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A Family of Circulatory Computer Models Developed to Analyse and Predict Physiopathological Events: Applications to Mechanical Circulatory and Ventilatory Assistance

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The aim of this work is to present a family of circulatory computer models suitable to be used for analysis and prediction. Circulatory models can reproduce many circulatory phenomena for several practical applications referable to the main functional sectors of analysis and prediction. Of course, the models are different in relation to the phenomena to be represented. An important issue is the possibility to represent the artero-ventricular interactions and the effects, in different ventricular conditions, of the influence of mechanical ventilatory and circulatory assistance. In these models of human cardiovascular system, the influence of mechanical ventilation was introduced, changing the thoracic pressure to positive values. In the work, two different applications were presented: in the first the trends of the haemodynamic variables were analysed when mechanical ventilation of the lungs was applied for different values of mean intrathoracic pressures. In the second, were presented the effects on the haemodynamic variables of the left ventricular assist device (in particular a rotary blood pump) that aspirates blood from the left ventricle and ejects it into the aorta.

K e y w o r d s : Circulatory Model, Mechanical Ventilation, Ventricular Assist Device, Computer Simulation, Haemodynamics, Intrathoracic Pressure

1. Introduction

Circulatory models can reproduce many circulatory phenomena for several practical applications referable to the main functional sectors of analysis and prediction [1, 2]. Of course, the models are different in relation to the phenomena to be repre-

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sented. An important issue is the possibility to represent the artero-ventricular interactions and the effects of mechanical circulatory and ventilatory assistance. The aim of this work is to present a family of circulatory computer models suitable to be used for analysis and prediction. This family of circulatory computer models can be used for:

1. Research.
2. Testing and evaluation.
3. Education.

Considering the aims of their application, the design criteria chosen for the realisation are following:

— Flexibility, that consist in the possibility to modify easily the basic structure according to the specific needs.

— Modelling, lumped parameter models of the circulation was chosen. Reproduction of the Starling's law of the heart was realised by variable elastance models.

— Graphical presentation of data, simple and exhaustive.

— Mechanical circulatory assistance: simple connection of heart assistance (Left Ventricular Assist Device, Right Ventricular Assist Device, Bi-Ventricular Assist Device, Intraaortic Balloon Pump and Hemopump).

— Mechanical ventilatory assistance: possibility to reproduce, by intrathoracic pressure, its effects on haemodynamic and ventricular energetic variables.

Mechanical heart assistance has the aim to improve general circulatory conditions. If it is used for heart recovery, has the additional aim to improve coronary circulation and unload the failing ventricle supporting, in this way, its recovery. Among the devices used for heart recovery, an important role is played by non-pulsatile devices as their characteristics make their use rather simple and competitive in comparison to other devices such as intraaortic balloon pump (IABP). Hemopump HP31 device (Medtronic, Inc., Minneapolis, Minnesota, USA) is among them: it is a miniature rotary blood pump introduced into the ventricular cavity through the valve. This ventricular assist device (VAD) aspirates the blood from the left (right) ventricular cavity and ejects it into the aorta (pulmonary artery). This device can be considered as a sequential pump to the left (right) ventricle.

In this study, according with Bai's works [3,4], was modelled Hemopump type HP31. This VAD can be operated at seven different rotational speeds ranging from 17000 to 26000 rpm, with an increment of 1500 rpm.

2. Methods

Figure 1 shows the general structure of different sections of the cardiovascular system [1, 5, 6]. The nomenclature is presented in Table 1. The basic structure was constantly updated resulting in creation of a library of models for several circulatory compartments, heart assist devices (like intraaortic balloon pump, left ventricu-

