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Role and Applications of Circulatory Models in Cardiovascular Pathophysiology

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Circulatory models are relevant for research, education and testing of prosthetic devices/components. Independently of its structure that can be numerical, physical or hybrid the models can be used in different areas of cardiovascular pathophysiology. However, the models are often used to reproduce specific circulatory conditions instead of being used as "systemic" tools. That is to say, the models are used to evaluate the global effects of external disturbances such as pathologies, therapies, special environments or surgery on the circulatory system. Aim of this paper is to illustrate a family of circulatory models developed to represent the whole circulatory system in pathophysiological conditions describing some of the possible applications.

K e y w o r d s: modelling of the cardiovascular system, ventricular elastance, arterial elastance, heart assist device, mock circulatory system, lumped parameter model

1. Introduction

Circulatory modelling plays a significant role in the areas of research, education and prosthetic devices/components testing and development. The use of the circulatory modelling in this frame is both local and global. The models have been used to study the specific circulatory phenomena or evaluate the global effects of external disturbances (pathologies, therapies, special environments or surgery) on the circulatory system. In other words and just as an example, the circulatory modelling can be applied for studying the same prosthetic device and investigating its fluidodynamics or its effects on the whole circulatory system.

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The outlined above is as a matter of fact the expression of two different approaches to the circulatory modelling: the first one analyses and reproduces the details of a specific circulatory phenomenon [1–3], while the second one analyses and reproduces haemodynamic and volumetric phenomena often at the level of large vessels [3–6]. This implies that the models of the first type, while giving local and detailed information on the specific phenomenon, cannot be used to obtain information on the effects of the same phenomenon at a larger scale level. In contrast, the models simulating the whole circulatory system do not give details of the circulatory phenomena. They rather give a general overview of haemodynamics to evaluate, for example, the trends of the main haemodynamic variables evidencing the critical ones [7] that should be the subject of the more accurate investigations/simulations. On the other hand, the models developed so far are tailored to the specific application both for their structure (numerical or physical) [4–9] and for the chosen representation of the circulatory system [4, 6, 10, 11].

For the above reasons, the results obtained with different models are hardly comparable. The possible solution to this problem is the development of a modelling platform flexible enough to be easily adapted to different experimental conditions considering anyway carefully any restriction to the model usage scope. To fulfil this approach, it is evidently needed a comprehensive model able to represent the whole circulatory system, built in such a way that some of its parts can be easily replaced if and when a deeper detail is necessary.

An important aspect of the comprehensive circulatory models is their capability to reproduce, in addition to haemodynamics, the artero-ventricular interaction: the concepts of the end-systolic ventricular elastance and the effective arterial elastance [12] can be used to model, analyze, interpret and resume the ventricles behaviour and its interactions with the arterial system.

To summarise, the use of the circulatory models as practical clinical, research and/or educational tools makes simplicity of use and flexibility their main requirements. However, simplicity of use and flexibility are two features that can be hardly found together in a circulatory model and are the pre-requisite to develop a model that can be treated as a modelling platform in the sense that it can be easily adapted to different needs in different environments. The goal of this paper is among others to illustrate how a family of lumped parameter circulatory models, aimed at performing a global analysis of the circulatory system, was developed. These models and their applications are the first step towards construction of a modelling platform in the sense stated above.

Among the common features of these models there is reproduction of the Starling's law of the heart by the variable elastance model. They are based on different structures (numerical, physical and hybrid) [13–15] and can be easily adapted to different applications that range from the mechanical heart assist devices testing [16] to the haemodynamics study in specific environmental conditions (breath-hold diving) [17] and the beating heart surgery [11].

2. Materials and Methods

2.1. Modelling Circulatory Pathophysiology

The use of the end-systolic ventricular elastance and the effective arterial elastance [12] provides the analytical tools necessary to study and model circulatory pathophysiology in the meaning of a comprehensive analysis. Nevertheless, there are some questions to be answered to develop models of practical usage, namely, complexity of the model, structure and technical solutions. The questions are not trivial as the answers can influence the future model usage heavily. Finding the answer to the above question one should keep in mind that the "connective tissue" is the model usage: even in the case of models intended to a well defined application area (study and reproduction of global relationships inside the circulatory system), the contours of their usage can be undefined, therefore the best solution is a flexible model that can be adapted to wide variety of different situations.

2.2. Complexity of the Model

Taking the above paragraph into consideration, the complexity of the model is a critical issue and is often a compromise between accuracy and ability to identify model parameters, and manage the variables involved in the simulation. The model complexity should be therefore tuned to the specific needs while keeping the model as simple as possible. If the model is developed to reproduce, for example, hepatic circulation, it should not include redundant details necessary in other applications. In other words, organization (and complexity) of the model depends strictly on the intended application. A proper design and organization of the model would permit to adapt it easily to the specific application. Again, the flexibility should be one of the main features of the model. The passage from a complex model to a simpler one (or from simple to more complex) implies of course use of the different models: what is important in our opinion that the model has a modular structure (the flexibility requirement) permitting to replace parts of the model when and if needed. We applied this concept extending it to the model structure developing the models defined as hybrid [13,18–21].

According to what was said above, it was necessary to chose a base circulatory model (Fig. 1) where the circulatory system is divided into seven main sections: left and right hearts, systemic and pulmonary circulation (arterial and venous), coronary circulation. The model shown in Fig.1 can be easily adapted and modified into more complex one [6] where the systemic arterial and venous circulation sections are expanded into a more complex and accurate representation. A legend of all variables is reported in Table 1.

2.3. Structure of the Model

The second question evokes the problem of the model structure. The circulatory modelling is traditionally based on two types of structures: numerical and hydraulic.

