TECHNISCHE UNIVERSITÄT WIEN

Master Thesis

Assembly and control of a pulsatile Mock Circulation

carried out for the purpose of obtaining the degree of Diplom-Ingenieur (DI)
submitted at TU Wien, Faculty of Mechanical and Industrial Engineering, by

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Vienna, September 2022

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Acknowledgements

I would like to thank Professor Gföhler and Professor Angeli for their guidance and suggestions given to me for the completion of this thesis and Christoph for helping me with whatever I needed and taught me a lot of things.

Also I would like to thank Harald, Helmuth, Herman and my friends Adam and Alexandros for sharing their technical expertise with me and helping me overcome many obstacles.

And finally I would like to thank my mother Katerina, my father Giannis and my sister Eleni whose support was priceless all through this period.

Abstract

The rapid aging of global population in synergy with a constant deterioration of nutrition quality and lifestyle choices in the last decades has resulted in a massive increase in patients suffering from acute cardiovascular diseases. This means that more and more people are in need of mechanical support systems as part of their medical treatment. A large category of these systems is ventricular assist devices (VADs) which main function is to increase the blood perfusion in the organs of people with critically reduced stroke volume. The aim of this thesis work was to assembly and control a modular pulsatile mock circulation circuit that will simulate the conditions existing in the systemic circulation of the human body and be used to test the performance of VADs. A system was designed and built that was able to achieve aortic flows up to 4 L/min under physiological aortic and ventricular pressure values in a range of heart rates from 40 to 150 bpm with the option to retrieve these values in real time and post process them for further analysis. In addition to that pathological conditions could be simulated by alternating parameters such as the vascular compliances and resistances and the motor profile building the pressure differential into the hydraulic system.

Die rasche Alterung der Weltbevölkerung in Verbindung mit einer ständigen Verschlechterung der Ernährungsqualität und der Lebensweise in den letzten Jahrzehnten hat zu einem massiven Anstieg der Zahl der Patienten mit akuten Herz-Kreislauf-Erkrankungen geführt. Dies hat zur Folge, dass immer mehr Menschen mechanische Unterstützungssysteme für ihre medizinische Behandlung benötigen. Eine große Kategorie dieser Systeme sind ventrikuläre Unterstützungssysteme (VAD), deren Hauptfunktion darin besteht, die Durchblutung in den Organen von Menschen mit kritisch reduzierten Schlagvolumen zu erhöhen. Das Ziel dieser Arbeit war es, einen modularen pulsierenden Scheinkreislauf aufzubauen und zu kontrollieren, welcher die Bedingungen des systemischen Kreislaufes des menschlichen Körpers simuliert und zur Prüfung von VADs verwendet werden kann. Es wurde ein System entwickelt und gebaut, wo unter physiologischen Aorten- und Ventrikel druckwerten Strömungsgeschwindigkeiten in der Aorta bis zu 4 L/min erreicht werden konnten. Die Herzfrequenzen waren zwischen 40 bis 150 bpm. Die Werte konnten in Echtzeit abgerufen und für weitere Analysen verwendet werden. Darüber hinaus können pathologische Bedingungen simuliert werden, indem Parameter wie die Gefäßkompetenzen und -widerstände, sowie das Motorprofil, das die Druckdifferenz in das hydraulische System aufbaut, verändert werden

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List of Abbreviations

AoF	Aortic Flow
CAD	Cardiac Assistive Device
CVS	Cardiovascular System
ECAD	Extra-corporeal Assistive devices
EDV	End Diastolic Volume
EF	Ejection Fraction
ESV	End Systolic Volume
ET	Ejection Time
H-MCL	Hybrid - Mock Circulatory Loop
IABP	Intra-Aortic Balloon Pump
LVEF	Left Ventricular Ejection Fraction
MCL	Mock Circulatory Loop
M-MCL	Mechanical- Mock Circulatory Loop
N-MCL	Numerical - Mock Circulatory Loop
PVR	Pulmonary Vascular Resistance
SVR	Systemic Vascular Resistance
VAD	Ventricular Assistive Device

1. Introduction

Cardiovascular diseases are a class of diseases that affect the cardiovascular system and if not treated can lead to premature death. It is estimated that around 20 million people globally lose their life due to implications caused by cardiovascular diseases every year making them the leading cause of death worldwide. Many of these deaths can be prevented by the adoption of a healthier lifestyle by the patient. In this case, an improved lifestyle means more exercise, healthy eating and minimization of tobacco and alcohol consumption (A.Roth, 2019). However, at some severe cases, these lifestyle changes cannot improve the health condition of the patient and medical intervention is required. This intervention might include medication to regulate blood pressure, surgical intervention in the form of coronary bypass surgery, stent or pacemaker insertion or even a total heart transplant when the heart of the patient is unable to supply with blood the vital organs of the body. Unfortunately, there is a great mismatch between the demand for heart transplants and available organs. This is why engineers in coordination with physicians strive to develop devices that can replace or assist the function of the heart and extend the lifetime of patients that are either not eligible for a heart transplant or they cannot find one available. The two main categories of devices that are designed to support failing hearts are the total artificial and ventricular assistive devices (VADs). In this thesis, emphasis will be given on the latter category and specifically on the assembly and control of a pulsatile mock circulation that can be used to test the functionality of VADs. Firstly, however a short introduction on the main parts and functions of the cardiovascular system, the cardiac cycle in addition to the indicators used to judge its health will be presented to set the basis for further discussion regarding the aforementioned type of intervention.

1.1 Human Circulation

The human circulation or cardiovascular system is the system that permits blood to circulate and transport nutrients (such as amino acids and electrolytes), oxygen, carbon dioxide, hormones, and blood cells to and from the cells in the body to provide nourishment. It also helps in fighting diseases, stabilize temperature and pH and maintain homeostasis. It consists of four main components the heart, the blood vessels, the lungs and the blood itself. The cardiovascular system is divided into two sub circuits, the systemic and the pulmonary circulation (Saladin, 2011).

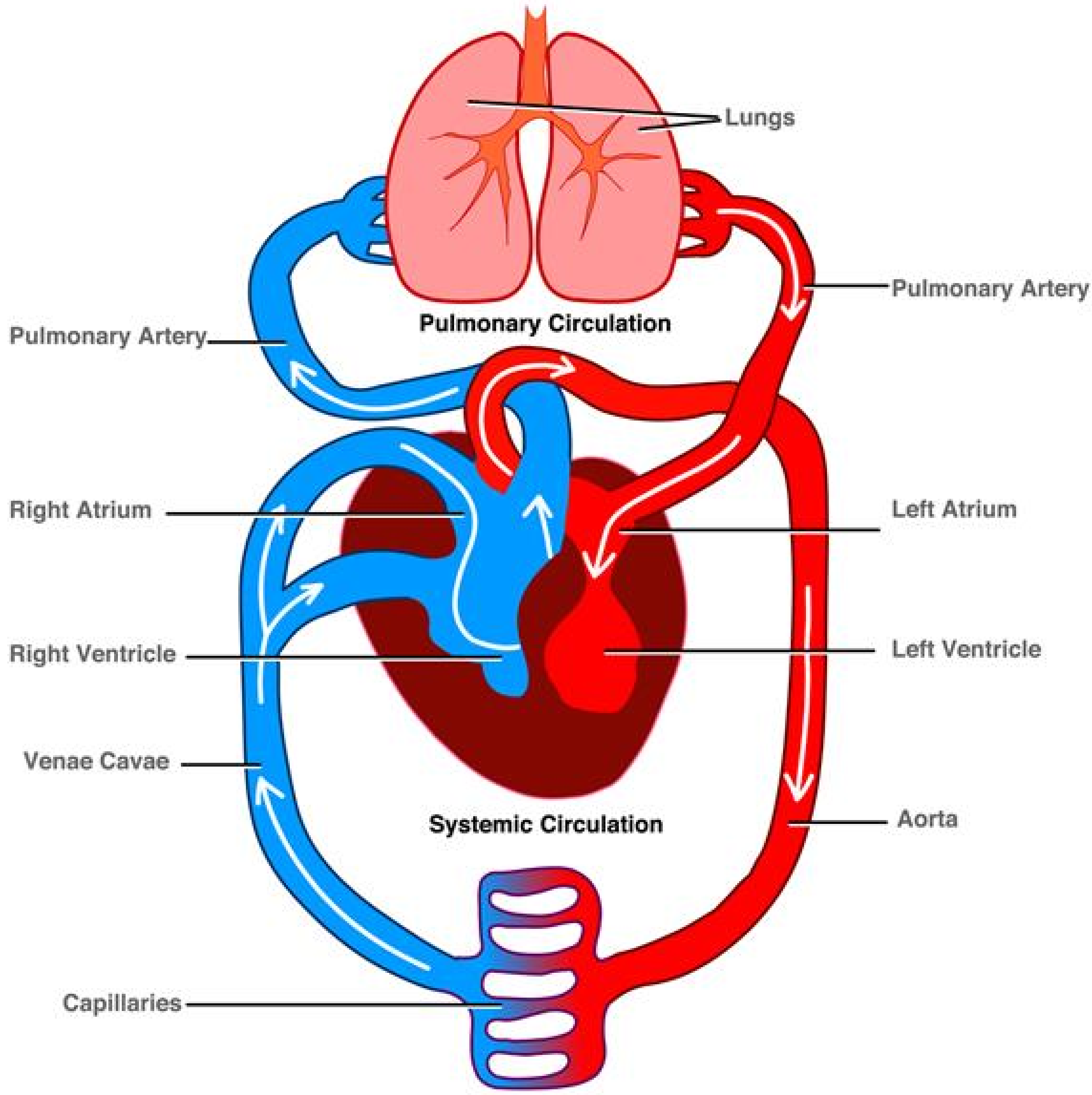


Figure 1 - 2 Main features of Systemic and Pulmonary Circulation (Shalom Education, 2022)

1.1.1 Systemic vs Pulmonary Circulation

Both systemic and pulmonary circulations are powered by the pulsatile contraction of the heart but have different functions. The pulmonary circulation receives deoxygenated blood (mark as blue in Figure 1 - 1) from the heart and its main functions are to reoxyganate the blood stream passing through the lungs and absorb all the carbon dioxide present in the blood. On the other hand, the systemic circulation receives oxygenated blood (mark as red in Figure 1 - 1) from the heart and transports it all through the body via the arteries. This blood releases oxygen and nutrients to the cells of the organs when passing though the smallest sized branch of the arterial tree, the capillaries. Then the deoxygenated blood travels through the venous side of the system back to the heart to close the circle. (Lawton, 2019)

1.1.1.1 Structure and Function of the Heart

The hearts is a muscular organ, which has the task to pump blood through blood vessels around the body. It is located in the middle compartment of the chest and is protected by the bones of the thorax. It is enclosed in a protective sac called pericardium which contains a small amount of fluid. The wall of the heart is consisted of three layers. The outer layer, the epicardium is made up from elastin rich loose connective tissue and its main function is that it acts as a protection layer from trauma or friction for the heart under the pericardium. It also contains the coronary blood vessels, which oxygenate the tissues of the heart. The middle layer is the myocardium or cardiac muscle that constitutes the main tissue of the wall of the heart. It is an involuntary striated muscle, which is composed by cardiac muscle cells joined by intercalated discs, which are encased by collagen fibers and other substances that form the extracellular matrix. Cardiac action potentials electrically stimulate the heart muscle cells myofilaments in a process called excitation contraction coupling, which is, responsible for the continuous beating of the heart in one's lifetime. The third and inner layer making up the heart wall is the endocardium which lines the chambers of the heart with endothelial cells similar to the ones of the blood vessels. Its main functions is to provide protection to the valves and heart chambers and control myocardial function (Betts, 2013).

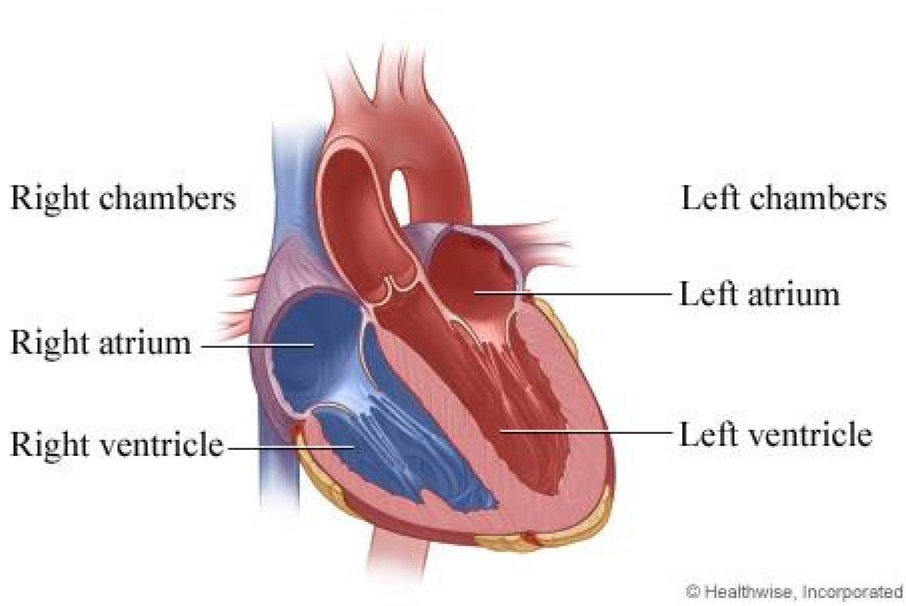


Figure 1 - 2 Chambers of the Heart (Healthwise, 2022)

1.1.1.2 Chambers of the Heart

The heart is divided into two segments, left and right which are consequently further subdivided into two chambers (Figure 1 - 2). The top chamber of each segment is called atrium and the bottom chamber is called ventricle. The right ventricle pumps deoxygenized blood towards the lungs while the left ventricle pumps blood to the systemic circulation. The left atrium receives oxygenated blood from the lungs whereas the right atrium receives deoxygenized blood from the rest of the body. Ventricles have thicker walls in comparison to the atria a property that allows them to perform more work by pumping out blood in greater quantities (Guyton, 2020).

1.1.1.3 Heart Valves

Heart Valves are fibrous flaps of tissue located between the heart chambers. Heart consists four valves one for each chamber of the heart. They are responsible for keeping blood moving through the heart in the right direction. They are passive, one-way valves that open and close according to the blood pressure differential on each side. Valves between the atria and the ventricles are known as the right and left atrioventricular valves, otherwise known as the tricuspid and mitral valves respectively. Valves between the ventricles and the great arteries are known as the semilunar valves. The aortic valve is found at the base of the aorta, while the pulmonary valve is found at the base of the pulmonary trunk (Guyton, 2020).

1.1.1.4 Blood Vessels

Blood vessels are the conduits through which blood is distributed to body tissues. The vessels make up two closed systems of tubes that begin and end at the heart. The smaller system, the pulmonary vessels, transports blood from the right ventricle to the lungs and back to the left atrium. The larger system, the systemic vessels, carries blood from the left ventricle to the tissues in all parts of the body and then returns the blood to the right atrium. Based on their structure and function, blood vessels are classified as either arteries, capillaries, or veins (Guyton, 2020).

1.1.1.4.1Arteries

Arteries always carry blood away from the heart. Pulmonary arteries transport blood that has a low oxygen content from the right ventricle to the lungs. Systemic arteries transport oxygenated blood from the left ventricle to the body tissues. Blood is pumped from the ventricles into the aorta and then towards large elastic arteries that branch repeatedly into smaller and smaller arteries until the branching results in microscopic arteries called arterioles. The arterioles play a key role in regulating blood flow into the tissue capillaries. Only about 10% of the total blood volume is in the systemic arterial system at any given time.

Arteries consist of 3 layers, the innermost layer is called tunica intima (also called tunica interna) and is a simple squamous epithelium surrounded by a connective tissue basement membrane with elastic fibers. The middle layer, the tunica media, is primarily smooth muscle and is usually the thickest layer. It does not only provide support for the vessel but also changes its diameter to regulate blood flow and blood pressure. This property of the arteries to distend and increase their volume with increasing transmural pressure is called compliance and is of particular significance in cardiovascular physiology. The outermost layer, which attaches the vessel to the surrounding tissue, is the tunica externa or tunica adventitia. This layer is connective tissue with varying amounts of elastic and collagenous fibers. The connective tissue in this layer is quite dense at the point where it is adjacent to the tunica media, but it changes to loosen connective tissue near the periphery of the vessel (Khan, 2006).

1.1.1.4.2 Capillaries

Capillaries, the smallest and most numerous of the blood vessels, form the connection between the vessels that carry blood away from the heart (arteries) and the vessels that return blood to the heart (veins). The primary function of capillaries is the exchange of substances between the blood and tissue cells (Khan, 2006).

1.1.1.4.3 Veins

Veins carry blood toward the heart. After blood passes through the capillaries, it enters the smallest veins, called venules. From the venules, it flows into progressively larger and larger veins until it reaches the heart. In the pulmonary circuit, the pulmonary veins transport oxygenated blood from the lungs to the left atrium of the heart. Systemic veins transport blood from the body tissue to the right atrium of the heart. This blood has a reduced oxygen content because the oxygen has been used for metabolic activities in the tissue cells. The walls of veins have the same three layers as the arteries. Although all the layers are present there is less smooth muscle and connective tissue. This makes the walls of the veins thinner in comparison to arterial walls something that is related to the fact that blood pressure is lower in veins and as a result, there is no need to sustain the increased stresses that arteries do (Khan, 2006).

1.1.1.5 Blood

Blood is a non-Newtonian body fluid responsible for the transportation of oxygen and nutrients into the cells as well as for the removal of metabolic waste from the cells. It is consisted mainly of the blood plasma which is mainly water. Various proteins, ions and hormones that are in charge for various functions of the human body are suspended in this plasma. Additionally, it contains white blood cells, which are the immune system cells that are responsible for protecting the body against infectious diseases and foreign invaders and red blood cells whose main function is to carry oxygen into the cells and carbon dioxide out of them. The quantity, morphology and mechanical properties of the red blood cells are of vital importance since they can affect the viscosity of blood. This can have detrimental effects on the cardiovascular system state since it affects factors such as the friction between blood and vessel walls, the rate of venous return, organ perfusion but also the work required from the heart to pump blood into the body (M. Baskurt, 2007).

1.1.1.6 Lungs

Despite the fact that lungs are the main organ of the respiratory system, they cannot be excluded when considering the human blood circulation. There are two lungs, the right and the left both of them located inside the thoracic cavity anterior of the spine on either side of the heart. The right and left lungs are divided into sections called lobes, which are further subdivided into segments and then lobules. The lungs are part of the lower respiratory tract that begins at the trachea and branches into the bronchi and bronchioles which receive air breathed in via the conducting zone. The conducting zone ends at the terminal bronchioles. These divide into the respiratory bronchioles of the respiratory zone which divide into alveolar ducts that give rise to the alveolar sacs that contain the alveoli, where gas exchange takes place between them and the capillaries of the pulmonary circulation system.

The anatomic and physiologic continuity of the lungs with the heart and vessels intuitively suggests that impairments in any component of lung function may influence cardiovascular health. This suggestion has been proven clinically with studies made on patients suffering from chronic obstructive pulmonary disease (COPD) that have shown that these individuals are more prone to suffering from coronary artery disease, arrhythmias and heart failure (Sergio H.R. Ramalho, 2021).

1.1.1.7Vascular Compliance

The ability of a blood vessel to expand and contract according to changes of transmural pressure is called compliance. It depends on the material and morphological properties of the vessel. Arteries having to sustain greater transmural pressures possess more muscle and collagen fibers in comparison to veins, which contain more elastin. This means that veins are more compliant and hence show larger extension of their cross section for the same increase of transmural pressure in comparison to the arteries as seen in Figure 1 – 3.

Compliance is simply defined mathematically as the ratio of change in volume over a change in pressure across the vessel

$$C = \frac{\Delta V}{\Delta P} \qquad (1)$$

Another conclusion that can be drawn by looking at Figure 1 – 3 is that compliance tends to decrease for all blood vessels as pressure increases (curve slope decreases with increasing pressure). This happens because as pressure increases and therefore the relative volume of the vessels increase more collagen fibers are deployed hence increasing the stiffness of the vessel. The dotted line curves represents the compliance of the veins and arteries when there is vascular smooth muscle contraction, which is also a factor that reduces compliance. The opposite effect can be observed at the case of vascular muscle relaxation. This means that a single vessel does not have a single compliance value but multiple depending on the vascular muscle activity. It can be deducted that by manipulating the vascular compliance of the blood vessels blood flow rates and pressure profiles can be also controlled to a great extent. The concept of vessel compliance as it has become apparent is crucial to the design of a mock circulation system and is broadly considered on this thesis. We will consider the vascular compliance of the arteries and the veins separately (Klabunde, 2021).

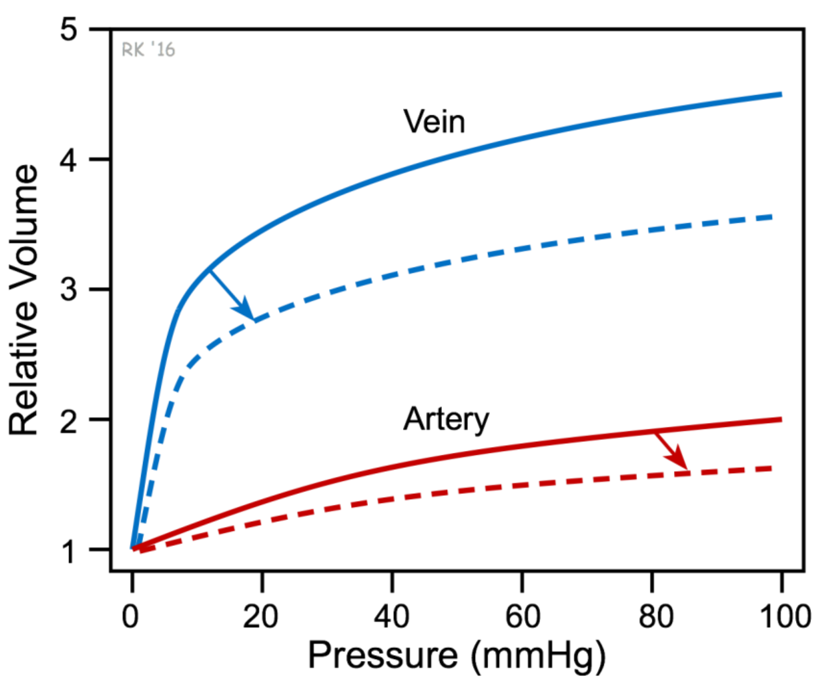


Figure 1 - 3 Relative Volume change over Pressure variation inside blood vessels

1.1.1.7 Vascular Resistance

Vascular resistance is defined as the resistance experienced by blood as it flows through the vessels during circulation. The higher the vascular resistance the higher the pressure differential the heart has to generate in order to achieve a certain flow rate. The mathematical definition of the resistance *R* of a vessel or circulation loop is simply given by the ratio of the pressure differential *ΔP* across it over the flow *Q* through it. Hence, it is written as

$$R = \frac{\Delta P}{Q} \tag{2}$$

The human body strives to maintain homeostasis through vasoconstriction and vasodilation which reduce or increase the diameter of the blood vessels conditions which either increase or decrease vascular resistance respectively.

