On Aortic Blood Flow Simulations
Scale-Resolved Image-Based CFD

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Scale-Resolved Image-Based CFD

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Cover: Colorful Display of turbulent kinetic energy in an aortic coarctation
Nobody climbs mountains for scientific reasons. Science is used to raise money for the expeditions, but you really climb for the hell of it.

Sir Edmund Hillary (1919-2008)
Abstract

This thesis focuses on modeling and simulation of the blood flow in the aorta, the largest artery in the human body. It is an accepted fact that abnormal biological and mechanical interactions between the blood flow and the vessel wall are involved in the genesis and progression of cardiovascular diseases. The transport of low-density lipoprotein into the wall has been linked to the initiation of atherosclerosis. The mechanical forces acting on the wall can impede the endothelial cell layer function, which normally acts as a barrier to harmful substances. The wall shear stress (WSS) affects endothelial cell function, and is a direct consequence of the flow field; steady laminar flows are generally considered atheroprotective, while the unsteady turbulent flow could contribute to atherogenesis. Quantification of regions with abnormal wall shear stress is therefore vital in order to understand the initiation and progression of atherosclerosis.

However, flow forces such as WSS cannot today be measured with significant accuracy using present clinical measurement techniques. Instead, researches rely on image-based computational modeling and simulation. With the aid of advanced mathematical models it is possible to simulate the blood flow, vessel dynamics, and even biochemical reactions, enabling information and insights that are currently unavailable through other techniques. During the cardiac cycle, the normally laminar aortic blood flow can become unstable and undergo transition to turbulence, at least in pathological cases such as coarctation of the aorta where the vessel is locally narrowed. The coarctation results in the formation of a jet with a high velocity, which will create the transition to turbulent flow. The high velocity will also increase the forces on the vessel wall. Turbulence is generally very difficult to model, requiring advanced mathematical models in order to resolve the flow features. As the flow is highly dependent on geometry, patient-specific representations of the in vivo arterial walls are needed, in order to perform an accurate and reliable simulation.

Scale-resolving flow simulations were used to compute the WSS on the aortic wall and resolve the turbulent scales in the complex flow field. In addition to WSS, the turbulent flow before and after surgical intervention in an aortic coarctation was assessed. Numerical results were compared to state-of-the-art magnetic
resonance imaging measurements. The results agreed very well, suggesting that the measurement technique is reliable and could be used as a complement to standard clinical procedures when evaluating the outcome of an intervention.

The work described in the thesis deals with patient-specific flows, and is, when possible, validated with experimental measurements. The results provide new insights to turbulent aortic flows, and show that image-based computational modeling and simulation are now ready for clinical practice.
Populärvetenskaplig beskrivning

Den vanligaste dödsorsaken i Sverige och övriga delar av västvärlden är hjärt- och kärlsjukdomar. Förutom riskfaktorer som t.ex. rökning, diabetes och bukfetma finns det även en koppling mellan hjärt-kärlsjukdomar och blodflöde. De delar i kärlsystemet där blodet har en onaturlig effekt på kärlväggen sammanfaller ofta med områden med åderförfettning, _ateroskleros_, dvs. inlagring av fett och kolesterol i kärlväggen. Vad är då en onaturlig effekt?


Det är här modellering och simulering av blodflöden kommer in. Denna avhandling beskriver hur man med hjälp av avancerade matematiska modeller kan bestämma hur det yttersta cellagret påverkas av blodflödet. Vanligtvis är blodflödet laminärt, dvs. välvordmat och effektivt, men vid sjukdomsfall där förträngningar av kärl eller hjärtklaffar lokalt minskar tvärsnittsareaen kan flödet övergå till att bli turbulent. Ett turbulent flöde karaktäriseras av oregelbundenhet och är, sett ur ett energiperspektiv, ineffektivt. Dessutom kommer ett turbulent flöde att resultera i komplexa friktionskrafter på väggen, med både varierande riktning och storlek. En noggrann och korrekt kvantifiering av dessa krafter är mycket viktiga för att förstå uppkomst och utveckling av olika hjärt- och kärlsjukdomar.

Parallellt med beräkningar krävs mätningar på patienter. En patient som un-
dersöktes led av en förträngning på aortan som påverkade både blodflödet och krafterna på kärlväggen. Patienten undersöktes både före och efter operation för att kunna utvärdera ingreppet. Förträngningen hade tvingat fram en övergång från laminärt till turbulent flöde och beräkningar visade bland annat att det turbulent flödet minskade efter en operation där förträngningen vidgades. Resultaten jämfördes med en ny experimentell teknik för turbulensmätningar och överensstämmelsen mellan beräkningar och mätningar var mycket god. Detta innebar att mätmetoden är mycket lovande och att den efter ytterligare studier skulle kunna användas i en klinisk tillämpning som komplement till traditionella undersökningsmetoder.

Arbetet som är beskrivet i avhandlingen visar potentialen av att använda modellering och simulering av biologiska flöden för att få kliniskt relevant information för diagnos, operationsplanering och/eller uppföljning av ingreppet på en patientspecifik nivå.
This thesis was carried out at the Division of Applied Thermodynamics and Fluid Mechanics, Department of Management and Engineering, Linköping University.

I would like to thank my main advisor Matts Karlsson for introducing me to the wonderful field of image-based computational fluid dynamics, and for being a never-ending source of new thoughts and bright ideas. Somehow we managed to cherry-pick the best ones, and I am both proud and pleased with the outcome. Thank you!

Writing scientific research articles is a team effort and none of the articles in this thesis would have been published without my skilled colleagues and co-authors. A big thank you goes to Roland Gårdhagen, Fredrik Carlsson, Johan Renner, Tino Ebbers and Jan Engvall for their hard work and valuable input. Dan Loyd is greatly acknowledged for his thoughts and comments on the draft of this thesis. I would also like to take the opportunity to express my gratitude to my friends and colleagues at the Division of Applied Thermodynamics and Fluid Mechanics for the valuable discussions and good company during these five years. In addition, I would like to acknowledge the people I got to know at IEI, IMT and CMIV who in different ways also contributed to this work.

Besides doing fancy research and colorful pictures, I have also been teaching in courses ranging from basic thermodynamics to aerodynamics and computational fluid mechanics. Teaching and interacting with more than 500 students from all over the world has been both fun and enlightening, and for that I thank you all.

Last, but not least, I would like to express my sincere gratitude to my family and friends for always being there when I need them, and for reminding me that there is another reality outside the university. A very special thank you goes to my wife Karin for your love and affection - `Without You I’m Nothing’.

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November 2012
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List of Papers

This thesis is based on the following five papers, which will be referred to by their Roman numerals:

I. Quantifying Turbulent Wall Shear Stress in a Stenosed Pipe Using Large Eddy Simulation
   Roland Gårdhagen, Jonas Lantz, Fredrik Carlsson and Matts Karlsson
   *Journal of Biomechanical Engineering*, 2010, 132, 061002

II. Quantifying Turbulent Wall Shear Stress in a Subject Specific Human Aorta Using Large Eddy Simulation
    Jonas Lantz, Roland Gårdhagen and Matts Karlsson
    *Medical Engineering and Physics*, 2012, 34, 1139-1148

III. Wall Shear Stress in a Subject Specific Human Aorta - Influence of Fluid-Structure Interaction
     Jonas Lantz, Johan Renner and Matts Karlsson

IV. Large Eddy Simulation of LDL Surface Concentration in a Subject Specific Human Aorta
    Jonas Lantz and Matts Karlsson
    *Journal of Biomechanics*, 2012, 45, 537-542

V. Numerical and Experimental Assessment of Turbulent Kinetic Energy in an Aortic Coarctation
   Jonas Lantz, Tino Ebbers, Jan Engvall and Matts Karlsson
   Submitted for publication

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Abbreviations

$\alpha$  Womersley number
$\phi$   Generic flow variable
CAD    Computer Aided Design
CFD    Computational Fluid Dynamics
CFL    Courant-Friedrichs-Lewy condition
CT     Computed Tomography
DNS    Direct Numerical Simulation
FSI    Fluid-Structure Interaction
KE     Kinetic Energy
LDL    Low-Density Lipoprotein
LES    Large Eddy Simulation
MIP    Maximum Intensity Projection
MRI    Magnetic Resonance Imaging
OSI    Oscillatory Shear Index
PC-MRI Phase Contrast Magnetic Resonance Imaging
Pe     Péclet Number
PWV    Pulse Wave Velocity
RANS   Reynolds Averaged Navier Stokes
Re     Reynolds Number
RMS    Root-Mean-Square
RSM    Reynolds Stress Model
Sc     Schmidt Number
SGS    Subgrid-Scale Model
$T_i$  Turbulence intensity
TAWSS  Time-Averaged Wall Shear Stress
TKE or $k$ Turbulent Kinetic Energy
US     Ultrasound
WALE   Wall-Adapting Local Eddy-Viscosity Subgrid-Scale Model
WSS    Wall Shear Stress
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Chapter 1

Introduction

The purpose of the human cardiovascular system is to transport oxygenated blood from the lungs to the rest of the body, and in addition, transport nutrients, hormones, waste products and other important substances around the blood stream. Diseases related to the cardiovascular system is the most common cause of death, both in Sweden and worldwide [1]. During 2010, 41% of women and 39% of men in Sweden had cardiovascular disease as the underlying cause of death [2].

There is a close connection between some cardiovascular diseases and blood flow [3], and in order to understand the genesis and progression of these diseases, accurate description and assessment of blood flow features are crucial. While non-invasive measurement techniques are getting more and more advanced, accuracy and resolution are still a limiting factor. Flow features such as wall shear stress, which depend on the velocity gradient at the arterial wall, cannot be measured with a significant accuracy using present measurement techniques. Additionally, complex biological systems and individual variability makes it difficult to use imaging and experiences from larger groups to provide information on a single individual patient [4].

This is where modeling and simulation of physiological flows come in. Where today’s measurement techniques are limited in spatial and temporal resolution, mathematical models representing physiological flow situations are, in essence, only limited by computer power. With computational fluid dynamics (CFD) it is possible, at least in theory, to simulate not only healthy and diseased conditions but also what-if scenarios, for example to determine the optimal location of a stent or to predict the outcome of a surgery, on an individual basis. As noted by Taylor et al [5], CFD could be a powerful tool, "[...] surpassing experimental fluid mechanics methods to investigate mechanisms of disease, and design and evaluation of medical devices and therapeutic interventions". These opportunities are still in its infancy, and necessary steps in terms of accuracy and validation are required before it can be used on a clinical basis. Robust methods are essential,
CHAPTER 1. INTRODUCTION

not only for reliable results but also for convincing the (sometimes conservative) physician about the possibilities of CFD modeling and simulation.

Modeling physiological flows is difficult. The difficulties arise from both physics and physiology; the flow may be transitional or even turbulent in some cases, which calls for the need of advanced turbulence models to accurately predict the flow features. At the same time, each patient is unique in terms of vascular geometry and flow, introducing the need for patient-specific geometries and boundary conditions in the flow model. Thus, in order to use modeling tools to simulate flows on a clinical level, measurements of each patient has to be made. This can be done with magnetic resonance imaging (MRI) or computer tomography (CT). While both image modalities are non-invasive, CT uses ionizing radiation and is unable to quantify flow, making MRI the natural choice in cardiovascular flow research. Image-based CFD refers to the use of image material from a measurement technique, such as MRI, in a numerical flow simulation.

