Hemodynamics of Cerebral Aneurysms: Physiology and Numerical Simulations

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Dissertation submitted to obtain the Master’s Degree in Biomedical Engineering

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February 2011
I would like to start by expressing my sincere gratitude to Prof. Adélia Sequeira, for giving me the opportunity to work with her, not only in this thesis, but also over the past three years. Both her kindness and wisdom are remarkable, and I will always be thankful for believing in my work and proposing me new challenges.

To Prof. Jorge Campos, for providing me the anatomical geometries, which were a crucial aspect of this work, and for the medical feedback.

A special thanks to Doutora Alexandra Moura. For her knowledge and almost daily support, that guided me throughout this work. I am profoundly grateful for her words of encouragement in the most frustrating moments and for her tremendous patience and dedication. Obviously, none of this could have happened without her.

I also like to thank Alberto Gambaruto for the time he spent processing the geometries used in this work, and also for the insightful comments, that improved the quality of this thesis.

A big thanks to all my friends and colleagues for all the funny times throughout these years.

To my parents, sister and grandmother, for the unconditional support and for always being there when I needed the most. There is nothing more important to me than my family.

To Madalena, the most wonderful and precious gift I received last year.

At last, I would like to thank Miguel, especially for his (almost) never ending patience and constant care. You are my rock!


Resumo

O objectivo deste estudo foi determinar o impacto da escolha do modelo matemático, e de variações geométricas, na hemodinâmica no interior de um aneurisma. Efectuou-se uma comparação exaustiva, sistemática, quantitativa e qualitativa, usando geometrias 3D idealizadas e reais de aneurismas saculares cerebrais. Foram avaliadas as diferenças resultantes do uso de dois tipos de modelos fluidos, Newtoniano e não-Newtoniano inelástico (Carreau), regime estacionário ou pulsátil, e condições de fronteira distintas nas secções computacionais de saída. As últimas incluem condições standard sobre a tenso normal, bem como o acoplamento com modelos reduzidos 1D ou 0D, simulando o sistema cardiovascular, no sentido da modelação geométrica de multi-escala. Os efeitos hemodinâmicos da presença de vasos laterais também foi analisada, com base na inclusão ou exclusão, quer através de modelos 3D ou de modelos reduzidos.

De um modo geral, as simulações numéricas mostraram ser bastante sensíveis às alterações analisadas neste trabalho, tanto para os modelos, como para a geometria. Foram observadas variações substanciais nas diferentes geometrias. Para além disso, na maior parte dos casos, as diferenças entre as soluções estacionárias e pulsáteis foram mais significativas do que as diferenças entre as duas leis da viscosidade do fluido, mostrando a importância das simulações pulsáteis. Os resultados demonstram uma semelhança considerável ao considerar a geometria com os vasos laterais ou a geometria truncada acoplada com modelos reduzidos nas secções de saída. Apesar de o modelo 0D aqui considerado se ter mostrado insuficiente para simular a circulação sistémica, é possível concluir que em alguns casos os modelos reduzidos podem ser usados para simular os efeitos dos vasos laterais em geometrias reais.

Palavras chave: Aneurismas cerebrais, dinâmica computacional de fluidos, metodologia de multi-escala geométrica, geometrias idealizadas, geometrias específicas de pacientes.
Abstract

The purpose of this study was to assess the impact of the mathematical model choice, and geometrical variations, in the hemodynamics inside an aneurysm. Exhaustive and systematic quantitative and qualitative comparisons were carried out, using both idealized and patient-specific 3D geometries of saccular aneurysms. The differences between using two fluid models, Newtonian and inelastic non-Newtonian (Carreau), steady or pulsatile flow regimes, and distinct boundary conditions at the downstream computational sections, were evaluated. The latter include standard normal stress boundary conditions, as well as the coupling with 1D or 0D reduced models for the cardiovascular system, in the framework of the so-called 'geometrical multiscale approach’. Furthermore, the influence of the presence of side branches was analyzed, by neglecting or including them, either through 3D or reduced models.

Overall, the numerical simulations were very sensitive to the modeling and geometrical changes analyzed in this work. Substantial variations in using different geometries were observed. Moreover, in most cases, the differences between the steady and unsteady solutions were more significant than the differences between the two fluid viscosity laws, showing the importance of unsteady simulations. Results demonstrate a remarkable resemblance between considering a wide geometry, with side branches, or a clipped geometry coupled to reduced models at the downstream sections. Even though the 0D model here considered has shown to be not sufficient in accounting for the systemic circulation, it is possible to conclude in some cases of realistic geometries the reduced models can be used to simulate the effects of the side branches.

Keywords: Cerebral aneurysms, computational fluid dynamics, geometrical multiscale approach, idealized geometries, patient-specific geometries.
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<th>Description</th>
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<tr>
<td>0D</td>
<td>Zero-dimensional</td>
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<td>1D</td>
<td>One-dimensional</td>
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<td>3D</td>
<td>Three-dimensional</td>
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<td>3DRA</td>
<td>Three-Dimensional Rotational Angiography</td>
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<td>CTA</td>
<td>Computerized Tomography Angiography</td>
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<td>DSA</td>
<td>Digital Subtraction Angiography</td>
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<tr>
<td>FSI</td>
<td>Fluid-structure interaction</td>
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<td>GON</td>
<td>Gradient oscillatory number</td>
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<td>IA</td>
<td>Intracranial aneurysm</td>
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<tr>
<td>MRA</td>
<td>Magnetic Resonance Angiography</td>
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<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<td>NO</td>
<td>Nitric oxide</td>
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<td>OSI</td>
<td>Oscillatory shear index</td>
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<td>RBC</td>
<td>Red blood cells</td>
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<td>SMC</td>
<td>Smooth muscle cells</td>
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<td>SR</td>
<td>Size ratio</td>
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<td>Wall shear stress gradient</td>
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Chapter 1

Introduction

1.1 Motivation

Heart diseases, cancer, and stroke, are, respectively, the three leading causes of death in developed countries. Among other reasons, hemorrhagic strokes may occur in result of the rupture of an aneurysm, which, in the majority of the cases, and unlike most medical conditions, is a sudden event, with no warning signs. Nowadays, aneurysms still represent a frightening and devastating silent threat, not only due to their association with high prevalence and mortality rates, but also because they are the greatest cause of long-term disabilities. Thus, aneurysms have a significant impact on cost and overall state of health care, and the understanding of the fundamental aspects of their pathophysiology and treatment is a subject of great importance, both nationally and globally, highly contributing to the progress of the modulation of the complex phenomena associated with these pathologies.

Generally, an aneurysm is a localized pathological dilation of the wall of a blood vessel, due to the congenital or acquired structural weakening of the wall media, and potentially results in severe complications, or even sudden death, through pressing on adjacent structures, thrombus formation or rupturing causing massive hemorrhage [32]. The natural history of this pathology is far from being fully understood, mainly because of the paucity of temporal investigations, which is related to the fact that aneurysms are rarely detected before rupture. Intracranial aneurysms are dynamic structures, with constantly changing morphologic features, so, in order to have a better understanding of the modifications that lead to rupture, those properties should be examined over time [53]. Every year a large amount of new studies are made, covering the multiple aspects of the aneurysm genesis, development and eventual rupture, from a cellular level to a macroscale point of view. These investigations provide valuable and thorough information while incite for even more detailed and comprehensive analysis. In fact, the intricacy of aneurysms is reflected on the intensive multi-faceted and multi-disciplinary effort to understand the development of this disease. The professionals involved in these studies can have completely distinct background areas, spanning
from clinicians to mechanical or biomedical engineers, molecular biologists, mathematicians, and so many others.

Currently, the investigations use a variety of methodologies, from *in vitro* to *in vivo* models, but a great percentage is based on mathematical modeling and numerical simulations of blood flow, since it is now well established that blood flow dynamics play a major role in the development of cardiovascular pathologies, like aneurysms [84]. Inherited and acquired factors may be involved in the aneurysmal initiation but specific hemodynamic characteristics, such as oscillatory shear stress, elevated pressure, long cell residence time and flow impingement, i.e. collision between the inflow jet and the aneurysmal wall, are known to be closely related with the aneurysmal environment [15]. These evidences demonstrate the importance of a detailed comprehension of the local blood flow conditions, which can be useful for diagnostic and treatment purposes. The substantial evolution of non-invasive neuroimagiological techniques both allows for the acquisition and processing of more accurate and detailed medical images, on the other hand, increasing advances of high performing computers and efficient numerical algorithms leads to even more precise numerical results. The most recent simulations use these medical data to approximate individual specific situations and to model physical quantities, like wall shear stress (WSS) and complex blood flow velocity fields while connecting individual hemodynamic factors to clinical events. In the past, all numerical models used idealized geometries that simulate the hemodynamic quantities in a generalized way but these methods fell short since, ultimately, each aneurysm is a unique case, with a singular geometry, location, relationship with the surrounding environment, and hemodynamic behavior, which is heavily dependent not only on its own geometry but also the parent vessel. Hence the importance of these patient specific image-based geometry computational simulations. They also enable to predict hypothetical specific surgical interventions and the variation of desired flow conditions in a fast and inexpensive way. However, the use of mathematical models and numerical simulations to study and comprehend blood flow behavior and cardiovascular pathologies, such as intracranial aneurysms (IA), is still a very challenging task and a field of active research [84]. A statistical analysis of a wide range of realistic models would have a great value, but the reliable *in vivo* measurement of some of the parameters is still very difficult to obtain with current techniques, interfering with the validation of the numerical results. Also, the realistic simulation of the local and global events, that have such a significant influence in the development of aneurysms, represents a computational challenge because of the diversity and intricacy of the human arterial system, not only in terms of its geometry but also the functional interactions that take place between several entities.

### 1.2 Objectives

Although there is a considerable number of methodologies that have been used to study the development of vascular diseases, such as aneurysms, it is yet to be described an ideal model, that takes...
into account all the particular parameters that influence the real aneurysmal environment. In this work, we will present an overview of the current notions and theories concerning the aneurysmal physiology and will focus our attention in the study of the blood flow behavior in a portion of the arterial tree that includes an intracranial aneurysm, provided from a real patient through medical acquisition. In order to do so we present a mathematical and numerical methodology that evaluates the flow and pressure fields in idealized and realistic aneurysm geometries. This methodology uses efficient algorithms to couple three-dimensional (3D) Newtonian and non-Newtonian models for the aneurysm area [29] with one-dimensional (1D) hyperbolic [27] or non-dimensional (0D) models [43] that simulate the blood circulation in the circle of Willis. We also aim to analyze the impact of several flow variables, like the WSS and its spatial and temporal variations, in the development of aneurysms.

1.3 Methodology

We have chosen to implement the geometrical multiscale modeling, in which we will exploit the combination of two models, with different complexities, due to the fact that the current technology is not advanced enough to simulate the whole cardiovascular tree using full complex and accurate models, since this implies an elevated computational cost. This methodology allows us to simulate, at a reduced cost, the local aneurysmal environment and its surrounding vessels, at different dimensional scales, giving more emphasis, and consequently more accuracy, to the solution of the problem in the aneurysmal portion. This is the area that requires more detailed data and, because of that, it is approximated using a three-dimensional model, that describes the pressure and velocity fields in a very precise way. With the use of medical images, the area of interest is chosen and truncated from the rest of the 3D domain, which is taken into account at the artificial sections using the reduced model, by means of boundary and compatibility conditions. We use a 1D or 0D scheme as the reduced models, which resort to some simplifying assumptions in order to provide averaged quantities for the pressure and velocity fields. The 3D model describes the blood flow using 3D equations for incompressible Newtonian and non-Newtonian fluids, capturing the shear-thinning behavior of blood viscosity. Though it is well known that the mechanical interaction between the blood flow and the compliant vessel wall is relevant in the blood flow propagation phenomenon, the 3D model is constructed as a fixed domain, neglecting the wall displacements.

The realist geometry is obtained using the rotational Computerized Tomography Angiography technique in a subject with an aneurysm in the circle of Willis. In fact, aneurysms are most commonly located at the branching points of the major arteries of this ring-like arterial structure, with a bigger incidence in the anterior circulation. The image processing encompassed the image segmentation, surface extraction, and surface smoothing, and we also resort to visualization softwares. The numerical algorithms are implemented in C++, in the scope of the finite element library LifeV.
1.4 Thesis outline

This thesis is divided into 6 chapters. It starts with the present introduction where the motivations and purposes of this work are enunciated. Chapter 2 reviews the different features concerning the physiology of aneurysms, their initiation and growth, the local blood flow characteristics, as well as the current techniques in treatment and medical imaging acquisition. Chapter describes the used 1D mathematical model and displays numerical results obtained with this model. Chapter 3 includes a review of the current techniques in this area, the formulations of the 3D mathematical model used in this work, and the coupling strategies. The applied image processing techniques are also discussed in this chapter. In chapter 4, numerical results obtained using the introduced methodology are presented and discussed. Finally, in chapter 5 the conclusions are drawn and some future perspectives are suggested.
Chapter 2

About Intracranial Aneurysms

In this Chapter, the current literature suits as a foundation to present the principal features and state of the art knowledge of the initiation, growth and rupture of IA. We start by introducing the statistical analysis and classification of this pathology and by describing the characteristics and complexity of the cerebral arterial walls. Both the current treatment and image acquisition techniques are revised and the dynamic features of the blood flow are presented. Then, we approach the diverse factors that may have some influence in the development of aneurysms and illustrate the pathologic mechanisms involved in the developmental stages.

2.1 Epidemiology

On the basis of several autopsy and angiography series, it is estimated that 0.4 to 6% of the general population harbors one or more IA, and, on average, the incidence of an aneurysmal rupture is of 10 per 100,000 population per year, and tends to increase in patients with multiple aneurysms [75, 49]. More precisely, IA cause an estimated 28,000 cases of subarachnoid hemorrhage annually in North America [22] and in 30% of the patients there is a development of multiple aneurysms [96]. The incidence of IA is predominant in female patients and in subjects with ages greater than 50 years [94]. The tendency generally increases to about 8 to 9% if a person has more than one familial case and for first-degree relatives the risk is even higher [96]. Moreover, patients with familial aneurysms are prone to share identical aneurysm locations and rupture age with their relatives, which is usually at a younger age than those with non-familial cases [57]. Pregnant women have an increased rate of aneurysm incidence, about 1 in 1,100 to 1 in 25,000, because of pregnancy related physiologic changes in the arterial wall, such as thickening of the media, loss of normal corrugation of elastic, and hypertrophy and hyperplasia of smooth muscle cells fibers [6]. Despite considerable advances in diagnostic and surgical techniques, ruptured aneurysms are associated with high rates of mortality. Several studies report that more than 50% of the patients with ruptured IA die or become severely disabled from the resultant subarachnoid
hemorrhage within the first hospitalization, and if left untreated, another 30% die as a result of a rebleeding in the next decade [22]. This means that only a small percentage of the patients survive a ruptured IA with minor manifestations and to make matters worse, once an aneurysm has ruptured, there is a very high re-bleeding rate. In terms of the IA site, autopsy and angiography studies revealed that 24% of the IA are located on the anterior communicating artery (ACA), 30% are located on the middle cerebral artery (MCA), 42% are located on the internal carotid artery (ICA), and only 10% are located on the posterior circulation [75].

2.2 Structural and etiological classification

Aneurysms are often classified as being either true or false aneurysms, and depending on how focal is the point of weakness in the vessel wall, true aneurysms may be divided into saccular, fusiform and dissecting aneurysms, having distinctive shapes and sizes, which are not specific for any clinical complication [51].

False aneurysms involve the rupture of the wall and the formation of an extravascular hematoma, bounded by extravascular connective tissue, which contiguously communicates with the interior of the vessel. On the other hand, true aneurysms involve all three layers of the attenuated arterial wall.

Saccular or berry aneurysms, which encompass 90% of the encountered aneurysms [34], are characterized by a development of a spherical evagination connected to the vessel by a neck. These berry-like aneurysms involve only a vascular portion and are commonly related to thrombus formation. In the case of fusiform aneurysms, the expansion of the vessel wall has a diffuse elongated shape and occurs in large segments of the vessel walls.

According to their relative position to the parent vessel, aneurysms may also be classified as terminal, lateral or bifurcation aneurysms [15].

There are several classes of aneurysms according to the predisposition disease associated with the vessel wall weakness and aneurysm formation [51, 52]. In the aorta, the two most common disorders that predispose to the formation of aneurysms are atherosclerosis and hypertension. Atherosclerotic aneurysms are common in the abdominal portion of the aorta, while hypertension is a greater factor in the initiation of aneurysms located in the ascending aorta. Intracranial aneurysms are mostly associated with hemodynamic stresses at bifurcation sites, but congenital defects may also contribute to their initiation. Although referred to as congenital aneurysms, they are only developed after birth due to media defects at sites of bifurcation. In fact, aneurysms are absent in neonates [86]. Microaneurysms or Charcot-Bouchard aneurysms also affect the cerebral vessels. These miniature aneurysms generally arise numerously from small arteries. Aneurysms may also be secondary to other conditions, such as trauma, inflammation/infection and neoplasia, which include those that are originated as a result of syphilis and arteritis. Syphilitic aneurysms, a more often rare complication nowadays, usually appear in the ascending aorta and arch of the aorta,
while aneurysms caused by vasculitis tend to be located in the renal and mesenteric vessels, leading to local ischemia. Infectious aneurysms are originated from embolization of a septic thrombus, as an extension of an adjacent suppurative process or by infectious organisms, such as bacteria and fungi. On the other hand, the embolization of tumor cells causes the destruction of the vessel wall by tumoral infiltration, leading to oncotic aneurysms. Though reports on cerebral oncotic aneurysm are rare, the most frequent primary neoplasms are cardiac myxoma, choriocarcinoma, and bronchogenic carcinoma [39].

False aneurysms are usually due to trauma but occasionally occur because of an infection or a tumor, and can rupture very easily.

2.3 Anatomy and histology of cerebral arteries

Aneurysms could arise from any blood vessel across the vascular network but they are primarily located in the arteries, more precisely, in different segments of the aorta, referred to as aortic aneurysms, and even more frequently in the intracranial arteries supplying the brain, referred to as cerebral, or intracranial, aneurysms. Intracranial arteries have an increased tendency to develop aneurysms when compared to extracranial arteries because of certain histopathologic and embryological differences in the wall, and hemodynamic factors [96]. Moreover, IA are most likely to be encountered on or close to the circle of Willis, see Figure 2.1, an important polygonal-like arterial network, particularly in apices of the bifurcation of first and second order arteries and curved arterial segment [101].

This polygonal-like arrangement of arteries located at the base of the brain is extremely important since it supplies the blood to all the brain territories and equalizes the pressure and blood flow volume between the two sides of the brain [34]. Furthermore, the circle of Willis creates redundancies in the cerebral circulation in a way that if one artery is occluded or missing the blood
Figure 2.2: Non-pathological arterial wall [51]

is redistributed through the circle of Willis maintaining the blood perfusion at a reasonable level to avoid stroke and ischemia [2]. As a matter of fact, in about 50% of the population at least one artery is absent or partially developed [56] and this variations in the circle of Willis play some role in the development of IA [47].

When a cerebral vessel wall develops an aneurysm it becomes a vessel in a pathological state. It is required a detailed knowledge of the healthy wall vessel and comparative experiments of healthy and diseased vessels in order to fully understand the mechanics that lead to the aneurysm formation.

The walls of the large vessels are made up of three layers or tunicas, known as intima, media and adventitia, surrounding the lumen, through which the blood flows [91], see Figure 2.2.

Each of these layers plays an important role in the overall strength and elasticity of the vessel. In general, the arteries can be classified as elastic or muscular. The former are the ones with larger radii and closer to the heart, such as the aorta and the carotid arteries, and the latter are located in the peripheral districts, such as most of the cerebral arteries. The elasticity of the blood vessels increases with the proximity to the heart and depends on its structure and composition whereas the stiffness of the wall is considerably regulated by the activity of the single layer of vascular endothelial cells that covers the intima at the luminal side. Endothelial cells form a semi-permeable barrier that prevents blood elements from adhering to the luminal surface and allows access to the wall to various substances [54]. This monolayer of cells adhere to a protein-rich layer called the basal lamina that covers a sub-endothelial layer composed of connective tissue, elastic fibrils, and collagenous bundles. The intima thickens and stiffens with age, resulting in the augmentation of its contribution to the mechanical properties of the arterial wall. Moreover, atherosclerosis may also cause pathological changes in the wall intima and alter its mechanical behavior.

The media layer is mostly formed by a 3D network of smooth muscle cells (SMC), elastic sheets, elastic fibrils, and collagenous bundles embedded in an extracellular matrix. Like the dynamic
resistance, most of the mechanical properties of the vessel wall are determined by the proportions of the different components of this layer, which are dependent on the location of the vessel in the arterial tree. In fact, elastin fibers account for the elastic behavior of the wall in response to the pressure effect, being able to stretch up to 250% of its original length, while collagen fibers can prevent excessive dilation, since their modulus of elasticity is about 1000 times larger than elastin [54]. In the cardiovascular system, the elasticity decreases towards the peripheral circulation because of the dissipation of the elastic fibers in this direction [91]. Usually, intracranial arteries do not possess any elastic layers in the media and have an absent median muscular layer at the apex of their bifurcations [54].

The intima and the media are separated by a layer of elastin called internal elastic lamina while the external elastic lamina separates the media from the outer adventitial layer. The internal elastic lamina is a predominant feature of muscular arteries but may not be present in the elastic ones. On the other hand, the cerebral arteries, as well as all small vessels, are characterized by an almost loss of the external elastic lamina [49].