Table 1. Nomenclature of the parameters and variables used in the model

	Resistance [$mmHg \cdot cm^{-3} \cdot sec$]	Compliance [$cm^3 \cdot mmHg^{-1}$]	Inertance [$mmHg \cdot cm^{-3} \cdot sec^2$]	Pressure [mmHg]	Flow [$l \cdot mmHg^{-1}$]
LEFT (RIGHT) HEART SECTION					
Left input (output) valve	Rli (Rlo)				
Right input (output) valve	Rri (Rro)				
Left (right) atrium		Cla (Cra)		Pla (Pra)	
Left input (output) flow					Qli (Qlo)
Right input (output) flow					Qri (Qro)
Left (right) ventricle				Plv (Prv)	
SYSTEMIC SECTION					
Systemic arterial section [7, 8]					
Systemic arterial section	Rvs	Cvs		Pvs	
PULMONARY SECTION					
Pulmonary arterial section	Rap – Rcp	Cap	Lap	Pap	
Pulmonary venous section		Cvp		Pvp	
Mean Thoracic Pressure				Pt	
ASSIST DEVICES					
Hemopump					
Left Ventricular Assist Device (LVAD)					
Right Ventricular Assist Device (LVAD)					
Intraaortic Balloon Pump (IABP)					

lar assist device, right ventricular assist device, bi-ventricular assist device and Hemopump) and assisted ventilation. Feedbacks were introduced to control peripheral resistances and ventricular function.

In Figure1 the following sections are presented: the left and right ventricle and the left and right atrium sections, the systemic-arterial and venous and the pulmonary arterial and venous sections. When necessary, it is possible to add to the network the coronary circulation. When pathological conditions are reproduced it is possible to insert the intraaortic balloon pump or ventricular assist device. The VAD presented in this work is a pneumatic device that produces a pulsatile flow; it can be inserted in series or in parallel to the left natural ventricle. It is possible to reproduce also the effects of bi-ventricular assistance with two pneumatic VAD. Finally it is also possible to simulate a rotary blood pump that produces a continuous flow. This pump is the Hemopump HP31 that takes blood from the ventricle and ejects it into the artery. Hemopump may be used as the left or right ventricular assist device and as bi-ventricular assist device.

