

## A prototype compartmental model of blood pressure distribution

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### ABSTRACT

We consider a system of differential equations, the behavior of whose solutions possesses several properties characteristic of the blood pressure distribution. The system can be used for a compartmental modeling [R. Bellman, *Mathematical Methods in Medicine*, in: *Series in Modern Applied Mathematics*, vol. 1, World Scientific Publishing Co., Singapore, 1983; J.A. Jacquez, *Compartmental Analysis in Biology and Medicine*, Elsevier, New York, 1972] of the cardiovascular system. It admits a unique bounded solution such that all coordinates of the solution are separated from zero by positive numbers, and which is periodic, eventually periodic or almost periodic depending on the moments of heart contraction. Appropriate numerical simulations are provided. Some of the results were announced at The Fifth International Conference on Dynamic Systems and Applications held at Morehouse College, Atlanta, in 2007 [M.U. Akhmet, G. Bektukhambetova, On modeling of blood pressure distribution, in: *Proceedings of the Fifth International Conference on Dynamic Systems and Applications* held at Morehouse College, Atlanta, USA, May 30–June 2, 2007, *Proc. Dyn. Syst. Appl.*, 5 (2008) 17–20].

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### 1. Introduction and preliminaries

A living organism can be considered as a complex system of nonlinear oscillating structures of different origins. The system as an integrity is a “constellation” of all of its oscillations. The oscillators are connected with each other to build oscillating chains. The essential task of controlling processes in a living organism is to sustain the oscillating activity of certain significantly unstable elements in such a way that the amplitudes of their oscillations do not become excessively large or excessively small. It is, therefore, natural to assume that the data of oscillations should be considered as one of the most important sources of information about the condition of the organism.

The movement of any fluid in a certain direction is the result of pressure differences in the starting and ending points of the system. The difference of pressure in heart chambers and in the aorta, and in the aorta and outgoing blood vessels, is the cause of blood flow in an organism. In the last decades there has been an increase of intensive investigations of blood pressure in respect of its connections with other parameters of the cardiovascular system [1–14]. At the same time we should recognize that due to the nonlinear properties of blood vessel walls and their variability along the length of a vessel the relation between actual oscillations of pressure and of blood volume [6,10,13] is very complex, and consequently, it is reasonable to consider the distribution of blood pressure out of its connection with other parameters, particularly blood volume. There are many different approaches to the problem of modeling cardiovascular dynamics, including, for example, modeling of the coupling mechanisms as a system of differential equations with delay [5,15] or as a system of

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ordinary differential equations [8,9,14]. Compartmental models have been effectively applied to investigate different types of processes in chemistry [16], medicine [15,17–19], epidemiology [20], ecology [21], and pharmacokinetics [4,17,22,23]. The idea of compartments makes our investigation more abstract. In particular, we do not specify the physiological meaning of the compartments nor do we specify the number of these parts. Only compartments which have an essential influence on the aortic pressure are considered.

It is obvious that all parts of the cardiovascular system should be involved if, let us say, the blood flow problem is investigated, because the total volume of the blood is constant with time, but the pressure could be discussed locally, as, for example, in [8,9], where blood pressure for only a compartment is studied. In this paper we focus on the interactions of the blood pressure of several parts of the system, but not all of them. We suppose that there exists, as a consequence of the blood flow, a mutual interaction of blood pressure in different parts of the system. One of them, the systemic arterial pressure, should be singled out, as it is disturbed impulsively with large simultaneous inflow of blood in the time of heart contraction. Other compartments of the system do not directly undergo this impulsive action, so their change is continuous. We want to note that in this paper we consider exclusively the aorta and the parts of the cardiovascular system interacting with the aorta through blood pressure, that is, only compartments belonging to the systemic circulation are considered. The blood pressure in the pulmonary artery also changes impulsively, and the differential equation system we propose can therefore also be used to model the pressure in this artery and its neighboring compartments. However, we leave this out of our discussion.

The goal of our paper is not to build a final model of the cardiovascular system, but rather to introduce a system of differential equations, in which one coordinate is perturbed impulsively and other coordinates exhibit a continuous change, thus having certain properties characteristic of the actual blood pressure behavior. The results obtained now need qualitative experimental confirmation. We hope that our results will serve as a basis for further experimental and clinical studies, which can lead to better understanding of the cardiovascular system.

Let  $\mathbb{Z}$ ,  $\mathbb{N}$  and  $\mathbb{R}$  be the sets of all integers, natural and real numbers, respectively,  $\mathbb{R}_+ = [0, \infty)$ , and let  $\|\cdot\|$  be the Euclidean norm in  $\mathbb{R}^n$ ,  $n \in \mathbb{N}$ .

We denote  $C_0$  the aorta and arteries, and  $P_0$  blood pressure in  $C_0$ . Let  $C_i$ ,  $i = \overline{1, m}$ , be other vessels and organs, which adjoin  $C_0$ , and have an essential influence on fluctuations of  $P_0$ , and  $P_i$ ,  $i = \overline{1, m}$ , the blood pressure values in compartments  $C_i$ ,  $i = \overline{1, m}$ .