Fibroblasts and nerve fibers are the main components of the outermost layer of the vessels and are responsible for the production of collagen fibers and the innervation of smooth muscle cells, respectively. The thickness of the adventitia depends on the artery type and in cerebral arteries it is almost absent.

Overall, the entire arterial wall is thinner in cerebral arteries [101].

2.4 Aneurysm treatment

A patient with an unruptured IA may think that treatment is synonym of playing safe, but any treatment option has some associated risks. Before deciding whether or not to treat an aneurysm it is necessary to weight the risk of rupture against the risks inherent in the procedure, which is often difficult because of limited diagnostic criteria. Computational techniques may be used to turn this process easier, by using computational fluid dynamics based methods to simulate the hemodynamic consequences of interventional procedures in patient specific geometries [63]. The choice of approach is based on an individual analysis concerning the size, location, and shape of the IA along with the patient’s symptoms and general healthy. The hemodynamic conditions in the aneurysmal region are also relevant when planning treatment [44]. Currently, the main surgical options for the treatment of IA are direct clipping, and endovascular therapy, including coiling and proximal ligation or trapping of aneurysms with or without the use of bypass [61, 96], but in some cases the short and long term monitoring without operating is the most appropriate choice.

The microsurgical clipping is the most routine and definite procedure but since it is an open surgery procedure it is also the most invasive one. In order to cut off the aneurysm blood supply its base or neck is tightly closed by clamping it with a metallic clip. The clip has the strength, shape, and size necessary to prevent the blood from flowing into the intra-aneurysmal structure
and to insure that the blood circulates once again properly through the parent vessel, without further damaging the arterial wall [61].

The endovascular procedures have greatly evolved and they require the insertion of an catheter in the vascular system which then reaches the region of the aneurysm in the brain. These methods are specially profitable when aneurysms are difficult to access by open surgery but they may induce vessel dissection, stroke, and intra-operative aneurysm rupture in up to 5% [1]. The aim of endovascular surgery is to induce thrombosis by filling the aneurysmal sac with platinium coils. This technique includes the use of mechanical agents like balloons, electrolytically detachable coils and coated coils. Other experimental procedures physical agents like RF probes, laser light, and chemical agents like biocompatible adhesives and magnetically controlled compounds [34]. A stent may also be introduced inside the parent vessel, across the aneurysmal portion, in addition to coil embolization, in order to assist the coil retention or to promote intra-aneurysmal thrombosis [1].

Other indirect surgical techniques include the proximal ligation and trapping of the aneurysm. The endovascular proximal ligation technique consists of occluding the parent artery adjacently to the aneurysm, e.g. by permanently placed balloons or using coils, while trapping of the aneurysm consists of introducing detachable balloons in the main artery above and below the aneurysm. Presently, these procedures are rarely used. When the patient cannot tolerate the vessel occlusion by inadequate colateral circulation, an arterial bypass can be used in the therapeutic approach.

2.5 Medical image acquisition

Brain aneurysms are rarely detected at early stages, which is the most alarming feature of this disease. Thus, they are mostly identified only after they have either ruptured or become fully developed and reached a dangerous size. Besides that, in many cases the aneurysm is randomly found in an incidental exam. Unruptured aneurysms are currently detected in only 10% of the patients, from which a small portion are detected by chance and the majority owe its discovery to symptoms related to the compression of adjacent brain structures, which usually happens in the case of bigger aneurysms. Nonetheless, unruptured brain aneurysms are being detected more frequently with the use of current neuroimaging techniques, such as Digital Subtraction Angiography (DSA), Three-Dimensional Rotational Angiography (3DRA), Magnetic Resonance Angiography (MRA), and Computerized Tomography Angiography (CTA) scans. The incidence of hemorrhage from an unruptured aneurysms is an uncertain event but these techniques provide substantial imaging of the aneurysm condition, which is imperative to decide on whether or not to treat the unruptured aneurysm. These imagiologic methods are unable to provide accurate quantitative measures of intra-aneurysmal hemodynamics parameters, but instead they produce a direct representation of the intra-aneurysmal flow structure [18].

Although it has a 0.5% risk of permanent neurologic complications [59], the selective angiographic technique is considered the gold standard for evaluation of the cerebral vasculature and
the extent of its malfunctions because of its unsurpassed resolution [33]. The tomographic and resonance techniques are so far not as sensitive nor specific [59].

2.5.1 Digital Subtraction Angiography (DSA)

An angiography is an invasive procedure that produces images, using X-ray imaging methods, which show the blood vessels in a comprehensive, sensitive and specific manner. Since the blood vessels are not seen on the plain X-ray, the blood vasculature is distinguished from the background through the administration of a bolus of iodine-based contrast agent into the bloodstream, which is most commonly inserted through the femoral artery using a catheter that is then fed into the specific arteries of interest. Usually, a mathematical subtraction technique is used in order to increase the contrast between the background features and the blood vessels. In the DSA procedure, two images are taken, one without the contrast agent and another after injection of the contrast agent. The increased attenuation from the blood vessels is overcome by using the first image to suppress the attenuations from the surrounding tissues, such that the resulting images only contain the vessels lumen. Images produced from DSA have very high spatial resolution, and have the capacity to screen vessels with diameters down to 100µ m [98]. The risks associated with this vital component in diagnosis of vascular conditions are very low but not negligible. The major complications include cerebral infarction, formation of a hematoma or pseudoaneurysm at the puncture localization, and renal failure [80]. In addition, although this radiographic technique provides a relatively quick and efficient means for the diagnosis of aneurysms, it may not show the real extent of an aneurysm when there is a clot and the final result is a two-dimensional projection of the aneurysm region which limits the accurate determination of the presence and geometry of the aneurysm lumen or neck. This drawback can be overcome using techniques that produce 3D images, i.e. 3DRA, CTA, and MRA.

2.5.2 Three-Dimensional Rotational Angiography (3DRA)

Using a 3DRA, a series of X-ray images projection of the blood vessels may be acquired from any orientation by continuously rotating the C-arm on which the X-ray tube and image detector are mounted at both ends. The acquisition at a sufficiently high number of angles allows for the 3D reconstruction of the blood vessels, which enables the visualization of the 3D data from any angle. The 3D image volume reconstruction uses the same mathematical procedure as the computed tomography though when comparing the two approaches, 3DRA allows more exact depiction of anatomical details [38].

2.5.3 Computed Tomography Angiography (CTA)

CTA enhances the spiral CT scan with a contrast dye injected into a vein, which allows for 3D imaging highlighting the blood vessels. In this technique, the X-ray imaging methods and an
interpretive computer are used in order to obtain two-dimensional projections of the cross-sectional area of an anatomical region of interest. Basically, a thin beam of X-rays is produced by an X-ray tube, attenuated by the patient, and measured by an X-ray detector, over a large number of angles. The patient is slowly translated through the gantry, at the same time that X-ray tube rotates continuously around the patient. For each angle, \( \theta \), the measured intensity profile, \( I_\theta \), depends on the distribution of the linear attenuation coefficient, \( \mu \), in the \( xy \)-plane, and can be transformed into an attenuation profile using the unattenuated intensity of the X-ray beam, \( I_0 \). This attenuation profile is the projection of the function \( \mu(x, y) \) along the angle \( \theta \) and gathering all the projections results in a 2D dataset called sinogram, which is constructed using a Radon transform. Each point of each scanned slice can be reconstructed using a 2D-Fourier transform.

After several scans, the cross-sectional images yield anatomical information at different depths, and a 3D visualization may be obtained by stacking the two-dimensional projections. The obtained image is a representation of the X-ray attenuation properties of the body. CTA detects tissue and bone structure, and since blood is very dense, it images very clearly on a CTA scan, so thrombosed and partially thrombosed aneurysms can be easily detected. IA usually appear as rounded areas of hyperdensity in close proximity to the circle of Willis [34].

2.5.4 Magnetic Resonance Angiography (MRA)

A magnetic resonance angiography may be obtained using time-of-flight (TOF-MRA) and phase contrast (PC-MRA) angiography techniques, and even though it does not require the injection of an opaque dye, Gd-DTPA is often administrated to increase the signal difference [98]. The anatomy of the vessels is acquired using the former technique whilst the latter also provides directional-flow images. MRA relies is based on magnetic resonance imaging (MRI), which is a nonionizing technique that provides 3D data, with an excellent soft-tissue contrast and high spatial resolution (1mm) [98]. Despite these strong capabilities, the major drawbacks when using an MRI machine are its slow temporal resolution, when compared, for example with CT, and the inability to detect small aneurysms. During a MRI scan the patient is placed inside a strong magnet, which generates an homogeneous magnetic field, typically with 1.5T to 3T, denoted \( B_0 \). \( B_0 \) interacts with hydrogen nuclei, or protons, which are forced to precess coherently around its axis at the Larmor frequency, producing a net magnetization effect. Supplying a radiofrequency (RF) pulse with Larmor frequency to the system produces an electromagnetic field and when its ceases the protons in different tissues return to their equilibrium state at different rates, and this difference is detected. The formation of the 3D signal requires three basic processes: the slice selection, the phase-encoding, and the frequency-encoding. Finally, the analog signal is amplified and digitalized, and the final image is obtained using an inverse two-dimensional Fourier transform. The TOF-MRA relies on a short echo time, i.e the time between the initial RF pulse and the maximum in the echo, and flow compensation, whereas in the PC-MRA the phase of the MRI signal is manipulated.
by varying magnetic fields, called bipolar pulses. The TOF-MRA partly saturates low velocity blood flow, resulting in better contrast images yielded from the PC-MRA technique.

In magnetic resonance images an unclotted portion of an aneurysm reveals a negative flow defect or signal void in the lumen of the parent vessel whilst the clotted or thrombosed portions are areas of decreased signal intensity [34].

2.6 Dynamic properties of blood flow

The cardiovascular system can be considered a closed blood distribution network with multiple branches, constituted by three interrelated components: blood, the heart, and blood vessels. It has the essential purpose of delivering blood to all the organs in the human body, so that it can maintain an optimal environment.

The blood is the only liquid connective tissue and it has many vital functions, but mainly delivers oxygen and nutrients to all tissues, drains metabolic waste products, defends the body against infection, transports hormones through the vascular system, and helps regulate the pH of body fluids [91]. This very complex fluid constitutes about 8% of the total body weight and its composition consists of an intricate of cellular deformable elements with different concentrations, namely, red blood cells (erythrocytes), white blood cells (leucocytes), and platelets, suspended in a fluid component called plasma that contains electrolytes and organic molecules. Because of their high concentration, the red blood cells (RBC) are the main contributors to the mechanical properties of blood, and consequently the rheology of blood is largely affected by the state of the RBC, which can range from 3D structures to dispersed individual cells, at different shear rates [81]. The nature and behavior of blood is not only dependent on the fluid properties, but also on other mechanical factors, including the forces exerted on the fluid, the fluid motion, and the boundary conditions of the vessel geometry. Moreover, the blood viscosity also dictates its behavior. According to these features, the blood flow may be characterized as steady or pulsatile, Newtonian or non-Newtonian, and laminar or turbulent.

2.6.1 Steady versus pulsatile

Fully developed flows are described by velocity and pressure fields, with all kinematic quantities independent from the axial coordinate, but this ideal behavior is never achieved in the vascular system. Two relevant particular cases are the steady flow, governed by the Poiseuille solution, and the time-periodic flow, governed by the Womersley solution. In most of the vascular system, blood flow has pulsatile behavior, that varies in different sites of the arterial tree, due to the repeated, rhythmic mechanical pumping of the heart [50]. This means that the blood flow is an unsteady flow and because of that the time dependence should not be neglected.

The Womersley solution for a pulsatile flow in straight or tapered cylinders is a reasonable
approximation to model blood flow in the arterial network [100]. In this case the flow rate at the inlet varies with time in a periodic manner, and at sufficient distance from the inlet, the velocity only has an axial component, function of radius. Generally, the Womersley velocity profile is not parabolic and, even though the total volume flow always remains positive, there is a boundary layer of reversed flow close to the wall. This inversion is important in the characterization of pulsatile flow and is featured in the blood flow when the viscous traction forces are opposite to the dominant flow direction [87]. Even so, the blood flow is often considered in a steady state, depending only on the spatial position, since an unsteady flow is usually much more complex than a steady one. In this case, the blood flow is approximated by the Poiseuille solution for steady flow and the velocity profile is parabolic, with flow direction parallel to the vessel wall. This is a simplification and does not correspond to the general physiological situation, however, in a long circular cylinder after a reasonable distance the fluid tends to be parabolic, and in small arteries, sufficiently distant from the heart, the flow is predominantly steady.

The parabolic velocity profile of steady flow is given by
\[ v(r) = v_0 \left[ 1 - \left( \frac{r}{R} \right)^2 \right] \quad 0 \leq r \leq R \] (2.1)
where \( v_0 \) is the velocity of the central layer and \( R \) is the luminal vessel radius. The Poiseuille law establishes the relation between steady flow and pressure gradient,
\[ \Delta p = \frac{8\mu Q l}{\pi R^4} \] (2.2)
in which \( l \) is the tube length, \( Q \) is the flow rate, given by \( Q = \pi R^2 v_0 \), and \( \mu \) is the fluid viscosity.

In terms of the unsteady flow, a Fourier Series may be used to decompose the flow rate curves into Fourier coefficients \( Q_n \),
\[ Q(t) = \sum_{n=0}^{N} Q_n e^{i\omega nt}. \] (2.3)
which, after being applied in the Womersley equation, are used in the definition of the Womersley velocity profile for the axial component of velocity,
\[ v(r, t) = \frac{2Q_0}{\pi R^2} \left[ 1 - \left( \frac{r}{R} \right)^2 \right] + \sum_{n=1}^{N} Q_n \frac{1 - J_0(\beta_n r)}{\beta_n J_0(\beta_0)} e^{i\omega nt} \] (2.4)
where $\omega$ is the angular frequency, $J_0$ and $J_1$ are Bessel functions of the first kind, and $\beta_n = i^{3/2} \alpha_n$ with $\alpha_n = R \sqrt{(n\omega)/\nu}$ and $\nu = \mu/\rho$ as the kinematic viscosity, with $\rho$ as the density. The transformation of the kinematic viscosity into a dimensionless parameter results in the Womersley number which is a predictor for the onset of unsteady flow, see Section 4.4.

### 2.6.2 Newtonian versus non-Newtonian

As mentioned before, the RBC play an important role in the blood characterization, and when they are dispersed, the blood can be modeled as a Newtonian inelastic fluid. Still, blood properties such as shear thinning, thixotropy and viscoelasticity, resemble non-Newtonian fluids [77], and it has been proven that the blood behavior is similar to these viscoelastic fluids. The viscosity of a Newtonian fluid is constant during flow, i.e. is independent of kinematic quantities, and has a linear relationship with shear stress, defined by

$$\tau = \mu \dot{\gamma}$$

(2.5)

where $\tau$ is the shear stress and $\dot{\gamma}$ is the strain rate. On the other hand, the behavior of non-Newtonian fluids dictates the non-linear relationship between the shear stress and the shear rate, and the dependence of shear stress not only on shear rate but also on normal strain. Moreover, in these fluids the viscosity can also change during flow, being a function of the shear rate, i.e. $\mu(\dot{\gamma})$.

The viscosity of blood is variable, leading to differences in the shear stress along the arterial wall. Indeed, in large arteries the instantaneous shear rate over a cardiac cycle has drastic variations, up to two orders of magnitude [82]. Apparently, at high shear rates the viscosity of the blood decreases as red blood cells tend to deform and to align with the flow field and at low shear rates the viscosity increases as RBC form clusters [50]. The decreasing viscosity with shear rate is an important blood property named shear-thinning behavior.

Despite the evidences, since the blood flow in sufficient large non-pathological arteries has high shear rate, over 100$s^{-1}$, it is reasonably acceptable to simulate its behavior using simplified Newtonian models. This assumption is not valid when the shear rate is lower than 100$s^{-1}$, which is the case of small arteries, veins, capillaries, and aneurysms or stenosis [93]. In these areas filled with slow flows, the non-Newtonian models are much more suited for an approximation of blood flow.

Even when an aneurysm arises in a large artery, the flow in that area tends to acquire non-Newtonian properties due to the presence of large stable regions of slowly recirculating blood flow [74], but some authors like [15] consider that IA flows can be fairly modeled using the Newtonian assumption.
2.6.3 Laminar versus turbulent

Generally, blood velocity field has a laminar regime flowing parallel to the vessel centerline but under conditions of high flow during the systole period of the cardiac cycle, particularly in the ascending aorta and in stenotic or aneurysmal arteries, the flow can be disrupted and acquire turbulent features, that may include recirculation sites, also known as vortices. Curves and branches across the vascular network also generate secondary flows.

Laminar flow has a parabolic velocity profile and turbulence occurs when fluctuating velocity components are found in both the axial and nonaxial directions [10]. The onset of turbulence can be predicted using the Reynolds number, see Section 4.4. Pulsatile flows become turbulent for Reynolds numbers larger than 2000, specially during decelerating systole or near the end of systole [5]. Over one cardiac cycle, the maximum value of this parameter can range from 6000 to $< 10^{-3}$, in transport from the heart to the periphery [34].

2.7 Inherited and acquired factors

Inherited and acquired risk factors have been associated with the aneurysmal initiation [96], such as genetics, biochemical disorders of collagen metabolism, immature collagen, enzymatic destruction of the vessel wall through the action of elastase and collagenase, and preexisting health conditions [34]. Since the incidence of idiopathic IA is age dependent and they tend to develop at points where the hemodynamic stress forces are greatest, which is mostly at irregular arterial geometries such as tortuous segments, bends, and bifurcations [34], they can be considered acquired lesions. A genetic background may also contribute to the development of an aneurysm, as evidenced by the elevated prevalence of IA in patients suffering from inherited disorders, such as polycystic kidney disease and aortic coarctation, and by the cases of familial IA [57]. The evidence of a congenital influence in some IA suggests that specific genes may contribute to this pathogenesis. Actually, there are evidences that suggest that a genetic locus for IA lies within or close to the elastin gene locus on chromosome 7 [68]. Type III collagen deficiency was also associated with IA, revealing
the importance of connective tissue disorders like Ehlers-Danlos syndrome (type IV) [71].

Exogenous factors like cigarette smoking, alcohol and drug abuse, or medications known to facilitate the generation of atherosclerosis and elevated blood pressure have shown some correlation with the prevalence of IA [49], and despite the fact that in most cases the catalyst for the rupture of the aneurysm remains unknown, some factors like hypertension, strong emotions, blood thinner medications, as well as recreational drugs and smoking tend to increase the risk of rupture [59, 80].

2.8 Hemodynamic factors

The strong tendency for the arise of aneurysms at bifurcations and regions of strong curvatures has lead to the hypothesis that the particular flow features encountered in those sites play an important role in the aneurysm development, inciting the characterization of the complex hemodynamics in such regions [36, 60, 62, 102]. In fact, hemodynamics and the genesis of vascular diseases are believed to be fairly related through the action of mechanical parameters on and near the vessel wall, such as WSS and its derivatives, like the wall shear stress gradient (WSSG), the oscillatory shear index (OSI), and the gradient oscillatory number (GON). The luminal side of blood vessels is constantly exposed to WSS, which is a fluid mechanical tangential force per unit of area generated by blood flow across the endothelial surface, with the purpose of retarding the flow. The lumen diameter and histological structure of the arterial wall are regulated by this hemodynamic stress. Chronic increase of blood flow, and consequently WSS, induces the expansion of the internal diameter so that mean shear stress can establish its basal values, whereas low flow or blood viscosity, leads to the decrease of WSS and the luminal diameter [58]. WSS plays an important role in the development of some vascular diseases, since both excess and lack of this stimulus can generate pathological changes in the arterial wall, through the reaction that it induces on endothelial cells [9]. Increasing evidences suggest that the focal combination of high WSS and WSSG plays an important role in the aneurysmal initiation, by inducing the endothelial-dependent excessive production of vasoactive molecules, such as nitric oxide (NO), a potent vasodilator [28, 60]. The neck of the aneurysm is the location that registers the maximum WSS, in result of high flow velocity and velocity gradient near the wall of the neck [89]. Besides that, aneurysms are usually located at high WSS sites, like bifurcations, and can be created in animals through systemic hypertension and high-flow blood. A study [5] has shown that the formation of an aneurysm may be linked to the combination of variations of WSS vectors in magnitude and direction, and local elevation of static pressure around impingement areas inside saccular aneurysms, more specifically, in these regions a low WSS area is surrounded by a band of high WSS.

In terms of the aneurysm progression, there are two main theories. One that links the aneurysm growth to increased blood flow effects [89] and another that shows that aneurysms are most likely to grow in regions with low shear stress [9, 45]. This results in an ongoing low/high shear stress controversy, similar to what happens in the atherosclerosis case. According to the low-flow theory,
high WSS potentially causes the initial damage in the arterial wall, and progressive changes in the aneurysm shape result in the focal decrease of the WSS, which lead to mechanobiologic processes that result in the aneurysm evolution. The other possible explanation is that the increased WSS causes destructive remodeling that leads to a disturbance of the equilibrium between the blood pressure forces and the internal wall stress forces, resulting in the progressive dilation of the wall.

2.9 Pathogenesis of aneurysm formation, growth and rupture

Despite the continuous progress in the medical research field and the wide range of studies on the pathogenesis of aneurysms, the exact developmental stages are far from being thoroughly comprehended because of the scarcity of studies with a significant amount of patients and long-term follow-up [46], mostly due to the fact that the majority of aneurysms are only detected in an advanced stage. Ultimately, this leads to a poor overall understanding of the formation of an aneurysm, and the natural history of aneurysms is based on insufficient studies with considerable differences on the results. Yet, the pathological formation of an aneurysm is believed to be a multifactorial process, resulting from complex interactions.

