Characterization of Blood Flow in a Capillary Tube

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CHARACTERIZATION OF BLOOD FLOW IN A CAPILLARY TUBE

By

Tammy Lynn Ladner

A Thesis
Submitted to the Faculty of
Mississippi State University
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for the Degree of Master of Science
in Computational Engineering
in the Bagley College of Engineering

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Tammy Lynn Ladner

2007
To better understand how platelets behave when exposed to high shear stress, computational fluid dynamic (CFD) models for single-layer (uniform and constant) viscosity flow and two-layer (two distinct regions of different viscosities) viscosity flow were developed. The single-layer model, which represents common standard practice, did not predict the pressure drop correctly; the error produced from using the single-layer model was approximately 95%. However, the two-layer model produced results that were within 6% of the experimental results. Experimental results used to validate CFD models were obtained from data gathered by researchers at University Medical Center (UMC) in Jackson, MS. Using Fluent R 6.2, simulations were performed that showed the characteristics of blood flow in a long stenosis. The beginning of the development of a blood damage model was also investigated. This thesis could provide researchers with information that will eventually allow the prediction of platelet activation and hemolysis.
DEDICATION

This thesis is dedicated to my parents, David and Gail Ladner, my sisters, Melissa Peterson and Amy Ladner, my grandfather, Delmer Ladner, and my wonderful fiancé, George Threadgill. Without their love and support, I would not have made it this far.
ACKNOWLEDGMENTS

I would like to take this time to express my sincere gratitude to all of the people who helped make this thesis possible. First of all, thanks to my twin sister, Amy, who shared every grueling moment with me, from start to finish. Through choosing the Computational Engineering program to writing my thesis, she was with me through it all. To Dr. John Ker-mode, thank you for performing all experimental data presented in this thesis. Without it, I would still be twiddling my thumbs. To Dr. Marina Kameneva, thank you for providing us with the blood viscosity data as related to hematocrit. A very sincere and heartfelt thanks to Dr. Greg Burgreen; without his guidance and patience, I never would have been able to finish this project. I also must acknowledge the National Science Foundation; through their financial support (grant number: 0443903), this research was possible. And last, but not least, I would like to thank God for giving me the strength, courage, and sanity needed to pursue a Masters degree in Computational Engineering.
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LIST OF SYMBOLS, ABBREVIATIONS, AND NOMENCLATURE

$Re$ Reynolds number (in tube flow)

$Q$ flow rate ($m^3/s$)

$V$ velocity for given flow rate (m/s)

$\Delta P$ pressure drop (N/m$^2$)

$Ht$ Hematocrit of blood; usually percent

$D$ internal diameter of tube

$\mu$ viscosity of fluid (kg/m-s)

$\rho$ density of fluid (kg/m$^3$)

$r_c$ core radius

$r_o$ radius of shear tube

$\mu_c$ viscosity of core region

$\mu_o$ viscosity of outer (wall) region

$\rho_c$ density of core region

$\rho_o$ density of outer (wall) region

$\tau$ shear stress (N/m$^2$)

$\gamma$ strain rate ($s^{-1}$)
CHAPTER 1
INTRODUCTION

Biomedical devices have been used in the cardiovascular system for many years. Often times these devices save or extend the lives of patients who use them. Unfortunately, though, in many cases these devices can cause dangerous pathological complications triggered by non-physiological conditions acting on the blood flowing through these devices. One such disease leading to non-physiological flow conditions is atherosclerosis, which can result in rapid thrombosis formation that can lead to strokes and heart attacks. According to the Centers for Disease Control and Prevention, heart disease is the leading cause of death in the United States—28.3% of the recorded deaths in 2003 were attributed to this disease [22]. Due to this fact, now more than ever, researchers need to focus time on designing and improving reliable cardiovascular devices.

More than forty years of research has been dedicated to studying hemocompatibility issues, i.e., blood-biomaterial surface interactions. However, in comparison, very little attention has been given to studying the fluid dynamic aspects of blood damage. Studying these interactions could provide new insights into the mechanisms of blood damage, thereby enabling further progress in the design, evaluation, and improvement of cardiovascular devices.
1.1 Background

Biomedical devices have been used for many years in the cardiovascular system. Prosthetic heart valves, vascular grafts, ventricular assist devices, blood pumps, artificial hearts, vascular stents, and catheters are just a few of such devices. Some of these listed are temporary, or short-term, devices such as catheters and blood pumps. But others are long-term devices, such as stents and heart valves. Although these devices are meant to, and often do, extend or save the lives of the patients that use them, dangerous pathological complications can arise due to the less than optimal performance of the devices [18]. Some of these devices can lead to significant clinical problems such as thrombosis and infection [18] [3]. Each year in the United States alone, approximately 120,000 prosthetic heart valves are implanted in patients; in all of these replacement prostheses, thromboembolism, primarily caused by platelet activation, is the leading reported complication [7] [24]. Another class of cardiovascular devices, total artificial hearts (TAH), such as the Jarvik-7 TAH, when implanted for long periods of time, also leads to several complications such as thromboembolism, stroke, and infection [15].

1.1.1 Composition and Flow Characteristics of Blood

Blood is composed of 55% plasma, by volume, and 45% formed elements, by volume [34]. There are three major types of formed elements: red blood cells (RBCs), platelets, and white blood cells (WBCs). Red blood cells, which are biconcave and discoid in shape, make up about 95%, by cell count, of the formed elements and measure about 6-8 µm in diameter. Platelets comprise approximately 4.9% and have a diameter of about 2 µm.
White blood cells make up the remaining 0.1% of the formed elements and usually measure about 10 µm in diameter. Because of this very small percentage of platelets and white blood cells, their effect on the macroscopic flow of blood has been reported to be negligible [13].

Hematocrit (Ht) is the percent by volume of whole blood that is composed of red blood cells; it is essentially a measure of the number and the size of RBCs. Figure 1.1, obtained from [27], shows a depiction of blood and its components. The average for human hematocrit is approximately 35-45% Ht.

![Figure 1.1](image)

Hematocrit: Components of Blood

RBCs tend to migrate to the center of flow, and a RBC-depleted layer develops near the wall—this migration is known as hydrodynamic lift effect [1] [11]. Because of this
hydrodynamic lift effect on RBCs, plasma along with platelets are displaced towards the near-wall region, and consequently are exposed to high shear stresses. According to Kroll et al., platelet activation in some patients can be a direct result of the higher than physiologic shear stresses ($\geq 50 \text{ dynes/cm}^2 \approx 5 \text{ N/m}^2$) created at, for example, the closure of mechanical heart valves or in the impeller of a rotary blood pump [26]. It has been shown that platelet activation depends not only on the level of shear stress, but also on the length of time a platelet is exposed to that level of shear stress. Hellums found an inversely proportional relationship to the level of shear stress and the threshold exposure time [33] [21]. The exact relationship remains an open and active area of research.

