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OBJECT-ORIENTED MODELING AND SIMULATION OF THE CLOSED LOOP CARDIOVASCULAR SYSTEM BY USING SIMSCAPE

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Abstract

The modeling of physiological systems via mathematical equations reflects the calculation procedure more than the structure of the real system modeled, with the simulation environment SIMULINK$_{TM}$ being one of the best suited to this strategy. Nevertheless, object-oriented modeling is spreading in current simulation environments through the use of the individual components of the model and its interconnections to define the underlying dynamic equations. In this paper we describe the use of the SIMSCAPE$_{TM}$ simulation environment in the object-oriented modeling of the closed loop cardiovascular system. The described approach represents a valuable tool in the teaching of physiology for graduate medical students.

Keywords: Object-Oriented Modeling, Hierarchical Modeling, SIMULINK$_{TM}$ Simulation Language, SIMSCAPE$_{TM}$ Simulation Language, Cardiovascular System.

1. Introduction

There are a considerable number of specialized and general-purpose modeling software applications available for biomedical studies. A non-exhaustive list of such tools is provided in Tomaseth [1], divided into structure-oriented and equation-oriented applications. A general purpose simulation environment that is also often used for physiological modeling is MATLAB-SIMULINK$_{TM}$ [2]. However, this software follows a causal modeling approach and requires explicit coding of mathematical model equations or representation of systems in a graphical notation such as block diagrams, which is quite different from common representation of physiological knowledge.

In the same way, acausal and object-oriented approaches can offer many advantages in biomedical research both for the building of complex multidisciplinary models when dynamics are given by a set of differential algebraic equations (DAEs) and for the exchange of modeling knowledge [3]. The object-oriented approach has been made possible by using the modeling environment MODELICA$_{TM}$ [4,5] and the MATLAB$_{TM}$-based modeling module SIMSCAPE$_{TM}$ [2,6] together with the linked domain libraries SIMELECTRONICS$_{TM}$, SIMHYDRAULICS$_{TM}$, and SIMMECHANICS$_{TM}$. Both integrated environments are software tools that are ideally suited as architectural description languages for complex systems, which allow the system, subsystem, or component levels of a whole physical system to be described in increasing detail. In this way, individual components of the system's model and its interconnections describe the underlying dynamic equations by allowing the design of the model to start from the inherent structure of the physical system [7].

While the MODELICA$_{TM}$ environment has been used for a long time in different fields of engineering [8] with proven results in biomedical system modeling [9-11], few results have been reported using the SIMSCAPE$_{TM}$ tool instead.

Cardiovascular modeling presents a particular challenge in that it requires both a multi-scale and a multi-physics approach [12,13]. Several models of the closed loop cardiovascular system have been developed, ranging from mathematical ones based on dynamic equations [14-16] to physical electronic circuit models [17-19]. Software tools based on hierarchical block diagrams have also been applied to the description of cardiovascular systems [20-22]. In fact, in the Physiome project [23,24], a formal description of different physiological systems is realized and this has enabled the development of tools such as the JSim and CellML languages, with Quantitative Human Physiology (QHP) being the most extensive and recent development [25-26] Actually, graphic visualization environments have been developed for modeling and simulation of physiological systems as is described in McLoone et al. [27], including SIMULINK$_{TM}$ as a development tool.

In the same way, acausal simulation tools have also been used for modeling and control of the cardiovascular system, and in fact MODELICA$_{TM}$ applications can be found in the literature [28] and recently even a web-based multimedia application has been developed by using the SIMULINK$_{TM}$ and MODELICA$_{TM}$ environments to perform interactive simulations in the cardiovascular control field [29].

In this paper we describe the use of the SIMSCAPE$_{TM}$ simulation environment for object-oriented modeling of the closed loop cardiovascular system. For this task we have followed an acausal hierarchical structure whose validity has been previously assessed to represent the cardiovascular dynamics as a multi-compartmental system constituted by the arterial and venous tree together with the heart pump. Results obtained during simulation in both physiological and pathological conditions provide a physiological interpretative key to the patient´s hemodynamic behavior during steady state and transient induced changes, and comparisons have been made with a SIMULINK$_{TM}$ realization.

Glossary

U	isovolumetric pressure (mmHg)
q	ventricle blood flow ($cm^3\ s^{-1}$)
P	ventricular pressure (mmHg)
ΔP	pressure drop across heart valve (mmHg)
V	ventricular volume (cm^3)
E	ventricular elastance ($mmHg\ cm^{-3}$)
R	resistance ($mmHg\ s\ cm^{-3}$)
L	inertance ($mmHg\ s^2\ cm^{-3}$)
C	compliance ($mmHg^{-1}\ cm^3$)
S	Ideal valve (diode)
a	Normalized activation function
t	time (s)

Subscripts

L	left
R	right
in	inflow
out	outflow
v	ventricular
o	initial
i	index

lp	linearization point
p	peak value
s	systolic
d	diastolic
m	myocardial viscosity
c	cardiac
sim	simulation

2. Methods

As a first approach, we can consider the cardiovascular system as a closed loop circuit constituted by two circuits in series (systemic/pulmonary circulation) with the heart pump configured by two ventricles with two valves each.

The model used here is based on previous studies by Avanzolini et al [14], where an electric model for the cardiovascular system is proposed (Fig. 1). The use of the analogy will enable us to define the voltage, current, charge, resistance, and capacitance in the electronic circuit as equivalent to the blood pressure, flow, volume, resistance, and compliance in the cardiovascular system.

/ Figure 1 here /

2.1. Model of the Closed Loop Cardiovascular System

According to the description of the cardiovascular model by Avanzolini et al [14], we can relate every element of the analog circuit with its analogous anatomic property of the circulatory system. On ~~the~~ one hand, each ventricle will be described as an isovolumetric time-dependent pressure generator in series with a time-varying elastance and a resistance. The unidirectional character of the inlet and outlet heart valves is modeled by an ideal diode in series with an electrical resistance. The atrial elastic

characteristics are included in the venous compliances, which are modeled as capacitances in the circuit. On the other hand, the systemic and pulmonary circulations will be simply described by an RLC two-stage network, where resistances and inductances represent inertial and viscous properties of the blood flow, while capacitances correspond to the elastic properties of the vessel walls.

Although the whole cardiovascular model can be represented with a set of nonlinear equations describing its dynamics [Avanzolini et al 1988], with a state vector characterized by twelve state variables $\bar{x}(t) = \{x_1(t), \ldots, x_{12}(t)\}$ representing volume variations, compartmental pressures and inter-compartmental pressures (Table 1), the present paper focuses on the multi-compartmental acausal approach; hence we will describe every component of the cardiovascular system as a unique mesh of our analogical electrical circuit. Besides, the modeling efforts can be substantially reduced by reusing previously defined similar components. In this way, the essence of the modeled reality and the simulation models are much more legible and much less prone to mistakes.

/ Table 1 here /

2.1.1. Left and Right Ventricles Modeling

According to the results of Avanzolini et al [30], we have considered the linearization of the systolic pressure-volume-flow surface to represent each ventricle's behavior. In Fig. 2 we show the electrical meshes relative to the left and right ventricles.

/ Figure 2 here /

In this way, each ventricle can be approximated by an isovolumetric pressure generator $U(t)$ in series with both a time-varying elastance $E(t)$ and a resistance R, and these two elements are used to establish the dependence of ventricular pressure on the volume $V(t)$ and the rate of volume variation $\frac{dV}{dt}$, respectively.

Therefore, by assuming a constant elastance E_d during the diastole, the ventricular pressure is given by

$$P_v(t) = \begin{cases} U(t) + E(t) \cdot \big(V(t) - V_{lp}\big) + R_m \dfrac{dV}{dt} & systole \\ E_d(V(t) - V_{lp}) & diastole \end{cases} \tag{1}$$

where V_{lp} is the volume at the linearization point, while $U(t) = U_0 a(t)$ is the isovolumetric pressure at volume V_{lp} with peak value U_0, and $E(t) = E_d + E_s a(t)$ is the diastolic plus time-varying systolic elastance, with the normalized activation function being $a(t)$ in both cases. Finally, R_m is the resistance due to the myocardium viscosity.