Blood flow features are affected by the geometry, but not only in the vicinity of the area of interest, but also upstream and downstream the blood vessel. Effects such as wave reflections, wall distensibility, and flow branching all affect the flow, and may need to be considered in a flow model. Simplifications can sometimes be made; the assumptions of a rigid arterial wall and that blood behaves like a Newtonian fluid are the two most common. However, it is important to understand how these simplifications affect the result. Recent advances in computer hardware and numerical methods has made it possible to simulate complex flow problems, including transitional and turbulent flows that are related with cardiovascular disease [5]. The goal of any simulation determines the amount of simplifications that can be made, and thus, requires a thorough understanding of both the fluid mechanics and the physiology of the cardiovascular system.

This thesis focuses on modeling and simulation of blood flow in the human aorta. The aorta has a complex shape, characterized by curvature, bending and tapering. With the addition of branching vessels, a highly complicated three-dimensional flow is obtained, even in healthy subjects. In a diseased environment the flow may become even more complex with the transition to turbulent flow. Accurate modeling of these types of flows may be crucial for understanding the progression and genesis of cardiovascular diseases, or when evaluating different surgical options. Modeling may also be used for intervention planning and evaluation of the outcome of a surgery. Obviously, computational modeling can and will provide a useful tool in clinical practice. The challenge is to translate the opportunities and possibilities available in computational simulations to the clinic [3].
Chapter 2

Aims

The goal of the research described in this thesis was to model and quantify the blood flow in the human aorta, considering both healthy subjects and patients. It is believed that much can be gained in a clinical environment if image-based computational modeling and simulation can be used for diagnose, intervention planning, and/or treatment follow-up. Specifically, the following aims were addressed:

- Use advanced computational models, in particular large eddy simulation (LES) for simulating turbulent flows and fluid-structure interaction (FSI) for simulating wall motion, in order to quantify aortic blood flow in both healthy subjects and patients.

- Simulate the flow-dependent transport of a passive scalar, e.g. low-density lipoprotein (LDL) and correlate its accumulation on the arterial wall to flow features and locations prone to develop cardiovascular disease.

- Apply the gained knowledge on a patient with an aortic coarctation before and after surgery to evaluate the change in blood flow due to the intervention, and by doing so take computational modeling one step closer to clinical practice.
Chapter 3

Physiological Background

3.1 The Circulatory System

The circulatory system in humans include three important parts: a heart, blood and blood vessels. The heart pumps the blood through the vessels in a loop, and the system is able to adapt to a large number of inputs as the demand on circulation varies throughout the body, day and life. The circulatory need is e.g. different between rest and exercise, and in different body positions.

During systole, the left ventricle in the heart contracts and ejects the blood volume into the aorta. The blood pressure in aorta increases and the arterial wall is distended. After the left ventricle has relaxed, the aortic valve closes and maintains the pressure in the aorta while the blood flows throughout the body. The blood continues to flow through smaller and smaller arteries, until it reaches the capillary bed where water, oxygen, and other nutrients and waste products are being exchanged, and is then transported back to the right side of the heart through the venous system. The right side of the heart pumps the blood to the lungs for oxygenation, which then enters the left side of the heart again, closing the loop [6].

3.2 Anatomy of the Aorta

The blood leaves the left ventricle of the heart during systole and is ejected through the aortic valve into the ascending aorta. After the ascending aorta the blood deflects into (normally) three larger branching vessels in the aortic arch which supplies the arms and head, or makes a 180-degree turn and continues through the descending and thoracic aorta towards the abdomen.

The parts of the aorta all have different shapes, in terms of bending, branching and tapering, creating different flow fields. The flow behavior in the ascending aorta is characterized by the flow through the aortic valve, and the curvature can
CHAPTER 3. PHYSIOLOGICAL BACKGROUND

Figure 1: Schematic figure of the largest artery in the human body, the aorta.

create a skewed velocity profile. The flow in the arch is highly three-dimensional, with helical flow patterns developing due to the curvature, and unsteady flows can be created as a result of the branching vessels. The flow patterns that are created in the ascending aorta and arch are still present in the descending aorta, where local recirculation regions may appear as a result of the curvature and bending of the arch.

The aortic wall is elastic in its healthy state, and will deform due to the increase or decrease in blood pressure. The wall consists of three layers: intima, media, and adventitia. Regardless of the contents of each layer, the arterial wall is made up out of four basic building blocks: endothelial cells, elastic fibers, collagen fibers, and smooth muscle cells [6]. All blood vessels are lined with a single layer of endothelial cells that are in direct contact with the blood flow. The elastic fibers are mainly made up of elastin and are, as the name suggests, responsible for the elastic properties of the vessel; elastin fibers are capable of stretching more than 100% under physiological conditions. Collagen fibers on the other hand, are only capable of stretching 3-4% and together with the elastin, determines the compliance and distensibility of the artery. Finally, the smooth muscle cells are muscle fibers which, when activated can contract the wall to change the vessel diameter and, thus, change blood pressure. When they are relaxed they do not contribute significantly to the elastic properties. Arteries are thicker than veins due to a larger amount of smooth muscle cells in the walls.
3.3 Cardiovascular Disease and Blood Flow

Blood flow characteristics are involved either directly or indirectly in the initiation and progression of some cardiovascular diseases. In particular, highly oscillating, disturbed, or turbulent flows, which are uncommon in normal healthy persons, can introduce adverse effects to the heart or blood vessel [7–10].

It is now common knowledge that blood flow affects the endothelial structure, which, in turn, may initiate vascular diseases such as atherosclerosis or aneurysms. Atherosclerosis is an ongoing inflammatory response to local endothelial dysfunction initiated by one or several factors, such as abnormal wall shear stress levels, hypertension, oxidative stress, and elevated low-density lipoprotein levels [3, 11–13]. Research on the importance of blood flow in the development of atherosclerosis have been performed since the late 1960’s to early 1970’s [14, 15], but a complete understanding of the disease is still lacking. The influence of flow on the endothelial cell layer is believed to be correlated to the development and progression of atherosclerotic disease [9, 10, 15, 16]. Formation and development of aortic aneurysms are highly dependent on the structural integrity of the arterial wall, making hemodynamics an important factor when characterizing the biomechanical environment [17]. Aortic dissection is another disease that is highly flow dependent; the blood flow creates a fake lumen between the intima and media layers in the wall, causing the formation of a stenosis or even occlusion of the vessel. Carotid artery dissection is a common cause of stroke among young and middle-aged persons [18].

Flow characteristics can also be used as an indicator of cardiovascular disease; a common example is the turbulent blood flow through an aortic valve stenosis, where the fluctuating pressure levels produce sounds (heart murmurs) that can be heard in a stethoscope. Normally, turbulent or highly disturbed flow are considered abnormal and are often an indication of a narrowed blood vessel or a stenotic heart valve, which by decreasing the cross-sectional area increases the flow velocity and triggers a transition to turbulence. The turbulent kinetic energy is a measure of the amount of turbulent fluctuations, and high values indicate a very energy ineffective flow, as energy from the mean flow is lost to feed the turbulent fluctuations, which in turn increases the heart work load to maintain the flow rate [19]. This also applies to constrictions such as coarctations or stenoses, which introduce additional pressure losses over the constriction. In essence, any flow that departs from the energy efficient laminar characteristics to a disturbed turbulent flow, will introduce a higher workload on the heart and vessels.

The force that affects the vessel wall consists of two components: the blood pressure and wall shear stress. The blood pressure acts in the normal direction to the wall, while the wall shear stress acts tangentially. Blood pressure is normally on the order of 1000 times larger than the wall shear stress. However, endothelial
CHAPTER 3. PHYSIOLOGICAL BACKGROUND

cells are much more susceptible to the frictional shear force than the pressure, making them very sensitive to local flow conditions. They have been shown to align with flow direction if the shear magnitude is steady and large enough, while they become randomly orientated and take on a cobblestone shape in low or oscillating wall shear regions [8, 20, 21].

Although there are several risk factors (including both environmental, genetic and biological) linked to the development of atherosclerosis, the disease is often localized to certain vascular regions, such as in the vicinity of branching or highly curved vessels and arterial stenoses [22]. These are locations where nonuniform blood flows are present, creating a locally very complex wall shear stress pattern. Regions experiencing low and/or oscillating shear stress has been shown to be more prone to develop atherosclerotic lesions [8, 11, 15, 22–27], possibly due to the fact that the permeability of the endothelial cell layer can be shear dependent [11, 28, 29]. High levels of wall shear stress has been found to be atheroprotective, but a strict definition of high and low values is difficult to define [22].

In addition to low and oscillating shear stress, elevated low-density lipoprotein (LDL) surface concentration and increased particle residence time of the flow field could promote mass transport into the vessel wall, especially if the wall permeability is enhanced due to abnormal wall shear stress. Increased particle residence time occurs in regions with recirculating flow or very slowly moving fluids [30, 31]. Increased levels of low-density lipoprotein has been shown to promote the accumulation of cholesterol within the intima layer of large arteries [32, 33]. There is a small flux of water from the blood to the arterial wall, driven by the arterial pressure difference, which can transport LDL to the arterial wall. The endothelium presents a barrier to LDL, creating a flow-dependent concentration boundary layer. This concentration polarization is interesting, as regions of elevated LDL are co-located with low shear stress regions [13], suggesting a relationship between accumulation and flow dynamics. Studies in humans and animals indicate that the flux of LDL from the plasma into the arterial wall depends both on the concentration and the permeability at the plasma-arterial wall interface [34].

3.4 Medical Imaging Modalities

In clinical practice there are, in general, three different techniques used for cardiovascular imaging: Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and Ultrasound (US).

CT has the advantage of providing a very high resolution of lumenal geometries, and also has the ability to detect different materials due to the fact that the absorption of x-rays change with the material. However, CT is based on ionizing
3.4. MEDICAL IMAGING MODALITIES

radiation and uses contrast agents to distinguish between the lumen and surrounding tissue. Also, the technique is unable to measure flow, and is therefore not the method of choice for studies in blood flow research [11].

Ultrasound is non-invasive, has an excellent temporal resolution and is perhaps the most widely available clinical imaging technique. A high-frequency beam is transmitted into the body and the resulting echoes are collected and used to produce an image. Normally, flow velocity measurements only yield one value per lumenal cross-section. Thus, flow wave forms are normally obtained with the assumption of a known velocity profile (normally Hagen-Poiseuille), which may be far from in vivo flow conditions [3, 35]. Additionally, the image quality is very dependent on the proximity of the transducer to the vessel, making US limited to superficial vessels. Despite these drawbacks, it is commonly used in clinical practice as it is a relatively cheap method compared to CT and MRI, making it useful for screening examinations.

The method of choice for studying cardiovascular flows is MRI [3, 11]. There are no ionizing radiation and both flow and geometry can be measured. The technique is based on the detection of magnetization arising from the nucleus of hydrogen atoms in water. Radio frequencies are used to change the alignment of the magnetization vector, and the time it takes for the magnetization vector to return to its original position after the radio frequency signal has been shut off will indicate what kind of tissue that returns the signal to the receiver. Phase Contrast MRI (PC-MRI) is a technique that images the flowing blood inside the vessel, and thereby gives both velocity and geometrical information. The name comes from the fact that the velocity signal is encoded in the phase of the complex MRI signal. The technique can measure all three velocity components [36], and has also recently been shown to being able to quantify turbulent kinetic energy [37].

