic properties of blood pressure also have a significant impact on the state of the cardiovascular system. For example, inhibition of the baroreceptor control mechanism increases the daily level of BP and increases the intensity of its short-term oscillations. Thus, the need to build adequate models of the cardiovascular system that allow us to trace the dynamic behavior and regulation of BP through a complex chain of interacting organs and systems comes to the fore. The construction of mathematical models based on the numerical values of specific experimentally obtained parameters makes it possible to correctly assess the changes occurring in the body for those cases when direct measurements are not possible or involve a risk for the subject [1].

The development of a full-fledged model of the dynamic work of the cardiovascular system is extremely difficult. This is primarily due to the fact that not only individual organs contribute to this complex process, but also the activity of the entire body as a whole. At the same time, the time scales of the oscillations of the cardiovascular system include fractions of a second or seconds (for pacemakers, baro- and chemoreceptors, respiratory activity), minutes (for the renin-angiotensin system), hours (for renal regulation, the influence of ambient temperature, blood viscosity), and even days and months (due to the season activity).

Rhythms in each of these frequency ranges can exhibit very complex behavior. At the same time, direct measurement of the values of parameters that characterize the regulation of rhythms (which are described in more detail below) is difficult, and sometimes impossible without direct intervention in the cardiovascular system, which is practically unrealizable in standard studies. That is why mathematical modeling of the dynamic behavior of the cardiovascular system is sometimes the only way to study the processes at a qualitative level.

11.2 Materials and Methods

Studies of complex multicomponent systems are accompanied by attempts to build models of these objects. As new knowledge about such objects is gained, their models develop, improve and become more complex, starting with representations in the form of high-quality structural diagrams. Modeling is of particular importance in physiology and medicine, since the study of the functioning and interaction of the systems of regulation of the human body, in particular, the circuits of the nervous regulation of the work of the cardiovascular system, is of fundamental and applied importance [8].

Figure 11.1 shows a conceptual physiological model of the behavior of the baroreceptor regulation circuits for increasing (solid lines) and decreasing (dotted lines) blood pressure (BP). Let's consider in more detail the process of rising BP. When the pressure in the artery is significantly reduced, the intensity of baroreceptor stimulation also decreases. This leads to a decrease in afferent impulses in the solitary nucleus (SN) of the medulla oblongata. In this case, the following processes occur.

Increased tone of sympathetic innervation from the vasomotor center (VC). Stimulation of VC leads, firstly, to an increase in the stimulation of vasoconstrictors, which leads to vasoconstriction—narrowing of veins and arterioles and, consequently, to an increase in total peripheral vascular resistance (TPVR), decrease in volumetric blood flow (VBF) [9], as well as the movement of a large volume of blood from peripheral blood vessels to the heart cavities, what causes them to stretch. As a result, heart rate (HR) and cardiac output (CO) increase, allowing the heart to pump more blood;