The activation function represents the time-dependence of the isovolumetric pressure given by

$$a(t) = \begin{cases} \dfrac{1 - \cos(2\pi\, t_m/t_s)}{2} & \text{if } t_m < t_s \\ 0 & \text{if } t_m > t_s \end{cases} \tag{2}$$

where t_s and t_c are systolic and cardiac periods defined by $t_s = 0.16 + 0.3t_c$ and $t_m = mod(t, t_c)$.

Particularizing these results to the right and left compartments, it is possible to describe the isovolumetric pressure generator for each ventricle by

$$U_R(t) = U_{pR}\, a(t) \tag{3}$$

$$U_L(t) = U_{pL} a(t)$$

where U_{pR} and U_{pL} represent the right and left peak isovolumetric pressures at volume V_{lp}, while the time-varying elastances are defined as

$$E_R(t) = E_{dR} + E_{sR}\, a(t) \tag{4}$$

$$E_L(t) = E_{dL} + E_{sL} a(t)$$

where E_{dR} and E_{sR} are the right diastolic and systolic elastances, and E_{dL} and E_{sL} are the corresponding left heart values.

The input blood flow from systemic circulation to the right heart is regulated by the diodes $S_2 - S_3$ in series with the resistances $R_4 - R_5$, respectively, and these nonlinear elements model the tricuspid and the pulmonary valves respectively through

$$S_2(t) = \begin{cases} 1 & \text{if } \Delta P_2(t) > 0 \\ 0 & \text{otherwise} \end{cases} \tag{5}$$

$$S_3(t) = \begin{cases} 1 & \text{if } \Delta P_3(t) > 0 \\ 0 & \text{otherwise} \end{cases}$$

where $\Delta P_2(t)$ and $\Delta P_3(t)$ are functions depending on the regulatory functions $U_R(t)$ and $E_R(t)$ related by Kirchhoff's second law applied to the mesh in Fig. 2.a, so that

$$\Delta P_2(t) = x_5(t) - U_R(t) - x_6(t)\, E_R(t) \tag{6}$$

$$\Delta P_3(t) = U_R(t) + x_6(t)\, E_R(t) - x_7(t)$$

where $x_5(t)$ and $x_7(t)$ are the steady variables which represent the right atrial pressure and pulmonary venous pressure, respectively, and $x_6(t)$ is the right ventricular volume time-variation during the systole. At this point, we can define both the right ventricular inflow and outflow by using Ohm's law, so we have

$$q_{inR}(t) = \frac{\Delta P_2(t) S_2(t)}{R_4} \tag{7}$$

$$q_{outR}(t) = \frac{\Delta P_3(t) S_3(t)}{R_{mR} + R_5}$$

The right heart model is completely defined by the right ventricular pressure resulting from the application of Kirchhoff's second law in the electrical model of Fig. 2.a, so that

$$P_{vR}(t) = U_R(t) + E_R(t) x_6(t) - R_{mR} q_{outR}(t) \tag{8}$$

In the same way, the input blood flow from pulmonary circulation to the left heart is regulated by the diodes $S_4 - S_1$ in series with the resistances $R_8 - R_1$, respectively, and these nonlinear elements model the mitral and the aortic valves, respectively, through

$$S_4(t) = \begin{cases} 1 & \text{if } \Delta P_4(t) > 0 \\ 0 & \text{otherwise} \end{cases} \tag{9}$$

$$S_1(t) = \begin{cases} 1 & \text{if } \Delta P_1(t) > 0 \\ 0 & \text{otherwise} \end{cases}$$

where $\Delta P_1(t)$ and $\Delta P_4(t)$ are functions depending on the regulatory functions $U_L(t)$ and $E_L(t)$ related by Kirchhoff's second law applied to the mesh in Fig. 2.b, so that

$$\Delta P_1(t) = U_l(t) + x_{12}(t)E_l(t) - x_1(t) \tag{10}$$

$$\Delta P_4(t) = x_{11}(t) - U_L(t) - x_{12}(t)E_L(t)$$

where $x_{11}(t)$ and $x_{12}(t)$ are the steady variables which represent the left atrial pressure and aortic pressure, respectively, and $x_{12}(t)$ is the left ventricular volume time variation during the systole. Similarly, we can define both the left ventricular inflow and outflow by using Ohm's law, so we also have

$$q_{inL}(t) = \frac{\Delta P_4(t) S_4(t)}{R_8} \tag{11}$$

$$q_{outL}(t) = \frac{\Delta P_1(t) S_1(t)}{R_{mL} + R_1}$$

Finally, the left heart model is completely defined by the left ventricular pressure resulting from the application of Kirchhoff's second law in the electrical model of Fig. 2.b, so that

$$P_{vL}(t) = U_L(t) + E_L(t)x_{12}(t) - R_{mL}q_{outL}(t) \tag{12}$$

2.1.2. Circulatory Network Modeling

The systemic and pulmonary circulations are described by RLC two-stage networks where inductances and resistances represent inertial and viscous properties of the blood flow, while capacitances correspond to the elastic properties of the vessel walls. The high pressure arterial sections of the systemic and pulmonary circulation are then characterized by a two-compartment model $C_1 - C_2$ and $C_4 - C_5$, respectively, separated from the corresponding low pressure venous sections C_3 and C_6 by the systemic and pulmonary peripheral resistances R_3 and R_7, respectively (Fig. 3).

/ Figure 3 here /

2.1.3. Steady-State Variables

The behavior of the whole cardiovascular model is given by a set of first-order non-linear differential equations in the form

$$\frac{dx_i}{dt} = \emptyset_i(x_1, x_2, \dots, x_{12}, t) \quad , \; i = 1,..12 \tag{13}$$

where $\bar{x}(t) = \{x_1(t), \dots., x_{12}(t)\}$ is known as the steady-state vector already defined in Table 1, and the particular relationship for each nonlinear function $\overline{\emptyset}(t) = \{\emptyset_1(t), \dots., \emptyset_{12}(t)\}$ is given in Table 2, with a explicit set of initial conditions $\bar{x}(0) = \{x_{1_0}, \dots., x_{12_0}\}$.

/ Table 2 here /

2.2. Causal and Acausal Modelling Approach

Interconnection of the blocks in SIMULINK$_{TM}$ reflects the calculation procedure rather than the actual structure of the modeled reality. Signals are transmitted through links between individual blocks and the signals serve to transfer values of individual variables from the output of one block to inputs of other blocks. Input information is processed in the blocks to output information. This is the so-called causal modeling.

However, in describing the model it is important that its actual structure captures the physical essence of the modeled system especially well. Therefore, acausal notation of models is starting to be used, so that the interconnection of individual components of the model describes the system equations directly.

SIMSCAPE$_{TM}$ is a MATLAB$_{TM}$-based, oriented-object physical modeling language that enables the user to create models of physical components using an acausal modeling approach [2]. From a modeler point of view, 'oriented-object' means that one can build a model similar to a real system by taking the components and connecting them into a model. These physical components can be connected through exactly defined interfaces (connectors) in which variables used for connection are defined, so that only connectors falling in the same connector classes can be connected. In this way the connections can be thought of as one of the key features of oriented-object modeling, enabling both effective model reuse and hierarchical modeling by connecting basic physical components into more complicated ones, until a top-level model is achieved.

This language is designed for use under the MATLAB$_{TM}$ and SIMULINK$_{TM}$ environments, because it can benefit from MATLAB$_{TM}$ functions and SIMULINK$_{TM}$ blocks. This multi-domain simulation environment can also be linked to specific domain libraries such as SIMPOWERSYSTEMS$_{TM}$, SIMMECHANICS$_{TM}$ and SIMHYDRAULICS$_{TM}$ [2], among others, all of which run under MATLAB$_{TM}$.

