Blood flow modeling and mass transport in the human aorta

Ανάπτυξη μοντέλων ροής και μεταφοράς μάζας στην αορτή

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Abstract

Atherosclerosis is a disease of cardiovascular system and is usually located within large arteries. It is a major cause of death and mortality and it is related to over 12 million deaths annually affecting nearly all people in the modern world. It is a disease that involves the circulation of low density lipoproteins –LDLs (a main carrier of cholesterol) within the blood stream. These eventually accumulate in the cell wall of large and medium sized arteries to form plaques or atherosclerotic patches gradually narrow the lumen and gradually become the site of bleeding and thrombus formation.

It is well known that atherosclerotic lesions in the arterial wall develop at certain sites in the human arterial system such as along the inner walls of curved segments and the outer walls of arterial bifurcations. This phenomenon is called the localization of atherosclerosis. As the early event leading to the genesis of atherosclerosis is the accumulation of atherogenic lipids such as low density lipoproteins (LDLs) within the arterial wall, mass transport between the blood and the artery wall must play an important role in the genesis and development of atherosclerosis.

In the present study we investigate the correlation of luminal surface LDL concentration \( c_w \) distribution with the distribution of wall shear stress (WSS) and the effects of both non – Newtonian behavior and pulsation of blood flow on the distributions of luminal surface LDL concentration along the wall of the human aorta. The dependence of viscosity and diffusivity and the local density are incorporated in the single and two phase flow models rendering these quantities position dependent. Then we compared the predictions of a single phase model with those of the two phases one under both steady flow and realistic pulsatile flow conditions using a human aorta model constructed from CT images. Then local hemodynamics studied by using computational fluid-dynamics (CFD) applied to realistic geometric model of the aorta. It is therefore important to solve the problem of accurately reconstructing geometric models from CT image in order to gain accuracy in CFD computations and predictions.

The present numerical study revealed an adverse correlation between wall shear stress and the luminal surface LDL concentration in the aorta. The results indicate that the luminal surface LDL concentration depends not only on the local wall shear stress but also on both the global and local flow patterns. Also the results showed that under steady flow conditions, although the shear thinning non – Newtonian nature of blood could elevate wall shear stress (WSS) in most regions of the aorta, especially in areas with low wall shear stress, it had little effect on luminal surface LDL concentration \( c_w \) in most regions of the aorta. Nevertheless, it could significantly enhance \( c_w \) in areas with high luminal surface LDL concentration through the shear depended diffusivity of LDLs. The pulsation of blood flow could significantly reduce \( c_w \).
in these disturbed places. In conclusion the shear shining non – Newtonian nature of blood has little effect on LDL transport in most regions of the aorta, but in the atherogenic – prone areas where luminal surface LDL concentration is high its effect is apparent. Similar is the effect of pulsatile flow on the transport of LDLs.
ΠΕΡΙΛΗΨΗ

Η αθηροσκλήρωση είναι μία νόσος του καρδιαγγειακού συστήματος και βρίσκεται συνήθως μέσα σε μεγάλες αρτηρίες. Πρόκειται για μια σημαντική αιτία θανάτου και η θνησιμότητα της σχετίζεται με πάνω από 12 εκατομμύρια θανάτου ετησίως, η οποία επηρεάζει σχεδόν όλους τους ανθρώπους στο σύγχρονο κόσμο. Είναι μια ασθένεια που περιλαμβάνει την κυκλοφορία των χαμηλής πυκνότητας λιποπρωτεϊνών-LDLs (ένας κύριος φορέας της χοληστερόλης) εντός της κυκλοφορίας του αίματος. Η χαμηλής πυκνότητας πρωτεϊνές συσσωρεύονται στο αρτηριακό τοίχωμα των μεγάλων και μεσαίων μεγέθους αρτηριών και σχηματίζουν πλάκες ή αθηρωματικά μπαλώματα, τα οποία σταδιακά προκαλούν στένωση του αυλού και έπειτα δημιουργούνται αιμορραγία στην περιοχή, με αποτέλεσμα το σχηματισμό θρόμβων.

Είναι γνωστό ότι οι αθηροσκληρωτικές βλάβες στο αρτηριακό τοίχωμα αναπτύσσονται σε συγκεκριμένες περιοχές στο ανθρώπινο αρτηριακό σύστημα, όπως κατά μήκος των εσωτερικών τοιχωμάτων των καμπυλωτών τμημάτων και των εξωτερικών τοιχωμάτων των αρτηριακών διακλαδώσεων. Αυτό το φαινόμενο ονομάζεται localization of atherosclerosis. Καθώς το πρώιμο συμβάν που οδηγεί στη γένεση της αθηροσκλήρωσης είναι η συσσώρευση των αθηρογόνων λιπιδίων όπως είναι οι λιποπρωτεϊνές χαμηλής πυκνότητας (LDLs) εντός του αρτηριακού τοιχώματος, η μεταφορά μάζας μεταξύ του αίματος και του τοιχώματος της αρτηρίας διαδραματίζει σημαντικό ρόλο στην ανάπτυξη της αθηροσκλήρωσης.

Στη συνέχεια, συγκρίνουμε τα αποτελέσματα του μονοφασικού μοντέλου με το διφασικό μοντέλο, τόσο υπό σταθερή ροή όσο και υπό ρεαλιστικές συνθήκες παλμικής ροής, χρησιμοποιώντας ένα ανθρώπινο μοντέλο αορτής κατασκευασμένο από CT εικόνες. Τέλος, μελετάμε τη τοπική αιμοδυναμική με τη χρήση υπολογιστικής ρευστοδυναμικής (CFD) που εφαρμόζεται στο ρεαλιστικό γεωμετρικό μοντέλο της αορτής. Επομένως, είναι σημαντικό να λύσουμε το πρόβλημα της ακρίβειας στην ανακατασκευή του ρεαλιστικού μοντέλου από την εικόνα CT, προκειμένου να έχουμε ακρίβεια στους CFD υπολογισμούς και στα αποτελέσματα.
Η παρούσα αριθμητική μελέτη έδειξε ένα αντίστροφο συσχετισμό της διατμητικής τάσης του τοιχώματος και της συγκέντρωσης των LDL στην επιφάνεια του αυλού στην αορτή. Τα αποτελέσματα, επίσης έδειξαν ότι η συγκέντρωση των LDL στην επιφάνεια του αυλού εξαρτάται όχι μόνο από την τοπική διατμητική τάση του τοιχώματος αλλά και από τα ολικά και τοπικά πρότυπα ροής. Επίσης, τα αποτελέσματα έδειξαν ότι κάτω από συνθήκες σταθερής ροής, η μη - Νευτώνεια φύση του αίματος αυξάνει τη διατμητική τάση του τοιχώματος (WSS) στις περισσότερες περιοχές της αορτής, ιδιαίτερα στις περιοχές με χαμηλή διατμητική τάση και έχει μικρή επίδραση στη συγκέντρωση των LDL (c_w) στην επιφάνεια του αυλού, στις περισσότερες περιοχές της αορτής. Παρ’ όλα αυτά, μπορεί να ενισχύσει σημαντικά το c_w στις περιοχές με υψηλή συγκέντρωση των LDL στην επιφάνεια του αυλού μέσω της εξαρτώμενης διατμητικής διάχυσης των LDLs. Η παλμικότητα της ροή του αίματος μπορεί να μειώσει σημαντικά το c_w σε αυτές τις διαταραχμένες θέσεις. Εν κατακλείδι, η μη - Νευτώνεια συμπεριφορά του αίματος έχει μικρή επίδραση στη μεταφορά των LDL στις περισσότερες περιοχές της αορτής, αλλά στις αθηρογόνες - επιρρεπείς περιοχές όπου η συγκέντρωση LDL στην επιφάνεια του αυλού είναι υψηλή τα αποτελέσματα είναι εμφανή. Παρόμοια είναι η επίδραση της παλμικής ροής στη μεταφορά των LDLs.
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1 Clinical Problem

Atherosclerosis is a disease of cardiovascular system and is usually located within large arteries. It is a major cause of death and mortality and it is related to over 12 million deaths annually affecting nearly all people in the modern world. It is a disease that involves the circulation of low density lipoproteins – LDLs (a main carrier of cholesterol) within the blood stream. These eventually accumulate in the cell wall of large and medium sized arteries to form plaques or atherosclerotic patches gradually narrow the lumen and gradually become the site of bleeding and thrombus formation.

The typical anatomical structure of an arterial wall is shown schematically in Fig. 1. going from the lumen to the most external layer, a large artery is comprised of the following five layers: glycocalyx, endothelium, intima, media, and adventitia. The luminal glycocalyx is a thin layer of macromolecules which is believed to cover the plasma membrane of a single layer of endothelial cells, and the entrance of the intercellular junctions. The thickness of the glycocalyx is usually less than 100 nm (average thickness 60 nm) \cite{[2, 3]}. Immediately in contact with the glycocalyx is the endothelium, a single layer of endothelial cells, which are elongated in the direction of blood flow. Endothelial cells are interconnected through intercellular junctions. Internal elastic lamina (IEL), an impermeable elastic tissue with fenestral pores, is lying between intima and media. In contrast to the media, which contains alternating layers of smooth muscle cells and elastic connective tissue, the intima is mainly comprised of proteoglycan and collagen fibers. The media layer is surrounded by loose connective tissue, the adventitia, in which there are capillaries (lymphatic and vasa vasorum). Except via transport from luminal blood supplies, proteins can be transported from the adventitia to the media through the vasa vasorum \cite{[1]}.  

Fig. 1. Transverse section of a large artery
Fatty streaks are the earliest visible sign of atherosclerosis. They are subendothelial accumulations of large, lipid-containing cells called foam cells (Low Density Lipoproteins-LDL and cholesterol). Later, fibrous plaques or atheroma form, which are the cause of the clinical manifestation of atherosclerosis. These plaques consist of an accumulation of monocytes, macrophages, foam cells, T lymphocytes, connective tissue, tissue debris, and cholesterol crystals. The pathogenesis of atherosclerosis remains unexplained. The current hypothesis is that endothelial damage could be the primary event and the reaction to it may eventually lead to plaque formation [4].

The formation and progression of plaques are influenced by a number of risk factors, such as hypertension, smoking, hyperlipidemia, diabetes mellitus and hyperhomocysteinemia which can be controlled. It is not clear whether Chlamydia infection plays an important part in the pathogenesis of atherosclerosis or whether it perhaps even triggers its development .Risk factors that cannot be influenced are age, male sex and genetic predisposition .Subordinate factors are overweight and sedentary or stressful lifestyle . However the disease cannot be prevented by simple maintenance of one’s cholesterol, lipid levels, and blood pressure. A major role also plays biomechanical factors that are innate to all humans [4, 5].
The consequences of plaque deposition are narrowing of the lumen which results to reduced blood flow that can lead to ischemia. Especially, in the coronary arteries where myocardial infarction can cause heart failure leading to cardiac death. Other consequences of plaque formation are stiffening of the vessel wall (calcification), thrombus formation that obstructs the residual lumen and can cause peripheral emboli (e.g. cerebral infarction, stroke) as well as bleeding into the plaques (additional narrowing by the hematoma) and the vessel wall. Thus weakened, the wall may be stretched (aneurysm) and even rupture, with dangerous bleeding into the surrounding tissues, for example, from the aorta or cerebral vessels (massive intracerebral bleeding stroke) [4]. However with medication and lifestyle changes, such as a healthy diet, exercise, and quitting smoking, plaques may slow or stop growing or even shrink slightly with aggressive treatment. Moreover in patients with severe cases of atherosclerosis, doctors can open up blockages (stenting) from atherosclerosis, or go around them (bypass surgery) by using invasive techniques. Stenting opens up a blocked artery and helps reducing symptoms, although it does not prevent future heart attacks. While with bypass surgery surgeons take a healthy blood vessel from the patient to bypass a segment blocked by atherosclerosis [6].

As mentioned before there are a lot of risk factors associated with atherosclerosis, but the concentration of cholesterol in blood is considered to be the most important factor since the plaques are rich in lipid [7, 8, 9]. However the localization of atherosclerotic lesion in a human arterial tree cannot be explained by considering only lipid metabolism [10]. Atherosclerotic plaques in humans form preferentially in specific locations in the human vascular tree. Regions that have the highest probability to form lesions are the ones where the wall shear stress is low. Clinical and postmortem anatomical studies revealed that atherosclerotic lesions in humans develop preferentially at certain sites such as the inner wall of curved segments and the outer walls of bifurcations of relatively large arteries, where blood flow is likely to be disturbed by the occurrence of flow separation and formation of complex
secondary and recirculation flows. [11, 12, 13, 14]. In addition another important factor involved in the localization of atherogenesis is oxygen flux. Hypoxia has been shown to cause damage to the endothelial barrier, resulting in inter-endothelial gaps, leading to increase arterial wall permeability to macromolecules [15]. Moreover hypoxia also induces endothelial cell apoptosis, which can facilitate LDL transport into the arterial wall through leaky junctions [16]. On the contrary hyperoxia has been shown to have the effect on the regression of atherosclerotic plaques. [17]. These suggested that fluid mechanical factors are involved in the localized genesis and development of atherosclerosis in man and that is a phenomenon worthy to be studied.

Statistical results showed that four primary regions in the body are the most common sites of plaque formation. The coronary arteries, major branches of the aortic arch such as the carotid arteries, the visceral branches of the abdominal aorta such as the renal arteries, and the terminal branches of the abdominal aorta such as the femoral arteries, are the principal regions where plaques form in humans. Such sites are particularly of clinical interest because these arteries supply the heart, the brain, and other organs essential for homeostasis. Any lesion that could disrupt blood flow to such organs may result in significant morbidity or mortality.

![Fig. 4. Formation atherosclerotic plaque in aortic arch](image)
1.1 Recent Studies

*Shigeo Wada and Takeshi Karino [10]* studied the interrelationship among the sites of low wall shear stress (WSS), the sites of high LDL surface concentration, and the sites of atherosclerotic wall thickening in a vessel of complex geometry considering the semipermeable nature of the vascular endothelium. That means that the endothelium allows the passage of water and ions dissolved in it but not macromolecules. The chosen vessel for this work was a multiple bend of a human right coronary artery, in which the flow is locally disturbed by the formation of complex secondary and recirculation flows.

A three dimensional mesh model of the vessel used in the computational analysis of blood flow and transport of LDL was constructed using the shape of the multiple bend taken from a photograph of a transparent human right coronary artery.

It was assumed that the flow is steady, the arterial wall is rigid and blood is an incompressible Newtonian fluid with a viscosity, $\mu = 3.5 \text{ mPas}$ and a density, $\rho = 1.05 \times 10^3 \text{ kg/m}^3$. Thus the blood flow can be described by the continuity and Navier-Stokes equations:
\[ \nabla \cdot \mathbf{v} = 0 \]  
(1)

\[ \rho (\mathbf{v} \cdot \nabla) \mathbf{v} = -\nabla P + \mu \nabla^2 \mathbf{v} \]  
(2)

where \( \mathbf{v} \) is a velocity vector consisting of three components, namely \( u, v, w \) for \( x, y, z \) direction, and \( P \) is blood pressure.

These equations are solved under the following boundary conditions:

\[ u = 2u_0 \left[ 1 - \left( \frac{r}{R_0} \right)^2 \right], v = 0, w = 0 \quad \text{at} \; x = 0 \]  
(3)

\[ P = 0 \quad \text{at} \; \ell = L \]  
(4)

\[ \frac{\partial u}{\partial z} = 0, \frac{\partial v}{\partial z} = 0, w = 0 \quad \text{at} \; z = 0 \]  
(5)

where \( u_0 \) is the mean velocity of blood at the inlet, \( r \) is the radial distance from the central axis of the vessel, and \( R_0 \) is the radius of the vessel at the inlet.

One more important condition is that the vessel wall is uniformly water permeable and the filtration velocity \( V_w \) was assumed to be \( 4 \times 10^{-5} \text{mm/s} \).

\[ \mathbf{v} = V_w \mathbf{n} \]  
(6)

where \( \mathbf{n} \) is a unit vector normal to the vessel wall and \( r \) is a radial distance from the center of each cross section.

Finally, wall shear stress was evaluated at each node on the vessel wall by calculating the velocity gradient in the direction normal to the vessel wall and multiplying it by the viscosity of blood.

In flowing blood small macromolecules such as LDL, spherical molecules (diameters= 21 – 26 nm, densities 1.006 – 1.063 \times 10^3 \text{kg/m^3}), are transported by being carried by the flowing blood itself and also by molecular diffusion. Steady state mass transport of LDL in flowing blood can be described by

\[ \mathbf{v} \cdot \nabla C - D \nabla^2 C = 0 \]  
(7)
where C is the concentration of LDL, and D is the diffusivity of LDL. Using the Stones-Einstein equation, the diffusivity of LDL was estimated to be $5 \times 10^{-6} \text{mm}^2/\text{s}$ in blood at a body temperature of $37^\circ \text{C}$.

By solving Eqs (1) and (2) which govern blood flow, the velocity vector $\mathbf{v}$ was obtained.