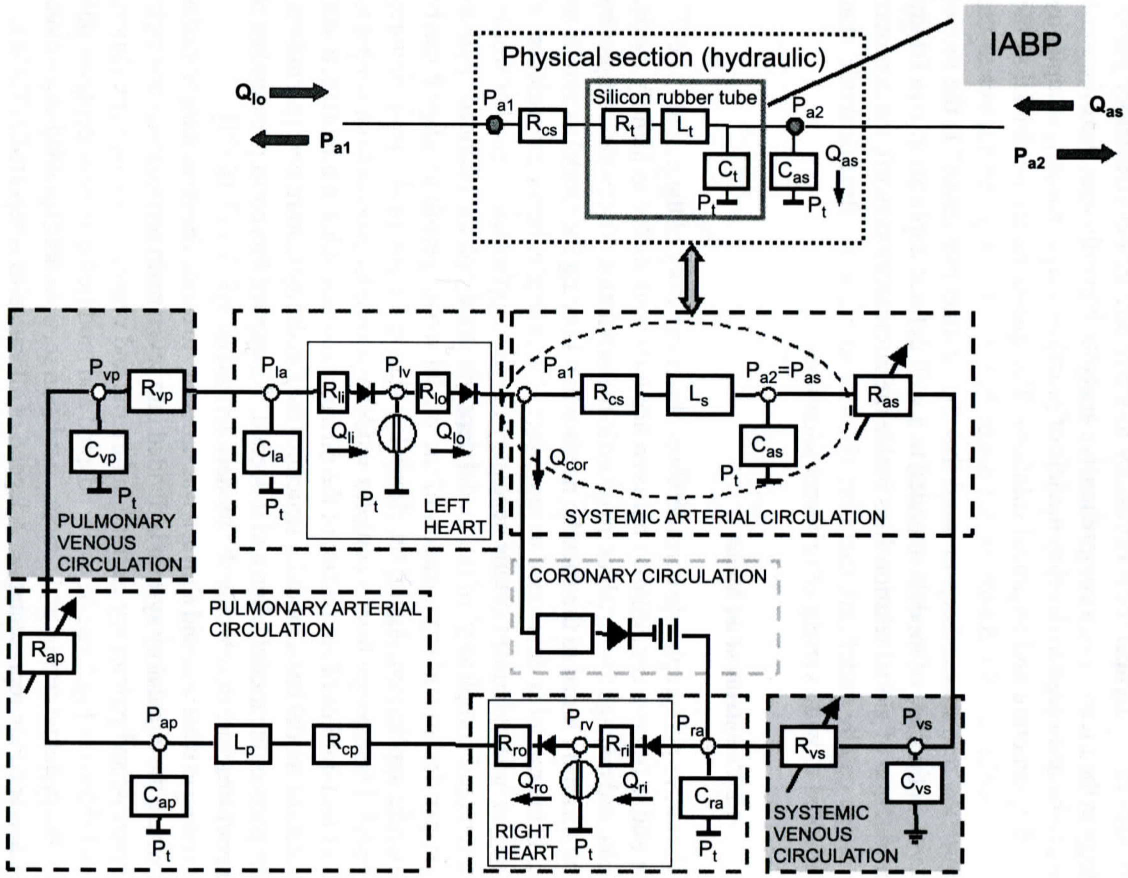

Fig. 1. Electric equivalent of the basic closed loop model of circulation. The circulatory system is divided into seven main sections (including coronary circulation) part of five function blocks: left and right heart, systemic, pulmonary and coronary circulation. Each of these sections can be easily modified or replaced

Table 1. Nomenclature

Abbreviations	Variables
HR	Heart rate
CO	Cardiac Output
AOP	Aortic pressure
P_t	Intra-thoracic pressure
E_{maxl}/E_{maxr}	Left/Right maximum time-varying elastance
V_{0l}/V_{0r}	Left/Right ventricular rest volume
P_{la}/P_{ra}	Left/Right atrial pressure
C_{la}/C_{ra}	Left/Right atrial compliance
R_{li}/R_{ri}	Left/Right ventricular input resistance
R_{lo}/R_{ro}	Left/Right ventricular output resistance
P_{lv}/P_{rv}	Left/Right ventricular pressure
V_{edl}/V_{edr}	Left/Right ventricular end-diastolic volume
V_{esl}-V_{es}/V_{esr}	Left/Right ventricular end-systolic volume
Q_{li}/Q_{ri}	Left/Right ventricular input flow
Q_{lo}/Q_{ro}	Left/Right ventricular output flow
P_{a1}/P_{a2}	Pressures at the interfaces (output of the left ventricle/C_{as})
P_{as}/P_{ap}	Systemic/Pulmonary arterial pressure
P_{assys}	Systolic systemic arterial pressure
L_s/L_p	Systemic/Pulmonary inertance
R_{cs}/R_{cp}	Systemic/Pulmonary characteristic resistance
C_{as}/C_{ap}	Systemic/Pulmonary arterial compliance
R_{as}/R_{ap}	Systemic/Pulmonary arterial resistance
Q_{as}	Peripheral systemic resistance flow
P_{vs}/P_{vp}	Systemic/Pulmonary venous pressure
C_{vs}/C_{vp}	Systemic/Pulmonary venous compliance
R_{vs}/R_{vp}	Systemic/Pulmonary venous resistance
R_{cor}	Total coronary resistance
k	Coupling factor for coronary model
IABP	Intra-aortic balloon pump
$R_t/L_t/C_t$	Resistance/inertance/compliance of the silicon rubber tube used in the hybrid model
γ	Blood density
V_l, α, h_v	Ventricular length/ventricular rotation angle/effective height of the blood column
T_{bl}	Total body length
H_p/l_t	Position of the heart in relation to total body length/position of the heart
β/h_b	Trendelenburg rotation angle/height of the corresponding blood column
Pat.	Pathology
IABP	Intra-aortic balloon pump
R_p, P_{at}	Parameters used to characterize the ventricle (equivalent to total resistance and atrial pressure respectively
E_a, R_T, P_{es}	Effective arterial elastance, total resistance, end systolic pressure
T	Cardiac cycle duration

Choice of the structure depends strictly on the type of application. Normally, hydraulic models are used to test physical devices while numerical models are preferred to simulate specific circulatory phenomena with better accuracy. What one can add is that in general the numerical models are less expensive and more accurate than the hydraulic ones and, on the other hand, are the only way to test physical devices limiting the use of complex and non-ethical animal experiments. Another solution developed at our labs is the use of models with a hybrid structure [15,18–21]. Usually in the hybrid models a numerical model of the circulation is the base as in Fig. 1: a part of numerical model can be replaced by a physical section or the model itself can be interfaced with a physical device, according to the essentials of the specific experiment. The block diagram in Fig. 2 illustrates and resumes these concepts. In fact it is possible to replace one of the five blocks composing the original numerical model of Fig.1 with a physical model (that can be hydraulic, electrical or pneumatic one) or interface the same numerical model with a physical device.