In SIMSCAPE$_{TM}$, a model is a collection of physical blocks which must be appropriately connected to define the dynamic system. The specific connection diagram together with the conservation laws applied determines the system dynamic equations. Physical blocks can be of a very distinct nature, ranging from electric to mechanical, hydraulic, and thermal, and its constitutive parameters can be modified easily by double-clicking on them. Lines are used to transfer physical signals from one block to another, in contrast with SIMULINK$_{TM}$. These physical blocks are arranged in Physical Libraries which are accessed in the main SIMSCAPE$_{TM}$ window, while physical block parameters can also be defined from the MATLAB$_{TM}$ workspace.

The construction of the physical block diagram starts with the assembly of each of the physical componentes which define the system model by gathering appropriate components from the Physical Block Libraries [6]. Figure 4 shows the Electrical Library, which is composed of three sub-libraries termed the Electrical Elements, Electrical Sensors, and Electrical Sources libraries.

/ Figure 4 here /

The Physical Network approach supports two types of variables (Fig. 5.a), effort variables (e_A, e_B), which are measured with a sensor connected in parallel to a component with respect to a reference, and flow variables (f_{AB}), which are measured with a sensor connected in series to a component.

There are different ports associated to the SIMSCAPE$_{TM}$ blocks, namely conserving and signal ports, which differ from the SIMULINK$_{TM}$ standard ports. The conserving ports represent physical connections and relate physical variables among physical blocks, and the connection lines that connect these ports together are bidirectional lines that carry effort and flow variables rather than signals. The sum of effort variables in a closed loop is null, while the sum of flow variables flowing into a branch point equals the sum of all its values flowing out (Fig. 5.b).

/ Figure 5 here /

There are several types of conserving ports in SIMSCAPE$_{TM}$, each with effort and flow associated variables, which are listed in Table 3.

/ Table 3 here /

The signal ports transmit signals between blocks with units associated with them, usually specified along with the parameter values in the block, unlike SIMULINK$_{TM}$ signals, which are dimensionless. Associated with these types of ports are the sensor and actuator blocks. SIMSCAPE$_{TM}$ is equipped with a Physical Signal Library which enables linear and nonlinear operators, functions, lookup tables, and so on to be implemented in case a relationship is not available in SIMSCAPE$_{TM}$ to implement a

determined component. In order to manage the signal inputs and outputs to and from the physical block diagram, it is necessary to use converter blocks to connect SIMSCAPE$_{TM}$ diagrams to SIMULINK$_{TM}$ sources and scopes.

Finally, it must be emphasized that 'ode15s' and 'ode23t' are the only numerical integration methods allowed by SIMSCAPE$_{TM}$ to run the model [2].

2.2.1. SIMSCAPE$_{TM}$ Model of the Cardiovascular System

The electronic circuit shown in Fig. 1 is the base model used for the SIMSCAPE$_{TM}$ model hereby developed. This circuit has been realized by dragging the necessary components which are available in the SIMSCAPE$_{TM}$ Library Browser. In Fig. 6 the SIMSCAPE$_{TM}$ model for the cardiovascular system is shown.

/ Figure 6 here /

On the other hand, the voltage sources $U_R(t)$ and $U_L(t)$ and the elastances $E_R(t)$ and $E_L(t)$ have been modeled by two independent SIMSCAPE$_{TM}$ subsystems V_6 and V_{12} in Fig. 7 according to Eqs. (2), (3), and (4). Figure 7 depicts the SIMSCAPE$_{TM}$ implementation diagrams for the right and left ventricles, both including the normalized activation function $a(t)$ that models the excitation–contraction mechanical effects in the vessel walls of the heart.

/ Figure 7 here /

2.2.2. SIMULINK$_{TM}$ Model of Cardiovascular System

Once the description of the steady state variables has been done, we can implement the causal model in SIMULINK$_{TM}$ as a simple translation of the dynamic state equations defined in Table 2 to the appropriate code. So, to gain an easier comprehension of the block-diagrams language, we have subdivided the whole system into representative parts by using subsystems and labeling and coloring the flow variables in order to differentiate them. We have employed the 'ode45' routine, which is the default method for solving ordinary differential equations (ODE) in SIMULINK$_{TM}$. Figure 8 shows the general structure of the SIMULINK$_{TM}$ diagram corresponding to the cardiovascular model.

/ Figure 8 here /

A SIMULINK$_{TM}$ subsystem for the cardiovascular model has been created ('Steady Var' Block) in order to integrate each first derivative variable $\frac{dx_i}{dt}$, i =1…12 imposing the relevant initial conditions x_{i0} , i =1…12, where the output signal is the steady state variables $x_i(t), i$ =1…12. In the same way, a SIMULINK block has been designed to synthesize the normalized activation function $a(t)$ described by Eq. (2) which is a periodic function with period $\frac{t_s}{t_m}$ ('Impulse Function' Block).

As we commented previously, the main benefit of using SIMSCAPE$_{TM}$ as compared to SIMULINK$_{TM}$ is the identification of the physical elements that characterize the model. This acausal modeling approach allows modifications to be made to each component in a more intuitive and simple way than when causal block diagrams are used. In fact,

despite the nonlinearity of the cardiovascular model of Avanzolini et al [30], it is extremely easy to follow the proper branches of the circuit in order to identify the very different parts of the cardiovascular system. We can clearly appreciate up to eight subsections that are made up of either RLC stages or RC-diode stages, due to the compartmental strategy used to model the cardiovascular system.

3. Results and Discussion

The results have been obtained by applying the full cardiovascular model depicted in Fig. 7 under both physiological and pathological conditions, assuming the validation tests previously performed with physiological data by Avanzolini et al [30] and McInnis et al [31].

3.1. Results on Physiological Conditions

Figure 9 shows the aortic pressure (x_1), right venous-atrial pressure (x_5), left ventricle outflow (q_{outL}) and right ventricle inflow (q_{inR}) respectively, obtained under normal conditions for the set of patient's parameters detailed in Avanzolini et al [30]. The initial values for the cardiovascular compartments at the start of the simulation and the parameters referring to a normal circulatory condition in a patient are included in Table 4.

/ Table 4 here /

/ Figure 9 here /

Both the qualitative and the quantitative behavior obtained with the SIMSCAPE$_{TM}$ model can be considered satisfactory. In particular, the arterial pressure waveform exhibits a quite realistic dicrotic wave ~~plateau~~ after aortic valve closure, due essentially to inertial effects, while no backflow is present in the left ventricle outflow due to unidirectional valve modeling.

3.2 Results on Increased Systemic Resistance

In the presence of changes in peripheral resistance, the intrinsic regulatory mechanisms play an important role in keeping the balance between the left and right outputs at the heart.

Figure 10 shows the cardiovascular response to ~~an increase in blood viscosity due to~~ a doubling of the peripheral systemic resistance (R_3) during the diastole. An increase in aortic pressure of 36%, causing a corresponding decrease in both the left stroke volume and the right atrial-venous pressure, can be observed. Thus, the right filling pressure is reduced, which according to the Frank-Starling law determines a decrease in right stroke volume of 25% to balance the left one until a new steady condition is reached.

/ Figure 10 here /

3.3 Results on Physical Exercise Condition

The physical exercise condition has been modeled by decreasing the systemic and pulmonary resistance values by about 60%. This means, in physiological terms, that the

blood flow will increase as a consequence of greater oxygen transfer from the lungs (pulmonary resistances R_6 and R_7) to muscles (systemic resistances R_2 and R_3). We have also augmented the peak values of the isovolumetric pressure generators by 15%, considering an increase in the valves and vessel walls pressure.

As shown in Fig. 11, the mean aortic pressure decreases slightly at the same time as the right venous atrial pressure increases.

/ Figure 11 here /

3.4 Results on Aortic Insufficiency

In order to create a severe aortic insufficiency condition, the aortic resistance R_1 has been reduced to 60% of its normal value, whilst the diode S_1 has also been adjusted so that the aortic valve does not show a non-return valve response, irremediably compelling the aortic valve to fail.

