T.C.
BAHÇEŞEHİR UNIVERSITY

DESIGN OF LEFT VENTRICLE FOR CARDIOVASCULAR SYSTEM MOCK CIRCUIT

Master's Thesis

EMİR GÖKBERK EKEN

İSTANBUL, 2014

(This Page Left Blank)

THE REPUBLIC OF TURKEY
BAHÇEŞEHİR UNIVERSITY

FACULTY OF ENGINEERING

DEPARTMENT OF MECATRONICS ENGINEERING

DESIGN OF LEFT VENTRICLE FOR CARDIOVASCULAR SYSTEM MOCK CIRCUIT

Master's Thesis

EMIR GÖKBERK EKEN

Supervisor: PROF. M. EROL SEZER

İSTANBUL, 2014

THE REPUBLIC OF TURKEY
BAHCESEHIR UNIVERSITY

THE GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES
M.S. BIOENGINEERING

Name of the thesis: **Design of Left Ventricle for Cardiovascular System Mock Circuit**
Name/Last Name of the Student: **Emir Gökberk EKEN**
Date of the Defense of Thesis: **15/01/2014**

The thesis has been approved by the Graduate School of Natural And Applied Sciences.

Doc. Dr. Tunç BOZBURA
Graduate School Director

I certify that this thesis meets all the requirements as a thesis for the degree of Master of Arts.

Prof. Dr. M. Erol SEZER
Program Coordinator

This is to certify that we have read this thesis and we find it fully adequate in scope, quality and content, as a thesis for the degree of Master of Arts.

Examining Comittee Members	Signature
Thesis Supervisor Prof. Dr. M. Erol SEZER	----------------------------------
Thesis Co-supervisor Doc. Dr. A. Kamuran KADIPAŞAOĞLU	---------------------------------
Member Dr. Serap AYDIN	----------------------------------

ABSTRACT

DESIGN OF LEFT VENTRICLE
FOR CARDIOVASCULAR SYSTEM MOCK CIRCUIT

Emir Gökberk Eken

Bioengineering

Supervisor: Prof. Dr. M. Erol SEZER

January, 2013, 82 pages

Heart disease is founded as the highest cause of death in the world. These loses can reduce by improving heart valves, ventricular assist devices (VADs), total artificial hearts, heart and lung machines etc. All these medical devices have to be tested on cardiovascular mock circuits (CVMCs) before starting clinical testing.

At 1975 Donovan et al. designed and built a complete mock circulation for testing artificial hearts but, atria or ventricles wasn't include to system. This CVMC has been the basis for many. Timms et al. (2010) designed and constructed a CVMC which includes both systemic and pulmonary circulatory systems. They accomplished to produce left ventricular pressure but, they couldn't prevent lagging in aortic pressure. Aortic valves opening and closing times or wrong resistance values may cause this problem. For prevent this problem more accurate heart valves may use and resistance may optimize with feed-back control of proportional control valves.

Objective in this study was to design and build CVMC which is drivable with an elastance based feed-back control for simulate heart functions in various conditions. CVMC virtually designed by using Solidworks based on results which are obtained in the Simulink model. Pressure and flow inputs and check valve outputs are implemented into system by using dSPACE control card. CVMC operated successfully with compressed air and check valves. However, results are indicated a leaking problem of heart valves.

Key Words: Cardiovascular Mock Circuit, VAD and Heart valve test

ÖZET

DESIGN OF LEFT VENTRICLE FOR CARDIOVASCULAR SYSTEM MOCK CIRCUIT

Emir Gökberk Eken

Biyomühendislik

Tez Danışmanı: Prof. Dr. M. Erol SEZER

Ocak, 2013, 82 sayfa

Kalp hastalıklarından kaynaklı ölümler hala dünyadaki en yüksek sayıdaki ölüm sebebidir. Bu kayıplar kalp kapakçıkları, ventrikül destek üniteleri (VADs), yapay kalpler, kalp-akciğer makinaları vs. Geliştirilerek azaltılabilir. Ancak bütün bu araçlar kılinik testler öncesinde kardiovasculer mock düzenekleride (CVMC) test edilmelidir.

Donovan ekibi 1975 yılında kalp kapakçıklarının denenmesi amacıyla CVMC dizayn edip kurdular fakat, kulakçık ve karıncıklar sisteme dahil edilmemişti. Bu sistem bir çok yenisi için temel niteliği taşımaktadır. 2010 yılında Timms ve ekibi sistemic ve pulmoner tarafların bulunduğu bir CVMC dizayn edip kurdular. Bu sistemle sol karıncık basıncını başarılı bir şekilkde elde etmelirne karşın aort basıncının gecikmeli olarak elde edilmesini engelliyemediler. Bu probleme aort kapakçığının zamanında açılıp kapanamaması yada direnç değerlerinin optimum olmaması sebep olmuş olabilir. Bu problemi engellemek için daha iyi kalp kapakçıkları seçilerek, dirençlerde geri-besleme konrollü, doğrusal akış vanalarıyla optimize edilebilinir.

Kalp fonksiyonlarını çeşitli durumlara yerine getirebilicek, geri-beslemeli elastansla kontrol edilebilicek bir CVMC dizayn edip kurmak bu projenin amacıdır. Bunun için Matlabdeki simülasyonlardan elde edilen verilerle, SolidWorks de sanal dizaynı yapıldı. Basınç, akış bilgileri ve çek valflerini kontrolleri dSpace kontol borduna yerleştirldi. CVMC hava basıncı kullanılarak başarlı birşekilde işletildi. Ancak soruçlar kalp kaçakçıklarının kaçırdığına işaret etti.

Anahtar Kelimeler: Kardiovasculer Mock düzeneği, Kalp Kapakçığı ve VAD testleri

CONTENTS

FIGURES

TABLES

ABBREVIATIONS

ADC	:	Analog to Digital Converter
AHF	:	Acute Heart Failure
Ao	:	Aorta
AV	:	Aortic Valve
C	:	Compliance
CHF	:	Chronic Heart Failure
CO	:	Cardiac Output
CVMC	:	Cardiovascular Mock Circuit
DAC	:	Digital to Analog Converter
GUI	:	Graphical User Interface
HF	:	Heart Failure
HR	:	Hearth Rate
I/O	:	Input/output
IVC	:	Isovolumetric or Isovolumic contraction
IVR	:	Isovolumetric or Isovolumic relaxation
LA	:	Left Atrium
LV	:	Left Ventricle
MAP	:	Mean Aortic Pressure
MCA	:	Mechanical Circulatory Assistance
MV	:	Mitral Valve
PA	:	Pulmonary Artery
PA	:	Pulmonary Artery
PC	:	Pulmonary Capillary
PE	:	Potential Energy
PV	:	Pulmonary Venous
PVA	:	Pressure Volume Area
PVR	:	Pulmonary Vascular Resistance
RA	:	Right Atrium
RTI	:	Real-time Interface
RV	:	Right Ventricle

SAP	:	Systolic Aortic Pressure
SC	:	Systemic Capillary
SV	:	Stroke Volume
SVR	:	Systemic Vascular Resistance
SW	:	Stroke Work
T	:	Cardiac Cycle Length
TV	:	Tricuspid Valve
VAD	:	Ventricular Assist Device

SYMBOLS

Explanation		Symbol	Units	
			SI	Conventional
Pressure	:	P	Pa	mmHg
Volume	:	V	m^3	m^3
Length	:	L	cm	m
Radius	:	r	cm	m
Diameter	:	d	cm	m
Mathematical constant	:	π	[dimensionless]	[dimensionless]
Difference	:	Δ	[dimensionless]	[dimensionless]
Dynamic viscosity	:	μ	Pa.s	$N.s/m^2$
Volumetric flow rate	:	Q	m^3 /s	mL/min
Resistance (Hydraulic)	:	R	$Pa.s/m^3$	mmHg.min/mL
Compliance	:	C	m^3/Pa	$m^3/mmHg$
Elastance	:	E	Pa/m^3	mmHg/mL

1. INTRODUCTION

1.1 OBJECTIVE

The objective of this study is to design, build and control a hydraulic/pneumatic Cardiovascular Mock Circuit that can be used as a test platform to evaluate the performance of left-ventricular assist devices. The mock circuit is required to replicate the dynamics of human cardiovascular system, especially, the pressure-volume relationship of the left ventricle with sufficient accuracy.

1.2 MOTIVATION

The heart is essentially a mechanical pump that circulates blood through the body and the lungs at a certain rate. National Institute for Clinical Excellence defines heart failure as "a complex syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the heart to function as a pump to support a physiological circulation.”[1] Acute heart failure (AHF) is defined as the rapid or progressive beginning of symptoms of heart failure. AHF can be often cured with treatment (Teerlink 2008). Chronic heart failure (CHF) is a long-term condition in which the heart cannot eject required amount of blood out into the body over an extended period, e.g. months to years.

CHF causes the death of more than two million people in the European Union and more than five million people in Europe each year. Fifty percent of coronary heart disease death occurs before age 75 and 15 percent occurs before age 65 in Europe.[2] More than five million adults between ages 40 to 70 year of age in the USA have heart failure, and every year more than half-a-million new cases occur. According to the 2002 World Health Organization Report, 11.8 percent of males and 10.5 percent of females in the world population had troubles from heart disease.

The only known solution to CHF is heart transplantation. However, donated organs are

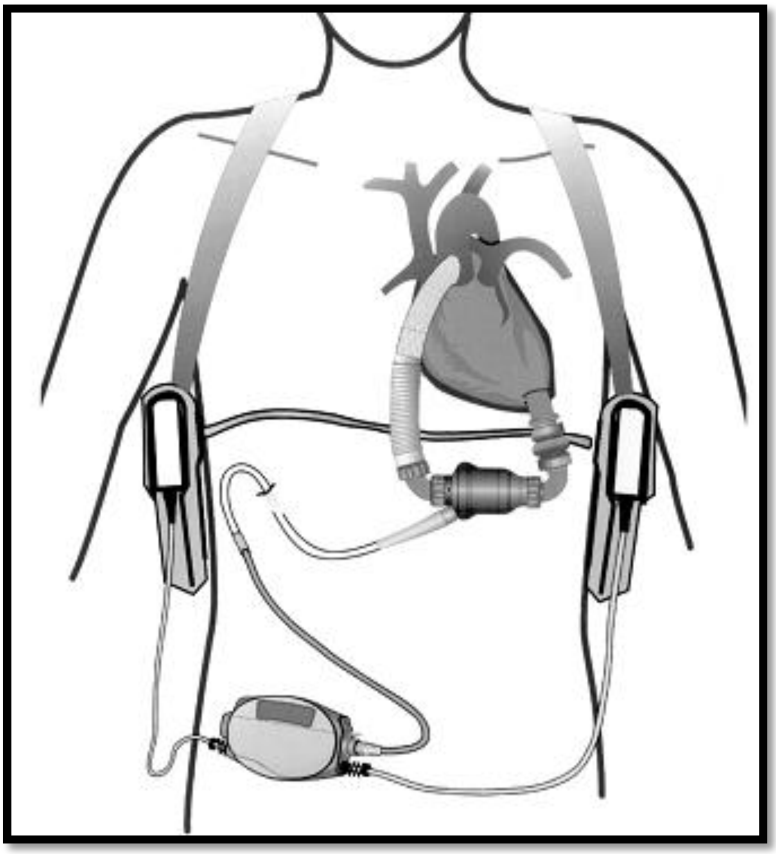
---

[1] *National Institute for Clinical Excellence “Chronic heart failure – Management of chronic heart failure in adults in primary and secondary 2003 care.” London*

[2] *Annual Report 2009 by European Hearth Network*

limited, but the number of patients waiting for a heart transplant is increasing with the population. Implantable heart pumps were invented in order to keep alive CHF patients until a suitable donor is found (Bridge to Transplant). Since most of the CHF cases are due to left ventricle failure, the most widely used heart pumps are left ventricular assist devices (LVAD) that pump blood from the left ventricle to the aorta.
(See Figure **1.1**).

Figure 1.1: HeartMate II LVAD as Bridge to Transplant System in Patients Body



Source: Bartley P. Griffith, et al. Heartmate ii left ventricular assist system: from concept to first clinical use. The Annals of Thoracic Surgery, 2001.

Over the years, LVADs developed from simple and bulky suction pumps to smaller size continuous flow pumps as summarized in Table 1.1.

The first LVAD in Turkey was designed in 2010 (Kucukaksu 2003, pp. 114-20). A second prototype is currently being developed at Bahçeşehir University. As in all LVAD designs, the prototype has to be subjected to extensive performance tests, first in simulators, and then in animals, before being offered into service. This thesis is a result of our efforts to develop such a Mock circuit to be used for performance tests of the LVAD being developed.

Table 1.1: VAD devices, generations, manufacturers and types.

Device	**Generation**	**Manufacturer**	**Type**
Novacor	Generation 1	World Heart	Pulsatile
HeartMate XVE	Generation 1	Thoratec	Pulsatile
HeartMate II	Generation 2	Thoratec	Continuous axial flow
HeartMate III	Generation 2	Thoratec	Continuous axial flow
Jarvik 2000	Generation 2	Jarvik Heart	Continuous axial flow
MicroMedDeBakey VAD	Generation 2	MicroMed	Continuous axial flow
VentrAssist	Generation 3	Ventracor	Continuous centrifugal flow
HVAD	Generation 3	HeartWare	Continuous centrifugal flow
DuraHeart	Generation 3	Terumo	Continuous centrifugal flow

1.3 A REVIEW OF PREVIOUS CARDIOVASCULAR MOCK CIRCUITS

CVMCs are used as a mechanical representation of human cardiovascular system in vitro. Early versions of CVMCs were built for testing artificial heart valves. CVMCs can also be used for testing of total artificial hearts, artificial lungs and many other artificial organs. In these systems stepping motors are used to create an artificial heart beat (Pantalos et al. 2004, pp. 37-46).

Kolff et al. (1959) constructed a mock circuit which consisted of both pulmonary and systemic sides. Compressed air was used to operate ventricles, and also to obtain pressures of aortic and pulmonary arterial chambers. No resistance valves were used in this study.

Donovan et al. (1975) designed and built a complete mock circulation for testing new artificial heart designs in an artificial environment. However, they didn't include atria or ventricles, which limited the cardiovascular device testing capabilities. This device used acrylic material to build chambers to model aortic, systemic venous, pulmonary arterial, pulmonary venous and ventricular components. This cardiovascular mock circuit has been the basis for many CVMCs since.

Verdonck et al. (1992) designed and built a complete mock circulation for testing mitral valves. For this reason aortic and mitral valves in the system could change easily. The silicone left ventricle and latex atrium were both anatomically shaped, and mounted in water filled Plexiglas tanks where the pressures are controlled by an external circuit. This CVMC was later used by Vandenberghe et al. in 2003 to estimate the hydrodynamic performance of the PUCA II LVAD (Vandenberghe 2003, pp. 743-752).

Baloa et al. (2001) studied control of cardiovascular mock circuit by using the elastance-based control. This study used the elastance of the ventricle to change control output and developed a new strategy. The authors concluded that this design was successful in simulating different cardiac conditions.

Koenig et al. (2004) produced a systemic mock circulation to test pulsatile and continuous ventricular assist devices (VADs). A mock ventricle was created of ellipsoid shape with mounts for the aortic and mitral valves. This system was used with a pressure chamber to replicate desired pressure values. Arterial resistance was realized by a latex tube in the system. However, the pulmonary circulation to complement the systemic side was not included in the system.

Pantalos et al. (2004) constructed a CVMC to replicate the Frank-Starling response for several situations. In this system, flexible polyurethane was used for produce both the atrium and the ventricle. A polyurethane aorta was connected to the ventricle. Pressure-volume loops representing natural situations were produced. The primary limitation of this system was not having a pulmonary vasculature mock circulatory system.

Gregory S.D. (2004) designed a mock circuit that used compliancebased control. However, the circuit didn't accurately replicate the elastic nature of the ventricle.

Timms et al. (2005) designed and constructed a complete CVMC for testing of VADs. The purpose of this study was to design and construct a CVMC that was capable of replicating several situations. This mock loop was not shown to produce accurate pressure and flow data for several situations. Limitations in this study were mainly due to use of slow check valves that model the natural heart valves.

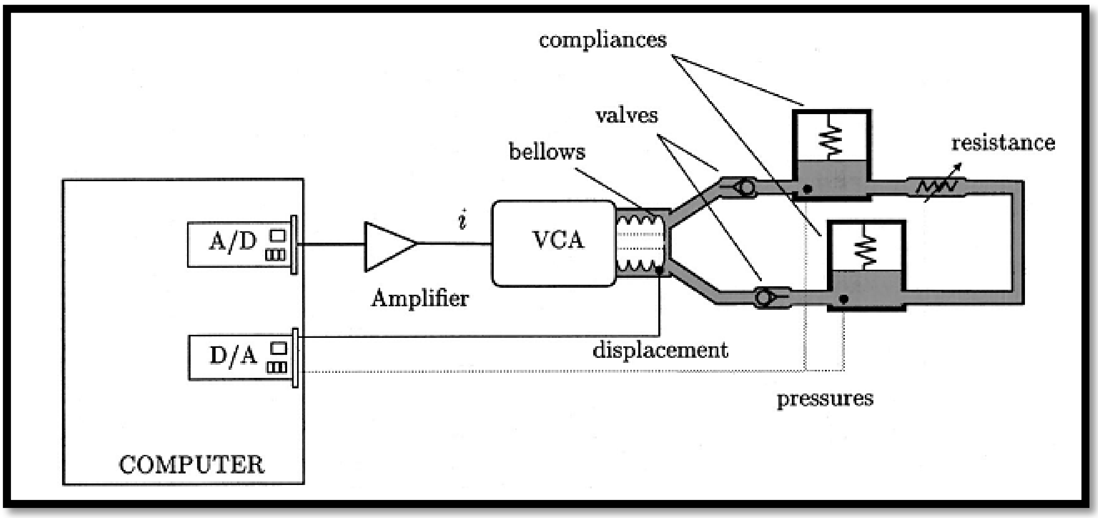
Timms et al. (2010) designed and constructed a CVMC which included both systemic and pulmonary circulatory systems. However, the system was not accurately replicating the human cardiovascular system. There was a lag between left ventricular and aortic pressures. Aortic valve's opening and closing times might have caused this problem.

1.3.1 Elastance-Based Control of CVMCs

In 2001, L.A Baloa, J.R Boston and J.F Antaki designed an elastance-based control of a Mock circulatory system that consists of Aorta, LV and LA. They defined a volume function of LV and determined desired end-systolic pressure (P_{es}) by calculating the elastance from (Eq. 1-1). Control algorithms were implemented digitally by using 12-bit digital to analog board (see Figure 1.2).

$$E_{es} = \frac{P_{es}}{(V_{es} - V_0)} \qquad \text{(Eq. 1-1)}$$

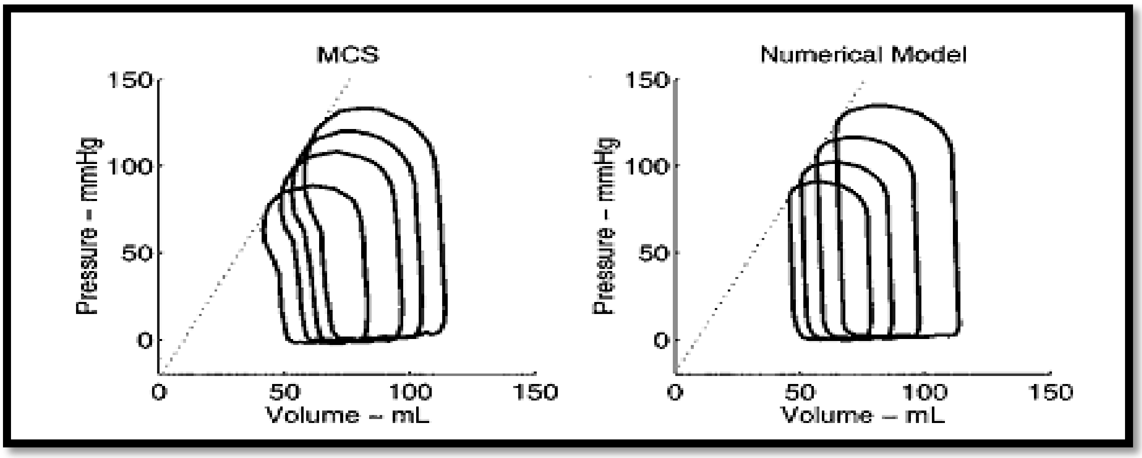
Figure 1.2: Mock Circulatory System diagram used by Baloa (2001)



Source: Baloa, L., J. Boston, and J. Antaki, Elastance -based control of a mock circulatory system. Annals of Biomedical Engineering, 2001. 29: p. 244-251.

Results of the experimental PV-loop were similar with the numerical model except the volume increase during IVR shown in Figure 1.3. Frank-Starling response was modeled in the experiment and results of afterload, preload and contractility changes were similar to normal heart. Dysfunctional heart was not simulated in this experiment.

