A MINIMAL CARDIOVASCULAR SYSTEM HAEMODYNAMIC MODEL FOR RAPID DIAGNOSTIC ASSITANCE

Bram W. Smith[1], J. Geoffrey Chase[2], Geoffry M. Shaw[3] and Roger Nokes[2]

Department of Mechanical Engineering, University of Canterbury, New Zealand
Dept of Intensive Care Medicine, Christchurch Hospital, New Zealand
Department of Civil Engineering, University of Canterbury, New Zealand

Characterising circulatory dysfunction and choosing a suitable treatment is often difficult, and time consuming. This paper outlines a numerically stable minimal model of the human cardiovascular system (CVS) specifically aimed for rapid, on site modelling to assist in diagnosis and treatment. A minimal number of governing equations and a realistic valve law are used to accurately capture trends in CVS dynamics. The model is shown to have long-term stability and consistency with non-specific initial conditions. Results show that the model adequately provides appropriate magnitudes and trends for a variety of physiologically verified test cases.

Keywords: Biomedical control, Biomedical systems, Nonlinear models, Physiological models

1. INTRODUCTION

Heart foundation statistics show cardiovascular disease is the leading cause of death amongst Australians, accounting for 40% all deaths in 1998. Often it is difficult for health professionals to diagnose and select a suitable treatment for these conditions, and they must rely solely on their experience and intuition. For patients in a critical condition, such as those under intensive care, the longer it takes to diagnose and treat a problem the more the patients condition can deteriorate, and the less chance of recovery. The goal of this research is to develop a computer model of the human cardiovascular system that can be used to assist medical staff in the key areas of understanding, rapid diagnosis and therapy selection.

With an appropriate model, medical staff can gain a better understanding of CVS function by varying parameters to simulate a variety of dysfunctions, such as stiff heart walls or blocked arteries. A model whose parameters have been identified to match a specific patient could be used to assist diagnosis and treatment by comparing model outputs simulating various CVS dysfunctions and therapies to make a best choice. More specifically, by measuring various physiological parameters such as blood pressure, heart rate, stroke volume and ventricular pressures, the governing elastances, resistances and PV relationships for a given patient's haemodynamics can be determined. Hence, the performance of a patients CVS will be rapidly identified, enabling comment on any irregularities found and the simulated testing of several potential therapies.

It is intended that the model fulfil the following aims:

- Model parameters can be relatively easily identified for a specific patient.
- Although quantitatively exact results are not necessary, accurate prediction of trends with changes in parameters or therapy is required.

These goals ensure the model is practical and effective as a diagnostic aid.

Most current approaches to modelling the human CVS can be grouped into either Finite Element (FE) or Pressure Volume (PV) approaches. FE techniques

[1] Research Assistant, University of Canterbury
[2] Sr. Lecturer, University of Canterbury
[3] Consultant, Christchurch Hospital

offer accurate results, but require immensely detailed inputs such as muscle fibre orientations, structures and mechanical properties (Peskin, 1992; Legrice, 1997). Limitations on the availability of detailed in vitro patient specific data and computational power mean that FE methods are not well suited as rapid diagnostic tools.

PV methods divide the CVS system into a series of elastic chambers separated by resistances, and inductors simulating inertial effects where required. Each elastic chamber models a section such as the ventricles, the atria, or the aorta, each with their own pressure-volume relationship. Only a minimal number of parameters, such as chamber elastances and arterial resistances, are required to create such a model. These models can be solved on modern, commonly available desktop computers in very reasonable times suitable for immediate feedback.

This paper outlines a stable "Minimal Model" approach to the CVS modelling problem using a minimal number of governing equations. Problems with long-term divergence and dependence on accurate initial conditions, caused by too many governing equations over-defining the model, were encountered with other similar models (e.g. Chung, 1997). The minimal model is developed starting with a simple single ventricle system and progressively adding complexity. The emphasis is on using the minimal amount of parameters and complexity required to model the essential dynamics and trends.

