Simulation and Development of a Mock Circulation Loop with Variable Compliance

Masters Thesis

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Abstract

Heart disease is attributed as the highest cause of death in the world. Although this could be alleviated by heart transplantation, there is a chronic shortage of donor hearts and so mechanical solutions are being considered. Currently, many Ventricular Assist Devices (VADs) are being developed worldwide in an effort to increase life expectancy and quality of life for end stage heart failure patients. Current pre-clinical testing methods for VADs involve laboratory testing using Mock Circulation Loops (MCLs), and in vivo testing in animal models. The research and development of highly accurate MCLs is vital to the continuous improvement of VAD performance.

The first objective of this study was to develop and validate a mathematical model of a MCL. This model could then be used in the design and construction of a variable compliance chamber to improve the performance of an existing MCL as well as form the basis for a new miniaturised MCL.

An extensive review of literature was carried out on MCLs and mathematical modelling of their function. A mathematical model of a MCL was then created in the MATLAB/SIMULINK environment. This model included variable features such as resistance, fluid inertia and volumes (resulting from the pipe lengths and diameters); compliance of Windkessel chambers, atria and ventricles; density of both fluid and compressed air applied to the system; gravitational effects on vertical columns of fluid; and accurately modelled actuators controlling the ventricle contraction. This model was then validated using the physical properties and pressure and flow traces produced from a previously developed MCL.

A variable compliance chamber was designed to reproduce parameters determined by the mathematical model. The function of the variability was achieved by controlling the transmural pressure across a diaphragm to alter the compliance of the system. An initial prototype was tested in a previously developed MCL, and a variable level of arterial compliance was successfully produced; however, the complete range of compliance values required for accurate physiological representation was not able to be produced with this initial design.
The mathematical model was then used to design a smaller physical mock circulation loop, with the tubing sizes adjusted to produce accurate pressure and flow traces whilst having an appropriate frequency response characteristic.

The development of the mathematical model greatly assisted the general design of an \textit{in vitro} cardiovascular device test rig, while the variable compliance chamber allowed simple and real-time manipulation of MCL compliance to allow accurate transition between a variety of physiological conditions. The newly developed MCL produced an accurate design of a mechanical representation of the human circulatory system for \textit{in vitro} cardiovascular device testing and education purposes. The continued improvement of VAD test rigs is essential if VAD design is to improve, and hence improve quality of life and life expectancy for heart failure patients.
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<th>Definition</th>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>Cross sectional area of pipe</td>
</tr>
<tr>
<td>$A_c$</td>
<td>Cross sectional area of compliance chamber pipe</td>
</tr>
<tr>
<td>AoP</td>
<td>Aortic pressure</td>
</tr>
<tr>
<td>Bpm</td>
<td>Beats per minute</td>
</tr>
<tr>
<td>c</td>
<td>Speed of sound</td>
</tr>
<tr>
<td>C</td>
<td>Compliance</td>
</tr>
<tr>
<td>EDV</td>
<td>End diastolic volume</td>
</tr>
<tr>
<td>ESV</td>
<td>End systolic volume</td>
</tr>
<tr>
<td>g</td>
<td>Gravitational constant</td>
</tr>
<tr>
<td>HR</td>
<td>Heart rate</td>
</tr>
<tr>
<td>K</td>
<td>Spring constant</td>
</tr>
<tr>
<td>$K_a$</td>
<td>Bulk modulus of air</td>
</tr>
<tr>
<td>L</td>
<td>Inertiance</td>
</tr>
<tr>
<td>LAP</td>
<td>Left atrial pressure</td>
</tr>
<tr>
<td>LVP</td>
<td>Left ventricle pressure</td>
</tr>
<tr>
<td>LVP$_{ed}$</td>
<td>End diastolic left ventricle pressure</td>
</tr>
<tr>
<td>LVP$_{es}$</td>
<td>End systolic left ventricle pressure</td>
</tr>
<tr>
<td>m</td>
<td>Mass</td>
</tr>
<tr>
<td>$m_a$</td>
<td>Mass of air</td>
</tr>
<tr>
<td>mL</td>
<td>Milli-Litres</td>
</tr>
<tr>
<td>MAP</td>
<td>Mean aortic pressure</td>
</tr>
<tr>
<td>MCL</td>
<td>Mean circulatory pressure</td>
</tr>
<tr>
<td>MPAP</td>
<td>Mean pulmonary artery pressure</td>
</tr>
<tr>
<td>MPQ</td>
<td>Mean pulmonary flow rate</td>
</tr>
<tr>
<td>$m_{reg}$</td>
<td>Mass of air from regulator</td>
</tr>
<tr>
<td>MSQ</td>
<td>Mean systemic flow rate</td>
</tr>
<tr>
<td>Q</td>
<td>Flow rate</td>
</tr>
<tr>
<td>$Q_c$</td>
<td>Flow rate into compliance chamber</td>
</tr>
<tr>
<td>$Q_{in}$</td>
<td>Flow into subsystem</td>
</tr>
<tr>
<td>$Q_{out}$</td>
<td>Flow out of subsystem</td>
</tr>
<tr>
<td>$Q_{reg}$</td>
<td>Flow of air from regulator</td>
</tr>
<tr>
<td>$P_a$</td>
<td>Air pressure</td>
</tr>
<tr>
<td>$P_{AP}$</td>
<td>Pulmonary artery pressure</td>
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<tr>
<td>$P_c$</td>
<td>Compliance chamber pressure</td>
</tr>
<tr>
<td>$P_{in}$</td>
<td>Pressure into subsystem</td>
</tr>
<tr>
<td>$P_{L loss}$</td>
<td>Pressure loss due to inertiance</td>
</tr>
<tr>
<td>$P_{loss}$</td>
<td>Pressure loss</td>
</tr>
<tr>
<td>$P_{out}$</td>
<td>Pressure out of subsystem</td>
</tr>
<tr>
<td>PQ</td>
<td>Pulmonary flow rate</td>
</tr>
<tr>
<td>$P_{reg}$</td>
<td>Pressure from regulator</td>
</tr>
<tr>
<td>$P_{R loss}$</td>
<td>Pressure loss due to resistance</td>
</tr>
<tr>
<td>PVP</td>
<td>Pulmonary venous pressure</td>
</tr>
<tr>
<td>R</td>
<td>Resistance</td>
</tr>
<tr>
<td>$R$</td>
<td>Universal gas constant</td>
</tr>
<tr>
<td>RAP</td>
<td>Right atrial pressure</td>
</tr>
<tr>
<td>$R_{reg}$</td>
<td>Regulator resistance</td>
</tr>
<tr>
<td>Rt</td>
<td>Compliance chamber resistance</td>
</tr>
<tr>
<td>RVP</td>
<td>Right ventricle pressure</td>
</tr>
<tr>
<td>s</td>
<td>Seconds</td>
</tr>
<tr>
<td>SQ</td>
<td>Systemic flow rate</td>
</tr>
<tr>
<td>SVP</td>
<td>Systemic venous pressure</td>
</tr>
<tr>
<td>SVR</td>
<td>Systemic vascular resistance</td>
</tr>
<tr>
<td>VAD</td>
<td>Ventricular assist device</td>
</tr>
<tr>
<td>$V_{air}$</td>
<td>Volume of air</td>
</tr>
<tr>
<td>$V_c$</td>
<td>Volume of fluid in chamber</td>
</tr>
<tr>
<td>$V_{reg}$</td>
<td>Volume of air from regulator</td>
</tr>
<tr>
<td>x</td>
<td>Position of centre of mass</td>
</tr>
<tr>
<td>$\ddot{x}$</td>
<td>Double derivative of centre of mass</td>
</tr>
<tr>
<td>$\rho_a$</td>
<td>Density</td>
</tr>
<tr>
<td>$\rho_c$</td>
<td>Density of air</td>
</tr>
<tr>
<td>$\rho_{reg}$</td>
<td>Density of fluid</td>
</tr>
<tr>
<td>$\mu$</td>
<td>Density of air from regulator</td>
</tr>
<tr>
<td>$\rho_{air}$</td>
<td>Viscosity</td>
</tr>
</tbody>
</table>
Statement of Authorship

The work contained in this thesis has not been previously submitted for a degree or diploma at any other higher education institution. To the best of my knowledge and belief, the thesis contains no material previously published or written by any other person except where due reference is made.

Shaun Gregory

2008
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Medical engineering first became a career goal of mine following the death of my grandfather due to cancer. He remains a big part of my life, and I dedicate the work carried out in this Masters to him. I would like to thank everyone who has helped me progress to the completion of this degree.
Chapter 1

Introduction

Mock Circulation Loops (MCLs) are vital for the \textit{in vitro} testing and development of Ventricular Assist Devices (VADs). As well as testing VADs, MCLs have many more applications. They can be used for the testing and refinement of heart valves, total artificial hearts, artificial lungs, vascular grafts and intra-aortic balloon pumps. Tissue engineering of heart valves and other preliminary studies on the cardiovascular system can also be achieved with MCLs. MCLs are also a useful education tool as haemodynamic parameters such as cardiac output and blood pressures can be observed in real-time.

Heart disease is recognised as the highest cause of death in the world, resulting in the need for donor hearts \cite{1}. In the USA alone, around 40,000 patients require a heart transplant per year, while there are only around 2,000 donors annually \cite{2}. This donor shortage creates a need for a bridge-to-transplant device to keep the patient alive while a donor is being found.

This problem is currently being addressed by the development of ventricular assist devices. Some of these devices assist only the left or right side of the heart (LVADs and RVADs), while others assist both sides of the heart (BiVADs). While these devices are adequate to keep patients alive and organs reasonably perfused while a donor heart is located, research continues in an effort to improve designs. To assist with the testing procedures of developing VADs, mock circulation loops are used. MCLs are required to test VADs by FDA regulations; however, they do not replace \textit{in vivo} trials \cite{3}.

Early versions of mock circulation loops were primarily used for testing artificial heart valves. These systems consisted of pulse duplicators driven by stepping motors to create an artificial heart beat \cite{4}. Current devices vary from simple, non-pulsatile loops to complex systems mimicking the natural haemodynamics of the human circulatory system incorporating features such as compliance, resistance, fluid inertia, pulsatile flow, multiple VAD attachments etc. Many mock circulation loops consist
of only a systemic circulation, and hence can only be used for testing LVADs. Current complete circulation loops are often limited in their functions and excessive size. This creates a need for a new highly developed, compact mock circulation loop for testing VADs and for other applications such as teaching cardiac physiology.

The design of a new mock circulation loop must incorporate several factors. Easy alteration of haemodynamic parameters such as resistance, compliance, heart rate, and contractility is vital for efficient, repeatable VAD testing. Reproduction of the Frank Starling mechanism, which relates the heart’s ability to increase contractility with an increase in venous return, is an important factor in producing a physiologically accurate model of the human circulation. The ability to easily incorporate mechanical assistance is also a critical feature of a MCL. A mathematical model of a mock circulation loop would be useful for the optimization of the system in the design phase. This model will enable the selection of appropriate piping dimensions to generate the correct impedance for each section of the MCL in order to produce accurate physiological haemodynamics under all simulated conditions.
1.1 Aims

The aim of this thesis was to present the development of a mathematical model of a mock circulation loop, which was then used to assist in the design of a variable compliance chamber and a complete physical mock circulation loop.

The specific aims of this study were to –

- Conduct an extensive review of literature in the field of mock circulation loops,
- Develop a mathematical model of a mock circulation loop to assist the design of a new loop,
- Validate the mathematical model against a previous mock circulation loop,
- Design and construct a variable compliance chamber for use on a mock circulation loop,
- Test and validate the variable compliance chamber,
- Use the mathematical model and variable compliance chamber to assist in the design of a compact mock circulation loop.
1.2 Scope

The scope of this study involved the development and validation of a mathematical model of a mock circulation loop. A variable compliance chamber was to be developed and tested with a current mock circulation loop. The mathematical model, created in the MATLAB / SIMULINK environment, was then used to design, but not construct, a compact mock circulation loop for use in ventricular assist device testing and for educational purposes.
Chapter 2

Background and Literature Review

To provide a detailed understanding of what is required for the design of a new mock circulation loop, research was conducted into the human circulatory system and all of its components.

2.1 The Circulatory System

Deoxygenated blood returns to the heart from the body into the right atrium. It continues to flow through the tricuspid valve into the right ventricle, where it is then pumped through the pulmonary valve into the pulmonary artery. The pulmonary artery bifurcates to supply blood to both the left and right lung via the arterioles and finally the capillaries in the lungs, where the blood is oxygenated and flows through the pulmonary veins into the left atrium. From there the blood travels through the mitral valve into the left ventricle, where it is pumped under high pressures through the aortic valve and into the aorta. Following this, the circulatory system branches into many arteries that carry the oxygenated blood to the body. Blood then flows back to the heart through the systemic venous system. Any flow from the upper body flows into the right atrium via the superior vena cava, while the flow from the lower body travels into the right atrium via the inferior vena cava. From this point, the cycle of blood through the body starts over to continually supply oxygenated blood to the whole body.

2.2 The Cardiac Cycle

Cardiac function occurs in cycles, where each cycle can be divided into two portions; diastole and systole. Diastole is the stage where the ventricle relaxes and fills with blood, while systole is the process of forcing the blood out of the ventricle. These portions can then be broken down into smaller phases, as shown in Figure 1.

Phase 1 is known as Atrial Contraction where the atrium contracts to such a degree that the pressure gradient across the atrioventricular (AV) valve is sufficient for blood to flow quickly into the ventricle. This contraction provides a small increase in
venous pressure while accounting for about 10-20% of ventricular filling in normal heart function. An “atrial kick” can be seen in cases with high atrial contractility, such as exercise, which can cause up to 40% of ventricular contractility to occur during this stage. After atrial contraction, in the same phase, the atrial pressure falls and the valves begin to close. By this stage the ventricle has reached maximum volume, known as end diastolic volume (EDV).

Isovolumetric contraction occurs in Phase 2. This process involves the ventricle contracting, causing a rapid increase in pressure, while the volume remains constant. The ventricle becomes more spherical and pushes the AV valve back into the atrium slightly after it has closed. This, accompanied with continuous venous return, increases the atrial pressure.

The third phase is rapid ejection. This occurs when the pressures inside the ventricle exceed that of the pulmonary artery and the aorta, causing the valves to open and blood to flow out of the ventricles. Ventricular pressure stays a small amount higher than aortic / pulmonary pressure during this stage while a rapid decrease in ventricular volume can be noticed. Atrial pressure is reduced during this phase due to the base of the atrial chamber being pulled downward and increasing in volume.

Phase 4, reduced ejection, occurs when the rate of ejection falls. The ventricular pressure falls just below that of the aortic / pulmonary pressure, but flow continues for a short time due to the inertia of the blood. The atrial pressure rises slowly during this phase from venous return.

Isovolumetric relaxation occurs in Phase 5. In this phase, the ventricular pressure falls well below that of the aortic / pulmonary pressures, and the valves suddenly close. This valve closure causes a small amount of backflow and is represented by the
dicrotic notch in the pressure waveform, which is a small rise in the aortic / pulmonary pressures. During this phase the volume of the ventricle remains constant as all of the valves are closed. This volume is known as end systolic volume (ESV) and is usually about 50mL in the left ventricle. As can be seen in Figure 1, the atrial pressures continue to rise. This is due to continuous venous return during this stage.

The sixth phase is known as rapid filling. This phase is caused by the ventricular pressures dropping below that of the atrial pressures. This causes a rapid inflow of blood into the ventricles, while the pressures continue to drop in the ventricles due to the ventricle walls still relaxing. The atria pressures drops fairly rapidly as the volume of the atria are decreased. Aortic pressure decreases gradually, a property of both the aortic compliance and systemic vascular resistance, as blood flows through the systemic circulation. Phase 7, reduced filling, occurs as the ventricles continue to fill with blood. The compliance of the walls decreases as the volume of the ventricle increases, causing the rate of filling to slow. Atrial pressure continues to rise as it is filled while the aortic pressure falls due to blood continuing into the systemic circulation [5].

2.3 Mock Circulation Loops

Mock circulation loops are used as a mechanical representation of the human cardiovascular system for in vitro testing of artificial heart valves, pulsatile and continuous flow ventricular assist devices, total artificial hearts, aortic balloon pumps, and almost any other cardiovascular device. Basic systems can consist of a pre-load chamber to deliver constant flow and a resistance valve to alter the pressure drop, however new systems have been developed including features such as physiologically accurate pulsatile flow, compliance, resistance, fluid inertia, atrial contraction, systemic and pulmonary circuits, cardiovascular device insertion, septal defects, valve regurgitation, and many more. An extensive background and literature review into mock circulation loops and the human cardiovascular system is presented.

The first mock circulation systems were primarily used for testing artificial heart valves and consisted of pulse duplicators driven by stepping motors to create an artificial heart beat [6]. Many of these systems include transparent, flexible ventricles for valve flow visualisation [7-12].
An example of a MCL is the system designed by Cornhill et al. (1977) [13], for the purpose of testing prosthetic aortic heart valves. This system used a collapsible silicone bag in a pressurised airtight box for a mock left ventricle which was supplied with pulses of compressed air, controlled by a solenoid valve. With characteristic impedance, total arterial capacitance and peripheral resistance incorporated, the system reproduced appropriate conditions for the testing of artificial heart valves, however failed to simulate atrial systole and ignored inertial effects.

An early mock circulation loop designed by Kolff et al. (1959) [14] consisted of both systemic and pulmonary sides. The ventricles were operated by use of compressed air, while the pressures in the aorta and pulmonary artery were obtained by tall columns of water (82cm or 60mmHg for aorta and 26cm or 20mmHg for PA). The diastolic pressure could be changed by altering the height of the fluid column. These columns created an undesirable effect of excessive inertia which had to be overcome to move fluid up the tube. This was overcome by surrounding the bottom part of the tube with a pressurised air chamber to assist with the flow up the tube. A single flow meter was used as it was said that the flow must be the same in both sides at all times, even though slight changes can be seen at times before levelling out. No resistance valves were used in this study as the resistance was seen to increase with increased flow, and no attempt to simulate vessel compliance was mentioned.

Reul et al. (1974) [15] constructed a systemic mock circulation loop using flexible tubing for the aorta and all of its branches. This system was suspended in a water filled Perspex box which is connected to a Windkessel chamber with adjustable air volume for compliance. Separate resistances were applied for each branch of the system by a tube membrane. The system was driven by a cam which supplies a pulsatile pressure to the mock ventricle, and inertiance is accounted for by appropriately dimensioning the aorta and its branches. Although this system displayed a suitable mock version of the systemic circulatory system, it did not include a method of connecting and testing of VADs.

Donovan et al. (1975) [16] designed and built a complete mock circulation loop that has been replicated many times since its conception. It was designed for testing new artificial heart designs in vitro, however did not include atria or ventricles which limits the cardiovascular device testing capabilities of the rig. This device used ½
10 inch acrylic sheet to make a box, with several smaller compartments situated inside to replicate aortic, systemic venous, pulmonary arterial, pulmonary venous and ventricular components. This system was fairly compact with dimensions of 605mm wide, 403mm high and 202mm deep. This mock circulation loop showed positive results when compared to a calf model, and has been the basis for many mock circulation loops since.

A mock circulation loop was developed by Scotten et al. (1979) [17] for evaluation of mitral valve prostheses. A transparent mock ventricle was created which is driven by a cam which pushes fluid in a sealed chamber that includes the ventricle. This method gave a solution to finding the volume of the ventricle with respect to time by examining the cam position and cross sectional area with respect to time. The ventricle pumped into a compliant latex rubber aorta, and then to resistance and compliance elements. Resistance was simulated by use of cellulose fibre water filters with pore sizes of 5 and 50μm for characteristic and peripheral resistance respectively. The lengths of these filters, and hence the resistance value, could be altered by insertion into a plastic tube while the mock circulation loop was in operation, however this produced a discretely variable resistance rather than a continuously variable system. Compliance was obtained by a volume of air trapped above the resistance elements. Transparent materials were used for the ventricle, hydraulic chamber, and working fluids to gain flow visualisation through the valves. This mock loop successfully produced pressure and flow results which allowed for detailed flow visualisation to be completed.

Rosenborg et al. (1981) [18] summarised the design and evaluation of the commonly repeated Pennsylvania State University Mock Circulatory System. This system, first designed in 1971 for use on *in vitro* testing of VADs, has been refined in many ways since it was first introduced. It included features such as resistance, compliance, inertia, systemic and pulmonary circulation, VAD connections and adjustable cardiac conditions. The values chosen for reproduction in the mock circulation loop with a cardiac output of 5L/min, MAP of 100mmHg, MPAP of 15mmHg, mean LAP of 7.5mmHg and mean RAP of 2.2mmHg are shown in Table 1. While resistance and compliance values were based on those seen in a healthy male, inertia values were incorrectly assumed to be equal for systemic and pulmonary circulations. This mock
circulation loop has shown adequate results when representing the human circulatory system and provides a suitable method for the in vitro testing of blood pumps prior to animal testing.

<table>
<thead>
<tr>
<th>Systemic resistance</th>
<th>Pulmonary resistance</th>
<th>Systemic capacitance</th>
<th>Pulmonary capacitance</th>
<th>Systemic Inertiance</th>
<th>Pulmonary Inertiance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.36 mmHg.s/mL</td>
<td>0.14 mmHg.s/mL</td>
<td>1.33 mL/mmHg</td>
<td>4.4 mL/mmHg</td>
<td>0.0158 mmHg.s²/mL</td>
<td>0.0158 mmHg.s²/mL</td>
</tr>
</tbody>
</table>

Table 1 - Mock circulation loop parameters chosen by Rosenborg et al. (1981).

Verdonck et al. (1992) [19] created a mock circulation loop for testing of mitral valves, which was later altered [7]. This system had the ability to easily replace the mitral and aortic valves. Fluid entered the system from a preload reservoir representing the lungs, into two rigid pulmonary veins, which carry the fluid through the replaceable mitral valve. From the left ventricle, the fluid travelled through the replaceable aortic valve into the afterload system consisting of a Windkessel chamber for compliance and a hydraulic resistor. A venous reservoir was then included to obtain a constant venous pressure of 5 mmHg. The silicone left ventricle and latex atrium were both anatomically shaped and mounted in water filled Perspex housing where the pressures are controlled by an external circuit. The amount of pressure delivered to the ventricle was determined by a feedback system, which was given a model pressure-time diagram which was used to control the amount of air to obtain a model pressure-time curve as close as possible. Positive pressures were induced for systole while negative pressures were used to simulate diastole, resulting in physiologically inaccurate ventricle filling. This mock circulation loop was later used by Vandenberghe et al. (2003) [20] to assess the hydrodynamic performance of an intra-arterial LVAD.

To investigate the effects of extracorporeal membrane oxygenation (ECMO), Trittenwein et al. (1998) [21] designed a simple neonatal mock circulation loop. This loop was required to mimic the neonatal circulation, and produce lower cardiac output with decreased heart rate as seen in the natural situation. This mock circulation was tested by simulating conditions of hypovolemia (volume depletion of mock loop), enhanced arterial resistance, a combination of the two, and low cardiac output. The
authors concluded that this mock circulation loop is a valuable tool in demonstrating several cardiac conditions in neonates, however cannot replace clinical studies due to the inability to replicate the reaction of the patient and medication effects. While promising results were recorded for this system, the lack of a pulmonary circulation resulted in inaccurate simulated ventricle preload and made the rig incapable of simulating right / biventricular heart failure in neonates.

Many different arrangements of mock circulation loops are in existence. They can differ from basic two element Windkessel models, to more advanced 5 element Windkessels. Sharp et al. (1999) [22] conducted a study into the benefits of several of these, and used this study to construct a mock circulation loop to compare with natural human results, the popular Donovan loop, and the Penn State mock circulation loop. A computer analysis of RC, RCR, RLRC, and RCLRC models was conducted, where R stands for a resistance, C for a compliance and L for an inertiance component. The results of this study showed that as each element was added to the design, an improvement was made when comparing to human data. When the fourth element was added, only a slight improvement over the three element design was noted, while the addition of a fifth element improved the circuit significantly. Due to the common nature of the RCR model, and the difficulty of construction of an RCLRC model, the results of the simulation were ignored and RCR was chosen to take to a physical model stage. This was seen to compare favourably against the Donovan and Penn State models when being measured against human data. It is thought by the authors that the Penn State system included small diameter (2.54cm) elements in the system which caused an undesirable effect on the inertial properties of the mock loop.

A study was conducted by Baloa et al. (2001) [23] into the elastance-based control of a mock circulation loop. This concept used the elastance, defined as the instantaneous ventricular pressure versus ventricular volume, of the ventricle to develop a new control strategy for mock circulation loops. The maximum value for elastance was taken at the point of end systole, and can be interpreted as a measure of ventricular contractility. Resistance and compliance were both changed manually in this system, and the values used for this study were –
Load resistance 1.83 mm.Hg.s/mL
Arterial compliance 1.37 mL/mmHg
Pulmonary venous compliance 6.74 mL/mmHg

The authors concluded that this design was successful in using elastance-based control to change the contractility of the ventricular chamber, resulting in a new way of reproducing difference cardiac conditions in a mock circulation loop for the evaluation of cardiac assist devices. While the contractility of the ventricle was controlled, inertial effects in the ventricle and circulation were ignored, while only a systemic circulation was simulated.

Fiore et al. (2003) [24] designed a mock ventricle of natural shape for use in the study of mitral valve surgical correction. This study involved creating a flexible mock ventricle and observing the shape changes of this ventricle throughout the cardiac cycle. This information was then intended to be used for creating a suitable mock ventricle for the study of fluid dynamics of ventricular filling. The end systolic shape of the ventricle was chosen for reproduction in this model. This was chosen so that as the ventricle fills, it will stretch but keep a similar shape, whereas if the end diastolic volume was chosen, it would be forced to contract and potentially buckle in a shape that may not represent the true shape of a ventricle in systole. Finite element modelling was used to construct the shape of the ventricle, which had an end systolic volume of 71mL. The shell thickness of the model was 0.21mm, while the structure was reinforced with 5 bands. Cardiac function was simulated by applying a negative pressure around the mock ventricle to induce ventricular filling until the ejection fraction reached a value of 0.55. Values of wall curvature were taken from 7 sections along the mock ventricle and compared with that seen in literature. It was found that the inaccuracy of this system did not exceed 3.5%, and was concluded that this design displays a similar behaviour to that of a natural left ventricle. The mock ventricle represented the correct shape for a healthy male, however the larger ventricle volumes seen in conditions such as dilated cardiomyopathy could not be replicated in this system, resulting in only one physiological condition being reproducible in this system.
An infant mock circulation for educational simulation was created by Goodwin et al. (2004) [25]. This study replicated the cardiovascular parameters for the infant, which can be seen along with the adult values displayed in the study, in Appendix 1.