Figure 12 shows the aortic pressure evolution during this condition. Comparing this with Fig. 9, it can be seen that the aortic pressure shows a noticeable increase in its peak value. However, the most significant change in this magnitude occurs in its shape, since the secondary peak, at the beginning of the diastole, is largely reduced and practically disappears. This is due to the malfunction of the aortic valve, which offers no resistance to the return flow from the aorta. The aortic return flow is also depicted in Fig. 12, where each cycle presents a period in which the outgoing ventricle flow is negative,

allowing the blood flow to return to the left ventricle because the valve cannot prevent outgoing fluid from getting back in.

/ Figure 12 here /

3.5 Results on Hypervolemia

A case of hypervolemia with a sudden rise of the blood volume from 1.4 s to 8 s has also been included. A larger amount of blood results in a fluid inertance augmentation, so that the inductances L_1 and L_2 have been progressively increased up to an extra 80% from their original values during the blood injection period.

In conclusion, a large increase in the aortic pressure is observed within a rather short transition time, where the highest values attained are as shown in Fig. 13. While the blood volume rises, the aortic pressure at the beginning of the diastole rises enormously as a consequence of overwhelming return flow, which the aortic valve tries to prevent from passing through. This effect can be seen in the deformation illustrated in Fig. 13. In any case, the pressures balance out due to the different regulation mechanisms. In fact, as the aortic pressure rises, the right-atrial venous pressure decreases, yielding a sufficiently stable configuration.

/ Figure 13 here /

4. Summary

We have illustrated the difference between modeling the physiologic system using block-oriented simulation tools and SIMSCAPE$_{TM}$. The model of the cardiovascular system chosen was very simple, distinguishing only the main components of systemic and pulmonary circulations, which were described in accordance with the classical Guyton models [12]. This simple structure was consistent with the aim of the study, which was to highlight the use of analogy in the study of the cardiovascular function through the use of object-oriented simulation software such as SIMSCAPE$_{TM}$.

While SIMULINK$_{TM}$ reflects a calculation procedure to describe the system's structure in order to solve the derivatives of the state variable equations of the model, SIMSCAPE$_{TM}$ enables this structure to be organized as components with well defined connections, so that the system dynamics are embedded in the connection diagram. The depiction of the model in this acausal simulation environment ~~thus~~ resembles the physical reality of the modeled world more closely than the classical interconnected block schemes in SIMULINK$_{TM}$. SIMSCAPE$_{TM}$ describes the system behavior much better than SIMULINK$_{TM}$ does. Simulation models are more legible in SIMSCAPE, ~~and therefore SIMSCAPE$_{TM}$ is~~ which can be considered a very suitable tool to model physiological systems.

The simulation results obtained are in agreement with those previously obtained by Avanzolini et al [14]. Apart from the simulations described above (change in peripheral resistance, physical exercise, aortic insufficiency, hypervolemia), it is possible to simulate a great many different pathological conditions such as hemorrhage, hypertension, heart failure, valvular pathologies, renal diseases, and so on, just by

updating either the structure or the parameters of the cardiovascular model in terms of the analog electronic circuit. In this way, the use of SIMSCAPE$_{TM}$ facilitates the software implementation of both physiological and pathological scenarios in cardiovascular simulation as compared to direct electronic designs of Rupnik et al [17] and Podnar et al 2004 [18] or block-oriented software by McLoone et al 2011 [27]. Besides, the SIMSCAPE$_{TM}$ environment allows the use of the complete set of MATLAB$_{TM}$ Toolboxes and can interact with SIMULINK$_{TM}$, sharing its functionality through the complete set of its Libraries. In this sense, it has superior performance to MODELICA$_{TM}$, which doesn't provide such functionality.The described approach represents also a valuable tool in the teaching of physiology for graduate medical students.

Future works consider the short and long term pressure control mechanisms involved in the cardiovascular control, namely the baroreceptor mechanism and the renal regulation, respectively, in order to improve physicians' understanding of the feedback loop control mechanisms underlying the cardiovascular system. Also, the development of a SIMSCAPE$_{TM}$ Physiological Library for the building of cardiovascular and respiratory models is currently under construction.

References

[1] K. Thomaseth, Multidisciplinary modelling of biomedical systems, Comput. Methods Programs Biomed. 71 (2003) 189-201.

[2] MATLAB 2010, /http://www.mathworks.com/

[3] M. Hakman, T. Groth, Object-oriented biomedical system modelling:/The rationale, Comput. Methods Programs Biomed. 59 (1999) 1-17.

[4] S.E. Mattsson, H. Elmquist, M. Otter, Physical system modelling with Modelica, Control Eng. Practice 6 (1998) 501-510.

[5] D. Bruck, H. Elmqvist, H. Olsson, S.E. Matteson, Dymola for multi-engineering modelling and simulation, in: Proc. 2nd Int. Modelica Conference, Germany (2002) 551-558.

[6] J. Fernandez de Canete, C. Galindo, I. Garcia-Moral, System engineering and automation. An interactive educational approach, Springer-Verlag, 2011.

[7] G. Zauner, D. Leitner, F. Breitenecker, Modeling structural dynamic systems in MODELICA/Dymola, MODELICA/Mosilab and AnyLogic, in: Proc. Int. Workshop on Equation-Based Oriented Languages and Tools, 2007.

[8] M. Tiller, Introduction to physical modeling with modelica, Kluwer Ac. Press, 2001.

[9] F.E. Cellier, A, Nebot, Object-oriented modeling in the service of medicine, in: Proc. 6th Asia Simulation Conference, Beijing, China (2005) 33-40.

[10] J. Kofranek, Design of educational simulators, what is behind the curtain, in: MEFANET report Inst. Biestatistic and Analysis Univ. Masarykova (2008) 60-72.

[11] J. Fernandez de Canete, P. Del Saz Huang, First-principles modeling of fluid and solute exchange in the human during normal and hemodialysis conditions, Comput. Biol. Med. 40 (2010) 740-750.

[12] A.C. Guyton, J.E. Hall, Textbook of medical physiology, 9th Edition, W.B. Saunders, New York, NY, 1996.

[13] R.M. Berne, M.N. Levy, Cardiovascular physiology, Mosby, St. Louis, 1997.

[14] G. Avanzolini, P. Barbini, A. Cappello, G. Cevenini, CACDS simulation of the closed-loop cardiovascular system, Int. J. Biomed. Comput. 22 (1988) 39-49.

[15] R.S. Srinisavan, J.I. Leonard, R.J. White, Mathematical modeling of physiological states, in: Space Biology and Medicine, Huntoon, Antipov, Grigoriev (eds), vol. 3, American Institute of Aeronautics and Astronautics, Reston, VA (1996) 559-594.

[16] C.F. Rothe, J.M. Gersting, Cardiovascular interactions: an interactive tutorial and mathematical model, Am. J. Physiol. Adv. Physiol. Educ. 26 (2002) 98–109.

[17] M. Rupnik, F. Runovc, D. Sket, M. Kordas, Cardiovascular physiology: simulation of steady state and transient phenomena by using the equivalent electronic circuit, Comput. Meth. Prog. Bio. 67 (2002) 1–12.

[18] T. Podnar, F. Runovc, I. Milisav, M. Kordas, Simulation of some short-term control mechanisms in cardiovascular physiology, Comput. Biol. Med. 34 (2004) 35–49.

[19] M. Sever, T. Podnar, F. Runovc, M. Kordas, Analog simulation of two clinical conditions: (1)Acute left ventricle failure; (2) exercise in patient with aortic stenosis, Comput. Biol. Med. 37 (2007) 1051 – 1062.

[20] J. Kofranek, L.D. Anh, H. Snaselova, R. Kerekes, T. Velan, GOLEM – multimedia simulator for medical education, in: L. Patel, R. Rogers, R. Haux (Eds.), Proceedings of the 10th World Congress on Medical Informatics, IOS Press, London (2001) 1042–1046.

[21] G.M. Raymond, E. Butterworth, J.B. Bassingthwaighte, JSIM: Free software package for teaching physiological modeling and research. Exp. Biol. 280 (2003) 102-107.

[22] S.R. Abram, B.L. Hodnett, R.L. Summers, T.G. Coleman, R.L. Hester, Quantitative circulatory physiology. An integrative mathematical model of human mathematical model of human physiology for medical education, Adv. Physiol. Educ. 31 (2007) 202–210.

