NUMERICAL IMPLEMENTATION OF A CONTINUUM PLATELET AGGREGATION MODEL

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by
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Abstract

A continuum stress transport model of platelet aggregation from the literature [14], [16], [15], and [18] is presented and solved numerically. The model is a single-scale reduction of a multi-scale model and utilizes the incompressible Navier-Stokes equations with a Newtonian constitutive relationship to govern blood flow. Other field variables including platelet and chemical activator concentrations exist with partial differential equations governing their transport. The platelet aggregation model is closely related to the model of the viscoelastic Oldroyd-B fluid, which is discussed. The focus of this thesis is on the numerical solution of the Oldroyd-B equations and the equations comprising the platelet aggregation model using a finite volume formulation within an existing open source Computational Fluid Dynamics platform. Pressure-velocity coupling is achieved using the PISO Algorithm while the remaining model equations are solved sequentially. In the first class of simulations, the flow of an Oldroyd-B fluid is solved within a two dimensional planar domain. The viscous and elastic properties of the fluid are varied in an effort to observe the model’s resulting behavior. Exact solutions for the transient and steady-state flow of an Oldroyd-B fluid are used for the purpose of validating the numerical approach. Numerical solutions are observed to correspond well with exact solutions for a range of parameter sets. Solution divergence is observed under certain conditions, specifically for fluids with high Weissenberg numbers and elastic moduli. In the second class of simulations, the platelet aggregation model is solved within the same domain as the Oldroyd-B simulations. Clot growth is observed but solution divergence occurs in the presence of growth of the model’s stress tensor field. By limiting certain model parameters it is shown that numerical stability can be improved. Using this approach, the sensitivity of results to various model parameters is investigated. Finally, a preliminary investigation of the application of the model to the clinically important case of clot growth within stagnant and recirculating flows is presented.
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A.2 Dimensional units used within OpenFOAM for model parameters. 1 kgmol = 1000 mol. 86
List of Symbols

\( \eta_s \) solvent dynamic viscosity
\( \eta_p \) polymer dynamic viscosity
\( \eta_o \) total dynamic viscosity
\( \psi \) solvent viscosity ratio
\( \lambda \) relaxation time
\( \tau \) elastic stress tensor
\( D \) deformation rate tensor
\( \rho \) fluid density
\( \mu \) fluid viscosity
\( D_c \) chemical activator diffusivity
\( D_{n} \) non-activated platelet diffusivity
\( K \) chemical activator degradation rate constant
\( A \) chemical activator release rate
\( \alpha_0 \) inter-platelet link formation rate constant
\( \alpha_2 \) cohesive stress formation rate constant
\( \beta \) breaking rate
\( R(c) \) platelet activation rate function
\( C_{th} \) threshold chemical activator concentration
\( C_o \) initial injury zone chemical activator concentration
\( I \) identity matrix
\( \nabla \cdot \) divergence operator
$\nabla$ gradient operator
$\nabla^2$ laplacian operator
$\frac{\partial}{\partial t}$ partial time derivative operator
$tr$ trace operator
$p$ fluid pressure
$u$ fluid velocity
$\phi_a$ activated platelet concentration
$\phi_n$ non-activated platelet concentration
$c$ chemical activator concentration
$z$ inter-platelet link concentration
$\sigma$ cohesive stress tensor
$Wi$ Weissenberg number
$Re$ Reynolds number
$E$ elasticity number
$G$ elastic modulus
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Chapter 1

Introduction

1.1 Review of Relevant Literature

1.1.1 Haemostasis and Thrombosis

1.1.1.1 Definitions and Clinical Implications

The blood clotting process, or haemostasis, is essential to life. When injury to a blood vessel occurs, platelets bind to the damaged site and a clot forms in order to seal off the opening preventing blood loss. Through similar biological mechanisms, an unwanted blood clot, or thrombus, can also form under certain circumstances within the bloodstream. Thrombosis occurs in situations where clotting is not necessary and in fact detrimental to the patient and therefore different than regular haemostasis. One condition that can lead to thrombus formation is atherosclerosis. Plaque that builds up over time causes a local narrowing of the blood vessel. These regions can develop blood clots which may grow to fully block flow or break away (embolize) and travel downstream. The surfaces of artificial blood contacting devices are often prone to the formation of a thrombus as well. Such devices include heart pumps, replacement heart valves, stents, and in general any foreign artificial device implanted in the blood stream. Clots which form over these devices also can partially or completely impede blood flow through a vessel, and possibly embolize.

As a thrombus grows it decreases the quantity of oxygen supplied to cells and organs downstream of the clotting site. Furthermore, if embolization occurs the now separated clot can travel and become lodged in narrower vessels, causing a sudden and dramatic decrease in oxygen supply to cells and organs downstream of the lodging point. Depending on the blood vessel in question, thrombosis can cause heart attack, stroke, and pulmonary embolism, by reducing oxygen transport to the heart, brain, and lungs respectively. According to the American Heart Association, as of 2006, an estimated 17.6 million American adults suffered from coronary heart disease, leading to one in every six deaths [2]. In 2006, stroke occurred in 6.4 million American adults causing one in every 18 deaths that year [2]. Pulmonary embolism caused 8,702 deaths in the U.S. in 2007
Based on its implications there exists a need to study thrombosis and the blood clotting process. Specifically, there is interest in the theoretical modeling and computer simulation of thrombosis and thromboembolism. One potential application of numerical thrombosis modeling is optimizing the design of blood contacting devices in order to minimize thrombus formation on such devices. Various numerical approaches from the literature are presented in section 1.2. In the following sections a general overview of the mechanisms of haemostasis and thrombosis is presented.

1.1.1.2 Biological Mechanisms

Human blood is composed of roughly one half plasma and one half red blood cells. Several other cells exist suspended in the plasma, including platelets which play a major role in haemostasis and thrombosis. Blood platelets are introduced into the bloodstream by megakaryocytes which reside in the bone marrow [23]. Platelets average 2-5 microns in diameter with a thickness of 0.5 microns [29]. Platelets exist in the blood for 7-10 days before they are replaced [29]. During haemostasis, platelets generally become adhesive and bind to the injured portion of a vessel, then they cohere with other nearby activated platelets, and finally coagulation or solidification of the platelet aggregate occurs. These processes are outlined in the following sections.

![Platelet](image)

**Figure 1.1.** Platelet photographed using a low-voltage, high-resolution scanning electron microscope with a 30,000X magnification. Figure reproduced from [29].

Adhesion describes the initial action of circulating platelets binding to the injured portion of a vessel wall during haemostasis. When a vessel wall is damaged platelets initially bind to the exposed subendothelial collagen [23]. The mechanism of adhesion of platelets to the collagen
depends on the existing fluid velocity gradients. Under high fluid shear rates, the multimeric plasma protein, von Willebrand factor aids in platelet adhesion by adhering to collagen of the subendothelium and to the GPIb/V/IX receptor on platelets [23]. In the presence of low fluid shear rates, platelets adhere directly to exposed collagen [23]. With wall adherent platelets present, the stage is set for the platelet aggregation process.

Immobilized platelets can secrete certain chemicals such as adenosine diphosphate (ADP) and serotonin which stimulate nearby circulating platelets [23]. High concentrations of these chemical agonists in regions adjacent to the aggregate, lead to activation of surrounding resting platelets which can subsequently bind to the platelet network. The GPIIb/IIIa platelet receptor plays an important role in platelet aggregation by connecting activated platelets via fibrinogen [23]. In addition, fibronectin is believed to contribute to aggregation under high shear though the specific mechanisms are not completely understood [22]. Interestingly, at high shear rates, non-activated platelets can actually aggregate with von Willebrand factor playing a major role [34]. Platelet aggregates tend to lack structural integrity when compared to a coagulated blood clot. In general, increased aggregate solidification and stability occurs next as a result of the coagulation cascade.

The coagulation cascade represents a complex series of reactions leading to the reinforcement of the platelet network by fibrin fibers. Thrombin, an enzyme crucial to coagulation, is responsible for the conversion of fibrinogen into fibrin [7] resulting in clot solidification. Two different pathways are often used to describe the process of coagulation. The extrinsic pathway is governed by tissue factor (TF), a membrane protein abundantly present in cells surrounding the vascular bed” [7]. Through this pathway, plasma factor VII/VIIa is introduced to tissue factor in the presence of vascular injury, which is believed to commence the coagulation cascade in vivo [27], [7]. The intrinsic pathway consists of plasma FXI, FIX, and FVIII and is generally believed to contribute to the amplification of the coagulation cascade [27], but can also initiate the process [7]. The intrinsic pathway, however, is not present in the coagulation response following vessel damage [7]. In contrast to normal haemostasis, evidence exists that thrombosis may occur in part due to tissue factor that circulates within the bloodstream [36], [27].

The biochemical aspects of haemostasis and thrombosis are complex and although research has afforded us much knowledge over the years, many issues remain to be understood. It is not the intention of this thesis to provide an exhaustive review of these processes and the resources cited in this section should be referred to for a more inclusive description of haemostasis and thrombosis.

1.1.1.3 A Fluid Mechanical Perspective

In addition to complex biochemistry, blood flow itself has profound effects on thrombus formation both within the human vasculature and on the surfaces of artificial blood contacting devices. Two specific situations in which the local blood flow characteristics tend to promote thrombosis and clot formation are discussed next.
Platelet adhesion and aggregation are often promoted in locations with high fluid velocity gradients. This fact has been demonstrated multiple times in the experimental literature. Baumgartner and Sakariassen [3] performs experiments flowing citrated rabbit blood over rabbit aorta subendothelium. Here, platelet surface coverage was shown to increase with increasing shear rate and perfusion time. One clinical condition leading to the development of large shear rates is the stenosed vessel. A vessel stenosis is a local reduction in the area seen by the flow and often presents as an atherosclerotic plaque, which is a fatty deposit that develops on the vessel wall. These plaques are prone to thrombus formation and the resulting ischemic conditions. A vessel stenosis can promote platelet aggregation directly [24] or by atherosclerotic plaque rupture [24], [41], [8]. Figure 1.2 shows a ruptured atherosclerotic plaque and the resulting thrombus that developed.

![Figure 1.2. Plaque cap rupture and the resulting formed thrombus. Figure reproduced from [8].](image)

In the case of atherosclerosis, exposure to the thrombogenic components of the plaque promote thrombosis. Lassila et al. [25] performs blood perfusion experiments over 0 percent, 55 percent, and 80 percent stenoses. Both in vitro and in vivo experiments present with concentrated thrombus formation at the peak of the stenosis. Although elevated shear rate is known to enable platelet aggregation and thrombus formation, regions of especially low shear tend to have a similar effect.

Regions of flow stasis and recirculation can promote platelet aggregation and thrombosis. This fact is presumably due to the decreased advective transport of haemostatic components such as platelets and chemical agonists within these regions. One example of recirculating flow which occurs clinically is within the region distal to a vessel stenosis [41]. Another clinical condition leading to the development of stagnant flow within the human vasculature is the aneurysm, which is the local enlargement of a blood vessel. One implication of aneurysms is bursting of the
vessel and subsequent blood loss, however, for aneurysms which remain intact, a local increase in flow area and fluid deceleration is observed. In this manner, flow stagnation and recirculation can occur. Rayz et al. [33] performs patient specific Computational Fluid Dynamics studies on intracranial aneurysm geometries. Here, it is found that regions of numerically predicted low flow velocity and low shear stress present with thrombus formation in the patient follow up analysis. Narracott et al. [30] performs in vitro experiments flowing hypercoaguable milk through a sharp contraction expansion geometry. Results presented with clot deposition on the downstream side of the area reduction. Figure 1.3 shows a schematic of typical results observed in [30].

![Image](image.png)

**Figure 1.3.** Schematic of experimental geometry and milk clot formation observed in [30]. Figure reproduced from [30].

In unpublished research performed by the Pennsylvania State University Bioengineering Department, pulsatile blood flow over a three dimensional backward facing step geometry presents with clot formation within the recirculating flow region on the downstream side of the step. In Chapter 5 a theoretical platelet aggregation model is numerically solved under flow conditions similar to those used in these experiments in a preliminary investigation of the application of the theoretical model to the prediction of experimental results.

### 1.1.2 Numerical Thrombosis Models

Numerical prediction of blood clot formation is a research area important to the biomedical field. Generally, there is interest in accurately predicting thrombosis due to its serious implications on device performance and patient health. One particular application of numerical thrombosis modeling is improved design of artificial blood contacting devices such as ventricular assist devices and heart valves. Clots that form on these devices present a risk to patients utilizing them. A numerical model capable of predicting clot formation could potentially be used to design these devices such that thrombosis is minimized.

#### 1.1.2.1 Discrete Models

Several thrombosis models represent biological cells discretely. Discrete models offer the potential to more accurately capture the physics of thrombus formation, much of which occur at a smaller scale. However, computational time is often significant when compared to continuous models due to the large number of particles that may be required for simulation.
One such model outlined in [13] uses a Dissipative Particle Dynamics Method. Here, the fluid and platelets are represented by discrete mesoscale particles. Newton’s second law is employed to describe the motion of these particles due to the various forces acting upon them. Repulsive, dissipative (viscous), and random forces are calculated and account for interaction between particles. In addition, an attraction force between activated platelets and the nearby wall and a fluid driving force are both present in the model. When an activated platelet comes within a prescribed distance of the wall the attraction force is applied through the presence of a linear spring connecting the platelet and the wall. In this model a platelet becomes activated when in the presence of some minimum chemical agonist concentration. Chemical agonist concentrations are governed by convective-diffusive partial differential equations which are solved over a finite element grid.

A multi-scale approach presented in [42] predicts platelet and blood cell aggregation using a Discrete Cellular Potts Model, while blood flow and coagulation reactions are governed by continuous partial differential equations. In the Cellular Potts Model, several different types of cells are defined, including quiescent and activated platelets, platelets with high fibrin level, blood cells, and plasma. Each cell contains multiple pixels each of which are assigned an index that defines the cell’s current state. With each iteration a random pixel undergoes an index change and the change in effective energy of the system is calculated. The probability of index change acceptance is calculated using a Monte Carlo-Boltzmann Acceptance Rule. Cell properties such as size, position, and type are subsequently modified based on the system energy change, which is calculated from flow pressure and velocity. Platelets are activated upon reaching the injury site or if their ADP concentration surpasses some prescribed threshold value. Upon platelet activation thrombin is released thus promoting fibril generation and subsequently stiffening the thrombus.

1.1.2.2 Lattice Boltzmann Method Based Models

The Lattice Boltzmann Method is becoming more prevalent especially for fluid flow simulations with complex boundaries. The LBM, outlined in [4] uses kinetic models to capture the most fundamental microscopic behavior such that macroscopic quantities like velocity and pressure fields are accurately modeled by macroscopic equations, i.e., the Navier-Stokes Equations. The motion of and interaction between discrete particles are viewed as particle distribution functions. The dependent variables that arise in the LBM are average particle distributions as opposed to the pressure and velocity fields present in the continuum Navier-Stokes equations. The LBM is a promising approach for complex and changing boundaries and therefore has been applied in several instances to the modeling of blood clot formation.

Harrison et al. [19] implements the Lattice Boltzmann Method for computation of clot formation in enzymatically activated milk flowing in a stenosed vessel. In the model, fluid residence time is calculated and when a fluid node achieves some prescribed residence time it immediately becomes a solid node. In addition a node must be adjacent to a wall or solid node and have a shear stress
below some specified value in order for solidification to occur.

Tamagawa et al. [38] implements the Lattice Boltzmann Method for the computation of clot formation with a backwards facing step geometry. Both steady and pulsatile flow fields are considered. This approach tracks activated fibrinogen as a concentration. Thresholds for activated fibrinogen concentration, shear rate, and wall proximity are employed for the purpose of predicting clot location and subsequently enforcing changes in boundary conditions. The results presented in [38] for both steady and pulsatile flow predict adhesion initiation on the downstream side of the step near the reattachment point and are in agreement with visual observations.

1.1.2.3 Continuum Mechanics Based Models

Continuous models of thrombosis exist in the form of partial differential equations governing the field variables related to thrombosis, with the Navier-Stokes equations used to predict the haemodynamics. Computationally, solutions to such models are not as expensive as their discrete counterparts. However, molecular interactions between cells are more difficult to capture in continuum based models.

One such model developed by Aaron Fogelson is in the form of a closure approximation to a full multi-scale model of platelet aggregation [14], [16], [15], [18]. In the model, Blood is assumed to be a continuous homogeneous Newtonian fluid of constant density and viscosity. Platelets, both activated and non-activated, and a general chemical agonist are incorporated in the model using scalar transport equations for the concentrations of each. Stress tensor transport equations are incorporated and represent platelet aggregates. These stress tensor fields are coupled with the fluid motion through their addition to the momentum equation as source terms. Regions of adequate stress present as zero flow regions, and in the model, they represent platelet aggregates.

