Hydraulic Characteristics and Flow-field Related Hemocompatibility of Rotary Blood Pump Designs

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(Dr. sc. ETH Zurich)

presented by

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The successful completion of my PhD thesis would not have been possible without the input and support of a number of people that are very important to me and my work. I would like to take the chance to thank some of them in the following.

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Abstract

Rotary blood pumps (RBPs) are implanted into patients with end-stage heart failure to support the left heart by pumping blood from the left ventricle to the aorta. Although the survival rate of patients supported with RBPs has increased substantially over the last decades, patients still suffer from a high incidence of adverse events such as infection, major bleeding or cerebral strokes. Many of these adverse events can be linked to the hemocompatibility of the RBP. And hemocompatibility, in turn, is closely related to the flow conditions in the RBP.

The design of RBPs is based on the same principles as industrial turbomachinery. Whereas design rules and guidelines for turbomachinery design in industrial applications have been collected and refined over many decades, specific design knowledge for RBPs is rare and subjected to additional requirements different from industrial application. These requirements include the sufficient hemocompatibility of the pumps and the operation under dynamic conditions of the clinical application. Thus, this thesis aims to contribute to the design knowledge for RBPs in those two areas.

The overall objective of this thesis is twofold: (I.) to model and compare the hydraulic behavior of RBPs under realistic pressure conditions of the cardiac cycle and (II.) to relate effects of typical RBP design parameters to indicators of hemocompatibility. In order to obtain repeatable and accurate in vitro experiments, a viscosity control was implemented into a mock circulation. The results of this thesis have implications for the design and testing of new RBPs, but also for the modeling and analysis procedures of existing RBPs.

To investigate the hydraulic characteristics of implantable RBPs, an universal mathematical model of the static and dynamic hydraulic pump behavior was developed. This model was then used to systematically compare four current RBPs at clinically relevant, dynamic operating conditions. The model structure was based on principles of
turbomachinery, including the low and backflow region, and it proved to be applicable to each of the investigated RBP.

To investigate the influence of the design parameters of an RBP on hemocompatibility indicators, an RBP design was developed using industrial guidelines. Selected design parameters of this RBP design were varied systematically and the resulting effects on flow field and hydraulic performance were simulated using computational fluid dynamics. The flow fields were analyzed based on Eulerian and Lagrangian features, shear stress histograms and six indicators of hemocompatibility. Potentially damaging shear stress conditions were found for larger gap size and a higher number of blades. The extent of stagnation and recirculation zones was reduced with lower numbers of blades and a semi-open impeller, but it was increased with smaller clearance gaps. The Lagrangian hemolysis index showed a negative correlation with hydraulic efficiency and no correlation with the Eulerian threshold-based metric for hemolysis.

In order to obtain repeatable and accurate in vitro experiments for the previously mentioned investigations, the control of the fluid viscosity was implemented in an existing mock circulation. This accounts for evaporation and temperature changes as well as for mimicking different viscosities of blood. The implemented viscosity control was then used for investigating an implantable RBP at different viscosities in the range of blood viscosities of patients with heart assist devices. For average support conditions, the influence on the measured head pressure was negligible, whereas the measured motor current deviated noticeably for higher speeds.
Zusammenfassung

Rotatorische Blutpumpen (RBPs) werden bei Patienten mit schwerer Herzinsuffizienz eingesetzt. Obwohl die Überlebensrate der mit RBPs unterstützten Patienten in den letzten Jahrzehnten erheblich gestiegen ist, leiden Patienten immer noch unter starken Nebenwirkungen wie Infektionen, schweren Blutungen oder Schlaganfällen. Viele dieser Nebenwirkungen können auf die mangelnde Hämokompatibilität der RBPs zurückgeführt werden, welche wiederum in engem Zusammenhang mit den Strömungsverhältnissen innerhalb der RBPs steht.


Zur Untersuchung der hydraulischen Eigenschaften implantierbarer RBPs wurde zum einen ein allgemeingültiges mathematisches Modell entwickelt, welches das statische und dynamische Pumpenverhalten beschreibt, und zum anderen ein systematischer Vergleich von vier RBPs unter klinisch relevanten, dynamischen Betriebsbedingun-
gen durchgeführt. Die Modellstruktur basiert auf den Prinzipien der Turbomaschinen, schließt den Niedrig- und Rückflussbereich mit ein, und ist auf jede der untersuchten RBPs anwendbar. Das ermittelte hydraulische Verhalten der RBPs zeigte keinen charakteristischen Unterschied zwischen Axial- und Radialpumpen. Für die simulierten Unterstützungsbedingungen wurde eine stark variierende Flusspulsativität beobachtet und bei partiellen Unterstützungsbedingungen trat bei drei der vier untersuchten RBPs Rückfluss auf.


Nomenclature

The following list explains the acronyms and abbreviations as well as Greek and Latin symbols used in the dissertation. They are listed in alphabetic order. Pressure analyses are performed in Pa, but are stated and depicted as mmHg (1 mmHg = 133.32 Pa) as this is the common convention in the field of rotary blood pumps and in the clinical environment.

Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD</td>
<td>Computer aided design</td>
</tr>
<tr>
<td>CFD</td>
<td>Computational fluid dynamics</td>
</tr>
<tr>
<td>HF</td>
<td>Heart failure</td>
</tr>
<tr>
<td>HM3</td>
<td>HeartMate 3</td>
</tr>
<tr>
<td>HMII</td>
<td>HeartMate II</td>
</tr>
<tr>
<td>HTx</td>
<td>Heart transplantation</td>
</tr>
<tr>
<td>IRP</td>
<td>Industrial rotary pump</td>
</tr>
<tr>
<td>LA</td>
<td>Left atrium</td>
</tr>
<tr>
<td>LV</td>
<td>Left ventricle</td>
</tr>
<tr>
<td>LVAD</td>
<td>Left ventricular assist device</td>
</tr>
<tr>
<td>MC</td>
<td>Mock circulation</td>
</tr>
<tr>
<td>NYHA</td>
<td>New York Heart Association</td>
</tr>
<tr>
<td>OMM</td>
<td>Optimal medical management</td>
</tr>
<tr>
<td>RA</td>
<td>Right atrium</td>
</tr>
<tr>
<td>RBP</td>
<td>Rotary blood pump</td>
</tr>
<tr>
<td>RMSE</td>
<td>Root mean square error</td>
</tr>
<tr>
<td>RV</td>
<td>Right ventricle</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SOH</td>
<td>Shut-off head</td>
</tr>
<tr>
<td>VWF</td>
<td>von Willebrand factor</td>
</tr>
</tbody>
</table>
### Latin Symbols

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a)</td>
<td>Static parameter of hydraulic pump model</td>
<td>(mmHg/rpm(^2))</td>
</tr>
<tr>
<td>(A)</td>
<td>Cross sectional area</td>
<td>(m(^2))</td>
</tr>
<tr>
<td>(A_{gap})</td>
<td>Surface of gap between impeller and housing</td>
<td>(m(^2))</td>
</tr>
<tr>
<td>(A_{total})</td>
<td>Total surface area of the impeller surface</td>
<td>(m(^2))</td>
</tr>
<tr>
<td>(A_{WSS&gt;1Pa})</td>
<td>Area of the impeller surface exposed to (WSS &gt; 1) Pa</td>
<td>(m(^2))</td>
</tr>
<tr>
<td>(c)</td>
<td>Meridional discharge velocity</td>
<td>(m/s)</td>
</tr>
<tr>
<td>(C)</td>
<td>Empirical constant for HI calculation</td>
<td>(-)</td>
</tr>
<tr>
<td>(u_2)</td>
<td>Circumferential velocity</td>
<td>(m/s)</td>
</tr>
<tr>
<td>(H)</td>
<td>Head pressure</td>
<td>(mmHg)</td>
</tr>
<tr>
<td>(H_{dyn})</td>
<td>Dynamic head pressure</td>
<td>(mmHg)</td>
</tr>
<tr>
<td>(H_{Eul})</td>
<td>Eulerian head pressure</td>
<td>(mmHg)</td>
</tr>
<tr>
<td>(H_{fri})</td>
<td>Head pressure due to fluid friction loss</td>
<td>(mmHg)</td>
</tr>
<tr>
<td>(H_{inc})</td>
<td>Head pressure due to incidence loss</td>
<td>(mmHg)</td>
</tr>
<tr>
<td>(H_{rec})</td>
<td>Head pressure due to recirculation loss</td>
<td>(mmHg)</td>
</tr>
<tr>
<td>(H_{per})</td>
<td>Head pressure loss over periphery</td>
<td>(mmHg)</td>
</tr>
<tr>
<td>(HI)</td>
<td>Hemolysis index</td>
<td>(-)</td>
</tr>
<tr>
<td>(I)</td>
<td>Current</td>
<td>(A)</td>
</tr>
<tr>
<td>(I_{Thres})</td>
<td>Fraction of fluid volume with scalar shear stress above a threshold</td>
<td>(%)</td>
</tr>
<tr>
<td>(I_{WSS&gt;1Pa})</td>
<td>Relative area of the impeller surface exposed to (WSS &gt; 1) Pa</td>
<td>(%)</td>
</tr>
<tr>
<td>(k_n)</td>
<td>Constants of turbomachinery equations</td>
<td>(-)</td>
</tr>
<tr>
<td>(k_{inf})</td>
<td>Constant for inflection flow rate</td>
<td>(mmHg/rpm(^2))</td>
</tr>
<tr>
<td>(K)</td>
<td>Gain</td>
<td>(cP/W)</td>
</tr>
<tr>
<td>(K_P)</td>
<td>Proportional constant</td>
<td>(-)</td>
</tr>
<tr>
<td>(K(s))</td>
<td>Transfer function of PI controller</td>
<td>(-)</td>
</tr>
<tr>
<td>(L)</td>
<td>Constant for fluid inertia</td>
<td>(mmHgs/L)</td>
</tr>
</tbody>
</table>
## Nomenclature

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$L_{\text{per}}$</td>
<td>Constant for fluid inertia of periphery</td>
<td>(mmHg s$^2$/L)</td>
</tr>
<tr>
<td>$n$</td>
<td>Pump speed</td>
<td>(rpm)</td>
</tr>
<tr>
<td>$\mathbf{n}$</td>
<td>Normal of $A_{\text{gap}}$</td>
<td>(-)</td>
</tr>
<tr>
<td>$N_k$</td>
<td>Number of points on the kth particle trajectory</td>
<td>(-)</td>
</tr>
<tr>
<td>$N_p$</td>
<td>Number of particle trajectories</td>
<td>(-)</td>
</tr>
<tr>
<td>$p_n$</td>
<td>Coefficients for quadratic fit of slope</td>
<td>(-)</td>
</tr>
<tr>
<td>$p_{\text{sta}}$</td>
<td>Static pressure</td>
<td>(-)</td>
</tr>
<tr>
<td>$p_{\text{tot}}$</td>
<td>Total pressure</td>
<td>(-)</td>
</tr>
<tr>
<td>$P_{\text{hydr}}$</td>
<td>Hydraulic power</td>
<td>(W)</td>
</tr>
<tr>
<td>$P_{\text{mech}}$</td>
<td>Mechanical power</td>
<td>(W)</td>
</tr>
<tr>
<td>$P(s)$</td>
<td>First order lag element</td>
<td>(-)</td>
</tr>
<tr>
<td>$q$</td>
<td>Flow rate</td>
<td>($L$/min)</td>
</tr>
<tr>
<td>$q_{\text{cor}}$</td>
<td>Corrected flow rate after calibration</td>
<td>($L$/min)</td>
</tr>
<tr>
<td>$q_{\text{des}}$</td>
<td>Design flow rate</td>
<td>($L$/min)</td>
</tr>
<tr>
<td>$q_{\text{inf}}$</td>
<td>Inflection flow rate</td>
<td>($L$/min)</td>
</tr>
<tr>
<td>$Q$</td>
<td>Flow rate</td>
<td>($L$/min)</td>
</tr>
<tr>
<td>$Q_{\text{est}}$</td>
<td>Estimated flow rate</td>
<td>($L$/min)</td>
</tr>
<tr>
<td>$Q_{\text{leak}}$</td>
<td>Leakage flow rate</td>
<td>($m^3$/s)</td>
</tr>
<tr>
<td>$Q_{p,\text{est}}$</td>
<td>Estimated flow rate over periphery</td>
<td>($L$/min)</td>
</tr>
<tr>
<td>$Q_{\text{pump}}$</td>
<td>Pump flow rate</td>
<td>($m^3$/s)</td>
</tr>
<tr>
<td>$Q(t)$</td>
<td>Volume flow rate</td>
<td>($m^3$/s)</td>
</tr>
<tr>
<td>$r$</td>
<td>Spearman’s rank correlation coefficient</td>
<td>(-)</td>
</tr>
<tr>
<td>$R_{\text{rec}}$</td>
<td>Constant recirculation losses</td>
<td>(mmHg/($L$/min)$^2$)</td>
</tr>
<tr>
<td>$R_1$</td>
<td>Static parameter of hydraulic pump model</td>
<td>(mmHg/ (rpm/($L$/min))$^2$)</td>
</tr>
<tr>
<td>$R_2$</td>
<td>Static parameter of hydraulic pump model</td>
<td>(mmHg/ (rpm/($L$/min))$^2$)</td>
</tr>
<tr>
<td>$s$</td>
<td>Slope</td>
<td>(-)</td>
</tr>
<tr>
<td>$\overline{s}$</td>
<td>Position vector</td>
<td>(m)</td>
</tr>
<tr>
<td>$SPWV$</td>
<td>Local spanwise vorticity</td>
<td>(1/s)</td>
</tr>
<tr>
<td>$SPWVI$</td>
<td>Spanwise vorticity index</td>
<td>(1/s)</td>
</tr>
<tr>
<td>$SS$</td>
<td>Shear stress</td>
<td>(Pa)</td>
</tr>
<tr>
<td>$t$</td>
<td>Time</td>
<td>(s)</td>
</tr>
<tr>
<td>$T$</td>
<td>Torque on rotor</td>
<td>(Nm)</td>
</tr>
</tbody>
</table>
### Nomenclature

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Unit(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_i$</td>
<td>Proportional constant</td>
<td>(-)</td>
</tr>
<tr>
<td>$T_s$</td>
<td>Sampling time</td>
<td>(s)</td>
</tr>
<tr>
<td>$v$</td>
<td>Velocity</td>
<td>(m/s)</td>
</tr>
<tr>
<td>$\mathbf{v}$</td>
<td>Fluid velocity vector</td>
<td>(m/s)</td>
</tr>
<tr>
<td>$V_{\text{total}}$</td>
<td>Total volume of fluid in the pump</td>
<td>(mL)</td>
</tr>
<tr>
<td>$V_{\tau&gt;\text{Thresh}}$</td>
<td>Fluid volume with scalar shear stresses above the prescribed threshold</td>
<td>(mL)</td>
</tr>
<tr>
<td>$WSS$</td>
<td>Wall shear stress</td>
<td>(Pa)</td>
</tr>
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</table>
# Greek Symbols

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$</td>
<td>Empirical constant for HI calculation</td>
<td>(-)</td>
</tr>
<tr>
<td>$\beta$</td>
<td>Empirical constant for HI calculation</td>
<td>(-)</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>Discharge angle</td>
<td>($^\circ$)</td>
</tr>
<tr>
<td>$\eta$</td>
<td>Hydraulic efficiency</td>
<td>(%)</td>
</tr>
<tr>
<td>$\psi$</td>
<td>Temperature</td>
<td>($^\circ$C)</td>
</tr>
<tr>
<td>$\mu$</td>
<td>Viscosity</td>
<td>(cP)</td>
</tr>
<tr>
<td>$\rho$</td>
<td>Density</td>
<td>(kg/m$^3$)</td>
</tr>
<tr>
<td>$\sigma_{ij}$</td>
<td>Viscous shear stress components</td>
<td>(Pa)</td>
</tr>
<tr>
<td>$\tau$</td>
<td>Scalar shear stress</td>
<td>(Pa)</td>
</tr>
<tr>
<td>$\tau_s$</td>
<td>Time constant</td>
<td>(s)</td>
</tr>
<tr>
<td>$\varphi(\mathbf{\bar{s}}; t)$</td>
<td>Angle formed by velocity and vorticity vector</td>
<td>(rad)</td>
</tr>
<tr>
<td>$\mathbf{\omega}(\mathbf{\bar{s}}; t)$</td>
<td>Vorticity vector</td>
<td>(1/s)</td>
</tr>
<tr>
<td>$\Omega$</td>
<td>Angular speed</td>
<td>(rad/s)</td>
</tr>
</tbody>
</table>
1 Introduction

1.1 Heart failure and left ventricular assist devices

This section puts left ventricular assist devices (LVADs) into context with heart failure (HF) and possible treatments. First, the anatomy and functionality of the healthy human heart is explained, giving an overview of the most important terminologies used. A discussion on HF, its epidemiology, its symptoms and classifications, and current therapy options follows. Finally, the history, state-of-the-art technology, and current limitations of LVADs are described in detail.

1.1.1 Healthy heart

The human heart is divided into the right and the left heart. The right heart pumps deoxygenated blood through the lungs (pulmonary circulation) and the left heart pumps oxygen-rich blood through the peripheral organs (systemic circulation). Figure 1.1 shows the schematic anatomy of the human heart, partly cut open to reveal the ventricles, atria and valves.

During each cardiac cycle, the heart muscle contracts and relaxes to realize the pumping function, which is enabled by the unidirectional valves. The two phases of the cardiac cycle are called systole (heart contraction and blood ejection) and diastole (heart relaxation and blood filling) [2]. The left atrium (LA) and right atrium (RA) are chambers connected to the respective ventricle. They work as a weak primer pump by helping to move blood into the respective ventricle and thereby allowing the heart to fill an additional 20% in volume [3]. The stroke volume, which is defined as the blood volume each ventricle ejects with one contraction, is about 70 mL for the healthy human
1 Introduction

Figure 1.1: Anatomy of the human heart with the ventricles, atria, valves and the connecting arteries and veins. In this drawing, the heart is partly cut open to reveal the four heart valves; the hatched surface marks the cut tissue. The systemic circulation is colored in red: Oxygenated blood is pumped from the pulmonary veins through the left atrium (LA) into the left ventricle (LV) and from there into the aorta. The pulmonary circulation is colored in blue: Deoxygenated blood is pumped from the superior and inferior vena cava through the right atrium (RA) into the right ventricle (RV) and from there into the pulmonary arteries. Figure modified with permission from Ochsner [1].

Heart at rest. This is about 60% of the blood volume in the ventricle at the end of diastole [3]. This percentage is called the ejection fraction.

Figure 1.2 illustrates the pressure curve in aorta and left ventricle (LV) as well as the flow rate between LV and aorta through the aortic valve during one cardiac cycle. At the beginning of systole, the pressure in the LV rises until it surpasses the aortic pressure. Due to the pressure difference, the aortic valve opens and blood starts flowing.
1.1 Heart failure and left ventricular assist devices

![Graph showing cardiac cycle with pressure and flow characteristics](image)

**Figure 1.2:** Cardiac cycle with qualitative curves of pressure and flow characteristic of the left ventricle (LV) in systole and diastole. The pressure in the aorta (blue) and in the LV (red) are displayed in the top graph based on the Wiggers diagram [3]. The flow rate through the aortic valve is displayed in the bottom graph, derived from measurements with magnet resonance imaging [4].

into the aorta. Before the start of the diastole, the LV pressure falls back under the aortic pressure again. This leads to a short period of backward flow through the aortic valve, followed by a sudden stop of flow when the valve closes again [3]. The LV then relaxes and its pressure decreases rapidly until the mitral valve opens and the filling of the LV starts. During that period, the LV pressure stays almost constant. At the end of diastole, the filling of the LV is supported by the contraction of the LA, which causes the small bulge to form just before the onset of the next cardiac cycle as a result of the pressure increase and subsequent decrease.

The maximum flow rate through the aortic valve and the ascending aorta is around 20 L/min [4]. The averaged flow rate is called cardiac output and is about 5 L/min for a healthy adult with normal body weight. The maximum pressure a ventricle achieves with each con-
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traction differs for the LV and the right ventricle (RV) due to the high systemic resistance and low pulmonary resistance. In its normal state, the LV has a maximum systolic pressure of 120 mmHg, while the RV only reaches 25 mmHg [2]. This difference in load is also anatomically and pathologically evident; for example the LV has thicker walls and is more prone to HF.

1.1.2 Heart failure

HF describes the pathological condition in which the heart is not able to pump a sufficient amount of blood to meet the demand of the body. Typically a myocardial abnormality, meaning an abnormal change of form or function of the heart muscle, causes systolic or diastolic ventricular dysfunction [5]. Abnormalities can be caused by different conditions such as coronary artery disease, valve disease, high blood pressure, diabetes or heart defects present at birth. Affected individuals show symptoms such as fatigue, breathlessness and ankle swelling (as a consequence of fluid retention). Diagnostic signs include LV dilatation, increased right atrial pressure, lung congestion or valve regurgitation [6]. HF can affect both ventricles, the left HF is the most common type and often the cause of right HF. [7].

One way of classifying left HF is by the ejection fraction of the LV. If the ejection fraction is above 50%, it is called HF with preserved ejection fraction [6]. This is characterized by impaired filling of the ventricle during diastole and increased filling pressure. The LV loses the ability to relax normally and the heart muscle stiffens substantially. If the ejection fraction is below 40% it is called HF with reduced ejection fraction [6]. This is characterized by impaired discharging of the LV due to improper contraction in systole and an enlarged LV.

