Simulations of the Cardiovascular System Using the Cardiovascular Simulation Toolbox

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―――― **Abstract** ――――

In the present document, six mathematical models of the cardiovascular system are studied and implemented in MATLAB® R2013a using an updated version of the Cardiovascular Simulation Toolbox proposed by O. Barnea at the Tel-Aviv University. All the mathematical models are based on electrical lumped-parameter analogies. The results of the simulations are compared with a list of expected hemodynamic parameters and contrasted with laboratory values.

1 Introduction

Simulation with lumped-parameter models is one of the traditional approaches to model the cardiac system. After the development of the Windkessel models by O. Frank in 1899 [6], several mathematical models based on equivalent circuits have been proposed. One of the efforts to build a complete set of equivalent models for cardiovascular simulations has been made by O. Barnea *et al.* [1] at the Tel-Aviv University. His team developed a Cardiovascular Simulation Toolbox for MATLAB® R14. This open-source tool is conformed by a set of 21 individual lumped-parameter electrical models. Complex models of the circulatory system can be achieved by interconnecting blocks and signals.

Barnea's library of models was no longer supported by the recent releases of MATLAB® because the original toolbox was built using the Power Systems Blockset™, and it was replaced by the SimPowerSystems™ module for Simulink®. In a previous publication [11] we showed our efforts to update Barnea's toolbox to the newer releases of MATLAB®, and published an updated version currently working in MATLAB® R2013a.

In this document, we implement six mathematical models in MATLAB® R2013a using this updated version of the Cardiovascular Simulation Toolbox, in order to obtain the hemodynamic parameters of healthy persons. The numerical results of this work are compared with reference hemodynamic parameters obtained at specialized laboratories [10] [7] [4]. The most important parameters used to compare simulations in this work are the cardiac output (CO), the blood flow or aortic flow (AQ) and the arterial pressure (AP).
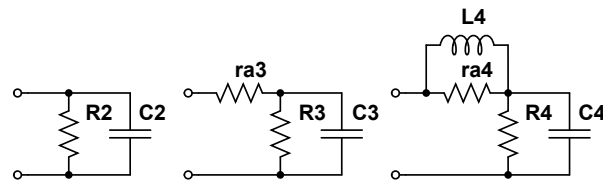
■ **Figure 1** The Windkessel models of second, third and fourth order.
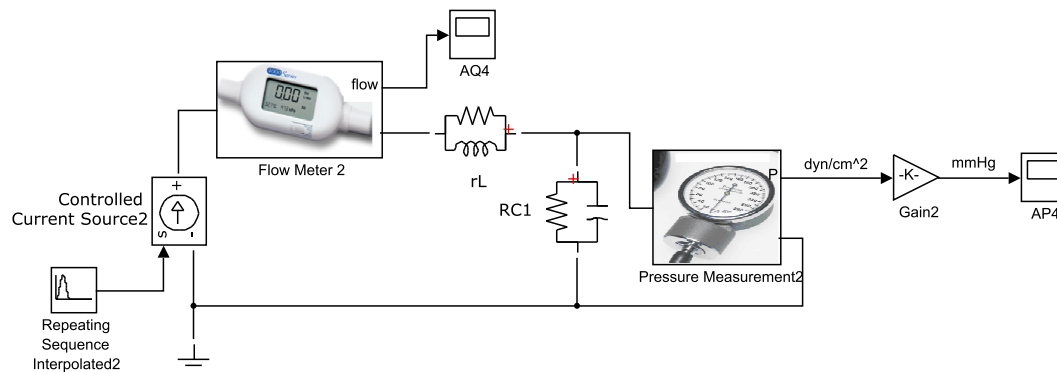
■ **Figure 2** Windkessel model of fourth order, implemented in Simulink® using blocks from the Cardiovascular Simulation Toolbox [15].