In this thesis we will distinguish between aortic and peripheral resistance, aortic being the one produced by the aorta and peripheral the one from the distal blood vessels (V.Fuster, 2004).

1.2 The Cardiac Cycle

The cardiac cycle is defined as the sequence of alternating contractions and relaxations of the atria and ventricles in order to pump blood all over the body. Its period is the time occurring between two consecutive heartbeats. The cardiac cycle is further divided into two sub-periods, namely contraction and relaxation or systole and diastole respectively. Systole is the sub-period when blood is pumped into circulation through contraction of the heart and diastole is the sub-period where heart chambers are filled with blood.

Figure 1-4 gives information about the four signals that are critical in describing the performance of the heart during the cardiac cycle.

The 1st subplot (starting from the top) depicts the pressure profile inside the aorta (AP), the left atrium (LAP) and the left ventricle (LVP)

The 2nd subplot indicates the left ventricular volume (LVV)

The 3rd subplot is an electrocardiogram (ECG) of the heart

The 4th subplot portrays the timestamps when the heart valves are opening and closing, producing sounds.

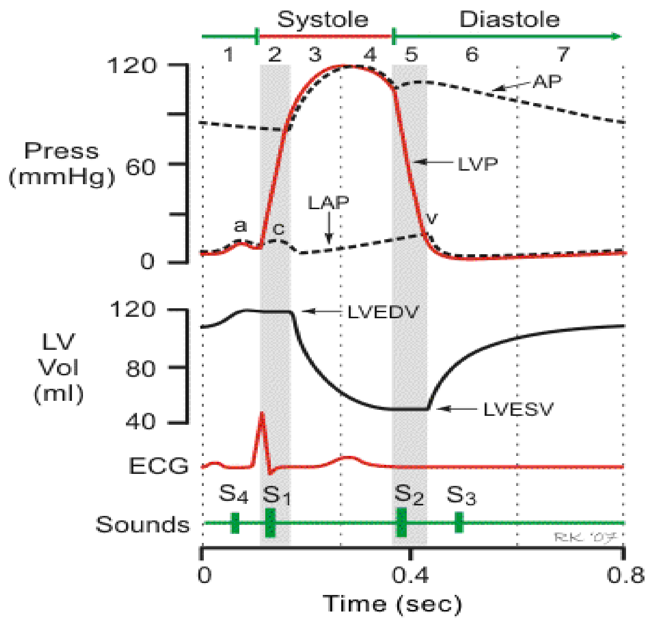


Figure 1 - 4 Characteristic parameters of heart function over a cardiac cycle; from top to bottom – i) aortic and ventricular pressure, ii) left ventricular volume, iii) ECG signal profile, iv) heart valves sounds

As it can be seen these subplots are subdivided into 7 phases called the phases of the cardiac cycle and are named according to the behavior of the heart at this particular timestamp. They are the following.

1) Atrial depolarization/contraction

2) Isovolumetric Contraction

3) Rapid Ejection

4) Reduced ejection

5) Isovolumetric Ejection

6) Rapid Ventricular filing

7) Reduced filling

The cycle begins with phase 1 where the pacemaker cells of the sinoatrial node (SA node) fire and stimulate the atria to depolarize. This depolarization is designated by the small wave seen in the ECG signal called as the P Wave. This has as an effect the rise of left atrial pressure (LAP) because of the contraction caused by the increased electrical activity which results in more blood being pumped into the left ventricle. As the contraction of the atria completes atrial pressure begins to fall which causes a reversal of the pressure gradient across the atrioventricular valves causing them to close. This is depicted by the mark *S1* in the sound subplot. This gives rise to the 2nd phase of the cycle, the isovolumetric contraction which designates the start of the systole. At the beginning of this phase, the electrical depolarization of the ventricles (QRS complex) is already midway its action. This leads to the contraction of the ventricles and to the rapid increase of the ventricular pressure (LVP). The fact that the heart valves are closed implies that there is no exchange of blood between the atria and the ventricles meaning that the pressure in the chambers increases with the volumetric volume remaining constant (left ventricular end diastolic volume (LVEDV) is the maximum volume of blood LV holds before ejection). When ventricular pressures exceed the pulmonary and aortic ones the semilunar valves open and blood is ejected towards the circulation in a rapid rhythm as depicted by the steep negative slope on the LVV subplot. This is the 3rd phase of the cardiac cycle and is known as Rapid Ejection. However, when the ventricle repolarizes as the T wave initiates, ventricular pressure starts to fall. As a result, the rate at which blood is pumped into the aorta decreases (phase 4) until it drops to zero when the aortic pressure (AP) surpasses the ventricular one, thus leading to the closure of the semilunar valves causing the S2 sound and the initiation of the 5th phase known as isovolumetric relaxation. During this phase, the ventricles are isolated and their volume increases without any blood volume exchange. This has as a result the rapid pressure drop inside the left ventricle. Meanwhile blood is ejected into the atria in order to prepare for the supply of the ventricles in the next heartbeat. When ventricular pressure drops below the atrial pressure the atrioventricular valves open and blood flows from the atria to the ventricles at a decreasing rate. This phase is the ventricular Rapid Filling (phase 6) and it is followed by the 7th and last phase known as Reduced filling where the ventricles continue to fill with blood and expand but become less compliant as intraventricular pressure rises. This has as an effect a reduced filling rate until around 90% of the ventricle is filled with blood by the end of the phase. The whole cycle repeats itself with the depolarization of the atria that indicates the start of the next cycle (Klabunde, 2021).

1.3 Cardiovascular System Health Indicators

Heart along with the brain are the most crucial of the vital organs. Even small deviations from physiological functioning can lead to shock or death. This is the reason there are several health indicators that help physicians judge whether the individual needs immediate or long-term medical intervention of any sort.

1.3.1 Aortic Blood Pressure

Measuring blood pressure is the easiest and quickest way to estimate cardiovascular health since it can be measured by anybody even at home. Although the value of blood pressure is affected by dozens of parameters such as activity, percentage of salt in the blood, drugs, stress levels etc., diastolic and systolic pressures that are frequently over 90mmHg and 140mmHg respectively, are considered high and this condition is clinically significant and is called hypertension.

Hypertension is directly correlated with damaged and narrowed arteries and the existence of aneurysms. Damaged and narrowed arteries can eventually lead to limited blood supply to vital organs and at severe cases to the obstruction of an artery. Aneurysms are formed when arterial walls are weakened through sustained high blood pressure and if ruptured they can induce a life threatening internal bleeding.

In addition to the arterial system, hypertension is extremely harmful to the heart. It can lead to coronary artery disease, enlarged left heart or heart failure all of which can lead to heart attack and sudden cardiac death.

Blood pressure is a brilliant indicator of cardiovascular health but it does not provide specific information on what is exactly problematic with it at cases where pharmacological intervention and lifestyle changes are inadequate for the improvement of the cardiovascular system function.

Hence, physicians use additional methods to better judge the health of the cardiovascular system and more specifically the heart.

1.3.2 Electrocardiography

Electrocardiography is the process where 12 electrodes are attached on the limbs and chest skin area of the patient in order to produce a graph called electrocardiogram (ECG) which depicts how the electrical activity of the heart fluctuates over time.

The physician has the opportunity to detect various abnormalities regarding the function of the heart that are not apparent through a simple aortic blood pressure measurement, such as cardiac rhythm disturbances, inadequate coronary artery blood flow as well as electrolyte disturbances.

This diagnostic tool is extremely powerful and physicians can use it in combination with other diagnostic tools, to discover the source of the abnormality for each distinct patient. However, at some cases the physician wants to get information regarding hemodynamic parameters of the heart such as the stroke volume, the ejection fraction, etc (Lilly, 2016)

1.3.3 Stroke Volume, Ejection Fraction and Cardiac Output

In Cardiovascular physiology, the Stroke Volume (SV) is defined as the amount of blood pumped out of the left ventricle in one beat. It is an indicator of the mechanical performance of the heart. It can be calculated by subtracting echocardiogram-acquired measurements of left ventricular end systolic volume (ESV) from end diastolic volume (EDV) which are the volumes of blood presented in the left ventricle just before the initiation of the diastole and systole respectively. Another way to calculate it is by finding the product of the average aortic flow (AoF) during systole and the ejection time (ET).

So

$$SV = EDV - ESV \tag{3}$$

or

$$SV = AoF \ x \ ET \tag{4}$$

By multiplying the product of SV with the heart rate (HR) the Cardiac Output (CO) is figured out which is basically the amount of blood pumped from the heart in one minute. Normal values of CO are 4-8L/min for a healthy 70kg individual. Values below 3L/min are considered critically low and require medical intervention

Finally another parameter that gives physicians information about the operational condition of the heart is the Ejection Fraction (EF). It is the volumetric fraction of blood ejected over the total volume present in a chamber (LV is of interest in our case) in one contraction. EF is used as a measure of pumping efficiency of the heart and also to classify heart failure types and their severity. Mathematically the left ventricular ejection fraction (LVEF) can be calculated by dividing SV over EDV.

Hence,

$$LVEF = \frac{\mathrm{SV}}{\mathrm{EDV}} \ x \ 100 \tag{5}$$

Normal values of LVEF are between 55% and 75%. Damage to the myocardium occurred either from myocardial infraction or from cardiomyopathy could compromise hearts performance and reduce the ejection fraction. An LVEF value below 30% is considered critically low (Feher, 2016).

1.4 Classification of Heart Failure

Classifying the extent to which a heart is malfunctioning is crucial when it comes to choosing the optimum medical intervention a patient needs to receive. There have been various classification systems used over different countries, however one of the most widely used is the classification made by The American College of Cardiology (ACC) and the American Heart Association (AHA). In this classification system, the patients are divided into four classes that define the stage of heart failure.

In the following table these four classes are presented along with common intervention methods suggested for the patients of each class.

ACC/AHA Stage	Symptoms	Treatment
(A)	The patient is at high risk of heart failure but has no symptoms of failure or signs of structural heart disease.	The patient is strongly advised to exercise regularly, treat high blood pressure and lipid disorders, quit smoking and alcohol and take prescribed medications in the case of existing coronary artery disease.
(B)	Structural heart disease.	The patient should receive medication to treat high blood pressure. In case of coronary artery or valve disease the option of surgery should be considered.
(C)	Structural heart disease with prior or current symptoms of heart failure.	Diuretics may be prescribed; dietary sodium should be restricted and weight should be monitored. A pacemaker or an implantable cardioverter defibrillator may be recommended in the case of chronic arrhythmia.
(D)	Refractory heart failure requiring specialized interventions.	Heart transplant or VADs should be considered if surgery is an option. Otherwise continuous infusion of intravenous inotropic drugs or research therapies should be implemented.

Table 1 of ACC and AHA Heart Failure Classification - Stages of Heart Failure and Their Treatments
(PennMedicine, 2021)

In the context of this thesis, the stage (D) of the ACC/AHA is of particular interest and more specifically patients that have a severe heart failure but are neither good candidates for a heart transplant nor a transplant is available, or the heart failure is temporary. In these cases, a VAD is a solution that can significantly improve the quality of life of the patient and extend his/her life expectancy.

1.5 VADs

1.5.1. Patients eligible for a VAD

The application of a VAD is applied in one of the following three cases

i) The patient is waiting for a heart transplant.

In this case the patient is eligible for a transplant but there is not one available. A VAD can be implanted temporarily while the patient is waiting for a donor heart to become available. The VAD can radically improve the blood perfusion to organs and increase the chances of survival until heart transplant surgery. This case is called *"bridge to transplant."*

ii) The patient is not eligible for a heart transplant because of age or other conditions.

At some cases the patient is not a good candidate for a heart transplant either because he/she is too old or due to medical conditions such as an active infection, cancer diagnosis, organ impairment, medical obesity etc. all of which make an operation of such complexity extremely risky. (Heart *Transplant Criteria | Tampa General Hospital*, n.d.)

Therefore, in this case a VAD can significantly improve the quality of life of a patient. This treatment is called *"destination therapy."*

iii) The patient's heart function can become normal again.

There are cases that heart failure is judged by the doctor to be temporary. At these cases, a VAD is a better solution than a heart transplant. The VAD is implanted until it is judged that the heart is able to adequately supply the organs with blood without the need of artificial mechanical assistance. A great example of such cases are patients that have undergone heart surgery and require assistance for a couple of weeks until the heart is back to normal function. This case is called *"bridge to recovery"* (MayoClinic, 2021).

1.5.2 Function and Types of VADs

There are plenty of different VADs available today that are used to treat patients according to their needs. They are divided into 2 main categories depending on whether the pumping unit is inside or outside the body (extra-corporeal). The former ones are called percutaneous and are positioned inside the aorta several centimeters under the subclavian artery and the latter category is called bypass. The bypass models had been used for long time and present the most reliable solution to support patients during open-heart surgeries. Extra-corporeal Assistive devices have shown great survival rates and continuously decreasing hemolysis as the models evolve. On the negative side, the surgical procedure is lengthy and requires total anesthesia an issue that hinders the application at patients who cannot afford to stay too long in the surgery room.

On the other hand, percutaneous VADs can effectively support the left ventricle and increase organ perfusion with the benefit of a quick, simple and minimally invasive implantation method. This has as a result the decrease of leg ischemia and strokes occurrences as well as lower rates of hemolysis observed during and post-surgery.

Despite the obvious advantages, a percutaneous VAD device has over the bypass one there are still many challenges that need to overcome to make them safer and more efficient. A main problem with percutaneous VADs is that due to the position they are inserted (inside the aorta), an abrupt stoppage of their operation can lead to the trapping of blood between the aorta and the ventricle and hence minimum perfusion of blood to organs. This ischemic shock can lead to organ failures and in some cases to death. Hence reducing the size of the VAD without making compromises on the augmentation levels it can provide to the cardiac output is a top priority design criterion of VAD manufacturers. In addition to that, the quantity and design of moving parts is another major issue. Percutaneous VADs rotors can rotate up to 40000rpm in order to achieve the essential output flow at such a small size (Dennis Taylor, 2016). This means that they are susceptible to mechanical failure due to fatigue and wear. The component of the VADs that is particularly susceptible to wear is the bearing of the impeller. In order to avoid these modes of failure engineers have implemented the use of magnetic and hydrodynamic bearings since in this case there is no direct contact between the moving parts allowing them to have lower friction wear and vibration than traditional bearings

Lastly, another thing that has to be carefully considered when designing a VAD device is the method of actuation of the pump. Hemopump, the first ever percutaneous VAD used a DC motor located outside the body to drive the pump unit. The transmission of motion between the motor and the pump was achieved by a flexible shaft encapsulated by a shallow catheter. Another device that progressed the development of VADs was the TandemHeart where both the pump and actuating unit were placed extra corporeally using two catheters that drew blood from the right atrium and released it to the left atrium. This offered significant benefits to the cardiac output, systolic blood pressure and venous oxygen saturation, but the dimensions of the catheters proved to be a discouraging factor for the extended use of TandemHeart due to the regular occlusions of two large blood vessels. A 3rd device that revolutionized the design of VADs is the Abiomed Impella which was the first device to actually have both the pump and motor units inserted into the body. The motor unit is externally controlled by a control panel connected to the motor through cables immersed into a catheter. It is minimally invasive and hence the patient can benefit from it by facing a lower risk of ischemia, however due to the fact that the motor is directly coupled to the pumping unit there is the possibility of blood entering into the motor which can lead to abrupt pump failure (Karabegovic, 2017).

Despite the improved performance of the VADs serious adverse events still occur during VAD implementation. According to Papaioanou between 2015 and 2019 16.4 % percent of the deaths caused in patients with VAD support were due to multisystem organ failure, 15.6% due to neurological dysfunction and 12.5% due to heart failure. Thus, ongoing research is needed to enhance VADs as a solution to the increasing donor shortage (T. Papaioannou, 2021)

In order to develop new improved VADs testing rigs that can simulate the conditions present in the cardiovascular systems are required. These test rigs in the greater field of Cardiac Assistive Devices (CADs) are called Mock Circulatory Loops (MCLs).

1.6 Mock Circulations Used in the Past

The Mock Circulatory Loop plays a key role in the design, development and in vitro assessment of VADs and other CADs (e.g. vascular stents, heart valves, and Intra-Aortic Balloon Pumps (IABP)). In vitro studies are preferred over in vivo studies when quantitative investigation and adoption of specific, controlled, physiological parameters are needed. Moreover, in vitro studies do not require ethical approval and are much more cost-effective than animal studies. Therefore, MCLs are widely used prior to in vivo studies. The MCL aims to mimic the structure and function of the native cardiovascular system (CVS) by providing a realistic test-bench for performance assessment. It simulates hemodynamic parameters like heart rate, ventricle contractility, peripheral resistance, arterial compliance, and fluid inertance under healthy and various degrees of pathological conditions. These parameters are adapted to obtain physiological pressure and flow waveforms. MCLs are employed to study, for example, the fluid balance between the systemic and pulmonary circulation of an adult patient, the timing of IABP inflation, the unloading effect of a rotary blood pump and to study the hemodynamics of artificial heart valves, extracorporeal life support or biventricular assist devices.

1.6.1 Three types of Model Approaches

Three different types of MCLs exist: firstly, the mechanical MCLs (M-MCLs), which simulate the CVS using mechanical and hydraulic components. M-MCLs were the first type of MCLs developed. They represent the ventricles with hydraulic pumps, the arterial compliance by water and air-filled, reservoirs (or flexible tubes), and the resistance is simulated by obstructions of the flow path. M-MCLs can test various CADs and pathological conditions. However, the fixed design limits the range of applications.

Numerical models of the CVS develop in parallel to M-MCLs, in which the CVS is described with mathematical expressions. They have absolute reproducibility, controllability and are more flexible than M-MCLs. However, they neglect or simplify physiological aspects and complex properties of the CVS (e.g. wave travel and turbulence).

Merging N-MCLs and M-MCLs defines a third group of MCLs: hybrid MCLs (H-MCLs). In an H-MCL the numerical and mechanical parts run alongside and communicate with each other in real-time using a numerical-hydraulic interface. The H-MCL can describe cardiovascular characteristics that are too difficult to represent with mechanical components using computer algorithms and provides a hydraulic platform to connect the physical prototypes of CADs. Within the next few years, H-MCLs are likely to become an essential test-bench for CADs development.

1.6.2 Early Beginnings

When scientists firstly began to turn lumped parameter models of electrical components into physical test rigs consisted of hydraulic components certain tendencies occurred as to how the hydraulic equivalents will be represented. Windkessel chambers or flexible tubes were mainly used to represent the compliance of the vessels, obstructive elements, throttles or swing check valves were used to represent the resistance to flow caused by the arteries and the inertance of the system was adjusted by changing the density of the fluid used or the dimensions of the tubes.

Donovan, 1975 who developed a system that used two Windkessel containers in order to simulate the systemic and pulmonary circulations separately did one of the preliminary works on MCLs. Reul H et al, 1974 managed to approximate the geometry and elastic properties of the arteries by developing a hydro mechanical model of the arterial systemic circulation to study the hemodynamic properties of the arterial system.

1.6.3 Advances

The early models of M-MCLs were driven using pneumatic and hydraulic pumps. Verdonck et.al., 1992 though developed silicon models of the left atrium and ventricle, which were placed into a water filled housing where a feedback system was used to control its pressure. The system successfully regulated ventricular contraction and relaxation as well as left ventricular pressure and heart rate. The introduction of computer control gave the opportunity to researchers to simulate a range of rest, exercise and pathological conditions using the same system just by altering the command sent to the motor driving the pump used. Timms DL, 2011 developed an M-MCL that simulated normal and heart failure at rest by adjusting mean arterial pressure, heart rate, SVR, PVR and aortic compliance. They managed to achieve cardiac outputs between 2.7 L/min and 5.15 L/min and successfully used the system for VADs performance assessment.

Computer controllable ventricles gave the chance to researches to implement the Frank-Starlings mechanism into their MCLs in order to describe the interaction between the CADs and the CVS more accurate. One of the first to achieve that were Yokoyama et al who linearly related the elastance of the left ventricle to ventricular volume and pressure using the time varying Suga-Sagawa model. Linear elastances between 0.56 to 1.75 mmHg/ml which could regulate the preload and afterload response of the left ventricle both at healthy and heart failure conditions.

The next step to the evolution of MCL was the inclusion of anatomical models into them in order to achieve flow visualization but also increase accuracy by choosing to use higher order Windkessel models of the systemic and pulmonary circulation. This would allow researchers to also test patient specific 3d printed left ventricles and asses the viability of CADs in vitro by taking advantage of the modular design nature of this kind of MCLs. Kolyva C, 2012 designed a particularly complex anatomical model of the aorta and 12 of its largest branches. In this model, syringes of varying air volume were used in order to simulate local compliances and capillary tubes of different sizing were placed at the outlet of each branch to simulate the resistance effect. In another attempt, Knoops PGM, 2017 and his team developed an anatomical model of the pulmonary trunk with two generations of bifurcations and showed the possibility to study the heamodynamic response of the system for patient and pathology specific cases.