Another classification of HF pertains to the severity of the symptoms. This commonly used classification is the functional classification of the New York Heart Association (NYHA), dividing the different degrees of severity in four classes [8]. Patients of NYHA Class I have the best functional capacity and no limitation of physical activity. Class IV patients are not able to carry out any physical activity without discomfort, and HF symptoms may even be present at rest.
1.1 Heart failure and left ventricular assist devices

HF affects about 2% of the population worldwide, with prevalence increasing significantly in elderly people. Approximately half of the overall HF population has HF with reduced ejection fraction. Of these patients, approximately 10% have advanced symptoms, so-called end-stage heart HF, and are classified NYHA class IIIb-IV [9]. The resulting patient cohort is in consideration for several therapeutic treatments, including the implantation of rotary blood pumps (RBPs). In the following, the different therapy options are described and compared.

1.1.3 Therapy options

The first treatment method that is commonly followed by clinicians is optimal medical management (OMM), which includes a combination of different medications with the aim of decreasing the workload of the heart. Medication can include diuretics that increase the excretion of water from the body, beta blockers that decrease blood pressure by, among others, lowering the heart rate at rest, and angiotensin-converting-enzyme inhibitors that decrease systemic resistance by widening the blood vessels.

If medical therapy does not suffice, the gold standard option is heart transplantation (HTx), where the heart of a deceased organ donor is implanted into the patient. Worldwide, over 5,000 patients receive a transplant per year [10]. However, the annual demand for HTx outweighs the supply of donor hearts by a large margin [9].

If a donor heart is unavailable or patients are ineligible for HTx, the implantation of an LVAD is the therapy of choice. LVADs assist the failing heart by providing additional blood flow from the LV to the aorta. The largest registry for the implantation of such devices [11] reports around 3,000 patients per year who receive an LVAD implant. However, the actual number, including implantations in all clinical centers not represented in this registry, is probably higher. The most common application is for patients to receive an LVAD as a destination therapy (40%). The next most frequent device strategies are bridge to transplant (29%) and bridge to candidacy (30%), which means the patient is still waiting to become eligible for transplantation [11].
Figure 1.3 shows a comparison of the most recent statistics [10, 12] on survival rates over time for the three therapy options for end-stage HF. Two-year survival is 41% for OMM, 70% for LVAD support and 78% for HTx. While over this two-year period survival of LVAD patients is close to the gold standard of HTx, the survival rate for a six-year period differs drastically, with 67% survival for heart transplant patients [10] and 32% survival for LVAD patients [13].

![Figure 1.3: Comparison of the most recent statistics on survival of end stage HF patients (NYHA Class IIIb to IV) that received one of the three therapy options: Optimal medical management (OMM), Implantation of a left ventricular assist device (LVAD) [12], [12] or heart transplantation (HTx) [10]. 1-year and 2-year survival is indicated as a percentage next to each curve. The device used for LVAD support is the HeartMate II.](image)

### 1.1.4 History of left ventricular assist devices

The development of LVADs has been evolving greatly over the last six decades. First generation LVADs were volume displacement devices,
1.1 Heart failure and left ventricular assist devices

whereas by now the focus has shifted almost entirely to rotary pumps (second and third generation devices).

Volume displacement pumps commonly incorporate a pneumatically or electrically actuated membrane or pusher plate in a rigid housing, and unidirectional valves at the inlet and outlet of the pump. Due to their size, these kinds of pumps are usually paracorporeal, which means the device is resting outside of the body (for instance on the patient’s chest or belly), or implanted into the abdominal cavity. In 1966, the first device of this kind was successfully implanted into a human by Dr. Michael DeBakey and his team [14], and in 1989, one of the first commercial LVAD developments with the Novacor LVAS (Baxter Healthcare Corp, Oakland, CA, USA) was implanted as a bridge to heart transplant [15].

Volume displacement pumps deliver a pulsatile flow that is more similar to that of the native ventricle. However, low survival rates for stroke-free patients and device failure [16] as well as disadvantages such as lack of durability, reduced mobility due to large driving consoles, and high rates of infection due to the large percutaneous cannulas have limited their use. Nevertheless, a few of the volume displacement pumps are still in use today, like the BerlinHeart Excor (BerlinHeart, Berlin, Germany), which is especially suitable for children and has been implanted in over 2,000 patients worldwide [17].

Over the last three decades, RBPs have gained importance and have largely replaced volume displacement pumps. Survival rates for patients with RBPs are 30% higher than for patients with pulsatile pumps and RBPs promise a better quality of life with higher mobility and fewer adverse events [16]. RBPs have a spinning turbodynamic impeller and are fully implantable due to their smaller size. In 1988, the HemoPump was the first rotary pump to be used in a human [18].

RBPs can be divided into the so called second and third generations LVADs. The second generation uses mechanical bearings that have either a conventional shaft going through impeller and housing or a mechanical ball and cup bearing, while the third generation LVADs use a fully levitating impeller with no mechanical contact bearing between impeller and housing during normal operation [19]. Technical approaches that enable the levitation of the impeller are passive magnetic bearings, used for instance in combination with either hy-
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drodynamic or active magnetic bearings. These bearing systems are supposedly preferable to mechanical bearings, as these are expected to contribute to poor hemocompatibility due to very high shear stresses in the bearings and due to frictional heating. Nevertheless, second generation devices such as the HeartMate II (HMII) have been successfully used for over a decade and have proven durable [19].

Figure 1.4 shows the progression of miniaturization in the past 27 years. RBPs (second and third generation devices) brought a revolution for the treatment of HF and almost fully replaced the use of pulsatile devices. The number of implantations of RBPs is steadily increasing [13] and now accounts for 97% of LVADs implanted in the last five years [13]. Further details about the most current RBPs that are in clinical use, including three third generation devices, are given in Section 1.2.2.

Figure 1.4: Progression of miniaturization of LVADs over a time period of 27 years. All devices are from the company Abbott (Abbott Park, IL, USA), former Thoratec (Pleasanton, CA, USA), and are capable of providing full support of over 5 L/min: (A) HeartMate XVE, (B) Thoratec PVAD, (C) Thoratec IVAD, (D) HeartMate II (HMII), (E) HeartMate 3 (HM3). The first three devices (A-C) are pulsatile pumps, D is a second-generation axial-flow rotary pump and E a third-generation radial-flow rotary pump. Reprinted from Schumer et al. [20] with permission of Oxford University Press.
1.1 Heart failure and left ventricular assist devices

1.1.5 Limitations of LVAD support

In the healthy heart, the pressure in the aorta changes from systole to diastole by about 40 mmHg. When the LVAD is set to a low level of support in interaction with the pathological heart, the aortic pressure variation is 10-30 mmHg (and even less for higher levels of LVAD support) [21]. This reduced pulsatility in the aorta does not mimic the normal physiology and drastically reduces peak flow rates and flow pulsatility. The limitations do not only result from these abnormal pressures and flow rates but also from the introduced artificial surfaces and supraphysiological shear rates in the LVAD, among other factors. The limitations of therapy with LVAD support either lead to severe complications and hospital readmissions or even death.

With the current survival rates of 70% after two years of LVAD support, the greatest risks of death are neurologic events like strokes, multisystem organ failure and infections [13]. Strokes can either be ischemic as the result of a blood vessel being obstructed by a blood clot and therefore cutting off oxygen supply to the respective tissue, or hemorrhagic when a weakened blood vessel ruptures [7]. Multisystem organ failure may follow a combination of other complications and is set off by sepsis and inadequate support [22]. Infections most commonly appear at the site where the driveline of the LVAD penetrates the skin, which presents an open wound throughout LVAD therapy. Infections are treated with antibiotics; if these are unsuccessful, a surgical procedure for LVAD exchange or driveline repositioning is necessary [23].

Not only the survival rate, but also the complications that the surviving patients experience while being under LVAD support, are of concern. During the first two years of LVAD support only 20% of patients remain free from major adverse events [13]. An adverse event is an undesired medical occurrence that is relevant in the context of the treatment but does not necessarily have a causal relationship to the LVAD implantation. The most common adverse events are internal bleeding, infection and cardiac arrhythmia [13]. The most common form of bleeding is in the gastrointestinal tract. Commonly, anticoagulation is reduced as a reaction which, in turn, can lead to a higher rate in thromboembolic complications [24]. Arrhythmia, the third most
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frequent adverse event, is a disturbance of the regular sinus rhythm that may occur from suction events during which the inlet cannula of the LVAD touches the ventricular wall [22].

The limited hemocompatibility of current LVADs is a major factor in causing the afore-mentioned limitations, which manifest themselves as complications and adverse events. Next to artificial material and heat generation, hemocompatibility is said to be related to the unphysiological flow-field with high shear stresses, turbulences, stagnation zones and diminished pulsatility of RBPs. These factors and their implications are further discussed in Section 1.2.4.

1.2 Characteristics of rotary blood pumps

In this section, we first define different classifications and notations for RBPs. Then, a selection of current RBPs used for experiments throughout this thesis is introduced. The hydraulic behavior under dynamic boundary conditions is explained next and finally, we connect the flow field in an RBP to its hemocompatibility.

1.2.1 Terminology

Based on the angle between inflow into and outflow from the impeller, one can differentiate between axial-flow, mixed-flow and radial-flow pumps. In axial-flow pumps, the blood enters and exits the impeller in the same direction, parallel to the impeller’s axis of rotation. In radial-flow pumps, often referred to as centrifugal pumps, the blood exits the impeller in a radial direction, or a $90^\circ$ angle to the rotation axis. A mixed-flow pump is somewhere between the two and has elements of both [25].

Figure 1.5 shows the meridional section, which is an unfolded cut along the blade through the impeller and housing, and the plan view of a radial-flow impeller without housing. An impeller design with a bottom shroud and a top shroud, as shown in the drawing is called a closed impeller. Two variations on this design are without a top shroud (semi-open impeller) or without any shroud (open impeller). The clearance gap is the gap between either the upper edge of the
blade and the housing (in a semi-open design) or between the top shroud and the housing (in a closed design). The cavity between two adjacent blades, the primarily channel for blood flow, is called blade channel.

When describing local effects in the impeller we note four additional important terms: The face of the blade leading in rotation direction is the pressure side, while the opposite blade surface, which experiences lower pressure, is the suction side. The leading edge is the edge of the blade that first contacts the fluid when entering the impeller, while the edge on the other end is the trailing edge.

Figure 1.5: Meridional section and plan view of a radial-flow pump with closed impeller. The same notation holds true for axial-flow pumps. The basic geometry sketch is adapted from Gülich [26] and the here used annotation is also modified.

1.2.2 Current rotary blood pumps

Four implantable RBPs and one extracorporeal RBP that represent a diverse sample of clinically used LVADS are introduced. These include the two implantable RBPs that so far have the highest number of implantations worldwide. All four of the implantable RBPs are the subject of investigation in Chapter 2, and one extracorporeal and one of the implantable RBPs were used for experiments in Chapter 4.
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Implantable RBPs

The four implantable RBPs are two axial-flow and two radial-flow pumps. The rationale for the choice of devices was their relevance in current clinical use on the one hand, their diversity regarding their hydraulic characteristics - steepness of the HQ curve and pump design (axial-flow vs radial) - on the other.

The two radial-flow pumps are the HVAD (Medtronic/Heartware, Minneapolis, MN, USA) and the HeartMate 3 (HM3, Abbott/Thoratec, Abbott Park, IL, USA). The HVAD uses a hydrodynamic and passive magnetically-levitated bearing. It is one of the most widely used LVADs worldwide, with implantation numbers exceeding 10,000 patients [27]. Its first human implantation dates back to 2006, whereas the HM3 is a comparably new LVAD, with the first in-man implantation in 2014 [28]. So far, the HM3 has been implanted in over 500 patients [19] and has promising clinical results, with no reported case of pump thrombus [29]. It uses an active magnetic bearing with large flow paths between housing and impeller of at least 500 µm [30].

The two axial-flow pumps are the HMII (Abbott /Thoratec, Abbott Park, IL, USA) and the Incor (BerlinHeart, Berlin, Germany). The HMII, as shown in Figure 1.6, is the most widely used and studied LVAD [18] due to the high number of patients treated (over 25,000 implantations) [31] and the long clinical availability (the first human implantation was conducted in 2000) [28]. HMII is considered a second generation LVAD due to the mechanical contact areas of the ball-cup bearing, whereas the other three pumps are third generation pumps due to their levitating impeller with no mechanical contact point during stationary operation [18]. The Incor has been implanted about 500 times, with the first in human implantation being carried out in 2002. It was the first implantable LVAD with active magnetic bearing that received market approval (Foster, 2018).

Extracorporeal RBPs

An extracorporeal RBP differs from an implantable RBP in several aspects. It is used for mechanical circulatory support and extracorporeal membrane oxygenation, both in acute cases for several hours and up to several weeks for an extended support [33]. The housing and
1.2 Characteristics of rotary blood pumps

The drive unit of such an RBP are not bound to the size restriction of the cavity in the human body, and the durability requirements are lower compared to implantable RBPs.

The Deltastream DP2 (Medos Medizintechnik AG, Stolberg, Germany), one example of an extracorporeal RBP, is a mixed-flow RBP with diagonal flow path [34]. Unlike implantable RBPs that have blood-contacting surfaces made from titanium alloy and ceramics, the Deltastream DP2 has a housing and impeller made from polycarbonate, which are exchangeable as one unit. The bearing of the impeller is realized with a one-sided shaft, and the energy transmission for rotation is done by magnetic coupling.

We focus on implantable RBPs in the following discussion of operating conditions and flow-field related hemocompatibility of RBPs.

1.2.3 Static and dynamic operation

The impeller of an RBP transfers energy to the fluid, resulting in the generation of fluid flow and/or an increase in static pressure. The
achieved flow rate is dependent on the pressure level that has to be overcome [26], which is the pressure difference from pump inlet to pump outlet - also called head pressure. This dependency differs for different pump designs and is characterized by a curve, displaying the head pressure (H) over flow rate (Q) for a constant pump speed. Figure 1.7 illustrates such a curve with the corresponding signal of head pressure over time. A single curve for one speed is called the HQ curve; several curves at different speeds spread over the relevant operating range form the HQ diagram.

Figure 1.7 additionally shows a dynamic head pressure signal over time in the form of a sine wave. This input in head pressure does not lead to a trajectory along the HQ curve as one would intuitively expect, but instead leads to an elliptic trajectory around the static curve in a counter-clockwise direction [35]. Dynamic changes in either pressure or speed lead to delayed changes in flow rate due to fluid inertia. The dynamics changes of the cardiac cycle are also manifested in this form, with a hysteresis around the static HQ curve [36].

1.2.4 Flow-field related hemocompatibility

Common adverse events as described earlier in Section 1.1.5 are gastrointestinal bleeding, device thrombosis, and stroke. These adverse events are commonly thought to be related to limited hemocompatibility and its consequences, such as hemolysis, von Willebrand factor (VWF) degradation and platelet activation. Diminished pulsatility also plays an important role. [24].

The blood in an RBP is exposed to non-physiological shear stresses due to high rotational speeds of the spinning impeller, small clearances between moving and stationary parts and turbulence in the flow field. These high shear stresses lead to the rupture of red blood cells (hemolysis) on the one hand and the activation of platelets (as part of the coagulation cascade) on the other. Zones of stagnation and recirculation may lead to the forming of a blood clot. This may result in a pump thrombus that adheres to the housing or the impeller and partly or fully blocks the function of the pump, or to thromboembolic events such as a ischemic stroke if the clot is flushed through the pump into the systemic circulation.
1.2 Characteristics of rotary blood pumps

Clinically, an abrupt increase of pump thrombus with the HMIII [37] was seen. One might relate the occurrence of pump thrombus to the applied strategy of using lower speeds and thus lower flow rates, as the flow field of the HMIII pump has been shown to become disturbed at lower speeds and therefore lower flow rates [38, 39]. These observations from an RBP being used at an off-design point might indicate that the disturbed flow fields at off-design flow rates relate to disadvantageous treatment outcomes. However, it must be noted that this relates to an average flow rate during a cardiac cycle, whereas the actual flow rate changes continuously depending on the boundary conditions and is thus unknown. These observations from an RBP being used at an off-design point might indicate that the disturbed flow fields at off-design flow rates relate to disadvantageous treatment outcomes.

Even lower shear stress levels than those critical for hemolysis or platelet activation can still be supraphysiological and therefore lead to a conformational change of the VWF [40], which is a large pro-


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tein involved in the coagulation cascade that stops bleeding. Clinical findings have also shown that patients that suffer from bleeding also acquired von Willebrand disease [41], but the causality is unclear.

It is important to understand which flow rates occur in an implanted RBP at typical support situations, and more specifically, which flow rates dominate over one cardiac cycle, to be able to evaluate the flow-related hemocompatibility at the most realistic operating points. Important influences of flow on hemocompatibility that need to be investigated are the effects of the pump flow - namely non-physiological flow conditions such as elevated shear stress, turbulence and stagnation zones.

1.3 Comparison to industrial rotary pumps

Industrial rotary pumps (IRPs) are used for transporting liquids by raising a certain volume flow to a specified pressure level. The main components of such a pump comprise a housing, the pump shaft and bearing, and the impeller. Their applications include water storage, drainage, cooling supply, fire pumps, chemical processing or water turbines for power plants [26, 42]. Depending on the application, they can be designed for high loads, such as head pressures of up to 5,000 m water column (368,000 mmHg), and flow rates up to 60 m$^3$/s (3.6 Mio L/min) [26].

Designers of IRPs benefit from a large amount of collected experimental data, analytical approximations and established pump design rules that have been improved and refined over many decades. This knowledge is manifested in textbooks for pump design [26, 43, 44]. These, however, do not cover the special requirements and design objectives of the hydraulic design of RBPs, as they are not important to IRPs [25]. Still, design guidelines for IRPs are a good starting point when designing an RBP.

In the following, the similarities and, more prominently, some selected differences between IRPs and RBPs are described, and the implications for RBP design are discussed. For this comparison, only the more narrow group of implantable RBPs is considered.
1.3 Comparison to industrial rotary pumps

1.3.1 Similarity in the Cordier diagram

Based on similarities of turbomachines with high efficiencies, the Cordier diagram represents the general relation between the non-dimensional variable for speed and impeller diameter. The Cordier diagram displays data points for IRPs that had an optimal design and therefore achieved high efficiencies, from data collected over 60 years ago [43]. It uses the universally true relationship for IRPs between specific speed and specific diameter. The specific variables are used in pump theory to facilitate comparable, non-dimensional analysis.

Figure 1.8 shows the analytical and experimental Cordier curve from the literature. This diagram is still used today to define the optimal pump type based on the performance requirements in the design point, and to choose the rotor diameter or speed for best achievable efficiency [45]. Figure 1.8 also contains the calculated values for the four implantable RBPs based on their operational and geometric parameters. One can see that all four pumps meet the analytic curve for turbodynamic pumps quite closely. Based on this result, the underlying relationships for a rough performance estimation is similar between IRPs and RBPs.

1.3.2 Differences to RBPs

RBPs differ from IRPs in several aspects. A selection of the most prominent differences from literature is presented and discussed in the following: Size, bearing concept, working fluid, Reynolds number, operating conditions, design objectives, hydraulic efficiencies and leakage flow through clearance gap.

Size

RBPs have reached small sizes to fit in the cavity of the human thorax. Impeller diameters of the devices presented previously (1.2.2) range from 12 to 34mm [32]. RBPs can thus be seen as miniaturized IRPs [25].
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Figure 1.8: Cordier diagram with specific speed over specific diameter. The analytical and experimental cordier curve for rotary pumps [43] is compared with the entries of the four implantable RBPs (HVAD, HM3, HMII, Incor).

Bearing concept

RBPs can either have a contactless bearing through a combination of a passive magnetic bearing with a hydrodynamic or active magnetic bearing, or a mechanical ball-and-cup bearing. Thus, RBPs usually do not have a sealing to seal the rotating shaft from the stationary housing, as do IRPs. For IRPs, this leads to the consideration of sealing and lubrication designs. For RBPs, however, the contactless bearing concepts in particular, lead to severe restrictions in the freedom for the impeller design, due to the placement of passive magnets and grooved surfaces for hydrodynamic bearing placement in or on the impeller. For some RBPs, such as the HVAD, considerations regarding the placement of the hydrodynamic bearing surfaces and the passive magnets supposedly dominated the design of the impeller.
1.3 Comparison to industrial rotary pumps

Working fluid

The working fluid of RBPs is blood, which exhibits non-Newtonian behaviour. More specifically, viscosity decreases with increasing shear rates. This effect reaches its saturation for higher shear rates, as they are apparent in large blood vessels with shear rates above $100 \text{s}^{-1}$, where viscosity is shown to be constant [46]. The viscosity of blood is dependent on the hematocrit, which is the volume percentage of red blood cells in the blood. With pathological hematocrits down to 20% within the first months after LVAD implantation [47], the blood viscosity can range from 2.1 to 3.8 cP [48]. For the small gaps between blades and housing of an RBP, a cell migration effect has been observed [49], which means that the concentration of red blood cells in the gap decreased. This has been observed when the gap decrease from 200 to $50 \mu m$, but the mechanisms leading to the demixing processes of blood are still poorly understood [49].

