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Modeling and flow control for a left ventricular assist device

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Abstract

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List of Symbols

Abbreviations

A-V valve	Atrioventricular valve
BTB	Bridging to decision
BTR	Bridging to recovery
BTT	Bridging to transplantation
BVAD	Biventricular Assist Device
CO	Cardiac Output
CVDs	Cardiovascular Diseases
CVS	Cardiovascular System
DT	Destination therapy
EDV	End-diastolic volume
ESV	End-systolic volume
HR	Heart rate
HTx	Heart transplantation
IMACS	International Mechanically Assisted Circulatory Support
INTERMACS	Interagency Registry for Mechanically Assisted Circulatory Support
LVAD	Left Ventricular Assist Device
MCS	Mechanical Circulatory Support
RWTH Aachen	Rheinisch-Westfälische Technische Hochschule Aachen
SL valve	Semilunar valve
SV	Stroke Volume
VADs	Ventricular Assist Devices
WHO	World Health Organization

1 Introduction

1.1 Motivation and goal

1.2 Thesis structure

2 Medical Fundamentals

Comprehension of the physiology of the human heart and the cardiovascular system is an important prerequisite to the work addressed in this thesis. Therefore, the basics of these topics will be explained in this chapter.

2.1 Cardiovascular System

The fundamental task of the cardiovascular system is to supply all organs with blood. The human cardiovascular system is divided into two components, the systemic circulation and the pulmonary circulation. As shown in Figure 2.1, which represents the percentage distribution of the blood over the circulatory system, the systemic circulation is supplying blood flow to all tissues and organs apart from the lungs. [Hal16]

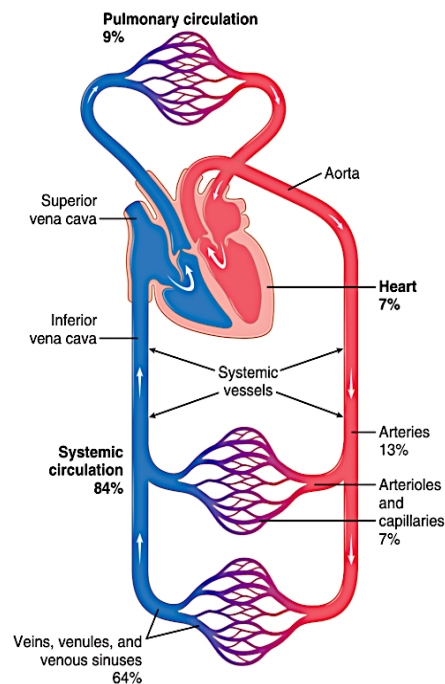


Figure 2.1: Blood distribution in the circulatory system [Hal16].

The center of the cardiovascular system is the heart. The heart itself consists of two mechanical pumps, which are functionally connected in series but are united in one organ. It is separated into two sides, which themselves are divided into an atrium and

a ventricle each. The atria act as weak primer pumps needed to provide blood flow to the ventricles.[SLH11] Both, the atria and the ventricles are surrounded by the myocardium, which acts as the working muscle of the heart. Through the contraction of the myocardium, blood is pumped into the circulatory system.[SK07] The left ventricle is pumping oxygenated blood through the aorta into the systemic circulation. There, the oxygen stored in the blood is delivered to the organs. The blood, now low in oxygen, is then led into the right atrium through the inferior and superior vena cava. From the right atrium, the deoxygenated blood then enters the right ventricle. Afterwards it is directed into the pulmonary circulation via the pulmonary artery. After the blood is oxygenated in the lungs, it is returned to the left atrium through the pulmonary vein.[SLH11] In addition to the atria and the ventricles each side of the heart has an atrioventricular (A-V) valve, as well as a semilunar (SL) valve. The A-V valve of the left heart is called the mitral valve, the one of the right heart is referred to as the tricuspid valve. The aortic valve and pulmonary valve are the SL valves of the left and right heart, respectively. The valves determine the direction of blood flow and thus prevent backflow. [SK07] Figure 2.2 provides a graphic overview of the anatomy of the heart and the course of blood flow through the heart.