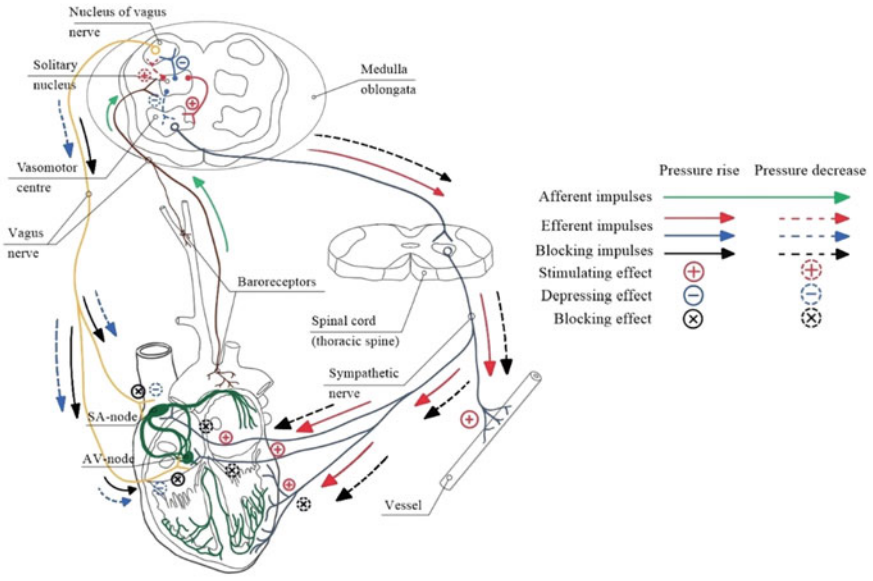

Fig. 11.1 Conceptual physiological model of baroreceptor regulation circuits

secondly, an increase in the stimulation of nerve nodes and fibers that innervate the heart, which leads to an increase in the HR [10].

Decreased tone of parasympathetic innervation from the nucleus of the vagus nerve (NVN). The depressing signal from the SN to the NVN helps to reduce the activity of the parasympathetic nervous system (PNS), which sends inhibitory signals to the heart, which allows the sympathetic nervous system (SNS) to increase the HR without hindrance. Thus, until BP rises to a normal value, control over BP regulation is completely transferred to the SNS. Thus, with increasing pressure, the following parameters change:

- Heart rate increases;
- Cardiac output increases;
- Total peripheral vascular resistance increases;
- Volumetric blood flow decreases;
- Blood pressure increases.

When BP rises strongly, the intensity of baroreceptor stimulation also increases. This leads to an increase in afferent impulses in the SN of the medulla oblongata. In this case, the opposite processes occur.

To build a model describing the relationship between arterial pressure and pulse wave velocity, a transition was made from Frank's Windkessel hydrodynamic model [11, 12] to Frank's electrical model. The simplest two-element model consists of resistance R, which corresponds to the total peripheral resistance (TPR) of the arteries, and capacity C, which acts as an elastic reservoir. Models based on electrical analogies are an effective way to analyze hemodynamic processes in the human body. In this case, the known equations of the electrical circuit theory can be applied, effective for calculations using modern circuit modeling programs, which allow to visualize the solutions of differential equations [13–15]. The result of solving problems related to the analysis of circulatory processes by means of equivalent electrical circuits, with the proper degree of adequacy of the model used and the choice of boundary and initial conditions known from experimental data, sufficiently correspond to the real hemodynamic processes occurring in the human body. The program of circuit modeling MicroCap 12, intended for analysis and modeling of processes in electric circuits, has been used for the analysis of processes of the developed electrical model.

Figure 11.2 shows diagrams, explaining the model, known as Frank's Windkessel (WK): in hemodynamic (Fig. 11.2a) and electrodynamic (Fig. 11.2b) representations. In these schemes, resistance R corresponds to TPR, which is taken as the sum of all individual resistances of different microcirculation sections, which gives the resistance of the entire vascular bed, with the main resistance to flow in the arterial system set by the smallest arteries and arterioles. Capacity C is the total arterial elasticity (or arterial compliance), which is determined mainly by the elasticity of large (conducting) arteries—the smaller the artery, the more insignificant its elasticity and greater resistance. R_Z is the characteristic impedance of the aorta, which allows relating concentrated two-element model and pulsatile pressure wave propagation through the arterial system.

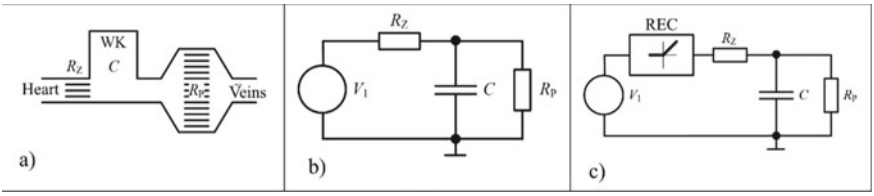

Fig. 11.2 Explanation of the WK model: in hemodynamic **a**, standard **b**, and modified electrodynamic **c** representation

The three-element model, given the statistics accumulated in recent years, is much more accurate in reflecting the relationship between arterial blood pressure and blood flow, especially in the lower frequencies.