1.1.2 Blood-Biomaterial Compatibility

Forty years of research has been performed on hemocompatibility issues related to cardiovascular devices. Hemocompatibility tests evaluate the effects of foreign substances on blood or blood components. Since the materials used in developing biomedical devices are often off-the-shelf polymers and metals, care must be taken to see that they possess qualities similar to endothelial cells that line blood vessel walls–they should ideally possess the appropriate strength, elasticity, corrosion resistance, etc. [33]. Ratner addressed several issues that must be considered when choosing a material that is “blood compatible” [28]:

1. Are there low levels of platelet adhesion?
2. Are there low levels of platelet activation?
3. What is the lowest level of anticoagulant that will be needed in conjunction with the material?
4. Is the blood-surface interaction time low?
5. Are there few flow disturbances?
6. What is the purity of the material?
7. What is the stability of the chemical composition of the material?
8. Can the material be readily fabricated?
9. Can the material be readily sterilized?

In order to truly develop a blood compatible material, all of these questions must be considered. At this point in time, although much research has been done in this area, no material has been developed that is completely inert towards blood. Many researchers advocate that devices that are coated with endothelial cells would possess all necessary qualities of a “blood compatible” device; however, even with all of the research done in this area, much more research still needs to be performed [19].

1.1.3 Fluid Dynamic Aspects of Blood Damage using CFD

Only recently have researchers begun investigating the fluid dynamic aspects of blood damage using CFD. Several examples of using CFD in the cardiovascular area are presented. Burgreen et al successfully modeled a rotary blood pump using modern CFD analysis that emphasized the use of CFD as a development tool for device improvements to rotary blood pumps [8]. Arvand et al also used CFD to study blood damage resulting from a rotary pump [2]. His goal was to develop and validate a new hemolysis model, which he found to be in good agreement with experimental results of blood damage estimation. Hemolysis is simply defined as the breaking of RBCs; it is sometimes referred to as RBC, or erythrocyte, lysis. Song et al evaluated stress-induced hemolysis occurring in a
left ventricular assist device (LVAD) in the form of an implantable centrifugal pump. The accumulated data of shear stress and time levels, obtained using a Lagrangian particle-tracking method, allowed the investigators to estimate the cellular damage that resulted from flowing through the artificial device [32]. Similar CFD studies by this same group were performed in order to design an impeller for an early prototype of the HeartQuest LVAD [10]. These studies focused on three major areas of blood damage: high shear regions, stagnation points and possible flow separation regions. Curtas et al, based on their analysis, found an improved design for the impeller that appeared to have little, if any, damaging effect on the blood [10]. All of the research mentioned above had one key aspect in common: the primary reason of using CFD to investigate blood damage was to provide device designers and researchers with a clearer understanding of optimal and/or suboptimal characteristics to the design.

In summary, although many years of research has been devoted to the study of blood flow and also to biomaterial hemocompatibility issues as concerned with cardiovascular devices, little attention has been given to actually applying CFD to study flow-induced blood damage that arises from use of these devices. Much more research needs to be performed in the cardiovascular biofluids area; specifically, it is anticipated that the use of CFD models to develop and/or optimize devices will prove to be both time saving and cost effective. This thesis focuses on improved modeling blood flow as pertaining to blood damage models.
1.2 Objectives

The research discussed in this thesis attempts to increase the understanding of the fluid dynamics of blood damage as related to mechanical devices used in the cardiovascular system. To accomplish this, four objectives were identified:

1. Develop and validate a microchannel flow device to study the dynamics and function of platelets subjected to pathophysiological flow conditions. This in vitro microscale device will be designed to isolate specific types of fluid dynamic related damage to platelets. It will mimic in vivo fluid dynamic conditions typical of occlusive arterial disease and cardiovascular mechanical prostheses. CFD will be employed to simulate the detailed fluid dynamics of the device.

2. Develop an experimental protocol for obtaining the pressure drop across the microdevice. The purpose of developing this protocol is to provide data for validating our computational model. Matching the computationally obtained pressure drop to the experimental microscale device is our primary validation criteria for the CFD model.

3. Develop mathematically-based engineering models of blood flow that can lead to the development of blood damage models.

4. Begin characterization of blood damage as related to current results. Blood damage models should be able to predict damage induced from destructive fluid mechanical stresses commonly found in cardiovascular environments such as cardiovascular prostheses and occlusive arterial disease. One example of a blood damage model is shear-induced lysis of platelets.
In the development of an experimental model, a microscale device was designed. Then in order to validate preliminary computational studies, the pressure drop across the microdevice needed to be obtained. Once the device and pressure drop protocol were developed, experiments were run using human blood. All experiments were performed by a group of researchers, Dr. John Kermode, Associate Professor of Pharmacology, and his lab assistants, from University of Mississippi Medical Center (UMC) in Jackson, Mississippi.

2.1 Microscale Device Development

The microscale device developed for the experiments was composed of many smaller constituitive pieces. The basic structure is simple, consisting of lengths of tubing of two differing diameters connected by special fittings. This configuration was chosen because of its simplicity, inexpensiveness to fabricate, and because preliminary calculations showed that it would adequately mimic the flow parameters (shear rates, shear stress, etc.) that arise from occlusive arterial disease and cardiovascular mechanical prostheses. All parts used for the microdevice were purchased from UpChurch Scientific, Inc (Oak Harbor, WA). The larger diameter tube was 0.040 inches (1016 µm) internal diameter with an outer diameter of $\frac{1}{16}$ inches (UpChurch 1538), and the smaller diameter tube was 0.005
inches (127 µm) internal diameter with an outer diameter of \( \frac{1}{32} \) inches (UpChurch 1576). In order to connect the smaller tube to the larger tube, a Microtight adapter (UpChurch P-881) was used. All parts ordered were fabricated from Poly-Ether-Ether-Ketone, or PEEK. A schematic of the microdevice with all tubing length dimensions is shown in Figure 2.1.

![Figure 2.1](image)

**Figure 2.1**

Microscale Device

### 2.2 Pressure Drop Experimental Setup

After the device was designed and assembled, it was necessary to develop an approach to measure the pressure drop across the shear tube. It was decided that a differential pressure transducer would be the most appropriate device for obtaining the measurements. The transducer selected for these studies was a variable reluctance differential pressure transducer (Validyne DP 15-TL) from Validyne Engineering Corporation (Northridge, CA), which allows a pressure drop to be obtained through the use of two ports, a high pressure side port and a low pressure side port. To obtain the pressure drop, in pounds per square inch (psi), from the transducer, a carrier demodulator (Validyne CD-379) was used. The fluid in the system was introduced and pressure pumped via a syringe pump (Harvard
HP4400) from Harvard Apparatus (Holliston, MA). The pressure drop experimental setup is found in Figure 2.2. More details about the device will be discussed in the following sections.

![Pressure Drop Experimental Setup](image)

**Figure 2.2**

**Pressure Drop Experimental Setup**

### 2.3 Calibration and Priming of Setup

The transducer was calibrated according to the Validyne instruction manual. After calibration, the transducer was primed using a glycerol solution. Glycerol was used for priming because blood entering the transducer could cause severe corrosion of the ports, which would eventually result in incorrect pressure readings. Each port and all port connections had to be carefully primed to remove all air from the system because entrapped air could offset the zero calibration.
During priming of the high pressure side port, the syringes S-1 and S-2 were filled with 40% and 100% glycerol solutions, respectively; all shut-off valves, except SO-1, were closed; and the high pressure side port bleed screw was loosened. To prime the high pressure side port arm, 40% glycerol was injected until all air bubbles were visibly removed satisfactorily from the system. The bleed screw was then tightened, and SO-1 is closed. For priming of the high pressure side port leg, SO-2 and SO-4 were opened, and the plug from the blood loading tube was removed. The 100% glycerol solution was introduced to the system until the solution began to discharge from the blood loading tube. All shut off valves were then closed again; the high pressure side port and all respective connections were considered to be primed. The P-760 union was then submerged in a solution of 100% glycerol, and the tube connected to the union was removed and replaced by a plug (UpChurch P-551). The entire system pressure transducer subsystem was then connected to the P-760 union on the negative port side of the device.