1.1 Windkessel models (WK)

The first Windkessel model model was proposed by O. Frank in 1899 [6]. The simplest model is the second order Windkessel model (WK2) and includes a single resistor R and a single capacitor C that are the equivalent lumped parameters of the systemic circulatory system. On 1930 Ph. Broemser and O. Ranke [2] added a third circuit element r used to describe the input impedance of the aorta. This model is called the third order Windkessel model (WK3). The final model of four elements (WK4) was proposed to improve the dynamic response of the circuit and it includes an inductance L, describing the inertia of blood. The circuit representations of the Windkessel models are shown in Figure 1.

To simulate this model, the input flow of the left ventricle is required. We assumed a sinusoidal pulsing function, as described in [8]. The model calculates the mean arterial pressure (MAP), to calculate the cardiac output.

The models of Figure 1 are implemented in Simulink® using different blocks from the Cardiovascular Simulation Toolbox [15] and some extra blocks from the SimPowerSystems™ library. The block diagram of the fourth-order Windkessel model using Barnea's toolbox is presented in Figure 2.

The simulation results of the three Windkessel models are presented in Figure 3, which is a graphic describing the arterial pressure as a function of time. Constants required for the parameters of the elements are from M. Hlaváč [8].

Based on the results from Figur 3 the mean arterial pressure is calculated, and then divided by the total peripheral resistance (TPR) in order to obtain the mean aortic flow (MAQ). The cardiac output is calculated multiplying by 60. Results of these calculations are presented on Table 1 with the results of the other models.
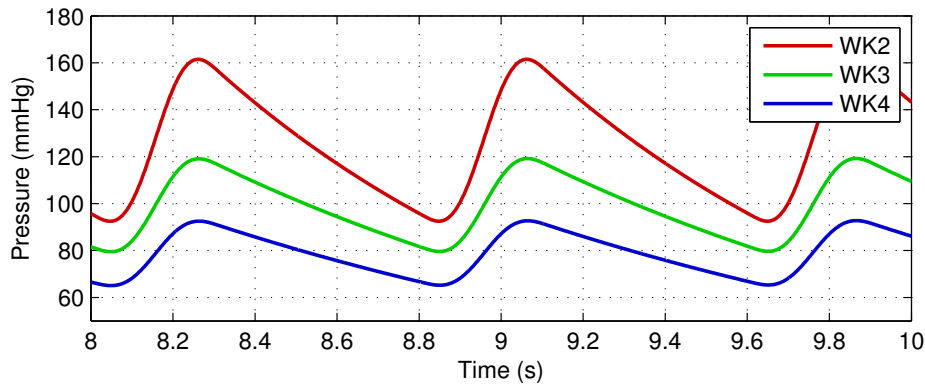
■ **Figure 3** Arterial pressure as a function of time for the Windkessel models.
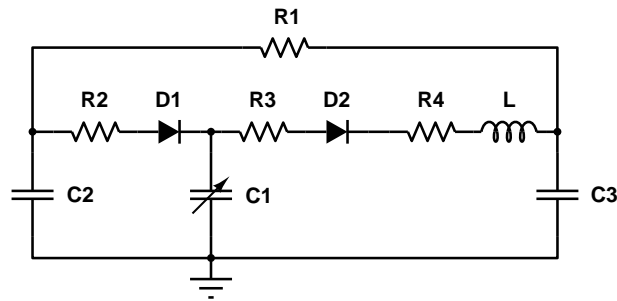
■ **Figure 4** Circuit diagram for A. Ferreira model [5].

1.2   Lumped-parameter model of A. Ferreira

The model of A. Ferreira [5] is shown in Figure 4. The left ventricle C1 is described with a variable capacitor, because the walls of the heart chambers are elastics, and the elastance changes over time across the cardiac cycle. The left atria is described by the capacitance C2. The peripheral circulatory system is described by R1 and C3. Also the model includes the mitral valve, described by D1 and R2, and the aortic valve formed by D2 and R3. The resistor R4 models the input impedance of the aorta, and the inductance L describes the inertia of blood. Mitral valve and aortic valve are described with thyristors, switched with control signals to enable or block the blood flow in one direction.