And the following boundary conditions were imposed on the transport equation:

\[
C = C_0 \text{ at } x = 0 \\
\frac{\partial C}{\partial \zeta} = 0 \text{ at } \zeta = L \\
\frac{\partial C}{\partial z} = 0 \text{ at } z = 0 \\
V_w C_w - D \frac{\partial C}{\partial n}_{r=R} = K C_w
\]

They calculated various hemodynamic properties of blood flow for different Reynolds numbers. At $R_e = 500$ and $R_e = 900$ they observed the formation of standing recirculation (adverse flow) zone adjacent to the inner wall of the second bend between points of flow separation, S, and stagnation, P. In these regions the wall shear stress was low. However at $R_e = 200$ the formation of a recirculation zone did not occur.

![Fig. 6. Detailed flow patterns in the multiple bend obtained at an inflow Reynolds number, $R_e = 500$ by tracing the paths of fluid elements that were chosen to depict the characteristics of the flow in this vessel (panel A), and the distributions of fluid velocity and wall shear stress in the common median plane of the multiple bend (panel B). A flow pattern and a contour map of the fluid velocity in the cross section of the vessel are also shown in the figure, respectively, in the right and left halves of the cross section at each location where a velocity distribution is shown. Arrows at S and P indicate separation and stagnation points, respectively. Arrows outside of the flow pattern in the cross section of the vessel indicate the direction of the flow along the vessel wall. Numbers at the outside of the vessel indicate the values of wall shear stress evaluated at each location.](image)
As it concerns the LDL surface concentration, they found out that at $R_e = 500$ the LDL concentration remained almost the same as that at the inlet in most regions of the vessel, except of two regions, where the concentration of LDL was locally elevated. These regions were located on the inner walls of the mild first and acute second bends, where as it was mentioned before, the flow was slow and the wall shear stress was relatively low. They found out generally that the surface concentration of LDL was elevated at locations where wall shear stress was low, presenting a sharp increase as the wall shear stress decreased from 1-0 Pa (see fig.7).

![Fig.7. The relationship between wall shear stress and surface concentration of LDL at $R_e = 500$. Note that the surface concentration of LDL which corresponds to a certain value of wall shear stress is not only one, indicating that the surface concentration of LDL at a location is dependent not only on the value of wall shear stress at that location but also some other factors such as flow patterns which determine the paths of fluids elements and the times they spend in regions of high and/or low wall shear stress until they reach the particular location in the vessel.](image)

In addition they studied factors that affect the surface concentration of LDL. The first one was the *Reynolds number*. By carrying out the same calculations as at $R_e = 500$ for $R_e = 200$ and 900 they found that the surface concentration of LDL was elevated at the same regions. However at $R_e = 200$ the region of high surface LDL concentration was wider than at $R_e = 500$. At $R_e = 900$ the region of high surface concentration of LDL was much smaller compared to the one at $R_e = 500$, as well as the surface concentration itself. The second factor was the *water filtration velocity* at the vessel wall. They calculated the surface concentration of LDL using three different values for water filtration velocity and observed that both the area of the region of high surface concentration and the surface concentration of LDL itself greatly increased as water filtration velocity increased. Another factor is the *size of lipoproteins*. In human plasma there are other lipoproteins except the LDL macromolecules.
such as VLDL, HDL and VHDL with different densities. All these lipoproteins have also different molecular size and weight. As a result there diffusivity in blood differs to one to another. It was found out that at \( R_e = 500 \) the area of surface concentration and the surface concentration itself were increased in cases of large molecules such as VLDL and LDL, whose diffusivities were low in contrast to cases of smaller molecules such as HDL and VHDL. The last factor is the \textit{fluid viscosity}, because it is used in the estimation of the diffusivity of LDL in flowing blood by the Stones-Einstein equation. Hence it affects the degree of concentration polarization of LDL.

This analysis can be also extended to cases of arterial stenoses, bifurcations, end-to-end and end-to-side anastomoses and uneven surface of endothelium in order to investigate the relationship between the flow and LDL surface concentration.

Another interesting study by Xiao Liu, Fang Pu, Yubo Fan, Xiaoyan Deng, Deyu Li and Shuyu Li [18] was done to verify the hypothesis that the helical flow observed in the aorta may have a great influence on the distribution of luminal surface LDL concentration. As a result it may suppress or even eliminate areas of flow stagnation in order to prevent the accumulation of atherogenic lipids on the luminal surfaces of the ascending aorta and the aortic arch. They also investigated the effects of aortic torsion, branching, taper, and curvature on the flow pattern and the luminal surface LDL concentration.

From the acquisition of 1.5 Tesla MRI images from a healthy male which included slices of the ascending aorta, the aortic arch and a majority portion of the descending aorta, four models were created.

\textbf{Model 1}: was created to mimic the human aorta with all geometrical features intact.
\textbf{Model 2}: was made the same as model 1 but without the branches.
\textbf{Model 3}: was constructed with the torsion of the aorta removed.
\textbf{Model 4}: had the same feature as that of model 3, but with the tapering removed along the model.
It was assumed that the flow is steady, the arterial wall is no-slip rigid and blood is an homogenous incompressible Newtonian fluid with a viscosity, $\mu = 3.5 \times 10^{-3} \text{kg/m} \cdot \text{s}$ and a density, $\rho = 1.05 \times 10^3 \text{kg/m}^3$. Thus the blood flow was described by the continuity and Navier-Stokes equations (1), (2). Two boundary conditions for the Navier-Stokes equations were implied. The first was that at each of the three aortic arch branches, 5% of flow volume was allowed to be ejected. The second was a flat inlet flow velocity profile was used, assuming the time average $Re = 790$ (velocity is 0.1 m/s). The mass transport of LDLs in flowing blood was described by the following equation:

$$\bar{u}^2 \nabla c - D \Delta c = 0 \quad (12)$$

where $c$ is the concentration of LDLs and $D$ is the diffusion coefficient of LDL in blood, assumed to be $4.8 \times 10^{-12} \text{m}^2/\text{s}$.

The boundary conditions for the mass transport equation were

**BC-1 inlet:** \[ c = c_o \quad (13) \]

**BC-2 outlet:** \[ \frac{\partial c_n}{\partial n} = 0 \quad (14) \]

**BC-3 wall:** \[ \nu_w - D \left( \frac{\partial c}{\partial n} \right) = \dot{m} \quad (15) \]

where $c_o$ is the LDL concentration in the bulk flow, $\nu_w$ is the filtration velocity of LDL across the vessel wall ($\nu_w = 4 \times 10^{-8} \text{m/s}$), and $c_w$ is the concentration of LDLs at the
luminal surface of the artery. Suffice n indicated the direction normal to the boundary, and \( \hat{n} \) was assumed to be 0.

The results of velocity profiles for model 1 showed at the entrance the axial velocity profile was flat, at the front part of the ascending aorta (slice A) the flow was skewed toward the inner aortic wall and remained the same till the midway of the ascending aorta (slice B). At the entrance of the aortic arch (slice C), skewness of the flow shifted toward between the inner wall and the posterior wall, and the distribution of axial velocity became relatively uniform there. This uniformity was enhanced at the middle part of the aortic arch (slice D) and the skewness of the flow shifted to the posterior wall. At the exit of aortic arch (slice E) the axial velocity became uneven with a clearer skewing of the velocity profile toward the anterior wall. Finally the skewness shifted to the outer wall of the descending aorta. In general, the position of the peak axial velocity rotated clockwise in the aortic arch. The velocity profile for model 2 was similar to that for model 1, but it was greater at the location beyond the branches. For model 3 blood flow was highly skewed toward the inner wall, and this effect was moving along the median plane to the outer wall in the descending aorta. For model 4 the velocity profile resembled that of model 3, but blood velocity was smaller. In addition only in model 4 the reversed axial flow was detected in the middle part of the aortic arch.
For model 1 they observed secondary flows at the inner and posterior walls of the ascending aorta, and a small vortex near the anterior wall (slice A). At the middle portion of the ascending aorta, the secondary flow was strengthened with two vortexes formed along the anterior and posterior walls (slice B). In the aortic arch the secondary flows became stronger and the anterior wall vortex grew bigger. In the arch (slices C, D and E) it was observed the formation of helical flow, which was then attenuated in the descending aorta (slice F). The secondary flow pattern for model 2 was very similar to model 1, hence, the branches on the aortic arch had little effect on the formation of secondary flows in the aorta. The simulation in model 3 showed that without torsion the helical flow which was observed in the aortic arch would not appear in a curved tube. The secondary flow pattern in model 4 resembled that in model 3, except that at slice E, there were formed four vortexes instead of two. Thus, the aortic taper seemed that it could stabilize the flow blood in the aorta.

The distribution of luminal surface LDL concentration was estimated for the four models. For model 1 the highest surface LDL concentration ($c_w$) in the whole aorta was observed at the area from the distal end of the aortic arch to its apex (region B). The second highest $c_w$ was in the entry area of the brachiocephalic artery (region A), whereas $c_w$ in the neighboring areas of the other two branches (region D) was relatively low. The third highest $c_w$ was located in region C of the descending aorta.

![Diagram of the aorta showing the distribution of luminal surface LDL concentration](image)

*Fig. 10. Distribution of luminal surface LDL concentration in the 4 models, showing that in model 1, regions A, B, and C have relatively severe polarization of LDL, region D with its neighboring areas including 2 of the branches are spared from high LDL polarization and the ascending aorta has an even distribution of luminal surface LDL concentration with relatively low concentration of LDLs at the luminal surface of the artery ($c_w$). $c_w$: LDL concentration in the bulk flow.*
The distribution of the luminal surface of LDL concentration in model 2 was similar to the one of model 1, except in the descending aorta where $c_w$ was generally lower for model 2. For model 3 the distribution of $c_w$ along the outer wall of the ascending aorta was uneven when compared to model 2 and in the descending aorta LDL concentration polarization turned more severe. Finally for model 4 the effect of the absence of aortic taper led to a great increase in luminal surface LDL concentration. Especially in all the inner wall of the descending aorta, where $c_w$ was 50% higher than the LDL concentration in the bulk flow, $c_o$.

As it is shown in figure 11 the two lowest WSS areas were located at regions A and B, respectively and the highest WSS area was located at the flow divider of the brachiocephalic left common carotid branch. There were two other places where the WSS were relatively high, at the entrance of the left subclavian artery and along the anterior wall of the aortic arch.

It was showed an adverse correlation between the distribution of luminal surface LDL concentration and the distribution of WSS. However the $c_w$ distribution seems to be affected by other factors too, such as flow pattern itself. An indicative example of that is region D where although it was the area with the lowest $c_w \equiv c_o$, the WSS there, was not the highest in the aorta. For model 2 the WSS distribution resembled that of model 1, except in the descending aorta where WSS was generally higher compared to model 1 leading to reduced $c_w$. The removal of aortic torsion resulted in a bigger area of WSS in the ascending aorta.
causing an uneven distribution of $c_w$ there, and the decrease of the value of WSS in the descending aorta causing the increase of $c_w$. Finally without arterial taper the WSS was generally lower when compared to the other models leading to enhanced $c_w$ in the whole model.

As a conclusion, the helical flow in the aorta has an important physiological significance in the circulation. The helical flow induced by aortic torsion may stabilize the flow of blood in the aorta, reducing the flow disturbance and suppressing the separation of flow. Thus the polarization of LDLs in the aortic arch decreases. Moreover the helical flow seems to suppress severe polarization of LDLs at the entrances of the three arterial branches of the arch, hence, protecting them from atherogenesis. It was found out that another important feature of the aorta is the taper, which can stabilize the blood flow. Without this feature the helical flow might not move beyond the arch and reaching the beginning part of the descending aorta. The last feature is the branches of the aorta. Without them, the wall shear stress was higher and the surface concentration of LDL in the descending aorta was generally lower.

Another study was done by G.C Bourantas, E.D. Skouras, V.C. Loukopoulos, V.N. Bourganos and G.C. Nikiforidis [56] to investigate the effects of the two-phase blood flow behavior and the pulsation of blood flow on the distribution of luminal surface of LDLs concentration and oxygen flux along the wall of the human aorta. The flow simulation was based on the three-dimensional incompressible Navier - Stokes and continuity equations (1), (2). First, the blood was assumed as an incompressible and Newtonian fluid. Then, the non-Newtonian blood flow assumption is applied using the Carreau model, in order to calculate the blood viscosity with increased accuracy.

The mass transport of LDLs was modeled by the convection-diffusion equation. The diffusion coefficient of LDLs in blood was obtained from the Stokes–Einstein equation, which is dependent on the blood viscosity which, in turn, is a function of shear rate. The transport of oxygen was modeled by convection–diffusion equations coupled with oxygen transport by hemoglobin. A time-dependent flat inlet flow velocity profile was used for the pulsatile flow simulation (see Fig. 31). The time-average velocity was applied to the steady flow simulation. In this study the blood flow was considered as two-phase. The principle difference compared with a single-phase model is the appearance of the volume fraction for each phase, as well as mechanisms for the exchange of mass, momentum, and energy between the phases. In the two-phase Newtonian hemodynamic model, the continuous phase is plasma, which can be
considered a Newtonian fluid to a very good approximation. The predominant particulate phase suspended in the plasma consists of red blood cells (RBCs) having a hematocrit, $H$, or volume fraction, $\varepsilon_{RBC}$, in the normal range of 35-50%. Platelets and white blood cells constitute an aggregate volume fraction less than 1%.

The continuity equation for each phase ($k=\text{plasma, RBCs}$) was given by:

$$\frac{\partial (\rho_k \varepsilon_k)}{\partial t} + \nabla \cdot (\rho_k \varepsilon_k \mathbf{u}_k) = 0 \quad (16)$$

where $\rho$ is the density, $\varepsilon$ is the volume fraction, $t$ is time and $\mathbf{u}$ is the velocity. The sum of the volume fractions for each phase must sum to one.

The momentum equation for each phase ($k=\text{plasma, RBCs}$) was given by:

$$\frac{\partial (\rho_k \varepsilon_k \mathbf{u}_k)}{\partial t} + \nabla \cdot (\rho_k \varepsilon_k \mathbf{u}_k \mathbf{u}_k) = \rho_k \varepsilon_k \mathbf{g} - \varepsilon_k \nabla p + \nabla \cdot \varepsilon_k \mathbf{\tau}_k + \sum_{l \neq k} \beta_{kl} (\mathbf{u}_l - \mathbf{u}_k) + \mathbf{F}_k \quad (17)$$

The terms of the RHS of Eq. (17) represent gravity $\mathbf{g}$, shear stress $\mathbf{\tau}_k$, pressure $p$, drag force between the carrier fluid and particulates, and external forced $\mathbf{F}$, such as virtual mass, rotational and shear lift, electric and magnetic (usually not present). In the drag force, $k$ and $l$ represent plasma or RBCs, and $\beta_{kl}$ are the interphase momentum exchange coefficients.

In the two-phase model, blood was assumed flowing in the center of the vessel with viscosity of the blood 4 cP and 45% hematocrit. The rest of the fluid volume was considered as thin phase located near the vessel walls, having low velocity and approximately unit viscosity (1cP). Predefined average pressure values were used as inlet and outlet boundary conditions for both the RBCs and the plasma, and a zero-slip velocity boundary condition was employed for both RBCs and plasma. No mass transfer was considered between phases. The model was reconstructed human aorta based on CT images from a healthy individual. They found out that the distribution of WSS in the aorta for both Newtonian and non-Newtonian simulations was quite similar, but the values of WSS were significantly different for the two cases. As it concerns the LDL transport, it was estimated that the non-Newtonian blood flow had a little effect when compared to the Newtonian behavior in most parts of the aorta but it significantly affected regions with high luminal surface LDL concentration by increasing $c_w$ through the shear dependent diffusivity. In addition it was observed that the non-Newtonian nature of blood had little effect on the oxygen transport in most parts of the aorta, except for the regions
with low oxygen flux, where oxygen flux could be suppressed significantly. On the contrary, it was found out that the pulsatile flow could enhance oxygen flux notably in most areas, especially in those predisposed to flow disturbance. However the pulsation had a little effect on the surface LDL concentration in most regions of the aorta, except the regions with high luminal $c_w$, where there $c_w$ was reduced considerably. As conclusion, the shear thinning non-Newtonian nature of blood may be treated as pro-atherogenic, while the pulsation of blood flow may be considered anti-atherogenic.

2 Introduction to fundamental medical principles

2.1 Blood

Blood is an essential, life-sustaining fluid. Total blood volume correlates with the (fatfree) body mass (Table below) and average 3.6 L in women and 4.5 L in men. The blood’s tasks include transporting various substances (O$_2$, CO$_2$, nutrients, metabolic products, vitamins, electrolytes, etc.), the transport of heat (heating, cooling), signal transmission (hormones), and buffering as well as defense against foreign materials and microorganisms [19].

| Total Blood | Blood volume (L) | $\leq 0.041 \cdot \text{kgKG} + 1.53$; $\geq 0.047 \cdot \text{kgKG} + 0.86$ |
| Erythrocytes | Hematocrit ($\text{L eryth}$/L$_\text{blood}$) | $\leq 0.40 - 0.54$; $\geq 0.37 - 0.47$ |
| Leukocytes | Number ($10^9$/L$_\text{blood} = 10^9$/μL$_\text{blood}$) | $\geq 4.6 - 6.2$; $\leq 4.2 - 5.4$ |
| Thrombocytes | Hemoglobin (g/L$_\text{blood}$) | $\leq 140 - 180$; $\geq 120 - 160$ |
| Plasmproteins | Number ($10^9$/L$_\text{blood} = 10^9$/μL$_\text{blood}$) | $3 - 11$ (of which 63% granuloc., 31% lymphoc., 6% monoc.) |
| | (g/L Serum) | $\geq 170 - 360$; $\leq 180 - 400$ |
| | (g/L Serum) | $66 - 85$ (of which 55–64% albumin) |

Table. 1. Correlation between total blood and body mass

The blood cells (Table above) are involved in this, the erythrocytes being responsible for O$_2$ and CO$_2$ transport and a part of pH buffering. Among the leukocytes, the neutrophil granulocytes (neutrophils) are responsible for nonspecific immune defenses, and the monocytes and lymphocytes for specific immune reactions. The thrombocytes (platelets) are
important for hemostasis. The ratio of blood cell volume to total blood volume is called *hematocrit* (Hct). More than 99% of the Hct is made up of erythrocytes [19].