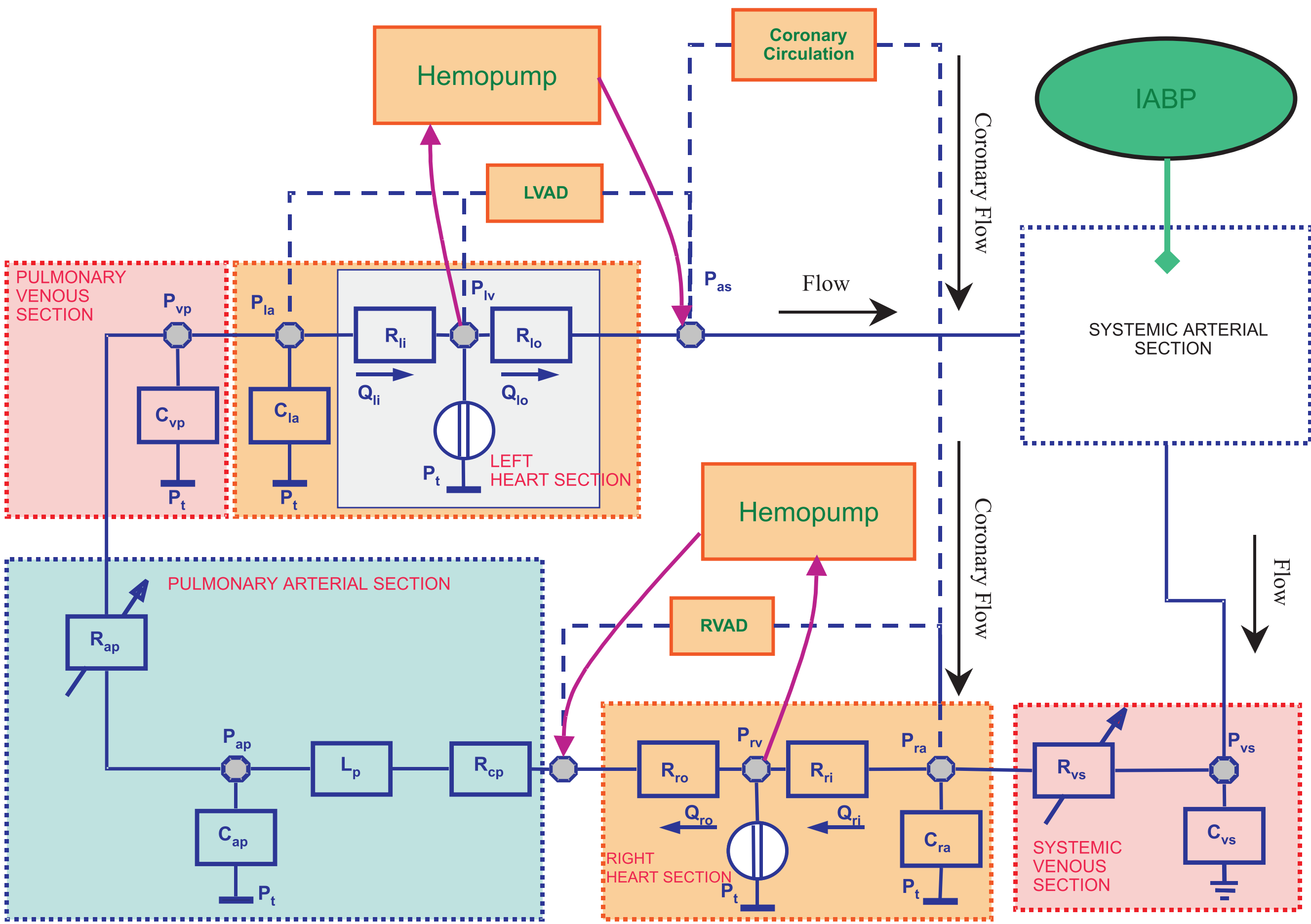

Fig. 1. General structure of different sections of the cardiovascular system. Systemic arterial section is described in literature [7, 8]. LVAD (RVAD) is the left (right) ventricular assist device. IABP is the intraaortic balloon pump

Changing the mean intrathoracic pressure value, the effect of mechanical ventilation of the lungs can be simulated. The mechanical ventilation is frequently used alone in emergency situations or simultaneously with ventricular assist devices.

The model chosen to represent the Starling's law of the heart for each ventricle is based on the variable elastance model, modified according to Suga and Sagawa's studies [9]. The heart contraction and ejection phase and the ventricular filling are represented by equations reported in literature [1, 5, 6].

As far as the circulatory system is concerned, its basic structure is a lumped parameter structure where windkessel models are widely used.

For the coronary model (Fig. 2), it is possible to chose between two different models. The simple model (the upper panel) consists of a diode and a resistance [10]. The complex model (the lower panel) consists of five sections that are the coronary arterial input resistance, the coronary arterial and venous microcirculation, the myocardial compliance and the coronary venous resistance [11]. The nomenclature is represented in Table 2. Both the models are connected to the systemic arterial section and to the right atrium.

The models of heart assist device can be characterised by the different insertion point in the circulatory network. For the pneumatic ventricular assist device, de-