[23] J.B. Bassingthwaighte, Strategies for the Physiome project. Ann. Biomed. Eng. 28 (2000) 1043-1058.

[24] NSR Physiome Models, 2010, [Online] http://www.physiome.org/Models/

[25] R.L. Hester, T.G. Coleman, R. Summers, A multilevel open source integrative model of human physiology, FASEB J. 22 (2008) 756-758.

[26] A mathematical model of integrated human physiology, 2010 [Online], http://www.hummod.org/

[27] V.I. McLoone, J.V. Ringwood, B.N. VanVliet, Graphical simulation environments for modelling and simulation of integrative physiology, Comput. Meth. Prog. Bio. 102(3) (2011) 295-304.

[28] J. Kofranek, M. Matejak, P. Privitzer, M. Tribula, Causal or acausal modelling: labour for humans or labour for machines, in: Proceed. Technical Computing Prague, Prague (2008) 124-140.

[29] J. Kofranek, S. Matousek, J. Rusz, P. Stodulka, P. Privitzer, M. Matejak, M. Tribula, M. The Atlas of physiology and pathophysiology: Web-based multimedia enabled interactive simulations, Comput. Meth. Progr. Bio. (in press) 2011.

[30] G. Avanzolini, P. Barbini, A. Cappello, A. Cevese. Time-varying mechanical properties of the left ventricle. A computer simulation, IEEE T. Biomed. Eng. 32 (1985) 756-763.

[31] B.C. McInnis, Z.W. Guo, P.C. Lu, J.C. Wang, Adaptive control of left ventricular bypass assist devices, IEEE T. Automat. Contr. 30 (1985) 322-329.

Table 1. Set of state variables with equivalent quantities corresponding to the cardiovascular model

State Variable	Electric System	Cardiovascular System
x_1	Voltage C_1	Aortic pressure
x_2	Current L_1	Blood flow in arterial systemic circulation
x_3	Voltage C_2	Systemic pressure
x_4	Current L_2	Blood flow in venous systemic circulation
x_5	Voltage C_3	Right venous atrial pressure
x_6	Charge E_R	Right ventricle volume
x_7	Voltage C_4	Pulmonary venous pressure
x_8	Current L_3	Blood flow in arterial pulmonary circulation
x_9	Voltage C_5	Pulmonary pressure
x_{10}	Current L_4	Blood flow in venous pulmonary circulation
x_{11}	Voltage C_6	Left venous atrial pressure
x_{12}	Charge E_L	Left ventricle volume

Table 2. Set of Dynamic Sate Equations corresponding to the Cardiovascular Model

$$\frac{dx_1}{dt} = \frac{1}{C_1}\left(\frac{S_1(t)\Delta P_1(t)}{R_l + R_1} - x_2\right) \quad (14)$$

$$\frac{dx_2}{dt} = \frac{1}{L_1}(x_1 - R_2 x_2 - x_3) \quad (15)$$

$$\frac{dx_3}{dt} = \frac{1}{C_2}(x_2 - x_4) \quad (16)$$

$$\frac{dx_4}{dt} = \frac{1}{L_2}(x_3 - R_3 x_4 - x_5) \quad (17)$$

$$\frac{dx_5}{dt} = \frac{1}{C_3}\left(x_4 - \frac{S_2(t)\Delta P_2(t)}{R_4}\right) \quad (18)$$

$$\frac{dx_6}{dt} = \frac{S_2(t)\Delta P_2(t)}{R_4} - \frac{S_3(t)\Delta P_3(t)}{R_r + R_5} \quad (19)$$

$$\frac{dx_7}{dt} = \frac{1}{C_4}\left(\frac{S_3(t)\Delta P_3(t)}{R_r + R_5} - x_8\right) \quad (20)$$

$$\frac{dx_8}{dt} = \frac{1}{L_3}(x_7 - R_6 x_8 - x_9) \quad (21)$$

$$\frac{dx_9}{dt} = \frac{1}{C_5}(x_8 - x_{10}) \quad (22)$$

$$\frac{dx_{10}}{dt} = \frac{1}{L_4}(x_9 - R_7 x_{10} - x_{11}) \quad (23)$$

$$\frac{dx_{11}}{dt} = \frac{1}{C_6}\left(x_{10} - \frac{S_4(t)\Delta P_4(t)}{R_8}\right) \quad (24)$$

$$\frac{dx_{12}}{dt} = \frac{S_4(t)\Delta P_4(t)}{R_8} - \frac{S_1(t)\Delta P_1(t)}{R_1 + R_l} \quad (25)$$

Table 3. List of physical conserving ports in SIMSCAPE$_{TM}$

Physical Port Type	Effort Variable	Flow Variable
Electrical	Voltage	Current
Mechanical Translational	Velocity	Force
Mechanical Rotational	Angular Velocity	Torque
Hydraulic	Pressure	Flow Rate
Thermal	Temperature	Heat Flow

Table 4. Initial values of state variables and parameters of the cardiovascular model

Parameter		Value
x_{1_0}	Initial aortic pressure (mmHg)	71.112
x_{2_0}	Initial blood flow in arterial systemic circulation (cm^3s^{-1})	8.880
x_{3_0}	Initial systemic pressure (mmHg)	70.516
x_{4_0}	Initial blood flow in venous systemic circulation (cm^3s^{-1})	67.337
x_{5_0}	Initial right venous atrial pressure (mmHg)	3.328
x_{6_0}	Initial right ventricle volume (cm^3)	105.520
x_{7_0}	Initial pulmonary venous pressure (mmHg)	13.417
x_{8_0}	Initial blood flow in arterial pulmonary circulation (cm^3s^{-1})	0.786
x_{9_0}	Initial pulmonary pressure (mmHg)	13.393
x_{10_0}	Initial blood flow in venous pulmonary circulation (cm^3s^{-1})	23.836
x_{11_0}	Initial left venous atrial pressure (mmHg)	11.294
x_{12_0}	Initial left ventricle volume (cm^3)	112.760

U_{pL}	Left peak isovolumic pressure (mmHg)	50.000
U_{pR}	Right peak isovolumetric pressure (mmHg)	24.000
E_{dL}	Left elastance while diastole (mmHg cm^{-3})	0.100
E_{sL}	Left elastance while systole (mmHg cm^{-3})	1.375
E_{dR}	Right elastance while diastole (mmHg cm^{-3})	3.000E-02
E_{sR}	Right elastance while systole (mmHg cm^{-3})	0.328
R_{mL}	Left myo. viscosity resistance (mmHg s cm^{-3})	8.000E-02
R_{mR}	Right myo. viscosity resistance (mmHg s cm^{-3})	1.750E-02
R_1	Aortic valve resistance (mmHg s cm^{-3})	3.7511E-03
R_2	Aortic-systemic resistance (mmHg s cm^{-3})	6.7501E-02
R_3	Systemic resistance (mmHg s cm^{-3})	1.000
R_4	Tricuspid valve resistance (mmHg s cm^{-3})	3.751E-03
R_5	Pulmonary valve resistance (mmHg s cm^{-3})	3.751E-03
R_6	Pulmonary artery resistance (mmHg s cm^{-3})	3.3761E-02
R_7	Pulmonary resistance (mmHg s cm^{-3})	0.101
R_8	Mitral valve resistance (mmHg s cm^{-3})	3.751E-03
L_1	Aortic-systemic inertance (mmHg s^2 cm^{-3})	8.250E-04
L_2	Systemic inertance (mmHg s^2 cm^{-3})	3.600E-03
L_3	Pulmonary artery inertance (mmHg s^2 cm^{-3})	7.500E-04
L_4	Pulmonary inertance (mmHg s^2 cm^{-3})	3.080E-03
C_1	Aortic compliance ($mmHg^{-1}$ cm^3)	0.220
C_2	Arterial systemic compliance ($mmHg^{-1}$ cm^3)	1.460
C_3	Venous systemic compliance ($mmHg^{-1}$ cm^3)	20.000
C_4	Pulmonary artery compliance ($mmHg^{-1}$ cm^3)	9.000E-02
C_5	Arterial pulmonary compliance ($mmHg^{-1}$ cm^3)	2.670
C_6	Venous pulmonary compliance ($mmHg^{-1}$ cm^3)	46.700
t_c	Cardiac period (s)	0.800