Koenig et al. (2004) [26] produced a systemic mock circulation to test continuous and pulsatile ventricular assist devices. A Starling responsive loop was used to test haemodynamic and ventricular pressure-volume loop responses at different levels of assist for pulsatile and continuous flow devices. A mock ventricle was created of hemi-ellipsoid shape with semi-rigid dome with mounts for the aortic and mitral valves. This system was controlled by a pressurised chamber to obtain the desired heart rate and pressures. Ventricular pressure and volume was monitored by use of a high fidelity pressure-volume conductance catheter. A coronary vasculature was included in this system. A resistance element was included by a compliant latex tube in a sealed chamber. This chamber was supplied with pressures from the driveline which also supplied the ventricle, with smaller pressures to produce the appropriate level of coronary flow. The primary limitation of this study was the absence of a pulmonary circulation to complement the systemic side. The volume catheter was also prone to error depending on its position in the ventricle.

Pantalos et al. (2004) [4] aimed to construct a mock circulation loop to mimic the Frank Starling response in normal, heart failure, and partial recovery situations. Table 2 shows the values chosen for reproduction in the mock circulation loop by Pantalos. This system incorporated a flexible polyurethane atrium and ventricle. The ventricle was situated inside a pressurization chamber with a semi-rigid dome for mounting inflow and outflow valves, however was not anatomically shaped to produce accurate flow dynamics in the ventricle. This configuration allowed for atrial or ventricular apex inflow and aortic outflow cannulation. A high fidelity pressure-volume catheter was used for monitoring pressure and volume with respect to time and was placed inside the mock ventricle via the outflow valve. A polyurethane aorta was connected to the ventricle and leads to the systemic and coronary vasculature and inertial effects were accounted for in the cross sectional area and length of the tubing. Pressure volume loops representing natural situations were produced, while this system can be shown to mimic the Frank Starling response for all conditions. This mock circulation loop produced accurate haemodynamic waveform magnitudes and morphology for all
testing conditions and could be used for testing of cardiac devices. The primary limitations of this system involve not having a pulmonary vasculature and noise in the aortic pressure waveform due to valve closure. This mock circulatory system was then used by Glower et al. (2004) [27] to evaluate an artificial vasculature device (AVD) and Koenig et al. (2004) [26] to investigate haemodynamic and pressure-volume responses to continuous and pulsatile ventricular assist devices.

Parameter Normal Heart failure Recovery

<table>
<thead>
<tr>
<th>Mean Aop (mmHg)</th>
<th>95</th>
<th>65</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO (L/min)</td>
<td>5.0</td>
<td>3.0</td>
<td>4.0</td>
</tr>
<tr>
<td>LVPed (mmHg)</td>
<td>2-5</td>
<td>15-25</td>
<td>10-15</td>
</tr>
<tr>
<td>DLP (mmHg)</td>
<td>210</td>
<td>80</td>
<td>150</td>
</tr>
<tr>
<td>Arterial resistance (mmHg.s/mL)</td>
<td>1.218</td>
<td>2.023</td>
<td>-</td>
</tr>
<tr>
<td>Compliance (ml/mmHg)</td>
<td>1.4</td>
<td>0.3</td>
<td>-</td>
</tr>
<tr>
<td>Inertiance (mmHg.s^2/ml)</td>
<td>0.02</td>
<td>0.05</td>
<td>-</td>
</tr>
<tr>
<td>Characteristic impedance (mmHg.s/ml)</td>
<td>65</td>
<td>1066</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 2– Values chosen for reproduction in mock circulation by Pantalos et al. (2004). [4]. AoP – Aortic pressure; CO – Cardiac output, LVPed – End diastolic left ventricular pressure, DLP – driveline pressure for ventricle.

A systemic mock circulation with coronary vasculature was constructed by Litwak et al. (2005) [28] for use in a study on aorta outflow graft location with pulsatile and continuous flow VADs. The parameters presented in Table 3 show the values used to represent normal and heart failure conditions in the mock circulation. This mock loop consisted of an atrium and ventricle, both made of flexible polymer sacs with the ventricle situated in a pressure chamber. Ventricular cannulation was achieved via the apex of the ventricle and into the aorta. A coronary and systemic vasculature, including the carotid artery, was included while an artificial aorta was connected downstream of the mock ventricle and into the mock vasculature. The inclusion of a coronary circulation and carotid artery improve the accuracy of a cardiovascular simulation, however the venous return from these structures was ignored without a
pulmonary circulation. Phasic coronary resistance was achieved by a compliant latex tube inside a pressure chamber driven by the same pressure pulse as the ventricle source, with a lower pressure. This resulted in an elevated coronary resistance during ventricular systole, and reduced coronary resistance during diastole resulting in a biphasic coronary waveform which produces the majority of coronary flow during diastole.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal function</th>
<th>Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mmHg)</td>
<td>95</td>
<td>65</td>
</tr>
<tr>
<td>CO (L/min)</td>
<td>5.0</td>
<td>3.0</td>
</tr>
<tr>
<td>LVPed (mmHg)</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>LVV (mL)</td>
<td>75-150</td>
<td>215-280</td>
</tr>
</tbody>
</table>

Table 3– Values chosen by Litwak et al. (2005), for mock loop study. MAP – Mean arterial pressure, CO – Cardiac Output, LVPed – End diastolic left ventricular pressure, LVV – Left ventricular volume.

Liu et al. (2005) [29] constructed a complete mock circulation loop for the testing of continuous flow LVADs and can be seen in Figure 2. The ventricles were simulated by semi-ellipsoidal shaped silicone diaphragms in pressure chambers which received pulses of compressed air for systole while a slight negative pressure was applied for diastole. Check valves were used to achieve uni-directional flow. Clear tygon tubing was used to connect all components in the loop, while the VAD was connected to the loop via the apex of the mock ventricle and the systemic arterial tank. Testing was conducted with the loop under several different conditions including healthy resting, healthy sleeping, healthy

![Figure 2 - Mock circulation loop by Liu et al. (2005)](image_url)
exercise, congestive heart failure (CHF), resting, and partially recovered CHF resting. The pressure and flow values chosen to simulate these conditions are shown in Table 4. This mock circulation loop was sufficient for testing continuous flow LVADs under various heart rates and contractility. Due to the inability to mimic the Frank Starling response in this system it could not be used to provide an accurate prediction of LVAD performance in the transition of activity levels and left ventricular failures.

<table>
<thead>
<tr>
<th></th>
<th>Health/Rest</th>
<th>Healthy/Sleep</th>
<th>Healthy/Exercise</th>
<th>CHF/Rest</th>
<th>Partially recovered</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVPED</td>
<td>5.1</td>
<td>5.4</td>
<td>6.9</td>
<td>24.6</td>
<td>21.2</td>
</tr>
<tr>
<td>MAP</td>
<td>95</td>
<td>81</td>
<td>115</td>
<td>54</td>
<td>69.5</td>
</tr>
<tr>
<td>MVP</td>
<td>8.2</td>
<td>7.8</td>
<td>7.8</td>
<td>7.2</td>
<td>8.8</td>
</tr>
<tr>
<td>CO</td>
<td>5.2</td>
<td>4.7</td>
<td>10.3</td>
<td>3.2</td>
<td>4.0</td>
</tr>
<tr>
<td>PLVP-PAOP</td>
<td>-1.8</td>
<td>1.4</td>
<td>20.5</td>
<td>1.8</td>
<td>-2.1</td>
</tr>
</tbody>
</table>

Table 4– Values chosen for simulation by Liu et al. (2005). LVPED – left ventricular end diastolic pressure (mmHg), MAP – mean arterial pressure (mmHg), MVP – Mean venous pressure (mmHg), CO – Cardiac output (L/min), PLVP-PAOP – the difference between peak left ventricular

A complete mock circulation loop for testing of VADs was constructed by Timms et al. (2005) [3]. The aim of this study was to design and construct a new MCL that was capable of reproducing normal and heart failure conditions. This rig was seen to adhere to the Frank Starling law, however with no method of measuring ventricular volume; it could not be quantitatively measured. This mock loop was shown to produce accurate pressure and flow data for normal and heart failure conditions with a wide range of variable parameters. Limitations in this study involve the use of heavy brass swing check valves for use in replacing the natural heart valves, restriction of flow in the pulmonary circuit due to a small flow meter orifice, and the inability to measure ventricular volume with respect to time.

A hybrid mock circulation loop was designed by Kozarski et al. (2003) [30]. This system used features of current hydraulic and electrical models of the simulation, and
combined them to form a low cost, accurate system. A flow generator was used to convert incoming electrical signals into the appropriate flow for the hydraulic side of the loop. The hydraulic components represented in this study consist of a characteristic resistance, inertiance, and arterial compliance.

While many MCLs have been previously developed, features such as a pulmonary circulation, accurate representation of fluid inertia, variable compliance and adhering to the Frank Starling law are often ignored. A MCL capable of testing a large range of cardiovascular devices under various physiological conditions requires many components such as systemic and pulmonary circulations, variable vascular resistance, variable arterial compliance, venous compliance, attachment sites for mechanical support and pressure, volume and flow sensors.

2.4 Blood Volume

The majority of blood in the human body is stored in the veins. This is due to the compliant nature of the veins in comparison to the arteries, which allows the veins to hold significantly more blood. Table 5 illustrates the volume of blood in the primary vessels of the body.

<table>
<thead>
<tr>
<th>Vessels</th>
<th>Total Blood Volume (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic</td>
<td></td>
</tr>
<tr>
<td>Veins</td>
<td>64</td>
</tr>
<tr>
<td>Large veins</td>
<td>(39%)</td>
</tr>
<tr>
<td>Small veins</td>
<td>(25%)</td>
</tr>
<tr>
<td>Arteries</td>
<td>15</td>
</tr>
<tr>
<td>Large arteries</td>
<td>(8%)</td>
</tr>
<tr>
<td>Small arteries</td>
<td>(5%)</td>
</tr>
<tr>
<td>Arterioles</td>
<td>(2%)</td>
</tr>
<tr>
<td>Capillaries</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total in systemic vessels</strong></td>
<td><strong>84</strong></td>
</tr>
<tr>
<td>Pulmonary vessels</td>
<td>9</td>
</tr>
<tr>
<td>Heart</td>
<td>7</td>
</tr>
<tr>
<td><strong>Total blood volume</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Table 5 - Vessel blood volume by Seeley et al. (2003). [31]

Bevegard et al. (1960) [32] conducted a study on the effect of body position on circulation at rest and exercise, paying particular attention to stroke volume. Ten
healthy male subjects were used for this study with right heart catheterization obtained through the brachial artery. Standing, sitting and the supine position (laying down, face up) were all examined at different levels of exercise. Cardiac output in resting conditions averaged at 7.89 L/min for supine position and 5.85 L/min for sitting position while the highest workload due to exercise produced averages of 17.93 L/min and 15.94 L/min for the same positions respectively. Stroke volume varied for different positions with an average of 115.7mL for the supine position and 70.0mL while sitting. The mean increase in stroke volume when going from rest to work in the sitting position was recorded at 51%. With a change of posture from supine to sitting positions at rest, it was noted that the pulse rate increased and the stroke volume decreased significantly. It was found that the filling pressures of the right ventricle were unchanged during the transition from rest to exercise in the sitting position, while the absolute diastolic pressure in the right ventricle decreased during exercise in the supine position.

The neonatal mock circulation loop constructed by Mitsui et al. (1998) [33] had a total volume of 200mL, which is equal to the blood volume of a 2.7kg neonate, and was achieved by use of 3 elastic tubing segments simulating the main venous, central vein, and right atrium components.

Loh et al. (2004) [34] presented a detailed study of the design of a mock circulation loop and the parameters chosen for resistances, compliances, ventricular volumes, and system gains. Values of 10mL and 315mL for residual ventricular volume and maximum ventricular volume respectively were chosen for this study.

2.5 Blood Flow

Flow through the circulatory system is primarily laminar, with turbulent flow seen in the heart and where the arteries branch. It is usually measured in litres per minute (L/min) and typical values are around 5L/min for a healthy adult at rest and 2-3L/min for a heart failure situation [3]. The flow of blood in a vessel is related to the pressure difference in that vessel, and the resistance of that vessel (R). Blood will always flow from an area of higher pressure (P₁) to an area of lower pressure (P₂). The flow of blood through a vessel (Q) can be represented as –
\[ Q = \frac{P_3 - P_2}{R} \] (2.1)

The amount of blood pumped out of the heart per minute is known as the cardiac output (CO). This can be found by multiplying the heart rate by the stroke volume.

### 2.6 Frank Starling Law

The Frank Starling law states that the heart has an intrinsic capability of increasing its force of contraction and therefore stroke volume in response to an increase in venous return [5]. Deconstructed, this law states that what goes into each ventricle must come out, and that the heart is a loop that does not leak fluid. It also states that as more blood is pumped into the ventricle, the heart works harder to eject more blood and hence resist backflow. Figure 3 demonstrates that as more blood enters a ventricle, the ventricular preload (EDV) increases. This causes an increase in force of contraction leading to a larger stroke volume of the heart to maintain a constant ESV.

### 2.7 Blood Pressures

An important value for the evaluation of mock circulation loops, as well as humans, is pulse pressure. This is the difference between systolic and diastolic pressures, with typical values of 120mmHg and 80mmHg respectively [31]. Pulse pressure is primarily influenced by stroke volume and compliance levels. With an increase in stroke volume, and/or a decrease in vascular compliance, the pulse...
pressure will increase. If stroke volume is decreased and/or vascular compliance increased, the pulse pressure will decrease. As the blood flows away from the heart, the pulse pressure is gradually damped, resulting in an almost non-existing difference in the arterioles.

Mean arterial pressure (MAP) is the average pressure over one cycle taken from the aorta and is slightly less than the average of systolic and diastolic pressures. This is due to slightly less time spent in systole (about 40%) compared to diastole (about 60%). MAP can also be found by multiplying the CO by the peripheral resistance (PR). This shows that the MAP is directly affected by a change in heart rate, stroke volume, and peripheral resistance. Mean pressures throughout the body can be seen in Figure 4.

The natural pressures for resting condition used by Timms et al. (2005) [3] when considering mock circulation loop design can be seen in Table 6.

<table>
<thead>
<tr>
<th>Region of circulatory system</th>
<th>Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left atrial (LAP)</td>
<td>8-10</td>
</tr>
<tr>
<td>Left ventricular (LVP)</td>
<td>0-120</td>
</tr>
<tr>
<td>Left ventricular end diastolic (LVP_{ED})</td>
<td>8</td>
</tr>
<tr>
<td>Aortic (AoP)</td>
<td>120/80</td>
</tr>
<tr>
<td>Mean arterial (MAP)</td>
<td>93</td>
</tr>
<tr>
<td>Right atrial (RAP)</td>
<td>3</td>
</tr>
<tr>
<td>Right ventricular (RVP)</td>
<td>0-25</td>
</tr>
<tr>
<td>Right ventricular end diastolic (RVP_{ED})</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary arterial (PAP)</td>
<td>25/10</td>
</tr>
<tr>
<td>Mean pulmonary arterial (MPAP)</td>
<td>15</td>
</tr>
<tr>
<td>Mean circulatory (P_{mc})</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 6 - Pressure values used by Timms et al. (2005).
2.8 Compliance

Compliance is the tendency for blood vessel volume to increase as the blood pressure increases [31]. Compliance is inversely related to stiffness, meaning that a high level of compliance results in a vessel wall stretching easily. It can be expressed by the equation –

$$\text{Compliance} = \frac{\text{Change in volume (mL)}}{\text{Change in pressure (mm Hg)}}$$ (2.2)

The compliance of the veins is approximately 24 times greater than that of arteries [31]. This gives the veins the ability to hold large amounts of blood in comparison to arteries. Ventricular compliance influences the ventricle’s pressure volume curve. If the compliance of the ventricle is decreased, this increases the end diastolic pressure for any given end diastolic volume. This is represented in Figure 5.

Donovan et al. (1975) [16] obtained compliance by using a trapped volume of air above the circulatory fluid in each chamber. The values used for compliance in this study were: 10 mL/mmHg for the systemic venous chamber, 1 mL/mmHg for the pulmonary arterial chamber, 5 mL/mmHg for the pulmonary venous chamber, and 1 mL/mmHg for the systemic arterial chamber, but were variable by changing the volume of air above the fluid.

A mock circulation loop was designed by Garrison et al. (1994) [35] for use in haemolysis studies associated with VADs. This loop was required to be free of air and contain only biocompatible materials so that blood could be used as the working fluid. A small volume was also required so that only one unit of blood would be required for each study. It was designed so that less than one unit of blood plus 200mL of saline could fill two of these mock circulation loops, so that one control loop and one test loop could be used. The compliance chambers used in this design
consisted of two 70mL sacs and a sealed chamber. The chamber was just large enough to fit one full, and one empty sac inside. Blood would flow into the bottom sac while a set pressure would be applied to the top sac to provide a relatively constant pressure as the volumes of the two sacs changed. The blood sac would fill while the air sac empties during systole, while the reverse occurred during diastole. The compliance of the sack was limited by the small volume of the chamber limiting volume changes, and hence compliance. This feature was used for venous and aortic compliance, and resulted in the required pulse pressures to simulate natural compliance.

Marcus et al. (1994) [36] conducted a study using 70 healthy subjects to determine arterial compliance values and compare the two and three element Windkessel models. The haemodynamic profile of the normal population results can be seen in Table 7.

A compact mock circulation system was required for use in the study of cardiac performance in microgravity by Woodruff et al. (1997) [37]. It was chosen to use the Penn State mock circulatory system as a base and significantly reduce the size and weight of the compliance chambers. The new design can be seen in Figure 6, and included a new spring design to reduce size and weight. A conical seat is used to centre the spring and accommodate for many different spring diameters. Target values of 1 and 10 mL/mmHg for arterial and venous compliance respectively, and the spring constants were chosen according to the following equation –

\[ K = \frac{A_c^2}{C} \]  

(2.3)

where \( K \) is the spring constant, \( A_c \) is the area of the piston, and \( C \) is the desired value of compliance. To allow for a variable compliance, spring values were chosen at 0.5, 1, and 1.5 mL/mmHg for arterial compliance, and 5, 10, 15 mL/mmHg for the venous compliance. Availability of springs led to a limitation in this study where approximations were made, giving close but not exact values for the desired spring constants, and hence compliance values. The process of changing springs for each variation in compliance resulted in inefficient testing procedures, since the MCL must be shut down and restarted after the new spring is installed, resulting in potential shifts of other MCL parameters during this time. The new compliance chamber design
produced a weight reduction of 47% and a volume reduction of 64% compared with the original Penn State design.

---

Measured parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>122 ± 13</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>83 ± 10</td>
</tr>
<tr>
<td>Mean blood pressure (mmHg)</td>
<td>91 ± 11</td>
</tr>
<tr>
<td>Stroke volume (mL)</td>
<td>84 ± 15</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>68 ± 10</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>5.68 ± 1.11</td>
</tr>
</tbody>
</table>

Model (derived) parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total vascular resistance (mmHg.sec/mL)</td>
<td>1.387 ± 0.34</td>
</tr>
<tr>
<td>Arterial Compliance (2 element WK) (mL/mmHg)</td>
<td>1.57 ± 0.38</td>
</tr>
<tr>
<td>Arterial Compliance (3 element WK) (mL/mmHg)</td>
<td>1.23 ± 0.30</td>
</tr>
</tbody>
</table>

Table 7– Haemodynamic profile of normal population by Marcus et al. (1994)

Compliance was obtained by Arabia et al. (1984) [38] (Figure 7) and later by Ferrari et al. (1998) [39] by use of a spring capacitor. The values of systemic arterial, systemic venous, pulmonary arterial, and pulmonary venous compliance used by Arabia et al. were 3.6, 82.5, 4.8 and 10mL/mmHg respectively. The simplified equations used in an earlier study by Ferrari et al. for solving the spring constant for a given value of compliance can be seen in Appendix 2 [40]. The concept of using a spring for compliance was repeated by Pantalos et al. (2004) [4]. This design used a spring loaded piston on a roll sock diaphragm to obtain the required amount of compliance.

A study on the effect of increasing aortic compliance to ventricular performance was conducted by Kolh et al. (2000) [41]. The aim of this study was to investigate left
ventricular contractility and energetic cost of cardiac ejection when an increase in aortic compliance was applied. Pressure and flow catheters monitored the state of the heart while a 60mL air chamber was connected to the aorta perpendicular to the direction of blood flow by a short cannula to achieve extra compliance. The results achieved in this study showed that in normal hearts, the effect of increasing aortic compliance on contractile function is minimal, while the energetic cost of the heart was significantly reduced.

![Figure 6 - Compact spring compliance chamber by Woodruff et al. (1997).](image)

Lick et al. (2001) [42] furthered a previous study on an artificial lung by including several adjustments, one of them being a compliance chamber. Previous in vivo studies of an artificial lung being developed produced a 50% immediate right heart failure resulting in death. Modifications to the initial design included an inflow separator, inflow compliance chamber, and a modification to the outlet geometry. The method of obtaining a compliance chamber in this study was to include a solvent-cast, polyurethane bulging segment encased in open-faced housing so that no pressures would be generated externally of the chamber. This chamber was passive by accepting the stroke volume by filling the bulge without significant elastic expansion, however required MCL shutdown for changing the diaphragm, and hence compliance. Significantly improved results were noted in the next in vivo trials due to the design modifications.

![Figure 7 - Spring compliance chamber by Arabia et al. (1984).](image)
Dumont et al. (2002) [43] created a pulsatile bioreactor for the tissue engineering of an aortic valve. This system employed a variable compliance chamber that was achieved by altering the pressure of the air above the water in a chamber. Assuming the change in volume in the chamber due to the pressure change is negligible, this design would give a variable compliance. The mock loop constructed by Dumont only represents the systemic circulation, and the concept of this compliance chamber would not be suitable for a full mock circulation due to the changing in pressures of the whole system when varying compliance. Values of 0.4-1.2 mL/mmHg were used as the range of compliance in this study. Limitations in this study included not having a pulmonary circulation, negative flows seen in the system, while only a small range of conditions are shown to be producible by using this mock loop.

Papaioannou et al. (2002) [44] conducted a study on the effect of arterial compliance on the effectiveness of intra-aortic balloon counterpulsation using a mock circulation loop. The compliance was simulated by a Windkessel chamber with a variable air volume. As compliance is given by $C = - \frac{dV}{dP}$, the isothermic air process is assumed by $PV = \text{constant}$, giving the formula for compliance as $C = \frac{V}{P}$. This allowed the value for compliance to be found by the volume and pressure of the air above the fluid in the chamber. Tests were conducted by varying the levels of compliance between 1.05-2.62 mL/mmHg, the mean aortic pressures between 55, 75 and 105 mmHg, and the heart rate between 80, 100 and 120 bpm. Flow rate was kept constant at 2.6 L/min. The results of this study showed that arterial compliance is a major factor influencing the performance of intra-aortic balloon counterpulsation, regardless of the pressure level and heart rate. When arterial compliance was increased, an increase in left ventricle stroke volume of up to 6% was recorded for systolic dysfunction, while no change was recorded for diastolic dysfunction. Left ventricle systolic work was decreased by 4% in systolic and 11% in diastolic dysfunction, indicating that a small reduction in arterial stiffness could improve left ventricle performance.

A compliance chamber using a flexible rubber wall was created by Bustamente et al. (2003) [45]. Situated distal to the ventricle, the chamber consisted of mostly clear plastic, with one wall made of a flexible rubber diaphragm to dampen then pulse pressures. This diaphragm was removable to allow for a new material of different
stiffness if the compliance was required to be changed, however required MCL shutdown and discretely variable compliance depending on diaphragm elasticity. Positive results were recorded with this chamber while the flexible tubing used to make up the circulation also assisted with obtaining continuous flow by capillary level.

Haft et al. (2003) [46] developed an artificial lung compliance chamber and tested this design in a basic mock circulation. The mock circulatory model ignored inertiance and adjustable resistance elements, relying on the resistance of the tubing and the pulsatile flow VAD which pumped fluid through the system. A reservoir simulating the right atrium was kept at an elevated height to deliver a constant pressure into the VAD, which delivered the fluid into the compliance chamber and then in series to the artificial lung. The compliance chamber, shown in Figure 8, was made of a flaccid polyurethane bag in an airtight box which receives compressed air to alter the compliant nature of the bag. The pressure in the chamber was varied between 0 and 16mmHg, and the volume of the chamber was also varied between values of 50, 100, 250 and 500mL. Values for zero harmonic impedance \(Z_0\), equivalent to resistance, and first harmonic impedance \(Z_1\), where most of the pulsatile flow is seen, were found for this study to compare to values found in healthy human subjects. Typical values for a healthy human subject were said to be 1 and 0.5 Wood units (mmHg.min/L) for \(Z_0\) and \(Z_1\) respectively. Pneumatic compression of the compliance chamber reduced \(Z_1\) for all chamber volumes, with the lowest value recorded while using the 250mL chamber at 12mmHg. Compression above 12mmHg elevated \(Z_1\) while reducing \(Z_0\) for all chamber volumes. By using a stented compliance reservoir, this effect was reduced. The minimum pulsatility was recorded with the 250mL chamber at 14mmHg. It was found that applying an external pressure to the compliance element maximized the value of compliance and altered its time scale by augmenting diastolic emptying and maximizing capacitance.

Figure 8 - Compliance element used by Haft et al. (2003).
before systole. In this example, the application of pressure reduced the cross sectional area of the tubing, resulting in an increased resistance. This was seen as the pressure rose above the “left atrial” pressure, demonstrated by the increase in $Z_0$. A stented compliance chamber reduced this affect by limiting the amount that the tubing could collapse. Limitations of this study include a fixed pump rate and stroke volume, the use of water rather than blood or glucose solution and the exclusion of separate resistance, compliance and inertiance elements.

The arterial compliance used in the study by Fiore et al. (2003) [24] was part of the hydraulic side of the hybrid system. This was to improve the quality of pressure measurements by reducing the effect of mechanical and hydrodynamic disturbances. The value chosen for the compliance was 1.2mL/mmHg. An additional arterial compliance was added to the electrical circuit, which could be altered to give a variable compliance value.

Loh et al. (2004) [34] chose the following values for compliance –

<table>
<thead>
<tr>
<th>Compliance Type</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic</td>
<td>37 mL/mmHg</td>
</tr>
<tr>
<td>Chamber / Left ventricular</td>
<td>1832 mL/mmHg</td>
</tr>
<tr>
<td>Pulmonary venous / atrial</td>
<td>6.74 mL/mmHg</td>
</tr>
</tbody>
</table>

It can be seen that the value for aortic compliance used by Loh is significantly higher than other values seen in the literature. The left ventricular compliance also appears to be excessively high.