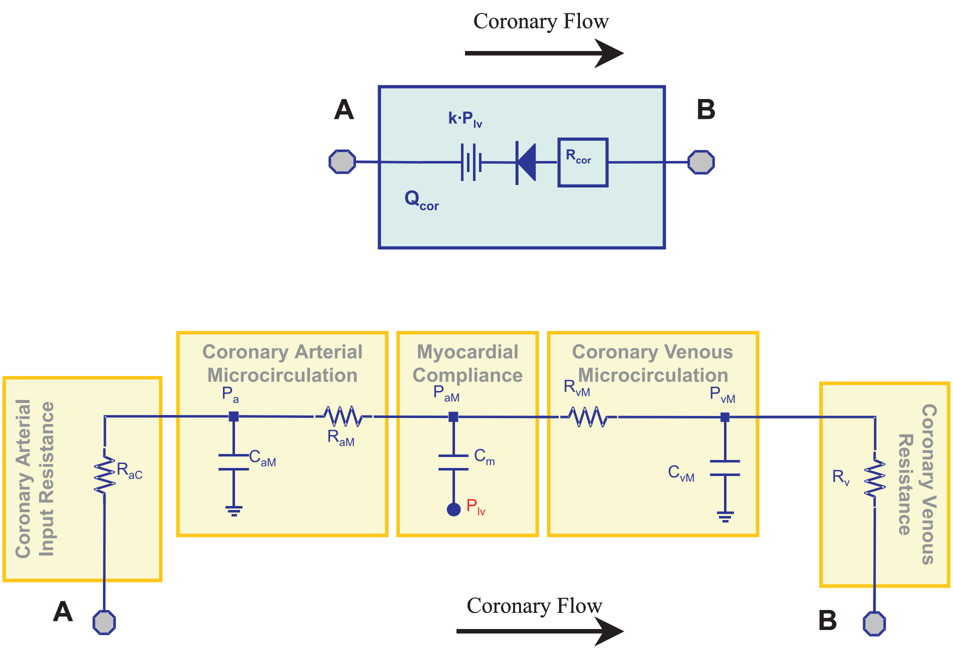

Fig. 2. Electrical analogue of the coronary models. The upper (lower) panel shows the simple (complex) model. The full nomenclature of the electric analogue is reported in Table 2. In both the models the input (point A) was connected to the systemic arterial pressure (Pas — see Fig. 4), the output (point B) was connected to the right atrial pressure (Pra — see Fig. 4).

Table 2. Nomenclature of the parameters and variables used in the coronary models

	Resistance [mmHg·cm^{-3}··sec]	Compliance [cm^3·mmHg^{-1}]	Pressure [mmHg]	Constant	Flow [l·mmHg^{-1}]
SIMPLE MODEL					
Coronary Resistance	Rcor				
Left ventricular pressure			Plv		
Coronary flow					Qcor
Constant				K	
COMPLEX MODEL					
Coronary arterial input compartment	RaC				
Coronary arterial microcirculation compartment	RaM	CaM	Pa		
Myocardial compartment		Cm	PaM – Plv		
Coronary venous microcirculation compartment	RvM	CvM	PvM		
Coronary venous compartment	Rv				

scribed in the previous papers [12, 13], it is possible to choose between the parallel and the serial connection. In the parallel connection, the device aspirates blood from the atrium, in the serial connection it aspirates blood from the ventricle. In this model of pneumatic ventricle, the filling and ejection phases are represented separately. Parallel VAD can be used for bi-ventricular assistance.

The intraaortic balloon pump is represented as a flow generator. The model reproduces filling and emptying of a balloon considering, when present, its elastic properties [14]. For a pneumatic ventricular assist device and an intraaortic balloon pump (IABP), it is possible to set several variables, such as the filling and emptying pressures and timing. Hemopump HP31 is a serial rotary blood pump that aspirates blood from the ventricle and ejects it into the artery. It is simulated as a flow generator, and it can be used for the left or right ventricle or for bi-ventricular assistance. In the model, it is possible to set different rotation speeds [3, 4].

The software presented in this work (its name is CARDIOSIM©) runs on any personal computer under the Windows system. It is implemented using the Visual Basic language. The structure of the model can be easily modified using its wide library of models. The set of the presented variables can be easily modified. It is possible to program experiments with constant afterload or constant peripheral resistance. Graphical presentation of the data is performed in terms of the time courses, average values in the cardiac cycle, ventricular work cycles. Ventricular energetic variables (External Work, Pressure Volume Area, Potential Energy, Oxygen Consumption (VO_2) and Cardiac Mechanical Efficiency [CME=EW/VO_2]) [9] are among the computed data. It is possible to simulate mechanical heart assistance. Mechanical ventilation (MV) of the lungs can be simulated controlling the mean intrathoracic pressure value [6, 12, 13].

In this work, two different applications of the CARDIOSIM© software are presented: in the first application a MV of the lungs with three different value of the intrathoracic pressure was simulated, in the second a pathological condition (like heart failure) was reproduced and successively a LVAD was applied with two different rotational speed.