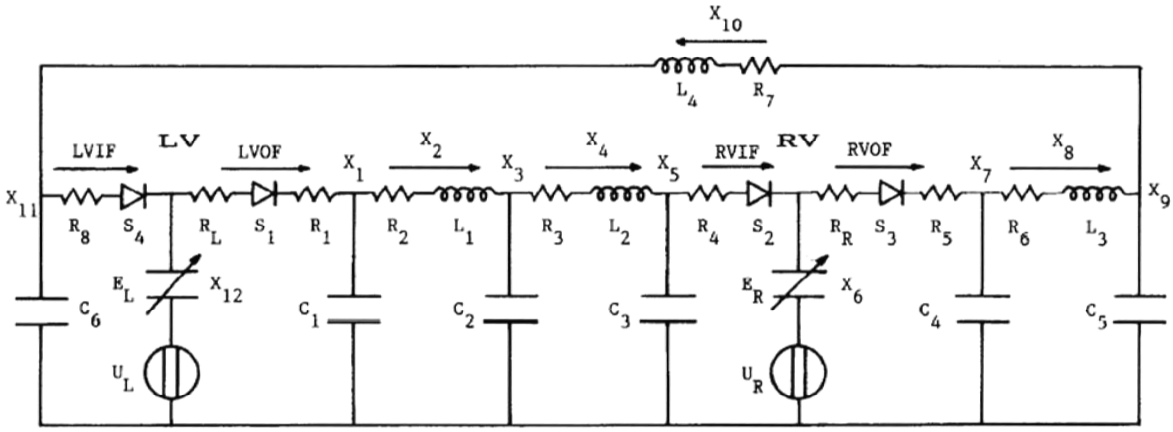
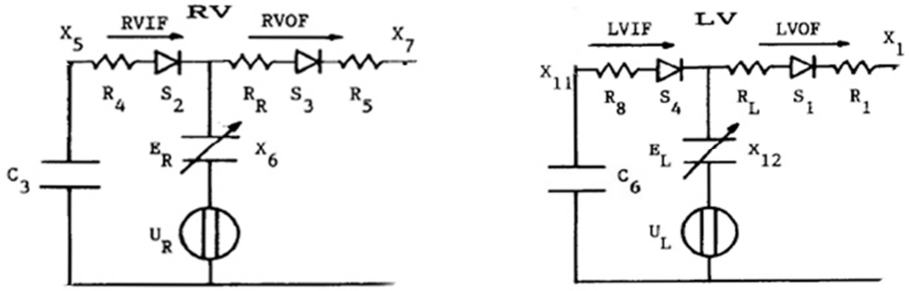
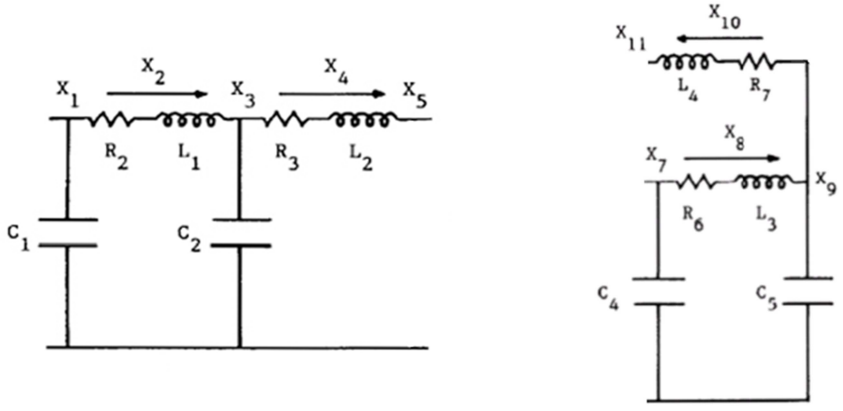


Fig. 1. Electronic model of the closed loop cardiovascular system



(a) (b)

Fig. 2. Right (a) and left (b) ventricles analogue models



(a) (b)