2. MODEL STRUCTURE AND DEFINITION.

The model presented is intended to simulate the essential haemodynamics of the cardiovascular system including the heart, and the pulmonary and systemic circulation systems, as shown in Figure 1. The full model presented is shown in Figure 2, where two ventricles are shown along with additional chambers for both the systemic and pulmonary systems. The atria have not been added as they contribute only minimally to the main cardiac trends and can be easily added for more specific cases. The ventricles are coupled to account for important ventricular interaction dynamics due to the septum and pericardium.

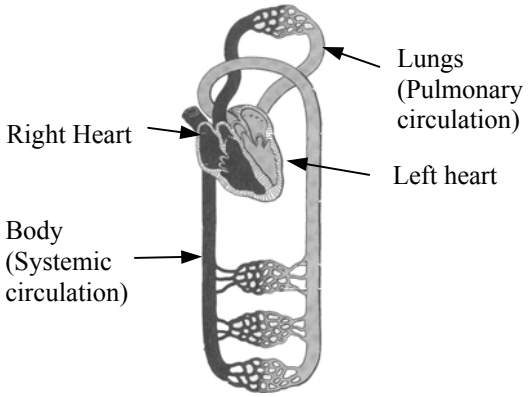

Fig. 1. Diagram of the heart and circulation system. (Guyton, 1991)

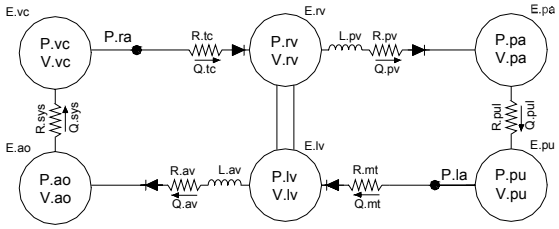

Fig. 2. The presented closed loop model of the cardiovascular system.

In Figure 2, resistances (R) simulate the resistance on the blood passing through the arteries or valves between elastic chambers. Inductors (L) model the effects of inertia, which are only included where the blood goes through large changes in velocity, such as around the valves where velocity pulses between zero and a peak value (Melchoir, 1992). Diodes show the location of the one-way valves at the inlet and exit of the ventricles.

2.1. Single Chamber model

The single elastic chamber shown in Figure 3 was analysed first to understand the dynamics of a single active chamber such as a ventricle. This model is similar to the Windkessel circuits in the literature, but with a simple elastic chamber rather than a capacitor (e.g. Tsitlik, 1992). Resistors (R) and inductors (L) at the inlet and outlet of the chamber model the resistance and inertial effects on flow entering or exiting the chamber.

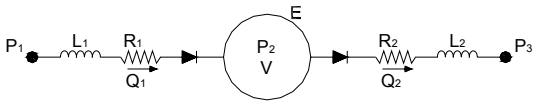

Fig. 3. Single chamber model

2.2. The PV diagram

PV diagrams, such as shown Figure 4, are used extensively in the medical profession, and importantly, doctors are familiar with and comfortable using PV diagrams to plot and analyse ventricular function. The two main characteristics of the PV diagram are the lines plotting the End Systolic Pressure-Volume Relationship (ESPVR) and the End Diastolic Pressure-Volume Relationship (EDPVR). These lines define the upper and lower limits respectively of time varying ventricular elastance during the cardiac cycle.

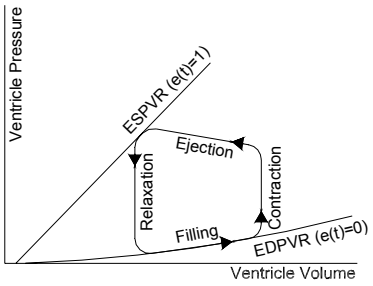

Fig. 4. Schematic PV diagram.

Equations approximating the ESPVR and EDPVR lines are widespread throughout the literature (Maughan, 1987; Chung, 1997; Beyar, 1987). The most commonly used relationships are defined below (Chung 1997; Beyar 1987):

$$P_{es}(V) = E_{es}(V - V_d) \tag{1}$$

$$P_{ed}(V) = A(e^{\lambda(V - V_0)} - 1) \tag{2}$$

where Equation (1) is the linear relationship between the end systolic pressure (P_{es}) and volume (V) with elastance (E_{es}) and intercept (V_d), and Equation (2) plots the non-linear relationship between end diastolic pressure (P_{ed}) and volume (V) with the additional parameters A, λ, and V_0.