1.6.4. Hybrid Mock Circulation Loops

The continuous need for more accurate MCLs is forcing many scientists to follow the H-MCL approach and design systems where numerical models interact at real time with the physical model thus achieving a simulation closer to the physiological case. However achieving a fast and accurate numerical- physical-CAD interface is not easy and requires a bunch of sensors, actuators and fast responding control systems working simultaneously. Ferrari GF, 2005 created a numerical-hydraulic interface using a DC motor driven gear pump as an actuator and using atrial and arterial pressure values as input to the numerical model. The model instantly calculated the desired output flow at this pressure level and directly sends a command to the DC motor in order to control the flow output of the gear pump in the hydraulic circuit. This H-MCL was then used to test various VADs and IABPs. A more advanced system from Ochsner G, 2013 included the baroceptor response in the evaluation of VAD performance. In this H-MCL, SVR and PVR were adapted when pressure in the arterial system changed, but without a change in the heart rate. In a more sophisticated system based on the mathematical description of Ursino, Fresiello et al managed to affect heart rate, SVR and venous volume after a change in mean pressure in order to test IABP timing on baroreceptor activity and the VADs performance (Cappon F, 2021).

2 The Assistocor Project

As briefly discussed in the end of the previous chapter there are various factors that affect the performance of a VAD device and an improvement on one aspect of the design many times means the deterioration of another design criterion. This is why the research on the topic and the development of new devices has not stopped since the development of the first successfully implantation of an LVAD designed by Domingo Liotta and Dr Micheal E.DeBakey.

Inspired by this a group scientists from TU Wien in coordination with scientists from the Medical University of Vienna, founded by FFG[1] designed a novel percutaneous VAD (Assistocor) with the aim to offer a reliable solution to patients with heart problems.

This chapter will present a summary of the advantages, potential disadvantages of the actual VAD developed and the testing environment designed to test its performance

2.1 General Idea

The main goal of the Assistocor team was to design and manufacture a miniscule turbine driven heart catheter pump, inserted with minimal invasion that would assist patients suffering from temporary cardiac failure (BiofluidsLabTUWien, 2021).

Additionally, it was decided to be employed in synergy with an IABP to maximize oxygen perfusion and increase cardiac output through afterload reduction. IABPs are gas filled cylindrical polyurethane balloons that are inserted in the aorta and are actively deflated in systole and inflated in diastole. This cycle has as a result the reduction of afterload during systole due to a vacuum created on the area of the proximal area of the descending aorta that reduces aortic pressure and hence increases blood flow while the inflation of the balloon during diastole results into higher blood perfusion of the coronary arteries.

2.1.1 Helium Actuation and Magnetic Coupling

Helium was chosen as the gas medium used to drive the turbine since it offers some great advantages in comparison with CO_2 which was mainly used so far. Helium is the gas of the periodic table with the smallest density meaning it can maintain a lower Reynolds number and hence a laminar flow profile at higher speeds. This results to reduced pressure losses due to friction and hence higher overall efficiency in comparison with other gases, enabling the team to design a VAD that can give high flow rates at a smaller dimension. Another reason Helium was a perfect candidate for use in the device was the fact that due to its low viscosity it rapidly flows through the long connection tubes that lead to the IABP, hence it has a quicker response to the commands given by the system control. The fact that only one catheter will be used to drive the turbine coupled pump and expand the IABP is extremely beneficial since it considerably saves space making the device less invasive and easier to insert and put into operation. Furthermore one control system is needed to control both the VAD and the IABP simplifying the control design.

[1] https://www.ffg.at/

On the other hand, Helium has a decreased solubility in blood in comparison to other gases that could potentially be used such as CO_2 meaning that a potential rupture of the balloon or leakage from the turbine unit or the connecting tubes would intensify the consequences of gas embolization (Stouffer, 2017). Therefore, increased attention was given on hermetically securing all the parts of the device in contact with blood. A magnetic coupling is used to transmit the kinetic energy of the turbine to the pump that plays a vital role in this sealing of the unit. However, this gave rise to a new challenge that was the fact that barebone magnets could not offer adequate coupling to the pump. In order to deal with this issue the designers used additional elements of very high magnetic permeability to strengthen the magnetic field produced and therefore achieve adequate coupling and in the meantime hermetical separation between the turbine and the pump. (Karabegovic, 2017)

2.1.2 Cooling Effect

Heat generated by implantable devices can have an extremely adverse effect on the tissue surrounding it. Even a small blood clot that could interfere with the impeller of a motor driven VAD can increase the load on the motor leading to increased amount of heat dissipated on the nearby blood and tissue (Gardner Yost, 2016). The cooling of the device is therefore of extreme importance. In the Assistocor unit friction forces created between the Helium and the turbine blades inevitably generate heat. However the fact that the gas pressure drops as it passes through the turbine decreases its temperature hence creating an overall cooling effect that both extends the lifetime of the system and benefits the recovery of the patient. This poses a significant advantage of Assistocor over motor driven VADs.

2.1.3 Building Elements and General Characteristics

As seen in Figure 2- 1 the Assistocor device consists of multiple small-scale elements that require elaborate manufacturing processes to be produced. The max efficiency of the turbine unit is at 160000 rpm meaning that a gearing unit should be used to drop down the rotational speed of the pump, which has an optimal working point of 39700 rpm. The extremely high speeds generated by both the pump and turbine means that bearings used to hold their shafts into place must be designed very carefully. In this case, the designers have implemented one hydrodynamic bearing for each unit, which means that there is no direct contact, and hence no sliding friction between the moving parts. This significantly affects service life and minimizes noise and vibrations. What is also apparent is the slender shape of the device. It has a maximum diameter of 6mm and a length of 45mm allowing it to be placed comfortably in the ascending aorta where it gets into contact with blood inside the left ventricle using an inlet cannula that goes through the aortic valve. Despite its minute size the high operating speed allows to produce up to 2.5 L /min.

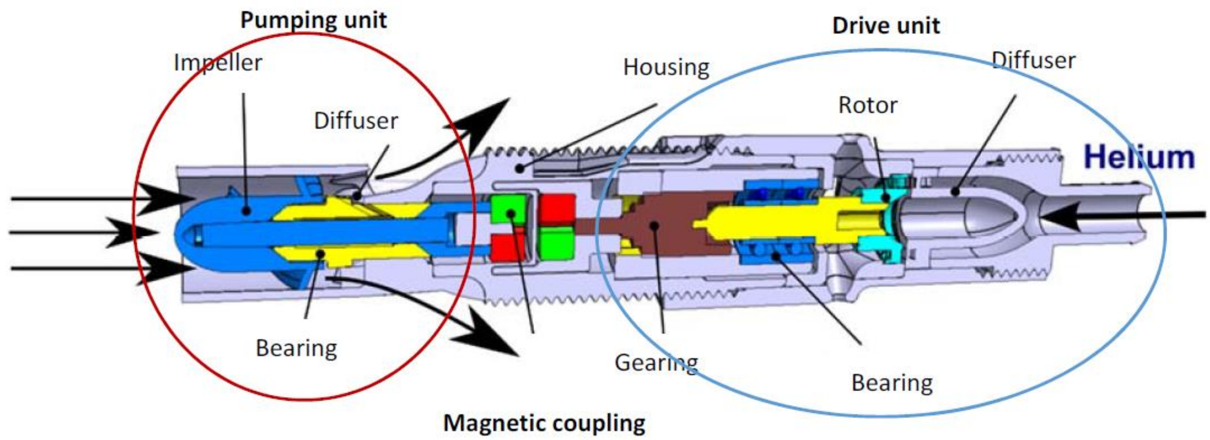


Figure 2- 2 Section View showing main internal components of the heart pump (Karabegovic, 2017)

2.2 Objectives of the Thesis

This thesis aimed to upgrade the mock circulation system build by Karabegovic in 2016 in order to simulate the conditions prevailing in the systemic circulation. The idea was to maintain most of the components used but also decrease the size and complexity of the electronic control panel, change sensors where appropriate and implement improvements on the software controlling the circulation to get results that are more accurate. A design criterion of great importance is that the setup is modular and easily modifiable in case the user needs to change one or more modules in the future.

At the end, the mock circulation system should be able to simulate successfully the ventricular and aortic pressure profiles and amplitudes as well as the aortic flow rate for heart frequencies ranging from 40 to 150 bpm and aortic flow levels from 1 L/min to 8 L/min. In addition various pathological regimes shall be able to be simulated.

This can give the opportunity to perform in vitro tests for the Assistocor pump, other VADs as well as test the durability of heart valves, IABPs or artificial arteries under pulsatile flow conditions.

3 Materials and Methods

3.1 Choice of type of Circulation

As discussed since the development of the first M-MCL, the complexity and simulation accuracy of MCLs has increased dramatically even though still today there are some limitations to the flexibility and reproducibility of the models. In parallel, N-MCLs have become more competent and offer a high flexibility and reproducibility to the user, however they still lack the ability to test a physical prototype device or even simulate complex hemodynamic effects. This is why nowadays scientists are mainly using hybrid systems to reproduce a wide range of physiological but also pathological conditions including rest exercise, heart failure, hypertension, valve insufficiencies etc. This enables them to test various CADs and observe the effect they have in the pressure and flow profiles at various part of the circulation system and observe their performance at continuously changing conditions. What is also extremely important is to design and build a system that meets ones demands. In our case, a system was desired that will be used initially as the testing platform for the Assistocor VAD developed by TU Wien, with the intention to use it for testing of other assisting devices such as stents, aortic valves and VADs by doing minor modifications on the hydraulic circuit. An M-MCL was chosen since in our case the main design criterion is to build an MCL that will be able to simulate the aortic, ventricular pressure profiles as well as the aortic flow profile and also monitor the effect a LVAD has on these parameters. Henceforth, it was decided that a H-MCL that would be able to mimic the pressure and flow profiles at predefined positions in the real circulation would be too complicated and expensive to construct and would not offer any significant benefits in comparison to the M-MCL.

3.2. Function and main components

The way the mock circulation works is by the introduction of a stream of compressed air into a vessel, which is partially filled with water and air. This vessel simulates the left ventricle of the heart and is separated from the rest of the system by two valves. The air stream is fed at such a way that it creates conditions similar to the ones existing in the left ventricle and as a result pushes water into the rest of the system when the pressure in the vessel exceeds the pressure outside of it. The amplitude of pressure head and frequency of pulsation governed by the air stream along with the regulation of certain resistive and compliance elements downstream of the vessel are the factors that can be controlled in order to achieve the desired result. What follows is a detailed description of all the elements that form the system to clarify things further.

3.2.1Motor – Cylinders Assembly

The power required to drive the system is provided by a Kollmorgen AKM32H-ANCNC-00 DC motor that has 0.62 kW power and can generate a peak torque of 7.26 Nm. This motor is coupled with a Festo DNCE-40-300-BS-12.7 P-Q electric cylinder with a 30cm stroke length. On the piston end of the electric cylinder a Heschen pneumatic cylinder is coupled. This cylinder has a stroke length of 20 cm and an effected cross sectional area of $0.01m^2$ giving a maximum stroke volume of 2 L. The main reason that a motor-electric cylinder assembly is used to drive the pneumatic cylinder instead of compressed air entering through solenoid valves is the increased accuracy of motion ensured by the encoder of the motor.

Figure 3- 5 Representation of Motor – Electric Cylinder – Pneumatic Cylinder Assembly

3.2.2 Left Ventricle Vessel

The vessel that represents the physical entity of the left ventricle is a closed aluminum cylinder with a height of 28 cm and a diameter of 18 cm. The vessel is filled with a water/air mixture. The compressible air models the contraction of the ventricle by pushing or sucking water out and into the ventricle. This is achieved since the top of the vessel is connected via a 1'' PVC tube with the pneumatic cylinder in order to regulate the pressure inside it. The vessel has one inlet and one outlet orifice that let it deliver and receive water from the rest of the system depending on whether the pressure gradient is positive or negative. Another property of the vessel is that it has a valve through which air can be pumped into it and thus preloading it, a feature that gives us the opportunity to regulate pressure conditions as well as the air-water ratio existing on the vessel initially. It is vital that the vessel is air tight to ensure no pressure losses occur during operation which could hinder the accuracy of the simulation.

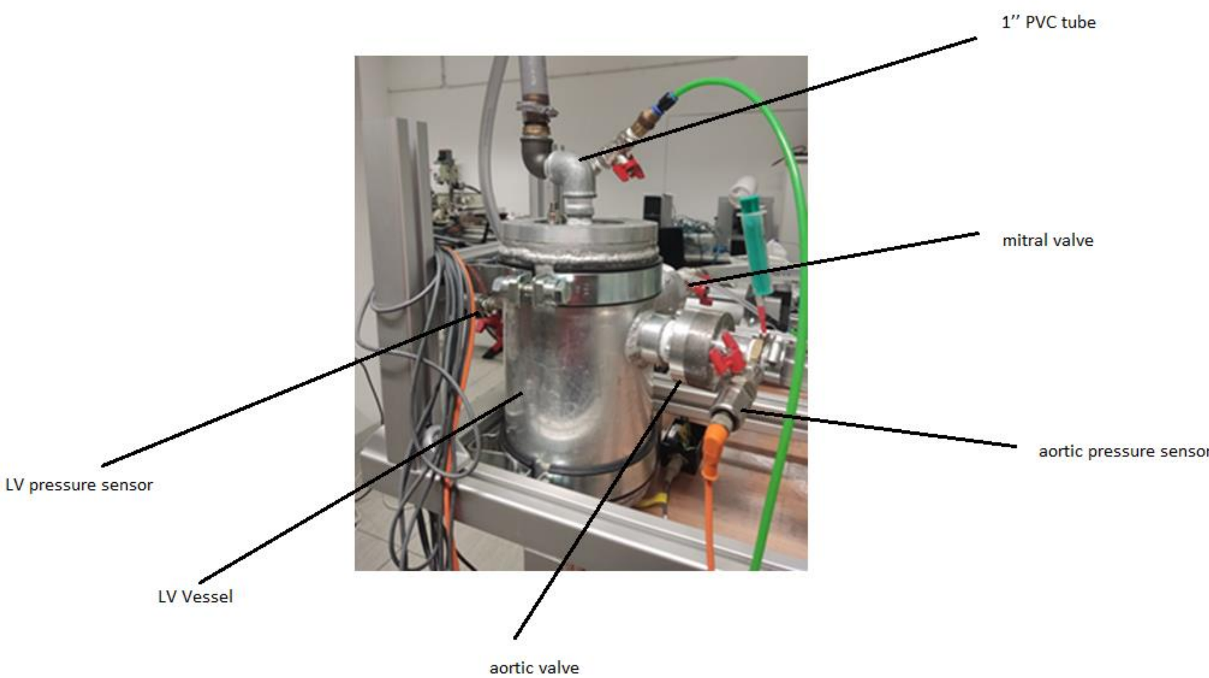


Figure 3- 6 Depiction of Left Ventricle Vessel with aortic and ventricular pressure sensors visible

3.2.3 Aortic Resistance- Peripheral Resistance

All fluids flowing through a tube will face resistance from the walls of that tube while flowing through it. Blood is not an exception to this rule and also experiences frictional forces while travelling through the arterial and venous systems. In order to produce a realistic representation of the conditions existing in the cardiovascular system, certain resistive elements had to be introduced in the mock circulation system that will resemble the total resistance exerted on the blood both in the aortic and peripheral part of the system.

Assuming that blood vessels have a quasi-circular cross section, their resistance can be determined using the following equation

$$R_{vessel} = \frac{8nL}{\pi R^4} \tag{6}$$

where n is the viscosity of the fluid, L the length of the vessel segment and R is the radius of the vessel.

Reasonably assuming that the viscosity of blood remains almost constant during circulation, it can be deducted that the two factors affecting the resistance in flow is the length of the vessel and its radius. Hence, ideally we would use cylindrical hydraulic resistances of adjustable length and radius, however this is not very practical in our case since a large range of resistances are required for our testing. As a result, it was initially decided to use 2 flat metallic plates placed opposite to each other as such that by screwing the 2 screws that connect them the tube which they encircle will be squeezed. This squeezing action has as a result the decrease of the cross section of the tube in the area of compression. In this case, the equation giving the resistance of an elliptical cross section tube is given by the following equation

$$R_{squeezed\ tube} = \frac{12nL}{ab^3} \tag{7}$$

where a is the height of the squeezed tube and b is the width.

It is understood that by having a stable plate width and manipulating the distance between the two plates we can theoretically get an infinite set of a values and hence resistances.

Therefore, the plates that were initially used had a width of 4 cm and could be squeezed until a is practically zero and consequently the resistance was infinite and no flow was induced in the system.

After certain experiments, it was decided to gradually decrease the width of the plates. The reason was that the resistive element was acting as the reflection point of the forward pressure wave caused by ventricular blood ejection. The existence of this reflection point (dicrotic notch) is vital to the physiological operation of the cardiovascular system and in vivo this reflection is occurring by the reflection of the wave on the blood vessel bifurcations. What was observed during testing was that in order to achieve the dicrotic notch in the aortic pressure profile a significant reduction on the distance between the 2 plates on the periphery was required. However, this setting was compromising significantly the magnitude of the aortic flow. Hence, it was decided to gradually decrease the length of the peripheral resistance using 3D printed adaptors that could easily change and used for new sets of tests. It was discovered that the aortic flow increased significantly using this strategy without compromises on the pressure profiles of the left ventricle and the aorta.

3.2.4 Aortic Compliance-Peripheral Compliance Vessels

Vascular compliance is the ability of the blood vessels to contract and expand passively due to changes of transmural pressure. This property has significant effects on the development of the pressure and flow profiles in the heart and the rest of the cardiovascular system and has to be taken into account when designing the mock circulation. The two main compliances that have to be considered is the aortic and the peripheral compliances, which will account for the compliance of the arteries and veins respectively.

Generally speaking hydraulic compliance is the ratio between the extent of volumetric change over the pressure change required to cause this change in volume.

Hence, the general compliance equation is as following

$$C = \frac{dV}{dp} \tag{8}$$

It was decided that aortic compliance would be simulated by a cylindrical reservoir with closed top that is partially filled with water and partially with air. The idea behind this selection is that as the water pressure will be increased through the strokes of the pneumatic cylinder the water level in the cylinder will increase thus decreasing the volume available for air in the closed container. This as a result will increase the pressure of the trapped air and hence push the water level down thus resembling the effect experienced by blood when blood vessels are stiffened due to elevated blood pressure.

What is substantial is to determine the parameters that the compliance depends on so it can be easily regulated while testing

In the equation below V_0 is the initial amount of water in the reservoir, V_{in} the amount of water that has entered after a time period *Dt* and *V* the total inner volume of the reservoir. Additionally, p_0 is the initial pressure at the water surface level and *p* is the pressure after time *Dt*.

So substituting into equation (1) we get the following

$$C = \frac{V_0 + V_{in} - V_0}{p - p_0} \tag{9}$$

However, assuming that air behaves as an ideal gas we can claim that

$$p_0(V - V_o) = p(V - V_0 - V_{in}) \tag{10}$$

Solving for *p* and substituting into equation (2)

We get $$C = \frac{V_{in}}{p_0 \frac{V-V_0}{V-V_0-V_{in}} - p_0} = \frac{V-V_0-V_{in}}{p_0} \approx \frac{V-V_0}{p_0}$$

Since V_{in} is very trivial in comparison to $V - V_o$

This result points out that aortic compliance depends only on the initial volume of water as well to the initial pressure of the air in the reservoir.

The case for the peripheral compliance is slightly different since in this case the pressure of the blood is technically zero in comparison with the arterial pressure. Hence, the compliance reservoir is represented by an open top cylindrical reservoir where the water is in contact with air in atmospheric pressure.

Let *A* be the area of the reservoir, *ρ* the density of the water and *dh* the change in liquid level after a pressure change *dp* using equation (1)

$$C = \frac{dV}{dp} = \frac{Adh}{\rho g dh} = \frac{A}{\rho g} \tag{11}$$

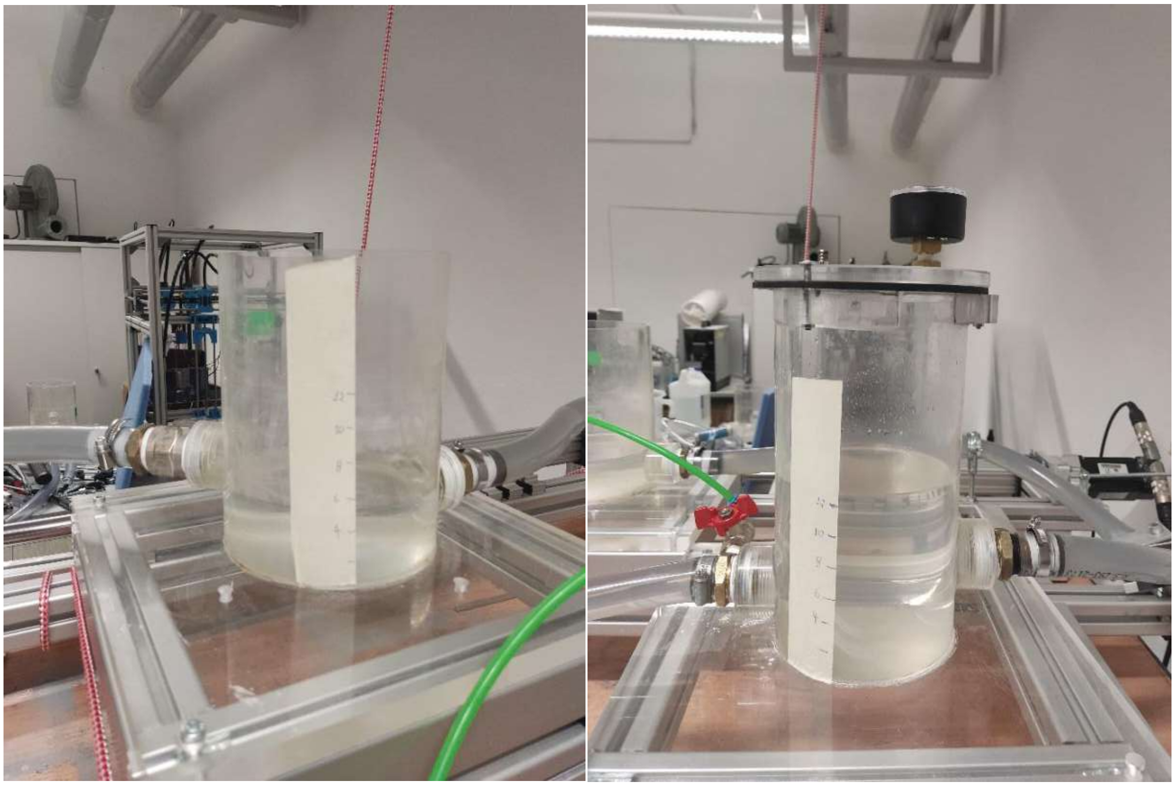
This shows that peripheral compliance depends only on the cross-sectional area of the cylinder, the density of the liquid used as a medium in the system and the gravitational acceleration constant and not in the initial pressure as in the case of the aortic compliance.