Fig. 3. Systemic (a) and pulmonary (b) circulation analogue models

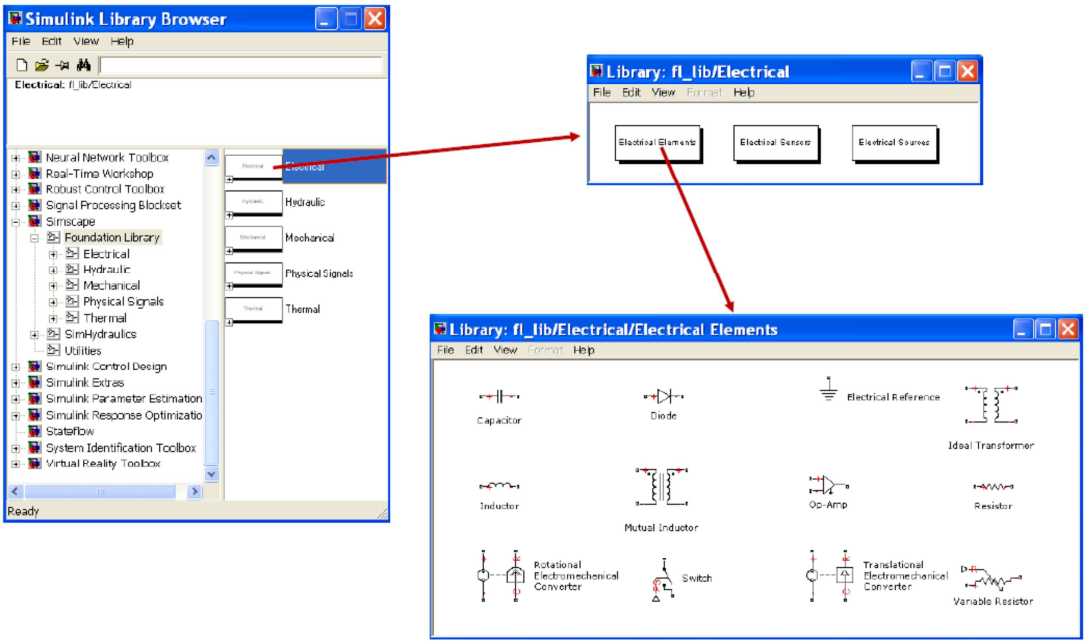


Fig. 4. The SIMSCAPE$_{TM}$ Electrical Library

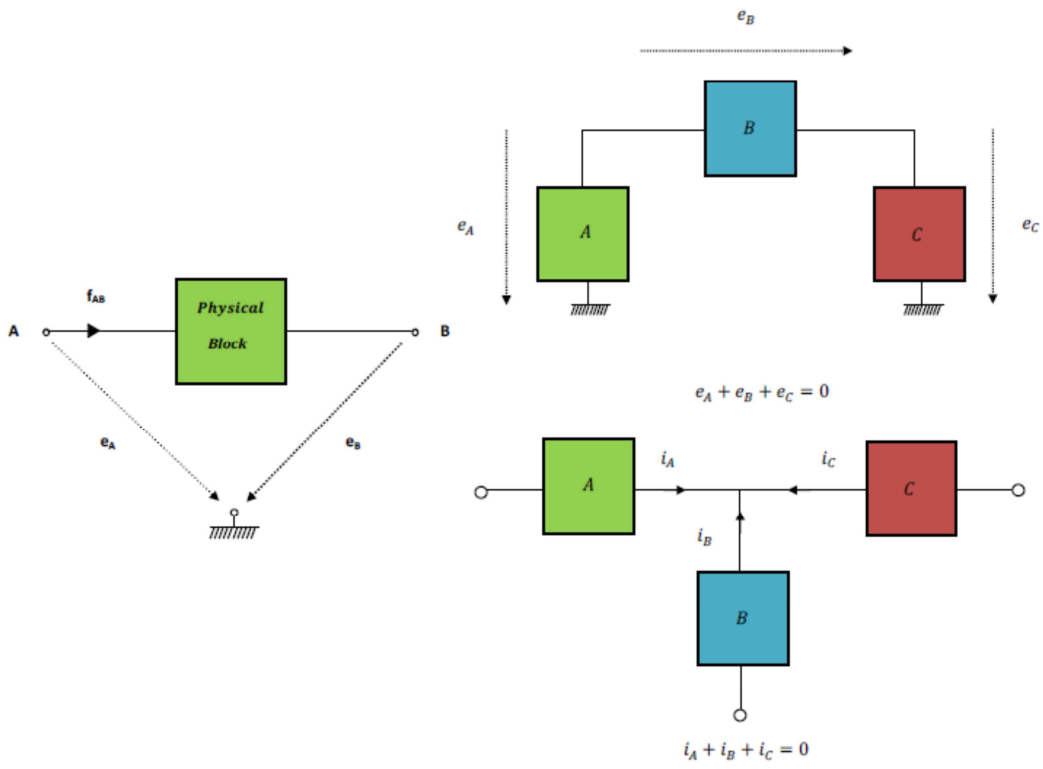


Fig. 5. Physical block diagrams in SIMSCAPE$_{TM}$ (a) effort and flow variables for each SIMSCAPE$_{TM}$ component (b) conservation laws

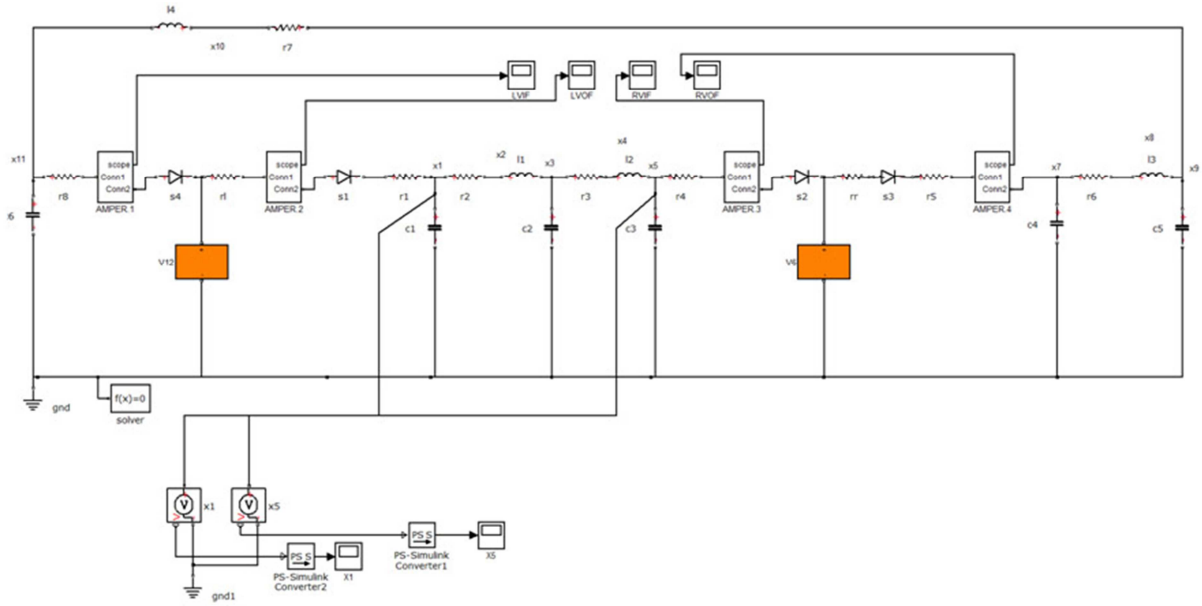


Fig. 6. The SIMSCAPE$_{TM}$ model of the cardiovascular system

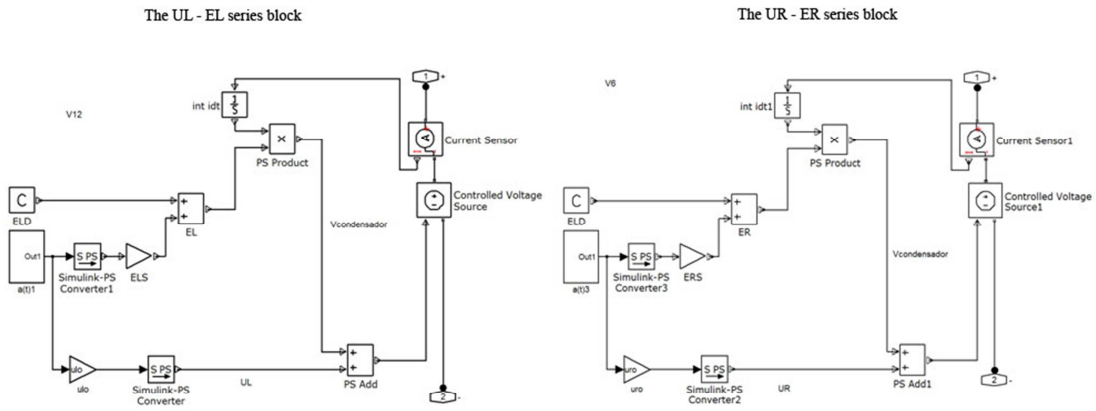


Fig. 7. The SIMSCAPE$_{TM}$ subsystems $U_R(t) - E_R(t)$ and $U_R(t) - E_R(t)$ to model the isovolumetric pressure generators of each ventricle