![Figure 1.4](image.png)

Figure 1.4. Contours of strain in thrombi growing over a stenosed geometry. Dark corresponds to high strain, and pale corresponds to low strain. Figure reproduced from [16].

Sorensen et al. [37] presents a convection-diffusion transport model of platelet activation and deposition. The model is based off of Fogelson’s work but includes a more in depth analysis of the biochemistry of thrombosis. The model includes transport of resting and activated platelets, platelet released and platelet synthesized agonists, prothrombin, thrombin, and antithrombin III. In contrast to Fogelson’s model which uses stress tensor fields to represent platelet adhesion and cohesion, [37] employs surface-flux boundary conditions to model adhesion and cohesion. Sorensen’s model does not incorporate fluid thrombus coupling as it assumes a velocity field which does not vary with time and which is not impacted by the remainder of the model. In this
respect the model is geared toward surface interactions rather than clot growth and the resulting fluid thrombus coupling.

Goodman et al. [17] presents a model focusing on low shear conditions which is governed by a series of convection-diffusion reaction equations. Here initial platelet adhesion, thrombus growth, fluid dynamic coupling with the thrombus, and embolization are all predicted. Agonist induced platelet activation is modeled after [37]. In the model a thrombus is represented by increasing the viscosity of grid cells where clotting is predicted to exist. Embolization is accounted for by removing the thrombus completely when the fluid forces acting upon it reach some predefined threshold value.

1.1.3 OpenFOAM: An Open Source CFD Software

1.1.3.1 Overview of the Code

All numerical analyses in the present study are performed using OpenFOAM (Open Field Operation and Manipulation) [31]. OpenFOAM is an open source Computational Fluid Dynamics package. OpenFOAM is a C++ library and is distributed free of cost under the GNU General Public License. Although commonly referred to as a CFD package OpenFOAM can more generally be described as a finite volume based numerical analysis package. It is distributed with a variety of applications called solvers which solve differential equations modeling various problems related to fields including fluid mechanics, electromagnetism, and finance. One major advantage of OpenFOAM is the fact that users have complete access to the source code, which provides flexibility and facilitates general physical modeling through code modification. In the present study, for example, OpenFOAM is used to solve partial differential equations governing thrombus formation, a process which is strongly dependent on fluid motion. To accomplish this task a pre-existing Navier-Stokes solver is modified to solve several additional scalar and tensor thrombosis related transport equations while including their coupling to the Navier-Stokes equations. Another advantage of OpenFOAM is its high level construction, which enables calculations and manipulations to be performed using physically meaningful language. OpenFOAM has a growing user base and is applied to a variety of fields including the biomedical field.

1.1.3.2 OpenFOAM’s Application to Biological Systems

Fluid mechanics is a research area important to the biomedical field. Fluid flows of the circulatory and respiratory systems are often studied due to the crucial role they play in the proper functioning of the human body. As with general fluid mechanics, biofluid mechanics is often studied using numerical approaches. OpenFOAM has been employed to study biomedical flows in several instances.

The human circulatory system can fall victim to a variety of medical conditions. Aneurisms, which have been previously discussed represent a serious condition of the circulatory system. Due to increased vessel wall strains, aneurisms carry the risk of rupture and subsequent internal
bleeding. Rau et al. [32] uses OpenFOAM to calculate blood flow through the junction of the anterior cerebral arteries and the anterior communicating artery. Specifically, the haemodynamic effect of several flow rate differentials between the left and right anterior cerebral arteries is calculated resulting in increased wall shear stress at expected aneurism locations. Ventricular Assist Devices are often implanted into patients suffering from heart failure in an effort to restore blood flow to the body’s cells and organs. In work performed at Penn State University, [43], [45], [44], blood flow characteristics in the end-to-side anastomotic graft of both pediatric and adult VADs is investigated using OpenFOAM.

The respiratory system can be afflicted with a variety of diseases as well. The fluid mechanics of the respiratory system is important to the understanding and treatment of these diseases. Asthma and similar respiratory conditions are often treated with inhalation therapies. With such treatments, medication is inhaled and deposited within the airway. Cui and Gutheil [6] investigates airflow through an idealized mouth-throat geometry using a large eddy simulation approach within OpenFOAM. A Lagrangian particle tracking method is also implemented and particle deposition onto the walls of the airway is simulated, showing good comparison with experimental results. In work performed at Penn State University motivated by the study of canine olfaction, [28] investigates various internal flows using OpenFOAM.

1.2 Present Study Claim

Of the previous classes of numerical approaches to thrombosis modeling, a continuum mechanics based approach is chosen for use in the present study. Specifically, Fogelson’s single-scale continuum model of platelet aggregation is employed. The focus of the present work is on clot formation within geometries possessing length scales on the order of millimeters, where this model is pertinent. Ultimately, there is a desire to predict thrombosis within cardiac devices, many of which are on this same scale. Fogelson’s treatment of blood as one homogenous Newtonian fluid simplifies computations but is not applicable to flow within the microvasculature. The present study focuses on large length scale computations and therefore Fogelson’s model is applicable and the advantages of the simple treatment of blood flow can be exploited. Another aspect of the model making it favorable is the continuous representation of platelet concentrations and other variables which enables them to be computed using well established numerical methods similar to those employed for the flow solution itself. One particularly important aspect of a thrombosis model is its ability to incorporate a dynamic solid boundary within a flow field. Numerically, this can be achieved in many ways. For example, dynamically changing the computational grid can incorporate such behavior, but becomes more computationally expensive. One appealing aspect of this model is its ability to include a dynamic solid boundary in the presence of a grid which does not change in time. Grids employed with Fogelson’s model need not be complex, a major contributing factor to its use in this work.

The objective of the work presented here is to implement the aforementioned theoretical model
within OpenFOAM. In the present study it is shown that the continuous partial differential equations of Fogelson’s platelet aggregation model are closely related to the Oldroyd-B model of viscoelastic fluids. Within a range of parameter sets the Oldroyd-B fluid model can be solved accurately using OpenFOAM’s implementation of the Finite Volume Method. Stability becomes a concern at both high Weissenberg numbers and high elastic moduli. The platelet aggregation model can also be solved stably within a range of parameter values and limiting the platelet stress tensor helps greatly with solution convergence.

1.3 Present Study Agenda

In the present study, Fogelson’s continuous model of platelet aggregation is first presented and summarized. Its relationship to the viscoelastic Oldroyd-B fluid model is then discussed. The numerical methods employed for the solution of the PDEs in this work are presented next. As a validation of the numerical approach, the Oldroyd-B equations are solved under transient conditions within a two dimensional planar channel. Numerical results are compared to available exact solutions. Finally, the platelet aggregation model equations are solved within a similar geometry with a specified wall injury to initiate the clot. Various model parameter values are explored for the purpose of gaining a qualitative understanding of the model’s behavior. Finally, a summary of the conclusions drawn is presented accompanied by general suggestions for future direction of the work.
Chapter 2

Description of a Continuum Stress Transport Platelet Aggregation Model

2.1 Model Development

The continuum model presented here aims to predict platelet aggregation, a major component of thrombosis. Platelet aggregation is the process by which blood platelets become activated and bind to each other as well as to the vessel wall. These binding sites, or aggregates, create the framework for a blood clot. The model used here is based on work done by Dr. Aaron L. Fogelson from the University of Utah and others over the past several years [14], [16], [15], [18]. The stress transport models used in this thesis are a single-scale reduction of the full multi-scale continuum model presented in [14] and [16]. Details of the closure approximation enabling the reduction from the multi-scale model to a single-scale model can be found in [16] and are briefly discussed in the following sections.

In Fogelson’s multi-scale model of platelet aggregation, blood is assumed to be a continuous homogeneous Newtonian fluid of constant density and viscosity. The incompressible Navier-Stokes equations are employed to model the blood flow itself. Platelets, both activated and non-activated are incorporated in the model using scalar transport equations for the concentrations of each. A scalar transport equation for a single chemical activator, which promotes platelet activation, is also included. When non-activated platelets are in the presence of this chemical activator they become activated and subsequently secrete chemical activator of their own. Two length scales arise in the model, one on the order of the vessel size (millimeters) and the other on the order of platelet size (microns). A transport equation for the number of elastic links connecting activated platelets exists and is the only equation in the model to incorporate transport at both spatial scales. Link breaking and formation rates are also included in this equation.
Finally, a cohesion force density is calculated in the model based on the distribution and stiffness of elastic links. The cohesion force density is added as a body force source term to the Navier-Stokes equations in order to represent the presence of a platelet aggregate and the solid boundary such an aggregate imposes on the velocity field. The cohesion force density can also be represented as the divergence of a stress tensor, $\sigma$, termed the cohesive stress tensor. This formulation becomes important in the single-scale model. The integral of the elastic link function over the micro-scale spatial variable, $z$, represents the concentration of elastic links and it too plays an important role in the single-scale model.

The multi-scale nature of the full model comes with increased computational expense. The work presented in this thesis focuses on the single-scale reduction of the multi-scale model. In the single-scale model, the transport equations for activated platelets, dormant platelets, and chemical activator from the multi-scale model remain. The transport equation for the elastic link function is recast into a transport equation for $\sigma$. In order to remove the dependence of this equation on the micro-scale, two assumptions are made by Fogelson:

1. inter-platelet links have a constant stiffness.
2. the link breaking rate, $\beta$ is a function of the trace of the cohesive stress tensor divided by the link concentration, or equivalently the average link energy.

With these assumptions in place, dependence on the micro-scale is removed completely. The latter assumption is termed the closure approximation and it allows the link breaking rate to depend on a representation of the link length without explicitly incorporating the micro-scale spatial variable. Specifically, the trace of the stress tensor divided by the link concentration represents the average energy per link. The correspondence between the single and multi-scale model results depend on beta’s functional form and is discussed in [18]. In this thesis Fogelson’s reduced single-scale model is termed the Approximate Closure Model and is described in the following section.

### 2.2 Approximate Closure Stress Transport Platelet Aggregation Model (ACM)

#### 2.2.1 Description of Model Equations

The Approximate Closure Model is comprised of Equations 2.1 through 2.7 below. Equations 2.1 and 2.2 represent conservation of momentum and mass, respectively, for an incompressible fluid with constant viscosity. It should be noted that a new source term, $\nabla \cdot \sigma$ appears on the right hand side of the momentum equation. Here, $\sigma$ is the cohesive stress tensor. $\nabla \cdot \sigma$ is a body force and when added to the momentum equation, as in Equation 2.1, couples the velocity field to the cohesive stress tensor. Specifically, in this model, the goal is to bring the flow to zero velocity in regions where a blood clot is forming. Physically, a blood clot grows presenting
a changing no-slip boundary, thereby altering the flow field. The ACM captures this coupling without actually requiring a change in the grid or geometry of the computational domain, which is a major advantage of the approach.

\[ \rho \frac{\partial u}{\partial t} + \rho (u \cdot \nabla)u = -\nabla p + \mu \nabla^2 u + \nabla \cdot \sigma \quad (2.1) \]

\[ \nabla \cdot u = 0 \quad (2.2) \]

Equation 2.3 governs the transport of dormant (non-activated) platelets. \( \phi_n \) represents the concentration of non-activated platelets in the blood. In this thesis, platelet concentrations are represented with dimensions of number of platelets per unit volume. Non-activated platelets are transported in space by advection with the velocity field, \( u \) and by diffusion where \( D_n \) is the constant diffusivity of non-activated platelets. In addition, non-activated platelets are removed from the blood at a rate equal to their activation. Physically, when a single dormant platelet is activated, one non-activated platelet is removed from the blood and one activated platelet is added, though the total number of platelets does not change. \( R(c)\phi_n \) is the platelet activation rate and \( R(c) \) is an increasing function of the chemical activator concentration \( c \), which reflects the fact that in spatial regions that have high concentrations of chemical activator, platelet activation occurs more readily. In the ACM, this agonist induced activation is the only platelet activating mechanism.

\[ \frac{\partial \phi_n}{\partial t} + (u \cdot \nabla)\phi_n = D_n \nabla^2 \phi_n - R(c)\phi_n \quad (2.3) \]

Equation 2.4 governs the transport of activated platelets. \( \phi_a \) represents the concentration of activated platelets in the blood. Activated platelets are transported in space by advection with the velocity field, \( u \). The source term on the right hand side of Equation 2.4 represents the addition of activated platelets to the blood via platelet activation.

\[ \frac{\partial \phi_a}{\partial t} + (u \cdot \nabla)\phi_a = R(c)\phi_n \quad (2.4) \]

Equation 2.5 governs the transport of chemical activator in the blood. \( c \) represents the concentration of chemical activator in the blood and is represented in dimensions of mols per unit volume. Chemical activator is transported in space by advection with the velocity field, \( u \) and by diffusion where \( D_c \) is the constant diffusivity of the chemical activator. The model assumes that chemical activator is generated at a rate proportional, by \( A \), to platelet activation. Physically, this source term represents secretion of chemical activator by activated platelets. Large activation rates will lead to high concentrations of activated platelets in a given region and therefore a high concentration of chemical activator will be present in that region due to secretion. Furthermore,
the model allows for the degradation of chemical activator with time, where $K$ is the constant degradation rate of the chemical activator.

$$\frac{\partial c}{\partial t} + (\mathbf{u} \cdot \nabla)c = D_c \nabla^2 c + AR(c)\phi_n - Kc \quad (2.5)$$

Equation 2.6 governs the transport of the cohesive stress tensor, $\sigma$ which has dimensions of force per unit area. It should be noted that for simulations in this thesis the stress is represented on a per unit density basis thereby changing the dimensions to length squared per time squared. $\sigma$ is transported in space by advection with the velocity field, $\mathbf{u}$. the remaining terms in Equation 2.6 result from Fogelson's closure approximation. Equation 2.6 was derived from a more general multi-scale model into the single scale form presented here as previously described. It can be seen from the third term on the right hand side of Equation 2.6 that activated platelets present a source of platelet aggregation. Here $I$ is the identity matrix and $\alpha_2$ is a constant. $\beta$ represents the rate of destruction of inter-platelet bonds. As a result of the closure approximation $\beta$ is a function of the trace of $\sigma$ divided by $z$. $z$ is the link concentration and is described in the following.

$$\frac{\partial \sigma}{\partial t} + (\mathbf{u} \cdot \nabla)\sigma = \sigma \nabla \mathbf{u} + (\sigma \nabla \mathbf{u})^T + \alpha_2 \phi_2^2 I - \beta \sigma \quad (2.6)$$

Equation 2.7 governs the transport of the inter-platelet link concentration, $z$, which is a scalar quantity and is represented with dimensions of number of links per volume. $z$ is transported in space by advection with velocity, $\mathbf{u}$. Source and sink terms similar to those seen in the transport equation for $\sigma$ can be found in Equation 2.7, with $\alpha_0$ equal to a constant.

$$\frac{\partial z}{\partial t} + (\mathbf{u} \cdot \nabla)z = \alpha_0 \phi_a^2 - \beta z \quad (2.7)$$

### 2.2.2 Platelet-Wall Adhesion

Two additional transport equations are presented in [16] and [15] which consider platelet-wall adhesion as an entity separate from cohesion. This formulation requires a combined Lagrangian and Eulerian representation at the wall. In this thesis, platelet-wall interactions are not represented in this manner. Here, platelet wall bonding is simulated by specifying a nonzero chemical activator concentration in the grid cells near the wall within a specified injury zone. The fluid velocity is zero at the wall an so advection of haemostatic components in these injury grid cells is low enough to allow aggregation to be initiated. At this point the clot grows as if it were actually fixed to the wall as it should be from a physical standpoint, though manually limiting advection within the clot is required to achieve this behavior as described in detail in Chapter 5.
2.2.3 Applications and Limitations of the ACM

As with the full scale model from which it was derived the Approximate Closure Model is intended for thrombosis prediction only in the body’s larger vessels. Blood can be assumed a continuous Newtonian fluid only in vessels with length scales much larger than those of the cells and particles which comprise it. With the ACM, initiation of a clot is achieved through the prescription of an injury zone. This requirement implies that the model includes no mechanism for predicting where within a given geometry a clot is likely to form, but instead focuses on the actual growth of a clot with time.