2.3. Cardiac Driving Function

The contractions of the cardiac muscle are modelled by a time varying chamber elastance that varies between a minimum value defined by the EDPVR and a maximum value defined by the ESPVR. A driving function, e(t), that varies approximately sinusoidally between 0 and 1 drives the changes in elastance to make the heart pump (Chung, 1997). Combining the driver definition with Equations (1) and (2) produces an equation for the chamber pressure (P_2):

$$P_2(V,t) - e(t)Pes(V) + (1 - e(t))Ped(V) \tag{3}$$

$$e(t) = \sum_{i=1}^{N} A_i e^{-B_i(t - C_i)2} \qquad 0 \le e(t) \le 1 \tag{4}$$

Equation (3) is now the governing equation for the time dependent pressure volume relationship in an active elastic chamber such as a ventricle. Equation (4) defines the driver function used here with parameters N=1, A=1, B=80 and C=0.27.

2.4. Fluid Flow Rate Definitions

When the effects of inertia are not included, the equation for the flow rate (Q) is Poiseuille's equation (Fung, 1990; Beyar, 1987; Chung, 1997; Olansen, 2000).

$$Q_1 = \frac{P_2 - P_1}{R_1} \tag{5}$$

where the resistance (R) is defined by Poiseuille's equation as $R = \pi r_0^4 / 8\mu l$ with variables for radius (r_0), fluid viscosity (μ), and artery length (l).

Equation (5) allows discontinuous changes in flow rate, meaning the flow rate can change instantaneously, ignoring inertial effects on the fluid. When inertial effects are added, the equation of motion for the flow becomes a second order differential equation:

$$\frac{dQ_1}{dt} = \frac{P_1 - P_2 - Q_1 R_1}{L_1} \tag{6}$$

With the governing equations for flow rate, the rate of change of volume in the chamber is simply calculated as the inflow minus the outflow:

$$\frac{dV}{dt} = Q_{in} - Q_{out} \tag{7}$$

Thus, the dynamics of a single ventricle model with resistances and inertial effects are defined by Equations (6) and (7). Given volume (V) and time (t), the pressure in the chamber ($P_2(V,t)$) can be calculated using Equation (3). The flow rates are then calculated using either Equation (5) or Equation (6), and from the flow rate, the rate of change of volume is calculated using Equation (7).

2.5. Two ventricle model with interaction

Ventricular interaction has a significant impact on cardiovascular dynamics, and is caused by both the septum and the pericardium. The septum is a flexible common wall between the left and right ventricle, and the pericardium is an inelastic wall that encapsulates the entire heart. The double lines between the left and right ventricles in the full model of Figure 2 indicate the coupling due to ventricular interaction. Figure 5 shows the cardiac geometry employed, and defines the necessary volume and pressure variables.

The Volumes shown in Figure 5 and defined in Table 1 include the 2 ventricle volumes, and 3 free wall volumes of the ventricles and septum. The free wall volumes, V_{lvf}, V_{rvf} and V_{spt}, are not chamber volumes, but are defined to capture the deflection of the cardiac free walls relative to the ventricle volumes.

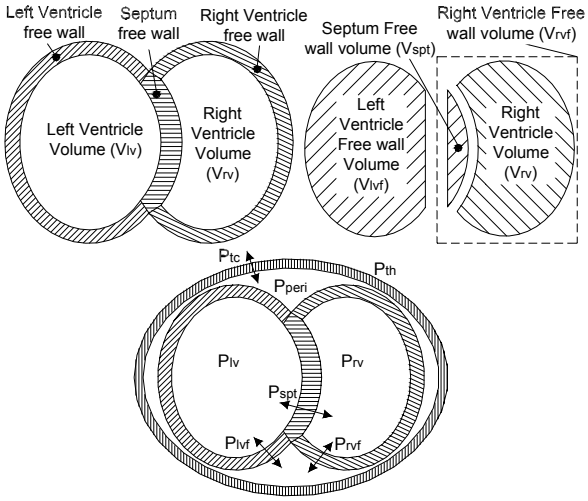

Fig. 5. Septum, pericardium, left and right ventricle, and free wall volumes and pressures of the heart.

Table 1 Volume Variables.