Initiation

The aneurysmal wall is the result of variations of the healthy arterial wall, instead of a completely new tissue. Early stage aneurysm formation is related to the recruitment of collagen fibers and elastin breakage, which explains the stiffness of aneurysmal walls. There is an almost complete loss of elastic fibers and the internal elastic lamina is discontinued at the entrance of the aneurysm sac or after a short distance towards inside the aneurysm [49]. Histological evidences suggest that the development of an IA begins with a deformation of a section of arterial wall into a bleb, without a distinct neck region, and then into a fully shaped aneurysm with an identifiable neck [101].

How and why IA first develop is intimately related to interaction between the biological processes of the blood vessel wall and high-flow hemodynamic forces [84]. Arteries are living organs sensitive to hemodynamic conditions, constantly adapting and changing in function of flow and pressure variations [50]. Like platelets and RBC, endothelial cells discriminate among different types of flow patterns and are physiologically stimulated by stress, i.e. blood pressure acting normal to the cell surface and WSS acting tangentially. Endothelial cells respond to stress through an active adaptive process that leads to modifications in their morphology, function and gene expression [8, 25]. Moreover, WSS promotes the elongation and alignment of endothelial cells nuclei in the direction of the local flow pattern [25] and the secretion of vasodilation and anticoagulation mediators, such as NO. The alterations in endothelial secretion and synthesis of collagen, elastin, and connective tissue proteases influence the neighboring smooth muscle cells from the media layer.
This continuous process of microstructural adjustment called remodeling allows the blood vessels to accommodate to physiological conditions through the thickening and thinning of the wall, while maintaining the integrity and resistance. This arterial wall stabilizing process, dependent on the WSS, requires a non destructed endothelial layer [58], and since there are no evidences that the wall weakening that leads to the formation of aneurysms relies only on excessive elevations of peak pressure [84], the vessel wall has to suffer some damaging changes, which are most likely generated by the local increased WSS. The excessive elevation of the stresses acting on the arterial wall, which may result from the different known risk factors, potentially leads to a fatigue-like remodeling process in the elastic layer, resulting in the focal enlargement of the arterial wall. The fact that intracranial arteries have a defective elastic layer and lack an external elastic lamina explains the increased number of aneurysms in these arteries when compared to extracranial arteries of similar size [80]. Moreover, the susceptibility to suffer this destructive remodeling process is magnified at the apices of the cerebral bifurcations because of their particular hemodynamics and these sites are the most propitious to undergo a permanent dilation due to their attenuated muscular layer.

Thus, abnormal hemodynamic stresses origin arterial wall defective biological responses whereas hypertensive blood pressure and genetic factors affecting the elastin/collagen metabolism appear to be an aggravation factor to the formation process of an aneurysm rather than a causal one [54, 86]. Hypertension is not essential but it induces significant changes in the blood-flow distribution, and consequently, in the WSS and mechanical stress distribution in the aneurysmal wall [89].

**Development**

The rate of expansion of an aneurysm is not gradual nor similar in all the cases. In fact, it has been reported that some aneurysms grow steadily whereas others grow quite promptly until they reach a certain size, slowing down the enlargement process afterwards [54]. The knowledge of the velocity at which the aneurysm develops is crucial for the clinical management of a patient with this potentially lethal condition and has lead to an intense investigation on the characterization of the specific variation patterns of the flow shear stresses acting on the endothelial cells, due to their possible influence on the enlargement rate.

According to the high-flow effects theory, the destabilization of the tissue remodeling in consequence of the high WSS plays a major important role in the aneurysmal growth. The high WSS causes the overexpression of NO and the subsequent reduction of the medial layer, related to the destruction of SMC in consequence of their apoptosis [48], and unbalance in the constant adaptation of the wall leads to the permanent weakening of the vessel wall. The blood flow pressure effect in the debilitated wall induces its distention and the abnormal blood shear stress field incites the aneurysm growth, with stretching of collagen and elastin fibers of the media and adventitia. On the other hand, the low-flow theory denotes that low flow within the aneurysm induces localized blood flow stagnation, which causes spatial disorganization, proliferation and apoptosis of endothelial
cells [9] and the dysfunction of the NO released by the action of the shear stress elevation [84]. The destabilization of NO promotes the clustering of RBC, as well as the accumulation and adhesion of both platelets and WBC in the intima, which becomes damaged and allows the infiltration of WBC and fibrin [84]. The vessel becomes progressively weaker as the inflammation degenerates the wall.

Some microscopical studies have shown that the wall becomes thinner in result of the decreased number of endothelial cells, the degenerative changes in the internal elastic lamina leading to its absence or severe fragmentation, and the thinning or disappearance of the tunica media [85]. Other microscopical studies have shown the cellular and fibrinous infiltrate in walls of unruptured aneurysms [20], promoting its importance in the aneurysm wall weakening process. Despite the described loss of the elastic lamina, a secondary elastic lamina can develop as the aneurysm enlarges [49].

Rupture

The rupture of an aneurysm cannot be interpreted merely as its mechanical enlargement until the forces produced by the wall structural components are supplanted by the wall tension resulting from the pulsatile internal blood flow. Indeed, the aneurysmal wall is even able to repair itself, under certain conditions. Like in the previous developmental stages, the hemodynamic stresses are thought to be highly correlated to the rupture phenomenon and despite the evidences suggesting that the bleeding probability is depend on the size, shape, location, presence of previous rupture from another aneurysm, and symptoms that it manifests, no current method can precisely determine if an aneurysm is prone to rupture. In some cases when the wall starts to succumb, a warning leak may occur and a small amount of blood is released. These signs anticipate the final rupture of an IA and the release of the subarachnoid hemorrhage.

In the unruptured aneurysm dome the wall tension is moderately low and uniformly distributed but when it ruptures, the wall tension is increased and concentrated around possibly existing bleb-like formations on the dome [7], which have been identified as risk factors for aneurysm rupture. In terms of flow patterns, unruptured aneurysms usually have large flow impingement regions and simple stable flows, whereas ruptured aneurysms are most likely to have more complex unstable flows, small impaction zones, higher inflow rates at the aneurysmal neck, and, consequently, higher maximum intra-aneurysmal WSS [15, 14]. Rupture occurs almost always at the bottom of the dome [20], and when a daughter aneurysm is present, the rupture frequently takes place there [95]. On the other hand, regions in IA with low velocity flow and low WSS are particularly prone to thrombus formation [74] due to the accumulation of platelets, which could either stop the bleeding, cause additional stress to the wall, or even allow recanalization of blood through small channels, favoring the aneurysm growth.

The rupture of the aneurysm wall does not necessarily occurs when it reaches a reasonable
size, actually it has been shown that small aneurysms can lead to devastating consequences and large aneurysms can be quite stable [53]. Moreover, giant aneurysms tend to promote intra-aneurysmal thrombosis, which could consequently reduce the rupture probability. Nevertheless, clinical studies suggest that aneurysm rupture is associated with significant changes in size [46] and many aneurysm geometric parameters, such as neck width, dome width, aneurysm shape, aspect ratio (height/neck width), and bottleneck factor (dome width/neck width), have been pointed out as predictors of rupture [53]. Aspect ratio is though to be one of the strongest factors, and aneurysms with a narrowed neck and a long depth, i.e. with high aspect ration, have a higher risk of rupture [53, 95, 99]. Aneurysms are specially dangerous when the aspect ratio is greater than 1.6, which is a common flow characteristic in the geometry of ruptured aneurysms [95]. This high aspect ratio aneurysms are prone to have localized, slowly rotating flow, or even blood stagnation, narrow inflow jets and smalls concentrated impaction zones in the dome of the aneurysm, which is thought to degenerate the arterial wall, leading to eventual rupture. A new parameter called size ratio (SR), defining the ratio between maximum aneurysm height and average parent vessel diameter, is thought to present an even stronger correlation with IA rupture. In fact, a retrospective analysis demonstrated that 77% of ruptured aneurysms showed an SR of more than 2, and 83% of unruptured aneurysms showed an SR of 2 or less [92], findings that were consistent with the results from a complementary computational study. The contact constraints between the aneurysm and the surrounding structures, such as bone or nerves, called the perianeurysmal environment, also dictate the evolution of the aneurysm and influences the possible aneurysm rupture [79]. Moreover, the perianeurysmal environment may have a protective effect for the aneurysm since it can locally decrease the stresses, stabilizing the aneurysm [83].
Chapter 3

The 1D mathematical model

A 1D model of the human artery was originally proposed by Euler in 1755 [23] and resulted in a basic system of two non-linear partial differential equations for the conservation of mass and momentum for an inviscid flow. Nevertheless, only in the 1970s the first solution of the linearized 1D model was provided. Since then, 1D models for blood flow have been widely applied [2, 27]. They provide a fair description of the flow motion in arteries and the mechanics of its interaction with the wall displacement, under a few simplifying assumptions. In this work we will adopt the approach proposed in [27], where the 1D model is obtained by means of a simplification of the 3D incompressible Navier-Stokes equations coupled with a structure model for the vessel wall. More precisely, the 1D model accounts for the evolution, in time and in the vessel axial direction, of the mean quantities: flow rate, mean pressure, and area. This model has been successfully applied in a previous study [65], in which it was implemented in MATLAB®. There, the evolution in time and in the axial coordinate of the mean quantities over the major the arteries of the human circulatory system was analyzed. Namely, it was studied the wave propagation of blood from the heart to the circle of Willis. Some pathological situations have also been tested and in all cases the model showed consistent results.

3.1 The equations

This basic model is deduced assuming that an artery is a cylindrical compliant tube, with axial symmetry and fixed cylinder axis. The velocity components orthogonal to the axial one are neglected and the wall displacements are only accounted for in the radial direction. Moreover, no body forces are considered and the pressure, $P(t, z)$, is assumed constant on each axial section. The area of each cross-section $S$ is given by $A(t, z) = \int_S d\sigma$ and its mean velocity is defined as $\bar{u} = A^{-1} \int_S u_z d\sigma$, where $u_z$ is the axial velocity. The area, $A$, the averaged pressure, $P$, the mean flux, $Q = A\bar{u}$, are the unknown variables to be determined.

Integrating the Navier-Stokes equations on a generic cross-section $S$, and after a few simplifi-
cations explored in [27], the reduced 1D form of the continuity and momentum equations for the flow in blood arteries is given, for all $t \in I$, by

\[
\begin{align*}
\frac{\partial A}{\partial t} + \frac{\partial Q}{\partial z} &= 0, \\
\frac{\partial Q}{\partial t} + \alpha \frac{\partial}{\partial z} \left( \frac{Q^2}{A} \right) + \frac{A}{\rho} \frac{\partial P}{\partial z} + K_r \left( \frac{Q}{A} \right) &= 0,
\end{align*}
\]

where $z$ is the axial direction, $L = b - a$ denotes the vessel length, $K_r$ is the friction parameter, $\alpha$ is the momentum flux correction coefficient, also known as Coriolis coefficient, defined by $\alpha = \frac{\int_{-\infty}^{\infty} u^2 dz}{\bar{A} \bar{u}^2}$, and $\rho$ is the fluid mass density. For a parabolic profile, the friction parameter has the relation $K_r = 8 \pi \mu$ [27], which is the value generally used in practice. The Coriolis coefficient is set to $\alpha = 1$, corresponding to a flat profile [27], in order to simplify the analysis. The density $\rho$ and the fluid dynamic viscosity $\mu$ are considered constant.

The previous system of two equations for the three unknown variables $A$, $Q$ and $P$ needs to be closed. In order to do that, a relation linking the area to the pressure should be provided, considering the vessel wall mechanics. There are a few ways to do this. Here we choose to use a pressure-area algebraic relation. In this hypothesis the inertial terms are neglected and there is a dominance of the elastic stresses in the circumferential direction- these are two realistic assumptions concerning the blood circulation analysis. A complete mechanical model for the structure of the vessel wall would lead to a much more complex problem, in which the displacement and the force applied by the fluid pressure would be connected through a differential equation.

Assuming that $P_{ext}$ is the external pressure exerted by the organs outside the vessel, the pressure may satisfy the general relation

\[
P(t, z) - P_{ext} = \psi(A(t, z); A_0(z), \beta(z)), \text{ with } \frac{\partial \psi}{\partial A} > 0 \text{ and } \psi(A_0; A_0, \beta) = 0.
\]

Thus, the pressure depends not only on the wall displacement, through the cross-sectional area $A$, but also on the reference cross-sectional area $A_0$ and on a set of parameters $\beta = (\beta_0, \beta_1, \ldots, \beta_p)$ describing the mechanical and physical properties of the vessel wall. The function $\psi$ must be defined for all $A > 0$, and $A_0 > 0$, and the range of variation of $\beta$ depends on the chosen mechanical model for the vessel wall. Furthermore, the external pressure is assumed to be equal to zero, as it is often done [27].

By exploiting the linear elastic law for the wall mechanics of a cylindrical vessel, and employing the relation $\eta = \frac{\sqrt{A} - \sqrt{A_0}}{\sqrt{\pi}}$, we obtain the simplest pressure-area relation possible, which will be the one used in this work:

\[
\psi(A; A_0, \beta_0) = \beta_0 \frac{\sqrt{A} - \sqrt{A_0}}{A_0},
\]

where $\beta$ is identified with the single parameter

\[
\beta_0 = \frac{\sqrt{\pi h_0 E}}{1 - \xi^2},
\]

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being \( h_0 \) the wall thickness, \( E \) the vessel wall Young, or elasticity, modulus and \( \xi \) the vessel wall Poisson ratio. \( \beta_0 \) is constant along \( z \) only when \( E \) or \( h_0 \) are constant, since both \( E \) and \( A_0 \) may be functions of \( z \).

Other pressure-area algebraic relations, or even more complex differential relations can be used [27].

By choosing relation (3.3), the pressure may be eliminated from the momentum equation and system (3.1) becomes hyperbolic, with two distinct eigenvalues (see [27, 65]) for the characteristic analysis of system (3.1):

\[
\lambda_{1,2} = \bar{u} \pm c_1, \tag{3.5}
\]

where \( c_1 = c_1(A; A_0; \beta) = \sqrt{\frac{2}{\rho A_0}} \frac{\partial c_1}{\partial A} \) is the speed of the propagation of waves along the artery. The eigenfunctions, or characteristic variables, corresponding to the eigenvalues \( \lambda_{1,2} \) are defined by

\[
W_{1,2} = \bar{u} \pm \int_{A_0}^{A} \frac{c_1(\tau)}{\tau} d\tau. \tag{3.6}
\]

In the case of relation (3.3), the parameter \( c_1 \) and the characteristic variables, have the following expressions

\[
c_1 = \sqrt{\frac{\beta}{2\rho A_0}} A^\frac{4}{4}, \tag{3.7}
\]

\[
W_{1,2} = \bar{u} \pm 4 \sqrt{\frac{\beta}{2\rho A_0}} \left( A_1^\frac{4}{4} - A_0^\frac{4}{4} \right). \tag{3.8}
\]

Notice that \( W_{1,2} = 0 \) for \( A = A_0 \) and \( Q = 0 \). By inverting the previous expression, the flow rate and the cross-section area may be written in terms of the characteristic variables as follows,

\[
Q = A \left( W_1/W_2 \right), \quad A = \left( \frac{2\rho A_0}{\beta_0} \right)^2 \left( \frac{W_1 - W_2}{4} + c_{1,0} \right)^4, \tag{3.9}
\]

where we define \( c_{1,0} = c_1(A_0) \).

Under physiological conditions, typical values of the flow velocity and mechanical characteristics of the vessel wall are such that \( c >> \bar{u} \), and consequently we have that \( \lambda_1 > 0 \) and \( \lambda_2 < 0 \), everywhere. This means that blood flows are under a sub critical regime, meaning that the flow velocity, \( Q \), is smaller than the wave velocity,\( c \). Furthermore, by manipulating system (3.1), we can write it in the conservative form,

\[
\frac{\partial U}{\partial z} + \frac{\partial F(U)}{\partial z} = B(U), \tag{3.10}
\]

where

\[
U = \begin{bmatrix} Q \\ A \end{bmatrix}, \quad F(U) = \begin{bmatrix} Q \\ \alpha \frac{Q^2}{4} + C_1 \end{bmatrix}, \tag{3.11}
\]

\[
B(U) = S(U) - \begin{bmatrix} 0 & \frac{\partial C_1}{\partial A_0} \frac{dA_0}{dz} + \frac{\partial C_1}{\partial \beta} \frac{d\beta}{dz} \\ \frac{\partial C_1}{\partial A_0} \frac{dA_0}{dz} + \frac{\partial C_1}{\partial \beta} \frac{d\beta}{dz} & 0 \end{bmatrix}, \quad S(U) = \begin{bmatrix} 0 \\ K_r \left( \frac{Q}{4} \right) + \frac{A}{\rho} \frac{\partial \psi}{\partial A_0} \frac{dA_0}{dz} + \frac{A}{\rho} \frac{\partial \psi}{\partial \beta} \frac{d\beta}{dz} \end{bmatrix}. \tag{3.12}
\]
The parameter $C_1$ is the primitive of $c_1^2$ with respect to $A$, so that $C_1(A; A_0, \beta) = \int_{A_0}^{A} c_1^2(\tau; A_0, \beta) d\tau$, and is given by the expression

$$C_1 = \frac{\beta}{3 \rho A_0} A^2,$$

(3.13) when using the relation (3.3). In this work, the variation of cross area at rest, $A_0$, and of the vessel wall physical parameters, $\beta$, in space, i.e., with $z$, will be neglected. This means that the tapering of the vessels as well as variations of the Young modulus in each vessel will not be taken into account. Using the $C_1$ expression (3.13), and neglecting the variation of $A_0$ and $\beta$ with $z$, the previous matrices simplify as follows,

$$F(U) = \left[ \begin{array}{c} \frac{Q}{\alpha} A + \frac{\beta}{3 \rho A_0} A^2 \end{array} \right], \quad B(U) = \left[ \begin{array}{c} 0 \\ -K_r \frac{Q}{\alpha} \end{array} \right].$$

(3.14)

### 3.2 Numerical discretization

Subsequently, the 1D model (3.10) is numerically discretized in time and space. We do that by means of a second order Taylor-Galerkin scheme. It consists in using the Lax Wendroff scheme to discretize in time, and in using the finite element method to obtain the space approximation. This discretization can be considered a finite element counterpart of the Lax-Wendroff scheme, which has a very good dispersion error characteristic and is easily implemented [27].

#### 3.2.1 Time discretization: The Lax-Wendroff scheme

The Lax-Wendroff scheme is obtained using a Taylor series of the solution $U = [Q, A]^T$ truncated at the second order. Let us divide the time interval into subintervals $I_n = (t^n, t^{n+1})$ for $n = 0, \cdots, M - 1$ such that $I = [0, T] = \bigcup_{n=0}^{N-1} I_n$, and where $t^n = n\Delta t$ with $\Delta t = t^{n+1} - t^n$ the time step (which will be considered to be constant). Denoting $U^{n+1} = U(t^{n+1})$, the Taylor expansion of $U$ up to the second order is

$$U^{n+1} \approx U^n + \Delta t \frac{\partial U^n}{\partial t} + \frac{\Delta t^2}{2} \frac{\partial^2 U^n}{\partial t^2}.$$

(3.15)

Noticing that from equation (3.10) we have

$$\frac{\partial U}{\partial t} = -B - \frac{\partial F}{\partial z},$$

(3.16)

and thus,

$$\frac{\partial^2 U}{\partial t^2} = B \left( \frac{\partial F}{\partial U} + \frac{\partial}{\partial z} \left( \frac{\partial F}{\partial z} \right) B + \frac{\partial}{\partial U} \left( \frac{\partial F}{\partial z} \right) \right).$$

(3.17)

Introducing the flux Jacobian $H = \frac{\partial F}{\partial U}$, and the source Jacobian $B_U = \frac{\partial B}{\partial U}$, we finally obtain the time semi-discrete expression...
\[ U^{n+1} = U^n - \Delta t \frac{\partial}{\partial z} \left[ F^n + \frac{\Delta t}{2} H^n B^n \right] + \Delta t \left[ B^n + \frac{\Delta t}{2} B_U^n B^n \right] - \frac{\Delta t^2}{2} \left[ B_U^n \frac{\partial F^n}{\partial z} - \frac{\partial}{\partial z} \left( H^n \frac{\partial F^n}{\partial z} \right) \right], \quad n = 0, \ldots, M - 1 \]  

(3.18)

where

\[ H(U) = \frac{\partial F}{\partial U} = \begin{bmatrix} 0 & 1 \\ -\alpha \frac{Q^2}{h} + \frac{\beta}{\pi \rho A} \Delta z & 2 \alpha \frac{Q}{h} \end{bmatrix}, \quad B_U = \frac{\partial B}{\partial U} = \begin{bmatrix} 0 & 0 \\ K_\rho \frac{Q}{h} & -K_\rho \frac{1}{h} \end{bmatrix}, \]  

(3.19)

and where \( U^0 \) is the initial condition.

**Remark 1** The Lax-Wendroff scheme is an explicit method, thus entailing a time step limitation in order to guarantee the stability. In this case, it can be shown that a CFL condition of

\[ CFL = \frac{\sqrt{3}}{3} \]  

(3.20)

must be verified, i.e., \( \Delta \leq \frac{\sqrt{3} h}{3} \), where \( h \) is the spacial spacing [27]. Typically, the time step will be very small (the order of \( 10^{-4} \) or \( 10^{-5} \)), to guarantee that this CFL condition is verified.

