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A MATHEMATICAL CARDIOVASCULAR MODEL WITH PULSATILE AND NON-PULSATILE COMPONENTS

AURELIO DE LOS REYES V AND FRANZ KAPPEL

Abstract. In this study, two existing mathematical cardiovascular models, a non-pulsatile global model and a simplified pulsatile left heart model were investigated, modified and combined. A global lumped compartment cardiovascular model was developed that could predict the pressures in the systemic and pulmonary circulation, and specifically the pulsatile pressures in the the finger arteries where real-time measurements can be obtained. Linking the the average flow with a pulsatile flow is the main difficulty. The left ventricle is assumed to be the source of pulse waves in the system. Modifications were made in the ventricular elastance to model the variations of the stiffness of heart muscles during stress or exercise state. The systemic aorta compartment is added to indicate pressure changes detected by the baroreceptors acting as a control mechanism in the system. Parameters were estimated to simulate an average normal blood pressures during rest and exercise conditions.

Introduction

In Kappel and Peer (1993) [4], a cardiovascular mathematical model has been developed for the response of the system to a short term submaximal workload. It is based on the four compartment model by Grodin's mechanical part of the cardiovascular system. It considers all the essential subsystems such as systemic and pulmonary circulation, left and right ventricles, baroreceptor loop, etc. Included in the model are the basic mechanisms such as Starling's law of the heart, the Bowditch effect and autoregulation in the peripheral regions. The basic control autoregulatory mechanisms were constructed assuming that the regulation is optimal with respect to a cost criterion. The model provided a satisfactory description of the overall reaction of the cardiovascular-respiratory system under a constant ergometric workload imposed on a test person on a bicycle-ergometer. Further studies have been done to include the respiratory system, see Timischl (1998) [13]. The model was also extended and used to describe the response of the cardiovascular-respiratory system under orthostatic stress condition, see for

Key words and phrases. pulsatile cardiovascular model, left ventricular elastance, baroreceptor loop, regulation of the cardiovascular system, stabilizing control.

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example Fink et al. (2004) [5] and Kappel et al. (2007) [3].

A simple lumped parameter cardiovascular model was developed by Olufsen et. al (2009) [10]. The model utilizes a minimal cardiovascular structure to close the circulatory loop. It consists of two arterial compartments and two venous compartments combining vessels in the body and the brain, and a heart compartment representing the left ventricle. The model was used to analyze cerebral blood flow velocity and finger blood pressure measurements during orthostatic stress (sit-to-stand).

The aim of this study is to construct a global cardiovascular model combining pulsatile and non-pulsatile components that predicts the pressures in the systemic and pulmonary circulation, and specifically the pulsatile pressures in the the finger arteries where real-time measurements can be obtained. Basically, a pulsatile left heart model is adapted from the works of Olufsen, et al. (2009) [10] and is integrated in the global non-pulsatile model by Kappel and Peer (1993) [4].

1. Modeling the Cardiovascular System

The cardiovascular model presented here is depicted in Figure 1. It includes arterial and venous pulmonary, left and right ventricles, systemic aorta, finger arteries, and arterial and venous systemic compartments. In the compartments, pressures and compliances are denoted by P and c, respectively. The resistances are denoted by R. In the right ventricle, Q stands for the cardiac output and S for the contractility. The subscripts stand mainly for the name of the compartments. That is, $ap, vp, lv, sa, fa, as, vs$, and rv correspond respectively to the arterial pulmonary, venous pulmonary, left ventricle, systemic aorta, finger arteries, arterial systemic, venous systemic and right ventricle compartments. Also, subscripts mv and av denote the mitral valve, respectively aortic valve. Moreover, sa_1 and sa_2 as subscripts for R (i.e., R_{sa_1} and R_{sa_2}) correspond to two different resistances connecting the systemic aorta to finger arteries and systemic aorta to arterial systemic compartment, respectively.

Figure 2 shows the combined cardiovascular model depicting the parts of (Kappel) non-pulsatile and (Olufsen) pulsatile left heart model including the modifications made. The systemic aorta compartment is added for it is the site of the baroreceptor loop. A finger artery compartment is included to reflect measurements of pulsatile pressures.

The model is mathematically formulated in terms of an electric circuit analog. The blood pressure difference plays the role of voltage, the blood flow plays the role of current, the stressed volume plays the role of an electric charge, the compliances of the blood vessels play the role of capacitors,