The working fluid of IRPs is commonly a Newtonian fluid with low viscosities similar to that of water (1 cP at room temperature).

Reynolds number

The Reynolds number is the ratio of inertial forces to viscous forces in a fluid, and is used to predict flow patterns in different situations of fluid flow. Reynolds numbers for RBPs are only occasionally reported. Smith et al. reports average Reynolds numbers of $7.6 \times 10^4$ [50], whereas Bertram reports a range from $2.5 \times 10^4$ to $4.5 \times 10^4$ [51]. This is relatively low compared to IRPs that show Reynolds numbers between $10^6$ and $10^8$ [26] and the difference may have significant impact on the flow field in general and on the scaling effects from IRPs to RBPs [50].

Operating conditions

Commonly, a design point in the range of 5L/min and a mean head pressure of around 80mmHg are assumed for RBPs [32]. IRPs can have flow rates and head pressures that are orders of magnitude higher [26]. Furthermore, the application of IRPs is stationary with a constant speed against a constant head pressure. Dynamic operations, which include the effects of the fluid inertia, only play a minor role
in the process of starting up the pump, which is why dynamic conditions are not well investigated. RBPs are also operated at constant speeds, whereas the head pressure changes dynamically in every heart cycle in such way that the resulting flow rate dynamically changes in a wide range, as shown in Section 1.2.3. This dynamic operating range of RBPs implies that the optimization for only one design point is not applicable, and that the bearing technology and the motor must be able to handle dynamically varying loads during standard, all day operation.

Design objectives

Antaki et al. [52] derives 39 design objectives for the development of a pediatric RBP, which are also applicable to RBPs in general. He divides the objectives into the five categories: anatomic fit, performance, biocompatibility, reliability and manufacturability. Following such a high number of design objectives makes the design considerations complex. Moreover, several of the design objectives are contradictory, such as low hemolysis index and inherent recirculating [52].

Although the design objectives of IRPs go beyond meeting the operating point (a certain pump head and flow rate) at maximum possible efficiency rates, they are dwarfed by the complexity of design objectives for RBPs.

Hydraulic efficiencies

Hydraulic efficiency is defined as the ratio of mechanical input power to hydraulic output power. IRPs commonly have hydraulic efficiencies above 80%, and, depending on the design of the pump, efficiencies of up to 95% can be reached [53].

For RBPs, there is no general knowledge about achievable efficiencies, and specific values of state-of-the-art RBPs are rarely published. A simulation study showed an efficiency of 32% for the HVAD and 25% for the HMI [54]. In-vitro measurements for the early stage development of the HM3 show hydraulic efficiencies of up to 30% [55]. Other less well-known studies were published with pump efficiencies of 24% [56, 57] and 27% [58] hydraulic efficiency.
1.3 Comparison to industrial rotary pumps

The big difference in currently attainable hydraulic efficiencies between RBPs and IRPs leaves either a lot of optimization potential for the RBP design or suggests that there are some systematic reasons why the limit of hydraulic efficiencies for RBPs is lower than for IRPs.

Smith et al. (2004) [50] analyzed anonymized performance data for RBPs in a variety of applications. Maximum efficiencies of 65% were achieved. Since this study found much higher efficiencies, and because it was conducted before the rise of implantable RBPs, one has to assume that the bearing concepts, size and support duration of the tested RBPs differ substantially from RBPs considered for implementation today. In a more recent study by Mozafari et al. [59] with optimized pump geometries, high efficiencies of up to 70% were also achieved. However, very narrow gaps of 25 µm were selected and the bearing concept was not mentioned; as a result, this study also lacks comparability.

Small size alone cannot be the decisive factor for the limited efficiency, as higher values were reported in design variation studies for RBPs of comparable size [50, 59].

All requirements considered, hydraulic efficiencies of RBPs are not as high as those for IRPs.

**Leakage flow through clearance gap**

Leakage flow can occur through the clearance gap between impeller and housing and its flow direction is opposite to the main flow path.

Minimal clearance gap sizes between impeller and housing for the investigated RBPs are 22, 100, 130 and 500 µm for HVAD [60], HMII [32], Incor and HM3 [61], respectively. The clearance gap of the Incor is based on the author’s own measurements, as an official value has not been published. If one calculates the ratio of clearance gap to blade outlet height, the values are 0.25, 4, 8 and 14% for HVAD, Incor, HMII and HM3, respectively. Most of these values are comparably high, as efficient IRPs exhibit a clearance ratio of less than 1% [26].

In addition to the clearance gap above the impeller, some of the RBPs have a secondary flow passage through the center of the impeller which enables good washout of the bottom gap between housing and
impeller, but also leads to an additional another leakage flow. The main and the additional flow paths are exemplary illustrated for the HM3 in Figure 1.9. They are similar to the ones of the HVAD.

Consequently, with larger clearances, efficiency suffers [53]. This may partly explain the results presented in the previous section. Leakage flow in RBPs is somewhat desirable for good washout and the prevention of thrombus formation [62].

![Figure 1.9](image-url): Leakage flow passages above and below the HM3 impeller, as indicated by the black arrows. Grey arrows mark the main flow path due to the pumping function. The sketch of the HM3 is cut off, showing only the lower part of the pump.

### 1.3.3 Implications for pump design

When comparing RBPs and IRPs, one can find differences that might be a matter of scaling or not fully exploited design potentials on the one hand. On the other hand, differences might result from the different application and its imposed requirements. Surely, the multiple design objectives, contactless bearing concept, non-Newtonian working fluid, dynamic operating condition and lower Reynolds numbers make RBPs distinguishable from IRPs. The fact that no in-depth design knowledge is available for RBPs clearly shows a need to further add specific design knowledge for RBPs to the existing knowledge for IRPs. Overall, this could prevent many trial and error iterations.
1.4 Objective and contribution of this thesis

The overall objective of this thesis is to model and compare the hydraulic behavior of RBPs under realistic pressure conditions of the cardiac cycle (first study) and to relate effects of typical RBP design parameters to indicators of hemocompatibility (second study). To make the in-vitro testing environment used throughout this thesis more realistic and reproducible, an additional objective was to control the viscosity of the working fluid and thus accurately mimic different viscosities of blood (third study).

This thesis contributes to the design and testing knowledge for RBPs and has implications for the design of new RBPs and also for a better understanding of existing RBPs. The differences between RBPs and IRPs and the lack of explicit design knowledge for RBPs

that are especially critical in the development of implantable devices, where many of the hemocompatibility requirements receive their final validation either in in-vivo trials or, even later, in clinical studies.

For this thesis, we devote special attention to some of the differences in design objectives for RBPs and IRPs, namely the design for sufficient biocompatibility or, more precisely, hemocompatibility and operation under dynamic operating conditions matching clinical application.

Previous RBP design research of a similar orientation as this thesis has investigated the implications of specific devices currently in development, but a few studies also provide more general knowledge by comparing a larger number of designs: For example, Smith et al. [50] collected and compared the efficiency and performance curves for several anonymized designs in vitro. Mozafari et al. [59] varied the blade number and the blade outlet angle of a conceptual RBP to investigate their effect on efficiency in vitro and the effect on hemolysis in a CFD simulation. Korakianitis et al. [45] varied a number of geometric design parameters of a conceptual RBP and compared the dimensionless characteristics of specific speed and specific diameter. Chan et al. [62] investigated relationship between leakage flow rate and the dimensionless representation of geometric and performance parameters.
have been discussed in the previous section. As one of the design objectives of RBPs, hemocompatibility is a contributor to complications and adverse events related to LVADs. The flow field is strongly believed to influence their hemocompatibility. Regarding performance as another design objective of RBPs, the hydraulic behavior under dynamic pressure conditions matching clinical application determines the resulting flow rate and subsequently the flow field in the pump.

The detailed objectives and contributions are described in the following section for each of the studies. In the following main chapters, the original content from the published or accepted studies is presented.

First study - Chapter 2

The objective of the first study was to characterize and compare the hydraulic characteristics of several current implantable RBPs under clinically relevant dynamic operating conditions. This is the first study in which four current implantable RBPs were compared using the same setup. The main focus was on analyzing the flow rate occurring in a cardiac cycle resulting from either full support conditions in severe heart failure or partial support conditions for more healthy patients. It is assumed that large deviation from the design flow rate is related to increased disturbance of the flow field with respective consequences for hemocompatibility.

One aim was to define a mathematical model that universally represents the static and dynamic hydraulic behavior of RBPs. Several models have been introduced for modeling specific pumps of either axial-flow or radial-flow type and these are mainly based on empirics, but not all include dynamic behavior and none model negative flow rates. Unique to our approach is that the defined model covers the full range down to low negative flow rates, is applicable independent of the pump type as well as the specific pump design, and takes explicitly existing phenomena of pump theory described in the literature into account.

Another aim was to clearly differentiate between the hydraulic characteristics of the pump itself and the periphery that connects the pump to the aorta and the LV.
1.4 Objective and contribution of this thesis

This study has been published in *IEEE Transactions on Biomedical Engineering* and can be cited as follows:


Second study - Chapter 3

The objective of the second study was to determine the effects of typical design parameters of an RBP on indicators of hemocompatibility using a simulation of computational fluid dynamics (CFD). Considered metrics for hemocompatibility based on the velocity and shear field were Lagrangian and Eulerian indicators of hemolysis, thrombogenicity factors and von Willebrand Factor (VWF) degradation. Analysis was done with a quantitative comparison of achieved values for the overall design on the one hand, and with a qualitative analysis of the local effects using visualization of the streamlines, high shear stresses and low flow zones on the other.

In order to make the results transferable and reproducible, a universal baseline impeller and respective housing was designed according to the guidelines for turbomachinery design, using the boundary conditions of size and hydraulic performance of today’s RBPs. The resulting design was manufactured with 3D-printing and tested on a mock circulation for validation of the hydraulic results of the simulation model.

Isolated changes of single design parameters allowed the investigation of the correlation of the different hemocompatibility metrics. Therefore, another aim of this study was to investigate whether metrics meant to relate to the same hemocompatibility issue lead to similar results. Additionally, the correlation of the hemocompatibility metrics with hydraulic characteristics such as achieved flow rate, hydraulic efficiency and leakage flow rate was analyzed.

This study was published in *Annals of Biomedical Engineering* and can be cited as follows:
1 Introduction


**Third study - Chapter 4**

The objective of the third study was to make the testing environment for ventricular assist devices more realistic and reproducible by making it possible to accurately mimic different viscosities of blood in a MC. MCs are test benches that allow researchers to analyze the interaction of LVADs with the simulated human physiology through a hardware interface. Commonly, a glycerol-water mixture is used as the working fluid. In the two previous studies outlined above, the MC was used for its intended purpose but also for the more simple purpose to apply controlled static and dynamic pressure signals to identify the hydraulic characteristics of RBPs. The first and the second study both made use of the viscosity control feature.

The aim of this study was to implement and test the control of viscosity and show its potential and limitations. To do this, the temperature dependency of the viscosity of the glycerol-water mixture was used to change hematocrit for the same mixture by inducing changes in temperature. A new method of flow probe calibration was introduced and the dependency on viscosity, temperature and flow rate itself was mapped using linear regression. The implemented control shows the influence of a varying viscosity in the range of realistic hematocrits on the static hydraulic characteristics of an RBP on the one hand and on the static power characteristics of an RBP on the other. This study addresses whether and under which conditions a viscosity control is crucial or only has a minor influence.

This study was published in *Artificial Organs* and can be cited as follows:
1.4 Objective and contribution of this thesis

2 Hydraulic Characterization of Implantable Rotary Blood Pumps

The content of this chapter has been accepted for publication in IEEE Transactions on Biomedical Engineering.

2.1 Introduction

LVADs have become the therapy of choice for the treatment of end-stage HF if donor hearts are not available or patients are ineligible for HTx [5]. Survival rates are at 70% after two years of LVAD support and only 20% of these patients remain free from major adverse events such as infection, major bleeding events, or cerebral strokes [13]. Consequently, the patient’s quality of life is limited [65] and the costs of the therapy remain high due to hospital readmissions and follow-up care [66]. Current research focuses on (RBPs), as they represent 97% of the LVADs implanted during the last five years [13]. The causes of the high incidence of adverse events with RBPs and, more specifically, the influence of their inherent hydraulic characteristics on the clinical outcome are part of an ongoing discussion [28, 67].

The static hydraulic characteristics of RBPs depend on the pump type (axial flow, radial flow or mixed forms) and the individual pump geometry. The flow rate as the output of an RBP results from its hydraulic characteristics, the pump setting (rotational speed), and the hemodynamic boundary conditions (head pressure) at the interface of the pump and the cardiovascular system. The relation of flow rate \( Q \) and head pressure \( H \) at constant speeds is described with static performance curves in the so-called HQ diagram. Axial-flow pumps, which make up for two thirds of LVAD implantations in the USA [13], are regarded to have a rather steep HQ curve compared to the rather flat HQ curve common for radial-flow pumps [68], which are
2 Hydraulic characterization of implantable rotary blood pumps

also referred to as centrifugal pumps. An RBP with a flat HQ curve is more pressure-sensitive, which means the same change of head pressure leads to a larger change in flow rate than for a pump with a steep HQ curve.

Remarkably, the HQ diagrams for the same pump measured by different researchers vary substantially. Figure 2.1 shows the relationship of head pressure and flow rate for a radial RBP (HVAD, Medtronic, Minneapolis, MN, USA), published by different research groups [36, 48, 69–71]. The resulting flow rate at a head pressure of 80 mmHg ranges from 4.7 to 8.3 L/min. The obvious differences between the HQ curves can have various reasons, such as varying viscosities of the working fluid, tubing length and curvature, position of the pressure sensors as well as accuracy and calibration of flow and pressure sensors.

Next to the static properties, the dynamic properties of an RBP contribute to the overall pump performance. Together with the steepness of the HQ curve, the fluid inertia in the pump strongly influences its dynamic properties. In the clinical setting, dynamic changes in head pressure result from the pulsatile LV pressure caused by the remaining heart function and the arterial pressure. This leads to a frequency-dependent attenuation of the flow rate following a head pressure change, that causes a hysteresis around the static HQ curve [72].

When considering the pump hydraulics in the implanted situation, one needs to additionally take into account that there are peripheral components connected to the RBP: The length, diameter, and curvature of cannulas, connectors and outflow grafts influence its hydraulic resistance and the fluid inertia. Therefore, the output flow rate is diminished in static as well as in dynamic conditions compared to investigations looking solely at the pump.

As an additional factor contributing to the hydraulic pump performance in the clinical arena, the pump speed is set by the clinician to achieve the desired extent of support. In full support at higher pump speeds, the cardiac output is generated by the pump and not delivered through the aortic valve. By contrast, in partial support at lower speeds the cardiac output is additionally ejected through the aortic valve at a lower pump output. In recent years, the strategy of
operating RBPs at lower speeds and therefore lower pump flow rates was pursued to achieve aortic valve opening and to treat patients with less advanced heart failure [73].

The hydraulic characteristics have been modelled mathematically for axial-flow RBPs [35,74-76] and radial-flow RBPs [69,77-80] to develop flow rate estimation algorithms and to simulate hemodynamic influences. All the mathematical models have in common that the head pressure at zero flow is modelled with a quadratic relationship to pump speed as described by the Euler equation from turbomachinery [35]. Other than that, the terms of each model are based on empirics and vary greatly, in fact only two out of the ten referenced models use the same mathematical equation [35,77]. The periphery was considered in one of the models [79] and the dynamics were considered in half the models [35,69,74,75,77]. None of the models cover the region of negative flow rate.

All these variations in static and dynamic properties, model structure and periphery described above render a direct comparison of different pumps difficult. This difficulty highlights the need for a standardized approach to compare the characteristics and hemodynamic influences of RBPs with each other.

In our study, we aimed at an improved mathematical model of the hydraulic pump behavior on the one hand and at a systematic comparison of four current RBPs at clinically relevant, dynamic operating conditions on the other hand. Therefore, we first developed a mathematical model for RBPs that covers the region of negative flow rates based on physical principles described in turbomachinery theory. With this model, we experimentally identified the static and dynamic properties of four RBPs that are most commonly used clinically, including their periphery. Secondly, we compared the four RBPs regarding their hydraulic properties in conditions that are comparable to the clinical setting. In this way, we highlighted the impact of the hydraulic properties of an RBP on flow conditions and discuss the potential consequences for hemocompatibility.
2 Hydraulic characterization of implantable rotary blood pumps

Figure 2.1: Relation of head pressure to flow rate for the HVAD at stationary conditions of 3000 rpm described by six different research groups. Most studies show experimental results [48, 70, 71, 76], two present mathematical models derived from measurements [36, 69]. While most of the experiments were conducted with a blood-analog fluid like dextrose solution or a glycerol-water mixture, one also used heparinized porcine blood [76].

2.2 Methods

Four implantable RBPs were investigated in this study. Two radial-flow and two axial-flow pumps were selected to achieve a representative diversity of currently used LVADs in terms of pump type and bearing technology. The radial-flow pumps are the hydrodynamically and passive magnetically levitated HVAD (Medtronic, Minneapolis, MN, USA) and the active magnetically levitated HM3 (Abbott, Abbott Park, IL, USA). The two axial-flow pumps are the HMIII (Abbott, Abbott Park, IL, USA) with a mechanical ball-and-cup bearing, and the Incor (BerlinHeart, Berlin, Germany) with an active magnetic bearing.
2.2 Methods

First, we present the experimental setup and the identification procedure, then we introduce the physical principles from turbomachinery before we integrate them in the mathematical models for the hydraulics of pump and periphery. Finally, we introduce the numerical model of the cardiovascular system used for evaluating and comparing the hydraulic pump behavior.

2.2.1 Experimental setup

To identify the static and dynamic hydraulic properties of different LVAD systems, a test bench setup presented earlier [81] was adapted. Two pressure-controlled fluid reservoirs constituted the physical interface to the blood pump under evaluation. The fluid reservoirs were connected via a bidirectional backflow pump (‘Water Puppy’ self-priming bilgepump 24V, Xylem Jabsco, Hoddesdon, UK), which controlled the fluid level in the reservoirs. The temperature was adjusted to \(37 \pm 0.5^\circ\text{C}\) to keep the working fluid (47 mass-% glycerol) at a viscosity of \(3 \pm 0.1 \text{cP}\), which was constantly monitored with a viscometer [48]. The flow rate through the blood pump was measured with a clamp-on flow probe (TS410/ME-11PXL, Transonic Systems, Ithaca, NY, USA). The pressures were measured directly before and after the blood pump (at less than 20 mm distance), as shown in Figure 2.2 (TruWave, Edwards Lifesciences, Irvine, CA, USA) and in the reservoirs (PN2009, IFM Electronic GmbH, Essen, Germany). All sensors were calibrated before the experiments using the calibration procedures described earlier [48].

The pump periphery such as inlet and outlet elbows or grafts were mimicked by 3D-printed cannulas of similar geometry and additional tubing. Tygon tubing with clinically relevant dimensions with a length of \(200 \pm 10 \text{mm}\) and an inner diameter of \(12.7 \text{mm}\) was used. The elbow connectors for the two axial-flow pumps were reverse-engineered and a small access hole for the pressure measurement was included. The connectors were then 3D-printed from photopolymeric resin (FullCure 720, Objet-Stratasys Inc., Eden Prairie, MN, USA), which resulted in small deviations of the inner diameter compared to the original connectors by a maximum of 7%. Figure 2.2 shows the setup for each of the pumps with connectors and tubing attached to the pressure
reservoirs. For the radial-flow pumps (see top row of Figure 2.2), we defined the head pressure over the periphery from the pump outlet (D) to the outlet reservoir (G). For the axial-flow pumps (see bottom row of Figure 2.2), the pressure drop over the two elbow connectors (B) was additionally included. This was achieved by adding up the pressure difference between reservoir (F) and pressure transducer (C), and between pressure transducer (D) and reservoir (G).

The setup permits the application of static and dynamic test signals to the inlet and outlet of the pump, respectively, as well as hardware-in-the-loop simulations of the cardiovascular system in real time where the LV and aortic pressure were applied to the fluid reservoirs [81].
2.2 Methods

2.2.2 Experimental procedure

Static identification

For the static identification, a staircase ramp of the head pressure was performed for each pump at four speeds (see Figure B.1 in the Appendix B). The head pressure over the two fluid reservoirs ranged from a negative pressure of $-30$ to $30 \text{mmHg}$ above shut-off head (SOH). The step-width of the staircase ramp was modified depending on the shape of the HQ curve, varying from $2 \text{mmHg}$ for the flat regions to $10 \text{mmHg}$ in the steep regions, which resulted in a range of 20–47 steps per staircase ramp over all pumps. The duration of each step was $15 \text{s}$ to achieve stationary conditions.

Dynamic identification

The input for the dynamic identification experiments was a sinusoidal sweep in head pressure, with a logarithmic increase of frequency from $0.1$ to $20 \text{Hz}$ over a time frame of $200 \text{s}$. The dynamic experiments were repeated three times for each of the four speeds with three different mean operating points and amplitudes, defined relative to the respective SOH at a certain speed: 1) $75\% \text{SOH} \pm (25\% \text{SOH} + 5 \text{mmHg})$; 2) $50\% \text{SOH} \pm (50\% \text{SOH} + 5 \text{mmHg})$; 3) $25\% \text{SOH} \pm (25\% \text{SOH} + 5 \text{mmHg})$.