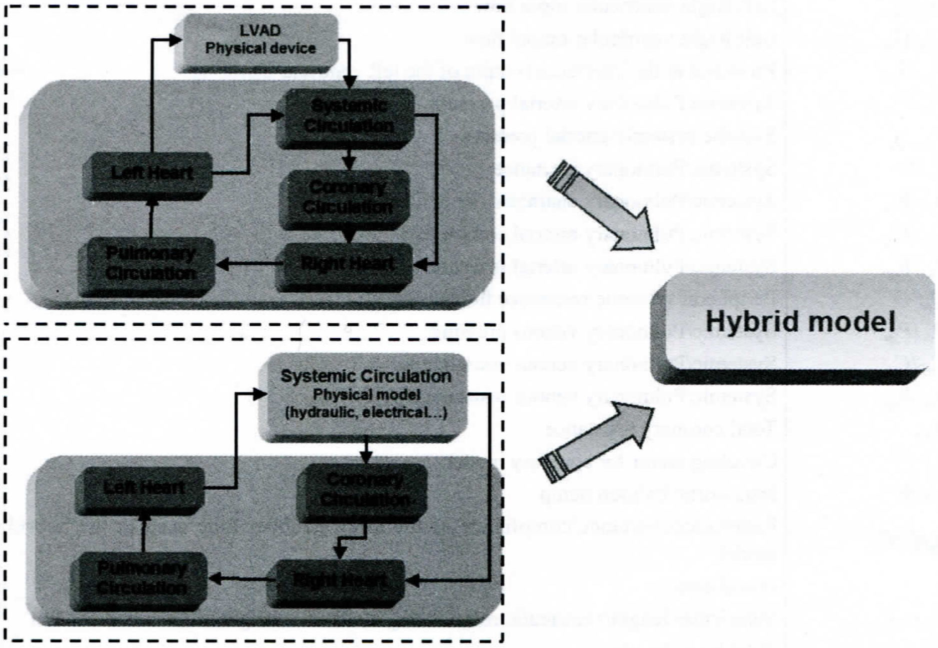

Fig. 2. General approach to circulatory hybrid modelling: an existing numerical circulatory model is transformed into a hybrid model by connecting the model to a physical device (LVAD) or replacing a circulatory district with a physical model that can be hydraulic or electrical one

2.4. Technical Solutions

This paragraph illustrates shortly the technical solutions adopted to develop the family of the circulatory models at our lab. Even if it is true that, for example, in the case of numerical models any programming language could be used to develop a circulatory model, the issue requires some comments. In the light of two issues: the ability to transform the model into hybrid one and the model portability the choice of the programming language is not irrelevant. The first remark is obvious; the second one is connected with the ability to develop models that the end user can adapt to his/her specific needs. This issue will be treated again in the conclusions. It is clear, however, that the choice of the programming language can influence this feature.

2.4.1. Numerical Models

The family of numerical models developed in our labs is based on two different software platforms: Visual Basic® and LabVIEW™. The first one originates from the former C++ platform and is used in research and educational applications [13, 23–24]. The software package includes the model of several mechanical heart assist devices and permits simulation of the assisted ventilation. The LabVIEW™ based models are included in the recently developed family of the circulatory models [11, 18–22]. The choice of LabVIEW™ was determined by the process control capabilities of this language: they are especially useful in the case of hybrid applications. In both software platforms the models share the same features – the most important is reproduction of the Starling's law of the heart with variable elastance models.

2.4.2. Hydraulic Model

The model [14] was developed with the aim of testing and studying the mechanical heart assistance: its structure corresponds to the schematics of Fig.1 (the base model) apart from the coronary circulation. In this case, the variable-elastance model was created using an algorithm based on invariance of the ventricular volume waveform (that can be normalized) [14, 25].

2.4.3. Hybrid Models

The numerical model corresponding to the basic structure of Fig. 1 was modified in a hybrid model by replacing some elements with physical structures that can be electrical or hydraulic. The interfaces between numerical and physical parts were carried out using electronic circuits in the case of numerical-electrical hybrid models [21] and DC motor driven gear pumps in the case of the numerical-hydraulic models [15]. In the case of numerical-hydraulic hybrid model, the upper part of Fig. 1 shows how the systemic arterial tree of the numerical model was replaced by the hydraulic structure: two pressures (P_{a1}, P_{a2}) are acquired from the physical circuit and used to solve the equations in the numerical model. The numerical model in turn computes two flows (Q_{lo}, Q_{as}) that are applied (through the DA converter) to the servo amplifiers controlling the gear pumps at the two interfaces. Figure 3 shows the corresponding hardware block diagram.