In this paper we suppose that the pressure variables satisfy the following system of differential equations with impulses:

$$\begin{aligned} \frac{dP_0(t)}{dt} &= -k_0P_0 - g_0(P_0 - P_1, P_0 - P_2, \dots, P_0 - P_m), \\ \frac{dP_1(t)}{dt} &= -k_1P_1 + g_1(P_0 - P_1), \\ \frac{dP_2(t)}{dt} &= -k_2P_2 + g_2(P_0 - P_2), \\ &\dots\dots\dots \\ \frac{dP_m(t)}{dt} &= -k_mP_m + g_m(P_0 - P_m), \\ \Delta P_0|_{t=\theta_i} &= I_0 + J_0(P_0), \end{aligned} \quad (1)$$

where  $\Delta P_0|_{t=\theta_i} \equiv P_0(\theta_i+) - P_0(\theta_i)$ ,  $P_0(\theta_i+) = \lim_{t \rightarrow \theta_i+} P_0(t)$ .

The following assumptions for (1) will be needed throughout the paper:

(C1) real constants  $I_0$ ,  $k_i$ ,  $i = \overline{0, m}$ , are positive;

(C2)  $J_0$ ,  $g_i$  are real valued functions,  $J_0(0) = 0$ ,  $g_i(0) = 0$ ,  $i = \overline{1, m}$ ,  $J_0(z) > 0$ ,  $g_i(z) > 0$ , if  $z > 0$ ,  $g_0(0, 0, \dots, 0) = 0$ ,  $g_0(z_1, z_2, \dots, z_m) > 0$ , if  $z_j > 0$ ,  $j = \overline{1, m}$ ;

(C3) the functions  $J_0$ ,  $g_i$ ,  $i = \overline{0, m}$ , satisfy the Lipschitz condition

$$\begin{aligned} |g_i(z^1) - g_i(z^2)| &\leq l_i|z^1 - z^2|, \quad i = \overline{1, m}, \\ |g_0(z_1, \dots, z_m) - g_0(w_1, \dots, w_m)| &\leq l_0 \sqrt{\sum_{i=\overline{1, m}} |z_i - w_i|^2}, \\ |J_0(z^1) - J_0(z^2)| &\leq l_j|z^1 - z^2|; \end{aligned} \quad (2)$$

(C4) there exists a number  $\omega > 0$ , such that  $i\omega \leq \theta_i < (i+1)\omega$ ,  $i \in \mathbb{Z}$ ;

(C5) there exist positive real constants  $m_i$ ,  $i = \overline{0, m}$ ,  $m_j$  such that

$$\begin{aligned} \sup_{z \geq 0} g_i(z) &= m_i, \quad i = \overline{1, m}, & \sup_{z_j \geq 0, j=\overline{1, m}} g_0(z_1, \dots, z_m) &= m_0 \\ \sup_{z \geq 0} J_0(z) &= m_j. \end{aligned} \quad (3)$$

We assume that atmospheric pressure has zero value. Since pressures cannot be negative, the main goal of our paper is to find the conditions which guarantee the existence of bounded positive solutions. Moreover, the coordinates of the solutions are separated from zero by some positive constants, and eventually the first coordinate must be larger than any another. The solutions should be exponentially stable under certain conditions, and their various oscillatory properties (periodicity, eventual periodicity, almost periodicity) according to the particular properties of the sequence of moments  $\theta_i$ .

Differential equations such as (1) as a model of the physiological process are developed using models, which can be found, for example, in [4,5,8,9,12] and many others. To clarify this, we shall describe the two following models.

In [9] the following differential equation is considered for the peripheric blood pressure  $P_p$ :

$$\frac{dP_p}{dt} = -\frac{1}{RC}P_p + \frac{1}{C}Q(t), \quad (4)$$

where  $C$  is the total arterial compliance,  $R$  the arterial resistance, and  $Q(t)$  the continuous blood flow. The formula for the continuous blood flow evaluation is given by  $Q(t) = \frac{P_0(t) - P_p(t)}{r}$ , where  $P_0$  is the systemic arterial pressure, and  $r$  is the aortic impedance. As we suppose that the systemic arterial pressure is larger than the blood peripheric pressure,  $Q(t)$  is a positive function.

For the systemic arterial pressure the following differential equation with impulses has been discussed in [8]:

$$\begin{aligned} \frac{dP_0}{dt} &= -\frac{1}{RC}P_0, \quad t \neq \theta_i, \\ P_0(\theta_i+) - P_0(\theta_i) &= \frac{V_j}{C}, \end{aligned} \quad (5)$$

where  $\theta_i = iT$ ,  $i \in \mathbb{Z}$ , are prescribed moments,  $P_0(\theta_i+)$  is the right limit's value,  $V_j$  are the stroke volumes, and  $C$  is the systemic arterial compliance.

It is natural to consider cardiovascular problems using discontinuous dynamics theory. One of the interesting approaches which should be mentioned is the method of circle mappings [3,7] for cardiac arrhythmias. In [2] we consider the extended form of Eq. (5) for the systemic arterial pressure, and we investigate the problem of existence of positive periodic and almost periodic solutions, oscillations of the equation. The case when the moments of heart contraction are not prescribed, but are caused by a certain value of the systemic arterial pressure, has also been investigated.

We have further developed the models of our predecessors in several ways:

(1) The nonlinear perturbations caused by interactions are used in the model, both in differential equations and the impulsive part of the model. Function  $g_0(P_0 - P_1, P_0 - P_2, \dots, P_0 - P_m)$  is positive since the outflow from the aorta to neighboring compartments reduces the systemic arterial pressure; all differences in the function are assumed to be positive. Nonlinearities  $g_i(P_0 - P_i)$ ,  $i = 1, m$ , are positive, when the differences again are positive, since the differences generate inflow into compartments, which naturally implies the rise of pressure. Every function  $g_i(P_0 - P_i)$  does not depend on  $P_j$ ,  $j \neq i$ , since we assume that there is no essential mutual interaction between compartments.