Windkessel model assumes that during diastole, when the arterial valve is closed, pressure will decrease exponentially with a time constant $\tau = RC$. Diastolic aortic pressure P_{DIA} (when the valve is closed) can be described by an exponential relationship:

$$P_{DIA}(t) = P_{SIS} \cdot e^{-\frac{t}{RC}}, \tag{11.1}$$

where P_{SIS} is the maximum systolic pressure.

The problem of return flow to the left ventricle (LV) was solved using an additional nonlinear link (Fig. 11.2c), simulating LV valve operation of the heart and corresponding to a single half-period rectifier (REC) with the function of the following form:

$$\begin{cases} (P - P_V) \leq 0, K_{REC} = 0, \\ (P - P_V) \geq 0, K_{REC} = 1. \end{cases} \tag{11.2}$$

where PV is the value of pressure at the input of the rectifier, P is the value at its output, K_{REC} is its transfer coefficient.

11.3 Results

The developed model allows us to study the effect of heart rate variability on blood pressure values without any feedbacks (arterial baroreflex, regulation of total peripheral resistance, etc.). This is a significant simplification of the conceptual model given earlier, but it still allows a qualitative assessment of the processes taking place. Figure 11.3a shows the section of a 10s cardiorhythmogram (CRG) used in the simulation.

Heart rate here varies between 67 and 116 beats per minute, with a total of 11 complete cardiac cycles. This CRG corresponds to a series of consecutive heartbeat

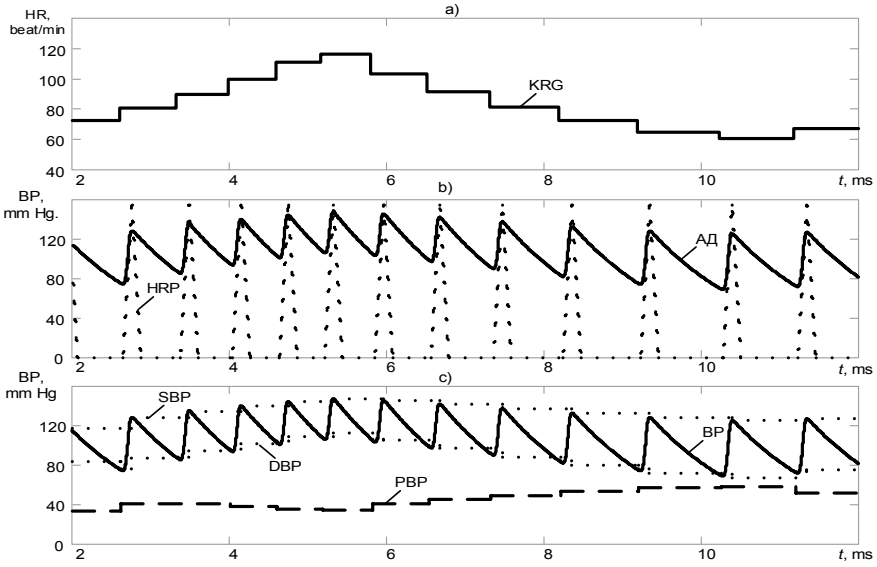

Fig. 11.3 Simulation results: **a** section of the cardiorhythmogram (CRG); **b** heart rate pulse (discontinuous curve) and BP signal (solid curve); **c** BP signal (solid curve), envelope of local maxima—graph of BP beat-to-beat values (discontinuous curve), envelope of local minima—graph of BP beat-to-beat values (discontinuous curve), graph of PBP values (dashed curve)

pulses (HBP) (Fig. 11.3b, discontinuous curve). For clarity, they are presented with normalized values, in the model their source is a voltage generator. As a result of the HBP action on the RC circuit with a nonlinear element the ABP signal is formed, presented in Fig. 11.3b (solid curve). Local maxima of this curve correspond to systolic blood pressure (SBP) beat-to-beat values, minima—to diastolic blood pressure (DBP). The plots corresponding to these beat-to-beat SBP and DBP values are shown in Fig. 11.3c (discontinuous curves). Beat-to-beat values of SBP and DBP, like beat-to-beat values of heart rate, have variable character and vary in the following ranges: from 117 to 147 mm Hg for SBP, from 67 to 112 mm Hg for DBP. In the same figure there is a graph of pulse blood pressure (PBP, dashed curve), which is the difference between systolic and diastolic arterial blood pressure.