Priming of the low pressure side port and its connections was very similar to priming the positive port with a few minor differences. First, the outflow plug was removed when priming the low pressure side port leg with 100% glycerol solution. Secondly, the pressure transducer subsystem was not removed after priming; closing SO-3 was sufficient to prevent backflow of the glycerol (or blood) into the syringes on the low pressure side of the system. The low pressure side port and all connections were considered to be primed.

The final step in the priming process was to remove any glycerol that was introduced to the blood perfusion path. This was accomplished by filling the 8-mL Harvard syringe with isotonic saline and perfusing this through the blood perfusion path and the blood loading
tube. All shut-off valves were closed for this process. Another 8-mL syringe of isotonic saline was perfused through the blood path again just to ensure that no glycerol remained in the blood perfusion path. The device was then deemed fully primed and was ready for of blood experiments.

2.4 Pressure Drop Experiments

Blood was drawn from presumably healthy donors into an anticoagulant solution to prevent the blood from clotting in the tube. The anticoagulant used was Phe-Pro-Arg-chloromethylketone (PPACK), which is a direct inhibitor of thrombin that does not have any direct effect on the platelets, and it does not perturb the concentration of calcium in the plasma. The final concentration of PPACK in the blood was 40 µM.

All shut-off valves were first closed, and the plug was removed from the blood loading tube. The outflow plug remained in place. The 8-mL Harvard syringe was then filled at a rate of 12 mL/min with 8 mL of blood from the loading tube. A five minute waiting period was required. The first minute was used to ensure that the syringe was filled before plugging the blood loading tube. The four additional minutes allowed the blood in the syringe to warm to 37°C. At that time, the plug was removed from the outflow tube, and SO-3 and SO-4 were then opened. Forced perfusion of blood was started, and the output from the pressure transducer was observed throughout the perfusion. The experimental pressure drop recorded was the pressure reading after 4-mL of blood was perfused through the system; however, in most cases, the pressure readings were relatively stable throughout most of the perfusion period.
CHAPTER 3

EXPERIMENTAL RESULTS

It is well known that pressure drop is directly related to the flow rate, temperature, and hematocrit of blood. The results shown in Table 3.1 were obtained using the device setup from Figure 2.1 and blood with normal hematocrit levels and two different blood temperatures. The room temperature was approximately 26°C on the day this experiment was performed. Table 3.1 confirmed that pressure drop in the device does depend on the temperature of the blood. It also confirmed that pressure drop increased as flow rate increased. All subsequent experiments were performed at 37°C since that is the average normal internal body temperature of warm blooded mammals.

Table 3.1

Room Temperature vs 37°C Pressure Drop Measurements

<table>
<thead>
<tr>
<th>Flow Rate (mL/min)</th>
<th>26°C</th>
<th>37°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>123 psi</td>
<td>102 psi</td>
</tr>
<tr>
<td>8</td>
<td>260 psi</td>
<td>225 psi</td>
</tr>
<tr>
<td>12</td>
<td>405 psi</td>
<td>320 psi</td>
</tr>
</tbody>
</table>

The results obtained from the same device setup at different flow rates and hematocrits are shown in Table 3.2. Data confirmed that pressure drop was dependent on hematocrit.
as hematocrit increased, pressure drop increased. Note from Table 3.2, two different experiments were performed with 40% Ht. At 41% and 45% Ht, some experimental results do not follow correct trends. For example, for 41% Ht and 4 mL/min, a pressure drop larger than 123 psi is expected; however, a pressure drop of 102 psi was recorded—this is considered outlying data and was disregarded from further analysis. For this reason, CFD simulations will focus on blood with 40% Ht at flow rates of 4, 8, 10, and 12 mL/min.

Table 3.2

Results at Various Flow Rates and Hematocrits

<table>
<thead>
<tr>
<th>Flow Rate (mL/min)</th>
<th>40% Ht (Exp #1)</th>
<th>40% Ht (Exp #2)</th>
<th>41% Ht</th>
<th>45%Ht</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>62 psi</td>
<td>57 psi</td>
<td>N/A</td>
<td>57 psi</td>
</tr>
<tr>
<td>4</td>
<td>121 psi</td>
<td>123 psi</td>
<td>102 psi</td>
<td>116 psi</td>
</tr>
<tr>
<td>6</td>
<td>170 psi</td>
<td>181 psi</td>
<td>N/A</td>
<td>175 psi</td>
</tr>
<tr>
<td>8</td>
<td>231 psi</td>
<td>239 psi</td>
<td>225 psi</td>
<td>262 psi</td>
</tr>
<tr>
<td>10</td>
<td>295 psi</td>
<td>306 psi</td>
<td>N/A</td>
<td>333 psi</td>
</tr>
<tr>
<td>12</td>
<td>360 psi</td>
<td>381 psi</td>
<td>320 psi</td>
<td>378 psi</td>
</tr>
</tbody>
</table>
A CFD model was developed to predict blood flow in the capillary tube (the microdevice). In order to validate the CFD model, the computational pressure drop was compared to that of the experimental data. This chapter describes the model geometry, the software, and with the model equations used to perform the CFD.

4.1 Computational Model Geometry

The schematic of the geometry being used for the computational model is found in Figures 4.1-4.4. The geometry consisted of a simple sharp inlet reduction to a small diameter tube and a sudden sharp expansion back to an exit tube of the same diameter as the inlet tube. The grid consisted of an unstructured, axisymmetric grid with an anisotropic “viscous” node distribution at the wall to account for boundary layer effects.

Figure 4.1
Microdevice Mesh Geometry
Figure 4.2
Axisymmetric Geometry

Figure 4.3
Sharp Inlet Reduction

Figure 4.4
Detail of Viscous Meshing
4.2 Model Equations using Fluent® 6.2

The CFD simulations were run with the commercial CFD software Fluent® 6.2 developed by Fluent Inc (Lebanon, NH). A second-order upwind scheme was chosen and is known to produce more accurate results than a first order scheme. The solver used a segregated pressure-based solver as the solution algorithm and a control-volume-based technique. The simulations also use a laminar flow field. The equations used in Fluent to model the flow are described below [12].