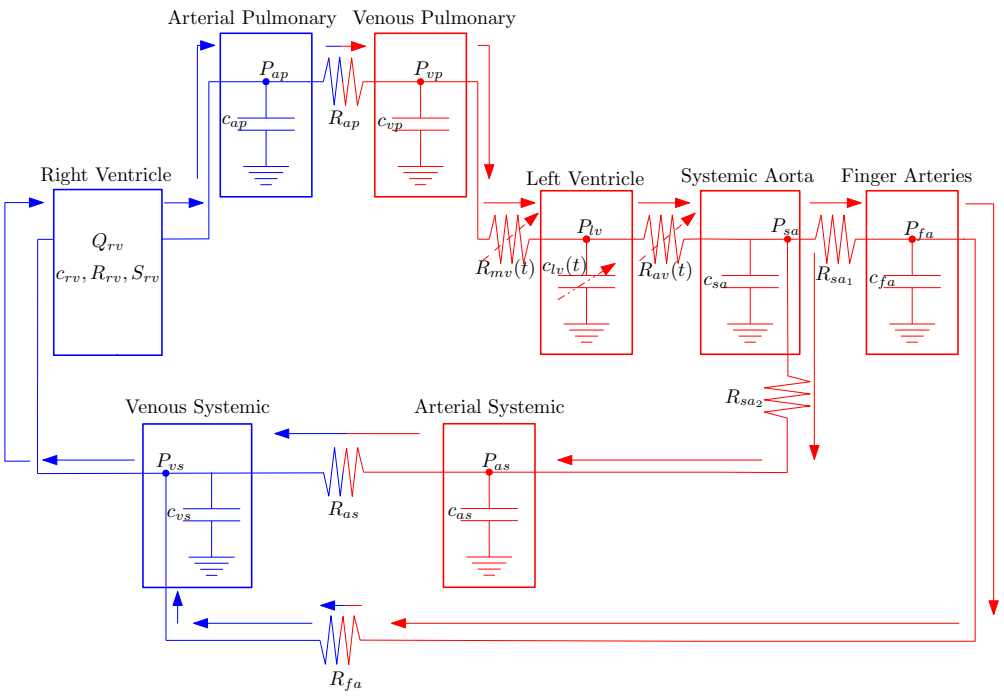


FIGURE 1. The electric analog of the global pulsatile model depicting the blood flow in the pulmonary and systemic circuit including the systemic aorta and finger arteries compartment.

and the resistors are the same in both analogies. The stressed volume in a compartment is the difference between total and unstressed volume (i.e., the volume in a compartment at zero transmural pressure). Thus, stressed volume is the additional volume added to the unstressed volume when positive transmural pressure causes a stretching of the vascular walls.

The basic assumptions of the modeling process are given as follows:

- The vessels in the arterial and venous parts of the systemic or pulmonary circuits are lumped together as a single compartment for each of these parts. Each compartment is considered as a vessel with compliant walls in which its volume is characterized by the pressure in the vessel. Hence, these vessels are called *compliance vessels*.

- The systemic peripheral or pulmonary peripheral region is composed of capillaries, arterioles, and venules which are lumped together into a single vessel. These vessels are considered to be pure resistances to blood flow and characterized only by flow through the vessel. Therefore, these vessels are called *resistance vessels*.

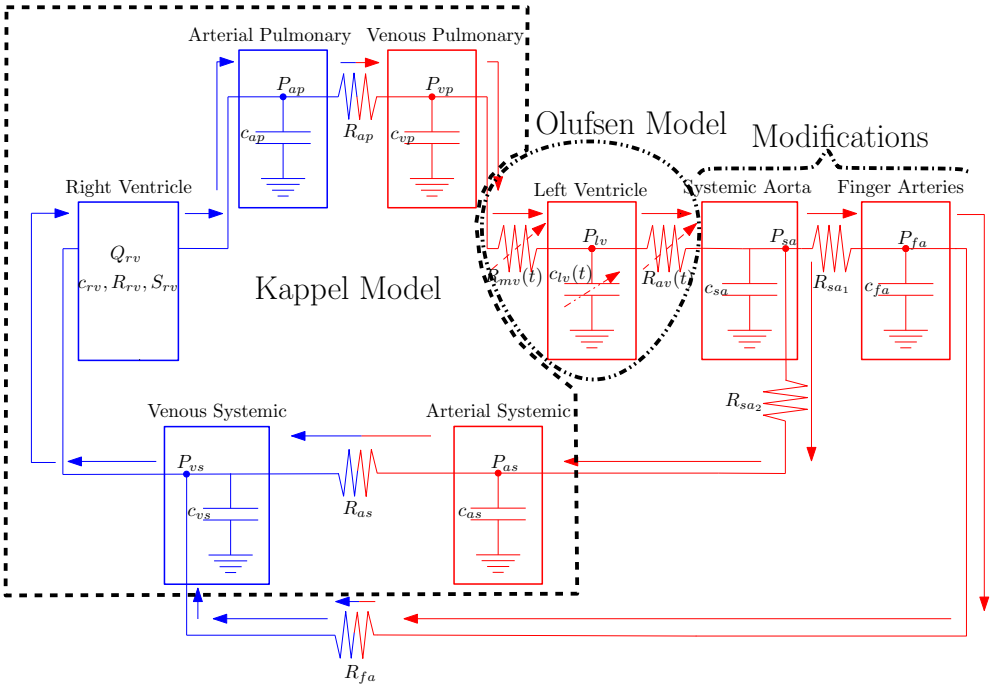


FIGURE 2. The cardiovascular model showing the (Kappel) non-pulsatile global model, (Olufsen) pulsatile left heart model and the model modifications.

- The atria are not represented in the model. It is assumed that the right atrium is part of the venous systemic compartment and the left atrium is part of the venous pulmonary compartment.