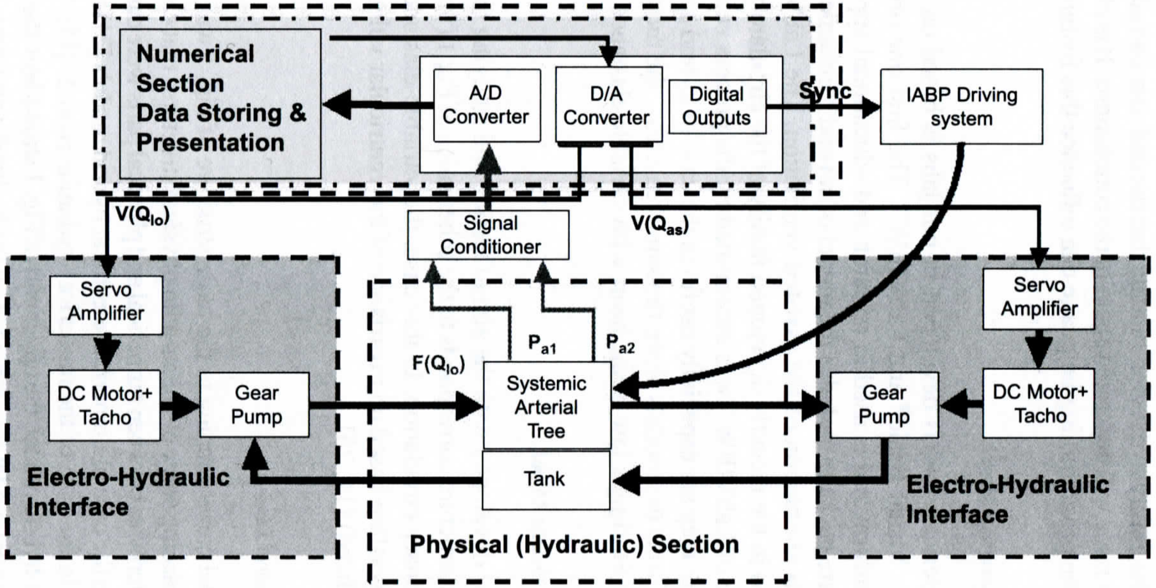

Fig. 3. Hardware block diagram of the numerical/hydraulic hybrid circulatory model

3. Applications

Before starting the description of some applications for this family of the circulatory models, it is necessary to give a few general comments. All the models of the family are based on a rather simple structure. However, the simplicity is their strength. Using the circulatory models in practical applications and especially in clinical environment one must pay attention to the price to be paid in terms of the model accuracy to have a tool simple and flexible enough to be practically usable. Our attempt is aimed at developing of the circulatory models dependent on a limited number of parameters and if possible, as it was noted above, on parameters that allow giving a global description of the circulatory system. Such models are simple enough to be used in the environments where accurate and complex tuning of the model is not possible. The models can be used to estimate the trend of critical haemodynamic variables and to suggest the haemodynamic variables to be monitored.

The block diagram in Fig. 4 shows schematically the main existing applications of this family of circulatory models. The common features of the whole family permit to consider the models as entities independent of the structure.

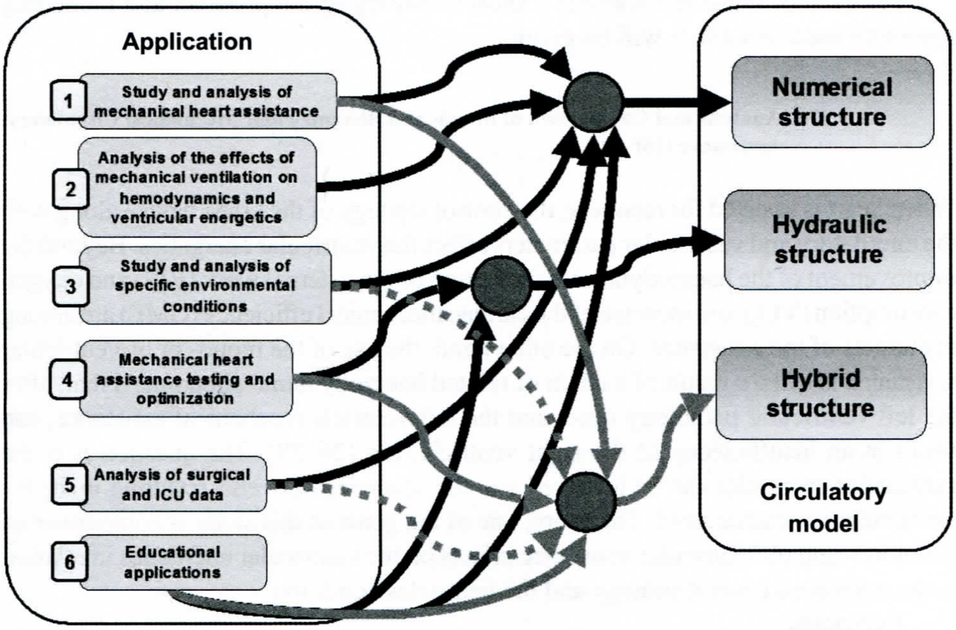

Fig. 4. Family of circulatory models: block diagram of the applications. The numbers correspond to the numbers reported in Table 2. The continuous arrowed lines point at existing applications, the dashed arrowed lines point at planned applications

The applications can be roughly divided into three groups:

- Evaluation and optimization of the mechanical circulatory and ventilatory assistance [16, 23, 24].
- Reproduction, study and evaluation of the specific circulatory conditions [7, 17, 22].
- Educational applications.

As it can be seen from Fig. 4, most of the applications are based on a numerical structure. This is not a matter of chance as the use of physical and hybrid models should be and is limited to specific applications where a totally or partly physical model is needed. The block diagram in Fig. 4 shows what way, at least in our experience, the circulatory modelling can be a tool used in many different circulatory conditions. For the majority of the applications depicted in Fig. 4, the basic circulatory model (Fig. 1) was modified by adapting it to the specific application.

As mentioned above, many of the applications outlined in Fig. 4 have been realized by modifying the basic structure shown in Fig. 1. Table 2 resumes all the applications together with the circulatory model structure and the main changes applied to the basic model to fulfil the specific application requirements.

The next and last part of this paper is devoted to describe certain selected applications.

For each of these applications a short summary of the problem and modelling approach used to solve it will be given.

3.1. Analysis and Comparison of Mono- and Bi-ventricular Mechanical Circulatory Assistance [16]

When heart is assisted for recovery, the control strategy of the assist device along with the circulatory and ventricular parameters affect the ventricular energetics. Beyond the improvement of the haemodynamics, reduction of the external work (EW) and oxygen consumption (VO_2) and increase of the cardiac mechanical efficiency (CME) are among the targets of the assistance. On the other hand, the use of the mono- or bi-ventricular assistance is often a result of a chain of related haemodynamic phenomena that, after the left ventricular pathology onset and the left ventricle mechanical assistance, can result in an insufficiency of the right ventricle, too [26–29]. The question is if the ventricular energetics can be involved into the sequence of events resulting in the bi-ventricular assistance need. Therefore, one of the goals of this study is comparison of the mono- and bi-ventricular assistance effects on the ventricular energetics in relation to the assistance control strategy and the ventricles condition.