The image material obtained from MRI is useful when making computer models of cardiovascular flows, as it provides both the geometry and proper flow boundary conditions. Additionally, image data for validation of simulation results are also made available. However, compared to numerical models the resolution is coarse, especially near the walls. Wall shear stress would be desirable to measure with MRI, see e.g. [38], but as the near-wall velocity gradient cannot be resolved with sufficient accuracy, estimations of MRI-based wall shear stress will be inaccurate [39, 40]. Instead, numerical models are used extensively to resolve local wall shear stress patterns and other hemodynamic parameters.
Chapter 4

Modeling Cardiovascular Flows

4.1 Governing Equations

The motion of a fluid is governed by the following conservation laws [41, 42]:

- Conservation of mass
- Conservation of momentum
- Conservation of energy

The first law states that mass cannot be created nor destroyed. The second law states that the rate of change of momentum equals the sum of the forces on a fluid particle, and is described by Newton’s second law. The third law states that the rate of change of energy is equal to the rate of change of heat addition and work done on a fluid particle, and is the first law of thermodynamics. If the motion of a fluid is only affected by phenomena on a macroscopic scale and molecular effects can be ignored, it is regarded as a continuum. A fluid element therefore represents an average of a large enough number of molecules in a point in space and time. On a continuum level, the fluid element is the building block on which the conservation of mass, momentum, and energy apply to.

Throughout the text an incompressible, isothermal fluid is assumed. This assumption is often justifiable for liquids under normal pressure levels, such as water and blood. Conservation of mass for an incompressible fluid results in the following volume continuity equation for a fluid element:

\[ \nabla \cdot \mathbf{u} = 0 \]  

(1)

where \( \mathbf{u} \) is the velocity vector. Equation 1 implies that an equal amount of mass that enters a volume also must leave it. Conservation of energy states that total amount of energy is constant over time within a system or control volume. In an
CHAPTER 4. MODELING CARDIOVASCULAR FLOWS

 Isothermal system the conservation law balances the amount of energy lost due to work done by the system with the change in internal energy of the system.

The rate of change of momentum of a fluid element can be described as:

\[ \rho \left( \frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) \]  \( (2) \)

where \( \rho \) is the density of the fluid and \( t \) time. The rate of change of momentum balances the forces acting on the fluid element. The forces are usually divided into two types: body and surface forces. Body forces could e.g. be gravity, centrifugal, Coriolis, or electromagnetical forces, while surface forces are typically pressure and viscous forces. Body forces are introduced through a source term \( S \), while surface forces are included through the stress tensor \( \sigma \). For a Newtonian fluid, where the viscosity is constant, the stress tensor becomes:

\[ \sigma = -\nabla p + \mu \nabla^2 \mathbf{u} \]  \( (3) \)

which is the sum of pressure and viscous forces. Here \( p \) is the pressure and \( \mu \) the viscosity of the fluid. The stress tensor and body forces balances the rate of the change of momentum [42], yielding the Navier-Stokes equations:

\[ \rho \left( \frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) = -\nabla p + \mu \nabla^2 \mathbf{u} + S \]  \( (4) \)

The first term on the left hand side of Equation 4 describes the transient acceleration while the second term is the convective acceleration. The terms on the right hand side are a pressure gradient, a viscous term, and a source term accounting for body forces. Together with the continuity equation, Equation 1, and proper initial and boundary conditions they form a complete description of a fluid’s velocity and pressure fields, \( \mathbf{u}(x, t) \) and \( p(x, t) \).

4.2 Flow Properties

Flows can be categorized as either steady or transient, and laminar or turbulent. A steady (time-independent) type of flow can be present in predominantly smaller arteries in the human body, far away from the pumping heart. But, even in larger arteries a steady flow assumption can be useful, as it can provide initial insights and information when modeling physiological flows. However, the flow in the aorta and other larger vessels are pulsatile due to the pumping motion of the heart, and a transient approach is therefore needed to accurately capture time-dependent blood flow features.
An important parameter in fluid mechanics is the Reynolds number \((Re)\), which is a measure of the ratio of inertial to viscous forces, defined as:

\[
Re = \frac{\rho U L}{\mu}
\]

where \(\rho\) and \(\mu\) have been defined earlier and \(U\) and \(L\) are characteristic velocity and length scales in the flow, respectively. In hemodynamic flows, \(U\) is the mean velocity while \(L\) is the diameter of the blood vessel. The Reynolds number is very often used in dimensional analysis when determining dynamic similarities between two flows, but can also be used to quantify flow regimes. Empirical studies have found that steady, fully developed flow in circular pipes is laminar when the critical Reynolds number is below a value on the order of 2300 [43]. There is no well defined limit when the flow is fully turbulent, but it is normally assumed to be above the critical Reynolds number. For pulsating flows the transition to turbulence is often at higher critical Reynolds numbers [44], as the accelerating phase in the pulse tend to keep the flow structured, while the flow breaks up in disturbed and chaotic features during the decelerating phase.

The flow in larger arteries is often assumed to be laminar [45–48], based on both experience from measurements and a discussion on the range of Reynolds numbers present. Fully developed turbulence is rarely seen in healthy humans [49]. However, the flow in the aorta can be in the transitional regime between laminar and turbulent flow, especially during the deceleration phase where flow instabilities can occur. Measurements based on both hot-wire anemometry and MRI supports the idea that healthy subjects can have transitional or slightly turbulent flows in the aorta [50–52]. In patients with certain cardiovascular diseases, fully turbulent flows are not uncommon. Normally, an aortic stenosis or stenosed heart valve will introduce turbulence as direct consequence of the narrowing of the cross-sectional area, which, in turn makes the flow velocity increase and trigger turbulence. Heart murmurs are a consequence of turbulent flow, where the severity of the murmurs is directly linked to the amount of narrowing of the cross-sectional area in the heart valve.

Despite an intuitive feeling of turbulence and several decades of research on the topic, a precise definition of turbulence is not easy to define [53, 54]. A turbulent flow contains eddies which are patterns of fluctuating velocity, vorticity and pressure. These eddies exists over in wide range of scales in both space and time, where the larger eddies contains the most energy, which is passed down to smaller and smaller eddies through the cascade process. At the smallest eddies the effect of viscosity becomes dominant and the energy finally dissipates into heat. Some of the characteristics of turbulent flow are [53, 54]:

- High Reynolds number: transition to turbulence occur at large Reynolds numbers, due to flow instability. The non-linear convective term in the
CHAPTER 4. MODELING CARDIOVASCULAR FLOWS

Navier-Stokes equations becomes dominant over the viscous term, increasing the sensitivity to instability which otherwise is damped by the viscous term. This is evident in high Reynolds-number flows, which are in essence inviscid.

- Randomness: a turbulent flow has a very large number of spatial degrees of freedom and is unpredictable in detail, but statistical properties can be reproducible if the turbulence is considered ergodic, i.e. that statistical properties can be calculated from a sufficiently large realization.

- Wide range of scales: turbulent flows contain a wide range of spatial and temporal scales, with spatial scales superimposed in each other. Energy is transferred from the large energy-carrying scales through the cascade-process to the small scales where it is dissipated into heat by viscosity. The smallest scales are several orders of magnitude larger than the molecular free path, making turbulence a continuum phenomenon. The dynamic behavior of the flow involves all scales.

- Dissipation: As energy is dissipated (smeared out) at the smallest scales by viscosity, a continuous supply of energy from the larger scales is needed to feed the turbulence. If the energy is cut off the flow will return to a laminar state as the Reynolds number decrease.

- Diffusivity: Turbulent flow is highly diffusive, as indicated by the increase of mixing and diffusion of momentum and heat transfer.

- Nonlinearity: small disturbances in a well-structured flow can grow fast and result in an unstable flow.

- Small-scale vorticity: as vorticity is defined as the curl of the velocity field, the derivatives will depend on the smallest scales of velocity, making the spatial scale of vorticity fluctuations the smallest in the turbulent range of scales. This scale is called the Kolmogorov scale and here the energy input from the larger scales are in exact balance with the viscous dissipation.

Due to the random behavior of turbulence, it usually needs to be treated with statistical tools [54]. For non-laminar but not fully turbulent flows, it can be said to be disturbed, and a laminar flow assumption may not be suitable, as transitional effects can play a major role in the flow behavior. In addition, cardiovascular flows are often pulsatile and the effects from both inertial and viscous forces are important. The flow in large vessels is highly three-dimensional and can have strong secondary flows, especially in diseased vessels [11].
4.3 Flow Descriptors

Flow can be described and quantified in a large number of ways, and here a few descriptors for turbulent flows are presented. A flow variable \( \phi \) can be decomposed into a mean and a fluctuating part, as:

\[
\phi(x, t) = \bar{\phi}(x) + \phi'(x, t)
\]

where the overbar represents the mean value and the prime the fluctuating part. Further, the mean or time average of the flow variable is defined as:

\[
\bar{\phi}(x) = \frac{1}{\Delta t} \int_{0}^{\Delta t} \phi(x, t) dt
\]

where \( \Delta t \) is a sufficiently long time. The (time) average of the fluctuating part, by definition, is zero:

\[
\bar{\phi'}(x) = \frac{1}{\Delta t} \int_{0}^{\Delta t} \phi'(x, t) dt \equiv 0
\]

The spread of the fluctuating part \( \phi'(x, t) \) around the mean \( \bar{\phi}(x) \) can be described by the variance and root-mean-square (RMS) values:

\[
(\bar{\phi'}(x))^2 = \frac{1}{\Delta t} \int_{0}^{\Delta t} (\phi(x, t) - \bar{\phi}(x))^2 dt
\]
CHAPTER 4. MODELING CARDIOVASCULAR FLOWS

\[ \phi'_{RMS}(x, t) = \sqrt{\left[ \phi'(x, t) \right]^2} = \sqrt{\frac{1}{\Delta t} \int_0^{\Delta t} (\phi(x, t) - \overline{\phi}(x))^2 dt} \]  

(10)

where the decomposition in Equation 6 has been used. A turbulent velocity fluctuation in a steady flow is plotted in figure 3, where it is obvious that while the mean value of the fluctuations is zero (by the definition, Equation 8), the RMS values are not.

In a pulsating flow, the decomposition in Equation 6 instead becomes:

\[ \phi(x, t) = \langle \phi \rangle (x, t) + \phi'(x, t) \]  

(11)

where \( \langle \phi \rangle (x, t) \) represents phase-average instead of the time-average. The phase average operator \( \langle \cdot \rangle \) is defined as:

\[ \langle \phi \rangle (x, t) = \frac{1}{N} \sum_{n=0}^{N-1} \phi(x, t + nT) \]  

(12)

where \( N \) is the number of cardiac cycles and \( T \) the (constant) period of the cardiac cycle. Thus, the phase-average is the mean value of \( \phi \) over \( N \) number of cycles, at each time during the cardiac cycle. Note that the decompositions defined here are valid for any flow variable, including wall shear stress. A purely laminar flow does not exhibit any random fluctuations and the decomposition would therefore not render any fluctuating components. Besides variance and RMS, the third and fourth order moments (known as skewness and kurtosis) can be obtained by changing the exponents in Equation 9 from 2 to 3 or 4, respectively.