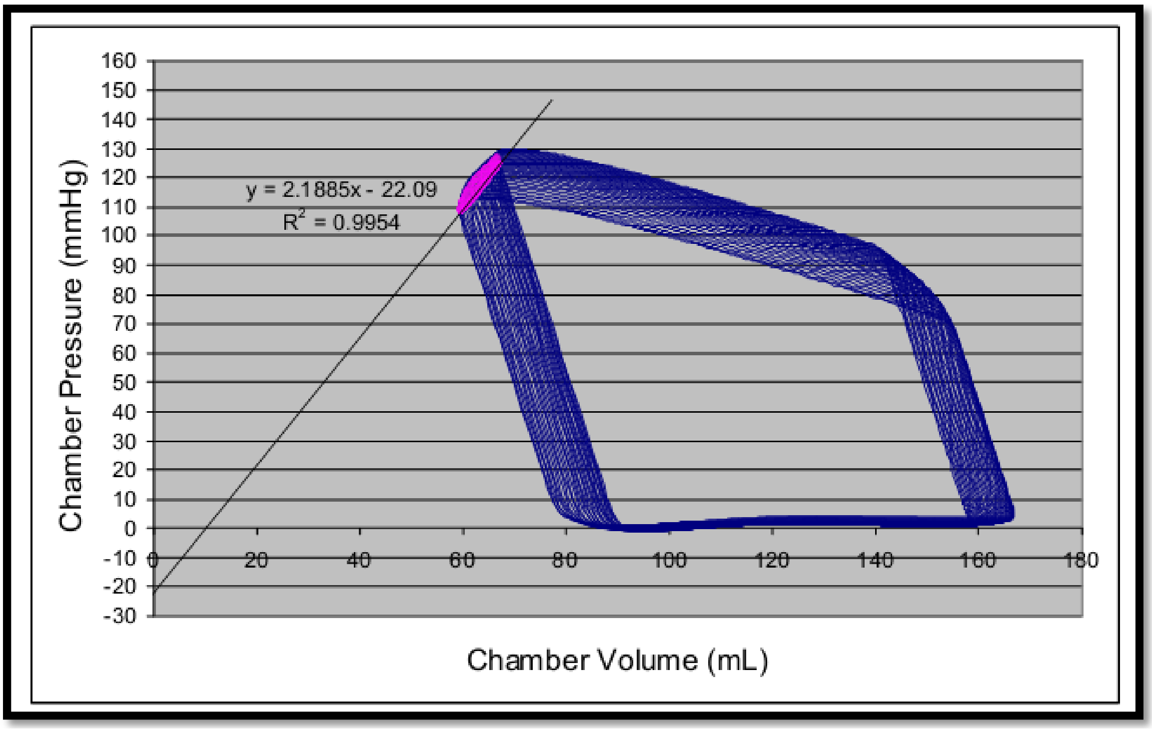
Figure 1.3: Response of PV loops to change in preload.



Source: Matthew Loh and Yih-Choung Yu, "Feedback control design for an elastance-based mock circulatory system," in Proc. 2004 American Control Conf. (Boston, Massachusetts, June 30 – July 2, 2004.

Mathew Loh and Yih-Choung Yu published an article about feedback control mechanism for Mock circulatory system in 2004. Aim was to design a feedback control to simulate sufficient (healthy) and insufficient conditions of heart according to elastance of the left ventricle. They implemented pulmonary circulation into the Mock circuit model, and test results showed that when E_{es} in the simulation was changed from 0.5 (dysfunctional condition, below 25 percent of its nominal value) to 3.8 (extremely functional condition, beyond 70 percent of the nominal value), error of the produced E_{max} was less than 3 percent, independent of preload and afterload. Physiologically meaningful pressure volume and flow waveforms were produced. However, IVR and IVC stages were not produced accurately (shown Figure 1.4)

Figure 1.4: Example Result of M. Loh (et al.) paper in 2004



Source: Matthew Loh and Yih-Choung Yu, "Feedback control design for an elastance-based mock circulatory system," in Proc. 2004 American Control Conf. (Boston, Massachusetts, June 30 – July 2, 2004.

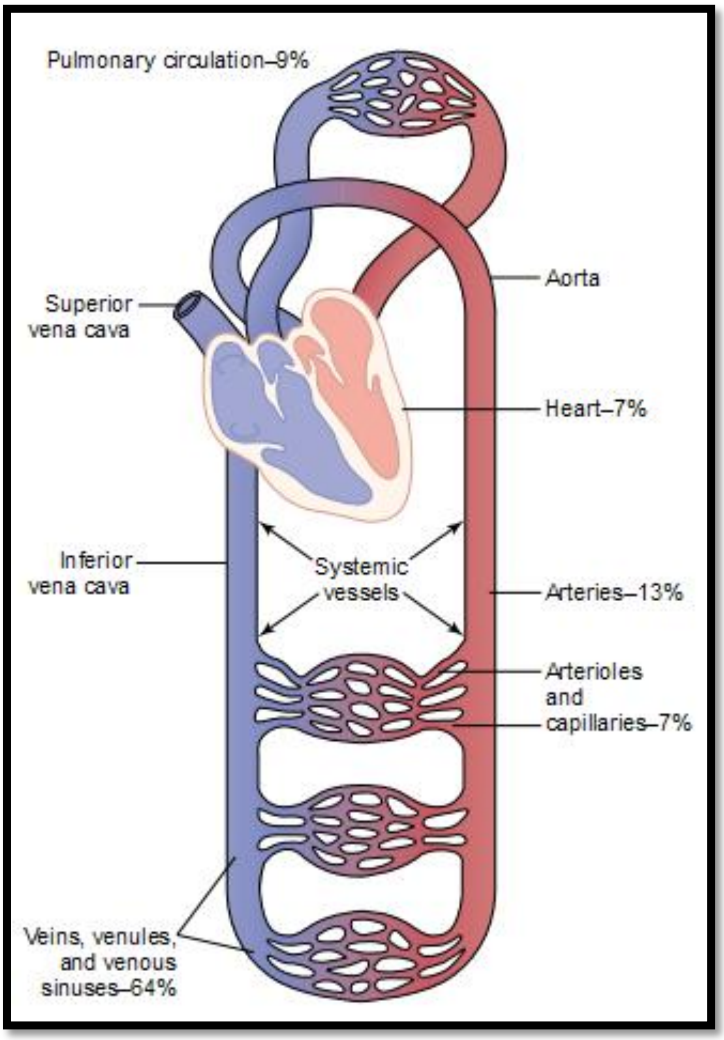
1.4 OUTLINE OF THESIS

The reminder of the paper is structured as follows. The next two sections give a general information about Human Cardiovascular System and Cardiovascular Mock Circuits (CVMC) which is context of this study. Followed by desired functions and design criteria's are discussed. Afterwards, the research methodology and materials are explained. At the end results, discussion and conclusion are presented.

2. HUMAN CARDIOVASCULAR SYSTEM

The human cardiovascular system (CVS) is a closed circuit in which blood pumped by heart circulates. Basic components of the CVS are the heart, consisting of the left and right atria and ventricles and four unidirectional valves, the aorta, and systemic and pulmonary arteries, capillaries and veins, as shown in Fig. 2.1 together with the distribution of the total blood volume among these components.

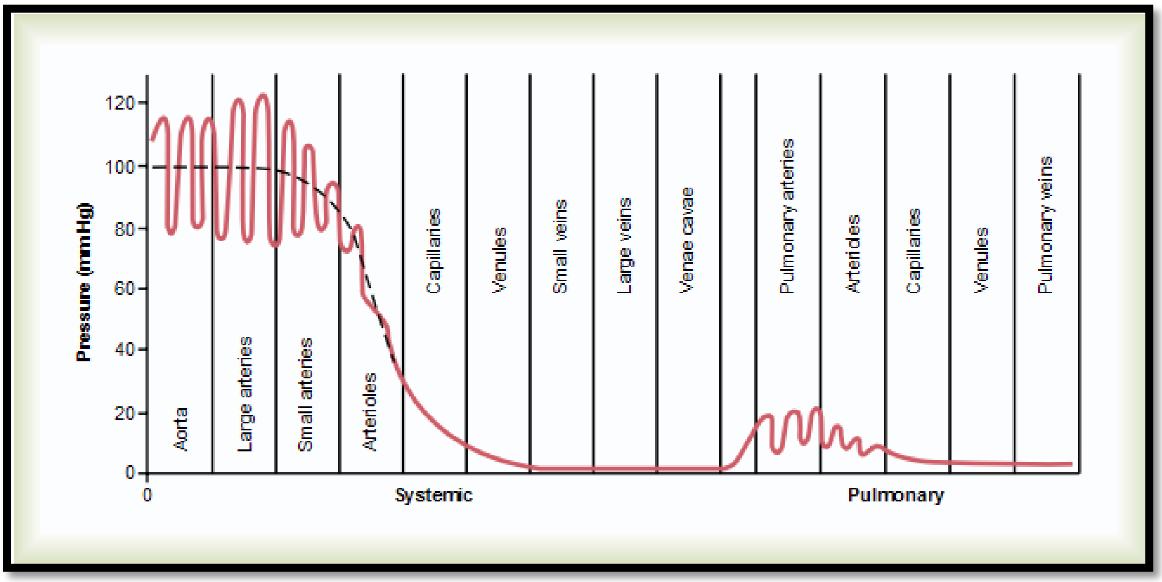
Figure 2.1: Distribution of blood in the different parts of the circulatory system.



Source: Textbook of Medical Physiology 11th ed by Arthur C. Guyton, John E. Hall. Copyright at 2006 by Elsevier Inc.

Among the most significant variables of the CVS from a physiological perspective are blood pressures and flow rates at different parts of the system. Typical blood pressure values in a healthy CVS are summarized in Fig. 2.2. Although it is essentially a distributed-parameter system, lumped-parameter models (physical or virtual) are often adequate to replicate CVS physiology. In such models, the passive components such as the aorta, arteries and veins are represented as interconnected storage elements and the heart as an active pump. In the following, we present the input/output characteristics of various elements of a hydraulic/pneumatic model of CVS.

Figure 2.1: Normal blood pressures in the different portions of the circulatory system when a person is lying in the horizontal position



Source: Textbook of Medical Physiology 11th ed by Arthur C. Guyton, John E. Hall. Copyright at 2006 by Elsevier Inc.

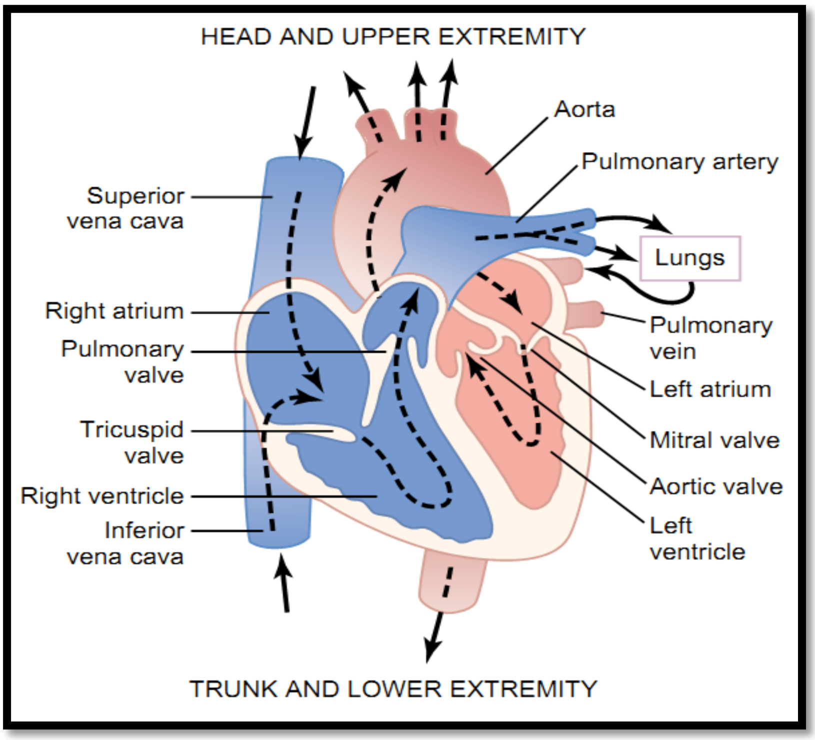
2.1 THE HEART

The heart can be considered as a pair of pulsatile pumps that synchronously receive blood from a low pressure reservoir and deliver it to a high pressure reservoir at a given rate (See Figure 2.1). Circulation through the pulmonary arteries, capillaries and veins is realized by the RV and the circulation through the systemic arteries, capillaries and veins is realized by the LV.

Right atrium (RA) receives deoxygenated blood returning from the body via superior and inferior vena cava, while left atrium (LA) receives oxygenated blood from the lungs via the pulmonary veins. Blood flows from the RA into the right ventricle (RV) through the tricuspid valve (TV), and at the same time from the LA into the left ventricle (LV) through the mitral valve (MV). It is then pumped from the RV through the pulmonary valve (PV) into pulmonary arteries supplying the lungs, and from the LV through the aortic valve (AV) into the aorta (Ao). Blood oxygenated in the lungs flows through the pulmonary veins back into the LA, and blood in the Ao flows through the high resistance systemic arteries and the low resistance systemic veins back into the RA. At this point, the circulatory cycle starts over to continually supply oxygenated blood to the whole body.

Since the total pulmonary resistance is almost five times lower than that of the total systemic resistance, the pressures are proportionally higher in the LV compared to RV in order to realize the same flow rate across each pump.

Figure 2.3: Structure of the heart, and course of blood flow through the heart chambers and heart valves



Source: Textbook of Medical Physiology 11th ed by Arthur C. Guyton, John E. Hall. Copyright at 2006 by Elsevier Inc.

2.1.1 The Cardiac Cycle

The cardiac cycle starts from the beginning of one heartbeat and ends at the beginning of the next heartbeat, and consists of four phases. Only the cycle in the LV will be explained below for simplicity, the cycle in the RV being exactly the same, except for the differences in the names of the anatomic structures involved.

The first phase is called diastole. Diastole includes rapid inflow of blood into the LV from the LA through the MV, diastasis and atrial kick. Rapid inflow is caused when the ventricular pressure falls below the atrial pressure (P_{LA}). As a result, the MV valve opens and blood flows into the ventricle rapidly as ventricular pressure keeps falling due to the continued relaxation of the ventricular wall. Diastasis is the period during which the heart is completely relaxed and the inflow rate is slowed down. Towards the end of diastole, the atrium contracts, increasing the pressure inside and forcing the remaining blood into the ventricle. This is called the atrial kick.

The second phase of the cardiac cycle is isovolumetric (or isovolumic) contraction (IVC). As the ventricle contracts, the pressure inside the left ventricle (left ventricular pressure, P_{LV}) rapidly increases and forces the closure of the MV. P_{LV} continues to rise until it reaches the level of the pressure inside the aorta (Aortic pressure, P_{Ao}). During this short period of rapid pressure rise, left ventricular volume (V_{LV}) doesn't change because both AV and MV are closed. As soon as P_{LV} surpasses P_{Ao}, AV opens, blood starts to flow into the aorta, V_{LV} begins to drop and IVC ends.

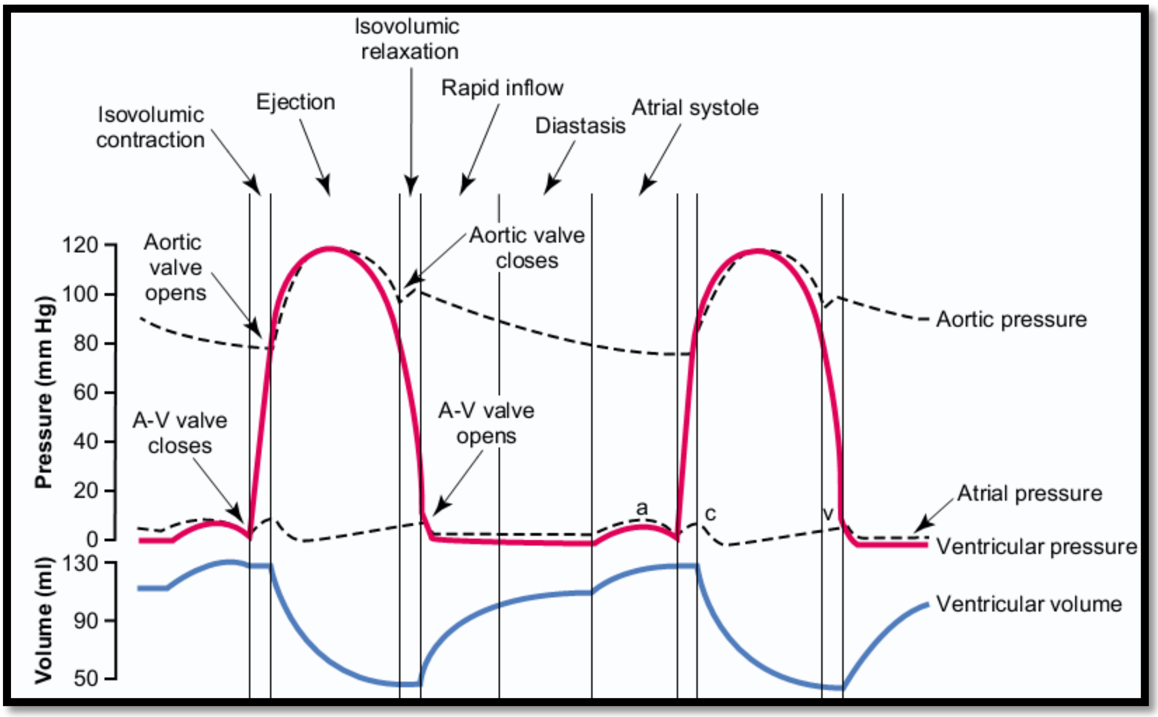
The third phase is called systole. Systole consists of two parts. These are rapid ejection and deceleration. Rapid ejection begins when P_{LV} exceeds P_{Ao} at which time the aortic valve (AV) opens and blood starts to flow into the aorta. During this period, P_{LV} remains slightly higher than P_{Ao} in order to create flow (Q_{LV}) through the AV. However, as V_{LV} decreases so does $P_{LV.}$ Reduced ejection occurs when P_{LV} is just below P_{Ao}, but blood flows into Ao because of inertia of blood itself. The atrial pressure rises slowly during this phase.

The fourth and last phase is Isovolumetric relaxation (IVR), which occurs when P_{LV}

falls rapidly below P_{Ao} and aortic valve closes.

The phases of the cardiac cycle are illustrated in Figure 2.4 for the LV in terms of the time variations of P_{LV}, P_{Ao}, P_{LA}, and V_{LV}. All phases listed for LV are also valid for RV with lower pressure values.

Figure 2.4: Events of the cardiac cycle for left ventricular function, showing changes in left atrial pressure, left ventricular pressure, aortic pressure and ventricular volume.



Source: Textbook of Medical Physiology 11th ed by Arthur C. Guyton, John E. Hall. Copyright at 2006 by Elsevier Inc.

2.1.2 The Pressure-Volume Loop

The cardiac cycle can also be described by plotting variation of P_{LV} against V_{LV} as shown in Figure 2.5. Such a plot is called the pressure-volume-loop (PV-loop).

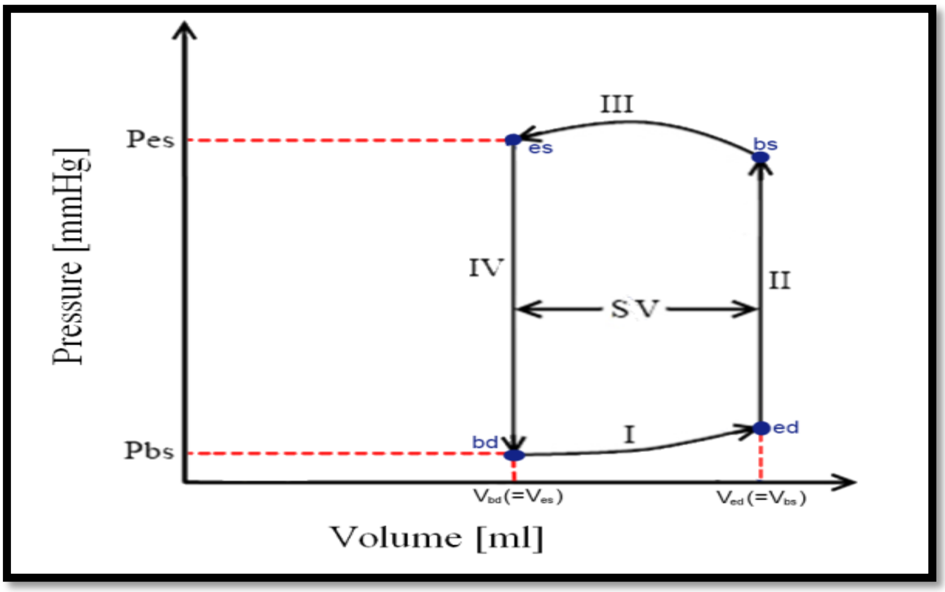
Phase I of the cardiac cycle, the filling period (diastole), corresponds to the lower part of the PV-loop, and is characterized by an increase of V_{LV} from a typical end-systolic value of about 45-50 milliliters (V_{es}) to a typical end-diastolic value of about 115-120 milliliters (V_{ed}), accompanied with a slight increase in P_{LV} from about 1-2 mmHg (P_{bd}) to an end-diastolic value of about 5-6 mmHg (P_{ed}).

During Phase II, the isovolumetric contraction period, P_{LV} rapidly increases from P_{ed} to the diastolic aortic pressure value, which is about 80 mmHg (P_{bs}), while V_{LV} remains constant at V_{ed} as both AV and MV are closed. This phase corresponds to the right vertical portion of the PV-loop.

Phase III, the ejection period (systole), corresponds to the upper portion of the PV-loop. This phase begins when the aortic valve opens. P_{LV} continues to rise, but since blood flows out from the left ventricle into the aorta, V_{LV} decreases. After reaching a maximum value of about 120 mmHg, P_{LV} starts to decrease as the heart muscles start to relax. Ejection phase ends when P_{LV} is balanced with P_{Ao} at a typical end-systolic value of about 110 mmHg (P_{es}), at which instant AV closes with V_{LV} at a minimum (V_{es}).

In Phase IV, which corresponds to the left vertical portion of the PV-loop, P_{LV} drops rapidly from P_{es} to P_{bd} with V_{LV} constant at V_{es} (isovolumetric relaxation), until the MV opens and the cycle restarts.

Figure 2.1: Volume-pressure diagram, demonstrating changes in volume and pressure during the normal cardiac cycle.