Airtight tanks with a trapped volume of air above the fluid were chosen for the compliance mechanism by McMahon et al. (1971) [47], Swanson et al. (1977) [48], Gabbay et al. (1978) [49], Cassot et al. (1985) [50], Bowles et al. (1991) [51], Knierbein et al. (1992) [52], Schima et al. (1992) [53], Orime et al. (1994) [54], Andrade et al. (1999) [55], Ayre et al. (2003) [56], Haft et al. (2003) [46], Athanasssiou et al. (2005) [57], Litwak et al. (2005) [28], Liu et al. (2005) [29] and Avrahami et al. (2006) [58]. These chambers are capable of producing continuously variable levels of compliance, however require MCL shutdown for each compliance
change. The volumes of the chambers used by Litwak et al. (2005) were 4.9, 43.6, 5.6 L for systemic arterial, systemic venous, and pulmonary compliances respectively. An air valve is incorporated in the top of the chamber to alter the volume of air and hence the compliance value. The equation used for gaining the correct compliance values in this study is –

\[
C = \frac{dV_{\text{fluid}}}{dP_{\text{fluid}}} = \frac{V_{\text{air}}}{P_{\text{air}}} = \frac{V_{\text{tank}} - A_{\text{tank}}h_{\text{fluid}}}{P_{\text{fluid}} - \rho gh_{\text{fluid}}}.
\]  

(2.4)

where \( C \) is the compliance, \( V_{\text{air}} \) is the volume of air in the tank, \( P_{\text{air}} \) is the absolute pressure of air in the tank, \( V_{\text{tank}} \) is the volume of the tank, \( A_{\text{tank}} \) is the cross-sectional area of the tank, \( P_{\text{fluid}} \) is the absolute pressure of the fluid in the tank, \( h_{\text{fluid}} \) is the height of fluid in the tank, \( \rho \) is the density of the fluid, and \( g \) is the acceleration due to gravity. In the case of the aortic pressure, where the usual value for \( P_{\text{fluid}} \) would vary between 120mmHg and 80mmHg, a value for \( P_{\text{fluid}} \) is set at 100mmHg. The values chosen in this study for systemic arterial and venous compliance were 2.2mL/mmHg and 50mL/mmHg respectively.

Hassani et al. (2007) [59] developed a mathematical model for the study of aortic aneurysms. This highly detailed model included compliance, inertia and resistance elements. The equation used by Hassani et al. for defining the compliance of an elastic vessel was –

\[
C = \frac{3\pi R^3 Z}{2 Eh}
\]

(2.5)

Where \( C \) represents the compliance, \( R \) the radius of the vessel, \( Z \) the length of the vessel, \( h \) the thickness of the vessel, and \( e \) the elastic modulus of the vessel.

Timms et al. (2005) [3] achieved atrial compliance by using an open to air chamber which changes the volume of fluid in response to venous return. This created a change in pressure due to the height of the fluid, hence changing the level of compliance. Aortic, systemic vascular, pulmonary arterial and pulmonary vascular compliances were achieved by using a fluid filled chamber with a trapped volume of air. The volume of air in the chamber operates in the same manner as a spring, and could be changed to give a variable compliance. This value could only be changed
while the loop was not running. The values of compliance for a natural heart at rest which were chosen for reproduction in the Timms loop can be seen in Table 8.

<table>
<thead>
<tr>
<th>Compliance chamber</th>
<th>Compliance value (mL/mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic</td>
<td>1-2</td>
</tr>
<tr>
<td>Systemic vascular</td>
<td>10-200</td>
</tr>
<tr>
<td>Pulmonary arterial</td>
<td>2-4</td>
</tr>
<tr>
<td>Pulmonary vascular</td>
<td>4-6</td>
</tr>
</tbody>
</table>

Table 8 - Natural compliance values shown by Timms et al. (2005).

Stergiopulos et al. (1994) [60] conducted a study into current methods of estimating arterial compliance, and compared these results to that of a previously developed mathematical model including 55 arterial segments modelling the major arteries. Fluid friction, fluid inertia and nonlinear compliance were all accounted for in this model. Four 2 element Windkessel (WK) methods were employed including the time decay method, the area method, the two-area method, and the pulse pressure method, while three 3 element WK methods were analysed including the three-element WK fit method, the low-frequency impedance method, and the integral method. The time decay and area methods were both highly dependent on the length and conditions of the diastolic phase, causing errors when higher heart rates were applied. It was noted that all methods based on the two element WK generally produced errors of less than 10%, much more accurate than the three element WK models which strongly overestimated the compliance. It was shown that the non-linear compliance element, compared to that of a linear system, had little effect on the results. The most accurate method was shown to be the pulse pressure method, with a maximum error of 17% over a variety of conditions including high and low heart rate, hypertension, and exercise conditions. The most accurate three element WK method was the fit method, with errors between 15-40%. The integral method was seen to be the most inaccurate method of estimating arterial compliance, with errors ranging from 25-105%. Each method required several parameters of the circulation to be known. The least restrictive of these was the two-area method, which only requires the instantaneous pressure and flow through the artery. It was shown that the three element WK model can represent the arterial system accurately; however the parameter values are incorrect. A conclusion was drawn that a two element WK model is a much better
representation of the systemic arterial tree at low frequencies, while a three element WK is required at high frequencies [60, 61].

Segers et al. (1999) [62] later concluded that the pulse pressure method was the most consistent method for estimating total arterial compliance by comparing the *in vivo* results of the pulse pressure method with the area method and the stroke volume-to-pulse pressure ratio.

While many methods of simulating vascular compliance have been successful in previous MCLs, no device exists that provides a continuously variable compliance with no significant effect on vascular resistance that can be altered while the MCL is in operation. Therefore, the development of a continuously variable compliance chamber would greatly enhance the ability to test the performance of cardiovascular devices during the transition from one physiological state to another.

### 2.9 Resistance

The resistance to blood flow has a significant effect on the circulatory system. As arteries and veins decrease in radius (r), their resistance (R) increases. The viscosity (η) of blood and the length of the artery (L) also influence the resistance, which can be modelled by the equation –

\[ R \propto \frac{nL}{r^4} \quad (2.6) \]

The aorta exhibits very little resistance to the flow of blood, and so only a very small pressure drop can be seen from the point at which blood enters the aorta, and the point of exit. Meanwhile, parts of the systemic circulation such as the smaller arteries and the arterioles, show a high level of resistance, and produce a significant pressure drop on the blood.

The body has the ability to change the resistance to flow by constricting or dilating the arteries. Constriction increases resistance causing less blood to flow through that artery, forcing it to go elsewhere, while dilation produces the opposite effect.
The resistance to blood flow by the whole systemic circulation is known as systemic vascular resistance (SVR) and is primarily determined by blood vessel diameters. If the central venous pressure is known, SVR can be calculated by –

\[ SVR = \frac{MAP - CVP}{CO} \]  

(2.7)

If CVP is not known, it can be assumed to be 0, as it is usually around this value.

Resistance is primarily obtained by using a pinch valve in conjunction with flexible tubing. The valve is usually lowered by an electrical signal to occlude the valve, resulting in a variable level of resistance. This feature has been used in many previous studies [3, 28, 43, 45, 63, 64].

Donovan et al. (1975) [16] used an innovative form of obtaining resistance (Figure 9) in the design of a complete mock circulation loop. Pulmonary and systemic resistance was obtained by a plate which rotated about a pivot to occlude the flow tube. The value of resistance depended on the angle of rotation. The angle of rotation of the plate was controlled by a lever arm connected to a bellows which was situated inside the chamber filled with water at a specified pressure. When the pressure in the aortic / pulmonary arterial chambers increased, the pressure difference across the bellows forced the bellows to contract, which pulled on the lever arm and rotated the valve plate about the pivot. This caused the valve plate to move giving a greater cross-sectional area for the fluid to travel through the flow tube, and hence lower resistance, which also served to lower the arterial
pressure. The systemic resistance system operated in the same manner as the pulmonary resistance; however an extra spring was present in parallel to the bellows to allow for the higher pressure on the systemic side.

The method of supplying resistance chosen by Trittenwein et al. (1998) [21] and later by Liu et al. (2005) [29] was by using sintered aluminium oxide porous blocks, which had appropriate permeability to represent the characteristic impedance and the peripheral resistance. The resistance value was adjusted by a sliding plate moving over the porous material to block or unblock some of the pores.

Resistance was calculated by Scotten et al. (1979) [17] using the following equations

\[ \Delta P = R \cdot Q \] \hspace{1cm} (2.8)

\[ R = \frac{\Delta P L_R \pi}{\mu \pi A_R^2} \] \hspace{1cm} (2.9)

Where \( \Delta P \) is the pressure drop, \( R \) is the resistance, \( Q \) is the volumetric flow rate, \( \mu \) is the fluid viscosity, \( L_R \) is the effective length of the resistor tubing and \( A_R \) is the area of the resistance tubing. The method of applying resistance (Figure 10) to this mock circulation loop was by several small, flexible tubes that could be compressed by a flat plate. The more the flat plate compressed the tubing, the higher the resistance value. A slightly different concept was employed by Ferrari, who chose a system that obtains its resistance by a slide that moved up and down to block the flow through a pipe. The resistance in this system could be adjusted by either choosing a resistance value which moved the slide, or by choosing a mean arterial pressure, which provided feedback to the slide to obtain the desired result.

A constant and variable resistance was chosen for use in the neonatal mock circulation loop constructed by Mitsui et al. (1998) [33]. The variable component
consisted of an inflatable cuff surrounding elastic tubing while a screw clamp represented the constant resistance.

Patel et al. (2003) [65] obtained resistance for a systemic mock circulation by use of a 1.5 inch gate valve. The resistance values chosen for simulation of healthy and congestive heart failure were 0.85 mmHg.s/mL and 1.2-1.4 mmHg.s/mL respectively. This system was shown to accurately mimic the human systemic circulation for testing of LVADs.

Resistance was obtained by Pantalos et al. (2004) by use of a chamber which contains open cell foam of different densities for peripheral and proximal components according to the required value of resistance. This foam can be compressed by sealed pistons to adjust the value of resistance to flow. The values for resistance in the natural circulation used by Timms et al. (2005) can be seen in Table 9 [66, 67].

<table>
<thead>
<tr>
<th>Resistance</th>
<th>Rest</th>
<th>Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR</td>
<td>1.463</td>
<td>1.800</td>
</tr>
<tr>
<td>PVR</td>
<td>0.106</td>
<td>0.160</td>
</tr>
</tbody>
</table>

*Table 9– Resistance values used by Timms et al. (2005).*

2.10 Inertiance

Inertia relates to the property of an object to resist a change in motion. As blood flows through the circulatory system, its pulsatile nature requires constant changes in motion. This can be represented in a mock circulation loop by incorporating an inertiance component in the model. By finding the correct values for the volume of fluid being moved in each section of the circulatory system, and representing these values on the mock loop with pipe lengths and diameters, an inertial component can be achieved.

The circulatory system is frequently modelled by the Windkessel model. This system incorporates features such as resistance, compliance, and inertiance and represents these as electrical drawings. Many mock circulation loop simulations use a three element Windkessel model, which includes characteristic resistance \( R_c \), arterial compliance \( C \), and a peripheral resistance \( R_p \). Four element Windkessel models
also include an inertial component \( (L) \). Three and four element Windkessel models are shown in Figure 11.

![Three-element windkessel and Four-element windkessel](image)

**Figure 11 - Three and four element Windkessel models by Stergiopulos et al. (1999).**

Stergiopulos et al. (1999) [68] reported that the inertiance of a tapered arterial segment \( (L_i) \) can be found by –

\[
L_i = \frac{l_s^3 c_u \rho \cdot dx}{A}
\]  
\( (2.10) \)

Where \( \rho \) is the blood density, \( l_s \) is the segment length, \( A \) is the cross sectional area and \( c_u \) is a coefficient that accounts for a non-flat velocity profile, equalling 4/3 for low frequencies. Inertiance in series and parallel are calculated in the same manner as spring constants, with inertiance in series being calculated by the sum of all inertiances, and parallel situations being calculated by –

\[
\frac{1}{L_{i+2}} = \frac{1}{L_1} + \frac{1}{L_2}
\]  
\( (2.11) \)

Noble et al. (1968) conducted a study on the contribution of blood momentum to left ventricular ejection in dogs. This study was conducted by placing pressure transducers in the aorta and left ventricle, and a flow probe in the aorta. Controls were noted first and showed that the ventricular pressure was higher during the early ejection period, with the aortic pressure increasing above ventricular pressure in the last 30-50% of ejection. An aortic occlusion device was then placed around the aorta, with the theory that when the aorta was fully occluded during late systole, the ventricular pressure would drop if the flow was primarily dependent on blood momentum. As the aorta was being occluded by the device, which required about 20 milliseconds to fully close, a spike was seen in the ventricular pressure trace, followed
by a distinct reduction in pressure. This result proved that blood momentum has a significant effect on ejection. One limitation in this study was the occlusion site. When this study was conducted it was not possible for the authors to find a way of occluding the aorta at the valve site in a very small amount of time, so occlusion was obtained on the ascending aorta.

Many current systems use a 3 element Windkessel model consisting of a characteristic resistance, arterial compliance, and a peripheral resistance. Scotten et al. (1979) [17] used the following equations to solve for the required inertiace –

\[
\Delta P = \phi \left( \frac{dQ}{dt} \right) \\
\phi = \rho \frac{L_1}{A_1}
\]

Where \(\Delta P\) is the change in pressure, \(\phi\) is the inertiace, \(Q\) is the volumetric flow rate, \(t\) is time, \(\rho\) is fluid density, \(L_1\) is the length of the pipe and \(A_1\) is the cross sectional area of the pipe. The values for the inertiace in certain areas of the mock circulation loop were too small to be measured experimentally, and a more complex method was later described. This method included inertiace effects by placing them upstream of the compliance chambers, where the flow is much more pulsatile. Inertiace effects were reduced by shortening the length of the tubing upstream of the compliance chambers.

Stergiopulos et al. (1999) [68] aimed to find the difference in flow and aortic pressure measurements between the three and four element Windkessel models in dogs, humans and a mock circulation. An example of the results obtained can be seen in Figure 12, showing a significant difference in accuracy between the two models. It was concluded in this study that the four element Windkessel model represented aortic pressure and flow measurements with greater than the three element model.
Ferreira et al. (2003) [69] conducted a study using 26 human subjects comparing the three and four element Windkessel models’ ability to estimate arterial compliance. It was found that adding the fourth element, an inertial component, resulted in an improved representation of the arterial compliance. The results presented in this literature review demonstrate that MCL designs must include inertial components in the design of the system for more accurate pressure and flow magnitudes and waveforms.

2.11 Baroreceptor Reflex

Baroreceptors work to control short term pressure changes. They are sensitive to stretch, and are positioned along the walls of most arteries in the neck and thorax [31]. A sudden increase in blood pressure causes the baroreceptors to respond. Through a series of signals by the nervous system, peripheral blood vessels are dilated and blood pressure and heart rate both decrease. A decrease in blood pressure leads to an opposite effect on the blood vessels, blood pressure and heart rate. This effect can be seen when a person stands after being seated. The pull of gravity on the blood cause a significant drop in blood pressure in the neck and thorax, often resulting in dizziness. This is regulated by the baroreceptor response which quickly re-establishes appropriate blood pressure to the desired regions.

2.12 Mathematical Modelling and Computer Simulation

Dynamic performance of a system is often neglected in the design phase. The analysis of the system is often expensive and time consuming before the system is constructed. Using simulation packages, process systems can be evaluated in a small amount of time and at a low cost. In order to model a system using a simulation package, a good knowledge of control is required, as well as a highly detailed knowledge of the system. The reasons given by Bustamante et al. (2007) [70] for simulating a system were for the design of regulation and control systems, and to predict the performance of the system. A simulation must include all components which have any effect on the dynamic behaviour of the system, while having the ability to change model parameters that may influence the system, and must follow mass, momentum and energy conservation principles, and state equations.
Assumptions can be made in the simulation providing only a negligible effect is given, such as one-dimensional flow through a system. Validation of the model can be performed by comparing the results using other recognised software, or by those of a similar physical model.

### 2.12.1 Cardiovascular System Modelling

Cardiovascular system models have been developed for analysis in a variety of studies. A computer model of the human cardiovascular system was created by Wu et al. (2003) [71] for evaluating a physiological controller. The cardiovascular system was modelled as an electric circuit analogue with resistance, compliance and inertiance properties taken into account. The ventricles were modelled as nonlinear capacitors. Total peripheral resistance (TPR) was modelled as a variable resistance in this case, and could be adjusted to represent the change in resistance under heart failure conditions. Positive results were obtained from this model, and it was then used to analyse a physiological controller system.

A detailed electric circuit analogue version of the human systemic arterial tree was described by Westerhof et al. (1969) [72]. This study aimed at constructing and evaluating a model of the arterial tree to improve a previous study. It was found that each segment of the arterial tree can be represented by an electric circuit analogue which accounts for resistance, compliance and inertiance. The example used by Westerhof is shown in Figure 13, with the symbol representations listed in Appendix 3.

Westerhof used the model to represent each arterial branch in the model, and combined these to form a representation of the systemic circulatory system. It was concluded that this model produced flow and pressure measurements closely representing that of a natural situation. A later study by Westerhof et al (1971) [73], involved design and evaluation of a hydraulic mock circulation loop using the previous principles. Resistance values were calculated by:

\[
R_1 = 8. \mu \frac{l}{\pi r^4} 
\]  
(2.14)

\[
R = 8. \mu \frac{l}{\pi r^4 N} 
\]  
(2.15)
where $R_1$ is resistance through one tube, $R$ is the resistance when using $N$ tubes in parallel, $\mu$ is the viscosity of the fluid, $l$ is the length of the tube, and $r$ is the radius of the tube. Resistance was obtained by using several small orifices that could be blocked or opened by movement of a slide.

A circulatory simulation circuit (Figure 14) was designed to test the Wankel type semipulsatile left ventricular assist pump in conjunction with in vivo trials by Mitsui et al. (1998) [33]. In this computerized model, the ventricles were represented by a simple capacitor, and the pumping function was altered by changing this capacitance value. Resistance, capacitance and inertiance are all included in this study and are shown in Table 10.
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compliance</td>
<td></td>
<td>Resistance</td>
<td></td>
</tr>
<tr>
<td>Left ventricular</td>
<td>8.0D, 0.1S</td>
<td>Descending aorta</td>
<td>0.5</td>
</tr>
<tr>
<td>Ascending aortic</td>
<td>0.8</td>
<td>Upper extremities + head</td>
<td>3.0</td>
</tr>
<tr>
<td>Peripheral arterial</td>
<td>1.0</td>
<td>Lower extremities + abdomen</td>
<td>1.2</td>
</tr>
<tr>
<td>Systemic vein + right atrium</td>
<td>400</td>
<td>Coronary artery</td>
<td>10D, 1000S</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>8.0D, 0.5S</td>
<td>Peripheral vessels of lung</td>
<td>0.12</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>3.0</td>
<td>Tricuspid valve</td>
<td>0.01</td>
</tr>
<tr>
<td>Pulmonary vein + left atrium</td>
<td>50</td>
<td>Pulmonary valve</td>
<td>0.04</td>
</tr>
<tr>
<td>Inertiance</td>
<td></td>
<td>Mitral valve</td>
<td>0.01</td>
</tr>
<tr>
<td>Descending aorta</td>
<td>0.01</td>
<td>Aortic valve</td>
<td>0.04</td>
</tr>
<tr>
<td>Peripheral vessels of lung</td>
<td>0.002</td>
<td>Blood volume in whole body</td>
<td>4500</td>
</tr>
</tbody>
</table>

Table 10 - Parameter values used by Mitsui et al. (1998). Compliance in mL/mmHg, Inertiance in mmHg.s²/mL, Resistance in mmHg.s/mL and Blood volume in mL. S and D denote systolic and diastolic values respectively.

Figure 15– Circulatory system presented by Vollkron et al. (2002).
A detailed cardiovascular system with left ventricular support was developed using Simulink by Vollkron et al. (2002) [74]. This model was based on current literature, previous simulations, \textit{in vitro} and \textit{in vivo} data. The model used for this system can be seen in Figure 15, while the parameters used are presented in Table 11.

The boundaries for cardiac contraction and pressure volume loops were produced by both the end diastolic (EDPVR) and end systolic (ESPVR) pressure volume relations, with the ESPVR being found in a look-up table while EDPVR was defined by –

\[
E_d = a e^{b(V-V_0)} \quad \text{(mmHg)}
\]  

(2.16)
Where V is the Ventricular volume, V₀ is the initial ventricular volume, while a and b are constants equal to 0.006 and 0.046 respectively for the left ventricle, and 0.003 and 0.046 respectively for the right ventricle. No precise pressure-volume loops for the right ventricle could be found for this data, so an in vitro experiment comparing left and right ventricle pressure volume loops on dogs was used. The ventricular contraction was achieved by the following equations –

\[ a(t)_{\text{rise}} = \sin \left( \frac{t\pi}{2T_{\text{rise}}} \right) \]

(2.17)

for the rising edge and -

\[ a(t)_{\text{fall}} = 1 - \left[ \sin \left( \frac{t\pi}{2T_{\text{fall}}} \right) e^{\left( \frac{T_{\text{fall}}}{T_{\text{fall}}} \right)} \right] \]

(2.18)

for the falling edge, where

\[ T_{\text{rise}} = 0.833 \times T_{\text{systole}} \text{ and } T_{\text{fall}} = T_{\text{systole}}e^{T_{\text{rise}}} \]

(2.19)

Left and right atrial contractions were included in this model by including time variant capacitances. The systemic and pulmonary circulations were represented by lumped parameter models with resistance, compliance and inertiance. The system was seen to include stiff differential equations, so Matlabs ODE15s routine was used to solve the model. Validation was performed by comparing data from the model to that in literature and previously obtained in vitro and in vivo results. Parameter variations were evaluated in comparison with in vivo results, and finally a left ventricular assist device was added to the model and validated with in vivo data. A flow chart showing the validation process can be seen in Figure 16. The shape and values of the pressure and flow vs time traces produced by the model closely matched those seen in the literature and in vivo results, while accurate pressure-volume loops were also produced. It was noted that pressure-volume loops are an important feature in the validation of models such as this, as they are highly sensitive to inconsistencies of impedance and time-dependant contraction parameters. This model is currently being used to investigate different strategies for physiological control.
A concentrated parameter model of the complete circulation was developed by Korakianitis et al. (2006) [75] to study the dynamic function of the human circulation. This study used magnetic resonance imaging (MRI) technology to obtain ventricle shapes and suitable inputs to the numerical models. The ventricles were modelled by using a variable elastance, while the heart valves were modelled to include features such as pressure differences, frictional forces and vortex effects. Resistance,
compliance and inertia were also incorporated in this model. A schematic of the full circulation can be seen in Figure 17 which includes compliance, resistance and inertia properties. The values used for each segment in this study can be seen in Appendix 4.

Figure 17 - Schematic of full circulation used by Korakianitis et al. (2006)

This model was further developed by Shi et al. (2007) [76], by inserting a VAD model to investigate the performances of several different types of pumps. Impeller pumps with constant flow, counterpulsation, and copulsation were modelled, along with displacement pumps using counterpulsation or copulsation, and a reciprocating-valve pump using copulsation. All of these pumps were connected to the circulation in parallel, except for the reciprocating-valve pump which is connected in series in the ascending aorta. The model was first used with healthy parameters with no VAD connection to validate the model. The maximum elastance of the heart was then reduced from 2.5mmHg/mL to 0.5mmHg/mL to create a heart failure situation, and mechanical assistance was switched on. The results of this study showed that the impeller device produces only small pulsatility in arterial pressure and flow, while the displacement and reciprocating-valve pump produce noticeable pressure and flow pulses. The displacement pump required the most power input, while the impeller pump required the least. It was noted that if the displacement or impeller pumps were required to provide 100% assistance to the circulation, the aortic valve would remain
closed which could lead to an aortic valve fusion. This was not the case with the in-series reciprocating-valve pump. The model was shown to accurately represent the natural cardiovascular system with mechanical assistance, and produced results previously seen from \textit{in vivo} and \textit{in vitro} studies.

Hassani et al. (2007) \cite{59} developed a mathematical model of the complete cardiovascular system to study the effects of aortic aneurysms and renal artery stenosis on hypertension and ruptured arteries. An electronic circuit was used to represent the human cardiovascular system including resistance, inertia, compliance and pressures. This model was highly detailed and consisted of 42 separate elements (Table 12) to represent the heart, arteries and veins. Ventricle contraction was modelled by time-variable voltage sources while the heart valves were modelled by ideal diodes. The viscosity and density of blood used in this model was 0.0035Pa.s and 1050kg/m$^3$ respectively. The model was seen to be highly stable by nearly reaching a steady state by the second cycle. Pulse pressure values produced by this model were seen to be fairly close to those seen in previous literature, while several conclusions were drawn from the model results which support clinical data.

An advanced model of the circulatory system including an artificial heart was developed by Ding et al. (1994) \cite{77}. This system included the features discussed in previous literature such as resistance, compliance and inertia, while also developing complex reflex control systems such as the baroreceptor response and nonlinear vessel compliance. A control system was developed to model an artificial heart connected to the natural circulatory system. A pulse frequency modulated (PFM) control technique was used, with the measured pulmonary and systemic venous pressures being the inputs. These inputs were compared to the previously stated desired values, which provided a feedback to change the outputs of stroke volume and heart frequency. The simulation was tested and the authors concluded that the performance of the artificial heart in the model could be achieved with the use of a PFM control scheme.

A mathematical model was created by Vrettos et al. (2005) \cite{78} to find the effect of arterial compliance on the power requirements of the heart. A basic 3 element Windkessel model was employed in this model, including a characteristic and
peripheral resistance and compliance. It was found that an increase in compliance minimizes the power consumed by the arterial system, and that compliance cannot be ignored when investigating the power requirements of the heart. Limitations with this study included the inertiance of the system being neglected and the assumption that all pressures and flows in the arterial system are stationary.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>DESCRIPTION</th>
<th>R(Ω)</th>
<th>L(µH)</th>
<th>C(µF)</th>
</tr>
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<tr>
<td>2</td>
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<td>0.1</td>
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<td>47.533</td>
<td>0.0906</td>
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<td>3.135</td>
<td>0.0577</td>
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<td>10.1</td>
<td>0.0524</td>
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<td>47.533</td>
<td>0.0906</td>
</tr>
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<td>0.0125</td>
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<td>6.24</td>
<td>3.4072</td>
<td>0.0125</td>
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<td>Inferior Mesenteric</td>
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<td>0.00561</td>
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<td>72</td>
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<td>1.4</td>
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<td>71</td>
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<td>32</td>
<td>Vein 1</td>
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<td>-</td>
<td>210</td>
</tr>
<tr>
<td>33</td>
<td>Vein 2</td>
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<td>450</td>
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<tr>
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<td>0.1</td>
<td>216.45</td>
</tr>
<tr>
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<td>Right Ventricle</td>
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<td>0.1</td>
<td>150</td>
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<td>1</td>
</tr>
<tr>
<td>D</td>
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<td>4</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>E</td>
<td>Pulmonary Artery 3</td>
<td>8</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>F</td>
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<td>-</td>
<td>27</td>
</tr>
<tr>
<td>G</td>
<td>Pulmonary Vein 2</td>
<td>1</td>
<td>0.1</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 12 - Electrical specifications of each cardiovascular segment by Hassani et al. (2007).