2.3 Approximate Closure Model as an Oldroyd-B Fluid

2.3.1 Equivalence of the ACM and Oldroyd-B Fluid

In the following presentation it is shown that Fogelson’s Approximate Closure Model of platelet aggregation is identical to the Oldroyd-B model of viscoelastic fluid flow when certain conditions are imposed. A more detailed analysis of viscoelastic fluid flow is presented in [18]. Here we restrict our discussion to the Oldroyd-B model which bears a direct relationship to the Approximate Closure Model of platelet aggregation which is also discussed in [18]. Starting with the Approximate Closure Model, if all scalar transport equations are removed and both the breaking rate and activated platelet concentration are held constant represented by $\beta_o$ and $\phi_{a,o}$ respectively, we arrive at the following system of equations.

\[
\rho \frac{\partial u}{\partial t} + \rho (u \cdot \nabla)u = -\nabla p + \mu \nabla^2 u + \nabla \cdot \sigma \quad (2.8)
\]

\[\nabla \cdot u = 0 \quad (2.9)\]

\[
\frac{\partial \sigma}{\partial t} + (u \cdot \nabla) \sigma = \sigma \nabla u + (\sigma \nabla u)^T + \alpha_2 \phi_{a,o}^2 I - \beta_o \sigma \quad (2.10)
\]

As discussed in [18], the steady-state solution to Equation 2.10 under zero velocity gradient is as follows,

\[\sigma = \frac{\alpha_2 \phi_{a,o}^2}{\beta_o} I \quad (2.11)\]

In order to ensure that the stress is zero when the velocity gradient is zero, this term, which acts like an extra pressure can be subtracted defining a different stress tensor as follows,

\[\tau = \sigma - \frac{\alpha_2 \phi_{a,o}^2}{\beta_o} I \quad (2.12)\]
Substituting σ as defined by Equation 2.12 into Equation 2.10 and reducing yields the following equation.

$$\frac{\partial \tau}{\partial t} + (u \cdot \nabla)\tau = \tau \nabla u + (\tau \nabla u)^T + \frac{\alpha_2 \phi_{a,o}}{\beta_o} (\nabla u + \nabla u^T) - \beta_o \tau \quad (2.13)$$

The only remaining step to bridge the platelet aggregation model with the Oldroyd-B viscoelastic fluid model is to recast the equation in terms of the notation often used in the viscoelastic literature. Specifically, the relaxation time, solvent viscosity, polymer viscosity, and deformation rate tensor are defined respectively as follows.

$$\lambda = \frac{1}{\beta_o}$$

$$\eta_s = \mu$$

$$\eta_p = \frac{\alpha_2 \phi_{a,o}^2}{\beta_o^2}$$

$$D = \frac{1}{2} (\nabla u + \nabla u^T)$$

Using the viscoelastic notation given above, Equation 2.13 becomes Equation 2.16 below, which is the form often found in the viscoelastic fluid literature.

$$\rho \frac{\partial u}{\partial t} + \rho (u \cdot \nabla)u = -\nabla p + \eta_s \nabla^2 u + \nabla \cdot \tau \quad (2.14)$$

$$\nabla \cdot u = 0 \quad (2.15)$$

$$\frac{\partial \tau}{\partial t} + (u \cdot \nabla)\tau = \tau \nabla u + (\tau \nabla u)^T + \frac{\eta_p}{2D} \frac{\eta_p}{\lambda} 2D - \frac{1}{\lambda} \tau \quad (2.16)$$

Equations 2.14 through 2.16 comprise the system of equations governing the incompressible flow of an Oldroyd-B fluid. Equations 2.14 and 2.15 are the familiar conservation of momentum and mass for an incompressible fluid. Equation 2.16 governs the transport of the elastic stress tensor, τ. The addition of τ to the momentum equation contributes elasticity to the fluid, while the familiar diffusive term contributes viscosity. In contrast to the purely viscous Newtonian fluid, an Oldroyd-B fluid possesses both viscous and elastic behavior, representing energy dissipation and storage respectively. It is important to note that in contrast to the simple relationship for the viscous stress, the constitutive relationship for the elastic stress is represented by an evolution
equation which must be solved in order to determine this elastic stress.

2.3.2 Differences Between the ACM and Oldroyd-B Fluid Model

As previously mentioned the system of equations governing the motion of an Oldroyd-B fluid present some key differences from those comprising Fogelson’s Approximate Closure Model of platelet aggregation. The first difference being the fact that in the ACM, the breaking rate and activated platelet concentration are variable. In the model of an Oldroyd-B fluid, variable breaking rate and activated platelet concentration correspond to a variable relaxation time and polymer viscosity. Both of these parameters, however, are constant in the Oldroyd-B model. This implies that the ACM represents an Oldroyd-B fluid whose elasticity and viscosity are allowed to vary in space and time. A second difference is the fact that the Oldroyd-B equations lack the transport of any scalar quantities while the ACM possesses evolution equations governing the transport of chemical activator, dormant platelets, activated platelets, and inter-platelet links. These two differences are in fact related. Specifically, the solution of the equations for chemical activator and dormant platelets determine the source term due to platelet activation in the activated platelet transport equation. The subsequent solution of the activated platelet transport equation then determines the value of this variable. Likewise, the variation of the breaking rate is determined from the cohesive stress and inter-platelet link concentration transport equations. Essentially the solution of the scalar transport equations in the ACM determines the variation of the breaking rate and activated platelet concentration whose analogs in the Oldroyd-B model are constant.

Another key difference between the models lies within which stress tensor is added to the momentum equation. In the ACM the cohesive stress tensor, $\sigma$, is added while in the Oldroyd-B fluid, the elastic stress tensor, $\tau$, is used. The two are related by Equation 2.12. We note that the equation given in Fogelson’s ACM governs the transport of $\sigma$ while the equation often found in the viscoelastic literature, Equation 2.16 governs the transport of $\tau$. Solutions to the ACM to be presented in later chapters indicate that the cohesive stress tensor, $\sigma$, achieves large values within the region representing a blood clot and is essentially zero within the remainder of the flow field. We therefore interpret the zero velocity region representing the clot as an Oldroyd-B fluid whose elastic stress is equal to the inter-platelet cohesive stress minus the extra pressure defined in Equation 2.11 and the remainder of the flow representing normal blood as a Newtonian fluid. Although the stress transport equation is solved over the entire computational domain, regions outside the clot have zero activated platelet concentration and cohesive stress and therefore the elastic stress tensor, $\tau$, is zero as can be seen from Equation 2.12. Therefore, the elastic stress is zero outside the clot and Newtonian blood flow is present.

2.3.3 Numerical Stability and the High Weissenberg Number Problem

The Weissenberg number is a dimensionless parameter that arises in the Oldroyd-B equation system and is defined as the ratio of the polymer relaxation time to the fluid time scale [39].
The Weissenberg number is defined as follows, where $U$ and $L$ represent the characteristic fluid velocity and length scales respectively.

$$Wi = \frac{\lambda U}{L}$$

Stability of numerical approaches has been shown on numerous occasions to be dependent upon this parameter. Specifically, upper limits on this parameter for the achievement of stable solutions are observed and the issue is often termed the High Weissenberg Number Problem (HWNP). The HWNP is a result of the form of the stress equation and can be shown to be independent of both the tensorial nature of the stress equation and the elastic stress coupling to the momentum equation [11]. Fattal and Kupferman [11] demonstrates that higher Weissenberg number convergence can be obtained by recasting the constitutive equations in terms of the matrix logarithm of the conformation tensor. Other methods to help overcome the HWNP exist, one of them being the FENE-P penalization. The FENE class of models imposes a finite extensibility of polymer chains whereas the pure Oldroyd-B fluid possesses polymer chains which can extend to infinite lengths, an unphysical result.
Chapter 3

OpenFOAM: Model Numerical Implementation and Case Structure

3.1 CFD General Overview

Computational Fluid Dynamics, CFD, refers to the field of science concerned with developing approximate solutions to the governing equations of fluid mechanics using numerical methods. These equations are usually in the form of partial differential equations governing the conservation of mass, momentum, energy, and species. Typical dependent variables include velocity, pressure, temperature, and species concentration, which at one spatial scale, depend most generally on three spatial dimensions and time. Equations are often written in an Eulerian frame of reference where the transport of the dependent variables is observed within a specified region or domain. Depending on the problem at hand the governing equations can take on many forms. In the present study the Navier-Stokes equations are solved which govern the incompressible flow of a Newtonian fluid. The additional model equations from Chapter 2 are solved in conjunction with the Navier-Stokes equations using the methods outlined in this chapter.

The first step in a CFD problem is discretization. Ultimately, the problem is broken down from the continuum level into discrete components. The spatial domain is broken down by defining a computational grid or mesh and the time domain is reduced to a collection of time steps. The governing PDEs must too be discretized reducing to a system of algebraic equations. Employing boundary and initial conditions enables the solution of this equation system to be obtained. The equation system must then be solved, typically using an iterative procedure. Solutions to the field variables now exist at each location in space and time. The techniques used in this thesis for this general process are described in the remaining portions of this chapter.
3.2 OpenFOAM and the Finite Volume Method of Discretization

OpenFOAM employs the Finite Volume Method of spatial discretization. The Finite Volume Method requires that the spatial domain is divided into a collection of control volumes. These control volumes must not overlap and they must fill the entire computational domain. Every control volume face belongs to exactly one other control volume unless the face lies on a boundary. Dependent variable values are solved for at each control volume center. Figure 3.1 below represents an arbitrary control volume, \( P \) and its relation to an example neighboring control volume in one dimension.

![Figure 3.1. Schematic of control volumes in the finite volume method. Control volume faces are in lower case while control volume centers are in upper case.](image)

The fundamental idea behind the Finite Volume Method is that each term in the model PDEs is integrated over each control volume in the computational mesh. In the following sections the discretization of each of the four general terms that arise in the model equations will be described. These four terms are the convective, diffusive, temporal and source terms. Much of the following work is taken from [12], which discusses computational approaches to fluid dynamics problems and [31], which discusses OpenFOAM’s implementation of numerical analyses. In the following analysis Gauss’ Theorem (Equation 3.1) and the Midpoint Rule (Equation 3.2) are used and as such they are stated here for reference.

\[
\int_V (\nabla \cdot F) \, dV = \int_S (F \cdot \hat{n}) \, dS = \int_S f \, dS \quad (3.1)
\]

\[
\int_{S_k} f \, dS = \tilde{f}_k S_k \approx f_k S_k \quad (3.2)
\]

3.2.1 Convective Term

A convective term arises in all of the platelet aggregation model equations except the continuity equation. The convective term is of the form
(\mathbf{u} \cdot \nabla)\phi \quad (3.3)

But can alternatively be written in conservative form as

$$\nabla \cdot (\phi \mathbf{u}) \quad (3.4)$$

Here \( \phi \) is a scalar quantity that is transported by the velocity field. The conservative form of the convective term is integrated over an arbitrary control volume and Gauss’ Theorem is invoked yielding

$$\int_V (\nabla \cdot \phi \mathbf{u}) dV = \int_S (\phi \mathbf{u} \cdot \hat{n}) dS \quad (3.5)$$

Here \( \mathbf{u} \) is the velocity field vector and \( \hat{n} \) is the unit outward normal vector. The integral on the right hand side of Equation 3.5 is approximated using the midpoint rule as follows

$$\int_S (\phi \mathbf{u} \cdot \hat{n}) dS \approx \sum_k (\phi \mathbf{u} \cdot \hat{n})_k S_k \quad (3.6)$$

Here \((\phi \mathbf{u} \cdot \hat{n})_k\) is the value of \((\phi \mathbf{u} \cdot \hat{n})\) at the center of face \(k\) and \(S_k\) is the surface area of face \(k\). The face-centered value of \(\phi\) is needed in terms of its value at the control volume center which is accomplished by interpolation. Various interpolation methods are available in OpenFOAM and in the present study one of the simpler methods is employed. Upwind interpolation approximates the face centered values as follows.

$$\phi_k = \begin{cases} \phi_P & \text{for } (\mathbf{u} \cdot \hat{n})_k > 0 \\ \phi_Q & \text{for } (\mathbf{u} \cdot \hat{n})_k < 0 \end{cases} \quad (3.7)$$

Upwinding has the advantage of improving numerical stability, specifically by reducing sharp gradients in the dependent variable fields. However, it is only first-order accurate and presents solutions with numerical diffusion. This error can be viewed as an additional diffusive transport of the field variable and although it reduces the accuracy of calculations it is responsible for solution smoothing and improved stability previously described. Numerical diffusion is an artifact of the inaccuracy of upwind interpolation and therefore not representative of the physical model being solved. Reduction of this diffusive behavior can be achieved by using finer grids. In this thesis, upwind interpolation for the advection of all field variables is used exclusively due to the unstable nature of the stress transport equation being solved. However, in Chapter 4 we show through comparison with exact solutions for the flow of an Oldroyd-B fluid, that accurate results can be obtained using first-order upwinding.
3.2.2 Diffusive Term

The diffusive term is of the form

\[ \nabla \cdot \nu \nabla \phi \quad (3.8) \]

Integrating over a control volume and employing Gauss’ Theorem and the Midpoint Rule yields

\[ \int_V (\nabla \cdot \nu \nabla \phi) \, dV = \int_S (\nu \nabla \phi \cdot \hat{n}) \, dS \approx \sum_k (\nu \nabla \phi \cdot \hat{n})_k S_k \quad (3.9) \]

\( \nabla \phi \) at the cell face must be expressed in terms of cell centered values of \( \phi \). This approximation is achieved using linear interpolation as follows.

\[ (\nabla \phi)_k \approx \frac{\phi_Q - \phi_P}{b} \quad (3.10) \]

3.2.3 Temporal Term

A temporal term arises in each of the model equations except for the continuity equation and is of the form

\[ \frac{\partial \phi}{\partial t} \]

Here, \( \phi \) can be any one of the model field variables excluding pressure. This term is integrated over an arbitrary control volume as follows

\[ \frac{\partial}{\partial t} \int_V \phi \, dV \approx \frac{(\phi_P V_P)^{n+1} - (\phi_P V_P)^n}{\Delta t} \quad (3.11) \]

Here, \( \phi_P \) is the cell centered value of \( \phi \), \( V_P \) is the volume of cell \( P \), and \( \Delta t \) is the time step or the discrete portion of the temporal domain being considered. \( n + 1 \) represents the current time level at which the field variables are being solved for and \( n \) represents the previous time level at which all field variables are known.

3.2.4 Source Term

Source terms encompass any remaining terms that do not fall under any of the three preceding categories. In this thesis all source terms are treated explicitly. Explicit treatment implies that at a given time level each term is calculated using the most recent field values.
3.3 Solution Time Advancement

At this point we have completed the discretization of the model PDE terms which can be grouped together to yield the discrete forms of the model equations. A general form for the discrete model equations is given in Equation 3.12.

\[
\frac{(\phi P V_P)^{n+1} - (\phi P V_P)^n}{\Delta t} + C\phi + D\phi = Q_P 
\]  

(3.12)

Here, the first term on the left hand side is the discretized temporal derivative from Equation 3.11. \(C\phi\) and \(D\phi\) represent the discrete convective and discrete diffusive terms respectively. \(Q_P\) is the discrete form of the source term. The discrete form of the model equations, Equation 3.12, must now be integrated over time in order to advance the solutions in time.

\[
\int_{t}^{t+\Delta t} \frac{(\phi P V_P)^{n+1} - (\phi P V_P)^n}{\Delta t} \, dt + \int_{t}^{t+\Delta t} (C\phi + D\phi) \, dt = \int_{t}^{t+\Delta t} Q_P \, dt 
\]  

(3.13)

The spatially discretized terms can be evaluated at the current time level, the previous time level, or a combination of the two. The time level at which the spatial terms are evaluated determines the temporal discretization scheme. Euler Explicit and Euler Implicit for example, evaluate the spatial terms at the previous and current time levels respectively. The Crank Nicholson Method which is used exclusively in this thesis evaluates the spatial terms at both time levels. This method employs the trapezoid rule, is second order accurate, and is unconditionally stable. The final form of the discretized model equations using the Crank Nicholson Method is given in Equation 3.14.

\[
\frac{(\phi P V_P)^{n+1} - (\phi P V_P)^n}{\Delta t} + C\left(\frac{\phi^{n+1} + \phi^n}{2}\right) + D\left(\frac{\phi^{n+1} + \phi^n}{2}\right) = Q_P^n 
\]  

(3.14)

The solution of Equation 3.14, which is an algebraic equation, is carried out at time level \(n + 1\) for each of the model equations. Solution of the algebraic system is described in the following section. During the solution of each model equation, with the exception of the special treatment of the momentum and continuity equations, only the variable being transported for that specific equation is treated as an unknown. All other model dependent variables are considered to have known values equal to their most recent solution. This type of solution method is referred to as sequential and is described in more detail in the section titled Model Solution Algorithm.

3.4 Solution of Algebraic System

As previously stated, Equation 3.14 is actually an algebraic equation. Specifically it contains unknowns which include the variable value, \(\phi\) (velocity, cohesive stress etc.) at control volume
\( P \) as well as their values at various neighboring control volumes. In general this equation will have more than one unknown and therefore its solution is unattainable. However, Equation 3.14 exists for every control volume \( P \) in the computational domain, thereby creating a system of \( N \) equations in \( N \) unknowns where \( N \) is the number of control volumes or grid cells in the computational domain. Solution of this system of equations yields the values of \( \phi \) at the center of every control volume in the computational domain or equivalently the field of \( \phi \). Furthermore, this system of equations is solved at each time step within the simulation and therefore dependent variable fields exist at fixed locations in time.