1.1. **Blood Volume in the Compartment.** For each compartment, we associate the pressure $P(t)$ and the volume $V(t)$ of the blood. Assuming linear relationship between the transmural pressure and the total volume, we have

$$V(t) = cP(t), \tag{1}$$

where c represents the compliance of the compartment which is assumed to be constant. In this case, the unstressed volume is zero and the stressed volume equals the total volume in the compartment. Generally, the total volume in the compartment can be expressed as

$$V(t) = cP(t) + V_u, \tag{2}$$

where V_u denotes the unstressed volume. A more physiologically realistic approach is to consider that the relation between pressure and total volume is $V = f(P)$, which is nonlinear. In this case, the unstressed volume is given by $V_u = f(0)$ and the compliance, $c(P)$ at pressure P is $f'(P)$ assuming

smoothness on f.

For simplicity, we used (2) assuming $V_u = 0$ in most of the compartments except in the left ventricle. This is mainly to avoid introduction of additional parameters which cannot be observed directly. This however introduces a modeling error that needs to be considered for further investigations.

1.2. **Blood Flow and Mass Balance Equations.** The blood flow is described in terms of the mass balance equations, that is, the rate of change for the blood volume $V(t)$ in a compartment is the difference between the flow into and out of the compartment. For a generic compartment, we have

$$\frac{d}{dt}(cP(t)) \;=\; F_{in} - F_{out}, \tag{3}$$

where c denotes the compliance, $P(t)$ the blood pressure in the compartment and F_{in} and F_{out} are the blood flows into and out of the compartment, respectively. The loss term in the compartment is the gain term in the adjacent compartment. Also, the flow F between two compartments can be described by Ohm's law. That is, it depends on the pressure difference between adjacent compartments and on the resistances R against blood flow. Thus we have the relation

$$F \;=\; \frac{1}{R}\left(P_1 - P_2\right), \tag{4}$$

where P_1 and P_2 are pressures from adjacent generic compartments 1 and 2, respectively.

The blood flow out of the venous systemic compartment is the cardiac output $Q_{rv}(t)$ which is the blood flow into the arterial pulmonary. The cardiac output generated by the right ventricle is

$$Q_{rv}(t) \;=\; HV_{str}(t), \tag{5}$$

where H is the heart rate and $V_{str}(t)$ is the stroke volume, that is the blood volume ejected by one beat of the ventricle. Following the discussions given in Batzel et. al (2007) [1], the cardiac output of the right ventricle can be expressed as

$$Q_{rv}(t) \;=\; H\frac{c_{rv}P_{vp}(t)a_{rv}(H)f(S_{rv}(t),P_{ap}(t))}{a_{rv}(H)P_{ap}(t)+k_{rv}(H)f(S_{rv}(t),P_{ap}(t))}\;. \tag{6}$$

In our previous simulations, we used the function $f(S_{rv}(t), P_{ap}(t))$ be given by

$$f(S_{rv}(t),P_{ap}(t)) \;= \tag{7}$$
$$0.5\left(S_r(t)+P_{ap}(t)\right) - 0.5\left(\left(P_{ap}(t)-S_r(t)\right)+0.01\right)^{1/2}\;.$$

This function is used by Timischl (1998) [13]. This function chooses the minimum value between S_{rv} and P_{ap} at a specific time point t. Recently,

we approximate the $min(S_r, P_{ap})$ (t is omitted for brevity) by the smooth function

$$f_\epsilon(S_r, P_{ap}) = \begin{cases} S_r & \text{if } 0 \leq S_r \leq (1-\epsilon)P_{ap}, \\ -\dfrac{1}{4\epsilon P_{ap}} S_r^2 + \dfrac{1+\epsilon}{2\epsilon} S_r - \dfrac{(1-\epsilon)^2}{4\epsilon} P_{ap} & \text{if } (1-\epsilon)P_{ap} < S_r \leq (1+\epsilon)P_{ap}, \\ P_{ap} & \text{if } S_r > (1+\epsilon)P, \end{cases} \tag{8}$$

where $\epsilon < 0$ is arbitrarily small. Also,

$$k_{rv}(H) = e^{-(c_{rv}R_{rv})^{-1}t_d(H)} \quad \text{and} \quad a_{rv}(H) = 1 - k_{rv}(H)\ , \tag{9}$$

and

$$t_d(H) = \frac{1}{H^{1/2}}\left(\frac{1}{H^{1/2}} - \kappa\right)\ , \tag{10}$$

where κ is in the range of $0.3 - 0.4$ when time is measured in seconds and in the range of $0.0387 - 0.0516$ when time is measured in minutes.

Moreover, the change in the volume in the left ventricle $dV_{\ell v}(t)/dt$ as modeled in [10] is

$$\frac{dV_{\ell v}(t)}{dt} = \frac{P_{vp}(t) - P_{\ell v}(t)}{R_{mv}(t)} - \frac{P_{\ell v}(t) - P_{sa}(t)}{R_{av}(t)} \tag{11}$$

where $P_{vp}(t), P_{\ell v}(t)$ and $P_{sa}(t)$ are respectively, the blood pressures in the venous pulmonary, left ventricle and systemic aorta compartments and the time-varying elastances $R_{mv}(t)$ and $R_{av}(t)$ in the mitral valve and aortic valve, respectively.