2.2.3 Principles from turbomachinery

To derive a universally applicable structure for a model of the RBP hydraulics, the relationship between the well-known principles from turbomachinery and the link to our final model are introduced in the following. Corresponding to a common convention in the field of RBPs and in the clinical environment we used the head pressure ($H$), the flow rate ($Q$), and the pump speed ($n$) with the units mmHg ($1 \text{mmHg} = 133.32 \text{Pa}$), L/min, and revolutions per minute (rpm), respectively.
2 Hydraulic characterization of implantable rotary blood pumps

Theoretic head pressure

Independently of pump type, the Euler head equation defines the theoretical head pressure $H_{Eul}$ of a rotary pump for incompressible fluids. The variables contained are the meridional discharge velocity $c_{m2}$, the circumferential velocity $u_2$, the discharge angle $\beta_2$, and the density $\rho$ [44]. For the hydraulic model, we transformed this equation such that all variables that are independent of the flow rate and the speed are summarized in two constants ($k_1, k_2$):

$$H_{Eul} = \rho u_2 (u_2 + c_{m2} \cot \beta_2) = k_1 n^2 - k_2 nQ$$

(2.1)

Friction loss

The theoretical head pressure in Equation 2.1 is reduced by fluid friction and incidence losses. The fluid friction losses $H_{fri}$ quadratically increase with the flow rate [44] and can be combined in a single term with the constant $k_3$:

$$H_{fri} = k_3 Q^2$$

(2.2)

Incidence loss

When the pump is operated off the design point, a deviation of flow angle and blade angle occurs and causes flow detachment at the leading and trailing edge of the blade. This results in eddy and separation losses, which are commonly referred to as incidence losses. The resulting head pressure loss $H_{inc}$ can be modeled by a constant $k_4$ and the variable $q_{des}$ for the design flow rate [44]. As the design flow rate $q_{des}$ is linearly dependent on pump speed [53], we generalized the head pressure loss with three constants ($k_5-k_7$):

$$H_{inc} = k_4 (Q - q_{des})^2 = k_5 Q^2 - k_6 nQ + k_7 n^2$$

(2.3)

Part-load recirculation

The combination of the theoretic head pressure $H_{Eul}$ (2.1) and hydraulic losses $H_{fri}$ (2.2) and $H_{inc}$ (2.3) does not yet lead to a model that
2.2 Methods

is applicable in praxis [44]. An omitted effect is the part-load recirculation in the blade channels, which start at medium flow rates (below the design flow rate) and intensify towards zero flow rate. These recirculations, especially at the outer radius of the impeller inlet section, partly block the blade channel and thus lead to a change in the effective diameter of the blade channel. This effect results in an increase in head pressure that can be described partly by a quadratic relation to the decreasing effective diameter at the inlet section [53]. Therefore, assuming the effective diameter decreasing linearly with a decreasing flow rate, we approximate the head pressure increase $H_{rec}$, starting at the transition between full and part load with

$$H_{rec} = \begin{cases} 0, & Q > q_{inf} \\ R_{rec} (Q - q_{inf})^2, & Q < q_{inf}. \end{cases} \quad (2.4)$$

The inflection flow rate $q_{inf}$ further indicates a linear relationship to the speed, and was identified individually for each pump:

$$q_{inf} = k_{inf} n \quad (2.5)$$

with a constant value of $k_{inf}$.

**Fluid inertia**

It was previously shown that the dynamic change in head pressure $H_{dyn}$ in an RBP can be captured by a term related to the first derivative of the flow rate [35, 69, 75, 77] as in

$$H_{dyn} = L \frac{dQ}{dt} \quad (2.6)$$

with the constant $L$ for the fluid inertia.

**2.2.4 Hydraulic models for pump and periphery**

To derive a universally applicable hydraulic model structure for RBPs, in the following we combine the effects previously described.
Pump model

To obtain the head pressure $H$ over the pump, we combined the equations by subtracting (2.2), (2.3), (2.6) and adding (2.4) from and to the Euler head (2.1), respectively:

$$H = H_{Eul} - H_{fr} - H_{inc} - H_{dyn} + H_{rec} \quad (2.7)$$

The resulting equation is

$$H = an^2 + R_1nQ - R_2Q^2 - L \frac{dQ}{dt} + \begin{cases} 0, & Q > q_{inf} \\ R_{rec}(Q - q_{inf})^2, & Q < q_{inf} \end{cases} \quad (2.8)$$

with the new constants $a$, $R_1$, and $R_2$ that result from combining the parameters $k_1$ to $k_7$.

For flow rate estimation, we discretized 2.8 using the linear forward approximation of the derivate and then resolving it to

$$Q_{est}(k + 1) = Q_{est}(k) + \frac{T_s}{L} \left( an^2 + R_1nQ_{est}(k) - R_2Q_{est}(k)^2 \right. \\
- H(k) + \begin{cases} 0, & Q_{est}(k) > q_{inf} \\ R_{rec}(Q_{est} - q_{inf})^2, & Q_{est}(k) > q_{inf} \end{cases}. \quad (2.9)$$

The index $k$ ranges from 1 to the number of samples acquired minus 1. The initial value of $Q_{est}$ has to be set and $T_s$ is the sampling time.

Model of periphery

The behavior of the periphery was consolidated in one equation assuming a hydraulic loss due to fluid friction and a frequency-dependent behavior due to inertia, which leads to

$$H_{per} = -L_{per} \frac{dQ}{dt} + \begin{cases} -R_{per}Q^2, & Q < 0 \\ R_{per}Q^2, & Q > 0 \end{cases}. \quad (2.10)$$
The discretization was executed according to 2.9 and leads to

\[
Q_{p,est}(k+1) = Q_{p,est}(k) + \left( \frac{T_s}{L_{per}} \right) - \left( H(k) \right) + \begin{cases} 
-R_{per}Q_{p,est}(k)^2, & Q_{p,est}(k) < 0 \text{L/min} \\
R_{per}Q_{p,est}(k)^2, & Q_{p,est}(k) > 0 \text{L/min} 
\end{cases}. \quad (2.11)
\]

### 2.2.5 Identification process

The static parameters \((a, R_1, R_2, L, R_{per}, k_{inf})\) and the dynamic parameters for fluid inertia \((L, L_{per})\) were determined over the entire operating range of pump speed, flow rate, and head pressure for each of the four pumps. The pressure head was measured separately for the pump and its periphery according to the positioning of the pressure sensors shown for each pump in Figure 2.2. The measured pressure \(p_{sta}\) in the tubing and the connectors was corrected with the hydrodynamic pressure calculated based on the Bernoulli equation to obtain the total pressure

\[
p_{tot} = p_{sta} + \rho \left( \frac{Q}{A} \right)^2 \quad (2.12)
\]

with the density \(\rho\) and the cross-sectional area \(A\) at the location of the pressure measurement.

**Static identification**

For each static measurement, the last 5 seconds of the flow rate and the head pressure signal of every staircase step were averaged for further signal processing. Using a simplex search algorithm [82], \(k_{inf}\) was iteratively optimized with the root mean square error (RMSE) between the respective estimated and measured signal as the objective function. In each iteration the constants \(a, R_1, R_2, R_{per}\), were fitted using the least squares method.
Dynamic identification

To identify the dynamic parameters $L$ and $L_{\text{per}}$ the flow rate and head pressure signals of the sinusoidal sweep measurements were low-pass filtered with a cut-off frequency of 25 Hz. For each of the 12 measurements (3 operating points for each of the 4 speeds), the inertia $L$ resp. $L_{\text{per}}$ was iteratively identified using a simplex search method and the RMSE as the objective function. The results of each of the measurements were used for a 12-fold cross-validation [83], which yielded the average values of RMSE and $L$ resp. $L_{\text{per}}$ for each pump including the respective standard deviation (SD).

2.2.6 Evaluation and comparison of hydraulic pump properties

A numerical model of the cardiovascular system was used to generate the input signals and boundary conditions for comparing the hydraulic behavior of the four pumps.

Numerical model of the cardiovascular system

A numerical model of the cardiovascular system in combination with the hydraulic model of the RBP was implemented in MATLAB/Simulink (The MathWorks, Natick, MA, USA) to mimic realistic physiological conditions of full support (aortic valve closed) and partial support (aortic valve opens). The heart was modeled according to Colacino et al. [84] with a time-varying elastance and non-linear end-systolic as well as an end-diastolic pressure-volume relationship. The ventricular function and the cardiovascular parameters were adjusted to meet patient data of Gupta et al. [85] a heart rate of 91 bpm, a left atrial pressure of 13 mmHg, a mean aortic pressure of 84 mmHg, and a right atrial pressure of 10 mmHg. Finally, the cardiac contractility and the pump speed (HVAD) were adjusted such that a flow rate of 5 L/min was achieved during full support [85] and of 3 L/min during partial support [86] while maintaining a cardiac output of 5 L/min in both support conditions.
2.3 Results

Comparison of hydraulic behavior

The resulting support conditions were used to compare the pumps. For the static comparison, the inertia was not considered, therefore the speed was chosen such that the HQ curve of the pump including periphery is forced through the average operating point. For the dynamic comparison, the speed of each pump was adjusted such that the same operating point was achieved on average over one cardiac cycle. The resulting loop in the HQ diagram was displayed for each pump with and without periphery and augmented by the respective static models. In order to quantify and visualize the time duration at a certain flow rate, the flow rate for each pump was displayed in a histogram.

2.3 Results

2.3.1 Model of pump and periphery

Model parameters

In Table 2.2 the parameters identified for all pumps and their respective periphery are listed. The model 2.8 derived was applicable to all four pumps independently of axial-flow or radial-flow type.

Model accuracy

The models of the hydraulic pump characteristics accurately mimic the static measurement results with an average RMSE of $2.6 \pm 0.5$ mmHg over all pumps (see also Figure B.1). If the hydraulic model (2.8) is identified without part-load recirculation (2.4) and therefore the inflection point is not mapped, the RMSE almost doubles to $5.1 \pm 1.5$ mmHg. If only positive flow rates are considered, a model without part-load recirculation performs only slightly worse with an RMSE of $3.2 \pm 1.1$ mmHg. For the dynamic identification, the cross validation revealed an average RMSE was $0.38 \pm 0.14$ L/min. For three of the pumps, the parameter $L$ showed only small deviations for different operating points with an average SD of $1.2$ mmHg·s$^2$/L; whereas in the HVAD a larger SD of $4.4$ mmHg·s$^2$/L was observed.
2 Hydraulic characterization of implantable rotary blood pumps

Table 2.1: RMSE for the static and the dynamic identification of pump and periphery. Static RMSEs are given in mmHg and dynamic RMSEs in L/min.

<table>
<thead>
<tr>
<th>System</th>
<th>Model</th>
<th>Unit</th>
<th>HVAD</th>
<th>HM3</th>
<th>HMII</th>
<th>Incor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump</td>
<td>Static</td>
<td>mmHg</td>
<td>2.5</td>
<td>3.4</td>
<td>2.2</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>Dynamic</td>
<td>L/min</td>
<td>0.43 ± 0.18</td>
<td>0.39 ± 0.15</td>
<td>0.36 ± 0.17</td>
<td>0.19 ± 0.06</td>
</tr>
<tr>
<td>Periphery</td>
<td>Static</td>
<td>mmHg</td>
<td>1.2</td>
<td>1.3</td>
<td>1.6</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>Dynamic</td>
<td>L/min</td>
<td>0.40 ± 0.19</td>
<td>0.32 ± 0.15</td>
<td>0.24 ± 0.12</td>
<td>0.17 ± 0.06</td>
</tr>
</tbody>
</table>
Table 2.2: Parameters identified for the hydraulic model of the pumps 2.8 and their respective periphery 2.10. The inertia $L$ is indicated with a standard deviation (SD) of the cross-validation results.

<table>
<thead>
<tr>
<th>System</th>
<th>Parameter</th>
<th>Unit</th>
<th>HVAD</th>
<th>HM3</th>
<th>HMII</th>
<th>Incor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump</td>
<td>$k_{inf}$</td>
<td>(L/min)/rpm</td>
<td>$1.470 \cdot 10^{-4}$</td>
<td>$2.596 \cdot 10^{-4}$</td>
<td>$3.593 \cdot 10^{-4}$</td>
<td>$3.981 \cdot 10^{-5}$</td>
</tr>
<tr>
<td></td>
<td>$a$</td>
<td>mmHg/rpm$^2$</td>
<td>$1.331 \cdot 10^{-5}$</td>
<td>$3.458 \cdot 10^{-6}$</td>
<td>$9.536 \cdot 10^{-7}$</td>
<td>$2.774 \cdot 10^{-6}$</td>
</tr>
<tr>
<td></td>
<td>$R_1$</td>
<td>mmHg/(rpm·L/min)</td>
<td>$-8.732 \cdot 10^{-4}$</td>
<td>$7.295 \cdot 10^{-4}$</td>
<td>$3.209 \cdot 10^{-4}$</td>
<td>$-1 \cdot 10^{-3}$</td>
</tr>
<tr>
<td></td>
<td>$R_2$</td>
<td>mmHg/(L/min)$^2$</td>
<td>$0.7667$</td>
<td>$2.245$</td>
<td>$0.864$</td>
<td>$1.774$</td>
</tr>
<tr>
<td></td>
<td>$R_{rec}$</td>
<td>mmHg/(L/min)$^2$</td>
<td>$4.762$</td>
<td>$3.580$</td>
<td>$3.070$</td>
<td>$3.753$</td>
</tr>
<tr>
<td></td>
<td>$L$</td>
<td>mmHg·s / L</td>
<td>$18.74 \pm 4.37$</td>
<td>$17.00 \pm 1.16$</td>
<td>$22.97 \pm 1.20$</td>
<td>$32.88 \pm 1.29$</td>
</tr>
<tr>
<td>Periphery</td>
<td>$R_{per}$</td>
<td>mmHg/(L/min)$^2$</td>
<td>$1.093 \cdot 10^{-1}$</td>
<td>$1.244 \cdot 10^{-1}$</td>
<td>$3.833 \cdot 10^{-1}$</td>
<td>$3.154 \cdot 10^{-1}$</td>
</tr>
<tr>
<td></td>
<td>$L_{per}$</td>
<td>mmHg·s$^2$ / L</td>
<td>$14.15 \pm 4.75$</td>
<td>$13.38 \pm 1.39$</td>
<td>$20.30 \pm 1.59$</td>
<td>$18.35 \pm 0.84$</td>
</tr>
</tbody>
</table>
Figure 2.3 shows the typical static and dynamic behavior of the model derived in comparison to in-vitro measurements. The model tracks the measured flow signals over one cardiac cycle with only small deviations.
2.3 Results

![Graph showing flow rate (L/min) vs. head pressure (mmHg) for Static behavior (1800 rpm, 2400 rpm, 3000 rpm, 3600 rpm) and Flow rate (L/min) vs. Time (s) for Dynamic behavior with model and measured data.]

**Figure 2.3:** Comparison of in-vitro measurements with the mathematical model developed for the HVAD under static (left) and dynamic conditions (right). Dynamic behavior is indicated for one cardiac cycle in partial support at 2100 rpm.

### 2.3.2 Comparison of hydraulic pump properties

#### Numerical model of the cardiovascular system

Figure 2.4 shows the resulting signals of ventricular and aortic pressure (top row) and pump flow rate in relation to head pressure (bottom row) for one cardiac cycle. The average operating point of the RBP for full support was 5 L/min and 63 mmHg and for partial support 3 L/min and 45 mmHg. The minimum and maximum head pressure for full support were 40 and 78 mmHg and for partial support −1 and 88 mmHg, respectively. The HQ loops are passed through in counterclockwise direction.

#### Static properties

Figure 2.5 indicates the static periphery models for all four pumps and illustrates an exemplary comparison of the HQ curves of pumps with and without periphery. The periphery pressure losses at a flow rate of 8.1 L/min, which is the maximum flow rate achieved in peak systole in partial support for all pumps, are highest for the two axial-flow pumps with 24 mmHg (Incor) and 27 mmHg (HMII). At the same flow rate, the two radial-flow pumps have a periphery pressure loss of 8 mmHg.
Figure 2.4: One cardiac cycle of the full-support and partial-support condition simulated. The top row shows aortic and LV pressures, the bottom row shows exemplary the relation of head pressure and flow rate through the LVAD. The letters refer to different points in time of the cardiac cycle: A) start of systole with the closing of the mitral valve, B) start of diastole, C) mitral valve opens. For partial support, the time point B) corresponds to the closing of the aortic valve.

(HM3) and 9 mmHg (HVAD).

Figure 2.6 shows the static hydraulic pump models including the periphery for full support and partial support. The axial-flow pump HMIII without periphery indicates the flattest HQ curve in the average operating point with a steepness of −9.5 and −5.2 mmHg/(L/min), closely followed by the HVAD with −9.8 and −6 mmHg/(L/min) for full and partial support, respectively. In the higher flow regions, the HVAD and the HMIII with periphery indicate similar hydraulic properties. The increase in the head pressure at lower flow rates probably
2.3 Results

Figure 2.5: Resulting model of the pressure loss due to the respective periphery of each pump. The graph on the right side shows exemplarily the effect of the periphery on the HQ curve. Here, the HM3 at 5400 rpm and the HMII at 9100 rpm are shown for solely the pump (solid lines) and the pump with periphery (dashed lines).

due to part-load behavior (2.10) is most pronounced in the HMIII. The steepness at the average operating point for each pump with and without periphery is listed in Table B.1.

Dynamic properties

Figure 2.7 shows the HQ loops of each pump for one cardiac cycle, which display substantial differences between the pumps, between full and partial support, as well as with and without periphery. In full support, the flow pulsatility, defined as the difference between minimum and maximum flow rate, ranges from 1.2 L/min for the Incor to 3.2 L/min for the HVAD. In partial support, the flow pulsatility is highest (9.1 L/min) for the HVAD and lowest (4.1 L/min) for the Incor. The HVAD and the HMIII, featuring the flattest HQ relationships, indicate the highest deviation of flow pulsatility between the dynamic HQ curves and the static ones (see Table B.2). The static and dynamic changes due to the periphery are largest in these pumps as well.

Figure 2.8 shows the histograms of the flow rate for one cardiac cycle in full and partial support, as presented in Figure 2.7. During partial support, for all pumps more than half of the cardiac cycle is taking place at flow rates of less than 2.5 L/min. For the HVAD, even flow
Hydraulic characterization of implantable rotary blood pumps

Figure 2.6: Resulting static models for the pumps including periphery at full and partial support. The average operating point for full support is defined at 5 L/min and 63 mmHg, for partial support it is 3 L/min and 45 mmHg, respectively. The speeds that were set to achieve those operating points for the HVAD, HM3, HMII and Incor for full support are 2600, 5400, 9100 and 7400 rpm, and for partial support are 2000, 4000, 7200 and 5400 rpm, respectively. All speeds are rounded to 100 rpm.

rates below 1 L/min make up for 44% of the cardiac cycle, whereas in the Incor the flow rate never falls below this value. During partial support, flow rate values below zero were reached during diastole for all pumps except the Incor.

For all pumps and support modes, the histogram peaks at both edges of the distribution. If those edges are characterized as the highest and the lowest 10% of flow range, they account for about 50% of the cardiac cycle, the same for both partial and full support.

2.4 Discussion

In this study, the static and dynamic hydraulic behavior of four clinically used RBP-equipped pumps was characterized with the same experimental pro-
Figure 2.7: HQ loop of each pump for one cardiac cycle in full and partial support. The top row shows the response to the physiological boundary condition of full support, the bottom row displays partial support. Each graph contains the dynamic HQ loop of the pump and of the pump including periphery, as well as the corresponding static HQ curve in dashed lines, respectively. The speeds set to achieve those operating points for the HVAD, HM3, HMII and Incor for full support are 2600, 5500, 9200 and 7400 rpm, and for partial support are 2200, 4500, 7400 and 5600 rpm, respectively. All speeds are rounded to 100 rpm.
toool and compared to each other. The newly developed hydraulic model is discussed in the following, with an emphasis laid on part-load recirculation. We compare the hydraulic characteristics of the four RBPs, elaborate the differences between axial-flow and radial-flow pump types in terms of flow pulsatility and discuss the potential implications for hemocompatibility.

2.4.1 Model of pump and periphery

Our modelling approach was based on principles that are well described in turbomachinery literature. The same model was applicable for both axial-flow and radial-flow pumps, and the validation results did not show a tendency to yield better fits for one or the other pump type. The overall RMSEs for the dynamic models are comparable to those published in other studies that focused on a single pump [35]. We can deduct that a model based on turbomachinery theory covers the characteristics of an RBP satisfactorily.

The resulting model structure without part-load consideration was similar to models presented earlier [35, 69, 74, 75, 77]. In addition, our approach also covers the low and negative flow region with a high accuracy: The hydraulic model developed was split at the inflection point of the HQ curve and an additional term was added towards lower flow rates, mimicking expected part-load recirculation. The position of the inflection point $q_{rec}$ varies with speed and for each pump (see also Figure B.1). Such behavior and the resulting shape of the HQ curve are well known in conventional pump theory and are specifically common for axial-flow pumps. Radial-flow pumps typically show an inflection point around a flow rate of zero [44], but can also shift into the low-flow region depending on the specific blade and volute geometry [53]. This inflection point has also been described in the RBP context for another axial-flow pump, the MicroMed-DeBakey pump [35], however, it was not incorporated into a model. If the part-load recirculation and the resulting inflection point is not taken into account, the average estimation error almost doubles and varies strongly between the investigated pumps.