Solutions of equation systems can be broken down into two general classes, direct and indirect methods. Direct methods solve the system exactly such that there is no difference between the obtained solution and the actual solution to the system. Some common methods include Gauss Elimination and LU Decomposition. Such methods have the advantage of improved accuracy but become too computationally expensive for many modern CFD problems. Indirect methods calculate the solution to the system of equations using an iterative procedure and as such there is always some difference between the obtained solution and the exact solution to the system. This difference is defined as the iteration error. Direct methods, for example, always have an iteration error of zero. In this thesis, iterative procedures are used exclusively. The general algebraic system of equations to be solved can be represented by the following.

\[
A\phi = Q \quad (3.15)
\]

Here, \( A \) and \( Q \) are both known and represent the square coefficient matrix, and right hand side column vector respectively. \( \phi \) is the column vector of variables being solved for at each grid cell. For a general system of equations solved iteratively, the following equation applies, where \( n \) is the current number of iterations.

\[
A\phi^n = Q - \rho^n \quad (3.16)
\]

Here, \( \phi^n \) is the calculated value of \( \phi \) on the \( n^{th} \) iteration and \( \rho^n \) is defined as the residual on the \( n^{th} \) iteration. As the residual is forced to zero Equation 3.16 approaches Equation 3.15 and the exact solution to \( \phi \) is recovered. In OpenFOAM, residual tolerances are defined at run time, where the tolerance represents the residual value below which the iterative procedure is stopped.

The equation systems to be solved for the platelet aggregation and Oldroyd-B models are linearized (see Section 3.5). OpenFOAM offers a variety of iterative methods for the solution of linear systems of equations. In this thesis, the Preconditioned Conjugate Gradient and Preconditioned Bi-Conjugate Gradient methods are elected for symmetric and asymmetric matrices respectively. Specifically, the Preconditioned Conjugate Gradient method is used for the solution of the pressure equation and the Preconditioned Bi-Conjugate Gradient Method is used for the solution of all other field variables. The Diagonal Incomplete Cholesky preconditioner is used for
the pressure equation and the Diagonal Incomplete LU preconditioner for all remaining variables.

### 3.5 Model Solution Algorithm

The algorithm used to solve Fogelson’s platelet aggregation model and the Oldroyd-B fluid model can be broken down into three general portions. That is, within a given time step, the algorithm consists of the following three steps.

1. simultaneous solution of the incompressible Navier-Stokes equations and the continuity equation using OpenFOAM’s implementation of the PISO (Pressure Implicit with Splitting of Operators) Algorithm
2. sequential solution of the remaining model equations
3. explicit update of stress term in momentum equation

#### 3.5.1 Pressure Velocity Coupling and the PISO Algorithm

The PISO algorithm, originally developed by [21] is a common method used to solve the Navier-Stokes equations for transient problems. Specifically, the goal of the PISO Algorithm is to calculate a velocity and pressure field that satisfy both the conservation of mass and momentum at each simulation time step. Within each time step, the pressure equation is solved using the most recent velocity field. Solution of the velocity field and pressure field are repeatedly computed until the conservation laws are satisfied.

#### 3.5.2 Sequential Solution of Platelet Aggregation Related Equations

With the velocity field known at the current time step the remaining model equations are to be solved. The scalar and tensor transport equations from the platelet aggregation model and the tensor transport equation from the Oldroyd-B fluid model have several non-linear terms. In this thesis, during the solution of a particular transport equation, all other variables except for the one governed by the equation in question are considered to be known and equal to their most recently calculated values. In this manner, the partial differential equations become linear thus simplifying their solution and reducing computational expense. For the Oldroyd-B fluid model there is only one equation in addition to the momentum and continuity equations. For the Approximate Closure Model of platelet aggregation, however, several additional equations exist and are solved in the following order.

\[
\text{chemical activator transport equation} \\
\downarrow \\
\text{non-activated platelet transport equation}
\]
3.6 OpenFOAM General Case Structure

In OpenFOAM, solutions are generated by executing applications called solvers. Once a particular solver is chosen all user input exists within one parent directory often referred to as the case directory. Parameters within a given case may vary depending on the solver. A case using the incompressible laminar flow solver icoFoam, will be presented here as an example of the OpenFOAM case structure. Although, other solvers may contain more parameters, an icoFoam case will suffice to demonstrate OpenFOAM’s general case structure. A typical case directory contains three directories titled 0, constant, and system. The resulting directory tree is presented in Figure 3.2.

![Figure 3.2. Schematic of OpenFOAM case structure.](image)

The 0 directory contains information regarding the dependent field variables. For icoFoam these are pressure \( p \), and velocity \( U \), where lowercase and capital letters are used to denote scalars and vectors respectively. Inside 0, two files exist named \( p \) and \( U \) which contain the grids boundary names, boundary conditions, and the initial conditions. An independent boundary condition is
specified for each boundary name. Within p and U dimensions for each field variable are specified using the seven primary dimensions.

The constant directory contains a file named transportProperties and a directory named polyMesh. Model constants are included in transportProperties. For icoFoam the kinematic fluid viscosity is the only constant present and its value and dimension is specified in transportProperties. The polyMesh directory contains files that define the grid for a given case. The five files, boundary, faces, neighbour, owner, and points exist in ployMesh and represent lists of mesh entities. These five files define the spatial discretization and geometry of the case.

The final directory found in the case directory is titled system and it contains three files which control many of the numerical parameters. The file controlDict, for example, allows the user to choose various parameters such as time step size, frequency with which to write data, and solution time duration. The file fvSchemes, also exists in the system directory and defines the various temporal and spatial discretization schemes. Each term from the equations being solved is listed here with a chosen discretization scheme. The final file located in the system directory is titled fvSolution. Parameters pertaining to the iterative solution of the discretized model equations and solution algorithm are defined in fvSolution. For example, matrix preconditioners and residual tolerances are prescribed here.

Following execution of a solver, multiple time directories are added to the case directory. For example, the directory titled 10 holds the solution at a time of ten seconds. The number of time directories depends on the chosen data write frequency and solution time duration. Each time directory contains data files with all field variable values for every grid cell in the mesh.
Chapter 4

Simulation Results for Flow of an Oldroyd-B Fluid

As previously discussed, the approximate closure model of platelet aggregation is equivalent to the Oldroyd-B model of a viscoelastic fluid under the conditions of constant activated platelet concentration, constant breaking rate, and removal of the associated scalar transport equations. In this chapter, the flow of an Oldroyd-B fluid is calculated numerically under varying conditions for the pressure driven flow through a two-dimensional planar channel. Simulations are performed using the equation form present in the viscoelastic literature and the form used in Fogelson’s platelet aggregation model. The purpose of this chapter is to validate the time-accurate solution of the Oldroyd-B equations using the computational methodology presented in Chapter 3. In addition, the dependence of numerical stability on various model parameters is investigated.

4.1 Steady State Poiseuille Newtonian Flow

For the start up flow of a resting Oldroyd-B fluid exposed to a constant pressure gradient. A linear pressure field is imposed as an initial condition and the pressure is solved for using the PISO Algorithm previously discussed. In order to obtain this pressure field a steady-state pressure driven Newtonian flow is computed using a density, viscosity, steady-state centerline velocity, and channel height equal to those used in [18] for the background flow applied with the platelet aggregation model. Here, the Reynolds number is based on the steady-state centerline velocity and channel separation resulting in a value of 25. In the present study, the Reynolds number is based on the steady-state average velocity and half the channel separation resulting in a value of 8.3. This different Reynolds number definition is elected because it is used in the viscoelastic literature [10] for similar simulations. Viscous and elastic properties are selected as described in the following case studies and they are not selected based on values which are physically relevant to platelet aggregation. A schematic of the geometry and coordinate system is given in Figure 4.1.
4.1.1 Exact Solution

This case study aims to predict steady laminar flow in a two-dimensional rectangular fixed wall channel through numerical solution of the incompressible Navier-Stokes equations. An analytical solution to the incompressible Navier-Stokes equations for this case can be derived under the following assumptions and conditions.

1. Constant fluid density and viscosity
2. Steady-state flow (variables do not change with time)
3. Fully developed flow (velocity does not change with respect to the streamwise direction)
4. Two-dimensional flow (z-component of velocity and changes wrt z-direction in velocity are zero)
5. Constant pressure gradient in $x$ direction and zero pressure gradient in $y$ and $z$ directions

Assumptions 3 and 4 reduce the three-dimensional incompressible continuity equation to the following.

$$ \frac{dv}{dy} = 0 $$

Here, $v$ is the y-component of velocity. Therefore $v$ is constant over the entire flow field. The no-slip boundary condition requires that all components of the fluid velocity be zero at the top and bottom walls and so $v$ must be zero everywhere. It follows that the velocity field is unidirectional in $x$. Under the preceding assumptions and results, the Navier-Stokes equations reduce to

$$ 0 = \mu \frac{d^2 u}{dy^2} - \frac{dp}{dx} \quad (4.1) $$

A simple separation of differentials and integration leads to a general solution for velocity that
is quadratic with $y$. Application of the no-slip boundary condition

$$u(-h) = u(h) = 0$$

leads to the following solution for the velocity profile.

$$u(y) = U_{max}(1 - (y/h)^2) \quad (4.2)$$

where

$$U_{max} = \frac{3}{2} U_{avg}$$

and

$$U_{avg} = -h^2 \frac{dp/dx}{3\mu} \quad (4.3)$$

4.1.2 Computational Grid

Simulations are performed on three successively refined two dimensional grids. All grids in this thesis are constructed using Pointwise grid generation software. Grid spacing is uniform with orthogonal control volumes each having an aspect ratio of unity. Each of the three grids is defined by a single parameter $N$, with grids consisting of $N-1$ control volumes in the vertical direction and $5N-1$ control volumes in the horizontal direction. $N$ is equal to 10, 20, and 40, on the coarse, medium, and fine grids respectively. The grid has dimensions, $h$ equal to 0.0005 m and $L$ equal to 0.005 m. The grid is one cell deep in the $z$ direction and equations are not solved in this direction.

4.1.3 Boundary and Initial Conditions

Four separate boundaries are defined excluding the two boundaries in the $z$ direction. The inlet boundary is specified to have a horizontal velocity distribution equal to the analytic steady-state solution described above with $U_{max}$ equal to a value of 0.1 m s$^{-1}$ which was used in [18], while the pressure at the inlet is forced to have zero gradient in the direction normal to the boundary. The parabolic velocity inlet profile is specified using groovyBC, an open source contribution to the OpenFOAM toolbox that facilitates a range of complex boundary condition specifications. At the outlet boundary, the pressure and velocity component gradients in the direction normal to the boundary are set to zero. Both the top and bottom walls represent no slip boundaries with all velocity components set to zero. Finally, the pressure gradient in the direction normal to each
wall is set to zero. Initially, both the velocity and pressure fields are set to zero for all control volumes.

4.1.4 Case Study 4.1: Newtonian Flow at Re = 8.3

For these simulations, only the steady-state pressure and velocity solutions are desired, however the solution is carried out using the time accurate transient stress transport solver without actually solving the stress equation. Time steps of 0.0004 s, 0.0002 s, and 0.0001 s are used on the coarse, medium, and fine grids respectively, forcing the maximum Courant number to a value of 0.8 on all three grids. Simulations are carried out to a steady-state. The computed steady-state velocity profile matches well with the analytic solution given in Equation 4.2. Numerical results from all three grids are presented along with the analytic solution in Figure 4.2. Results on all three grids are satisfactory and almost no change is observed between the medium and fine grids. Numerical results in Figure 4.2 are taken from the streamwise center of the computational domain. The streamwise pressure distribution decreases linearly as expected. The pressure drop is linear on all three grids, however the calculated inlet pressure is slightly lower than the expected value of 16 Pa on coarser grids. This expected value is calculated using Equation 4.3 with an average velocity equal to two thirds of the centerline velocity supplied with the inlet profile. Figure 4.3 shows the streamwise pressure solution at the domain’s vertical center on the three grids with the exact solution based on an inlet pressure of 16 Pa. As with the velocity profile, the pressure distribution on the medium grid is observed to agree well with the analytic solutions.

4.2 Start Up Flow of an Oldroyd-B Fluid

The next scenario to be considered is the start up flow of an Oldroyd-B fluid initially at rest. An initially resting Oldroyd-B fluid is instantaneously exposed to a constant pressure gradient, which drives a transient fully developed flow settling upon a steady-state. In the following sections the exact solution and numerical results for such a flow are presented. Specifically, it is demonstrated that the numerical solver is capable of predicting accurate solutions for both the time accurate evolution and steady-state distribution of Oldroyd-B fluid flow through a two dimensional channel. As is shown in the following sections the stability and accuracy of numerical solutions depend on the parameters selected to represent the fluid.

4.2.1 Exact Solution

Exact solutions are an excellent tool for the validation of numerical codes as they provide a correct result with which to compare computations and are independent of the model’s ability to capture the physics at hand. For the two dimensional planar pressure driven flow of an Oldroyd-B fluid, the steady-state flow field is identical to the steady-state analytical solution for Poiseuille flow derived above with a viscosity equal to \( \eta_0 \), the sum of the polymer and solvent viscosities. Furthermore, the transient temporal evolution of the flow field admits an exact solution. This
Figure 4.2. Steady-state velocity profile computed on all three grids with exact solution. Data sampled at horizontal center of computational domain.

Figure 4.3. Streamwise pressure distribution at the centerline ($y=0$). Results presented on all three grids with exact solution.
solution is presented in [10] and was originally derived by [40]. It is reproduced here in its final form omitting details of the derivation. The following assumptions and conditions apply.

1. Fully developed flow (velocity and elastic stress does not change with respect to the streamwise direction)
2. Two-dimensional flow in $x$ and $y$
3. Pressure gradient in $x$ direction is constant and zero in the $y$ direction

The exact solution for the temporal evolution of the start up portion of the flow is given in [10] in terms of dimensionless variables and the same is done here. The nondimensional velocity, time, and plate separation are defined respectively as follows.

$$U = \frac{u}{U_{avg}} \quad T = \frac{t}{\lambda} \quad Y = \frac{y}{h}$$

The Reynolds number, Weissenberg number, and elasticity number are defined respectively as follows. The velocity field is unidirectional in $x$.

$$Re = \frac{\rho U_{avg} h}{\eta_0} \quad Wi = \frac{\lambda U_{avg}}{h} \quad E = \frac{Wi}{Re} = \frac{\lambda \eta_0}{\rho h^2}$$

The final solution for the start up flow is given by

$$U(T,Y) = 1.5(1 - Y^2) - 48 \sum_{n' = 1}^{\infty} n^{-3} \sin\left(\frac{1}{2} n(1 + Y)\right) e^{-\frac{\pi n T}{4}} G(T)$$

Where,

$$n = (2n' - 1)\pi \quad \alpha_n = 1 + \frac{1}{4} \beta E n^2 \quad \gamma_n = 1 - \frac{1}{4} (2 - \beta) E n^2$$

The parameters $\beta_n$ and $G(T)$ depend on the sign of $\alpha_n^2 - En^2$ as follows.

$$\beta_n = \begin{cases} \sqrt{\alpha_n^2 - En^2} & \text{for } \alpha_n^2 - En^2 > 0 \\ \sqrt{En^2 - \alpha_n^2} & \text{for } \alpha_n^2 - En^2 < 0 \end{cases}$$

and

$$G(T) = \begin{cases} \cosh\left(\frac{1}{2} \beta_n T\right) + \frac{\pi}{\beta_n} \sinh\left(\frac{1}{2} \beta_n T\right) & \text{for } \alpha_n^2 - En^2 > 0 \\ \cos\left(\frac{1}{2} \beta_n T\right) + \frac{\pi}{\beta_n} \sin\left(\frac{1}{2} \beta_n T\right) & \text{for } \alpha_n^2 - En^2 < 0 \end{cases}$$
Thus far exact solutions have been presented for both the start up and steady-state velocity fields of an Oldroyd-B fluid in a two dimensional planar channel under the influence of a constant pressure gradient. Steady-state solutions for the \( xx \), \( xy \), and \( yy \) components of the elastic stress tensor are given in [9]. We reproduce them here as they too are used to validate the numerical approach taken in this thesis. The steady-state fully developed distribution of the \( xx \), \( xy \), and \( yy \) components of the elastic stress are as follows.

\[
\tau_{xx} = \frac{8\eta_o \lambda U_{max}^2}{h^4} y^2 \\
\tau_{xy} = \tau_{yx} = -\frac{2\eta_o U_{max}}{h^2} y \\
\tau_{yy} = 0
\]

### 4.2.2 Computational Set Up

A variety of simulations are performed for the case of start up flow for an Oldroyd-B fluid. Parameters are varied between simulations and simulations are performed by solving both forms of the Oldroyd-B model described in Chapter 2, that is using transport equations for both \( \tau \) and \( \sigma \). The computational set up for all cases, however, is identical and described here. The grids employed are identical to those described for the steady-state Poiseuille flow from the preceding section. The no-slip boundary condition is applied at both walls for velocity. The gradient of each velocity component in the direction normal to both the inlet and outlet boundaries is specified to be zero in order to allow unimpeded flow through the computational domain. Zero pressure gradient normal to both walls is specified and the inlet and outlet boundaries are forced to have a constant pressure equal to the value calculated there for the steady-state solution of Poiseuille flow on the same grid from the preceding section. The value of pressure at each control volume comprising the grid is specified to be equal to the steady-state solution for Poiseuille flow on the same grid at time \( t = 0 \). In this manner the pressure distribution throughout the channel remains unchanged throughout the simulations thereby satisfying the constant pressure gradient condition. The fluid is initially at rest and therefore the velocity is set to zero for all control volumes in the grid at \( t = 0 \). Each component of the elastic stress tensor field, \( \tau \) is set to zero initially for all grid cells. \( \sigma \) is specified to have an initial value based on Equation 2.12 with each component of \( \tau \) set to zero for consistency. The parameters in Equation 2.12 are converted to those used in the Oldroyd-B fluid model using the relations presented in Chapter 2. The gradient of each component of both stress tensors is set to zero at all four boundaries.