In the fluid phase of blood, called plasma, electrolytes, nutrients, metabolic products, vitamins, gases and proteins are held in solution.

The blood cells are formatted in the *red bone marrow* in adults and in the *spleen and liver* in the fetus. These contain *pluripotent stem cells* that, under the effect of hematopoietic growth factors, differentiate into myeloid, erythroid, and lymphoid precursor cells. These stem cells reproduce in such a way that their stock is maintained throughout life. While the lymphocytes that originate from the lymphoid precursors still require further *maturation* (partly in the thymus, partly in the bone marrow) and are later on formed in the spleen and the lymph nodes (*lymphopoiesis*), all other precursor cells proliferate and mature up to their final stage in the bone marrow (*myelopoiesis*), until they finally pass from there into the blood. The three most important types of blood cells, as mentioned before, are erythrocytes, leukocytes and *thrombocytes* (platelets) [19].

Erythrocytes (red blood cells [RBCs]) reach the bloodstream as nucleus-free and mitochondria-free, disc-shaped cells. They can be severely deformed within the blood capillaries, which greatly facilitate both their passage and the exchange of substances and gases with the surrounding tissues. Erythrocytes contain a large amount of hemoglobin (Hb). Hemoglobin is the iron-containing oxygen transport metalloprotein in the red blood cells of all vertebrates as well as the tissues of some invertebrates. Hemoglobin in the blood carries oxygen from the respiratory organs (lungs) to the rest of the body (i.e. the tissues) where it releases the oxygen to burn nutrients to provide energy to power the functions of the organism, and collects the resultant carbon dioxide to bring it back to the respiratory organs to be dispensed from the organism [19].

Leukocytes or white blood cells are cells of the immune system involved in defending the body against both infectious disease and foreign materials. The body possesses *nonspecific*, *congenital*, and (interlinked) *specific, acquired, or adaptive* immune defenses against microorganisms (bacteria, viruses, fungi, parasites) and against macromolecules identified as being “foreign”. Fragments of pathogens and large-molecular foreign bodies represent antigens to which the specific defense system reacts with the *activation* and *proliferation* of monospecific T and B lymphocytes (T cells and B cells). B cells differentiate to plasma cells which produce antibodies. It is their task to: 1) neutralize, 2) opsonize antigens, and 3) activate the complement system. These highly specific mechanisms of the immune defense serve to *recognize* the particular antigens whose elimination is then accomplished in a
relatively nonspecific way. In addition, the antigen (with B and T memory cells) is held “in memory”. Nonspecific defense is served by dissolved or humoral defense substances, such as lysozymes and complement factors as well as phagocytes, i.e., especially macrophages (formed in tissue from immigrating monocytes) and neutrophil leukocytes, or neutrophils. The phagocytes take up the pathogen (endocytosis), damage it and “digest” the pathogen with their lysosomal enzymes (lysis) \[19\].

Thrombocytes are nucleus-free cytoplasmic bud-like particles split off from the megakaryocytes in bone marrow. They circulate in the blood of mammals and are involved in hemostasis, leading to the formation of blood clots \[19\].

### 2.2 Heart and Circulation

The circulatory system is an organ system that passes nutrients (such as amino acids, electrolytes and lymph), gases, hormones, blood cells, etc. to and from cells in the body to help fight diseases, stabilize body temperature and pH, and to maintain homeostasis. This system may be seen strictly as a blood distribution network, but some consider the circulatory system as composed of the cardiovascular system, which distributes blood, and the lymphatic system, which distributes lymph. The main components of the human cardiovascular system are the heart, blood, and blood vessels \[23, 47\].

![Fig.12 The circulatory system](image)
2.3 Anatomy of the heart

The heart is a hollow, four-chambered, muscular organ that is specialized for pumping blood through the vessels of the body. It weighs about 5% of the body weight. The heart is located in the mediastinum, where it is enclosed in a loose-fitting serous sac called the pericardial sac or parietal pericardium. The pericardial sac consists of two layers. The inner, serous layer of the pericardial sac of the secretes pericardial fluid the lubricates the surface of the heart, and the outer fibrous layer of the pericardial sac has the protective and separative and pulmonary vessels. About two-thirds the heart is to the left (the subject’s left) of the midsagittal plane with its apex or cone-shaped end, pointing downward, in contact with diaphragm. The base of the heart is the broad superior end, where the large attached.

The heart wall consist of three layers the epicardium, the myocardium and the endocardium.

The epicardium is made of serous membrane of connective tissue, covered with epithelium and including blood capillaries, lymph capillaries and nerve fibers and it acts as a lumbricative outer covering.

The myocardium is cardiac muscle tissue, separated by connective tissues and including blood capillaries, lymph capillaries and nerve fibers. It functions as a contractile to eject blood from the heart chambers.

The endocardium is a serous membrane of epithelium and connective tissues, including elastic and collagenous fibers blood vessels and specialized muscle fibers. It works as a lubricative inner lining of the chambers and valves.

The heart is a four chambered, double pump. It consists of upper-right and upper left atria, that pulse together, and lower-right and lower-left ventricles, which also contract together. The atria are separated by the thin muscular interatrial septum, while the ventricles are separated by the thick, muscular, interventricular septum. Two antroventricular valves, the bicuspid and tricuspid valves, are located between the chambers of the heart and semilunar valves are present at the bases of the two large vessels (the pulmonary trunk and the aorta) that leave the heart [48].
2.4 Cardiac cycle

The resting heart rate is 60–80 beats per minute. A cardiac cycle therefore takes roughly 1 second. It can be divided into four distinct phases: (I) contraction phase and (II) ejection phase, both occurring in systole; (III) relaxation phase and filling phase (IV), both occurring in diastole. At the end of phase IV, the atria contract (phase IVc). Electrical excitation of the atria and ventricles precedes their contraction. The cardiac valves determine the direction of blood flow within the heart, e.g., from the atria to the ventricles (phase IV) or from the ventricles to the aorta or pulmonary artery (phase II). All cardiac valves are closed during phases I and III. Opening and closing of the valves is controlled by the pressures exerted on the two sides of the valves [19].

Near the end of ventricular diastole, the sinoatrial (SA) node emits an electrical impulse, marking to the beginning of the P wave of the ECG (Fig.14-A1-phase IVc). This results in atrial contraction (Fig.14-A4) and is followed by ventricular excitation (QRS complex of the ECG). The ventricular pressure then starts to rise (Fig.14 A2-blue line) until it exceeds the atrial pressure, causing the atroventricular valves (mitral and tricuspid valves) to close. This marks the end of diastole [19].

The isovolumetric contraction phase now begins. With all valves are closed, the ventricles now contract, producing the first heart sound (Fig.14-A6), and the ventricular pressure increases rapidly. The semilunar valves (aortic and pulmonary valves) now open because the
pressure in the left ventricle (Fig.14-A3-blue line) exceeds that in the aorta (black broken curve) at and the pressure in the right ventricle exceeds that in the pulmonary artery.

During the ejection phase, the pressure in the left ventricle and aorta reaches a maximum of ca. 120 mmHg (systolic pressure). In the early phase of ejection (IIa or rapid ejection phase), a large portion of the stroke volume (SV) is rapidly expelled (Fig.14-A4) and the blood flow rate reaches a maximum (Fig.14-A5).

Myocardial excitation subsequently decreases (T wave of the ECG, Fig14.A1) and ventricular pressure decreases (the remaining SV fraction is slowly ejected, phase IIb) until it falls below that of the aorta or pulmonary artery, respectively. This leads to closing of the semilunar valves, producing the second heart sound (Fig.14-A6).

The first phase of ventricular diastole or isovolumetric relaxation now begins (phase III; ca. 60 ms). The atria have meanwhile refilled, mainly due to the suction effect created by the lowering of the valve plane during ejection. As a result, the central venous pressure (CVP) decreases (Fig.14-A3, falls from c to x). The ventricular pressure now drops rapidly, causing the atrioventricular valves to open again when it falls short of atrial pressure.

The filling phase now begins (phase IV; ca.500ms at rest). The blood passes rapidly from the atria into the ventricles, resulting in a drop in CVP (Fig.14-A3, point y). Since the ventricles are 80% full by the first quarter of diastole, this is referred to as rapid ventricular filling (Fig.14-phaseIVA; A4). Ventricular filling slows down (phase IVb), and the atrial systole (phase IVc) and the awave of CVP follows (Fig14-A2,3). At a normal heart rate, the atrial contraction contributes about 15% to ventricular filling. When the heart rate increases, the duration of the cardiac cycle decreases mainly at the expense of diastole, and the contribution of atrial contraction to ventricular filling increases.

The heart beats produce a pulse wave (pressure wave) that travels through the arteries at a specific pulse wave velocity (PWV): the PWV of the aorta is 3–5 m/s, and that of the radial artery is 5–12 m/s. PWV is much higher than the blood flow velocity (V), which peaks at 1 m/s in the aorta and increases proportionally to (a) decreases in the compliance of aortic and arterial walls and (b) increases in blood pressure[19].
Fig. 14 Action phases of the heart (cardiac cycle)
2.5 Aorta

Aorta is the blood vessel carrying blood from the heart to all the organs and other structures of the body. At the opening from the left ventricle into the aorta is a three-part valve that prevents backflow of blood from the aorta into the heart. The aorta emerges from the heart as the ascending aorta, turns to the left and arches over the heart (the aortic arch), and passes downward as the descending aorta. The left and right coronary arteries branch from the ascending aorta to supply the heart muscle. The three main arteries branch from the aortic arch and give rise to further branches that supply oxygenated blood to head, neck, upper limbs, and upper part of the body. The descending aorta runs down through the posterior centre of the trunk past the heart, lungs, and esophagus, through an opening in the diaphragm, and into the abdominal cavity [24].

In the chest the aorta, as it descends, gives off branches to the pericardium, the sac that encloses the heart, the connective tissues of the lungs, the bronchi, which carry air from the windpipe into the lungs, the esophagus, part of the diaphragm and the chest wall [24].

In the abdominal cavity the aorta gives off a number of branches, which form an extensive network supplying blood to the stomach, liver, pancreas, spleen, small and large intestines, kidneys, reproductive glands, and other organs. At the level of the fourth lumbar vertebra, which is about even with the top of the hip bones, the aorta divides into the right and left common iliac arteries, the principal arteries to the legs [24].
The aorta is an elastic artery, and as such is quite distensible. Mean arterial blood pressure is highest in the aorta and mean arterial pressure diminishes across the circulation from aorta to arteries to arterioles to capillaries to veins back to atrium: the difference between aortic and right atrium pressure accounts for blood flow in the circulation [25].

The aorta consists of a heterogeneous mixture of smooth muscle, nerves, intimal cells, endothelial cells, fibroblast-like cells, and a complex extracellular matrix. The vascular wall consists of several layers known as the tunica adventitia, tunica media, and tunica intima. The intima is a monolayer of endothelial cells that lines the lumen of the vessel. This layer is in direct contact with the flowing blood in the aorta. The media is a layer of smooth muscle cells and elastic lamina. The smooth muscle component does not dramatically alter the diameter of the aorta but rather serves to increase the stiffness and viscoelasticity of the aortic wall when activated. The adventitia is an outer layer of fibrous tissue that stabilizes the aorta against the surrounding organs. These elastic fibers allow the expansion of the aorta due to pressure of blood flowing through it [5].

Aortic pressure is highest at the aorta and becomes less pulsatile and lower pressure as blood vessels divide into arteries, arterioles, and capillaries such that flow is slow and smooth for gases and nutrient exchange [25].
2.6 Fluid Dynamic – Basic principles

A Fluid is a substance which deforms continuously, or flows, when subjected to shearing forces. If a fluid is at rest there are no shearing forces acting. All forces must be perpendicular to the planes which they are acting. When a fluid is in motion shear stresses are developed if the particles of the fluid move relative to one another. When this happens adjacent particles have different velocities. If fluid velocity is the same at every point then there is no shear stress produced: the particles have zero relative velocity.

Consider the flow in a pipe in which water is flowing. At the pipe wall the velocity of the water will be zero. The velocity will increase as we move toward the centre of the pipe. This change in velocity across the direction of flow is known as velocity profile and shown graphically in the figure below:

Fig.16 Structure of aorta
Because particles of fluid next to each other are moving with different velocities there are shear forces in the moving fluid i.e. shear forces are normally present in a moving fluid. On the other hand, if a fluid is a long way from the boundary and all the particles are travelling with the same velocity, the velocity profile would look something like this:

Fig. 17. Velocity profile in a pipe

and there will be no shear forces present as all particles have zero relative velocity [20].

2.6.1 Compressible vs. incompressible flow

All fluids are compressible to some extent, that is, changes in pressure or temperature will result in changes in density. However, in many situations the changes in pressure and temperature are sufficiently small that the changes in density are negligible. In this case the flow can be modeled as an incompressible flow. Otherwise the more general compressible flow equations must be used.
Mathematically, incompressibility is expressed by saying that the density \( \rho \) of a fluid parcel does not change as it moves in the flow field, i.e.

\[
\frac{D\rho}{Dt} = 0
\]  
(17)

where \( D/Dt \) is the substantial derivative, which is the sum of local and convective derivatives. This additional constraint simplifies the governing equations, especially in the case when the fluid has a uniform density.

For liquids, whether the incompressible assumption is valid depends on the fluid properties (specifically the critical pressure and temperature of the fluid) and the flow conditions (how close to the critical pressure the actual flow pressure becomes) [21, 22].

2.6.2 Viscous vs. inviscid flow

Viscous problems are those in which fluid friction has significant effects on the fluid motion. The Reynolds number, which is a ratio between inertial and viscous forces, can be used to evaluate whether viscous or inviscid equations are appropriate to the problem. Stokes flow is flow at very low Reynolds numbers, \( Re < 1 \), such that inertial forces can be neglected compared to viscous forces. On the contrary, high Reynolds numbers indicate that the inertial forces are more significant than the viscous (friction) forces. Therefore, we may assume the flow to be an inviscid flow, an approximation in which we neglect viscosity completely, compared to inertial terms. This idea can work fairly well when the Reynolds number is high. However, certain problems such as those involving solid boundaries may require that the viscosity be included. Viscosity often cannot be neglected near solid boundaries because the no-slip condition can generate a thin region of large strain rate (known as Boundary layer) which enhances the effect of even a small amount of viscosity, and thus generating vorticity. The standard equations of inviscid flow are the Euler equations. One often used model, especially in computational fluid dynamics, is to use the Euler equations away from the body and the boundary layer equations, which incorporates viscosity, in a region close to the body. The Euler equations can be integrated along a streamline to get Bernoulli’s equation. When the flow is everywhere irrotational and inviscid, Bernoulli’s equation can be used throughout the flow field. Such flows are called potential flows [21, 22].
2.6.3 **Steady vs. unsteady flow**

When all the time derivatives of a flow field vanish, the flow is considered to be a **steady flow**. Steady-state flow refers to the condition where the fluid properties at a point in the system do not change over time. Otherwise, flow is called unsteady. Whether a particular flow is steady or unsteady, can depend on the chosen frame of reference. For instance, laminar flow over a sphere is steady in the frame of reference that is stationary with respect to the sphere. In a frame of reference that is stationary with respect to a background flow, the flow is unsteady.

Turbulent flows are unsteady by definition. A turbulent flow can, however, be statistically stationary.

The random field $U(x, t)$ is statistically stationary if all statistics are invariant under a shift in time. This roughly means that all statistical properties are constant in time. Often, the mean field is the object of interest, and this is constant too in a statistically stationary flow. Steady flows are often more tractable than otherwise similar unsteady flows. The governing equations of a steady problem have one dimension fewer (time) than the governing equations of the same problem without taking advantage of the steadiness of the flow field \([21, 22]\).

2.6.4 **Laminar vs. turbulence flow**

Turbulence is flow characterized by recirculation, eddies, and apparent randomness. Flow in which turbulence is not exhibited is called laminar. It should be noted, however, that the presence of eddies or recirculation alone does not necessarily indicate turbulent flow—these phenomena may be present in laminar flow as well. Mathematically, turbulent flow is often represented via a Reynolds decomposition, in which the flow is broken down into the sum of an average component and a perturbation component.

It is believed that turbulent flows can be described well through the use of the Navier–Stokes equations. Direct numerical simulation (DNS), based on the Navier–Stokes equations, and makes it possible to simulate turbulent flows at moderate Reynolds numbers. Restrictions depend on the power of the computer used and the efficiency of the solution algorithm. The results of DNS have been found to agree well with experimental data for some flows.