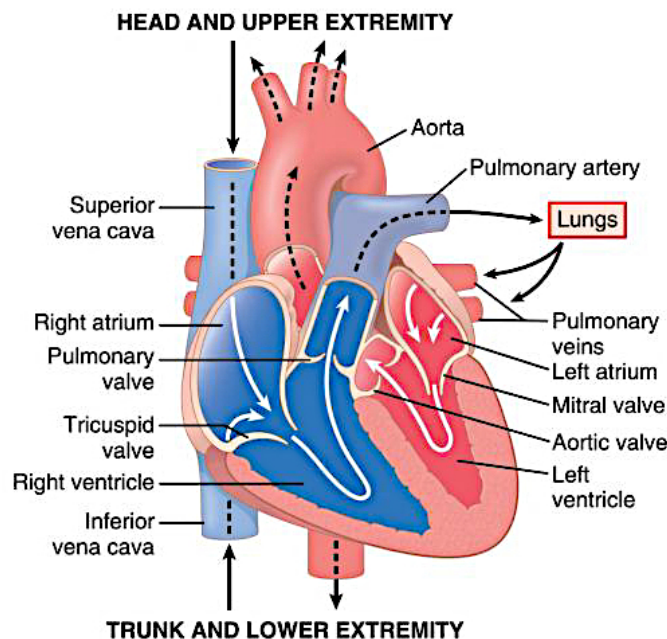


Figure 2.2: Anatomy of the human heart [Hal16].

The amount of blood pumped through the two sides of the heart is equal at all times. This value is called cardiac output (CO). It is calculated by multiplying the heart rate (HR) and the stroke volume (SV). For an average adult at rest, with a heart

rate of approximately 70min^{-1} and a stroke volume of 70ml , this leads to

$$CO = HR \times SV = 70\text{min}^{-1} \times 70\text{ml} = 5\frac{\text{l}}{\text{min}} \quad (2.1)$$

In case of maximum physical load, for a stroke volume of 110ml and a heart rate of 190min^{-1} , the cardiac output can increase to up to $20\frac{\text{l}}{\text{min}}$. [SLH11]

The cardiac cycle describes the events that occur during the time-span of one heart-beat. It is triggered by an electrochemical action potential originating from the sinus node. The cycle is divided into four phases. Figure 2.3 illustrates these action phases and events of the cardiac cycle for the left ventricle. During the period of