The amount of blood ejected from the LV during Phase III is called the stroke volume (SV):

$$Stroke\ Volume\ (SV) = \qquad \text{(Eq. 2-1)}$$

$$End\ Diastolic\ Volume\ (V_{ed}) - End\ Systolic\ Volume\ (V_{es})$$

Total amount of blood ejected in one minute is the average flow-rate out of the LV (measured in liters per minute), and is called the Cardiac Output (CO). Thus

$$\mathbf{Cardiac\ Output}\ (\mathbf{CO}) \qquad \text{(Eq. 22-1)}$$

$$= \mathbf{Stroke\ Volume}(\mathbf{SV})\ \mathbf{x}\ \mathbf{Heart\ Rate}\ (\mathbf{HR})$$

2.1.3 The Frank – Starling Mechanism

The heart has the ability of increasing its contraction force and, as a result, its stroke volume. The Frank-Starling law states that as more blood flows into the ventricle due to an increase in the left-atrial pressure, the heart works harder to pump more blood out. Dependence of the stroke volume, and hence the cardiac output on the left-atrial pressure is illustrated by the graph in Figure 2.6.

2.1.4 Elastance and Compliance of Ventricles

Blood pumped from the atrium to the ventricle during diastole increases the volume of the ventricle and stretches the muscle fibers in ventricle wall. Stretched muscle fibers behave like a spring and create a force that manifests itself as pressure inside the ventricle during systole. Dependence of pressure on volume is characterized by the elastance of the ventricle:

$$E = \frac{\Delta P}{\Delta V} \quad \text{(Eq. 2-3)}$$

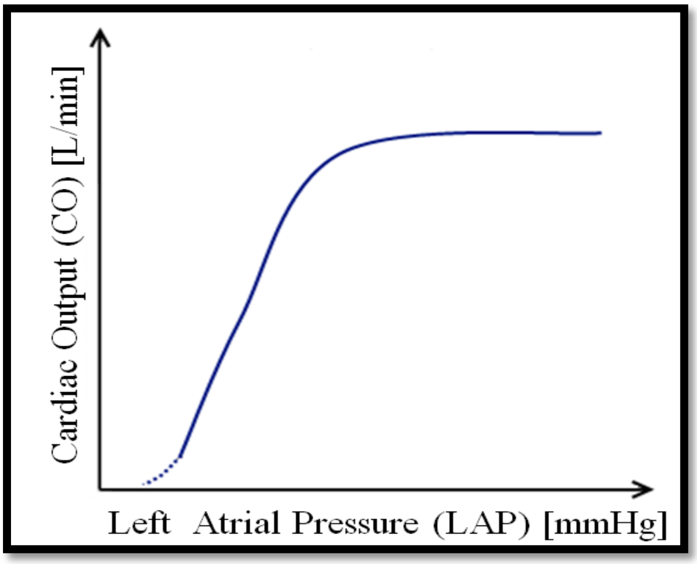
Thus, of the two LVs with different elastances, the one with a higher elastance creates a higher pressure than the one with a lower elastance for the same amount of the increase in the volume.

On the other hand, increase in the volume of the ventricle during diastole can be interpreted as a response to the pressure change caused by blood inflow. Dependence of volume on pressure is characterized by the compliance of the ventricle:

$$C = \frac{\Delta V}{\Delta P} \quad \text{(Eq. 2-4)}$$

Thus, although elastance and compliance are reciprocals of each other, elastance is an active property of the ventricle measuring its ability to create contractile force, while compliance is a passive property measuring its capacity to absorb flow.

Figure 2.6: Effect on the cardiac output (CO) curve of left atrial pressure (LAP)

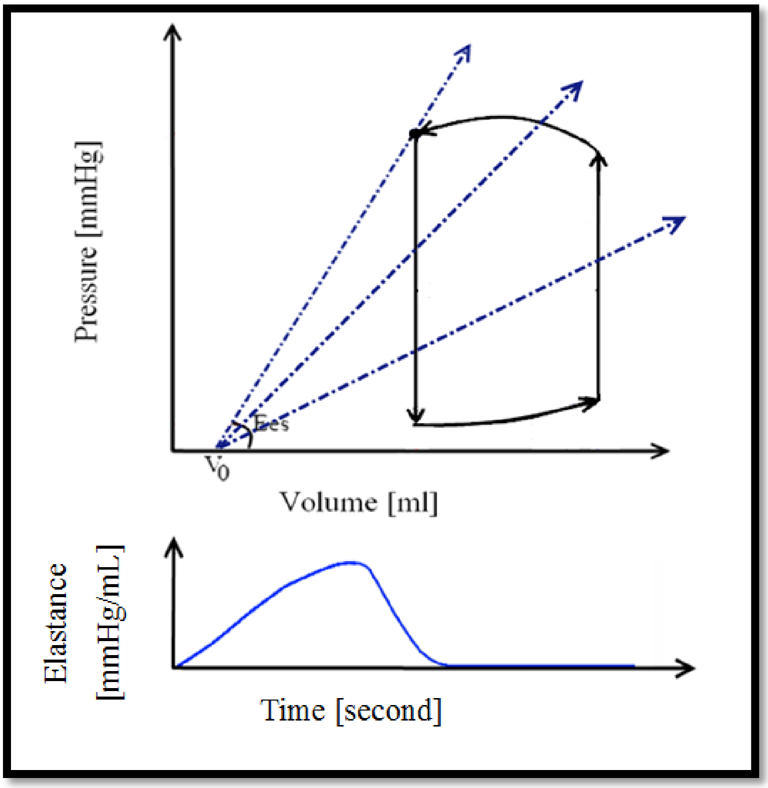


Source: Textbook of Medical Physiology 11th ed by Arthur C. Guyton, John E. Hall. Copyright at 2006 by Elsevier

2.1.5 Time-Varying Elastance Model of the LV

A trace of the PV-loop starting from the right bottom corner (begin contraction) describes the change of the LV elastance during the cardiac cycle as illustrated in Figure 2.7. The elastance-time curve thus obtained is often used in modeling the LV as a storage element (reservoir or capacitor) with a prescribed time-varying capacity.

Figure 2.7: Pressure-Volume Loop and Elastance-Time Curve



2.1.6 Heart Valves

Four valves, the mitral valve between LA and LV, the aortic valve between LV and Ao, the tricuspid valve between RA and RV, and the pulmonary valve between RV and the pulmonary artery provide unidirectional flow of blood in the CVS as

$$\text{LA} \rightarrow \text{LV} \rightarrow \text{Ao} \rightarrow \text{Body} \rightarrow \text{RA} \rightarrow \text{RV} \rightarrow \text{Lungs} \rightarrow \text{LA}$$

Although the operation of the heart valves involves some nonlinear dynamics, they are usually modeled as resistive elements with nonlinear flow-pressure characteristics

$$Q = \begin{cases} G\Delta P, & \Delta P \geq 0 \\ 0, & \Delta P \leq 0 \end{cases} \qquad \text{(Eq. 2-5)}$$

2.2 THE CIRCULATORY SYSTEM

The circulatory system consists of the passive components of the CVS each of which can be modeled as combination of a storage element together with a resistive and possibly an inertial element.

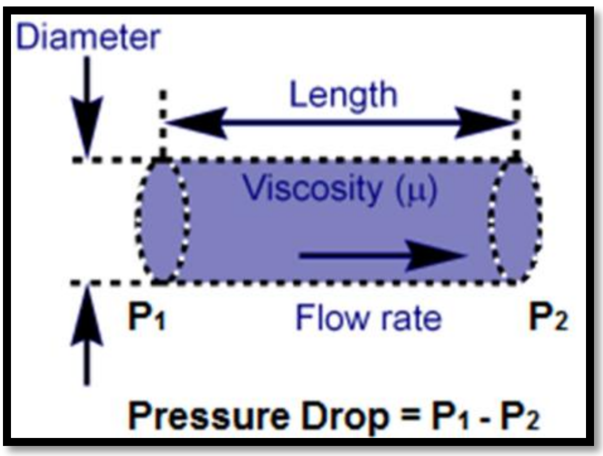
Hydraulic resistance in vessels is defined as the slope of the pressure-flow relationship obtained by measuring vascular pressure at several fluid flow rates **(**Scott DA 1996, p. 331). It is calculated in terms of the length (L) and the radius (r) of the pipe, and the viscosity(μ) of the fluid as

$$\Delta P = \frac{8\mu L}{\pi r^4} Q \qquad \text{(Eq. 2-6)}$$

The parameters used in Eq. 2-6 are illustrated in

Figure 2.2:.

Figure 2.2: Pressure – Flow relationship value references on the pipe



Inertial effects are due to the force (pressure) needed to accelerate blood in the vessels. Referring to

Figure 2.2:, inertance coefficients can be determined as

$$\Delta P = \frac{\rho L}{\pi r^2} \frac{dQ}{dt} \qquad \text{(Eq. 2-7)}$$

Table 2.1 below summarizes the compliance, resistance and inertance coefficients associated with major components of the circulatory system

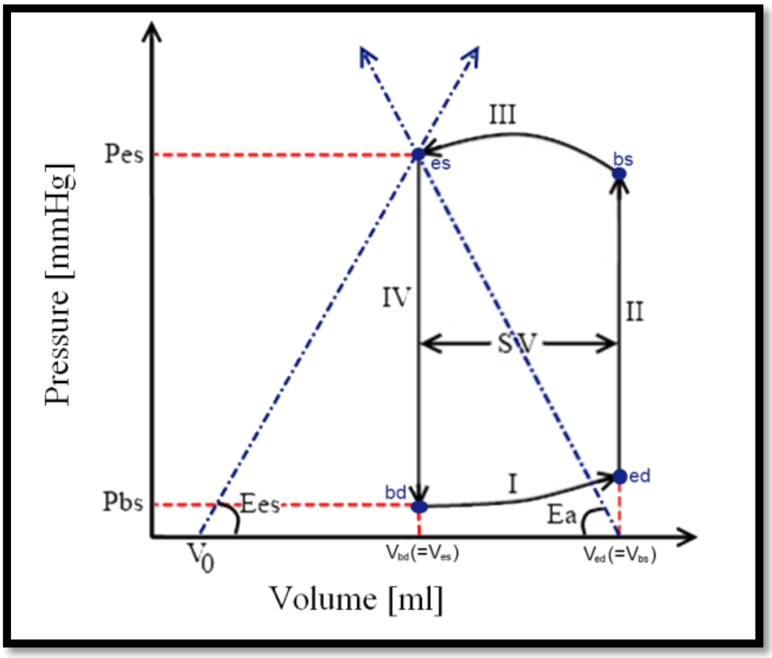
Table 2.1: Coefficients of Circulatory System Components

Component	Compliance (mL/mmHg)	Resistance (mmHg.s/mL)	Inertia (mmHg.s^2/mL)	Volume (mL)
LA	8	$7e^{-4}$	$5.4\ e^{-4}$	40
LV	11	$7e^{-4}$	$5.4\ e^{-4}$	40
Ao	1.5	$1e^{-4}$	$1.2\ e^{-4}$	715
SV	20	$4e^{-4}$	$9.7\ e^{-4}$	2785

2.3 VENTRICULAR-ARTERIAL COUPLING

Interactions between the LV and ventricular-arterial coupling (arterial system) are key factors for cardiovascular function. Ventricular arterial coupling is evaluated more frequently in the level of pressure-volume ratio of effective arterial elastance (EA), end-systolic elastance (EES) (see Figure 2.3). EA as the final volume of the systolic pressure / stroke can calculate, while EES ideal evaluated using data obtained from a pressure-volume curves during acute change bias.

Figure 2.3: Elastance of LV and Aorta in P-V loop



3. DESIGN AND IMPLEMENTATION OF A CARDIOVASCULAR MOCK CIRCIUT

Design of a CVMC involves

a) compiling the requirements (design criteria)
b) deciding on the physical structure of the CVMC
c) modeling the components of the CVMC and setting up the model parameters
d) simulating the model on computer and iterating on the model parameters until realistic results are obtained
e) implementing the model, together with actuators and sensors, in the physical environment
f) operating the physical model and tuning the physical parameters until satisfactory performance is achieved

In this section we present our work on each of the tasks listed above.

3.1 DESIGN CRITERIA

3.1.1 Physical Design Criteria

a) Size: The CVMC must be implementable on a table top.

b) Modularity: Components of the CVMC must be simple, replaceable and standardized as much as possible. The structure must allow addition of new components should a need arise.

c) Durability: CVMC must include minimum number of mechanical parts.

d) Set-up and Calibration: CVMC must be easy to set-up and components must be easy to calibrate.

3.1.2 Functional Design Criteria

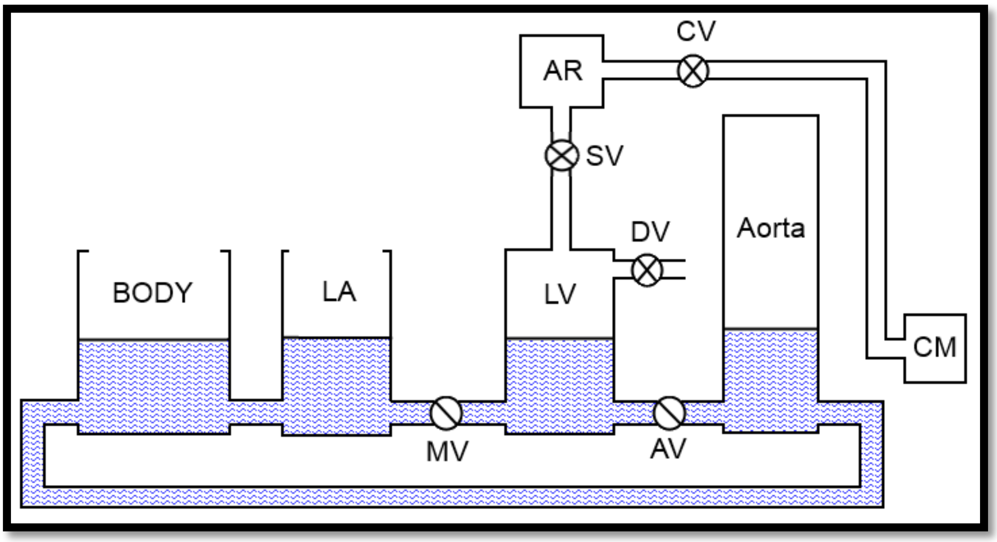
a) Both the virtual (computer) design and the physical model must have realistic pressure and flow characteristics.

b) Active components of the system must be controllable to implement exercise and CHF modes.

3.2 PHYSICAL STRUCTURE

Giving priority to physical design criteria, we decided to omit the left right ventricle from the model, and condense the rest of the circulatory system to three components, representing the aorta, the body and the left atrium. This resulted in the simple hydraulic model shown in Fig. 3.1 that consists of four cylindrical chambers, the three mentioned components plus one representing the left ventricle. In addition to these main components, we included mitral and aortic valves, and a pneumatic drive mechanism for the left ventricle, which consists of an air supply (compressor), an air reservoir that provides power to drive the LV, and several unidirectional air valves to control the drive mechanism.

Figure 3.1: Physical Structure of the CVMC



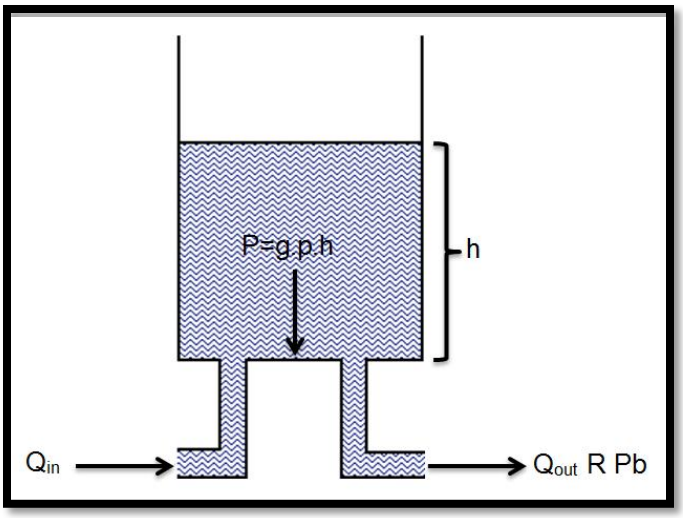
3.3 COMPONENT CHARACTERISTICS

In CVMCs, water is circulated instead of blood. An open reservoir is used to represent the low-pressure LA, and closed reservoirs are preferred for high-pressure Ao and Bo to avoid excessively high water levels.

3.3.1 Open Chambers

A typical open chamber is shown in Figure 3.2. Using the relations

Figure 3.2: Open reservoir parameters



$$P = \rho g h = \frac{\rho g}{A} V \qquad \text{(Eq. 3-1)}$$

$$\dot{V} = Q_{in} - Q_{out} \qquad \text{(Eq. 3-2)}$$

$$Q_{out} = \frac{P - P_{out}}{R} \qquad \text{(Eq. 3-3)}$$

where h is the water level, V is the water volume, P is the pressure at the bottom (inlet) of the tank, P_{out} is the load (outlet) pressure Q_{in} and Q_{in} are the inflow and outflow rates, respectively, ρ is the water density, g is the gravitational acceleration constant, A is the cross-sectional area of the chamber, and R is the hydraulic outlet resistance, the dynamic model of the chamber is obtained as

$$\dot{P} = -\frac{1}{CR} P + \frac{1}{C}\left(Q_{in} + \frac{P_{out}}{R}\right) \qquad \text{(Eq. 3-4)}$$

where

$$e = \frac{1}{C} = \frac{\rho g}{A} \qquad \text{(Eq. 3-5)}$$

is the elastance of the chamber.

3.3.2 Closed Chambers

The model of typical closed chamber is shown in Fig. 3.3 is obtained, using Eq. (3.2), Eq. (3.5), and the relation

$$(P_{air} + P_{atm})(V_T - V) = P_{atm}(V_T - V_o) \qquad \text{(Eq. 3-6)}$$

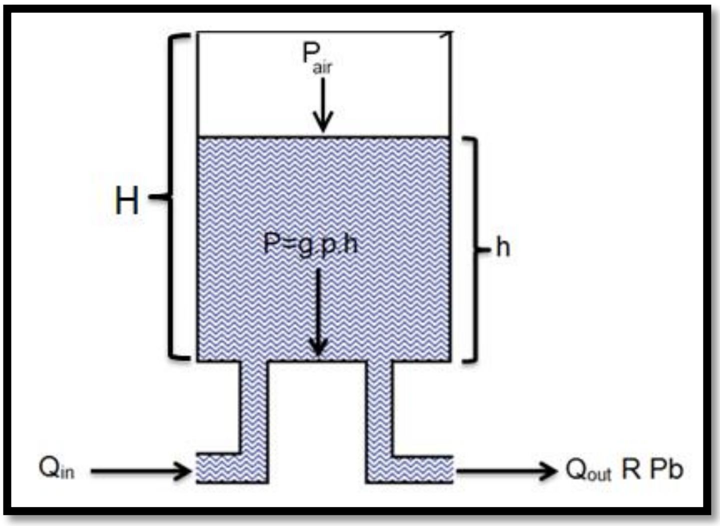
where P_{atm} is the atmospheric pressure, V_T is the total chamber volume, and V_o is the water volume corresponding to $P_{air} = 0$, as

$$P = \frac{V - V_o}{V_T - V} P_{atm} + \frac{\rho g}{A} V \qquad \text{(Eq. 3-7)}$$

From Eq. (3.7), instantaneous elastance of the component at an operating volume is calculated as

$$e(V) = \frac{\partial P}{\partial V} = \frac{V_T - Vo}{(V_T - V)^2} P_{atm} + \frac{\rho g}{A} \qquad \text{(Eq. 3-7)}$$

Figure 3.3: Closed reservoir parameters



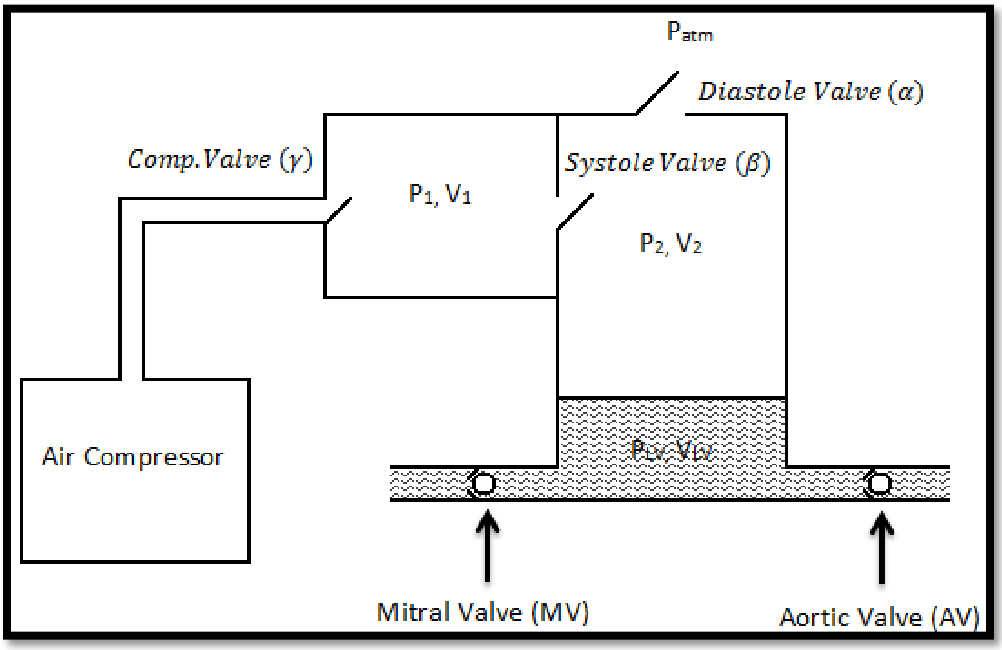
3.3.3 Left Ventricle (LV)

The model of the LV is shown in Fig. 3.4. Contraction of the LV is realized by pumping pressurized air from the reservoir chamber (chamber #1) into the LV chamber (chamber #2) through the systole valve (β), and the relaxation by releasing air from the LV chamber into atmosphere through the diastole valve (α). During diastole, used air of the reservoir is resupplied by the compressor through the compressor valve (γ) for the next cycle. Timing of the valves is shown in the following Table 3.1. Equations describing the LV model are given as follows.