### 4.2.3 Pressure Solution

Solution of the governing equations is carried out using the methodology described in Chapter 3. That is, the pressure-velocity coupling is resolved using the PISO Algorithm and the resulting velocity field is assumed constant during the subsequent solution of the stress transport equation. The coupling of the stress back to the momentum equation is performed in an explicit manner. It should be noted that an alternative method to solving the equations of motion for an Oldroyd-B
fluid exposed to a constant pressure gradient is to simply define a constant pressure gradient within the momentum equation. This method removes the need for pressure-velocity coupling and in fact no pressure field is solved for. For the case of Poiseuille start up flow this approach is perfectly appropriate, however in this thesis we aim to solve these equations in the presence of a flow field which changes as a result of a growing blood clot. Such a dynamic problem will require the solution of a pressure field whose gradient will be variable. We validate the model for the simpler start up flow in this chapter using the PISO Algorithm for pressure-velocity coupling because it will be necessary for the clot growth simulations.

4.2.4 Case Study 4.2: Poiseuille Flow at \( \text{Wi} = 1 \) and \( \psi = 1/9 \)

In the following study, \( \psi \), the solvent viscosity ratio, is chosen to be \( 1/9 \) which is a common value used in the literature \[10\]. The solvent viscosity ratio is defined as follows.

\[
\psi = \frac{\eta_s}{\eta_s + \eta_p}
\]

A Weissenberg number of unity is selected and along with \( \psi \) it is fixed for a grid refinement study. The solvent viscosity is set to 0.004 \( \text{kg m}^{-1}\text{s} \) equivalent to the viscosity used for the Newtonian simulations from the preceding section. The polymer viscosity and relaxation time are selected to be 0.032 \( \text{kg m}^{-1}\text{s} \) and 0.0675 s respectively in order to obtain the appropriate values for \( \psi \) and \( \text{Wi} \). Simulations are performed on each of the three successively refined grids using a time step of 0.0002 s, 0.0001 s, and 0.00005 s on the coarse, medium, and fine grids respectively thereby settling on a maximum Courant number of 0.044. Simulations are carried out to a time of 10 seconds though a steady-state is reached much earlier.

4.2.4.1 Results for Start Up Flow

Numerical results from solving both forms of the model equations are nearly identical and all results presented in this chapter use the stress equation from the platelet aggregation model. First results are presented for the temporal evolution of the velocity field. The fluid velocity oscillates due to the elastic nature of the flow and is eventually damped out by the dissipative effects of the viscosity. Figure 4.4 shows the numerically computed temporal evolution of the centerline velocity on all three grids along with the exact solution. The average velocity used in all figures is calculated using \( \eta_0 \) and the pressure gradient based on a pressure of 16 Pa at the inlet. The numerical results are observed to converge to the exact solution with decreasing grid spacing. It is also noted that very little difference exists between solutions on the medium and fine grids. The centerline velocity maintains a positive value at all times, however this behavior is not a requirement as will be shown in the following sections where the velocity is observed to change direction during the oscillating portion of the flow history. From Figure 4.4 it can be seen that the steady-state velocity at the centerline is equal to one and a half times the average
velocity based on the sum of the polymer and solvent viscosities thereby satisfying the exact solution.

![Temporal Evolution of Centerline Velocity](image)

**Figure 4.4.** Temporal evolution of centerline velocity computed on all three grids. Exact solution plotted for comparison.

Figures 4.5 and 4.6 show velocity profiles at two different times during the start up portion of the flow. Numerical results for all three grids and the exact solution are presented. Figure 4.7 presents velocity profiles at four successive times during the start up flow calculated on the medium grid along with the exact solutions. Finally, Figures 4.8 and 4.9 present the temporal evolution of $\tau_{xx}$ and $\tau_{xy}$ at the centerline, wall, and midline (midway between the two), calculated on the medium grid.

### 4.2.4.2 Results for Steady State Flow

In this section results for the steady-state distributions of elastic stress and velocity are presented. Figures 4.10 and 4.11 show the steady-state elastic stress profiles at the streamwise center of the domain. It can be seen that correspondence with the exact solution is strong near the centerline with increasing deviation toward the walls. One possible reason for this behavior is the choice of boundary condition on stress at the wall. The zero-gradient boundary condition at a no-slip wall physically represents impermeability. In other words, each scalar stress tensor component is incapable of passing through the wall and though this is appropriate for certain applications of mass transport it may lack physical realism for the stress tensor field. One alternative method for defining the stress tensor field at solid walls is the calculation of the stress components based
Figure 4.5. Velocity profile at 0.025 seconds computed on all three grids. Solutions taken from horizontal center of domain. Exact solution plotted for comparison.

Figure 4.6. Velocity profile at 0.06 seconds computed on all three grids. Solutions taken from horizontal center of domain. Exact solution plotted for comparison.
Figure 4.7. Velocity profile at several different times computed on the medium grid. Solutions taken at the horizontal center of the domain. Exact solution plotted for comparison.

Figure 4.8. Temporal evolution of the \(\tau_{xx}\) component of the elastic stress tensor computed on the medium grid.
on the local velocity gradient. Dou and Phan Thien [9] numerically solves the flow of an Oldroyd-B fluid over a cylinder running perpendicularly through a channel. Here, the momentum and constitutive equations are solved in order to develop expressions for the elastic stress components at the wall in terms of the velocity gradient. These expressions are employed as boundary conditions at the walls. Such an approach might offer improvements in the accuracy of the calculated stress field over the simple boundary condition specification used in this thesis. Analytical expressions, however, may not be obtainable for certain flow situations. Figure 4.12 shows the steady-state velocity profile at the streamwise center of the computational domain.

Overall, it is found that the numerical approach is satisfactory for the preceding flow conditions. However, not all parameter sets provide such solutions. In the following two sections we present Oldroyd-B fluid start up flow simulations with varying parameters. The goal of these analyses is to gain insight into the behavior, particularly in terms of stability, of the model of an Oldroyd-B fluid and any parallels that may be drawn to the platelet aggregation model. The solvent viscosity, fluid density, and pressure gradient are not varied as they represent the background blood flow within which the platelet aggregation model is to be solved. The only remaining parameters to vary are the polymer viscosity, $\eta_p$ and relaxation time, $\lambda$. 
Figure 4.10. Steady-state profile of the $xx$ component of the elastic stress tensor computed on all three grids. Exact solution plotted for comparison. Solutions taken at horizontal center of computational domain.

Figure 4.11. Steady-state profile of the $xy$ component of the elastic stress tensor computed on all three grids. Exact solution plotted for comparison. Solutions taken at horizontal center of computational domain.
4.2.5 Case Study 4.3: Poiseuille Flow at variable Relaxation Time

In this case study the relaxation time, \( \lambda \) is varied while fixing all other parameters at their values from the preceding section. As such, \( \psi \) remains equal to 1/9 and the Weissenberg number changes based on the choice of relaxation time. Starting at a relaxation time equal to 0.0675 s used in the previous case study its value is incrementally increased and decreased by a factor of ten. The six chosen values are given in Table 4.1 along with the resulting Weissenberg numbers and elastic moduli. It is found that at increasing Weissenberg number, simulations become unstable resulting in divergent solutions. This expected result is consistent with the literature as described in Section 2.3.3. At particularly low values of \( Wi \) solutions diverge as well. This problem therefore can not be due to the HWNP. As the Weissenberg number decreases the elastic modulus increases and therefore simulations show that upper limits on both the Weissenberg number and elastic modulus may exist for achieving stable solutions. In the following, we present results for the temporal evolution of the centerline velocity. The remainder of the simulations performed in this chapter use the medium grid which is not explicitly stated in figure legends. Furthermore, the remaining figures in this chapter are in terms of the dimensional velocity and time, rather than their non-dimensional forms. This approach is taken because the steady-state average velocity and relaxation time are variable depending on the simulation. These two quantities are used as velocity and time scales in the preceding section when plotting results for velocity and time.
respectively. Therefore, in order to facilitate comparison between figures from simulations with different polymer viscosities and relaxation times, results are plotted in terms of dimensional quantities. Figures 4.13 and 4.14 show the centerline velocity evolution at Weissenberg numbers of 0.01 and 0.1. At a Weissenberg Number of 0.01 no oscillations in the velocity are observed. The low Weissenberg number here is achieved through a low relaxation time, which is a measure of the elasticity of the fluid. Oscillations in the centerline velocity and elastic stress fields disappear for this low relaxation time and the fluid behaves in a viscous manner with a strictly increasing centerline velocity that damps out to a steady-state value. This behavior can be observed in Figure 4.13. A relaxation time of zero represents the purely viscous Newtonian fluid. As the relaxation time is increased, oscillations present with larger velocities achieved at higher relaxation times. This behavior is shown in Figure 4.14. Additionally, from Figures 4.13 and 4.14 it can be seen that the time required to reach a steady-state increases with relaxation time. Figures 4.15 through 4.18 show the temporal evolution of the nonzero components of the elastic stress tensor at the horizontal center of the domain. Results at the centerline walls and midlines are presented. The midline is defined as the vertical location midway between the wall and centerline. \( \tau_{xx} \) is symmetric about the centerline and therefore only the stress at the centerline upper midline and upper wall is plotted, whereas for \( \tau_{xy} \) all five locations are plotted. It can be seen that similarly to the velocity field for \( Wi = 0.01 \) the elastic stress components do not oscillate. Additionally, it can be seen that as with the velocity evolution, oscillations in the elastic stress tensor components increase in magnitude with increasing relaxation time. As can be seen, both nonzero stress components reach a steady-state value at these two Weissenberg numbers.

The simulations performed in this case study are carried out to a time of 10 seconds which is well beyond the time required for the velocity to reach a steady-state. At the three higher Weissenberg numbers of 10, 100, and 1000, solutions diverge prior to 10 seconds. At a Weissenberg number of 10 the computed centerline velocity corresponds well with the exact solution out to its steady-state value as can be seen in Figure 4.19. The elastic stress tensor, however, is incapable of settling upon a steady-state value as it does at lower Weissenberg numbers. Figures 4.20 and 4.21 show the temporal evolution of the elastic stress components. Even by later times the \( xx \) component of the elastic stress tensor does not reach a steady-state and simulations eventually

<table>
<thead>
<tr>
<th>( \eta_p ) (kg ( m ) ( s ))</th>
<th>( \lambda(s) )</th>
<th>( \psi )</th>
<th>( Wi )</th>
<th>( G ) (Pa)</th>
<th>Solution Convergence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.032</td>
<td>0.0000675</td>
<td>0.111</td>
<td>0.001</td>
<td>474</td>
<td>solver failure by ( t = 0.007 ) seconds</td>
</tr>
<tr>
<td>0.032</td>
<td>0.000675</td>
<td>0.111</td>
<td>0.01</td>
<td>47.4</td>
<td>converged solution to ( t = 10 ) seconds</td>
</tr>
<tr>
<td>0.032</td>
<td>0.00675</td>
<td>0.111</td>
<td>0.1</td>
<td>4.74</td>
<td>converged solution to ( t = 10 ) seconds</td>
</tr>
<tr>
<td>0.032</td>
<td>0.675</td>
<td>0.111</td>
<td>10</td>
<td>0.0474</td>
<td>solver failure by ( t = 6.7 ) seconds</td>
</tr>
<tr>
<td>0.032</td>
<td>6.75</td>
<td>0.111</td>
<td>100</td>
<td>0.00474</td>
<td>solver failure by ( t = 0.875 ) seconds</td>
</tr>
<tr>
<td>0.032</td>
<td>67.5</td>
<td>0.111</td>
<td>1000</td>
<td>0.000474</td>
<td>solver failure by ( t = 1.885 ) seconds</td>
</tr>
</tbody>
</table>
Figure 4.13. Temporal evolution of centerline velocity at $Wi = 0.01$. 

Figure 4.14. Temporal evolution of centerline velocity at $Wi = 0.1$. 
Temporal Evolution of Elastic Stress: \( Wi = 0.01, \psi = 1/9 \)

**Figure 4.15.** Temporal evolution of \( xx \) component of the elastic stress at \( Wi = 0.01 \).

Temporal Evolution of Elastic Stress: \( Wi = 0.1, \psi = 1/9 \)

**Figure 4.16.** Temporal evolution of \( xx \) component of the elastic stress at \( Wi = 0.1 \).
Figure 4.17. Temporal evolution of $xy$ component of the elastic stress at $Wi = 0.01$.

Figure 4.18. Temporal evolution of $xy$ component of the elastic stress at $Wi = 0.1$. 

Temporal Evolution of Elastic Stress: $Wi = 0.01, \psi = 1/9$

Temporal Evolution of Elastic Stress: $Wi = 0.1, \psi = 1/9$
fail, presumably due to the high Weissenberg number problem. At Weissenberg numbers of 100 and 1000 solutions diverge as well, however, neither the centerline velocity or the elastic stress tensor reaches a steady-state prior to solver failure in these cases. The final case not yet discussed is for a Weissenberg number of 0.001. Simulations at this Weissenberg number present with rapidly divergent solutions. It is expected that these results are not due to the high Weissenberg number problem. Furthermore it is noted that for this case the elastic modulus is the highest value achieved in this case study. Combined with results from the next case study in which the polymer viscosity is varied it is observed that large values for the elastic modulus seem to present with rapidly divergent solutions. Though, it should be noted that the exact reason for simulation failure is currently unclear and there may be a more representative stability parameter than the elastic modulus.

![Temporal Evolution of Centerline Velocity: Wi = 10, ψ = 1/9](image)

**Figure 4.19.** Temporal evolution of centerline velocity at Wi = 10.

### 4.2.6 Case Study 4.4: Poiseuille Flow at Variable Polymer Viscosity

In this case study, all parameters are identical to those used in Case Study 4.2 except for the polymer viscosity, which is varied. Varying the polymer viscosity changes the steady-state average velocity of the flow and therefore, the Weissenberg number changes in addition to ψ. Table 4.2 shows the polymer viscosities used in this case study along with the associated Weissenberg numbers and elastic moduli.
Figure 4.20. Temporal evolution of $\tau_{xx}$ component of elastic stress tensor at $Wi = 10$.

Figure 4.21. Temporal evolution of $\tau_{xy}$ component of elastic stress tensor at $Wi = 10$. 
We first present results for a polymer viscosity of zero. For this case the elastic stress is zero for all time. The Weissenberg number for this case is meaningless as there is no elastic stress. Furthermore, in the absence of elastic stress the fluid behaves in a purely Newtonian manner. Plots of the centerline velocity evolution and the steady-state velocity profile are given in Figures 4.22 and 4.23. Numerical results correspond well with exact solutions. These results show that in the absence of elastic stress, the steady-state flow is identical to that calculated in Cases Study 4.1.

![Temporal Evolution of Centerline Velocity: $Wi=9, \psi=1$](image)

**Figure 4.22.** Temporal evolution of centerline velocity at zero polymer viscosity.

Results for polymer viscosities of 0.004 kg/m·s, 0.076 kg/m·s, 0.396 kg/m·s, 0.796 kg/m·s are presented next.