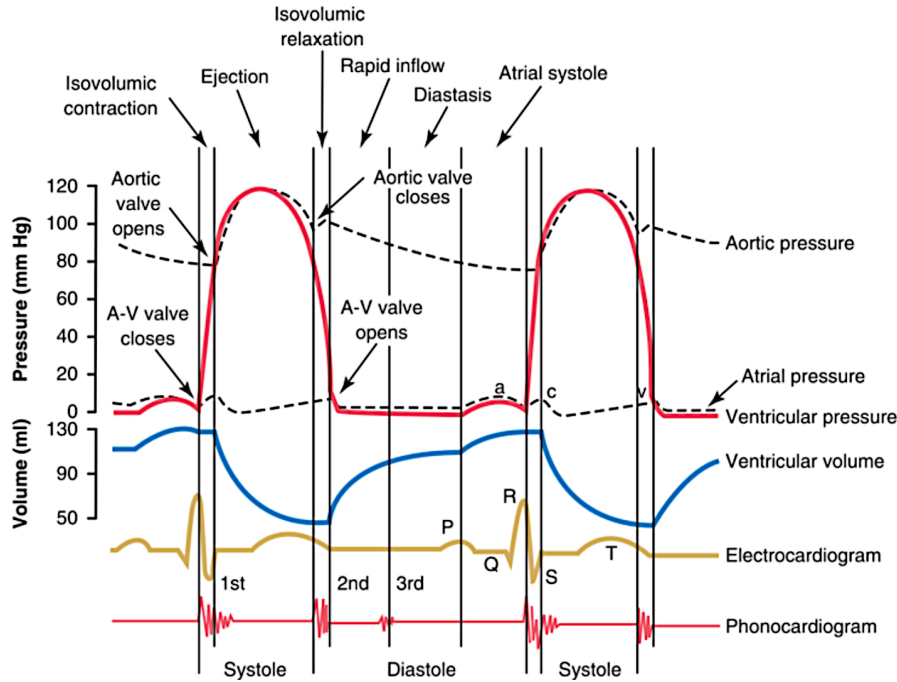


Figure 2.3: Action phases of the cardiac cycle based on the example of the left ventricle [Hal16].

isovolumic contraction, the ventricular pressure increases. For the left ventricle, the pressure increases from about 4-6 mmHg to 80 mmHg. The pressure values for the right ventricle are much lower. This increase is happening as a direct result of the ventricular contraction. The A-V valves, as well as the SL valves, are closed during this process. This leads to a constant blood volume in the ventricles. As soon as the ventricular pressure exceeds the arterial pressure the pulmonary and aortic valves open and blood can flow into the aorta and the pulmonary artery. This phase is called ejection phase, as the blood is ejected into the circulatory system. The period

of isovolumic contraction in combination with the ejection phase describes ventricular systole.[SLH11] During the systole the blood volume in the ventricle decreases by 55-60%, resulting in an end-systolic volume (ESV) of about 40-50 ml [Hal16]. Due to the contraction of the myocardium, the ventricular pressure keeps increasing for a while before decreasing again as the relaxation of the myocardium sets in. As soon as the outflow of the blood ends, the semilunar valves close, initiating the period of isovolumic relaxation. During this period pressure in the ventricles is decreasing, while the blood volume is constant. When the pressure in the atrium exceeds the ventricular pressure, the A-V valves open. This leads to blood flowing into the ventricles until the pressure level in the atria and the ventricles is equalized.[SLH11] This phase is referred to as the period of rapid filling of the ventricles. Combined with the isovolumic relaxation it represents the diastole. The end-diastolic volume (EDV) is about 110-120 ml.[Hal16] While, at rest, the diastole lasts about twice as long as the systole, above a heart rate of 150min^{-1} , the two phases are about equal [SLH11].

The pumping mechanism of the left ventricle can be illustrated well using a pressure-volume diagram (P-V diagram). For the construction of the P-V diagram first the relationship between the left ventricular volume and the ventricular pressure during diastole and systole, as displayed in Figure 2.4a, has to be discussed. The blue