Symbol	Description
V_{lv}	Left ventricle volume
V_{rv}	Right ventricle volume
V_{lvf}	Left ventricle free wall volume
V_{rvf}	Right ventricle free wall volume
V_{spt}	Septum free wall volume
V_{pcd}	Pericardium volume

The left ventricle free wall volume from Figure 5 is simply the left ventricle volume less the septal volume. Similarly, the right ventricle free wall volume is the sum of the right ventricle volume, and the septum volume.

$$V_{lvf} = V_{lv} - V_{spt} \tag{8}$$

$$V_{rvf} = V_{rv} + V_{spt} \tag{9}$$

The pericardium volume is the sum of the ventricle volumes, or the sum of the ventricle free wall volumes.

$$V_{pcd} = V_{lv} + V_{rv} = V_{lvf} + V_{rvf} \tag{10}$$

The total volume of the pericardium defined in this model excludes the volume of the atria, and the myocardium.

The pressures defined for the two-ventricle model and shown schematically in Figure 5 are listed in Table 2.

Table 2. Pressure Variables.

Symbol	Description
Plv	Pressure in the left ventricle
Prv	Pressure in the right ventricle
Pperi	Pressure in the pericardium
Pth	Pressure in the thoracic cavity
Plvf	Pressure across the left ventricular free wall
Prvf	Pressure across the right ventricular free wall
Pspt	Pressure across the septum free wall
Ppcd	Pressure across the pericardium wall

The left and right ventricle and pericardium chamber pressures are defined:

$$P_{lv} = P_{lvf} + P_{peri} \tag{11}$$

$$P_{rv} = P_{rvf} + P_{peri} \tag{12}$$

$$P_{peri} = P_{pcd} + P_{th} \tag{13}$$

The septum pressure, using Equations (11) and (12), is therefore defined:

$$P_{spt} = P_{lv} - P_{rv} = P_{lvf} - P_{rvf} \tag{14}$$

Contraction and relaxation of the heart occurs as a result of free wall thickening. Hence, the left and right ventricle and septal free wall pressures (P_{lvf}, P_{rvf} and P_{spt}) are calculated using Equation (3). For example the pressure in the left ventricle free wall is given as:

$$P_{lvf} = e(t)E_{es,lvf}(V_{lvf} - V_{d,lvf}) + (1-e(t))A_{lvf}(e^{\lambda_{lvf}(V_{lvf} - V_{0,lvf})} - 1) \tag{15}$$

Finally, the pressure across the passive wall of the pericardium is defined by the nonlinear PV relationship (Chung, 1997):

$$P_{pcd}(V) = A_{pcd}(e^{\lambda_{pcd}(V_{pcd} - V_{0,pcd})} - 1) \tag{16}$$

The pressures calculated using these equations are used to calculate the flow rates into and out of the cardiac chambers.

2.6. Full Closed system loop model

To capture more of the major governing haemodynamics, the circulation must be closed so that fluid can flow around the entire loop, as in Figure 2. Two elastic chambers are added each for the systemic and pulmonary systems with a resistance between. Each chamber is modelled using the linear PV relationship in Equation (1). With the output of each cardiac chamber connected to the inlet of the other, peripheral elastances and resistances capture the basic dynamics of the pulmonary and systemic circulation.

3. DYNAMIC SYSTEM MODELS & SIMULATION

The dynamics of each chamber modelled with no inertial effects are governed by the ordinary

differential equation in Equation (7), requiring only the volume as a state variable ($\underline{x}$=[V]). With the incorporation of inertial effects into the model, the flow (Q) is governed by the first order ODE of Equation (6). To run this model, both inflow and outflow rates must become additional state variables, adding two more states ($\underline{x}$=[V Q_1 Q_2]).

3.1. The Valve Law

In models where inertia is not included and the governing flow is defined by Equation (5), the valves are simulated simply by setting the flow rate to zero when the pressure gradient is positive. However, when inertial effects are included in the model, the flow rate (Q) is now governed by a first order ODE, and setting the flow rate to zero will create a discontinuity, causing an unstable numerical solution. To solve this problem, the state vector is changed while solving.