3. Results

Figure 3 shows one of the possible outputs of the software presented. Three different particular graphical presentations can be observed. They are:

1. The vascular tone index (VTI) window, in which the relationships between the cardiac index (CI) and the total peripheral resistance (TPR) is presented [15, 16].
2. The window, in which the wedge (CWP) and CI relationship is shown [15, 16].
3. The ventricular function index (VFI) window, where the left ventricular systolic work (LVSW) and the central venous pressure (CVP) relationship are presented [15, 16].

In the same figure, in the upper panel, the left (left panel) and right (right panel) ventricular pressure volume loop, during the cardiac cycle, are presented. In the lower panel the instantaneous left ventricular and systemic arterial pressure curves during the cardiac cycle are presented. In Figure 3 two columns are also present, they represent respectively the command panel (left side) and the mean values panel, in which the mean values during the cardiac cycle of pressures and flows, the stroke volume and the end systolic (diastolic) volume for both ventricles are reported.

A particular application of the model's family is the reproduction of ventilatory assistance controlling the mean intrathoracic pressure (Pt). For this example, the network assembled like in Fig. 4 (see Table 3) was chosen, in which there are: the left and right heart, the coronary section, the systemic arterial section, the splanchnic venous and peripheral circulation, the extrasplanchnic venous and peripheral circulation, the peripheral and venous circulation in the active muscle compartment, the systemic thoracic veins section [17, 18] and the pulmonary arterial, peripheral and venous sections [19]. During this simulation the Hemopump (represented in Fig. 4) was not applied.

Starting from these choices for the circulatory network, the effects of MV of the lungs on some haemodynamic variables by changing the mean intrathoracic pressure value from Pt = 0 mmHg to Pt = –2 mmHg and to Pt = +5 mmHg were simulated. Table 4 shows the results of our simulation on the haemodynamic variable. In general, when Pt changes from 0 mmHg to –2 mmHg, all the variables presented (except right atrial pressure-Pra) increase, when Pt changes from 0 mmHg to +5 mmHg all the variables (except Pra) decrease. These results are in a good agreement with the data reported in literature. Analysing Table 4, it is possible to observe