To implement this model in Simulink® a new block was designed for the Cardiovascular Simulation Toolbox. The block is a variable non-linear capacitor, where the capacitance can be adjusted using an external elastance function. This elastance function is described by A. Ferreira *et al.* [5] and it is composed of exponential functions. The new block is based on the existent polynomial capacitor, but a multiplier was added and the polynomial block removed, in order to include the external signal that modulates the compliance of the block.

The model of A. Ferreira calculates the instantaneous arterial pressure in the same way as the Windkessel models, and then calculates the mean arterial pressure and the cardiac output. In this simulation, cardiac output has a value of 4.64 L/min. This value is included in Table 1 with the other results of this simulation.
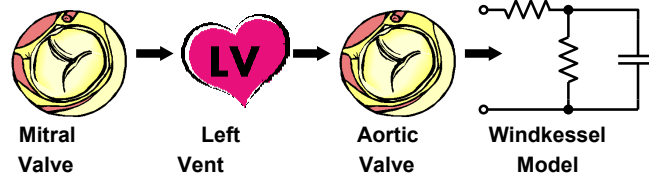
The Simulink® implementation of the electrical model of A. Ferreira is presented in Figure 5. Simulation results for the model of A. Ferreira can be appreciated in Figure 6.
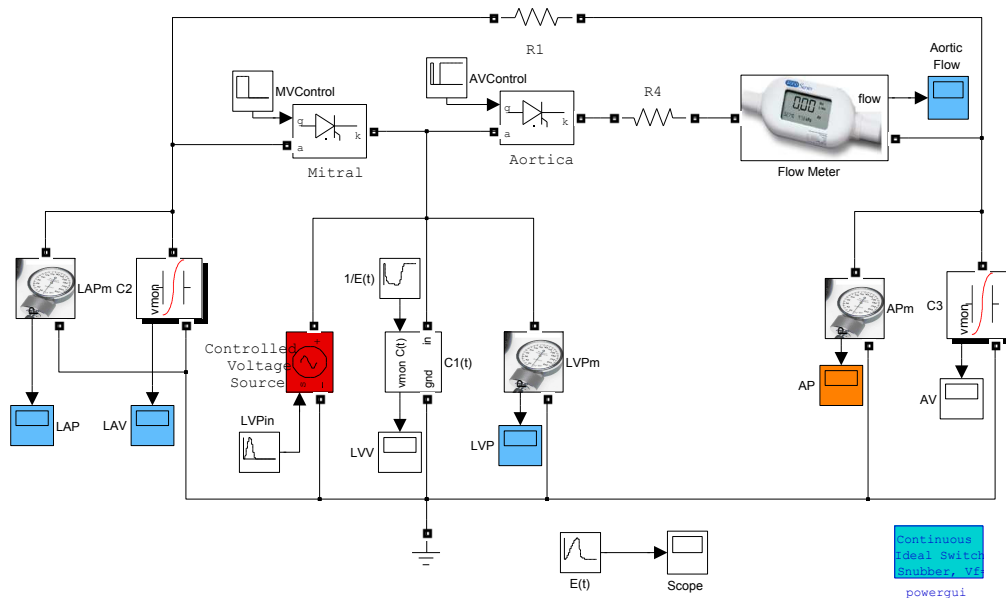
Figure 5 Simulink® implementation of the electrical model of A. Ferreira.
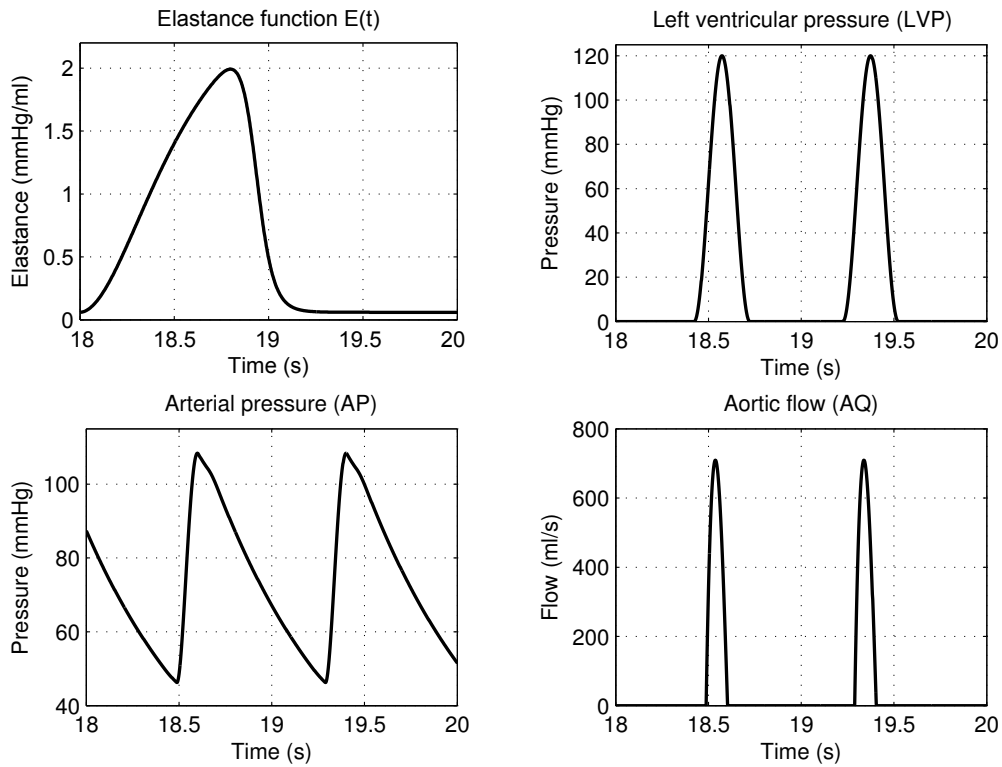
Figure 6 Simulation results of A. Ferreira model.