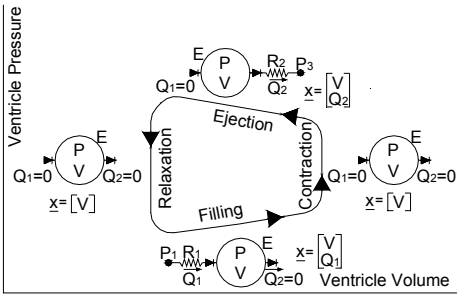

Fig. 6. The 3 states of a single elastic chamber during the cardiac cycle.

Figure 6 shows the three states for a single cardiac chamber during the cardiac cycle, and each associated state vector ($\underline{x}$). For example, during the transaction from isovolumetric contraction to ejection, the system changes state from having just volume (V) in the state vector, to including out flow rate (Q_2).

To change the state of the system, the state variables employed are triggered to change when either a flow rate or a pressure gradient becomes negative. When a flow rate (Q) becomes negative, it is removed from the state vector to account for the valve closing in the absence of flow. Alternatively, when a pressure gradient becomes negative, the associated flow rate is reincluded in the state vector to account for the valve opening. Hence, the valve law for the model presented is "close on flow, open on pressure" where the valve opens on a negative pressure gradient, but is delayed from closing on a positive pressure gradient due to the inertia of the blood, per physiological observation (Opie, 1998).

3.2. Ventricular interaction

When simulating ventricular interaction, the following steps are taken at each iteration using the current volumes (V_{lv} and V_{rv}) to find their rates of change:

- Calculate the pressure in the pericardium from the total volume. ($V_{tot} = V_{lv} + V_{rv}$)
- Numerically solve he following equation, derived from equations (1)-(3) and (14), to find V_{spt}:

$$\begin{aligned} &eE_{es,spt}(V_{spt}-V_{d,spt})+(1-e)P_{o,spt}(e^{\lambda_{spt}(V_{spt}-V_{o,spt})}-1) \\ &=eE_{es,lvf}(V_{lv}-V_{spt}-V_{d,lvf})+(1-e)P_{o,lvf}(e^{\lambda_{lvf}(V_{lv}-V_{spt}-V_{o,lvf})}-1) \\ &-eE_{es,lvf}(V_{rv}+V_{spt}-V_{d,rvf})+(1-e)P_{o,rvf}(e^{\lambda_{rvf}(V_{rv}+V_{spt}-V_{o,rvf})}-1) \end{aligned} \quad (17)$$

- Given V_{spt},V_{lvf} and V_{rvf}, values of P_{lvf} and P_{rvf} can be determined.
- Use the values of P_{lvf}, P_{rvf} and P_{peri} to calculate P_{lv} and P_{rv}.
- With P_{lv} and P_{rv}, it is now possible to calculate flow rates, and thus, rates of change of ventricular volumes (V_{lv} and V_{rv}).

The initial volumes are approximated based on normal heart function and the initial flow rates are calculated using Equation (5). Alternatively, the results from a previously run model can be used as the initial conditions for a new model.

4. PHYSIOLOGICAL VERIFICATION

When tested, the closed loop model was shown to have no dependence on initial conditions, with different initial conditions converging to the same solution after a period of about two heartbeats. Long-term stability was also verified over a period of 40 seconds, or about 66 heartbeats.

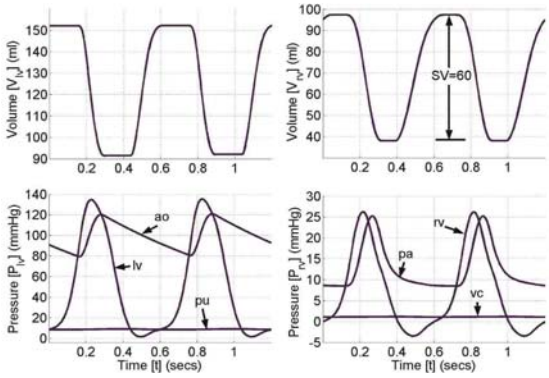

Fig. 7. Simulation results for closed loop model with inertia and ventricular interaction.

The patient parameters used in this model are based on those found in the literature, and manipulated to produce model outputs comparable to an average human (Burkhoff, 1993; Chung, 1997). Figure 7 shows the output pressures and volumes for this model while Figure 8 plots the deflection of the septum wall as a result of ventricular interaction.