For two-dimensional axisymmetric geometries, the continuity equation is given by

\[
\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x} (\rho v_x) + \frac{\partial}{\partial r} (\rho v_r) + \frac{\rho v_r}{r} = S_m
\]  

(4.1)

where \( x \) is the axial coordinate, \( r \) is the radial coordinate, \( v_x \) and \( v_r \) are the axial and radial velocities, respectively, and \( S_m \) is a source term that denotes any mass sources added to the system. Similarly, the axial and radial conservation of momentum equations are given by

\[
\frac{\partial}{\partial t} (\rho v_x) + \frac{1}{r} \frac{\partial}{\partial x} (rp v_x^2) + \frac{1}{r} \frac{\partial}{\partial r} (r \rho v_r v_x) = - \frac{\partial p}{\partial x} + \frac{1}{r} \frac{\partial}{\partial x} \left[ \tau \left( \frac{2}{3} (\nabla \cdot \mathbf{v}) \right) \right] + \frac{1}{r} \frac{\partial}{\partial r} \left[ \frac{\rho v_r}{\partial r} + \frac{\partial v_x}{\partial x} \right] + F_x
\]  

(4.2)

\[
\frac{\partial}{\partial t} (\rho v_r) + \frac{1}{r} \frac{\partial}{\partial x} (r \rho v_x v_r) + \frac{1}{r} \frac{\partial}{\partial r} (r \rho v_r^2) = - \frac{\partial p}{\partial r} + \frac{1}{r} \frac{\partial}{\partial x} \left[ \tau \left( \frac{2}{3} (\nabla \cdot \mathbf{v}) \right) \right] - 2 \frac{v_r}{r^2} + \frac{2}{3} \frac{\mu}{r} (\nabla \cdot \mathbf{v})
\]  

\[+ \rho \frac{v_r^2}{r} + F_r
\]

(4.3)
where
\[ \nabla \cdot \vec{v} = \frac{\partial v_x}{\partial x} + \frac{\partial v_r}{\partial r} + \frac{v_r}{r} \]  \hspace{1cm} (4.4)

and \( \mu \) is molecular viscosity, \( p \) is static pressure, \( F \) is external body forces, and \( v_z \) is the swirl velocity, which is set to zero in the present study. Gravitational body forces are neglected due to the high flow rates and the concomitant short time passage through the device. There is negligible gravitational settling of the formed elements during time frames measured in only tens of microseconds.

It is also important to note that the flow was modeled as a continuum and not as particulate flow. For this reason, the standard Navier Stokes equations were solved neglecting all microscopic effects. Modeling blood flow as a continuum is by far the most common practice today, and the choice to innovate within this continuum framework was made with a view of pragmatically advancing biofluid simulation for the majority of the biomedical community.
CHAPTER 5
DETERMINATION OF THE VISCOSITY OF BLOOD

The experimental data obtained from the researchers at UMC did not report the viscosity of blood; instead, the hematocrit of the blood was provided. In order to conduct the CFD analysis, a relationship between hematocrit and viscosity needed to be obtained. Dr. Marina Kameneva from the University of Pittsburgh experimentally determined a relationship between hematocrit and viscosity for human blood at 37°C. Her results are shown in Figure 5.1, obtained from [25]. It is well known that the viscosity of blood depends not only on hematocrit but also on shear rate [13]. At low shear rates, RBCs tend to stack together similar to a stack of coins; this causes the viscosity to increase and a non-Newtonian constitutive relationship in blood. This stacking is referred to as rouleaux formation and cannot withstand shear stresses exceeding 1 dyne/cm², which is equivalent to 0.1 N/m² [6]. Figure 5.2, obtained from [30], shows a rouleaux formation. Since the shear stress levels from the current simulations far surpass 0.1 N/m², rouleaux formation was not taken into consideration in this study. The minimum shear stress in this study was estimated to be approximately 680 N/m² as will be shown in Section 8.1.
Figure 5.1

Viscosity vs. Hematocrit

Figure 5.2

Rouleaux Formation
In this chapter, the computational results from the single-layer and two-layer viscosity models simulations will be reported. These results were found to not match our desired experimental data. Hence, some physical aspects of blood flow will be discussed in order to deduce, formulate, and validate a two-layer viscosity model approach. Finally the two-layer viscosity model results will be reported.

6.1 Single-Layer Viscosity Model

6.1.1 Single-Layer Viscosity Model Setup

The first series of CFD simulations that attempted to match the experimental results involved a single-layer viscosity model. This model simply consisted of constant viscosity and constant density throughout the entire system. This is standard practice in CFD modeling of blood flow. Figure 6.1 gives an idea of how this simulation is set up inside the shear tube.

6.1.2 Single-Layer Viscosity Model Results

The results obtained from Fluent for the single-layer viscosity model are found in Table 6.1. Comparing these results to the average value of the pressure drop found in
Table 3.2, one can see that the error produced from the computational simulations is large, approximately 95% for each of the flow rates. From Table 6.1, it becomes apparent that this model is inappropriate for capillary tube class of flows. Therefore possible causes of these large deviations were investigated with a view of reducing these errors.

Table 6.1

Results at Various Flow Rates for 40% Ht using Single-Layer Model

<table>
<thead>
<tr>
<th>Flow Rate (mL/min)</th>
<th>40% Ht CFD</th>
<th>40% Ht Exp’t Avg</th>
<th>% Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>233.96 psi</td>
<td>122 psi</td>
<td>91.77</td>
</tr>
<tr>
<td>8</td>
<td>474.6 psi</td>
<td>235 psi</td>
<td>101.96</td>
</tr>
<tr>
<td>10</td>
<td>597.32 psi</td>
<td>300.5 psi</td>
<td>98.78</td>
</tr>
<tr>
<td>12</td>
<td>721.6 psi</td>
<td>370.5 psi</td>
<td>94.76</td>
</tr>
</tbody>
</table>

6.2 Single-Layer Viscosity Model Issues

There are many physical aspects of blood flow that might affect pressure drop in small diameter tubing. Laminar flow is characterized by smooth particle pathlines, and turbulent flow occurs when flow particles move chaotically about the flow chamber and do not follow a rigid path [14]. Laminar to turbulent flow transition is a common occurrence in
tubes when the flow passes through an expansion or constriction. Having knowledge of
the Reynolds number for each flow rate helps confirm validate or reject whether this tran-
sition may be occurring. Other physical aspects that may be considered are the Fahraeus
Effect and the Fahraeus-Lindqvist Effect. Each of these physical phenomena are discussed
below.

6.2.1 Laminar to Turbulent Transition

It has been found that in circular microtubes with diameters between 50 and 247
µm, laminar to turbulent transition occurs at critical Reynolds numbers between ≈ 1800-
2000 [31], which is slightly different than that in regular circular tubes where the critical
Reynolds number ranges between ≈ 2100-2500 [5] [14]. The Reynolds number of the
current study can be found using Equation (6.1).

\[ Re = \frac{\rho V D}{\mu} = \frac{V D}{\nu} \]  \hspace{1cm} (6.1)

Using the diameter of the model simulations, \( D = 0.000127 \text{ m} \), the Reynolds numbers
at the various flow rates can be found in Table 6.2. The second column shows the Reynolds
number that is produced from the single-layer flow cases with a viscosity of 0.0038 kg/m-
s, which corresponds to that of blood with 40% hematocrit. The third column shows an
extreme Reynolds number calculated assuming single-layer flow with a viscosity of 0.0015
kg/m-s, which matches that of cell-free plasma at 37°C. Since all of the Reynolds numbers
calculated are much lower than the critical Reynolds number, regardless of the flow rate or
the particular viscosity chosen, we conclude that laminar to turbulent transition does not
occur in the current studies, i.e., the flow is fully laminar.
Table 6.2
Reynolds Number at Various Flow Rates

<table>
<thead>
<tr>
<th>Flow Rate (mL/min)</th>
<th>$\rho = 1050; \mu = 0.0038$</th>
<th>$\rho = 1025; \mu = 0.0015$</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>2.89</td>
<td>7.14</td>
</tr>
<tr>
<td>8</td>
<td>5.77</td>
<td>14.27</td>
</tr>
<tr>
<td>10</td>
<td>7.21</td>
<td>17.84</td>
</tr>
<tr>
<td>12</td>
<td>8.66</td>
<td>21.42</td>
</tr>
</tbody>
</table>

6.2.2 Fahraeus Effect

The next phenomenon that we considered was the Fahraeus effect, which states that when blood flows from a large diameter tube through a smaller (capillary) tube, the average hematocrit of the capillary blood is less than that of the blood in the larger tube [4] [16]. Since the single-layer viscosity model did not take this physical phenomenon into effect, either this effect, by necessity, must be neglected or else another model must be hypothesized to account for it. The net effect of the Fahraeus effect is realized if the average viscosity is taken across the shear tube.