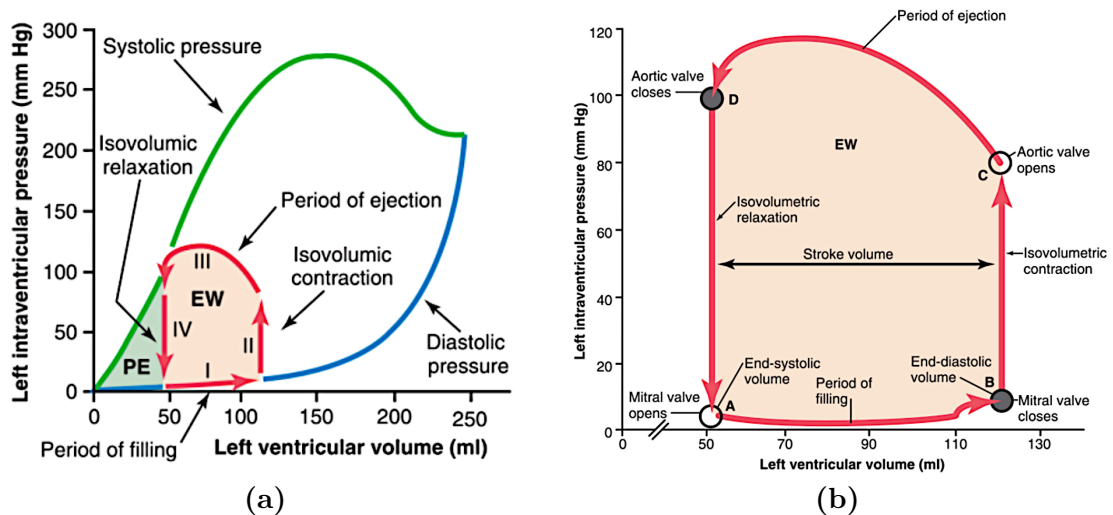


Figure 2.4: (a)Working diagram of the left ventricle with the P-V diagram. (b) Close-up P-V diagram. [Hal16]

curve representing the *diastolic pressure* is calculated by gradually filling the heart with higher blood volumes and then measuring the diastolic pressure just before ventricular contraction occurs. It is describing the heart's mechanical properties

when the myocardium is in a relaxed state. The green curve in Figure 2.4a, named *systolic pressure*, is plotted by measuring the systolic pressure over varying filling volumes for constant ventricle volumes. The red lines in Figure 2.4a and Figure 2.4b indicate the cardiac cycle and its four action phases, as described above. The line between points A and B in Figure 2.4b depicts the period of rapid filling. The isovolumic contraction is represented through line II in Figure 2.4a, respectively between points B and C in Figure 2.4b. The ejection phase is represented through III in Figure 2.4a and the line referred to as IV represents the period of isovolumic relaxation. The area of the work diagram, marked with EW in Figure 2.4 is a measure of the work done by the heart. Knowledge of the P-V diagram is an important prerequisite in understanding myocardial diseases, such as heart failure. [SLH11]

2.2 Heart failure

The World Health Organization (WHO) names cardiovascular diseases (CVDs) as the global number one cause of death. In 2016 about 17.9 million people died from CVDs, which represent 31% of all global death that year.[Wor20]

In the case of heart failure, the heart is unable to provide the required amount of blood flow to the cardiovascular system in order to supply all organs and tissue with oxygen. Heart failure does not directly represent a disease but rather a clinical syndrome. Nevertheless, the symptoms of different forms of heart failure are very similar and eventually manifest themselves in a decreased cardiac output. One acute consequence of heart failure, for example, is the feeling of shortness of breath. In the long term, however, severe heart failure can also lead to muscle weakness and a lack of concentration.

According to [SLH11], heart failure can be attributed to either systolic dysfunction or diastolic dysfunction. Systolic dysfunction can manifest itself in several ways. One is a reduced contractility and stroke volume of the heart. Causes may be, for example, a coronary artery disease that limits oxygen supply or a preceding myocardial infarction. Secondly, there may be increased pumping resistance due to an outflow obstruction. This can be the result of arterial hypertension, among other things. Furthermore, cardiac arrhythmias or a heart attack can lead to systolic dysfunction. Figure 2.5a displays the variation of the P-V diagram between a normal functioning heart (dotted line) and one impaired by heart failure with a systolic dysfunction (solid line). In diastolic functional impairment, the dysfunction is evident in the course of the filling phase. This can be triggered, among other things, as a result of reduced compliance of the myocardium due to hypertrophy or fibrosis. The change in the P-V diagram for diastolic heart failure is illustrated in Figure 2.5b.