1.3. **Opening and Closing of the Heart Valves.** In order to model the left ventricle as a pump, the opening and closing of the mitral and aortic valves must be included. During the diastole, the mitral valve opens allowing the blood to flow into the ventricle while the aortic valve is closed. Then the heart muscles start to contract, increasing the pressure in the ventricle. When the left ventricular pressure exceeds the aortic pressure, the aortic valve opens, propelling the pulse wave through the vascular system [6].

Rideout (1991) [11] originally proposed a model of the succession of opening and closing of these heart valves. A piecewise continuous function was later developed by Olufsen et al., see for example [6] and [10]. This function represents the vessel resistance which characterized the *open* valve state using a small baseline resistance and the *closed* state using a value of larger

magnitudes. The time-varying resistance is given as

$$
\begin{aligned}
R_{mv}(t) &= \min\left(R_{mv,open} + e^{(-2(P_{vp}(t)-P_{lv}(t)))}, 10\right) , \\
R_{av}(t) &= \min\left(R_{av,open} + e^{(-2(P_{lv}(t)-P_{sa}(t)))}, 10\right) ,
\end{aligned} \tag{12}
$$

where $R_{mv}(t)$ and $R_{av}(t)$ are the time varying mitral valve and aortic valve resistances, respectively. The first equation suggests that when $P_{lv}(t) < P_{vp}(t)$, the mitral valve opens and the blood enters the left ventricle. As $P_{lv}(t)$ increases and becomes greater than $P_{vp}(t)$, the resistance exponentially grows to a large value. A similar remark can be deduced from the second equation. The value 10 is chosen to ensure that there is no flow when the valve is closed and remains there for the duration of the closed valve phase. The open and closed transition is not discrete. An exponential function is used for the partially opened valve, with the amount of *openness* [10].

In our previous simulations we used the time-varying mitral and aortic resistances given in (12). For simplicity purposes, we assumed that the time dependent resistances $R_{mv}(t)$ and $R_{av}(t)$ are given by

$$
\begin{aligned}
R_{mv}(t) &= \begin{cases} \infty & \text{for } P_{lv}(t) > P_{vp}(t), \\ R_{mv,open} & \text{for } P_{lv}(t) \le P_{vp}(t), \end{cases} \\
R_{av}(t) &= \begin{cases} \infty & \text{for } P_{lv}(t) < P_{sa}(t), \\ R_{av,open} & \text{for } P_{lv}(t) \ge P_{sa}(t). \end{cases}
\end{aligned} \tag{13}
$$

This means that when the left ventricular pressure is greater than the venous pulmonary pressure (i.e., $P_{lv}(t) > P_{vp}(t)$), the mitral valve resistance is too large that flow to the left ventricle is impossible. This is the state when the mitral valve is closed. As soon as the left ventricular pressure reaches the venous pulmonary pressure, the mitral valve opens and the blood flows to the left ventricle. In this case, the mitral valve resistance is assumed to be a constant value. The mitral valve remains open as long as left ventricular pressure is less than the venous pulmonary pressure. Similarly, when the left ventricular pressure is less than the pressure in the aorta, the aortic valve is closed and its resistance is too large making the blood flow to the systemic aorta compartment impossible. When left ventricular pressure reaches the systemic aortic pressure, the aortic valve opens and remains open as long as it exceeds the systemic aortic pressure. Here, the blood flows from the left ventricle to the systemic aorta compartment with the aortic resistance assumed to be constant during this duration.

1.4. **Time-Varying Elastance Function.** The slope of a pressure-volume curve which has pressure on the y-axis and volume on the x-axis is called the *ventricular elastance* or simply the *elastance*. It is a measure of stiffness

of the ventricles. Elastance and compliance are inverse of each other.

According to Ottesen et al. (2004) [7], the relationship between the left ventricular pressure $P_{\ell v}$ and the stressed left ventricular volume $V_{\ell v}(t)$ is described by

$$P_{\ell v}(t) = E_{\ell v}(t)\left(V_{\ell v}(t) - V_d\right) \ , \tag{14}$$

where $E_{\ell v}(t)$ is the time-varying ventricular elastance and V_d (constant) is the ventricular volume at zero diastolic pressure.