Researchers may use the models to simulate and further investigate the dynamic interaction between different pumps and the cardiovas-
2.4 Discussion

cular system. For ease of implementation, the static and dynamic models of the four pumps are made available in the supplementary material as MATLAB functions. Further, the detailed identification protocol described in this study may contribute to a standardized approach to make future identifications of hydraulic pump characteristics comparable.

2.4.2 Comparison of hydraulic pump properties

No characteristic distinction was found between the hydraulic pump behavior of the axial-flow and the radial-flow pumps investigated in this study. Without periphery, both the steepest and the flattest HQ curve at the average operating point belong to the axial-flow pumps, whereas inclusion of the periphery leads to the HMII having the flattest curve closely followed by the HVAD. The resulting HQ curve for the HVAD is within the range of HQ curves introduced in Fig. 1 and compares most closely to the results of Granegger et al. [69]. The flow pulsatility of the pumps with periphery varies greatly among the pumps but is similar for the HVAD and the HMII. Clinical observations [87] confirm the latter finding, with no significant differences for the two pumps in overall hemodynamic effects. This result contrasts with the widespread view, that flat HQ curves and high flow pulsatilities relate only to radial-flow pumps, and vice versa [68].

The static influence of the periphery is more pronounced for axial-flow than for radial-flow pumps. In the HMII and the Incor, the hydraulic loss is larger by a factor of 3.2 and 2.7, respectively, compared to the average loss observed in the two radial-flow pumps. This can be explained by geometric differences of the periphery between the investigated radial-flow and axial-flow pumps, specifically the radius of the curvature of the elbow connectors [44]. To achieve the desired output flow rate, the hydraulic losses of the periphery are accounted for by increasing the speed of the pump. Therefore, the efficiency of the system decreases and the blade tip velocity increases. The latter leads to higher shear forces compared to the same pump without periphery losses and consequently potentially higher blood damage. It must be noted that in clinical usage the pump and the elbow connectors are
Figure 2.8: Histogram of the flow rate of each pump during one cardiac cycle in full and partial support. The top row shows the response to the physiological boundary condition of full support, the bottom row displays partial support. The dashed line marks the flow rate of 0 L/min. Note that the scales of the y-axis for partial and full support differ for a better visualization of the distribution. All speeds are rounded to 100 rpm.
treated as a unit, however, in future development these results may be considered to optimize the system’s hydraulic characteristics.

However, not only the overall steepness of the HQ curve is of importance, but also its shape. Whereas the steepness of the HMIII is similar to that of the HVAD in the higher flow region, the HMIII indicates an increase in pressure at lower flow rates. The inclusion of this flow region in the model reveals the low-flow and backflow properties including residence times within this flow regime, which is important for a cardiac cycle at low average flow rates, for example partial support. During partial support the flow range shifts such that a large portion of the operating time is at low off design flow rates. For example, the HVAD runs 44% of the operating time at flow rates of below 1 L/min, due to the flat HQ curve in the low-flow region. This is similarly pronounced in the HMIII with 42%, whereas the Incor does not reach the negative-flow region at all. As the operating condition was chosen based on the average patient condition with a SD of 0.4 L/min [86], one can expect a shift of the flow rate further into the negative region in many cases.

Higher flow pulsatility leads to higher arterial pulse pressure, as well as enhanced adaptations to pre- and afterload changes, which is often considered beneficial [68]. The flow pulsatility determined based on the static HQ curve overestimates the flow pulsatility observed with the dynamic model. This overestimation is more pronounced when the lower limit of the flow rate of a cardiac cycle falls into the flat region of the HQ curve. This indicates that a flat HQ curve in combination with the fluid inertia of the system attenuate flow pulsatility and needs to be considered especially for pumps aiming at a high pressure sensitivity [88].

Several indicators in scientific literature support the hypothesis that the operating conditions of the pump are of considerable importance for the hemocompatibility of the device. Yang et al. [39] suspected that the increase in thrombus formation in an axial-flow RBP might be related to the lower speed strategy with the aim of facilitating aortic valve opening. The REVIVE-IT study [73] investigated the partial support of patients with less advanced HF, with RBPs at lower speed settings. The study was discontinued because equipoise with the optimal medical treatment was not reached due to the occurrence of
major adverse events. In both cases, the pump was operated at lower flow rates, which are far off its regular design point.

In our study, we found that during one cardiac cycle, half of the time is spent in the highest and the lowest 10% of the range of the flow rate. The shape of the histogram that peaks at both edges of the distribution, indicating a prolonged residence time in the extrema, has also been observed in in-vivo studies [89, 90]. These findings suggest that not only the flow field at the mean flow rate but also at the extrema need to be thoroughly assessed when analyzing flow characteristics of RBPs. The investigation of the flow field at lower flow rates becomes inevitable, when acknowledging that in partial support the flow rates are below 2.5 L/min during half of the cardiac cycle for all investigated pump. Such studies could be used to analyze blood trauma and thrombotic potential through stagnation zones, increased residence times and backflow.

2.4.3 Limitations

The study has several limitations that mainly result from the accessibility of the actual pump speed signal and the difficulty to resemble the periphery from the clinical application in an in-vitro setup. In our study, we assume that the set pump speed is equal to the actual pump speed. However, in reality, changing flow results in small deviations of the set and actual speed signals which may influence the dynamic behavior of the hydraulic model [69]. We mimicked the bent cannulas with 3D-printed photopolymeric resin and the graft used for implantation with Tygon tubing. The patient’s individual anatomy and the implantation approach lead to the graft length and curvature, which can vary greatly [91, 92]. Therefore, the difference in surface, rigidity, length, curvature and transitions between connecting elements strongly influence the measured hydraulic losses and inertia.

In our study, the viscosity of the fluid was fixed to 3 cP which mimics an hematocrit of 31% [48]. This hematocrit is close to the typical hematocrit of a VAD patient [93]. We neglect on the one hand, that the hematocrit varies from patient to patient and on the other hand, that blood is a non-Newtonian fluid with a shear-dependent viscosity.
2.5 Conclusion

It has been demonstrated that a universal modeling approach based on principles of turbomachinery is feasible for both radial-flow and axial-flow RBPs. The suggested standardized identification procedure revealed greatly varying hydraulic properties between pumps, independent of the pump type. The hydraulic properties are strongly affected by its periphery as well as the overall dynamic properties. In clinical practice, the steepness and the shape of the static HQ relationship needs to be considered especially if a low flow strategy (e.g., partial support) is envisaged and backflow is to be avoided. For future investigations of the flow field of an RBP, not only the mean flow rate but more importantly the extrema of the flow rate distribution need to be thoroughly assessed.
3 Blood Pump Design Variations and Their Influence on Hydraulic Performance and Indicators of Hemocompatibility

The content of this chapter has been published in *Annals of Biomedical Engineering*.

3.1 Introduction

LVADs are the main treatment option for patients with end-stage HF if HTx is not possible. Even though LVADs are increasingly implanted as destination therapy, patients still suffer from high rates of adverse events [94]. Many of these, such as bleeding, thrombosis and stroke, are thought to be closely related to the flow conditions within the LVAD. These flow conditions are determined to a large extent by the pump design, which suggests that its optimization would translate to fewer adverse events and improve patients’ quality of life.

Among the existing pump types, turbodynamic pumps are most widely used for LVADs. Several experimental and numerical frameworks have been devised for their optimization. Studies such as those by Wu et al. [58,95] and Arvand et al. [96] shed light on the impact of different impeller designs and clearance gap sizes, while others have focused on developing automated optimization frameworks [97,98]. Yet, for designers, it is important to gain insight into the impact of single design parameters independently. Building on the vast collective know-how on generic turbodynamic pumps, Mozafari et al. systematically investigated the impact of variations in geometry [45,59]. The latter study [59] focused on hydrodynamic performance, investigating the influence of geometry on a metric for hemolysis.
Computational LVAD design studies reporting on hemocompatibility have typically focused on hemolysis [57, 99–101] represented by a hemolysis index (HI), which incorporates a weighted integration of shear stresses and exposure times. However, despite being widely used, HI performs poorly in predicting experimentally measured hemolysis values [102]. Its value derives from providing insight into the shear stress history as a general indicator of potential damage to blood cellular components, which may be of use for comparative studies. Thrombus formation as another major aspect of hemocompatibility is driven by multiple factors, including platelet activation and slow blood flow conditions. While an assessment of the latter is indeed feasible, direct computational prediction of platelet activation is currently not possible. Therefore, computationally determinable surrogates have been suggested to serve as alternatives [103, 104]. In general, views on the best surrogate metric of hemocompatibility diverge and validated models for predictions of measured values remain a challenge. This may be one reason why metrics applied for assessing blood damage differ between studies on LVAD geometry.

In this study, we provide a comprehensive investigation of selected design parameters in view of their hydrodynamic performance and hemodynamic characteristics. Our geometry is based on an industrial pump design guideline [26], starting from which we investigate the effect of alterations in clearance gap, number of blades, and shroud design. We use computational fluid dynamics (CFD) simulations that are validated experimentally regarding hydraulic performance to assess the flow fields within the pump, as well as Lagrangian particle tracks to characterize the stress exposure of blood cellular components flowing through the device. These analyses are further supplemented by the classical HI and other metrics proposed to correlate with platelet activation, thrombus formation, or acquired von Willebrand disease. Collectively, these results shed light on the impact of gap size, blade number and shroud design on shear stress exposure and flow stagnation, both of which were shown to have implications in terms of blood damage and thrombosis potential.
3.2 Material and Methods

3.2.1 Baseline pump design

The impeller and the housing were designed according to the industrial design guideline for centrifugal pumps by Gülch [26]. Starting with six input parameters that describe the desired operating conditions and impeller topology, the design process is broken down into 21 steps, involving 65 equations and look-up tables, which ultimately result in fully constrained geometries of the impeller and housing. Details on this process are given in Appendix A.1.

The first three input parameters that describe the desired operating conditions were maintained constant for all designs performed in this study: Operating rotational speed and head pressure were set to 3000 rpm and 100 mmHg, respectively. The design flow rate as an input to the design guideline was iteratively increased until, for our baseline geometry, an effective flow rate of 4-5 L/min was achieved in the CFD simulation. The chosen speed and head pressure correspond to that of HVAD (Medtronic/Heartware, Minneapolis, MN, USA), a clinically used LVAD that produces a flow rate of 5 L/min against a head pressure of 106 mmHg at 3000 rpm [48]. The simulated effective flow rate in the retained baseline geometry was 4.4 L/min.

The remaining three input parameters for the impeller topology, namely clearance gap size (defined as the distance between the tip of the blades and the housing), number of blades and shroud design, were chosen based on the recommendations given in Gülch [26]. They are listed in Table 3.1 and Table 3.2 under “base”. Figures 3.1A and 3.1B show the Computer-aided design (CAD) drawings of the resulting pump, featuring a priming volume of 11 mL and an impeller with 32 mm diameter. Since the character of this study is conceptual, the design process was free of any constraints imposed by bearing and actuation systems.

3.2.2 Design variations

Starting with the baseline design as the initial configuration, clearance gap size, number of blades, and shroud type were varied independently
3 Influence of Blood Pump Design Variations

Figure 3.1: A: Side-view of the Computer-aided design (CAD) model of cut-open housing and impeller design that served as baseline for the CFD simulation, B: Top-view of the CAD model of baseline impeller and cut-open housing.

(Table 3.1). These variations resulted in a total of eight simulated designs, including the baseline design. Table 3.2 shows the combination of parameters for each variant. Parameter ranges were chosen based on literature and existing technology. For the size of clearance gap, we selected a lower bound of 50 µm and an upper bound of 500 µm based on the dimension of the smallest gaps between impeller and housing of the HVAD [32] and the HM3 (Abbott/Thoratec, Abbott Park, IL, USA) [61], respectively. The number of blades was varied from four as seen in a number of clinically used LVADs, including the HVAD and HM3, up to seven in order to investigate the suggested range of 5 to 7 blades based on the specific speed of our pump design [26].

In the third variation, the influence of the presence or absence of a top shroud was examined. A semi-open design has a bottom shroud but no top shroud (like the HVAD), whereas a closed design has both bottom and top shrouds (like the HM3). In both designs, we kept the blade height constant. Therefore, the housing of the closed design was slightly larger to maintain the desired clearance gap, resulting in a 1.6% increase of the priming volume.
**Table 3.1**: Investigated geometry parameter values. The clearance gap size, number of blades and shroud design were investigated independently, varying one parameter at a time while the others were maintained at their baseline value (underlined values).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clearance gap size</td>
<td>50, 150, 300, 500 µm</td>
</tr>
<tr>
<td>Number of blades</td>
<td>4, 5, 6, 7</td>
</tr>
<tr>
<td>Shroud design</td>
<td>Semi-open, closed</td>
</tr>
</tbody>
</table>
Table 3.2: Combinations of geometry parameters for each simulated design. Only one parameter was varied at a time for each of the three parameters: clearance gap, number of blades and shroud design. The baseline design (base) is the same for each of the three variations. This resulted in a total of eight individual designs (including the baseline design) that were evaluated in CFD simulations.

<table>
<thead>
<tr>
<th>Variant</th>
<th>Clearance gap</th>
<th>Number of blades</th>
<th>Shroud design</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
<td>base</td>
</tr>
<tr>
<td>Clearance gap</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>size (µm)</td>
<td>50</td>
<td>150</td>
<td>300</td>
</tr>
<tr>
<td>Number of blades</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Shroud design</td>
<td>semi-open</td>
<td>semi-open</td>
<td>semi-open</td>
</tr>
</tbody>
</table>
3.2.3 Computational fluid dynamics simulations

CFD simulations were carried out for the eight different designs to evaluate their hydrodynamic performance and associated hemodynamics. The geometries were imported into the commercial CFD package StarCCM+ (Siemens, Munich, Germany). Polyhedral grids were generated using the same settings for all configurations, including a 4-element boundary layer along the walls and a local mesh refinement in the clearance gap, ensuring that it contained a minimum of twelve cell layers. The resultant grid sizes ranged between 4.7 and 7.6 million cells.

The three-dimensional unsteady Reynolds-averaged Navier-Stokes equations were solved using the k-ω-SST turbulence model and implicit second order temporal discretization. Blood was modelled as a Newtonian fluid with a viscosity of 3.5 mPa·s and a density of 1060 kg/m³ [105]. This simplification was considered acceptable, as the non-Newtonian properties of blood, such as shear-thinning, become negligible at high shear rates (> 100 s⁻¹) [106] such as those typically found in LVADs. The rotation of the impeller was implemented as a rigid body motion with a set speed of 3000 rpm. Pressure boundary conditions were set at the inlet and outlet with a user-defined function such that a constant static head pressure of 100 mmHg was kept between inlet and outlet of the pump.

The simulations were carried out with a convergence criterion of 10⁻⁴ for the residual errors and a time step of 5·10⁻⁵ s, corresponding to less than 1° rotation per time step at 3000 rpm. The simulations were run for five rotations after the flow rate had stabilized, and only the fifth cycle was used for the analysis. Grid and time step independence were confirmed for pressure, velocity, and shear stresses as reported in Appendix A.2.

To probe blood cell paths through the pump, we implemented a Lagrangian particle tracking with passive advection. The particles had a diameter of 5 μm and a density of 1125 kg/m³, which are representative of the dimension and density of red blood cells. A total of 6332 particles were seeded 4 mm downstream of the inlet in a uniform spatial distribution during four consecutive time steps.
3 Influence of Blood Pump Design Variations

3.2.4 Validation

To validate the numerical simulations, the hydraulic performance of the baseline pump design was also assessed experimentally. The baseline design was complemented with features for motor shaft integration resulting in only slight geometric changes to the bottom of the housing below the impeller, which was assumed to have no impact on the fluid dynamics. This design was then 3D-printed using photopolymeric resin (FullCure 720, Objet-Stratasys Inc., Eden Prairie, MN, USA) in a polyjet printer (Objet Eden 350 V, Objet-Stratasys Inc) with a layer thickness of 16 µm. We investigated the surface roughness of the printed material with a confocal laser microscope (VK-X260K, Keyence International, Mechelen, Belgium) for different inclinations relative to the printing axis, obtaining a mean Ra value of 5 µm. A brushless motor (EC-max 40, 120 W, Maxon Motor AG, Sachseln, Switzerland) was used for actuation. The impeller was mounted directly on the motor shaft through press fit. The 3D-printed pump was connected to the test bench [81] with two pressure-controlled fluid reservoirs, and the resulting flow rate was measured at the pump inlet as illustrated in Figure 3.2. The head pressure over the pump was measured with two in-line pressure sensors (TruWave, Edwards Lifesciences, Irvine, CA, USA) connected to the inlet and the outlet of the pump.

3.2.5 Analyses

Table 3.3 summarizes the metrics used to compare the various design options in terms of hydrodynamic performance and hemodynamic characteristics.

To gain better understanding of the relation between design features and potential blood damage, we investigated the flow fields qualitatively and quantitatively. To this end, we visualized the regions with low velocities, potentially prone for platelet aggregation and thrombus formation [107], considered disturbances of the flow field, investigated the location of zones with high shear stresses and compared histograms of medium and high shear stresses and exposure times along the Lagrangian particle tracks. We also analyzed six metrics
Figure 3.2: 3D-printed baseline pump design on the motor platform, connected to the test bench [81] for experimental validation.
Table 3.3: Summary of the analyzed hydrodynamic and hemocompatibility metrics, their implementation, and their suspected implication for blood pumps.

Nomenclature: 
- $Q(t)$: volume flow rate [m$^3$/s], $t$: time [s], $T_{2\Pi}$: time period for one rotation [s], $\mathbf{V}$: fluid velocity vector [m/s], $\mathbf{A}_g$: normal of $A_{gap}$ [ ], $A_{gap}$: surface of gap between impeller and housing [m$^2$], $P_{mech}$: mechanical power [W], $P_{hyd}$: hydraulic power [W], $\Omega$: angular speed [rad/s], $T$: torque on rotor [Nm], $H$: head pressure [Pa], $\tau$: scalar shear stress obtained from Equation 3.1 [Pa], $\mathbf{V}_s$: fluid volume with scalar shear stresses above the prescribed threshold [mL], $V_{total}$: total volume of fluid in the pump [mL], VWF: von Willebrand factor, WSS: wall shear stress [Pa], $A_{total}$: total surface area of the impeller surface [m$^2$], $\mathbf{A}_{WSS>1\text{Pa}}$: area of the impeller surface exposed to $WSS>1\text{Pa}$ [m$^2$], $SPWV$: local spanwise vorticity [1/s], $\mathbf{s}$: position vector [m], $\mathbf{\nu}$(s,t): vorticity vector [1/s], $\phi(s,t)$: angle formed by velocity and vorticity vector [rad], $N_k$: number of points on the kth particle trajectory [ ], $N_p$: number of particle trajectories [ ], $\alpha, \beta, C$: empirical constants [108].

<table>
<thead>
<tr>
<th>Metric</th>
<th>Implementation</th>
<th>Implication</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump flow rate ($Q_{pump}$) [m$^3$/s]</td>
<td>$Q_{pump} = \frac{1}{T_{2\Pi}} \int_0^{T_{2\Pi}} Q(t) dt$</td>
<td>Suitability for full pump support of patient</td>
<td></td>
</tr>
<tr>
<td>Leakage flow rate ($Q_{leak}$) [m$^3$/s]</td>
<td>$Q_{leak} = \mathbf{V} \cdot \mathbf{A}_{gap}$</td>
<td>Efficiency losses</td>
<td></td>
</tr>
<tr>
<td>Hydraulic efficiency ($\eta$)</td>
<td>$\eta = \frac{P_{mech}}{P_{hyd}} = \frac{Q_{pump}H}{\mathbf{V}_s}$</td>
<td>Hydraulic design</td>
<td></td>
</tr>
<tr>
<td>Relative fluid volume with scalar shear stress above a threshold $I_r&gt;\text{Thres}$</td>
<td>$I_r&gt;\text{Thres} = \frac{V_r&gt;\text{Thres}}{V_{total}}$</td>
<td>Hemolysis (Thres = 150 Pa)</td>
<td>[103]</td>
</tr>
<tr>
<td>Relative area of low WSS on the impeller surface ($I_{WSS&lt;1\text{Pa}}$)</td>
<td>$I_{WSS&lt;1\text{Pa}} = \frac{A_{WSS&lt;1\text{Pa}}}{A_{total}}$</td>
<td>Platelet activation (Thres = 50 Pa)</td>
<td>VWF cleavage (Thres = 9 Pa)</td>
</tr>
<tr>
<td>Spanwise vorticity index ($SPWVI$) [1/s]</td>
<td>$SPWVI = \sum_{k=1}^{N_p} \frac{1}{N_p} \sum_{j=1}^{N_j} SPWV_{k,j}$</td>
<td>Platelet activation status</td>
<td></td>
</tr>
<tr>
<td>$SPWV$</td>
<td>$SPWV(\mathbf{k}t) = \mathbf{\nu}(\mathbf{k}t) \sin(\phi(\mathbf{k}t))$</td>
<td></td>
<td>[104]</td>
</tr>
<tr>
<td>Hemolysis Index ($HI$)</td>
<td>$HI = \frac{1}{N_p} \sum_{k=1}^{N_p} C \left( \sum_{j=1}^{N_j} \Delta t_{k,j} \beta^{\alpha} \right)^a$</td>
<td>Hemolysis</td>
<td>ref [108, 110]</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>0.7650</td>
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<tr>
<td>$\beta$</td>
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<tr>
<td>$C$</td>
<td>$1.8 \cdot 10^{-6}$</td>
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proposed in literature to assess blood damage potential that quantify Eulerian and Lagrangian characteristics of the simulated flow fields. Spanwise vorticity and hemolysis index \((HI)\) were integrated over all particle tracks. All other metrics, Eulerian in nature, were computed at each time step and averaged over the last rotation.