Two notes:

- In the application developed some years ago the pneumatic ventricles were used as the assist devices [16]. Even if this type of assist devices is out of date, many considerations expressed in that paper stay valid for any type of the parallel (atrio-aortic connection) pulsatile mechanical assistance.

- The specific problem of studying the mechanical circulatory assistance with a physical device suggested applying a hydraulic model of the circulation [14]. The model corresponds functionally to the schema shown in Fig.1 except the coronary circulation and a more detailed model of the systemic circulation [30].

To analyze the mechanical assistance, we had to take into consideration that during the assistance the ventricular contractility can vary (up and down) and in addition the interaction between the ventricle and the assist device depends on the assistance execution, i.e., its control strategy. We made an attempt at defining an analytical tool able to put together these different factors and to show graphically their effects on the ventricular energetics. It resulted in the following procedure:

- The variable elastance model of the ventricle was characterized as a function of the filling pressure (P_{at}) and the peripheral resistance (R_p). For each pair of values $P_{at} - R_p$ the EW, VO_2 and CME were calculated.
- Each group of experiments was repeated for different values of the ventricular E_{max} assuming that E_{max} is a measure of the ventricular contractility [12]. In our opinion such solution is a realistic assumption for the parallel mechanical assistance in spite of some recent doubts [31].
- The result of this simulation was three families of surfaces representing, respectively, EW, VO_2 and CME as a function of P_{at} and R_p with E_{max} as a parameter. The surfaces obtained in this way were normalized and coupled (EW–VO_2 and CME–VO_2). The EW–VO_2 and CME–VO_2 surfaces intersect along lines that move leftwards with decreasing E_{max}. As an example, the EW–VO_2 surfaces for two different values of ventricular elastance (1 and 4 mmHg·cm^{-3}) are shown in Fig. 5. The CME–VO_2 surfaces behave exactly in the same way [16]. The EW surfaces' maximum corresponds to the conditions of the maximum power transfer to the load [12].
- The ventricle state can be described by the working point P_0 defined by P_{at} and R_p on the EW, CME and VO_2 surfaces as it is sketched in the same Fig. 5.

Two remarks:

1) The position of the working point P_0 in relation to each pair of the surfaces is important as each intersection line is the locus of points corresponding respectively to the compromise between minimum oxygen consumption, minimum external work and maximum cardiac mechanical efficiency.

2) The position of the working point P_0 depends on the ventricle state, the circulatory network and the assistance execution. The latter can be taken into account considering that its action modifies the filling pressure (P_{at}) and can be "seen" from the ventricle as a change of the peripheral resistance that can be computed using the residual cardiac output from the natural ventricle and the arterial pressure resulting from the joint action of the assistance and the natural ventricle. In conclusion, the working point P_0 moves along a path (Fig. 5) that, *inter alia*, depends on the assistance control strategy. The same path in the different ventricular conditions produces different effects from the energetics point of view.

Table 2. Circulatory model structure for different applications

Appl.# (Fig. 4)	Description	Model structure	Changes to the basic model	Reference
1	2	3	4	5
1	Study and analysis of the mechanical heart assistance. Evaluation of the mechanical circulatory assistance effects (LVAD, BVAD, IABP, Rotary blood pump) on the hemodynamics and ventricular energetics.	Numerical	Application developed using the CARDIOSIM package. In most cases the basic structure of Fig.1 was used.	23, 24
1	Study and analysis of the mechanical heart assistance. Comparison of the parallel and in series LVAD assistance.	Hybrid	Coronary circulation model is missing. A more complex model of the systemic arterial circulation (including a silicon rubber model of the aorta) was adopted. A hybrid model of the left ventricle replaced the ventricular model in a hydraulic circulatory model.	19
2	Analysis of the mechanical ventilation effects on hemodynamics and ventricular energetics, including the mechanical circulatory assistance joint effect	Numerical	Application developed using the CARDIOSIM package. Compliances corresponding to the circulatory areas inside the thorax were polarized with a value corresponding to the mean intra-thoracic pressure.	23, 24
3	Study and analysis of the specific environmental conditions. Simulation of the breath-hold diving. Reproduction of the "diving reflex". Study of hemodynamics during the breath-hold diving. Identification of the critical variables.	Numerical	Compliances corresponding to the circulatory areas inside the thorax were polarized at a value corresponding to the mean intra-thoracic pressure at breath-hold and during diving. Systemic venous compliance was polarized at a value corresponding to the depth.	17
3	Study and analysis of the specific environmental conditions. Simulation of the breath-hold diving.	Hybrid	Planned application. Transformed into hybrid model by replacing the systemic and pulmonary arterial circulation model with the hydraulic model exposed to the diving pressure.	

4	Mechanical heart assistance testing and optimization. Analysis of the interaction of several mechanical heart assist devices (LVAD, RVAD, BVAD, IABP) with the ventricle and the circulatory system. Study of the changes in the ventricular energetics and the hemodynamics in relation to the device control strategy.	Hydraulic	Coronary circulation model is missing. A more complex model of the systemic arterial circulation (including a silicon rubber model of the aorta) was adopted	14–16
4	Mechanical heart assistance testing and optimization. Analysis of the interaction IABP with the ventricle and the circulatory system. Study of the IABP timing effects on the hemodynamics.	Hybrid	Transformed into hybrid model by replacing the systemic arterial circulation model with the hydraulic model including two lumped components and a silicon rubber tube for the IABP insertion	15
5	Analysis of the surgical and ICU data. Reproduction and analysis of the hemodynamics phenomena during the beating heart surgery (heart lifting) and the Trendelenburg maneuver. Estimation of the coronary flow.	Numerical	Hydrostatic effects of the heart lifting and the Trendelenburg maneuver were taken into account polarizing the ventricles and systemic venous compliance at a value corresponding to rotation angle of the heart and the surgical bed.	11
5	Analysis of the surgical and ICU data.	Hybrid	Planned application. Transformed into hybrid model acquiring the clinical data on line.	
6	Educational applications. Demonstration of the mechanical assistance and the breath-hold diving for physicians and perfusionists.	Numerical	Open and closed loop versions of the model were used.	
6	Educational applications. Mechanical assistance use in demonstration and training for physicians and perfusionists.	Hydraulic	A closed loop hydraulic version of the model was used.	
6	Educational applications.	Hybrid	Transformed into hybrid (numerical-hydraulic and numerical-electric).	