Table 3.1: Timing of the pneumatic LV valves

Pneumatic Valve	Systole		Diastole
	Contraction	Relaxation	
α	OFF	OFF	ON
β	ON	OFF	OFF
γ	OFF	OFF	ON then OFF

Figure 3.4: Left ventricle parameters



During IVC:

$$
\begin{aligned}
(P_1\dot{V}_1) &= -\beta(P_1 - P_2) \\
(P_2\dot{V}_2) &= \beta(P_1 - P_2)
\end{aligned}
$$

During relaxation:

$$(P_2\dot{V}_2) = constant$$

During diastole:

$$
\begin{aligned}
(P_2\dot{V}_2) &= -\alpha(P_2 - P_{atm}) \\
(P_1\dot{V}_1) &= \begin{cases} \gamma(P_c - P_1), & P_1 < P_{10} \\ 0, & P_1 \geq P_{10} \end{cases}
\end{aligned}
$$

3.3.4 Pipes (Tubes)

Connection between chambers was provided by using flexible transparent Tygon® tubes that are modeled as

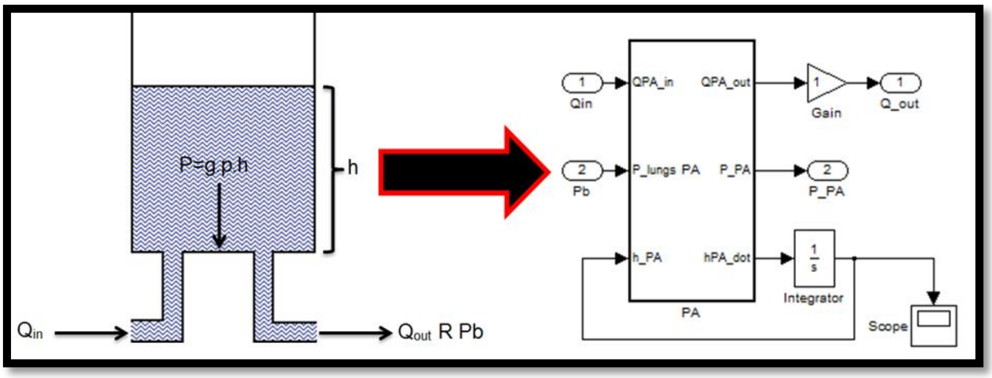
$$q = G\Delta P \quad \text{(Eq. 3-4)}$$

3.4 METHOD

MATLAB/SIMULINK (The Mathworks, Natick, MA, and U.S.A) was used to simulate CVMC in visual environment.

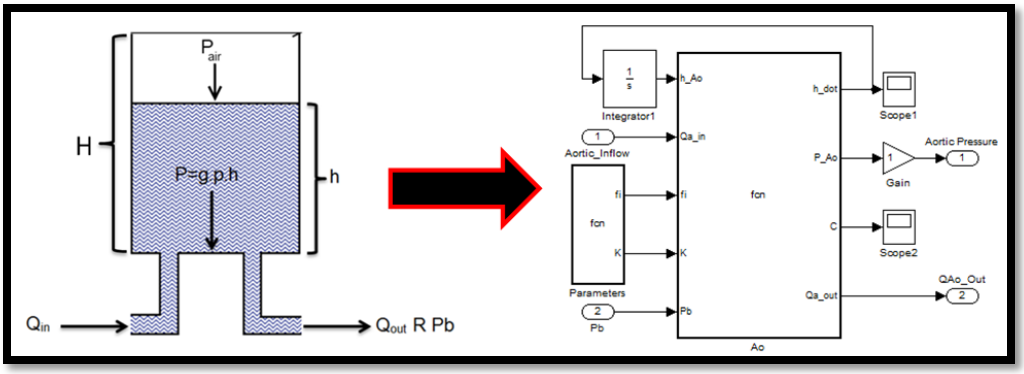
To model the CVMC, subsystems for Left Ventricle (LV), Aorta (Ao), Body and Right Atrium (RA) were created. The pressure and flow output of each system was calculated using the flow output from the previous subsystem and the pressure output from the following subsystem. Simulink diagrams and associated codes for open and closed reservoirs are given in Figure 3.5 and Figure 3.6, respectively.

Figure 3.5: Simulink diagram of open reservoirs




```
function [QPA_out,P_PA,hPA_dot]= PA(QPA_in,P_lungs,h_PA)
r=.0375;
A=pi*(r^2);
P_PA=9810*h_PA;
R_PA_btw_lungs=(16)*133.32*60*(10^2)/5;
QPA_out=(P_PA-P_lungs)/R_PA_btw_lungs;
hPA_dot=(QPA_in-QPA_out)/A;
end
```

Figure 3.6: Simulink diagram of closed reservoirs




```
function [h_dot,P_Ao,C,Qa_out]= fcn(h_Ao,Qa_in, fi,K,Pb)
q = 1000;
g = 9.81;
H_Ao = 1;
A_Ao=pi*(0.03^2);
R=10^6;
P_Ao=(q*g*h_Ao)+(fi*A_Ao*q*g*(H_Ao^2));
Qa_out=P_Ao-Pb/R;
h_dot=(Qa_in-Qa_out)/A_Ao;
V=A_Ao*H_Ao;
Vt=h_Ao*A_Ao;
C=((V-Vt)^2)/(K+((V-Vt)^2));
end
```

3.5 IMPLEMENTATION CARDIOVASCULAR MOCK CIRCUIT

3.5.1 CVMC CONTROL

CVMC requires a control mechanism. It was vital that the parameters which control the CVMC could be easily changed. dSPACE (dSPACE GmbH, Germany) is a hardware and software package that supports the tools for control of check valves by collected real-time pressure and flow data from transducers and flow-meter.

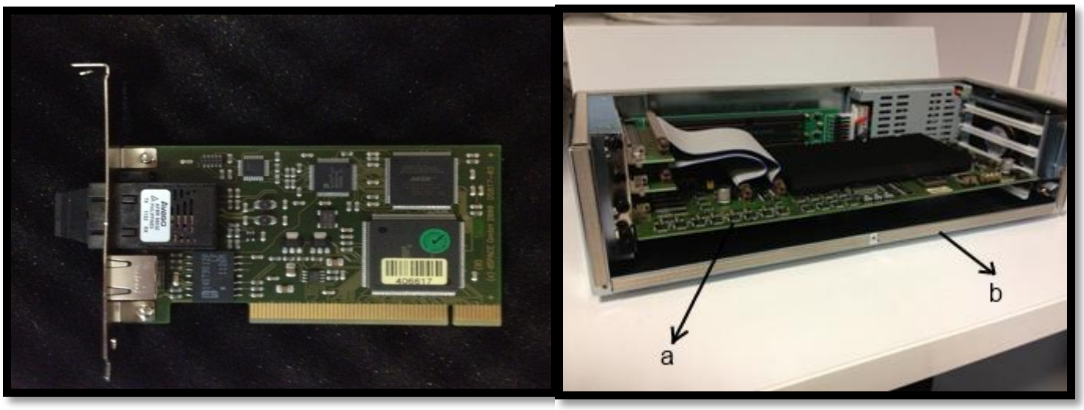
3.5.1.1 Hardware Installation of dSPACE Advanced Control Kit 1103

dSPACE DS817 PCI Controller Board and PPC control card (see Figure 3.7) provides data transfer between computer and dSPACE. Real-Time Interface (RTI) provides Simulink® blocks for graphical I/O configuration. Controller board provides to configure all I/O graphically, insert the blocks into a Simulink block diagram, and generate the model code via Simulink.

DS1103 control card, placed into DS814 PX4 case which has serial port communication module is attached, shown in Figure 3.7(ii). DS817 PCI card is placed into computer's PCI socket as shown in Figure 3.8.

Figure 3.7: dSPACE DS817 PCI Controller Board (left)

(a) PPC control card (b) DS814 PX4 Case and Serial Port Interface (right)



dSPACE CLP1103 Single-Board-Hardware has 20 analog to digital converters (ADC) input, 8 digital to analog converts (DAC) output, Digital I/O sub-d connector and serial interfaces. ADCs are used as input connections from pressure transducers and flow-meters. DACs are used as output connections from MATLAB/Simulink to check valves and proportional control valves.

Figure 3.8: Position of DS817 PCI card inside the computer

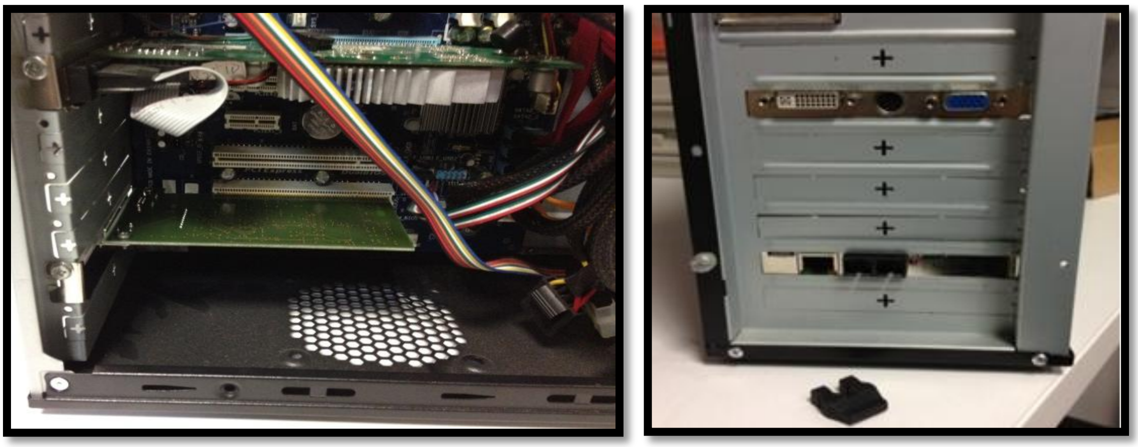


Figure 3.9: Single Board Hardware of CLP1103

DS817 PCI card is connected to DS814 PX4 case, via high speed optic cable. Also CLP1103 Single Board Hardware's data transmitting cables (P1, P2, P3) connected to DS814 case as shown in the Figure 3.10.

Figure 3.10: CLP1103 data transmitting cables

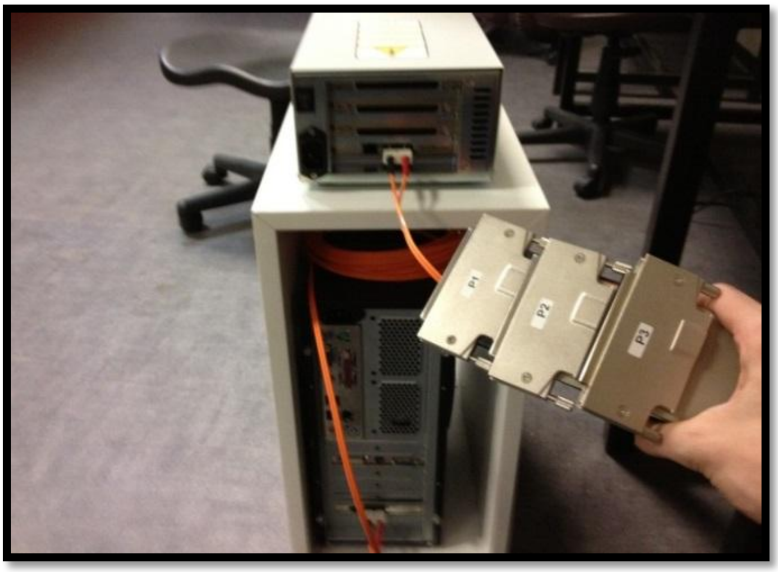
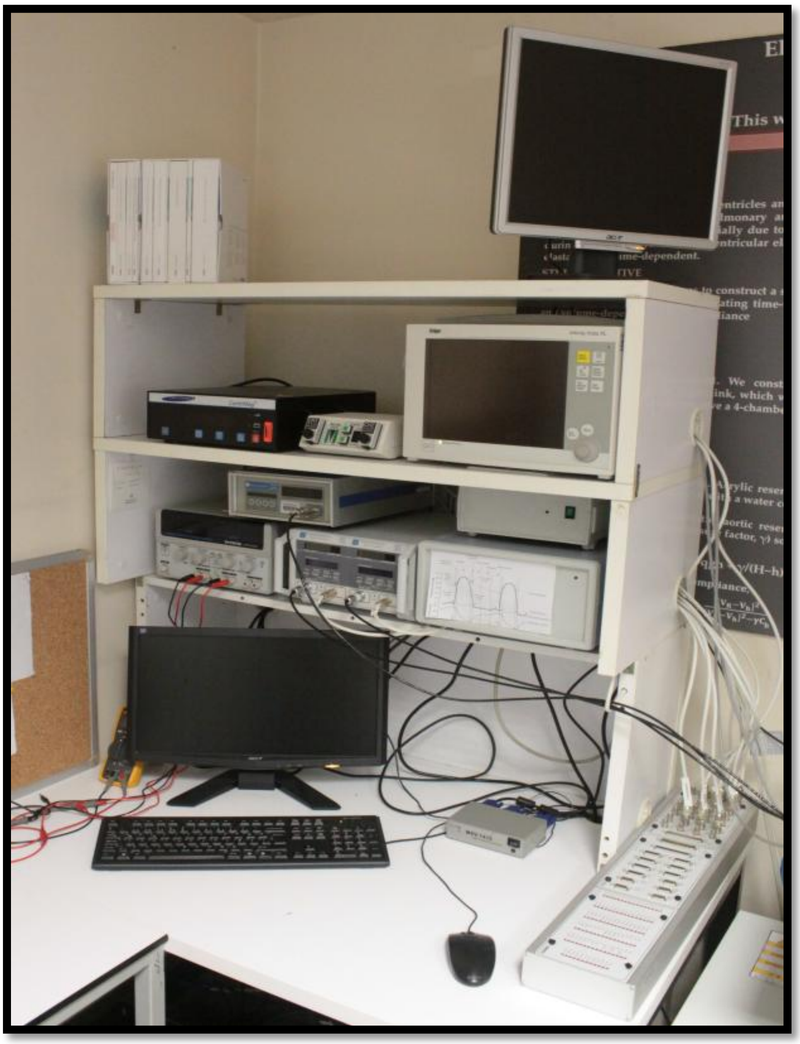


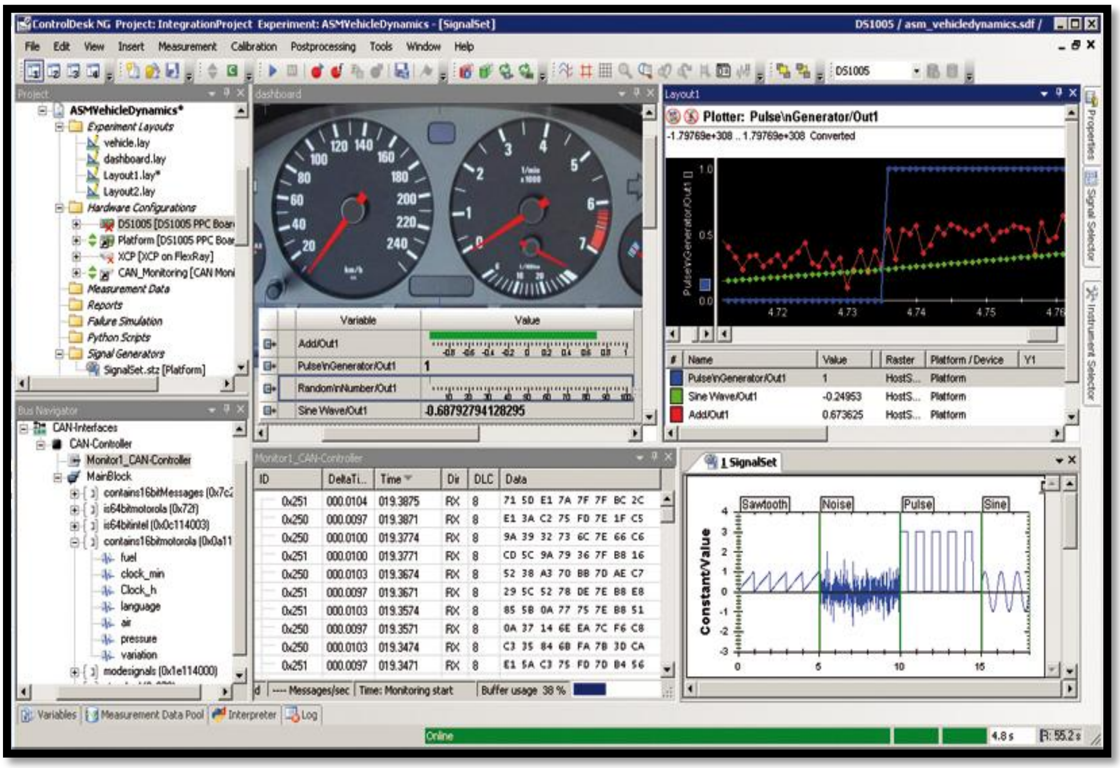
Figure 3.11: General View of the Workspace



3.5.1.2 Software Installation of Control Desk

For the graphical user interface (GUI) Control Desk software was used (shown in the Figure 3.12). Control Desk allows the user to change parameters in real time and reading input and output values simultaneously. Also Control Desk provides data acquisition to compare results after tests.

Figure 3.12: Control Desk Example Screen



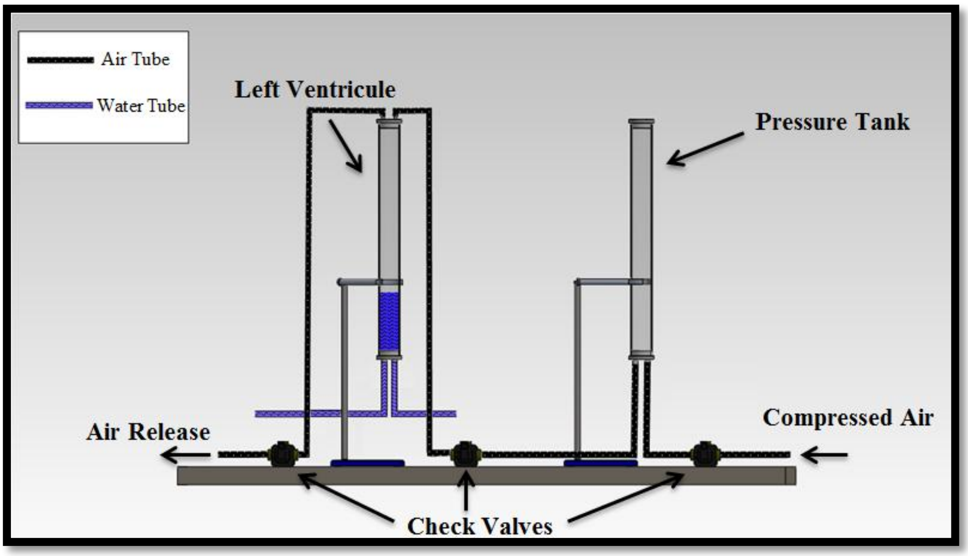
3.5.2 CVMC VIRTUAL DESIGN

By using the results obtained in the Simulink model of a Cardiovascular Mock Circuit (CVMC), a new CVMC was virtually designed to produce accurate pressure and flow diagrams. The new CVMC was required to replicate the human circulatory system.

SolidWorks (DassaultSystèmes, Vélizy, France) is 3D CAD (Computer Aided Design) program is used to design the product before production. SolidWorks was used to design three air/water chambers and chamber for left ventricle (LV).

3.5.2.1 The Ventricle

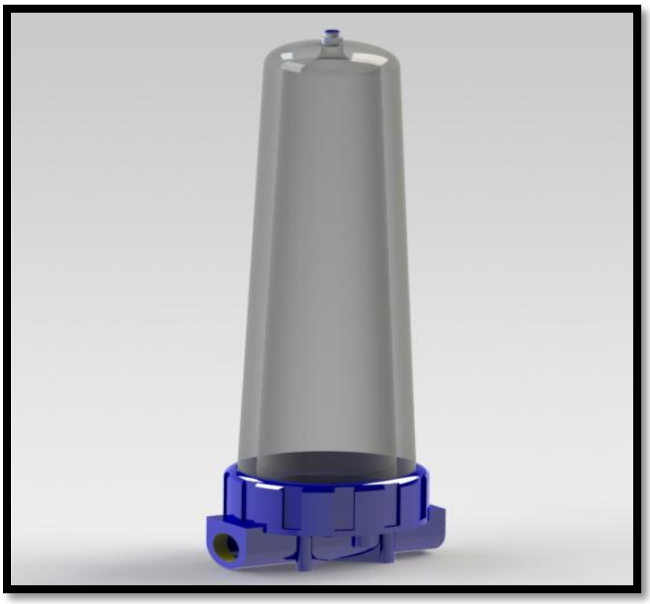
Figure 3.13: Left Ventricle Pneumatic System Design



3.5.2.2 The Chamber

The four chambers which are Left Atrium (LA), Aorta (Ao), Pulmonary Artery (PA) represented by transparent, horizontal chambers with one hole at the top for air transfer and two holes at the bottom of the chamber for fluid flow.