Central to most blood damage models are the fluid shear stresses experienced by blood cells and plasma proteins as they flow through the device. The scalar shear stress, \(\tau\), was calculated from the viscous shear stress components, \(\sigma_{ij}\), according to Bludzuweit et al. [105]:

\[
\tau = \left( \frac{1}{6} \sum (\sigma_{ii} - \sigma_{jj})^2 + \sum \sigma_{ij}^2 \right)^{1/2}
\] (3.1)

Reynolds stresses were not included in the scalar shear stress since blood damage models available in literature are based on viscous stresses only [111].

\(HI\) was calculated as a power law of the scalar shear stresses and exposure time [110] (see corresponding equation in Table 3.3) using constants by Heuser and Opitz [108] as presented before [102]. Values of \(HI\) were integrated along each particle track based on the recorded shear stress histories, and were then averaged to derive the total \(HI\) for blood flowing through the LVAD. Variation in the number of seeded particles above 6332 (tested range 156-9498) did not result in significant changes in the computed \(HI\).

We further determined the overall volumes of fluid in which fluid shear stress is above the threshold suspected for VWF cleavage \((\tau > 9 \text{ Pa})\), platelet activation \((\tau > 50 \text{ Pa})\) and hemolysis \((\tau > 150 \text{ Pa})\) [103], respectively. Enhanced VWF cleavage and the successive loss of its high molecular weight multimers is believed to be one of the main causes for bleeding complications in LVAD patients [112]. Areas of very low wall shear stress \((WSS)\) on the rotor surface \((WSS < 1 \text{ Pa})\) were derived to assess the potential risk of platelet deposition [109]. The Lagrangian spanwise vorticity index \((SPWVI)\) was shown numerically to correlate well with the platelet activation status [104]. This correlation was originally reported for prosthetic heart valves, but since the principles behind shear stress-induced effects on blood
components are comparable for blood pumps, an application in this field seems reasonable [113].

To test for association between blood damage indices suggested in literature, we calculated the nonparametric rank correlation coefficients (Spearman’s rho) using the IBM SPSS Statistics 23 software (IBM Corporation, Armonk, USA). P-values below 0.05 were considered indicative of statistical significance. We checked visually for the absence of non-monotonic relations.

### 3.3 Results

The influence of design parameter variation on pump flow rate and hydraulic efficiency is shown in Figure 3.3. The pump flow rate ranged between 3.2 and 5.7 L/min, and the hydraulic efficiency between 38 and 53%. With 4.4 mL/min of flow at 100 mmHg, the baseline geometry achieved an efficiency of 47%. The variation of the clearance gap led to the most substantial effects, followed by the change in shroud design.

![Figure 3.3: Computed flow rate and hydraulic efficiency plotted for variations of clearance gap size, number of blades and shroud design. The baseline configuration is marked by filled symbols. When one parameter was varied, the remaining two parameters were kept at baseline value. Note that the vertical axes depicting flow rate and efficiency have ranges of 3-6 L/min and 35-55%, respectively.](image-url)
3.3 Results

Relative changes in hemocompatibility indicators are shown in Figure 3.4. In this figure, all indices are normalized by their respective value in the baseline geometry to allow for a direct comparison of the relative impact of the various design variations. The numerical data, without normalization to the baseline geometry, is listed in Appendix A.3. Fractions of fluid volume with shear stress values above a threshold, $I_{\tau>150\text{Pa}}$, $I_{\tau>50\text{Pa}}$, and $I_{\tau>9\text{Pa}}$, were in the range of 0.006-0.049%, 1.1-2.2%, and 14.4-16.6% of the total fluid volume, respectively.

Table 3.4 shows Spearman’s rank correlation coefficients ($r$) between all derived metrics of pump performance and hemocompatibility. Strong positive correlations were found between $HI$ and $I_{\tau>50\text{Pa}}$ ($r = 0.74$, $p = 0.037$), and between $SPWVI$ and $I_{\tau>9\text{Pa}}$ ($r = 0.86$, $p = 0.007$). A strong negative relation was observed between $HI$ and efficiency ($r = -0.71$, $p = 0.047$). None of the other correlations were found to be significant.

3.3.1 Clearance gap size

From the smallest clearance gap of 50 µm to the largest one of 500 µm, the flow rate decreased by 43% and the efficiency decreased by 28% (Figure 3.3). Although the flow rate steadily declined from 5.7 to 3.2 L/min, the efficiency remained constant at 53% for the two smaller gaps (50 and 150 µm), and only declined for larger ones, reducing to 38% for a gap of 500 µm.

Figure 3.5A depicts the fluid volume exposed to high shear stresses ($SS$) which in Figure 3.4 was shown to be minimal for medium gap sizes (150, 300 µm). Yet, $HI$ steadily increased with increasing gap size. In contrast, smaller gaps led to larger regions of low speeds (<0.5 m/s, Figure 3.5B). $SPWVI$ was lowest for medium-sized gaps (Figure 3.4). Larger clearance gaps induced significant flow disturbances on the suction side of the blade as shown by streamlines seeded just above a blade, whereas for the small clearance gap (50 µm) streamlines seeded at the same position were almost undisturbed (Figure 3.5C). The number of particles exposed to medium (> 50 Pa) and high (> 150 Pa) $SS$ increased substantially for the large gap (Figure 3.5D).
3 Influence of Blood Pump Design Variations

Figure 3.4: Effect of change in clearance gap size (50 to 500 µm), number of blades (4-7), and shroud design (semi-open or closed) on hemocompatibility indicators. Hemocompatibility indicators are grouped into three categories according to their suspected implications: (1) Hemolysis indicators are $HI$ and $I_{τ>150Pa}$. (2) Thrombosis potential is indicated by $I_{τ>50Pa}$, rotor surface with $I_{WSS<1Pa}$ and $SPWVI$. (3) Bleeding potential due to VWF cleavage is assessed with $I_{τ>9Pa}$. All indices are normalized by their respective values in the baseline configuration. Numerical values are listed in Appendix A.3. Dashed frames indicate baseline configuration.
Table 3.4: Spearman’s rank correlation coefficients for the hydrodynamic and hemocompatibility metrics obtained by CFD simulations.

Nomenclature: \( r \): rank correlation coefficient, \( \eta \): hydraulic efficiency, \( Q_{\text{leak}} \): leakage flow rate, \( \tau \): scalar shear stress, \( I_{\tau>150\text{Pa}} \), \( I_{\tau>50\text{Pa}} \) and \( I_{\tau>9\text{Pa}} \): fraction of fluid volume with scalar shear stresses above 150, 50 and 9 Pa, respectively, \( WSS \): wall shear stress, \( I_{WSS>1\text{Pa}} \): relative area of the impeller surface exposed to \( WSS>1\text{Pa} \), \( HI \): hemolysis index, \( SPWVI \): spanwise vorticity index. Statistically significant correlations are underlined. \( *p<0.05, **p<0.01 \).

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<tr>
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<th>( \eta )</th>
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<th>( I_{\tau&gt;150\text{Pa}} )</th>
<th>( I_{\tau&gt;50\text{Pa}} )</th>
<th>( I_{\tau&gt;9\text{Pa}} )</th>
<th>( I_{WSS&lt;1\text{Pa}} )</th>
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<tbody>
<tr>
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<td>( 0.233 )</td>
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<td>( 0.74^* )</td>
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<td>( p)-value</td>
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<td>( SPWVI )</td>
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<td>( 0.86^{**} )</td>
<td>( 0.19 )</td>
<td>( 0.41 )</td>
<td>( 1 )</td>
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<td></td>
<td>( p)-value</td>
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Figure 3.5: Visualization of the effects of change in clearance gap size from 50 to 500 µm. A: Localization and extent of areas of high shear stress ($\tau > 150$ Pa). B: Regions with low velocities ($v < 0.5$ m/s) along the meridional section of the flow channels inside the pump. The velocity threshold of 0.5 m/s was chosen for best visual representation of possible stagnation zones. C: Flow structures represented by streamlines seeded with a randomized distribution in the clearance gap above one of the blades. D: Histograms of the exposure times to shear stresses above 50 and 150 Pa. With the 50 µm clearance gap, 1049 (16.8%) and 364 (5.8%) of the seeded particles experienced SS above 50 and 150 Pa, respectively, compared to 2560 (40.2%) and 669 (10.5%) with the 500 µm gap.
In contrast, large gaps reduced the maximum SS that particles were exposed to (Appendix A.4).

### 3.3.2 Number of blades

Increasing the blade number from four to seven increased the pump flow rate from 4.0 to 4.6 L/min (+15%), but did not affect efficiency (variation within ±1%, Figure 3.3). The values of $I_{\tau>50Pa}$ and $I_{\tau>9Pa}$ increased marginally with an increasing number of blades (Figure 3.4). In contrast to $I_{\tau>50Pa}$, the thrombosis indicators $I_{WSS<1Pa}$ and $SP-WVI$ increased to 3.5-fold and 1.9-fold when the blade count was increased from 4 to 7. Stagnation zones with low velocity (Figure 3.6b) increased with the number of blades and aggregated for higher blade numbers at the suction side of the blades. Exposure times to medium and high SS were almost unaffected, with a slight shift towards longer exposure to medium stresses for seven blades (Figure 3.6c).

### 3.3.3 Shroud design

Compared to the semi-open impeller, the closed impeller yielded higher hydraulic efficiency and flow rate (Figure 3.3). In the semi-open design, high SS occurred in the clearance gap, a behavior that was effectively suppressed by the closed design (Figure 3.7a). The closed design also reduced the size of the low-velocity zones near the blades (Figure 3.7b), but gave rise to stagnation zones at the corner edges where blades and shroud meet. The closed impeller radically reduced the amount of fluid exposed to SS above 150 Pa, but moderately increased the amount of fluid exposed to mid-range SS above 50 Pa, and more than tripled the value of low WSS $I_{WSS<1}$ (Figure 3.4). Similarly, substantially fewer particles were exposed to high SS for the closed design, while simultaneously, exposure time to medium SS increased (Figure 3.7c).
Figure 3.6: Visualization of the effects of change in the number of blades from 4 to 7. A: Areas of high shear stress ($\tau > 150 \text{ Pa}$). B: Regions with low velocities ($v < 0.5 \text{ m/s}$) along the meridional section of the flow channels inside the pump. The velocity threshold of 0.5 m/s was chosen for best visual representation of possible stagnation zones. C: Histograms of the exposure times to shear stresses above 50 and 150 Pa. With 4 blades, 2552 (40.3%) and 557 (8.8%) of the seeded particles experienced SS above 50 and 150 Pa, respectively, compared to 2835 (44.8%) and 651 (10.3%) with 7 blades.
Figure 3.7: Visualization of the effect of a semi-open vs. closed shroud design. (a) Areas of high shear stress ($\tau > 150$ Pa). B: Regions with low velocities ($v < 0.5$ m/s) along the meridional section of the flow channels inside the pump. The speed threshold of 0.5 m/s was chosen for best visual representation of possible stagnation zones. C: Histograms of the exposure times to shear stresses above 50 and 150 Pa. With the semi-open design, 2435 (38.5%) and 611 (9.7%) of the seeded particles experienced $SS$ above 50 and 150 Pa, respectively, compared to 2111 (33.0%) and 171 (2.7%) with the closed design.
3.3.4 Validation

We compared simulated and measured pump performance with the baseline geometry, finding good agreement between the two modalities. For a speed of 3000 rpm and a head pressure of 100 mmHg, the simulated flow rate was 4.4 versus 4.9 L/min in the experiments, which corresponds to a difference of 10.3%. Figure 3.8 shows the experimental measurements of the relation between head pressure and flow rate at a rotational speed of 3000 rpm. A curve shape that is typical for radial pumps can be observed, flatter at low and steeper at high flow rates. The difference between experimentally measured and simulated flow rates is high in the low flow region (< 5 L/min) with 19.7% RMSE compared to only 2.4% in the high flow region (> 5 L/min).

![Figure 3.8](image)

**Figure 3.8:** Experimental measurements and simulation results of the hydraulic performance of the baseline design at a rotational speed of 3000 rpm.

3.4 Discussion

In this study, we performed systematic variations of design parameters in a centrifugal blood pump. Using CFD, we analysed their effects on the flow field and multiple metrics of hydraulic performance. Explo-
3.4 Discussion

sure to elevated shear stress and exposure duration have been shown to damage and/or activate the cellular components of blood including erythrocytes, thrombocytes [103] and leukocytes [114]. According to Virchow’s triad of thrombus formation, zones of low flow require attention. Despite the evidence for flow induced blood damage, validated models for predictions of measured values of damage remain a challenge. While indices such as the numerically derived hemolysis index often provide an integrated view on specific flow features, they should not be interpreted as predictors of measured blood damage. We, therefore, use them here in combination with detailed analysis of the flow fields and particle tracks to shed light on the influence of each independent design variation on the extent of cell exposure to potentially damaging or activating hemodynamic environments.

In the choice of clearance gap size, designers face conflicting requirements: Aiming for high hydraulic efficiency calls for small gaps, whereas minimization of maximum SS and suspected washout performance would suggest larger gaps. In our geometries, smaller gap sizes indeed increased the maximum SS (Appendix A.4). However, firstly, the total fluid volumes exposed to high SS ($I_{τ>150 Pa}$) were comparable for 50 and 500 µm gaps (Figure 3.4) and, secondly, smaller gaps induced cell screening, an effect also observed experimentally by Antaki et al. [49], such that only half as many particles effectively experienced these high SS in the 50 µm gap compared to the 500 µm gap (5.8 vs. 10.5% of the tracks, Figure 3.5D). Larger gaps on the other hand gave rise to substantial flow disturbances in the fluid path (Figure 3.5c), increasing SS and vorticity. As a result, volumes exposed to medium SS ($I_{τ>50 Pa}$) generally increased with gap size. These medium SS volumes, with sizes two to three orders of magnitude larger than those with SS above 150 Pa, affected about 40% of the particles in the 500 µm gap setup vs. only 17% in the 50 µm gap configuration (Figure 3.5D). Increased vorticity content in the main particle paths is reflected by the increase in SPWVI with the largest gap size. Combined, the noted changes in SS histories led to lower HI in smaller gaps, which is consistent with previous results [100]. In contrast, Wu et al. [57] reported minimal HI at 100 µm compared to clearance gaps of 50 and 200 µm. Different to our study, they studied the effect of gap size prescribing a constant flow rate. While a well
validated metric of hemolysis remains to be established, all qualitative and quantitative indicators investigated here suggest that by minimizing the number of cells exposed to high and medium stresses, smaller gaps may be expected to yield lower hemolysis than larger ones. This is also consistent with experimental observations [101]. $SS > 50 \text{ Pa}$ and higher $SPWVI$ have been proposed as indicators of platelet activation. However, whether the noted reduction in $I_{r>50 \text{ Pa}}$ and $SPWVI$ (Figure 3.4) in the 50µm gap compared to the 500µm gap geometry do translate into reduced activation remains to be demonstrated. One major drawback of the smaller gaps is certainly the close to three-fold increase in regions of low $WSS$ and flow separation with low velocities on the pressure side of the blades. Strategies to avoid stagnation regions should thus be devised in accordance to the retained gap size. The gap size also affected the location of potential flow stagnation regions, shifting from the pressure side in the 50µm to centrally in the vanes in the 500µm gap (Figure 3.5B).

Compared to gap size variations, varying the number of blades had more blunted effects. While there was a clear increase in volumes exposed to high $SS$ with 7 blades compared to 4, $SS$ histograms were almost unaffected, showing for 7 blades only a slight shift towards longer exposure times to medium stresses (Figure 3.6C). Consistent with these marginal changes in $SS$ exposures, $HI$ was also marginally affected. The $SPWVI$ increased with the number of blades, as did the regions of potential flow stagnations ($I_{WSS<1 \text{ Pa}}$, Figure 3.4) due to flow separation at each blade (Figure 3.6B). Collectively, the decreased $SS$, vorticity indices and extent of potential stagnation zones point to fewer blades as being advantageous in terms of potential hemocompatibility. However, it should be noted that for fewer than 5 blades this comes at the cost of a decrease in pump flow rate.

In contrast to the above, shroud design variations yielded conflicting observations. Compared to the semi-open design, a closed shroud drastically reduced exposure to high $SS$ but increased exposure time to medium $SS$ (Figure 3.7C). The number of particles affected by medium $SS$ was one order of magnitude larger than to the peak $SS$. $HI$ was slightly lower for the semi-open configuration reflecting the opposite evolution of exposures to high and medium $SS$. However, without further data, no conclusion can be drawn on the integrated
3.4 Discussion

effect of these two changes on net hemolysis. Both platelet activation indicators suggested slightly preferable behaviour for the semi-open shroud. The semi-open compared to the closed design resulted in a smaller overall area of low WSS.

Overall, statistical analysis revealed that high efficiency correlates with low $HI$ ($r = -0.71$, $p = 0.047$). Indeed, more efficient pumps have fewer recirculation zones, flow disturbances and lower leakage flow, all of which contribute to higher shear stresses or longer exposure times and thereby higher $HI$. This finding is consistent with the experimental data of Mozafari et al. [59]. Lack of correlation between $HI$ and $I_{>150Pa}$ ($r = -0.12$, $p = 0.78$) highlights that in the considered geometries, peak $SS$ only reflects a small part of particles’ $SS$ histories, which are dominated by medium stresses as indicated by the correlation of $HI$ and $I_{>50Pa}$ ($r = 0.74$, $p = 0.037$) and the areas under the histograms in Figure 3.5D. The two metrics that have been suggested to indicate platelet activation, $I_{>50Pa}$ and $SPWVI$, did not correlate ($r = 0.21$, $p = 0.61$) in our study.

The computational approach employed in this study has limitations. First and foremost, all design variations were tested against a constant head pressure. The consideration of pulsatile conditions would be an important next step, acknowledging not only the physiological pulsations in the cardiovascular system, but also LVAD-inherent features such as washout algorithms as in the HM3 [115]. Secondly, while the blood damage indicators used in this study are widely employed in cardiovascular modelling, they remain explorative. They substantially simplify complex biological mechanisms [102, 116] and often perform poorly when evaluated against experimental data [102]. We, therefore, used them here to probe integrated flow characteristics rather than as predictors of measured blood damage. Quantification of true hemolysis or platelet activation potentials requires further investigation. Further effects, such as the interaction between blood and the pump material are also critical for thrombogenesis [117] and hemocompatibility. Biological advances in its understanding and modelling could significantly enhance the predictive power of CFD models. Finally, we investigated an approach presented recently, which links $SPWVI$ to platelet activation [104]. We applied this metric to Lagrangian tracks of particles with properties similar to erythrocytes.
3 Influence of Blood Pump Design Variations

(diameter 5 µm, density 1125 kg/m$^3$) rather than platelets (1 µm, simulated as massless) as used in the original work. Even though this might slightly alter the flow paths, the major characteristics of the tracks are expected to remain unaffected. However, the SPWVI lacks a thorough experimental validation. Thus, the prediction of platelet activation remains challenging and requires further investigation.
4 Control of the Fluid Viscosity in a Mock Circulation

The viscosity control is a prerequisite to parts of the experiments described in Chapter 2 and Chapter 3. The content of this chapter has been published in *Artificial Organs*.

4.1 Introduction

Despite significant clinical and technical developments, HF remains one of the major health challenges in developed countries [118]. For end-stage HF, the only option next to HTx is the implantation of a LVAD. A MC allows the in vitro investigation, development and testing of LVADs. Instead of blood, the majority of MCs [35, 81, 119–126] use an aqueous-glycerol solution to mimic the viscosity of blood in the human body.

The viscosity of human blood mainly depends on the hematocrit [46], whereas the viscosity of an aqueous-glycerol solution depends on its mixture ratio and temperature. In this study, viscosity is defined as the dynamic viscosity that yields a measure of internal resistance to flow. Viscosity has the unit centipoise (cP) which is equal to millipascal-second (mPa-s). The viscosity of blood shows a non-Newtonian behavior, meaning that the viscosity decreases with increasing shear rates. Because the aqueous-glycerol solution is a Newtonian fluid and therefore independent of the shear rate, the shear-thinning effect cannot be mimicked. However, since this effect only plays a role in the microcirculation [46] it can be neglected for large vessels such as the aorta. The average hematocrit for a healthy patient is about 40%, with extreme values ranging from 15% (anemia) to 65% (polycythemia) [3]. The hematocrit of LVAD patients is commonly measured in the range of 30-40% [93]. During surgery and within the
first months after surgery, lower values down to about 20% are observed [47]. This range of hematocrits results in blood viscosities of 2.1-3.8 cP.