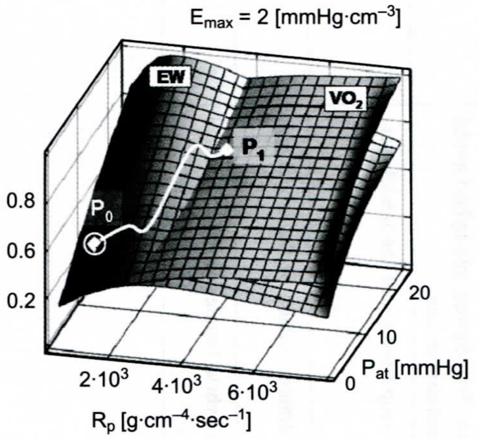

Fig. 5. Characterisation of the ventricular model as a function of filling pressure (P_{at}) and peripheral resistance (R_p) in terms of ventricular energetics (EW, VO_2, CME) with E_{max} as a parameter. The data are normalized and arranged in the coupled surfaces (EW–VO_2, CME–VO_2). P_0 is the working point. Presented EW–VO_2 surfaces correspond to two values of E_{max}: 1 and 4 mmHg·cm^{-3}. Line grid surface corresponds to EW data. The white line shows a possible path of the working point during mechanical circulatory assistance

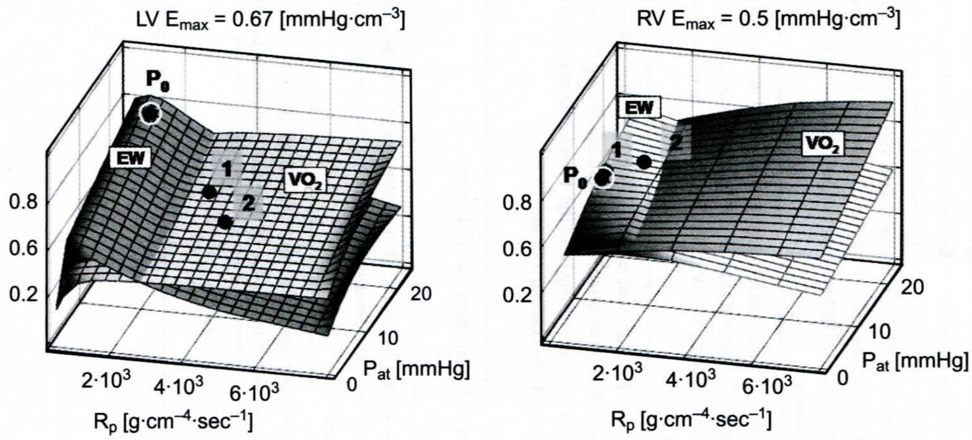

Fig. 6. Results of the simulation showing on the left EW–VO_2 surfaces for the pathological left ventricle (E_{max} = 0.67 mmHg·cm^{-3}) the working points corresponding to the situation before the LVAD assistance (P_0) and during the assistance changing its onset time in relation to ventricular contraction beginning. The corresponding surfaces for the right ventricle are shown on right side: the conduction of the assistance modifies energetic conditions of the right ventricle

As mentioned before, the working points that lie in the vicinity of the intersection lines correspond to the best compromise between the EW and VO_2 reduction and the CME increase. Depending on the left ventricular assistance execution, the position of the right ventricular working point may be closer or farther to the intersection line. This implies that the right ventricle, depending on the conduction of the left ventricular assistance, might work in good or bad conditions in relation to its energetics as it can be seen in the example reported in Fig. 6 where, after simulating a pathological condition of the left ventricle (left side of Fig. 6), the latter was assisted modifying the level of assistance. One of the possible situations of the right ventricle is reproduced in the right side of the same Fig. 6: it is seen the effect of LVAD assistance conduction on the right ventricular energetics. It could be interesting to analyze statistically the incidence of the onset of the right ventricular assistance need in relation to the left ventricular assistance execution. To improve the ventricular simulation accuracy, the original model of the left ventricle was later replaced by a hybrid one. In this case, therefore, the original hydraulic circulation model was transformed into the hybrid one by replacing one of its components (the left ventricle) by a numerical one [18–19].

3.2. Numerical Simulation of the Haemodynamic Effect of the Heart Displacement in the Beating Heart Surgery [7]

Haemodynamic instability, mostly due to the vertical lifting of the heart, is usually observed during beating heart surgical procedures. The primary aim of this application was to develop a tool, based on a digital computer model of the circulation, to supply clinicians with information that allows estimating the haemodynamic changes during the beating heart surgery. Usually, the beating heart surgery implies the heart displacement and use of the Trendelenburg manoeuvre [11] to correct the effects of the heart displacement. The application was developed on basis of the hypothesis that the effects of heart displacement and the Trendelenburg manoeuvre are mostly due to the hydrostatic phenomena determined by the *preload* changes with the heart vertically lifted [32]. Therefore, the vertical heart lifting and the corrective action (the Trendelenburg position) in the model are described in relation to the hydrostatic pressure changes. It is assumed that the angles α and β are the heart and the bed rotation angles in relation to the horizontal line (Fig. 7). The effect of the vertical heart lifting is described assuming that the hydrostatic pressure P_h corresponding to the height h_v (depending on the angle α) hinders the ventricular filling. The height h_v is equal to the ventricular length V_l (assumed to be 6 cm) when the heart is perfectly vertical. It is assumed that the blood density γ is equal to 1060 $kg \cdot m^{-3}$.