According to results of performed modeling, the following preliminary conclusions can be made by visual comparison of plots with HR, SBP, DBP and PBP beat-to-beat values:

1. For the given model parameters (and as it was mentioned above, in the absence of feedback), the HR variability has a significant impact on the BP variability.
2. Systolic and diastolic BP are directly proportional to HR.
3. Pulse pressure is inversely related to HR.
4. The effect of HR on systolic and diastolic BP is manifested in varying degrees. In other case, pulse pressure values would remain constant.
5. HR affects diastolic blood pressure more than systolic blood pressure.

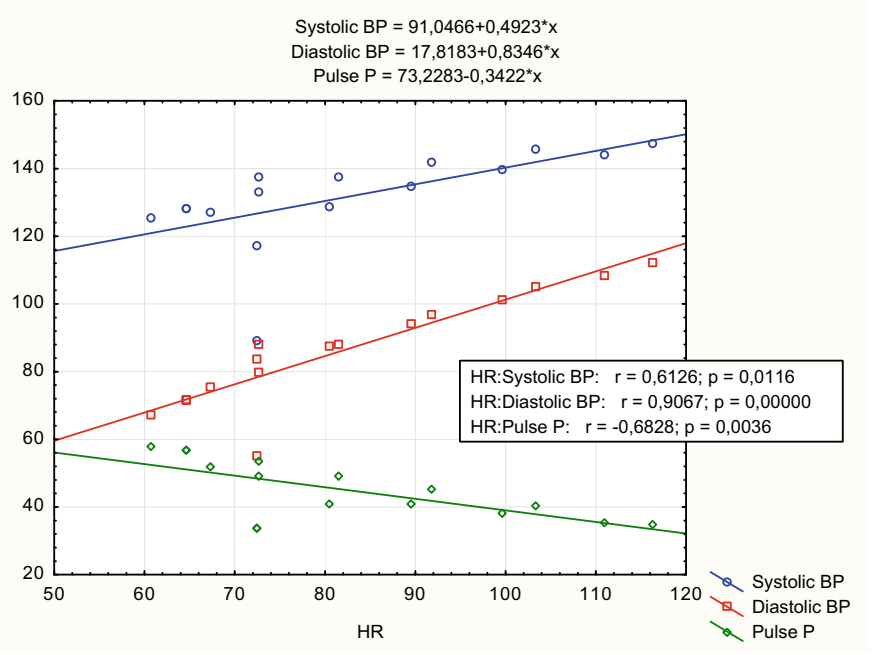

Fig. 11.4 Dependences of SBP, DBP and PBP on HR. We also present the parameters of linear approximation (above), correlation coefficient (r) values and p-values

The variants for the signals considered on Fig. 11.3 are shown in Fig. 11.4, these are dependences of beat-to-beat values of SBP, DBP and PBP on HR.

The corresponding parameters of linear approximation (above), correlation coefficient values (r) and p- values (results calculated using Statistica software) are shown in the same figure. The numerical values of the correlation coefficients confirm our preliminary findings: correlation coefficients, r are sufficiently high ($r > 0.6$) and significant ($p < 0.05$), with the highest correlation coefficient being the correlation between DBP-HR, and the negative one being the correlation between PBP-HR (Fig. 11.4).

11.4 Conclusion

Thus, the obtained simple model allows studying the dependence of beat-to-beat arterial blood pressure values on HR and other basic parameters of the system hemodynamics only on the basic level. Accordingly, further studies would be connected with the study of the influence of the model main parameters on the dependence of HR-BP: among others are the values of HRP amplitude, total peripheral resistance, elasticity (capacitance) and internal resistance. The next stage of the study should

be the refinement and complication of the model due to consecutive introduction of feedback loops, first of all, arterial baroreflex and regulation of total peripheral resistance.

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