In [10], the time-varying elastance function $E_{\ell v}(t)$ is given by

$$E_{\ell v}(t) = \begin{cases} E_m + \dfrac{E_M - E_m}{2}\left[1 - \cos\left(\dfrac{\pi t}{T_M}\right)\right], & 0 \le t \le T_M \\ E_m + \dfrac{E_M - E_m}{2}\left[\cos\left(\dfrac{\pi}{T_r}\left(t - T_M\right)\right) + 1\right], & T_M \le t \le T_M + T_r \\ E_m, & T_M + T_r \le t < T \ . \end{cases} \tag{15}$$

This is a modification of a model developed by Heldt et al. (2002) [2]. Here, T_M denotes the time of peak elastance, and T_r is the time for the start of diastolic relaxation. These are both functions of the length of the cardiac cycle T. These parameters are set up as fractions where $T_{M,frac} = T_M/T$ and $T_{r,frac} = T_r/T$. Moreover, E_m and E_M are the minimum and maximum elastance values, respectively. The above elastance function (15) is sufficiently smooth. Its derivative can be easily computed as follows

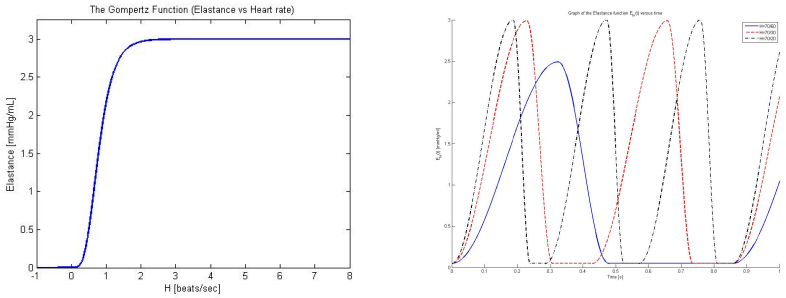
$$\frac{dE_{\ell v}(t)}{dt} = \begin{cases} \dfrac{E_M - E_m}{2}\left[\dfrac{\pi}{T_M}\sin\left(\dfrac{\pi t}{T_M}\right)\right], & 0 \le t \le T_M \\ \dfrac{E_M - E_m}{2}\left[-\dfrac{\pi}{T_r}\sin\left(\dfrac{\pi}{T_r}\left(t - T_M\right)\right)\right], & T_M \le t \le T_M + T_r \\ 0, & T_M + T_r \le t < T \ . \end{cases} \tag{16}$$

In our model, further modifications of the elastance function in (15) has been done. The maximum elastance E_M can be interpreted as a measure of the contractile state of the ventricle, see [8] and [12]. For normal resting heart, E_M can be a parameter constant. However, during exercise state, the contractility of the heart muscles may vary and could depend on the heart rate. That is, an increase in heart rate may result to an increase ventricular elastance. Thus we considered E_M as a function dependent on the heart rate H. Such function must be positive-valued, bounded and continuous. We chose the Gompertz function for $E_M(H)$, a sigmoidal function given by

$$E_M(H) = a\exp(-b\exp(-cH)) \ , \tag{17}$$

where a, b, c are positive constants. The constant a determines the upper bound of the function, b shifts the graph horizontally and c is the measure of the steepness of the curve.

In Ottesen (2004) [7] and Olufsen et al. (2009) [10], $E_M = 2.49$ [mmHg/mL]. Figure 3(a) depicts the maximum elastance curve where constants a, b and c were estimated obtaining $E_M = 2.4906$ [mmHg/mL] at $H = 70/60$ beats per second.



(a) (b)

FIGURE 3. (a) The maximum elastance E_M expressed as a sigmoidal function dependent on the heart rate H. (b) The elastance function with varying heart rates.

Since, E_M is now H-dependent, T_M which is the time of peak elastance should be H-dependent as well. We considered T_M as the time for systolic duration which is defined by the Bazett's formula given by

$$T_M = \frac{\kappa}{H^{1/2}} \,. \tag{18}$$

Figure 3(b) depicts the elastance function with varying heart rates. As the heart rate increases, the maximum elastance value increases as well. Notice also the decrease in the time for peak elastance and the smaller support of the elastance curve.

1.5. **Filling Process in the Right Heart.** The filling process in the right ventricle depends on the pressure difference between the filling pressure and the pressure in the right ventricle when the inflow valve (tricuspid valve) is open. Following Batzel et al. (2007) [1], the blood inflow into the right ventricle is given by

$$\frac{dV_{rv}(t)}{dt} \;=\; \frac{1}{R_{rv}} \left(P_v(t) - P_{rv}(t)\right), \tag{19}$$

where $V_{rv}(t)$ is the volume in the right ventricle at time t after the filling process has started, $P_v(t)$ is the venous filling pressure, $P_{rv}(t)$ is the pressure

in the right ventricle, and R_{rv} is the total resistance to the inflow into the right ventricle.

As in [1], it is assumed that $P_v(t)$ is constant during the diastole, $P_v(t) \equiv P_v$, the end-systolic volume at the end of a heart beat equals the end-systolic volume of the previous heart beat and the compliance c_{rv} of the relaxed ventricle remains constant during the diastole.