In our case the aortic compliance vessel has a height of *250mm* and a diameter of *150mm*. That gives a total inner volume of *V= 250 x* $\frac{\pi 150^2}{4}$ *= 4.4 L*

For a trial where the volume of the vessel is halfway full with water, $V - V_0$ *=2.2 L.* Assuming that the pressure at the water surface is atmospheric initially then p_0 *= 1 bar* giving an aortic compliance of *2.2 L/bar.*

As far as the peripheral compliance is concerned this remains constant independent of the height of the water inside the compliance vessel. In our case $A = \pi r^2 = \pi\ x\ 8.5^2\ cm^2$ = 230 cm^2. Since our working fluid is water and the experiments are performed in nearly sea level altitude *ρ=1000kg* $/m^3$ and g*= 9.81* m/s^2 hence giving a peripheral compliance of *0.0023 L/bar*, three orders of magnitude lower than the aortic, a result that is expected since peripheral veins are much less elastic than arteries hence a lower volume increase is induced over the same pressure differential across the vessel.

This way the compliances can be calculated before the start of each experiment and can be inserted into analogous electrical models in order either to validate the model or be used to predict the system's behavior when other parameters are modified.



(a) *(b)*

Figure 3- 7 Reservoirs depicting peripheral (a) and aortic (b) compliances

3.2.5 Tubing

The material chosen for connections between the left ventricle and the compliance reservoirs was 1'' PVC tubes. The main advantages of these tubes is that they are inexpensive, durable, lightweight and can be adjusted to hydraulic fittings really easily and quickly using tube clamps. The 1'' diameter was chosen because it resembles well the diameter of the aorta which is on average around 2.5-3.5cm.

3.2.6 Metallic Base

It was decided to build a metallic base that would support the three main reservoirs used and connect them with the motor-piston assembly using ITEM aluminum profiles.

The main reason that the two units have to be connected is that the electrical cylinder can attain extremely high acceleration especially when stroking forward to simulate the isovolumetric contraction period of the cardiac cycle. This period can last *0.05s* or less and since by that time the pressure of the system should have reached *70%* of its peak value it means that the piston of the cylinder might have covered around *20cm* in the forward direction. Using simple kinematic equations, it can be deduced that the piston can reach accelerations higher than *100* m/s^2. Bearing in mind that the moving mass of the piston is *0.65kg* using Newton's 2nd law we can deduce that *65N* of force can be generated in high amplitude tests. The force that opposes the motor piston assembly to move forward is the frictional forces between the supports of the frame and the wooden table surface.

The combined weight of the motor-piston assembly along with its support is *12kg* and assuming a static coefficient of friction of *0.4-0.6* between the plastic support legs and the wooden surface, we get a static frictional force opposing the motion between *48N* and *72N,* which do not guarantee that the assembly will not move. However, by connecting the motor assembly with the rest of the system (left ventricle, reservoirs, water, tubing, and frame) another *20kg* are added increasing the total mass of the unit to *32kg* and hence resulting to frictional forces between *130N* and *190N* significantly increasing the stability of the system. This is important because a moving setup adversely effects the service life of the moving components of the motor and the electric cylinder but also causes air and water turbulence inside the system adding noise to the signal and hence making the simulation less accurate.

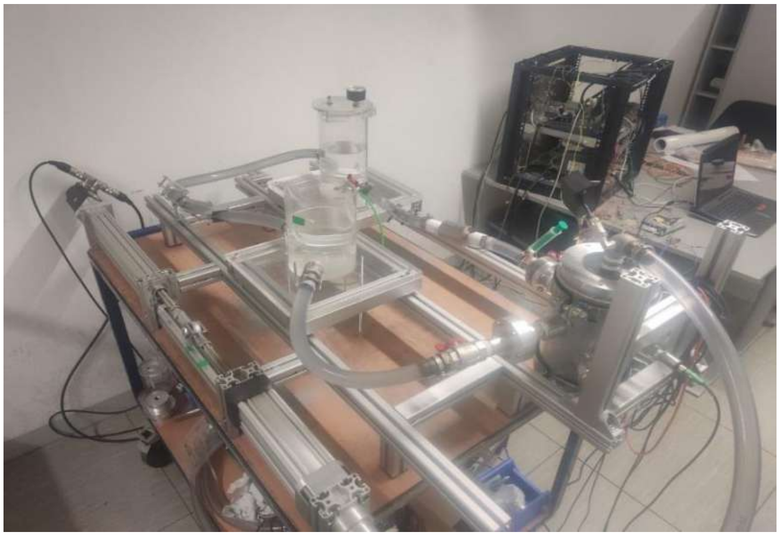


Figure 3- 8 Depiction of the metallic base and components of the Mock Circulation circuit

3.2.7 Valves

As aforementioned heart valves are an integral part of the cardiovascular system and their properties affect the behavior of the system in a big way. Since our system considers only the left ventricle out of the 4 heart chambers only the aortic and mitral valves are embedded in the design. The valves used for the purposes of this thesis are manufactured by Edwards Lifesciences which are medically approved and can simulate the performance of the physiological ones in close proximity. They can be used in lengthy experiments without a significant increase in the mean pressure across the valve. They are fixed into two special designed adaptors that can accommodate valves of diameters ranging from *21mm* to *27mm*.

(a) *(b)*

Figure 3- 9 Aortic Valve (23mm) (a) and metallic adaptor (b) enclosing the valve with aortic pressure sensor depicted just after it

3.3 Measuring Devices

There are three main parameters that give us information about the mechanical performance of the heart, these being the ventricular pressure, the aortic pressure and the aortic flow.

This means that two pressure sensors and one flow sensor are necessary to gain information about these values.

3.3.1Measurement of Pressure

In order to measure the ventricular and aortic pressures two Telemecanique XLMPM00GD71F *0-10V, 0-1 bar* analog pressure sensor were used. The pressure sensors were placed at the same height to avoid any initial pressure discrepancies that could arise from excess hydraulic head. The pressure magnitude inside the left ventricle rarely exceeds *0.25 bar* so the pressure range is adequate.

In the previous setup the Gefran TK-N-1-Z-B04U-V and the Gefran TK-N-1-Z-B25D-M-V were used which have higher pressure ranges for the same voltage range meaning they were less precise and hence the XMLPM00GD71F was chosen over them.

3.3.2Measurement of Flow

For the flow measurement, the IFM SM6000 magnetic-inductive flow meter was used. The main advantages of this flow meter is that it has a measuring range from *0.1 L/min* to *25 L/min* with an accuracy of *0.05 L/min* which covers perfectly our working conditions. In addition, the fact that it has a *0-10V* analog output suits our purposes since data acquisition can be performed using the same analog module used for the pressure sensors making the control design simpler and more cost effective.

3.4 Control apparatus and Method

The program that runs the application has been written with the LabVIEW software of National Instruments. The program is uploaded to cRIO 9074 real-time embedded industrial controller when connection is achieved from the PC to the controller via an Ethernet cable. Below the general control schematic is depicted.

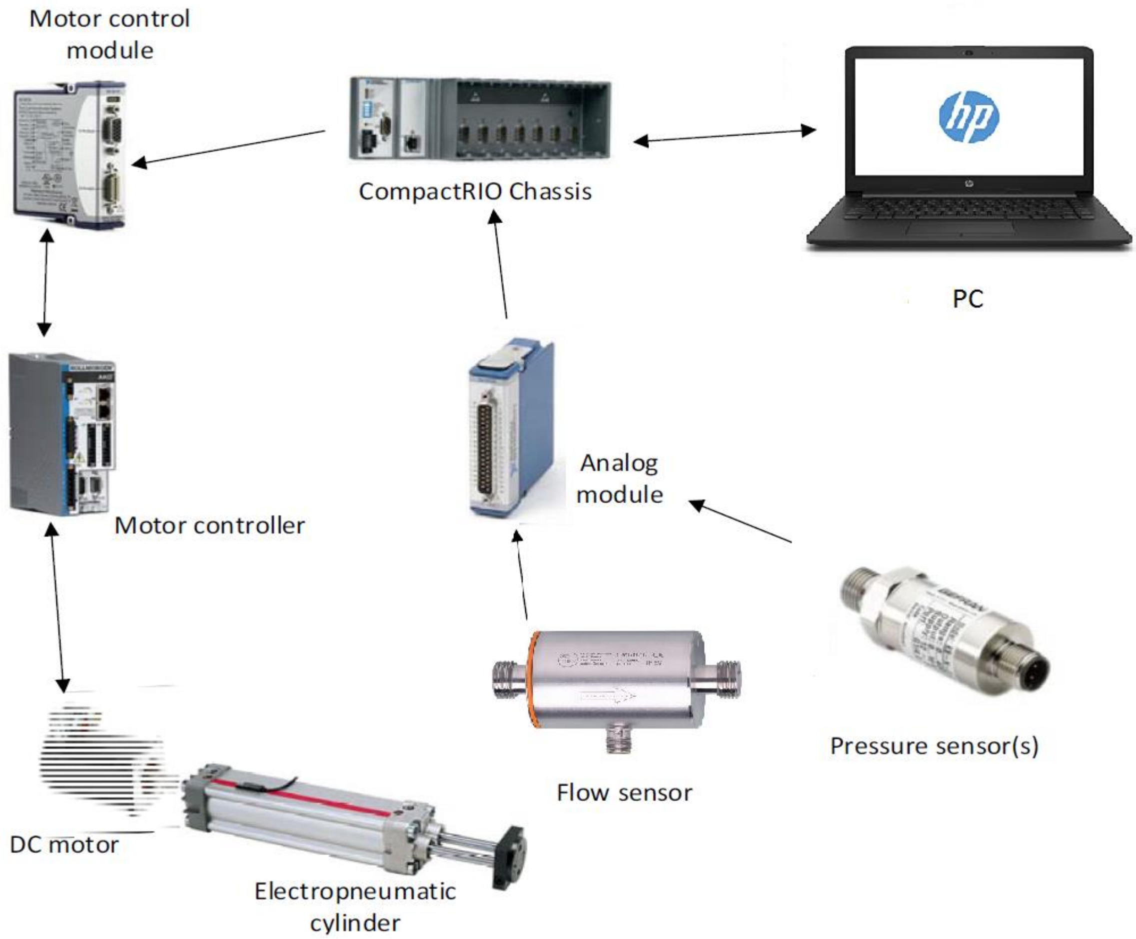


Figure 3- 10 Representation of components communicating for the supervision and control of the system

As seen in the control schematic the motor is controlled by the AKM servo driver which is commanded by the NI 9516 motor control module that is embedded into the cRIO 9074. Using the NI softmotion module in Scan Engine mode the position reference information is transferred to the motor control controller every 10ms. There is a unique motion table for each pumping frequency. Another factor that can be also controlled programmatically is the amplitude of the piston stroke. That means that the heart rate and periodic motion of the piston can be modified during runtime to meet the desired result

As far as the ata Acqusition of the pressure and flow profiles is concerned this is done at *500Hz* using the NI 9205 Analog module which is also embedded in the cRIO 9074. The data are graphically depicted and evaluated on the screen of the PC in real time.

Finally, there is the option to save data such as the motor position, the ventricular pressure, the aortic pressure and flow at timestamps lagging each other *0.002s* and save them in an excel file for post analysis.

3.5 Selection of Motor Profile

The motor profile basically simulates the ventricular pressure profile. In vivo the pressure profile of the ventricular pressure looks like a rectified sine wave with about 40% of the time being spent in systole and 60% in diastole with the percentage of time spent in systole increasing as the heart's frequency increases.

Various profiles were tested in order to find the one that better resembles the conditions present in the cardiovascular system.

The motor module NI 9516 can update the position of the motor every 0.01s. This means that at a frequency of 60 bpm where the pressure profiles are repeated every 1 second, 100 data points can be used to define the motor position which in turn will affect the shape of the pressure profiles.

For the initial experiments the motor profile designed by Karabegovic was used (Figure 3-11)

This profile has one main advantage. It is less steep than the physiological profiles and hence requires smaller acceleration of the electric and pneumatic cylinder shafts meaning that their moving components face less wear and the setup can withstand longer testing sessions. However, it doesn't closely resemble the profile of the physiological case and hence was disregarded after some testing sessions which nevertheless gave useful feedback for the rest of the experiments.

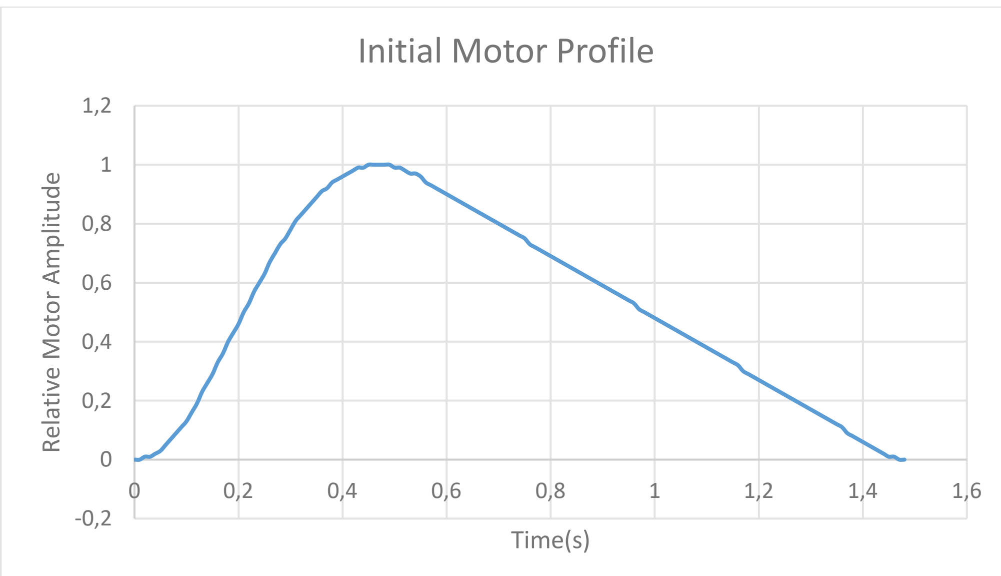


Figure 3-12 Initial Motor profile used by Karabegovic

Next, attempts were made to create a motor profile that would better simulate the pressure profile of the left ventricle. The profile depicted in Figure 3-13 was designed. This profile accurately resembles the pressure profiles but cannot give rise to sufficient flow and synchronously simulate the dicrotic notch effect no matter how much the resistance and compliances vessels parameters are manipulated.

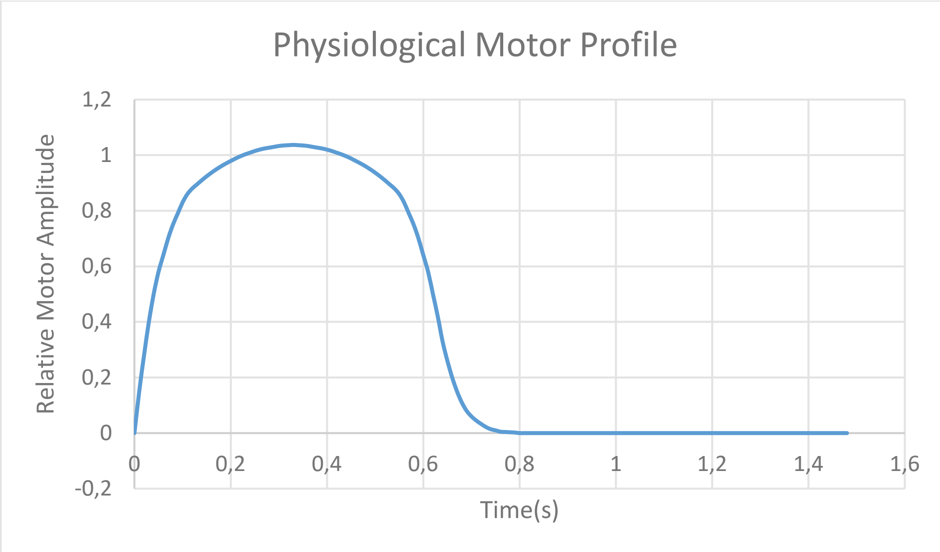


Figure 3-14 Improved Motor Profile representing physiological heart beat more realistically

Hence, it was decided to design a profile where the motor would stay longer in the ejection phase hence creating a larger plateau at the peak of the motor position. This increases the flow as the area under the *Relative Motor Amplitude vs Time curve* is proportional to the stroke volume and hence the Aortic flow produced by the system.

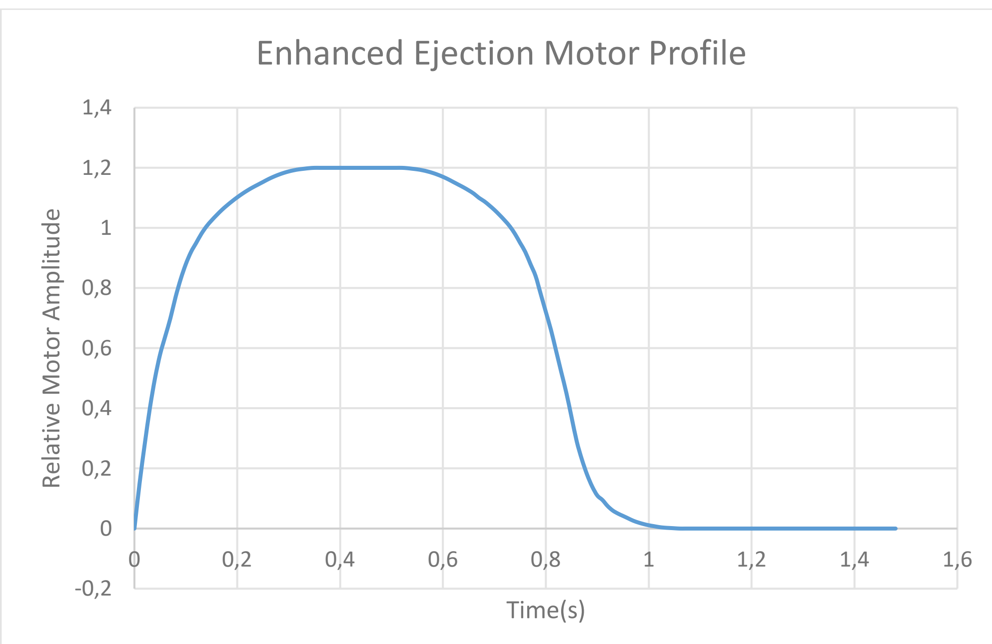


Figure 3- 15 Motor profile with longer ejection phase created to enhance stroke volume

3.6 Resistance plates improvement

Flow resistance is a fundamental parameter in fluid flow and its regulation is crucial when designing a hydraulic system. As aforementioned, it was decided to use two parallel plates to control the flow rate of the mock circulation. The initial choice was plates with a width of *40mm.* However early test sessions revealed that it was impossible to achieve a regime that would successfully simulate the pressure profile of the circulation system and simultaneously achieve a flow rate that would resemble the cardiac output of a healthy adult. Therefore, as theory suggested it was decided to reduce the resistance gradually and observe the behavior of the system. It was thought that the most economic and quick way to achieve this was to manufacture a metal beam of *10mm* thickness and then adjust 3D printed adaptors on it so the user could change the resistance of the system according to his or her needs. The comparison between the two configurations is shown in Figure 3- 16.

(a) *(b)*

Figure 3- 17 Thin (a) vs Thick (b) hydraulic resistance plates

The impact this change had at the flow is apparent in Figure 3- 18 where the aortic flow for two resistance plates settings is plotted over time. The blue line is the setting where the resistance plate has a width of 1.5mm whereas the orange line is the setting where the plate is at highest value of 40mm. It is observed that the flow (proportional to the area under the curve) is almost doubled in the small width setting underlining the importance of carefully choosing the parameters to achieve the desirable flow and pressure profiles.