<table>
<thead>
<tr>
<th>$\eta_p$ (kg/(m·s))</th>
<th>$\lambda$ (s)</th>
<th>$\psi$</th>
<th>$Wi$</th>
<th>$G$ (Pa)</th>
<th>Solution Convergence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.0675</td>
<td>0.0005</td>
<td>0.045</td>
<td>0.045</td>
<td>converged solution to $t = 10$ seconds</td>
</tr>
<tr>
<td>0.004</td>
<td>0.0675</td>
<td>0.001</td>
<td>0.009</td>
<td>0.009</td>
<td>solver failure by $t = 0.08$ seconds</td>
</tr>
<tr>
<td>0.076</td>
<td>0.0675</td>
<td>0.05</td>
<td>0.45</td>
<td>1.13</td>
<td>converged solution to $t = 10$ seconds</td>
</tr>
<tr>
<td>0.396</td>
<td>0.0675</td>
<td>0.01</td>
<td>0.09</td>
<td>5.87</td>
<td>converged solution to $t = 10$ seconds</td>
</tr>
<tr>
<td>0.796</td>
<td>0.0675</td>
<td>0.0005</td>
<td>0.045</td>
<td>11.8</td>
<td>converged solution to $t = 10$ seconds</td>
</tr>
<tr>
<td>3.996</td>
<td>0.0675</td>
<td>0.0001</td>
<td>0.009</td>
<td>59.2</td>
<td>solver failure by $t = 0.08$ seconds</td>
</tr>
<tr>
<td>7.996</td>
<td>0.0675</td>
<td>0.0005</td>
<td>0.0045</td>
<td>118.5</td>
<td>solver failure by $t = 0.015$ seconds</td>
</tr>
</tbody>
</table>

Table 4.2. Parameter values and simulation results for variable polymer viscosity simulations. Elastic modulus is defined as the ratio of the polymer viscosity to the relaxation time.
Figures 4.24 through 4.27 show the temporal evolution of the centerline velocity. Results indicate that for sufficiently low values of polymer viscosity the numerically predicted centerline velocity agrees well with the exact solution but discrepancies occur at higher polymer viscosities. Simulations performed at the two even higher polymer viscosities listed in Table 4.2 present with rapidly divergent solutions. As the polymer viscosity is increased the Weissenberg number decreases and so we reason that these numerical instabilities are not caused by the HWNP. As the polymer viscosity increases, the elastic modulus increases representing a stiffer fluid, indicating that as with Case Study 4.3 there may be some upper limit on this parameter for a given numerical solver. As the polymer viscosity decreases, the Weissenberg number increases, yet simulations converge out to the maximum simulation time of 10 seconds at the lowest possible polymer viscosity. The lowest polymer viscosity used in these simulations, other than $\eta_p = 0 \frac{kg}{m \cdot s}$ yields a Weissenberg number of 4.5. Therefore, the reason why there is no high Weissenberg number instability in this case study is presumably because the choice of parameters does not allow the Weissenberg number to rise to an unstable value as in Case Study 4.3. Simulations and exact solutions show that the largest amplitude of the velocity decreases with increasing polymer viscosity. In addition, for these simulations, where only the polymer viscosity is varied, the time taken for the velocity to settle upon its steady-state value appears to remain unchanged. For these four values of polymer viscosity the elastic stress is observed to reach a steady-state value. Figures 4.28 and 4.29 show the elastic stress evolution at a polymer viscosity of $0.796 \frac{kg}{m \cdot s}$. 

Figure 4.23. Steady-state velocity profile at zero polymer viscosity.
Figure 4.24. Temporal evolution of centerline velocity at a polymer viscosity of 0.004 kg/m·s.

Figure 4.25. Temporal evolution of centerline velocity at a polymer viscosity of 0.076 kg/m·s.
Figure 4.26. Temporal evolution of centerline velocity at a polymer viscosity of $0.396 \text{ kg m}^{-1}\text{s}$. 

Figure 4.27. Temporal evolution of centerline velocity at a polymer viscosity of $0.796 \text{ kg m}^{-1}\text{s}$. 
Figure 4.28. Temporal evolution of $\tau_{xx}$ component of elastic stress at a polymer viscosity of 0.796 kg m$^{-1}$ s$^{-1}$.

Figure 4.29. Temporal evolution of $\tau_{xy}$ component of elastic stress at a polymer viscosity of 0.796 kg m$^{-1}$ s$^{-1}$.
Chapter 5

Clot Growth Simulations in a Pressure Driven Flow

In this chapter the Approximate Closure Model of platelet aggregation is solved numerically under the influence of a pressure driven flow in a two-dimensional planar channel. The background flow is identical to the flow generated in the steady-state Poiseuille flow case study presented in Chapter 4. Here, we generate the flow on a grid of length of 0.004 m which is slightly shorter than those used in Chapter 4. This change is made in order to decrease simulation time noting that the fully developed flow field itself is identical because the plate separation is the same as that used in Chapter 4. Another difference with the grid used in this chapter is the addition of near wall refinement of grid cells. Wall adjacent grid cells have a thickness of 10 microns in the cross flow direction, and the number of cells in the cross flow direction is 39. There are 79 uniformly spaced grid cells in the stream-wise direction. A time step of 0.0001 seconds is used for all parallel plate simulations in this chapter. In addition to parallel plate studies, fluid flow and clot growth within a two-dimensional backward facing step geometry is simulated. The purpose of this study is to evaluate the model’s applicability to clot growth within recirculating flows which are known to promote thrombus formation.

5.1 Model Parameter Selection

In this section the selection of model parameters is presented. Accepted values exist for many of the parameters in the Approximate Closure Model of platelet aggregation and as such are adopted for use in this thesis. However, the choice of some parameters is less straightforward and in some instances different values are tested in order to gain an understanding of the sensitivity of results to changes in the parameters.
5.1.1 Diffusion Coefficients and ADP Release Rate

Constant diffusion coefficients exist for five of the equations in the model, the Navier-Stokes equations, the non-activated platelet transport equation, and the chemical activator transport equation. For the Navier-Stokes equations this parameter is the kinematic viscosity of blood, which is defined as the dynamic viscosity, $\mu$, divided by the density, $\rho$. These values are selected to be $0.004 \frac{\text{kg}}{\text{m s}}$ and $1000 \frac{\text{kg}}{\text{m}^3}$ respectively which are the values adopted in [18]. Wootton and Ku [41] also suggests a value of $0.004 \frac{\text{kg}}{\text{m s}}$ for the dynamic viscosity of blood for normal hematocrit. The diffusivities of dormant platelets and chemical activator (ADP) are taken from [37] who predicts platelet activation and deposition using a model based on Fogelson’s transport equations, but does not predict the alterations in the flow field caused by the growing thrombus. The adopted value for the ADP release rate, $A$, from the chemical activator transport equation used in [37] is also borrowed for use in this thesis.

5.1.2 Platelet Activation Rate Function

The functional form of the platelet activation rate function, $R(c)$ must be chosen. One might expect that physically, $R$ would be some increasing function of $c$. Such a philosophy is adopted by [37] and borrowed for use in this thesis. Sorensen et al. [37] assumes that $R$ increases linearly with chemical activator concentration above some chemical concentration threshold, $C_{th}$. For a chemical activator concentration below $C_{th}$, $R$ is zero. Although [37] allows for the inclusion of multiple agonists using a weighted average, only one chemical agonist, ADP, is considered here. The functional form of $R$ is as follows.

$$R(c) = \begin{cases} \frac{c}{C_{th}t_{act}} & \text{for } \frac{c}{C_{th}} \geq 1 \\ 0 & \text{for } \frac{c}{C_{th}} < 1 \end{cases}$$

Here $t_{act}$ is the characteristic time constant for platelet activation and is taken to be equal to 1 second by [37]. The same value is used in this thesis.

5.1.3 Link Breaking Rate Function

The breaking rate, $\beta$ is a function of the trace of the stress tensor divided by the inter platelet link concentration within the framework of the approximate closure model. This quantity physically represents the average energy stored within an inter-platelet link at the location in space and time. Some of the simulations performed in this chapter use a breaking rate which is a function of this average energy per link and others use a constant breaking rate. The functional form used in this thesis for the breaking rate depending on the average link energy is as follows.

$$\beta = \beta_{min} + Q \frac{Tr(\sigma)}{z}$$
\( \beta_{\text{min}} \) is chosen somewhat arbitrarily with stability as the primary concern. The numerical algorithm fails for sufficiently low values of beta and since \( Q \) and the energy per link are both positive, the breaking rate never falls below \( \beta_{\text{min}} \) using this formulation. In addition the breaking rate is increased with the energy per link as is expected physically. Simulations show that the energy per link is relatively constant within the clot and largest near the surface of the clot which is expected physically due to the large shear rates present there. \( Q \) is selected such that the breaking rate within the clot is roughly equal to \( \beta_{\text{min}} \) and simulations show that by increasing \( Q \) the breaking of inter-platelet links at the surface of the clot is increased thereby decreasing clot growth. Numerical stability becomes an issue at high values of the breaking rate and so the breaking rate is forced to remain below some maximum value which is chosen based upon the admission of stable solutions. The values for each parameter used in this thesis from Fogelson’s Approximate Closure Model of platelet aggregation are summarized in Table 5.1.

**Table 5.1.** Parameters which are not varied throughout simulations and their adopted values.

<table>
<thead>
<tr>
<th>Model Parameter</th>
<th>Adopted Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( D_n ) (m²/s)</td>
<td>1.58x10⁻¹³</td>
</tr>
<tr>
<td>( D_c ) (m²/s)</td>
<td>2.57x10⁻¹⁰</td>
</tr>
<tr>
<td>( A ) (kgmol/platelet)</td>
<td>2.4x10⁻²⁰</td>
</tr>
<tr>
<td>( t_{\text{act}} ) (s)</td>
<td>1</td>
</tr>
<tr>
<td>( C_{\text{th}} ) (kgmol/m³)</td>
<td>2x10⁻⁶</td>
</tr>
<tr>
<td>( \mu ) (kg/m/s)</td>
<td>0.004</td>
</tr>
<tr>
<td>( \rho ) (kg/m³)</td>
<td>1000</td>
</tr>
</tbody>
</table>

### 5.2 Boundary and Initial Conditions

The boundary and initial conditions for the field variables in the platelet aggregation model are summarized in Tables 5.2 and 5.3 respectively. Boundary and initial conditions on all variables are identical for all simulations performed in this chapter.

The boundary conditions on pressure and velocity are the same as for the background flow generation previously described. Boundary conditions on the cohesive stress tensor are the same as those used for both stress tensors in the Oldroyd-B simulations performed in Chapter 4. At the walls, platelet, chemical activator, and link concentrations are specified to have a gradient of zero in the direction normal to the wall at the walls. A gradient normal to the wall of zero implies that diffusive transport cannot exist through the wall. Advective transport must too be zero as the velocity is zero at the wall, and therefore transport through the wall is removed. Physically, this Neumann specification represents an impermeable wall. As such, we assume that that platelets, chemical activator, and inter-platelet links do not penetrate the vessel wall. Zero
Table 5.2. Summary of boundary conditions used in platelet aggregation model simulations. The direction normal to the boundary is denoted by \( n \). 1 kgmol = 1000 mol.

<table>
<thead>
<tr>
<th>Field Variable</th>
<th>Walls</th>
<th>Inlet</th>
<th>Outlet</th>
</tr>
</thead>
<tbody>
<tr>
<td>velocity (( \frac{m}{s} ))</td>
<td>( u_i = 0 )</td>
<td>( \frac{du_i}{dn} = 0 )</td>
<td>( \frac{du_i}{dn} = 0 )</td>
</tr>
<tr>
<td>pressure (( \frac{m^2}{s^2} ))</td>
<td>( \frac{dp}{dn} = 0 )</td>
<td>( p = 0.0128 )</td>
<td>( p = 0 )</td>
</tr>
<tr>
<td>cohesive stress (( \frac{m^2}{s^2} ))</td>
<td>( \frac{d\sigma_{ij}}{dn} = 0 )</td>
<td>( \frac{d\sigma_{ij}}{dn} = 0 )</td>
<td>( \frac{d\sigma_{ij}}{dn} = 0 )</td>
</tr>
<tr>
<td>activated platelet concentration (( \frac{\text{platelets}}{m^3} ))</td>
<td>( \frac{d\phi_a}{dn} = 0 )</td>
<td>( \frac{d\phi_a}{dn} = 0 )</td>
<td>( \frac{d\phi_a}{dn} = 0 )</td>
</tr>
<tr>
<td>non-activated platelet concentration (( \frac{\text{platelets}}{m^3} ))</td>
<td>( \frac{d\phi_n}{dn} = 0 )</td>
<td>( \phi_n = 1.5 \times 10^{14} )</td>
<td>( \frac{d\phi_n}{dn} = 0 )</td>
</tr>
<tr>
<td>chemical activator concentration (( \frac{\text{kgmol}}{m^3} ))</td>
<td>( \frac{dc}{dn} = 0 )</td>
<td>( dc = 0 )</td>
<td>( dc = 0 )</td>
</tr>
<tr>
<td>inter-platelet link concentration (( \frac{\text{links}}{m^3} ))</td>
<td>( \frac{dz}{dn} = 0 )</td>
<td>( dz = 0 )</td>
<td>( dz = 0 )</td>
</tr>
</tbody>
</table>

Table 5.3. Summary of initial conditions used in platelet aggregation model simulations. *Chemical activator concentration is nonzero for grid cells in the specified injury zone as previously discussed. 1 kgmol = 1000 mol.

<table>
<thead>
<tr>
<th>Field Variable</th>
<th>Initial Condition for all Grid Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>velocity (( \frac{m}{s} ))</td>
<td>steady-state Poiseuille solution</td>
</tr>
<tr>
<td>pressure (( \frac{m^2}{s^2} ))</td>
<td>steady-state Poiseuille solution</td>
</tr>
<tr>
<td>cohesive stress (( \frac{m^2}{s^2} ))</td>
<td>( \sigma_{ij} = 0 )</td>
</tr>
<tr>
<td>activated platelet concentration (( \frac{\text{platelets}}{m^3} ))</td>
<td>( \phi_a = 0 )</td>
</tr>
<tr>
<td>non-activated platelet concentration (( \frac{\text{platelets}}{m^3} ))</td>
<td>( \phi_n = 1.5 \times 10^{14} )</td>
</tr>
<tr>
<td>chemical activator concentration (( \frac{\text{kgmol}}{m^3} ))</td>
<td>( c = 0^* )</td>
</tr>
<tr>
<td>inter-platelet link concentration (( \frac{\text{links}}{m^3} ))</td>
<td>( z = 0 )</td>
</tr>
</tbody>
</table>

gradient normal to the outlet boundary is specified on these four variables. Such a specification implies that the variable value does not change across the boundary. In this way, the outlet boundary represents an extension of the vessel. The dormant platelet concentration is specified to have a constant value at the inlet boundary representing the fact that dormant platelets at this background concentration are flowing into the domain. This concentration is also used as an initial condition for all grid cells in the domain. Activated platelets, chemical activator, and platelet links are specified as zero at the inlet representing the fact that none are expected to be flowing within the blood prior to clotting. It should be noted that activated platelets may be present in the blood and such a condition is employed in [37]. The initial condition for both activated platelets and inter-platelet links is zero for all grid cells in this thesis. Chemical activator is specified to have a concentration of zero for all grid cells initially except for the injury zone which covers specific wall adjacent cells. The initial chemical activator concentration specified in the injury zone is denoted by \( C_o \).
5.3 Case Study 5.1: Effects of $\beta$, $\alpha_2$, and $C_0$

In the following case study the relative effects of $\beta$, $\alpha_2$, and $C_0$ on simulation results are investigated. For these simulations, a constant breaking rate is used in order to remove some parameters from the model and simplify the sensitivity study. For a constant breaking rate, $Q$ is equal to zero, and the platelet link concentration no longer effects the rest of the model, as its only coupling to the other transport equations is through a breaking rate that varies with the average energy per link. Therefore, we set $\alpha_0$ to zero forcing the link concentration, $z$, to remain at its initial condition of zero for all time. Employing the adopted values from Table 5.1, the aforementioned three parameters remain the only ones left to vary.

First some limiting cases are discussed as they indicate upper and lower bounds on parameter values. For an $\alpha_2$ of zero, a clot can never form. In this instance the source term in the stress equation representing stress formation due to activated platelets is zero. As such, the stress field remains zero for all time because the initial condition on the stress is zero for all components and no other mechanism exists in the model for initiating stress production. Specifically, the two source terms containing the velocity gradient and the breaking term remain zero because they contain the stress tensor at a value of zero. Nonzero values of $\alpha_2$ which are sufficiently low are also found to produce no clot growth. As previously described, clot initiation in this thesis is achieved by specifying grid cells at time $t = 0$ which have some nonzero value of chemical activator concentration $C_0$. In order for this method to produce a clot, stress production must be rapid initially such that the fluid velocity is sufficiently halted to reduce the flow of constituents and enable further stress production. $\alpha_2$ must therefore be large enough to achieve this rapid stress production and in the event it is not, clots fail to form and an unaffected steady-state Poiseuille flow prevails. Conversely, for increasing values of $\alpha_2$ the cohesive stress becomes too large and solutions diverge. In the following simulation results, a range of $\alpha_2$ values are presented which generate clot producing results. The value for the initial chemical concentration in the injury zone, $C_0$, must be at least as large as the threshold chemical concentration in order to enable platelet activation. Therefore, we only select $C_0$ values which are greater than $C_{th}$ in order to facilitate clot growth. The actual values chosen for the three parameters are selected somewhat arbitrarily with the main goal of generating results that demonstrate the full range of model behavior, namely zero clot growth to solution divergence. Figure 5.1 shows the breakdown of parameter combinations used in this case study. All cases are carried out to 5 seconds in time which is sufficiently long to demonstrate the desired behavior. In the following, the observed results for the variation of each parameter while the other two are held constant are discussed.