### 3.2.2 Space discretization: the finite element method

In order to apply the finite element method, the length \( L \) of the vessel is subdivided into \( N \) elements, each of \( h_i \) size, with \( i = 0, \ldots, N \). In the case of the 1D model, we will consider uniform meshes meaning that the elements size will be constant and equal to \( h \). We will also consider in this case linear (P1) finite elements. Let \( V_h(a, b) \) be the space of piecewise linear functions, in each element, continuous in the space interval \([a, b]\). We consider \( V_h(a, b) = [V^n_h(a, b)]^2 \), while \( V^n_h(a, b) = [V^n_0(a, b)]^2 \) is the subset of \( V_h \) with functions equal to zero in \( z=a \) and \( z=b \). The discrete continuity and momentum equations are rewritten by taking test functions of the form \( \psi_j = [\psi_j, 0]^T \) and \( \psi_j = [0, \psi_j]^T \), respectively. Thus, we need to find the solution \( U^{n+1}_h \in V_h(a, b) \), for \( n \geq 0 \), such that \( U_h(z, t) = \sum_{i=0}^{N} U_i(z, t) \psi_i(z, t) \), with \( \psi_i \) the linear finite element nodal function for each node. The final finite element solution for the area and flow rate is obtained by finding, for the interior nodes, \( U^{n+1}_h = \sum_{i=0}^{N} U^{n+1}_i(z) \psi_i(z) \), satisfying the following expression for the interior nodes, for each time step,

\[
\begin{align*}
(U^{n+1}_h, \psi_j) &= (U^n_h, \psi_j) + \Delta t (F^n + \frac{\Delta t}{2} H^n B^n, \frac{\partial \psi_j}{\partial z}) + \Delta t (B^n + \frac{\Delta t}{2} B^n U^n B^n, \psi_j) - \frac{\Delta t^2}{2} (H^n \frac{\partial F^n}{\partial z}, \frac{\partial \psi_j}{\partial z}) - \frac{\Delta t^2}{2} (B_U^n \frac{\partial F^n}{\partial z}, \psi_j), \quad j = 1, \ldots, N, \quad n = 0, \ldots, M - 1,
\end{align*}
\]  

(3.21)

being \( U^n_h \) a suitable approximation of the initial data and where \( (u, v) = \int_0^L u \cdot v \, dz \) is the inner product in \( V_h(a, b) \). In [65] can be found the detailed matricial expressions of (3.21) for the area and flow rate.
3.3 Initial, boundary, and compatibility conditions

Finally, the system must be supplemented with proper initial, $U_0^n$ and boundary conditions for the solution $U_{h}^{n+1}$, at the boundary points $z = a$ and $z = b$.

The initial conditions are the following ones,

$$A(0, z) = A^0, \quad Q(0, z) = Q^0, \quad \text{with } a \leq z < b. \quad (3.22)$$

In the present work, the initial conditions were taken $A^0(z) = A_0$, and $Q^0(z) = 0$. As mentioned in the characteristic analysis in Section 3.1, in physiological conditions blood flows under a sub-critical regime. This implies that the two eigenvalues of system (3.10) have opposite signs, meaning that there is one characteristic traveling forward, and another traveling backward (see Figure 3.1).

Because of this, we have to impose exactly one boundary condition at each extremity of the vessel, being the number of characteristics entering the domain through each boundary [72].

The boundary conditions are presented in their general form as functions of $A$ and $Q$,

$$\phi_1(A(t), Q(t)) = h_1(t), \text{ at } z = a, \quad \text{and } \phi_2(A(t), Q(t)) = h_2(t), \text{ at } z = b.$$  \hspace{1cm} (3.23)

However, the discretized model, requires two conditions for each boundary node to solve the system, corresponding to $Q_{h}^{n+1}$ and $A_{h}^{n+1}$, both at $z = a$ and $z = b$. Thus, we need to provide two additional conditions, which have to be compatible with the problem. These compatibility conditions can be obtained by means of the outgoing characteristic at each boundary [72]. The characteristic variables are constant along the characteristic lines. So, in order to find the value of the outgoing characteristic variable at the boundary point, we just need to find the foot of the characteristic line at the previous time step, in which the value of the outgoing characteristic will be the desired one. Since usually the foot of the characteristic is not a mesh nodal point, the value of the outgoing characteristic is found through interpolation [72].

Notice that, according to definitions (3.5) and (3.6), $W_1$ is the entering characteristic at $z = a$, thus being the outgoing characteristic $z = a$, and vice-versa for $W_2$ (see Figure 3.1).

Thus, the compatibility conditions are given by:

$$W_2(Q_{h}^{n+1}(a), A_{h}^{n+1}(a)) = W_2(Q_{h}^{n}(z_a), A_{h}^{n}(z_a)) - \Delta t K_r \frac{Q_{h}^{n}(z_a)}{(A_{h}^{n}(z_a))^2}, \quad \text{at } z = a, \quad (3.23)$$

and

$$W_1(Q_{h}^{n+1}(b), A_{h}^{n+1}(b)) = W_1(Q_{h}^{n}(z_b), A_{h}^{n}(z_b)) - \Delta t K_r \frac{Q_{h}^{n}(z_b)}{(A_{h}^{n}(z_b))^2}, \quad \text{at } z = b, \quad (3.24)$$
Figure 3.2: Schematic representation of the coupling (left), branching (middle), and merging between 1D models.

with the corresponding foot of the outgoing characteristic lines given by

\[ z_a = a - \Delta t \frac{Q_n^a(a)}{A_n^a(a)} + \sqrt{\frac{\beta}{2\rho A_0}} (A_n^a(a))^\frac{3}{4}, \]

(3.25)

\[ z_b = b - \Delta t \frac{Q_n^b(b)}{A_n^b(b)} - \sqrt{\frac{\beta}{2\rho A_0}} (A_n^b(b))^\frac{3}{4}. \]

(3.26)

The solution for the exterior nodes of the domain may then be achieved through the solutions of a 2x2 non linear system (for more details see \[65\]). Nevertheless, it is necessary to insure that the functions \( \phi_i, i = 1, 2 \) do not depend only on the exiting characteristic, i.e. \( \phi_1(A(t), Q(t)) \neq \phi(W_2(t)) \) and \( \phi_2(A(t), Q(t)) \neq \phi(W_1(t)) \). Typically, the inflow condition of \( \phi_1 \), at \( z = a \), is a flux \( (\phi_1(A,Q) = 0) \), or a total pressure \( (\phi_1(A,Q) = \bar{p} + \rho \frac{Q}{2}) \), while the outflow condition, at \( z = b \), is \( \phi_2(A,Q) = 0 \), with \( \phi_2 = W_2 \), meaning that there is no incoming characteristic at \( z = b \), corresponding to a completely absorbing boundary condition at the outflow point.

### 3.4 Coupling 1D models together

One of the greatest advantages of the 1D models is their low computational cost, hence their capacity of describing blood flow in a global way, like studies of the whole circle of Willis \[2\], or the 55 main arteries of the human vasculature \[27\]. They also allow to carry out studies of the pulse arterial propagation in several different scenarios, like the presence of stents, or the amputation of a member, and the global impact of changes in the artery properties.

The coupling between two or more vessels (to simulate for instance bifurcating or merging arteries) is done based on a domain decomposition technique \[72\], where the continuity of the fluxes and of the total pressure is prescribed at the coupling points. For instance, the coupling of two tubes at the interface point is carried out imposing \( Q_1 = Q_2 \), and \( P_1^i = P_2^i \), where \( Q_1 \) and \( Q_2 \) are the fluxes flowing from the outlet section of the first tube to the inlet section of the second tube, respectively, and \( P_1^i \) and \( P_2^i \) are the pressures from the outlet section of the first tube and the inlet section of the second tube, respectively (see Figure 3.2 a)). Again, these are two conditions for the two tubes, but each tube requires two conditions, at the interface point. So, two additional compatibility conditions are needed. As compatibility for the coupling interface we impose the
continuity of the characteristics [27, 65]:

\[
\begin{cases}
W_1^1(A^1, Q^1) - W_1^1 = 0, \\
W_2^2(A^2, Q^2) - W_2^2 = 0,
\end{cases}
\] (3.27)

where \(W_1^1\) and \(W_2^2\) are the values of the outgoing characteristic variables \(W_1\) and \(W_2\), at the interface point, respectively, and \(W_1^1(A^1, Q^1)\) and \(W_2^2(A^2, Q^2)\) denote the relations (3.23) and (3.24) computed at the interface. Taking into account the pressure-area algebraic relation (3.3), this leads to the final non-linear system for the coupling, to be solved using the Newton’s method,

\[
\begin{cases}
Q_2 - Q_1 = 0, \\
\frac{Q_1}{A_1} + 4\sqrt{\frac{\beta_1}{\rho_1 A_{o_1}}} (A_1^1 - A_{o_1}^1) - W_1^1 = 0, \\
\frac{Q_2}{A_2} - 4\sqrt{\frac{\beta_2}{\rho_2 A_{o_2}}} (A_2^1 - A_{o_2}^1) - W_2^1 = 0.
\end{cases}
\] (3.28)

The branching case follows the same principals enunciated in the coupling case, such that at the interface we need to impose the continuity of fluxes and total pressure, through \(Q_1 = Q_2 + Q_3\) and \(P_{t1} = P_{t2} = P_{t3}\), where \(Q_1, Q_2\) and \(Q_3\) are the fluxes at the interface point of tube 1, tube 2 and tube 3, respectively, while \(P_{t1}, P_{t2}\) and \(P_{t3}\) are the respective total pressures (see Figure 3.2 b)).

Again, in order to obtain all the unknown parameters at the interface we need three additional compatibility conditions, which will consist in imposing the continuity of the characteristics, as for the coupling case [27, 65].

Similarly, the merging case interface conditions are \(Q_1 + Q_2 = Q_3\), and \(P_{t1} = P_{t2} = P_{t3}\) (see Figure 3.2 c)), and the compatibility conditions are once more the continuity of the computed, and extrapolated characteristics [27, 65].

### 3.5 Numerical results

As mentioned before the 1D hyperbolic model was tested under physiological and pathological conditions. In all tests a sinusoidal flux was given as an inflow, describing the periodic action of the heart, and an absorbing boundary condition, \(W_2 = 0\) (3.29) was prescribed at the outflow section.

Preliminary simulations were performed involving simple cases, such as the segmentation of the left common carotid artery into two halves, the bifurcation of the left common carotid artery into the left internal carotid artery and the left external carotid artery, and the merging of the two vertebral arteries into the basilar artery. Since these tests validated the proper implementation of the model and the most common couplings [65], more complex simulations afterwards were carried out.
In order to reach an absolute physiological condition we imposed an inflow wave with characteristics as similar as possible to the real blood flow wave leaving the left ventricle, and used a time domain corresponding to a heartbeat. Thus, a sine function with a maximum value of $Q = 485 \text{ ml/s}$, taken from [2], was prescribed to model the systolic period (0.3 s). The diastolic period (0.45 s) was simulated by imposing the inflow value to be zero. Besides that, the arteries described in the simulations had realistic parameters taken from [27].

The coupling of eighteen major arteries of the human vascular system is displayed in Figure 3.3. There we can see that the difference between the magnitudes of the blood flow among the arteries is noticeable. The flow rate has its peak value when it enters the aorta, with almost 500 ml/s, but when it reaches the right cerebral posterior artery the maximum value never even reaches 1 ml/s. There is also a substantial difference when the aorta branches into the brachiocephalic and the aortic arch, which would be expected due to the radial difference between the arteries, $r_{aorta} = 1.38 \text{ cm}$ and $r_{brachiocephalic} = 0.62 \text{ cm}$. This difference is also illustrated in Figure 3.4. In this case we demonstrate that even though the flux in the aortic arch is much more significant than the one in the brachiocephalic artery, the pressure values suffer a minor variation, which is related to the fact that we imposed the mean total pressure continuity across the bifurcation.

The comparison of the wave propagation across the left common carotid artery bifurcation, applying the inflow condition at the beginning of the aorta and directly at the beginning of the carotid artery is depicted in Figure 3.5. The inflow flux is prescribed directly in the carotid artery has a maximum value of $Q = 14 \text{ ml/s}$. The overall situation is analogous, with a minor discrepancy
Figure 3.5: Flow rate at the branching of the left common carotid, imposing the inflow flux at the beginning of the aorta artery (left), and at the beginning of the left common carotid artery (right).

Figure 3.6: Effect on the flow rate of the introduction of a stent in the middle of an artery in the maximum values, due to the little dissipation across the arteries inherent to the model.

In order to test a pathological situation, the presence of a stent in an artery was evaluated, coupling three segments of one vessel, such that the distal and proximal segments have the same physical characteristics, and the middle one has a higher Young modulus, \( E \), simulating the stiffness of the device. Three different values for the elasticity parameter where considered, \( E = 100.10^6 \text{ g/cms}^2 \), \( 1000.10^6 \text{ g/cms}^2 \), and \( 10000.10^6 \text{ g/cms}^2 \). The results for the flow rate are displayed in Figure 3.6. The remaining parts of the artery have a Young modulus of \( E = 10.10^6 \text{ g/cms}^2 \). The introduction of the stent resulted in an evident change on the wave propagation across the artery, giving rise to reflecting waves at the upstream part of the vessel, before the stent. Also, with the increment of the Young modulus, the compliance of the stent segment decreases giving rise to a flattening and a floating effect on the blood flux.
Chapter 4

The 3D mathematical model

This chapter focuses on the mathematical and numerical simulations of blood flow in vascular geometries, in particular in aneurysmal arteries. We start by revising the current relevant methodologies used in the study of the development of aneurysms, and describe the adopted procedure for the image processing scheme. The 3D Navier-Stokes equations, as well as the generalized Newtonian fluid equations, are derived to model blood flow. Thus, the initial and boundary conditions are addressed, including the description of non standard boundary conditions for the artificial sections, such as the coupling between the 3D and the 1D models. Afterwards, we provide the formulation for the numerical discretization both in space and time of the 3D problem. Finally, several hemodynamic indicators, derived from the velocity field, are introduced.

4.1 State of the art

IA have been studied for a long time, and the first descriptions of these lesions are contained in ancient Egyptian, Greek, and Arabic literature [61]. During the last three decades, detection of unruptured IA and treatment of ruptured aneurysms has increased considerably because of the advances in diagnostic techniques, and the more active treatment policy. Though it is still virtually impossible to prevent an IA from forming, the continuous research in this subject is leading to substantial improvements in the outcome of patients with aneurysms.

The different aspects of IA are studied under investigations that can range from the analysis of the influence of genetics [68], cellular mechanisms [48], and hemodynamics [9], to the examination and improvement of the clinical practice [61].

The current studies resort to a variety of methods, like animal models, in vitro vascular phantoms, and computational simulations. The various methodologies approximate as much as possible the real aneurysmal environment and may be successfully used to substantiate theories concerning not only the pathologic formation, but also the consequences on the blood field and possible outcome of a surgical intervention.
Animal models have been created to estimate flow patterns under different flow conditions [3, 25, 48, 60, 78]. However, the unpredictable nature of aneurysms and the variety of the anatomy of diseased human arteries, make the in vivo studies fairly problematic. Besides that, aneurysms do not naturally occur in non-humans. They have to be artificially induced in such studies, so that the hemodynamic features are as close as possible to the normal range of human aneurysms.

In vitro models may use either mathematically idealized geometry models [8], or casts of post-mortem specimens [41]. These models are able to provide detailed measurement of hemodynamic variables, but they are unsatisfactory when it comes to extrapolate those results to directly predict the particular intra-aneurysmal flow pattern of a real clinical case [84]. In fact, in the case of the cadaveric specimens, despite providing patient specific information, they only enable a retrospective analysis. The obstacle when using these methods to predict the aneurysmal behavior relies in the fact that blood flow inside an aneurysm may display a wide range of patterns, strongly depending not only on the specific geometry of the aneurysm, but also the connected vessels [17]. A study concerning the carotid artery bifurcation [62], has revealed obvious differences not only in the vascular physiognomy, but also in the hemodynamic patterns, such as flow rate and WSS, between two realistic models and between the realistic models and an idealized one.

Until recently, all vascular computational studies were based on idealized, generic models of vascular anatomy, or approximations of in vivo image based geometries [11, 93]. Nevertheless, they failed to simulate the real state of a specific patient. Nowadays, with the advances of medical image acquisition and scientific computing, patient specific computational models are becoming the favorite approach for many researchers, including medical doctors, to study hemodynamic factors in aneurysms. Unlike idealized models, they are not useful to perform systematic parametric studies [102], but they provide valuable tools to reproduce comparative studies. Also, they allow to obtain realistic patient-specific flow patterns, constituting a reliable tool for the comprehension and prediction of aneurysm formation and rupture. The realistic geometries are constructed using data acquired from imagiology techniques such as MRA [9, 44, 45, 62], 3DRA [13, 15, 17, 63, 92] and CTA [5, 29]. The patient-specific based vascular modeling was first introduced in the end of the 1990s [87], and since then the evolution in the realistic vascular computational modeling field has been remarkable. The most sophisticated computational models are able to reproduce small portions of the human cardiovascular system, using fully coupled fluid-structure interaction patient-specific features [7, 64, 90]. Realistic computational based models have the ability to reflect the heterogeneity of the cardiovascular system, and to thoroughly study particular aspects of the aneurysm hemodynamics in a non invasive way by readily and inexpensively changing the desired conditions of the problem. The use of patient-specific computational geometries enables an accurate and detailed estimation of the flow field and WSS, among others, which, in turn, consents the examination of anatomic and physiologic differences between different models. These informations contribute to gain a better understanding of the genesis and development of aneurysms, and might
be applied for diagnostic and surgical planning purposes.  

Current patient-specific image-based computational models are able to realistically reproduce the major intra-aneurysmal flow structures displayed in conventional angiography [18]. However, a few studies have shown their association with modeling uncertainties, concerning not only variations in the mathematical model but also in the geometrical acquisition and reconstruction [29, 30, 31, 55]. Also, these models still cannot be applied to populational studies. Nevertheless, as imaging techniques progressively provide images with higher resolution, the number of experimental and numerical tests using realistic geometries is becoming more pronounced. Another major problem relies on the in vivo validation of the computational results, because of the practical difficulties associated with the reliable measurement of hemodynamic quantities, such as WSS, and the requirement of complementary imagiologic studies [16]. Nonetheless, Computational Fluid Dynamics (CFD) remains the easiest way of obtaining quantitative and qualitative values of hemodynamic indicators, such as WSS, which are known to be strongly related to arterial pathologies [84]. Even image-based CFD models, that use some simplifications, are able to provide profitable clinical data [62].

Computational simulations of the human circulatory system carried out along the past years were performed under a wide range of considerations, using different definitions for the rheology and geometry. Depending on the level of detail and specifications required, the model can consist of many simplifications or can be very complex and detailed. 3D models are the most accurate ones. They apply the 3D Navier-Stokes or more complex fluid equations, coupled or not to a model for the structure of the arterial wall, to provide thorough information about the hemodynamic field. Ideally, the cardiovascular system would be completely modeled using 3D realistic geometries, but this is still not computational feasible, nor such a wide 3D patient-specific geometry can be acquired. Often, detailed information is necessary only in specific areas of interest. Thus, one way to reduce the heaviness of the problem is to use 3D geometries only in the domain of interest, and account for the rest of the circulatory system by resorting to reduced, 0D or 1D, formulations [27, 64, 69, 82]. In particular, as described in Chapter 3, 1D models interpret the circulatory system as cylindrical structures and resort to a 1D coupled system of nonlinear partial differential equations to provide transversally averaged values for the pressure, cross sectional area and flow rate at each time step [27]. The 0D or lumped parameter models are the simplest ones. They resort to electric circuits to represent the blood flow in compartments such as the heart, the venous bed or the pulmonary circulation [97]. The strategy of coupling the different dimensional mathematical models, 3D, 1D and 0D, each with a particular level of detail, to model the whole, or just a part of the cardiovascular system, is the so called geometrical multiscale modeling [27]. This approach has been broadly used, although only few works can be found in the context of coupling reduced models with 3D non-Newtonian ones [82, 43].

It is well established that the specifications of the mathematical models to describe the blood
flow have an impact in the achievement of accurate numerical simulations. A patient-specific model should take into account not only a realistic geometry, but also the vessel wall motion, the blood rheology, and realistic inflow and outflow boundary conditions. However, in some situations the blood flow complexity is reasonably approximated by models that make use of simplifying assumptions, such as considering blood as a Newtonian fluid, or assuming steady-state blood flow. These reductions translate into a significant diminution of the computational effort required for the numerical simulations, and have been demonstrated to have a small effect in the variation of the flow patterns compared with changes in the reconstructed geometries [14, 15, 30, 55]. Still, not all studies confirm the primary influence of the geometrical uncertainties over the rheological models [29]. For instance in [66], the effect of non-Newtonian rheology is pointed out as being explicitly based on the particular flow rate and geometry under study. The geometry and rheology of the aneurysmal environment is quite intricate, and in order to decrease the variability and uncertainty inherent to these simulations, one should consider using complex constitutive models. Since the earliest studies that relate the shear-thinning nature of blood to the aggregation of RBC [19], and the blood behavior to viscoelastic fluids [88], many investigations were performed using non-Newtonian assumptions, like shear-thinning, viscoelastic [4], and yield stress models [16].