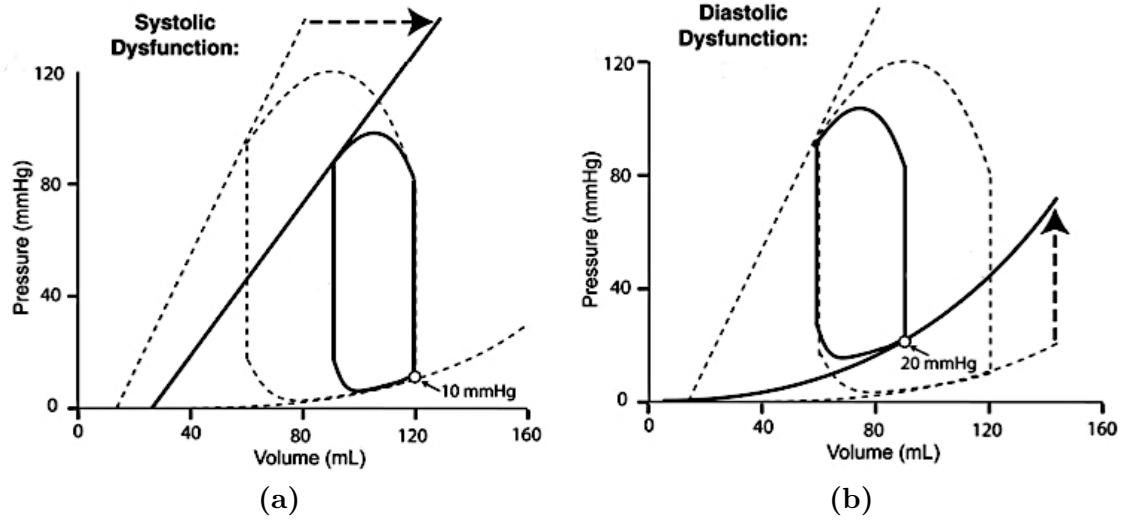


Figure 2.5: P-V diagram for heart failure in cases of (a) a systolic dysfunction and (b) a diastolic dysfunction according to [KR15].

For the treatment of heart failure, drug therapy using beta-blockers is initially targeted in most cases. However, if this is not successful, the use of ventricular assist devices can be a useful alternative in order to relieve the heart and provide sufficient blood flow. [SLH11]

2.3 Ventricular Assist Devices

Despite the fact that heart transplantation (HTx) still is the gold standard for treatment of patients with terminal heart failure [Sch10] ventricular assist devices (VADs), as a kind of mechanical circulatory support (MCS) technology, are becoming more and more important in treating patients with CVDs. There are two reasons for this. On the one hand, CVDs are gaining in importance due to demographic change. On the other hand, there is an increasing shortage of donor organs. [DMH19]

2.3.1 Therapeutic objective

Traditionally the therapeutic goals of VAD treatment can be divided into three categories: *bridging to transplantation* (BTT), *bridging to recovery* (BTR) and *destination therapy* (DT). However in some cases also the classification into *bridging to*

INTERMACS Score	NYHA	Patient condition	Survival time
1	IV	critical cardiogenic shock	hours
2	IV	increasing catecholamine demand	days
3	IV	stable under inotropics	a week
4	IV	frequent decompensation	weeks-month
5	IV	rest discomfort/ not resilient	weeks-month
6	IV	rest discomfort/ merely resilient	month
7	IIIb	merely resilient	one year survival rate: 50-70%

Table 2.1: Relation between INTERMACS Score, NYHA-classification, patient condition and approximate survival time based on [Eif18]

decision (BTD) and *bridging to transplantability* are mentioned as well. The decision for one of these goals is based on the type of CVD and the condition the patient is in, when receiving VAD assistance.[KSS⁺11] An overview on the relation between the INTERMACS Score, the New York Heart Association(NYHA)-classification and the patient’s condition is presented in Table 2.1. The INTERMACS Score, which is based on data from patients which have received VAD treatment, links the need for a VAD and the appropriate time frame in which the devices needs to be implanted. It is of high importance in the decision of the therapeutic objective for VAD treatment. [DMH19]