Gisolf et al. (2004) [79] conducted a study to compare the internal jugular veins with an alternative route for the venous return from the brain in supine, sitting and standing positions. A mathematical model was developed and can be seen in Figure 18. The model inputs were central venous pressure (CVP) and cerebral blood flow velocity
(CBFV). Several assumptions were made in this model, such as blood flow into the brain is equal to blood flow out of the brain, zero pulsatility, identical jugular veins, and modelling the alternative vertebral venous plexus route solely as a resistance. The jugular veins were modelled in ten segments with the nine most cranial containing a variable resistor and capacitor, while the final segment contained only a variable resistor. Gravity is taken into account in this model to simulate the different positions of the subject. Physiological data obtained from ten healthy subjects was used to test the model. The model was verified with ultrasound to capture the cross sectional area of the right internal jugular vein of the patients. It was found that the internal jugular veins were the main source of blood drainage from the brain in the supine position, while raising the CVP in this position further increased the jugular vein volume. In the standing position, the model showed a collapse in jugular vein volume, and an increased flow through the vertebral venous plexus, which decreased with increasing CVP. The model was verified by the results of the ultrasound. One limitation in this study was the modelling of the vertebral venous plexus as a resistor with no capacitance properties.

This review of literature on simulation of cardiovascular systems demonstrates the importance and capabilities of simulating physical systems. While many simulations have been previously conducted on the cardiovascular system, the simulation of MCLs has been ignored. For improved design of an MCL, a simulation of the physical system should be conducted to obtain more haemodynamically accurate results.
2.12.2 PHYSBE

One of the earlier simulations of the cardiovascular system is known as “PHYSBE, A Physiological Simulation Benchmark Experiment”. This model is a lumped parameter, non-linear system representing the flow of blood, and its properties such as nutrients and heat etc, throughout the body and back to the heart. Features such as compliance, resistance, pressure, volume, flow, heat, etc. are all included in this simulation. This mathematical model was later converted into a Simulink model, and has since been modified several times for various purposes [81].

2.12.3 Frequency Response

A frequency response analysis allows the designer to observe the response of the output signal in relation to a variable frequency input signal. This analysis can be performed on a MCL simulation to observe the response of the system over a variety of heart rates. Frequency response analysis can be performed analytically, however the complex mathematics often involved in this process often leads engineers to rely on experimental frequency/time domain analysis. By using the experimental method, it can be difficult to optimize the design of the system and may limit the amount of control parameters compared to a simulation model. Once a model is developed, parameters can be easily adjusted and repetitive simulations can be carried out to obtain the frequency response of the system. Non-linear modelling is easier, quicker and more flexible in Simulink compared to developing a code [82].

Ly et al. (2003) [83] presented a study on the analytical frequency response approach using the Matlab-Simulink environment for a dc-dc converter without small-signal linearization. A model was developed for this system, and a small signal was sent to the input of the system. By applying Fast Fourier Transform (FFT) techniques, the transfer function response, \( V_{\text{in}}/V_{\text{out}} \), could be found. Ly et al. performed a time domain simulation with sinusoidal signals of various frequencies added to the system. An FFT was then completed on the time domain data and the frequency response of \( V_{\text{in}}/V_{\text{out}} \) was stored. Different input frequencies were then applied and the frequency response for each was recorded. Accurate results were obtained using this simulation for the frequency response characteristics of a dc-dc converter.
2.13 Ventricular Assist Devices (VADs)

Approximately one in five people develop some degree of heart failure in their lifetime, and with a limited number of donor hearts available, a mechanical solution is often required [84-87]. The solution to this donor shortage appears to be in the form of a ventricular assist device (VAD), which is used to assist the failing heart of a patient by unloading the heart. This is achieved by blood flowing from the left or right atrium or ventricle into the VAD, which then pumps the blood into an artery (pulmonary or aorta). The tube that connects the patient to the pump is known as the cannula, and the positioning of this cannula can greatly affect the performance of the pump. Obstruction of this cannula can be fatal, with evidence of partial cannula obstruction being applied by the patient simply sitting at a certain angle. Clinical experience has shown that an implanted VAD can assist in the recovery of the patient, such as improving renal function and reducing pulmonary hypertension [88]. VADs can also be used as a destination therapy for patients who are not transplant candidates.

The first clinical experience with a VAD was reported by Dr Michael DeBakey in 1963, four years before the first heart transplant. The first mechanically assisted patient died; however an improved device was implanted 3 years later, with the patient being successfully weaned from support and discharged following myocardial recovery [87].

Ventricular assist devices are currently being used as a bridge to transplant (BTT) or bridge to recovery (BTR). With the continued development of these devices, it is hoped that a more permanent solution can be obtained. A detailed investigation into VAD (Heartmate vented electric device, Thoratec, Pleasanton, California, U.S.A) success rates known as the REMATCH study was conducted over 3 years with over 120 patients being assigned to either VAD support or standard medical therapy across several medical centres. The results of this study produced a 48% reduction in risk of death, and improved quality of life for the VAD group compared to the medical therapy group. Serious adverse events were noted to be twice as likely in the VAD group with the most common being bleeding and infection at the drive line site [89].
Current ventricular assist devices can be classified into either pulsatile or rotary blood pumps. Early VADs were pulsatile, working off a positive displacement pump, and are known as first generation assist devices. Rotary blood pumps, which can be separated into axial or centrifugal flow pumps are known as second generation assist devices. Rotary blood pumps coupled with a hydraulically or electromagnetically suspended impeller are classified as third generation assist devices. These VADs reduce wear on the pump and damage to the blood cells while avoiding the need to create a large pocket for VAD placement which in turn creates less surgical trauma and blood loss.

Although significant progress has been made towards the development of VAD technology, major problems such as infection, thrombosis, bleeding and VAD failure are still present, demonstrating the need for an improved device. Before expensive animal and clinical trials are conducted, in vitro testing in MCLs must be completed. More accurate in vitro testing will lead to improved device refinement in the development stage and increase the efficiency of cardiovascular device development.

2.14 Conclusion

The aim of this literature review was to determine the areas of possible improvement in mock circulation loop design. Current mock circulation loops vary from simple continuous flow devices to those with accurate representations of ventricles, atria, vascular resistance, compliance and fluid inertia.

Five element mock circulation loops, with two resistance and compliance elements and one inertia element, were shown to produce the most haemodynamically accurate simulations of the circulatory system. Both systemic and pulmonary sides of the natural system are required to be replicated in order for an accurate simulation and for testing of many cardiovascular devices. Reproduction of several different cardiac conditions such as rest, heart failure and exercise is an important feature in the design of a mock circulation loop.

Accurate representation of the vascular resistance and fluid inertia in the cardiovascular system is vital in the development of a mechanical simulation. Arterial and venous compliance is also important to the function of the system, while
a variable arterial compliance would improve the efficiency and accuracy of cardiovascular device testing. Some previous mock ventricles have been based on correct anatomical shapes; however, expensive equipment for ventricle pressure and volume data acquisition is required. A simple rigid design would allow for accurate and inexpensive ventricle data acquisition, while allowing for VAD attachment through rigid connections.

A mathematical model would assist in the development of a MCL. A validated MCL simulation would provide the ability to observe the effect of altering pipe dimensions and pressure inputs on the simulated rig’s haemodynamics prior to construction of the physical rig. The Matlab / Simulink environment is an appropriate modelling system to use as it has been used extensively for cardiovascular system modelling.

This literature review summarises the characteristics required to design and construct a complete mock circulation loop. The information gathered in this report will enable the development of a mathematical model to assist in the design of a mock circulation loop, and concepts from various sources of literature will be combined to design and construct a variable compliance chamber. The mathematical model of a MCL and variable compliance chamber can then be used to assist in the design phase of a physical MCL.
Chapter 3

Mock Circulation Loop Simulation

3.1 Aims

A simulation model was required to accurately mimic the function of a mock circulation loop. This model was to be used to improve the system by finding more suitable pipe dimensions for various components in the system. A frequency response analysis of the new mock circulation loop was required to observe the response of the system to increased heart rates. As several different frequencies are required to be reproduced in the mock loop due to heart rate simulations, a wide range of frequencies could be tested in this model and appropriate pipe sizes could be found.

3.2 Methods

The MATLAB / SIMULINK (The Mathworks, Natick, MA, U.S.A.) environment was chosen to simulate the mock circulation loop due to previous MATLAB experience and the ease of simulation using SIMULINK’s graphical block approach.

3.2.1 SIMULINK Models

The PHYSBE system was analysed at the start of this study to gain an understanding of how the human circulatory system can be modelled using the SIMULINK environment. It was noted that this model was not appropriate for the representation of a mock circulation loop which contains features such as vertical chambers influenced by gravity, pressure and inertial forces. The PHYSBE system does have a heat element included, representing the temperature of the blood as it flows through the body.

3.2.2 Mock Circulation Loop Model

A detailed model was required to simulate the function and assist in the design of a compact mock circulation loop. As components of the new MCL are similar to an older system developed by Timms et al. (2005) (Figure 19), parts of the SIMULINK model were based on that older system. This enabled model validation via the
application of set values of pipe lengths and diameters, regulator pressures, and observation of pressure and flow traces in the previously developed system.


3.2.2.1 Design

To model the MCL, subsystems for left atrium (LA), left ventricle (LV), left ventricle regulator (LVReg), aorta (Ao), systemic venous system (SV), right atrium (RA), right ventricle (RV), right ventricle regulator (RVReg), pulmonary arterial system (PA) and pulmonary venous system (PV) were created (Figure 20). The pressure and flow output of each system was calculated using the flow output from the previous subsystem and the pressure output from the following subsystem. A schematic of a subsystem can be seen in Figure 21, while a flow diagram is presented in Figure 22.
Figure 20 - Linked subsystems in mock circulation loop model.

Figure 21 - Parameters in each subsystem of mock circulation loop model. Note this figure represents a single subsystem with built in compliance.

Figure 22 - Flow diagram of subsystem in mock circulation loop simulation. Note the output flow and input pressure for each subsystem is determined by the flow from previous subsystems and pressure from following subsystems.
For each subsystem the outflow must be found, taking into account the input flow and the losses in the subsystem. From Figure 21, if $P_{\text{out}}$ is the pressure out of the subsystem, $P_{\text{in}}$ is the pressure into the subsystem, $P_{\text{loss}}$ is the pressure loss due to resistance and inertance effects, $P_{R\text{loss}}$ is the resistance pressure loss, $P_{L\text{loss}}$ is the inertance pressure loss, $R$ is the resistance of the horizontal piping, $Q_{\text{out}}$ is the flow out of the subsystem and $L$ is the inertance of the horizontal piping then:

\begin{align*}
P_{\text{out}} &= P_{\text{in}} - P_{\text{loss}} \quad (3.1) \\
P_{\text{loss}} &= P_{R\text{loss}} + P_{L\text{loss}} \quad (3.2) \\
\text{where} \quad P_{R\text{loss}} &= R \cdot Q_{\text{out}} \quad (3.3) \\
\text{and} \quad P_{L\text{loss}} &= L \cdot \frac{dQ_{\text{out}}}{dt} \quad (3.4)
\end{align*}

Sub (3.3) and (3.4) into (3.2)

\begin{align*}
P_{\text{out}} &= P_{\text{in}} - R \cdot Q_{\text{out}} - L \cdot \frac{dQ_{\text{out}}}{dt} \quad (3.5) \\
\text{Rearrange (3.5) to find } Q_{\text{out}} \\
Q_{\text{out}} &= \frac{\int (P_{\text{in}} - R \cdot Q_{\text{out}} - P_{\text{out}}) dt}{L} \quad (3.6)
\end{align*}

Following this, the pressure out of the subsystem must be found -

\begin{align*}
Q_{c} &= \frac{(P_{\text{in}} - P_{c})}{R_{t}} \quad (3.7) \\
\text{Rearrange (3.7) to find } P_{\text{in}} \\
P_{\text{in}} &= Q_{c} \cdot R_{t} + P_{c} \quad (3.8)
\end{align*}

Where $Q_{c}$ is the flow of fluid into the vertical chamber, $P_{c}$ is the pressure of the fluid inside the chamber at the base of the larger diameter pipe, and $R_{t}$ is the resistance of the piping into the vertical chamber.

$Q_{c}$ can be found by -

\begin{align*}
Q_{c} &= Q_{\text{in}} - Q_{\text{out}} \quad (3.9) \\
\text{Where } Q_{\text{in}} \text{ is the flow into the subsystem.}
\end{align*}

$P_{c}$ can be found by using the free body diagram (Figure 23) -

\begin{align*}
\sum F_{x} &= m \ddot{x} \quad (3.10)
\end{align*}
Differentiate (3.13) twice with respect to time to find \( \ddot{x} \). This function must be divided by 2 as \( x \) is found at the centre of mass of the fluid rather than the top of the body of fluid.

\[
\ddot{x} = \frac{1}{2A} \frac{dQ_c}{dt}.
\]  

(3.14)

Sub (3.12) and (3.14) into (3.11) to find \( P_c \)

\[
P_c = \frac{\rho_c}{2A} \frac{dQ_c}{dt} \left( V_c(0) + \int Q_c \, dt \right) + \rho_c \frac{g}{A} \left( V_c(0) + \int Q_c \, dt \right) + P_a.
\]  

(3.15)

Where \( m \) is the mass of the fluid in the vertical chamber, \( \ddot{x} \) is the double derivative of the position of the centre of mass, \( A \) is the cross sectional area of the vertical chamber, \( g \) is the gravitational constant, \( P_a \) is the pressure of the air above the fluid, \( \rho_c \) is the density of the fluid, \( V_c(0) \) is the initial volume of fluid in the chamber and \( x \) is the position of the centre of mass.

The pressure in the air must be found. For the ventricles, with air injection and venting, \( P_a \) can be found by -

\[
P_{reg} = P_a = Q_{reg} \cdot R_{reg}
\]  

(3.16)

\[
Q_{reg} = \frac{d}{dt} V_{reg}
\]  

(3.17)

Assume the air from the regulator has constant density.
\[ V_{reg} = \frac{m_{reg}}{\rho_{reg}} \]  
(3.18)

Sub (3.18) into (3.17)

\[ Q_{reg} \rho_{reg} = \frac{d}{dt} m_{reg} \]  
(3.19)

\[ m_a = m_a(0) + m_{reg} \]  
(3.20)

Differentiate (3.20) with respect to time

\[ \frac{d}{dt} m_a = \frac{d}{dt} m_a(0) + \frac{d}{dt} m_{reg} \]  
(3.21)

\[ \frac{d}{dt} m_a = \frac{d}{dt} m_{reg} \]  
(3.22)

Sub (3.19) into (3.22)

\[ \frac{d}{dt} m_a = Q_{reg} \rho_{reg} \]  
(3.23)

The density of air can be found by

\[ \rho_a = \frac{m_a}{V_a} \]  
(3.24)

Differentiate (3.24) with respect to time

\[ \frac{d}{dt} \rho_a = \frac{V_a \frac{d}{dt} m_a - m_a \frac{d}{dt} V_a}{V_a^2} \]  
(3.25)

Sub (3.23) into (3.25)

\[ \frac{d}{dt} \rho_a = \frac{Q_{reg} \rho_{reg} V_a - m_a \frac{d}{dt} V_a}{V_a^2} \]  
(3.26)

Using the equation for bulk modulus -

\[ K = \rho \cdot c^2 \]  
(3.27)

and

\[ c^2 = \frac{d \rho}{d \rho} \]  
(3.28)

Sub (3.28) into (3.27)

\[ \frac{d \rho}{d \rho} = \frac{\rho}{K} \]  
(3.29)

and

\[ \frac{d p_a}{dt} = \frac{d p_a}{d p_a} \cdot \frac{d p_a}{dt} \]  
(3.30)

Sub (3.29) into (3.30)

\[ \frac{d p_a}{dt} = \frac{p_a}{K_a} \cdot \frac{d p_a}{dt} \]  
(3.31)

Sub (3.31) into (3.32)

\[ \frac{p_a}{K_a} \cdot \frac{d p_a}{dt} = \frac{Q_{reg} \rho_{reg} V_a - m_a \frac{d}{dt} V_a}{V_a^2} \]  
(3.32)

Sub (3.24) into (3.32)
\[
\frac{m_a}{V_a K_a} \frac{dP_a}{dt} = \frac{Q_{reg} P_{reg}}{V_a} - \frac{m_a}{V_a} \frac{dV_a}{dt}
\]  
(3.33)

and

\[
Q_c = -\frac{dV_a}{dt}
\]  
(3.34)

Sub (3.34) into (3.33) and expand

\[
\frac{dP_a}{dt} = \frac{K_a Q_{reg} P_{reg}}{m_a} + \frac{K_a Q_c}{V_a}
\]  
(3.35)

Sub (3.16) into (3.35)

\[
\frac{dP_a}{dt} = \frac{K_a Q_{reg} (P_{reg} - P_a)}{R \cdot m_a} + \frac{K_a Q_c}{V_a}
\]  
(3.36)

Integrate with respect to time to find \( P_a \)

\[
P_a = \int \left( \frac{K_a Q_{reg} (P_{reg} - P_a)}{R \cdot m_a} + \frac{K_a Q_c}{V_a} \right) dt
\]  
(3.37)

Where \( P_{reg} \) is the pressure from the regulator, \( Q_{reg} \) is the flow of air from the regulator, \( R \) is the resistance of the regulator and connecting tubing, \( V_{reg} \) is the volume of air passed from the regulator to the chamber, \( m_{reg} \) is the mass of air passed from the regulator to the chamber, \( \rho_{reg} \) is the density of air from the regulator, \( m_a \) is the total mass of air in the chamber, \( m_a(0) \) is the initial mass of air in the chamber, \( \rho_a \) is the density of air in the chamber, \( V_a \) is the volume of air in the chamber, \( K_a \) is the bulk modulus of air, \( \rho \) is the density of air, \( c \) is the speed of sound in air and \( P \) is the pressure of the air. \( P_{reg} \) is simulated by a pulsing function multiplied by a gain which represents the user controlled regulator pressure.

As the compliance chambers are modelled as sealed Windkessel chambers, the ideal gas law can be used to find the air pressure –

\[
PV = mRT
\]  
(3.38)

\[
P_a V_a = m_a RT
\]  
(3.39)

\[
\frac{P_a m_a}{\rho_a} = m_a RT
\]  
(3.40)

\[
P_a = \frac{m_a}{V_a} RT
\]  
(3.41)

where

\[
m_a = V_a(0) \rho_a(0)
\]  
(3.42)

and

\[
V_a = V_a(0) - \int Q_c dt
\]  
(3.43)
Where $R$ is the universal gas constant, $T$ is the air temperature, $V_a(0)$ is the initial volume of air in the chamber and $\rho_a(0)$ is the initial density of air in the chamber. This will give the absolute pressure, so 760mmHg must be subtracted to obtain the gauge pressure.

The above equations can be used to accurately model the mock circulation loop; however resistance, inertia, and volume parameters must be known. As the aim of this model is to observe the system response to change in pipe dimensions, the lengths and radii of the pipes must be used as the input parameters to the model. A schematic of subsystem, showing lengths and radii, is shown in Figure 24. This is achieved by applying the following equations to obtain the parameters mentioned above –

\[
R = 8. \mu_c \cdot \pi \cdot \frac{l_h}{(\pi r_h^2)^2} \tag{3.44}
\]
\[
R_t = 8. \mu_c \cdot \pi \cdot \frac{l_{rt}}{(\pi r_{rt}^2)^2} \tag{3.45}
\]
\[
R_{reg} = 8. \mu_c \cdot \pi \cdot \frac{l_{reg}}{(\pi r_{reg}^2)^2} \tag{3.46}
\]
\[
L = \rho_c \cdot \frac{l_h}{\pi r_h^2} \tag{3.47}
\]
\[
A = \pi \cdot (r_v)^2 \tag{3.48}
\]

The mock circulation loop is filled to a zero level to zero the pressure and volume sensors. Following this, fluid is added to the system until the system pressure is equal to the central venous pressure, approximately 8mmHg. This added volume is the initial volume in the unsealed vertical chambers (atria and ventricles), $V_c(0)$, and can be found by –

\[
C = \frac{\Delta V}{\Delta P} \tag{3.49}
\]
\[
\Delta V = C \cdot \Delta P \tag{3.50}
\]

where $C$ is the compliance of the chamber found by -
\[
C = \frac{A}{\rho_c g} \tag{3.51}
\]

and $\Delta P$ is the CVP, therefore
\[
V_c(0) = \frac{A}{\rho_c g} \tag{3.52}
\]
The initial volume for the sealed compliance chambers can be found using the ideal gas law -

\[ P_a(0) V_a(0) = m_a RT \]  \hfill (3.53)

\[ V_a(0) = \frac{m_a RT}{P_a(0)} \]  \hfill (3.54)

and

\[ V_c(0) = V_{vertical\ chamber} - V_a(0) \]  \hfill (3.55)

where

\[ V_{pipe} = l_p \pi r_p^2 \]  \hfill (3.56)

The volume of air in the vertical chambers can be found by -

\[ V_a = V_{vertical\ chamber} - V_c(0) - \int Q_c \, dt \]  \hfill (3.57)

The mass of air in the vertical chambers can be found by -

\[ m_a = \rho_{reg} \int Q_{reg} \, dt + m_a(0) \]  \hfill (3.58)

where

\[ Q_{reg} = \frac{P_{reg} - P_{air}}{r_{reg}} \]  \hfill (3.59)

and

\[ m_a(0) = \rho_a(0) \cdot V_a(0) \]  \hfill (3.60)

The density of air from the regulator depends on the pressure of the air from the regulator, and can be solved by using the ideal gas law -

\[ P_{reg} V_{reg} = m_{reg} RT \]  \hfill (3.61)
The following constants apply -
\[ \rho_c = \text{constant} = 1000 \text{kg/m}^3 \]
\[ g = \text{constant} = 9.81 \text{m/s}^2 \]
\[ K_a = \text{constant} = 757.576 \text{mmHg} \]
\[ \rho_a(0) = 1.2 \text{kg/m}^3 \]

To prevent algebraic loops in the system, the resistance and inertiance elements for the horizontal pipes were modelled as a single transfer function. Using Laplace transforms, equation (3.5) can be written as –

\[
\frac{P_{\text{out}}(s) - P_{\text{in}}(s)}{Q_{\text{out}}(s) + L(sQ_{\text{out}}(s) - Q_{\text{out}}(0^+))} = R \quad (3.64)
\]

Now rearrange (3.64) to get

\[
P_{\text{out}}(s) - P_{\text{in}}(s) + LQ_{\text{out}}(0^+) = Q_{\text{out}}(s)(sL + R) \quad (3.65)
\]

Rearranging (3.65) gives

\[
\frac{P_{\text{out}}(s) - P_{\text{in}}(s) + LQ_{\text{out}}(0^+)}{(sL + R)} = Q_{\text{out}}(s) \quad (3.66)
\]

This can now be written as a transfer function

\[
Q_{\text{out}}(s) = \left[ P_{\text{out}}(s) - P_{\text{in}}(s) + LQ_{\text{out}}(0^+) \right] \left( \frac{1}{sL + R} \right) \quad (3.67)
\]

Where the \(1/(sL+R)\) is the transfer function implemented as the resistance and inertiance elements in SIMULINK.

Due to the loop nature of the system, a stiff Simulink solver was required to prevent perturbations in the system. The solver ode23s (stiff/Mod. Rosenbrock) was chosen to solve the equations used in the simulation.

### 3.2.2.2 Heart valves

The heart valves in this model were completed in two parts. The first part of the system is before the combined inertiance and resistance transfer function, and operates by applying limits to the output using a feedback system. As the transfer function operates as an integrator, a positive input will produce a positive output. If a negative input is then supplied, a positive output can still be observed, however if a continued negative input is supplied, the output will turn negative. As the input to the
system is the pressure difference, found by subtracting the subsystem pressure from the next subsystem pressure, this value can often be negative. When a positive pressure difference is returned, the transfer function output will gradually increase from a negative number to a positive number. This gradual effect is not an accurate representation of how a heart valve operates, as the valve should open as soon as the pressure difference becomes positive. This was corrected by eliminating the negative signal input to the transfer function with a subsystem directly before the transfer function. This subsystem collects feedback from the MCL segment outflow, and returns this value to a switch which disables negative flows. A positive flow is allowed through the system, while a negative flow creates an output signal of zero. Using this method, as soon as the pressure difference between the two segments is positive, the transfer function will return a positive output and immediately allow forward flow.

The second part of the valve system worked as a saturation control function, and was used as a backup in case the resistance or inertia elements in the transfer function caused a negative output. This saturation had an upper limit of infinity and a lower limit of zero to prevent backflow.

Each subsystem was then modelled using the equations derived above and can be seen in Appendix 5.

3.2.3 Model Validation
To ensure the results from this model were as accurate as possible, the model was validated against pressure and flow traces obtained from a previous mock circulation loop. Values of pipe lengths and diameters and regulator pressures were taken from the current physical model, and implemented in the mathematical model (Table 13). The code for the MCL model can be seen in Appendix 6.