The target performance metrics of the model were obtained from Guyton (1991). A typical ventricle stroke volume (SV) is about 60-70ml, and is marked on the graph. The aortic pressure in an average person is around 120 over 80mmHg as marked (ao), while a normal pulmonary artery pressure is about 25 over 8mmHg as marked (pa). The return pressure entering the right heart is typically around 0mmHg, but it can be negative since the pressure in the thoracic cavity is generally about -4mmHg. The return pressure to the left ventricle is typically 1-5mmHg. All of the magnitudes reported are comparable to expected values verifying the model assumptions and solution.

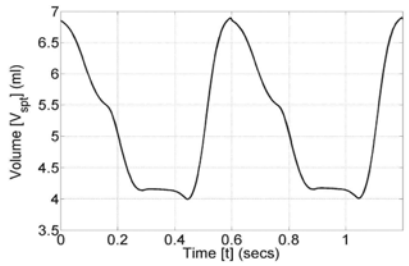

Fig. 8. Simulation output showing fluctuations in septum volume.

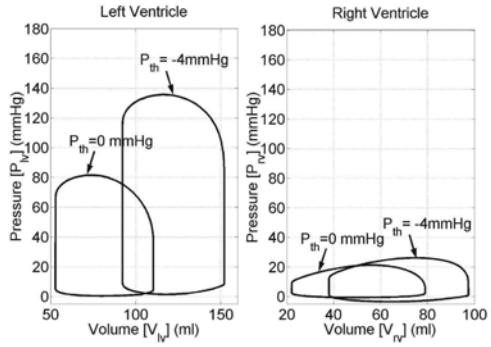

Fig. 9. PV profiles for closed loop model with normal thoracic pressure (P_{th}=-4mmHg), and high thoracic pressure (Pth=0mmHg).

A specific aim for the model is simulation of human heart function in response to changes in therapy and parameters. Tests to further validate the model were carried out comparing model outputs to specific changes with known physiological trends. Normal thoracic cavity pressure in humans is about -4mmHg, however if this pressure is increased, as occurs with a patient on a respirator during positive pressure breathing, cardiac output (CO) decreases (Guyton, 1991). Figure 9 shows the model output for both 0mmHg and -4mmHg thoracic pressure where the stroke volume, and thus the cardiac output, is decreased by 5% with the increased thoracic pressure. Figure 9 is presented as a PV diagram to more clearly illustrate these changes.

A second test shows the effect of changing the systemic circulatory resistance. Normally, increased resistance results in reduced cardiac output. Figure 10 shows that as systemic resistance is increased, stroke volume, and thus cardiac output, decreases. The simulation results also show an increase in aortic pressure from 120/80mmHg to 160/130mmHg when the systemic resistance is doubled mimicking the usual rise in blood pressure associated with the arteries becoming blocked, and the resulting increased resistance.

These results show the potential of this model for accurately simulating trends in the cardiovascular system in response to changes in therapy or physiology. With future development of the model, it is hoped that more subtle trends in CVS haemodynamics can be simulated.

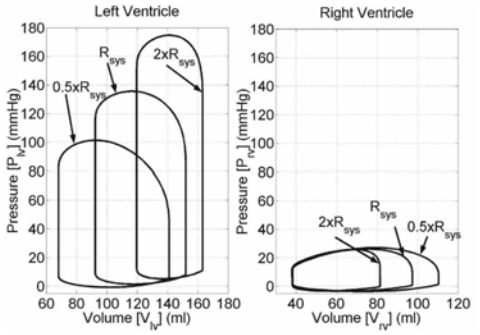

Fig. 10. Variation in ventricle PV profiles as a result of varying systemic resistance (R_{sys}).

5. CONCLUSION

The minimal model approach presented for modelling the CVS is shown to offer numerical stability and robustness. A means of modelling the valves is shown that accommodates inertial effects and avoids discontinuities and numerical instability while providing physiologically realistic performance. The closed loop system model was shown to accurately capture basic trends in human cardiovascular system function. The overall results show the significant potential of this approach to modelling the CVS system and, ultimately, in becoming an important diagnostic aid for critical and cardiac care health professionals.

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