6.2.3 Fahraeus-Lindqvist Effect

The Fahraeus-Lindqvist effect, directly related to the Fahraeus effect, states that in very small tubes ($\approx 300 \ \mu m$) the apparent viscosity decreases as tube diameter decreases. This is a direct effect resulting from the decrease in the tube hematocrit [13]. Recall that the tubes used in the current CFD simulations were only $127 \ \mu m$. From Figure 6.2, obtained from [16], it can be seen that for tubes of this diameter, the viscosity of blood is experimentally found to be approximately $3.4 \text{ cP} = 0.0034 \text{ kg/m-s}$, which is down from
the 4.0 cP viscosity originally introduced into the system [16]. Therefore, we can assume that for our current simulations, the apparent viscosity in the tube should decrease approximately 8.5% from the viscosity of the fluid that was originally introduced to the system. Using the viscosity of blood that corresponds to a 40% Ht, 0.0038 kg/m-s, and applying the 8.5% predicted decrease resulting from the Fahraeus-Lindqvist effect reduces the viscosity of blood inside the shear tube to approximately 0.0035 kg/m-s.

![Figure 6.2](image)

**Figure 6.2**

**Fahraeus-Lindqvist Effect**

Using the single-layer model CFD data with viscosity reduced to 0.0035 kg/m-s, shown in Table 6.3, a large error, averaging 80%, is still obtained. However, applying this modification does prove to better approximate the desired experimental values. Considering
the single-layer model with 4 mL/min flow rate and referring to Figure 6.3, the experimentally determined pressure drop cannot be obtained unless the viscosity decreases to approximately 0.00195 kg/m-s. That yields a 52% viscosity decrease in the shear tube, which is extremely larger than the predicted 8.5% decrease. Unfortunately, there is no rational physical basis for this type of viscosity approximation.

Due to the computational results being approximately 80% higher than the experimental results, even after applying the 8.5% decrease resulting from the Fahraeus-Effect, further investigation into causes of the Fahraeus-Lindqvist was investigated. According to Haynes, there are two areas thought to contribute to this well known phenomenon: cell migration effects and the sigma phenomenon [20]. Cell migration effects account for the fact that red blood cells tend toward the center of tube flow, forcing plasma and platelets toward the wall of the outer tube. The sigma phenomena accounts for the existence of unsheared laminae that causes the flow of the fluid to be calculated by a summation (hence...
Table 6.3
Results at Various Flow Rates for 40% Ht using the 8.5% F-L Correction

<table>
<thead>
<tr>
<th>Flow Rate (mL/min)</th>
<th>40% Ht CFD</th>
<th>40% Ht Exp’t Avg</th>
<th>% Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>214.07 psi</td>
<td>122 psi</td>
<td>75.46</td>
</tr>
<tr>
<td>8</td>
<td>434.26 psi</td>
<td>235 psi</td>
<td>84.79</td>
</tr>
<tr>
<td>10</td>
<td>546.55 psi</td>
<td>300.5 psi</td>
<td>81.88</td>
</tr>
<tr>
<td>12</td>
<td>660.26 psi</td>
<td>370.5 psi</td>
<td>78.21</td>
</tr>
</tbody>
</table>

the term sigma) rather than an integration [20]. Although the sigma phenomena was not investigated as part of the current research, it is assumed to be a reinterpretation of cell migration effects.

Because of the drastic differences between the experimental results and single-layer data, these naturally occurring phenomena, including the hydrodynamic lifting effects, a new two-layer blood viscosity model was developed in order to better simulate these naturally occurring phenomena in the cardiovascular system.

6.3 Two-Layer Viscosity Model

6.3.1 Two-Layer Viscosity Model Setup

In an attempt to better approximate the experimental data, a two-layer viscosity model was hypothesized. For this model, two regions in the shear tube were created with distinct viscosities and densities separated by a core radius, $r_c$. Figure 6.4 gives a better representation of how the two-layer viscosity model was set up within the shear tube. This model was setup in Fluent using several user-defined functions (UDFs), examples of which can be found in the appendix.
6.3.2 Previous Research Studies

Examples of this type of two-layer model is not without precedence. Previous studies modeling two-phase flow (RBC concentrated area and plasma-like area) has been performed by Cokelet and Goldsmith in vertical tubes [9]. Their studies focused on the hydrodynamic resistance of blood flow through microtubes with internal diameters of 55, 73, and 172 µm. Each of the tube lengths studied were 10 cm, and the flow rates ranged between 0.00003–0.0024 mL/min. The hematocrit of most of their studies was approximately 34% Ht. These parameters, using theory from Poiseuille’s Law [13] and Equation (6.2), results in shear stresses ranging between 0.104–0.272 N/m². The flow device setup and pressure drop protocol that they used can be found in Figure 6.5, obtained from [9].

\[ \tau_{rx} = \mu \frac{dv_x}{dr} = \mu \frac{(\Delta P)r}{2\mu L} = \frac{(\Delta P)r}{2L} = \frac{8\mu LQ}{\pi r^4} \frac{r}{2L} = \frac{4\mu Q}{\pi r^3} \]  \hspace{1cm} (6.2)

For comparison, recall that flow rates for the current study are 4–12 mL/min. These flow rates, along with the current viscosities used, produce wall shear stress values ranging from approximately 620–1900 N/m². The flow rates and shear stresses of this thesis are
Figure 6.5

Experimental Setup used by Cokelet and Goldsmith
much higher than those of Cokelet and Goldsmith. However, the main conclusions and implications developed by Cokelet and Goldsmith are believed to be applicable in this study’s device and hence quite relevant. Their findings include [9]:

1. Fahraeus Effect was successfully shown to appear in their experiments. That is, the ratio of the tube hematocrit to feed reservoir hematocrit decreased with decreasing steady flow.

2. Inward migration of RBCs and development of two-phase flow was due to the formation of rouleaux. This conclusion is attributed to the fact that their shear stresses at low flow rates were very close to 0.1 N/m², which is the yield shear stress required to break up rouleaux formation.

3. The minimum core radius decreased with decreasing hematocrit.

4. For feed hematocrits of 46% and 34%, the two phases were found to be distinct at $r_c \approx 0.85 r_o$ and $r_c \approx 0.75 r_o$, respectively.

5. At lower flow rates, a large portion of the center core region underwent plug flow, which is characterized by a blunted velocity profile.