1.6. **The Contractility of the Right Ventricle.** There is a heart mechanism called the *Bowditch effect*. It roughly states that changing the heart rate causes a concordant change in the ventricular contractilities. In this study, we adapted the model presented in Batzel et al. (2007) [1] (see also [4]). where sympathetic and parasympathetic activities were not considered directly. Thus, the variations of the contractilities can be described by the following second order differential equation

$$\frac{d^2 S_{rv}}{dt^2} + \gamma \frac{dS_{rv}}{dt} + \alpha S_{rv} = \beta H, \tag{20}$$

where α, β and γ are constants. This set-up guarantees that the contractility S_{rv} varies in the same direction as the heart rate H. Introducing the state variable $\sigma = \dot{S}_{rv}$ and transforming (20) into systems of first order differential equations, we have

$$\frac{dS_{rv}}{dt} = \sigma, \qquad \text{and} \qquad \frac{d\sigma}{dt} = -\alpha S_{rv} - \gamma\sigma + \beta H. \tag{21}$$

1.7. **The Autoregulation.** The role of autoregulation is to guarantee a sufficient blood flow in the the relevant tissues. The most efficient way to increase the blood flow in a tissue region locally is to increase the diameter of the arterioles in that region. These would in turn, decrease the resistance to blood flow. Thus, autoregulation can be done essentially by decreasing the resistance R_{as} in the relevant tissue. Also, in general, local dilation of the arterioles is influenced by substances which are set free locally due to increased functional activity of the organ or tissue region (functional activation). This mechanism is supported by a local metabolic regulation, where by-products of the local metabolism cause dilation of the arterioles. Following Peskin (1981) [9] we have

$$R_{as} \;=\; A_{\text{pesk}} C_{\text{v,O}_2} \;, \tag{22}$$

where A_{pesk} is a positive constant and $C_{\text{v,O}_2}$ is the concentration of O_2 in the venous blood in the capillary region..

In order to model the cardiovascular system response to a constant ergometric workload W imposed on a test person on a bicycle ergometer, the

following empirical formula for the metabolic rate is used:

$$M_{\mathrm{T}} \;=\; M_0 + \rho W \;, \tag{23}$$

where M_0 is the metabolic rate in the systemic tissue region corresponding to zero workload and ρ is a positive constant. As in Kappel and Peer (1993) [4] and related works, we have the relation

$$M_{\mathrm{T}} \;=\; F_s \left(C_{\mathrm{a,O_2}} - C_{\mathrm{v,O_2}}\right) + M_b \;, \tag{24}$$

where F_s denotes the blood flow in the arterial systemic region and $C_{\mathrm{a,O_2}}$ denotes the concentration of O_2 in the arterial blood which is assumed to be constant. Moreover, for the biochemical energy flow, we assume that it is directly proportional on the rate of change of $C_{\mathrm{v,O_2}}$,

$$M_b \;=\; -K \frac{d}{dt} C_{\mathrm{a,O_2}} \;, \tag{25}$$

where K is a positive constant. Equation (25) suggests that a positive amount of M_b is supplied whenever $C_{\mathrm{a,O_2}}$ is lowered.

Differentiating (22) and combining it with (24), (25), and the flow equation to the peripheral systemic region, we obtain the following differential equation for R_{as}:

$$\frac{dR_{as}}{dt} \;=\; \frac{1}{K}\left(A_{\mathrm{pesk}}\left(\frac{P_{as}-P_{vs}}{R_s} C_{\mathrm{a,O_2}} - M_{\mathrm{T}}\right) - \left(P_{as}-P_{vs}\right)\right) \tag{26}$$

In our model, we do not consider an autoregulation mechanism in finger arteries. This is due to the idea that in an ergometer bicycle test, the arms are hold in a fixed position. And hence, not directly involved in an exercise activity.

1.8. **The Model Equations.** The model can be described as a system of coupled first order of ordinary differential equations with state variables $x(t) = (P_{sa}, P_{fa}, P_{as}, P_{vs}, P_{ap}, P_{vp}, P_{\ell v}, S_{rv}, \sigma, R_{as})^T \in \mathbb{R}^{10}$, representing pressures in the systemic aorta, finger arteries, arterial systemic, venous systemic, arterial pulmonary and left ventricle compartments, right ventricular contractility and its derivative, and the arterial systemic resistance,

respectively. These are given by

$$
\begin{aligned}
\frac{dP_{sa}}{dt} &= \frac{1}{c_{sa}}\left(\frac{P_{lv}-P_{sa}}{R_{av}(t)} - \frac{P_{sa}-P_{fa}}{R_{sa_1}} - \frac{P_{sa}-P_{as}}{R_{sa_2}}\right),\\
\frac{dP_{fa}}{dt} &= \frac{1}{c_{fa}}\left(\frac{P_{sa}-P_{fa}}{R_{sa_1}} - \frac{P_{fa}-P_{vs}}{R_{fa}}\right),\\
\frac{dP_{as}}{dt} &= \frac{1}{c_{as}}\left(\frac{P_{sa}-P_{as}}{R_{sa_2}} - \frac{P_{as}-P_{vs}}{R_{as}}\right),\\
\frac{dP_{vs}}{dt} &= \frac{1}{c_{vs}}\left(\frac{P_{as}-P_{vs}}{R_{as}} + \frac{P_{fa}-P_{vs}}{R_{fa}} - Q_r\right),\\
\frac{dP_{ap}}{dt} &= \frac{1}{c_{ap}}\left(Q_r - \frac{P_{ap}-P_{vp}}{R_{ap}}\right),\\
\frac{dP_{vp}}{dt} &= \frac{1}{c_{vp}}\left(\frac{P_{ap}-P_{vp}}{R_{ap}} - \frac{P_{vp}-P_{lv}}{R_{mv}(t)}\right),\\
\frac{dP_{lv}}{dt} &= E_{lv}\left(\frac{\frac{dE_{lv}}{dt}P_{lv}}{{E_{lv}}^2} + \frac{P_{vp}-P_{lv}}{R_{mv}(t)} - \frac{P_{lv}-P_{sa}}{R_{av}(t)}\right),\\
\frac{dS_{rv}}{dt} &= \sigma,\\
\frac{d\sigma}{dt} &= -\alpha S_{rv} - \gamma\sigma + \beta H,\\
\frac{dR_{as}}{dt} &= \frac{1}{K}\left(A_{\text{pesk}}\left(\frac{P_{as}-P_{vs}}{R_s}C_{\text{a,O}_2} - M_{\text{T}}\right) - (P_{as}-P_{vs})\right),
\end{aligned}
\tag{27}
$$