The RMS of a velocity fluctuation can be measured experimentally, and in cardiovascular applications it can be performed \textit{in vivo} using hot-film anemometry [50, 55] which is a very invasive process. More recently, MRI techniques have been used to estimate the RMS values [56]. Other descriptors used to quantify...
4.3. FLOW DESCRIPTORS

Figure 4: Example of a temporal velocity signal during a cardiac cycle in a point in a constricted aorta. Notice how the velocity fluctuates in the deceleration phase in systole and the early parts of diastole, while being essentially undisturbed in the other parts of the cardiac cycle. In order to quantify the amount of disturbances in a numerical model, several cardiac cycles are needed to compute a phase-average, as described by Equations 11 and 12.

For the flow are the turbulent kinetic energy $k$ (or sometimes referred to as TKE) and turbulence intensity $T_i$. The turbulent kinetic energy is defined as:

$$k \equiv \frac{1}{2} \rho \left( u'^2 + v'^2 + w'^2 \right)$$

and represents the mean kinetic energy of the turbulent fluctuations in the flow. In the turbulent jet after an aortic coarctation, the turbulent kinetic energy can locally be on the order of 1000 Pa, while the kinetic energy is on the order of 5000 Pa, see e.g. Paper IV. The turbulence intensity is defined as the magnitude of the velocity fluctuations to a reference velocity:

$$T_i = \sqrt{\frac{2k}{u_{ref}}}$$

Values on the order of 1% is considered low, while 10% is considered high. Finally, the Womersley number $\alpha$ is often used as a measure of the unsteadiness of the flow, and it is defined as:

$$\alpha = r \sqrt{\frac{\omega}{\nu}}$$

where $r$ is the vessel radius, $\omega$ the frequency of the cardiac cycle and $\nu$ the kinematic viscosity of blood. For large vessels such as the aorta the Womersley number is in the range of 10-20 [57, 58], while it decreases significantly in the smaller vessels. For a large Womersley number the velocity profile is blunt, as the effect of viscosity does not propagate far from the wall. Therefore, in a highly pulsatile flow or in large vessels, the velocity profile takes on a plug shape, while for
smaller vessels where the Womersley number is small the velocity profile more closely resembles the classical Poiseuille profile [57].

### 4.4 Geometrical Representation

Image segmentation can be defined as the transformation of image material into a geometrical representation, such as a CAD surface. A variety of segmentation methods exist, which ranges in complexity from simple thresholding of image intensity to advanced pattern-recognition methods based on images of anatomical features.

In this thesis, the image material obtained from MRI measurements was transformed into a CAD surface using a cardiac image analysis software (Segment, http://segment.heiberg.se) [59]. It uses a level-set algorithm, with seed points placed at a few locations to increase segmentation speed and accuracy. Filtering functions were introduced to get a smooth surface, but was used with care; the final geometry closely resembled the original geometry and volume was conserved. Smaller vessels were not included, as the resolution was not sufficient to resolve them, and it was assumed that they did not contribute to the overall flow field.

![Image of heart and aorta with CAD surface](image.png)

Figure 5: *Left:* Maximum intensity projection (MIP) of the human heart, aorta and connecting arteries. *Center:* Resulting CAD surface after segmentation, including the three largest vessels leaving the aortic arch. *Right:* Close-up on the computational mesh in the inlet and ascending aorta. Notice the dense mesh resolution in the near-wall region.

When the CAD surface was created, it was discretized into control volumes. The size of each control volume (or mesh cell) determines the spatial resolution in the computational model and is therefore arbitrary. The more volumes in an area, the higher resolution. This comes of course with a prize, as the computational cost
increases with each volume. In general, a fine resolution is needed in areas with large gradients, such as near walls where the velocity profile goes from zero at the wall to the free stream velocity, or in highly disturbed flow regions. Accurate treatment of the near-wall flow is essential, as the shape of the velocity profile at the wall directly determines the wall shear stress and species concentration boundary layer [5]. Figure 5 shows an example of the near-wall resolution of a hexahedral mesh on the inlet in the ascending aorta, ensuring that the velocity gradient at the wall is resolved.

The choice of flow model also puts demands on the mesh resolution; for scale-resolving models (such as LES) both the local $y^+$ value and CFL number must be below 1, for accurate resolution of the turbulent flow features. The $y^+$ is a dimensionless distance from the wall to the first mesh cell, and a value less than unity ensures that the first mesh cell is inside the viscous sub-layer in the boundary layer. With a reasonable growth factor on the near-wall mesh elements, the entire boundary layer becomes resolved. The shape of mesh elements also affects solution accuracy; tetrahedral meshes are easy to create but might suffer from excessive numerical dissipation in shear layers or if they are highly skewed. Hexahedral mesh elements are harder to create in a complex geometry such as the aorta, but the mesh quality is greatly improved and errors due to numerical diffusion is decreased compared to a tetrahedral volume. Also, in general, the memory requirement and calculation time per tetrahedral mesh element is 50% more than a hexahedral cell [60].

When fluid-structure interaction was simulated (Paper III), the mesh resolution was coarser compared to the meshes when using a LES turbulence model. This was because a RANS approach was employed (see Section 4.9), which would not benefit from a finer resolution, as the turbulent effects were modeled instead of resolved. In addition, the arterial wall was meshed with 65 000 elements, with three elements dividing the wall thickness, putting serious demands on computer resources. Table 1 summarizes the details of the meshes used in this thesis.

<table>
<thead>
<tr>
<th>Paper</th>
<th>Application</th>
<th>Type of mesh</th>
<th># of cells</th>
<th>$y^+$</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>LES</td>
<td>Hexahedral</td>
<td>6 000 000</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>II</td>
<td>LES</td>
<td>Hexahedral</td>
<td>5 000 000</td>
<td>0.1-1</td>
</tr>
<tr>
<td>III</td>
<td>RANS+FSI</td>
<td>Hexahedral</td>
<td>500 000 + 65 000</td>
<td>&lt;1.5</td>
</tr>
<tr>
<td>IV</td>
<td>LES</td>
<td>Hexahedral</td>
<td>5 000 000</td>
<td>0.1-1</td>
</tr>
<tr>
<td>V</td>
<td>LES</td>
<td>Hexahedral</td>
<td>7 000 000</td>
<td>0.05-0.5</td>
</tr>
</tbody>
</table>
4.5 Blood Properties

From an engineering point of view, blood can be a very complex fluid. It consists of platelets and red and white blood cells suspended in a plasma. There has been significant research aimed at developing a constitutive model for all features of blood flow, but to date a full description is still not complete. The plasma acts as a Newtonian fluid with a constant viscosity, but due to the cellular content the whole blood acts as a non-Newtonian fluid, at least in small vessels and low shear rates. However, in large arteries such as the aorta, non-Newtonian effects are small and can generally be ignored. In general, blood behaves as a homogeneous Newtonian fluid in vessels with a diameter larger than 1 mm and shear rates over 100 s\(^{-1}\) \cite{6, 58}. Some popular non-Newtonian models are the Power-law, Casson, and Carreau-Yashuda models, which describes the relationship between blood viscosity and shear thinning as nonlinear, see Figure 6. For shear rates above 100 s\(^{-1}\), which are normally found in the aorta, the Casson and Carreau-Yashuda models approaches the Newtonian viscosity, which is normally set to 0.0035 Pa.s. Blood can be considered as incompressible with a density in the range of 1050-1060 kg/m\(^3\) \cite{61}. In this thesis the blood has been considered as Newtonian, as the shear rates were high enough and the cross-section of the aorta is large enough to prevent non-linear effects.

![Figure 6: Examples of shear rate dependency in three non-Newtonian blood viscosity models and a Newtonian viscosity for comparison. Notice how the Casson and Carreau-Yashuda models approaches the Newtonian viscosity at high shear rates.](image-url)
4.6 Boundary Conditions

The flow in a CFD simulation is driven by the boundary conditions, and accurate treatment is one of the most challenging problems when modeling cardiovascular flows [11, 62]. The boundaries of the computational domain are usually represented by inlets, outlets, and walls.

Inlets

Inlets are often prescribed with a time-dependent mass flow rate or velocity profile. Fully developed velocity profiles has been used extensively in the past, but this assumes a very long straight vessel upstream the location of the inlet, making undeveloped profiles very likely to exist in vivo [5]. Instead, as MRI can measure both geometry and flow, velocity profiles can be used as input for a patient-specific model [11]. Figure 7 shows three examples of measured velocity profiles in the ascending aorta, at maximum systolic acceleration, peak systole, and maximum deceleration. In this measurement the spatial resolution was about 25x25 pixels per cross-section and the temporal resolution 40 frames per cardiac cycle, or about 25 ms per frame. As the resolution in a CFD simulation usually is much smaller than that, some sort of interpolation technique in space and time must be employed.

![Figure 7: Velocity profiles measured by MRI in the ascending aorta. From left to right: maximum systolic acceleration, peak systole, and maximum deceleration.](image)

It is obvious that when patient-specific flows are of interest, measured velocity profiles should be included in addition to vessel geometry, to ensure that the correct flow field is being simulated. Normally only velocity profiles are specified, allowing turbulent quantities or unsteadiness develop from the transient velocity profile.

Outlets

A very common boundary condition is to use pressure on outlets. Since it is only the gradient of the pressure that is present in the incompressible Navier-Stokes
equations, Equation 4, the absolute pressure level in the model has to be specified. Therefore, pressure boundary conditions with the static pressure equal to zero is often used, making the pressure inside the model relative to that on the outlet, i.e. the pressure inside the domain will be an implicit result of the pressure on the outlet. If there are several outlets, the pressure values will determine the amount of flow through each outlet [11], and physiological waveforms should therefore be specified. In an incompressible model with rigid walls the wave speed becomes infinite, as opposed to a finite wave speed if the walls are allowed to deform due to the flow. Then, the wave speed can be approximated with the Moens-Korteweg equation:

\[ PWV = \sqrt{\frac{E h}{2r \rho}} \]  

where \( PWV \) is the pulse wave velocity, \( E \) is the Young’s modulus, \( h \) the wall thickness, \( r \) the radius of the vessel and \( \rho \) the fluid density. The underlying assumptions of the equation are that the vessel wall is thin, that the fluid is incompressible and that the wall stiffness is constant [63].

Prescribed pressure boundary conditions are only suitable when the wall is assumed to be rigid and the actual pressure level can be ignored. For FSI simulations, or when trying to predict the outcome of an intervention where the pressure is not known \textit{a priori}, other methods are needed [5]. The use of Windkessel models [64, 65] or more advanced arterial tree models [66] can be used to take into account the effects of wave reflections and attenuation of the pressure pulse from downstream locations. These lumped-parameter or 1-D models can account for both the peripheral and systemic resistance together with compliance effects of the downstream vessels [11].