### 6.3.3 Two-Layer Viscosity Model Results

The results obtained from Fluent for the two-layer viscosity model are found in Table 6.4. Here the computational parameters are $\rho_c$, $\mu_c$, $\rho_o$, $\mu_o$, $r_c$, and $r_o$, which were 0.004 kg/m-s, 1050 kg/m³, 0.0015 kg/m-s, 1025 kg/m³, 0.0000508 m = 0.80 $r_o$, and 0.0000635 m, respectively. Comparing these results to the average value of the pressure drop found in Table 3.2 for the 40% Ht experiments, one can see that the CFD data matches the experimental results to approximately 6% or less.
Table 6.4

Results at Various Flow Rates for 40% Ht using Two-Layer Model

<table>
<thead>
<tr>
<th>Flow Rate (mL/min)</th>
<th>40% Ht CFD (psi)</th>
<th>40% Ht Exp’t Avg (psi)</th>
<th>% Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>122.2</td>
<td>122</td>
<td>0.16</td>
</tr>
<tr>
<td>8</td>
<td>248.3</td>
<td>235</td>
<td>5.66</td>
</tr>
<tr>
<td>10</td>
<td>312.6</td>
<td>300.5</td>
<td>4.03</td>
</tr>
<tr>
<td>12</td>
<td>377.8</td>
<td>370.5</td>
<td>1.97</td>
</tr>
</tbody>
</table>
7.1 Poiseuille Flow

In order to better understand the two layer model, the behavior of the model was examined with respect to known theory as well as parametric variations of the model parameters. The behavior of the two-layer model compared to the known theory of Poiseuille’s Law, Equation (7.1) was investigated. Here $Q$ is flow rate in m$^3$/s, $\mu$ is viscosity in kg/m-s, $\Delta P$ is the pressure drop across the shear tube in N/m$^2$, $R$ is the outer tube radius in m, and $L$ is the length of the shear tube, 0.04 m. Both models reveal a linear relationship between pressure drop and flow rate, shown in Figure 7.1.

\[
Q = \pi \frac{2|\Delta P|}{L} \int R \left( rR^2 - r^3 \right) dr = \frac{|\Delta P|\pi R^4}{8\mu L} \tag{7.1}
\]

In order to better understand the single-layer model CFD data, theoretical pressure drop was also calculated, using Equation (7.1), for a viscosity of 0.0038 kg/m-s. This plot, shown in Figure 7.2, demonstrates the accuracy of Fluent predictions. Theoretical pressure drop for the two-layer model was not calculated due to the lack of a definitive viscosity. Equation (7.1) requires only one viscosity to accurately obtain a pressure drop and flow rate relationship.
Figure 7.1

CFD Pressure Drop vs. Flow Rate

Figure 7.2

Pressure Drop vs. Flow Rate Theoretical Comparison
Delving further, an investigation of the relationship between strain rate, $\gamma$, and radius was also produced, shown in Figures 7.3-7.6. A linear relationship best represents this data, further indicating that the linear shear stress/strain rate relationship of Poiseuille’s Law holds for both models. The reason for the wavy variations in the CFD data is most likely due to numerical averaging error. For the lower flow rates, the computational data follow the theoretical data very well; however, past the core radius line, the 12 mL/min flow rate shows that the computational data are higher than the theoretical data. These observed differences for the 12 mL/min flow rate may be attributed to data averaging and the larger flow gradient associated with the higher flow rate.

All theoretical data obtained for the single-layer model was obtained using Equation (7.2). For the two-layer model, a linear relationship can reasonably be expected; however, there should be two distinct slopes associated with the two distinct layers. Theoretical relationships for the two-layer flow simulations were obtained by applying Poiseuille’s Law separately to each of the regions. Equation (7.3) shows the mathematical formulas used for obtaining the theoretical data for two-layer model. For the lower flow rates, the computational data follow the theoretical data very well; however, past the core radius line, the 12 mL/min flow rate shows that the computational data are higher than the theoretical data. These slight differences for the 12 mL/min flow rate could be attributed to numerical issues arising from Fluent.

\[
\gamma = \frac{r(\Delta P)}{2\mu L} = \frac{r(\Delta P)}{2(0.0038)(0.04)}
\]  

(7.2)
\[ \gamma = \frac{r(\Delta P)}{2\mu L} = \begin{cases} 
\frac{r(\Delta P)}{2(0.0036)(0.04)} & \text{if } 0 \leq r \leq r_c \\
\frac{r(\Delta P)}{2(0.0015)(0.04)} & \text{if } r_c < r \leq r_o 
\end{cases} \] (7.3)

7.2 Pressure Drop Versus Core Radius Size

As can be seen from Figures 7.7 and 7.8, pressure drop is very much dependent on the size of the core radius. As the core radius size increases, the pressure drop also increases; it increases almost exponentially close to the wall of the shear tube. Similar trends are seen for the other flow rates. From this data, \( r_c = 0.8r_o \) produces results that best match the experimental data. This is in good agreement with the major conclusions from the research of Cokelet and Goldsmith found in Section 6.3.2 [9]. Thus, the two-layer model appears to be well grounded in a physiological foundation.
Figure 7.4
4 mL/min Two-Layer Strain Rate vs. Radius

Figure 7.5
8 mL/min Single-Layer Strain Rate vs. Radius
Figure 7.6

12 mL/min Two-Layer Strain Rate vs. Radius

Figure 7.7

4 mL/min Two-Layer Pressure Drop vs. Core Radius Size
7.3 Pressure Drop Versus Core Viscosity

Focusing on the 4 mL/min flow rate simulations, we find that pressure drop does slightly depend on the core viscosity, seen in Figure 7.9. As the core viscosity increases, the pressure drop also increases. Similar trends, although not presented here, were also seen for the higher flow rates. To obtain the data necessary to plot accurate figures, certain core viscosity values are used. Specifically, these values were: the viscosity of blood with 40% Ht, 0.0038 kg/m-s, 0.00342, 0.004, 0.00418, 0.00456, and 0.00494 kg/m-s. The core viscosity that produces the closest match to the desired pressure drop using \( r_c = 0.8 r_o \), from Section 7.2, is \( \mu_c = 0.004 \) kg/m-s, which is the standard accepted viscosity of blood at 37°C. Once again, there is a strong physical basis that underlies the currently selected values of the two-layer model parameters.
7.4 Pressure Drop Versus Outer Viscosity

From the two-layer model data, it was expected and found that pressure drop is heavily dependent on outer viscosity. As can be seen in Figures 7.10 and 7.11, there is a linear relationship between pressure drop and outer viscosity. Recall that the outer area of the shear tube is that region that is comprised mainly of RBC-depleted plasma and has a viscosity of 0.0015 kg/m-s at 37°C. The values of outer viscosity used to plot Figure 7.10 found below are: the viscosity of plasma at 37°C, 0.0015 kg/m-s, 0.00135, 0.00165, 0.0018, 0.00195, and 0.0021 kg/m-s. Using the values of $r_c$ and $\mu_c$ predicted from Sections 7.2-7.4 the outer viscosity value that best matches the experimental pressure drop is $\mu_o = 0.0015$ kg/m-s, and once more reflects a strong physical underpinning of the model.
Figure 7.10
4 mL/min Two-Layer Pressure Drop vs. Outer Viscosity

Figure 7.11
12 mL/min Two-Layer Pressure Drop vs. Outer Viscosity
7.5 Shapes of Velocity Profiles