Similar considerations are valid when the whole body is rotated: in this case, the hydrostatic pressure P_h is compensated by the hydrostatic pressure P_b depending on the angle β. It is assumed that the rotation centre is in the middle of the operating

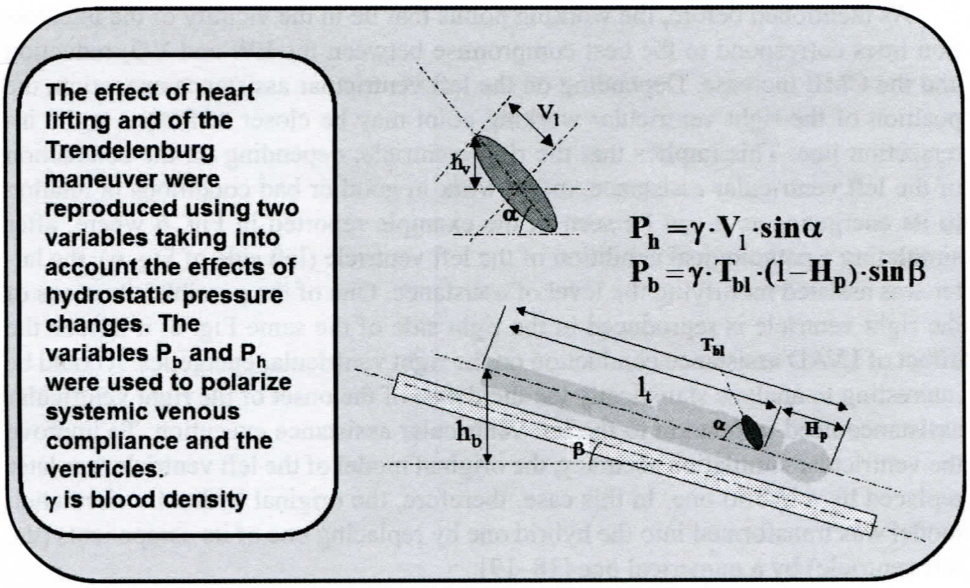

Fig. 7. Schema of the hypotheses done to simulate the heart lifting and the Trendelenburg manoeuvre. The two pressures P_h and P_b are used to polarize the ventricles and systemic venous compliance in the model of Fig. 1

table. The distance l_t is calculated from heart position H_p given as a percentage of the total body length T_{bl}.

In our experiments, performed on pigs, T_{bl} was set to 100 cm and H_p to 50%. The corresponding equations are reported in Fig. 7. In the model, the hydrostatic pressures P_h and P_b were represented by two pressure generators. The generators, added to the model of Fig. 1, polarized both the ventricles and the systemic venous compliance C_{vs}.

This model was used to analyze data originated from experiments with β-blocked and not β-blocked pigs. The model has shown capability to reproduce the haemodynamic data and predict trend of not measured variables such as coronary blood flow. Instead of analyzing the results of the simulation reported in the literature [7], it is interesting to focus on tuning the model. In fact, this is a central problem and its proper solution permits to apply rather simple model to a complex homodynamic situation. Another important note is that the model designed for the intensive care units or surgery can use a little number of variables acquired in those environments. The variables used in our case were the heart rate, the arterial pressure and the cardiac output. To tune the model we calculated the effective arterial elastance (total resistance divided by cardiac cycle duration) [12] according to the flow chart shown in Fig. 8. This procedure was applied to perform the automatic model tuning. HR is set manually but we carry out experiments with an algorithm to set HR automatically.

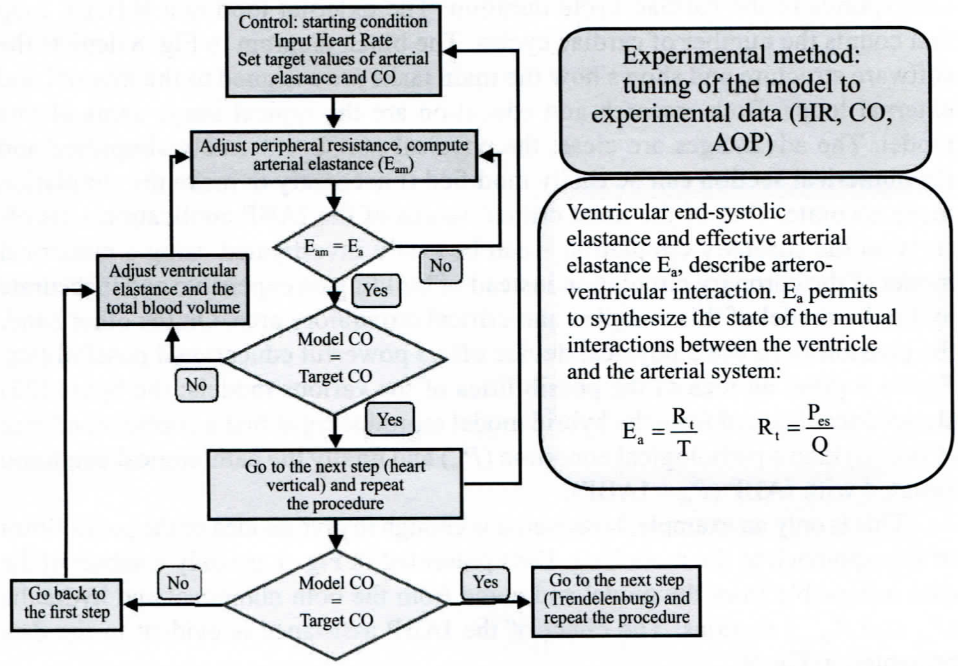

Fig. 8. Flow chart for the model tuning. This procedure was automatised and implemented into the model software

3.3. Hybrid Circulatory Model for IABP Testing [33]

For the purposes of this application the model shown in Fig. 1 was modified to permit the testing of IABP. In particular, the systemic arterial section was replaced by a physical circuit including a silicon rubber tube to permit the insertion of the intra-aortic balloon. The modified model is shown in the upper part of Fig. 1 and in Fig. 3.

Again, instead of exploring details of the simulation already reported in the literature [15], it is convenient to make some considerations about this hybrid application and the usage of this model.