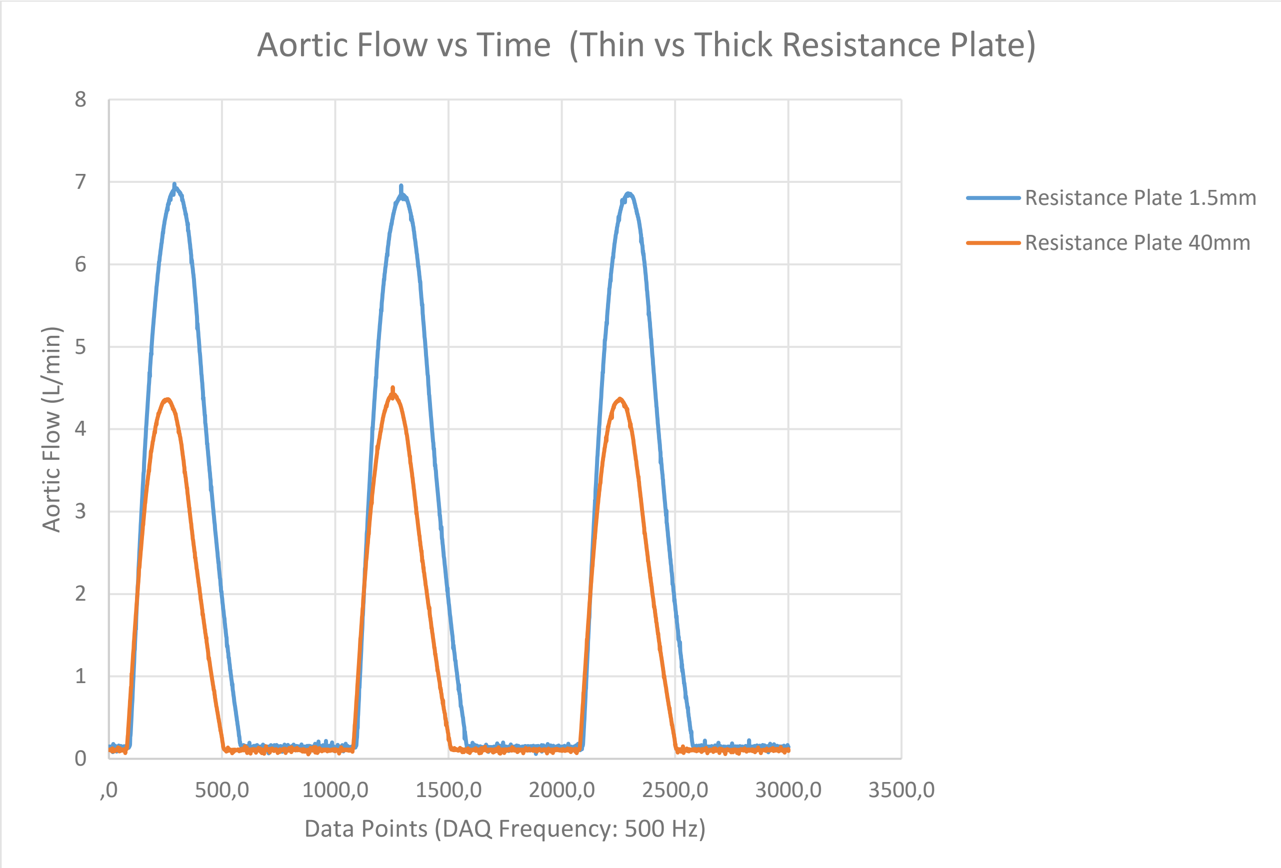


Figure 3- 19 Aortic Flow Profiles in 2 different resistance plate thickness (all other parameters remain constant)

3. 7 Aortic Compliance Improvement

Aortic compliance was found to be another parameter that has massive influence on the magnitude of the aortic flow. Initially the configuration that was used permitted a lot of air between the surface of the water inside the compliance vessel and the bottom surface of the vessel's top lid. This allowed the water to follow the path of least resistance (upwards) instead of forward towards the peripheral resistance plates and as a result, the cardiac output was reduced. It was thought that by decreasing the amount of air between the lid and the surface of the water the pressure of the air would increase considerably more and hence impose a higher resistance on the movement of the air in the vertical direction and thus increase the flow along the pipes and thus increase the cardiac output. This was achieved by designing and 3D printing a lid with a circular indentation on its bottom that is used to adjust cylinders of varying diameter and height on it thus regulating the effective volume of air present inside the vessel water interface.

The 3D printed part has a volume of 2L. This means that the effective inner volume of the vessel drops from 4.4 L to 2.4 L. The water volume of the system and hence of the aortic compliance vessel remains the same in both cases. So considering a case where the initial volume of water in the vessel is 2L and the initial pressure is at 1 bar we can deduce by using equation (10) that the aortic compliance value drops from $C_1 = \frac{4.4-2}{1} L/bar = 2.4\ L/bar$ to $C_2 = \frac{2.4-2}{1} L/bar = 0.4\ L/bar$. This manipulation increased the flow by up to over 200%. This is showcased in the results and discussion sections in detail.

(a) (b)

Figure 3- 20 (a) original aortic compliance vessel, (b) new aortic compliance lid with attached cylinders to reduce the volume of air in the vessel

3.8 Pneumatic Cylinder Improvement

An additional aspect of the previous design that had to be altered is the pneumatic cylinder used to supply with air the left ventricle and as a result initiate the flow in the system. Initially the Parker P1D-S063MS was used as an actuator. This cylinder has a bore diameter of *63mm* and a stroke amplitude of *160mm* meaning it can displace $31.2\ cm^3$ of air per each cm moved by the cylinder and a total of *0.5 L* at maximum stroke. This however was inadequate to induce the flow required in the system due to the large frictional forces met by the liquid during operation. It was decided to replace the Parker P1D-S063MS with a Heschen SC 100-250 PT1/2 which has a diameter of *100mm* and a stroke of *250mm* thus displacing $78.5\ cm^3$ per cm with the ability to reach *2L* at full stroke. This modification significantly increased the flow of aortic flow as seen in the Figure 3- 21 which compares the flow induced in the system by the cylinders with all the other parameters remaining the same.

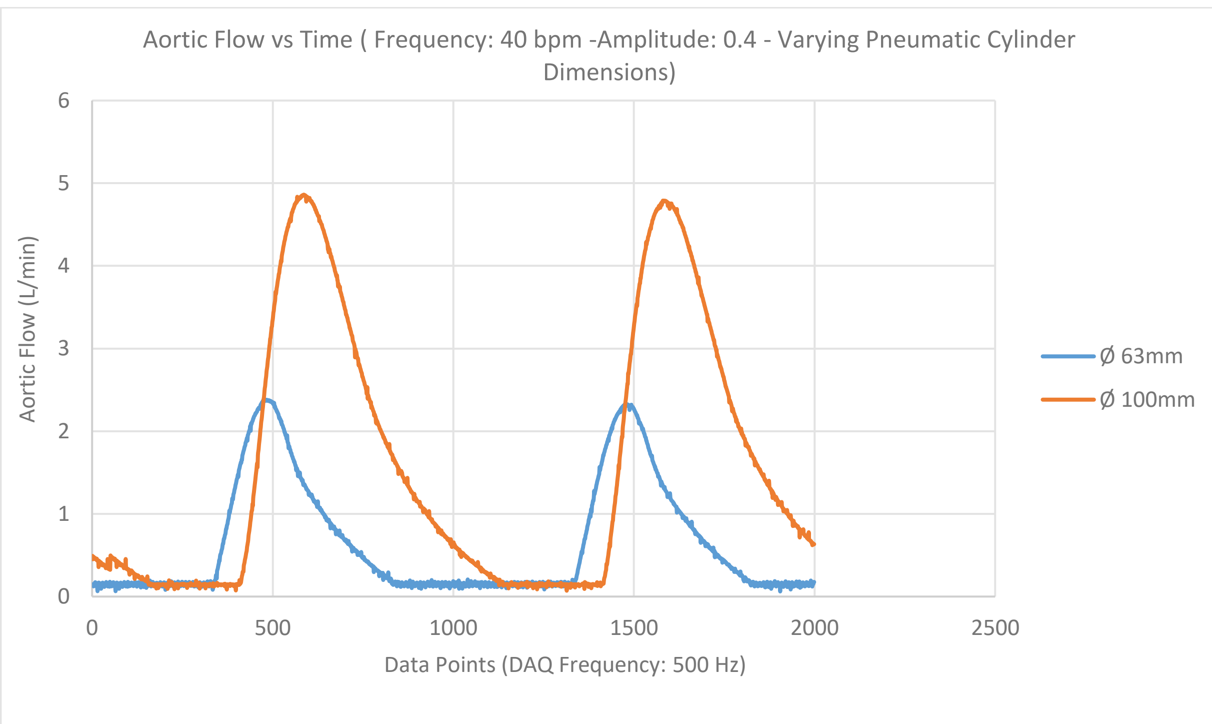


Figure 3- 22 Aortic Flow profiles for the two different pneumatic cylinders (all other parameters remain constant)

4. Results

The main objective of this Mock Circulation was to build a system that will be able to simulate the heart conditions at a range of frequencies and amplitudes under various compliance and resistance settings.

It was decided to perform a series of tests to investigate how reliable the system is and whether it responds realistically to the alterations of the parameters.

The LabVIEW program that controls the motor and collects real time data of pressure and flow has the added feature that it can export these data on an Excel sheet for further data processing.

Numerous experimental sessions were performed once the system was set. Various different resistive plates, aortic compliance lids and motor profiles were tested at a range of frequencies and amplitudes. The ones that are presented below are the ones that according to the author better simulate the conditions that a VAD would face if inserted inside the aorta of a patient.

For reference all the pressure values presented in the results have been transformed from bar to mmHg since this unit is more widely used in medicine. The flow values are in L/min. As far as the amplitude of the stroke of the pneumatic cylinder is concerned a 0.1 increase in the amplitude scale translates to 15mm extra displacement performed by the cylinder. So for example an amplitude of 0.8 interprets to a stroke of 120mm.

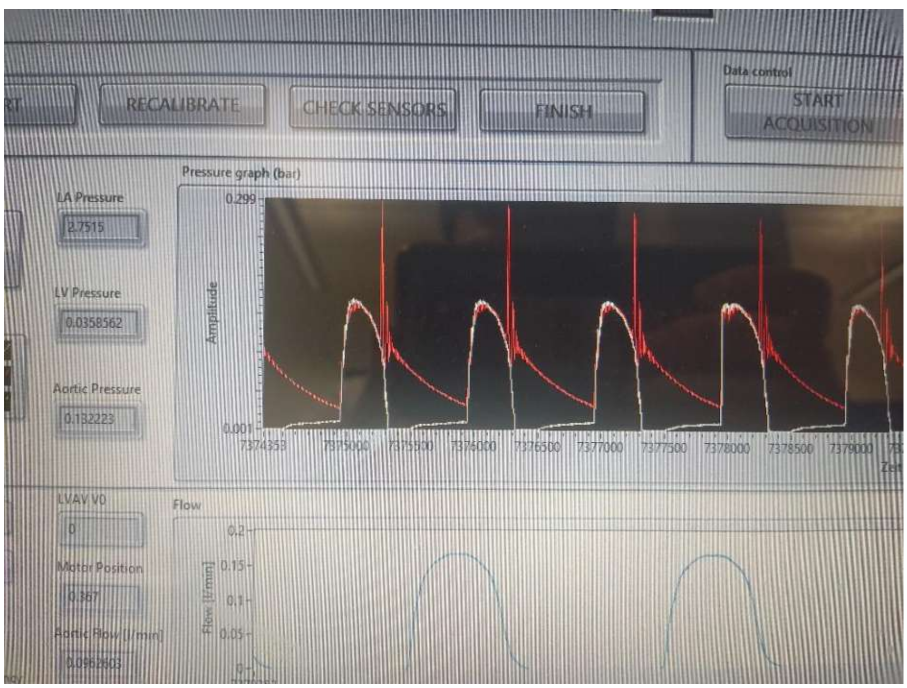


Figure 4 - 1 Depiction of LabVIEW software program while system is running

4.1 Constant Frequency-Varying Amplitude

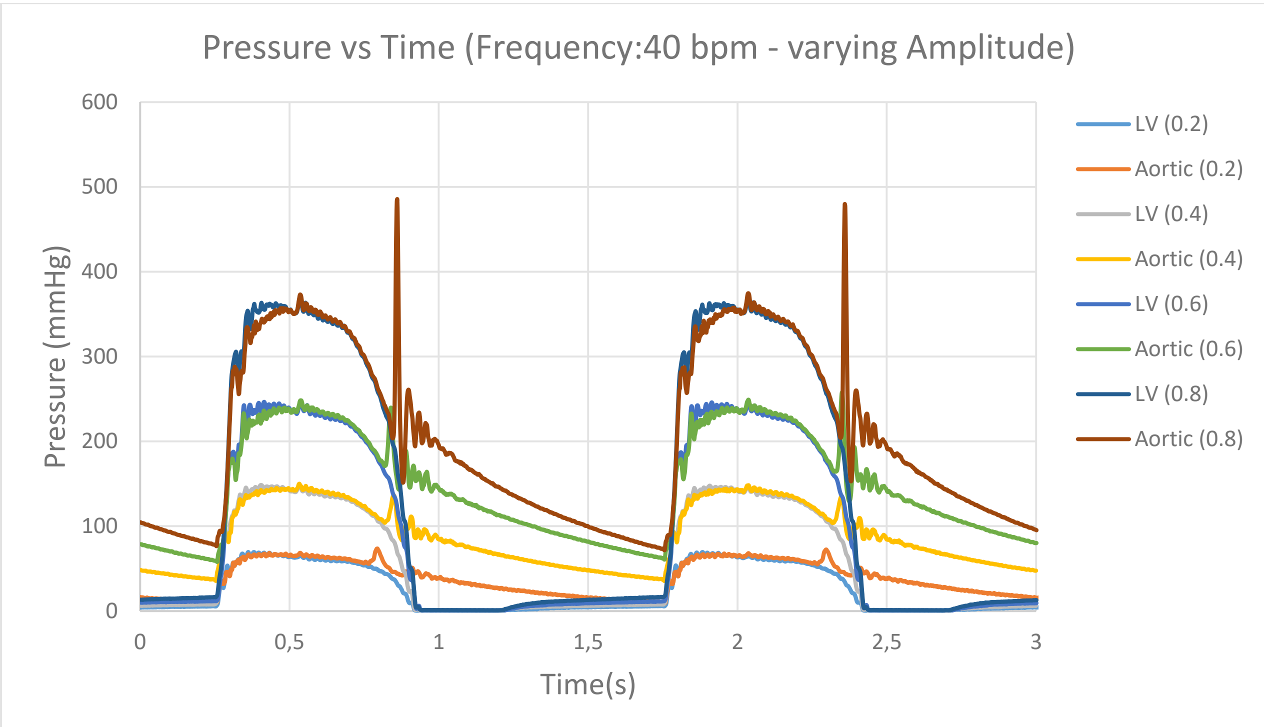


Figure 4 - 2 Aortic and Ventricular Pressure with Motor Amplitudes ranging from 0.2 to 0.8 and Frequency of 40bpm

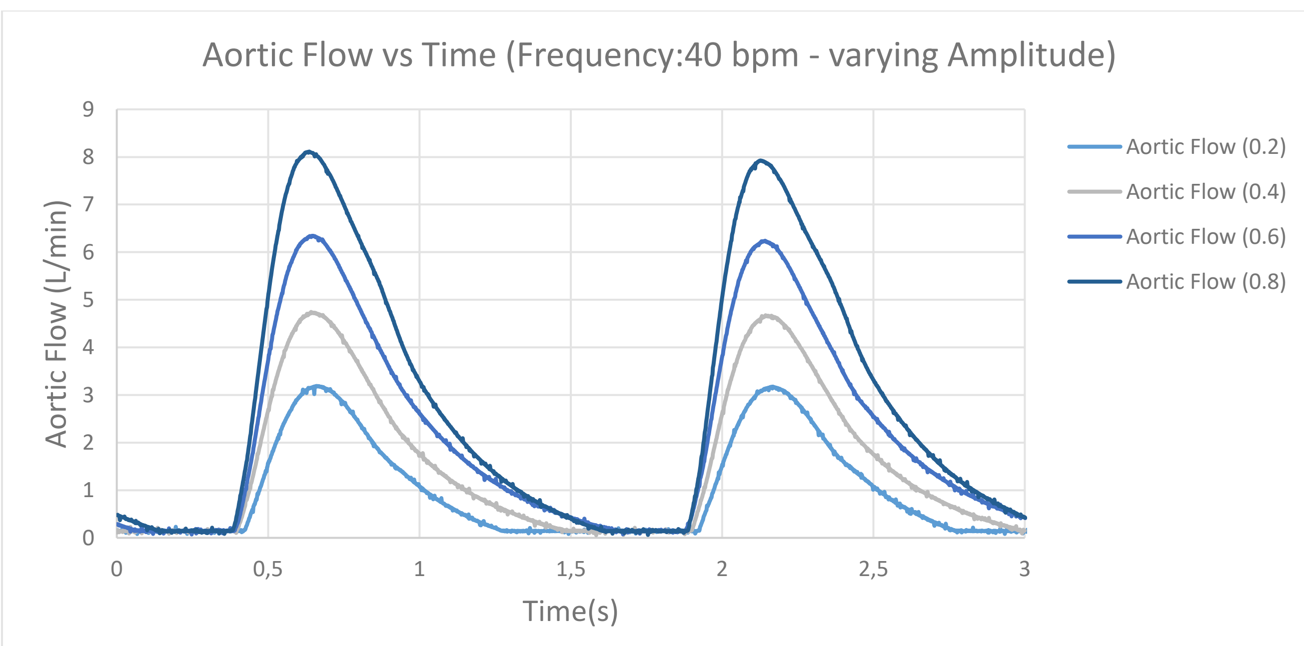


Figure 4 - 3 Aortic Flow with Motor Amplitudes ranging from 0.2 to 0.8 and Frequency of 40bpm

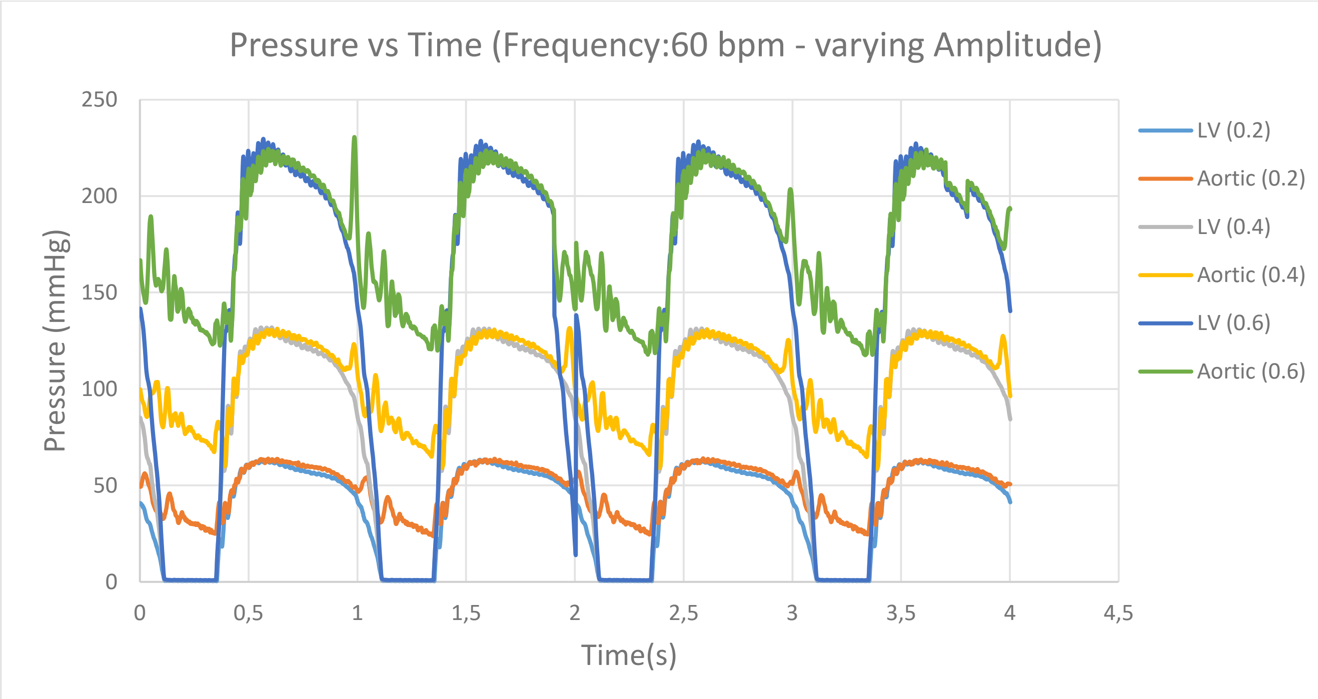


Figure 4 - 4 Aortic and Ventricular Pressure with Motor Amplitudes ranging from 0.2 to 0.6 and Frequency of 60bpm

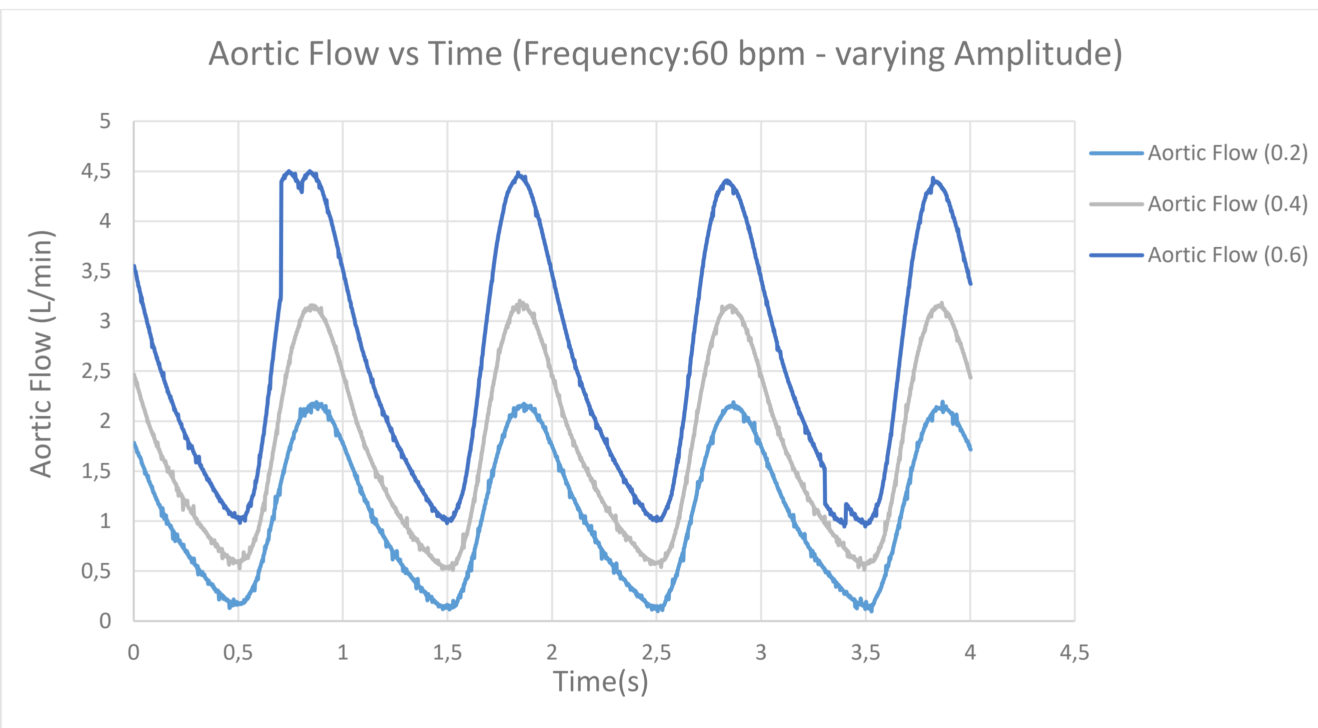


Figure 4 - 5 Aortic Flow with Motor Amplitudes ranging from 0.2 to 0.8 and Frequency of 60bpm