Figure 4.1 shows the varying viscosity of the working fluids used in several state-of-the-art MCs that have been published within the last seven years using an aqueous-glycerol solution with specified values of mixture ratio or viscosity [35, 81, 119–126]. When only the mixture ratio was specified, we used Cheng’s equation [127] to calculate the viscosity assuming a room temperature of 25 °C and a mixture ratio being given in mass-%. Note that the bottom x-axis displaying the equivalent hematocrit is a nonlinear axis, representing the relation of viscosity to hematocrit by Merrill [106] (Figure 4.2). The used viscosities range from 3.14 to 4.05 cP, corresponding to an equivalent hematocrit between 33.2 and 42%.

Not only are there differences between the viscosities of working fluids used in MCs, one can also observe temperature changes during prolonged experiments on an MC that influence the viscosity. We observed temperature changes of the fluid between 21 and 29 °C during long-term experiments on our own MC [81]. These changes occur mainly due to the heat dissipation of the actuators during long-term operation. They lead to a deviation of the viscosity by 24%, which results in a variation of the desired hematocrit from 37.4 to 27.6% for a fixed aqueous-glycerol solution. Such variations in return lead to varying experimental conditions when testing blood pumps, for example, a higher viscosity resulting in a reduced hydraulic performance of the pump under investigation.

Effecting a change in the viscosity in a controlled manner can also be a requirement for an MC. When developing a flow estimator, the accurate value of the viscosity is required as an input and needs to be altered to different viscosity values for the development and the validation of the estimation algorithm [128]. The same is true for parameter identification experiments for system modelling of blood pumps [129, 130]. Commonly, the viscosity is changed by exchanging the aqueous-glycerol solution for each desired viscosity, but this procedure is prone to errors due to remainders of the exchanged fluid in tubes and tanks that mix with the new fluid. Nestler et al. [129] and Moscato et al. [35] recommend that the fluid temperature be con-
4.1 Introduction

![Graph showing viscosity and equivalent hematocrit of working fluids in different mock circulations (MCs) [35, 81, 119-126]. The asterisk * marks the viscosities calculated from published mixture ratios according to Cheng’s equation [127] assuming a room temperature of 25°C. Note that the bottom x-axis displaying the equivalent hematocrit according to Merrill [106] is a nonlinear axis.](image)

Figure 4.1: Viscosity and equivalent blood hematocrit of working fluids in different mock circulations (MCs) [35, 81, 119-126]. The asterisk * marks the viscosities calculated from published mixture ratios according to Cheng’s equation [127] assuming a room temperature of 25°C. Note that the bottom x-axis displaying the equivalent hematocrit according to Merrill [106] is a nonlinear axis.

trolled in order to maintain or change to a certain viscosity. Additionally, there are several clinical and pathological scenarios where a dynamically changing viscosity and equivalent hematocrit can emulate a saline transfusion for instance, or the pathologically induced changes in hematocrit.

For all the above reasons, a control mechanism for the viscosity is desirable for reproducible and repeatable experimental conditions with a constant hematocrit or for changing the desired viscosity for experiments at different hematocrits. Freidberg et al. [130] report the need for changing the fluid viscosity in an MC and investigate a feed-forward control unit that automatically adds water or glycerol to
achieve a certain viscosity, but they concluded that the inaccurate and inconsistent viscosities of the base fluids would not allow achieving accurate viscosities. Their approach does not account for temperature and mixture changes through evaporation, which is an additional reason why temperature control alone would not be sufficient. To our knowledge there are no publications available about the implementation, the performance, or the experimental results of a closed-loop viscosity control system.

In this study we therefore present a method to control the viscosity of the working fluid of the MC by controlling the temperature of the fluid and measuring its viscosity. This method allows not only to maintain a certain viscosity, but also to change the viscosity and thus match the desired hematocrit. We present the implementation with a viscometer, the considerations regarding the calibration of the flow probe, the controller performance, and the experimental results, obtained with two RBPs connected to the MC. With these experiments, we address the question in which of the cases a viscosity control method for an MC is crucial for testing blood pumps and when it can be omitted due to marginal influence.

4.2 Methods

4.2.1 Viscosity equations

The relation between hematocrit and viscosity of blood has been described by several researchers through experiments and analytical equations of varying accuracy. Figure 4.2 shows the analytical relations of viscosity and hematocrit as modelled according to Einstein [46], Merrill [106]) and Pries et al. [131] in comparison to the experimentally deducted average values of Rand et al. for four hematocrits [132]. For all analytical equations, a plasma viscosity of 1.3 cP was selected according to Késmárky et al. [133]. Except for Einstein’s linear approach the analytic representations clearly match the experimental data well, for Merrill with a deviation of 6.3% on average and a maximum of 8.7%. For further calculations in this study, the equation of Merrill was selected.
For the aqueous-glycerol solution, the temperature and the mixture ratio of glycerol and water determine the viscosity and therefore the equivalent to a certain hematocrit. Cheng [127] proposes an empirical formula for the viscosity of an aqueous-glycerol solution. The relation of viscosity and temperature for one mixture ratio is a monotonously decreasing exponential function. The higher the temperature the less viscous the mixture is. Cheng’s formula is in good agreement with databases available in literature [127] and was therefore used throughout this study.

![Figure 4.2](image_url)

Figure 4.2: Analytical models of Merrill [106], Einstein [46], Pries et al. [131] and experimental results of Rand et al. [132] for representing the relation of the hematocrit of human blood to viscosity.

### 4.2.2 Viscosity control system

The existing hybrid MC described by Ochsner et al. [81] was extended to integrate and test the viscosity control method. This MC is based on a hardware-in-the-loop concept, where the human circulation is simulated in real time and the LV and aortic pressure are applied to two fluid reservoirs that form the physical interface to the blood pump to be tested. The fluid reservoirs are connected via a backflow pump, which yields a closed fluid circuit. The flow rate of the blood pump
is measured at the inlet and the value is fed back to the numerical cardiovascular model [84].

In order to control the viscosity, a viscometer (preliminary development version of inline viscometer DVP-0300, Rheonics Inc., Winterthur, Switzerland) is integrated as a sensor and two nozzle heater bands (Düsenheizband Mica 125 W, Brütsch/Rüegger Werkzeuge AG, Urdorf, Switzerland) are integrated as actuators. A temperature sensor alone would not account for undetected changes in the mixture ratio of the aqueous-glycerol solution. Nonetheless, temperature sensors (Temperature Probe 590-59AD07-302, Honeywell International Inc., Freeport, IL, USA) are mounted for safety functions such as over-heating and to detect any malfunction of the viscometer. Figure 4.3 shows the viscometer, the two nozzle heater bands, and the two temperature probes built into the existing MC.

The viscometer uses a vibrating resonator in the fluid and detects the damping of viscous dissipation by the fluid, which allows to determine the viscosity [134]. The viscosity value is transmitted from the viscometer once per second with an accuracy of ±3%, a reproducibility of 0.5%, and a signal discretization of 0.01 cP. It is mounted in-line
after the backflow pump, immersed in the working fluid, and fastened in such a way that vibrations from the MC are decoupled from the resonator. Prior to installation the viscometer was calibrated with Newtonian calibration oil (certified viscosity reference standard S6, CANNON Instrument Company, State College, PA, USA) in a temperature chamber with eight viscosities in the range of 1-10 cP. For each calibration measurement, the temperature was kept constant for 2 hours in order to guarantee a thermal equilibrium.

The two nozzle heater bands were mounted in series onto a steel pipe just ahead of the backflow pump, and the temperature probes were placed at the bottom of each fluid reservoir. The heater bands have a combined power of 250 W and they were connected in parallel. For better insulation, they were covered with heat paste and wrapped in motor insulation tape.

To assess the heat introduced through heat dissipation of the actuators of the MC, a long-term experiment was conducted with the heating element turned off. The actuators of the MC possibly prone to heat dissipation are the backflow pump (Moyno 500 Pumps-200 Series, Moyno, Inc., Springfield, OH, USA) that controls the fluid level in both chambers and the four solenoid inlet and outlet pressure valves (PVQ33-5G-23-01F, SMC Pneumatics, Tokyo, Japan) that change the air mass in the chambers to adjust the fluid pressure. For this experiment, the MC was operated with a pulsating head pressure mimicking the physiological operation mode with an average flow of 5 L/min. The MC was operated for several hours until a temperature equilibrium (± 0.2 °C) was reached and no further temperature changes were detected. The ambient room temperature was controlled at 23 ± 1 °C with a passive heat exchanger.

### 4.2.3 Calibration of flow probes

Variations in flow, temperature and viscosity influence the accuracy of flow measurements with the clamp-on flow probe (TS410/ME-11PXL, Transonic Systems, Ithaca, NY, USA). The flow probe is factory calibrated for a 40 volume-% aqueous-glycerol mixture at 23 °C with a resulting viscosity of 4.3 cP. Variations in viscosity and temperature lead to changes in the speed of sound of water, which in turn changes
the ultrasound transit time of the flow sensors. Additionally, we observed that the accuracy of the flow probe also changed depending on the flow rate.

All three parameters that influence the flow measurement were investigated experimentally in a test rig with a high-precision scale (ME 2002, Mettler Toledo, Greifensee, Switzerland). Figure 4.4 shows the test rig with all its components. A vertical tube with a length of 1.5 m is filled with fluid and is fed by a cone on top of it. At the bottom end of the tube the flow sensor is clamped, followed by a valve for setting different flow rates. The fluid leaving the tube is caught in a compartment sitting on the high-precision scale. The common calibration method is measuring the mass with the scale and comparing it to the volume flow of the flow probe, integrated over time. We introduced a new method by recording the mass flow rate continuously with the high-precision scale and comparing it to the volume flow of the flow probe. The volume flow can be calculated from the mass flow rate with the fluid density determined by the measured temperature and viscosity. Aqueous-glycerol solutions of four different mixture ratios (37, 44, 49 and 52 mass-% glycerol) were measured at four different temperatures (23, 29, 35 and 41°C) at four different flow rates (2, 4, 6 and 8 L/min), respectively. Each measurement was performed three times, which overall results in 192 measurement sets.

The experimental results were used to determine the coefficients of a polynomial correcting the flow measurements based on input flow, viscosity, and temperature. The measured flow \( q \) was corrected by the slope \( s \) resulting in \( q_{cor} \):

\[
q_{cor} = qs
\] (4.1)

With the method of least squares, the coefficients \( p_n \) were determined that have the least mean square error for all slopes \( s \) measured in the experiments. For example, for a quadratic fit this leads to the equation

\[
s = p_1 + p_2q + p_3q^2 + p_4\mu + p_5\mu^2 + p_6\vartheta + p_7\vartheta^2
\] (4.2)

with the coefficients \( p_1 \) to \( p_7 \), the flow inputs \( q \), the viscosity \( \mu \) and the temperature \( \vartheta \). The degree of the polynomial was chosen accord-
4.2 Methods

In the highest $R$-squared value. The difference achieved between $q_{cor}$ and $q$ for all measurement sets should yield a $p$-value $< 0.0001$ in the paired $t$-test for statistical significance. The Kolmogorov-Smirnov test indicates whether the data samples have a standard normal distribution, which is a requirement for validity of the paired $t$-test.

![Diagram](image)

**Figure 4.4:** Test rig for measuring the mass flow rate with a scale. The measured mass flow rate is used to calibrate the volume flow measured by the flow probe.

### 4.2.4 Controller design

To design the controller, we modelled the MC as an open-loop system, assuming a first-order lag element with heating power as input and viscosity as output. We ran heating power steps and measured the resulting step responses of the viscosity to determine the time constant $\tau_s$ and the gain $K$ of the first-order lag element $P(s)$ with the following transfer function:
4 Control of the Fluid Viscosity in a Mock Circulation

\[ P(s) = \frac{K}{\tau s + 1} \]  (4.3)

We verified the resulting transfer function by comparing simulated and measured step responses. The qualitative criterion for choosing the best match was a balance between stationary state error and rise time for both upwards and downwards steps. The transfer function that best mimics the behavior of the plant has the parameters \( K \) of \(-0.016\) cP/W and \( \tau \) of 4700 s.

To achieve the desired control behavior, we designed a PI controller with viscosity error as input and heating power as output. The transfer function of the PI controller \( K(s) \) is:

\[ K(s) = K_P (1 + \frac{1}{T_i}) \]  (4.4)

The proportional constants \( K_P \) and the integrator time constant \( T_i \) were chosen to achieve the best match of the following three specifications: (1) as fast as possible response with a steady-state error smaller than 0.03 cP resulting in an absolute hematocrit error of maximum 0.5%, (2) no overshoot because no active cooling actuator is integrated, and (3) robust behavior for different mixture ratios. An anti-reset windup was realized to clamp the integrator part when the controller output is beyond actuator saturation.

The controller was designed with the help of the idealized modeled plant, at first disregarding the restriction of the sensor resolution and the limited power of the heating actuator. Subsequently we added those restrictions to the modeled plant and we checked whether the resulting behavior still complies with the specifications. Finally the controller was verified in vitro for different steps of the set viscosity in the range of a hematocrit of 20-40%.

4.2.5 Blood pump performance assessment for various controlled viscosities

To investigate the severity of varying viscosities for the blood pump performance, the two centrifugal blood pumps Deltastream DP2 (Xenios AG, Stolberg, Germany) and HVAD (HeartWare Inc., Framing-
4.2 Methods

ham, MA, USA) were assessed at varying viscosities and speeds. The Deltastream DP2 pump was run at four speeds (3000, 3800, 4600, 5400 rpm) and the HVAD pump at four speeds (2000, 2500, 3000, 3500 rpm). The fluid viscosities were 2.15, 2.50, 2.89, 3.33 and 3.81 cP, respectively, such that hematocrits from 20 to 40% are mimicked in steps of 5% at a temperature of 30 ± 0.8 °C. This resulted in 20 combinations for each pump. For each combination, the head pressure was increased in steps of 10 mmHg every 10 s. The first 3 s were wait time to achieve stationary operation and then 7 s were recorded for calculating the mean value of flow and motor current for the respective speed and pressure.

The measurement data was corrected with the calibration slope for flow measurements (see Materials and Methods Section 4.2.3) and a compensation for the pressure loss through wall friction in the tubing. As the calibration of the flow probes was performed for 2-8 L/min, the analysis is performed only in this range. The head pressure was measured in the chambers and the blood pump was connected to the chambers via tubing made of Tygon E-3603. The wall friction in the tubing and the decrease in diameter from chamber to tubing lead to a pressure drop that decreases the measured performance of the pump. The combined length of the tubing before the inlet and after the outlet of the blood pump is 180 mm (HVAD) and 320 mm (Deltastream DP2). Experiments were conducted where the pressure loss was measured with tubing of the same length as used for the pumps for the different viscosities. The pressure difference was increased in steps of 2.5 mmHg every 10 s. The waiting time and recording time was the same as in the previous experiment. The resulting measurement of pressure loss for different flows was used for a fitted quadratic polynomial for correcting the head pressure of the pump.

For a qualitative assessment, pressure over flow (HQ curve) and the motor current over flow (IQ curve) at different pump speeds and viscosities were plotted. For a quantitative assessment, the deviations of pressure and motor current at different viscosities were measured at the common operating point of 5 L/min flow. The mean and maximum deviations between highest and lowest value were calculated.
4 Control of the Fluid Viscosity in a Mock Circulation

4.3 Results

The long-term experiment on the MC with the heating elements turned off reached a peak temperature of 28.4 °C after 410 min. The entire experiment was conducted for 500 min and the fluid temperature at the beginning was 24 °C. The rate of temperature increase for the first 60 min was roughly 0.02 °C/min.

![Graph](image)

Figure 4.5: Performance of integrated viscosity controller for different steps of set viscosity with a 44 mass-% aqueous-glycerol solution. The first panel shows the set (grey) and the actual viscosity (black), the second panel the measured temperature and the third panel the heating power of the nozzle heater bands.

Figure 4.5 shows the results of changes in the set values for the viscosity with the final implementation of the viscosity controller. The working fluid is a 44 mass-% aqueous-glycerol solution and the experiment was started from a room temperature of 24 °C. In this example the initial set point was 3 cP, followed by a step to 2.7 cP after 25 min and a step back to 3 cP after 38 min. All set points were chosen such that the required temperature was above the maximum temperature.
reached in the long-term experiment conducted without a heating element. The time from 3.8 to 3 cP was 16 min. When limiting the temperature range from 30 to 42 °C, an exemplary mixture ratio of 49 mass-% allows to mimic a hematocrit between 29 and 42%.

The implemented controller had no measurable steady-state error and kept the set values in a noise band of ± 0.03 cP. For a set point step of 0.3 cP, the settling time is 8.4 min, showing no overshoot behaviour. The parameters of the PI controller were set aggressively with $K_P$ of $-10^5$ W/cP and $T_i$ of 100 s. When the set value is reached, the heating power jumps between 0 and 100% heating power. The mixture ratio had no influence on the controller performance in the range tested. The time to attain a lower viscosity (3-2.7 cP – heating up in 8.4 min) is six times faster than doing the same step to a higher viscosity (2.7-3 cP – cooling down in 50.5 min), both in an error band of 0.03 cP.

The reduction of error in flow measurement achieved through the calibration of the flow probes is evident in Figure 4.6. The magnitude of the maximum error was reduced from 5.1 to 2.0% and the median error was cut from 1.2 to 0.4%. The quadratic polynomial used for the least-square regression proved to have a better fit with an $R^2$-squared value of 0.91 compared to a linear fit with an $R^2$-squared of 0.82. The polynomial parameters according to Equation 4.2 are: $p_1 = 0.9264, p_2 = 0.02087, p_3 = -0.00129, p_4 = 0.01574, p_5 = -0.00120, p_6 = -0.00308, p_7 = 0.00005$. The difference between the calibrated

![Figure 4.6: Percentage of error magnitude of flow probe measurements with and without calibration. Significant error reduction of $p < 0.0001$ analyzed by a paired $t$-test.](image)
4 Control of the Fluid Viscosity in a Mock Circulation

and not calibrated measurements is considered to be statistically significant. The paired $t$-test shows a $p$-value of $<0.0001$. According to the Kolmogorov-Smirnov test, both data samples have a standard normal distribution.

Figure 4.7 shows how different viscosities influence the hydraulic and electric performance of the two blood pumps HVAD and Deltastream DP2. The deviation of head pressure for different viscosities at 5 L/min for the HVAD and the Deltastream DP2 showed a mean value of 3.6 and 6.4 mmHg and a maximum value of 5 and 8.6 mmHg, respectively. The pressure loss through the wall friction in the tubing that is compensated in the measurement data is 2.1 mmHg and 2.8 mmHg for the same flow. The deviation of current for different viscosities at 5 L/min for the HVAD and the Deltastream DP2 has a mean value of 0.06 and 0.07 A and a maximum value of 0.1 and 0.1 A at the highest speed, respectively. In relative terms this deviation is 15 and 10% of the absolute current value measured at the lowest viscosity. For both pumps the lowest viscosity leads to the lowest current and the highest viscosity to the highest current at all measurement points. The different viscosity lines for each speed of the HVAD are evenly distributed, whereas the viscosity lines for the Deltastream DP2 show an irregular distribution. The higher the speed of the pump, the higher the absolute deviation in current for different viscosities.

4.4 Discussion

The viscosity controller implemented fulfills the set specifications. The aggressiveness of the controller in combination with the discretization of the signal of the viscometer in 0.01 cP steps led to the heating power operating in a binary fashion either at 0% or 100% power, while the requirement of a maximum stationary error of ± 0.03 cP is still fulfilled. The resulting binary operation either at full heating power or zero could also be realized with a simpler control algorithm, but the used PI control does make the control algorithm transferable to similar plants, no matter the restrictions of, for example, sensor resolution or actuator saturation.
4.4 Discussion

Compared to an MC without viscosity controller we are now able to accurately adjust to a certain viscosity to match the desired hematocrit. The time to reach a lower viscosity (heating up) is six times shorter than doing the same step to a higher viscosity (cooling down). A step to a higher viscosity means that the system needs to be cooled down, which is done solely passively by convective heat exchange with the ambient room temperature. For an experiment with a dynamically changing viscosity, an experimental design is therefore recommended that starts at high viscosities. For the viscosity controller implemented, the optimal mixture ratio for the aqueous-glycerol solution has to be chosen according to the targeted viscosity or viscosity range and the tolerated temperature or temperature range, respectively. As the slope of heat introduced through the actuators of the system is around $0.02^\circ$C/min, the minimum operating temperature for short experiments might be chosen just slightly above room temperature.

The here presented implementation of the viscosity controller in an existing MC has some hardware limitations, which in turn lead to limitations for the user of the viscosity control with long settling times depending on the use case. The settling time can vary from, for example, 5 min at startup for a matching mixture ratio of the aqueous-glycerol solution heated up to a temperature slightly above room temperature, to, for example, 21 min for a big viscosity step from 4 to 3 cP (from 41.8 to 31.3% hematocrit). The reason is the limited combined power of the heating bands of 250 W. If a faster response is required, the heater band should be replaced with a high power heater. Additionally, if viscosity steps from low to high viscosities (increase of hematocrit) are required for a study, the slow convective heat exchange with ambient room temperature is not practical and a cooling element should be added.