Focusing on the 4 mL/min flow rate single-layer viscosity model, the velocity profile produced from the CFD data is parabolic in shape as expected for laminar tube flow [14] [5]. This plot can be seen in Figure 7.12. To show the accuracy of Fluent, the velocity profile for the 4 mL/min flow rate using the single-layer model is plotted along with the theoretical velocity profile using the equation for velocity distribution for standard tube flow, Equation (7.4). From this figure, one can see that the computational data produced in Fluent matches the theoretical data to within 3%. Figure 7.13 shows the comparison between the single-layer viscosity model and the two-layer viscosity model. While the single-layer model predicts a parabolic velocity profile, the two-layer model produces a blunted profile, which is indicative of turbulent or laminar plug flow. One possible explanation is that since the RBCs tend toward the center of the tube, they will likely flow through the tube with plug flow characteristics. Figure 7.14 shows the comparison of velocity profiles at various flow rates for the two-layer viscosity model for $r_c = 0.8r_o$. It is concluded that as flow rate decreases, the velocity profile becomes more blunted. This is in agreement with experimental results found by Cokelet and Goldsmith [9], refer to Section 6.3.2, providing even further evidence that the two-layer model reflects physical reality.

$$V = \frac{(\Delta P)R^2}{4\mu L} \left[ 1 - \left( \frac{r}{R} \right)^2 \right]$$

(7.4)
Figure 7.12
12 mL/min Two-Layer Shear Stress vs. Core Radius Size

Figure 7.13
Two-Layer Model Velocity Profile Comparison
Figure 7.14

Two-Layer Model Velocity Profile Comparison
CHAPTER 8
PRELIMINARY CHARACTERIZATION OF BLOOD DAMAGE

To begin the characterization of a blood damage model, the shear stress magnitude and the exposure time to shear stress within the shear tube needs to be analyzed. Following this analysis, experimental results obtained at UMC and how their basic relationship to the computational results are discussed.

8.1 Shear Stress Follows Pressure Drop Trends

The average wall shear stress and strain rate values within the shear tube are found in Table 8.1. Focusing on the 4 mL/min flow rate, the average CFD shear stress over the shear tube can be deduced. This information is plotted in Figures 8.1 and 8.2. Values found in Table 8.1 do not agree with the experimental values obtained from Holme, et al who reported the shear rate obtained was approximately $10500 \, s^{-1}$ for an 80% occlusion that is approximately 0.5 inches long and 10 mL/min flow rate with $Re = 20$ [23]. Our results are approximately 100 times larger than these reported values. (The current microdevice can be thought representative of a small artery with an 87.5% occlusion that is approximately 1.5 inches long.) Possible explanations of this mismatch include, but are not limited to, numerical error produced by CFD, the way strain rate values were found experimentally compared to how Fluent calculates these values, or the differences in the length of the
occlusions. These strain rate and shear stress values are obviously in the nonphysiological range of the normal blood flow. Goldsmith and Turrito have stated that typical wall shear rates in blood vessels can range between 20-2000 s$^{-1}$, depending on how large or small the particular vessel is [17].

Table 8.1

Wall Shear Stress and Strain Rate Value for Two-Layer Model

<table>
<thead>
<tr>
<th>Flow Rate (mL/min)</th>
<th>shear stress (N/m$^2$)</th>
<th>strain rate (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>627.0128</td>
<td>418008.500</td>
</tr>
<tr>
<td>8</td>
<td>1257.730</td>
<td>838488.250</td>
</tr>
<tr>
<td>10</td>
<td>1575.683</td>
<td>1050452.500</td>
</tr>
<tr>
<td>12</td>
<td>1894.998</td>
<td>1263335.000</td>
</tr>
</tbody>
</table>

8.2 Newtonian Fluid

Since the shear rate in the current studies was determined to be much larger than 100 s$^{-1}$, non-Newtonian effects do not have to be considered [29], and so blood behaves as a Newtonian fluid, which is a fluid that follows Newton’s law of viscosity, Equation (8.1), where $\tau_{rx}$ represents shear stress in the x-direction on an area perpendicular to the r direction and $\frac{du_r}{dy}$ is the velocity gradient in the r-direction. The single-layer viscosity model produces a linear relationship between shear stress and strain rate, indicating that it is modeling a Newtonian fluid. This plot can be seen in Figure 8.4. Comparing this to the two-layer model in Figure 8.5, it can be seen that inside the core radius line, the data is very comparable to that of the single-layer model. However, outside the core radius line, the
Figure 8.1
4 mL/min Two-Layer Shear Stress vs. Core Radius Size

Figure 8.2
4 mL/min Two-Layer Shear Stress vs. Outer Viscosity
shear stress continues to develop a linear relationship but at a different rate and baseline. Since the viscosity is constant in the outer region of the shear tube, this linear Newtonian relationship is expected. Similar relationships are seen for all other flow rates.

\[ \tau_{rx} = -\mu \frac{dv_x}{dr} \]  

(8.1)

8.3 Exposure Time to Shear Stress

Since one major player in blood damage is the time duration of blood exposed to shear stress, the exposure time within the shear tube was analyzed. By observing Figure 8.6, one can see that exposure time increases as the radial location moves toward the outer wall of the shear tube. There is also a nontrivial increase in time exposure as the core radius size increases. Table 8.2 gives a brief listing of the major results. These data were found using
Figure 8.4
4 mL/min Single-Layer Shear Stress vs. Strain Rate

Figure 8.5
4 mL/min Shear Stress vs. Strain Rate
velocities predicted in Fluent and Equation (8.2). As can be seen in Figure 8.7, exposure
time increases as the shear tube wall is approached and increases as the flow rate decreases.

\[
t = \frac{\text{Length}}{\text{Velocity}} = \frac{L}{V} \tag{8.2}
\]

Table 8.2
Shear Stress Exposure Time at Various Flow Rates

<table>
<thead>
<tr>
<th>Flow Rate</th>
<th>( r = 0 )</th>
<th>( r = r_c )</th>
<th>( r = r_c + 0.5(r_o - r_c) )</th>
<th>( r = r_c + 0.75(r_o - r_c) )</th>
<th>( r = r_o )</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 (mL/min)</td>
<td>4.78 ms</td>
<td>8.72 ms</td>
<td>14.03 ms</td>
<td>26.38 ms</td>
<td>378 ms</td>
</tr>
<tr>
<td>8 (mL/min)</td>
<td>2.40 ms</td>
<td>4.36 ms</td>
<td>7.01 ms</td>
<td>13.21 ms</td>
<td>190 ms</td>
</tr>
<tr>
<td>10 (mL/min)</td>
<td>1.92 ms</td>
<td>3.48 ms</td>
<td>5.61 ms</td>
<td>10.57 ms</td>
<td>152 ms</td>
</tr>
<tr>
<td>12 (mL/min)</td>
<td>1.60 ms</td>
<td>2.90 ms</td>
<td>4.67 ms</td>
<td>8.81 ms</td>
<td>127 ms</td>
</tr>
</tbody>
</table>

8.4 Relationship to Blood Damage

According to experimental results obtained from UMC, Figure 8.8, platelet activation
occurs to some degree at all flow rates when using the 127 \( \mu \)m tubing. Platelet activation
was quantified by using the value of serotonin secretion, which is a common method
in determining platelet activation. The blue bars shown in Figure 8.8 were control ex-
periments that were performed using no shear tube. The experimental results show that
as the flow rate increases, more activation is observed. Based on the current computa-
tional simulations, the exposure time needed for platelet activation is higher at lower shear
stresses (lower flow rates). This is in very good agreement with previous findings from
other researchers [21][33].