Most flows of interest have Reynolds numbers much too high for DNS to be a viable option,\[^5\] given the state of computational power for the next few decades. Any flight vehicle large enough to carry a human (L > 3 m), moving faster than 72 km/h (20 m/s) is well beyond the limit of DNS simulation (Re = 4 million). Transport aircraft wings (such as on an Airbus A300 or Boeing 747) have Reynolds numbers of 40 million (based on the wing chord). In order to solve these real-life flow problems, turbulence models will be a necessity for the
foreseeable future. Reynolds-averaged Navier–Stokes equations (RANS) combined with turbulence provides a model of the effects of the turbulent flow. Such a modeling mainly provides the additional momentum transfer by the Reynolds stresses, although the turbulence also enhances the heat and mass transfer. Another promising methodology is large eddy simulation (LES), especially in the guise of detached eddy simulation (DES)—which is a combination of RANS turbulence modeling and large eddy simulation/21, 22/.

2.7 Properties of the blood flow

The geometry and the velocity gradients in every blood flow problem we study define the assumptions we make of the blood’s behavior as a fluid. Generally in arteries with diameters over 100 μm (such as aorta), blood can be considered as homogenous fluid. The reason is that the diameter and the distance of the red blood cells are greatly smaller than the diameter of the artery. For mediocre values of velocity such as the ones of a big artery, like aorta the Newtonian behavior of the fluid is a good assumption. The Newtonian behavior can also be assumed in problems with more complex geometry. In cases of arteries with diameter over 1 mm the viscosity of the blood can be considered independent of the diameter. The blood flow in the aorta can be assumed as laminar, except a part of it near the heart /26/.

Fig.19. Velocity of the blood vessels
3 Three-dimensional modeling of vascular structures

3.1 Introduction

Vascular modeling requires the wall position of the vessels to be extracted from medical images. In this chapter first it is introduced a technique for polygonal surface construction and clinical visualization from 3D images. Then parametric and implicit deformable models are referred, which are more advanced techniques and which are able to provide 3D models of the desired accuracy. Anatomic data on vascular structures in detail are provided by angiographic image acquisition techniques. The current techniques used for 3D representations are not suited for accurate geometric analysis and CFD computation, but are orientated to produce high-quality visual feedback.

3.2 Image acquisition

The basic imaging modalities used in clinical practice for the acquisition of 3D anatomy of vascular segments are mentioned.

3.2.1 Computed Tomography

Computed tomography (CT) is a technique for imaging cross-sections of a subject using series of X-ray measurements taken at different angles around the subject. The intensity of X-rays passing through the imaged body is attenuated according to the density of tissues encountered, so that the line integral of tissue density is measured. For each angle the source and the detector rotate around the subject and collect a row of X-ray measurements. The reconstructed image, contains attenuation values, called CT numbers and expressed by Hounsfield units (HU). Water is conventionally represented by zero (0) CT number.

\[
CT = K \frac{\mu - \mu_W}{\mu_W} \quad (18)
\]
where \( \mu \) is the linear attenuation coefficient of the voxel, \( \mu_w \) the linear attenuation coefficient of water and \( K \) a numerical constant quantity called magnifying or contrast factor. It usually has the value 1000.

As a result fat has negative values; connective tissue has low positive and calcium which has high positive CT numbers. The recent scanners used in clinical practice allow in-plane resolution \(< 0.5\text{mm}\) and slice thickness \(< 1\text{mm}\) of anatomical structures in a single breathhold. For vascular imaging contrast is used via intravenous injection. The HU values of the contrast enhanced images are positive values between that of connective tissue and that of calcium. For this reason an artery affected by atherosclerosis will be surrounded by connective tissue values and low contrast (lipid pools) and high contrast (calcified plaques), as we can see in figure 20.

![Fig. 20. Contrast-enhanced CT angiography image of the carotid bifurcations of a patient affected by severe atherosclerosis.](image_url)
CT angiography presents two main disadvantages, the X-ray dose absorbed by the patient and the contrast agents employed which are iodinated and could lead to intolerance problems [27, 28].

3.2.2 Magnetic Resonance

Magnetic Resonance (MR) is based on the measurement of relaxation times of the net magnetization vectors induced in tissues when a magnetic field at a given frequency is applied. More accurately the Larmor frequency of the applied field is equal to the one of the magnetic momentum of nuclei which tends to orientate along the direction of the field. In medical imaging the Larmor frequency of hydrogen nuclei is usually employed. When the applied magnetic field is terminated the magnetic momentum of hydrogen nuclei returns to equilibrium, and the net magnetization equals to zero again. The relaxation processes are exponential, and their time constants $T1$ and $T2$, which are characteristic of different tissues, can be measured. As a result, images represent proton density, $T1$, $T2$ or a combination of these quantities. Magnetic field gradients are used for spatial information, the purpose of these field gradients are slice selection (or volume selection) and position encoding within the selected slice (or volume). A fundamental advantage of MR is that until now no harmful effects of magnetic fields have been proven to be. Moreover in MR the orientation of imaging planes can be changed by the direction of gradients. The recent MR techniques allow <1mm resolutions within a single breathhold. However speed and resolution are higher in Computed Tomography. There are a few modalities available for 3D MR vascular imaging. The ideal technique for non-invasively acquisition of vessel geometry and wall thickness, both at the same time, is the black-blood technique. This technique produces high resolution images in which the vascular lumen is black and the vessel wall can be identified. However plaque-
mimicking artifacts can occur in regions of slow flow. Contrast agents can also be used to modify the magnetic properties of blood. For example gadolinium (Gd-DTPA) shortens T1 of blood, yielding fast high-contrast high-resolution acquisitions of vessel lumens, with image quality independent of blood motion. The disadvantage of using contrast agents is that it may occur intolerance problems, but compared to the substances used in CT angiography they are well tolerated. MR can also measure velocity components with phase contrast techniques. Acquisition is performed usually in straight vessels because in regions of complex flow patterns velocity measurements can be affected by artifacts [27, 28].

3.2.3 Ultrasound

Ultrasound imaging has been used in clinical practice for more than half a century. It is noninvasive, relatively inexpensive, portable, and has an excellent temporal resolution. The basic principle of ultrasound imaging is simple. A propagating wave partially reflects at the interface between tissues with different acoustic impedance. If these reflections are measured as a function of time, information is obtained on the position of the tissue if the velocity of the wave in the medium is known. Piezoelectric transducer is responsible for the generation of ultrasounds and the reception of the reflected waves. Ultrasound imaging is used not only to visualize morphology or anatomy but also to visualize function by means of blood and myocardial velocities. The principle of velocity imaging was originally based on the Doppler effect and is therefore often referred to as Doppler imaging. It accounts for the frequency shift of waves reflecting over flowing red blood cells. As a result velocity can be

![Maximum intensity projection of a Gd-DTPA enhanced MR angiography of the abdominal aorta of a 78-years-old patient.](image)
measured in real-time with high temporal resolution in a specific volume. However image resolution of ultrasound is quite lower compared to CT or MR angiography. Ultrasound is also limited to superficial vessels [27, 28].

![B-mode image of a normal heart in a four-chamber view showing the two ventricles (LV left ventricle; RV right ventricle), the two atria (LA left atrium; RA right atrium) and the origin of the aorta (outflow tract). Besides the anatomy of the whole heart, the morphology of the valves (e.g., mitral valve) can be visualized. (Courtesy of the Department of Cardiology).](image)

**3.2.4 Image storing format**

The acquired 3D images (usually stacks of 2D images) must be transferred to calculators for processing. The standard used for communication and storage of medical image data is the DICOM (DIgital COmmunication in Medicine) format. This format contains a great volume of information, the medical image data and information related to the acquisition, such as patient’s and investigator’s data, image number, image position, image resolution, acquisition time, acquisition modality and scan parameters [27].

**3.3 Contouring**

It is known that different tissues correspond to different gray levels. Contouring is a technique used for the reconstruction of 3D models of the vessel wall, which creates a surface in
correspondence with a given gray level of the acquired 3D image volume (Fig. 24). Contouring can be performed on 2D images constituting the 3D volume as well as directly on 3D images. The most commonly used contouring algorithm is the Marching Cubes [27].

![Image](image.png)

Fig. 24. Examples of contouring on a synthetic image (left) and on a angio-CT image. The contouring levels were chosen manually.

### 3.3.1 Marching Cubes

We assume a set of one voxel-wide cubes defined by eight neighboring voxels. We can identify the cubes intersected by the isosurface of interest as the ones in which some of the voxels are labeled *above* and the rest *below*. The concept of the Marching Cube algorithm is basically the fact that the *above* and *below* voxels of each cube can be partitioned by a set of triangles whose vertices lie on cube edges in different ways, called *cases*. For this reason a table of cases can be made containing all topological configurations of *above* and *below* voxels and triangles partitioning them, independent of the exact position of triangle vertices along cube edges (Fig. 25). In the contoured image the cubes are constructed, for each one of them surface construction can be performed, using the suitable surface configuration from the case table. The exact position of triangle vertices is computed by linear interpolation of voxel scalar values on cube vertices. The surface produced by marching through the whole image volume is therefore first-order sub-voxel accurate. For some cases there is a possibility of constructing more than one surface which partition *above* and *below* voxels, called *complementary cases*.

The complementary cases are generated from the base case by swapping *above* and *below* voxels. This possibility gives rise to ambiguity in surface construction, because an arbitrary
choice among ambiguous cases can change the surface topology (i.e. holes). The problem of ambiguity is usually resolved with the introduction of a set of rules which choose the suitable case according to the configuration of surrounding cubes [27, 29].

3.3.2 Limitations of isosurface extraction

In angiographic 3D images marching cubes algorithm can be applied to construct the isosurface located over the transition from vessel lumen to the surrounding tissue. The marching cubes technique gives good results for radiological visualization but for Computational Fluid Dynamics (CFD) and accurate geometric analysis presents some limitations. The most significant limitation is that the level of contouring affects the resulting surface which is a choice usually made by the operator. A fixed scalar level for vessel lumen boundary is not able to be defined because of the variability in gray-levels. This happens mainly because of the dependence of grey levels on acquisition modalities and on the physical features of the patient. In addition this variability is more intense near interfaces leading to great changes in geometric and topological features of the resulting surface even when the contouring level changes slightly, as it is shown in figure 26 and 27.

Fig. 25. Marching cube cases
Finally another limitation is the inability of reconstructing specific vessels of interest without their branching vessels and the absence of calcified plaques on the reconstructed CT images without first editing the source images [27].
3.4 Parametric deformable models

Absolute correspondence between tissues and gray levels is required in radiologic images in order to construct the isosurface of vessels by applying the marching cubes algorithm. Unfortunately the absence of this correspondence leads to construct models based on image features. Parametric deformable models belong to this category. These models are evolving in the image space and their deformations are described from the Lagrangian point of view [30].

3.4.1 Snakes

“Snakes” are active contours; they are a solution in the field of 2D image segmentation and shape retrieval [31]. A snake is a parameterized curve evolving on the basics of image features and internal constraints. Its description, in a Lagrangian frame, can be given as a function

\[ C = \frac{U}{s} \times R^+ \rightarrow R^2 \]  \hspace{1cm} (19)

where \( U \in R \) (e.g. \( U = [0,1] \)) and \( S \in U \) is curve parameterization. The evolution equation for snakes can be derived from the minimization of an energy functional

\[ E_{snakes}(C) = E_{smooth}(C) + E_{images}(C) \]  \hspace{1cm} (20)

where

\[ E_{smooth}(C) = \int_0^1 [w_1 |C_s|^2 + w_2 |C_{ss}|^2]ds \]  \hspace{1cm} (21)

is internal deformation energy (the first term controls snake tension, having the effect of reducing snake length, and the second term controls snake rigidity, producing a smoothing effect), and

\[ E_{image}(C) = \int_0^1 w_3 P(C)ds \]  \hspace{1cm} (22)
is driving energy, \( P(x) \) being a scalar potential function taking into account image features (e.g. \( P(x) = |\nabla I(x)| \), where \( I(x) \) is the scalar field of image gray values) and user-defined landmarks.

In order to minimize the functional \( E(C) \), the active contour \( C(s) \) must satisfy the Euler-Lagrange equation.

\[
-w_1 \frac{\partial C_s}{\partial s} + w_2 \frac{\partial^2 C_{ss}}{\partial s^2} + w_3 \nabla P(C) = 0 \tag{23}
\]

Instead of using an energy gradient descent algorithm to find a configuration which minimizes \( E_{snake} \), we can equally make the snake evolve in time toward a configuration satisfying the Euler-Lagrange equation, producing the evolution equation.

\[
\frac{\partial C}{\partial t} = w_1 C_{ss} - w_2 C_{ssss} - w_3 \nabla P(C) \tag{24}
\]

In 2D closed curves shrink because of their curvature evolving into a circle before transforming into one point. Snakes often start as closed lines surrounding regions of interest. Afterwards they shrink until driving energy makes them approach and stop on desired features. In some problems snakes can also start as small circles inside the areas of interest expand until image features are encountered. This strategy is more preferable in blood vessel modeling. Snakes are very popular in 3D vessel reconstruction. First vessel contours are extracted from 2D images, which constitute the 3D volume. Next the obtained profiles are used for the reconstruction of the 3D vessel surface. However it must be first assumed that the vessel wall is where the maximal difference of grey levels between the outside and the inside of the vessel lumen is. Then the evolution equation is used in this region to acquire a set of 2D contours. Although snakes for vessel modeling is a simple technique and it is characterized by high control on the results it has some limitations. Specifically due to the absence of alignment between the image slice direction and the vessel axis when segmentation of 3D structures is performed on 2D images, shape retrieval problems may occur. In addition the requirement of an operator to initialize the process makes the technique time demanding, especially in cases of complex branching vessels [27].
3.4.2 Balloons

The 3D equivalent of snakes is known as balloons and is described by the following equation:

\[ S: U \times U \times R^+ \rightarrow \mathbb{R}^3 \]  \hspace{1cm} (25)

where \( U \in \mathbb{R} \) and \( r, s \in U \) is surface parameterization, which we will assume orthonormal, so that

\[
\begin{align*}
|S_r| &= |S_s| = 1 \\
S_r \cdot S_s &= 0
\end{align*}
\]  \hspace{1cm} (26)

In 2D closed curves shrink because of their curvature evolving into a circle before transforming into one point. This doesn’t always apply in 3D where a surface does not always evolve into a sphere before transforming into one point. Therefore it is more preferable to inflate the 3D surface using an internal pressure term. This approximation is more easily applied because it only requires to define the center and the radius of a sphere located inside the 3D object, which is to be reconstructed. As a result the function of energy for balloons contains one more term, which is related to the balloon inflation.

\[ E_{balloon}(S) = E_{infl}(S) + E_{smooth}(S) + E_{image}(S) \]  \hspace{1cm} (27)

The corresponding evolution equation is

\[ \frac{\partial S}{\partial t} = w_1 G(S)N + w_2 (S_{rr} + S_{ss}) - w_3 \nabla P(S) \]  \hspace{1cm} (28)

where \( G(S) \) is scalar inflation speed (constant or depending on image features), \( N \) is outward surface normal and \( (S_{rr} + S_{ss}) \) is an average second-order smoothing term. The most important advantage of using balloons in vessel modeling is the direct processing in 3D geometry, which increases the speed and does not require an operator. Unfortunately in the present of great deformations, reparameterization has to be performed otherwise the excessive surface distortion would prevent the balloon from detecting the geometry of smaller structures [27].
3.5 Level Sets

Implicit models are scalar functions defined in $\mathbb{R}^2$ or $\mathbb{R}^3$ whose isosurface of level $k$ is the model of interest, and can be used instead of parametric deformable models. This model has no limitations on topology and great deformations, in contrast to the parametric deformable models. In the following paragraphs it is described the transition from the Lagrangian, which is used in solid mechanics to the Eulerian, which is used in fluid mechanics, related to model description. In this model the surface motion is described through the evolution of scalar field values at fixed points in space. Finally the level sets technique is introduced, which deals with the evolution equations for deformable implicit models, as well as some numerical details and the application of level sets to vessel modeling [27].

3.5.1 Localization of the evolution equation for deformable surfaces

A surface evolving in time $S: \mathbb{R}^2 \times \mathbb{R}^+ \rightarrow \mathbb{R}^3$ can be represented as an isosurface of level $k$, or $k$ level set, of a time-dependent scalar function $F: \mathbb{R}^3 \times \mathbb{R}^+ \rightarrow \mathbb{R}$, so that

$$S(t) = \{x | F(x, t) = k\} \quad (29)$$

Since $S$ remains the $k$ level set of $F$ over time,

$$\frac{\partial F(S, t)}{\partial t} = -\nabla F(S, t) \cdot \frac{\partial S}{\partial t} = -\left|\nabla F(S, t)\right| \frac{\partial S}{\partial t} \cdot N \quad (30)$$

where $N = \frac{\nabla F}{|\nabla F|}$ is the outward normal to level sets, supposed that the embedding function has lower values inside and higher values outside the model.