■ **Figure 7** Block diagram of the Windkessel model with the left ventricle [15].

1.3   Windkessel model coupled to left ventricle (WK+V)

The main problem with the Windkessel models is that they require information about the flow generated by the left ventricle. In many simulations this flow is approximated by a sinusoidal representation that does not reproduce exactly the waveform of real blood flow, and this represents an error source. In order to improve the accuracy, this model simulates the left ventricle using the varying elastance model, and couples the generated flow to a third-order Windkessel model to obtain the final results of mean arterial pressure and cardiac output. The block diagram of this model is shown in Figure 7.

The Windkessel model coupled to the left ventricle (WK+V) is similar to A. Ferreira's model because it uses an elastance function to describe the left ventricle, and connects it to a third order Windkessel model. The difference is that the left ventricle is characterized by a third order polynomial elastance function instead of the exponential function of Ferreira's model. This simulation is included as an example of the Cardiovascular Simulation Toolbox and here is implemented in MATLAB® R2013a. The implementation of this model is shown in Figure 8. Simulation results for this mathematical model are shown in Figure 9.

## 1.4   Systemic and pulmonary circulation model (2A2V)

This model proposed by O. Barnea *et al.* [15] in the Cardiovascular Simulation Toolbox includes the systemic and pulmonary circulation, both atria, ventricles and the four cardiac valves. This model also simulates the oxygen saturation in blood across the sections of the cardiovascular system. The model calculates the pressure and volume at multiple points and the pressure-volume loop can be obtained by plotting the pressure and the volume of the left ventricle.