where the time-varying resistances $R_{av}(t)$ and $R_{mv}(t)$ are given in equation (12), the cardiac output of the right ventricle Q_{rv} is given in equation (6) and other auxiliary equations such as for k_{rv} and a_{rv} are given in (9), the duration for diastole t_d is given in (10) and the right ventricular contractility S_r is given in (21).

2. Simulation Results and Discussions

Figure 4 shows the simulation results of the cardiovascular model (27) using the values of the parameters given in Table 1. Figure 4(a) depicts the rest equilibrium situation. Heart rate H is assumed to be 70/60 beats per second. The workload $W = 0$ Watt and the Peskin's constant $A_{\text{pesk=7.2276}}$ mmHg s/mL. The parameters are mostly taken from the literature and some are estimated to produce an average normal pulsatile pressures in the finger arteries which is 120/90 mmHg. Less pulsatility is observed in the arterial systemic compartment. In the venous pulmonary and arterial pulmonary compartments, the pulsatility is very small which is observed physiologically. Here, the contractility of the right ventricle is assumed to be constant

considering a rest normal condition. Furthermore, it is also observed numerically that when the heart rate is increased, pulsatility is increased. The blood pressures in most of the compartments except the venous systemic compartment increased. This is due to the Frank- Starling mechanism assumed in the filling process of the right ventricle as assumed in [1]. On the other hand, decreasing the heart rate produces the opposite result. Figure 4(b) shows the simulation for an exercise state with an elevated heart rate of $H = 95/60$ beats per second, a workload of $W = 50$ Watts and $A_{\text{pesk=12}}$ mmHg s/mL. Mean averages of the pressures are comparable to the results previously done in [4]. Long term simulations show that the states tend to periodic equilibrium both for rest and exercise situations.

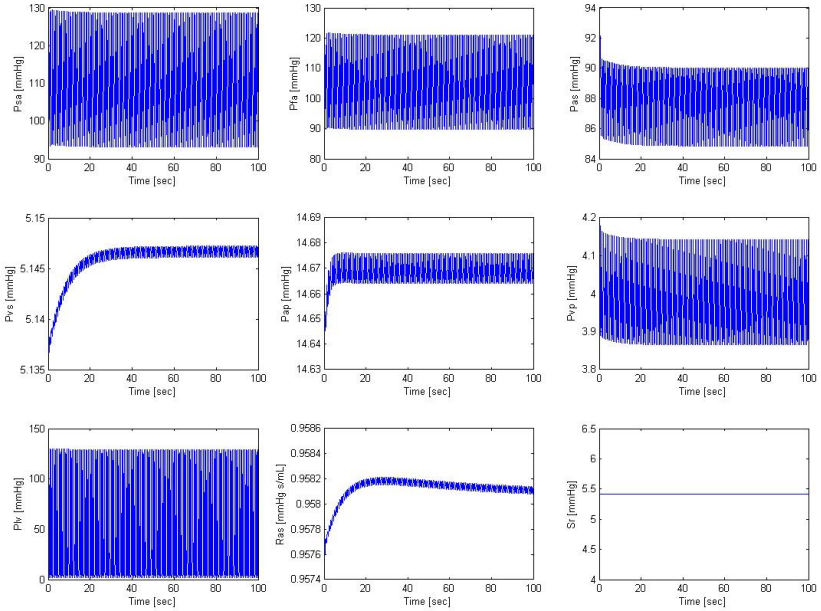
Parameter	Meaning	Value	Units
c_{sa}	Compliance of the systemic aorta compartment	1.5	mL/mmHg
c_{fa}	Compliance of the finger arteries compartment	0.085	mL/mmHg
c_{as}	Compliance of the arterial systemic compartment	3.25	mL/mmHg
c_{vs}	Compliance of the venous systemic compartment	850.95	mL/mmHg
c_{rv}	Compliance of the relaxed right ventricle	44.131	mL/mmHg
c_{ap}	Compliance of the arterial pulmonary compartment	25.15	mL/mmHg
c_{vp}	Compliance of the venous pulmonary compartment	200.75	mL/mmHg
$R_{mv,open}$	Resistance when the mitral valve is open	0.0025	mmHg s/mL
$R_{av,open}$	Resistance when the aortic valve is open	0.0025	mmHg s/mL
R_{sa_1}	Resistance between systemic aorta and finger arteries	0.4745	mmHg s/mL
R_{sa_2}	Resistance between systemic aorta and arterial systemic	0.25	mmHg s/mL
R_{fa}	Resistance between finger and venous systemic compartment	9	mmHg s/mL
R_{rv}	Inflow resistance of the right ventricle	0.002502	mmHg s/mL
R_{ap}	Resistance in the peripheral region of the pulmonary circuit	0.1097	mmHg s/mL
E_m	Minimum elastance value of the left heart	0.029	mmHg/mL
V_d	Unstressed left heart volume	10	mL
κ	Constant in the Bazett's formula	0.35	s
α	Coefficient of S_r in the differential equation for S_r	0.003969	s^{-2}
β	Coefficient of H in the differential equation for S_r	0.01841	mmHg/s
γ	Coefficient of $\dot{S}_r$ in the differential equation for S_r	0.021125	s^{-1}
a	Constant in the Gompertz function	3	mmHg/mL
b	Constant in the Gompertz function	10	1
c	Constant in the Gompertz function	3.415	s^{-1}
M_0	Metabolic rate in the systemic tissue region with zero workload	5.83	mL/s
ρ	Coefficient of W in (23)	0.183	mL/(s Watt)
$C_{\text{a,O}_2}$	O_2 concentration in arterial systemic blood	0.2	1
K	Constant in the formula for the biochemical energy flow	5465.9	mL