The circulatory model has the same specifications as other models of the family. It is a good example how the basic model shown in Fig.1 can be easily modified by replacing one or a few of its sections with a physical section, a hydraulic one in this case. Here, the main technical problem is how to ensure the real-time behaviour of the model and match the data from the numerical section and the hydraulic section. The software organization is a critical issue. It is based essentially on two nested loops: the internal one is a FOR loop with time of each step corresponding to the sampling time and the same time interval is used to solving the equations with the Euler method. All the time critical functions are placed inside the internal FOR loop. Execution time of the internal FOR loop corresponds to the cardiac cycle duration. The external loop is a WHILE loop that counts the number of cardiac cycles. The block diagram in Fig. 8 depicts the software structure and shows how the main tasks are assigned to the internal and external loops. Both research and education are the typical usage areas of this model. The advantages are clear: the physical part is extremely simplified and the numerical section can be easily modified if necessary to make the simulation more accurate. One of the most critical issues of the IABP application – its effects on the coronary circulation – can be easily investigated using a numerical model of the coronary circulation instead of building an expensive and inaccurate hydraulic model of this complex and critical circulatory area. On the other hand, the possibility to use a physical device offers powerful educational possibilities. Figure 9 gives an idea of the possibilities of the various models: the figure [33] shows data obtained from the hybrid model reproducing at first a control condition (Control) then a pathological condition (P_{at}) and finally the pathological condition assisted with IABP (P_{at} + IABP).

This is only an example; however, it is enough to give an idea of the possibilities of this approach to the modelling. Data presented in Fig. 9 are only a subset of the data achievable from the model and come from the both numerical and hydraulic (P_{as} and P_{assys}) sections. The effect of the IABP assistance is evident in the data presented in Fig. 9.

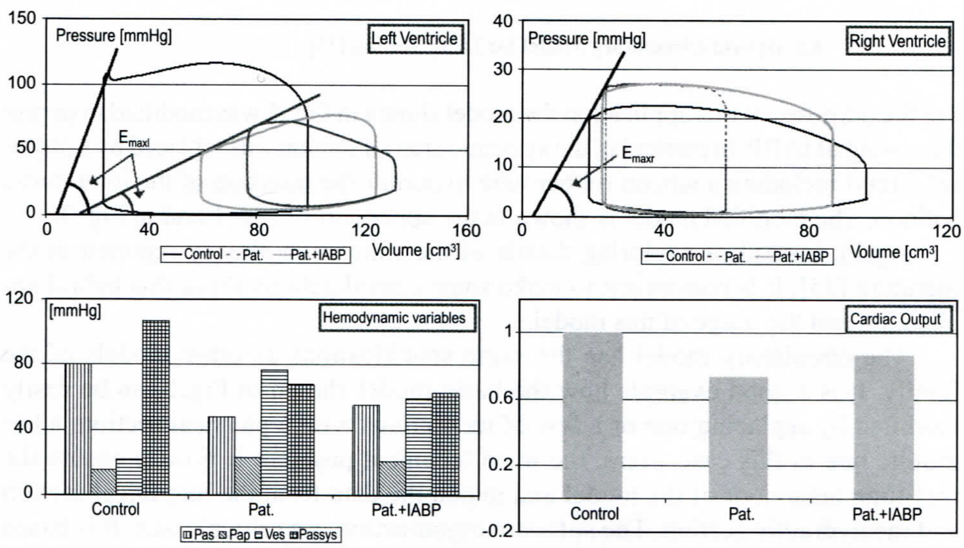

Fig. 9. Numerical-hydraulic hybrid model: results.

Upper part: the left and right ventricular work cycles show the transition from the Control to Pathological (Pat.) condition and the IABP assistance effects.

Lower part: haemodynamic data. Cardiac output is normalized to its value in the Control condition

4. Discussion and Conclusions

There are two basic considerations to be done: the first one is the approach to modelling. Capability to develop models that are able to give a global description of the circulatory system and the relationships inside the system permits to evaluate the global effects of external disturbances (drugs, prosthetic devices, pathologies, special environments) not prohibiting a more detailed analysis improving the representation of specific circulatory areas. The second consideration regards the usage of the models. *Inter alia* from a few examples reported in this paper, it is clear that the range of the possible applications is quite large and that it is therefore not easy to use the same model in different applications. However, an adequate design of the model together with the possibility to adapt its structure to the specific needs can simplify the modelling process by opening the way to the idea of a modelling platform usable for different applications. The use of the numerical circulatory models that can be easily transformed into hydraulic structures using the hybrid approach opens in fact the way to a wide set of applications.

Another important and connected note regards the final model usage: in fact, if the model is developed for research or a specific application where the end-user and the developer of the model are often the same, the model structure and its simplicity are not so important. On the contrary, if the challenge is to make the circulatory modelling a practical tool that allows replacing at least part of animal experiments or supports decision-making in the clinical environment, simplicity, standardization or flexibility become of the primary importance.

So, the discussion focuses again on the model usage. The application areas of circulatory modelling, at least in the meaning defined above, can be summarized in three main issues: research, development and testing, clinical application and education. As it was mentioned in the introduction, these three main issues have undoubtedly some common requirements but many different requirements as well. The question is if it is convenient to develop a common modelling platform to be applied indifferently to all the application areas outlined above. The answer lies in the level of compromise that can be acceptable, especially in case of the models intended for the clinical environment. In the last case the operating conditions of the models are often unpredictable when compared to the corresponding operating conditions in the case of research, device testing and, partially, educational applications. In our opinion, having in mind the keywords of simplicity and flexibility and accepting that the use of the models in clinical or special environments includes a procedure of tuning the model to the specific starting circulatory conditions, a compromise in the meaning stated above is possible. The model developed this way should be able to "react" to the disturbance irrespectively if it is a device, a drug, a surgical action or a change in environmental conditions [22].

What we are trying to do in developing the family of the circulatory models outlined in this paper is just to put together the tesserae to create a flexible and multipurpose modelling platform that will include in the future also an indispensable respiratory model [34] able to interact with the circulatory one. Also in this case, the approach will be necessarily gradual starting from respiratory mechanics and adding, on the basis of experimental needs, other features such as gas exchange and transport. Another important aspect of the modelling platform is the introduction of neural controls: again they could be part of the model modular structure. Barocontrols for peripheral resistance control were already introduced in the basic version of the model. It is planned to do the same for the more complex versions [6] that are being progressively introduced into the model in the form of a software library.

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