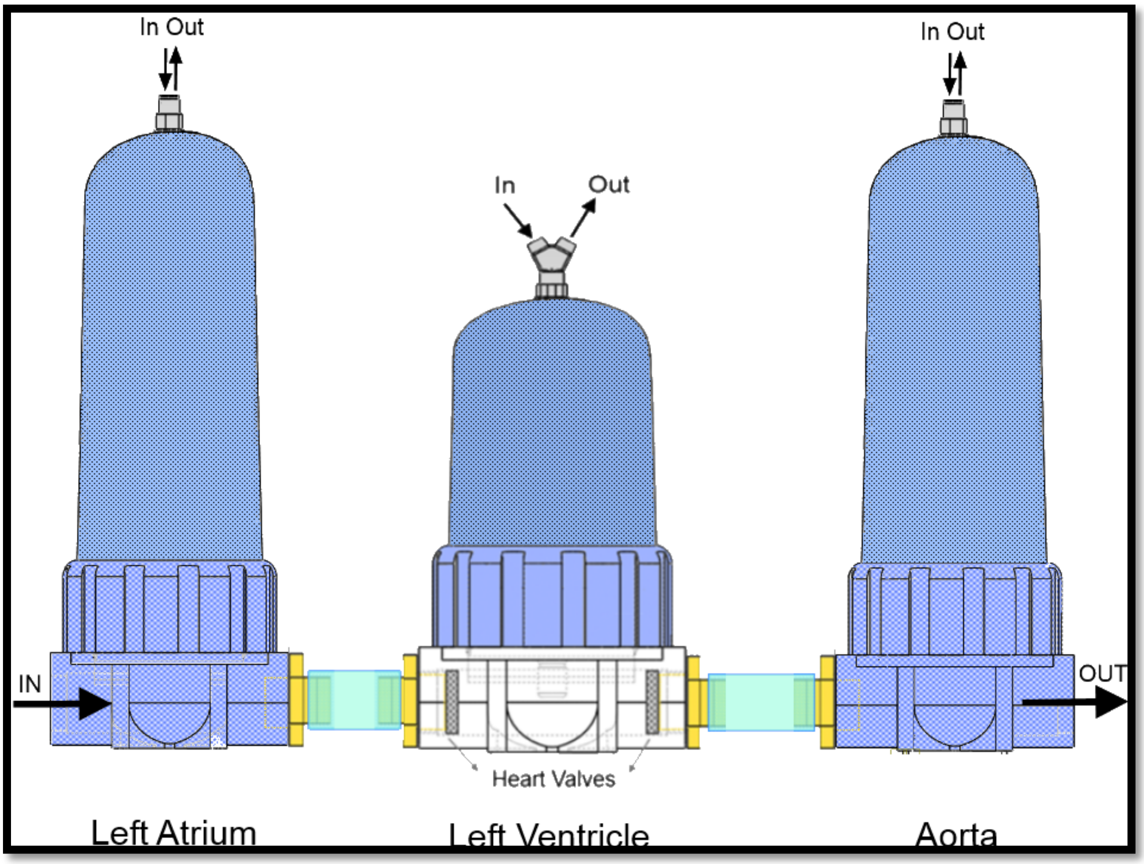
Figure 3.14: Solidworks Drawing of Designed Chamber



3.5.2.3 Aorta, LV and LA

Aorta, LV and LA connected each other by using Tygon tubes and artificial heart valves placed both side of LV.

Figure 3.15: Left Ventricle Drawing



3.5.3 CVMC MECHANICAL BUILDING

By using the results obtained in the Simulink model and Solidworks drawings of a Cardiovascular Mock Circuit (CVMC), a new CVMC was mechanically built to produce accurate pressure and flow diagrams. The new CVMC was required to replicate the human circulatory system.

CVMC is designed with four chambers for simplify system. However, this system can improve to eight chamber with adding other chambers.

Figure 3.16: Solidworks Design of CVMC.

3.5.3.1 Heart Valves

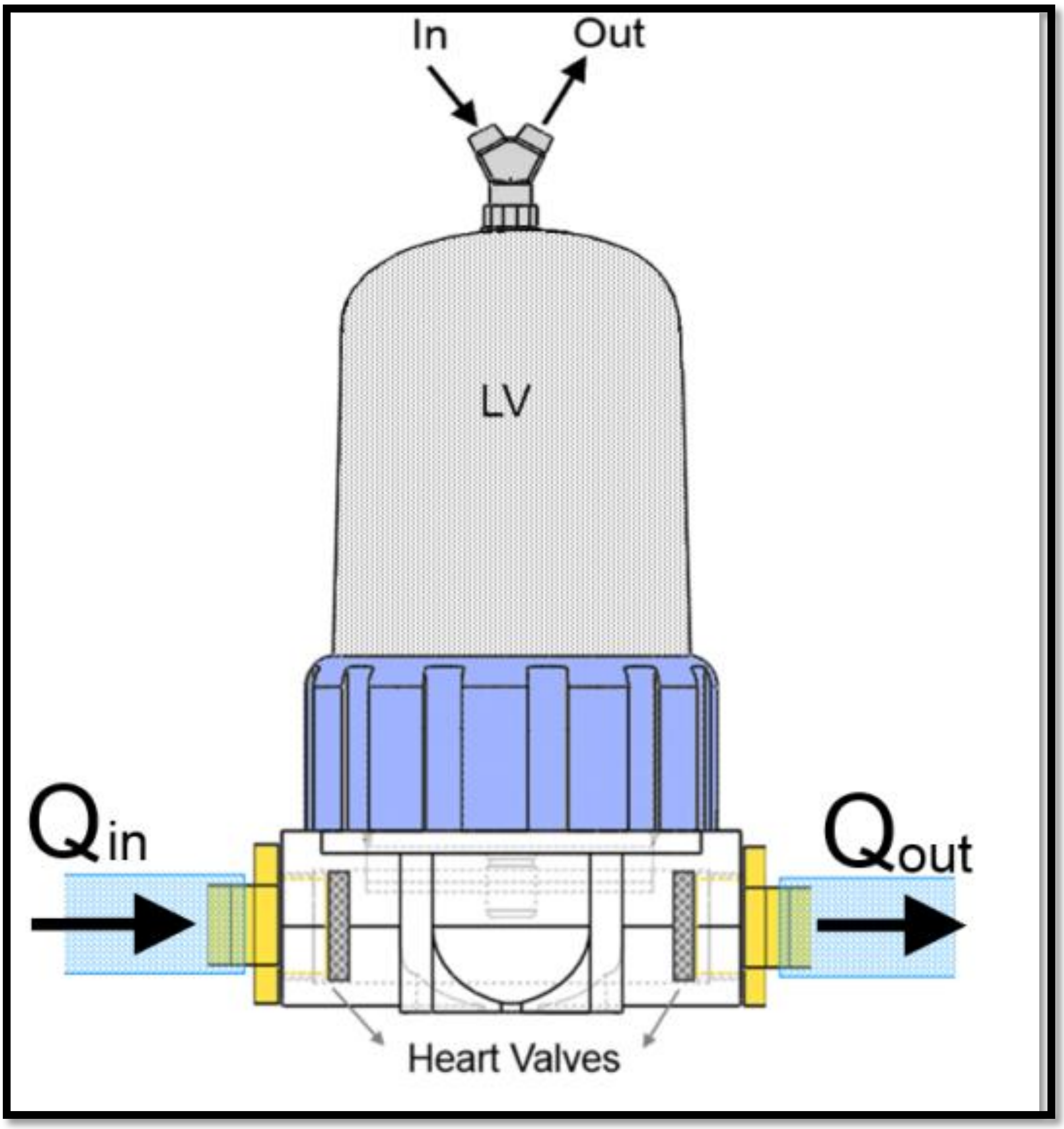
For simulate heart valves St. Jude artificial heart valves was used. St. Jude mechanical heart valve is shown in the Figure 3.17. Both Aortic and Mitral valves are standard cuff-polyester types. Aortic valve (AV) tissue annulus diameter is 29 mm, Mitral valve (MV) tissue annulus diameter is 25 mm, and material is pyrolytic carbon and woven polyester cuff.

Figure 3.17: **St. Jude Mechanical Heart Valve**

Source: Mechanical Aortic Valve Replacement Options For Patients. [ONLINE] Available at: http://www.heart-valve-surgery.com/heart-surgery-blog/2008/09/10/mechanical-aortic-valve-replacement-options/. [Accessed 11 December 2013].

Artificial heart valves are placed both side of LV. In that way mitral valve is connected between LA and LV and Aortic valve is connected between LV and Aorta. (see Figure 3.18)

Figure 3.18: Assembly of Heart Valves, Aortic Valve and Mitral Valve



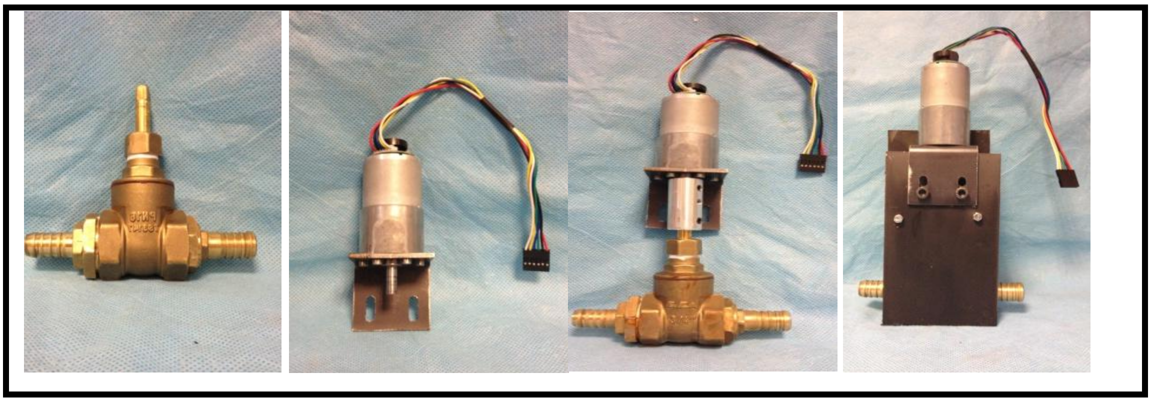
3.5.3.2 Proportional Control Valves

Resistance has to be replicated by mock circuit. Resistance of each section in the CVMC is determined by the length and cross-sectional area of the pipe. However, the Systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) changes are more than other resistances. That problem cause's need for a variable level of resistance. This was achieved by design and manufacture of proportional control valve which shown in Figure 3.19.

Figure 3.19: Proportional Control Valve

Outlet tube of Aorta (3/4" diameter) is connected to proportional flow valve serially. DC motor (131:1 Metal Gear motor 37Dx75L mm with 64 CPR Encoder) which has high torque-low speed properties (80 rpm x 18 kg/cm @ 12 Volt) is connected to top of the valve via coupling. Motor and valve fixed to metal frame. dSPACE controlled driver is used for obtain variable resistance by changing inside diameter of valve, directly proportional to rotation time and direction.

Figure 3.20: Proportional Control Valve Parts and Body



Proportional Control Valve (PCV) is used to control mean Aortic Flow (Q_{Ao}) constant. For obtain instantaneous resistance value (R_{PCV}) pressure difference between PCV (ΔP) and PCV output flow (Q_{PCV}) data taken from physical systems divided to each other ((Eq. **3-5** and (Eq. **3-6**.) Desired flow (Q_d) divided with ΔP gives desired resistant (R_d) ((Eq. **3-8**). Differences between these resistances gives resistance error (R_e) (Eq. 3-9).

$$\Delta P = P_{Ao} - P_{Pa} \qquad \text{(Eq. 3-5)}$$

$$P_{Ao} - P_{Pa} = R_{PCV} \text{ x } Q_{Ao} \qquad \text{(Eq. 3-6)}$$

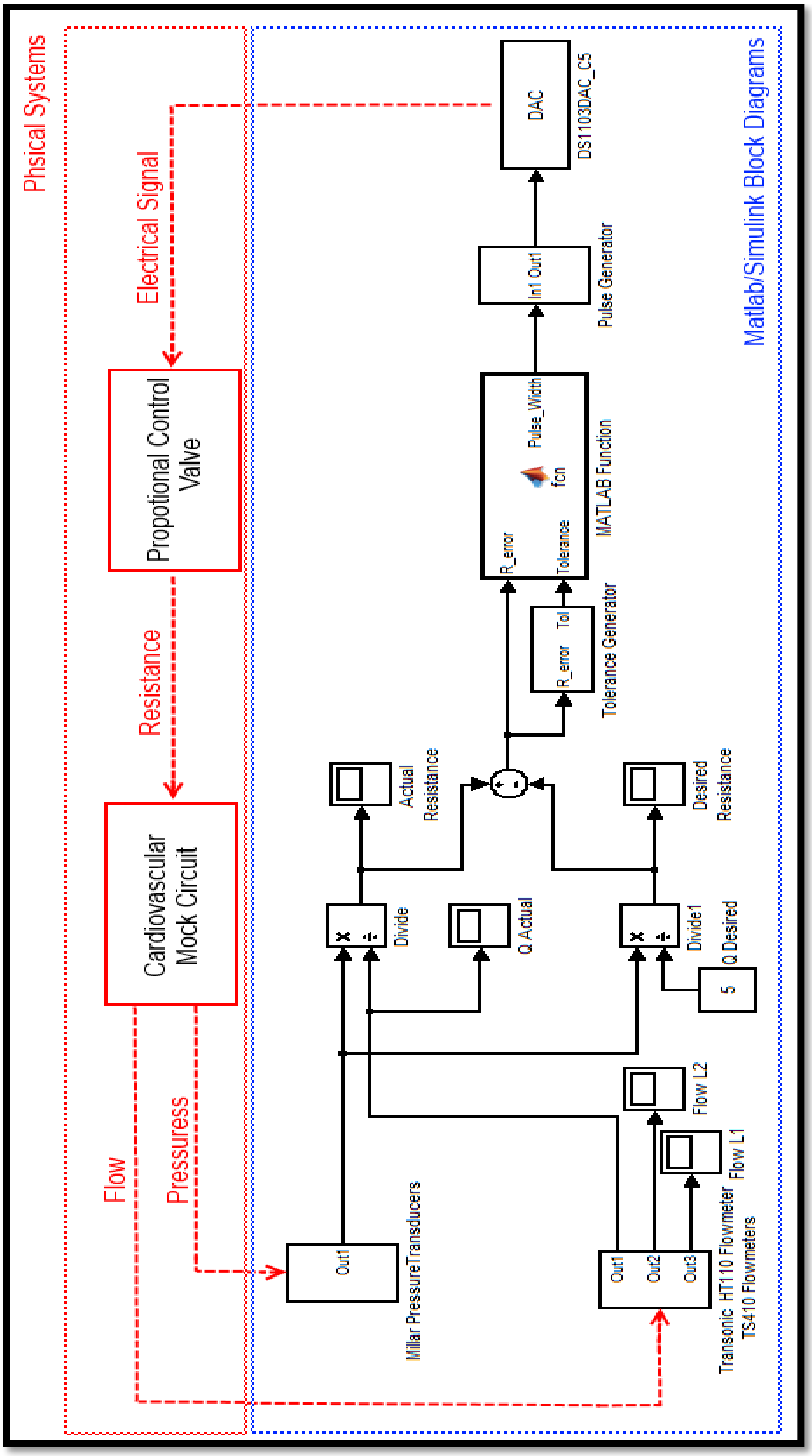
$$R_{PCV} = P_{Ao} - P_{Pa} \ / \ Q_{PCV} \qquad \text{(Eq. 3-7)}$$

$$R_d = P_{Ao} - P_{Pa} \ / \ Q_{dk} \qquad \text{(Eq. 3-8)}$$

$$R_e = R_{RCP} - R_d \qquad \text{(Eq. 3-9)}$$

If error is bigger than tolerance value, square wave voltage created from PWM (Pulse Wight Modulation) block based on error value for drive dc brushless motor. Matlab/Simulink blocks and physical system diagrams shown in Figure 3.21.

Figure 3.21: Matlab/Simulink blocks and physical system diagrams



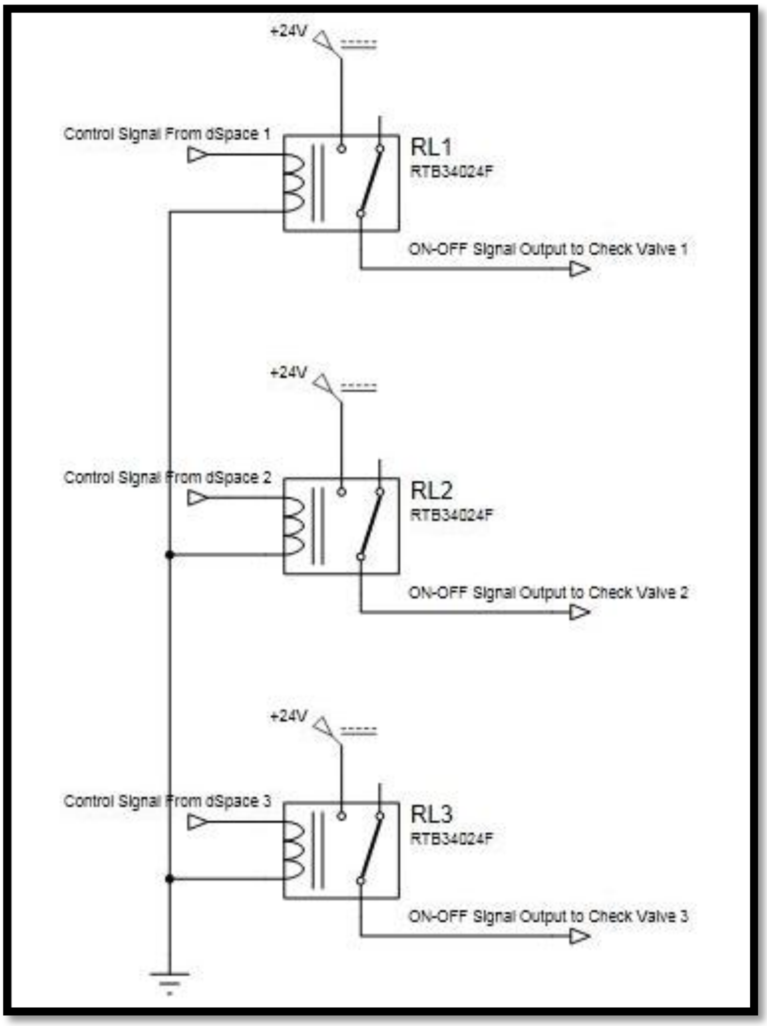
3.5.3.3 Check Valves

Pneumatic check valves (see Figure 3.22) are used for control air flow in the LV system as a Diastole valve, systole valve and compression valve which are shown in Figure 3.22 were used as three pneumatic check valves in shown positions. Check valves needs air pressure and +24V to change status. However, dSPACE output range is between -10V to +10V. For solve this problem, relays are used because relays can change status with +5V which is in range of dSPACE output voltage. Circuit of relays shown in Figure 3.23.

Figure 3.22: Pneumatic Check Valve

Souce: Poppet Valves-Systematıc. [ONLINE] Available at http://systematic.com.tr/pdf/1,2%20DI%C5%9ETAN%20P%C4%B0LOTLU%20POPPET%20VALF%20N.A.pdf. [Accessed 11 December 2013].

Figure 3.23: Check Valves Relay Circuit



3.5.3.4 Pressure Sensors

Millar Pressure Sensors

Millar PCU-2000 (Millar Instruments Inc., Canada) 2 channel pressure transducer control unit (see Figure 3.24) is used for measure instantaneous pressure at the bottom of LV and Aorta chambers for more obtain accurate pressure data. Catheter type SRP3705 model pressure transducers connected with PEC-10C type cables to Millar PCU-2000.

Figure 3.24: Millar PCU-2000 (a) front view (b) back view

(a) (b)

1/4 inch stereo type socket and BNC connector used for assemble cable which shown in Figure 3.25 (c). This cable takes pressure data from Millar PCU-2000 to dSPACE analog to digital converter (ADC) input.