(2) The equations for the compartments are derived from Eq. (4) for peripheric blood pressure. The nonnegative differences  $\frac{P_0(t) - P_i(t)}{r_i}$  are replaced by the nonlinear functions  $g_i(P_0 - P_i)$ .

(3)  $I_0$  is a constant part of the instantaneous change of systemic arterial pressure.

(4) Condition (C5) is chosen, assuming that the results obtained in our investigation can be interpreted for the blood pressure system activated by an artificial pacemaker, or for the case when fluctuations are regular. That is, we exclude the case when the set of points of discontinuity may have so-called accumulation points.

We must also note that our results can be easily reconsidered when condition (C5) is replaced by condition  $0 < \mu \leq \theta_{i+1} - \theta_i \leq \mu_1 < \infty$  or by the condition of existence of  $\limsup_{T \rightarrow \infty} \frac{i(t_0, t_0 + T)}{T} = p$ , where  $i(t_0, t_0 + T)$  is the number of elements  $\theta_i$  in the interval  $(t_0, t_0 + T)$ , and  $p$  is a nonnegative real number, uniform for all  $t_0 \in \mathbb{R}$ .

The mathematical background of our investigation, the theory of impulsive differential equations, has been developed in [24–29]. The results of the paper concerning eventual periodicity, positiveness of solutions, and domination of a coordinate over all other coordinates, are new. The role of the impulsive action as the one determining the relations is investigated for the first time. We are aware that in reality the role of the impulses is diminished, for example, by delays, and we plan to continue the investigation of the interactions of blood pressure levels in different parts of the cardiovascular system in our future papers.

The paper is organized in the following manner. In the next section we find the conditions for the equation such that there exists a unique solution bounded on the whole  $\mathbb{R}$ . The solution is periodic, almost periodic, or eventually periodic if the sequence of discontinuity moments has an appropriate property. Section 3 contains the results on the stability and positiveness of the solutions. In the last section we specify the choice of the moments of discontinuity such that they may be determined artificially by a particular map, and by the initial moment. In this case the approach can be considered as a way to discuss the pacemaker's design. Appropriate numerical simulations are provided.

## 2. Bounded, periodic, eventually periodic and almost periodic solutions

In this section we shall prove that the system admits oscillating solutions. The existence of an eventually periodic solution is proved for the first time. The assertions about the discontinuous periodic and almost periodic solutions are specified versions of general theorems of the theory of impulsive differential equations [25,28,29].

First, let us define the solutions of system (1).

A left continuous function  $P(t) : R \rightarrow R^{m+1}$  is in the set  $\mathcal{PC}(R)$ , if it is continuous on  $R$ , except at the points  $\theta_i, i \in Z$ , where its first coordinate may have discontinuities of the first kind, and is left continuous.

A function  $P(t) \in \mathcal{PC}(R)$  is a solution of (1) if:

- (1) the differential equation is satisfied for  $P(t), t \in R$ , except at the points  $\theta_i, i \in Z$ , where it holds for the left derivative of  $P(t)$ ;
- (2) the jump equation is satisfied by  $P_0(t)$  for every  $i \in Z$ .

We shall also need the following set of functions.

A left continuous function  $P(t)$  is in the set of functions  $\mathcal{PC}(R_+)$ ,  $R_+ = [t_0, \infty), t_0 \in R$ , if it is continuous on  $[t_0, \infty)$  except at the points  $\theta_i, t_0 \leq \theta_i < \infty$ , where its first coordinate may have discontinuities of the first kind.

A solution  $P(t) = (P_0(t), P_1(t), \dots, P_m(t))$  of (1) on  $[t_0, \infty)$  is a function in  $\mathcal{PC}(R_+)$  such that:

- (1) the differential equation is satisfied for  $P(t)$  on  $R_+$ , except at the points  $\theta_i, \theta_i > t_0$ , where it holds for the left derivative of  $P(t)$ ;
- (3) the jump equation is satisfied by  $P_0(t)$  for every  $i, \theta_i > t_0$ .

One can easily show, using the theory of impulsive differential equations [28,29], that under the aforementioned conditions a solution  $P(t, t_0, \pi_0), (t_0, \pi_0) \in R \times R^{m+1}, \pi_0 = (\pi_0^0, \pi_0^1, \dots, \pi_0^m)$ , of (1) exists and is unique on  $[t_0, \infty)$ .

One can also find that the solution satisfies the following integral equation:

$$\begin{aligned}
 P_0(t) &= e^{-k_0(t-t_0)}\pi_0^0 - \int_{t_0}^t e^{-k_0(t-s)}g_0(P_0(s) - P_1(s), P_0(s) - P_2(s), \dots, P_0(s) - P_m(s))ds \\
 &\quad + \sum_{t_0 \leq \theta_i < t} e^{-k_0(t-\theta_i)}(I_0 + J_0(P_0(\theta_i))), \\
 P_i(t) &= e^{-k_i(t-t_0)}\pi_0^i + \int_{t_0}^t e^{-k_i(t-s)}g_i(P_0(s) - P_i(s))ds, \quad i = \overline{1, m}.
 \end{aligned}
 \tag{6}$$

We say that a sequence  $\theta_i$  has the  $p$ -property,  $p \in N$ , if  $\theta_{i+p} = \theta_i + p\omega$  for all integers  $i$ . Moreover, we say that the sequence has the  $p$ -property eventually, if  $\theta_{i+p} - \theta_i \rightarrow p\omega$  as  $i \rightarrow \infty$ .