The equation (29) represents the embedding of an evolution equation for a parametric deformable surface $S(r, s, t)$, such as equation (28) into the evolution equation of a scalar function $F(x, t)$ whose $k$ level set is $S(t)$ [32]. The main advantage of this approach is that the embedded version of $S(t)$ relies only on local geometric properties of $F(x, t)$. Finally in order
to achieve localization the embedded version of the second part of the equation (28) must be expressed as differential expression on \( F(x, t) \), assuming that the \((r, s)\) parameterization of surface \( S(r, s, t) \) is orthonormal, i.e. follows equation 26.

The inflation term \( w_1 G(S)N \) in equation (4.10) rearranged to

\[
|\nabla F| w_1 G(x)N.N = w_1 G(x)|\nabla F| (31)
\]

The \( S_{rr} \) and \( S_{ss} \) of the smoothing term \( (S_{rr} + S_{ss}) \) of the equation (28) must be expressed as differential expressions on \( F(x, t) \). After calculations the final form of this term is given by the following equation

\[
|\nabla F| w_2 (S_{rr} + S_{ss}).N = -w_2 (F_{uu} + F_{vv}) = -2w_2 H(x)|\nabla F| (32)
\]

where \( H(x) \) is the mean curvature of level sets, which is invariant to rotations of the \((u, v)\) coordinates system within the tangent plane. The mean curvature of a surface at one point is defined as the mean value of the normal curvatures at the point, which in turn are the curvatures of the curve defined by the intersection of the surface with a plane perpendicular to each direction belonging to the tangent plane and passing in that point [27].

The last term, which is the driving term \( w_3 \nabla P(S) \), is rearranged to

\[
|\nabla F| w_3 \nabla P(x).N = w_3 \nabla P(x).\nabla F (33)
\]

Finally by collecting and summing the three previous terms, the localized level sets equation for \( F(x, t) \) yields:

\[
\frac{\partial F(x,t)}{\partial t} = -w_1 G(x)|\nabla F| + 2w_2 H(x)|\nabla F| + w_3 \nabla P(x).\nabla F (34)
\]
3.5.2 Level sets evolution equation

The equation (34) describes a deformable surface, such as a balloon following equation (28), embedded as a level set of a scalar field which is evolving in time. The greatest advantage of using this model instead of using the balloon model is that it can change its topology and deform without the need of reparameterization strategies. In addition when 3D images are processed, the equation (34) can be directly solved on the image. Next the inflation speed $G(x)$ and the attraction potential $P(x)$, which are image-based evolution terms are defined.

$$ G(x) = \frac{1}{1 + |\nabla I(x)|} \quad (35) $$

It is noted that when the image gradient increases the inflation speed decreases, which occurs near image features and

$$ P(x) = -|\nabla I(x)| \quad (36) $$

which defines the attraction potential areas. These two definitions are sufficient for 3D modeling of blood vessels from 3D angiographic images.

A slightly different form of equation 34 is

$$ \frac{\partial F(x,t)}{\partial t} = -w_1 G(x)|\nabla F| + 2w_2 G(x)H(x)|\nabla F| + w_3 \nabla P(x) \cdot \nabla F \quad (37) $$

where the second term in the right part of the equation is multiplied with $G(x)$, so that the smoothing effect is more intense in regions where the image gradient magnitude is low and less image features are present, while more surface details are allowed where $|\nabla I(x)|$ is higher [27].

3.5.3 Numerical approximation

One of the methods to solve equation 37 for blood vessel modeling reconstruction from 3D images is the numerical solution using finite difference method, with the image domain as structured grid for problem discretization. However some assumptions have to be made first. The equation (37) belongs to the class of Hamilton-Jacobi equations, with the following general form
\[
\frac{\partial F(x, t)}{\partial t} + \mathcal{H}(x, \nabla F(x, t)) = 0
\]  
(38)

In this particular case for level sets the Hamilton-Jacobi equation is taking the form

\[
\frac{\partial F(x, t)}{\partial t} = G(x, t) |\nabla F(x, t)|
\]  
(39)

which is a class of nonlinear hyperbolic partial differential equations. The equation is consider for the numeric approximation of the equation

\[
F(x, t + \Delta t) = F(x, t) + \frac{\partial F(x, t)}{\partial t} \Delta t
\]

\[
= F(x, t) + G(x, t) |\nabla F(x, t)| \Delta t
\]  
(40)

Unfortunately in hyperbolic equations the following problem may occur. After merging two level set fronts, a surface in which \(F(x)\) is not differentiated, may be produced. Because of the use of central two-sided finite differences in this region inaccurate results in the approximation of \(\nabla F(x)\) can be produced. This happens because of the calculation of the gradient value using the average value of the information from each side of first-order discontinuity. This inaccuracy can propagate to the other grid points in this area destabilizing the numerical solution. To move over this problem it is recommended the use of one-sided/upwind finite difference for the approximation of odd-order derivatives (proposed by Sethian et al. [29]). Specifically in the grid point \((i, j, k)\) on a grid of spacing \(h\), the central finite difference expression for the first derivative of \(F(x)\) is given by the Taylor expansion of \(F(x)\) around \(x_{ijk}\) up to the first order, resulting in

\[
F_x|_{x_{ijk}} \approx D_{ijk}^0 = \frac{F(i + 1, j, k) - F(i - 1, j, k)}{2h}
\]  
(41)

This expression contains contributions from both positive and negative directions. To separate them and take into account only the upstream contributions one-sided finite differences have to be applied. Upwind finite difference expressions for \(F_x|_{x_{ijk}}\) are
which are first-order accurate expressions.

It must be noted that the extension of equation 42 to the $y$, $z$ axes is straightforward.

However disadvantage of using one-sided derivatives occurs when the numerical viscosity is added to the hyperbolic equation. When the grid spacing tends to zero value ($h \to 0$), the solution converges to a specific solution, with a slow convergence while on the other hand for high order accuracy the convergence is faster [27].

Applying upwind finite difference for the level set approximation leads to

$$F(x, t + \Delta t) = F(x, t) - \left[ \max(G(x), 0) \nabla^+ + \min(G(x), 0) \nabla^- \right] \Delta t \quad (43)$$

where

$$\nabla^+ = \left[ \max(D_{ij,k}^+, 0)^2 + \min(D_{ij,k}^+, 0)^2 \right]^{1/2}$$

$$\max(D_{ij,k}^+, 0)^2 + \min(D_{ij,k}^+, 0)^2$$

$$\nabla^- = \left[ \max(D_{ij,k}^-, 0)^2 + \min(D_{ij,k}^-, 0)^2 \right]^{1/2}$$

$$\max(D_{ij,k}^-, 0)^2 + \min(D_{ij,k}^-, 0)^2$$

$$\max(D_{ij,k}^-)^2 + \min(D_{ij,k}^-)^2 \quad (44)$$

$$\max(D_{ij,k}^-)^2 + \min(D_{ij,k}^-)^2 \quad (45)$$
Finally in order $\Delta t$ from the equation $42$ to be stable, it must be equal or lower than a limit time step $[33]$. The limit time step is defined by the following equation:

$$\max\left(\frac{\partial F}{\partial t}\right) \leq \frac{h}{\Delta t}$$  \hspace{1cm} (46)

where the rate of change in the solution is not higher than the maximum velocity, modeled for a certain grid of spacing $h$. Substituting left-hand side with Equation $38$ yields a condition on $\Delta t$:

$$\Delta t \leq \frac{h}{\max (G(x, t)||\nabla F(x, t)||)}$$  \hspace{1cm} (47)

### 3.5.4 Sparse-field approach

As mentioned before the advantages of the embedding parametric deformable surface into a scalar function, are topology independence and the capability of presentation of great deformations. As a result a function which is defined on the whole image volume, it now needs to be described. Therefore the transition from model surface size to 3D image size increases the computational expensiveness and consequently makes difficult to have real time control on model evolution. To overcome this problem the sparse-field approach can be used (proposed by R.Whitaker – $[34]$). This method finds a set of voxels, called *active set*, which is intersected by the level set of interest (usually the 0 level set) at each time step. It also tracks two layers of voxels around the active set in order to compute the required derivatives (see figure 28).
Thus by applying this method the problem depends once again on model size and not on 3D image size. In addition the position of 0 level set can be evaluated from the function $F(x)$ and $\nabla F(x)$ of the voxels in the active set resulting to the sub-voxel accuracy computation of all differential and image-based quantities. The position is computed by Newton’s method with first order accuracy

$$\hat{x} = x - \frac{F(x)}{|\nabla F(x)|} N(x)$$

(48)

where $\hat{x}$ is the estimated zero-crossing position nearest to $x$.

At each time step $\tilde{t}$ the active voxels must have a value of $(x, \tilde{t}) \in \left[-\frac{1}{2} h, \frac{1}{2} h\right]$, where $h$ is the voxel spacing, since by definition the 0-level set must intersect the active voxels. The values of $F$ for two layers of voxels on each side of the active set are used because in equation 37 computation of up to second order derivatives is required. Voxel values for each inner (or outer) layer are computed from the value of the voxels of the neighboring layer by subtracting (or adding) $h$ to the minimum (or maximum) valued neighbor. For this reason, with the sparse-field method the embedding function is locally reinitialized to the signed distance function from $S(\tilde{t})$ at every iteration. In case a voxel in the active set is updated and its value becomes lower than $-\frac{1}{2} h$ (or greater than $+\frac{1}{2} h$), the voxel is moved from the active set to

Fig. 28. In the sparse field approach, level sets evolution is only computed for the set of voxels intersecting the contour of interest.
the adjacent inner (or outer) layer, and the opposite outer (or inner) layer voxel enters the active set. The same procedure is applied to the voxels belonging to the four neighbor layers.

3.5.5 **Application to blood vessel 3D modeling**

In blood vessel 3D modeling level sets can be used with great success with angiographic images showing the vessels of interest. Because of the inflation term of equation 37, single points turn into “spheres” which in the end merge with their neighbors. As the 0-level-set reaches the vessel wall the inflation term is deactivate while on the other hand the features attraction term is activated so that the 0 level set converge to gradient magnitude ridges. In case that level sets are initialized over an entire vessel tract with branches and vessels of different scales, a single set of parameters may not be enough for all scales. Moreover the use of one level sets evolution for a branching level tract has also difficulties because \( \Delta t \) depends on the gradient. More accurately if the gradient is low in one image region, \( \Delta t \) becomes smaller slowing down the evolution for the remaining part of the model. To overcome these problems the following approach is introduced. Using the dependence between evolution parameters and vessel scale, the level sets evolve into single vessels or into groups of vessels of similar scale. Next the functions \( F_i(x) \) from \( N \) single vessel evolutions merge and the model surface is extracted by contouring the merge function \( F_m(x) \) using the Marching Cubes algorithm. In the sparse field approach level sets represent the signed distance function from the 0 level set, with negative values inside the model and positive values on the rest of the

![Fig. 29. Level sets in the sparse field approach, showing the active layer and the four adjacent layers. The 0-level set is contoured.](image)
Therefore the merging of N level sets scalar field is done by selecting their minimum value

\[
F_m(x) = \min_{i \in [1,N]} F_i(x)
\]  

(49)

As a conclusion two important effects of this approach, where the evolution of level set is performed into vessels of similar scale must be noted. The first is the advantage of setting evolution parameters interactively with great ease. The second is that similar solution changes are computed over the area so that more adequate time step values are chosen by satisfying equation 46 resulting in the speeding up of evolution [27].

4 Computational hemodynamics

4.1 Introduction

The fluid dynamics problem is expressed by the Navier - Stokes equations. These are solved numerically by the finite element method. However the problem first has to be defined with appropriate rheologic parameters and boundary conditions. The purpose of this chapter is to present these concepts.

4.2 Navier - Stokes Equations

We make the assumptions that blood is a homogeneous, incompressible, constant-density and viscous fluid. We also don’t take in account gravity and thermal effects and vascular walls are modeled as non-permeable, rigid walls. As a result of these assumptions, the fluid dynamics problem is expressed by the conservation of mass and momentum, giving rise to the following system of partial different equations:

\[
\begin{aligned}
    u_{i,j} &= 0 \\
    \rho \frac{\partial u_i}{\partial t} + \rho u_j u_{i,j} &= -p_{,i} + \tau_{i,j,j}
\end{aligned}
\]  

(50)

where \(u_i\) the velocity, \(p\) is is pressure and \(\tau_{i,j}\) is the viscous stress tensors. The first equation describes mass conservation, and the second equation momentum conservation in the domain \(\Omega\). In Equation 4.1, \(u_i\) represents velocity, while \(p\) and \(\tau_{i,j,j}\) are pressure and viscous stress.
tensors respectively, which are the isotropic and deviatoric parts of the stress tensor 
\[ \sigma_{ij} = -p\delta_{ij} + \tau_{ij} . \]

The initial conditions of the system are:
\[ u_i(x_j, 0) = u_i^0(x_j) \quad x_j \in \Omega \quad (51) \]

And the boundary conditions are:
\[ u_i(x_j, t) = \bar{u}_i(x_j) \quad x_j \in \Gamma_D, t > 0 \quad (52) \]
\[ \sigma_i(x_j, t) = \sigma_{ij} n_i(x_j, t) = \bar{\sigma}_i(x_j) \quad x_j \in \Gamma_N, t > 0 \]

where \( n_j(x_j) \) is the outward oriented normal to the boundary, and \( \Gamma_D \) and \( \Gamma_N \) constitute a partition of the domain boundary \( \partial \Omega \).

For a viscous isotropic incompressible fluid the constitutive relation between \( \tau_{ij} \) and the strain rate tensor
\[ d_{ij} = \frac{1}{2} (u_{i,j} + u_{j,i}) \]
is of the type
\[ \tau_{ij} = 2\mu d_{ij} \quad (53) \]

where \( \mu \) is fluid viscosity. Replacing \( \tau_{ij} = 2\mu d_{ij} \) in equation of momentum conservation gives rise to the following equation:
\[ \rho \frac{\partial u_i}{\partial t} + \rho u_j u_{i,j} = -p_{,i} + \left[ \mu (u_{i,j} + u_{j,i}) \right]_{,j} \quad (54) \]

Assuming that viscosity is constant, the equation (3) turns into the Navier - Stokes equation:
\[ \rho \frac{\partial u_i}{\partial t} + \rho u_j u_{i,j} = -p_{,i} + \mu u_{i,jj} \quad (55) \]
We can see in the equation (4) a momentum time-dependence term $\rho \frac{\partial u_i}{\partial t}$, a momentum advection term $\rho u_j u_{i,j}$ and a momentum diffusion term $\mu u_{i,j,j}$.

### 4.3 Laws of blood rheology

The rheologic behavior of the fluid depends on the relationship between the deviatoric stress tensor and the strain rate tensor. We will mention two of blood rheology models.

#### 4.3.1 Newton’s Law

The Newton’s law is a linear relationship between stress and strain:

$$\tau_{ij} = 2\mu d_{ij} \quad (56)$$

where $\mu$ is constant and independent from kinematic quantities. In this model hematocrit and plasma protein concentration affects blood viscosity. If there is a blood sample analysis, blood viscosity can be determined with the data taken from the analysis and the use of empirical relationships [35, 36] as in [37]

$$\mu = \mu_{rel}\mu_{pl}$$

$$\mu_{rel} = (1 - 0.5H_t k)^{-2}$$

$$\log(k) = 1.3435 - 2.083H_t + 2.711H_t^2 - 0.6479H_t^3 \quad (57)$$

$$\mu_{pl} = 0.204 + 0.177C_p$$

where plasma protein concentration $C_p$ is expressed in g/dl and plasma viscosity $\mu_{pl}$ in cPoise. Otherwise, the blood viscosity takes the value of 3.5 centipoise [27]. The Newton’s law model has better result in large vessels e.g. aorta. Perktold et al. [38] pointed out how the errors deriving from employing a Newtonian model for blood yield non essential differences in flow characteristics and wall shear stress distributions.

#### 4.3.2 Carreau’s law

In domains with low shear rates and complex shear thinning blood rheology must be modeled accurately.
Models like this are named generalized Newtonian models and unlike the Newtonian model, the viscosity is not constant but it is a function of a shear rate:

$$\dot{\gamma} = \sqrt{2d_{ij}d_{ij}}$$  \hspace{1cm} (59)$$

take the name of generalized Newtonian models. A popular generalized Newtonian model is represented by the power law model [39], expressed by

$$\mu = \mu_0 K \gamma^{n-1}$$  \hspace{1cm} (60)$$

where $K$ is a constant. The power-law models the shear-thinning behavior for $n \leq 1$, but yields unphysical behavior for low and high shear rates, so that more sophisticated models are preferred, such as Casson’s [38].

One of the most used rheologic models for blood is Carreau’s law [39], expressed by the following equation:

$$\mu = \mu_\infty + (\mu_0 - \mu_\infty)(1 + K^2 \gamma^2)^{\frac{n-1}{2}}$$  \hspace{1cm} (61)$$

where $\mu_0$ and $\mu_\infty$ are low and high shear rate asymptotic values, and parameters $K$ and $n$ control the transition region. Parameter $\mu_\infty$ can be obtained with the same method used for viscosity in the Newtonian model. The other parameters can be derived by fitting experimental data [27].

4.3.3 Newtonian and non Newtonian fluids

4.3.3.1 Newtonian fluid

Even among fluids which are accepted as fluids there can be wide differences in behavior under stress. Fluids obeying Newton’s law where the value of $\mu$ is constant are known as Newtonian fluids. If $\mu$ is constant the shear stress is linearly dependent on velocity gradient. This is true for most common fluids [20].
4.3.3.2 *Non Newtonian fluid*

Fluids in which the value of $\mu$ is not constant are known as non-Newtonian fluids and there are several categories of these. These categories are based on the relationship between shear stress and the velocity gradient (rate of shear strain) in the fluid. These relationships can be seen in the graph below for several categories [20].