We used this model to obtain the hemodynamic parameters of a healthy person, considering a left-ventricular ejection fraction of 58.7% as suggested by Schlosser [14]. Adjusting the physical parameters of the atria and ventricles, we were also able to simulate the behavior of the cardiovascular system for a person suffering from systolic heart failure, with a left-ventricular ejection fraction of 24.6% [3].

Lumped-parameter models of the cardiovascular system in MATLAB® can be coupled with three-dimensional models, described in COMSOL® and simulated with finite element methods (FEM). Some examples of this coupling can be found in [12, 13].

The block diagram of the systemic-pulmonary model can be appreciated in Figure 10.

This model enables to obtain the pressure-volume loops for a healthy person, and also for a person suffering from systolic heart failure, as can be appreciated in Figure 11. The graphic from the left is obtained by running the default simulation of the model provided by O. Barnea, and it shows the cardiac cycle with the typical values expected for the subject. The complete set of parameters resulting from this simulation of the healthy system has been published in [11].
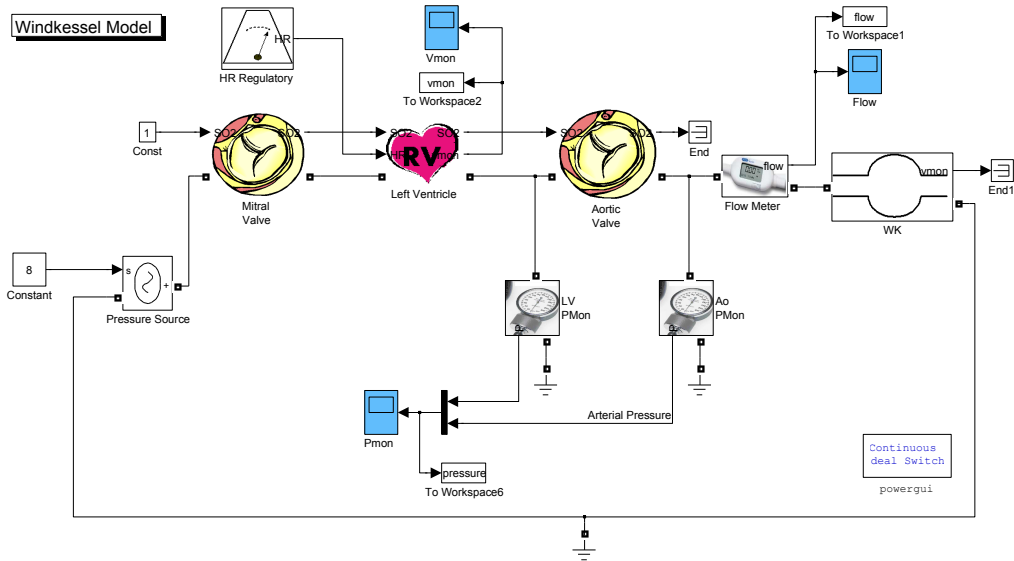
Figure 8 Simulation of the left ventricle coupled to a third order Windkessel model [1].
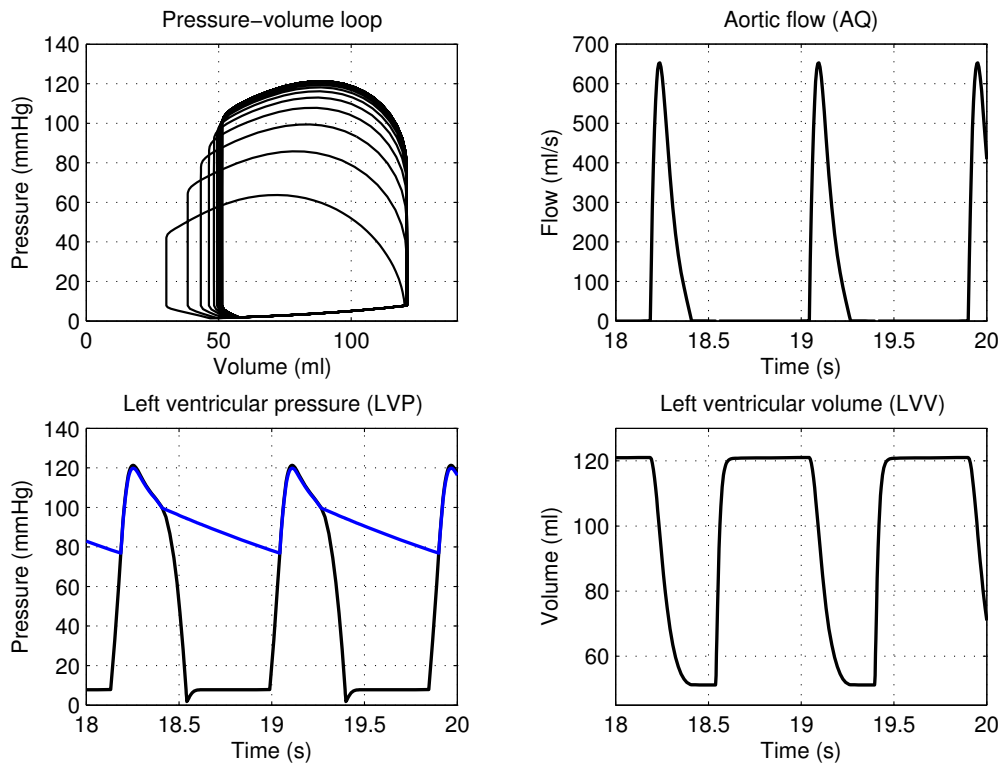
Figure 9 Simulation results of the WK+V model.