Figure 3.25: a) SPR 3705 Pressure Transducer b) PEC-10C cable c) Cable between Millar PCU and dSPACE

(a) (b) (c)

Calmed Pressure Transducers

Figure 3.26: Calmed® Pressure Transducers

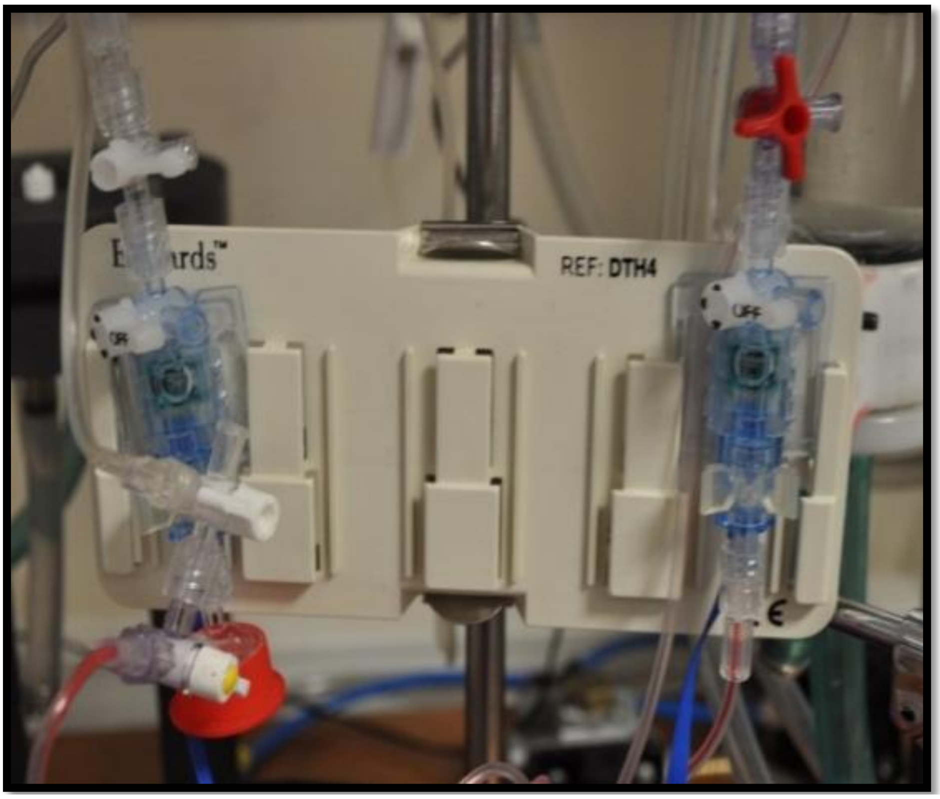
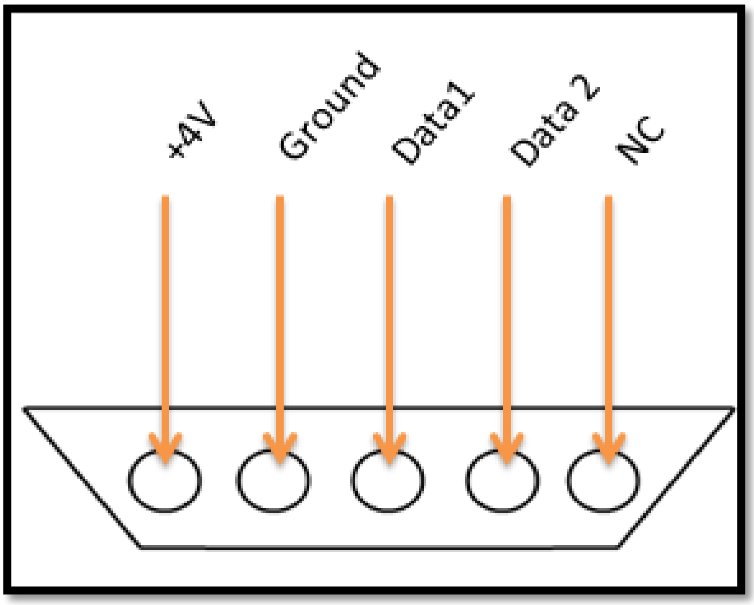
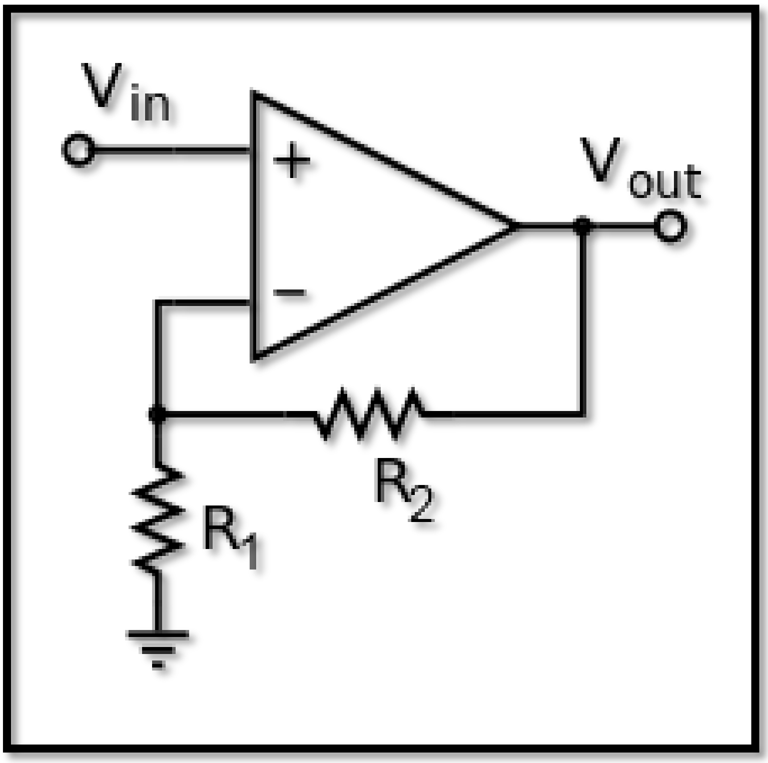


Figure 3.27: PBV connector of Pressure Transducers



Range of data voltages are measured from pressure transducers are between 0 and 5mV. That's why voltage amplified with analog amplifiers. As a amplifier Texas Instruments uA747C is used. Calculations of amplifier based on ideal pop-amp formula in (Eq. 3-10). Amplified voltage has to be between -10V and +10V for usability in the system and also protection of dSPACE hardware.

Figure 3.28: A Non-inverting Amplifier Circuit



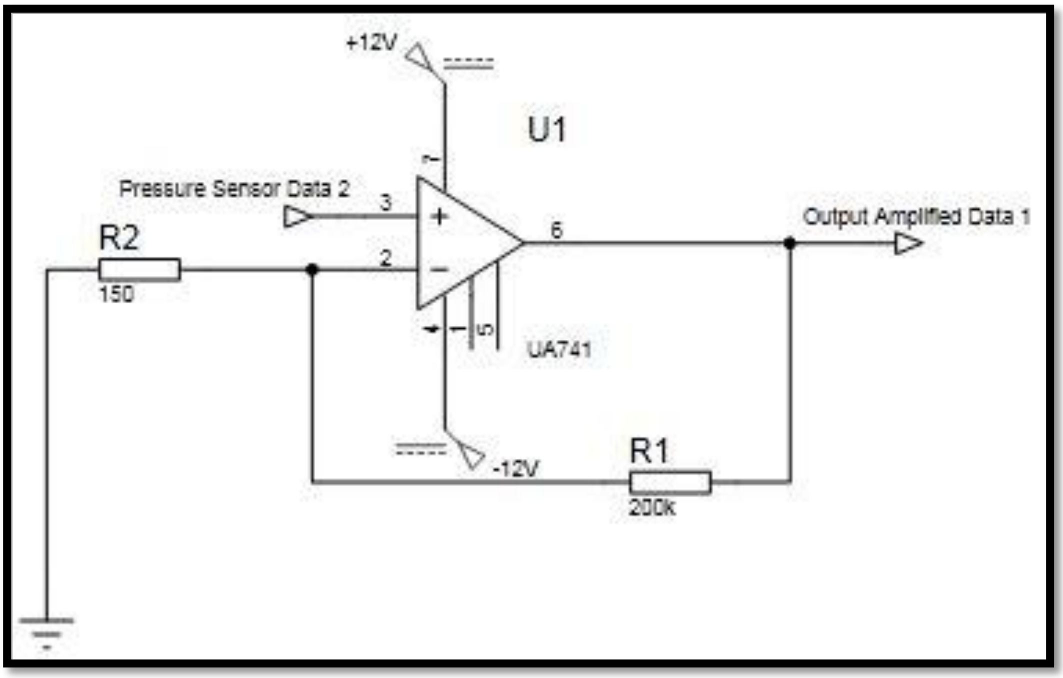
$$V_{out} = V_{in} + \frac{V_{in} * R_2}{R_1} \quad \text{(Eq. 3-10)}$$

$$V_{out_{max}} = 0.005V + \frac{0.005V * 200k\Omega}{150\Omega} \quad \text{(Eq. 3-11)}$$

$$= 6.672\,V$$

Amplifier circuit (shown in Figure 3.29) is constructed for each pressure transducer and output voltage is measured between 0V and +6.7V. Output voltage connected to computer for obtain pressure value.

Figure 3.29: Amplifier Circuit Design for Calmed® Pressure Transducers



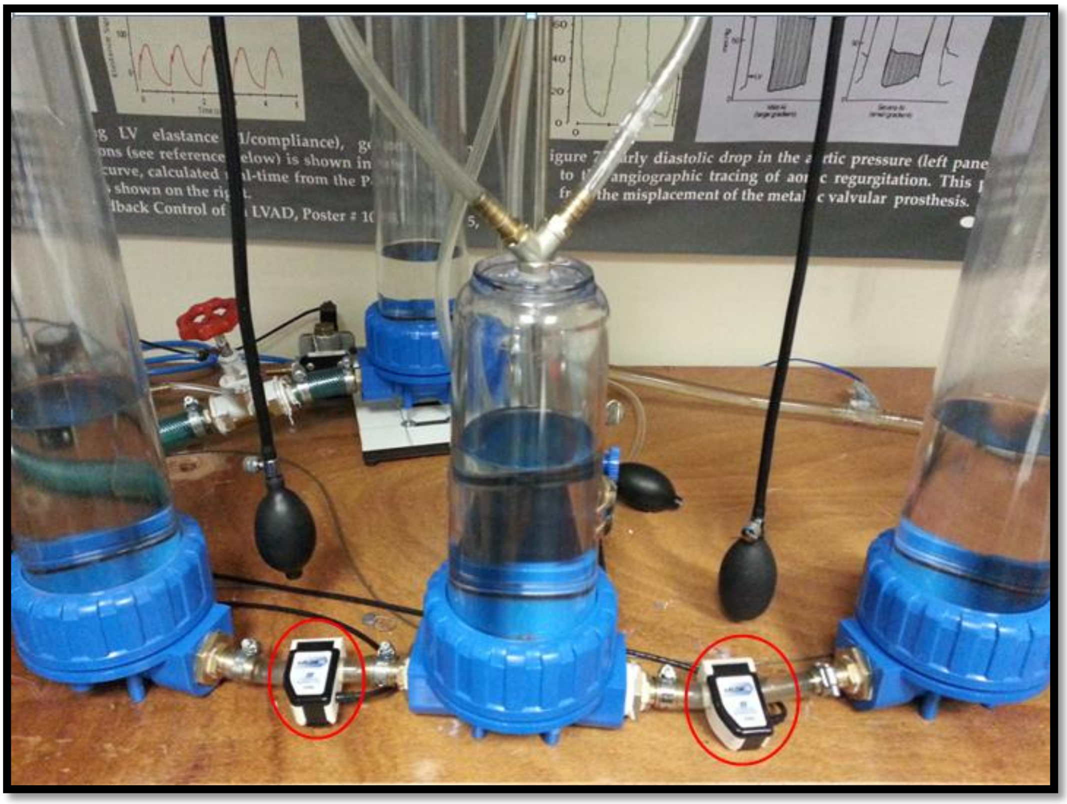
3.5.3.5 Flow Sensors

Analog flow data is obtained by using TS410 and HT110 bypass flow meter panel (Transonic Systems Inc., NY, USA), shown in Figure 3.30, and Transonic Systems Inc. ultrasonic flow meter sensor shown in Figure 3.32.

Figure 3.30: Transonic Systems TS410 Bypass Flow Meter Panel

Figure 3.31: Transonic Systems HT110 Bypass Flow Meter Panel

Figure 3.32: Transonic Systems Inc. Ultrasonic Flow Meter Sensor



3.5.3.6 Setkom Air Compressor

Setkom (Setkom LTD., Turkey, Bursa) Silent 20/2 model air compressor is used. Compressor working pressure range is between 0 to 8 bar and it has 100 lt. air tank.

Figure 3.33: Setkom Air Compressor

Source: SETKOM KOMPRESOR. 2013. [ONLINE] Available at: http://www.setkomkompresor.com/. [Accessed 11 December 2013].

3.5.4 CVMC DATA ACCUSATION

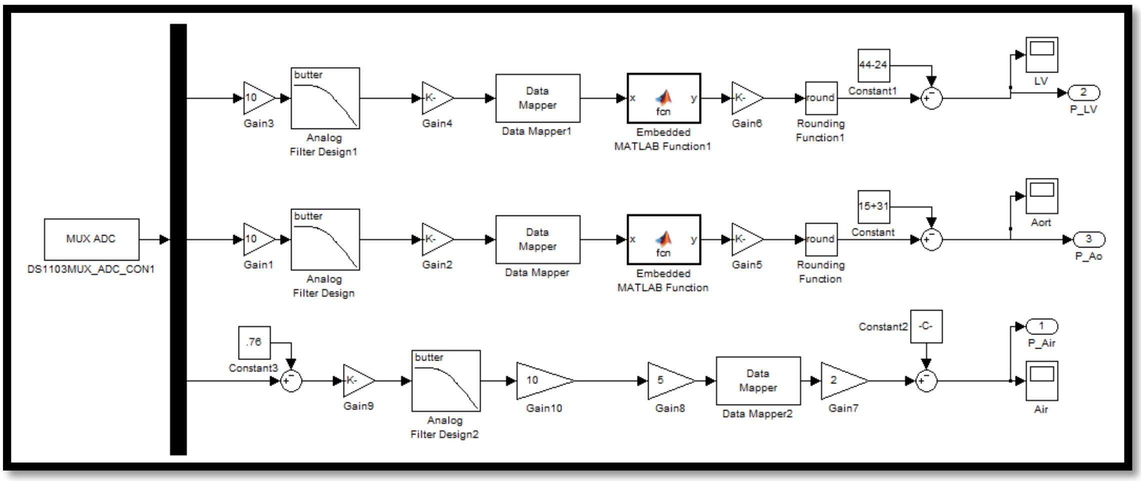
Simulink is a subprogram Matlab which is using of graphical block approach on computing environment. dSPACE software includes Simulink blocks which are designed for take inputs from CVMC via dSPACE to Simulink environment and gives outputs from Simulink to CVMC.

3.5.4.1 Pressure Input

Pressure input is obtained from using analog amplified pressure signal in dSPACE. Two different kinds of pressure transducers are used. Calmed® pressure transducers are used for measure Ao and LV pressures. In dSPACE analog amplified pressure signal amplified digitally by 10 times because of dSPACE's ADC inputs reduces signal by 10 times for circuit protection.

Digital pressure signal is filtered by "Analog Filter Design" box of Simulink for reduce noise and increase stability. Voltage of digital pressure signal measured and mapped by dSPACE. Measured data is compared with Dräger heart monitor, as taken as golden standard of measurement, by using MATLAB, curve fitting function and quadratic polynomial method. After mapping results are rounded and pressure values are obtained (see Figure 3.34).

Figure 3.34: Simulink Schematics of Calmed and Edwards Pressure Transducers



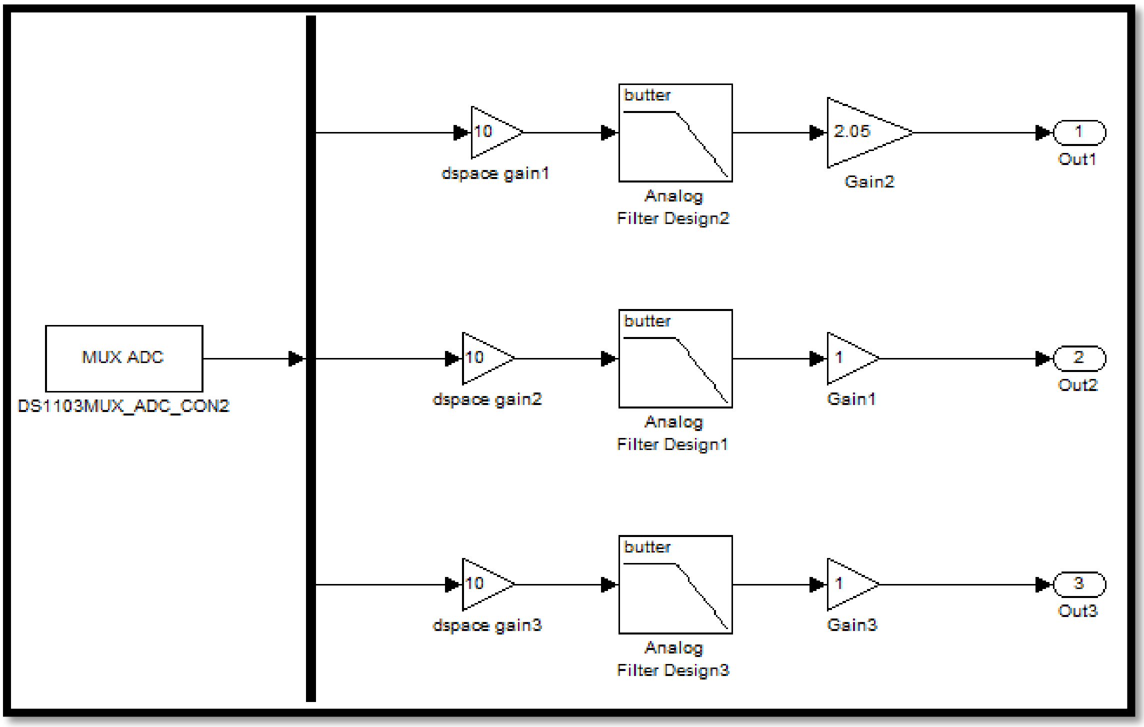
3.5.4.2 Flow and Volume Input

Analog flow data is obtained by using TS410 and HT110 bypass flow meter panel (Transonic Systems Inc., NY, USA), shown in Figure 3.30, and Transonic Systems Inc. ultrasonic flow meter sensor shown in Figure 3.32.Analog signal output of flow meter is transferred from analog output of TS410 and HT110 bypass flow meter panel to computer environment via dSPACE via BNC headed cable.

Figure 3.35: BNC headed cable

Digital data which is measured by dSPACE compared with flow values which are read from TS410 and HT110 Bypass Flow Meter Panel. MATLAB, curve fitting function, linear polynomial method is used for determine gain between flow value and digital flow data. Flow value is obtained as a L/min unit and converted to ml/sec (SI unit) by conversion gain. For finding volume value in chamber, flow value is integrated and summed with a initial volume.

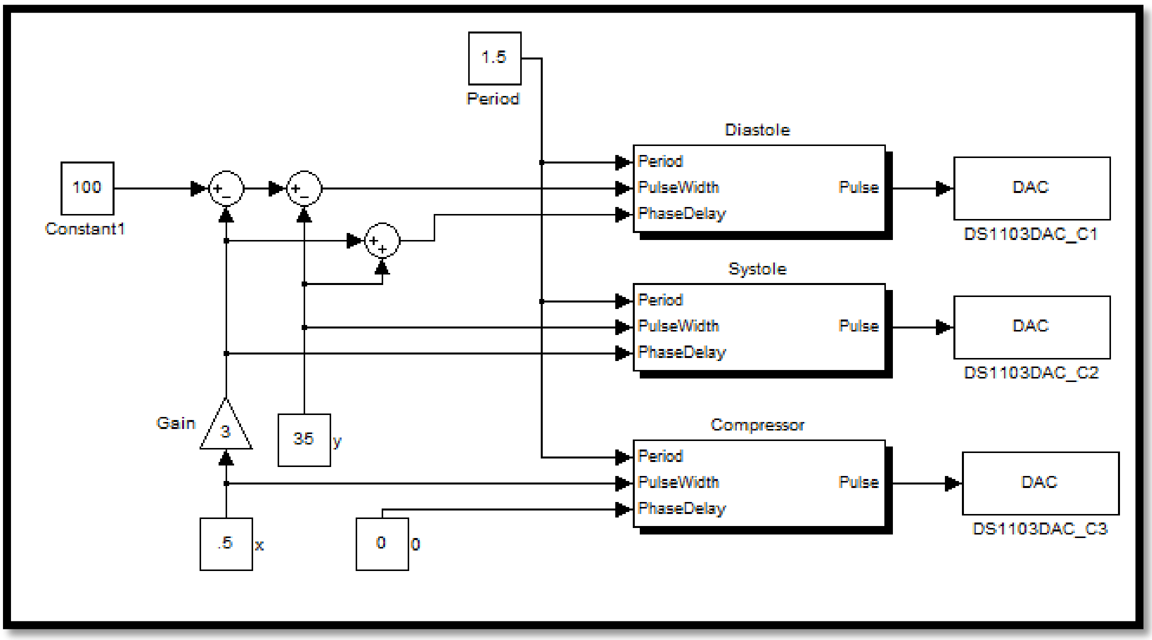
Figure 3.36: Simulink Schematics of Flow Sensor



3.5.4.3 Check Valve Control

Check valves are control by pulse signal generators. Opening time and duration are adjusted by hand. Changing timing of these time variables is provided to change diastole and systole duration, heart rate, elastance and stroke volume.

Figure 3.37: Simulink Schematics of Check Valves Controller



3.5.4.4 General Connection

Flow sensor, pressure transducers and check valves connected to each other as shown in Figure 3.38.