In the computational simulations, the resolution of the numerical problem is only achieved if proper boundary conditions are prescribed at the boundaries of the computational domain. In many cases the vessel is approximated by a fixed domain [17, 18]. This is a simplification that does not properly account for the complexity of the wall. In fact, studies reveal that arterial walls are nonlinear, anisotropic, viscoelastic, and heterogeneous materials [40]. Moreover, the pulse waves that characterize the blood flow across the arterial tree are entirely due to the mechanical interaction between the blood flow and the compliant vessel wall. The close relationship between the elastic properties of the arteries, and blood pulse is noticeable when a vascular prosthesis or stent is introduced in an artery, creating wave reflection in that area [65], as it has been also shown in the numerical results of Chapter 3. The modeling accounts for the wall compliance and is increasingly common in numerical models, by coupling the fluid equations with a constitutive model for the structure dynamics of the vessel wall [7, 26, 64, 90]. However, coupling the fluid and structure systems together is computationally very costly, and requires accurate measured data for the distension of the vascular structure, distribution of wall thickness and wall elasticity. This is one of the reasons why, in the geometrical multiscale modeling, the FSI problem is often only considered in the reduced models, and the 3D complex model uses a rigid structure that only includes the fluid characteristics. The computational costs inherent to 3D FSI simulations are another reason. Fixed geometry models are a reasonable approximation when the study is focused in the main features of the blood flow. Besides their simplicity, studies [21, 90] have shown that this type of models reproduce the same estimations as compliant models for a number of hemodynamic characteristics, such as the location and size of the flow impact zones, only with
some variations in the distribution of WSS. Indeed, many authors use rigid models and claim this is a fair approximation for localized studies [5, 14, 92]. Moreover, regarding the study at hand, the wall of an IA is mostly collagen, with a great loss of elastin, so it has little compliance and is approximately twice as stiff as the wall of a normal compliant vessel. Generally, the flowing blood only causes a minor movement of the vascular wall, when compared with the vessel diameter, and these radius changes become progressively smaller in the peripheral vessels. Nevertheless, there is still not a conclusive study about the importance of the rigid vessel wall approximation [15].

4.2 Image processing

In order to obtain the most realistic results possible, the geometries used in the numerical simulations were acquired using medical imaging techniques in human patients. The use of patient specific geometries is of great importance since the aneurysm hemodynamics depends heavily on its shape. Common medical imaging techniques are now able to provide high quality comprehensive 3D representations of the human anatomy. After the acquisition of the data coming from the imaging devise, it is necessary to translate it into viable information for computer models construction. The choice of different reconstruction procedures also contribute to the appearance of discrepancies in the numerical solutions of the flow field, in result of variances in the computed geometry [29]. The procedures involved in transforming the medical image into the virtual 3D arterial geometry for numerical simulations are image segmentation, 3D surface extraction, and surface smoothing. In this work, we will follow the approach advocated in [30].

4.2.1 Image segmentation

Factors like partial volume effects, movement of the patient, random noise, and complex flow patterns, are the main contributors to the heterogeneity of the acquired image. All these phenomena lead to a gray scaled image, instead of a plain white and black image.

The segmentation process consists in identifying volumes of interest through the pixelization, and posterior interpolation of the contours of the regions with similar intensity in each planar image along the stack [70]. It allows to delineate the foreground from the background, turning the gray scaled image into a binary one. In this work, after truncating the parent vessel at a certain location, we resort to the maximum intensity projection to do the segmentation. Afterwards, the Perona-Malik anisotropic diffusion method (see [30]) is applied to filter even more the selected region. At last, as a clustering technique, a constant threshold value $T$ of the pixel intensity is applied to define similar intensities, and consequently, to fully distinguish between the foreground and the background.
4.2.2 Surface extraction

After the segmentation, it is necessary to reconstruct the virtual model, which is carried out through interpolation. The interpolation of the medical data contours is a crucial step, since its insufficient resolution does not allow for the direct extraction of the surface of interest. Here, an implicit function formulation, described in [31], is used with cubic radial basis function interpolation, better known as Kriging. It permits a finer sampling of the image. The initial surface triangulation is obtained using linear interpolation and a marching tetrahedra algorithm for extracting the 3D surface (see [30]).

4.2.3 Surface smoothing

Due to the noise inherent to the imaging techniques, as well as geometrical inaccuracies created during surface triangulation, a surface smoothing is required to eliminate those unrealistic features, and to reverse the surface as close as possible to the real medical image.

Here, the reconstructed image is uniformly smoothed by using the iterative bi-Laplacian method (see [30]). Let \( L_i = \sum_{j=1}^{m_i} w_{ij} (v_j - v_i) \) be the discrete Laplacian at a given vertex \( v_i \), where \( v_i = (x_i, y_i, z_i) \), \( i = i, \ldots, n \), are the \( n \) vertices that constitute the triangular mesh, and \( v_j, j = 1, \ldots, m_i \), are the vertices neighbouring the vertex \( v_i \) in the triangulation. The weights \( w_{ij} = 1/m_i \), with \( m_i \) the number of neighbours of the vertex \( v_i \), are constrained such that \( \sum_{j=1}^{m_i} w_{ij} = 1 \). Then, the bi-Laplacian iterative scheme smooths the surface in following two sub-steps:

\[
\begin{align*}
    v_i^{k+1/2} &= v_i^k + \lambda L_i^k, \\
    v_i^{k+1} &= v_i^{k+1/2} - \lambda L_i^{k+1/2},
\end{align*}
\]

in which \( k \) is the iteration number. In this work we set \( \lambda = 0.6 \) [30]. If the bi-Laplacian method is iterated too many times, the surface may become idealized and loose some of its realistic small-scale geometrical features. Indeed, though further investigations are required to realize the true effects and proportions of the elimination of these small-scale features from the geometry, in [30] intensive smoothing shows evident reduction of the complex patterns of WSS.

4.3 The fluid equations

The most appropriate set of equations to simulate the blood flow in the vascular tree is the time-dependent fluid equations expressing the balance of linear momentum and the solenoidality of the velocity field, derived from the basic physical principles of conservation of the momentum and mass, respectively. It describes blood flow in vessels as an homogeneous, unsteady, and incompressible fluid, in terms of the velocity and the pressure fields.

Being \( \Omega \subset \mathbb{R}^3 \) an open bounded domain, the system of equations representing such fluid is
given by:
\[
\begin{aligned}
\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} - \frac{1}{\rho} \text{div} \sigma &= f^b, \\
\text{div} \mathbf{u} &= 0,
\end{aligned}
\]

where \( f^b \) represents the body forces, \( \rho \) is the fluid constant density, and the Cauchy stress tensor \( \sigma \) depends on the fluid velocity \( \mathbf{u} \) and may be generally represented as the sum of spherical and deviatoric parts [76]:

\[
\sigma(\mathbf{u}) = pI + \tau(\mathbf{u}).
\]

In the spherical part, \( p \) is the Lagrange multiplier connected to the incompressibility constraint, which defines the mechanical pressure for incompressible fluids, identified by \( p = p(\mathbf{x}, t) \), and \( I \) is the unitary tensor.

Definition (4.4) holds the assumption that the stress tensor only depends on the velocity gradient and the fluid mass density at a particular time, and is independent upon the previous history of the fluid deformations.

The deviatoric tensor \( \tau(\mathbf{u}) = \tau(\mu, D(\mathbf{u})) \) is also called the extra stress tensor, with \( D(\mathbf{u}) \) denoting the symmetric part of the velocity gradient (also called rate of deformation tensor, or strain rate tensor):

\[
D(\mathbf{u}) = \frac{1}{2}(\nabla \mathbf{u} + (\nabla \mathbf{u})^T).
\]

Using this notation, the balance of linear momentum can be rewritten as

\[
\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} + \frac{1}{\rho} \nabla p - \frac{1}{\rho} \text{div} \tau(\mathbf{u}) = f^b, \quad \text{in } \Omega, \forall t > 0,
\]

with \( \mathbf{u} \) and \( p \) the unknown fluid velocity and pressure, respectively.

A generic representation of \( \Omega \) is illustrated in Figure 4.1, with the boundary \( \Gamma_w \) denoting the physical artery wall, and \( \Gamma_i, i = 1, 2, 3 \), indicating the artificial boundaries. The latter are a set of non-natural boundaries, that delineate the computational domain, and define the interfaces between the truncated portion of the artery of interest, and the remaining circulatory system. The upstream sections are the ones closer to the heart, often called inflow sections, while the downstream are the ones closer to the systemic circulation, frequently named outflow sections.

### 4.3.1 Newtonian fluids

The definition of a constitutive relation for \( \tau(\mathbf{u}) \) is what models the rheological properties of the fluid. Under the assumption of incompressible Newtonian fluids, the Cauchy stress tensor is a linear isotropic function of the components of the velocity gradient, and is characterized by

\[
\sigma(\mathbf{u}, p) = -pI + 2\mu D(\mathbf{u}),
\]

with \( \mu \) the dynamic viscosity of the fluid.
where the viscosity \( \mu > 0 \) is constant, and \( 2\mu \mathbf{D}(\mathbf{u}) \) is the representation of \( \tau(\mathbf{u}) \).

Applying the previous constitutive relation to equation (4.6), and neglecting the external body forces, the Navier-Stokes equations for incompressible Newtonian fluids are then defined by

\[
\begin{cases}
\rho \frac{\partial \mathbf{u}}{\partial t} + \rho \mathbf{u} \cdot \nabla \mathbf{u} + \nabla p - \text{div}(2\mu \mathbf{D}(\mathbf{u})) = 0, \\
\text{div} \mathbf{u} = 0.
\end{cases}
\]

(4.8)

4.3.2 Generalized Newtonian fluids

The most general form of (4.4), for isotropic symmetric tensor functions, under the invariance requirements [76], is given by

\[
\sigma = \phi_0 \mathbf{I} + \phi_1 \mathbf{D} + \phi_2 \mathbf{D}^2,
\]

(4.9)

where \( \phi_0, \phi_1, \) and \( \phi_2 \) depend on the density \( \rho \), and on the three principal invariants of \( \mathbf{D} \), \( \mathbf{I}_D = \text{tr}(\mathbf{D}) \), \( \mathbf{I}_{ID} = ((\text{tr}(\mathbf{D}))^2 - \text{tr}(\mathbf{D}^2))/2 \) and \( \mathbf{III}_D = \text{det}(\mathbf{D}) \). For isochoric motions, we have \( \mathbf{I}_D = 0 \), and \( \mathbf{II}_D = -1/2\text{tr}(\mathbf{D}^2) \). The absorption of the function \( \phi_0 \) into the Lagrange multiplier leads to the following stress tensor definition for incompressible Reiner-Rivlin fluids

\[
\sigma = \alpha \mathbf{I} + \phi_1 \mathbf{D} + \phi_2 \mathbf{D}^2.
\]

(4.10)

By setting \( \phi_2 = 0 \), and \( \phi_1 \) constant, we obtain the relation for a Newtonian fluid, governed by the Navier-Stokes equations. Since a Reiner-Rivlin fluid, with \( \phi_2 \neq 0 \), does not correspond to any existent fluid under simple shear, the constitutive relation (4.10) is often used in the reduced general form, with \( \phi_2 = 0 \), and respecting the invariance requirements and the behavior of real fluids [76]:

\[
\sigma = -p \mathbf{I} + 2\mu(\mathbf{II}_D, \mathbf{III}_D) \mathbf{D},
\]

(4.11)

where \( \mu(\mathbf{II}_D, \mathbf{III}_D) \) indicates that the viscosity depends on the second and third invariants of \( \mathbf{D} \).

As \( \mathbf{III}_D = 0 \) in simple shear, as well as in other viscometric flows, it is reasonable to neglect the dependence of \( \mu \) on \( \mathbf{III}_D \). On the other hand, since \( \mathbf{II}_D \) is negative for isochoric motions, we introduce in the equation the positive metrics of the rate of deformation, \( \dot{\gamma} \equiv \sqrt{2\text{tr}(\mathbf{D}^2)} = \sqrt{-4\mathbf{II}_D} \),
also known as the shear rate, thus obtaining:

\[ \sigma = -pI + 2\mu(\dot{\gamma})D. \] (4.12)

This equation defines the constitutive equation for the generalized Newtonian fluids, being the equations of motion for these fluids of the form

\[ \begin{cases} \rho \frac{\partial u}{\partial t} + \rho u \cdot \nabla u + \nabla p - \text{div}(2\mu(\dot{\gamma})D(u)) = 0, & \text{in } \Omega, \forall t > 0 \\ \text{div}u = 0. & \end{cases} \] (4.13)

A variety of non-Newtonian viscosity functions \( \mu(\dot{\gamma}) \) can be used, only differing on the functional dependence of the viscosity on the shear rate. To model blood flow, we are interested in bounded viscosity functions of the form

\[ \mu(\dot{\gamma}) = \mu_\infty + (\mu_0 - \mu_\infty)F(\dot{\gamma}), \] (4.14)

where the constants \( \mu_0 \) and \( \mu_\infty \) are the asymptotic viscosities at zero, \( \mu_0 = \lim_{\dot{\gamma} \to 0} \mu(\dot{\gamma}) \), and infinity, \( \mu_\infty = \lim_{\dot{\gamma} \to \infty} \mu(\dot{\gamma}) \), shear rate, and \( F(\dot{\gamma}) \) is a continuous and monotonic function such that

\[ \lim_{\dot{\gamma} \to 0} F(\dot{\gamma}) = 0, \quad \lim_{\dot{\gamma} \to \infty} F(\dot{\gamma}) = 1. \] (4.15)

Thus, the definitions of function \( F(\dot{\gamma}) \) characterizes the generalized Newtonian model. In particular, we are interested in shear-thinning fluids, which is the main non-Newtonian characteristic exhibited by blood [77]. It means that the apparent viscosity decreases with increasing shear rates. This shear-thinning behavior of blood flows is mainly due to the RBC [77]. Table 4.1 was taken from [29] and shows several possible viscosity functions.

The values of the parameters there displayed, corresponding to an hematocrit \( H_t = 40\% \), and temperature \( T = 37C \) were obtained from in vitro blood experimental data. To set the parameters values, a non-linear least squares fitting was applied [29, 43]. Notice that, with such parameters, the viscosity functions in Table 4.1 are all shear-thinning.

Other generalized Newtonian models for blood viscosity, like the power-law and the Carreau-Yasuda model, have been frequently used to describe blood flow (for further detail on these models, see [77]). In this work, we follow [29], and use the Carreau viscosity function, with the parameters defined in Table 4.1.

### 4.4 Similarity parameters

In every simulation of the cardiovascular system, the main goal is to reproduce as close as possible not only the geometry, but also the vast flow characteristics. Thus, in order to ensure the dynamic similarity between the considered model and the real human system, a number of dimensionless parameters, known as the similarity parameters, are studied. Two important similarity parameters are the Reynolds and Womersley numbers.
### Table 4.1: Some generalized Newtonian models for blood viscosity and corresponding constants.

<table>
<thead>
<tr>
<th>Model</th>
<th>Viscosity Model</th>
<th>Model constants for blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carreau</td>
<td>( F(\dot{\gamma}) = (1 + (\lambda \dot{\gamma})^2)^{(n-1)/2} )</td>
<td>( \mu_0 = 0.456, \mu_\infty = 0.032 ) ( \lambda = 10.03s, n = 0.344 )</td>
</tr>
<tr>
<td>Cross</td>
<td>( F(\dot{\gamma}) = (1 + (\lambda \dot{\gamma})^n)^{-1} )</td>
<td>( \mu_0 = 0.618, \mu_\infty = 0.034 ) ( \lambda = 7.683s, n = 0.810 )</td>
</tr>
<tr>
<td>Yeleswarapu</td>
<td>( F(\dot{\gamma}) = \frac{1 + \log(1 + \lambda \dot{\gamma})}{1 + \lambda \dot{\gamma}} )</td>
<td>( \mu_0 = 1.10, \mu_\infty = 0.035 ) ( \lambda = 45.23s )</td>
</tr>
<tr>
<td>Oldroyd</td>
<td>( \mu(\dot{\gamma}) = \frac{\mu_0 + (1 + (\lambda_1 \dot{\gamma})^2)(\lambda_2 \dot{\gamma})}{1 + (\lambda_2 \dot{\gamma})^2} )</td>
<td>( \mu_0 = 0.426, \mu_\infty = \mu_0 \lambda_1^2 \lambda_2^{-2} ) ( \lambda_1 = 1.09s, \lambda_2 = 3.349s )</td>
</tr>
</tbody>
</table>

Figure 4.2: Apparent viscosity as a function of shear rate for whole blood at Ht = 40 %, T = 37\(^\circ\), obtained using a Contraves LS30 for low shear rates (\( \dot{\gamma} \leq 128s^{-1} \)) and a CMSM (\( \dot{\gamma} \geq 300s^{-1} \)).

#### 4.4.1 Reynolds number

The Reynolds number is used to predict transitions from laminar to turbulent flow. This is a similarity parameter for viscosity, and expresses the ratio of steady inertial forces to viscous forces within the fluid. The expression of the Reynolds number can be mathematically obtained from the dimensionless form of the incompressible fluid equations, in which each term is independent on the exact measurements of flow. Under the hypothesis that \( \mu \) is constant and the fluid is incompressible, and introducing the relation 2div(D(u)) = Δu + \nabla(div(u)), the momentum equation may be simplified as follows,

\[
\rho \frac{\partial \mathbf{u}}{\partial t} + \rho \mathbf{u} \nabla \mathbf{u} + \nabla p - \mu \Delta \mathbf{u} = 0, \quad \text{in } \Omega, \quad \forall t. \tag{4.16}
\]

We now introduce the dimensionless variables:

\[
\mathbf{u}' = \frac{\mathbf{u}}{U}, \quad t' = \frac{tU}{l}, \quad x' = \frac{x}{l}, \quad p' = \frac{p}{\rho U^2}, \tag{4.17}
\]
where $l$ defines a spatial scale, that in the blood flow case is considered the vessel diameter, and $U$ defines the average blood velocity, and the time and space derivatives, as function of the dimensionless variables $t'$ and $x'$,

$$\frac{\partial u'}{\partial t'} = U^2 \frac{\partial u'}{\partial t'}, \quad \nabla p = U^2 l \nabla p', \quad \Delta u = \frac{U}{T^2} \nabla u', \quad u \cdot \nabla u = \frac{U^2}{l^2} u' \cdot \nabla u'. \quad (4.18)$$

After a few algebraic calculations, the dimensionless momentum equation becomes [69],

$$\frac{\partial u'}{\partial t'} + u' \cdot \nabla u' = -\nabla p' + \frac{\mu}{U l} \Delta u', \quad (4.19)$$

in which the term $\frac{\mu}{U l}$ can be identified as the inverse of the Reynolds number, i.e.

$$Re = \frac{U l}{\mu}, \quad (4.20)$$

and

$$\frac{\partial u'}{\partial t'} + u' \cdot \nabla u' = -\nabla p' + \frac{1}{Re} \Delta u'. \quad (4.21)$$

If two arbitrary flows have two Reynolds numbers, $Re_1$ and $Re_2$, such that $Re_1 = Re_2$, and two spatial scales $l_1$ and $l_2$, such that they satisfy the relation $l_1 = \lambda l_2$, or $\frac{l_1}{\mu} = \frac{l_2}{\mu}^2$, $\lambda \in \mathbb{R}$, then they are considered dynamically and geometrically similar. A small Reynolds number ($Re << 1$) reflects the supremacy of viscous forces over inertial ones, meaning that the flow pattern is highly controlled by the local boundary. For a Reynolds number much less than one, which is the case of the capillary bed, it is reasonable to neglect convective acceleration terms. On the other hand, a large Reynolds number ($Re >> 1$) reveals the diminution of local boundary control on the flow pattern, resultant from the inertial dominance. An increased Reynolds number seems to increase the WSS and to decrease the wall pressure [73]. Normally, viscous stresses ($Re << 1$) tend to stabilize and organize the flow, and excessive inertial forces ($Re >> 1$) tend to disrupt organized flow, leading to spontaneous flow irregularity and eventually to turbulent behavior. Hence, the flow stability can be determined by the use of this parameter.

### 4.4.2 Womersley number

The non-dimensional form of the parameter $\alpha$ introduced in Section 2.6.1 is the so called Womersley number, which governs the relationship between unsteady inertial forces and viscous forces [100], and is given by

$$\alpha = \frac{D}{2} \sqrt{\frac{\mu}{\mu}} = \frac{D}{2} \sqrt{\frac{\frac{2\pi}{\mu T}}{\frac{\mu}{\mu T}}} \propto \frac{D}{\sqrt{\mu T}}. \quad (4.22)$$

where $D = 2R$ is the tube diameter, $T$ is the pulse period. Physically, the Womersley number is assumed to be the ratio between the tube diameter to the laminar boundary layer growth over the pulse period, since this growth can be considered proportional to $\sqrt{\mu T}$.

For very small $\alpha$ values, the velocity reaches a parabolic profile, as predicted by the Poiseuille solution (see Figure 2.3), because of the low frequency of pulsations. In fact, in some situations,
even unsteady flows are reasonable treated as quasi-static [77]. For high Womersley number, \( \alpha > 10 \), the velocity profile tends to flatten, as shown in Figure 2.3.

### 4.5 Hemodynamic indicators

In vascular simulations it is important to obtain the most possible information about the flow field, in order to better understand the vascular diseases. Thus, besides obtaining the velocity and pressure fields it is also relevant to get information about mechanical parameters. The most common indicators related to arterial diseases are defined, due to their believed influence in the origin and aggravation of many vascular pathologies, including aneurysms, on or near the wall [84]. The most sought hemodynamic indicators are the WSS and its derived measures, such as WSSG, OSI, and GON.

The WSS is the tangential component of the stress tensor, (4.4), on the wall, and is given by

\[
WSS = \sigma_n - (\sigma_n \cdot n)n = \tau_n - (\tau_n \cdot n)n,
\]

where \( n \) is the outward normal to the wall surface, and \( \sigma_n \) and \( \tau_n \) are the normal components of the stress and extra-stress tensors, respectively.