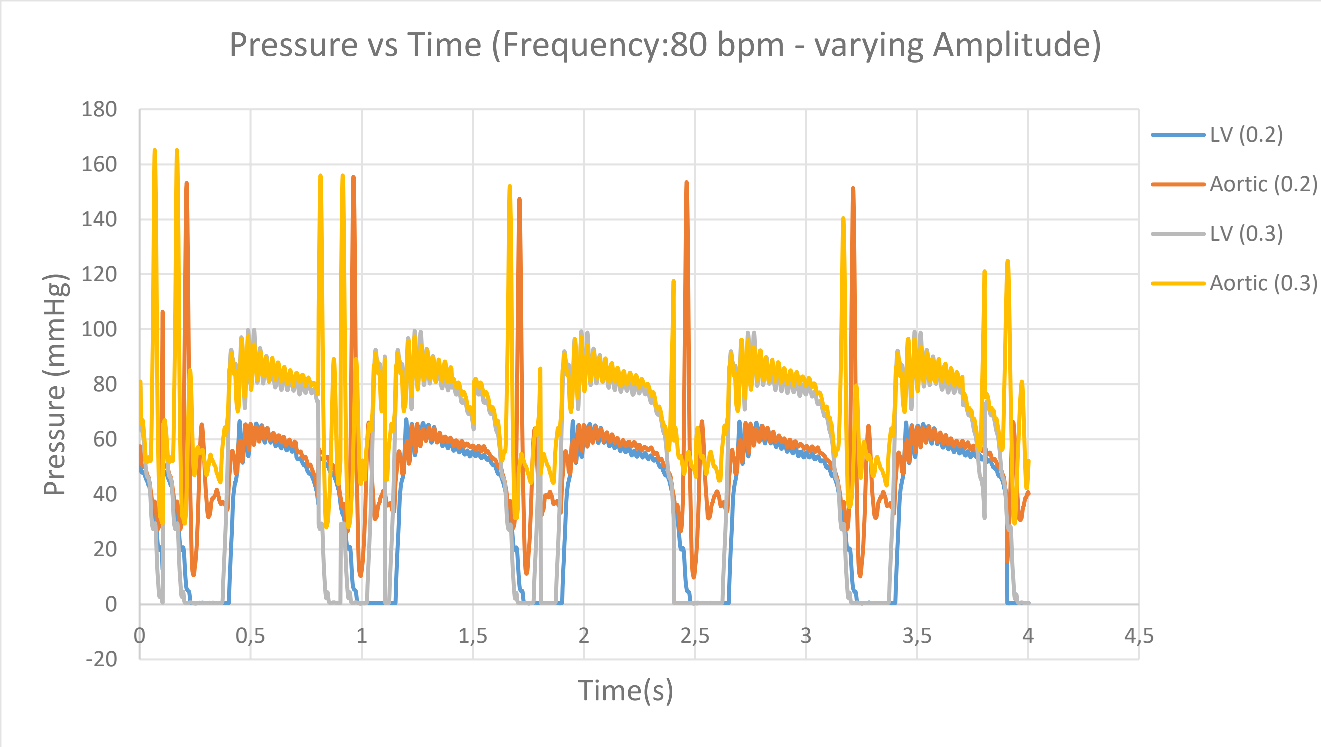


Figure 4 - 6 Aortic and Ventricular Pressure with Motor Amplitudes ranging from 0.2 to 0.8 and Frequency of 80 bpm

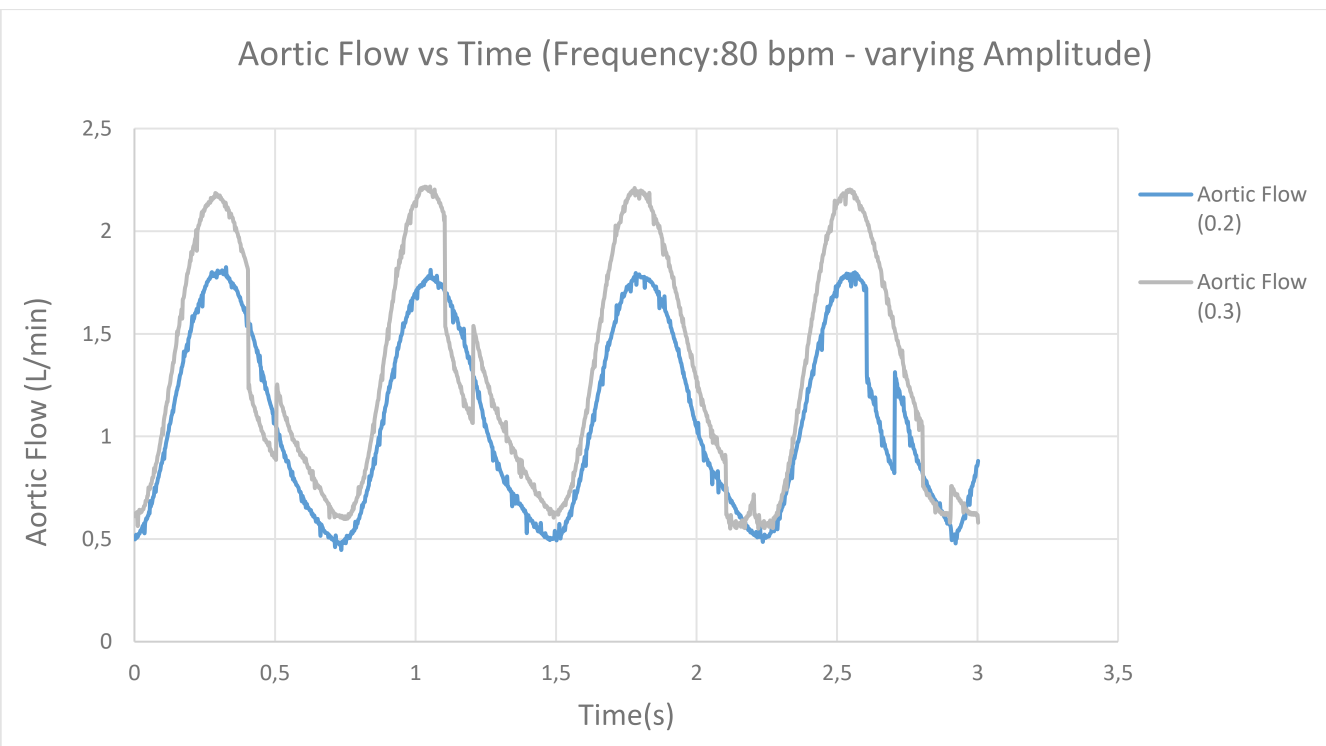


Figure 4 - 7 Aortic Flow with Motor Amplitudes ranging from 0.2 to 0.3 and Frequency of 80 bpm

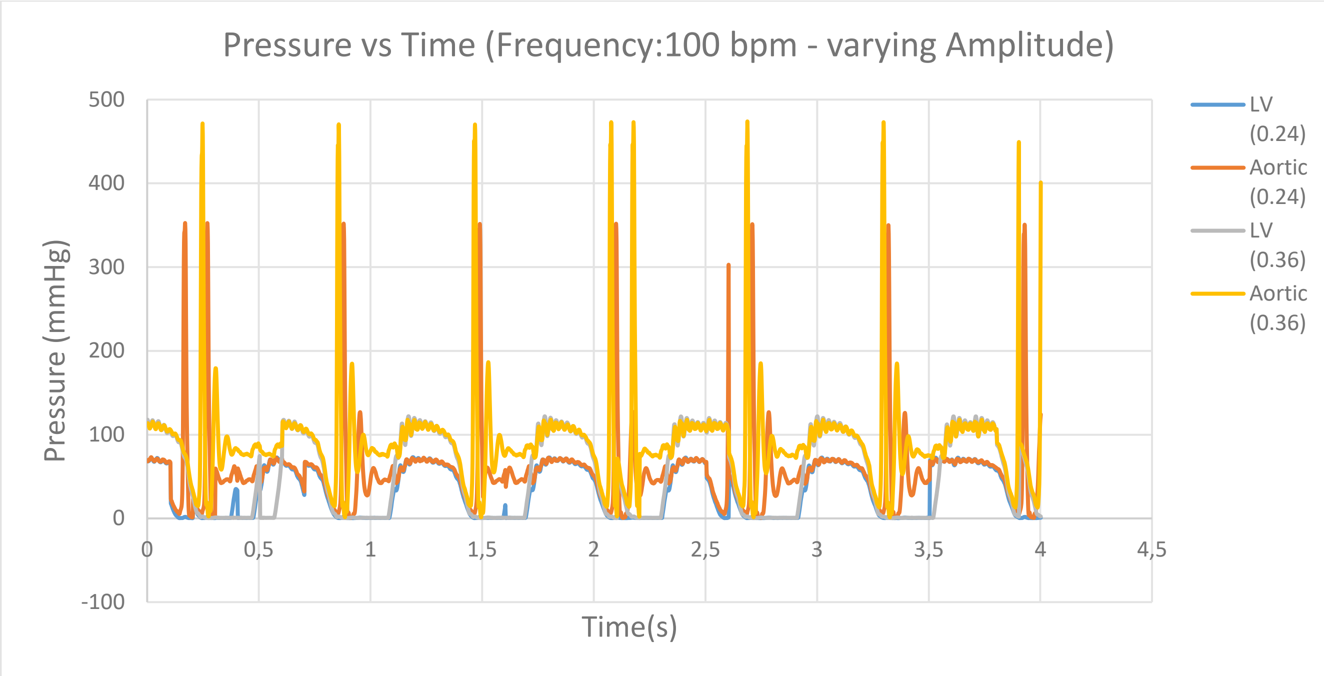


Figure 4 - 8 Aortic and Ventricular Pressure with Motor Amplitudes ranging from 0.24 to 0.36 and Frequency of 100 bpm

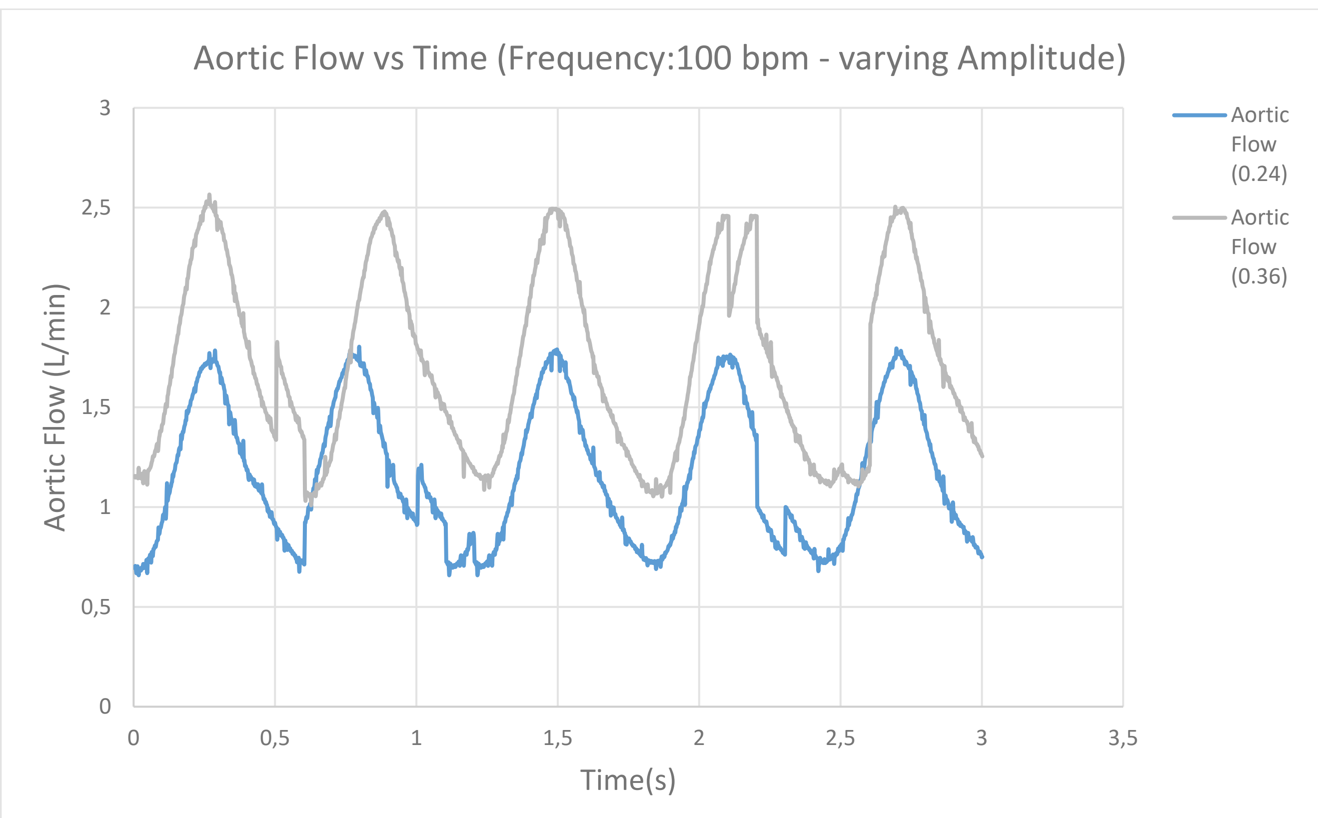


Figure 4 - 9 Aortic Flow with Motor Amplitudes ranging from 0.24 to 0.36 and Frequency of 100 bpm

4.2 Constant Amplitude- Varying Frequency

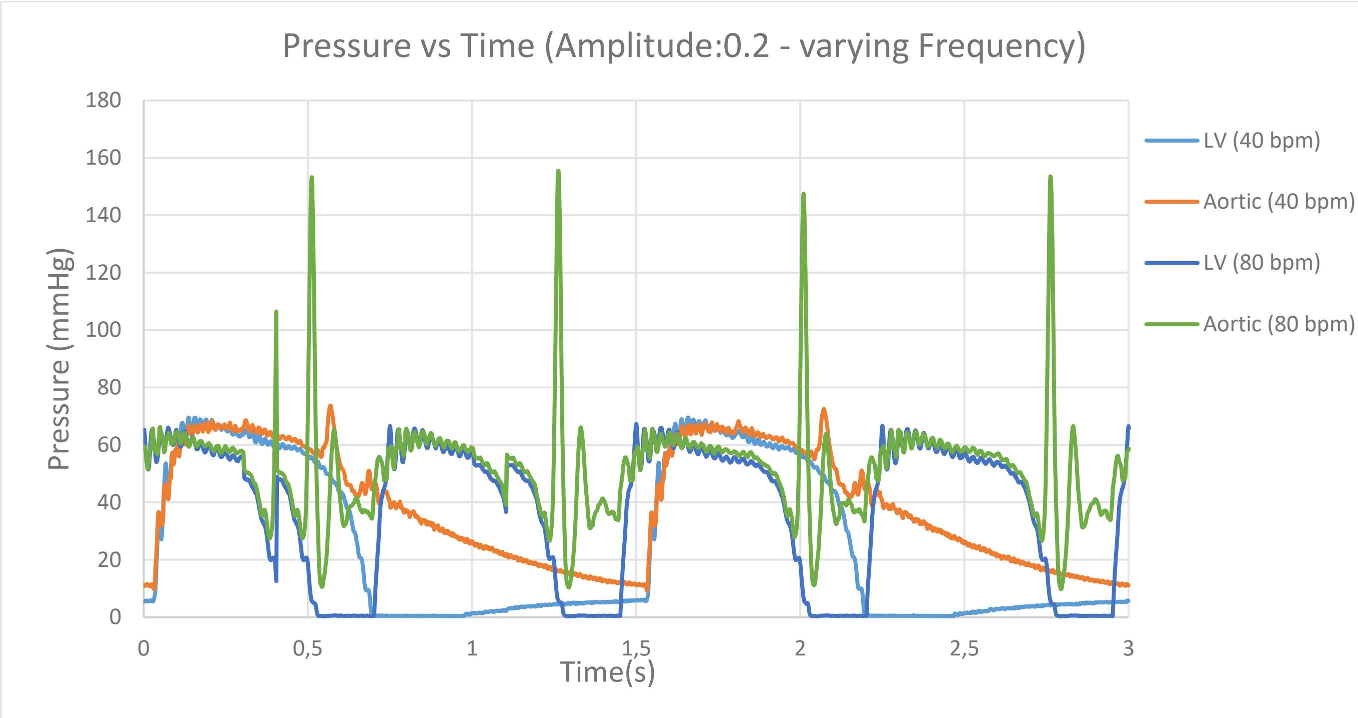


Figure 4 - 10 Aortic and Ventricular Pressure with Frequencies ranging from 40 bpm to 80 bpm and Motor Amplitude of 0.2

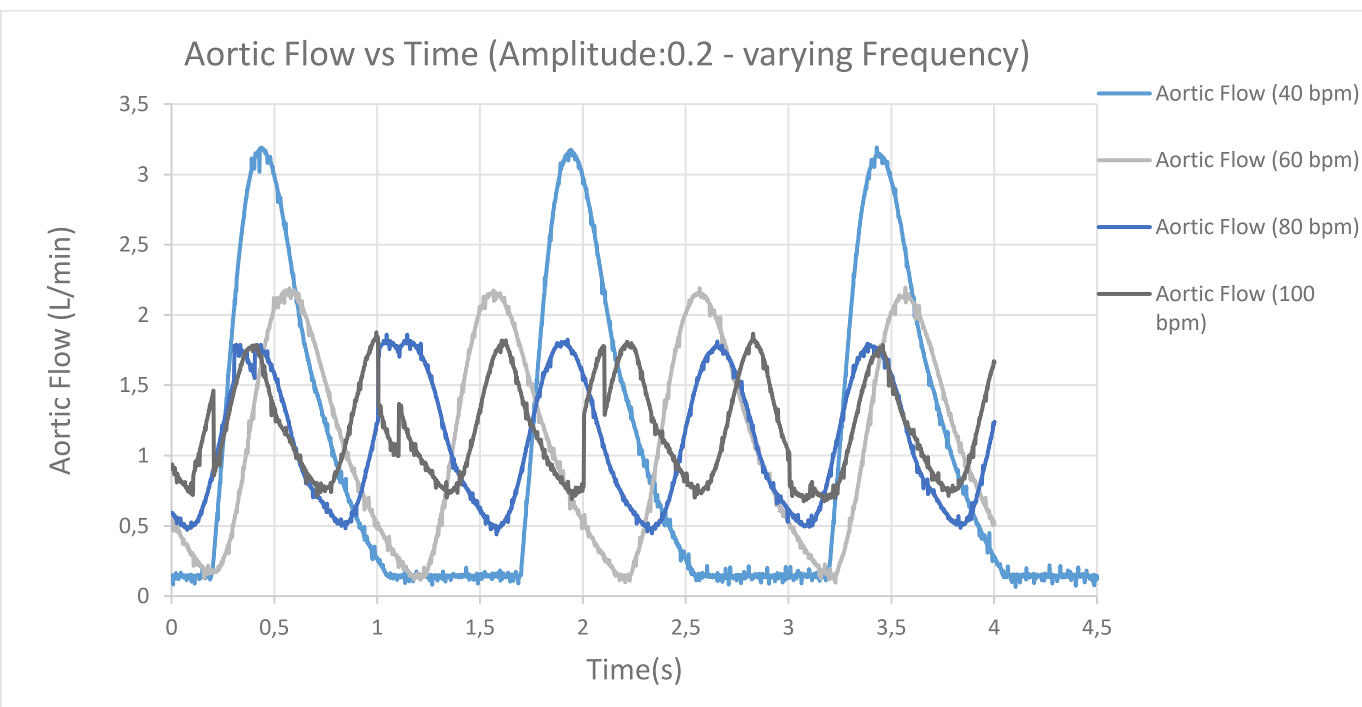


Figure 4 - 11 Aortic and Ventricular Pressure with Frequencies ranging from 40 bpm to 100 bpm and Motor Amplitude of 0.2