Consider a strictly ordered sequence of real numbers  $t_i, i \in Z$ . Denote  $t_j^i = t_{i+j} - t_i, i, j \in Z$ , and define the sequences  $\{t_j^i\}_i, i, j \in Z$ . Following [27,29], we call this family of sequences equipotentially almost periodic if for an arbitrary positive  $\epsilon$  there exists a relatively dense set of  $\epsilon$ -almost periods, common for all sequences  $\{t_j^i\}_i, j \in Z$ .

It is proved in [25] (see also [29]) that the family  $\theta_j^i, i, j \in Z$ , is equipotentially almost periodic if the sequence  $\theta_i - i\omega, i \in Z$ , is almost periodic. That is, if we chose an almost periodic sequence  $\xi_i, i \in Z$ , such that  $0 \leq \xi_i < \omega, i \in Z$ , then the sequence  $\theta_i$ , where  $\theta_i = i\omega + \xi_i, i \in Z$ , is equipotentially almost periodic.

Let  $[a, \hat{b}]$  be an oriented interval, that is  $[a, \hat{b}] = [a, b]$ , if  $a \leq b$ , and  $[a, \hat{b}] = [b, a]$ , if  $a > b$ .

We say that a function  $\phi(t)$  in  $\mathcal{PC}(R)$  is eventually  $p\omega$ -periodic if the sequence of discontinuities  $\theta_i$  has the  $p$ -property eventually, and

$$\lim_{t \rightarrow \infty} [\phi(t + p\omega) - \phi(t)] = 0,
 \tag{7}$$

for all  $t$  such that  $t \notin [\theta_i, \hat{\theta}_{i+p} - p\omega] \cap [\theta_{i+1}, \hat{\theta}_{i+p+1} - p\omega]$ .

Next, we shall give a definition from [27,29] which is slightly modified for our case.

A function  $\phi(t)$  in  $\mathcal{PC}(R)$  is a discontinuous almost periodic (d.a.p.) function if:

- (a) the function is uniformly continuous on the union of all intervals of the continuity  $(\theta_i, \theta_{i+1}), i \in Z$ ;
- (b) for every positive  $\epsilon$  there exists a relatively dense set  $\Gamma$  of almost periods such that if  $\gamma \in \Gamma$ , then  $\|\phi(t + \gamma) - \phi(t)\| < \epsilon$  for all  $t \in R$  such that  $|t - \theta_i| > \epsilon, i \in Z$ .

We may assume that

$$(C6) \quad L(l_0, l_1, \dots, l_m, l_j) = \sqrt{[\frac{l_0\sqrt{2m}}{k_0} + \frac{l_j e^{k_0\omega}}{1-e^{-k_0\omega}}]^2 + \sum_{i=1}^m \frac{l_i^2}{k_i^2}} < 1.$$

**Theorem 2.1.** *If conditions (C1)–(C6) are fulfilled, then there exists a unique solution of (1) bounded on  $R$  and:*

- 1. the bounded solution has the period  $p\omega$  if the sequence  $\theta_i$  has the  $p$ -property for a fixed  $p \in N$ ;
- 2. the bounded solution is an eventually  $p\omega$ -periodic function if the sequence  $\theta_i$  has the  $p$ -property eventually for a fixed  $p \in N$ ;
- 3. the bounded solution is a d.a.p. function if the sequence  $\theta_i - i\omega, i \in Z$ , is almost periodic.

**Proof.** We shall use the norm  $|\phi|_0 = \sup_R |\phi(t)|$  for scalar valued functions defined on  $R$ , and  $\|\phi\|_0 = \sup_R \|\phi(t)\|$  for vector-valued functions. Denote by  $\Omega$  a subset of  $\mathcal{P}\mathcal{C}(R)$  such that if  $\phi(t) \in \Omega$ ,  $\phi = (\phi_0, \phi_1, \dots, \phi_m)$ , then  $|\phi_0|_0 \leq \left(\frac{m_0}{k_0} + \frac{m_j e^{k_0 \omega}}{1 - e^{-k_0 \omega}}\right)$ ,  $|\phi_i|_0 \leq \frac{m_i}{k_i}$ ,  $i = \overline{1, m}$ .

One can easily verify that (1) has a bounded solution  $P(t)$  if and only if  $P(t)$  is a bounded on  $R$  solution of the following integral equation:

$$\begin{aligned}
 P_0(t) &= - \int_{-\infty}^t e^{-k_0(t-s)} g_0(P_0(s) - P_1(s), \dots, P_0(s) - P_m(s)) ds + \sum_{\theta_i < t} e^{-k_0(t-\theta_i)} (I_0 + J_0(P_0(\theta_i))), \\
 P_i(t) &= \int_{-\infty}^t e^{-k_i(t-s)} g_i(P_0(s) - P_i(s)) ds, \quad i = \overline{1, m}.
 \end{aligned}
 \tag{8}$$

Define on  $\Omega$  an operator  $T$  such that

$$\begin{aligned}
 (T\phi)_0(t) &= - \int_{-\infty}^t e^{-k_0(t-s)} g_0(\phi_0(s) - \phi_1(s), \dots, \phi_0(s) - \phi_m(s)) ds + \sum_{\theta_i < t} e^{-k_0(t-\theta_i)} (I_0 + J_0(\phi_0(\theta_i))), \\
 (T\phi)_i(t) &= \int_{-\infty}^t e^{-k_i(t-s)} g_i(\phi_0(s) - \phi_i(s)) ds, \quad i = \overline{1, m}.
 \end{aligned}
 \tag{9}$$

We can verify that  $T : \Omega \rightarrow \Omega$ . Take  $\phi, \psi \in \Omega$ . One can obtain that

$$\|T\phi - T\psi\|_0 \leq L(l_0, l_1, \dots, l_m, l_j) \|\phi - \psi\|_0,$$

and, consequently, condition (C6) implies that the operator is contractive. It is not difficult to check that the space  $\Omega$  is complete. Thus, there exists a unique solution of (1) from  $\Omega$ .