■ **Table 1** Results of the simulation of six mathematical models of the cardiovascular system, implemented with blocks from the Cardiovascular Simulation Toolbox and the SimPowerSystems$^{\text{TM}}$ toolbox.

Variable	WK2	WK3	WK4	WK+V	Ferreira	2V2A	Reference value
HR	75,00	75,00	75,00	70,00	75,00	75,00	$48 - 105$ [16]
CO	7,49	5,91	4,71	4,89	4,64	6,71	$4.0 - 8.0$ [4]
SV	99,87	78,80	62,80	69,81	61,87	89,45	$60 - 100$ [4]
MAP	124,83	98,54	78,49	-	-	116,83	$70 - 105$ [10]
SBP	161,49	119,25	92,76	119,86	108,39	143,89	$90 - 140$ [10]
DBP	92,50	79,60	65,23	76,87	46,24	68,35	$60 - 90$ [10]
LVEDV	-	-	-	121,00	-	152,47	$65 - 239$ [14]
LVESV	-	-	-	51,20	-	63,012	$16 - 143$ [14]
LVP	-	-	-	121,30	120,00	147,19	140 [9]
LVEf	-	-	-	57,69	-	58,67	$59,2 \pm 13,7$ [14]
RVEDV	-	-	-	-	-	152,85	$100 - 160$ [10]
RVESV	-	-	-	-	-	78,92	$50 - 100$ [10]
RVEDP	-	-	-	-	-	40,12	$15 - 25$ [10]
RVESP	-	-	-	-	-	2,17	$0 - 8$ [10]
RVEf	-	-	-	-	-	48,37	$40 - 60$ [10]

In order to simulate the cardiovascular system of a person suffering from systolic heart failure, we proceeded to decrease the elastances of the heart chambers, and increase the effective resistance of the cardiac valves, to describe a heart that cannot eject blood with the same effectiveness as a regular heart. This hardening of the heart was done by adjusting the model parameters in Simulink. The complete set of output parameters has been published also in [11].

Comparing the two diagrams shown in Figure 11, it can be observed that, when the person has a medical condition, the volume of blood in the left ventricle tends to increase, because the heart cannot eject the same volume per beat (the stroke volume is reduced). The stroke volume can be calculated from the plots by subtracting the maximum and minimum volumes. It can be appreciated that the stroke volume for the healthy simulation is higher than the stroke volume for the systolic heart failure.