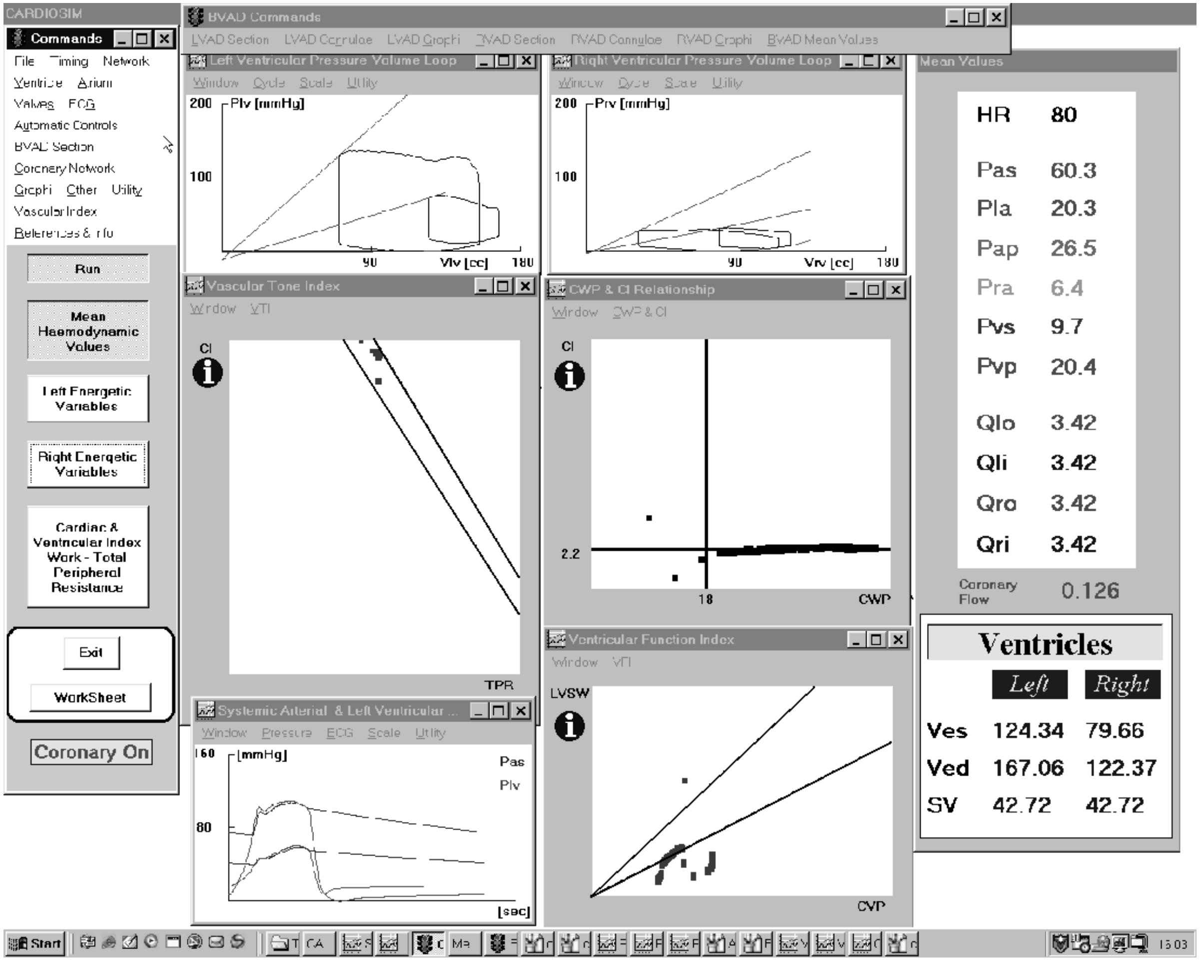

Fig. 3. One of the different outputs produced by CARDIOSIM© software. Left (right) ventricular pressure volume loop and pressures windows show the curves of two different circulatory conditions, produced when starting from the control condition (represented by the large cardiac loop) and after reducing the left and right ventricular elastance (condition represented by the small cardiac loop), like in pathological condition. VFI, VTI and CI-CWP windows show the different positions assumed from the working point in the passage from the control to a pathological condition

Table 3. Nomenclature of the parameters and variables used in Fig. 4

	Resistance [mmHg·cm^{-3}·sec]	Compliance [cm^3·mmHg^{-1}]	Inertance [mmHg·cm^{-3}·sec^2]	Pressure [mmHg]	Flow [l·mmHg^{-1}]
LEFT (RIGHT) HEART SECTION					
Left input (output) valve	Rli (Rlo)				
Right input (output) valve	Rri (Rro)				
Left (right) atrium		Cla (Cra)		Pla (Pra)	
Left input (output) flow					Qli (Qlo)
Right input (output) flow					Qri (Qro)
Left (right) ventricle				Plv (Prv)	
SYSTEMIC SECTION					
Systemic arterial section	Ras	Cas	Las	Pas	Qas
Splanchnic venous (peripheral) circulation	Rsv (Rsp)	Csv (Csp)		Psv (Psp)	Qsv
Extrasplanchnic venous (peripheral) circulation	Rev (Rep)	Cev (Cep)		Pev	Qev
Venous (peripheral) circulation in active muscle compartment	Rmv (Rmp)	Cmv (Cmp)		Pmv	Qmv
Systemic thoracic veins circulation	Rstv	Cstv		Pstv	
PULMONARY SECTION					
Pulmonary arterial section	Rap	Cap	Lap	Pap	Qap
Pulmonary peripheral (venous) section	Rpp (Rvp)	Cpp (Cvp)		Ppp (Pvp)	Qpp (Qvp)
Mean Thoracic Pressure				Pt	

Table 4. Effects of mechanical ventilation of lungs on the haemodynamic variables