The WSS is not easily measured for pulsatile flows, but for laminar steady flows in a straight tube with diameter \( d \), it is defined as

\[
WSS = \frac{32\mu Q}{\pi d^3},
\]

where \( Q \) is the cross sectional flow rate. Expression (4.24) can be very useful in some studies of the cardiovascular system [50], however it is very simplistic and it is hardly applied to study blood flow in complex geometries with pathologies, such as aneurysms. The numerical simulation is an excellent tool, to gather information on hemodynamic indicators, since once having the velocity flow field it is extremely easy to compute the WSS or its derived measures, contrary to \textit{in vitro} or \textit{in vivo} experiments.

From the WSS general expression, it is possible to obtain mathematically its highly important spatial variation through the relation

\[
WSSG = \sqrt{\left( \frac{\partial WSS}{\partial \zeta_1} \right)^2 + \left( \frac{\partial WSS}{\partial \zeta_2} \right)^2},
\]

where \( \tau_{\zeta_1} = \mu n \cdot \nabla (u \cdot \zeta_1) \) and \( \tau_{\zeta_2} = \mu n \cdot \nabla (u \cdot \zeta_2) \), being \( \zeta_1 \) and \( \zeta_2 \) the perpendicular unit tangent vectors to the surface.

The OSI and GON are wall parameters related to the unstationary flow. The OSI measures the cyclic oscillatory character of the WSS at every point from its predominant axial alignment, which has a correlation with the residence time of particles near the wall, and it is defined as

\[
OSI = \frac{1}{2} \left( 1 - \frac{\int_0^T WSS \, dt}{\int_0^T |WSS| \, dt} \right),
\]

where \( WSS \) is the wall shear stress.
where $T$ is the duration of the cycle. The OSI varies from 0 to $1/2$, corresponding to the best and worst temporal shear rate conditions, respectively.

The GON is similar to the OSI but regards the WSSG. It quantifies the degree of oscillating tension or compression forces through the relation

$$\text{GON} = 1 - \frac{|\int_0^T \text{WSSG} \, dt|}{\int_0^T |\text{WSSG}| \, dt}.$$  \hspace{1cm} (4.27)

It can vary between 0 and 1, increasing with the disturbance of tension or compression forces.

4.6 Boundary conditions

The prescription of proper initial and boundary conditions is a crucial step in the mathematical modeling and the numerical formulation of the vascular region of interest. After defining the initial condition, $u = u_0$, for $t = 0$ in $\Omega$, the fluid equations (4.8) and (4.13) are mathematically well defined and prepared to be solved by numerical methods only when the appropriate set of boundary conditions is imposed on the limits of the bounded domain $\Omega$. In particular, for the problem of blood flow in arteries, the computational domain consists of a truncated artery of the region of interest, containing the physical boundary, that is the artery wall, and the so called artificial boundaries, that are the cross sections originated from the truncation of the region of interest (see Figure 4.1). In order to obtain relevant computational simulations, we should impose physical boundary conditions on the vascular wall and set on the artificial sections boundary conditions accounting for the remaining parts of the cardiovascular system.

The classical conditions that we can prescribe on the boundary of $\Omega$, for all $t \in I$, are the Dirichlet and the Neumann, or natural, boundary conditions. For the fluid equations (4.8) and (4.13), the former corresponds to impose the velocity field, while the latter consists in imposing the normal stresses. Besides the Dirichlet and Neumann boundary conditions, it is also possible to prescribe an appropriate combination of these two, called Robin boundary condition.

4.6.1 The artery wall

On the physical boundary corresponding to the vascular wall, $\Gamma_w$, a no-slip condition is imposed, describing the complete adherence of the fluid with the wall. Thus, the following Dirichlet boundary condition is prescribed:

$$u = g, \quad \text{on } \Gamma_w, \quad \forall t > 0,$$  \hspace{1cm} (4.28)

where $g : I \times \Gamma_d \to \mathbb{R}^3$ is the velocity of the artery wall.

If a fixed geometry domain is considered, for all $t \in I$, then $g$ is set to be zero, $g = 0$, $\forall t \in I$. By choosing the rigid wall simplification, $(g = 0)$, we neglect the wall dynamics, which is a reasonable simplification in many cases [17, 18]. Moreover, the accurate acquisition of the arterial
wall properties is still a challenge. In spite of these drawbacks, it is possible to use solid mechanics models to describe the structure wall dynamics, which provide the structure wall velocity $\mathbf{g}$ to be imposed at the physical wall $\Gamma_w$ of the fluid domain. One possibility is the 3D model of hyperelasticity [24, 42].

4.6.2 The artificial sections

Much more difficult than the assessment of conditions for the natural existent boundaries, is to set proper conditions on the artificial sections. In this case, they can not be obtained from physical arguments, and can be a significative source of numerical inaccuracies during the resolution of the problem. Precisely, the issue relies on the fact that for those interfaces there is the need to account for the remaining parts of the arterial system, for which it is very difficult to obtain appropriate data. In this work, the remaining parts of the cardiovascular system are accounted for by resorting to the Geometrical Multiscale Approach. More precisely, the 3D model will be coupled with reduced, 1D or 0D, models at the artificial interfaces.

Defective boundary data Very often the available data provided from medical measurements or reduced (1D or 0D) models is expressed in terms of mean quantities such as the flow rate, $Q(t), t \in [0, T]$ or mean pressure, $P(t), t \in [0, T]$, rather than in pointwise quantities which are required for the 3D equations. Because of that, these mean average data are also known as defective conditions, and prevents a priori the achievement of a well posed 3D fluid problem. To simplify the notation, when imposing the mean pressure data to the fluid problem will be referred to as the mean pressure problem, whereas imposing the flow rate data will be referred to as the flow rate problem. Several approaches have been advocated to well pose the flow rate and the mean pressure problems. For instance, in [37] the mean pressure problem is overcome by imposing the mean pressure as a constant normal stress on the artificial section $\Gamma_i$ by means of the following Neumann boundary condition:

\[
\sigma(\mathbf{u}, p) \cdot \mathbf{n} = P_i, \quad \text{on } \Gamma_i, \quad t \in (0, T].
\] (4.29)

4.6.2.1 3D-1D coupling

To couple the 3D Navier-Stokes equations with the 1D hyperbolic model (3.1), we impose, at the coupling artificial boundary, $\Gamma_i$, with the 1D interface point $c$, (see Figure 4.3), the continuity of the flow rate and the mean pressure, for all $t \in [0, T]$,.

\[
\int_{\Gamma_i} \mathbf{u} \cdot \mathbf{n} d\gamma = Q_i^{1D}(c, t), \quad t \in [0, T]
\] (4.30)

\[
\frac{1}{|\Gamma_i|} \int_{\Gamma_i} pd\gamma = P_i^{1D}(c, t), \quad t \in [0, T]
\] (4.31)

The solution of the coupled problem is approximated in an iterative way, by resorting to a splitting strategy, i.e. each model is solved separately and yields the resultant information to the
Figure 4.3: Coupling scheme of the 3D and 1D model

other model. Thus, at each time step the 3D model returns pointwise data, which is integrated to
obtain the averaged quantities to be provided to the 1D model as a boundary condition at \( z = c \),
and, on the other hand, the 1D model provides the boundary conditions at the coupling sections of
the 3D in terms of average data. More precisely, in this work the coupling is performed by passing
the flow rate from the 3D to the 1D model, imposing (4.30) at the coupling of the 1D model, \( z = c \),
and by imposing the mean pressure, computed by the 1D model to the 3D model, considering the
defective condition (4.31) at the artificial coupling boundary, by means of condition (4.29).

The 3D-1D iterative coupling algorithm can be carried out explicitly or implicitly [64]. In
the explicit coupling, at each time step \( t_n \), the 3D model provides the flow rate computed at the
previous time step to the 1D model, and receives the mean pressure computed from the 1D model,
then moving forward to the next time step. This process is repeated for every time step, (see
Figure 4.3).

In the implicit coupling, subiterations between the 3D and 1D models are performed at each
time step, eventually using a relaxation parameter [64], until convergence between the 3D and 1D
flow rates at the coupling boundary is achieved, up to a given tolerance.

Due to the CFL condition (3.20), the 1D solver usually requires a smaller time step than the 3D
time advancing scheme. Also, the computational cost of the 3D problem makes it inconvenient to
use the 1D very small time steps on the 3D model. Thus, two different times steps are considered,
one for each model. The 1D model advances in time with the smaller time step, until it reaches
the 3D higher time step. Denoting \( t_n^{(m)} = t_{n-1} + m\delta t_{1D} \), such that \( t_n < t_n^{(m)} \leq t_{n+1} \), with \( \delta t_{1D} \)
the 1D time step, it is necessary to prescribe appropriate boundary conditions for the 1D model at
\( t = t_n^{(m)} \). Here we accomplish that by setting \( \phi_{1D}^{(m)} = \phi_{3D}^{(n-1)} \), where \( \phi_{1D} \) and \( \phi_{3D} \) is the boundary
data from the 3D and 1D models, respectively. Another possibility could be to interpolate the
boundary data, as described in [64, Chapter 3, p. 75].
4.6.2.2 3D-0D coupling

Lumped parameters models are derived from the 1D ones by furthering averaging in space [27], thus losing dependence from the spatial coordinates. Because of that they are also called 0D models. They are represented by a system of ODEs in time. They are analogous to electric circuits, where the flow rate can be identified with the current, the mean pressure with the voltage, and the 3D physical parameters, such as blood viscosity, blood inertia and wall compliance, with the lumped parameters resistance, inductance, and capacitance, respectively [27].

The 0D models can be used to represent compartments of the circulatory system, such as the heart action, or the resistance of the capillary bed. Hence, coupling 0D models to the 3D model allows to account for the global circulation. They can also be coupled to the 1D model, in order to have the proper resistance at the outflow boundaries, since a completely absorbing boundary condition, as described in Chapter 3, is not physiologic.

In the present study we will use simple 0D models, consisting only of a resistance, thus being just an algebraic relation between flux and mean pressure, through a resistance parameter: \( P = RQ \).

The choice of the resistance parameter \( R \) is done following [43]:

\[
R = \frac{\sqrt{\rho \beta}}{\sqrt{2} A_0^{5/4}}. \tag{4.32}
\]

This choice corresponds to impose the linear counterpart [43] of the absorbing boundary condition (3.29), directly on the 3D artificial section. Thus, the condition

\[
P = \frac{\sqrt{\rho \beta}}{\sqrt{2} A_0^{5/4}} Q \tag{4.33}
\]

is prescribed at the 3D artificial boundary, \( \Gamma_i \). As in [43], the averaged data condition (4.33) is imposed explicitly, that is,

\[
P^{(n+1)}_i = \frac{\sqrt{\rho \beta}}{\sqrt{2} A_0^{5/4}} Q^{(n)}_i, \quad \text{on } \Gamma_i, \tag{4.34}
\]

by means of a Neumann boundary condition (4.29).

4.7 Numerical approximation

The numerical solution of the fluid equations is reached using a discretization with respect to the time, and space domains.

4.7.1 Time discretization

The systems of partial differential equations, (4.8), and (4.13), are discretized in time using finite difference schemes. The time interval of interest \([0, T]\) is partitioned into subintervals, \( I^k = (t^k, t^{k+1}) \), \( k = 0, \ldots, N \), with \( t^0 = 0, t^N = T \), and constant time step \( \Delta t = t^{k+1} - t^k \). To solve the problem at \( t^{k+1} \), the solution at \( t^k \), or \( t^k - c, c = 1, 2 \) is known.
The finite difference schemes are obtained making use of the Taylor expansion formula. For the first order approximation, we get the implicit or backward Euler method:

\[
\frac{\partial u}{\partial t}(t^{k+1}) \approx \frac{u^{k+1} - u^k}{\Delta t},
\]

(4.35)

where \(u^k \approx u(t^k), k = 0, \cdots, N\). As second order approximation, the following backward difference formula, is obtained

\[
\frac{\partial u}{\partial t}(t^{k+1}) \approx \frac{3u^{k+1} - 4u^k + u^{k-1}}{2\Delta t}.
\]

(4.36)

In this case, besides the initial data \(u^0\), an additional second order initialization is needed to obtain \(u^1\).

Similarly, the backward difference formula of order 3 provides the approximation:

\[
\frac{\partial u}{\partial t}(t^{k+1}) \approx \frac{11}{6}u^{k+1} - 3u^k + \frac{3}{2}u^{k-1} - \frac{1}{3}u^{k-2}
\]

\[
\approx \frac{2\mu(\cdot)}{\Delta t}
\]

(4.37)

The later can be very memory consuming due to the necessity of storing the solutions of the previous three time steps. However, due to its third order, it provides a much better approximation, as long as a third order initialization of \(u^1\) and \(u^2\) is used.

The previous implicit time advancing schemes result in a non-linear system for the fluid equations, due to the convective term and the viscosity function, in the case of system (4.13), at each time step. For instance, using the backward Euler scheme the time discretization problem leads to, for all \(t \in [0, T]\),

\[
\begin{cases}
\rho \frac{1}{\Delta t}(u^{k+1} - u^k) + \rho u^{k+1} \cdot \nabla u^{k+1} + \nabla p^{k+1} - \text{div}(2\mu(\dot{\gamma})D(u^{k+1})) = 0, \\
\text{div} u^{k+1} = 0,
\end{cases}
\]

in \(\Omega\),

(4.38)

where \(\dot{\gamma}\) depends itself on the solution \(u^{k+1}\). Here, the convective term is linearized using the previous time step as follows:

\[
u^{k+1} \cdot \nabla u^{k+1} \approx u^k \cdot \nabla u^{k+1},
\]

(4.39)

as well as the viscosity function

\[2\mu(\dot{\gamma}^{k+1})D(u^{k+1}) \approx 2\mu(\dot{\gamma}^k)D(u^{k+1}).
\]

(4.40)

4.7.2 Space discretization

The space discretization is carried out through the FEM. In this context, the numerical approximation of the generalized Newtonian equations requires the reformulation of the differential problem, (4.8), (4.13), into a weak, or variational, form. In the sequel, the deduction of the variational formulation for the generalized Newtonian fluid equations in a rigid wall vascular domain is presented. Considering the Hilbert spaces \(M = L^2(\Omega_t) := \{q : \Omega_t \to \mathbb{R} : \int_{\Omega_t} |q|^2 < \infty\}\), and
\[ V = H^1_{\Gamma_0}(\Omega) := \{ \mathbf{v} : \Omega \to \mathbb{R}^3 : \mathbf{v} \in L^2, \nabla \mathbf{v} \in L^2, \mathbf{v}|_{\Gamma_0} = 0 \}, \]

the weak formulation is obtained by multiplying the differential equations, (4.8), (4.13), by suitable test functions \( q \in M \), and \( \mathbf{v} \in V \), integrating by parts over the domain \( \Omega \), and evoking the Green integration formula. We will assume two artificial sections with the following Dirichlet and Neumann boundary conditions:

\[ \mathbf{u} = \mathbf{g}, \quad \text{on } \Gamma^{in}, \quad (4.41) \]

\[ -p \mathbf{n} + 2\mu \mathbf{D}(\mathbf{u}) \cdot \mathbf{n} = \mathbf{h}, \quad \text{on } \Gamma^{out}. \quad (4.42) \]

The weak form of the equations ((4.8), (4.13)), (see for instance [72]), is thus to find \( \mathbf{u} \in V \), and \( p \in M \), such that for all \( \mathbf{v} \in V \), and \( q \in M \), we have,

\[
\begin{aligned}
\int_{\Omega} \rho \left( \frac{\partial \mathbf{u}}{\partial t} + (\mathbf{u} \cdot \nabla)\mathbf{u} \right) \cdot \mathbf{v} d\omega + \int_{\Omega} 2\mu \mathbf{D}(\mathbf{u}) : \mathbf{D}(\mathbf{v}) d\omega - \\
\int_{\Omega} p \text{div} \mathbf{v} d\omega - \int_{\Gamma^{out}} \mathbf{h} \cdot \mathbf{v} d\sigma &= 0, \quad (4.43)
\end{aligned}
\]

\[
\int_{\Omega} q \text{div} \mathbf{u} = 0.
\]

**Remark 2** In (4.43) the symmetry of the strain tensor \( \mathbf{D}(\mathbf{u}) \) was exploited, \( \int_{\Omega} 2\mu \mathbf{D}(\mathbf{u}) : \nabla \mathbf{v} = \int_{\Omega} 2\mu \mathbf{D}(\mathbf{u}) : \mathbf{D}(\mathbf{v}) \) as well as the definition of space \( V = H^1_{\Gamma_0}(\Omega) \), and of the boundary condition (4.42): \( \int_{\partial \Omega} (2\mu \mathbf{D}(\mathbf{u}) \cdot \mathbf{n} - pn) \cdot \mathbf{v} = \int_{\Gamma^{out}} (2\mu \mathbf{D}(\mathbf{u}) \cdot \mathbf{n} - pn) \cdot \mathbf{v} = \int_{\Gamma^{out}} \mathbf{h} \cdot \mathbf{v} \).

The FEM is a Galerkin method, requiring the discretization of the spatial domain \( \Omega^h \), and the introduction of two families, \( V_h | h > 0 \), and \( M_h | h > 0 \), of finite dimensional subspaces of \( V \) and \( M \), respectively. The problem is only solvable in the finite subspaces when these subspaces are accurately chosen, and when \( h \to 0 \) the approximate solutions converge to the solution of the system.

Thus, for each \( t \in [0,T] \), the purpose is to find an approximate solution \( \mathbf{u}_h(t) \in V_h \), and \( p_h(t) \in M_h \), such that, \( \forall \mathbf{v}_h \in V_h \), and \( \forall q_h \in M_h \),

\[
\begin{aligned}
\int_{\Omega} \rho \left( \frac{\partial \mathbf{u}_h}{\partial t} + (\mathbf{u}_h \cdot \nabla)\mathbf{u}_h \right) \cdot \mathbf{v}_h d\omega + \int_{\Omega} 2\mu \mathbf{D}(\mathbf{u}_h) : \mathbf{D}(\mathbf{v}_h) d\omega - \\
\int_{\Omega} p_h \text{div} \mathbf{v}_h d\omega - \int_{\Gamma^{out}} \mathbf{h} \cdot \mathbf{v}_h d\sigma &= 0, \quad (4.44)
\end{aligned}
\]

\[
\int_{\Omega} q_h \text{div} \mathbf{u}_h = 0.
\]

We consider finite element spaces on the domain \( \Omega^h \), associated with a triangulation \( \mathcal{T}_h \) of \( \Omega^h \), assuming that \( V_h \) and \( M_h \) are spaces of piecewise polynomial functions on each element of \( \mathcal{T}_h \). Moreover, the mesh \( \mathcal{T}_h \) is composed of elements of the same polyhedral shape, namely tetrahedral, and is regular and quasi-uniform [72]. The index \( h \) denotes the maximum diameter of the elements of the mesh.

The well posedness of the problem (4.44) requires that the spaces \( V_h \) and \( M_h \) satisfy the following
compatibility condition [72], for every \( t \in I \),

\[
\inf_{q_h \in M_h(Ω^p_h) \cap M_h(Ω^v_h)} \, \sup_{v_h \in V_h(Ω^p_h) \cap V_h(Ω^v_h)} \, \frac{\int_{Ω^p_h} q_h \text{div} v_h}{\|q_h\|_{L^2(Ω^p_h)} \|v_h\|_{H^1(Ω^v_h)}} \geq \beta_t,
\]

(4.45)

with the constant \( \beta_t > 0 \) independent from \( q_h, v_h \), and the mesh spacing \( h \). This is the so-called discrete inf-sup or Ladyzhenskaja-Babuska-Brezzi (LBB) condition [72], which establishes a relation between the test spaces for the velocity and pressure, and the singularity and stability of the solution in these spaces. The locking phenomenon for the velocity field, or spurious pressure modes, may occur if the approximation of the solution by piecewise polynomial functions on each element does not fulfill the discrete inf-sup condition [81]. Generally, the inf-sup condition is not verified when an equal order interpolation for both pressure and velocity is chosen. For that reason, the interpolation often used is piecewise quadratic elements for the velocity, and linear elements for the pressure \((P_2 - P_1)\), or of an extension of this technique \((P_1 \text{ iso } P_2 - P_1, \text{ or } P_2 \text{ bubble } - P_1)\).

One way to both verify the inf-sup condition and to use equal order, both velocity and pressure, for instance \( P_1 - P_1 \) finite elements, is by adding an interior penalty stabilization term [12]. In [72] other stabilization methods are described.