TABLE 1. The table of parameters.

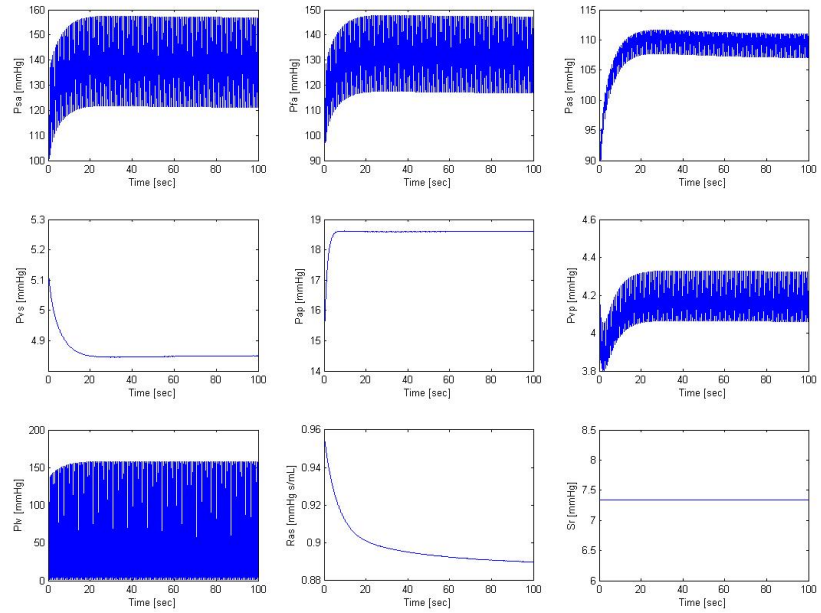
3. Ongoing and Future Work

A lot of considerations can be accounted to have a more holistic view of the overall behavior of the human cardiovascular system under specific conditions. The following are ongoing and future work on this area:

- to provide information for measurements such as the systolic and diastolic pressures in the fingers arteries



(a)



(b)

FIGURE 4. Simulations depicting the plots of the state variables at the heart rates (a) $H = 70/60$ beats per second and (b) $H = 95/60$ beats per second.

- to look into the relationship between the right ventricle contractility S_r and the left ventricle elastance E_M,
- to design a feedback law mechanism which controls the heart rate,
- to estimate and identify sensitive parameters,
- to investigate further the role of the unstressed volumes in the modeling process, and
- to include the respiratory system in the global pulsatile model.

Moreover, the model can be extended to describe the response of the cardiovascular system under orthostatic stress as in [5] and [3], and to study blood loss due to haemorrhage.

Note. This report has also been submitted to ÖAD (Österreichische Austauschdienst) Regionalbüro Graz. Part of this report will appear in "SEE doctoral studies in Mathematical Sciences"- Tempus Project Report in which Mr. de los Reyes gave an oral presentation entitled ***Modeling Pulsatility in the Human Cardiovascular System*** in the *Young Researchers in Mathematics Workshop* as part of the **Mathematical Society of South-Eastern Europe (MASSEE) International Congress on Mathematics (MICOM)** held in Ohrid, Macedonia on September 16-20, 2009. Preliminary results of this study have been presented in international conferences: **Federation of European Physiological Societies Meeting, FEPS 2009** in Ljubljana, Slovenia on November 12-15, 2009 and **2009 Joint Meeting of the Korean Mathematical Society and the American Mathematical Society**in Ewha Womans University, Seoul, Korea on December 16-20, 2009.

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