	Mean intrathoracic pressur [Pt = 0 mmHg]	Mean intrathoracic pressur [Pt = –2 mmHg]	Mean intrathoracic pressure [Pt = +5 mmHg]
Cardiac output [l/min]	4.98	5.14	4.34
Left ventricular end systolic volume [cm^{-3}]	101.36	107.2	86.63
Left ventricular end diastolic volume [cm^{-3}3]	172.49	180.55	148.58
Coronary flow [l/min]	0.212	0.219	0.185
Systolic aortic pressure [mmHg]	132.0	135.4	117.8
Diastolic aortic pressure [mmHg]	80.5	82.4	72.3
Mean arterial systemic pressure [mmHg]	92.6	94.9	82.9
Mean arterial pulmonary pressure [mmHg]	17.3	17.9	14.8
Mean peripheral pulmonary pressure [mmHg]	15.5	16.0	13.1
Mean right atrial pressure [mmHg]	4.1	3.7	5.8
Mean left atrial pressure [mmHg]	7.6	7.9	6.3

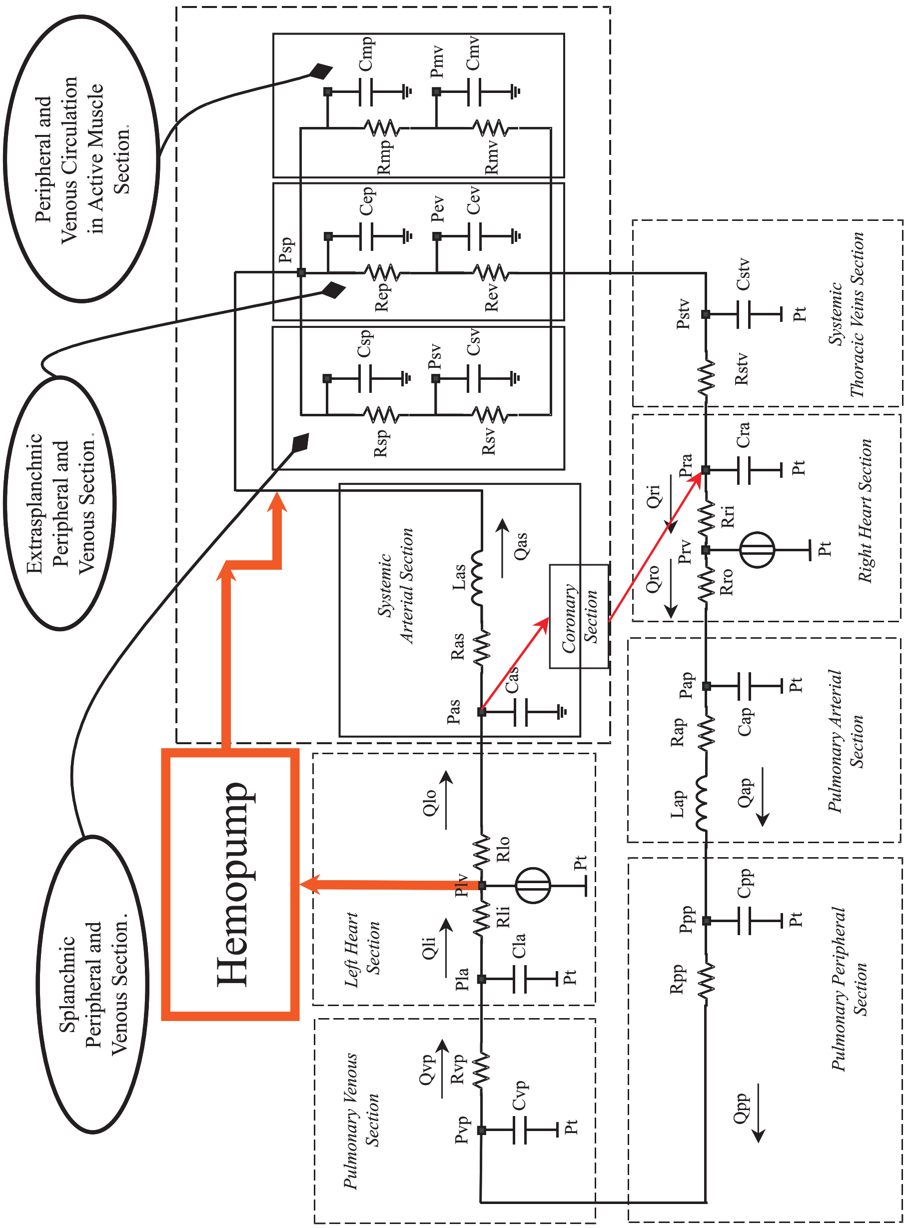

Fig. 4. Structure of the cardiovascular network chosen to simulate mechanical ventilatory and Hemopump assistance. The presented parameters are reported in Table 3.

that the trends are opposite when the intrathoracic pressure values are positive or negative.