5.3.1 Results for Variable $\beta$

In this section, the results for simulations performed at the three different breaking rates while holding $\alpha_2$ and $C_0$ constant are discussed. For simulations that converge out to 5 seconds clot heights or equivalently, occlusion percentage, is observed to decrease with increasing breaking
rate. For higher breaking rates links are broken and the stress is reduced more rapidly and such a result is expected. We also notice that values for the maximum elastic modulus and maximum magnitude of platelet stress during a given simulation are lower for larger breaking rates, again resulting from the increase in the sink term in the stress transport equation. As previously mentioned, some of the simulations performed in this case study present with divergent solutions prior to the specified ending time of 5 seconds. In these instances, larger breaking rates produce convergent solutions out to a later or equal time. Such results are ultimately expected as the breaking rate acts as a measure to control the growth of the platelet stress tensor. Figures 5.2 and 5.3 show the cohesive stress field at a breaking rate of 10 and 100 for a fixed initial injury zone chemical concentration and stress formation rate constant at a time of 0.5 seconds. Figures 5.4 and 5.5 present the resulting velocity fields.

5.3.2 Results for Variable $C_o$

Here we discuss the results for simulations performed at the three different initial injury zone chemical concentrations while holding the breaking rate and stress formation constant at constant values. Firstly, we notice that occlusion percentage increases for increasing values of $C_o$. This behavior is likely due to the fact that the platelet activation rate in the injury zone increases with increasing initial injury zone chemical activator concentration which in turn increases the activated platelet concentration. The activated platelet concentration feeds into the source term in the platelet stress transport equation and larger values of it increase clot growth. The maximum elastic modulus obtained during a simulation increases with $C_o$ and in some instances shows no change. Specifically, no or minimal further increase in the maximum elastic modulus is noticed when increasing $C_o$ from $3 \times 10^{-5}$ kmol/m$^3$ to $3 \times 10^{-4}$ kmol/m$^3$ in many cases. Simulations show that the maximum value for the magnitude of the cohesive stress tensor increases with $C_o$, but seems to level off. Specifically, in many instances, the maximum stress magnitude changes little.

\[
\beta = 10, 50, 100 \\
\alpha_2 = 10^{-27}, 10^{-26}, 10^{-25}, 10^{-24}, 10^{-23} \\
C_o = 3 \times 10^{-6}, 3 \times 10^{-5}, 3 \times 10^{-4}
\]
between the two higher values for initial injury zone chemical activator concentration. Increasing the initial chemical concentration in the injury zone causes simulations to diverge at earlier times as might be expected due to the increasing contribution to the platelet stress transport equation source term.

### 5.3.3 Results for Variable $\alpha_2$

Results for the effects of variations in the platelet stress formation rate constant, $\alpha_2$ are presented here. Increasing $\alpha_2$ while holding all else constant results in more occlusive clots for simulations that converge out to 5 seconds. Again, this behavior is likely due to the increase in the source term associated with the increase in $\alpha_2$. The maximum elastic modulus and platelet stress magnitude observed throughout the course of a given simulation increases with $\alpha_2$. Finally, solutions that diverge are observed to do so at earlier times for larger values of the platelet stress formation rate constant.

### 5.3.4 Numerical Stability Observations

The preceding results show that convergence is not always achieved. Results indicate that numerical instabilities revolve around the platelet stress tensor, and they arise when the stress becomes large. It was suggested in the previous chapter that two different mechanisms leading to divergent
solutions are present. One occurs at high Weissenberg number and low elastic modulus and the other at low Weissenberg number and high elastic modulus. The elastic modulus, $G$, is defined as follows.

$$G = \frac{\alpha_2 \phi_n^2}{\beta}$$

For the clot growth simulations in this chapter calculating the Weissenberg number is not straightforward. As previously discussed, in the case of the platelet aggregation model, the Oldroyd-B fluid exists only within the clot itself while a Newtonian relationship presides for the surrounding fluid. Therefore, no clear length scale is available. Furthermore, no velocity scale is apparent, because the viscosity is variable, depending on the activated platelet concentration. The Weissenberg number will vary in space and time in contrast to the simulations performed in Chapter 4.

The question of which of the two scenarios present in Chapter 4 is causing solutions to diverge here, remains. Although the Weissenberg number is not explicitly calculated, we know that the average velocity within the clot is low. This suggests a low Weissenberg number, however, the relaxation time and length scale could easily raise the Weissenberg number. From Tables 4.1 and 4.2 it can be seen that as the elastic modulus increases, the Weissenberg number decreases and
Figure 5.4. Top: velocity magnitude at 0.5 seconds simulation time. Bottom: corresponding velocity magnitude line contours. Breaking rate = $10^{1.5}$.

vice versa. The simulations presented in the current chapter are shown to diverge sooner with increasing elastic modulus, suggesting that the high Weissenberg number problem does not play a role. Although simulations are observed to diverge at increasing elastic modulus, the value of this parameter at which simulations fail changes dramatically. As the breaking rate and stress formation rate constant are varied, the maximum elastic modulus is observed to scale accordingly. For example, doubling the breaking rate from 50 to 100 generally halves the maximum elastic modulus. Similar results are seen for variations in $\alpha_2$. It is therefore concluded that there is no single value for the elastic modulus that indicates the presence of solution divergence over all parameter sets. However, for a given parameter set, solutions diverge readily when the elastic modulus becomes large. In addition, the elastic modulus is observed to increase with the stress field and therefore can be used to indicate the magnitude of the stress field. In the following section, this idea is used to limit the growth of the stress tensor field, thereby improving stability.

5.4 Model Modifications

5.4.1 Improved Stability Through a Limited Elastic Modulus

Using the computational methodology described in Chapter 3 we find that stability becomes an issue when solving the platelet aggregation model equations. Specifically, the platelet stress
Figure 5.5. Top: velocity magnitude at 0.5 seconds simulation time. Bottom: corresponding velocity magnitude line contours. Breaking rate = 100 $\frac{1}{s}$.

is observed to grow in an uncontrolled manner resulting in solution divergence and simulation failure. This growth in the stress field presents within the clot itself, while the surrounding Newtonian blood flow possesses zero platelet stress. In order to gain insight into the nature of the problem the source terms in the platelet cohesive stress transport equation, Equation 2.6 are investigated. The two terms with the velocity gradient present are expected to reduce to zero as the fluid velocity disappears within the clot and therefore are not expected to contribute significantly to the problem. The stress formation and depletion terms remain. The depletion term removes stress due to the breaking rate, $\beta$, of inter-platelet links. The formation of stress increases with activated platelet concentration as can be seen from the platelet activation source term in Equation 2.6, however there is no explicit mechanism for limiting this term within the clot as there is for the terms which contain the velocity gradient. This fact may contribute to the numerical instabilities observed during simulations. In [18] it is mentioned that if $\beta$ and $\alpha_2$ are changed proportionally, the elastic modulus of the clot will be constant which may be helpful for selecting physical parameters. In this thesis, the elastic modulus is limited to help with the growth of the platelet stress field instead. The elastic modulus is a representation of the ratio of the source to sink term in the stress transport equation, neglecting the terms containing the velocity gradient. Therefore, controlling it controls the growth of the platelet stress tensor. We place an upper limit on the elastic modulus. This value is not chosen to be the elastic modulus of an actual blood clot, rather it is selected based on the admission of stable solutions with the
additional requirement of achieving sufficiently low velocities within the clot.

The elastic modulus consists of three parameters. No impositions are made upon the breaking rate and it is calculated as a function of the energy per link as previously described. The breaking rate is shown to be useful for controlling clot growth in a physical manner. That is, link breaking increases with increasing energy per link. Placing restrictions upon the breaking rate could remove this important physical aspect of the model. We place no restrictions on the activated platelet concentration in order to allow its calculation to come purely from the solution of the activated platelet transport equation. The only remaining parameter, $\alpha_2$ is therefore modified in order limit the elastic modulus. Simulations are initialized by selecting $\alpha_0$ and $\alpha_2$. Within each simulation time step, $\alpha_2$ is recalculated as the minimum of the originally chosen value and the value at which the elastic modulus achieves its specified upper limit. In this way, if the originally selected value for $\alpha_2$ yields an elastic modulus below the specified maximum, no changes are made. Otherwise, $\alpha_2$ is reduced such that the elastic modulus remains at its specified upper limit. As $\alpha_2$ is reduced, its physical relevance is relinquished for the maintenance of stable solutions.

5.4.2 Stationary Clots Through the Removal of Advection

While the stress is able to reduce the flow within the clot essentially to zero in terms of the surrounding blood flow, there remains a nonzero velocity within the clot. As such, model variables within the clot are advected at this velocity. This advection causes the clot itself to have a net motion downstream, albeit at a much lower velocity than that present in the surrounding flow. A clot that slides along the wall in this manner is unphysical. In order to remove this behavior from the model we force the advection of all model variables except for fluid velocity to zero in the event the clot elastic modulus has reached the specified upper limit used for stability. Simulations show that regions where the elastic modulus has reached its maximum value provide a rough representation of the clot location and therefore field variables are not allowed to flow through the clot. It is important to note that no impositions are made upon the velocity field, and flow still exists through the clot. However, through the removal of advection, this flow does not affect the platelets, chemical activator, platelet links, and cohesive stress.

5.5 Case Study 5.2: Effectiveness of Model Modifications

In this short case study, the effects of the two model modifications are demonstrated. First, solutions from the previous case study at a breaking rate of $100 \frac{1}{s}$, stress formation rate constant of $10^{-24} \frac{kg \cdot m^5 \cdot links}{s^3}$, and initial injury zone chemical activator concentration of $3 \times 10^{-5} \frac{kgmol}{m^3}$ are presented. This simulation is observed to solve out to 5 seconds though instabilities in the velocity field present. Figures 5.6 and 5.7 show contour plots of the platelet stress tensor and the velocity respectively.

It can be seen that the clot itself has moved downstream considerably from the injury zone.
This behavior occurs due to reasons previously described. Furthermore, it can be seen that at 5 seconds the velocity field possesses a nonzero region within the clot. This behavior is often followed by solver failure. Simulations with a limited elastic modulus and no advection in the clot are performed for the same set of parameters to facilitate a direct comparison. A maximum elastic modulus of 20 Pa is selected which is large enough to sufficiently halt the flow yet small enough to control the stress field and stabilize the solution. This value for the maximum elastic modulus is used for the remainder of simulations in this thesis. Figures 5.8 through 5.10 show the solutions using the two model modifications.

It is clear from Figures 5.8 and 5.9 that, the clot no longer travels along the wall once advection is removed. It should be noted that in the beginning of the simulation before advection is limited due to the maximum elastic modulus being reached, the clot does move slightly from its original location but halts once advection is removed. Other criterion for the removal of advection could be employed to prevent this behavior, however, simulations are not observed to have significant initial movement and often times there is none at all. Although the clot is prevented from sliding along the wall, it is observed to grow downstream in and uncontrolled manner, which may not always be realistic. Methods for controlling this growth are presented in later sections. Limiting the elastic modulus has produced a well controlled stress field that does not rise high enough to cause instabilities in the velocity field. From Figure 5.8 it can be seen that the elastic modulus is observed to remain below the maximum value of 20 Pa. Some simulations show that the elastic modulus intermittently rises above the maximum specified value but it is always observed to remain near this value in regions where the limiting is in effect. It is concluded that the two model modifications presented here succeed in their respective goals. It should be noted that even with a limited elastic modulus, simulations are observed to become unstable, particularly at longer simulation times. Specifically, it is found that the stress tends to grow at the leading edge of the clot as well as at the outlet boundary near the wall. The latter problem is also observed in [18]. Simulations do show that stable solutions can be achieved out to a time on the order of...
Figure 5.7. Top: velocity magnitude at 5 seconds simulation time. Bottom: corresponding velocity magnitude line contours. Solutions generated without elastic modulus or advection limited.

minutes which is in the same regime as experimental observations.

5.6 Case Study 5.3: Effects of Variable Breaking rate

In this section a variable breaking rate is employed. Specifically, the breaking rate is a function of the average energy per link as assumed in Fogleson’s closure approximation previously discussed. Again the average energy per link is defined as the trace of the platelet stress tensor divided by the inter-platelet link concentration. The exact functional form used in this thesis is discussed in the beginning of this chapter and reproduced here.

\[
\beta = \beta_{\text{min}} + Q \frac{Tr(\sigma)}{z}
\]

For the simulations presented here, \(\beta_{\text{min}}\) is prescribed a value of \(100\ \frac{1}{s}\). This value is selected due to observations from Case Study 5.1. As previously discussed simulations are observed to behave more stably than at the two lower breaking rates. In addition, simulations performed at this constant breaking rate presented with evident clots with large enough values of \(\alpha_2\) and \(C_0\). Using a value of \(100\ \frac{1}{s}\) for \(\beta_{\text{min}}\) ensures that the breaking rate never falls below this value, and therefore potential stability issues at lower breaking rates are avoided. Furthermore, the intention
Figure 5.8. Elastic modulus (Pa) plot at 5 seconds simulation time. Solutions generated with elastic modulus and advection limited. Maximum elastic modulus = 20 Pa.

Figure 5.9. Cohesive stress magnitude at 5 seconds simulation time. Solutions generated with elastic modulus and advection limited. Maximum elastic modulus = 20 Pa. Cohesive stress normalized by fluid density.

is to compute a breaking rate that increases near the surface of the clot but remains at a value of $\beta_{\text{min}}$ within the clot itself. Physically, the energy per link should be roughly constant within the clot itself where the fluid forces are small. Near the clot surface, however, the platelet links are exposed to larger shear rates and therefore the energy within a given link should increase. It is here, that we want the breaking rate to increase above its minimum value in order to capture the fact that links at this location are more likely to break. Therefore, within the clot itself the energy per link should be small enough such that the second term in the formula for $\beta$ is small compared to $\beta_{\text{min}}$.

One main difference between the simulations performed here and those from the previous case study is that $\alpha_0$ can no longer be zero because the inter-platelet link concentration is now coupled to the remainder of the model through the breaking rate. Therefore, its calculation becomes important and it must be non-zero in order to predict a breaking rate above the minimum specified
Figure 5.10. Top: velocity magnitude at 5 seconds simulation time. Bottom: corresponding velocity magnitude line contours. Solutions generated with elastic modulus and advection limited. Maximum elastic modulus = 20 Pa.

value. A value of $3 \times 10^{-5} \, \text{kgmol m}^{-3}$ for the initial injury zone chemical activator concentration is selected and it is required that the breaking rate does not rise above $2000 \, \frac{1}{s}$. An upper limit is selected because we find that allowing the breaking rate to increase without limitation leads to divergent solutions. The value of $2000 \, \frac{1}{s}$ is shown to yield stable solutions though solutions may converge at higher values. Only three parameters, therefore, need to be selected. These parameters are $\alpha_2$, $\alpha_0$, and $Q$. The goal of this study is to investigate the ability of a variable breaking rate to control clot growth by reducing growth in regions where the energy per link is large. As observed in previous results, clots are generally predicted to grow downstream in addition to transverse to the flow. Even when limiting advection within the clot thereby removing the problem of clots moving along the wall, the clot still grows in the downstream direction. This behavior may not be physical in many instances and as we show in this study, a variable breaking rate tends to help with the problem.