Assume now that the sequence  $\theta_i$  has the  $p$ -property. Then, using the standard method, starting with a  $p\omega$ -periodic function from  $\Omega$ , we can, using the operator  $T$ , construct a sequence of  $p\omega$ -periodic approximations of the bounded solution, which is also  $p\omega$ -periodic.

Consider the case where  $\theta_i$  has the  $p$ -property eventually. In order to prove assertion (2) of the theorem, it is sufficient, according to the above discussion of boundedness of the solution, to prove that  $T\phi$  is eventually  $p\omega$ -periodic, if  $\phi$  is an eventually  $p\omega$ -periodic function.

Fix a positive number  $\epsilon$ . Since  $\theta_i$  has the  $p$ -property eventually, and  $\phi$  is eventually  $p\omega$ -periodic function, one can find positive numbers  $T_2 > T_1$  such that:

1. if  $t \geq T_2$  and  $\theta_i + \epsilon < t < \theta_{i+1} - \epsilon$  for some  $i \in Z$ , then  $\theta_{i+p} < t + p\omega < \theta_{i+1+p}$  and  $\|\phi(t + p\omega) - \phi(t)\| < \epsilon$ ;
2.  $2e^{-k_0(T_2-T_1)} \left[ \frac{m_0}{k_0} + \frac{m_j e^{k_0 \omega}}{1 - e^{-k_0 \omega}} \right] < \epsilon$ ,  $2e^{-k_0(T_2-T_1)} \frac{2m_i}{k_i} < \epsilon$ .

We have that

$$\begin{aligned}
 & |(T\phi)_0(t + p\omega) - (T\phi)_0(t)| \\
 &= \left| - \int_{-\infty}^{t+p\omega} e^{-k_0(t+p\omega-s)} g_0(\phi_0(s) - \phi_1(s), \dots, \phi_0(s) - \phi_m(s)) ds + \sum_{\theta_i < t+p\omega} e^{-k_0(t+p\omega-\theta_i)} (I_0 + J_0(\phi_0(\theta_i))) \right. \\
 &\quad \left. + \int_{-\infty}^t e^{-k_0(t-s)} g_0(\phi_0(s) - \phi_1(s), \dots, \phi_0(s) - \phi_m(s)) ds - \sum_{\theta_i < t} e^{-k_0(t-\theta_i)} (I_0 + J_0(\phi_0(\theta_i))) \right| \\
 &\leq \int_{-\infty}^{T_1} e^{-k_0(t-s)} 2m_0 ds + \sum_{\theta_i < T_1} e^{-k_0(t-\theta_i)} 2m_j + \int_{T_1}^t e^{-k_0(t-s)} l_0 \sqrt{2m} \|\phi(s + p\omega) - \phi(s)\| ds \\
 &\quad + \sum_{T_1 \leq \theta_i < t} e^{-k_0(t-\theta_i)} l_j \|\phi(\theta_{i+p}) - \phi(\theta_i)\| + \sum_{\theta_i < t} \int_{\theta_i - \epsilon}^{\theta_i + \epsilon} e^{-k_0(t-s)} 2m_0 ds \\
 &\leq \epsilon \left[ 1 + \frac{l_0 \sqrt{2m}}{k_0} + \frac{e^{\kappa \omega}}{1 - e^{-\kappa \omega}} (l_j + 4m_0 e^{k_0 \epsilon}) \right].
 \end{aligned}$$

Similarly, one can obtain that

$$|(T\phi)_i(t + p\omega) - (T\phi)_i(t)| \leq \epsilon \left[ 1 + \frac{l_i}{k_i} + 4m_i e^{k_0 \epsilon} \frac{e^{\kappa \omega}}{1 - e^{-\kappa \omega}} \right], \quad i = \overline{1, m}.$$

That is, there exists a unique eventually  $p\omega$ -periodic solution of (1).

Now assume that the sequence  $\theta_i - i\omega$  is almost periodic. From the previous discussion we see that to prove the existence of a d.a.p. solution we need only to verify that the function  $T\phi$  is d.a.p. if  $\phi$  is a d.a.p. function. By Lemma 35 of [29] (see also [25]), for a given positive  $\epsilon$  there exist a real number  $\nu$ ,  $0 < \nu < \epsilon$ , and relatively dense sets of real numbers  $\Gamma$  and integers  $H$ , such that:

1.  $\|\phi(t + \gamma) - \phi(t)\| < \epsilon$ ;
2.  $|\theta_k^h - \gamma| < \nu$ ,  $k \in Z$ ,  $h \in H$ ,  $\gamma \in \Gamma$ .