A new simulation, regarding the effects of Hemopump HP31 left assist device on haemodynamic variables, was reproduced using the network assembled in Fig. 4. The rotary pump aspirates blood from the left ventricle and ejects it into the aorta. Starting from the control pathological condition (like in heart failure), in which the left (right) ventricular elastance was fixed to Ev_{LEFT}=0 .6 mmHg·cm^{-3} (Ev_{RIGHT}=0.3 mmHg·cm^{-3}), the left (right) ventricular rest volume was fixed to Vo_{LEFT} = 20 cm^3 (Vo_{RIGHT} = 10 cm^3) and the heart rate was 70 bpm; LVAD with two different rotational speeds (17000 and 20000 rpm) was applied. Table 5 shows the effects of the Hemopump assistance on the haemodynamic variable.

In Table 5, how the haemodynamic variables changed when the pump was on with speed 17000 rpm can be seen:

1. A rise in the total cardiac output and a drop in the left cardiac output with a relative decrease in the oxygen consumption. This effect is typical of the Hemopump assistance.
2. A rise in the left telesystolic volume and a drop in the telediastolic volume.
3. A decrease in the left ventricular end diastolic volume.
4. A decrease (increase) in the right telesystolic (telediastolic) volume.
5. An augmentation in the coronary blood flow (also this aspect is typical of LVAD).

Table 5. Effects of Hemopump HP31 application on the haemodynamic variables

	Control [EvLEFT = = 0.6 mmHg·cm^{-3}] [VoLEFT=20 cm^{-3}]	Hemopump HP31 [17000 rpm]	Hemopump HP31 [20000 rpm]
Total flow (left ventricular + Hemopump HP31) [l/min]	2.55	3.18	3.42
Hemopump flow [l/min]	0.0	2.12	2.81
Left ventricular flow [l/min]	2.55	1.06	0.61
Left ventricular end systolic volume [cm^{-3}]	131.9	134.42	134.91
Left ventricular end diastolic volume [cm^{-3}]	168.31	161.2	157.73
Right ventricular end systolic volume [cm^{-3}]	90.35	83.79	81.17
Right ventricular end diastolic volume [cm^{-3}]	126.76	129.16	130.02
Coronary flow [l/min]	0.109	0.131	0.139
Mean splanchnic peripheral pressure [mmHg]	48.1	59.3	63.7
Systolic aortic pressure [mmHg]	71.0	73.5	73.7
Diastolic aortic pressure [mmHg]	44.3	57.3	62.3
Mean arterial systemic pressure [mmHg]	50.5	60.3	64.2
Mean arterial pulmonary pressure [mmHg]	18.5	15.6	14.6
Mean peripheral pulmonary pressure [mmHg]	17.5	14.4	13.3
Mean right atrial pressure [mmHg]	5.2	5.8	6.1
Mean left atrial pressure [mmHg]	13.5	9.4	7.9

6. A drop in the pulmonary and peripheral pressures.

7. A rise (drop) in the right (left) atrial pressure.

Analysing the data reported in Table 5, it is also possible to observe that when the pump rotational speed increased from 17 000 to 20 000 rpm the effects of assistance on the haemodynamic variables presented were much more evident.

4. Conclusions

In conclusion it can be stated that:

— These models of circulation can be useful in several applications to analyse the data, or to predict the effects of specific circulatory conditions or of mechanical circulatory and/or ventilatory assistance.

— Data presentation should be done in the clearest form to be helpful in practical applications.

— Availability of a library of circulatory models assures the maximum flexibility to adapt the whole model to the specific needs.

— Maximum efforts should be made to develop packages able to be run on any personal computer.

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