The goal of *bridging to transplantation* has a big relevance with patients in NYHA-IV Stadium which are showing hemodynamical instability. Due to a heart transplantation being the desired final treatment for these patients there must be no contraindication to HTx. In case the patient does show a contraindication, such as malignant tumors or an uncontrollable sepsis, the therapeutic objective changes from BTT to DT. In order for a treatment with a VAD as destination therapy being indicated all conservative treatment options need to be exhausted. Due to the ever-growing shortage of donor organs DT as a therapeutic approach in patients with heart insufficiency will become more relevant in the future even in cases usually suited for heart transplantation. [DMH19] There may occur some cases, in which at first a contraindication for HTx exists, which later on may dissolve. These indicate a therapy based on a *bridging to transplantability* goal. [KSS⁺11]

The indication for a *bridging to recovery* approach is twofold. Either the patient shows heart failure as a result of ischemia reperfusion damage or due to infectious genesis. In the first case the myocardium usually is able to recover within a few days, whereas in the second one the potential and the time necessary for recovery depends on how badly the tissue is damaged. In either scenario a weaning from the VAD is an essential part of therapy. [DMH19]

If a patient is admitted in cardiogenic shock and medical treatment is not sufficient, *bridging to decision* becomes a relevant form of therapy. By providing the patient with a VAD, a more accurate assessment of the patient's condition is possible. Based on this, the decision on further treatment can be thought through more thoroughly. [KSS⁺11]

2.3.2 Technology

Since the first artificial blood-pump has been implanted in 1963 [LHH⁺63] technology of VADs has improved significantly.

The general aim of ventricular assist devices is to provide mechanical support in pumping blood through the human body with the heart remaining inside the patient's body. Despite there being several types of VADs, all of them are working according to the same principle. Blood is taken from the circulatory system through the pump's inlet and ejected at another location via the outlet of the pump. [LW16] VADs are differentiated by three criteria: the localization of the device inside the human body, the flow profile and the implantation strategy.

Regarding the localization of the assistance device there are three types of VADs. With around 93% of all implemented devices the most commonly used ones are the left ventricular assist devices (LVADs). [DMH19] LVADs are placed inside the left ventricle, from where they are pumping blood into the aorta [GSL⁺03]. The second localization option is given by placing the device as a support for the right ventricle. These devices are therefore called right ventricular assist devices (RVADs). RVADs are positioned such that blood is taken from the right atrium and ejected into the pulmonary artery. [DMH19] In some cases RVADs in combination with the aforementioned LVADs are used to build a biventricular assist device (BVAD). This type of heart support is mainly used for more severe heart diseases with a high risk of developing right heart failure. [SH19]

The flow profile as the second criterion for VAD distinction is represented through pulsatile and continuous flow devices. Assistance with pulsatile devices can either be implemented to support the heart in a counter pulsation approach, working synchronous to the heart cycle, or as an asynchronous support. The most commonly known type of pulsatile device is a pneumatically driven pump ventricle. [LW16] However, according to the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) over 95% of all implanted devices are continuous flow devices [KPK⁺17]. These, in their most commonly used form, are electrically driven rotational blood pumps. A technological difficulty with these devices is the high probability of blood damage due to small gaps and very high rotational speed. In exchange for this problematic these devices enable a dynamic adaption to the patient's physiological needs by being able to quickly adjusting parameters like the

VAD type		Therapeutic objective	
LVAD	93%	DT	40%
BVAD	4%	BTD	30%
TAH	2%	BTT	29%
unknown	0.1%	others (BTR,...)	1%
RVAD	0.05%		

Table 2.2: Percentages of VAD types and therapeutic objectives in mechanical heart support based on [DMH19].

motor current. The possibility of keeping track of these signal characteristics furthermore makes it possible to detect malfunctions such like misplacement of the pump. [LW16]

Implantation of the VADs can be performed in one of three ways: paracorporeal, intracorporeal or percutaneous [DMH19]. For VAD systems which follow a paracorporeal approach, only the in- and outflow cannulas are located inside the human body. The cannulas are connecting the pump, which is located outside the body, with the ventricle and the vessels. Due to the pump being placed outside of the patients body, these systems provide the option for pediatric MCS. For most other systems this is not possible due to the device being too big to fit inside a child's body. [SBL19] One example for paracorporeal systems are the aforementioned pneumatically driven pump ventricles [LW16]. As far as the other two criteria for VAD differentiation are concerned, all combinations of localization and flow control are possible [SBL19]. As an example of a percutaneous device, [DMH19] names the Impella 2.5, which is a rotary blood pump with continuous flow used for left ventricular assistance. Table 2.2 illustrates the proportions of different VAD types and therapeutic goals using the International Mechanically Assisted Circulatory Support (IMACS) register.