Take the real number  $\nu$  such that  $\|\phi(t_1) - \phi(t_2)\| < \epsilon$  if  $t_1, t_2$  belong to the same interval of continuity of the function  $\phi(t)$  and  $|t_1 - t_2| < \nu$ . We have that if  $|t - \theta_i| > \epsilon$ ,  $i \in Z$ , then

$$\begin{aligned} & |(T\phi)_0(t + \gamma) - (T\phi)_0(t)| \\ &= \left| \int_{-\infty}^{t+\gamma} e^{-k_0(t+\gamma-s)} g_0(\phi_0(s) - \phi_1(s), \dots, \phi_0(s) - \phi_m(s)) ds + \sum_{\theta_i < t+\gamma} e^{-k_0(t+\gamma-\theta_i)} (I_0 + J_0(\phi(\theta_i))) \right. \\ &\quad \left. - \int_{-\infty}^t e^{-k_0(t-s)} g_0(\phi_0(s) - \phi_1(s), \dots, \phi_0(s) - \phi_m(s)) ds - \sum_{\theta_i < t} e^{-k_0(t-\theta_i)} (I_0 + J_0(\phi(\theta_i))) \right| \\ &\leq \int_{-\infty}^t e^{-k_0(t-s)} l_0 \sqrt{2m} \|\phi(s + \gamma) - \phi(s)\| ds + \sum_{\theta_i < t} e^{-k_0(t-\theta_i)} l_j \|\phi(\theta_{i+h}) - \phi(\theta_i)\| + \sum_{\theta_i < t} \int_{\theta_i-\epsilon}^{\theta_i+\epsilon} e^{-k_0(t-s)} 2m_0 ds \\ &\leq \epsilon \left[ \frac{l_0 \sqrt{2m}}{k_0} + \frac{2e^{k_0\omega}}{1 - e^{-k_0\omega}} (l_j + 4m_0 e^{k_0\epsilon}) \right] \end{aligned}$$

and

$$|(T\phi)_i(t + \gamma) - (T\phi)_i(t)| \leq \epsilon \left[ \frac{l_i}{k_i} + 4m_i e^{k_i\epsilon} \frac{e^{k_i\omega}}{1 - e^{-k_i\omega}} \right], \quad i = \overline{1, m}.$$

That is,  $T\phi$  is a d.a.p. function. The theorem is proved.  $\square$

### 3. Stability and positiveness

In this section we show that the bounded solution is exponentially stable, and that every coordinate of the solution is separated from zero by some positive number. Moreover, the first coordinate of the solution, which is the value of the systemic arterial pressure, is higher than any other pressure value. Some of the results of this section were discussed in [30].

Let us denote the solution bounded on  $R$  as  $\xi(t) = (\xi_0(t), \xi_1(t), \dots, \xi_m(t))$ . Next, we find the conditions for the positiveness of this solution. Assume additionally that

$$(C8) \quad \frac{m_0}{k_0} + \frac{m_i}{k_i} < I_0 \frac{e^{-k_0\omega}}{1 - e^{-k_0\omega}}, \quad i = \overline{1, m}.$$

Then, we obtain that

$$\xi_0(t) \geq I_0 \frac{e^{-k_0\omega}}{1 - e^{-k_0\omega}} - \frac{m_0}{k_0} > 0, \quad t \in R,$$

and

$$|\xi_i(t)| \leq \frac{m_i}{k_i}, \quad t \in R, \quad i = \overline{1, m}.$$

Hence,

$$\xi_0(t) - \xi_i(t) \geq I_0 \frac{e^{-k_0\omega}}{1 - e^{-k_0\omega}} - \frac{m_0}{k_0} - \frac{m_i}{k_i} = \delta > 0, \quad t \in R, \quad i = \overline{1, m}, \quad (10)$$

and using (8) again one can see that

$$\xi_i(t) \geq \frac{\bar{g}_i}{k_i} > 0, \quad t \in R, \quad i = \overline{1, m},$$

where  $\bar{g}_i$  is the minimal value of the function  $g_i(z)$  for  $z \in \left[ \delta, \frac{m_0}{k_0} + \frac{m_l e^{k_0\omega}}{1 - e^{-k_0\omega}} + \frac{m_i}{k_i} \right]$ .

The following assertion is proved.

**Theorem 3.1.** Assume that conditions (C1)–(C8) are valid. Then for the bounded solution  $\xi(t)$  of (1) there exist positive constants  $\nu_j$ ,  $j = \overline{1, m}$ ,  $\mu_i$ ,  $i = \overline{0, m+1}$  such that the inequalities  $\xi_0(t) - \xi_i(t) > \nu_j$ ,  $\xi_i(t) \geq \mu_i$  are valid for all  $i, j$ , and  $t \in R$ .

Let us give the definition of uniform exponential stability of the solution. Denote  $P(t) = P(t, t_0, P_0)$ , a solution of (1).

**Definition 3.1.** The solution  $\xi(t)$  is called uniformly exponentially stable if there exists a number  $\alpha \in \mathbb{R}, \alpha > 0$ , such that for every  $\epsilon > 0$  there exists a number  $\delta = \delta(\epsilon)$  such that the inequality  $\|P(t) - \xi(t)\| < \epsilon \exp(-\alpha(t - t_0)), \forall t \geq t_0$ , holds, if  $\|P_0 - \xi(t_0)\| < \delta$ .