Figure 3.38: Simulink Schematic of General Connection

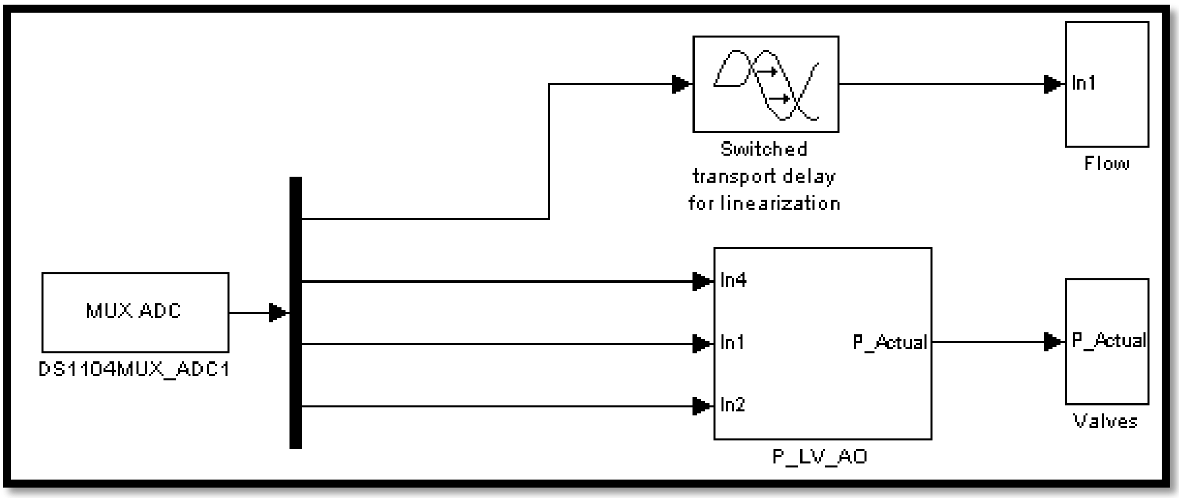
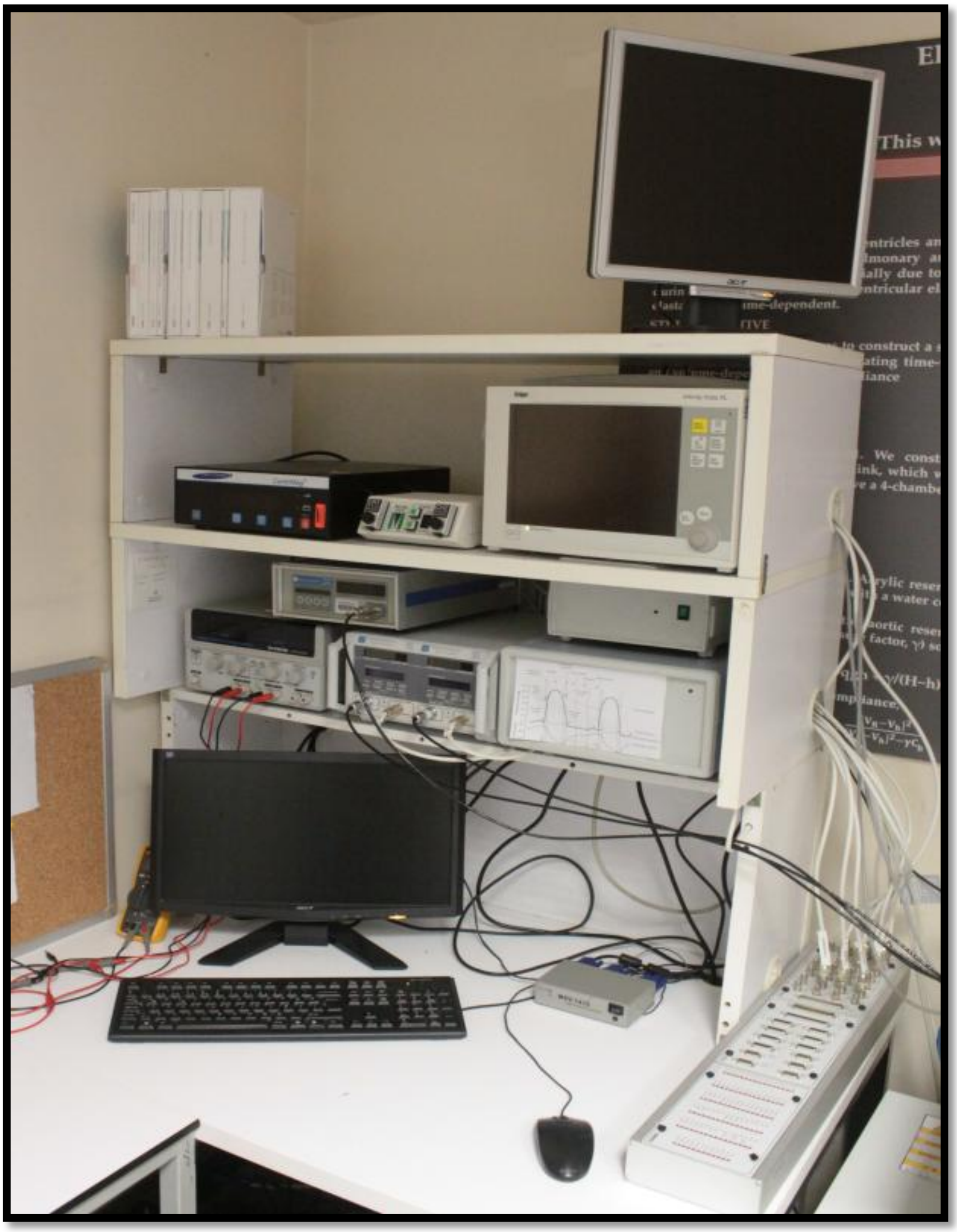


Figure 3.39: dSPACE connections of pressure transducers, flow meter and check valves

Figure 3.40: Workspace, heart monitor, dSPACE board, Flow-meter panel, amplifiers and power-supply.



3.5.4.5 CONTROLDESK Graphic Based User Interface (GUI)

CONTROLDESK provides a graphic based user interface (GUI) for observe Simulink system in real-time. CONTROLDESK is used for observe LV and Ao pressure, P-V loop, elastance control signal and other control parameters.

4. RESULTS

Results are obtained from Matlab/Simulink simulations given below. In Figure 4.1 water height versus time of open-air reservoir and in Figure 4.2 compliance of Aorta is shown.

Figure 4.1: Matlab/Simulink result of open-air reservoir

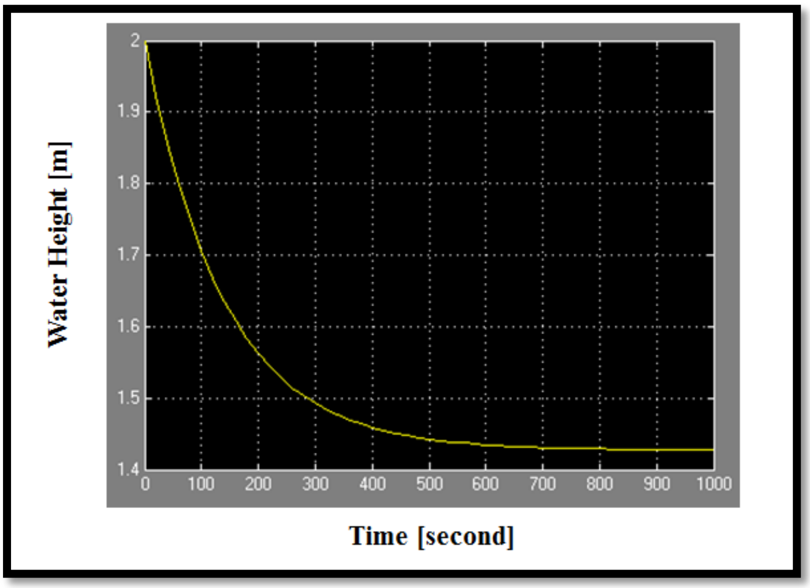
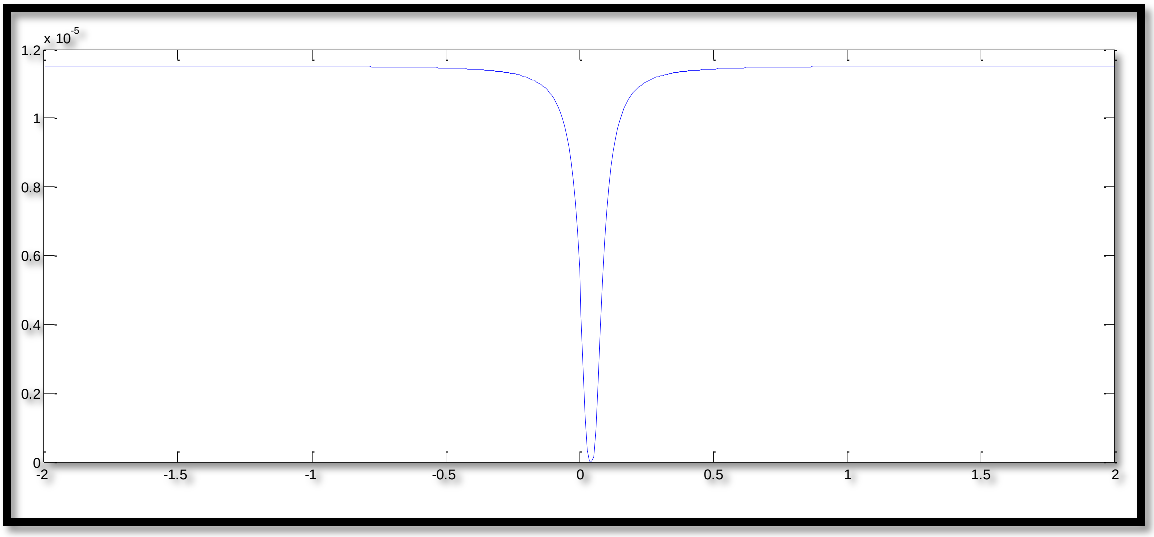


Figure 4.2: Simulation Result for Compliance of Aorta Chamber

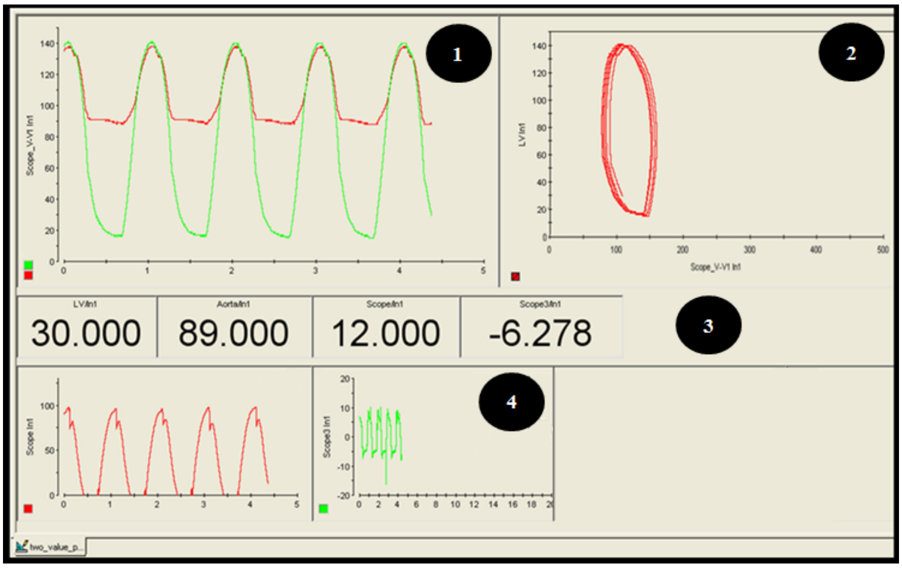


All result are obtained by using CVMC built in Bahçeşehir University, Bioengineering Research Laboratory. Four chamber CVMC shown in the Figure 4.3.

Figure 4.3: Built four chambers Mock circuit

The CVMC is successfully replicated heart physiology in vitro. Pressure values of LV and Ao and LV volume values are verified the ability of CVMC regenerate physical conditions stably and accurately.

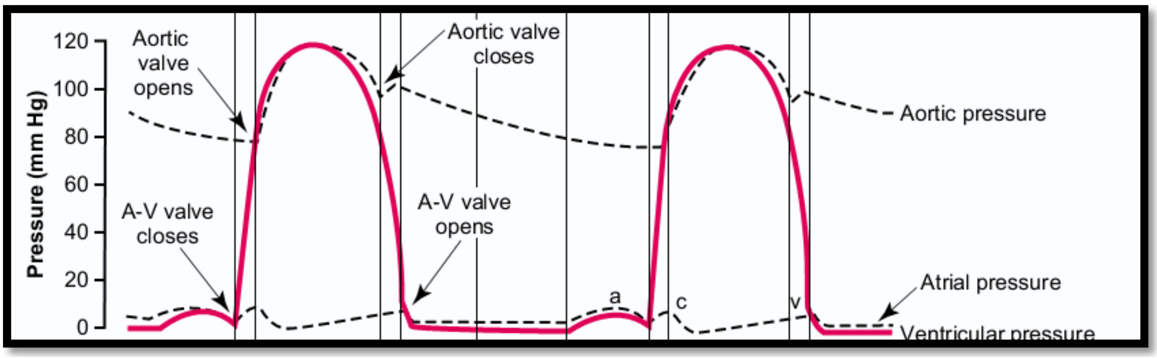
Figure 4.4: ControlDesk GUI



First part of the ControlDesk/GUI (Figure 4.4) shows P_{LV}(Green line)and P_{Ao} (Red line) which are obtained by Calmed pressure transducers via dSPACE. Second part shows P-V loop of heart, x axis is indicated LV volume and y axis is indicated LV pressure, in real-time. In third part in an order PLV, PAo, air-tank pressure and LV volume are numerically showed. At the bottom of the screen elastance based air-tank pressure and LV volume are showed by graphically.

4.1 LV AND AORTA PRESSURES

Figure 4.5: Ideal P_{LV}, P_{Ao} with Time Graph



Source: Textbook of Medical Physiology 11th ed by Arthur C. Guyton, John E. Hall. Copyright at 2006 by Elsevier Inc.

P_{LV} and P_{Ao} values recorded in real time and graphically displayed in Figure 4.7. In all results maximum pressures are slightly elevated from 120 mmHg to 130-140 mmHg. However, pressures can reduce by decreasing maximum air-tank pressure, means decreasing elastance.

Figure 4.6: Activation Signal of Check Valves in Initial Tests

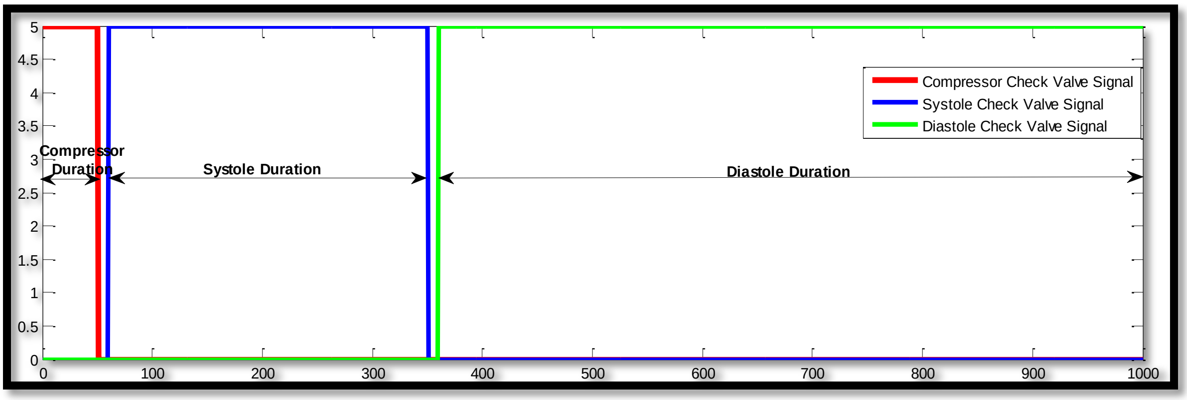


Table 4.1: Check Valve Signal Values and Results

Signal Values	Trial Number					
	1	**2**	**3**	**4**	**5**	**6**
Compressor Pulse Width	52	72	50	37	37	30
Compressor Pulse Delay	0	0	0	0	0	0
Systole Pulse Width	364	427	350	350	350	350
Systole Pulse Delay	80	88	50	140	140	10.5
Diastole Pulse Width	650	578	65	65	65	65
Diastole Pulse Delay	510	483	40	40	40	55
Period	1	1	1	1	1	1
Results	**1**	**2**	**3**	**4**	**5**	**6**
Flow Avag. (L/min)	3.07	3.4	2.4	3.14	2.16	2.46
Ao Pressure (mmHg)	134	150	116	130	120	125
	6	6	0	8	11	10
LV Pressure (mmHg)	115	135	80	125	120	122
	80	95	65	75	80	80

Figure 4.7: Recorded LV and Ao Pressures

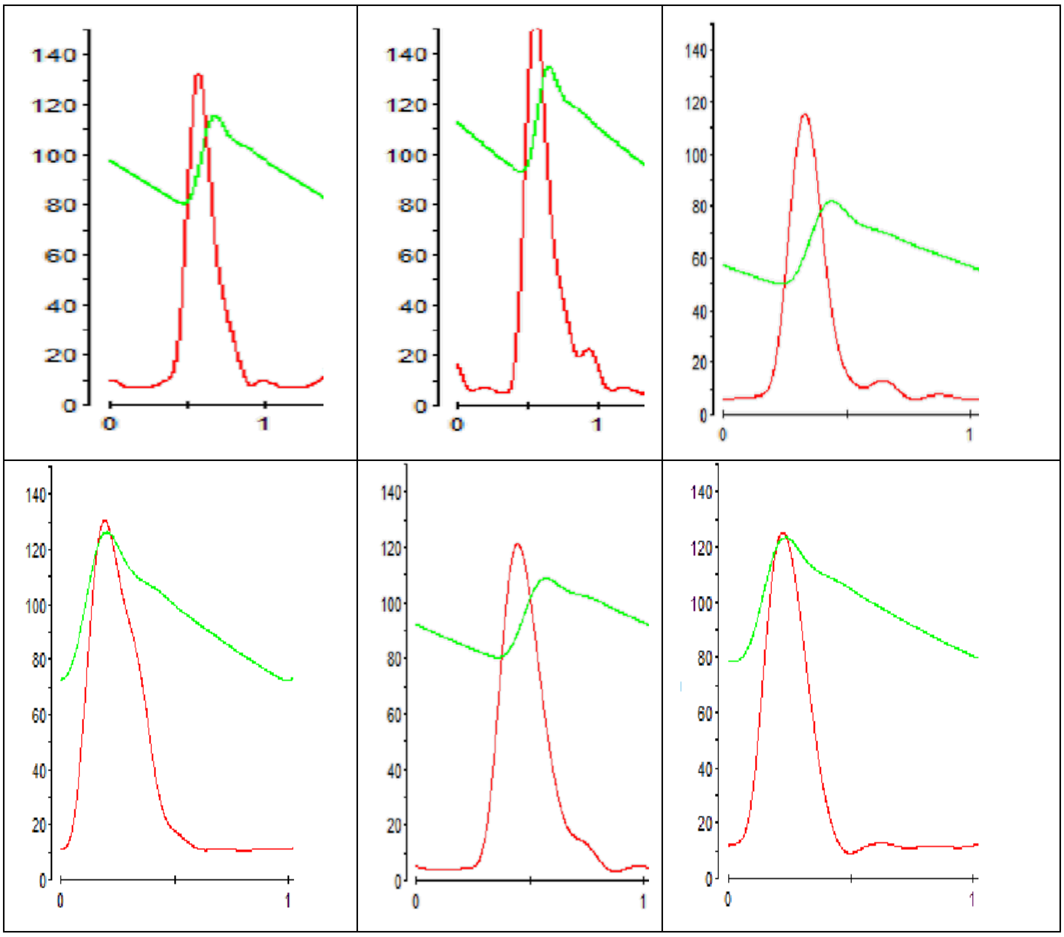
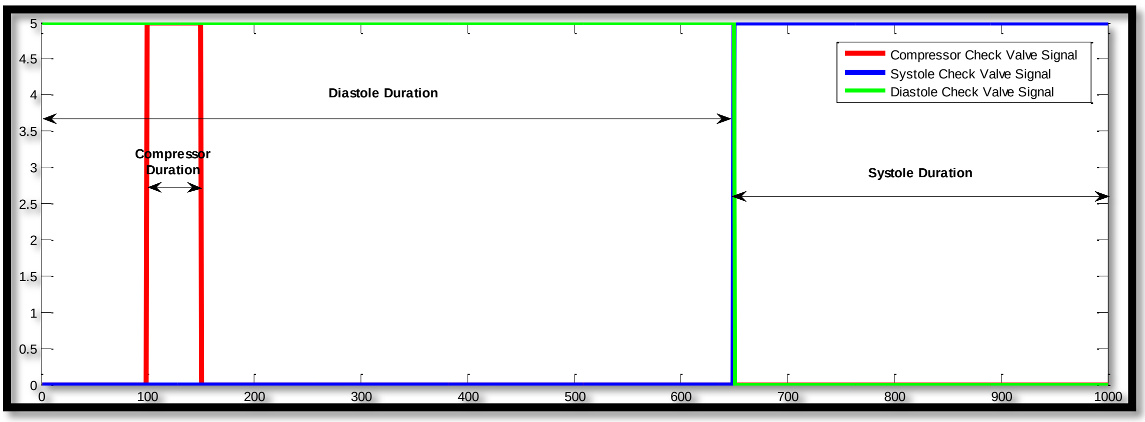


Figure 4.8: Optimized Activation Signal of Check Valves



As you can see from Figure 4.7 P_{Ao} increases before AV open and also P_{Ao} decreases rapidly after AV close. These results indicate AV leaking when it is closed. The presence of backwards flow across a closed cardiac valve is defined as valvular regurgitation (insufficiency).[3] In this project there is Aortic insufficiency and results are supported this finding. (See Figure 4.10)

Figure 4.9: Optimized LV and Aorta Pressures versus time

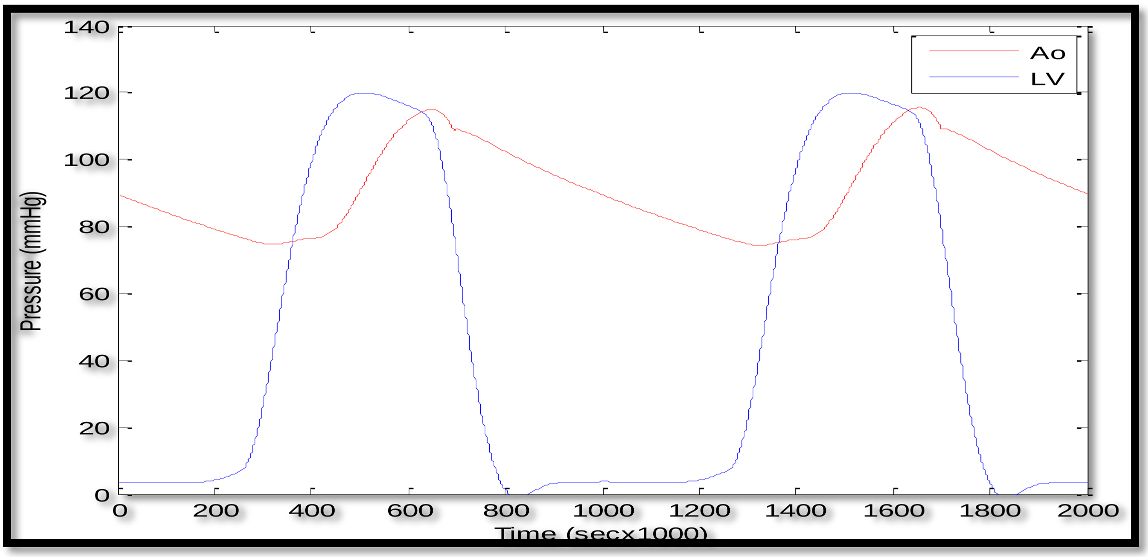
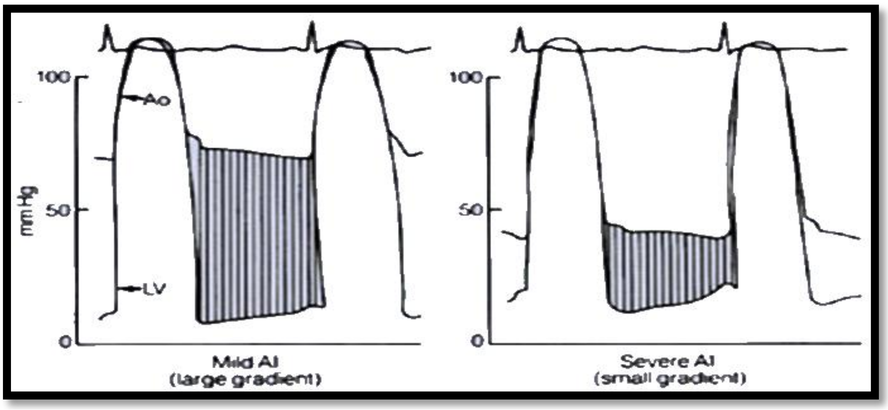


Figure 4.10: Pressure Relationships in Aortic Insufficiency



Source: Doppler Changes in Valvular Regurgitation. 2013 [ONLINE] Available at:http://www.echoincontext.com/doppler02/doppler02_02.asp. [Accessed 17 December 2013].