3 Technical Fundamentals

Since the main part of this thesis addresses the implementation of flow control algorithms for a left ventricular assist device, the basics of control theory and an introduction on iterative learning control will be presented here as well.

3.1 Control Theory

Since the field of control theory is very extensive, this section will only deal with the notation and structure of a standard control loop in general. Furthermore, the basic principles of a PI controller and an iterative learning control are discussed, since these are used within practical part of the thesis.

The basic task of control engineering is to influence a time-varying process from the outside with the goal that the process is executed in a predetermined manner. A control system is characterized in particular by the feedback of the controlled variable to the reference variable. The reference variable represents the state to be achieved. In theory, this is represented by a control loop with the components shown in Figure 3.1. The plant $G(s)$ transfers the actuating variable $u(t)$, as well as the influence of the disturbance $d(t)$, to the controlled variable $y(t)$. This variable is permanently compared with the reference variable $w(t)$ by means of a feedback. Which results in the control error

$$e(t) = w(t) - y(t) \quad (3.1)$$

The controller $G_c(s)$ then transfers the control error to the actuating variable again. The aim of the control loop is to achieve the smallest possible control error with the greatest possible damping. Since these goals contradict each other, a trade off must

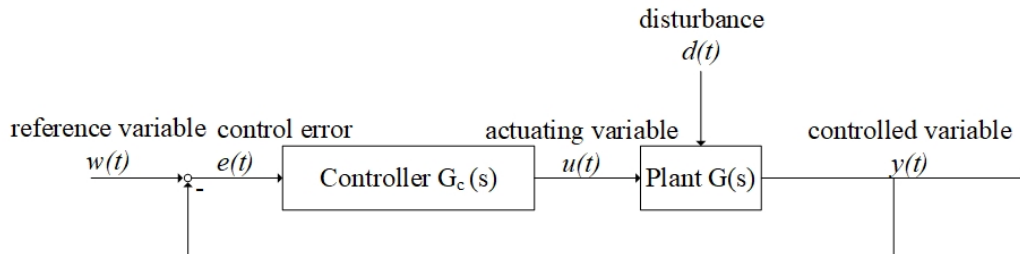


Figure 3.1: General structure of a control loop

always be accepted here.[ZR17]

However, there are some general requirements for the closed control loop, which have to be fulfilled. The first of which states that the closed loop needs to be stable. This is the case when the control loop responds to a finite excitation with a finite output signal. The second one is the requirement for disturbance rejection, stating that the controlled variable needs to follow the reference variable asymptotically, so that

$$\lim_{t \rightarrow \infty} e(t) = 0 \quad (3.2)$$

Another requirement is that the dynamic relationship between the reference variable $w(t)$ and the controlled variable $y(t)$ must satisfy specified quality requirements. The last requirement states that the first three requirements must be satisfied despite uncertainties in the plant. This requirement is called the Robustness requirement. More detailed information on these requirements can be found in [Lun10].

The plant corresponds to the part of the system in which the physical quantity to be controlled is influenced by the controller. The calculation of the controlled system is only possible in a few cases by setting up and solving differential equations. Due to this, the determination of the characteristic values of the controlled system is usually carried out experimentally. There are several basic types of plants. These are classified according to their dynamic behavior. As only the PT1 element is used in the practical part of this thesis, all other variations will not be discussed at this point. Detailed information on this topic can be found in [Lun10]. The PT_1 -element is the plant type which is most common in technical equipment.[Lun10] A PT_n -element, in its static state, reacts proportionally to the input value and has a distinct transition behavior. The index n describes the system order. A PT1 element therefore is a proportional delay element of first order. The time constant T enables an impression of the speed with which the system can react to changes at the input.