4.3 Varying Aortic Compliance

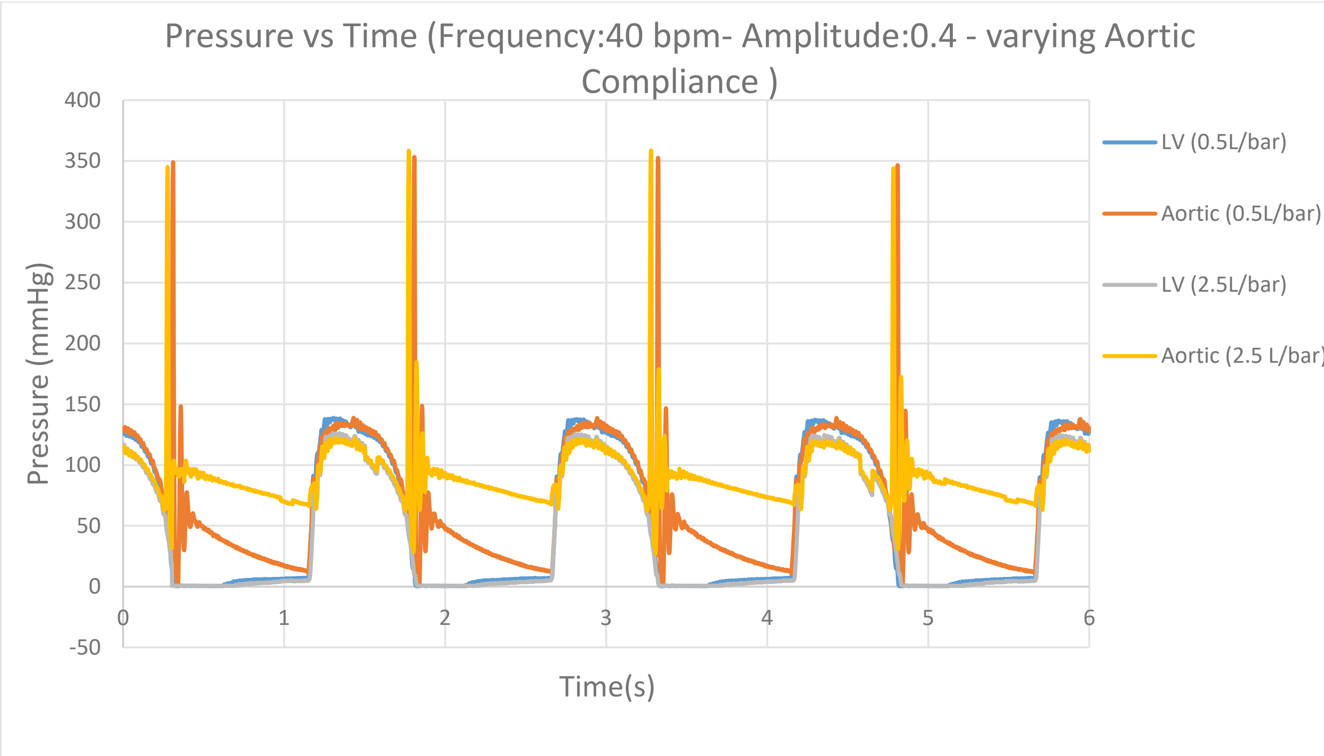


Figure 4 - 12 Aortic and Ventricular Pressure with compliances of 2.5 L/bar and 0.5 L/bar at Frequency of 40 bpm and Motor Amplitude of 0.4

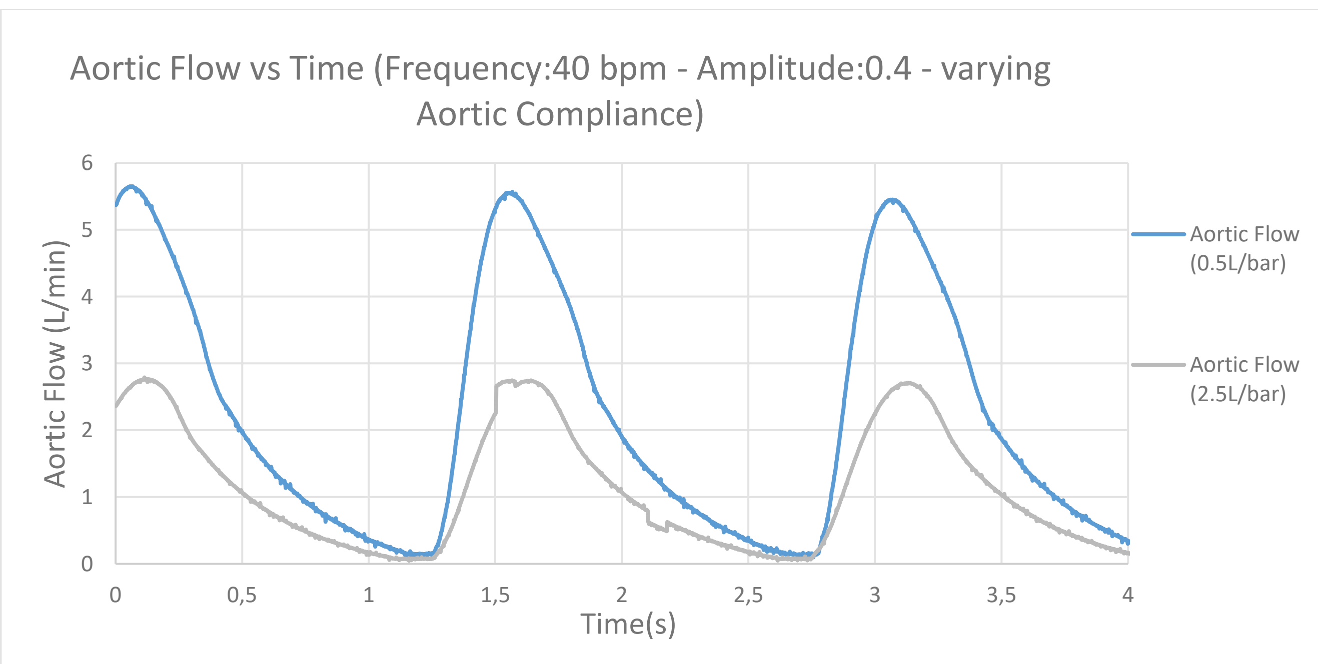


Figure 4 - 13 Aortic Flow with compliances of 2.5 L/bar and 0.5 L/bar, at Frequency of 40 bpm and Motor Amplitude of 0.4

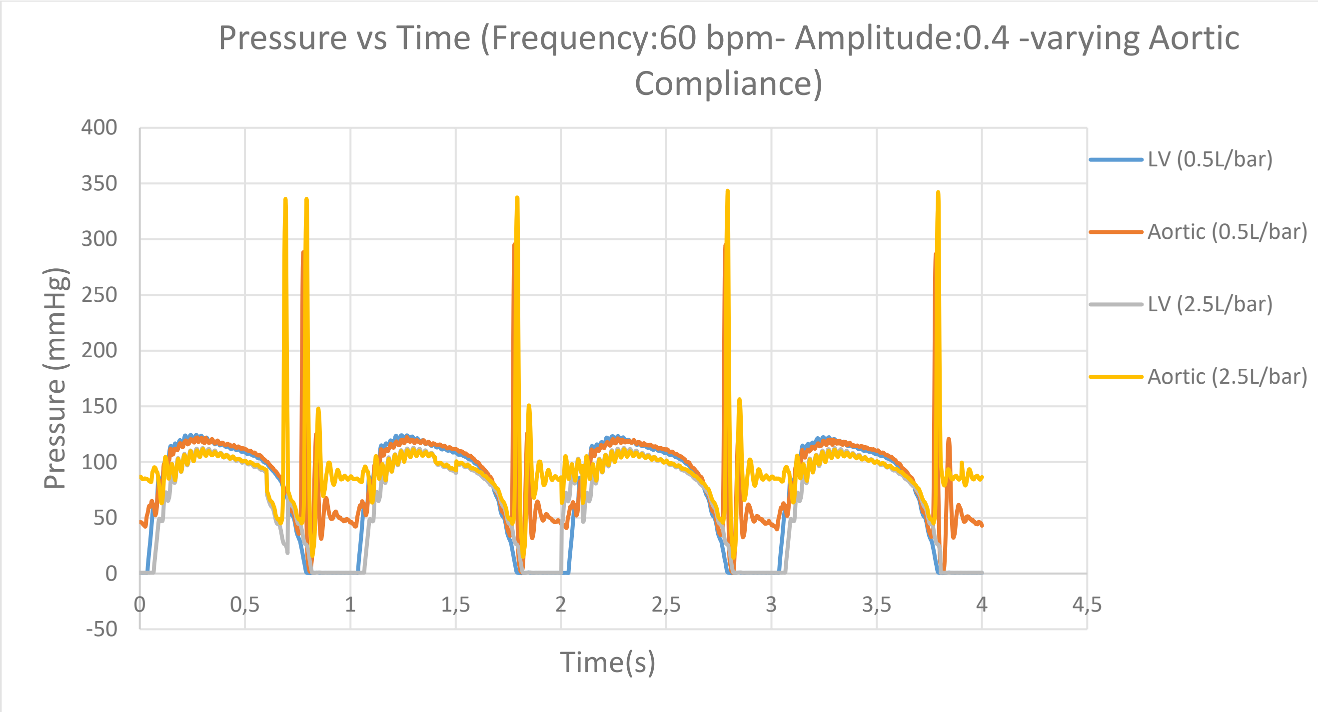


Figure 4 - 14 Aortic and Ventricular Pressure with compliances of 2.5 L/bar and 0.5 L/bar, at Frequency of 60 bpm and Motor Amplitude of 0.4

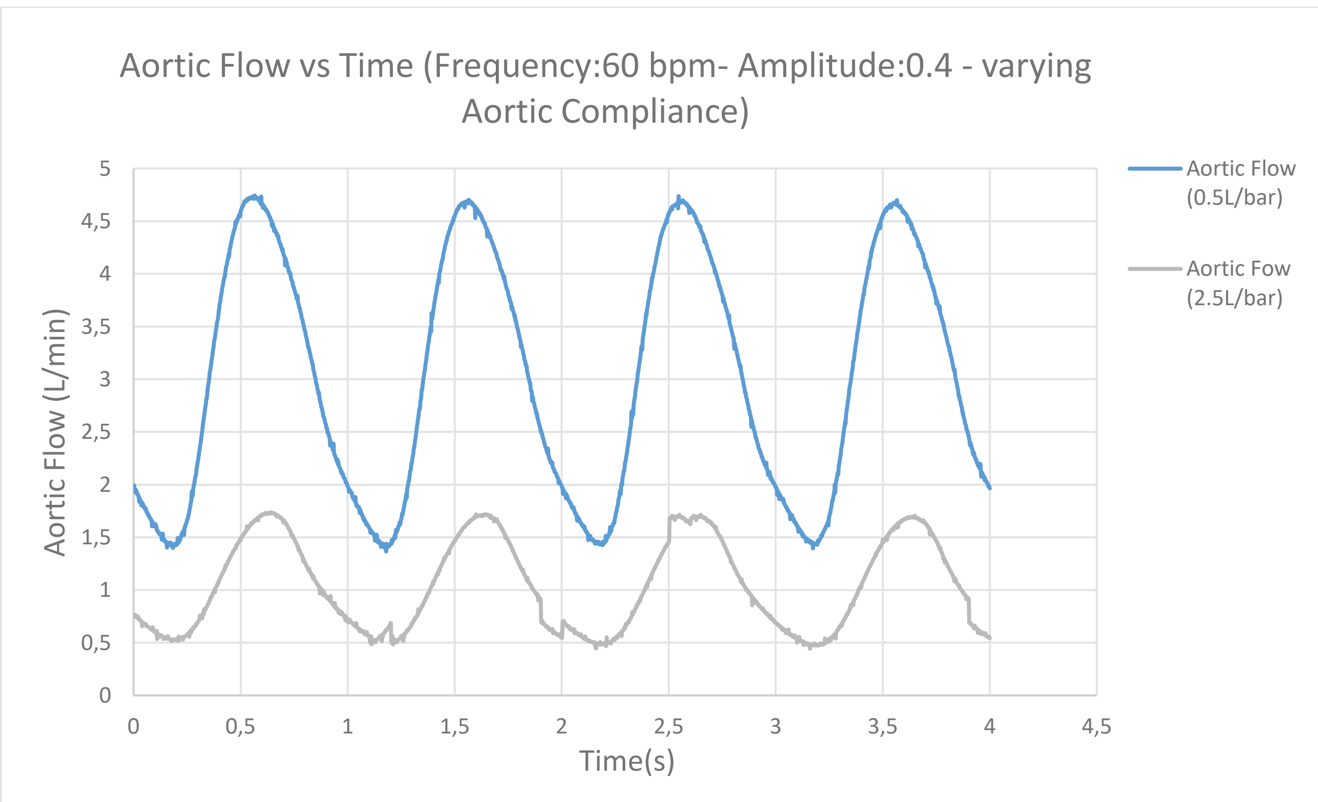


Figure 4 - 15 Aortic with compliances of 2.5 L/bar and 0.5 L/bar, at Frequency of 60 bpm and Motor Amplitude of 0.4

4.4 Varying Aortic Resistance

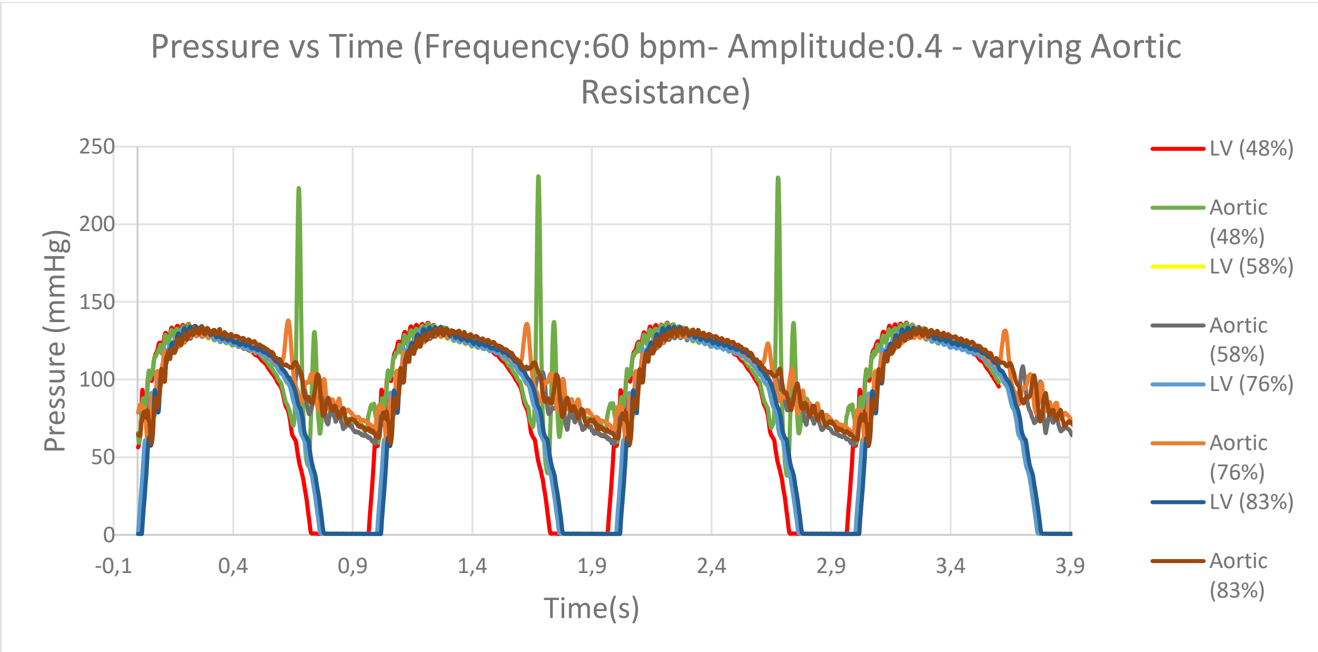


Figure 4 - 16 Aortic and Ventricular Pressure with Aortic Resistance ranging 48% to 83% non-constricted tube cross section, at Frequency of 60 bpm and Motor Amplitude of 0.4

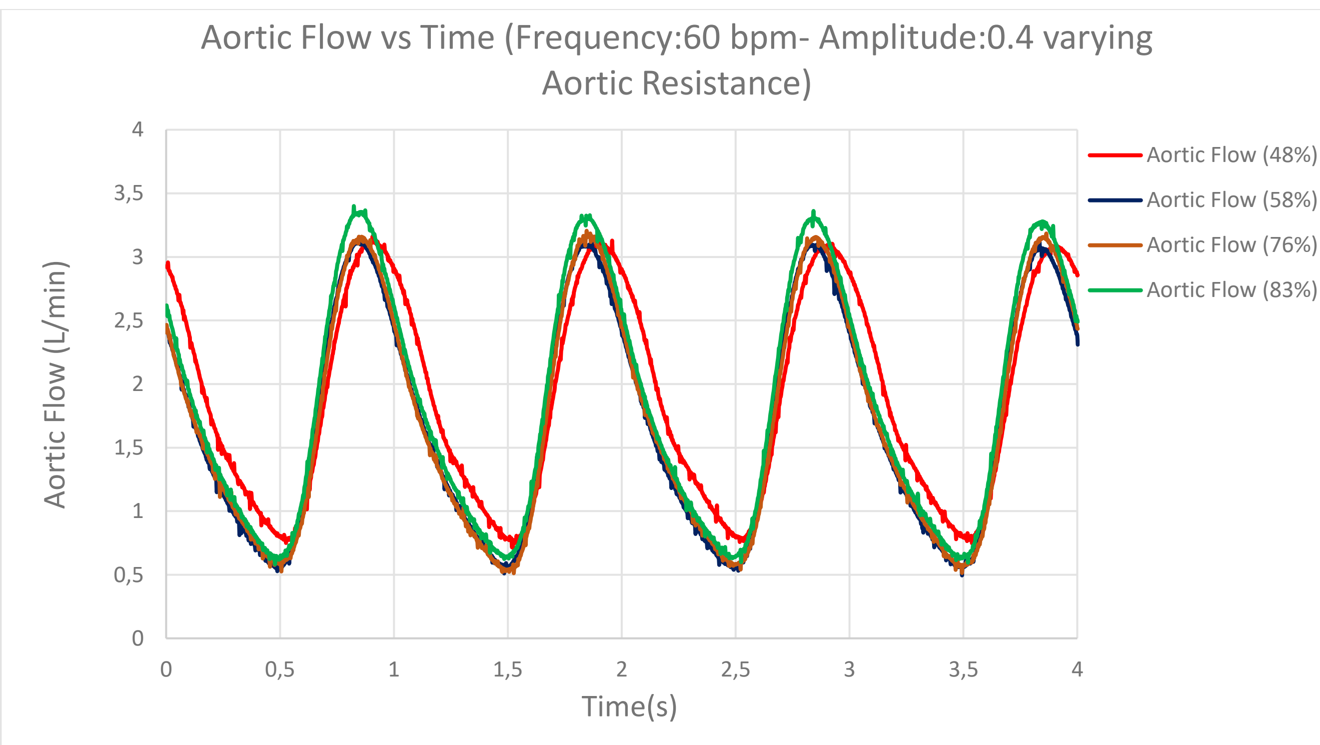


Figure 4 - 17 Aortic Flow with Aortic Resistance ranging from 48% to 83% non-constricted tube cross section, at Frequency of 60 bpm and Motor Amplitude of 0.4

4.5 Varying Peripheral Resistance

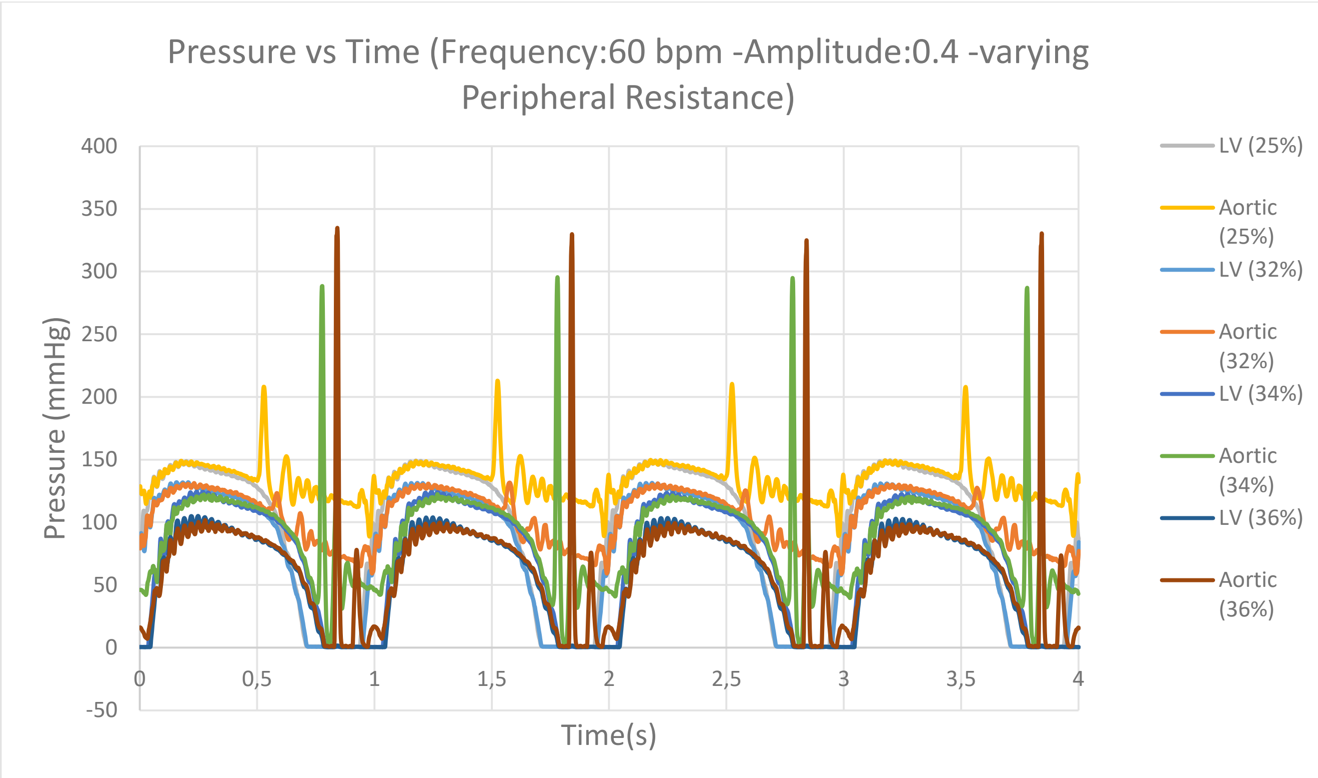


Figure 4 - 18 Aortic and Ventricular Pressure with Peripheral Resistance ranging from 25% to 36% non-constricted tube cross section, at Frequency of 60 bpm and Motor Amplitude of 0.4