After heart valves modifications and changing placement of Aortic pressure sensor

[3] Web source: `Doppler Changes in Valvular Regurgitation`
http://www.echoincontext.com/doppler02/doppler02_02.asp

delay on aortic pressure is prevented and results collected under three categories. These are (i) healthy, (ii) heart failure and (iii) end-stage heart failure.

4.2 LEFT VENTRICULAR VOLUME

Ideal volume is shown in the Figure 4.11Stroke volume (ΔV) in human normal physiology is approximately 70-80 ml. However, in ideal pressures CVMC produces less stroke volume than ideal (See Figure 4.12). That mean resistance between LV and Ao is higher than human physiology.

Figure 4.11: Ideal Left Ventricular Volume Change

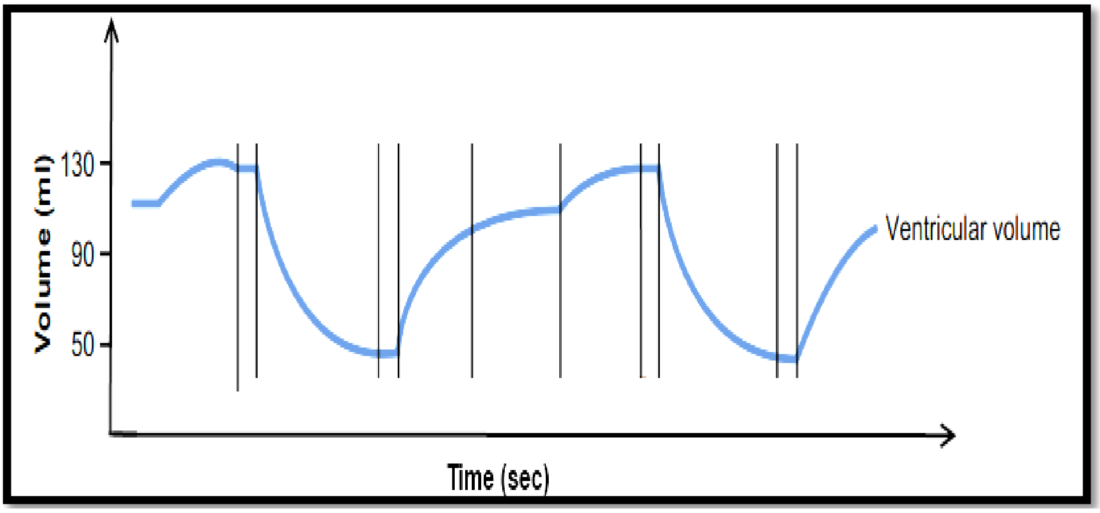
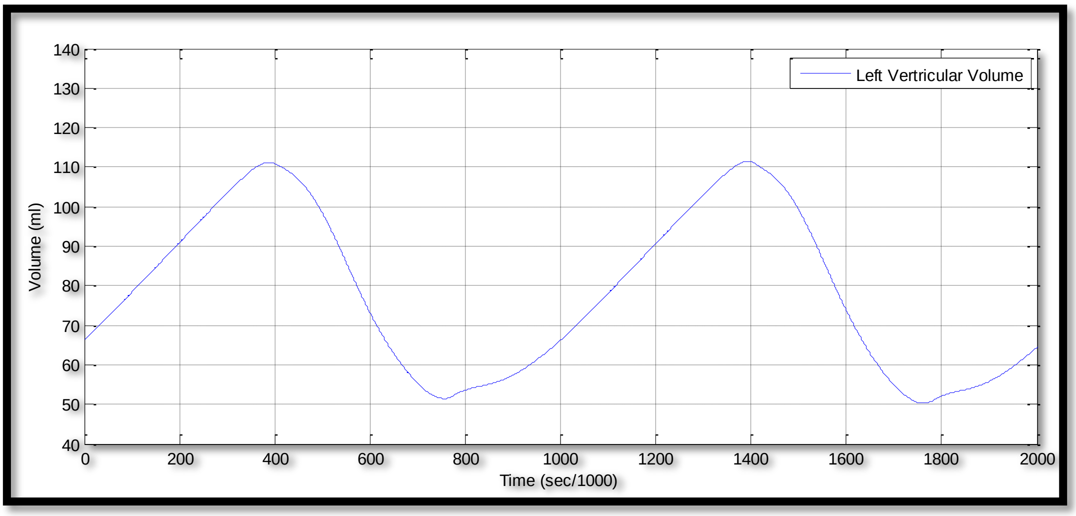
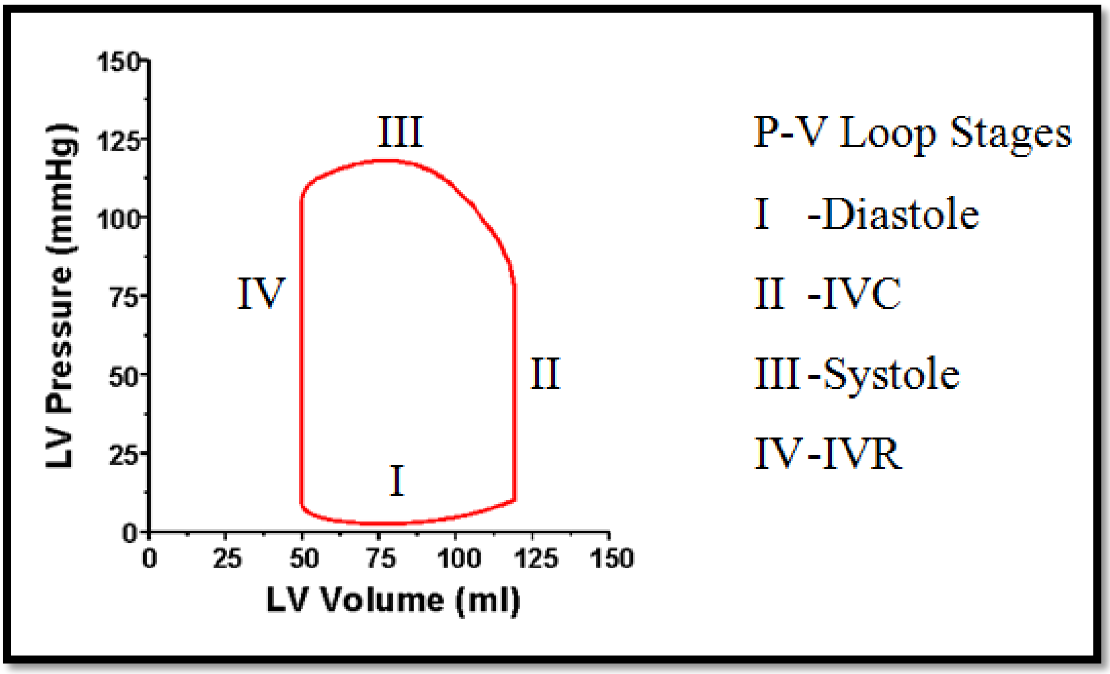


Figure 4.12: LV Volume Change produced by CVMC



4.3 P-V LOOP

Figure 4.13: Ideal P-V Loop for Healthy Human



Ideal P-V loop for healthy human is shown in the Figure 4.13 and some of the recorded p-v loops shown in the Figure 4.14**Error! Reference source not found.**As you can see in the recorded p-v loops IVC and IVR are not completely isovolumetric that results supports the theory about heart regurgitation (see Figure 4.15). Also stroke volume is not sufficient but stroke volume is in an acceptable range.

Figure 4.14: Recorded P-V Loop of CVMC

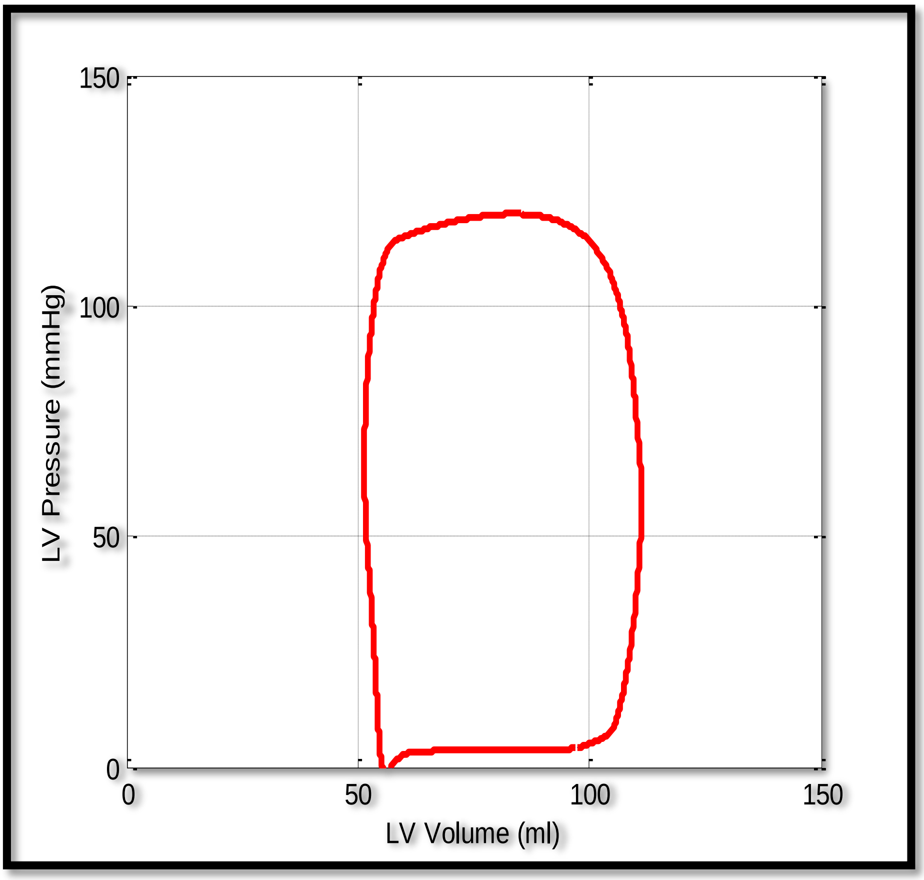
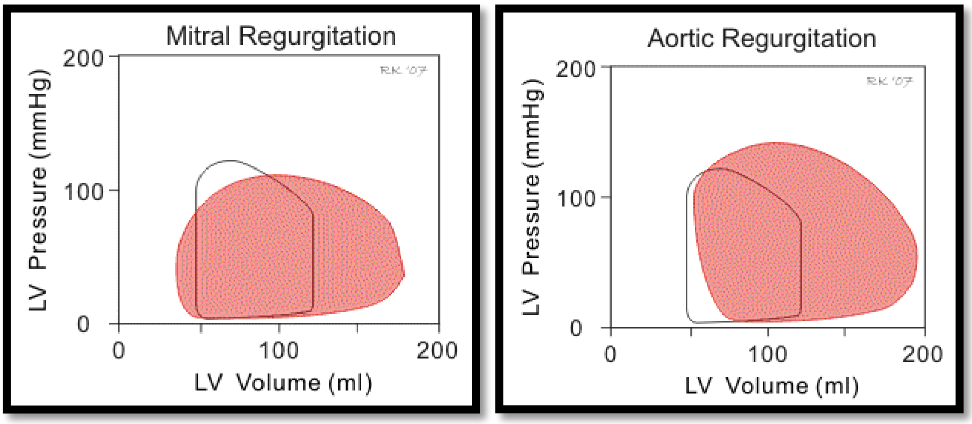


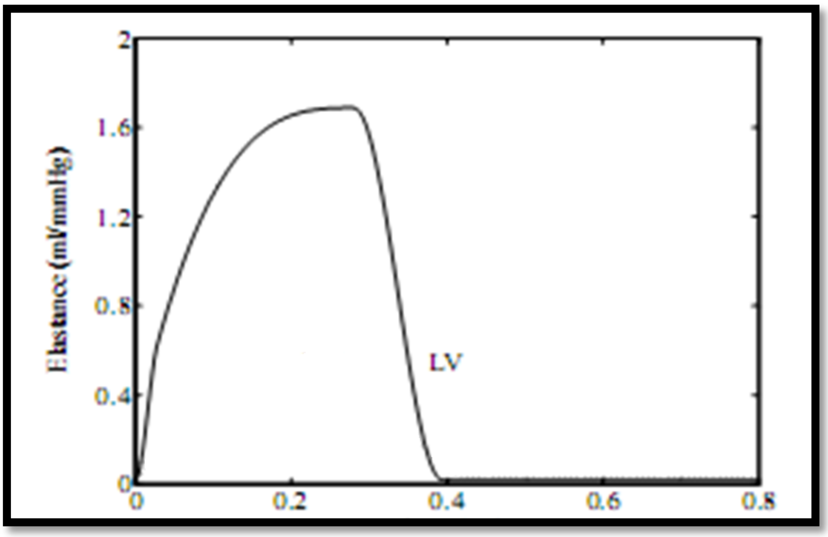
Figure 4.15: Mitral and Aortic Valve Regurgitation[4]



[4] Web Source: Aortic and Mitral Regurgitation http://www.cvphysiology.com/Heart%20Disease/

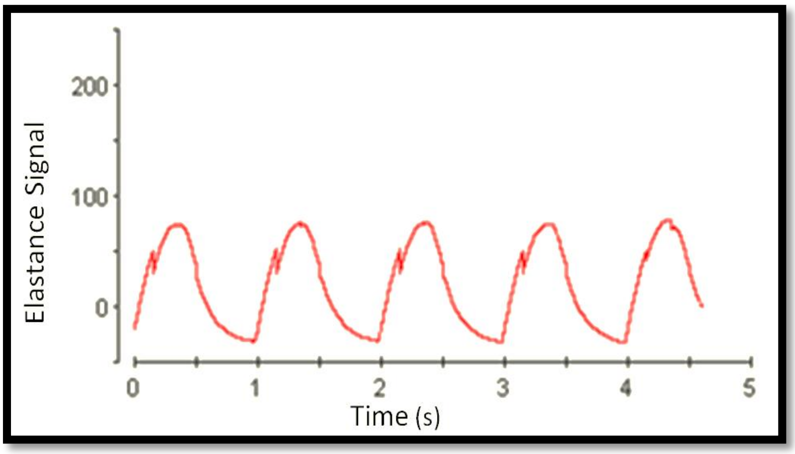
4.4 ELASTANCE

Figure 4.16: Ideal Elastance Graph



In CVMC, elastance is directly proportional to P_2 (LV air pressure, see Figure 4.17). That is the reason control algorithm based on controlling P_2.

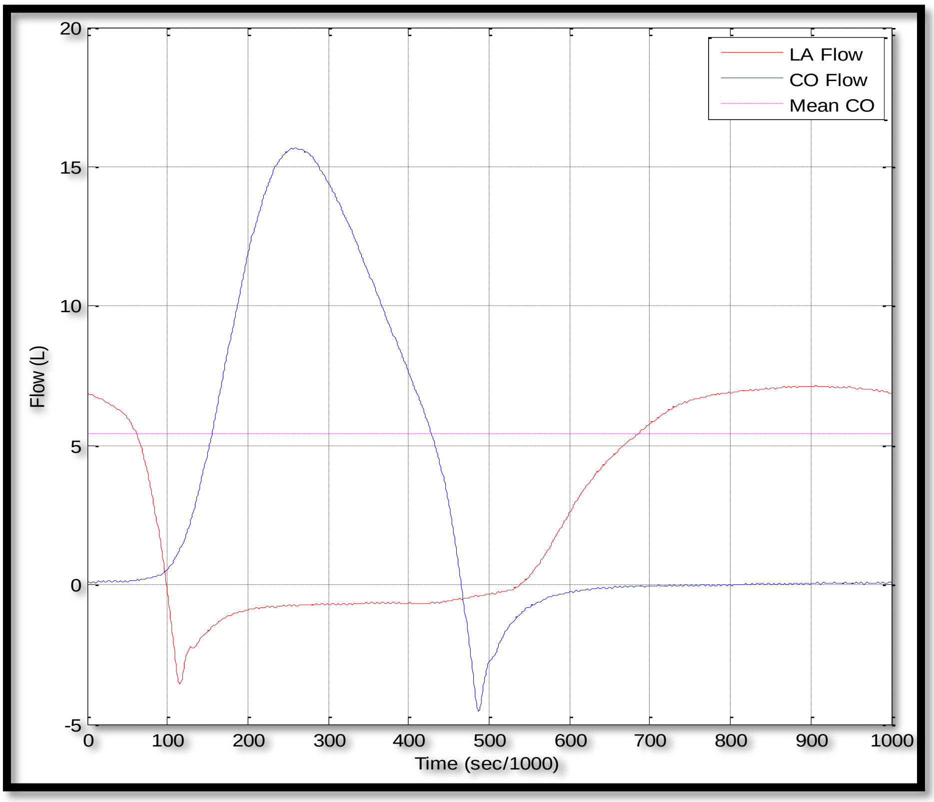
Figure 4.17: Created Elastance Signal for P_2



4.5 CARDIAC OUTPUT AND FLOW SIGNALS

Cardiac output and flow result shown in Figure 4.18. Mean Cardiac Output is above 5 L/min which is expected result.

Figure 4.18: Left Ventricle Input and Output Flow Signal



5. DISSCUSION AND CONCLUSION

CVMC has been designed to replicate pumping functions of heart in different conditions and characteristics of circulatory system. These conditions are could be rest, exercise, healthy and different types of diseases.

Cardiovascular mock circulation systems provide an easy and desirable way for testing cardiac devices during development process. For this reason system has to be portable, adjustable and most importantly trustable.

Recreate heart pumping function with controlling compressed air in the ventricle was successful. Results are comparable to heart functions but, system has to simulate different heart states and failure situations.

The shapes of the PV loops which are obtained with CVMC were similar to in vivo results. However, an increasing in volume was observed at the beginning of diastole and the end of the systole. The problem is artificial heart valves (AV- MV) are leaking when they are closed. This problem gives similar results with Aortic insufficiency.

REFERENCES

Books

Brian Kirby, 2010. Micro- and Nanoscale Fluid Mechanics: Transport in Microfluidic Devices. Edition. Cambridge University Press.

Bonow RO, Mann DL, Zipes DP, Libby P. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 9th ed. Philadelphia, Pa: Saunders Elsevier; 2011

Textbook of Medical Physiology 11th ed by Arthur C. Guyton, John E. Hall. Copyright at 2006 by Elsevier Inc.

Periodicals

Baloa, L., J. Boston, and J. Antaki, Elastance -based control of a mock circulatory system. Annals of Biomedical Engineering, 2001. 29: p. 244-251.

Donovan, F., Design of a hydraulic analog of the circulatory system for evaluating artificial hearts. Artificial organs, 1975. 3(4): p. 439-449.

Gregory SD, Simulation and Development of a Mock Circulation Loop with Varible Compliance, Master Thesis, Queensland University of Technology, 2009

Kolff, W., Mock circulation to test pumps designed for permanent replacement of damaged hearts. Cleveland Clinic Quarterly, 1959. 26: p. 223-226.

Koenig, S., et al.,Hemodynamic and pressure-volume responses to continuous and pulsatile ventricular assist in an adult mock circulation.ASAIO,2004.50: p.15-24.

Kucukaksu, First Turkish Experience with the MicroMed DeBakey VAD, (TexHeartInst J 2003;30:114-20)

Matthew Loh and Yih-Choung Yu, "Feedback control design for an elastance-based mock circulatory system," in Proc. 2004 American Control Conf. (Boston, Massachusetts, June 30 – July 2, 2004.

Pantalos, G., et al., Characterization of an adult mock circulation for testing cardiac support devices. ASAIO, 2004. 50(1): p. 37-46.

Scott DA, Fox JA, Cnaan A, Philip BK, Lind LJ, Palleiko MA, et al. Resistance to fluid flow in veins. J. Clin. Monit. 1996;12:331–337

Suga H. Ventricular energetics. Physiol. Rev. 1990; 70: 247–77.

Timms, D., et al., A complete mock circulation loop for the evaluation of left, right, and biventricular assist devices. Artificial organs, 2005. 29(7): p. 564-572.

Timms DL, Gregory SD, Greatrex NA, Pearcy MJ, Fraser JF, A compact mock circulation loop for the in vitro testing of cardiovascular devices, Artif Organs. 2011 Apr;35(4):384-91.

Verdonck, P., et al., Computer -controlled in vitro model of the human left heart. Med. & Biol. Eng & Comput., 1992. 30: p. 656-659.

Vandenberghe, S., et al., In vitro evaluation of the PUCA II intra-arterial LVAD. The International Journal of Artificial Organs, 2003. 26(8): p. 743-752.

Other Publications

Teerlink, John. Acute Heart Failure [Internet]. Version 17. Knol. 2008 Jul 28. From:http://knol.google.com/k/john-teerlink/acute-heart-failure/3fkxugmiumnks/1.