![Graph showing shear stress versus rate of shear strain](image)

Each of these lines can be represented by the equation

$$\tau = A + B \left( \frac{\delta u}{\delta y} \right)^n$$

(62)

where $A$, $B$ and $n$ are constants. For Newtonian fluids $A = 0$, $B = \mu$ and $n = 1$.

There is also one more - which is not real, it does not exist - known as the ideal fluid. This is a fluid which is assumed to have no viscosity. This is a useful concept when theoretical solutions are being considered - it does help achieve some practically useful solutions [20].
4.4 Boundary Conditions

The fluid dynamic problems require appropriate boundary conditions. Blood flow and wall shear stress patterns mainly depend on domain geometry. However inlet velocity profiles and flow waveform shapes affect wall shear stress distributions. These two effects are more intense when the flow’s Reynolds and Womersely numbers are high. Reynolds and Womersely numbers are given by the following equations:

\[ Re = \frac{\rho DU}{\mu} \]  \hspace{1cm} (63)

where D and U are the spatial dimension and velocity modulus, \( \mu \) is the viscosity and \( \rho \) the intensity of the fluid.

And

\[ Wo = \frac{D}{2} \sqrt{\frac{\omega}{\mu}} \]  \hspace{1cm} (64)

where \( \omega \) is the pulsation of the fluid, D is the spatial dimension and \( \mu \) is the viscosity of the fluid.

Reynolds number (Re) is a dimensionless number that gives a measure of the ratio of inertial forces to viscous forces and consequently quantifies the relative importance of these two types of forces for given flow conditions. They are also used to characterize different flow regimes, such as laminar or turbulent flow. Laminar flow occurs at low Reynolds numbers (Re<2300), where viscous forces are dominant, and is characterized by smooth, constant fluid motion. Turbulent flow occurs at high Reynolds numbers (Re>4000) and is dominated by inertial forces, which tend to produce chaotic eddies, vortices and other flow instabilities [40].

Womersely number (Wo) represents the ratio between transient inertial to viscous forces [27]. Boundary conditions (Equation 52) are velocity profiles or surface traction force on the inflow and outflow sections and zero velocity for the wall. Nevertheless it is difficult to acquire information about the inflow and outflow velocity distributions over the boundary even with the most recent acquisition techniques. Therefore velocity profiles for Newtonian fluids in circular-section rigid straight vessels under steady and pulsatile flow conditions are measurements from centerlines or section-averaged velocity measurement given by analytic solutions. If one of the following parameters velocity, pressure or flow rate is known then the
velocity profiles are expressed by Poiseuille equation in the case of steady flow condition and Womersley equation in the case of pulsatile flow conditions \[41\] when either centerline velocity, pressure or flow rate is known.

Another source to impose the boundary conditions of the reconstructed arterial domain are the physiologic conditions published in literature. However this approach has the disadvantage that the input flow waveform can vary significantly in morphology and magnitude, because of the in vivo changes of hemodynamic conditions (heart beat, flow rates) \[27\].

### 4.4.1 Patient - specific boundary conditions

The possibility of performing velocity measurements inside large arteries in vivo and non-invasively constitutes an important resource for the definition of patient specific boundary conditions. As pointed out above, the acquired flow waveforms have to be interpreted as a sample of a variety of conditions which depend on physical activity and posture. Moreover, clinical examinations are typically performed in the supine position, e.g. for technological reasons, which may have an influence on the resulting measurements. However, the prescription of boundary conditions acquired from the same subjects for which geometric modeling is performed constitutes a necessary step toward the study patient-specific local hemodynamics at a clinical level, because it accounts for the inter-subject variable unmodeled part of the circulation. Coupling such acquired data to mathematical models which simulate intra-subject physiologic variability will contribute to complete such clinical framework. As mentioned before there are a few in vivo acquisition techniques to provide data for the imposition of the boundary conditions. The two most commonly used non-invasive techniques are Doppler ultrasound and phase-contrast magnetic resonance employed to acquire velocity information for the prescription of patient-specific boundary conditions \[27\].

### 4.4.2 Acquisition of boundary conditions by Doppler ultrasound

This imaging modality is very good to characterize velocity waveforms for a number of reasons. First of all because of its temporal resolution (<15 ms) and its non-invasiveness. It is also less expensive compared to the other 3D imaging modalities. Finally unlike the other modalities the acquisition of data is not necessary to take place in supine position because of the geometry of the scanner.

Unfortunately there are disadvantages too. One of them is the position of the vessel (deep vessels). Also data from intracranial vessels cannot be acquired by Doppler ultrasound.
Instead, intracranial ultrasound can be used to provide an approximate measure of flow rates [27].

### 4.4.3 Acquisition of boundary conditions by phase-contrast magnetic resonance

Phase-contrast magnetic resonance angiograph provide images of the velocity distribution for a completely cardiac cycle [42]. This distribution is reconstructed from several frames acquired from different cardiac cycles [43]. The phase contrast acquisition sequences starts with the heart beat. Two images are produced from MR scan, the magnitude image which depicts anatomy and the phase image which contains velocity information. Then the magnitude image is segmented, so that the lumen is identified to derive velocity information in the same region from the phase image. As every imaging modality artifacts may be in MR images too. Therefore artifacts must be reduced so that phase contrast MR could be a useful velocimetry tool. First of all imaged sections must be located in regions of fully develop flow, otherwise it is possible to measure incorrect values of velocity (bifurcations, bendings) [44]. Misalignment between the imaging plane and the plane normal to flow direction can lead to errors in measured velocity values and distribution [27].

### 4.5 Finite-element approximation of Navier - Stokes equations

Once the problem has been defined with appropriate rheologic parameters and boundary conditions, the Navier-Stokes equations must be solved numerically. Several methods for the approximation of Navier-Stokes equations exist, the most popular being finite volumes (FV) [46] and finite elements (FE) [33].

We multiply the partial differential equation terms by arbitrary test functions $v$ and $q$ defined in proper test spaces $V$ and $Q$.

\[
\begin{align*}
\left\{ \begin{array}{l}
b(u) = 0 \\
a(u) + b(p) = f
\end{array} \right.
\end{align*}
\]

\[
\begin{align*}
\left\{ \begin{array}{l}
b(u, q) = 0 \\
a(u, v) + b(v, p) = (f, v)
\end{array} \right. 
\end{align*}
\]

(65)
Then we integrate the equation over the whole domain and apply the Green-Gauss theorem to shift one order of differentiation from the unknown function to the test function in second-order terms (i.e. momentum diffusion term in Navier-Stokes equation). The fluid dynamics problem is basically to define the functions \( v \in V \) and \( q \in Q \) so that the integral equations are satisfied \( \forall \, v \in V \) and \( \forall \, q \in Q \), where \( \alpha(\cdot) \) and \( b(\cdot) \) are proper integral expressions.

### 4.5.1 Spatial discretization

Equation (65) is in its integral form, but it is still an infinite dimensional problem. The continuum is now represented by functional spaces \( V \) and \( Q \) and not by \( \mathbb{R}^3 \). Using Galerkin method the problem is converted from infinite to finite dimension. To achieve that, approximate solutions \( u_h, p_h \) in finite functional subspaces \( V_h, Q_h \) of the original spaces \( V, Q \) must be found.

\[
\begin{align*}
u_h(x) &= \sum_{j=1}^{N_h} u_j \varphi_j(x) \\
p_h(x) &= \sum_{k=1}^{M_h} p_k \psi_k(x)
\end{align*}
\] (66)

Every function defined in \( V_h \) and \( Q_h \) can be expressed as a linear combination of finite numbers \( N_h \) and \( M_h \) of basics functions \( \varphi_j(x) \) and \( \psi_k(x) \), which are the only parameters now that depend on the spatial coordinate, because \( V_h \) and \( Q_h \) are finite. The coefficients \( u_j \) and \( p_k \) are the unknowns of the discrete problem, the nodal values of the solution. Then we substitute equation (6) into Navier-Stokes equations and the following equation is formed:

\[
\begin{align*}
\begin{cases}
b(u_h q_h) = 0 \\
\alpha(u_h, v_h) + b(v_h, p_h) = (f, v_h)
\end{cases}
\end{align*}
\] (67)

\( \forall \, v_h \in \mathcal{V}_h \) and \( \forall \, q_h \in \mathcal{Q}_h \).
The equation (67) is an algebraic nonlinear system in the \( N_h + M_h \) unknowns \( u_j \) and \( q_k \). When the finite functional subspaces, into which \( u_h \) and \( p_h \) are looked for as the space of continuous piecewise polynomial functions. It must be noted that the degree of the polynomials determines the order of the method’s accuracy. Due to this fact in FEM (Finite Element Method) the physical domain has to be discretized into elements whose nodes take the nodal value \( u_j \) and \( q_k \). Also the basis functions \( \varphi_j (x) \) and \( \psi_k (x) \) define the interpolation functions of FEM. It must be mentioned that the subspaces \( V_h \) and \( Q_h \) in a way to avoid that a \( q_h \) exists such that for every \( v_h \), \( b(v_h, q_h) = 0 \) [27].

4.5.2 Solution Technique

The equation (67) is a nonlinear algebraic system of equations with unknown variables \( v_h \) and \( q_h \) produced by finite element discretization must be solved to give the solutions. One solution technique is the commercial solver FIDAP [45] with a pressure-projection segregated solution strategy. For each iteration the pressure’s approximated value is computed from the momentum equation using the velocity field from the previous iteration. The next step is the computation of the velocity components from the momentum equation using the available field variables. Finally due to the mass conservation equation the computed velocity field must be adjusted in such a way to satisfy it. It must also be mentioned that time integration is needed to complete the Navier - Stokes approximation framework [27].

5 Methods

Computational fluid dynamics (CFD) have been used to investigate blood flows in the aorta due to their high resolution and straightforward representation of flow parameters.

Numerical solutions for blood pressure and velocity were obtained from Navier – Stokes and continuity equations using flow simulation software (ANSYS 13-\( \text{ANSYS} \)) and then various hemodynamic properties such as velocity profiles, paths of fluid elements, and wall shear stresses were evaluated.
5.1 Numerical approaches

We carried out a computational study on realistic, patient specific, three dimensional aorta geometry to investigate the interrelationship among the sites of low wall shear stress (shear rate), the sites of high LDL surface concentration, and the sites of atherosclerotic wall thickening in the vessel.

5.1.1 Analysis of blood flow

The flow simulation is based on the three-dimensional incompressible Navier-Stokes and continuity equations:

\[
\rho(\overline{u} \cdot \nabla)\overline{u} + \nabla p - \mu \Delta \overline{u} = 0
\]
\[
\nabla \cdot \overline{u} = 0
\]

For the non-Newtonian blood flow simulation, the Carreau model is used to calculate the blood viscosity.

The Navier–Stokes and mass conservation equation governing the fluid motion were solved using CFD commercial code ANSYS CFX.

5.1.2 Analysis of Mass Transport

LDLs are spherical molecules with diameter of 21-26 nm and densities of 1.006-1.063×10³ kg/m³. In flowing blood, such small macromolecules are transported both passively by being carried by the flowing blood itself and also voluntarily by molecular diffusion. Therefore, steady state mass transport of LDL in flowing blood can be described by

\[
v \cdot \nabla C - D \nabla^2 C = 0
\]

where C is the concentration of LDL, and D is the diffusivity of LDL. Using the Stokes–Einstein equation, the diffusivity of LDL was estimated to be 5 x 10⁻⁶ mm² / s in blood at a body temperature of 37°C. The velocity vector, v, was obtained by solving Navier–Stokes equations which govern blood flow.

Specifically, the mass transport of LDLs in blood is modeled by the convection–diffusion equation. The diffusion coefficient of LDLs in blood is obtained from the Stokes–Einstein equation, which is depended on blood viscosity that is a function of shear rate.
The transport of oxygen is modeled by convection–diffusion equation coupled with oxygen transport by hemoglobin.

5.1.3 Pulsatile Flow

A time-dependent flat inlet flow velocity profile is used for the pulsatile flow simulation (see fig. 31). The time-average velocity was applied to the steady flow simulation.

\[ \text{Fig. 31. Inlet flow waveforms of the aorta} \]

5.1.4 Multiphase hemodynamic model

In the two-phase Newtonian hemodynamic model considered here, the continuous phase is plasma, which can be considered a Newtonian fluid to a very good approximation [51]. The predominant particulate phase suspended in the plasma comprises the red blood cells (RBCs) having a hematocrit, \( H \), or volume fraction, \( \varepsilon_{RBC} \), in the normal range of 35–50\%. Platelets and white blood cells constitute an aggregate volume fraction less than 1\%. In the present work, RBCs are modeled more realistically since they control the blood rheology. This is important when modeling monocyte adhesion.

The continuity equation for each phase \( (k = \text{plasma, RBCs}) \) is given by

\[
\frac{\partial (\rho_k \varepsilon_k)}{\partial t} + \nabla \cdot (\rho_k \varepsilon_k \mathbf{u}_k) = 0
\]  

(4)

where \( \rho \) is density, \( \varepsilon \) is volume fraction, \( t \) is time, and \( \mathbf{u} \) is velocity. The sum of the volume fractions for each phase must sum to one. The momentum equation for each phase
\[(k = \text{plasma, RBCs})\text{ is given by}
\]

\[
\frac{\partial (\rho_k \varepsilon_k \mathbf{u}_k)}{\partial t} + \nabla \cdot (\rho_k \varepsilon_k \mathbf{u}_k \mathbf{u}_k) = \rho_k \varepsilon_k \mathbf{g} - \varepsilon_k \nabla p + \nabla \cdot \varepsilon_k \mathbf{t}_k + \sum_{l=1}^{\infty} \beta_{kl} (\mathbf{u}_l - \mathbf{u}_k) + \mathbf{F}_k \quad (5)
\]

The terms of the RHS of Eq. (5) represent gravity \(\mathbf{g}\), shear stress \(\tau_k\), pressure \(p\), drag force between the carrier fluid and particulates, and external forces \(\mathbf{F}\), such as virtual mass, rotational and shear lift, electric, and magnetic. In the drag force, \(k\) and \(l\) represent plasma or RBCs, and \(\beta_{kl}\) are the interphase momentum exchange coefficients.

### 5.2 Numerical implementation

In the present work, by using the ANSYS ICEM software we intervened in STL files. The STL segmented data, obtained from the imaging software, were fully imported into the advanced mesher, where all the segments of irrelevant surface portions were cut-off, leaving only the ones representing the aorta. Additional inlet and outlet surfaces were properly mounted at each opening of the arterial segment, with normal surface along the main flow direction. These inlet and outlet mouths were carefully attached to the respective wall segments and tightly tailored to the adjacent wall STL surfaces, in order to have consistent representation of the blood flow. Then we created the grid-mesh. All simulations for the idealized rigid aorta were carried out using the 3D computational domain. The problem of accurately reconstructing 3D models of vascular segments from volumetric angiographic images was addressed. The discretization of the domain volume into small elements is necessary. Meshing was achieved using also ANSYS ICEM software.
CFX (Computational Fluid Dynamics) was the last step before we run the code. At this stage we put the physical problem and set the boundary conditions on the ‘‘parts’’ (areas on the structure where created on the previous stage) and the flow-conditions of the material (blood). Specifically, we defined the blood as a fluid and then described the hemodynamic conditions in the human aorta.

The numerical solution methods use a finite volume, unstructured mesh, staggered grid arrangement. These scalar variables are located at the cell centers and the vector variables are located at the cell boundaries. The momentum equations are solved using a staggered mesh, while the continuity equations are solved using a donor cell method.