The new calibration method, where the mass flow rate is measured with a scale as reference, led to a reduction of the mean error to a third of the noncalibrated measurement. The influence on the resulting correction polynomial was most pronounced for the input parameters flow and temperature. For a permanent implementation, the calibration needs to be extended to negative flows and flow rates over 8 L/min. The influence of temperature on the performance of the blood pump to be tested should be considered as well, namely its power consum-
4 Control of the Fluid Viscosity in a Mock Circulation

ation and system efficiency. If the priority is an accurate temperature and small deviations in viscosity are tolerated, the controller may be adapted to the purpose of temperature control, while the viscosity sensor is used to determine whether the viscosity deviation can still be tolerated. For example, a temperature close to a body temperature of 37 °C can be chosen and therefore, future operating conditions for an implantable blood pump can be mimicked well.

When measuring the HQ curves, a ramp in head pressure was performed in steps of 10 mmHg. Together with the flatness of the HQ curves for low flows, this led to an area below 3 L/min where no or very few data points were available, because the change in head pressure from 0 to 3 L/min is below 10 mmHg. For an HQ curve with higher resolution at low flows, smaller steps in head pressure would have to be chosen.

The deviation of head pressure for the blood pumps tested is very low, which implies that the viscosity as a possible error source for a purely hydraulic assessment of the pump performance can be neglected. Considering the maximum values for investigated head pressures of up to 180 mmHg and common uncertainties of measurements, these deviations do not play an important role. This conclusion is in agreement with the results obtained in a study by Vidakovic et al. [135], in which the VentrAssist blood pump was assessed at different viscosities and no discernable changes to the HQ curves were reported from the flow rates and viscosities investigated.

Yet, the assessment of the power consumption is influenced remarkably by varying viscosities. For the same speed at a higher viscosity, a substantially higher motor current was measured in both pumps (see bottom row of Figure 4.7). This effect plays a role when flow estimators are developed, which are based on the motor current and speed of the blood pump [128] or in the process of parameter identification for a system model of a blood pump. The following example scenario shows the consequence for the flow estimation of the HVAD: If the viscosity is not taken into account and the model is built on a hematocrit of 40% while the patient’s hematocrit is only 20%, the error is 12% in current for an operating condition of 5 L/min and 110 mmHg head pressure. This leads to an estimated flow of 7.2 L/min instead of an actual flow of 5 L/min present.
4.5 Conclusion

A viscosity controller with heating actuators and a viscosity sensor has been incorporated into a MC. The benefits for in-vitro experiments with RBPs are boundary conditions that are repeatable and accurate. The experimental results for varying hematocrits showed that the changes in the hydrodynamic performance of RBPs are marginal, but the measured motor current at a high hematocrit can deviate from the measurement at a low hematocrit by up to 15%. Especially for the development of a flow estimator where the motor current is a model input, an integrated viscosity controller is a valuable contribution to an accurate testing environment.
Figure 4.7: Head pressure over flow (HQ curve in the top row) and current over flow (IQ curves in the bottom row) for the HVAD and the Deltastream DP2 pump at different viscosities and speeds. The viscosities are stated with their corresponding hematocrit values in the legend box. Note that scales of the y-axes for current in the bottom row differ.
5 Conclusion and Outlook

5.1 Conclusion

In this thesis, the hydraulic behavior of RBPs under realistic pressure conditions of the cardiac cycle was modelled and compared. Furthermore, effects of typical RBP design parameters were related to indicators of hemocompatibility. Last, a viscosity control for a MC was implemented and investigated. The results have implications not only for the design and testing of new RBPs, but also for the modeling and analysis procedures of existing RBPs.

The hydraulic characteristics of four implantable RBPs were investigated in interaction with simulated dynamic operation conditions for partial and full support conditions. The RBPs were characterized over their entire operating range with one experimental protocol and using the same setup. The chosen universal modeling approach for the hydraulic characteristics incorporated low to negative flows and was based on turbomachinery principles. It proved to be feasible with a good model fit for both axial-flow and radial-flow pump types. Validation results did not show a tendency to exhibit better fits for any particular pump type. The identified hydraulic behavior for the four implantable RBPs revealed a large variation in the hydraulic properties for the different RBPs. No common distinction of the static hydraulic behavior was found in the comparison of the axial-flow and radial-flow pumps, which contradicts a wide-spread assumption in the RBP research community. Our finding suggests that the hydraulic pump characteristics are more influenced by the individual pump design and geometry than by the pump type (axial-flow or radial-flow). The hydraulic loss of the periphery is on average three times as high for axial-flow pumps than for radial-flow pumps, which also means that the HQ curve for axial-flow pumps with periphery is considerably steeper at higher flow rates than without periphery. For both
full and partial support, half of the cardiac cycle is spent at the edges (highest and lowest ten percent) of the flow distribution. These findings suggest that not only the flow field at the mean flow rate but also the flow rate at the extrema needs to be assessed thoroughly. For partial support, three out of four investigated RBPs achieve negative flow rates during diastole, which means instead of the intended pumping direction, blood flow is reversed in the pump and flows back into the left ventricle. These findings suggest that the steepness and the shape of the HQ curve in the low and negative flow regions needs to be taken in particular consideration for a low flow strategy without backflow.

To investigate the effects of typical RBP design parameters on indicators of hemocompatibility, an RBP design was developed based on industrial guidelines and then selected design parameters were systematically varied. The investigated parameters were clearance gap, number of impeller blades and semi-open versus closed shroud designs. The resulting effects on flow field and hydraulic performance were simulated using CFD. As a result, potentially damaging shear stress conditions were associated with larger gap size and more blades. The extent of stagnation and recirculation zones was reduced with lower numbers of blades and a semi-open impeller, but increased with smaller clearance. Smaller clearances led to the highest efficiency. The closed impeller design drastically reduced peak shear stresses over 150 Pa. The Lagrangian hemolysis index showed a negative correlation with hydraulic efficiency. Therefore an optimization of RBPs for efficiency seems feasible when sufficient washout and the danger of pump thrombus with narrow gaps is also taken into account. The hemolysis index did not correlate with the commonly used Eulerian metric with shear stresses over 150 Pa, but instead correlated with shear stresses over 50 Pa. This suggests that, in the considered geometries, peak shear stresses reflect only a small proportion of particles considered in the shear stress history of the Lagrangian hemolysis index. Instead, this index seems to be dominated by medium shear stresses.

A viscosity controller with heating actuators and a viscometer has been incorporated into a MC to mimic the viscosity of blood. This was a necessary prerequisite for repeatable and accurate boundary conditions for the experiments in the two previously described studies. The
implemented viscosity control allows, for example, to change the viscosity in a corresponding hematocrit range between 29 and 42% with a temperature range of 30–42 °C. The experimental results for varying viscosities showed that the changes in the hydrodynamic performance of an RBP are marginal, but the measured motor current at a high viscosity can deviate from the measurement at a low viscosity by up to 15%. Especially for the development of a flow estimator where the motor current is a model input, an integrated viscosity controller is a valuable contribution to an accurate testing environment.

5.2 Outlook

The introduced model structure may serve as a standard for identifying the static and dynamic hydraulic behavior of RBPs in the future, or the already identified models for the four investigated pumps may serve as a rough orientation for similar pump designs. It would be desirable to extend the existing library of hydraulic RBP models with other current or upcoming pump designs, all identified under the same protocol and ideally on the same testbench setup for better comparability.

The identified hydraulic models for the four RBPs provided in this thesis can be used in interaction with a cardiovascular simulation for further studies, for example, to investigate other, more specific support cases such as pediatric support. Also, these models in interaction with a cardiovascular model can be used to produce realistic boundary conditions for fluid dynamics simulations. One study, that already built upon our up to this point unpublished hydraulic models, used the resulting pressure profile for the HM3 over one cardiac cycle as the boundary condition for a CFD simulation that investigates the hemodynamic characteristic of the cardiac pulsatility [136].

In future studies that use indicators of hemocompatibility for the analysis of RBPs, the differences and non-correlation between different metrics for hemocompatibility have to be taken into account. Specifically the Lagrangian and the threshold based Eulerian hemolysis indicator with a 150 Pa threshold did not correlate and therefore seem to predict different outcomes. Our results suggested that an Eulerian
5 Conclusion and Outlook

threshold of 50 Pa might be closer to the hemolysis index with respect to relative hemolysis comparison between different designs.

For future investigations of the effect of design variations, additional design parameters can be included like the blade exit angle and the blade wrap angle. An ongoing study is pursued in our group with the goal of finding the best combination of the design parameters for optimal efficiencies of an RBP. Here, an existing RBP design with active magnetic levitation will be used.
Appendix
A Blood Pump Design Variations

A.1 Resulting geometric design parameters

Industrial pumps differ from blood pumps in terms of size, flow rate, head pressure, efficiency, and Reynolds number [45] to where the application of industrial pump guidelines to LVADs constitutes an extension of their intended use. In our study, these differences caused discrepancies between the set design criteria and the actual operating points obtained in the CFD simulations: To achieve the desired pump flow rate of 4-5 L/min in CFD, we increased the targeted flow given as a design input up to 10 L/min. Similarly, the targeted hydraulic efficiency was set to 80%, which is close to the maximum for centrifugal pumps, but the values achieved only ranged between 38 and 53%, depending on the clearance gap and shroud design chosen.

Possible reasons for the discrepancies observed between design criteria and observed operating points are:

- **Clearance gap to impeller diameter ratio**
  The ratio of the clearance gap to the diameter of the impeller is substantially larger for a blood pump than for an industrial pump. Therefore, any losses due to the clearance gap are more relevant, which may be underestimated in guidelines derived based on larger pumps.

- **Sub-optimal constraints**
  If there is no danger of clogging the pump and if the fluid medium allows it, a closed shroud design is preferable over a semi-open design for efficiency reasons. In our study, we simulated a closed design with the relatively high clearance gap of 300µm. In combination with smaller clearance gaps, a higher efficiency is expected to be achieved.
Discarded leakage flow
The expected leakage flow rate as an input in the design process was set to zero. In an iterative design process, first CFD results of an actual leakage flow rate would be fed back into the calculation and would iteratively lead to more accurate results.

Absent downstream optimization
Designs based on the guideline are further optimized iteratively using CFD [26] and might achieve targeted efficiency values only after the optimization process.

Nonetheless, the resulting design in this study is comparable to clinical blood pumps with regard to impeller dimension, housing size, and hydraulic performance. The geometric output parameters based on the guideline are illustrated in Figure A.1, and the calculated values for the baseline design are listed in Table A.1.

A.2 Grid and time step independence studies
We conducted grid and time step independence studies on three line-probes located in crucial parts of our geometry: the first one spanned across the part of the pump directed towards the outlet, the second one followed a representative streamline within the vanes and the third one ran across the bottom gap between impeller and housing. The three locations are illustrated in Figure A.2. We investigated velocity (Figure A.3 and A.4), pressure (Figure A.5 and A.6) and shear stress (Figure A.7 and A.8) depending on different mesh sizes and time steps. For the grid independence study, a time step of $\Delta t = 5 \times 10^{-5}$ s was used. For the time step independence study, a mesh with 6.3 million cells was used. All simulations were performed on our baseline geometry with 4 blades, a semi-open impeller and 300 $\mu$m clearance gap. All other settings of the CFD simulation are described in the Methods section of the main manuscript.

Since the evaluation of shear stress along the streamline line-probe revealed some differences depending on the grid size, we additionally checked for independence of the resulting hemolysis index HI. HI was
A.2 Grid and time step independence studies

Table A.1: Geometric parameters of the baseline design as obtained from the guidelines for dimensioning the impeller and the volute casing.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Parameter</th>
<th>Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impeller</td>
<td><strong>d₁</strong> Diameter of impeller inlet</td>
<td>13.21</td>
<td>mm</td>
</tr>
<tr>
<td></td>
<td><strong>d₂</strong> Outer diameter of impeller</td>
<td>32.08</td>
<td>mm</td>
</tr>
<tr>
<td></td>
<td><strong>dₙ</strong> Hub diameter</td>
<td>0.80</td>
<td>mm</td>
</tr>
<tr>
<td></td>
<td><strong>b₁</strong> Width of the impeller inlet</td>
<td>6.21</td>
<td>mm</td>
</tr>
<tr>
<td></td>
<td><strong>b₂</strong> Width of the impeller outlet</td>
<td>2.90</td>
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<tr>
<td></td>
<td><strong>zₐ</strong> Number of impeller blades</td>
<td>5</td>
<td>[-]</td>
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<tr>
<td></td>
<td><strong>Rₐ</strong> Radius of curvature</td>
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<td></td>
<td><strong>zₑ</strong> Axial extension</td>
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<td><strong>g₁</strong> Short section to achieve flat pressure ditribution</td>
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<td><strong>εₐ</strong> Angle of the free blade at the trailing edge</td>
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<tr>
<td></td>
<td><strong>εₑ</strong> Angle of the bottom shroud at the trailing edge</td>
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<td><strong>εₑₑ</strong> Angle of the leading edge</td>
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<td><strong>β₂</strong> Outlet angle of impeller blade</td>
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<td>°</td>
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<td>**eₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑᵣ</td>
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<td>160.00</td>
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<td>Volute casing</td>
<td><strong>a₃</strong> Width of the throat area</td>
<td>9.15</td>
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<td><strong>d₃</strong> Inner diameter of the discharge nozzle</td>
<td>8.17</td>
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<td>17.76</td>
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<td><strong>b₃</strong> Height of the casing at the impeller outlet</td>
<td>5.79</td>
<td>mm</td>
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<td></td>
<td>**eₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑₑطور</td>
<td>0.64</td>
<td>mm</td>
</tr>
</tbody>
</table>
5.00 \times 10^{-5} for a mesh with 11.1 million cells compared to 5.07 \times 10^{-5} for a mesh with 6.3 million cells.
Figure A.2: Location of the three line-probes used for testing grid and time step independence: “Cross Outlet” (blue) runs across the part of the pump directed towards its outlet at half height of the channel. “Streamline” (red) runs along a streamline through the vane. “Bottom Gap” (green) runs across the gap below the impeller at half height of the total gap.
Figure A.3: Results of the grid independence study with respect to velocity. The three graphs represent the three geometric locations tested. The time step in these simulations was $\Delta t = 5 \times 10^{-5}$ s. The mesh with 6.3 million cells was chosen for the study. Position refers to the geometrical position on the line probe.
A.2 Grid and time step independence studies

Figure A.4: Results of the time step independence study with respect to velocity. The three graphs represent the three geometric locations tested. The grid size in these simulations was 6.3 million cells. $\Delta t = 5 \cdot 10^{-5}$ s was chosen for the study. Position refers to the geometrical position on the line probe.
Figure A.5: Results of the grid independence study with respect to pressure. The three graphs represent the three geometric locations tested. The time step in these simulations was $\Delta t = 5 \times 10^{-5}$ s. The mesh with 6.3 million cells was chosen for the study. Position refers to the geometrical position on the line probe.
A.2 Grid and time step independence studies

Figure A.6: Results of the time step independence study with respect to pressure. The three graphs represent the three geometric locations tested. The grid size in these simulations was 6.3 million cells. $\Delta t = 5 \times 10^{-5}$ s was chosen for the study. Position refers to the geometrical position on the line probe.
Figure A.7: Results of the grid independence study with respect to shear stress. The three graphs represent the three geometric locations tested. The time step in these simulations was $\Delta t = 5 \times 10^{-5}$ s. The mesh with 6.3 million cells was chosen for the study. Position refers to the geometrical position on the line probe.
A.2 Grid and time step independence studies

Figure A.8: Results of the time step independence study with respect to shear stress. The three graphs represent the three geometric locations tested. The grid size in these simulations was 6.3 million cells. $\Delta t = 5 \times 10^{-5}$ s was chosen for the study. Position refers to the geometrical position on the line probe.
A. Blood Pump Design Variations

A.3 Raw data hemocompatibility indicators (Figure 3.4)
Table A.2: Geometric parameters of the baseline design as obtained from the guidelines for dimensioning the impeller and the volute casing.

<table>
<thead>
<tr>
<th>Variation</th>
<th>Geometries</th>
<th>Hemolysis indicators</th>
<th>Thrombosis indicators</th>
<th>VWF cleavage</th>
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<td></td>
<td>Label acc. to Table 3.2</td>
<td>Geometry feature</td>
<td>$HI$</td>
<td>$I_{r&gt;150 Pa}$</td>
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<tr>
<td>Clearance gap size</td>
<td>I</td>
<td>50 μm</td>
<td>3.20E-05</td>
<td>4.80E-04</td>
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<td></td>
<td>II</td>
<td>150 μm</td>
<td>4.05E-05</td>
<td>3.82E-04</td>
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<tr>
<td></td>
<td>Baseline</td>
<td>300 μm</td>
<td>5.07E-05</td>
<td>3.64E-04</td>
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<tr>
<td></td>
<td>III</td>
<td>500 μm</td>
<td>5.51E-05</td>
<td>4.85E-04</td>
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<tr>
<td>Number of blades</td>
<td>IV</td>
<td>4 blades</td>
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<tr>
<td></td>
<td>V</td>
<td>6 blades</td>
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<td>VI</td>
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<td>Semi-open</td>
<td>5.07E-05</td>
<td>3.64E-04</td>
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<td>VII</td>
<td>Closed</td>
<td>5.59E-05</td>
<td>6.41E-05</td>
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</table>
A Blood Pump Design Variations

A.4 Maximum shear stress histograms

![Histograms of the maximal scalar shear stress experienced by each Lagrangian particle track depending on the clearance gap size.](image)

**Figure A.9:** Histograms of the maximal scalar shear stress experienced by each Lagrangian particle track depending on the clearance gap size. A: Clearance gap = 50 \( \mu \text{m} \) (geometry I). B: Clearance gap = 150 \( \mu \text{m} \) (geometry II), C: Clearance gap = 300 \( \mu \text{m} \) (geometry baseline), D: Clearance gap = 500 \( \mu \text{m} \) (geometry III). For optimal display, the x-axis shows maximum shear stresses between 0 and 500 Pa for all geometry variations. The maximum experienced shear stress was 694, 662, 486 and 418 Pa with the 50, 150, 300 and 500 \( \mu \text{m} \) gap sizes, respectively.
Figure A.10: Histograms of the maximal scalar shear stress experienced by each Lagrangian particle track depending on the number of blades. A: 4 blades (geometry IV), B: 5 blades (geometry baseline), C: 6 blades (geometry V), D: 7 blades (geometry VI). For optimal display, the x-axis shows maximum shear stresses between 0 and 500 Pa for all geometry variations. The maximum experienced shear stress was 468, 486, 440 and 414 Pa with 4, 5, 6 and 7 blades, respectively.
Figure A.11: Histograms of the maximal shear stress experienced by each Lagrangian particle track depending on the shroud design. A: semi-open impeller (geometry baseline), B: closed impeller (geometry VII). For optimal display, the x-axis shows maximum shear stresses between 0 and 500 Pa for all geometry variations. The maximum experienced shear stress was 486 and 303 Pa for the semi-open and closed shroud design, respectively.
B Hydraulic Characterization of RBPs

B.1 Static HQ curves

To get a visual impression of the model accuracy for all four pumps, Figure B.1 shows the static identification measurements performed in vitro in comparison to the respective hydraulic models.
Figure B.1: Static in-vitro measurements (black lines) compared to the respective mathematical models (grey thick line). The HQ curves are displayed at the pumps speeds that were used for the static and the dynamic identification. The coefficient of determination $R^2$ is displayed at the top right of each graph.
B.2 Flow pulsatilities

Table B.1 lists the flow pulsatilities derived for the four pumps for full support and partial support. The flow pulsatilities for the static and the dynamic model are compared.

Table B.1: Flow pulsatility for each pump in L/min measured for full and partial support in the static and dynamic model, respectively.

<table>
<thead>
<tr>
<th>Support</th>
<th>Model</th>
<th>HVAD</th>
<th>HM3</th>
<th>HMII</th>
<th>Incor</th>
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<td>Full support</td>
<td>static</td>
<td>3.9</td>
<td>1.9</td>
<td>4.1</td>
<td>1.3</td>
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<td></td>
<td>dynamic</td>
<td>3.2</td>
<td>1.8</td>
<td>3.0</td>
<td>1.2</td>
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<td>Partial support</td>
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<td>8.5</td>
<td>5.9</td>
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<td>dynamic</td>
<td>9.1</td>
<td>6.3</td>
<td>7.5</td>
<td>4.1</td>
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</table>

B.3 Steepness of HQ curves

Table B.2 lists the steepnesses measured in the static HQ curves at the respective average operating point of full and partial support for solely the pump and pump with periphery, respectively.

Table B.2: Steepness of the HQ curve in the static model at full and partial support in mmHg/(L/min), measured at the respective average operating point.

<table>
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<th>System</th>
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<th>HM3</th>
<th>HMII</th>
<th>Incor</th>
</tr>
</thead>
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<td>Full support</td>
<td>Pump</td>
<td>−8.7</td>
<td>−18.5</td>
<td>−5.7</td>
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<tr>
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<td>Pump with periphery</td>
<td>−9.8</td>
<td>−19.7</td>
<td>−9.5</td>
<td>−28.5</td>
</tr>
<tr>
<td>Partial support</td>
<td>Pump</td>
<td>−5.4</td>
<td>−10.5</td>
<td>−2.9</td>
<td>−16.1</td>
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<td></td>
<td>Pump with periphery</td>
<td>−6.0</td>
<td>−11.2</td>
<td>−5.2</td>
<td>−18.0</td>
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Bibliography


Bibliography


Bibliography


Bibliography


Bibliography


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