A simple model is the 3-element Windkessel model, represented by an electrical analog as a resistance in series with a resistance and a capacitance in parallel. Using a mass flow pulse as input, the Windkessel model can respond with a physiological pressure pulse. The values for the resistances and the capacitance determines the pressure pulse wave form and magnitude, and some sort of tuning or optimization is often needed [5, 63, 67].

**Walls**

The boundary conditions for the arterial walls can be assumed rigid, have a prescribed motion, or deform as a consequence of the fluid pressure. The walls can also be modeled as either smooth or rough, to account for surface roughness. Common for all wall boundary conditions in cardiovascular applications is that a no-slip condition is obeyed, meaning that frictional forces will create a boundary layer along the wall. Vessel walls are also normally assumed impermeable, at least
4.7 Fluid-Structure Interaction

The coupling of fluid and solid models is referred to as fluid-structure interaction, or FSI. Solving the FSI-equations can be done either in a monolithic or iterative way. In a monolithic solution, both the fluid and solid equations are solved in a single matrix, while in an iterative solution, forces and displacements are passed between two solvers through a common interface. The coupling can be one-way or two-way, where the former means that data is transferred from one solver to
CHAPTER 4. MODELING CARDIOVASCULAR FLOWS

the other, while in the latter data is transferred both ways between the solvers in a loop.

An example of an 1-way FSI case is when the fluid forces is passed to the solid model to calculate stresses and strains, but the deformations can be considered small enough to not influence the fluid. Therefore, information is only passed from the fluid to the solid case. In a two-way FSI case, the fluid forces is passed to the solid model which, in turn, responds by passing the resulting displacement back to the fluid model. In that way the fluid domain deforms and the new forces are passed to the solid model in an iterative manner.

\[ \rho_s \frac{\partial^2 d_s}{\partial t^2} = \nabla \cdot \sigma_s + f_s \]  

(17)

where subscript \( s \) denote solid, and \( \rho_s \) is the wall density, \( d_s \) represents the displacement vector, \( \sigma_s \) is the Cauchy stress tensor, and \( f_s \) is an externally applied body force vector. Boundary conditions on the FSI interface states that the velocities of the fluid and solid must be compatible and that the traction at the boundaries are in equilibrium. These boundary conditions are formulated as:

\[ u_s = u_f \]  

(18)

\[ \sigma_s \cdot \hat{n}_s = \sigma_f \cdot \hat{n}_f \]  

(19)

where \( u \) are velocities, \( \sigma \) are stress tensors and \( \hat{n} \) surface normals. Together with a constitutive relationship that relates the stress to the strain, the equation system can be solved.

Fluid-structure interaction has recently begun being used when modeling cardiovascular diseases. Some common applications are computing the flow in aortic aneurysms [71–79], stenotic arteries [80–84] and heart valves [85, 86]. Modeling deformation of the arterial wall requires knowledge about the wall structure. As described in Chapter 3, the arterial wall consists of several layers, each of which has different mechanical properties. Stresses and strains in the wall are related through a constitutive equation, where the most simple relationship is Hooke’s
4.7. FLUID-STRUCTURE INTERACTION

Law which relates the stress to the strain times a material constant called the Young’s Modulus. Researches have used both this linear relationship [83, 87–89], and also non-linear constitutive models such as Mooney-Rivlin [77, 86, 90–92], Ogden [81, 93], and Fung [94].

However, the non-linear constitutive models require knowledge about the residual stress that is present in real arterial walls, even in an unpressurized state. As the models often are based on experimental testing of actual real arteries, the (often unknown) residual stresses should be included in the model to yield reliable results. A shrink-stretch process can be employed, as in [95], where the wall is first shrunk and then pressurized with a diastolic blood pressure until it matches the original geometry. Besides problems with residual stresses, the wall material parameters should be considered patient-specific with different behaviors in healthy and diseased locations, making constitutive modeling a complex task.

In large healthy vessels such as the aorta, the wall is often modeled with a linear constitutive law [96], which, despite the approximations made, might be better than a rigid wall assumption. In this way, wall motion is included in the model without the problems that comes with residual stresses in a non-linear model. Therefore, as a first approximation the material mechanics of the wall was considered linear in this thesis, with a Young’s modulus on the order of 1 MPa. Paper III investigates the effect on the flow field from the wall motion using different values of the wall stiffness.

Another way of including wall motion in the simulation is to not model it at all, but instead prescribe a measured displacement [46, 97]. In that way the difficulties associated with residual stresses can be overcome and the correct wall motion is directly incorporated into the model. Besides the fact that stresses in the wall is not obtained with this method, there are other difficulties; the motion must be based on measurements (typically MRI, CT or US) all of which has a lower spatial and temporal resolution compared to the numerical model. Therefore, some sort of interpolation in time and space has to be employed, as the location of the wall between measurements is unknown.

Besides prescribing the wall motion, the effect of compliant vessels can be approximated by modeling the fluid as a compressible fluid, while keeping the walls rigid, as in [67]. They modeled the flow in a healthy aorta with FSI, rigid walls and as a compressible fluid. The compressible fluid was tuned to get the correct wave speed and their results showed that modeling the fluid to account for compliance yielded very similar results to a full-scale FSI simulation. The computational overhead was very low compared to the FSI simulation, suggesting that this kind of modeling might be useful in clinical practice.
4.8 Mass Transfer

Besides blood flow, the transport of species can be included in a flow model. Blood can be modeled as a multi-phase fluid where the interaction between all of the different components are accounted for. Particle flow can be either interacting with each other or non-interacting. A straightforward model for mass transport is to treat the species as a passive non-reacting scalar and solving a transport equation in addition to the Navier-Stokes equations:

\[
\frac{\partial C}{\partial t} + \nabla \cdot (uC) = \nabla \cdot (D \nabla C)
\]  

(20)

where \( C \) is the species concentration, \( u \) is the computed fluid velocity which is now known from the CFD simulation, and \( D \) the kinematic diffusivity. In this manner the mass transport is assumed to not affect the flow features, but is instead an implicit result of it - the species are just transported with the flow. Depending on the values of \( u \) and \( D \) the transport can be either dominated by convection or diffusion, and similar to the Reynolds number, the Péclet number quantifies the ratio of convection to diffusion:

\[
Pe = \frac{LU}{D}
\]  

(21)

where \( L \) is a characteristic length and \( U \) the velocity magnitude. When the Péclet number is larger than unity, convective effects dominate the mass transfer while for smaller values, diffusion controls the mass transfer. Species concentration is therefore a function of \( Pe \) [98]. In large blood vessels the transport is mainly dominated by convection, while in smaller arteries the diffusion can have a significant impact. The relative thickness of the hydrodynamic boundary layer to the concentration boundary layer can be quantified with the dimensionless Schmidt number, defined as:

\[
Sc = \frac{\nu}{D}
\]  

(22)

It is a measure of the ratio of momentum (viscous) diffusivity to the mass (molecular) diffusivity and is a function of fluid properties only. For gases the Schmidt number is on the order of unity, meaning that the hydrodynamic and concentration layers are equally thick, while for liquids the Schmidt number is several orders of magnitude higher, making the concentration layer very thin [99]. This puts additional constraints on the near-wall computational mesh resolution, as both boundary layers needs to be resolved. The concentration and hydrodynamic boundary layers are illustrated in Figure 10. The Schmidt number is analogous to the Prandtl number in convection heat transfer.
4.9. MODELING TURBULENT FLOW

In paper IV the transport of low-density lipoprotein (LDL) is modeled in a human aorta and the transport from the blood and to the arterial wall was investigated. As the actual aortic wall was not included in the simulation, a boundary condition which allows for mass transfer through the wall was set on the arterial surface. The net transport of LDL from the blood to the wall was modeled as the difference between the amount of LDL carried to the wall as water filtration and the amount diffusing back to the bulk flow. Due to the filtration flow of water into the wall and LDL rejection at the endothelium, a concentration polarization effect appears at the luminal side of the vessel wall. This boundary condition was modeled as:

\[ C_w V_w - D \frac{\partial C}{\partial n} \bigg|_{w} = K_w C_w \]  

(23)

where \( C_w \) is the concentration of LDL at the wall, \( V_w \) the water infiltration velocity, \( D \) the kinematic diffusivity, \( \partial C / \partial n \) the concentration gradient normal to the wall, and \( K_w \) a permeability coefficient for the wall. Numerical values for the coefficients were found in literature [100–102].

Figure 10: Schematic figure illustrating the hydrodynamic boundary layer thickness \( \delta \) and the concentration boundary layer thickness \( \delta_c \) of LDL particles. Relative boundary layer thickness is not to scale.

4.9 Modeling Turbulent Flow

The Navier-Stokes equations can fully describe all the details of any flow situation, making them very powerful even though they look relatively simple. But, as explained by Pope [43], their power is also their weakness, as all of the flow details are described, starting from the largest energy carrying turbulent scale governed by geometry, to the smallest scale where dissipation of energy occurs. Given the importance of turbulent flows in engineering applications, substantial research has been put into the development of numerical methods to capture the effects of turbulent flow features without needing to resolve all of the details. In general, the methods can be ordered in three groups: RANS, LES, and DNS, where the
two first models employ different approaches to avoid resolving all flow features, while in DNS all turbulent scales present in the flow are computed. Therefore, the computational cost also increases with the amount of details; RANS models are significantly cheaper to run compared to LES, while LES is significantly cheaper to run compared to DNS [54].

RANS Turbulence Models

In a RANS turbulence model the effort is put into modeling the effect of the turbulence on the mean flow quantities. This can be useful if the goal of a simulation is the mean or time-averaged values of e.g. velocity, but details about the turbulent fluctuations are not resolved. The decomposition introduced in Equation 6 is applied to the velocity and pressure as:

\[
\begin{align*}
    u_i &= \bar{u}_i + u'_i \\
    p &= \bar{p} + p'
\end{align*}
\]

Again, overbar represents an averaged quantity, while the prime denotes a fluctuating variable. The Navier-Stokes equations are then averaged, which yields an additional term called the Reynolds stress tensor that needs to be modeled in order to close the equations. In tensor notation, the Reynolds-Averaged Navier-Stokes (RANS) equations are:

\[
\frac{\partial \bar{u}_i}{\partial t} + \frac{\partial}{\partial x_j} \left( \bar{u}_i \bar{u}_j \right) = -\frac{1}{\rho} \frac{\partial \bar{p}}{\partial x_i} + \nu \left( \frac{\partial \bar{u}_i}{\partial x_j} + \frac{\partial \bar{u}_j}{\partial x_i} \right) - \frac{\partial u'_i u'_j}{\partial x_j} \tag{26}
\]