The model was then used to simulate conditions of rest, exercise and heart failure by changing the systemic vascular resistance, ventricle regulator pressure and arterial compliance. Resistance was changed by altering the radius in the pinch valves,
represented by the \( r_h \) value for both SVR (systemic) and PVR (pulmonary). Ventricle regulator pressure was changed by altering the \( P_{\text{reg}} \) value for either the left ventricle or right ventricle, while arterial compliance was altered by changing the length of the vertical chamber pipe (\( l_p \)) for either the Ao (systemic) or PA (pulmonary) systems (Table 14).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LA</th>
<th>LV</th>
<th>Ao</th>
<th>SVR</th>
<th>SVC</th>
<th>RA</th>
<th>RV</th>
<th>PA</th>
<th>PVR</th>
<th>PVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>( P_{\text{reg}} ) (mmHg)</td>
<td>0</td>
<td>122</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>26</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>( l_h ) (mm)</td>
<td>395</td>
<td>225</td>
<td>750</td>
<td>70</td>
<td>1200</td>
<td>395</td>
<td>125</td>
<td>750</td>
<td>70</td>
<td>1200</td>
</tr>
<tr>
<td>( r_h ) (mm)</td>
<td>16</td>
<td>16</td>
<td>12.5</td>
<td>1.01</td>
<td>12.5</td>
<td>16</td>
<td>16</td>
<td>12.5</td>
<td>2.2</td>
<td>12.5</td>
</tr>
<tr>
<td>( l_{\text{Rt}} ) (mm)</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>0</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>0</td>
<td>60</td>
</tr>
<tr>
<td>( r_{\text{Rt}} ) (mm)</td>
<td>25</td>
<td>25</td>
<td>12.5</td>
<td>0</td>
<td>16</td>
<td>20</td>
<td>25</td>
<td>12.5</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>( l_v ) (mm)</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>( r_v ) (mm)</td>
<td>25</td>
<td>25</td>
<td>50</td>
<td>0</td>
<td>75</td>
<td>20</td>
<td>25</td>
<td>50</td>
<td>0</td>
<td>50</td>
</tr>
<tr>
<td>( l_p ) (mm)</td>
<td>400</td>
<td>400</td>
<td>190</td>
<td>0</td>
<td>1000</td>
<td>400</td>
<td>400</td>
<td>450</td>
<td>0</td>
<td>750</td>
</tr>
<tr>
<td>( r_p ) (mm)</td>
<td>25</td>
<td>25</td>
<td>50</td>
<td>0</td>
<td>75</td>
<td>20</td>
<td>25</td>
<td>50</td>
<td>0</td>
<td>50</td>
</tr>
<tr>
<td>( l_{\text{reg}} ) (mm)</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>( r_{\text{reg}} ) (mm)</td>
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<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 13 - Physical parameters used for mock circulation loop simulation. \( P_{\text{reg}} \) – regulator pressure, \( l \) – length, \( r \) – radius, \((h)\) – horizontal pipe, \((\text{Rt})\) – vertical chamber entry pipe, \((v)\) – initial condition in vertical chamber pipe, \((p)\) – total vertical chamber pipe, \((\text{reg})\) – regulator attachment tube.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Rest</th>
<th>Exercise</th>
<th>Left Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR radius (mm)</td>
<td>1.01</td>
<td>1.10</td>
<td>0.95</td>
</tr>
<tr>
<td>PVR radius (mm)</td>
<td>2.2</td>
<td>3</td>
<td>2.2</td>
</tr>
<tr>
<td>Left ventricle regulator pressure (mmHg)</td>
<td>122</td>
<td>173</td>
<td>65</td>
</tr>
<tr>
<td>Right ventricle regulator pressure (mmHg)</td>
<td>26</td>
<td>37</td>
<td>41</td>
</tr>
<tr>
<td>Aorta ( l_p ) (mm)</td>
<td>190</td>
<td>110</td>
<td>100</td>
</tr>
<tr>
<td>Pulmonary artery ( l_p ) (mm)</td>
<td>450</td>
<td>240</td>
<td>240</td>
</tr>
<tr>
<td>Heart rate (beats per minute)</td>
<td>60</td>
<td>120</td>
<td>60</td>
</tr>
</tbody>
</table>

Table 14 - Parameters used in the mock circulation loop model to simulate rest, exercise and left heart failure.

### 3.2.4 Mock Circulation Loop Improvement

The MCL simulation model was used to alter the physical pipe dimensions to observe the change in pressure and flow traces for a healthy cardiac simulation. These traces were then compared to those seen in the literature, and through a series of iterative
trials a final set of parameters was developed to give a more accurate cardiovascular system representation (Table 15). A left atrial kick was added to assist left ventricle filling. Horizontal pipe lengths for the atria and ventricles were reduced to minimize the inertial effects between the heart chambers. Arterial compliance chamber entry pipe radius was also adjusted to produce a more physiologically accurate pressure waveform. To produce a more accurate left ventricle pressure, the regulator pressure was ramped up during the start of systole and down during the end of systole. This was achieved by varying the regulator pressure in 0.1 second increments. This time increment was chosen as it is the maximum response time for the regulators (ITV2030-012BS5, SMC Pneumatics, Brisbane, Australia) being used in the current physical MCL.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LA</th>
<th>LV</th>
<th>Ao</th>
<th>SVR</th>
<th>SVC</th>
<th>RA</th>
<th>RV</th>
<th>PA</th>
<th>PVR</th>
<th>PVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{\text{reg}}$ (mmHg)</td>
<td>40</td>
<td>126</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>26</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$l_h$ (mm)</td>
<td>25</td>
<td>25</td>
<td>440</td>
<td>70</td>
<td>560</td>
<td>25</td>
<td>25</td>
<td>100</td>
<td>70</td>
<td>440</td>
</tr>
<tr>
<td>$r_h$ (mm)</td>
<td>16</td>
<td>16</td>
<td>12.5</td>
<td>1.02</td>
<td>12.5</td>
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Table 15 - Physical parameters used for optimized mock circulation loop simulation

3.2.5 Frequency Response

To observe the response of the improved system over a variety of simulated heart rates, a subsystem was chosen for a frequency response analysis. Only the aorta subsystem was used as each subsystem is modelled in a similar way, so the trends seen in these results can be applied to the other subsystems. This was achieved by inputting a sine wave of amplitude one as the input pressure, a constant value of zero...
for the input flow, and observing the output pressure and flow. The frequency of the
sine wave was varied and the outputs observed. A Bode plot was then created for
both the output flow and output pressure, with gain vs frequency and phase vs
frequency plots being produced. The phase (seconds) was found by comparing the
position of the peaks for both the input and output signals while the gain (dB) was
found by -

\[ \text{Gain} = 10 \log_{10} \left( \frac{\text{output amplitude}}{\text{input amplitude}} \right) \]  

(3.68)

3.3 Results

3.3.1 Normal Heart Function

The results for the simulation of normal, healthy, resting heart function in the
mathematical model of the existing mock circulation loop over a full 30 second
simulation time are shown in Figures 25 to 28. The final two seconds of simulation
are shown in Figures 29 to 32 for closer detail. Abbreviations in these results include
LAP – left atrial pressure, LVP – left ventricle pressure, AoP – aortic pressure, MAP
– mean aortic pressure, SQ – systemic flow rate, MSQ – mean systemic flow rate,
RAP – right atrial pressure, RVP – right ventricle pressure, PAP – pulmonary artery
pressure, MPAP – mean pulmonary artery pressure, PQ – pulmonary flow rate and
MPQ – mean pulmonary flow rate.

Left ventricle pressures can be seen to have systolic and diastolic values of 122 and
8mmHg respectively. Aortic pressures oscillate between 81 and 123mmHg with a
mean value of 103mmHg, while left atrial pressures oscillate between 13 and
16mmHg. Mean systemic flow rate was recorded as 83mL/s with a maximum of
93mL/s and a minimum of 69mL/s.
Figure 25– Resting systemic pressure distribution from MCL simulation over 30 second simulation time. LAP - Left atrial pressure, LVP - Left ventricle pressure, AoP- Aortic pressure, MAP - Mean aortic pressure.

Figure 26– Resting systemic flow rate distribution from MCL simulation over 30 second simulation time. MSQ – Mean systemic flow rate, SQ – Systemic flow rate.
Figure 27 - Resting pulmonary pressure distribution from MCL simulation over 30 second simulation time. RAP - Left atrial pressure, RVP - Left ventricle pressure, PAP - Aortic pressure, MPAP - Mean aortic pressure.

Figure 28 - Resting pulmonary flow rate distribution from MCL simulation over 30 second simulation time. MPQ – Mean pulmonary flow rate, PQ – Pulmonary flow rate.
Figure 29 – Resting systemic pressure distribution from MCL simulation over final 2 seconds of simulation time. LAP - Left atrial pressure, LVP - Left ventricle pressure, AoP - Aortic pressure, MAP - Mean aortic pressure.

Figure 30 – Resting systemic flow rate distribution from MCL simulation over final 2 seconds of simulation time. MSQ – Mean systemic flow rate, SQ – Systemic flow rate.
Figure 31 - Resting pulmonary pressure distribution from MCL simulation over final 2 seconds of simulation time. RAP - Left atrial pressure, RVP - Left ventricle pressure, PAP- Aortic pressure, MPAP - Mean aortic pressure.

Figure 32 - Resting pulmonary flow rate distribution from MCL simulation over final 2 seconds of simulation time. MPQ – Mean pulmonary flow rate, PQ – Pulmonary flow rate.

The systolic and diastolic values for right ventricle pressure were seen to be 26 and 2mmHg respectively. A mean pulmonary artery pressure of 19mmHg was recorded with a pulse pressure of 16mmHg with an oscillation between 10 and 26mmHg. Right atrial pressures varied between 5 and 9mmHg while the pulmonary flow rate
oscillated between 51 and 106mL/s with a mean value of 83mL/s (approximately 5L/min).

The model was shown to take approximately 10 seconds to become stable, while an accurate mean value for arterial pressures and flow rates could be obtained by 20 seconds through the simulation.

### 3.3.2 Exercise

Figures 33 to 36 present the simulation of normal, healthy heart function during exercise in the mathematical model of the mock circulation loop. Left ventricle pressures values are shown to be 162 and 10mmHg for systole and diastole respectively. Aortic pulse pressures were 85mmHg with systolic / diastolic values of 191/106mmHg. MAP was steady at 147mmHg while left atrial pressures oscillated between 21 and 31mmHg. The aortic flow rate oscillated between 144 and 180mL/s while a mean value of 165mL/s (approximately 10L/min) was produced.

Systolic and diastolic pressures for the right ventricle were 35 and 3mmHg respectively. The pulmonary artery pulse pressure was 29mmHg with systolic / diastolic pressures of 42/13mmHg. Mean pulmonary artery pressure was shown to be at 27mmHg while right atrial pressure oscillated between 10 and 13mmHg. Pulmonary flow varied from 123 to 194mL/s with a mean value of 165mL/s.
Figure 33- Systemic pressure distribution for exercise conditions from MCL simulation over final 2 seconds of simulation time. LAP - Left atrial pressure, LVP - Left ventricle pressure, AoP - Aortic pressure, MAP - Mean aortic pressure.

Figure 34– Systemic flow rate distribution for exercise conditions from MCL simulation over final 2 seconds of simulation time. MSQ – Mean systemic flow rate, SQ – Systemic flow rate.
Figure 35 - Pulmonary pressure distribution for exercise conditions from MCL simulation over final 2 seconds of simulation time. RAP - Left atrial pressure, RVP - Left ventricle pressure, PAP - Aortic pressure, MPAP - Mean aortic pressure.

Figure 36 - Pulmonary flow rate distribution for exercise conditions from MCL simulation over final 2 seconds of simulation time. MPQ – Mean pulmonary flow rate, PQ – Pulmonary flow rate.

3.3.3 Heart Failure

These results, shown in figures 37 to 40, present the simulation of left heart failure in the mathematical model of the mock circulation loop. Left ventricle pressures can be seen to have systolic and diastolic values of 81 and 27mmHg respectively. Aortic
pressures oscillate between 47 and 83mmHg with a mean value of 67mmHg, while left atrial pressures oscillate between 30 and 32mmHg. Mean systemic flow rate was recorded as 43mL/s (approximately 2.5L/min) with a maximum of 51mL/s and a minimum of 33mL/s.

Systolic and diastolic values for right ventricle pressure were 41 and 1mmHg respectively. A mean pulmonary artery pressure of 33 was recorded with a pulse pressure of 19mmHg with an oscillation between 24 and 43mmHg. Right atrial pressures varied between 3 and 5mmHg while the pulmonary flow rate oscillated between 3 and 73mL/s with a mean value of 44mL/s.

Figure 37- Systemic pressure distribution for left heart failure conditions from MCL simulation over final 2 seconds of simulation time. LAP - Left atrial pressure, LVP - Left ventricle pressure, AoP - Aortic pressure, MAP - Mean aortic pressure.
Figure 38– Systemic flow rate distribution for left heart failure conditions from MCL simulation over final 2 seconds of simulation time. MSQ – Mean systemic flow rate, SQ – Systemic flow rate.

Figure 39- Pulmonary pressure distribution for left heart failure conditions from MCL simulation over final 2 seconds of simulation time. RAP - Left atrial pressure, RVP - Left ventricle pressure, PAP - Aortic pressure, MPAP - Mean aortic pressure.
3.3.4 Mock Circulation Loop Improvement

Figures 41 to 44 present the simulation of normal, healthy heart function in the mathematical model of the mock circulation loop after improvement of the system. Left ventricle pressures values are shown to be 120 and 8mmHg for systole and diastole respectively. Aortic pulse pressures were 40mmHg with systolic /diastolic values of 120/80mmHg. MAP was steady at 97mmHg while left atrial pressures oscillated between 8 and 20mmHg. The aortic flow rate oscillated between 71 and 95mL/s while a mean value of 83mL/s was produced.

Systolic and diastolic pressures for the right ventricle were 25 and 5mmHg respectively. The pulmonary artery pulse pressure was 15mmHg with systolic /diastolic pressures of 25/10mmHg. Mean pulmonary artery pressure was shown to be at 18mmHg while right atrial pressure oscillated between 5 and 10mmHg. Pulmonary flow varied from 54 to 105mL/s with a mean value of 83mL/s.
Figure 41– Improved systemic pressure distribution for resting conditions from MCL simulation over final 2 seconds of simulation time. LAP - Left atrial pressure, LVP - Left ventricle pressure, AoP - Aortic pressure, MAP - Mean aortic pressure.

Figure 42– Improved systemic flow rate distribution for resting conditions from MCL simulation over final 2 seconds of simulation time. MSQ – Mean systemic flow rate, SQ – Systemic flow rate.
3.3.5 Frequency Response

Figure 45 presents the frequency response characteristics for the aorta subsystem in the improved MCL simulation. Abbreviations in these results include s – seconds, and bpm – beats per minute.
A negative gain is present for all frequencies, indicating that the output of the subsystem will always be less than the input. The gain drops sharply from zero beats per minute until around 30 beats per minute when it begins to plateau. As frequency is increased, the rate of change of the gain decreases.

The phase difference is negative for all frequencies, demonstrating that the output pressure wave will always lag the input pressure wave. The phase lag decreases in magnitude sharply until around 60 beats per minute when it starts to plateau. As frequency is increased, the rate of change of the phase difference is decreased.

**Figure 45 - Frequency response characteristics of the aorta subsystem**

3.4 Discussion

For a mock circulation loop simulation, pressures and flows seen in a physical system must be accurately replicated in the model. This discussion focuses on the methods used in developing and testing the system, and the results produced.
3.4.1 Mock Circulation Loop Reproduction

An accurate representation of the physical mock circulation system was provided by a model that utilised mathematical equations for pressure and flow. Furthermore, inserting pipe lengths and diameters, input ventricle pressures, and a combination of known constants corresponding to those characterising the current physical system increased the accuracy, and demonstrated the modifiable nature of the simulation.

Comparison of the results (Figures 46, 47) produced by both the mathematical model and the physical representation of a previously developed MCL showed a good correlation between the pressure traces. The left ventricle pressure in the simulation includes a slight double pulse during systole which cannot be seen in the MCL. This is due to the length and radius of pipe which connects the left ventricle to the aorta, and can be eliminated by significantly reducing the length between the chambers. This inertial discrepancy also accounts for the aortic pressure rising before the ventricle pressure. The simulation produced a slight dip in LVP during the start of diastole due to the inertia of the fluid travelling out of the left ventricle. This can be reduced by decreasing the length of pipe between the left atrium and left ventricle to promote earlier left ventricle filling directly after the systolic period.

The aortic pressure wave produced accurate pulse pressures of 123/81mmHg and a fairly accurate sawtooth waveform. The systolic pressure of the aorta was slightly higher than that of the left ventricle, while the aortic pressure peaked shortly before the left ventricle. The increased aortic pressure can be seen in greater detail in exercise conditions, and is due to a combination of the fluid inertia between the ventricle and aortic subsystems and the high SVR following the aortic subsystem. This results in a high inflow and low outflow to the aortic subsystem, resulting in the aortic pressure exceeding that of the ventricle. These results were not repeated in the MCL, and can be eliminated in the simulation by reducing the length of pipe between the left ventricle and aortic compliance chamber.

The atrial pressure trace produced by the mathematical model followed the MCL atrial pressure very closely. The notch seen shortly after the start of left ventricle systole, produced due to the mitral valve closing, is reproduced however with a
reduced magnitude and duration. The model is incapable of reproducing these notches due to the valves being modelled as a perfect mechanical valve.

Figure 46 – Resting systemic pressure distribution from a) MCL simulation and b) Physical MCL system. LAP - Left atrial pressure, LVP - Left ventricle pressure, AoP- Aortic pressure, MAP - Mean aortic pressure.

Figure 47 – Resting pulmonary pressure distribution from a) MCL simulation and b) Physical MCL system. RAP - Right atrial pressure, RVP – Right ventricle pressure, PAP – Pulmonary artery pressure, MPAP - Mean pulmonary artery pressure.

Similar comparisons can be made with the pulmonary pressure results produced by the model. The double pressure pulse produced by the simulation was seen to accurately represent that seen in the MCL; however the arterial pressure was shown to rise faster than the ventricle pressure. The simulated right atrial pressure waveform oscillated in a sine-wave formation between 5 and 10mmHg which was not seen in the physical system. This is attributed to a low systemic venous resistance and can be eliminated by decreasing the systemic venous horizontal pipe radius.

The mathematical simulation of a previous MCL showed some limitations in its operation. Although pressure losses are mostly accounted for by representing the pipe
lengths and diameters, other losses were not accounted for. The pressure loss of a 90°
elbow, of which up to eight exist in the physical system, was not accounted for. The
loss of pressure caused by the fluid travelling along the horizontal pipe and into the
90° vertical chamber pipe, such as the ventricles or compliance chambers, was also
not modelled in this system. These pressures losses only have a slight impact on the
rig’s simulated haemodynamics, and thus were considered negligible for this study.
Additional pressure losses, caused by features such as elbows in the MCL, can be
accounted for in this system by applying a slight increase in the resistance of each
segment, a function of the pipe length or diameter. The current physical system
includes a variety of lengths and diameters of pipes in each subsystem which can vary
from 20mm to 40mm in diameter. The simulation, however, is modelled on the
assumption that all horizontal pipes in each section are the same diameter. Ideal
valves have been modelled in the simulation, as the effect of heavy mechanical check
valves was considered to have negligible effects on the results. This resulted in much
smoother simulation pressure traces compared to the physical system following valve
closure. Small oscillations in the pressure traces seen in the physical system, caused
by effects such as water hammer, were not able to be reproduced in the simulation,
resulting in a much smoother pressure waveform. Accurate modelling of the
mechanical check valves was considered beyond the scope of this study.

3.4.2 Mock Circulation Loop Improvement

The MCL simulation was improved by changing pipe dimensions and adding an atrial
kick and variable ventricle pulse pressure. The heart chambers and the aorta were
moved closer together to reduce the inertiance between the systems. This resulted in
the pressure traces closely following the pressures in the previous subsystem,
resulting in a much more physiologically accurate result. The improved systemic
pressure trace was compared to a natural systemic pressure trace (Figure 48).
Pressure and flow magnitudes produced by the improved simulation are shown
compared to natural values in Table 16.

The aortic pressure trace was adjusted by altering the aortic compliance chamber
entry pipe and the aortic compliance chamber pipe dimensions. This changed the
impedance of the system which resulted in a much more accurate aortic pressure
waveform. The aortic pressure followed the left ventricle pressure during systole
until the left ventricle pressure begins to drop. The fluid continued to flow until the aortic valve closes when the LVP and AoP reach approximately 105mmHg. Following this, the aortic pressure dropped until the next cardiac cycle begins.

The left ventricle pressure wave shown in the previous MCL system was too square and often produced a double pulse during systole. The double pulse was removed by reducing the distance between the left ventricle and the aortic compliance chamber. The square wave was altered to form a more curved pressure wave by adjusting the regulator pressure output in 0.1 second intervals, similar to adjusting the voltage on the regulator at the maximum response time.

Previous atrial pressures were shown to remain as a fairly flat line during the cardiac cycle. To accurately represent the human body, an atrial kick was introduced. This will also assist in left ventricle filling, which is particularly useful when the heart rate is increased. The small notch seen in the atrial pressure in the natural body shortly after ventricle systole is due to the left ventricle systolic pressure pushing the mitral valve back into the atrium. This is not achievable with this mechanical design due to the heart valves being modelled as rigid mechanical valves; however a very small notch can be seen in the model due to the valve closing.

![Figure 48 - Systemic pressures produced in a) the improved MCL simulation and b) a natural healthy condition. LAP - Left atrial pressure, LVP - Left ventricle pressure, AoP - Aortic pressure, MAP - Mean aortic pressure.](image)

The pressures shown in the improved MCL are close to that seen in the body, while the shapes of the pressure traces are also much more accurate than the previous system. Left atrial pressures are slightly higher in the model, which could be due to inaccurate initial volumes in the system. Pulmonary pressures were shown to be very
accurate to the natural situation; however the waveforms still showed a small left ventricle double pulse at the beginning of systole and a small pulse during the start of diastole. Flow rates for both systemic and pulmonary systems were shown to be 82mL/s which equates to 4.92L/min.

Limitations in the improved system can be seen by examining the results produced by the simulation. Similar to the MCL reproduction, all pressure losses have not been accounted for in the simulation, however accurate results can still be produced. Pipe dimensions chosen for the optimized system are not readily available and may have to be manufactured specifically for this purpose. While the LVP now presents a much more physiologically accurate waveform, the 0.1 second response time of the physical regulator limits how accurate this trace can become.

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<tr>
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Table 16 – Comparison of improved MCL model haemodynamics to a natural, healthy situation. LVP - Left ventricle pressure, AoP - Aortic pressure, MAP – Mean aortic pressure, LAP – Left atrial pressure, SQ – Systemic flow, RVP - Right ventricle pressure, PAP – Pulmonary arterial pressure, MPAP – Mean pulmonary arterial pressure, RAP – Right atrial pressure, RQ – Pulmonary flow rate.

3.4.3 Frequency Response

The frequency response of the improved system (Figure 49) was analysed to observe the output of the system compared to the input. As all the subsystems were modelled in a similar manner, with the exception of the ventricles with regulator inputs, only the aortic subsystem was analysed. Due to the input pressure being a sine wave and
the input flow being a constant, the ventricle regulators were eliminated to obtain an accurate sine wave pressure output. By excluding the regulators from the frequency response, the results will not be as accurate; however they can now be applied to the ventricle subsystems.

![Figure 49 - Frequency response characteristics of the aorta subsystem](image)

The gain vs frequency plot revealed that the output of each subsystem will be less than the input, providing there are no external pressure sources. This was expected as pressure losses due to the resistance and inertiance of the system are present, while the only pressure sources are the regulators for the ventricles. As the frequency increased, the magnitude of the gain was reduced. This indicated that the system allows low frequency waves through with only small losses, while high frequency waves result in a much smaller output.

A limitation with the frequency response analysis was only analysing a single subsystem rather than the whole system. Due to the heart valves, the ventricles and atria could not pass the full sine wave, as the negative regions would be cut off. If a
transfer function was found for the entire system, an accurate frequency response analysis could be performed; however this is beyond the scope of this study.

3.5 Conclusion

The aim of this study was to develop a mathematical model to accurately represent a physical mock circulation loop, and use this model to enhance the current system to produce more haemodynamically accurate results. The methods used to develop a mathematical simulation of a mock circulation loop produced an accurate representation of the previously developed physical system. The physical system was broken into ten subsystems to represent the four heart chambers, the systemic and pulmonary sides for arterial and venous systems, and the regulators which control the ventricle contraction.

The MATLAB/SIMULINK environment provided a simple method of modelling the system once the equations for pressure and flow through each subsystem had been derived. Using a simple code to define the system parameters, pipe lengths and diameters and input pressures could be easily changed to alter the system. Using this code, and the parameters from the physical system, results for pressure and flow could be easily obtained. Pressure and flow traces produced by the simulation compared closely to that found in the physical system when correct pipe dimensions and input pressures were applied.

By adjusting the basic parameters of the system such as pipe dimensions, input pressures and regulator outputs, the simulation was used to improve the physical model to produce more physiologically accurate pressure and flow waveforms. An atrial kick was also added by including another regulator in the system, and a significant improvement was shown in the pressure and flow traces for both the systemic and pulmonary sides. A basic frequency response analysis was carried out on this system, demonstrating attenuation in the output signal with increased input frequency.

By using this mathematical model to simulate the physical mock circulation loop, an enhanced system can be designed and constructed. Using this new system, a more
physiologically accurate test rig will be available to improve the design of cardiovascular devices and thus reducing the number of expensive animal and human trials required. The MCL model can also be used to assist in the design of a variable compliance chamber to observe the effect of altering chamber dimensions and to ensure appropriate haemodynamic results are produced.
Chapter 4

Variable Compliance Chamber

4.1 Aims

The compliance of an artery is defined as the change in pressure required to produce a change in volume within that segment. As a pulse of fluid travels into a vascular segment, the compliance of that segment determines how much it can expand. A higher compliance indicates a more “stretchy” vascular segment, and the segment will absorb a much higher volume of fluid with each pulse compared to that of a segment with low compliance. This feature of the circulatory system is vital in the development of a mock circulation loop.

Current mock circulatory systems include many different methods for simulating the compliance of the vascular system. Windkessel chambers are fairly common, and use a trapped volume of air above the MCL fluid to simulate compliance. The volume of air at atmospheric pressure above the MCL fluid is proportional to the level of compliance of that segment. A larger volume of air indicates a higher compliance. When operating the MCL, if the compliance of the system is required to be changed, the volume of air must be changed. This means the MCL is required to be shut down and set up again once the compliance has been changed. Other methods of modelling the compliance of the vascular system include the use of springs and flexible diaphragms. Similar to the Windkessel chamber, these systems require the MCL to be shut down and changed when a change in compliance is desired. By shutting down the MCL, it cannot be guaranteed that the system will return with the exact same parameters as the previous test, and therefore testing for a change in compliance with no other parameter changes can be difficult. The response of the MCL to a transient change in compliance cannot be observed with the current system.

To accelerate testing procedures, and to demonstrate the effect of a change in compliance when all other parameters are held constant, a system was required to produce a variable level of compliance. As the aortic compliance is the segment that was required to be varied most frequently, it was chosen to base the design on a
variable aortic compliance chamber. The size of the variable compliance chamber was also important; as the new MCL is to be used for teaching purposes so should be portable.

The aim of this chapter is to present the concept of producing a variable compliance using a flexible diaphragm in a Windkessel chamber. The non-linear displacement of the diaphragm can be controlled by altering the transmural pressure across the diaphragm by changing the air pressure in the chamber. The elasticity of the diaphragm between the air and fluid sections of the compliance chamber results in a smaller, and more physiological, aortic volume change when air is supplied to the system. This is an advantage over current systems that inject air into Windkessel chambers, which produce physiologically inaccurate aortic volumes.