The models also enable the verification of medical devices such as a intra-aortic balloon or a ventricular assist device. Any device model can be developed and coupled to this simulation, to study and observe the changes of the hemodynamic parameters as the response of the body after the medical device implantation. We have developed a dummy VAD block, as seen in Figure 10, but further development is required.

Table 1 includes the simulation results for the six mathematical models studied in this document. The list of output parameters consists of the following: Heart Rate (HR, bpm), Cardiac Output (CO, ml), Stroke Volume (SV, ml), Mean Arterial Pressure (MAP, mmHg), Systolic Blood Pressure (SBP, mmHg), Diastolic Blood Pressure (DBP, mmHg), Left Ventricular End-Diastolic Volume (LVEDV, ml), Left Ventricular End-Systolic Volume (LVESV, ml), Left Ventricular Pressure (LVP, mmHg), Left Ventricular Ejection Fraction (LVEf, %), Right Ventricular End-Diastolic Volume (RVEDV, ml), Right Ventricular End-Systolic Volume (RVESV, ml), Right Ventricular End-Diastolic Pressure (RVEDP, mmHg), Right Ventricular End-Systolic Pressure (RVESP, mmHg) and Right Ventricular Ejection Fraction (RVEf, %).
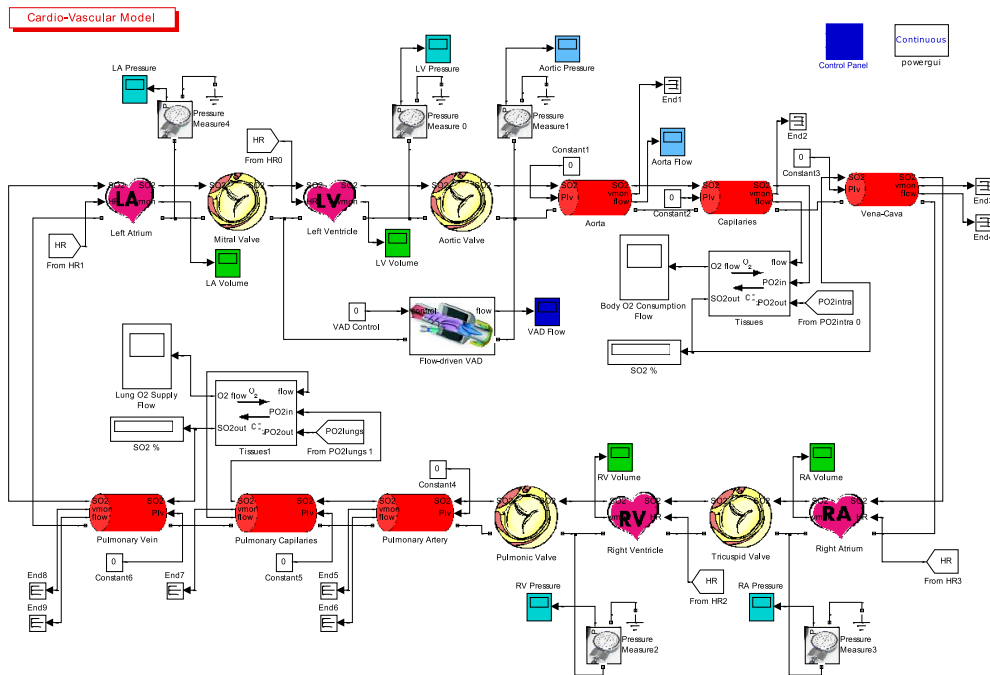
■ **Figure 10** Block diagram of the complete circulatory system using the Cardiovascular Simulation Toolbox [15]. This model considers systemic and pulmonary circulation, coupled to the four chambers of the heart.
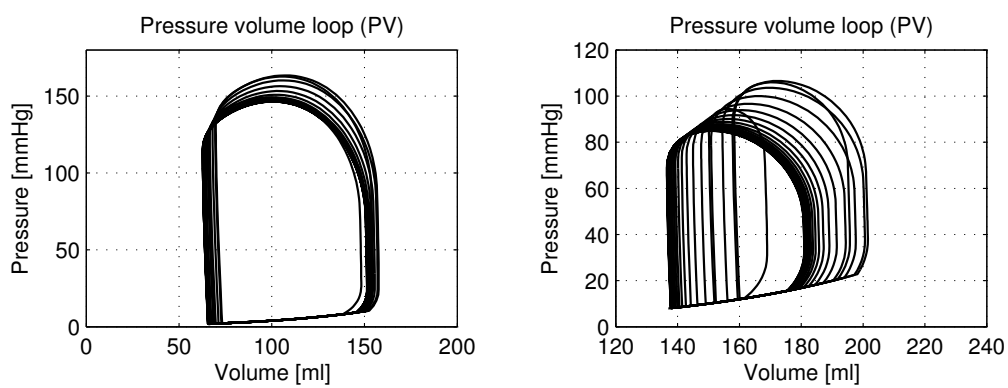
■ **Figure 11** Pressure-volume loops for the left ventricle in the 2A2V circulatory model, in normal health conditions (left, LVEf=58.7%) and with systolic heart failure (right, LVEf=24.6%).