Fix a positive number  $\sigma, 0 < \sigma < \min_{i=\overline{0,m}} k_i$ , denote  $m(l_0, l_1, \dots, l_m, l_j) = 1 - \max \left\{ \frac{l_0 \sqrt{2m}}{k_0 - \sigma} + \frac{l_j e^{(k_0 - \sigma)\omega}}{1 - e^{-(k_0 - \sigma)\omega}}, \frac{2l_i}{k_i - \sigma}, i = \overline{0, m} \right\}$ , and assume that the Lipschitz coefficients are small so that

$$(C9) \quad m(l_0, l_1, \dots, l_m, l_j) > 0.$$

**Theorem 3.2.** Assume that conditions (C1)–(C7) and (C9) are valid. Then the bounded solution  $\xi(t)$  of (1) is uniformly exponentially stable.

**Proof.** One can see that  $v(t) = P(t) - \xi(t), v = (v_0, v_1, \dots, v_m)$ , is a solution of the equation

$$\begin{aligned} \frac{dv_0}{dt} &= -k_0 v_0 + w_0(v), \\ \frac{dv_i}{dt} &= -k_i v_i + w_i(v_0, v_i), \quad i = \overline{1, m}, t \neq \theta_j, \\ \Delta v_0|_{t=\theta_j} &= u_0(v_0) \end{aligned} \tag{11}$$

where functions  $w_i, i = \overline{0, m}$ , and  $u_0$  satisfy the following conditions:

$$\begin{aligned} |w_0(v)| &\leq l_0 \sqrt{2m} \|v\|; \\ |w_i(v_i, v_0)| &\leq l_i (|v_i| + |v_0|), \quad i \in Z; \\ |u_0(v_0)| &\leq l_j |v_0|. \end{aligned}$$

Thus, the problem of the stability of  $\xi_0(t)$  is reduced to the stability of the zero solution of (11). Fix  $\epsilon > 0$  and denote  $K = K(l_0, l_1, \dots, l_m, l_j, \delta) = \frac{\delta}{m(l_0, l_1, \dots, l_m, l_j)}$ , where  $\delta \in \mathbb{R}, \delta > 0$ , and take  $\delta$  so small that  $K(l_0, l_1, \dots, l_m, l_j, \delta) < \epsilon$ . Assume, without loss of generality, that  $t_0 = 0$ . Let  $v(t, v_0)$  be a solution of (11) such that  $v(0, v_0) = v_0 = (v^0, v^1, \dots, v^m)$ .

Denote by  $\Psi$  a set of all functions  $\psi = (\psi_0, \psi_1, \psi_2, \dots, \psi_m)$ , defined on  $R_+ = [0, \infty)$ , such that: (1)  $\psi(0) = v_0$ ; (2)  $\psi(t) \in \mathcal{PC}(R_+)$ ; (3)  $|\psi_i(t)| \leq K \exp(-\sigma t)$  if  $t \geq 0, i = \overline{0, m}$ . Define an operator  $\Pi$  on  $\Psi$  such that, if  $\psi \in \Psi$ , then

$$\begin{aligned} (\Pi \psi)_0 &= e^{-k_0 t} v^0 + \int_0^t e^{-k_0(t-s)} w_0(\psi(s)) ds + \sum_{0 \leq \theta_i < t} e^{-k_0(t-\theta_i)} u_0(v_0(\theta_i)), \\ (\Pi \psi)_i &= e^{-k_i t} v^i + \int_0^t e^{-k_i(t-s)} w_i(v_0(s), v_i(s)) ds, \quad i = \overline{1, m}. \end{aligned} \tag{12}$$

We shall show that  $\Pi : \Psi \rightarrow \Psi$ . Indeed, for  $t \geq 0$  it is true that

$$\begin{aligned} |(\Pi \psi)_0| &\leq \exp(-k_0 t) \delta + \int_0^t \exp(-k_0(t-s)) l_0 \sqrt{2m} K \exp(-\sigma s) ds \\ &+ \sum_{0 \leq \theta_i < t} e^{-k_0(t-\theta_i)} l_j K \exp(-\sigma \theta_i) \leq \exp(-\sigma t) \left[ \delta + K \left( \frac{l_0 \sqrt{2m}}{k_0 - \sigma} + \frac{l_j e^{(k_0 - \sigma)\omega}}{1 - e^{-(k_0 - \sigma)\omega}} \right) \right] \leq K \exp(-\sigma t). \end{aligned}$$

Similarly,

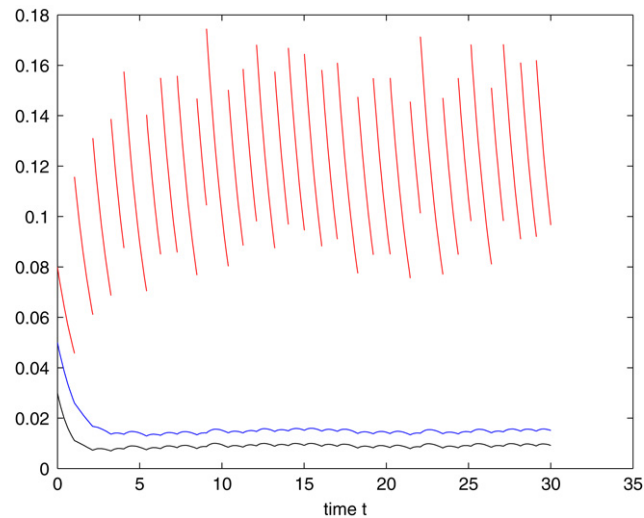
$$|(\Pi \psi)_i| \leq \exp(-\sigma t) \left[ \delta + 2K \frac{l_i}{k_i - \sigma} \right] \leq K \exp(-\sigma t), \quad i = \overline{1, m}.$$