4.2 Static diaphragm compliance testing

A diaphragm was tested statically to demonstrate the pressure volume curve of the system and find the region of transmural pressures which produce the largest range in compliance values. This test was carried out once and was used for an estimation of the diaphragm transmural pressure range which would result in a variable compliance. The simulation was not used for this estimation as the simulated compliance chambers were modelled on the Windkessel design, rather than that of a flexible diaphragm with variable transmural pressure.

4.2.1 Methods

A Windkessel chamber (Figure 50) uses a trapped volume of air, which simulates a spring, above the MCL fluid to simulate the compliance of the system. By placing a diaphragm between the air and fluid, a transmural pressure can be created. This transmural pressure will influence the displacement of the diaphragm. As the diaphragm stretches, a non-linear relationship will occur between the change in pressure and change in volume, resulting in a variable compliance.
4.2.1.1 Variable Compliance Chamber Design

The design of the variable compliance chamber required a method of air delivery to a chamber of air which sits above a flexible diaphragm. This diaphragm separates the air chamber from the MCL fluid chamber and creates a variable transmural pressure while ensuring that no air is pushed into the system. A connection to the MCL is also required, along with a method of collecting pressure data from the chamber.

4.2.1.2 Chamber

Two chambers are required for the design of the variable compliance chamber – one under the diaphragm for the MCL fluid, and one above the diaphragm for the compressed air which controls the diaphragm deflection. The size of the fluid chamber was designed to represent the natural volume of the aorta, in conjunction with the aortic tubing in the MCL. As the volume of the natural aorta is approximately 700mL, and the rest of the aortic section has a volume of 250mL, the chamber was required to have a volume of approximately 450mL. This compliance chamber is also being developed for use on a compact MCL for teaching purposes, so the design was required to be as small as possible to fit the finished MCL on a portable trolley. Due to the above size restrictions, a pipe inside diameter of 100mm
was chosen, with a height of 60mm allowing for approximately 470mL of fluid to exist in the chamber, depending on the stage of the cardiac cycle.

The air chamber was designed to allow for a large diaphragm deflection. As this part of the chamber is directly above the fluid chamber, the same pipe diameter, 100mm, was used. A height of 60mm was chosen to allow a fairly large change in transmural pressure. The two chambers were sealed by caps on each end, and in between the two chambers by rubber O-rings either side of the flexible diaphragm. They were then clamped together using tightly secured latches (Figure 51).

### 4.2.1.3 Diaphragm

Separating the air chamber from the fluid chamber is a flexible diaphragm. The deflection of this diaphragm will be controlled by the transmural pressure between the MCL pressure below the diaphragm and the regulated air pressure above the diaphragm. A highly flexible diaphragm is required to provide a wide range of volume changes with variable transmural pressure. Thin latex sheets, commonly used as dental dam, (thickness of 0.18mm, tensile strength of 24MPa) were chosen as the material for the diaphragm. This material is very flexible and durable. Butyl rubber, with a thickness of 0.8mm, was also tested as the diaphragm material, however was not flexible enough to produce the required volume changes in the aorta.
4.2.1.4 Air delivery

To obtain a variable transmural pressure, a compressed air supply must be attached to the compliance chamber air volume. Air delivery was achieved using a wall mounted compressed air source. This was passed through an electro-pneumatic regulator (ITV2030-012BS5, SMC Pneumatics, Brisbane, Australia), which allows a change in air delivery pressure when a change in voltage is applied. A small air chamber (approximate volume of 1L) was used between the regulator and the compliance chamber to dampen the air delivery and obtain smoother pressure curves. A 7mm inside diameter (ID) male tailpiece brass adaptor (Tony Powell hose & fittings, Brisbane, Australia) was used to attach the air delivery tubing to the air chamber via a threaded connection. Compressed air could then be added to increase the air chamber pressure, or vented to decrease air chamber pressure, resulting in a continuously variable transmural pressure. An exploded view of the final compliance chamber design is shown in Figure 52.

4.2.1.5 Data Collection

Monitoring the pressure in the chamber is vital for validating the system. To achieve this, a threaded connection was made into the fluid chamber below the diaphragm to allow for air to be drained from the fluid chamber. A clear PVC luer connector was attached via the threaded hole and was then connected to a 3 way stopcock for pressure monitoring and air drainage. A disposable pressure sensor (TOYODA SD10B-1, Gambro, Lakewood, CO, U.S.A.) and amplifier box (QUT, Brisbane, Australia) with full Wheatstone bridge and op-amp, that converts system pressure to voltage for data acquisition, was attached to the stopcock [3]. This voltage is then sent to a D-Space (DS1104, MI, USA) data acquisition card (DAC) which captures the voltage as a digital value. SIMULINK code then converts this value into a usable form of pressure (mmHg) by using a series of gains and offsets. The numerical value can then be displayed in real time using CONTROLDESK which can display it as a number in a text box or in a graph. The data can then be saved over a selected period of time and later plotted in MATLAB for data analysis. The change in volume in the chamber was measured by recording the volume of water injected into the chamber through a syringe.
4.2.1.6 Testing

The fluid chamber was filled with water to the top of the chamber and the diaphragm with rubber O-rings was put in place. The chamber was then clamped and the air chamber above the diaphragm left open to atmosphere. At this point the diaphragm was flat and the pressure sensor was calibrated to read 0mmHg. Water was then injected in accurate 20mL increments with a syringe into the fluid chamber through the 3 way stopcock. The resulting fluid chamber pressure was recorded after each injection. This was continued until the top of the diaphragm, now in an upwards dome shape, reached the top of the chamber. Water was then taken from the chamber until the zero point was reached. Water was then taken from the chamber in 20mL increments to produce negative transmural pressures until the bottom of the diaphragm, now in a downwards dome shape, reached the bottom of the chamber. The diaphragm was then gradually unloaded, and no elastic hysteresis was observed.

4.2.2 Results

Results were taken from the chamber to produce a transmural pressure vs volume trace. Table 17 presents the resulting pressure when a change in volume is applied. The trend of results is shown in Figure 53. The fluid pressure initially increased slowly when the first 60mL of fluid was added (0mL to 60mL), followed by a steep rise in pressure up until 260mL of fluid was added. Following this, the rate of change of pressure decreased until the maximum volume, 340mL, was reached. When negative pressures were induced, the fluid pressure dropped slowly, followed by a slight increase at about -60mL. Following this, the change in pressure per change in volume was fairly linear until the minimum volume of -200mL was reached.
<table>
<thead>
<tr>
<th>Added volume (mL)</th>
<th>Resulting Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-200</td>
<td>-43.3</td>
</tr>
<tr>
<td>-180</td>
<td>-37.9</td>
</tr>
<tr>
<td>-160</td>
<td>-30.2</td>
</tr>
<tr>
<td>-140</td>
<td>-25.2</td>
</tr>
<tr>
<td>-120</td>
<td>-21</td>
</tr>
<tr>
<td>-100</td>
<td>-16.1</td>
</tr>
<tr>
<td>-80</td>
<td>-11.1</td>
</tr>
<tr>
<td>-60</td>
<td>-6.4</td>
</tr>
<tr>
<td>-40</td>
<td>-2.9</td>
</tr>
<tr>
<td>-20</td>
<td>-1</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>1.4</td>
</tr>
<tr>
<td>40</td>
<td>2.2</td>
</tr>
<tr>
<td>60</td>
<td>3.9</td>
</tr>
<tr>
<td>80</td>
<td>7</td>
</tr>
<tr>
<td>100</td>
<td>12.2</td>
</tr>
<tr>
<td>120</td>
<td>18.3</td>
</tr>
<tr>
<td>140</td>
<td>24.9</td>
</tr>
<tr>
<td>160</td>
<td>31.4</td>
</tr>
<tr>
<td>180</td>
<td>36.7</td>
</tr>
<tr>
<td>200</td>
<td>41.3</td>
</tr>
<tr>
<td>220</td>
<td>45</td>
</tr>
<tr>
<td>240</td>
<td>47.9</td>
</tr>
<tr>
<td>260</td>
<td>50</td>
</tr>
<tr>
<td>280</td>
<td>51.6</td>
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<tr>
<td>300</td>
<td>52.8</td>
</tr>
<tr>
<td>320</td>
<td>53.6</td>
</tr>
<tr>
<td>340</td>
<td>54.3</td>
</tr>
</tbody>
</table>

Table 17 – Resulting pressures produced by adding 20mL increments of fluid to compliance chamber
4.2.3 Discussion

The compliance chamber was tested statically to observe the chamber’s response to a variable transmural pressure. As the fluid pressure was zeroed at the start of the test, the air pressure above the diaphragm was always zero (relative to the fluid pressure) throughout this test. This resulted in the pressure, presented in Figure 53, being represented as the transmural pressure across the diaphragm. Figure 53 was replotted with transmural pressure on the x-axis and volume on the y-axis, so that the variable compliance mechanism can be demonstrated (Figure 54). Figure 54 demonstrated that as the transmural pressure was increased from 0mmHg to approximately 20mmHg, the rate of change of volume decreased. Following this, the rate of change of volume became linear and eventually increased at a transmural pressure of approximately 40mmHg. A similar observation can be made for the results presented for negative transmural pressures. This indicates that if the transmural pressure is changed while the MCL is in operation, the change in aortic volume over the next cardiac cycle will change. As the compliance of the system, $C$, can be found by the change in volume $\Delta V$, divided by the change in pressure, $\Delta P$, this will create a variable compliance.
The largest volume change per unit change in transmural pressure is about the 0mmHg point. This indicates that the compliance of the system will be highest when the diaphragm is flat in the centre of the chamber. The lowest compliance should occur at the points where the transmural pressure vs volume trace is linear. This will occur between -30 and -10mmHg when the diaphragm is domed downwards, and 15 and 40mmHg when the diaphragm is domed upwards.

\[ C = \frac{\Delta V}{\Delta P} \]

4.2.4 Conclusion

Static testing of the flexible diaphragm with changing transmural pressures indicates that a variable compliance can be obtained with this system. The highest level of compliance is expected to occur when the diaphragm is flat at the centre point of the chamber, while the lowest compliance values are expected when the diaphragm is either upwards or downwards domed shaped. Dynamic testing of the chamber is required in a MCL to prove the chamber’s function.
4.3 Simulation of changing the cross sectional area in the compliance chamber

As the transmural pressure across the flexible diaphragm changed, the displacement of the diaphragm also changed. This resulted in the diaphragm changing from a flat shape with a small surface area, to a domed shape with larger surface area. The force generated by the fluid pressure is equal to the fluid pressure multiplied by the surface area. This force is also related to the spring constant (inverse of compliance) of the system, and the deflection of the surface. Due to this relation between the surface area and compliance, the MCL simulation was used to ensure the change in surface area in the dynamic MCL situation has no significant impact on the system compliance.

4.3.1 Methods

The parameters in the MCL simulation were adjusted to represent those currently seen in the physical MCL. The simulation was run and the systemic pressure trace was recorded. The cross sectional area of the aortic compliance chamber was then increased by increasing the radius of the chamber ($r_p$ and $r_v$), with the length of the chamber ($l_p$ and $l_v$) decreased to maintain the same initial air volume ($V_p$) and fluid volume ($V_v$) seen in the first test. To ensure correct results, this was repeated with the cross sectional area of the aortic compliance chamber increased further. The cross sectional area was computed and recorded for each case. The dimensions used in the simulation are presented in Table 18.

<table>
<thead>
<tr>
<th></th>
<th>Current MCL</th>
<th>Increased surface area</th>
<th>Further increased surface area</th>
</tr>
</thead>
<tbody>
<tr>
<td>$l_p$ (mm)</td>
<td>190</td>
<td>47.5</td>
<td>1.9</td>
</tr>
<tr>
<td>$r_p$ (mm)</td>
<td>50</td>
<td>100</td>
<td>500</td>
</tr>
<tr>
<td>$V_p$ (mm$^3$)</td>
<td>1.4923e6</td>
<td>1.4923e6</td>
<td>1.4923e6</td>
</tr>
<tr>
<td>$l_v$ (mm)</td>
<td>10</td>
<td>2.5</td>
<td>0.1</td>
</tr>
<tr>
<td>$r_v$ (mm)</td>
<td>50</td>
<td>100</td>
<td>500</td>
</tr>
<tr>
<td>$V_v$ (mm$^3$)</td>
<td>7.854e4</td>
<td>7.854e4</td>
<td>7.854e4</td>
</tr>
<tr>
<td>Area (mm$^2$)</td>
<td>7.854e3</td>
<td>3.1416e4</td>
<td>7.854e5</td>
</tr>
</tbody>
</table>

Table 18 – Parameters used in simulation for increasing compliance chamber cross sectional area. $l_p$ – length of air chamber pipe, $r_p$ – radius of air chamber pipe, $V_p$ – volume of air chamber pipe, $l_v$ – length of initial fluid chamber pipe, $r_v$ – radius of initial fluid chamber pipe, $V_v$ – volume of initial fluid chamber pipe.
Aortic pressure traces were compared to observe the change in compliance of the system due to changing compliance chamber cross sectional area.

### 4.3.2 Results

Results were taken from the simulation to ensure the changing surface area of the diaphragm would not alter the compliance of the system. Figure 55 presents the systemic pressure trace for each situation. Aortic pulse pressures have systolic and diastolic values of 123 and 81mmHg in each case. Left ventricular, left atrial and mean aortic pressure traces are of the same shape and magnitude for each test.

![Figure 55](image-url)

**Figure 55 – Simulated systemic pressure traces for**
a) **Current MCL**, b) **increased aortic compliance chamber surface area** and c) **Further increased aortic compliance chamber surface area**. LAP – Left atrial pressure, LVP – Left ventricle pressure, AoP – Aortic pressure, MAP – Mean aortic pressure.

### 4.3.3 Discussion and Conclusion

The changing surface area of the diaphragm, produced by changing transmural pressure, was modelled in the MCL simulation. Although the simulation did not accurately replicate the elastic nature of the diaphragm or the shape of deformation, an approximation was be made to observe the system response to changing compliance area. The results presented in Figure 55 demonstrated that no change in
compliance was recorded with a changing cross sectional area of the aortic compliance chamber in a dynamic situation.
4.4 Dynamic diaphragm compliance testing in a mock circulation loop

The diaphragm was tested dynamically to prove that the results obtained in the static compliance chamber testing could be reproduced in a MCL.

4.4.1 Methods

The chamber used for the static compliance chamber testing, presented in section 4.2, was used for dynamic testing in a MCL.

4.4.1.1 Mock Circulation Loop Setup

The previously developed MCL, explained earlier in this thesis, was used for testing the variable compliance chamber. This MCL used clear vertical chambers for the ventricles and atria, while the heart valves are modelled by mechanical check valves. Ventricle contractility was controlled by changing the input voltage to an electro-pneumatic regulator ((ITV2030-012BS5, SMC Pneumatics, Brisbane, Australia), while pulse period and length was controlled with a 3/2 solenoid valve (VT325-035DLS, SMC Pneumatics). The circulation was modelled as rigid piping, with lumped parameter Windkessel compliance elements representing the systemic venous, pulmonary arterial and pulmonary venous compliance. The systemic and pulmonary vascular resistances are also lumped parameter models and are represented by proportional control valves (EPV-375B, HASS Manufacturing, NY, U.S.A.) which can be computer controlled by inputting a voltage to raise or lower the resistance. The MCL was setup using both systemic and pulmonary systems.

4.4.1.2 Mock Circulation Loop Attachment

The mathematical model was used to determine an appropriate sized attachment from the fluid section of the compliance chamber to the MCL. This was achieved via a 25mm inside diameter vertical pipe that protrudes slightly into the base of the fluid chamber to allow a higher surface area for adhesive contact. The MCL attachment end was a 25mm ID threaded connection, which could be attached to the MCL via a T-section with connections for aortic inflow, compliance chamber inflow / outflow, and aortic outflow (Figure 56). The connection pipe from the MCL to the fluid chamber allowed both inflow during systole and outflow during diastole. The
previous aortic Windkessel compliance chamber was removed from the system and the new compliance chamber was attached.

### 4.4.1.3 Data collection

Pressure readings were also taken from the left ventricle and right atrium, while a mean aortic pressure was calculated from the pressure sensor in the fluid chamber. Systemic flows were recorded via a magnetic flow meter (IFC010, KROHNE, Netherlands) attached to the MCL directly after the variable aortic compliance chamber. The systemic vascular resistance (SVR) was calculated using the systemic flow rate (SQ) and mean right atrial (MLAP) and mean aortic (MAP) pressures in the MCL.

\[
\text{Resistance} = \frac{\Delta \text{Pressure}}{\text{Flow rate}}
\]

Therefore,

\[
\text{SVR} = \frac{\text{MAP} - \text{MLAP}}{\text{SQ}}
\]

### 4.4.2 Testing

The compliance chamber was attached to the mock circulation loop. Connections for air injection and data acquisition were made. To ensure that the compliance of the system was being changed by a change in diaphragm transmural pressure, tests were conducted with the diaphragm in three different positions. The MCL was started and contractility and resistance parameters were altered to achieve healthy resting conditions. The first test involved the diaphragm being pushed up near the top of the chamber during systole, resembling a fully stretched upwards dome shape. The second test involved changing the transmural pressure using the compliance chamber air regulator to create a small upwards dome, while the final test involved the diaphragm being in a fairly flat shape in the centre of the chamber.
Following the discrete tests, a transient test was conducted, also simulating healthy resting conditions. This test was carried out to observe the transient effect of changing transmural pressure on the system, and also to observe the system’s response to negative transmural pressures. This was achieved with a starting position where the diaphragm was close to maximum deflection upwards (Figure 57). The compliance chamber regulator voltage was then increased to reduce the diaphragm deflection until the diaphragm was flat. The regulator voltage was continually increased past the flat point until the point of maximum deflection was reached again, this time in a downwards direction. Data were recorded for the systemic pressures to observe the effect of changing diaphragm transmural pressure on the compliance of the system.

![Figure 57 – Diaphragm position in compliance chamber. a) Maximum deflection upwards, b) centre point (flat) and c) Maximum deflection downwards.](image)

4.4.3 Results

Results were taken from the system to verify the compliance chamber’s ability to alter the systemic arterial compliance.

4.4.3.1 Discrete change in compliance

Results for the discrete change in compliance can be seen over one cardiac cycle in Figures 58 to 60. Figure 58, with a large transmural pressure, demonstrated an aortic pulse pressure of 120/75mmHg, while left ventricle systolic and diastolic pressures were 120 and 6mmHg respectively. Mean aortic pressure was 95mmHg while compliance chamber air pressure oscillated between 40 and 82mmHg.
Figure 59 presents the results with a decreased transmural pressure. An aortic pulse pressure of 120/80mmHg is shown, while left ventricle systolic and diastolic pressures are 120 and 7mmHg respectively. Mean aortic pressure was 98mmHg while compliance chamber air pressure oscillated between 75 and 112mmHg.

Figure 60 presents the results with the smallest transmural pressure when the diaphragm was in the centre of the chamber. An aortic pulse pressure of 120/85mmHg is shown, while left ventricle systolic and diastolic pressures are 120 and 7mmHg respectively. Mean aortic pressure was 102mmHg while compliance chamber air pressure oscillated between 85 and 118mmHg.

![Graphs showing pressure tracings and comparisons](image)

**Figure 58** – Results for maximum upwards dome shaped diaphragm showing the a) systemic pressure trace and b) comparison between aortic pressure and compliance chamber air pressure. LVP – left ventricle pressure, AoP – Aortic pressure, MAP – Mean aortic pressure CP – compliance chamber air pressure.

![Graphs showing pressure tracings and comparisons](image)

**Figure 59** – Results for slightly upwards dome shaped diaphragm showing the a) systemic pressure trace and b) comparison between aortic pressure and compliance chamber air pressure. LVP – left ventricle pressure, AoP – Aortic pressure, MAP – Mean aortic pressure CP – compliance chamber air pressure.
4.4.3.2 Transient change in compliance

Results for the transient test are presented over a 35 second period and displayed in Figure 61 while detailed results are presented in Figure 62. Abbreviations in the results include LVP – left ventricle pressure, AoP – aortic pressure, MAP – mean aortic pressure, SQ – systemic flow rate, MSQ – mean systemic flow rate.

These results present normal heart function with continuously changing arterial compliance depending on the surface area of the diaphragm. Tests were conducted using a heart rate of 60bpm, while the left ventricle contractility was kept constant throughout testing. Initial left ventricle contractility and systemic vascular resistance parameters were adjusted to achieve an MAP of 100mmHg, AoP of 120/80mmHg, and a systemic flow rate of between 4.5 and 5L/min. When compliance chamber air pressure was increased, and hence the transmural pressure across the diaphragm decreased, the MAP increased to 105, while the aortic pressure changed to 120/95. Left ventricle systolic and diastolic pressures remained consistent at 120 and 7mmHg respectively. The flow rate initially increased from 4.6 to 5L/min, however decreased to 4.5L/min when the diaphragm was in the centre position.

Following a further increase in compliance chamber pressure past the centre point, the diaphragm was pushed downwards. This resulted in a negative transmural pressure. AoP was seen to return to 120/80mmHg, however MAP did not have time to return to...
the initial value of 95mmHg. Left ventricle pressures remained constant with systolic and diastolic pressures at 120 and 7mmHg respectively. The systemic flow rate initially decreased to 4.35L/min, however increased to a consistent mean value of 4.6L/min after the system had settled.

Figure 61 – Results for transient change in diaphragm deflection, a) systemic pressures and b) systemic flow rates. LVP – Left ventricle pressure, AoP – Aortic pressure, MAP – Mean aortic pressure, SQ – Systemic flow rate, MSQ – Mean systemic flow rate
Figure 62 – Systemic pressure trace for variation in compliance chamber diaphragm deflection for a) full deflection upwards, b) zero deflection (centre) and c) full deflection downwards. LVP – Left ventricle pressure, AoP – Aortic pressure, MAP – Mean aortic pressure

4.4.4 Discussion

For a simulated variable compliance, natural pressures and flows must be replicated in the mock circulation loop. This discussion focuses on the methods used in testing the system, and the results produced.

4.4.4.1 Discrete change in compliance

Pulse pressures of 120/75mmHg, 120/80mmHg and 120/85mmHg were simulated using the variable compliance chamber. By changing the pressure above the flexible diaphragm, the transmural pressure across the diaphragm is altered. This created a variable change in volume per change in pressure, as demonstrated in Figure 54.
transmural pressure over one cardiac cycle for each discrete test can be plotted to demonstrate the range of compliance values achievable in this chamber (Figure 63).

![Graph of transmural pressure over one cardiac cycle for each discrete test](image)

**Figure 63 – Transmural pressure traces for a) diaphragm in full upwards dome position, b) diaphragm in mid-dome position and c) diaphragm flat in centre of chamber.**

Pressure spikes were seen in the transmural pressure during the left ventricle isovolumetric relaxation period. This was possibly due to the aorta emptying fluid, which resulted in the air volume above the fluid chamber increasing. The increased volume in the air chamber produced a slight reduction in air pressure, causing the regulator to inject small amounts of air to compensate, resulting in small pressure spikes in the air pressure.

By observing the minimum and maximum transmural pressures for each result shown in Figure 60, the fluid chamber volume at these points can be approximated using Figure 54. An example of this is shown in Figure 64, where the change in volume is

108
calculated for the diaphragm in the full upwards dome position test. If the change in pressure in the aorta is known from the pulse pressures, and the change in aortic volume for each cardiac cycle is known, the compliance of the chamber can be found (Table 19).

### Table 19 – Calculation of compliance values for variable compliance chamber. \( P_P \) – Pulse pressure, \( \Delta A_o P \) – change in aortic pressure, \( \Delta P_T \) – Change in transmural pressure, \( \Delta V_T \) – Change in transmural volume, \( \Delta A_o V \) – Change in aortic volume, \( C_c \) – Calculated aortic compliance.

<table>
<thead>
<tr>
<th>( P_P ) (mmHg)</th>
<th>( \Delta A_o P ) (mmHg)</th>
<th>( \Delta P_T ) (mmHg)</th>
<th>( \Delta V_T ) (mL)</th>
<th>( \Delta A_o V ) (mL)</th>
<th>( C_c ) (mL/mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>120/75</td>
<td>45</td>
<td>43/24</td>
<td>209/137</td>
<td>72</td>
<td>1.6</td>
</tr>
<tr>
<td>120/80</td>
<td>40</td>
<td>11/-6</td>
<td>95/-58</td>
<td>153</td>
<td>3.8</td>
</tr>
<tr>
<td>121/85</td>
<td>36</td>
<td>5/-15</td>
<td>67/-96</td>
<td>163</td>
<td>4.5</td>
</tr>
</tbody>
</table>

The results shown in Table 19 demonstrate a large range of achievable aortic compliance values; however the change in volume for one cardiac cycle cannot be higher than the left ventricle stroke volume for a constant flow rate. At a systemic flow rate of 5L/min and a heart rate of 60 beats per minute, the stroke volume is approximately 83mL. These results indicated that the range of calculated compliance values was not correct, as the aortic change in volume was estimated at up to 163mL.
The inaccurate calculated volume changes were due to the dynamic nature of the system. The transmural pressure vs volume curve (Figure 54) was derived using a static chamber. For the transmural pressures recorded during dynamic testing, the diaphragm may not have had time to reach the same systolic position seen in the static test before the start of diastole. This resulted in smaller volume changes per cardiac cycle in the dynamic test. An improved method of measuring aortic compliance chamber volume changes would improve the accuracy calculating the range of compliance values produced by the chamber. To provide a more accurate range of the aortic compliance values produced by the variable compliance chamber, the change in volume was assumed to be equal to the left ventricle stroke volume, 83mL. The compliance was then be found by dividing this change in volume by the change in aortic pressure produced for each test, and compared with the previously calculated compliance values (Table 20). The compliance chamber produced a range of measured compliance values of 1.84 - 2.31mL/mmHg, much smaller than the compliance range previously calculated. The range of vascular compliance values could be increased with further investigation into diaphragm material selection or fine control of the electropneumatic regulator pressure to produce a larger change in transmural pressure over the cardiac cycle.

<table>
<thead>
<tr>
<th>Pp (mmHg)</th>
<th>∆P (mmHg)</th>
<th>∆V (mL)</th>
<th>Cm (mL/mmHg)</th>
<th>Ce (mL/mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>120/75</td>
<td>45</td>
<td>83</td>
<td>1.84</td>
<td>1.6</td>
</tr>
<tr>
<td>120/80</td>
<td>40</td>
<td>83</td>
<td>2.08</td>
<td>3.8</td>
</tr>
<tr>
<td>121/85</td>
<td>36</td>
<td>83</td>
<td>2.31</td>
<td>4.5</td>
</tr>
</tbody>
</table>

Table 20 – Improved calculation of achievable compliance values for the variable compliance chamber. Pp – Pulse pressure, ∆P – Change in pressure, ∆V - Change in volume, Cm – measured compliance values, Ce – calculated compliance values.