The right hand side can be rewritten as:

\[
\frac{1}{\rho} \frac{\partial }{\partial x_j} \left[ -\bar{p} \delta_{ij} + \mu \left( \frac{\partial \bar{u}_i}{\partial x_j} + \frac{\partial \bar{u}_j}{\partial x_i} \right) - \rho u'_i u'_j \right] \tag{27}
\]

where \(\delta_{ij}\) is the Kronecker delta. The first term inside the square brackets represents the mean pressure stress, while the second term is the mean viscous stress tensor. The last term is the Reynolds stress tensor, normally denoted \(\tau_{ij}\). It is a fictitious stress tensor and represents the average momentum flux due to turbulent velocity fluctuations. In fully developed turbulence, the Reynolds stresses can be several orders of magnitude larger than the mean viscous stress tensor [54]. As \(\tau_{ij}\) is unknown, additional information needs to be introduced in order to close the equations. In a RANS approach, this is usually done through the eddy-viscosity hypothesis proposed by Boussinesq in 1877, which relates the Reynolds stresses to the mean rates of deformation and an eddy-viscosity, as:

\[
\tau_{ij} = \frac{2}{3} k \delta_{ij} - \nu \left( \frac{\partial \bar{u}_i}{\partial x_j} + \frac{\partial \bar{u}_j}{\partial x_i} \right) \tag{28}
\]
where \( k = \tau_{kk}/2 \) or the turbulent kinetic energy, and \( \nu_t \) the eddy (or turbulent) viscosity. Combining Equations 26 and 28 yields:

\[
\frac{\partial \bar{p}_t}{\partial t} + \frac{\partial}{\partial x_j} \left( \bar{p}_t \bar{a}_{ij} \right) = - \frac{1}{\rho} \frac{\partial \bar{p}_t}{\partial x_i} + \frac{\partial}{\partial x_j} \left( \nu + \nu_t \right) \left( \frac{\partial \bar{a}_{ij}}{\partial x_j} + \frac{\partial \bar{a}_{ji}}{\partial x_i} \right)
\]  

(29)

where \( \bar{p}_t \) is a modified pressure: \( \bar{p}_t = \bar{p} + \frac{2}{3} k \). Closure is obtained by relating the eddy viscosity to the turbulent kinetic energy \( k \) and the turbulent dissipation rate \( \epsilon \) or the turbulence frequency \( \omega \), as:

\[
\nu_t = C_\mu \frac{k^2}{\epsilon} \tag{30}
\]

\[
\nu_t = \frac{k}{\omega} \tag{31}
\]

where \( C_\mu \) is a dimensionless constant. This means that two additional transport equations are introduced for either \( k \) and \( \epsilon \) or \( k \) and \( \omega \), forming the \( k-\epsilon \) \([103, 104]\) and \( k-\omega \) \([105]\) turbulence models. The additional transport equations contains model constants that have been adjusted to be as general as possible. Each of the models exists in a variety of versions, all with different strengths and weaknesses. The basic \( k-\epsilon \) model has been shown to be useful in the free-stream but does not perform well in regions with adverse pressure gradients. Contrary, the \( k-\omega \) model performs well close to the wall but is very sensitive to the value of \( \omega \) in the free-stream \([42]\). Menter \([106]\) and Menter \emph{et al.} \([107]\) proposed a hybrid turbulence model called SST \( k-\omega \) that combined the best features from both the \( k-\epsilon \) and \( k-\omega \) models. In the inner parts of the boundary layer it uses the \( k-\omega \) formulation, while it blends gradually to the \( k-\epsilon \) formulation in a free-stream.

A more advanced type of turbulence model that also use the RANS equations is the Reynolds stress model (RSM), but it does not make use of the eddy-viscosity approach to close the equations. Instead, the Reynolds stresses are computed directly using additional equations for each Reynolds stress component and with an equation for either \( \epsilon \) or \( \omega \) \([43, 108]\). The RSM model is particularly useful in highly swirling flows with anisotropic turbulence, which can be found in e.g. turbomachinery and compressors. However, the additional equations makes the RSM model more computationally expensive and harder to converge compared to the standard two-equation RANS models, and is therefore rarely used in simulations of cardiovascular flows.

### Large Eddy Simulation

Contrary to RANS, in a LES model the large scale turbulent motion of the flow is resolved, while the flow scales smaller than a filter width, e.g. the grid size,
CHAPTER 4. MODELING CARDIOVASCULAR FLOWS

is handled with a subgrid-scale model (SGS). The rationale behind LES is that the large scales transport most of the momentum, mass and energy, and are also more problem-dependent, i.e. more sensitive to the geometry and boundary conditions compared to the smaller scales, which become more universal and isotropic and thus easier to model [109]. Therefore most of the effects of the turbulent fluctuations can be resolved, and, in addition, LES models are better at handling transitional flows compared to RANS models [54]. The Navier-Stokes equations are filtered instead of averaged, and in a finite volume approach the scales smaller than the control volume are normally handled by the SGS model. Filtering the Navier-Stokes equations yields:

\[
\frac{\partial \tilde{u}_i}{\partial t} + \frac{\partial}{\partial x_j}(\tilde{u}_i \tilde{u}_j) = -\frac{1}{\rho} \frac{\partial \tilde{p}}{\partial x_i} + \nu \left( \frac{\partial \tilde{u}_i}{\partial x_j} + \frac{\partial \tilde{u}_j}{\partial x_i} \right)
\]  

(32)

where the tilde represents filtering and the term \( \frac{\partial}{\partial x_j}(\tilde{u}_i \tilde{u}_j) \) contains terms that are unknown. The following decomposition can be made [42]:

\[
\tilde{u}_i \tilde{u}_j = \tilde{u}_i \tilde{u}_j + \tau_{ij}
\]

(33)

where \( \tau_{ij} \) denotes the subgrid-scale stress. Applying Equation 33 to Equation 32 yields

\[
\frac{\partial \tilde{u}_i}{\partial t} + \frac{\partial}{\partial x_j} (\tilde{u}_i \tilde{u}_j) = -\frac{1}{\rho} \frac{\partial \tilde{p}}{\partial x_i} + \nu \left( \frac{\partial \tilde{u}_i}{\partial x_j} + \frac{\partial \tilde{u}_j}{\partial x_i} \right) - \frac{\partial \tau_{ij}}{\partial x_j}
\]

(34)

Unlike the Reynolds stresses in a RANS formulation, the sub-grid stresses in a LES formulation contains further information [42]. The stresses can be decomposed into a resolved and a unresolved part [110]:

\[
\tau_{ij} = L_{ij} + C_{ij} + R_{ij}
\]

(35)

where \( L_{ij} \) are the Leonard stresses due flow features on a resolved scale, \( C_{ij} \) are the cross stresses that arise from interaction between sub-grid eddies and resolved flow, and \( R_{ij} \) are the LES Reynolds stresses that arise from convective momentum transfer due to sub-grid eddies. However, while \( R_{ij} \) are invariant with respect to Galilean transformation, \( L_{ij} \) and \( C_{ij} \) are not [111], making the decomposition dependent on coordinate system. Therefore, in most practical applications the Leonard and cross-stresses are lumped together with the LES Reynolds stresses, and \( \tau_{ij} \) is solved in an eddy-viscosity approach similar to the RANS formulation [42, 109]. The subgrid-stresses are modeled using the filtered strain rate tensor and the sub-grid eddy viscosity \( \nu_{sgs} \) as:

\[
\tau_{ij} = \frac{1}{3} \tau_{kk} \delta_{ij} - \nu_{sgs} \left( \frac{\partial \tilde{u}_i}{\partial x_j} + \frac{\partial \tilde{u}_j}{\partial x_i} \right)
\]

(36)
Combining Equations 34 and 36 yields the LES equations with sub-grid viscosity:

\[
\frac{\partial \tilde{u}_i}{\partial t} + \frac{\partial}{\partial x_j} (\tilde{u}_i \tilde{u}_j) = -\frac{1}{\rho} \frac{\partial \tilde{P}}{\partial x_i} + \frac{\partial}{\partial x_j} \left( (\nu + \nu_{sgs}) \left( \frac{\partial \tilde{u}_i}{\partial x_j} + \frac{\partial \tilde{u}_j}{\partial x_i} \right) \right) \tag{37}
\]

Here the isotropic part of \(\tau_{kk}\) is not modeled, but instead added to the filtered static pressure: \(\tilde{P} = \tilde{p} + \tau_{kk}/3\). The SGS model is needed to introduce an additional physically correct dissipation rate (in forms of eddy viscosity) into the system, as the smallest scales are not resolved. Therefore, LES does not model the actual influence of the unresolved scaled, but instead the dissipation of turbulence into heat [54, 109]. Additionally, the SGS model must account for the interaction between filtered and unfiltered scales, which require some sort of empirical information, as a general description of turbulence is unavailable [43]. Thus, a true separation of scales is not possible, as there is interaction between the smallest and largest scales. In order to solve Equation 36, models for \(\nu_{sgs}\) are needed. In this thesis two different SGS models have been used: the Dynamic Smagorinsky-Lilly model [112, 113] and the Wall-Adapting Local Eddy-Viscosity (WALE) model [114]. Both correctly provides zero eddy-viscosity in laminar shear layers, which is important as cardiovascular flows can undergo transition from a purely laminar state to a disturbed and transitional behavior, and the model should not affect the laminar flow.

The eddy-viscosity in the WALE model is formulated as:

\[
\nu_{sgs} = (C_{wale} \Delta)^2 \left( \frac{(S_{ij}^d S_{ij}^d)^{3/2}}{(S_{ij}^s S_{ij}^s)^{5/2} + (S_{ij}^d S_{ij}^d)^{5/4}} \right) \tag{38}
\]

where \(C_{wale}\) is a model constant set to 0.5 based on results from homogeneous isotropic turbulence, \(\Delta\) is the cube root of the computational cell volume, and \(S_{ij}^d\) is the traceless symmetric part of the square of the velocity gradient tensor. The \(S_{ij}^d\) tensor can be rewritten in terms of filtered strain-rate \(\tilde{S}_{ij}\) and vorticity \(\tilde{\Omega}_{ij}\) as:

\[
S_{ij}^d = \tilde{S}_{ik} \tilde{S}_{kj} + \tilde{\Omega}_{ik} \tilde{\Omega}_{kj} - \frac{1}{3} \delta_{ij} (\tilde{S}_{mn} \tilde{S}_{mn} - \tilde{\Omega}_{mn} \tilde{\Omega}_{mn}) \tag{39}
\]

Details about the Dynamic Smagorinsky-Lilly model are presented in Paper I. As a comparison between the RANS and LES models, notice how similar Equations 26 and 28 looks to Equations 34 and 36. The differences are the averaging or filtering operation and the formulation of the eddy-viscosities \(\nu_t\) and \(\nu_{sgs}\). These subtle differences may greatly affect the resulting flow field, as LES is more likely to resolve flow features that are instead modeled in a RANS model. While \(\nu_t\) accounts for the entire influence of turbulence on the mean flow, \(\nu_{sgs}\) is only relevant for the scales smaller than the filter size. The numerical value of the eddy viscosity
CHAPTER 4. MODELING CARDIOVASCULAR FLOWS

in a LES model is very small compared to the eddy viscosity in a RANS model, making it confined to the smaller scales, leaving the larger scales to be resolved by numerics [54]. The sub-grid scale stresses only accounts for a fraction of the total stresses, making the overall flow field less sensitive to any modeling effect in the sub-grid scale model, compared to the modeling in a RANS turbulence model [111]. The eddy viscosity ratio, defined as the ratio of the eddy viscosity to fluid viscosity, can interesting to compute; for values less than unity, the dissipation in the flow model is handled mainly by actual viscous dissipation, while larger values indicates the need of additional dissipation obtained from the SGS or RANS turbulence model. In this thesis, eddy viscosity values were on the order of 0.5-10 for LES simulations, while it was on the order of 100-1000 for the RANS simulations in Paper III.