**Case 1: Comparison of non-Newtonian model with the Newtonian one under steady flow condition**

- Single Phase Newtonian model under steady flow

It was assumed that an arterial wall is rigid and blood is an incompressible Newtonian fluid with a viscosity \( \mu = 4 \text{ centipoises} \) and density \( \rho = 1050 \text{ kg m}^{-3} \). Under these assumptions, a steady flow of blood can be described by the continuity and Navier – Stokes equations.
## Domain Physics Table:

<table>
<thead>
<tr>
<th>Type</th>
<th>Fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Created Material</td>
</tr>
<tr>
<td><strong>Materials</strong></td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td></td>
</tr>
<tr>
<td>Fluid Definition</td>
<td>Material Library</td>
</tr>
<tr>
<td>Morphology</td>
<td>Continuous Fluid</td>
</tr>
<tr>
<td><strong>Settings</strong></td>
<td></td>
</tr>
<tr>
<td>Buoyancy Model</td>
<td>Non Buoyant</td>
</tr>
<tr>
<td>Domain Motion</td>
<td>Stationary</td>
</tr>
<tr>
<td>Reference Pressure</td>
<td>1 [atm]</td>
</tr>
<tr>
<td>Additional Variable</td>
<td>Concentration</td>
</tr>
<tr>
<td>Kinematic Diffusivity</td>
<td>5 [m^2 s^-1]</td>
</tr>
<tr>
<td>Option</td>
<td>Transport Equation</td>
</tr>
<tr>
<td>Turbulence Model</td>
<td>Laminar</td>
</tr>
</tbody>
</table>

Table 2: Single Phase Newtonian model under steady flow - Domain Physics

## Boundary Physics Table:

<table>
<thead>
<tr>
<th><strong>Boundary Inlet</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
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</tr>
<tr>
<td>Location</td>
<td>INLET</td>
</tr>
<tr>
<td><strong>Settings</strong></td>
<td></td>
</tr>
<tr>
<td>Additional Variables</td>
<td>Concentration</td>
</tr>
<tr>
<td>Additional Variables value</td>
<td>0.0013 [g cm^-3]</td>
</tr>
<tr>
<td>Option</td>
<td>Value</td>
</tr>
<tr>
<td>Flow regime</td>
<td>Subsonic</td>
</tr>
<tr>
<td>Mass and Momentum</td>
<td>Normal speed</td>
</tr>
<tr>
<td>Normal Speed</td>
<td>0.1 [m s^-1]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>OUTLET</td>
</tr>
<tr>
<td>Location</td>
<td>OUTLET</td>
</tr>
<tr>
<td><strong>Settings</strong></td>
<td></td>
</tr>
<tr>
<td>Flow Regime</td>
<td>Subsonic</td>
</tr>
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<td>Mass and Momentum</td>
<td>Average Static Pressure</td>
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<td>Pressure Profile Bend</td>
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<tr>
<td>Relative Pressure</td>
<td>0 [Pa]</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Boundary Wall</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>WALL</td>
</tr>
<tr>
<td>Location</td>
<td>AORTA</td>
</tr>
<tr>
<td><strong>Settings</strong></td>
<td></td>
</tr>
<tr>
<td>Additional Variables</td>
<td>Concentration</td>
</tr>
<tr>
<td>Option</td>
<td>Zero Flux</td>
</tr>
<tr>
<td>Mass and Momentum</td>
<td>No slip wall</td>
</tr>
</tbody>
</table>

Table 3: Single Phase Newtonian model under steady flow - Boundary Physics
• Single Phase non - Newtonian model under steady flow

It was assumed that an arterial wall is rigid and blood is a non - Newtonian fluid with density \( \rho = 1050 \text{ km}^{-3} \). For the non-Newtonian blood flow simulation, the Carreau model is used to calculate the blood viscosity.

*Carreau Model:* In this model, the relation between viscosity and shear strain rate \( \dot{\gamma} \), can be written as:

\[
\lambda_f = 3.313 \text{ s}; \quad \text{zero strain viscosity, } \mu_0 = 0.056 \text{ Pa.s}; \quad \text{infinite strain viscosity, } \mu_\infty = 0.00345 \text{ Pa.s}; \quad \text{and the empirical exponent, } n = 0.3568 [62].
\]

A non – Newtonian and Newtonian 3-D flow model for the description of hemodynamic in vascular vessels was developed. It used the principles of mass, momentum, and energy conservation based on the generalization of the well known Navier – Stokes Equations.
Domain Physics Table:

<table>
<thead>
<tr>
<th>Domain - Blood Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
</tr>
<tr>
<td>Location</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Materials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
</tr>
<tr>
<td>Fluid Definition</td>
</tr>
<tr>
<td>Morphology</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Settings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buoyancy Model</td>
</tr>
<tr>
<td>Domain Motion</td>
</tr>
<tr>
<td>Reference Pressure</td>
</tr>
<tr>
<td>Additional Variable</td>
</tr>
<tr>
<td>Kinematic Diffusivity</td>
</tr>
<tr>
<td>Option</td>
</tr>
<tr>
<td>Turbulence Model</td>
</tr>
<tr>
<td>Turbulent Wall Functions</td>
</tr>
</tbody>
</table>

Table 4: Single Phase non – Newtonian model under steady flow - Domain Physics

Boundary Physics Table:

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<tr>
<th>Boundary Inlet</th>
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</thead>
<tbody>
<tr>
<td>Type</td>
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<tr>
<td>Location</td>
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<tr>
<th>Settings</th>
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<tr>
<td>Additional Variables</td>
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<tr>
<td>Additional Variables value</td>
</tr>
<tr>
<td>Option</td>
</tr>
<tr>
<td>Flow Direction</td>
</tr>
<tr>
<td>Flow Regime</td>
</tr>
<tr>
<td>Mass and Momentum</td>
</tr>
<tr>
<td>Mass Flow Rate</td>
</tr>
<tr>
<td>Turbulence</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Boundary Outlet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
</tr>
<tr>
<td>Location</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Settings</th>
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</thead>
<tbody>
<tr>
<td>Flow Regime</td>
</tr>
<tr>
<td>Mass and Momentum</td>
</tr>
<tr>
<td>Relative Pressure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Boundary Blood Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
</tr>
<tr>
<td>Location</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Settings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional Variables</td>
</tr>
<tr>
<td>Option</td>
</tr>
<tr>
<td>Mass and Momentum</td>
</tr>
<tr>
<td>Wall Roughness</td>
</tr>
</tbody>
</table>

Table 5: Single Phase non – Newtonian model under steady flow - Boundary Physics
Case 2: Comparison of pulsatile non-Newtonian flow simulation with steady non-Newtonian flow simulation

- Single Phase non-Newtonian model under steady flow
The simulation was the same as described before

- Single Phase non-Newtonian model under pulsatile flow
It was assumed that an arterial wall is rigid and blood is a non-Newtonian fluid with density \( \rho = 1050 \text{ km}^3 \). For the non-Newtonian blood flow simulation, the Carreau model is used to calculate the blood viscosity as mentioned before.

The blood flow was assumed to be periodic. We used a sinusoidal flow waveform of 4.3 [g/s] ± 2.6 \( \sin (\frac{2\pi t}{t_p}) \) t [g/s] at the inlet with a period of \( t_p \) of 0.345 s and \( t = 0.005s \). The parameter \( t/t_p \) was used to describe a particular time in a cycle. The term \( t \) represents the time in seconds and \( t_p \) is the period of the flow cycle [62].

Then we introduced the equations that govern the flow pulsation in Ansys CFX:

Flow Rate = 4.3 [g/s] ± 2.6 \( \sin (\frac{2\pi t}{t_p}) \) t [g/s]

Furthermore, the model of turbulence was the Shear Stress Transport, because the pulsation of flow creates vortices. So this problem could not be mentioned in a laminar flow. Tests were made for laminar flow, but the results were incorrect.

Fig. 35. Shear Stress Transport
Domain Physics Table:

<table>
<thead>
<tr>
<th>Domain - Blood Domain</th>
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<tbody>
<tr>
<td><strong>Type</strong></td>
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<td><strong>Location</strong></td>
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<td><strong>Materials</strong></td>
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<td><strong>Fluid Definition</strong></td>
</tr>
<tr>
<td><strong>Morphology</strong></td>
</tr>
<tr>
<td><strong>Settings</strong></td>
</tr>
<tr>
<td><strong>Buoyancy Model</strong></td>
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<tr>
<td><strong>Domain Motion</strong></td>
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<tr>
<td><strong>Reference Pressure</strong></td>
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<tr>
<td><strong>Additional Variable</strong></td>
</tr>
<tr>
<td><strong>Kinematic Diffusivity</strong></td>
</tr>
<tr>
<td><strong>Option</strong></td>
</tr>
<tr>
<td><strong>Turbulence Model</strong></td>
</tr>
<tr>
<td><strong>Turbulence Wall Functions</strong></td>
</tr>
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</table>

Table 6: Single Phase non-Newtonian model under pulsatile flow - Domain Physics

Boundary Physics Table:

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<th>Boundary Inlet</th>
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</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
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<tr>
<td><strong>Location</strong></td>
</tr>
<tr>
<td><strong>Settings</strong></td>
</tr>
<tr>
<td><strong>Additional Variables</strong></td>
</tr>
<tr>
<td><strong>Additional Variables value</strong></td>
</tr>
<tr>
<td><strong>Option</strong></td>
</tr>
<tr>
<td><strong>Flow Direction</strong></td>
</tr>
<tr>
<td><strong>Flow Regime</strong></td>
</tr>
<tr>
<td><strong>Mass and Momentum</strong></td>
</tr>
<tr>
<td><strong>Mass Flow Rate</strong></td>
</tr>
<tr>
<td><strong>Turbulence</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Boundary Outlet</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
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<tr>
<td><strong>Location</strong></td>
</tr>
<tr>
<td><strong>Settings</strong></td>
</tr>
<tr>
<td><strong>Flow Regime</strong></td>
</tr>
<tr>
<td><strong>Mass and Momentum</strong></td>
</tr>
<tr>
<td><strong>Relative Pressure</strong></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Boundary Blood Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
</tr>
<tr>
<td><strong>Location</strong></td>
</tr>
<tr>
<td><strong>Settings</strong></td>
</tr>
<tr>
<td><strong>Additional Variables</strong></td>
</tr>
<tr>
<td><strong>Option</strong></td>
</tr>
<tr>
<td><strong>Mass and Momentum</strong></td>
</tr>
<tr>
<td><strong>Wall Roughness</strong></td>
</tr>
</tbody>
</table>

Table 7: Single Phase non-Newtonian model under pulsatile flow - Boundary Physics
5.2.1 Cases for Multiphase hemodynamic model

The Navier-Stokes equations (momentum and mass conservation) governing the fluid motion were solved utilizing the CFD commercial code ANSYS CFX. A multiphase non-Newtonian 3-D flow model for describing the hemodynamics in vascular vessels is developed. It uses the principles of mass, momentum, and energy conservation for each phase based on the generalization of the well-known Navier–Stokes equations [49, 50].

Case 3: Comparison of two phase non-Newtonian model with the two phase Newtonian one under steady flow condition

- Two Phase Newtonian model under steady flow

Blood, was considered as the first phase having viscosity of 4 centipoises. The rest of the fluid volume considered as thin and thick blood phases. The thin phase (plasma) located near the vessels walls as a film-like orientation (of height 20% relative to the radius of the inlet face of the vessel), having low velocity and approximate unity viscosity. On the other hand, the thick phase (RBCs) was considered as the predominant particulate phase suspended in plasma, having a hematocrit of 45%. The velocity of the RBCs was considered higher than that of the plasma, flowing at the center of the vessel.

Finally, predefined average pressure values were used as inlet and outlet boundary conditions for both the RBCs and the plasma, and a zero slip velocity boundary condition was employed for both RBCs and plasma. Also no mass transfer was considered between phases.

Domain Physics Table:

<table>
<thead>
<tr>
<th>Domain - Blood Domain</th>
<th>Fluid</th>
<th>Created Material</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Material Library</td>
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</tr>
<tr>
<td>Location</td>
<td>Continuous Fluid</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Materials</th>
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</thead>
<tbody>
<tr>
<td>Blood</td>
</tr>
<tr>
<td>Fluid Definition</td>
</tr>
<tr>
<td>Morphology</td>
</tr>
<tr>
<td>Water at 25°C</td>
</tr>
<tr>
<td>Fluid Definition</td>
</tr>
<tr>
<td>Morphology</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Settings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buoyancy Model</td>
</tr>
<tr>
<td>Domain Motion</td>
</tr>
<tr>
<td>Reference Pressure</td>
</tr>
<tr>
<td>Additional Variable</td>
</tr>
<tr>
<td>Option</td>
</tr>
</tbody>
</table>

| Kinematic Diffusivity | 2e-11[m^2 s^{-1}] |
| Kinematic Diffusivity | 5e-12[m^2 s^{-1}] |
| Homogenous Model      | True |
| Turbulence Model      | Laminar |

Table 8: Two Phase Newtonian model under steady flow - Domain Physics
Boundary Physics Table:

<table>
<thead>
<tr>
<th>Boundary Inlet</th>
<th>INLET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>INLET</td>
</tr>
</tbody>
</table>

**Settings**

- **Additional Variables**: Concentration
- **Additional Variables value**: 0.0013 [g cm^-3]
- **Flow Regime**: Subsonic
- **Mass and Momentum**: Normal Speed
- **Normal Speed**: 0.1 [m s^-1]
- **Fluid**: Blood
- **Volume Fraction**: Value
  - **Value**: 1-water.vf
- **Fluid**: Water
- **Volume Fraction**: Value
  - **Value**: step( sqrt( ( (xGlobal - areaAve(xGlobal)@Inlet)^2 + (yGlobal - areaAve(yGlobal)@Inlet)^2 + (zGlobal - areaAve(zGlobal)@Inlet)^2) / (area()@Inlet / pi) ) - ratio)

<table>
<thead>
<tr>
<th>Boundary Outlet</th>
<th>OUTLET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>OUTLET</td>
</tr>
</tbody>
</table>

**Settings**

- **Flow Regime**: Subsonic
- **Mass and Momentum**: Average Static Pressure
- **Pressure Profile Blend**: 5e-02
- **Relative Pressure**: 0 [Pa]
- **Pressure Averaging**: Average Over Whole Outlet

**Boundary Blood Domain**

<table>
<thead>
<tr>
<th>Type</th>
<th>WALL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>AORTA</td>
</tr>
</tbody>
</table>

**Settings**

- **Additional Variables**: Concentration
- **Option**: Zero Flux
- **Mass and Momentum**: No slip wall

Table 9: Two Phase Newtonian model under steady flow - Boundary Physics

- Two Phase non - Newtonian model under steady flow

For the non-Newtonian blood flow simulation, the Carreau model is used to calculate the blood viscosity (see figure 33).

**Carreau Model**: In this model, the relation between viscosity and shear strain rate,$\dot{\gamma}$, can be written as:

$$\lambda_f = 3.313 \ s; \ \text{zero strain viscosity, } \mu_0 = 0.056 \ Pa.s; \ \text{infinite strain viscosity, } \mu_\infty = 0.00345 \ Pa.s; \ \text{and the empirical exponent, } n = 0.3568 \ [62].$$
## Domain Physics Table:

<table>
<thead>
<tr>
<th>Domain - Blood Domain</th>
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</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
<td>Fluid</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>Created Material</td>
</tr>
</tbody>
</table>

### Materials

<table>
<thead>
<tr>
<th>Blood</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluid Definition</strong></td>
<td>Material Library</td>
</tr>
<tr>
<td><strong>Morphology</strong></td>
<td>Continuous Fluid</td>
</tr>
</tbody>
</table>

### Water at 25°C

<table>
<thead>
<tr>
<th>Fluid Definition</th>
<th>Material Library</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphology</strong></td>
<td>Continuous Fluid</td>
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</tbody>
</table>

### Settings

<table>
<thead>
<tr>
<th>Buoyancy Model</th>
<th>Non Buoyant</th>
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<tbody>
<tr>
<td><strong>Domain Motion</strong></td>
<td>Stationary</td>
</tr>
<tr>
<td><strong>Reference Pressure</strong></td>
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</tr>
<tr>
<td><strong>Additional Variable</strong></td>
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</tr>
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<tr>
<td><strong>Kinematic Diffusivity</strong></td>
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<tr>
<td><strong>Turbulent Wall Functions</strong></td>
<td>Automatic</td>
</tr>
</tbody>
</table>

Table 10: Two Phase non–Newtonian model under steady flow - Domain Physics
A non-Newtonian and Newtonian 3-D flow model for the description of hemodynamic in vascular vessels was developed. It used the principles of mass, momentum, and energy conservation based on the generalization of the well known Navier–Stokes Equations.
**Case 4: Comparison of two phase Newtonian model under steady and pulsatile flow condition**

Blood, was considered as the first phase having viscosity of 4 centipoises. The rest of the fluid volume considered as thin and thick blood phases. The thin phase (plasma) located near the vessels walls as a film-like orientation (of height ca 20% relative to the radius of the inlet face of the vessel), having low velocity and approximate unity viscosity. On the other hand, the thick phase (RBCs) was considered as the predominant particulate phase suspended in plasma, having a hematocrit of 45%. The velocity of the RBCs was considered higher than that of the plasma, flowing at the center of the vessel.

Finally, predefined average pressure values were used as inlet and outlet boundary conditions for both the RBCs and the plasma, and a zero slip velocity boundary condition was employed for both RBCs and plasma. Also no mass transfer was considered between phases.

- Two Phase non - Newtonian under steady flow

The simulation was the same as described before

- Two Phase non-Newtonian under pulsatile flow

It was assumed that an arterial wall is rigid and blood is a non - Newtonian fluid with density \( \rho = 1050 \text{ km}^3 \). For the non-Newtonian blood flow simulation, the Carreau model is used to calculate the blood viscosity as mentioned before.

The blood flow was assumed to be periodic. We used a sinusoidal flow waveform of \( 4.3 \text{ [g/s]} \pm 2.6 \sin (2 \pi t_p t) \text{ [g/s]} \) at the inlet with a period of \( t_p \) of 0.345 s and \( t = 0.005 \text{s} \). The parameter \( t/t_p \) was used to describe a particular time in a cycle. The term \( t \) represents the time in seconds and \( t_p \) is the period of the flow cycle [62].