Finally, the fully discrete problem for the first order time approximation consists in finding the solution \((u_h^{k+1}, p_h^{k+1}) \in V_h \times M_h\) such that, \( \forall v_h \in V_h \), and \( \forall q_h \in M_h \),

\[
\begin{aligned}
\int_{Ω^v_h} \rho \left( \frac{1}{\Delta t} u_h^{k+1} + u_h^k \cdot \nabla u_h^{k+1} \right) \cdot v_h + \int_{Ω^v_h} 2\mu(\gamma^k) \mathbf{D}(u_h^{k+1}) : \mathbf{D}(v_h) \\
- \int_{Ω^p_h} p_h \text{div} v_h = \int_{Ω^v_h} \rho \left( \frac{1}{\Delta t} u_h^k \right) \cdot v_h + \int_{\Gamma_{out}} h \cdot v_h, \\
\int_{Ω^p_h} q_h \text{div} u_h^{k+1} = 0.
\end{aligned}
\]

(4.46)

If one chooses to use the two-step backward difference scheme, then (4.46) becomes

\[
\begin{aligned}
\int_{Ω} \rho \left( \frac{3}{\Delta t} u_h^{k+1} + u_h^k \cdot \nabla u_h^{k+1} \right) \cdot v_h + \int_{Ω} 2\mu(\gamma^k) \mathbf{D}(u_h^{k+1}) : \mathbf{D}(v_h) \\
- \int_{Ω} p_h \text{div} v_h - \int_{\Gamma} (\sigma \cdot \mathbf{n}) \cdot v_h = - \int_{Ω} \rho \left( \frac{1}{\Delta t} 2u_h^k - \frac{1}{2} u_h^{k-1} \right) \cdot v_h,
\end{aligned}
\]

(4.47)

Finally, for the third order backward differentiation method, (4.46) becomes

\[
\begin{aligned}
\int_{Ω} \rho \left( \frac{11}{6\Delta t} u_h^{k+1} + u_h^k \cdot \nabla u_h^{k+1} \right) \cdot v_h + \int_{Ω} 2\mu(\gamma^k) \mathbf{D}(u_h^{k+1}) : \mathbf{D}(v_h) \\
- \int_{Ω} p_h \text{div} v_h - \int_{\Gamma} (\sigma \cdot \mathbf{n}) \cdot v_h = \int_{Ω} \rho \left( \frac{1}{\Delta t} 3u_h^k - \frac{3}{2} u_h^{k-1} + \frac{1}{3} u_h^{k-2} \right) \cdot v_h,
\end{aligned}
\]

(4.48)
Chapter 5

Computational simulations and discussion

This Chapter is dedicated to the numerical results performed in 3D geometries of aneurysms. The simulations were carried out for steady and unsteady flow of Newtonian and non-Newtonian fluid models. Exhaustive and systematic quantitative and qualitative comparisons were executed, using either idealized or realistic geometries. Besides testing the differences between the two viscosity functions, and between steady and pulsatile regimes, we also analyzed the differences in using different boundary conditions at the downstream sections, including side branches. After introducing important aspects related to the computational implementation of the problem, the inflow conditions and parameter definition are provided. Finally, the results are presented and discussed, first for the set of idealized geometries, and afterwards for the anatomical ones.

5.1 Inflow conditions and parameter definition

For each geometry, blood flow is studied using the 3D equations for both Newtonian and non-Newtonian Carreau models, and in both steady and pulsatile inflow regimes.

In the case of a steady inflow flux, the fluid was considered to be at an initial rest state, with zero velocity, and then to be ramped up to a steady state of flux \( Q = 4 \, \text{cm}^3\text{s}^{-1} \), such that

\[
Q_{\text{in}}^{\text{ramp}}(t) = \frac{t Q}{t_{\text{ramp}}} \quad \text{for } t < t_{\text{ramp}}, \tag{5.1}
\]

with \( t_{\text{ramp}} \) the time length of the ramp. The reference value for the inflow was chosen to match measurements performed in the internal carotid artery [67]. When a pulsatile flow is imposed as inflow boundary condition, the fluid also starts from a rest state with zero velocity, but it is described through a periodic sinus wave, representing the heart beat, such that

\[
Q_{\text{in}}(t) = 1 + \text{abs} \left( 4 \cdot \sin \left( \frac{t \pi}{0.4} \right) \right). \tag{5.2}
\]
In this case, the mean flow rate in time is approximately $Q = 3.5 \text{ cm}^3/\text{s}$. In Figure 5.1 can be seen the plots of the steady and unsteady inflow flux profiles versus time. All the simulations in this work, either steady or unsteady, were performed with a final time of 5 s, which proved to guarantee the steadiness of the solutions, i.e. the difference between two consecutive time steps (steady case) or two consecutive cycles (unsteady case) was negligible. In the unsteady case, all the results presented in the sequel correspond to the 12th cycle.

At each time step the inflow flow rate was imposed on the inflow cross section as a parabolic profile.

In all cases, the simulations were carried out using a time step of 0.01 s on the 3D model, while a time step of $0.5e^{-4}$ s was taken for the 1D model. Also in the 1D model, an absorbing boundary condition, $W_2 = 0$, was considered at the downstream section of the tube.

In order to correspond to typical values for the blood, the fluid density was set to $\rho = 1 \text{ g/cm}^3$, and the Newtonian constant viscosity was set to $\mu = 0.04 \text{ poise}$ [15]. The parameters of the Carreau model were chosen from [29, 43], as described in Table 4.1, i.e. $\mu_0 = 0.456 \text{ poise}, \mu_\infty = 0.032 \text{ poise}, \lambda = 10.03 \text{ s},$ and $n = 0.344$.

In all numerical tests, the finite element meshes are tetrahedral.

## 5.2 Idealized geometries

Prior to preforming patient-specific simulations, numerical tests were carried out in idealized geometries. Although hemodynamics is highly dependent on the geometry, and patient-specific geometries are required to study blood flow inside aneurysms, the idealized geometries allow for a better understanding of the impact of changing the fluid model or the computational geometry, as well as performing steady or unsteady simulations.

Since these were simple geometries, and consequently of lower computational cost than the realistic geometries, this was also an easier approach to conduct a series of validation and optimization tests.

The idealized geometries, displayed in Figure 5.2, consist of a cylindrical and curved tube...
with a saccular aneurysm, both with and without side branches rising from the aneurysm. Their dimensions, as well as the side branch location, are the ones proposed in [35], such that the parent vessel radius is 0.5 cm, the side branch radius is 0.25 cm, except in one case where it is 0.15 cm (Figure 5.2 e)), and the aneurysm radius is 0.8 cm. The parent vessel length is 6 cm and the side branch length is 1.6 cm, except in one case where it is 2.5 cm (Figure 5.2 e)).

5.2.1 Straight tube

The first numerical test consisted of a straight tube with a saccular aneurysm (Figure 5.2 a)). The mesh was composed of approximately 0.54 M elements, corresponding to a maximum size of 0.04 cm. The simulations of this test case were performed prescribing a standard homogeneous normal stress at the downstream section.

In Figure 5.3 are shown the results for the velocity magnitude, as well as the differences between the Newtonian and the non-Newtonian solutions. There is a significant difference between the two models, of the order of 10%. This difference is more evident in the unsteady solution, both at systole and diastole, suggesting that steady simulations tend to underestimate the differences between Newtonian and non-Newtonian models. Regarding the velocity magnitude, we can also observe a clear difference between the steady and unsteady solutions, especially at the diastole. This difference can be also perceived in the WSS distribution, depicted in Figure 5.4. Indeed, regarding the WSS magnitude, there are relevant differences of the steady solution not only with the diastolic solution, but also with the systolic one. For what concerns the differences between the two fluid models, although the steady solution shows locally bigger discrepancies, the unsteady one exhibits more variations globally. Specially at the diastole, there are dissimilarities around almost the whole aneurysm neck. In both cases, the WSS differences between the Newtonian and Carreau solutions arrive to 10%, which is significative. We have also analyzed the differences between the WSS magnitude of the steady solution, with the temporal mean of the WSS magnitude of the unsteady solution. In this case, the maximum difference between the steady and the unsteady average is 5%, both for the Newtonian and the non-Newtonian solutions, while the maximum difference between the WSS average of the Newtonian and the non-Newtonian models goes up to 7.5%. In Figure 5.5 are illustrated the WSSG at the systolic peak of the Carreau model, and its difference with the Newtonian model. We can see that the distinction between the two models
Figure 5.3: The velocity magnitude for the Newtonian model (left) and the Carreau model (middle), and the difference between the two models (right), at the steady state (top), at diastole (middle) and at the systolic peak (bottom).

...arrives to 5%, and is localized specially around the aneurysm neck. The WSSG distribution in the remaining cases were very similar to the depicted one. The OSI for both Newtonian and non-Newtonian models, together with their difference, are depicted in Figure 5.6. Although both models seem very similar, the differences are noticeable, being 100% in some regions. This is due to the fact that the OSI peaks occur in different places in each fluid model, in spite the fact that both models have OSI values different from zero near or in the aneurysm neck. This means that regarding this indicator, the choice of the fluid model is crucial. We also remark that unsteady simulations are essential, to arrive to such conclusion.

5.2.2 Straight tube with a side branch

Next, we considered the straight tube with a saccular aneurysm and a side branch (Figure 5.2 b)). The mesh was composed of approximately 0.52 M elements, corresponding to a maximum size of 0.04 cm. For this test case two types of outflow boundary conditions were prescribed at both outflow and side branch downstream sections: i) the standard homogeneous normal stress, and ii) the coupling with the 1D model. Regarding the velocity magnitude, the differences between steady and unsteady flow, and between Newtonian and Carreau models, are very similar to the previous numerical test. As before, the discrepancy between fluid models is more relevant in the unsteady solution, specially at the systolic peak, with a maximum difference of about 10%. Figure 5.7 displays the particle traces inside or close to the aneurysm. Using the same seeding coordinates for all cases, the particle tracing allows for a further analysis on the impact of using different solutions. There is a clear variation between the steady and unsteady solutions, yet, all cases
Figure 5.4: The WSS for the Newtonian model (left) and the Carreau model (middle), and the
difference between the two models (right), at steady state (top), at diastole (middle) and at the
systolic peak (bottom).

Figure 5.5: The WSSG for the Carreau model at the systolic peak (left) and the difference between
the Newtonian and the Carreau model at the systolic peak (right).

Figure 5.6: The OSI for the Newtonian model (left) and the Carreau model (middle), and the
difference between the two models (left).
describe some vorticity inside the aneurysm. This phenomenon is more noticeable during diastole, and much less evident in the steady solution, which tends to underestimate this recirculation. On the other hand it is almost absent in systole. In fact, when the velocity increases, during systole, the flow has less tendency to stagnate and recirculate inside the aneurysm, flowing more smoothly towards to outward sections. The WSS magnitude for the unsteady non-Newtonian solution, and its difference with the Newtonian one, is depicted in Figure 5.8. This Figure exhibits the WSS magnitude distribution from two different perspectives, showing that this parameter is persistently higher, along the parent vessel, at systole. Inside the aneurysm, the WSS is consistently low, at both systole and diastole. Despite the lower values at diastole, the dissimilarity between the Newtonian and the Carreau models is more noticeable, and the maximum difference goes up to 10% in the aneurysm neck region. In terms of the steady solution, although the Newtonian and the Carreau solutions were found to be apparently equivalent, the difference between the two solutions is very significative, rising up to 10% of the maximum WSS magnitude, see Figure 5.9. In this Figure we can also observe that the difference between the temporal mean of the WSS magnitude for the unsteady Newtonian and Carreau cases is also considerable, with a maximum value of 7.5%. However, the differences between the steady and unsteady solutions, for both Newtonian and Carreau models, are even more important, since they are less localized and rise up to 10%.

5.2.2.1 Comparing the 1D coupling with standard boundary conditions

In this section, we only display the results obtained with the Carreau model since we reach the same conclusions using the Newtonian one. The results obtained for the 3D-1D coupling, were performed using two 1D tubes of 5 cm length, each one coupled to each downstream section, i.e., to the outlets of the parent and the branching vessels. In both 1D models, the $\beta$ parameter, (3.4), was set to 945308.72, and 50 finite elements were considered.

In Figure 5.10 we compare the coupling of the 1D model at the outflow sections, with the standard homogeneous normal stress boundary conditions, of the velocity magnitude for the Carreau solution. Overall, there is an underestimation of the velocity field using the standard boundary condition. The major differences between the two cases are concentrated in the side branch of the aneurysm, rising up to 50% of the maximum velocity magnitude. With the 1D coupling we impose a non zero pressure at the downstream sections, which simulates the systemic circulation, and drives even more flow in those directions. The increase on the amount of blood flowing through the side branch, results in a higher recirculation inside the aneurysm for the coupling case. The differences that arise from using distinct boundary conditions are also illustrated in Figure 5.11, where we compare the WSS magnitude. There is a clear difference between the steady and unsteady cases, both for standard and 3D-1D solutions, along the whole geometry. The main variations are positioned in the aneurysm neck region and in the side branch, which reach more than 20%, specially in the steady regime, where there is an elevated difference within the aneurysm neck region.
Figure 5.7: The particle tracing for the Newtonian model (left) and the Carreau model (right), at the steady state (top), at diastole (middle) and at the systolic peak (bottom), using the same seeding points in each case.

Figure 5.8: The WSS for the Carreau model (left and middle), and the difference between the Newtonian and Carreau model (right), at diastole (top) and at the systolic peak (bottom).

The WSSG comparison between the two boundary conditions is depicted in Figure 5.12. We only show the variations for the unsteady solution, since the remaining cases are very similar to this one. Apparently, the WSSG for the standard and 1D coupling boundary conditions are very close, however the difference between the two solutions goes up to 10% in the aneurysm neck, and in the side branch. Moreover, this discrepancy is much more significant than the difference between the Newtonian and Carreau solutions. In the coupling case the difference reaches 10% but in a much more restricted area, while in the standard case the maximum value is only of 5%.
Figure 5.9: The WSS for the Newtonian model (left) and the Carreau model (middle), and the difference between the two models (left), at the steady state (top) and at the temporal mean for the unsteady state (bottom).

Figure 5.10: The velocity magnitude for the Carreau model using standard (left) and 3D-1D coupling boundary conditions (middle) and the difference between the two cases (right), at the steady state (top), at diastole (middle) and at the systolic peak (bottom).
Figure 5.11: The WSS for the Carreau model using standard (left) and 3D-1D coupling boundary conditions (middle) and the difference between the two cases (right), at the steady state (top), at diastole (middle) and at the systolic peak (bottom).

Figure 5.12: The WSSG for the Carreau model at the systolic peak and the difference between the Newtonian and Carreau, using standard (top) and 3D-1D coupling (middle) boundary conditions, and the difference between the two boundary conditions (bottom).
5.2.3 Curved tube

Besides the straight tube, we also considered the curved tube with a saccular aneurysm, illustrated in Figure 5.2 c). The 3D finite element mesh is composed approximately of 0.49M elements, with a maximum size of 0.04 cm. In this geometry, standard homogeneous normal stress boundary conditions were prescribed at the outflow section.

In Figure 5.13 the effects of using either steady or unsteady flow regimes, as well as Newtonian or non-Newtonian fluid, are shown through the velocity field variations. The overview of the whole geometry shows that the differences between the solutions are not only observed inside the aneurysm. In fact, there is a considerable difference in the velocity field between the steady and unsteady solutions also in the parent vessel. The disparity between the velocity magnitudes of the Newtonian and Carreau solutions is again significant, of the order of 10%, with a higher impact in the unsteady cases. In terms of the particle tracing, there is an obvious difference between each solution, though all of them present some level of vorticity inside the aneurysm. Moreover, the dissimilarity between Newtonian and Carreau models is more visible when looking at the particle tracing, where different flow structures occur, especially for the unsteady case. The difference between the OSI of the Newtonian and non-Newtonian solutions is plotted in Figure 5.14. The region of maximum OSI is about the same for both solutions. Nevertheless, there is a clear overestimation in the Newtonian solution, compared to the Carreau one. Comparing with the straight tube geometry, despite the higher OSI values, the difference between the two solutions is much smaller, of the order of 5%. Yet, this is a considerable value and reflects evident differences between the two models.

5.2.4 Curved tube with a side branch

To the simple curved tube was also added a side branch rising from the saccular aneurysm (Figure 5.2 d)). The mesh consisted of about 0.45 M finite elements, with a maximum size of 0.04 cm. In this test case both the coupling with the 1D model, and standard homogeneous boundary conditions, were applied at the downstream sections. The 1D tubes considered were both set with 5 cm length, $\beta =$, and 50 finite elements. Here we analyze the solutions for the Carreau model, the conclusions for the Newtonian one being similar.

The 3D-1D coupling was also tested in the previous curved geometry, without the side branch, and the discrepancies with the standard boundary condition were negligible. That was mainly due to the fact that we are considering a rigid model, so the sum of the fluxes on the artificial sections must be zero due to the incompressibility condition. For the previous test case, that was a very restrictive condition, since there is only one outflow boundary sections, and an inlet section where the velocity is prescribed. We observe, however, that when introducing the side branch, there is a clear distinction between the velocity fields for both boundary condition strategies, as illustrated.
Figure 5.13: The velocity magnitude for the Newtonian and Carreau models (left), the difference between the two models (middle), and the particle tracing for both models (right), at the steady state (top), at diastole (middle) and at the systolic peak (bottom), using the same seeding points in each case.

Figure 5.14: The OSI for the Newtonian model (left) and the Carreau model (middle), and the difference between the two models (left).
in Figure 5.15. Indeed, that difference is extremely relevant, specially at diastole, where it reaches 50% in the side branch area. These results demonstrate the importance of taking into account the side branches when studying blood flow. There is also a clear variation between the steady and unsteady solutions.

The WSS magnitude for each boundary treatment, and their differences, are depicted in Figure 5.16. At steady state, the maximum values are located at the aneurysm neck, where the flow of the parent vessel impacts. However, at systole, the higher values spread for a wider region around the aneurysm neck. In the side branch, the systolic solution presents higher values of the WSS, specially in the 3D-1D coupling case. Contrary to the velocity field observations, apparently there are very few differences between using standard and 3D-1D coupling boundary conditions. However, this is not true, since in all cases the WSS differences in the side branch are of the order of 10%. In the rest of the geometry the WSS differences are also considerable, specially at the region of the aneurysm opposite to the side branch, where the flow impacts.

Figure 5.17 displays the comparison of the OSI with both boundary treatments, for the Newtonian and Carreau solutions. The higher values are concentrated around the same area in all cases, but these are more widely spread when the Newtonian model is used. For both models, the coupling case presents the maximum values concentrated in a smaller region, while in the standard case there is also non-zero OSI in the side branch. This is translated in bigger localized differences between the Newtonian and non-Newtonian solutions, while the dissimilarity between the different boundary conditions is more global, although with lower values.
5.2.4.1 Comparative study of the different boundary treatments

Here, an exhaustive analysis regarding the boundary conditions was carried out, for this idealized geometry (Figure 5.2 d)). The 3D-1D coupling of the branching vessel was performed for several different 1D tubes, with different lengths. The goal was to compare the 1D couplings with the 3D-0D coupling, where the 0D is a resistance obtained by means of a 1D model of zero length, as described in Section 4.6.2.2. In addition, different values of the artery parameter $\beta$ were taken.

We have also considered, for comparison purposes, a branching vessel with different radius and length, as depicted in Figure 5.2 e). The following results correspond to the Newtonian model and steady flow regime.

Apart from the value of the $\beta$ parameter already used in the numerical tests of Sections 5.2.2.1, and 5.2.4, we have also considered for this comparative study a $\beta$ value fitted from numerical results. This new value for $\beta$ was obtained resorting to the pressure drop between the inflow and the outflow sections, for the steady state solution, and using the Neumann homogeneous outflow boundary condition. From such numerical result, the $\beta$ value was computed by determining the resistance $R$ in the formula $\Delta P = RQ$, where $\Delta P$ and $Q$ are known from the numerical solution, and using expression (4.33). From Figures 5.18 and 5.19, we can state that the fitted resistance solution is much more similar to the standard boundary condition one. This is expected, considering how the fitted $\beta$ was computed. In this case, in the parent vessel we have $\beta = 133.39$, while in the
side branch $\beta = 156.71$. This values are of a much lower magnitude compared with the one used previously, that was $\beta = 945308.72$, resulting in a decreased resistance at the downstream sections, and in a lower pressure drop between the side branch and the upstream section. The increased pressure drop due to the higher $\beta$ value (Figure 5.18 c)), implies an increase on the velocity of blood through the side branch, as observed in Figure 5.19 c). Moreover, despite using the same $\beta$ parameter, there is a higher similarity between the Neumann homogeneous outflow boundary condition and the 3D-0D coupling case, when compared to the 3D-1D coupling, specially, in the pressure plot (Figure 5.18 a), b) and d)).

We tested the reduction of the length of the 1D model using $L_{1D} = 2.5 \, cm$, and $L_{1D} = 0.5 \, cm$. The results depicted in Figure 5.18 d), f), and g), show that the pressure drop between the inflow section and the side branch increases as the 1D tube length decreases. Indeed, even though the 1D model is compliant and the 3D is not, the 1D model coupled to the 3D problem corresponds to an extension of the side branch, with the pressure drop approximately constant between the 3D inlet section, and the 1D outlet point. Thus, the pressure drop between the 3D upstream section and the 3D downstream side branch one, corresponds the pressure drop between the inflow point, and a middle point, which is as closer to the outflow point as the 1D model is shorter. Notice that this results are only valid since we consider rigid geometries. In fact, using the FSI formulation we would have a pressure wave traveling along the geometry, instead of a pressure drop between the artificial sections.

Finally, we tested the influence of the dimensions of the side branch. The solution for this dif-
Figure 5.18: Comparison between the pressure for the 3D model (a)), 3D-0D model (b)), 3D-1D with elevated resistance and $h_{1D} = 5 \text{ cm}$ (c)), 3D-1D with fitted resistance and $h_{1D} = 5 \text{ cm}$ (d)), 3D-1D with fitted resistance and $h_{1D} = 2.5 \text{ cm}$ (e)), 3D-1D with fitted resistance and $h_{1D} = 0.5 \text{ cm}$ (f)), and 3D model with elongated side branch (g)).

different geometry was obtained with homogeneous boundary conditions at the downstream sections. The reduction of the side branch radius induces a decrease of the flow rate through it, as it is expected and can be seen by comparing Figures 5.19 a) and g).