Given the increased resolution and smaller amount of turbulence modeling, LES may be well suited for computing cardiovascular flows [115], whereas common two-equation RANS models may be unsuitable or even unable to capture transitional and relaminarizing flows [3, 5]. However, modeling flows with LES comes at a high prize; the mesh and time step requirements in a LES simulation far exceeds the requirements needed for a RANS simulation, and, as a result the computational cost for a LES simulation can be orders of magnitude higher in terms of memory and computational time. The highest mesh requirements lie in resolving the boundary layers, which limits the use of LES in wall-bounded high-Reynolds number flows [43]. LES will likely not be able to give exactly the same results as DNS due to the sub-grid scale modeling, which affects higher-order statistics more than lower-order. Thus, compared to DNS, LES is normally reliable for first and second order moments and is able to reproduce basic flow structures [111], to a significantly lower computational cost.

Direct Numerical Simulation

In a direct numerical simulation, DNS, all flow scales are computed and there is no modeling performed at all. The Navier-Stokes equations are solved on meshes that are fine enough to resolve all relevant length scales, and the temporal resolution is fine enough to capture all transient fluctuations. Besides spatial and temporal resolution, a DNS normally use high-order numerical schemes to minimize numerical errors. Altogether, this comes with an enormously large computational cost, making it unpractical for most engineering types of flows, at least with the current supercomputer capacity. There are a few exceptions, where one example is Varghese et al. who performed DNS simulations of both steady and pulsatile flows in an idealized stenotic pipe [116, 117]. High-order DNS with patient-specific geometries and boundary conditions might become a reality in the future, but with the present computer power and numerical methods, only simple idealized models
4.9. Modeling Turbulent Flow

can be solved.

To conclude, there is little hope of finding an analytical theory of turbulence and current research is therefore aimed at developing numerical methods to calculate the relevant properties of turbulent flow [43].
Chapter 5

Results

5.1 Quantification of Aortic Wall Shear Stress

_Papers I-III_

Low and/or oscillating wall shear stress has been established as predictors of increased risk for the development of atherosclerosis [9, 10, 30, 118, 119]. In addition, turbulent flow has been shown to affect endothelial cell function [8], making turbulent flow and abnormal WSS interesting when studying cardiovascular diseases. In these papers, computational fluid dynamics were used to resolve the WSS on the aortic surface, as clinical measurement techniques have been shown to be unable to measure the near-wall velocity gradient with sufficient resolution [39, 40].

First, steady flow in an idealized circular vessel with a stenosis was investigated using LES. It is an well-known geometry (see Figure 11 and [120] for details) where both experimental measurements and DNS data are available. In an article by Gärdhagen et al. [121], it was shown that a LES model could replicate results from both DNS and experimental Laser Doppler Velocimetry, indicating that LES is suitable for this kind of physiological flows.

Figure 11: The geometry of the idealized vessel used in Paper I. Flow is from left to right and the length downstream the stenosis is 20 diameters to ensure that outlet effects does not affect the flow.

The fluid enters the idealized vessel as a laminar well-structured flow, but in the throat of the stenosis a transition to turbulence is triggered due to the increased
velocity. The flow situation is similar to *in vivo* flows such as aortic coarctations or stenotic heart valves, where turbulent flow often is present. To take cardiovascular flow quantification a step further, the turbulent WSS signal on the walls was decomposed into a mean and a fluctuating part (denoted with overbar and prime, respectively). Sampling was performed at every diameter downstream the stenosis and the decomposition reads:

\[
\text{WSS} = \overline{\text{WSS}} + \text{wss}'
\]

(40)

It was found that the magnitudes of the mean and the fluctuating parts could be almost as large in the reattachment region, where most disturbed flow was found. The fluctuations decreased in magnitude further downstream, while the mean part approached a constant value, as turbulent effects reduced. Conversely, a RANS-model showed no or very low WSS magnitude in the reattachment region, reflecting the RANS models inability to predict turbulent parameters, as well as the need for a scale-resolving turbulence model in these types of flows. Also, as fluctuations are modeled and not resolved in RANS models, a decomposition into a mean and a fluctuating part was not feasible.

The mean and fluctuating parts were further decomposed into axial and circumferential components. It is evident from the right plot in Figure 12 that there is a recirculation region from D =1-6, where the mean axial component is negative, then changes sign in the reattachment point and becomes directed in the main flow direction. The fluctuating components cannot discern the flow direction, as they fluctuate around the mean value. As expected from a well converged simulation the mean circumferential part was zero, i.e. there was no preferred circumferential flow direction that would influence the magnitude. However, the fluctuating circumferential component was always larger than the axial component showing that even though, on average, the mean value is zero the fluctuating values can be significant.

Clearly, turbulent flow creates complex WSS patterns with significant fluctuations, which can impair endothelial function. It was therefore decided to apply the WSS decomposition to the flow field in a real human aorta. Here, the flow was pulsating and phase-averages (denoted with \(<.>\)) were computed to get statistically convergent results. Surface renderings of the phase-averaged WSS magnitude \(<\text{WSS}>\), and the corresponding fluctuations WSS’ at maximum systolic deceleration are plotted in Figure 13. Large mean WSS values are obtained around the branches and locally in the descending aorta, while fluctuating WSS are present on the inner curvature of the descending aorta and locally in the branching vessels. However, there are large spatial (and temporal) gradients of mean and fluctuating WSS on the aorta, and as discussed in [122], these gradients can injure the endothelial cells by causing e.g. high cell turnover, leaky cell junctions, enhanced permeability, or even cell-cell bond rupture.
5.1. QUANTIFICATION OF AORTIC WALL SHEAR STRESS

In order to quantify the WSS during a complete heart beat, two locations upstream and downstream the third branching vessel on the aortic arch were selected and the decomposition were plotted over time together with the time-averaged WSS, see Figure 14. The results illustrate that while instantaneous mean WSS values can take on values that are significantly higher than the time-averaged WSS, there are times during the cardiac cycle when the fluctuations also can become elevated, especially during systole.

The oscillatory shear index (OSI) is a common measure of the cyclic departure of the WSS vector from its predominant alignment [123]. It is an integrated quantity, and here it was used in a novel way together with the time-averaged WSS as locations with elevated values of both variables were mapped back onto the aorta. In general, the OSI parameter only reached the maximum values when the time-averaged WSS was low, which is in line with other studies [48]. However, there were a few locations that experienced both elevated TAWSS and OSI values, and these points were mapped back onto the aorta. It was found that regions exhibiting both high TAWSS and OSI values were located in the vicinity of the branching vessels in the aortic arch, and on the inner curvature of the descending aorta. These locations are common sites of development of atherosclerosis [16, 123]. Here it was assumed that TAWSS values higher than 2 Pa was considered high if there was elevated OSI values at the same location.
Figure 13: Surface rendering of phase-averaged WSS magnitude (upper row) and fluctuating WSS (lower row) at maximum systolic deceleration. Notice the different color scale between magnitude and fluctuation.
5.1. QUANTIFICATION OF AORTIC WALL SHEAR STRESS

Figure 14: Two examples of instantaneous mean WSS (phase average, \(<WSS>\)), the corresponding fluctuating WSS (\(WSS'\)) and the time-averaged WSS (\(<TAWSS>\)) at two locations in a healthy human aorta. Data were sampled over several cardiac cycles to get a statistically convergent result. Left plot is located in front of one of the branching vessels in the aortic arch, while the right plot is located behind the same vessel.

Figure 15: Left: Time-averaged WSS plotted against oscillatory shear index. Values inside the dotted box were mapped back onto the aorta. Right: Locations on the aorta where elevated TAWSS and OSI values are present.
CHAPTER 5. RESULTS

The effect of wall compliance on the blood flow and WSS was investigated by performing FSI simulations on a healthy aorta by changing the wall stiffness. FSI modeling is a very computational intensive process due to the iterative matter in which information is passed between a fluid and a solid solver. Therefore, turbulent effects were modeled with a RANS turbulence model. The goal was not to resolve all the flow details, but instead try to assess whether how wall motion and propagating pressure/mass waves affected the overall WSS distribution. Three FSI cases were simulated with a Young’s modulus of 0.5, 0.75 and 1.0 MPa. These cases were compared with two rigid wall models which were extracted from the 0.5 MPa model at peak systole and late diastole, to fully investigate the effect of wall compliance, but also to assess whether the rigid wall assumption is sensitive to the measurement technique. As the geometry reconstruction is created from an average of several cardiac cycles during the MRI measurement, the wall motion will be blended in the MR images. Ideally, MRI measurements of the geometry would be performed at different times during the cardiac cycle, yielding a specific geometry at each time point. As this was not the case, the acquired geometry will most probably be diastolic dominant, as approximately 2/3 of the cardiac cycle is during diastole. In the FSI models the effect from the tissue surrounding the outer part of the aortic wall was modeled as an elastic spring.

As seen in Figure 16, time time-averaged WSS are almost identical between the five models, indicating that wall motion and finite wave speeds does not significantly affect time-averaged WSS, which is in line with other studies, see e.g. [67]. On the other hand, instantaneous WSS values were different between the rigid wall and FSI models, indicating that if instantaneous values are important to assess endothelial function, FSI modeling might be needed to fully capture and resolve near-wall details.
5.1. QUANTIFICATION OF AORTIC WALL SHEAR STRESS

Figure 16: Time-averaged WSS on five different models. Three FSI simulations with Young’s modulus 0.5, 0.75 and 1.0 MPa correspond to cases a-c, while cases d and e are two rigid wall models at sampled at peak systole and late diastole, respectively. The effect of wall motion has little effect on the time-averaged WSS.
5.2 Aortic Mass Transfer and LDL

(Paper IV)

The transport of low-density lipoprotein (LDL) was simulated as a passive (non-reacting) scalar using LES. The walls were permeable, allowing LDL to be transported from the blood and to the wall. With this boundary condition, a concentration polarization effect appeared, where regions of elevated LDL surface concentration were found to be co-located with areas of low shear stress, suggesting a relationship between LDL accumulation and flow dynamics. The results indicated that LDL accumulation was inversely proportional to the WSS magnitude, so in order to further assess the relation between WSS and LDL surface concentration, surface data from 50 consecutive cardiac cycles were plotted in the same figure, yielding approximately 2.5 billion data points to be post-processed, see Figure 18. Clearly, the WSS is inversely proportional to the LDL surface concentration.
5.2. AORTIC MASS TRANSFER AND LDL

concentration, as low WSS values can give elevated LDL levels, and vice versa. As the concentration levels are normalized with the inlet value, the figure shows that the surface has a higher LDL concentration compared to the bulk blood flow. The increase is approximately 5-10% of LDL on the surface, with some regions experiencing almost 25% higher concentration levels.