Then we introduced the equations that govern the flow pulsation in Ansys CFX:

\[
\text{Flow Rate} = 4.3 \text{ [g/s]} \pm 2.6 \sin (2 \pi t_p t) \text{ [g/s]}
\]
### Domain Physics Table:

<table>
<thead>
<tr>
<th>Domain - Blood Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
</tr>
<tr>
<td><strong>Location</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Materials</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood</strong></td>
</tr>
<tr>
<td>Fluid Definition</td>
</tr>
<tr>
<td>Morphology</td>
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<tr>
<td><strong>Water at 25°C</strong></td>
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<tr>
<td>Fluid Definition</td>
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<tr>
<td>Morphology</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Settings</strong></th>
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<tbody>
<tr>
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Table 12: Two Phase non – Newtonian model under pulsatile flow - Domain Physics
Boundary Physics Table:

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Table 13: Two Phase non–Newtonian model under pulsatile flow - Boundary Physics
6 Results

Case 1: Comparison of non-Newtonian model with the Newtonian one under steady flow condition

a) Wall Shear Stress Distribution

As shown in Figures 36 - 39, the distribution of WSS in the aorta for both Newtonian and non-Newtonian simulations is similar. For most regions, the value of the WSS is approximately in the range of 1.6 Pa. The two areas with the lowest WSS are located in Regions A and B. The WSS in most portions of the ascending aorta (from the inlet to the brachiocephalic artery) is about 0.5 Pa, relatively lower along the outer wall (Region C) when compared with the inner wall. Although the WSS distribution is similar for both the Newtonian and the non-Newtonian simulations, the values of WSS are significantly different for the two cases. The WSS for the non Newtonian simulation is generally higher than that for the Newtonian simulation, approximately 10% higher in most areas of the aorta, 20% higher along the outer wall of the ascending aorta, and more than 40% higher at most locations in Regions A and B.

Fig. 36. Wall Shear Stress for the Single Newtonian model under Steady flow (View1)
Fig. 37. Wall Shear Stress for the Single non-Newtonian model under Steady flow (View1)

Fig. 38. Wall Shear Stress for the Single Newtonian model under Steady flow (View2)
b) Luminal surface concentration of LDLs

Generally speaking, for the two cases $c_w$ in the ascending aorta is relatively even, but quite uneven in the aortic arch, the inner wall of which has a much higher $c_w$ than the outer wall, especially from the distal end of the aortic arch to its apex (Region B). Region B of the arch has the highest $c_w$. The second highest $c_w$ is located at Region A in the entry area of the brachiocephalic artery. The third highest $c_w$ is at Region C in the descending aorta. With a shear depended $D_{LDL}$, only in areas with high $c_w$ such as regions A and B, the percentage difference between the two cases is more than 15% in most other areas of the aorta $c_w$ is just slightly elevated (Figures 40 - 43).
Fig. 40. The distribution of $c_w$ for the Single Newtonian model under Steady flow (View1)

Fig. 41. The distribution of $c_w$ for the Single non-Newtonian model under Steady flow (View1)
Fig. 42. The distribution of $c_w$ for the Single Newtonian model under Steady flow (View2)

Fig. 43. The distribution of $c_w$ for the Single non-Newtonian model under Steady flow (View2)
c) \textbf{Correlation of C_w Distribution with the distribution of WSS}

Figure 44 shows the distributions of WSS for the single phase Newtonian model under steady state. The highest WSS was \( \sim 0.5 \) Pa and located at the flow divider of the brachiocephalic left common carotid branch. There were another two places where the WSS was relatively high. One was located at the entrance of the left subclavian artery (not showed in figure 44); the other was located in an area along the anterior wall of the aortic arch (not showed in figure 44). The two lowest WSS areas were located at regions \( A \) and \( B \), respectively. The WSS in most portions of the ascending aorta was about 0.5 Pa, and it was relatively lower along the outer wall when compared with the WSS along the inner wall.

The comparison of \( C_w \) distribution with the distribution of WSS showed an adverse correlation between the two (see figures 44 and 45), especially in areas with low WSS where \( C_w \) was elevated significantly. Nevertheless, the numerical results also revealed that although the WSS of the ascending aorta was relatively low, the luminal surface LDL concentration there was not particularly high. In addition region D in the aortic arch was the area with the lowest luminal surface LDL concentration, but the WSS at the region D was not the highest in the aorta. Therefore, the present study indicated that WSS was not the only factor that determined the distribution of \( C_w \). The luminal surface concentration was probably affected by other factors, such as flow pattern itself as well. The study of Shigeo Wada and Takeshi Karino\cite{10} showed that the surface concentration of LDL at a location is depended not only on the value of wall shear stress at that location but also several other factors such as global flow patterns which determine the paths of fluid elements and the times they spend in regions of high and/or low wall shear stress until they reach the particular location in the vessel although near – wall fluid velocity which determine the value of wall shear stress plays the most important role in concentration polarization of LDL.
Fig. 44. Wall Shear stress for the Single Newtonian model under Steady flow

Fig. 45. The distribution of $c_w$ for the Single Newtonian model under Steady flow
Case 2: Comparison of pulsatile non-Newtonian flow simulation with steady non–Newtonian flow simulation

a) Wall Shear Stress Distribution

Fig. 47 - 50 displays the distribution of time averaged WSS ($\overline{\text{WSS}}$) in the aorta. For most areas of the aortic outer wall, WSS for the pulsatile flow simulation is approximately 40% higher than that for the steady flow simulation. Along the inner wall, the difference becomes much higher, close to 80%. In areas where wall shear stress is relatively low such as at the entry area of the brachiocephalic artery (Region A) and the distal end of the aortic arch (Region B), the difference in wall shear stress between the pulsatile flow and its corresponding steady flow can be even high, reaching to as much as 500%.

Fig. 46 Wall Shear Stress for the Single phase non-Newtonian model under Steady flow (View2)
Fig. 47. Wall Shear Stress for the pulsatile nonNewtonian model for $T=0.345\text{s}$

Fig. 48. Wall Shear Stress for the pulsatile nonNewtonian model for $T/4$
Fig. 49. Wall Shear Stress for the pulsatile non-Newtonian model for T/2

Fig. 50. Wall Shear Stress for the pulsatile non-Newtonian model 3T/4
b) Luminal surface concentration of LDLs

Our simulation shows that for most areas of the aorta, pulsatility of blood flow has almost no effect on $c_w$. For these regions, the difference in luminal surface LDL concentration between pulsatile flow and its corresponding steady flow is only about 2% (Fig. 51 - 54). However, for the entry area of the brachiocephalic artery (Region A) and the distal end of the aortic arch (Region B), pulsatile flow can lead to a decrease of more than 10% in luminal surface LDL concentration from its corresponding value under steady flow condition.

Fig. 51. The distribution of $c_w$ for the Single non - Newtonian model under Steady flow (View1)
Fig. 52. The distribution of $c_w$ for the Single non-Newtonian model under pulsatile flow (View1)

Fig. 53. The distribution of $c_w$ for the Single non-Newtonian model under Steady flow (View2)
Fig. 54. The distribution of $c_w$ for the Single non-Newtonian model under pulsatile flow (View 2)

Fig. 55. The concentration gradient of $c_w$ for the Single non-Newtonian model under steady flow
Fig. 56. The concentration gradient of $c_w$ for the Single non-Newtonian model under pulsatile flow for $T=0.345s$

Fig. 57. The concentration gradient of $c_w$ for the Single non-Newtonian model under pulsatile flow for $T/4$
Case 3: Comparison of two phase non-Newtonian model with the two phase Newtonian one under steady flow condition

a) Wall Shear Stress Distribution

As shown in Figures 59 and 60, the distribution of WSS in the aorta for both Newtonian and non-Newtonian simulations is similar. For most regions, the value of the WSS is approximately in the range of 1.10 Pa. The two areas with the lowest WSS are located in Regions A and B. The WSS in most portions of the ascending aorta (from the inlet to the brachiocephalic artery) is about 0.6 Pa, relatively lower along the outer wall (Region C) when compared with the inner wall. Although the WSS distribution is similar for both the Newtonian and the non-Newtonian simulations, the values of WSS are significantly different for the two cases. The WSS for the non Newtonian simulation is generally higher than that for the Newtonian simulation, approximately 10% higher in most areas of the aorta, 20% higher along the outer wall of the ascending aorta, and more than 40% higher at most locations in Regions A and B.
Fig. 59. Blood Wall Shear Stress for the Two-Phase Newtonian model under Steady flow

Fig. 60. Blood Wall Shear Stress for the Two-Phase non-Newtonian model under Steady flow
Fig. 61. Water Wall Shear Stress for the Two Phase Newtonian model under Steady flow

Fig. 62. Water Wall Shear Stress for the Two Phase non-Newtonian model under Steady flow
b) Luminal surface concentration of LDLs

Generally speaking, for the two cases \( c_w \) in the ascending aorta is relatively even, but quite uneven in the aortic arch, the inner wall of which has a much higher \( c_w \) than the outer wall, especially from the distal end of the aortic arch to its apex (Region B). Region B of the arch has the highest \( c_w \). The second highest \( c_w \) is located at Region A in the entry area of the brachiocephalic artery. The third highest \( c_w \) is at Region C in the descending aorta. With a shear depended \( D_{LDL} \), only in areas with high \( c_w \) such as regions A and B, the percentage difference between the two cases is more than 15% in most other areas of the aorta \( c_w \) is just slightly elevated.

![Image of blood distribution](image_url)

Fig. 63. The distribution of blood \( c_w \) for the Two-Phase non-Newtonian model under steady flow
Fig. 64. The distribution of water $c_w$ for the Two-Phase non-Newtonian model under steady flow

Fig. 65. The water concentration gradient for the Two-Phase non-Newtonian model under steady flow
Case 4: Comparison of two phase non-Newtonian model under steady and pulsatile flow condition

a) Wall Shear Stress Distribution

Fig. 67 and 69 displays the distribution of time averaged WSS ($\overline{WSS}$) in the aorta. For most areas of the aortic outer wall, WSS for the pulsatile flow simulation is approximately 40% higher than that for the steady flow simulation. Along the inner wall, the difference becomes much higher, close to 80%. In areas where wall shear stress is relatively low such as at the entry area of the brachiocephalic artery (Region A) and the distal end of the aortic arch (Region B), the difference in wall shear stress between the pulsatile flow and its corresponding steady flow can be even high, reaching to as much as 500%.

Fig. 66. Blood Wall Shear Stress for the Two – Phase non-Newtonian model under Steady flow
Fig. 67. Blood Wall Shear Stress for the Two-Phase non-Newtonian model under Pulsatile flow

Fig. 68. Water Wall Shear Stress for the Two Phase non-Newtonian model under Steady flow
b) **Luminal surface concentration of LDLs**

Our simulation shows that for most areas of the aorta, pulsatility of blood flow has almost no effect on $c_w$. For these regions, the difference in luminal surface LDL concentration between pulsatile flow and its corresponding steady flow is only about 2% (Fig. 70 and 71). However, for the entry area of the brachiocephalic artery (Region A) and the distal end of the aortic arch (Region B), pulsatile flow can lead to a decrease of more than 10% in luminal surface LDL concentration from its corresponding value under steady flow condition.
Fig. 70. The distribution of blood $c_w$ for the Two-Phase non-Newtonian model under steady flow

Fig. 71. The distribution of blood $c_w$ for the Two-Phase non-Newtonian model under pulsatile flow
Fig. 72. The distribution of water $c_w$ for the Two-Phase non-Newtonian model under steady flow

Fig. 73. The distribution of water $c_w$ for the Two-Phase non-Newtonian model under pulsatile flow
7 Conclusion

It is well documented that abnormal LDL accumulation within the arterial wall plays important roles in the genesis and the progression of atherosclerosis [52, 53, 54]. In the present study, we numerically studied the effect for both single and two phases non Newtonian pulsatile blood flow on the transport of LDL in a reconstructed human aorta model based on CT images from a healthy individual. The present study showed that the distribution of wall shear stress in the aorta for both Newtonian and non Newtonian simulations is quite similar. The wall shear stress in most portions of the ascending aorta (from inlet to the brachiocephalic artery) is relatively lower along the outer wall when compared with that of the inner wall. Although the wall shear stress distribution is similar for both the Newtonian and the non Newtonian simulations, the values of wall shear stress are significantly different for the two cases. The study of Liu et al [18] showed that flow patterns of the tapered and the untapered aorta are almost identical, indicating that spiral flow pattern in the aorta was not caused by the existence of the three branches. The helical flow induced by the aortic torsion may facilitate the stabilization of the flow of blood in the aorta, reducing flow disturbance and suppressing the separation.

In the past years, localization of atherosclerosis has always been discussed in their strong relationship with wall shear stress due to the fact that they were found in regions of relatively low wall shear stress. However, the results from our present study raised a strong doubt in their relationship. The present numerical study revealed an adverse correlation between wall shear stress and the luminal surface LDL concentration in the aorta. The highest c_w of LDL tends to be located in areas with very low wall shear stress. Nevertheless, this correlation between wall shear stress and c_w is not clear – cut for certain regions of the aorta. For instance, there are two locations along the outer wall of the ascending aorta that have lower wall shear stress than other parts of the ascending aorta and even lower than most parts of the descending aorta. But c_w in the ascending aorta distributes quite uniformly and is much lower than that in the descending aorta. This implies that the luminal surface LDL concentration depends not only on the local wall shear stress but also on both global and local flow patterns. In this aspect our results are in good agreement with those of Wada and Karino [10], who’s also showed that the surface concentration of LDL is not dermined by wall shear stress (shear rate) but by near – wall flow patterns which determine the paths and the velocities of fluid elements and LDL to reach a particular site, and the duration of interactions and contact of
LDL with the vessel wall which might be important for the uptake of LDL by endothelial cells.

Also the results from the present study obtained revealed that the shear shear thinning non Newtonian nature of blood (Carreau model) and pulsatile flow had different impact on mass transport in the aorta. When compared to the Newtonian blood simulation the non Newtonian behavior of blood had little effect on LDL transport in most parts of the aorta but could significantly affect those regions with high luminal surface LDL concentration by elevating $c_w$ through the shear dependent diffusivity. Localized elevation of LDL concentration occurred at the regions A and B (see figure 46) were flow was stagnant and wall shear stress was low. The study of Wada and Karino [10] showed that the degree of elevation in surface concentration of LDL and the area of the region where the surface concentration of LDL was elevated varied as function of Reynolds number, water filtration velocity, and the size of macromolecules. Of these, it was, of course, water filtration velocity which played the most important role in this phenomenon since without a filtration flow of water at the vessel wall, no concentration polarization occurred in the vessel. Quite the contrary, the pulsation of flow played a minor role in most regions of the aorta. Since the concentration polarization of LDL occurs within a thin fluid layer adjacent to the vessel wall where fluid velocity is low and wall shear stress is low, the flow near the vessel wall would not be disturbance so much by the pulsatility of the mainflow under normal physiological conditions, and regions of high LDL surface concentration are formed at the same sites in both steady and pulsatile flow. Therefore the pulsation of flow affected those regions with high luminal surface LDL concentration by remarkably reducing $c_w$ there. The study of Liu et al./55/ showed that the non Newtonian nature of blood also had a little effect on oxygen transport in most parts of the aorta expect for these regions of low oxygen flux, where oxygen flux could be suppressed greatly. On the contrary, the pulsatile flow could significantly enhance oxygen flux in most areas, especially those predisposed to flow disturbance. Therefore, generally speaking, the shear thinning non Newtonian nature of blood may be pro – atherogenic while the pulsation of blood flow may be anti – atherogenic.

To predict non – Newtonian behavior of blood using Newtonian models, various "characteristic viscosity" assumptions for blood flows in larger arteries have been made. Our simulations demonstrated that when compared with the characteristic viscosity derived from the average shear rate in Poiseuille flow, the results obtained from infinite shear viscosity (3.45 cP) were closer to the non – Newtonian results. Our results are in good agreement with those of Liu et al. [55] and Bourantas et al. [56] but are different from the results of Chen and Lu [57], in the carotid artery. This is because, in contrast to the carotid
artery, the greater taper and flow of the aorta make the shear rate near the wall high enough so that the blood can be treated approximately as Newtonian fluid with infinite shear viscosity in most regions of the aorta under steady and pulsatile flow conditions.

Finally, the principle difference compared with a single-phase model is the appearance of the volume fraction for each phase, as well as mechanisms for the exchange of mass, momentum, and energy between the phases.

In comparison with Newtonian flow simulation, the shear thinning non–Newtonian nature of blood has little effect on the mass transport in most regions of the aorta except for the areas with low disturbance. The effect of flow pulsation on the transport of LDLs has a similar trend.

7.1 Limitations and future extension of the study

In the present study, owing to the computational difficulties, the arterial wall was simplified as an appropriate boundary condition (wall free model), which cannot provide any information on the concentration profiles within the wall. In the recent years several authors developed a new four–layer model for mass transport in the arterial wall coupled with mass transport in the arterial lumen, describing in a more efficient manner mass transport in the human aorta [1, 51, 58]. Also in the present study all the comparisons were based on only one image–based healthy human aorta. It is apparent that one case study is insufficient. However, it still can show the effects of non Newtonian and pulsatile flow on mass transport and the correlation of $c_w$ distribution with the distribution of WSS. For the comparison of the human aortas with geometric differences, the present comparison method to calculate percent difference is not suitable. The quantitative comparison approaches used for different carotid arteries could be used for the human aortas [59, 60].

In order to elucidate the role of pulsatile flow, the same constant flow volume outlet boundary conditions for steady flow were also used for the pulsatile flow, which was approximate to the real situation. Using person specific measurement of velocity profiles or multiscales model as boundary conditions may improve the present simulations [61].
8 References


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