Let  $\psi_1, \psi_2 \in \Psi$ . Then, we have that

$$\|\Pi \psi_1 - \Pi \psi_2\| \leq L(l_0, l_1, \dots, l_m, l_j) \sup_{t \geq 0} \|\psi_1 - \psi_2\|,$$

where the coefficient is described in (C7). Using the contraction mapping argument one can conclude that there exists a unique fixed point  $v(t, v_0)$  of the operator  $\Pi : \Psi \rightarrow \Psi$  which is a solution of (11). The theorem is proved.  $\square$

From (10) it follows that the bounded solution has the first coordinate larger than any other coordinate, and the attractiveness of the solution implies that any other solution in its neighborhood eventually has the first coordinate as its largest coordinate. Now, we can make some physiological conclusions: the normal state of the distribution of blood pressure is such that systemic arterial pressure is higher than any other pressure. The initial state may be odd, that is, the



**Fig. 1.** The graph of the first coordinate  $P_0(t)$  of the solution is shown in red, of the second coordinate  $P_1(t)$  in blue, and the third coordinate  $P_2(t)$  in black. The initial value of the first coordinate is larger than that of the second and third coordinates, and one can easily see from the graphs that our theoretical predictions are in full accordance with the properties represented by the figure: the solutions are separated from zero by some positive numbers, coordinate  $P_0(t)$  is always larger than  $P_1(t)$ ,  $P_2(t)$ , and we may suppose that the solution is approaching the discontinuous almost periodic solution of the system, as time increases. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

initial systemic arterial pressure may be lower than the pressure in a neighboring compartment, but after a certain period of time the state becomes normal. We may call this period the time of stabilization of a solution.

In order to carry out numerical simulations of the obtained theoretical results we consider the following equation:

$$\begin{aligned}
 P'_0 &= -0.5P_0 - 0.1(P_0 - P_1), \\
 P'_1 &= -0.7P_1 + 0.1(P_0 - P_1), \\
 P'_2 &= -1.2P_2 + 0.1(P_0 - P_2), \\
 \Delta P_0|_{t=\theta_i} &= 0.07,
 \end{aligned} \tag{13}$$

where  $\theta_i = i + \frac{1}{4}|\sin(i) - \sin(\sqrt{2}i)|$ . It is proved in [25] that the sequence  $\frac{1}{4}|\sin(i) - \sin(\sqrt{2}i)|$  is almost periodic. The theoretical part of the paper implies that system (13) has a discontinuous almost periodic solution.

As can be seen from Fig. 1, the solution  $P(t)$ ,  $P(0) = (0.08, 0.05, 0.03)$ , is approaching the almost periodic solution as time increases.

Fig. 2 shows that there exists a time of stabilization of a solution with initial value  $P(0) = (0.03, 0.5, 0.2)$  so that the first coordinate is smaller than the second and third ones at the initial moment  $t = 0$ .

#### 4. Conclusion

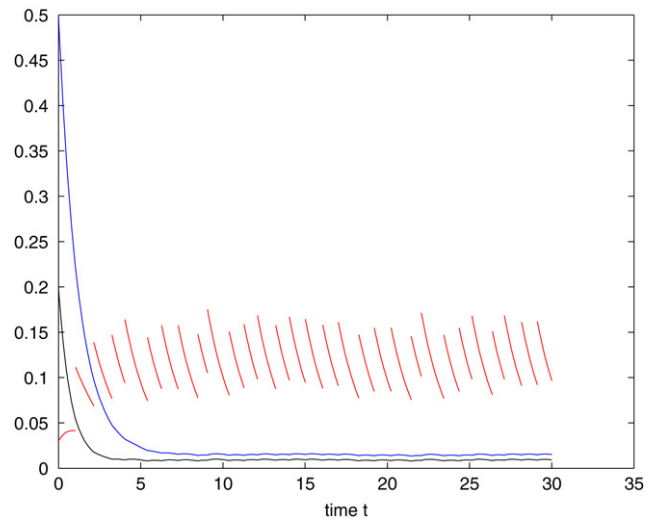
As follows from the preceding discussion, if system (1) satisfies certain conditions, then the systemic arterial pressure and the blood pressure in compartments oscillate, remaining positive. The shape of the oscillations depends on the behavior of the moments when contraction of the left ventricle takes place. The oscillations are asymptotically stable. That is, they do not react significantly to external perturbations.

From the results of our paper one can see that the strike type influence of the left ventricle contraction on the systemic arterial pressure is “softened” when it reaches the peripheral compartments through the connections of the system, so that the compartments’ oscillations are continuous. On the other hand, this influence is sufficiently large to sustain the positiveness of all coordinates and keep the aortic pressure higher than in any other compartment.

We believe that the proposed model can be developed further, using experimental results as well as the methods of the theories of functional differential equations, discrete equations, and so on, to obtain additional features of the regular behavior of blood pressure, as well as to investigate irregular (chaotic) processes in the system. The problem of the period-doubling and intermittency routes to the chaos can serve as an important theoretical tool in the studies of the arrhythmia processes.

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**Fig. 2.** We can see that despite the “odd” relation between the coordinates at the initial moment, the normal state is eventually achieved when coordinate  $P_0(t)$  is larger than  $P_1(t)$  and  $P_2(t)$ . The stabilization time of the solution is no more than 5 units. Again, we have the consistency of the theoretical result with the simulation observations.

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