4.4.4.2 Transient change in compliance

A transient test was completed to observe the system’s transient response to a change in diaphragm transmural pressure. While the LVP demonstrated small spikes during systole, possibly due to water hammer from the mechanical valves, values for systolic and diastolic LVP consistently showed an accurate representation of normal heart function under varying levels of compliance. Systolic times of 40% of the cardiac
cycle produced fairly accurate pressure waveforms that resemble those seen in the literature for a natural heart.

Measured compliance values were calculated from the pressure and flow results by finding the change in aortic pressure and the stroke volume from the flow rate. The aortic compliance varied from approximately 1.87mL/mmHg, at the start and end of testing, to 3mL/mmHg in the middle of the test.

The AoP had a slight lag from the LVP due to the inertiance of the fluid between the left ventricle chamber and the aortic compliance chamber. An accurate sawtooth waveform was observed for most tests. When the diaphragm was positioned in the centre point of the compliance chamber, the AoP was seen to increase slightly before systole due to the air pressure in the compliance chamber (Figure 62b). This result was not a physiologically accurate representation of the natural cardiovascular system. This is due to the regulator delivering a small amount of compressed air during diastole, which resulted in pressure being added to the system, similar to an aortic balloon pump. A valve could be used to prevent this extra pressure being added during diastole and promote normal aortic function.

The flow rate was shown to oscillate around 4.6L/min for each test. The increase in flow rate, which occurred while pushing the diaphragm from the maximum upwards deflection point to the flat centre point, occurred due to fluid being pushed out of the aorta and into the circulation. Following this, the centre point was reached and held for a small time, allowing the flow rate to settle to the initial value. When the diaphragm was then pushed down to maximum downwards deflection, the flow rate was initially increased again due to fluid being pushed out of the chamber again. Once more, the flow rate returned to 4.6L/min after a short settling period.

The systemic vascular resistance, calculated by subtracting MLAP from MAP and dividing by the flow rate, was noted to be approximately 1500dynes for all tests. This equates to 1.125mmHg.s/mL, which is an accurate representation of that seen in the literature (Table 21).
By reducing the pressure above the diaphragm, the upward deflection of the diaphragm is increased. If the starting point of the diaphragm is in the centre of the chamber, giving a flat diaphragm, decreasing the air pressure will result in a shift of the transmural pressure along the transmural pressure vs volume curve, and alter the compliance of the system. This also results in an increased aortic volume, which in turn decreases the volume in other sections of the mock circulation loop. End diastolic and systolic volumes for the aorta vary when using this compliance chamber. This result is not physiologically accurate, as the end diastolic volume of the aorta should remain constant with a change in compliance, while end systolic volume should decrease with an increasing stiffness.

<table>
<thead>
<tr>
<th>Author</th>
<th>Systemic Resistance (mmHg.s/mL)</th>
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</thead>
<tbody>
<tr>
<td>Rosenborg (1981)</td>
<td>1.3576</td>
</tr>
<tr>
<td>Marcus (1994)</td>
<td>1.04</td>
</tr>
<tr>
<td>Mitsui (1998)</td>
<td>1.7</td>
</tr>
<tr>
<td>Baloa (2001)</td>
<td>1.83</td>
</tr>
<tr>
<td>Vollkron (2002)</td>
<td>1.2</td>
</tr>
<tr>
<td>Goodwin (2004)</td>
<td>1.06</td>
</tr>
<tr>
<td>Pantalos (2004)</td>
<td>0.9136</td>
</tr>
<tr>
<td>Timms (2005)</td>
<td>1.097</td>
</tr>
<tr>
<td>Korakianitis (2006)</td>
<td>1.073</td>
</tr>
<tr>
<td>Mock Circulation loop with variable compliance</td>
<td>1.125</td>
</tr>
</tbody>
</table>

Table 21 - Comparison of systemic resistance between previous literature and calculated value from the mock circulation loop.

The change in air volume in the compliance chamber did not significantly alter the compliance of the chamber directly. The air volume was altered by a maximum of approximately 20%, producing a negligible change in arterial compliance.

**4.4.5 Conclusion**

Dynamic testing of the variable compliance chamber in a MCL was successful in simulating a small range of aortic compliance values in a healthy resting condition. Accurate systemic pressure traces were produced with compliance values varying
from 1.87 to 3mL/mmHg (pulse pressures of 120/75 to 120/95mmHg) by adjusting
the transmural pressure across the diaphragm.
4.5 Conclusion

The aim of this chapter was to produce a variable compliance chamber that could be easily controlled and replicate many different levels of arterial compliance. Simulations were carried out using the MCL model to ensure the cross sectional area of the compliance chamber had no effect on the rig’s haemodynamic results. A physical prototype was constructed using a flexible diaphragm to provide a variable transmural pressure in the chamber.

A previously developed mock circulation loop was used to test the new variable compliance chamber. This allowed a quick and accurate analysis of the chamber’s function by using the pressure and flow sensors already present in the physical system.

When the air pressure in the compliance chamber was adjusted by altering the compliance chamber regulator voltage, the transmural pressure across the diaphragm was altered and thus initial deflected position. This resulted in a shift along the transmural pressure vs volume curve for the system due to the non-linear properties of the diaphragm, which caused a change in aortic pulse pressures. A variable level of compliance was produced, capable of replicating aortic pulse pressures varying from 120/75mmHg to 120/95mmHg with a compliance range from 1.84 to 3mL/mmHg by adjusting the computer-controlled regulator. The required range of compliance values, approximately 0.5 to 7 mL/mmHg, was not capable of being produced by this chamber. However, with further development of the chamber, obtaining an increased range of compliance values is possible.

By improving this prototype device by investigating more appropriate material selection for the diaphragm, a final variable compliance chamber device can be achieved. This device will provide an accurate, repeatable method of adjusting the arterial compliance in a mock circulation loop while speeding up and improving the results of cardiovascular device testing procedures. The development of this chamber resulted in a more compact mechanism of representing arterial compliance, and will assist in the design of a compact MCL with variable compliance.
Chapter 5
Experimental Physical Mock Circulation Loop Design

5.1 Aims

By using the results obtained in the mathematical model of a mock circulation loop (MCL), a new MCL was developed to produce more accurate pressure and flow waveforms by improving pipe lengths and diameters to suit the range of frequencies being tested in VAD evaluation. The new MCL was required to accurately mimic the human circulatory system with features such as compliance, resistance, inertiance, contractility, pressures and flows that can be seen in a human model. This design was based on a previous model designed by Timms et al. (2005) [3]. The variable compliance chamber presented in Chapter 4 allowed for easy manipulation of arterial compliance while providing a much smaller MCL. This chapter outlines the design of the MCL, while the actual construction and validation of the device is beyond the scope of this study.

5.2 Methods

5.2.1 The Heart

The four heart chambers were represented by clear vertical pipes, with a tee section connecting the inflow, heart chamber and outflow. The four heart valves; the mitral valve, aortic valve, tricuspid vale and pulmonary valve, were all simulated by clear mechanical swing check valves (ALSCO, Lithia Springs, GA, U.S.A.) to prevent backflow (Figure 65).

5.2.2 Contractility

The contractility of the ventricles was mimicked by an injection of compressed air into the vertical chambers. By changing the voltage supplied to an electro-pneumatic...
regulator (ITV2030-012BS5, SMC Pneumatics, Brisbane, Australia), the amount of air delivered to the ventricle chamber could be increased or decreased, simulating a change in contractility. The compressed air was required to pass through a solenoid valve (VT325-035DLS, SMC Pneumatics) after the regulator and before the ventricle chamber. This solenoid valve was usually switched to open for 40% of the cardiac cycle, indicating a 40% systolic period, however this value can be changed. The remainder of the cardiac cycle was completed by venting the air from the ventricle to atmosphere, allowing for passive filling of the ventricle chamber during diastole.

An atrial kick was simulated in a similar way to the ventricle contraction. A systolic duration of 20% of the cardiac cycle is applied at a phase delay of 80% of the cardiac cycle, compared to the start of ventricle contraction. The contractility of the atrium is controlled using a manual regulator rather than the computer controlled system seen in the ventricles.

5.2.3 Blood Volume and Flow

To obtain an accurate representation of the human cardiovascular system, the volume for each MCL segment is required to accurately represent its natural counterpart. Values from the literature of an adult circulation were used for selecting pipe lengths and diameters in the new MCL. The MCL simulation was also used to assist with choosing appropriate pipe dimensions, shown in Table 22, for accurate volume representation. For situations such as congestive heart failure, where a higher left ventricle volume (LVV) is usually present, the MCL can be filled to a higher level to increase the LVV. Clear PVC pipe was chosen to construct the majority of the MCL so that the flow could be visualised throughout the system. Water will be used as the fluid in the MCL.

Recording the flow of water through the MCL is vital to in vitro VAD testing. Although the MCL is a closed loop system, a flow-meter is required on both the systemic and pulmonary sides of the MCL as a change in heart function on one side of the system does not instantly affect the other side. The systemic flow-meter should be placed after the aortic compliance chamber to record a smoother waveform than that seen between the left ventricle and the aortic compliance chamber. As the systemic
## Table 22—Physical mock circulation loop volumes compared to those seen in the literature for the unstressed volume of an average male. Note that heart volumes are representative of end diastolic volume.

<table>
<thead>
<tr>
<th>Anatomical Segment</th>
<th>Value in Literature (mL) [90]</th>
<th>Pipe Diameter (mm)</th>
<th>Pipe Length (mm)</th>
<th>Pipe Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left Heart</strong></td>
<td>50</td>
<td>32 50</td>
<td>50 20</td>
<td>40 39</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total = 79</td>
</tr>
<tr>
<td><strong>Systemic Arterial</strong></td>
<td>715</td>
<td>25 2.6 100 2.04</td>
<td>500 60 70</td>
<td>245 0.05 471 0.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total = 716</td>
</tr>
<tr>
<td><strong>Systemic Venous</strong></td>
<td>2785</td>
<td>25 25 150</td>
<td>600 35 35</td>
<td>294 17 2474</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total = 2785</td>
</tr>
<tr>
<td><strong>Right Heart</strong></td>
<td>50</td>
<td>32 50</td>
<td>50 20</td>
<td>40 39</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total = 79</td>
</tr>
<tr>
<td><strong>Pulmonary Arterial</strong></td>
<td>90</td>
<td>25 25 100 4.4</td>
<td>50 65 5 70</td>
<td>24 32 39 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total = 96</td>
</tr>
<tr>
<td><strong>Pulmonary Venous</strong></td>
<td>490</td>
<td>25 25 100</td>
<td>470 40 30</td>
<td>231 20 235</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total = 486</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4180</td>
<td>- -</td>
<td>- -</td>
<td>4241</td>
</tr>
</tbody>
</table>
resistance is much higher than the pulmonary resistance a 15mm orifice size was appropriate for the systemic flow-meter, however a 25mm orifice size was required for the pulmonary flow-meter. Due to the low flow rates in the MCL, a magnetic flow meter was required to produce accurate results. Both of these orifice sizes are available in a magnetic inductive flow meter (OPTIFLUX 1010 C/D, Krohne, Duisburg, Germany) with an error of less than 1% present at a flow rate of 5L/min. To convert this signal to a voltage, a signal converter can be used (IFC010C/D, Krohne, Duisburg, Germany).

As the device is required for teaching purposes, it was required to be portable. The overall size of the MCL was considered during the design phase, and was reduced to a maximum width, depth and height of 537mm, 635mm and 374mm respectively.

5.2.4 Compliance

The compliance of the MCL was required to accurately mimic the values seen in the human body. As the arterial compliance has a significant impact on patient haemodynamics, a variable arterial compliance was desired. This was achieved by using the variable compliance chamber developed and explained in Chapter 4 (Figure 66). Resting values for systemic arterial and pulmonary arterial compliance were chosen based on those seen in the human circulatory system and reported in the literature as 1.5mL/mmHg and 3mL/mmHg respectively, however these values can vary depending on the level of arterial stiffness due to heart and vascular disease.

As the venous compliance is not required to be variable and has a much larger value of compliance than the arterial segments, a different design of compliance chamber was required. As the mock circulation loop is required to be compact, the large Windkessel chamber seen in previous mock circulation loop designs is not appropriate. The use of a spring to simulate compliance has been successful, and the design used by Arabia et al. (1984) was compact and reliable. The basic principles of this design were used to develop systemic and pulmonary venous compliance chambers.
Spring constants were found using the following equation obtained from Woodruff et al. (1997) –

\[ K = \frac{A_c^2}{C} \]

Where \( K \) is the spring constant, \( A_c \) is the cross-sectional area of the compliance chamber, and \( C \) is the compliance.

Using desired values for systemic venous and pulmonary venous compliance based on values seen in the literature (20mL/mmHg and 5mL/mmHg respectively), and the cross sectional area of the compliance chamber pipe, the spring constants were calculated.

\[ K_{\text{systemic venous}} = 168 \text{ N/m} \quad \quad K_{\text{pulmonary venous}} = 674 \text{ N/m} \]

Allowing for maximum pressure changes of 10mmHg in both the systemic and pulmonary venous chambers, the maximum deflection of each spring could be calculated to give the desired spring length using Hooke’s law.

\[ \Delta x_{\text{systemic venous}} = 50 \text{ mm} \quad \quad \Delta x_{\text{pulmonary venous}} = 13 \text{ mm} \]

A loose, rubber diaphragm is used to separate the MCL fluid from the spring. These springs are seated on two cone shaped objects, which are attached to the top of the chamber and to the rubber diaphragm, in order to centre the spring in the chamber. A port is added to the bottom of the chamber which allows connection to the MCL for compliance chamber inflow and outflow. Luer connectors are attached to the compliance chamber both above and below the diaphragm to measure the MCL and air pressure in both locations. The luer connector below the diaphragm is attached as close to the diaphragm as possible, to allow the fluid chamber to be de-aired prior to testing. The top and bottom chamber components are held together tightly with latches and hooks, and sealed with a combination of the flexible diaphragm and rubber O-rings. Clear PVC is used as the material for most of the compliance chamber components to allow visualisation of how compliance works in the human body. The male tailpiece barbed connection for air delivery and latches are made of brass, while the O-rings are made of 0.8mm butyl rubber. Both variable and constant spring compliance chambers are shown in Figure 66.
Figure 66 – Models of a) Arterial compliance chamber, b) section view through centre of arterial compliance chamber, c) venous compliance chamber, d) section view through centre of venous compliance chamber.

5.2.5 Resistance

The resistance of each section in the MCL is determined by the length and cross-sectional area of the pipe. As seen in the literature, the systemic and pulmonary vascular resistance can change quite dramatically, giving the need for a variable level of resistance. This was achieved by the use of proportional control valves (Figure 67) placed directly after the flow-meter on the systemic and pulmonary side. The resistance of each side of the MCL is then given by the characteristic resistance of each section of pipe (Table 23) added to the resistance applied by the proportional control valve. These valves are controlled by supplying a voltage to the valve, which raises or lowers an occluder. A flanged connection on both the inflow and outflow of
the valve allows for connection to the MCL. Port sizes vary according to model and can be found in sizes ranging from \(\frac{1}{4}''\) to \(\frac{3}{4}''\). A port size of 3/8" (EPV-375B, HASS Manufacturing, NY, U.S.A.) was chosen for the systemic side while the largest size of \(\frac{3}{4}''\) (EPV-500B, HASS Manufacturing) was selected for the pulmonary side to allow for a lower resistance. While the venous resistances are much lower in the MCL compared to that in the literature, the arterial resistance can be increased to compensate.

### 5.2.6 Inertiance

The inertial effects of the human body were accounted for by selecting the appropriate pipe lengths and diameters. As inertance has the greatest effect on a system when high pressure changes are present, the inertance in the arterial segments are of great importance. Calculated inertance values are shown in Table 24.

### 5.2.7 Valve insufficiency

Heart valve regurgitation is simulated in the mitral and aortic valves and shown in Figure 68. This was achieved in the mitral valve by a connection to the left ventricle which passes through a computer controlled solenoid valve (VX2360-04-5D1, SMC Pneumatics, Brisbane, Australia) and one way check valve into the left atrium. The solenoid valve was implemented to switch the valve regurgitation on or off, while the one way check valve was to ensure MCL fluid does not flow from the atrium to the ventricle without passing through the mitral valve. Aortic valve regurgitation is simulated by a connection to the aorta which passes through another solenoid valve.
<table>
<thead>
<tr>
<th>Anatomical Segment</th>
<th>Value in Literature (mmHg.s.mL⁻¹) [3, 4, 18, 23, 25, 33, 36, 74, 75]</th>
<th>Pipe Diameter (mm)</th>
<th>Pipe Length (mm)</th>
<th>MCL Resistance (mmHg.s.mL⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left atrium Valve</td>
<td>0.003 - 0.01</td>
<td>32</td>
<td>25</td>
<td>6.5e⁻⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12</td>
<td>50</td>
<td>6.59e⁻⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total 0.00066</td>
</tr>
<tr>
<td>Left Ventricle Valve</td>
<td>0.008 - 0.04</td>
<td>32</td>
<td>25</td>
<td>6.5e⁻⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12</td>
<td>50</td>
<td>6.59e⁻⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total 0.00066</td>
</tr>
<tr>
<td>Systemic Arterial</td>
<td>0.9 - 1.83</td>
<td>25</td>
<td>500</td>
<td>3.5e⁻⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 - 12</td>
<td>70</td>
<td>9.22e⁻⁴ – 19.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total 0.00127 – 19.12</td>
</tr>
<tr>
<td>Systemic Venous</td>
<td>0.075 – 0.3</td>
<td>25</td>
<td>600</td>
<td>4.2e⁻⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total 0.00042</td>
</tr>
<tr>
<td>Right Atrium Valve</td>
<td>0.003 – 0.01</td>
<td>32</td>
<td>25</td>
<td>6.5e⁻⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12</td>
<td>50</td>
<td>6.59e⁻⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total 0.00066</td>
</tr>
<tr>
<td>Right Ventricle Valve</td>
<td>0.003 – 0.04</td>
<td>32</td>
<td>25</td>
<td>6.5e⁻⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12</td>
<td>50</td>
<td>6.59e⁻⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total 0.00066</td>
</tr>
<tr>
<td>Pulmonary Arterial</td>
<td>0.11 – 0.312</td>
<td>25</td>
<td>50</td>
<td>3.5e⁻⁵</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 - 12</td>
<td>70</td>
<td>9.22e⁻⁴ – 19.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total 0.00096 – 19.12</td>
</tr>
<tr>
<td>Pulmonary Venous</td>
<td>0.006 - 0.045</td>
<td>25</td>
<td>470</td>
<td>3.3e⁻⁴</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total 0.00033</td>
</tr>
</tbody>
</table>

Table 23 – Resistance of each segment for the physical mock circulation loop compared to those seen in the literature
<table>
<thead>
<tr>
<th>Anatomical Segment</th>
<th>Value in Literature (mmHg.s².mL⁻¹) [4, 18, 25, 33, 74, 75]</th>
<th>Pipe Diameter (mm)</th>
<th>Pipe Length (mm)</th>
<th>Inertiance (mmHg.s².mL⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic Arterial</td>
<td>0.0007 - 0.02</td>
<td>25</td>
<td>500</td>
<td>0.00764</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td>70</td>
<td>0.004642</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total 0.01228</td>
</tr>
<tr>
<td>Pulmonary Arterial</td>
<td>0.0017 - 0.01575</td>
<td>25</td>
<td>50</td>
<td>0.000764</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td>70</td>
<td>0.004642</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Total 0.005407</td>
</tr>
</tbody>
</table>

Table 24– Inertiance of each segment for the physical mock circulation loop compared to those seen in the literature

and check valve into the left ventricle. The solenoid valves included a 10mm port size, while the magnitude of the valve regurgitation can be altered by adjusting the resistance of the pipe between the two mock loop connections by increasing the connecting pipe length or decreasing the connecting pipe radius.

5.2.8 Septal defect

Septal defects were achieved between the atria and ventricles by the same piping connections to the heart chambers as the valve regurgitation connections. With computer controlled solenoid valves (VX2360-04-5D1, SMC Pneumatics,) the valve regurgitation could be switched off and a septal defect can be added. By opening either the atrial or ventricular septal defect solenoid valve, a defect is created and flow will travel between the two heart chambers. The magnitude of the septal defect can be adjusted by altering the resistance between the two heart chambers. Septal defect connections and the entire heart chamber assembly are shown in Figures 69 and 70 respectively.

5.2.9 Ventricular assistance

As one of the primary aims for developing the MCL is for in vitro VAD testing, the MCL-VAD interface is required to be replicated as accurately as possible. The connections made to the heart chambers for the valve regurgitation and septal defects are used in conjunction with small mechanical swing check valves to obtain cannulation to the left atrium, left ventricle, ascending aorta, right atrium, right
ventricle and pulmonary artery. By changing which solenoid valve is open, the site of VAD inflow cannulation can be altered. The inside diameter of the tubing from the MCL to the VAD was selected with an inside diameter of 15mm to allow for a large cannula, often used in pulsatile VAD support to promote sufficient VAD passive filling during diastole. To represent a wide range of cannula sizes, the resistance of the tube can be altered by either compressing the tubing or replacing it with tubing of a smaller inside diameter. Due to the wide range of VAD cannulae currently available, the tubing to the MCL was easily removable so that the cannulation can be changed to suit the VAD being tested.

5.2.10 Control

As the MCL is required for both VAD testing and teaching purposes, it was vital that the parameters which control the system could be easily changed. This was achieved through the use of a data acquisition card (DAC) (Figure 71), which collects real time data from the MCL and outputs control signals to the ventricle regulators, compliance chamber regulators, proportional control valves, and solenoids.

Twelve analog inputs to the DAC (LabJack UE9, Labjack, Lakewood, CO, U.S.A) from the MCL include pressure sensors from the left atrium, left ventricle, aorta, systemic venous chamber, right atrium, right ventricle, pulmonary artery and
pulmonary venous chamber. Flows from both sides of the MCL and left and right ventricular volumes complete the list of analog inputs. Six analog outputs from another DAC (LabJack U3-LV, Labjack) to the MCL include regulators to the left ventricle, right ventricle, aortic compliance chamber, pulmonary artery compliance chamber and resistance valves for both the systemic and pulmonary sides. One DAC combined with one terminal board (CB15, Labjack) allows for 16 analog inputs. Output blocks (LJTick-DAC, Labjack) connect to two of the DAC terminal board inputs and can produce two output signals of ±10 volts. Therefore to obtain twelve analog inputs, one DAC and one terminal board are required, while the seven analog outputs can be supplied by another DAC, one terminal board, and 4 output blocks.

The graphical user interface (GUI) for the MCL included three windows (Figure 72). The main window represented a schematic of the MCL with changeable parameter values to control the system. This window also included real-time pressure and flow measurements taken from the MCL and displayed in the appropriate area. For example, the left ventricle pressure (LVP) would be displayed in the LV box, and controlled by the value entered into the LV Voltage box. A list of features from the main screen and their description are given below. The secondary window was used for data collection and observation. Real-time graphs of systemic and pulmonary pressures, flows, resistance, ventricle volumes and input values were displayed and saved if required in this window. The third window allowed the user to zero all MCL inputs such as pressures, flows and volumes while setting up the MCL. This window also included adjustable gain and offset parameters for the MCL inputs. A flow diagram of the MCL control is shown in Figure 73, with a list of features displayed in Table 25.

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Figure 72 – MCL GUI including a) main window with MCL control and real-time pressure and flow measurements, b) data collection window with pressure and flow graphs and c) calibration window to allow the user to set the gains and offsets for input signals.

Figure 73 – Flow diagram of MCL control
<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA</td>
<td>Displays the systemic atrial pressure</td>
</tr>
<tr>
<td>LV</td>
<td>Displays the systemic ventricle pressure and volume</td>
</tr>
<tr>
<td>Ao</td>
<td>Displays the systemic arterial pressure</td>
</tr>
<tr>
<td>SQ</td>
<td>Displays the systemic flow rate</td>
</tr>
<tr>
<td>SVR</td>
<td>Displays the systemic vascular resistance</td>
</tr>
<tr>
<td>SV</td>
<td>Displays the systemic venous pressure</td>
</tr>
<tr>
<td>RA</td>
<td>Displays the pulmonary atrial pressure</td>
</tr>
<tr>
<td>RV</td>
<td>Displays the pulmonary ventricle pressure and volume</td>
</tr>
<tr>
<td>PA</td>
<td>Displays the pulmonary arterial pressure</td>
</tr>
<tr>
<td>PQ</td>
<td>Displays the pulmonary flow rate</td>
</tr>
<tr>
<td>PVR</td>
<td>Displays the pulmonary vascular resistance</td>
</tr>
<tr>
<td>PV</td>
<td>Displays the pulmonary venous pressure</td>
</tr>
<tr>
<td>LA Reg</td>
<td>Manual regulator controlling the contractility of the left atrium</td>
</tr>
<tr>
<td>RA Reg</td>
<td>Manual regulator controlling the contractility of the right atrium</td>
</tr>
<tr>
<td>LV Voltage</td>
<td>Inputs this value to the automatic regulator to change the left ventricular contractility</td>
</tr>
<tr>
<td>AoC Voltage</td>
<td>Inputs this value to the automatic regulator to change the aortic compliance</td>
</tr>
<tr>
<td>SVR Voltage</td>
<td>Inputs this value to the systemic proportional control valve to change the systemic vascular resistance</td>
</tr>
<tr>
<td>RV Voltage</td>
<td>Inputs this value to the automatic regulator to change the right ventricular contractility</td>
</tr>
<tr>
<td>PAC Voltage</td>
<td>Inputs this value to the automatic regulator to change the pulmonary arterial compliance</td>
</tr>
<tr>
<td>PVR Voltage</td>
<td>Inputs this value to the pulmonary proportional control valve to change the pulmonary vascular resistance</td>
</tr>
<tr>
<td>MV</td>
<td>Mitral valve - only allows forward flow from the left atrium to the left ventricle</td>
</tr>
<tr>
<td>AoV</td>
<td>Aortic valve – only allows forward flow from the left ventricle to the aorta</td>
</tr>
<tr>
<td>TrV</td>
<td>Tricuspid valve – only allows forward flow from the right atrium to the right ventricle</td>
</tr>
<tr>
<td>PuV</td>
<td>Pulmonary valve – only allows forward flow from the right ventricle to the pulmonary artery</td>
</tr>
<tr>
<td>S1</td>
<td>Solenoid valve controlling the systolic period and phase delay of left atrial contraction</td>
</tr>
<tr>
<td>S2</td>
<td>Solenoid valve controlling the systolic period and phase delay of left ventricle contraction</td>
</tr>
<tr>
<td>S3</td>
<td>Solenoid valve controlling the duration of air injection into the aortic compliance chamber</td>
</tr>
<tr>
<td>S4</td>
<td>Solenoid valve controlling the systolic period and phase delay of right atrial contraction</td>
</tr>
<tr>
<td>S5</td>
<td>Solenoid valve controlling the systolic period and phase delay of left ventricle contraction</td>
</tr>
<tr>
<td>S6</td>
<td>Solenoid valve controlling the duration of air injection into the pulmonary arterial compliance chamber</td>
</tr>
<tr>
<td>S7</td>
<td>When switched to open with a check box, allows flow from right atrium. Combined with an open S8 produces an atrial septal...</td>
</tr>
</tbody>
</table>
defect, or combined with an open S9 produces tricuspid valve regurgitation.