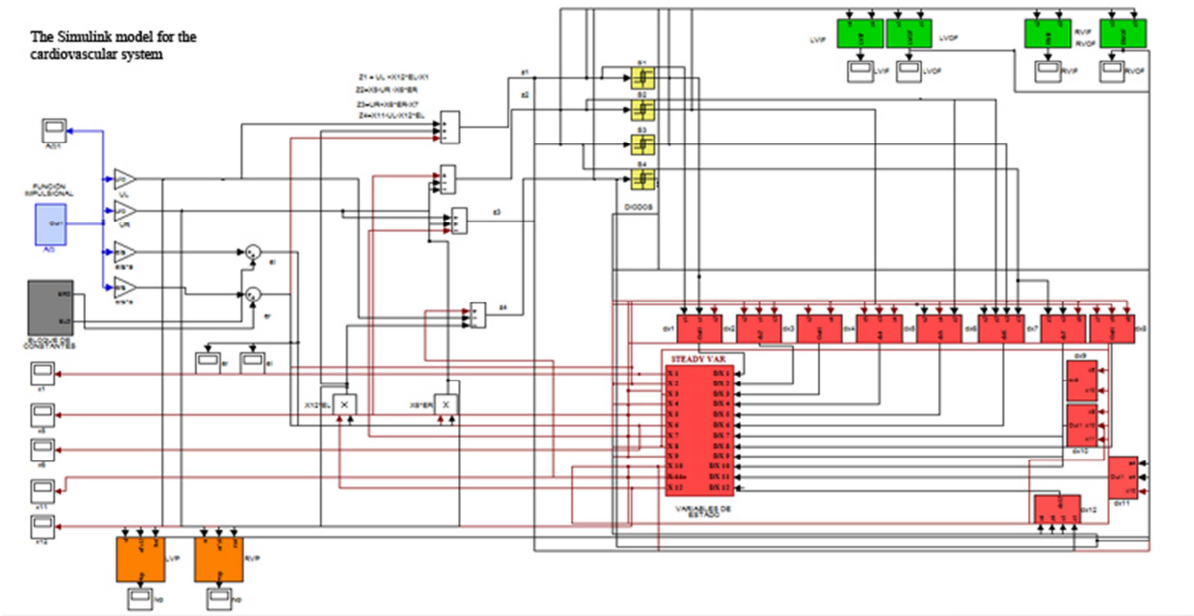


Fig. 8. SIMULINK$_{TM}$ model of the cardiovascular system

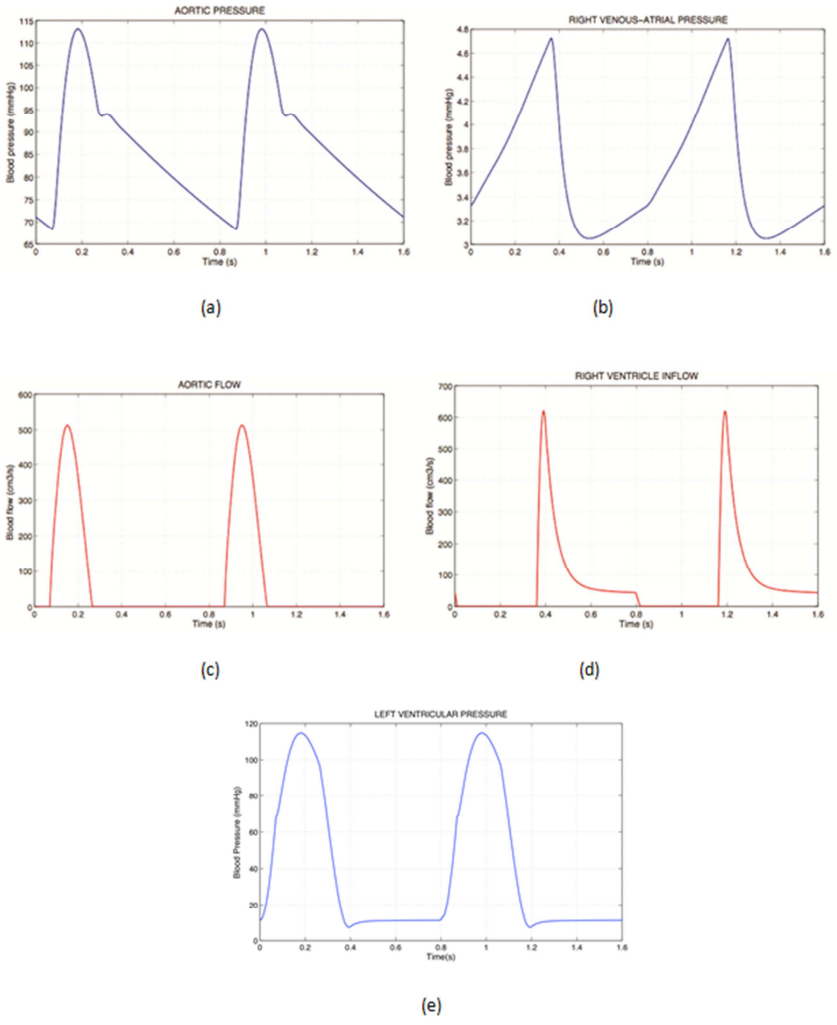
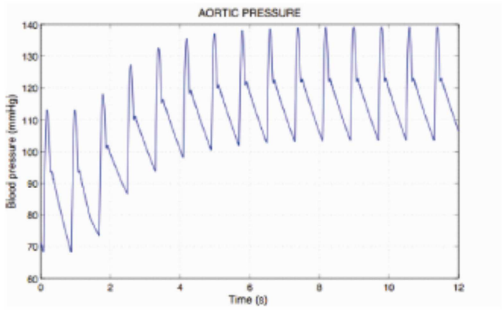
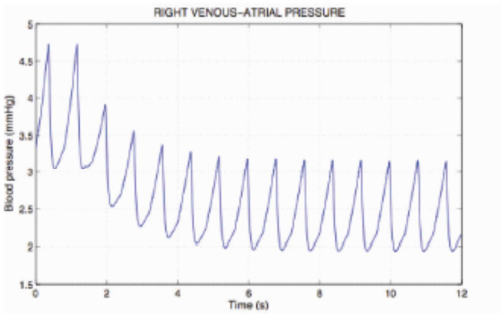


Fig. 9. Evolution under normal conditions (a) aortic pressure (b) right venous-atrial pressure (c) left ventricle outflow (d) right ventricle inflow (e) left venous-atrial pressure

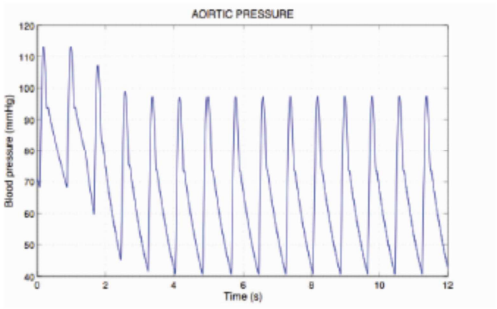


(a)

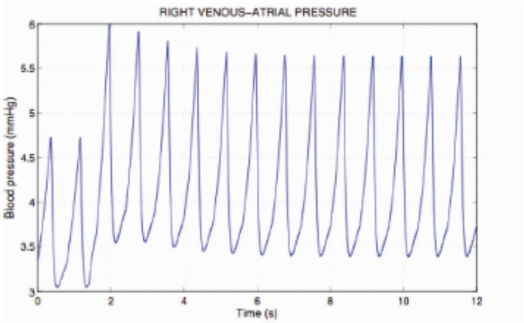


(b)

Fig. 10. Evolution after imposing a sudden change in value of resistance R_3 at 1.4 s simulation time (a) aortic pressure (b) right venous-atrial pressure

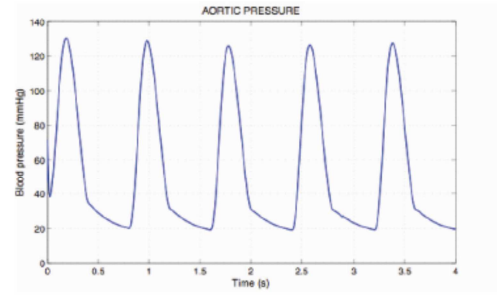


(a)

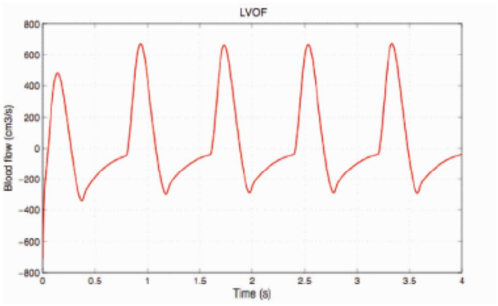


(b)

Fig. 11. Evolution after decreasing the systemic (R_2 and R_3) and pulmonary resistances (R_6 and R_7) values by about 60% and increasing the isovolumetric peaks U_{pR} and U_{pL} by 15% at 1.4 s simulation time (a) aortic pressure (b) right venous-atrial pressure

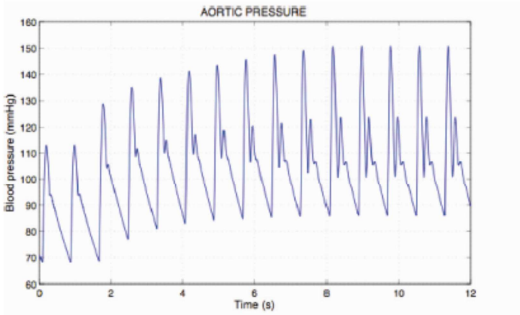


(a)

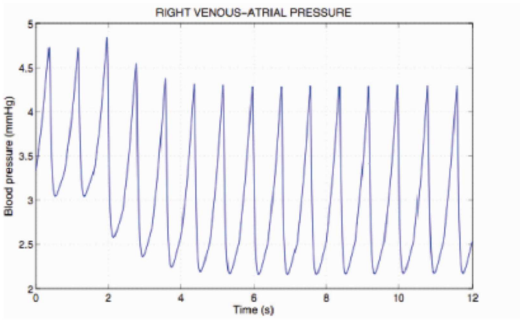


(b)

Fig. 12. Evolution with an insufficiency condition, with aortic resistance R_1 reduced to 60% of its normal value and murmur on the aortic valve S_1 (a) aortic pressure (b) left ventricular outflow



(a)



(b)

Fig. 13. Evolution during induced hypervolemia by increasing the inductances L_1 and L_2 by an extra 80% from 1.4 to 8 s (a) aortic pressure (b) right venous-atrial pressure