49
Figure 8.6

4 mL/min Exposure Time for $r_c = 0.8r_0$

Figure 8.7

Two-Layer Exposure Time for $r_c = 0.8r_0$
Also from the experimental results, there is significant RBC lysis at higher flow rates for the same size tubing, Figure 8.9. RBC lysis is also known as hemolysis, which refers to the breaking of RBCs and the consequent of hemoglobin release. Lysis does not appear to occur below flow rates of 6 mL/min. Again, we see an inverse relationship for shear stress exposure time and RBC lysis. This is due to the inverse relationship between exposure time and shear stress; so, higher shear stresses require less time to cause RBC lysis.
Figure 8.9

Red Blood Cell Lysis for Various Flow Rates
CHAPTER 9

CONCLUSIONS

Based on computational analysis presented in this paper and using experimental validation, it has been shown that, for capillary tube flows, a single-layer viscosity model, which is the standard practice in CFD blood flow modeling today, produced results that reflected approximately 95% error. A two-layer viscosity model was developed based on physical reasoning and was shown to predict pressure drop that matched experimental data to within 6% for all flow rates.

The first two objectives of this thesis were to develop and validate a microchannel flow device and to develop protocol for obtaining the pressure drop across this microdevice. This was successfully accomplished by creating the experimental microdevice along with the pressure drop protocol. The third objective was to develop mathematically-based engineering models of blood flow. This objective was achieved by the detailed CFD analysis performed using Fluent and by developing a novel two-layer viscosity model to model blood flow in capillary tubes. The final objective was to begin characterization of blood damage. This was successfully achieved by relating shear stress exposure time and shear stress levels obtained using CFD to the experimental data that showed the percentage of platelet activation and RBC lysis.
The information presented in this thesis, including the brief characterization of blood damage, should prove to be useful to cardiovascular device designers when developing or optimizing new devices. This research, though limited, can provide future researchers with information they could use in developing better cardiovascular devices. With the information presented here, designers could find a deeper understanding as to what physical design aspects should be considered when modeling blood flow in microsized channels as well as aspects that should be avoided in order to limit shear stress exposure time.
CHAPTER 10

FUTURE RESEARCH

For possible future extensions of this research, one could consider adding functionality to the model so as to definitively quantify platelet activation and RBC lysis. Also, modeling new geometries such as Figures 10.1 and 10.2 as a possible means to increase time exposure within a reasonably sized device would provide cardiovascular device designers more insight to developing different devices.

Figure 10.1

Optional Future Test Case
Figure 10.2

Optional Future Test Case
REFERENCES


APPENDIX

USER-DEFINED FUNCTIONS
two_phase.c
UDF for specifying 2-phase flow properties—density and viscosity of blood.
In this code, only the value for rad_core will change. For my studies, I used
rad_core = 0.10, 0.20,...,0.80,0.90*rad_outer.
*********************************************************************/

#include "udf.h" /* must be at the beginning of every UDF */

/* Define global constants. This makes the constants easier to change. */
#define blood_viscosity 0.0038 /* kg/m-s */
#define blood_density 1050 /* kg/m^3 */
#define plasma_viscosity 0.0015 /* kg/m-s */
#define PI_viscosity 0.004 /* kg/m-s core viscosity */
#define PI_density 1050 /* kg/m^3 core density */
#define PII_viscosity plasma_viscosity /* kg/m-s outer region viscosity */
#define PII_density 1025 /* kg/m^3 outer region density */
#define rad_outer 0.0000635 /* m */
#define rad_core (varies) /* m */
#define small_inlet 0.00 /* m */
#define small_outlet 0.040 /* m */

DEFINE_PROPERTY(cell_viscosity, c, t) 
{
  real mu; /* holds value of viscosity; returned at the end */
  real cell_pos[ND ND];

  C_CENTROID(cell_pos, c, t);
  if ((cell_pos[0] >= small_inlet) && (cell_pos[0] <= small_outlet))
  {
    if (cell_pos[1] <= rad_core) mu = PI_viscosity;
    else mu = PII_viscosity;
  }
  else mu = blood_viscosity;

  return mu;
}

DEFINE_PROPERTY(cell_density, c, t) 
{
  real rho; /* holds value of viscosity; returned at the end */
  real cell_pos[ND ND];

  C_CENTROID(cell_pos, c, t);
  if ((cell_pos[0] >= small_inlet) && (cell_pos[0] <= small_outlet))
  {
    if (cell_pos[1] <= rad_core) mu = PI_viscosity;
    else mu = PII_viscosity;
  }
  else mu = blood_viscosity;

  return mu;
}
C_CENTROID(cell_pos, c, t);
if ((cell_pos[0] >= small_inlet) && (cell_pos[0] <= small_outlet))
{
  if (cell_pos[1] <= rad_core) rho = P1_density;
  else rho = PII_density;
}
else rho = blood_density;

return rho;
}

/****************************************************************
  UDF for specifying 2-phase flow properties—density and viscosity of blood.
  In this code, only the value for PI viscosity (core area) will change. For my studies, I
  used PI viscosity = blood viscosity + 0.10, 0.00, 0.10,...,0.40*blood viscosity.
****************************************************************/

#include "udf.h" /* must be at the beginning of every UDF */

/* Define global constants. This makes the constants easier to change. */
#define blood viscosity 0.0038 /* kg/m-s */
#define blood_density 1050 /* kg/m3 */
#define plasma viscosity 0.0015 /* kg/m-s */
#define PI viscosity (varies) /* kg/m-s core viscosity */
#define PI density 1050 /* kg/m3 core density */
#define PII viscosity plasma viscosity /* kg/m-s outer region viscosity */
#define PII density 1025 /* kg/m3 outer region density */
#define rad_outer 0.000635 /* m */
#define rad_core 0.80*rad_outer /* m */
#define small_inlet 0.00 /* m */
#define small_outlet 0.040 /* m */

The remainder of the code is identical to that above.
UDF for specifying 2-phase flow properties—density and viscosity of blood. In this code, only the value for PII viscosity (outer area) will change. For my studies, I used PII viscosity = plasma viscosity ± 0.10, 0.00, 0.10,...,0.40*plasma viscosity.

#include “udf.h” /* must be at the beginning of every UDF */

/* Define global constants. This makes the constants easier to change. */
#define blood viscosity 0.0038 /* kg/m-s */
#define blood density 1050 /* kg/m^3 */
#define plasma viscosity 0.0015 /* kg/m-s */
#define PI viscosity blood viscosity /* kg/m-s core viscosity */
#define PI density 1050 /* kg/m^3 core density */
#define PII viscosity (varies) /* kg/m-s outer region viscosity */
#define PII density 1025 /* kg/m^3 outer region density */
#define rad outer 0.0000635 /* m */
#define rad core 0.80*rad outer /* m */
#define small inlet 0.00 /* m */
#define small outlet 0.040 /* m */

The remainder of the code is identical to that above.