<table>
<thead>
<tr>
<th>S8</th>
<th>When switched to open with a check box, allows flow from left atrium. Combined with an open S7 produces an atrial septal defect, or combined with an open S10 produces mitral valve regurgitation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>S9</td>
<td>When switched to open with a check box, allows flow from right ventricle. Combined with an open S10 produces a ventricular septal defect, or combined with an open S7 produces tricuspid valve regurgitation or when combined with an open S11 produces pulmonary valve regurgitation.</td>
</tr>
<tr>
<td>S10</td>
<td>When switched to open with a check box, allows flow from left ventricle. Combined with an open S9 produces a ventricular septal defect, or combined with an open S8 produces mitral valve regurgitation or when combined with an open S12 produces aortic valve regurgitation.</td>
</tr>
<tr>
<td>S11</td>
<td>When switched to open with a check box, allows flow from pulmonary artery. Combined with an open S9 produces pulmonary valve regurgitation.</td>
</tr>
<tr>
<td>S12</td>
<td>When switched to open with a check box, allows flow from aorta. Combined with an open S10 produces aortic valve regurgitation.</td>
</tr>
<tr>
<td>MCL START</td>
<td>Starts the mock circulation loop</td>
</tr>
</tbody>
</table>

Table 25– List of features in MCL control

### 5.2.11 Simulation of Cardiac Conditions

The mock circulation loop is required to be able to accurately reproduce a variety of cardiac conditions. The main examples of this are different degrees of rest, exercise and heart failure, with the haemodynamic parameters for these conditions listed in Table 26.

By changing the contractility, resistance and compliance of the MCL, the conditions of rest, exercise and heart failure can all be reproduced using the MCL. Conditions of an atrial septal defect, ventricular septal defect, mitral valve regurgitation and aortic valve regurgitation can all be achieved by opening a solenoid valve.
<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Exercise</th>
<th>Left Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVP&lt;sub&gt;sys&lt;/sub&gt; (mmHg)</td>
<td>120</td>
<td>160</td>
<td>80</td>
</tr>
<tr>
<td>LVP&lt;sub&gt;dias&lt;/sub&gt; (mmHg)</td>
<td>7</td>
<td>7</td>
<td>15-25</td>
</tr>
<tr>
<td>AoP&lt;sub&gt;sys&lt;/sub&gt; (mmHg)</td>
<td>120</td>
<td>160</td>
<td>75-80</td>
</tr>
<tr>
<td>AoP&lt;sub&gt;dias&lt;/sub&gt; (mmHg)</td>
<td>80</td>
<td>80</td>
<td>45-50</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>95</td>
<td>115</td>
<td>55-65</td>
</tr>
<tr>
<td>LAP (mmHg)</td>
<td>3-13</td>
<td>16</td>
<td>25</td>
</tr>
<tr>
<td>MCP (mmHg)</td>
<td>7</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>SQ (L/min)</td>
<td>5</td>
<td>10</td>
<td>2.5-3</td>
</tr>
<tr>
<td>LVV (mL)</td>
<td>50-133</td>
<td>50-133</td>
<td>150-192</td>
</tr>
<tr>
<td>RVP&lt;sub&gt;sys&lt;/sub&gt; (mmHg)</td>
<td>25</td>
<td>35</td>
<td>40</td>
</tr>
<tr>
<td>RVP&lt;sub&gt;dias&lt;/sub&gt; (mmHg)</td>
<td>4</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>PAP&lt;sub&gt;sys&lt;/sub&gt; (mmHg)</td>
<td>25</td>
<td>35</td>
<td>37</td>
</tr>
<tr>
<td>PAP&lt;sub&gt;dias&lt;/sub&gt; (mmHg)</td>
<td>10</td>
<td>10</td>
<td>26</td>
</tr>
<tr>
<td>MPAP (mmHg)</td>
<td>15</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
<td>2-7</td>
<td>15</td>
<td>15-18</td>
</tr>
<tr>
<td>RQ (L/min)</td>
<td>5</td>
<td>10</td>
<td>2.5-3</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>60</td>
<td>120</td>
<td>60</td>
</tr>
</tbody>
</table>

Table 26 – Approximate parameters used to determine conditions of rest, exercise and heart failure. LVPsys - Systolic left ventricle pressure, LVPdias - Diastolic left ventricle pressure, AoPsys - Systolic aortic pressure, AoPdias – Diastolic aortic pressure, MAP – Mean aortic pressure, LAP – Left atrial pressure, MCP – Mean circulatory pressure, SQ – Systemic flow, LVV – Left ventricle volume, RVPsys - Systolic right ventricle pressure, RVPdias - Diastolic right ventricle pressure, PAPsys - Systolic pulmonary artery pressure, PAPdias – Diastolic pulmonary artery pressure, MPAP – Mean pulmonary artery pressure, RAP – Right atrial pressure, RQ – Pulmonary flow, HR – Heart rate. [91]

### 5.2.12 Final Design

Natural features of the human cardiovascular system, such as resistance, compliance and fluid inertia, were all accurately represented in the new MCL. Pressure, flow and ventricle volumes were all able to be monitored to allow for accurate cardiovascular device testing and teaching purposes. Features such as an atrial kick and variable compliance chamber have been included to improve the accuracy of the system and allow for easier system manipulation. The final design can be seen in Figure 74.
5.3 Conclusion

Using the information gathered in the extensive literature review, the development of a variable compliance chamber, the results from the mathematical model, and the mock circulation loop design discussed above, a physiologically accurate model of the human circulatory system was designed.

Methods of obtaining physiological representations of arterial and venous compliance, vascular resistance, fluid inertia, blood volumes and heart function were developed and combined to form the design of a complete MCL. This rig was designed to reproduce the haemodynamics observed in a variety of healthy and pathological conditions such as rest, exercise, various degrees of left, right and biventricular heart failure, valvular and septal defects and mechanical circulatory assistance. A graphical user interface, combined with a data acquisition system, was designed to promote
efficient control of all components in the system while also being able to record pressures, flows and volumes throughout the MCL.

As the construction of this device was beyond the scope of this project, no results from the physical rig could be presented. However, once constructed and validated, this system can then used for *in vitro* cardiac device testing and teaching medical students and health professionals about the mechanics of the cardiovascular system and cardiovascular device operation.
Chapter 6

Conclusions and Future Research

This thesis is concluded by summarizing the conclusions drawn from each chapter presented and identifying potential future work.

6.1 Conclusions

The aim of this thesis was to present the development of a mathematical model of a mock circulation loop, which then assisted in the design of a variable compliance chamber and a complete physical mock circulation loop. An in-depth literature review assisted in the development of the mathematical model and the physical system by identifying the important issues and areas where others had not developed satisfactory solutions such as the variable compliance chamber. A mathematical model of an existing mock circulation loop was then developed, and validated by comparing pressure and flow results against those seen in the physical system. This model was then used in an iterative manner to improve the mock circulation loop by altering pipe diameters and input pressures to produce more physiologically accurate pressure and flow traces. The simulation was also used to assist in the development of a variable compliance chamber, which was then constructed and tested in a mock circulation loop. Finally, the mathematical model and variable compliance chamber were used in the design of a compact mock circulation loop for \textit{in vitro} cardiac assist device evaluation and for teaching purposes.

6.1.1 Literature Review

The literature review demonstrated the need for accurate cardiovascular assist device \textit{in vitro} testing equipment. Replication of features such as ventricle contractility, vascular resistance, inertiance and compliance and the Frank Starling mechanism were discussed in detail. Previous mock circulation systems were reviewed, while methods used and results obtained were analysed. A review was also conducted into mathematical simulations to gain an understanding of how physical systems can be modelled using the MATLAB / SIMULINK environment. Finally, a review of ventricular assist devices was conducted to demonstrate the requirement for an improved testing system.
6.1.2 Mock Circulation Loop Simulation

The mock circulation loop simulation was successful in the reproduction of pressure and flow results seen in a previously developed physical system. The model used parameters such as pipe dimensions, input pressures and a series of constants to model a physical system. Conditions for rest, exercise and heart failure were successfully replicated in the simulation by changing the same parameters that would be altered in the physical mock circulation loop. The simulation was then improved by adjusting pipe dimensions and input pressures to produce a more physiologically accurate result. The mock circulation loop simulation can be used as a valuable tool in the design of an improved physical system for the improved testing of cardiovascular devices.

6.1.3 Variable Compliance Chamber

A variable compliance chamber was developed using a compressed air supply and flexible diaphragm above the fluid in the aortic compliance chamber. This system successfully produced variable aortic pulse pressures by adjusting the transmural pressure across the diaphragm. Limitations with this design include a slight increase in aortic pressure before ventricle systole, incorrect end systolic and diastolic aortic volumes, and only a fairly small range of reproducible arterial compliance values. With further development of this device, a highly variable level of arterial compliance can be developed for use in a mock circulation loop, which will enable more efficient cardiovascular device testing.

6.1.4 Mock Circulation Loop Design

The design of a compact mock circulation loop was assisted by the mathematical model and the variable compliance chamber. Features such as systemic and pulmonary systems, ventricle contractility, an atrial kick, vascular resistance, systemic and venous compliance chambers, pressure and flow monitoring and data acquisition were all incorporated in the final design. This mock circulation loop will provide an accurate representation of the human cardiovascular system for teaching purposes, while also being a vital tool in cardiovascular device testing and development.
6.2 Future Research

The future research required to progress this study further in each section is outlined below.

6.2.1 Mock Circulation Loop Simulation

The mock circulation loop simulation was successful in providing an accurate representation of the physical system. However, several steps can be taken to further improve the simulation to obtain more accurate results.

- The pressure loss due to the eight 90° elbows should be included to give a more accurate representation of pressure loss in the system.
- The pressure loss due to the 90° tee sections used for the ventricles and compliance chamber entry pipes should be included.
- Improvements to the way the heart valves are modelled would give more accurate pressure traces. The valves modelled in this simulation were perfect mechanical valves, however the physical system includes brass swing check valves which take more time and energy to open and close.
- The model should be extended to include a variety of pipe dimensions in each subsystem, rather than relying on only one pipe length and radius for each subsystem.
- A graphical user interface (GUI) would be useful to accelerate simulation testing. This GUI would allow a selection of pipe dimensions and input parameters which, when run, would control the simulation. Displaying the calculated values for resistance and inertia for each subsystem after parameter changes would also be useful.
- The current proportional control valve, used to replicate vascular resistance, is modelled as a simple length and radius of tubing. This could be improved by implementing a function for the resistance of the valve depending on an input voltage, similar to the physical system. This would allow the user to simulate each condition from the physical mock circulation loop with more accuracy.
- The ventricle and atrial kick regulators could be improved by implementing a function for the delivery pressure depending on the input voltage supplied to the regulator. This would be an improvement on the current method which allows a selection of input pressures.
6.2.2 Variable Compliance Chamber

A variable level of aortic compliance was achieved using the variable compliance chamber. This device could be further improved and tested in more detail.

- An increased range of diaphragm transmural pressures is required to produce the required range of arterial compliance values for cardiovascular device testing. Diaphragm material selection requires further research to possibly assist in this task.

- The method of applying compressed air to the system produced some slight inaccuracy. The aortic pressure was often seen to increase slightly before the start of ventricle systole. This could possibly be improved by incorporating a solenoid valve to only inject air during ventricle systole rather than over the entire cardiac cycle.

- Following these improvements, testing should be carried out to ensure a large range of compliance can be achieved for a variety of different heart rates under different conditions of rest, exercise and heart failure.

6.2.3 Mock Circulation Loop Design

The design of a compact mock circulation loop using the mathematical model and variable compliance chamber was successfully completed. The final design is much smaller than the current physical system and should produce more physiologically accurate results for improved cardiovascular device testing. However this system has several avenues for future research.

- The pipe dimensions have been developed to obtain more accurate pressure and flow traces. The device needs to be constructed according to the details set out in this thesis. Following this, extensive testing needs to be completed to ensure the system can accurately replicate conditions such as rest, exercise and heart failure, while also being able to produce vascular defects such as valve stenosis and regurgitation.

- Heart valves could be improved by using mechanical artificial heart valves to reduce the size and weight of the current mechanical check valves.

- The mock circulation loop should be made modular so that components can be added or taken out with ease. This would enable different designs of
ventricles, compliance chambers and other features to be tested in the new system.

- The current ventricles are replicated using vertical PVC pipe. This system does not produce accurate ventricle inflow and outflow, and could be improved by developing a ventricle of the correct anatomical shape. This would be especially useful for flow visualisation studies.

- A change in position of a patient can result in a significant volume change in the highly compliant systemic venous system. A chamber should be attached to the systemic venous system which can take in or push out fluid to represent a change in position of the patient. This could be achieved by supplying pressure to the fluid in the chamber to push fluid out, or reduce the pressure to draw fluid in.

### 6.3 Summary

In conclusion, this thesis has developed a functional mathematical model of a mock circulation loop, which was then used to assist in the design and construction of a novel variable compliance chamber and a completed design for a new compact physical mock circulation loop.
Appendices

APPENDIX 1 – CARDIOVASCULAR PARAMETERS FOR THE ADULT AND INFANT BY GOODWIN ET AL.

APPENDIX 2 – EQUATIONS FOR FINDING THE SPRING CONSTANT FOR A GIVEN COMPLIANCE

APPENDIX 3 – REPRESENTATION OF SYMBOLS FOR STUDY BY WESTERHOF ET AL.

APPENDIX 4 – PARAMETERS FOR STUDY BY KORAKIANITIS FOR FIGURE 9

APPENDIX 5 – MOCK CIRCULATION LOOP MODEL SUBSYSTEMS

APPENDIX 6 – CODE FOR MCL MODEL
## Appendix 1 – Cardiovascular parameters for the adult and infant by Goodwin et al. [25]

<table>
<thead>
<tr>
<th>Part of circulation</th>
<th>Compartment</th>
<th>Parameter description</th>
<th>Adult value</th>
<th>Infant value</th>
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<tbody>
<tr>
<td>Total circulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrathoracic</td>
<td>Atria and ventricles</td>
<td>Heart rate</td>
<td>72</td>
<td>129</td>
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<tr>
<td></td>
<td></td>
<td>Average intrathoracic pressure</td>
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<td>-3.25</td>
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<td>Resistance to forward flow of the inflow tract</td>
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<td>0.006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mitral valve resistance</td>
<td>0.00300</td>
<td>0.006</td>
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<tr>
<td></td>
<td></td>
<td>Diastolic elastance</td>
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<td>0.733</td>
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<td></td>
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<td>Maximum systolic elastance</td>
<td>0.280</td>
<td>1.99</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unstressed volume</td>
<td>30.0</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Left atrium</td>
<td>Aortic valve and intrathoracic artery resistance</td>
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<td>0.016</td>
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<tr>
<td></td>
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<td>Diastolic elastance</td>
<td>0.0900</td>
<td>0.550</td>
</tr>
<tr>
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<td></td>
<td>Maximum systolic elastance</td>
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<td>28.4</td>
</tr>
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<td>Unstressed volume</td>
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<td>2.00</td>
</tr>
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<td>Intrathoracic arteries</td>
<td>Elastance</td>
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<td>7.76</td>
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<td>Unstressed volume</td>
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<td>Extrathoracic arteries</td>
<td>Blood flow inertia</td>
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<td>0.000200</td>
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<tr>
<td></td>
<td></td>
<td>Resistance</td>
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<td>Elastance</td>
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<td>3.02</td>
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<td>370</td>
<td>48.1</td>
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<td>Systemic peripheral vessels</td>
<td>Resistance</td>
<td>1.00</td>
<td>2.00</td>
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<tr>
<td></td>
<td>Extrathoracic veins</td>
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<td>Intrathoracic veins</td>
<td>Elastance</td>
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<td>0.00600</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tricuspid valve resistance</td>
<td>0.00300</td>
<td>0.00600</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diastolic elastance</td>
<td>0.0500</td>
<td>0.317</td>
</tr>
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<td></td>
<td></td>
<td>Maximum systolic elastance</td>
<td>0.150</td>
<td>0.63</td>
</tr>
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<td></td>
<td></td>
<td>Unstressed volume</td>
<td>30.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Pulmonary circulation</td>
<td>Right ventricle</td>
<td>Pulmonic valve and pulmonary artery resistance</td>
<td>0.00300</td>
<td>0.00600</td>
</tr>
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<td></td>
<td>Diastolic elastance</td>
<td>0.0570</td>
<td>0.348</td>
</tr>
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<td></td>
<td>Maximum systolic elastance</td>
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<td>2.09</td>
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<td></td>
<td>Unstressed volume</td>
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<td>3.0</td>
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<td></td>
<td>Elastance</td>
<td>0.233</td>
<td>1.27</td>
</tr>
<tr>
<td></td>
<td>Pulmonary arteries</td>
<td>Unstressed volume</td>
<td>50.0</td>
<td>6.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Resistance</td>
<td>0.110</td>
<td>0.220</td>
</tr>
<tr>
<td></td>
<td>Pulmonary peripheral vessels</td>
<td>Unstressed volume</td>
<td>350</td>
<td>45.5</td>
</tr>
<tr>
<td></td>
<td>Pulmonary veins</td>
<td>Elastance</td>
<td>0.0455</td>
<td>0.247</td>
</tr>
</tbody>
</table>
Appendix 2 – Equations for finding the spring constant for a given compliance

X = axial position of the piston
ΔV = volume variation
A = cross sectional area of the piston
ΔP = pressure drop (P_1-P_0)
F = axial force
Q = flow
C = compliance value
Q = C . (dP / dt)
ΔV = A . X
Q_1 – Q_2 = A . (dX / dt)
F = K . X
F = ΔP . A
Q_1 – Q_2 = (A^2 / K) . (dP_1 / dt)
C = A^2 / K
Appendix 3 – Representation of symbols for study by Westerhof et al.

R’\(n\), L’\(n\), C’ represent viscous and inertial properties of blood and the compliant properties of the arteries, respectively. (Primed quantities are used to indicate that they are given for unit length)

\[
R'_{n} = \frac{8\pi \eta}{S^2} \\
L'_{n} = \frac{\rho}{S} \cdot \frac{1}{2n-1} \\
C' = \frac{3\pi r^2 (a + 1)^2}{E(2a +1)}
\]

R’\(_o\) = resistance for correction of anomalous viscosity or to account for boundary layer of lower viscosity per unit length
n = 1, 2 up to at least 3 and at most 5, depending on the radius
R’\(_L\) = leakage for unit length through small branches
\(\eta\) = viscosity of blood
\(\rho\) = density of blood
\(S = \pi r^2\)
\(r\) = radius
\(a = r / h\)
\(h\) = wall thickness
\(E\) = Young’s modulus of the vessel wall

If the arteries are partitioned into segments of length \(\Delta z\) (\(\Delta z\) ranges from 2 to 7.5cm in the model), each segment can be replaced by the network of Fig. 7 by multiplying R’\(_o\), R’\(_n\), L’\(_n\) and C’ by \(\Delta z\) and dividing R’\(_L\) by \(\Delta z\).
### Appendix 4 – Parameters for study by Korakianitis for Figure 9

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left heart</strong></td>
<td></td>
<td><strong>Systemic circulation</strong></td>
<td></td>
</tr>
<tr>
<td>CQ&lt;sub&gt;ao&lt;/sub&gt; (ml/(s.mmHg&lt;sup&gt;0.5&lt;/sup&gt;))</td>
<td>350</td>
<td>Csas (ml/mmHg)</td>
<td>0.08</td>
</tr>
<tr>
<td>CQ&lt;sub&gt;mi&lt;/sub&gt; (ml/(s.mmHg&lt;sup&gt;0.5&lt;/sup&gt;))</td>
<td>400</td>
<td>Rsas (mmHg.s/ml)</td>
<td>0.003</td>
</tr>
<tr>
<td>E&lt;sub&gt;ls&lt;/sub&gt; (mmHg/ml)</td>
<td>2.5</td>
<td>Lsas (mmHg.s&lt;sup&gt;2&lt;/sup&gt;/ml)</td>
<td>0.000062</td>
</tr>
<tr>
<td>E&lt;sub&gt;ld&lt;/sub&gt; (mmHg/ml)</td>
<td>0.1</td>
<td>Csat (ml/mmHg)</td>
<td>1.6</td>
</tr>
<tr>
<td>P&lt;sub&gt;lv,0&lt;/sub&gt; (mmHg)</td>
<td>1.0</td>
<td>Rsat (mmHg.s/ml)</td>
<td>0.05</td>
</tr>
<tr>
<td>V&lt;sub&gt;lv,0&lt;/sub&gt; (ml)</td>
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<td>Lsat (mmHg.s&lt;sup&gt;2&lt;/sup&gt;/ml)</td>
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</tr>
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<td>E&lt;sub&gt;la,max&lt;/sub&gt; (mmHg/ml)</td>
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<td>Rsar (mmHg.s/ml)</td>
<td>0.5</td>
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<td>E&lt;sub&gt;la,min&lt;/sub&gt; (mmHg/ml)</td>
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<td>Rscp (mmHg.s/ml)</td>
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<td>P&lt;sub&gt;la&lt;/sub&gt; (mmHg)</td>
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<td>Rsvn (mmHg.s/ml)</td>
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<tr>
<td>V&lt;sub&gt;lv,0&lt;/sub&gt; (ml)</td>
<td>4.0</td>
<td>Csvn (ml/mmHg)</td>
<td>20.5</td>
</tr>
<tr>
<td><strong>Right heart</strong></td>
<td></td>
<td>Csvc (ml/mmHg)</td>
<td>1.5</td>
</tr>
<tr>
<td>CQ&lt;sub&gt;po&lt;/sub&gt; (ml/(s.mmHg&lt;sup&gt;0.5&lt;/sup&gt;))</td>
<td>350</td>
<td>Vlv0 (ml)</td>
<td>500</td>
</tr>
<tr>
<td>CQ&lt;sub&gt;hi&lt;/sub&gt; (ml/(s.mmHg&lt;sup&gt;0.5&lt;/sup&gt;))</td>
<td>400</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E&lt;sub&gt;rv,s&lt;/sub&gt; (mmHg/ml)</td>
<td>1.15</td>
<td>Cpas (ml/mmHg)</td>
<td>0.18</td>
</tr>
<tr>
<td>E&lt;sub&gt;rv,d&lt;/sub&gt; (mmHg/ml)</td>
<td>0.1</td>
<td>Rpas (mmHg.s/ml)</td>
<td>0.002</td>
</tr>
<tr>
<td>P&lt;sub&gt;rv,0&lt;/sub&gt; (mmHg)</td>
<td>1.0</td>
<td>Lpas (mmHg.s&lt;sup&gt;2&lt;/sup&gt;/ml)</td>
<td>0.000052</td>
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<td>Vrv0 (ml)</td>
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Appendix 5 – Mock circulation loop model subsystems

Figure 75 - Mock circulation loop system. This system includes all subsystems for the model.

Figure 76 - Atrial subsystem. This subsystem models the left / right atrium.

Figure 77 - Ventricle subsystem. This subsystem models the left / right ventricle.
Figure 78 - Arterial / Venous subsystem. This subsystem models the systemic and pulmonary venous and arterial systems.

Figure 79 - Regulator subsystem. This subsystem models the left / right ventricle regulator.

Figure 80 - Volume subsystem. This subsystem calculates the total volume and the volume in the vertical chamber for each MCL segment.

Figure 81 - Compliance subsystem. This subsystem calculates the pressure caused by the compliance of the vertical pipe for each MCL segment.
Figure 82 - Inertiance subsystem. This subsystem calculates pressure caused by the vertical inertiance for each MCL segment.

Figure 83 - Resistance subsystem. This subsystem calculates the pressure drop due to the connecting pipe between the horizontal and vertical sections for each MCL segment.

Figure 84 - Heart valve subsystem. This subsystem models the mitral, aortic, tricuspid and pulmonary valves.

Figure 85 - Mass delivery subsystem. This subsystem calculates the mass of air delivered to the ventricles from the regulators.

Figure 86 - Regulator volume subsystem. This subsystem calculates the volume of air delivered to the ventricles from the regulator.
## Appendix 6 – Code for MCL model

% Appendix 6 – Code for MCL model

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% %lh, rh are the length and radius of the horizontal pipes. 
% %lRt, rRt are the length and radius of the chamber entry pipes. 
% %lv, rv are the length and radius of the filled volume of vertical pipes. 
% %lp, rp are the length and radius of the total volume of vertical pipes.

```matlab
P0=8; 
Patm=760; 
L_cap = (pc./(2*((3.14159*((rv./10).^2)).^2)))*(100/133.32); 
V0c = ((lh.*((3.14159*rh.^2))+(lRt.*((3.14159*rRt.^2)))+lv.*((3.14159*rv.^2))))*0.001; 
V0t = ((lh.*((3.14159*rh.^2)))+(lRt.*((3.14159*rRt.^2)))+lp.*((3.14159*rp.^2))))*0.001; 
V0p = (lp.*((3.14159*rp.^2)))*0.001; 
M0a = (((lp./10).*((3.14159*(rp./10).^2)))-(lv./10).*((3.14159*(rv./10).^2)))*1.2e-6; 
C_cap = 1.((pc.*g./(3.14159*(rv./10).^2)))*(100/133.32); 
Rt=(8*0.000894*3.14159*(lRt./1000).*((3.14159*(rRt./1000).^2)).^2)*0.0000000750075; 
Rreg=(8*0.000894*3.14159*(lreg./1000).*((3.14159*(rreg./1000).^2)).^2)*0.00000000750075; ```
R = (8*0.000894*3.14159*(lh./1000)./(3.14159*(rh./1000).^2).^2)*0.00000000750075;
Rs = R(3)+R(4);
Rp = R(8)+R(9);
Vao = V0c(3)+V0c(4);
Vpa = V0c(8)+V0c(9);
L = (1000*(lh./1000)./(3.14159*(rh./1000).^2))*0.00000000750075;%good
Ls = L(3)+L(4);
Lp = L(8)+L(9);

%Filter Denominators

denS_inert_filt=conv([1/1e7 1],[1/1e6 1]);
denS_resist_filt=[1/1e8 1];
References