5.3 Pacient-specific geometries

This Section is dedicated to the analysis of the hemodynamics in anatomical geometries, corresponding to intracranial saccular aneurysms. Although the idealized geometries can be very useful to carry out quantitative comparative studies, clinical decision can only be based on patient-specific models. Two patient-specific geometries will be considered. In the first realistic geometry, we only consider the saccular aneurysm and the parent vessel (Figure 5.20 a)), which is a common approach in numerical simulations of aneurysms [29]. The effects of the side branches in the hemodynamics inside the aneurysm are considered in a second geometry, where the boundary conditions concerning the side branches are prescribed at the end of the side branch, Figure 5.20 b), or directly at the parent vessel, Figure 5.20 c). The anatomically realistic geometries of saccular aneurysms here presented, were reconstructed from in vivo rotational CTA scans of specific patients, provided by Prof. Jorge Campos and his team from the Faculty of Medicine of the University of Lisbon.
Figure 5.19: Comparison between the velocity magnitude for the 3D model (a)), 3D-0D model (b)), 3D-1D with elevated resistance and $h_{1D} = 5cm$ (c)), 3D-1D with fitted resistance and $h_{1D} = 5cm$ (d)), 3D-1D with fitted resistance and $h_{1D} = 2.5cm$ (e)), and 3D-1D with fitted resistance and $h_{1D} = 0.5cm$ (f)), 3D model with elongated side branch (e))

Figure 5.20: The set of realistic geometries, and highlight of the sections where the velocity magnitude was evaluated.
5.3.1 Saccular aneurysm

Several numerical simulations were performed in the geometry of Figure 5.20 a), corresponding to a cerebral saccular aneurysm located on the outer bend of the artery. A finite element mesh of about 0.85 M tetrahedra was employed, corresponding to a graded mesh with element size of 0.016 cm within the aneurysm, and maximum size of 0.04 cm. Concerning the boundary conditions, two strategies were followed for the outflow section: imposing the standard homogeneous normal stress; and coupling with a 1D model of 5 cm length, with $\beta = 945308.72$, and where 50 finite elements were used.

From the velocity magnitude inside the aneurysm, Figure 5.21, we can see that the differences between the unsteady and steady solutions are much more evident than the differences in using the Newtonian or non-Newtonian viscosity laws. Nevertheless, the variations between the Newtonian and Carreau models reach 10%. The dissimilarity of the two fluid models arise in different locations depending on the instant of the cardiac cycle. At diastole, the variations occur in the middle of the aneurysm, possibly due to recirculation effects, while during systole they are concentrated close to the wall. This explains the enormous variations of the WSS at systole for the two constitutive functions, as well as the much lower discrepancies of the WSS at diastole, Figure 5.22. Regarding the steady solution, the differences in the velocity magnitude of the Newtonian and Carreau models spread out through both the middle, and near the wall, of the aneurysm, resulting also in relatively high discrepancies on the WSS. From Figure 5.22, we also observe that the temporal mean of the WSS for the unsteady case is significantly smaller than the WSS of the steady solution. The dissimilarities of the steady and unsteady flow field of this results, demonstrate the importance of unsteady simulations in reproducing the hemodynamics. This is also clear form the particle tracing, Figure 5.21, where the flow structures, such as the impact, separation, and recirculation zones, are very distinct in systole and diastole, and also from the steady solution. In Figure 5.23 are plotted the differences of the WSS between the steady and the unsteady solutions, as well as the difference between the WSS of the steady solution using standard boundary conditions or the 3D-1D coupling, for the Carreau fluid model. It is unequivocal that the main distinctions occur for the diastolic solution, where a wide region of the artery has a dissimilarity of at least 20%. Also the systolic solution is significatively different from the steady one. In these two cases, the differences rise up to 50%. The dissimilarities with of the steady and time averaged unsteady WSS is not so obvious, but it still reaches 20%, and presents a large region with differences of at least 10%.

The test case which solution is closer to the steady one with standard outflow conditions, is the steady solution with the 1D coupling at the outflow, where differences of 0% occur in large regions of the geometry. This is expectable, and it is in accordance with the results already obtained for the idealized geometries. Indeed, the small influence of the 1D coupling here is related to the use of a rigid boundary condition, and the existence of only one outflow section.

Figures 5.24 a) and b) illustrate the WSSG for the Carreau steady solution, using both standard
Neumann homogeneous and 1D coupling boundary conditions. There are minor discrepancies between those two solutions, mainly located at the downstream of the parent vessel, after the aneurysm, being the WSSG very similar at upstream and within the aneurysm. The downstream discrepancies between the two boundary treatments are highlighted in Figure 5.24 c), where the WSSG differences appear mostly at downstream, rising up to 10%, being essentially zero in the aneurysm and at upstream. The variations in using Newtonian or Carreau models are depicted in Figures 5.24 d) and e), for the standard boundary condition and 3D-1D coupling cases, respectively. Again, the dissimilarities due to the fluid model in the 3D-1D coupling simulation occur in a wider region, specially at the downstream of the parent vessel, being similar to the ones of the homogeneous Neumann boundary condition within the aneurysm and upstream. Once more, we observe that the coupling with the 1D model has minor influence on the hemodynamics inside the aneurysm. However, the differences between using a Newtonian or non-Newtonian model are very relevant, being of the order of 10% at the part of the neck where the flow impacts, and arriving to 5% within the aneurysm.
5.3.2 Analyzing the presence of side branches

In order to study the effects of the main side branches in the aneurysm hemodynamics, a second patient-specific geometry was considered. First, the side branches were taken into account in the 3D anatomically realistic geometry, Figure 5.20 b). Afterwards, the side branches were clipped from the 3D geometry, Figure 5.20 c). The numerical simulations here carried out include steady and unsteady computations, as well as the use of Neumann homogeneous standard boundary conditions, and couplings both with 1D and 0D models. All the 1D models here applied have a length of 5 cm, where 50 finite elements are taken. For both 1D and 0D models, the $\beta$ parameters used were determined through expression (3.4), where the thickness of the wall $h_0$ is set to 10% of the vessel radius of the branch they are coupled to, or the radius of the hole, in the case of the clipped geometry Figure 5.20 c). The Young Modulus $E$ is set to $E = 1.e5$, and the Poisson
Figure 5.24: The WSSG for Carreau steady solution using both standard boundary condition (a)) and coupling with the 1D model (b)), the difference between the Newtonian and Carreau solutions for each boundary condition strategy (c) and d)), and the difference between the two conditions, using the Carreau solution (e)).

The ratio is set to $\xi = 0.5$, assuming the artery wall is incompressible. The numerical simulations on the clipped geometry, Figure 5.20 c), were carried out using a finite element mesh of around $1.2 \ M$ tetrahedra, corresponding to a maximum size of $0.04 \ cm$. Regarding the geometry with side branches, Figure 5.20 b), the simulations were executed using a graded mesh with element size of $0.03 \ cm$ within the aneurysm, and maximum size of $0.05 \ cm$, amounting to using around $1.2 \ M$ tetrahedral element. We present the results using the Carreau fluid model, and the unsteady flow regime.

Looking at the particle tracing in Figure 5.25, there is an obvious difference on the hemodynamics between systole and diastole, disregarding the boundary treatment. Whatever the boundary condition used, there is an increase of recirculation structures inside the aneurysm in the geometry with the side branches, at diastole, compared to the clipped geometry. The major differences between the several boundary strategies are mainly found at the downstream of the aneurysm, where in some cases, such as the 0D coupling in both geometries, there is an increase of recirculation zones, even in the parent, or side branch, vessels.

In the sequel, the results at the systolic peak will be analyzed. The solutions at the diastolic period lead to similar conclusions. In Figure 5.26 are illustrated the velocity magnitudes in the cross section of the saccular aneurysm represented in Figure 5.20. At first site, they are all very similar, regardless the geometry and the boundary conditions used. As expected, the high values of the velocity are concentrated in the region corresponding to the main vessel, whilst inside the aneurysm the reaches zero velocity, even in systole. Nevertheless, looking closely to the velocity differences between the several solutions, in Figure 5.27, discrepancies of at least 10% occur in large regions for some cases. Regarding the clipped geometry, the solutions using the 1D or 0D couplings are very close, the error being less than 2.5%. However, the discrepancies between those two and the solution obtained with the standard homogeneous boundary condition are much higher, reaching 20% on the neck of the aneurysm, although inside the aneurysm they are negligible. In what concerns the geometry with the side branches, the biggest dissimilarities happen between the solution with the standard boundary condition, and the 1D coupled solution. For this case, the
discrepancies almost reach 20% in the lumen of the parent vessel, and differences of at least 10% occur in a wide region, including inside the aneurysm. Contrary to the clipped geometry, in this case the solutions for the standard boundary condition and the 0D coupling are very similar, with differences lower than 2.5%, while the variations between the 1D and 0D coupled solutions are of the order of 10%. From these results, we conclude that coupling the geometry with side branches to the 1D model has a higher influence in the solution than coupling it with the 0D problem, suggesting that, in this case, the 0D coupling does not accurately incorporate the systemic circulation. On the other hand, in the clipped geometry, coupling the outflow sections with 0D or 1D models has the same impact, suggesting that, in this case, using the simplified 0D coupling is enough to account for the side branches. These results are in accordance with the velocity differences shown in Figure 5.28, where the variations obtained between the geometry with branches using standard and 0D coupling conditions and all the solutions obtained for the clipped geometry are similar (first and last rows of Figure 5.28). Analogously, the differences obtained between the clipped geometry with 1D and 0D coupling conditions and all the solutions obtained for the geometry with branches are also similar (second and last columns of Figure 5.28). One remarkable inference from the results in Figure 5.28 is that the solutions in the wider geometry, including the main side branches, using standard or 0D coupling conditions are closer to the clipped geometry solution using 1D or 0D coupling boundary conditions, than using standard ones. This corroborates the effectiveness of reduced models in accounting for the remaining parts of the cardiovascular system. Nevertheless, in localized regions, in the neck of the aneurysm and close to the wall, dissimilarities arrive to 10%.

The WSS for each geometry, using the three boundary condition strategies, is depicted in Figure 5.29. In all cases, there is a region of higher values, localized in the parent vessel, close to the aneurysm. Apparently, in the clipped geometry, the variations between each solution are negligible. This is not the case when the side branches are included in the geometry. In fact, there are clear differences in the side branches areas between using standard boundary conditions, and coupling either with a 1D or 0D model. These discrepancies are plotted in Figure 5.30, where we can see that, for the wider geometry including the side branches, the differences between each boundary condition reach 10% in the side branches. Despite this, the comparison between the standard boundary condition and the 3D-0D coupling, shows large regions of null WSS, which is agreement with the previous results, regarding the velocity field. Also for this geometry, there are higher discrepancies between the 3D-1D coupling and the standard boundary condition, than between the two coupling strategies. In the clipped geometry, the WSS difference between the standard boundary condition and both 3D-1D and 3D-0D coupling is very similar, reaching 10% in the parent vessel close to the region where the side branch was clipped. Once again, the solutions for both coupling boundary conditions are equivalent, such that the difference is almost zero throughout the whole geometry. One important observation from the WSS results is that the variations in using different boundary conditions on the clipped geometry are much less significant than in the
geometry including the side branches. This is particularly noticeable in the region of high WSS, such as in the parent vessel close to the aneurysm at the inside part of the vessel bend, and at the neck of the aneurysm, but also in the whole parent vessel and side branches. This suggests a higher sensibility of the WSS values to boundary condition variations in the wide geometry.

The WSSG for each case, and their differences, lead to the previous conclusions, and are illustrated in Figures 5.31 and 5.32. Again, the discrepancies between the solutions are more visible in the wider geometry, specially in the side branches, and on the regions of higher absolute values of the WSSG, which are located around the regions of high WSS. These differences reach 100% in some specific parts of the side branches. Remark that the differences between the two coupling cases in the clipped geometry are negligible in the whole geometry.

The OSI is depicted in Figure 5.33. Overall, the higher OSI values are concentrated in the parent vessel, just before the aneurysm close to the aneurysm neck, and in the aneurysm. Contrary to what happens in the WSS and WSSG, for the wider geometry there are elevated values in the side branches only in the standard boundary condition case. There is a relevant similarity between the OSI distribution of the solution on the wide geometry with the 0D coupling, and the clipped geometry using 0D or 1D coupling. This might suggest that the 1D, or 0D, model coupled to the clipped geometry proper accounts for the presence of the side branches. The differences between the 1D coupled solutions in the two geometries, clipped an wide (Figure 5.33 middle), can be due to the length of the 1D model, that in the case of the geometry with the side branches is added to the side branch length, which is not the case for the clipped geometry.

Following the previous results, the difference between each coupling approach in the clipped geometry is minor, not more than 5%, see Figure 5.34 top right. Accordingly, the results show similar discrepancies between the standard boundary condition and the 3D-1D or 3D-0D coupling, of the order of 20% in more than one region. On the other hand, in the wider geometry, the differences between the standard boundary condition and the 3D-0D coupling are very remarkable considering the results for the velocity, WSS, and WSSG. These occur mainly in the parent vessel and within aneurysm. This demonstrates the importance of analyzing the OSI as a hemodynamic indicator, other than the WSS and the WSSG. Indeed, if we had only taken into account the velocity field, or the WSS and WSSG, we would have concluded that the difference between this two cases is minimal, when in fact, they show discrepancies of the OSI in the order of 20% in more than one region. The higher dissimilarities are encountered in the difference between the standard boundary condition and the 3D-1D coupling for the geometry that considers the main side branches.
Figure 5.25: The particle tracing for the Carreau model, at diastole (left) and systole (right), using standard boundary conditions (first column), coupling with the 1D model (second column), and with the 0D model (third column), both for the clipped (top) and the wider (bottom) geometries, using the same seeding points in each case. The inflow section is on the left side and the outflow section is on top.

Figure 5.26: The velocity magnitude for the Carreau model using standard boundary conditions (first column), coupling with the 1D model (second column), and with the 0D model (third column), both for the clipped (top) and the wider (bottom) geometries.
Figure 5.27: The velocity magnitude difference, for the Carreau model, between using standard boundary conditions and coupling with the 1D model (first column and second column, with different scales), using standard boundary conditions and coupling with the 0D model (third column), and coupling with the 1D model and the 0D model (forth column), both for the clipped (top) and the wider (bottom) geometries.

Figure 5.28: The velocity magnitude difference, for the Carreau model, between using the two geometries, clipped (columns) and wider (rows), with the standard boundary conditions and coupling with the 1D model and 0D.
Figure 5.29: The WSS for the Carreau model using standard boundary conditions (first column), coupling with the 1D model (second column), and with the 0D model (third column), both for the clipped (top) and the wider (bottom) geometries.

Figure 5.30: The WSS difference, for the Carreau model, between using standard boundary conditions and coupling with the 1D model (first column), using standard boundary conditions and coupling with the 0D model (second column), and coupling with the 1D model and the 0D model (third column), both for the clipped (top) and the wider (bottom) geometries.
Figure 5.31: The WSSG for the Carreau model using standard boundary conditions (first column),
coupling with the 1D model (second column), and with the 0D model (third column), both for the
clipped (top) and the wider (bottom) geometries.

Figure 5.32: The WSSG difference, for the Carreau model, between using standard boundary
conditions and coupling with the 1D model (first column), using standard boundary conditions and
coupling with the 0D model (second column), and coupling with the 1D model and the 0D model
(third column), both for the clipped (top) and the wider (bottom) geometries.
Figure 5.33: The OSI for the Carreau model using standard boundary conditions (first column), coupling with the 1D model (second column), and with the 0D model (third column), both for the clipped (top) and the wider (bottom) geometries.

Figure 5.34: The OSI difference, for the Carreau model, between using standard boundary conditions and coupling with the 1D model (first column), using standard boundary conditions and coupling with the 0D model (second column), and coupling with the 1D model and the 0D model (third column), both for the clipped (top) and the wider (bottom) geometries.
Chapter 6

Conclusions

In this thesis, a CFD analysis was carried out to study the blood flow dynamics in cerebral aneurysms. An exhaustive comparative study was performed, with the goal of analyzing the impact of the mathematical model choice, the geometry variations, and the unsteadiness of blood flow, in the hemodynamics within the aneurysm. For this purpose, we started by considering idealized geometries. Since these are simplified, they provide more straightforward conclusions, leading to a better understanding of the effects of varying the fluid model, or the image reconstruction, in anatomical geometries. Afterwards, patient-specific geometries were also analyzed. We compared the influence of different flow regimes, both steady and unsteady, different flow viscosity laws, both Newtonian and Carreau, the presence or absence of side branches, the curvature of the main artery, and different boundary conditions. For each case the hemodynamics was analyzed through the pressure and the velocity fields, as well as hemodynamics indicators such as the WSS, and its variations, both in time, the OSI, and in space, the WSSG.

We have shown the importance of using unsteady simulations. There were major differences between the steady and unsteady solutions, just by examine the velocity field, or the WSS, even if the temporal mean of the unsteady solution was considered. Also, unsteady simulations allow for the analysis of a very important parameter, the OSI, which in some cases lead to conclusions not achievable by looking to other indicators. Moreover, in all cases, these differences are much more noticeable than the dissimilarities between the Newtonian and non-Newtonian fluid models, specially at diastole. By simplifying the blood flow pulsatile behavior, in most cases, there is also an underestimation of the velocity magnitude difference between the two fluid models, and of the flow structures inside the aneurysm. For both steady and unsteady solutions, independently of the indicator under consideration, the Newtonian model tends to provide overestimated values, compared to the non-Newtonian one. Moreover, considering the WSS of the unsteady solution, in most cases, the non-Newtonian effects are more visible at diastole, i.e., at low shear rate, as would be expected. In the case where this is not verified (Section 5.3.1), although the velocity magnitude shows more non-Newtonian effects at diastole, these are located at the middle of the aneurysm,
possibly due to recirculation, while at systole they are concentrated close to the wall, explaining the disparity between the solutions.

Concerning the boundary condition strategies, coupling with the 1D model proved to be inefficient in the cases where the main side branches were not taken into account. Since we are considering rigid geometries, the incompressibility of the fluid imposes the sum of the fluxes on the artificial sections to be zero. Thus, if there is only one inflow section and one outflow section, there is no flow division, and, even in the realistic case, the difference between using standard homogeneous normal stress at the downstream section or coupling it with a 1D model is minimal. In fact, in the geometries where the side branches are taken into account, those differences are very noticeable, due to the fact that by having flow division, the direction of the flow is not so restricted. Generally, considering the standard boundary condition at the outward sections results in an underestimation of the fluid quantities, comparing to the coupling case. The variations tend to arise specially at the side branches, where in some cases it reached 50% of the maximum value. This underestimation occurs for the velocity magnitude, WSS, and WSSG, but it is not verified for the OSI. In fact, there is even an overestimation of this indicator when the standard boundary condition is used. Hence the importance of considering as many indicators as possible when analyzing the hemodynamics inside the aneurysms. Only an intensive study can lead to reliable conclusions. This is true also for what regards the geometry under analysis. Indeed, the hemodynamics inside the aneurysm is highly dependent on the geometry of the vasculature, as we can notice in the differences between the straight and bend idealized geometries, as well as the patient-specific models here studied. Few aspects may be generalized, but others are very specific and variational. Thus, the conclusions achieved in this thesis for the patient-specific geometries, though in overall accordance with the idealized ones, might have some fluctuations if we consider different ones.

Overall, we conclude that, in the realistic geometries, there are considerable differences in the velocity magnitude between the steady and unsteady solutions. The dissimilarities between the velocity field at diastole and systole are located inside the aneurysm, and both upstream and downstream of the aneurysm, while the differences between using distinct boundary condition treatments are more concentrated in the downstream part of the main artery. In all cases, the higher values of velocity are located in the lumen of the parent vessel, and not within the aneurysm, which has always regions of zero velocity, even at systole. Both WSS and WSSG register higher values close to the aneurysm neck, or in the side branches when they are included, and lower values inside the aneurysm. The OSI higher values tend to appear not only in a different region of the parent vessel, close to the aneurysm neck, but also in the aneurysm. For the considered geometries, important variations arise from the inclusion, or not, of the main side branches. By ignoring the effects of the side branches, the recirculation inside the aneurysm tends to diminish, but even more importantly, there is a big similarity between the two coupling cases, i.e., the coupling with the
1D and the 0D models. From these results we conclude that, when using the simplified geometry without the side branches, the 0D coupling strategy is sufficient to account for the effects of the rest of the circulatory system. This is confirmed by the similarity between the solution for the wider geometry, with side branches, using standard or 0D coupling boundary conditions, and the solution for the clipped geometry, using either 1D or 0D coupling conditions. Although further tests are required, these results are very encouraging and lead to the conclusion that the reduced models coupled at the downstream sections of a clipped geometry can simulate the presence of the side branches. The similarity between both coupling strategies in the clipped geometry is corroborated for all the analyzed indicators, i.e., the velocity magnitude, the WSS, the WSSG, and the OSI. Notice that, the distinction between coupling each geometry with a 1D model is related to the length of the 1D tube, that is, the length of the side branch. Clearly, a comparative study between the length of the 1D model and the side branch poses an interesting future work, since, as we have seen from the comparative analyzes performed here, considering different sizes of the 1D model affects the pressure drop between the inflow and outflow sections, and thus the flow division. Considering the wider geometry, the remarkable similarity between velocity for the standard boundary condition, and the 0D coupling case, even if there are considerable differences on the OSI, can indicate that when using a more detailed geometry, the 0D model does not represent properly the impact of the systemic circulation. In this case the 1D model might better incorporate those effects. Overall, by accounting for the main side branches, the solutions for the velocity magnitude, WSS, WSSG, and OSI, show a higher sensitivity to variations of the adopted boundary condition strategy.

The artery wall dynamics was not taken into account in the results presented in this thesis. In order to account for the artery compliance, it is necessary to use FSI couplings, which are computationally very costly compared to the 3D rigid simulations, that are already computationally very demanding. Nevertheless, FSI simulations can be important, and further studies on the dissemblances between accounting or ignoring the effects of the wall movements in the hemodynamics inside aneurysms are required. Although this subject is beyond the scope of this thesis, some preliminary numerical simulations of FSI problems in aneurysms, using a linear elasticity model, were already performed, being the subject of ongoing work.
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