2 Analysis

Lumped-parameter electrical models of the cardiovascular system are an appropriate method to obtain several hemodynamic parameters of the circulation, and are a commonly used approach in many simulations.

Windkessel models of order 2, 3 and 4 are faster to produce results that the other models, and they require less computational power. These models are a good approximation to obtain the most general values and understand the basic behavior of the peripheral circulatory system, but they provide only the cardiac output and the arterial pressure.

The most versatile models are implemented with the Cardiovascular Simulation Toolbox because it presents excellent modularity and it is expandable with custom blocks. This characteristic permits to modify existent models in order to describe and simulate cardiac and circulatory diseases. The toolbox also can simulate existent lumped-parameter electrical models, such as the Windkessel models, the Ferreira model and many others.

We added a new block to the Cardiovascular Simulation Toolbox, describing a variable capacitor with an external compliance function C(t). This block was necessary to simulate Ferreira's model. The block enabled the use of the elastance function E(t) proposed on Ferreira's work.

Based on the results from Table 1 it can be observed that the 2A2V model calculates a higher number of parameters and it can obtain results for both ventricles. The other models have less precision and describe only the response of the systemic circulatory system to the input flow from the ventricle. The 2A2V model calculates the ejection fractions for both ventricles, and the results are compliant with the theoretical data.

3 Conclusions

We have implemented several models found in the literature using the Cardiovascular Simulation Toolbox from O. Barnea, in MATLAB® R2013a. The two models reviewed that can produce a pressure-volume loop are the WK+V and the 2A2V models. The other models do not generate sufficient information to calculate these diagrams.

In the Windkessel models, the comparison parameter is the cardiac output, and it can be appreciated how this value is close to the expected value when the order of the model is increased. These models are exact but they do not calculate any information about the behavior of the ventricles.

The numerical comparison of the models showed that the 2A2V simulation calculates the higher number of output parameters and has an adequate accuracy comparing with the expected laboratory values. The parameters of this model can be adjusted further to simulate illnesses and defects in the cardiovascular system, and several blocks can be added to the Cardiovascular Simulation Toolbox as they are required.

The models implemented in MATLAB® can be further improved by coupling the system with COMSOL® to increase numerical precision and produce realistic results.

We have used the 2A2V model to simulate the cardiovascular system of a healthy person, and also of a patient suffering from systolic heart failure, achieving a LVEf of 58.7% for the healthy cardiovascular system, and a LVEf of 24.6% for systolic heart failure, showing agreement with the expected parameters from Chatterjee *et al.* [3].

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