3.1.1 PI Controller

Chien Hrones Reswick

3.1.2 Iterative Learning Control

4 Identification

4.1 Sputnik VAD

The Sputnik VAD is an axial-flow blood pump, developed in a cooperative project of the National Research University of Electronic Technology, OJSC Zelenograd Innovation-Technology Center of Medical Equipment, FSBI "Academician V.I. Shumakov Federal Research Center of Transplantology and Artificial Organs", Ministry of Health of Russian Federation, DONA-M LLC and BIOSOFT-M LLC in 2009. [ST15]

This device is used for left ventricular assistance in patients with acute heart failure. The therapeutic objective in implantation of a Sputnik VAD is bridging to transplantation. The VAD is able to pump up to 10 liters of blood per minute with a continuous flow profile. The implantable pump weighs about 200 g, has a length of 81 mm and a maximum diameter of 34mm. It consists of a moving and a stationary part. The moving part, the impeller, which is a rotor with four blades, contains a permanent NdFeB-magnet which is actuated by a brushless DC motor. The rotor spins clockwise with speed values between 4000 – 10000rpm. An overview of the pumps specification is presented in Table 4.1 The stator is located inside a titanium

Blood flow	0-10 L/min
Rotational speed	4000-10000 rpm
Length	81 mm
Diameter	34 mm
Weight	200g

Table 4.1: Specifications of Sputnik VAD

housing with a 16 mm diameter. The stationary part of the pump consists of a flow straightener with three stationary blades and a flow diffuser with three twisted blades. The flow straightener is located in front of the rotor and straightens the incoming blood flow into the rotor. Behind the rotor, the blood is directed into the diffuser. Figure 4.1 depicts a cross-section of the Sputnik VAD and identifies it's individual components. The connection between the pump and the cardiovascular system is performed using in- and outflow cannulas, a felt ferule and vascular prosthesis which is sewed to the aorta. [ST15] The Sputnik VAD is powered using two lithium-ion batteries, fully loaded providing enough energy for up to eight hours of system support. The maximum charging time for the batteries is less than five hours. During this time the batteries can either be exchanged by another set of batteries or

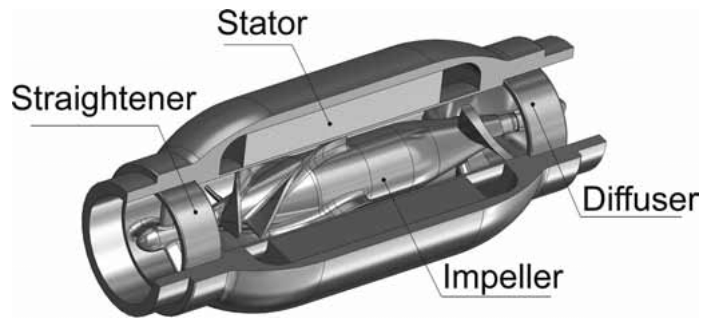


Figure 4.1: Cross-section of the Sputnik VAD from [ST16]

the system can be powered through connection to an AC network. A microprocessor-based driving unit is used to regulate the pump speed, manage the power supply and store parameter data. It is connected percutaneously to the pump with a up to 170 cm long and 5 cm wide lead. [ST15]

4.2 Hardware in the Loop Test Bench

4.3 System Identification

5 Flow Control

5.1 Controller Design

5.1.1 PI Controller

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5.1.2 Iterative Learning Control

5.1.3 Iterative Learning Control with varying iteration length

5.2 Evaluation

5.2.1 PI Controller

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5.2.2 Iterative Learning Control

5.2.3 Iterative Learning Control with varying iteration length

6 Conclusion and future work

A Appendix

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