In addition, near-wall flow affects both the velocity gradient (and thus the WSS) and the LDL concentration, as laminar flow regimes tend to create a stable concentration boundary layer while disturbed flow creates fluctuations in concentration levels. This was visualized by plotting the velocity magnitude along a line 5 mm normal to the surface into the flow domain for each time point in the cardiac cycle. By doing so, a spatio-temporal map of the near-wall flow was created. It was concluded that while the velocity closest to the wall was almost stationary, flow features at fractions of a mm from the wall greatly affected the WSS and LDL distribution, see Figure 19. Thus, the concentration boundary layer is sensitive to both the wall shear stress and flow effects from the bulk flow.
CHAPTER 5. RESULTS

Figure 19: Upper figure: LDL surface concentration and wall shear stress as a function of time, at a point on the outer side of the descending aorta. Lower figure: The near-wall velocity along a line directed normal to the surface at the same location. X-axis legend reads MA: systolic maximum acceleration, PS: peak systole, MD: systolic maximum deceleration, BD: beginning of diastole.
5.3 Turbulent Flow in an Aortic Coarctation

(Paper V)

The blood flow in a patient with an aortic coarctation was investigated before and after intervention. The intervention increased the cross-sectional area of the coarctation, resulting in a decreased pressure drop and increased flow rate. The turbulent kinetic energy (TKE) was evaluated using both MRI measurements and LES simulations, to complement traditional diagnostic tools when assessing the severity of the coarctation. Large TKE values indicate that energy is drawn from the mean flow to feed the turbulent fluctuations. In order to assess whether the current MRI methodology is able to estimate TKE \textit{in vivo}, a comparison between MRI and CFD was performed. Integrated values in a volume distal the coarctation was considered, and a very good agreement was found; the increase and decrease in TKE levels matched almost perfectly for both both the pre- and post-intervention models, while peak values differed slightly. The peak TKE values did not occur at peak flow rate when the Reynolds number reached its maximum value, but instead during the systolic deceleration phase, when the flow breaks up. A discussion whether a flow is turbulent or not based solely on Reynolds number may therefore not be ideal - features of the flow should considered be instead.

Differences between the MRI and CFD results can be a result of measurement errors and noise in the MRI-signal, and uncertainties in segmentation and boundary condition specification in the CFD model. Despite the two different methods to obtain TKE, the close agreement between CFD and MRI results give confidence.
that it can be used in a clinical context. However, further clinical studies are needed to quantify abnormal or dangerous TKE levels and whether integrated or local peak values are most important. CFD-computed TKE can provide additional information about the flow field, as the resolution is significantly higher compared to MRI measurements.

Figure 21: Volume renderings of a CFD simulation (left) and MRI measurement (right) of the turbulent kinetic energy in the pre-intervention case at peak flow rate.
Chapter 6

Discussion

The work described in this thesis focuses on disturbed, transitional and turbulent flow in the human aorta. The goal was to take image-based CFD of cardiovascular flows closer to clinical practice, as it is believed that it can provide additional information which is unavailable in traditional measurement techniques. Advanced models such as large eddy simulation and fluid-structure interaction were employed, to resolve the flow and compute hemodynamic parameters that can be useful for the understanding of cardiovascular diseases such as atherosclerosis or aortic coarctations.

Image-based CFD consists of two parts: acquisition of flow and geometry using a clinical image modality, and the actual CFD model. The transformation from image material to a geometrical representation is today routinely made, and flow measurements are normally accurate enough to be used as boundary conditions in the model. Even though fluid-structure interaction and scale-resolving flow modeling are being used more and more in cardiovascular studies, researchers still choose from one of the two; the computational cost for a unification of a scale-resolving turbulence model and FSI is still extremely expensive. This is the reason why a rigid wall assumption and/or a laminar flow or RANS-approach are common in the biofluid research community, even if there can be severe modeling errors and flow effects that are not resolved.

The decomposition of the wall shear stress vector into a mean and a fluctuating component was first investigated in an idealized stenotic vessel, and then applied to a subject-specific human aorta. Locations of turbulent WSS could be deducted, and it was discovered that the fluctuations could be as large as the time-averaged values during some parts of the cardiac cycle. The described methodology provides additional knowledge about the nature of the stress the endothelial cells are subjected to, as regions of turbulent WSS correlates with locations that are prone to atherosclerotic development. However, the relationship between fluctuating WSS and the development of vascular disease is not fully understood, and require
CHAPTER 6. DISCUSSION

further clinical trials. The WSS, and especially its fluctuating component, cannot be measured with significant accuracy using present measurement techniques, which calls for the need of image-based modeling and simulation. Note that a scale-resolving turbulence method is needed, as it was shown in Paper I that a simpler RANS method could yield unphysical results.

Another flow-related feature that cannot be measured with any present measurement technique is the flow-dependent transfer of LDL in the blood stream and accumulation on the luminal surface. Assuming that LDL can be seen as a non-reacting passive scalar in the blood, it was found that the blood flow features determine the accumulation and distribution of LDL on the arterial surface. The near-wall flow (and as a consequence, the WSS) affects the concentration boundary layer and, again, regions prone to atherosclerotic development seem to co-locate with regions of high LDL accumulation.

The turbulent kinetic energy before and after intervention was investigated using both CFD simulations and MRI measurements in an aortic coarctation. The numerical results agreed very well with experimental measurements, indicating that the measurement technique is robust. The CFD model was able to provide high resolution details of the turbulent flow field, and with the results it was possible to assess the impact of the intervention from a fluid dynamics point of view. It was seen that while the pressure drop decreased as a result of the increased cross-sectional area, the amount of turbulence (as quantified by TKE) did decrease, but it did not disappear. Turbulent flow is generally undesirable in the human body, and should therefore be avoided if possible. Thus, when evaluating the outcome of the intervention the measured change in turbulence level can be assessed, in addition to the pressure drop and mass flow rate that is normally considered.

Image-based CFD can provide parameters and variables that cannot be measured. Furthermore, as opposed to all measurement techniques, CFD can also be used as a predictive tool for treatment planning and intervention optimization. The combination of simulations and in vivo measurements provide information that would not otherwise be possible to obtain. Ideally, modeling and simulation could be used for diagnose, intervention planning and follow-up studies, which would then require both clinical studies and further development of numerical methods and models. The two latter, intervention planning and follow-up studies, are possible today, albeit with some limitations; optimization of surgical procedures using CFD are being done, even though it is still on a small scale. Follow-up studies would be able to provide data such as pressure and flow distributions, WSS maps, and TKE renderings that could be useful when assessing the outcome of a surgery. A very important factor to consider is uncertainty quantification, i.e. how a small uncertainty in the input to the model (e.g. noisy image data, boundary conditions, model resolution, etc.) affect the result. This can be done by perform-
ing a large number of simulations with small differences in input to assess the sensitivity of the output. Hence, a close collaboration in a team of physicians and experts in fluid mechanics and image modalities will be valuable, to fully exploit the possibilities of image-based CFD in cardiovascular flows.

The work described in this thesis takes image-based CFD from initial studies on idealized geometries, to the assessment of the outcome of an intervention on a patient. The methods have been shown to be robust and accurate, and with the tight integration of physics and physiology, simulated cardiovascular flows are now ready for the clinic.

**Outlook**

The use of image-based CFD in clinical environments is still in its infancy, but current research shows its importance and the use will certainly increase in the future. In order to gain confidence that numerical models are both reliable and provide important information, larger clinical studies should be made, in close cooperation with clinical staff. Relatively simple follow-up studies can already be performed, where the flow field can be assessed in detail. Recently, intervention planning using CFD has attracted attention, see e.g. [124–127] for numerical modeling of intervention planning of extra-cardiac Fontan surgery. The long-term goal of being able to predict the risk of developing a disease using CFD may become possible in the future, but it will certainly require further understanding (and mathematical modeling!) of physiological features such as growth and remodeling of arterial walls.

The models discussed in this thesis are mechanical and not biomechanical models. To be able to predict the initiation and progression of cardiovascular diseases, closer links between chemistry, biology, physiology, and mechanics are needed [5]. The vascular response in terms of growth and remodeling is important to fully understand pathophysiological mechanisms, calling for the need to increase the biological relevance in image-based computational modeling and simulation. Besides introducing more physics and physiology in the models, a solid understanding of the numerics and requirements for performing a reliable simulation is, and will continue to be crucial. As eloquently put by Roache [128]: it is a matter of solving the equations right, while solving the right equations.
Chapter 7

Review of Included Papers

Paper I


This paper focuses on non-pulsating turbulent flow through an idealized stenotic artery. Both RANS and LES models were used and the WSS vector was decomposed in a novel way into a mean and a fluctuating part. It was found that the turbulent WSS fluctuations were almost as large as the mean WSS in the immediate post-stenotic region, while the fluctuations decreased gradually further downstream. Another finding was that a simpler RANS-approach predicted completely different results compared to the LES model, indicating that RANS modeling of stenotic flows might not be suitable.

Paper II

Quantifying Turbulent Wall Shear Stress in a Subject Specific Human Aorta Using Large Eddy Simulation, Jonas Lantz, Roland Gårdhagen, and Matts Karlsson, Medical Engineering & Physics, 2012, 34, 1139-1148

This paper uses the decomposition introduced in Paper I in a subject-specific human aorta, and investigates how the mean and fluctuating WSS components changes at various locations in the aorta. Large eddy simulation was used and 50 cardiac cycles were simulated to ensure a statistically reliable result. Both elevated mean and fluctuating WSS values were found in the vicinity of the branches on the aortic arch, and the time-averaged WSS was found to be inversely proportional to the oscillatory shear index.
CHAPTER 7. REVIEW OF INCLUDED PAPERS

Paper III


In this paper the WSS distribution in a healthy human aorta was investigated using fluid-structure interaction. Three different values of the wall stiffness were used, to investigate the influence of the wall motion. In addition, two rigid wall models with different sizes were also included, to be able to estimate the influence of the rigid-wall geometries. Comparisons between simulation results and MRI measurements of descending aortic velocity profiles indicated a very good agreement between the simulations and measurements, while both the time-averaged WSS and the oscillatory shear index seemed unaffected by the wall motion. However, instantaneous WSS values were affected by wall motion, indicating that if instantaneous WSS values are important, it might be necessary to include fluid-structure interaction.

Paper IV

Large Eddy Simulation of LDL Surface Concentration in a Subject Specific Human Aorta, Jonas Lantz and Matts Karlsson, *Journal of Biomechanics*, 2012, vol. 45, 537-542

The mass transport of low-density lipoprotein (LDL) from the blood to the arterial wall was simulated and the influence of near-wall velocity patterns were investigated. An inverse relationship between time-averaged WSS and LDL surface concentration was found, where regions with high shear had a low surface concentration. It was also found that there were large temporal changes of LDL during a cardiac cycle, with decreasing values during systolic acceleration and a build-up phase during systolic deceleration and systole.

Paper V

Numerical and Experimental Assessment of Turbulent Kinetic Energy in an Aortic Coarctation, Jonas Lantz, Tino Ebbers, Jan Engvall, and Matts Karlsson, (submitted for publication)

The turbulent kinetic energy in an aortic coarctation before and after intervention was assessed using both MRI and CFD. It was shown that while the mass flow rate increased (and, thus, also the Reynolds number) after intervention as a result of decreased pressure drop, global TKE levels decreased. This suggests
that peak Reynolds number might not be suitable for estimation of the amount of turbulence in cardiovascular flows, but instead a quantity such as TKE could be considered. In addition, integrated values of TKE distal the coarctation showed very good agreement between the experimental data and numerical results. This means that MRI-measured TKE might be useful when determining the outcome of an intervention, while CFD results complement the experimental data, as the resolution is significantly higher in the numerical model.
Bibliography


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