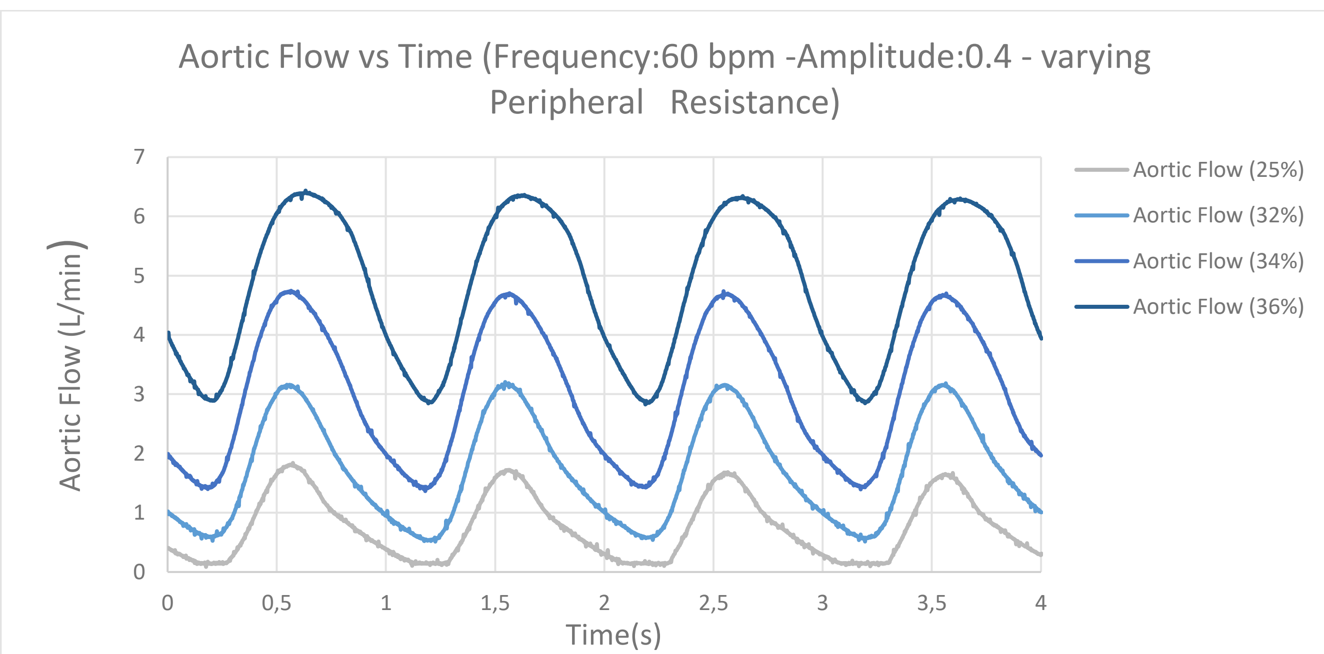


Figure 4 - 19 Aortic Flow with Aortic Resistance ranging from 25% to 36% non-constricted tube cross section, at Frequency of 60 bpm and Motor Amplitude of 0.4

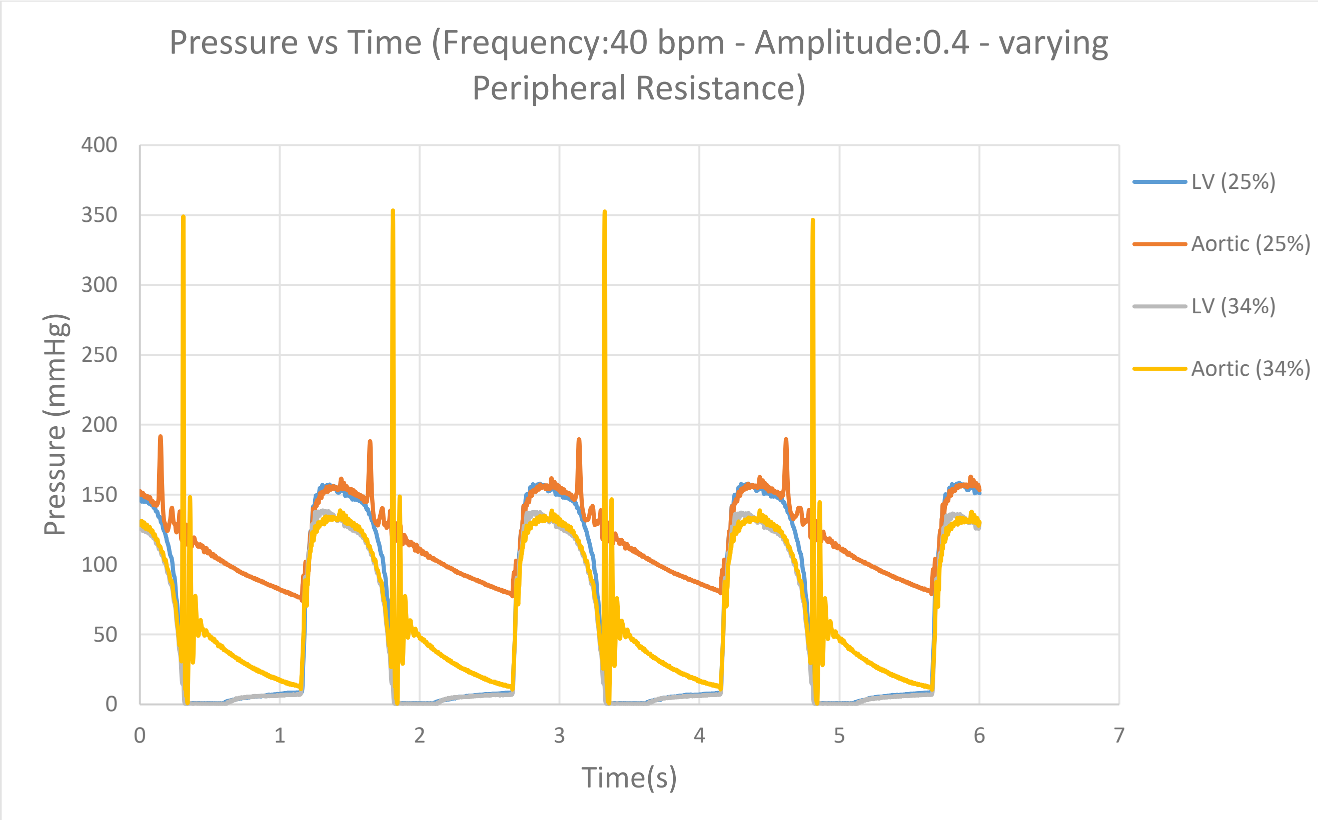


Figure 4 - 20 Aortic and Ventricular Pressure with Peripheral Resistance ranging from 25% to 34% non-constricted tube cross section, at Frequency of 40 bpm and Motor Amplitude of 0.4

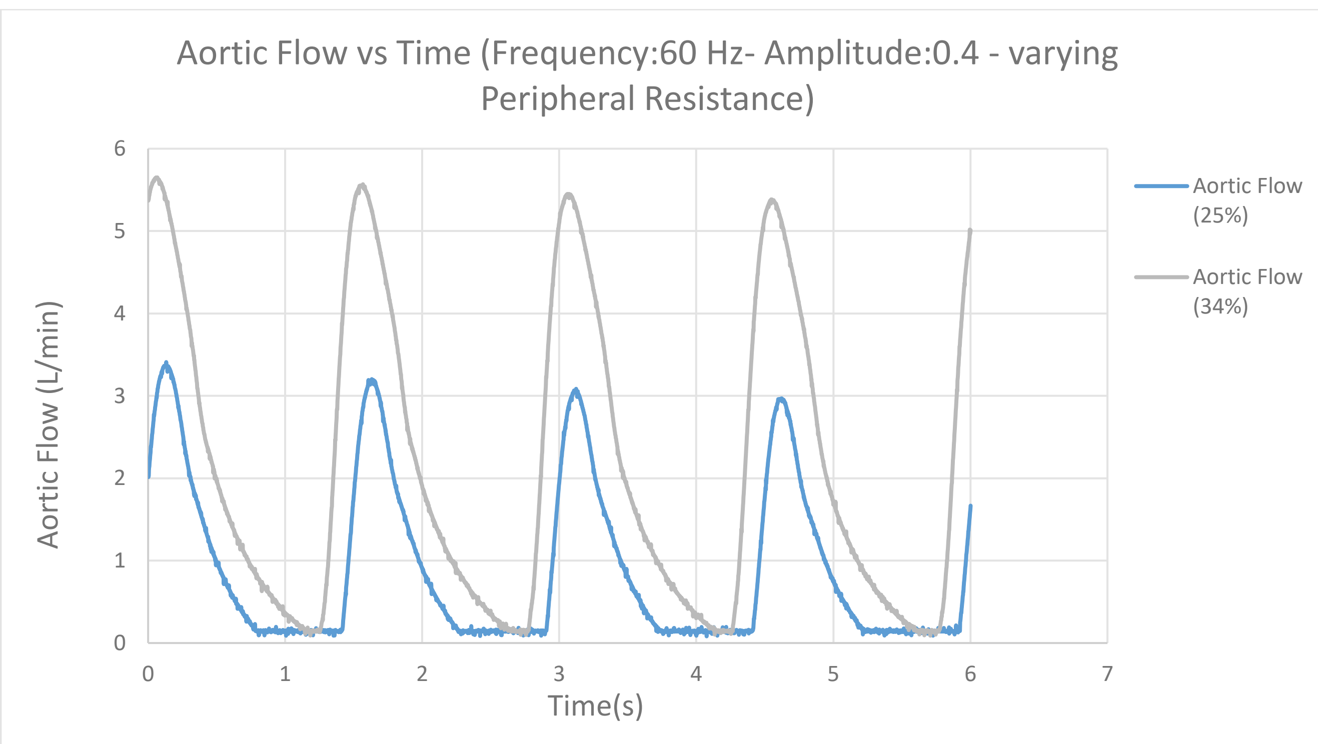


Figure 4 - 21 Aortic Flow with Peripheral Resistance ranging from 25% to 34% non-constricted tube cross section, at Frequency of 60 bpm and Motor Amplitude of 0.4

5. Discussion

5.1. Effect of Motor Amplitude on the System response

The Left Ventricular Vessel in addition to the pneumatic cylinder actuated by the motor form together the Left Ventricle of the heart which in vivo is responsible for sending blood to the systemic circulation when contracted. A contraction of higher amplitude implies a higher aortic flow if all other parameters remain constant. This behavior was expected from the system when the amplitude of the motor increases which has as an effect the decrease of the air volume present between the cylinder and the vessel and hence the increase of its pressure. This pressure increase translates into a higher pressure gradient that will result in an increase of the flow of water exiting the LV vessel. Looking at Figure 4 – 2 the aforementioned behavior is apparent; the pressure increases almost linearly with the amplitude. For example a frequency of 40 bpm and a relative amplitude of 0.2 result in peak pressures around 80 mmHg and a relative amplitude of 0.8 give peak pressures around 350 mmHg. This pattern is noticeable also at Figure 4 - 4, 4 - 6 and 4 - 8 where the influence the variations of amplitude have on higher frequencies is plotted. Figure 4 – 4 indicates the 60 bpm case and it is observed that the pressures arisen are very similar to the 40 bpm case for the equivalent relative amplitude. However, it can also be seen that there is no case for 0.8 amplitude in the Figure 4 - 4, 4 - 6 and 4 - 8. This is because as the frequency increases the speed and hence accelerations and thus momentum generated by the shaft of the electric cylinder pushing the pneumatic cylinder increases as well. This vigorous oscillating motion with high momentum shakes the whole structure and can lead to premature failure of the moving components of the set up. Hence it was decided not to test the system at very high amplitudes and frequencies for a prolonged period of time in order to prevent damages.

The pressure profile shapes of both the ventricular and aortic pressure are very similar to in vivo case and by finely tuning the amplitude, frequency and shape of motor profile we can achieve the desirable peak pressure values. One thing that is not desirable is the spikes in pressure that occur at the dicrotic notch fragment of the profile. The spikes even though they occur for several milliseconds can have values up to 4 times the value of the peak pressure as it is apparent in the 100 bpm case in Figure 4 - 8. This phenomenon is far less pronounced in bpm values of 60 or lower and almost disappears at lower amplitudes in these frequencies. It is believed to be related to a water hammer effect created by the reflection of the pressure wave causing the dicrotic notch on the aluminum holder that encloses the aortic valve. At lower amplitudes and frequencies they create a smaller impulse and hence a smaller spike peak.

Figure 4 - 3, 4 - 5, 4- 7 and 4 - 9 show how the aortic flow is affected by varying amplitude at frequencies of 40 bpm, 60 bpm, 80 bpm and 100 bpm respectively. What is noteworthy here is a mention on the shape of the aortic flow profile. Under physiological conditions between 60-80 bpm the aortic flow profile tends to look like a steep sinusoidal shaped curve that spans over 1/3 of the cycle and is around zero for the rest of the cycle. In our case, this is true only for the 40 bpm case. Additionally, this effect is more pronounced in the lower amplitudes. As the frequency and amplitude increase the aortic flow profile tends to become sinusoidal all over the cycle without getting down to zero at any point (Figure 4 - 5, Figure 4 – 7, Figure 4 - 9). This phenomenon has some potential explanations. Firstly, the amount

of time the system spends in systole is bigger than in vivo due to the fact that flow would be very low otherwise. Furthermore, the valves used might be a bit worn out due to their age and might not close flawlessly, hence water might leak out of the LV during diastole not allowing the flow to go down to zero. In any case the system manages to achieve a pulsatile flow which can be used to study the behavior of a LVAD.

By calculating the average value of the aortic flow the Cardiac Output (CO) of the heart can be found in L/min and then the Volume Stroke (VS) just by dividing the CO over the bpm value. The table below indicates the values of the CO and VS for different frequencies and amplitudes.

	Cardiac Output (L/min) / Stroke Volume (L)				
	Frequency				
Amplitude		40 bpm	60 bpm	80 bpm	100 bpm
	0.2	0.95 / 0.024	1.05 / 0.017	1.08 / 0.013	
	0.24	-	-		1.19 / 0.012
	0.3	-	-	1.32 / 0.016	
	0.36	-	-	-	1.68 / 0.017
	0.4	1.47 / 0.037	1.67 / 0.028	-	
	0.6	2.15 / 0.054	2.73 / 0.046	-	-
	0.8	2.70 / 0.067	-	-	-

Table 2 Cardiac Output and Stroke Volume over various Amplitude and Frequency settings

The table indicates that as the frequency increases the CO for the same amplitude increases and the SV decreases an observation that agrees with theory.

Under physiological conditions when the body tissues require more blood a series of events is triggered in order to increase the CO and among them the most crucial one is the increase of the heart rate (HR). However as this happens there is less time spend in diastole and hence less time for the ventricles to get filled with blood. This means that SV decreases even though the CO increases as it is also demonstrated in our system (A. Glynn, 2009).

5.2 Effect of Frequency on the System response

An attempt was made to plot the pressure and aortic flow profiles of cases with the frequency of pulse varying and all other parameters remaining the same. This is initially shown in Figure 4 - 10 where the frequencies of 40 bpm and 80 bpm have been plotted against each other. It is displayed that as the frequency increases the time of the cycle spent in diastole decreases comparably slightly more than the time spent in systole. This is confirmed by theory where it is stated that the systole/diastole ratio increases as the bpm increases (Occhetta, 2010).

Furthermore, it is also observed that as the frequency increases the spikes that occur in the dicrotic notch region have considerably higher amplitude. The main explanation could be the more severe water hammers taking place when the aortic valve closes in higher frequencies where the speed of the water is also higher.

Figure 4 - 12 indicates the aortic flow profile for four test runs at different frequencies at the same amplitude. It is apparent that there is a constant decrease in the peak aortic flow value per minute as the frequency increases even though the cardiac output increases with increasing frequency as it was discussed in the previous sub chapter. This decrease in peak aortic flow becomes less pronounced with increasing frequency. It is seen that the maximum peak amplitude is almost identical for the 80 bpm and 100 bpm cases.

5.3 Effect of Aortic Compliance on the System response

As mentioned in the theoretical background section compliance is the ability of a hollow organ to distend and increase its volume with increasing transmural pressure. It is a fundamental property of the arteries and veins but has a higher significance on the former ones. Figures 4-12 and 4-13, 4-14 and 4-15 indicate the pressure and aortic flow profiles at frequencies of 40 and 60 bpm respectively. Looking at Figures 4-12 and 4-13 it is apparent that the pressure profile is minimally affected by the variation of the aortic compliance. The pressure amplitude of the lower compliance case (0.5L) is slightly higher as expected since there is less volume accommodation during systole meaning that the pressure will increase more. Another difference is apparent on the time the dicrotic notch occurs. In the larger compliance case (2.5L) it occurs earlier on the cycle and has a higher amplitude. This might be explained by the fact that the magnitude of the reflective wave is lower in the lower compliance case since a higher percentage of the flow propagates forward as seen in Figures 4-13 and 4-15. As mentioned the momentum given by the pneumatic cylinder is the same in both testing scenarios meaning that the force of contraction is equal. However, it is pretty obvious that compliance has a huge effect on the magnitude of the flow. In the case were the residual air in the aortic vessel drops to 0.5 L the flow increases 2fold. This is validated by theory since the majority of the momentum of the water is propagated forward instead of dissipating radially when the compliance value is very high and the arterial system conduits are extended significantly.

5.4 Effect of Aortic Resistance on the System response

Aortic Resistance has a minimal effect on the system over a big range of values as seen in Figures 4-16 and 4-17. Strangling the piece of tube between the left ventricle and the aortic compliance slightly affects the pressure and aortic flow profiles. However, it is observed that the dicrotic notch region spikes tend to increase with increasing resistance.

5.5 Effect of Peripheral Resistance on the System response

As showcased in the Methodology section the peripheral resistance of the Mock Circulation greatly affects the profile of the flow. Small deviations can have massive implications on the shape and magnitude of the flow parameters. Figures 4 -18, 4-19 and Figures 4 -20, 4-21 display test runs done in 60 rpm and 40 rpm respectively at a constant amplitude with the resistance changing slightly with each different test run. The percentage values indicate the ratio between the constricted tube area over the tube area when no constriction has been applied. Hence the lesser the percentage, the lesser the area and therefore the larger the resistance applied to the flow. Looking at Figure 4-18 one can observe that as the resistance is increasing the peak amplitude of the pressure curve increases accordingly. Moreover, there is a tendency for the dicrotic notch region peaks to decrease in amplitude as resistance increases maybe because there is more damping. Another thing that is noteworthy is the fact that the dicrotic notch is shifting to the right (towards diastole´s zero ventricular pressure section) as the resistance decreases. Plus, the average (excluding the highest peak) amplitude of the dicrotic notch tends towards a zero value as the resistance increases.

Lastly when it comes to aortic flow it increases significantly with decreasing resistance. On the other hand, this comes with a drawback, that being that the profile of the flow turns sinusoidal and doesn’t stay to zero at all as it does in vivo. This phenomenon is even more noticeable with increasing frequency.

6. Conclusion and Future Work

Overall it can be stated that the system can simulate successfully the flow and pressure conditions existing in the high pressure side of the cardiovascular system over a small range of frequencies and amplitudes. It works well in frequencies of 60 bpm and lower and at a relative amplitude ranging from 0.2 to 0.6. When the frequency and amplitude increase the pressure magnitude gets way higher than the physiological case when the peripheral resistance is at the levels required to achieve the profiles experienced in vivo. That means that a larger pneumatic cylinder that could push more air though the system would not solve the problem. According to the author there are 3 main areas that attention should be given in order to improve the behavior of the system. Firstly, the air existing between the lid of the aortic compliance vessel and the surface of the water in the vessel should be minimized to decrease further the value of the aortic compliance. Observing the results it was obvious that aortic compliance was the parameter responsible for increasing the aortic flow the most without significantly increasing the pressure values something that is required by the system. Secondly, another thing that could potentially improve the behavior of the system is the replacement of the aortic valve with either a new medical valve or a mechanical check valve with a very low cracking pressure. During operation the piston of the pneumatic cylinder is rapidly drawn backwards during the isovolumetric phase of the cardiac cycle resulting to a significant amount of water being drawn from the aorta into the left ventricle. This obviously has as an effect the reduction of flow of water going forward and hence decreasing the average value of the aortic flow which is already lower than the anticipated value of 5 L/min. Thirdly what was also observed is the fact that even though the pneumatic cylinder can displace up to 2L of air per stroke it is still not enough to get an adequate flow. This is due to the fact that the plates consisting the peripheral resistance have to be really close to each other in order to offer an area that will reflect a large part of the forward moving pressure wave and create the effect of the dicrotic notch as measured in the aorta by the aortic pressure sensor. In vivo the dicrotic notch is realized by the reflection of the forward moving wave in the bifurcations of the arterial tree. Since in our system there is one single tube connecting all the elements of the system there are no bifurcations meaning that the resistive elements are the only areas where the reflection can occur. But this extremely strangulation of the tube adversely affects the flow. What is recommended in a future design is to modify the tubing in the exit of the aortic compliance so that there is at least one or multiple bifurcations that could create this reflecting effect. It is believed that this alteration might improve the behavior of the system substantially.

Furthermore, what also plays a factor to better simulate the behavior of the system is to do more testing with a liquid that better resembles the viscosity of the blood than water. A mixture of 40% glycerol and 60% water gives a viscosity of 4 cP which well into the 3.5-5.5 cP range that is considered normal (Elie Nader, 2019). Some early tests that were done using a water glycerol mixture showed a smoother signal with less noise in the dicrotic notch region but that coming at the cost of a slightly decreased overall aortic flow.

Moreover, there is the thought to replace the aluminum adapter embedding the aortic valve with an adapter made of a softer material such as Plexiglas or PVC, the reason being that in this way there will be more dampening of the reflected water wave coming from the peripheral resistance. This will decrease the amplitude of the pressure peaks observed in the aortic pressure wave signal and hence improve the overall quality of the simulation.

What is also suggested for future work is to create testing regimes that will simulate pathological conditions such as cardiac arrhythmias. A LVAD is implemented to treat people with severe heart failure meaning that the pressure and flow profiles of the cardiovascular system differ from these existing in a healthy individual. Therefore, the need to test the LVAD in various pathological conditions is of extreme importance.

Additional an electrical enclosure for the housing controls of the system consisting of the power supplies, electronic circuitry, the cRIO controller and the analog and digital I/O modules should be employed. That way it can be protected and be portable but on the same time keep its flexibility in case more sensors or modules need to be added on the system in the future.

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