5.6.1 Selection of $Q$ through Maximum Link Energy

In the first set of numerical experiments $Q$ is selected using experimental results from the literature to determine an approximation for the energy within a platelet link at rupture. Using this value in the equation for the breaking rate at a breaking rate equal to the maximum allowed value of $2000 \, \frac{1}{s}$, $Q$ is solved for. Therefore, the breaking rate is equal to its maximum
value at values of the energy per link which are equal to or greater than the determined value at link rupture. An approximate value for the energy per link at rupture is calculated as follows. Firstly, inter-platelet links from the model are approximated as fibrin strands. The development of fibrin within a clot results from coagulation which is not explicitly incorporated in the model and therefore an inconsistency exists. Fibrin strands are used to represent inter-platelet links during platelet aggregation in the model noting that the validity of this representation is currently unknown. Experimental results from [20] for the stress-strain relationship of an individual fibrin fiber are used. A typical stress-strain curve for a fibrin fiber is given. The stress varies nonlinearly with strain, however, here the relationship is approximated as linear by placing a line from the origin to the fracture point. It is assumed that the fiber deforms in an elastic (recoverable) manner up until fracture. Therefore the total elastic energy per unit volume stored in the fiber at fracture, $e$ is equal to the area under the stress strain curve.

$$e = \frac{1}{2} \epsilon_r S_r = 7\text{MPa}$$

Here, $\epsilon_r$ and $S_r$ represent the strain and stress at rupture respectively. These two values are approximated from the curve given in [20]. In order to determine the total energy within a platelet link at rupture, $T$, dimensions for a typical link are required. With known fiber dimensions, the volume of the fiber can be calculated and used to compute the total energy. Ryan et al. [35] performs measurements of various fibrin fiber parameters within generated clots. Results are borrowed from this publication for the mean measured diameter, $D = 93$ nm and length, $L = 2.4 \mu$m of fibrin fibers within one of the clots studied. The total energy within a typical fibrin fiber at rupture, $T$ is therefore approximated as follows.

$$T = \frac{e\pi D^2 L}{4} = 1.14 \times 10^{-13}\text{N} \cdot \text{m}$$

$Q$ is calculated as previously described using $T$, though $T$ is first normalized by the fluid density because in the numerical code the platelet stress tensor and therefore the energy per link is normalized in this manner. It is noted that the applicability of the aforementioned analysis is yet to be validated and the analysis is used in an effort to demonstrate that the model can predict values for the energy per link which are in a physiologically reasonable regime. Ultimately, the clot should stop growing once this maximum energy per link is reached, however, because of the representation of the breaking rate this condition is not satisfied. Specifically, the breaking rate reaches its maximum value at the experimentally determined maximum energy per link, though at this point the clot continues to grow outward. The reason for this behavior is likely due to the maximum imposed breaking rate not being large enough to overcome the platelet activation source term in the stress equation. One alternative is to define a breaking rate that grows infinitely as the maximum energy per link is approached and such a functional form is discussed in [18]. Once again, it is found that large values of the breaking rate lead to solver
failure and whether or not breaking rates large enough to halt clot growth can be obtained has not yet been tested. At this point values for \( \alpha_0 \) and \( \alpha_2 \) must be selected. For \( \alpha_2 \) a value of \( 10^{-18} \) \( \frac{\text{kg} \cdot \text{m}^5 \cdot \text{links}}{\text{s}^3} \) is arbitrarily selected and is shown to produce reasonably sized clots. Simulations are performed at varying values for \( \alpha_0 \) in an attempt to predict the energy per link near the surface of the clot at a value close to the maximum value determined from the experimental literature. For large values of \( \alpha_0 \) the calculated energy per link is observed to decrease. This result may be due to the fact that for large \( \alpha_0 \), the source term in the inter-platelet link transport equation is large and therefore a higher link concentration is calculated. The platelet link concentration is in the denominator of the energy per link equation and the energy per link therefore decreases. It is found that \( \alpha_0 \) equal to \( 10^{-5} \) \( \frac{\text{m}^3 \cdot \text{links}}{\text{s}} \) yields values of energy per link near the surface of the clot that are close to the experimentally calculated maximum value. Figures 5.11 and 5.12 show the energy per link and resulting breaking rate at 20 seconds of simulation time.

**Figure 5.11.** Plot of energy per link at 20 seconds simulation time. The stress tensor is normalized by the fluid density for numerical simulations and therefore so is the computed energy per link.

**Figure 5.12.** Plot of breaking rate at 20 seconds simulation time.
The energy per link is only calculated within and in the region surrounding the clot. The energy per link is computed as the trace of the stress tensor divided by the inter-platelet link concentration. Both of these fields are nonzero only in and around the clot, and zero outside the clot for all intents and purposes. However, they are not computed as identically zero outside the clot and the ratio of the two yields highly unphysical values in these regions. For this reason, the energy per link is only computed within and in the immediate vicinity of the clot. Ultimately, further outside the clot, there are no links and no energy and therefore there can be no energy per link. It can be seen from Figure 5.11 that the energy per link is highest near the surface of the clot and low within the clot itself. This makes physical sense due to the large and small shear forces present in these two regions respectively. Furthermore, the link breaking rate is observed to reach its maximum value near the surface of the clot where the energy per link is large. Within the clot, however, the breaking rate never rises above its minimum value, a result of the small energy per link present there. Figures 5.13 through 5.16 show the ADP and platelet concentration fields and the fluid pressure.

From Figure 5.14 it can be seen that within the clot the activated platelet concentration is large while in the surrounding flow it maintains a value of essentially zero. Furthermore, the activated platelet concentration within the clot is never observed to rise above the resting platelet concentration in healthy blood. Physically, this result is not expected as platelet aggregates represent an accumulation of platelets. Figures 5.14 and 5.15 demonstrate a balance between resting and activated platelets. Specifically, platelet activation represents the gaining of activated platelets and the loss of resting platelets. This behavior is observed in Figures 5.14 and 5.15 where a given spatial location with a high activated platelet concentration possesses a low resting platelet concentration and vice versa.
Figure 5.14. Plot of activated platelet concentration at 20 seconds simulation time.

Figure 5.15. Plot of non-activated platelet concentration at 20 seconds simulation time.

Figure 5.16. Pressure contour plot at 20 seconds simulation time. The clot represents a solid body and therefore the pressure within it does not have physical meaning.
5.6.2 Effect of variable $Q$

In the following case study the effects of $Q$ on model behavior are investigated. It has been shown that by imposing a breaking rate that increases with the average link energy, the breaking rate increases near the surface of the clot. Here it is shown that the selection of $Q$ has profound effects on clot size while holding all other parameters constant. The simulation from the previous study is used, except rather than selecting $Q$ based on the maximum energy per link, its value is varied. First some limiting cases are discussed. For $Q = 0$ the breaking rate is just a constant and clot growth is shown to proceed transverse to the flow direction as well as downstream as shown in previous results. For particularly large values of $Q$ we find that the maximum breaking rate of $2000 \, \frac{1}{s}$ is reached immediately within the clot and therefore growth in the transverse direction is restricted and a shallow clot grows in the downstream direction. This case is undesirable because no variation of breaking rate is observed with the energy per link. Essentially, $Q$ is so large that the maximum breaking rate is reached even for low values of the energy per link which occur within the clot. In the following, results for $Q$ at values of $10^{18}$ and $10^{19}$ are presented in order to demonstrate the effects of variable $Q$. All other parameter values are the same as in the previous case study where $Q$ is determined from the experimental maximum link energy. Simulations are carried out to 20 seconds in time. Figures 5.17 and 5.18 show the breaking rate distribution at 20 seconds simulation time for $Q = 10^{18}$ and $10^{19}$. Figures 5.19 and 5.20 show the resulting velocity fields at the same two values of $Q$ at 20 seconds.

![Figure 5.17. Plot of breaking rate at 20 seconds simulation time for small $Q$.](image)

From Figures 5.17 and 5.19 it can be seen that for the smaller value of the rate of increase of the breaking rate with the energy per link ($Q$) the clot is observed to grow significantly downstream by 20 seconds. Furthermore, the breaking rate is observed to rise above its minimum value at the surface of the clot but does not reach the imposed upper limit. In comparison, it can be seen from Figures 5.18 and 5.20 that at the higher value of $Q$ clot growth downstream is severely restricted. Physically, the breaking rate increases more rapidly with the energy per link resulting in a larger sink term in the stress equation, thereby controlling the downstream growth of the
clot. In this instance, it can be seen that the breaking rate’s upper limit is reached. Ultimately, the breaking rate shows potential for preventing the uncontrolled downstream growth observed in model simulations.
5.7 Case Study 5.4: Effects of Chemical Activator Degradation

Another potential mechanism for the inhibition of clot growth is the breakdown of chemical activator. In the event chemical agonists are broken down, platelet activation is decreased and can be eliminated if the chemical concentration drops enough. Coade and Pearson [5] experimentally measures the catabolism rates of ADP in whole blood demonstrating that ADP can be broken down. As mentioned previously, the platelet aggregation model used in this thesis incorporates chemical activator breakdown through the addition of a sink term in its transport equation. The sink term consists of a constant $K$ multiplied by the chemical concentration and it accounts for the degradation with time of the chemical activator. In order to gain insight into the behavior of this sink term a simplified version of the model is presented. Imagine, a uniformly distributed concentration of ADP in blood under stagnant conditions in the absence of platelets. In this instance, the advective, diffusive, and source term due to platelet secretion now drop out leaving the following ordinary differential equation.

\[ \frac{dc}{dt} = -Kc \]
The solution to this ODE is as follows, with $C_i$ equal to the uniform concentration present initially.

$$c(t) = C_i e^{-Kt}$$

It can be seen that for this simple case the ADP is predicted to degrade exponentially with time and remain uniform in space. In this section, the effects of $K$ on model results are investigated in the presence of diffusion, advection, and platelet secretion. Thus far $K$ has been set to zero for all simulations. Under the influence of a constant breaking rate results present with clots that continue to grow in the downstream direction even in the event that ADP has degraded below its threshold value, thus halting platelet activation. Simulations performed with a variable breaking rate and chemical degradation eventually stop growing all together. In addition, these clots are observed to fluctuate slightly in size during their growth but eventually settle upon a geometry that stops changing. These simulation results are presented next. The

**Figure 5.21.** Top: velocity magnitude at 50 seconds simulation time for small $K$. Bottom: corresponding velocity magnitude line contours.

simulation performed in the previous case study at $Q = 10^{19}$ is used as a starting point and various values for $K$ are tested. In the previous case study $K$ was equal to zero and the clot was observed to grow outward through the end of the simulation. In this section multiple values of $K$ are tested in order to investigate model behavior dependence on chemical degradation. In the
following, results at two different degradation rates are presented, noting that final clot size is observed to decrease with increasing $K$. The values of $0.05\frac{1}{5}$ and $1\frac{1}{5}$ are selected to demonstrate varying final clot sizes. It is noted that the correspondence between the selected values for $K$ and actual ADP degradation rates is not investigated, and this study is performed for the purpose of evaluating qualitative model behavior in the presence of some non-zero chemical activator degradation rate. Simulations are carried out to 50 seconds in time. Figures 5.21 and 5.22 show the velocity field at 50 seconds for two different degradation rates. As might be expected, the ADP concentration is observed to decrease with time. This degradation occurs more rapidly for larger values of $K$ and final clot sizes are observed to decrease with increasing $K$ as can be seen in Figures 5.21 and 5.22. Once the chemical concentration degrades below its threshold value for activation, platelet activation ceases. These two figures show the final clot sizes obtained during the simulations. Chemical activator degradation, therefore, is demonstrated to control and in fact inhibit altogether clot growth predicted by the model.

Figure 5.22. Top: velocity magnitude at 50 seconds simulation time for large $K$. Bottom: corresponding velocity magnitude line contours.
5.8 Case Study 5.5: Clot Growth Within a Backward Facing Step Geometry

As previously discussed, regions of flow stasis and recirculation tend to promote thrombus formation due to the low residence time experienced by platelets and clot constituents. The backward facing step is a benchmark geometry used in the field of fluid mechanics, both experimentally and computationally. Blood clots have been shown to develop on the downstream side of a backward facing step in the recirculation region in unpublished experiments performed by the Biengineering Department at Penn State University. A three-dimensional cylindrical geometry is used in the presence of pulsatile flow as described in [26]. In this thesis, a two-dimensional representation of this three dimensional geometry is developed in order to evaluate the platelet aggregation model’s applicability to this clinically important flow situation. The fluid properties used here are taken from [26]. In this section, preliminary numerical results for thrombus formation on the downstream side of the two dimensional backward facing step are presented.

5.8.1 Flow Geometry and Computational Set Up

In this section, the two dimensional geometry and computational domain used in this thesis are described. A schematic of the geometry and domain is given in Figure 5.23.

![Figure 5.23](image)

**Figure 5.23.** Schematic of flow geometry and computational domain. Figure not to scale.

Firstly, it is assumed that the flow is fully developed upon entering the computational domain and a parabolic velocity profile is supplied at the domain inlet as indicated in Figure 5.23. The inlet only spans the top 8.5 mm of the domain. The bottom 2.5 mm represents the step and this portion of the domain’s left hand boundary is defined as a no-slip wall with zero pressure gradient normal to the boundary. With this formulation, the computational domain is rectangular and the step itself is not evident. However, through the boundary conditions described, the presence of the step is modeled. the top and bottom of the domain are modeled as no-slip walls with zero pressure gradient normal to the boundaries. At the outlet boundary, the pressure and the gradient of each component of the velocity in the direction normal to the boundary is prescribed as zero. Finally at the inlet, a non-pulsatile parabolic velocity profile with a centerline velocity of
0.31 m/s is defined and the pressure gradient in the direction normal to the boundary is prescribed to be zero. The computational domain is 50 mm long which is determined to capture the full recirculation region.

5.8.2 Flow Solution

As in the previous studies, a background flow is required for the platelet aggregation model. For simplicity this flow is computed under steady (non-pulsatile) conditions. The pressure and all components of the velocity field are prescribed a value of zero initially. The flow field is computed using the thrombosis model in the absence of clot initiation. The steady-state results for velocity and pressure are presented in Figures 5.24 and 5.25. A pronounced flow recirculation region is observed to develop on the downstream side of the step. It is this region that the focus of the platelet aggregation model is on, as this is where clot formation is observed in the in vitro experiments. As in previous simulations, the pressure and velocity fields from Figures 5.24 and 5.25 are used as an initial condition for the platelet aggregation model simulations.

![Figure 5.24](image)

Figure 5.24. Top: steady-state velocity magnitude. Bottom: corresponding velocity magnitude line contours.

5.8.3 Platelet Aggregation Model Implementation

The first step to modeling clot formation is choosing a region in space to prescribe chemical activator for the initiation of the model. In the past this was done arbitrarily, but here it is known a priori that clotting is likely to take place on the downstream side of the step. Simulation results are very sensitive to the location of the initiation region. Simulations performed with chemical
activator placed at the corner where the bottom of the step meets the lower wall yield undesirable results. Specifically, the clot is observed to grow with the recirculating flow up the back of the step and upon meeting the shear layer at the top of the step the platelet stress is transported downstream in an uncontrolled and unphysical manner. However, placing chemical activator in the wall adjacent cells spanning the entire recirculation zone yields much more desirable results. This method is used for the simulation presented next. For this simulation, a constant breaking rate is used for simplicity and other model parameters are selected such that a clot forms rapidly. No chemical degradation is used and the maximum elastic modulus is prescribed to be 20 Pa. Results for the evolution of the stress and velocity are presented in Figures 5.26 and 5.27. The platelet stress initially develops along the walls of the recirculation zone where the chemical activator was initiated. As time evolves, the entire recirculation zone is observed to fill with clot which mirrors experimental results. Interestingly, downstream and transverse growth of the clot is observed locally at the far end of the recirculation zone before the entire recirculation zone is filled. This behavior may not be physical and results from the choice of initiation zone. The fluid velocity is observed to decrease in regions where the stress is high, and in this manner the flow recirculation is essentially eliminated (representing the clot). This study is performed as a preliminary investigation of the platelet aggregation model’s applicability to the prediction of clot growth within a recirculating flow. Early results do show potential, however, the model appears to be sensitive to the chemical initiation region’s location and further investigation of this result is necessary. In addition, though the numerical results mimic experimental observations, the

Figure 5.25. Top: steady-state pressure. Bottom: corresponding pressure line contours. Pressure is normalized by the fluid density.
physical nature of the chemical activator specification region is presently unclear.
Figure 5.27. Temporal evolution of horizontal component of velocity profile 10 mm downstream of the step near the center of the original recirculation zone. $H$ is equal to the step height.
Chapter 6

Concluding Remarks

In this chapter a summary of the conclusions drawn from the work performed in this thesis is presented with a discussion of suggested future direction of the research.

6.1 Model Numerical Behavior

Results from Chapter 4 indicate that solutions of two forms of stress transport equations associated with the Oldroyd-B fluid can be obtained accurately and stably over a range of parameter sets. Two extremes, however, are noticed that present with divergent solutions. Firstly, at large Weissenberg numbers, simulations fail. It is expected that this behavior occurs due to the High Weissenberg Number Problem described in the viscoelastic literature, although no analysis regarding the structure of the instabilities is performed in this thesis. For the Oldroyd-B simulations performed in Chapter 4, it is also noticed that solutions diverge at low values of Wi. This behavior is likely separate from the HWNP. As the Weissenberg number decreases the elastic modulus increases and based on this fact, the elastic modulus, $G$ is viewed as a qualitative indicator of stability for simulations not associated with a high Weissenberg number.

Results from Chapter 5, where only the platelet aggregation form of the stress transport equation is solved, indicate that simulation failure is associated with increasing elastic modulus, though the Weissenberg number is not calculated. Ultimately, the stress tensor grows to unstable values leading to solution divergence. This behavior is mirrored by an elastic modulus which grows as the stress tensor does. No fundamental stability upper limit on the elastic modulus exists over all parameter sets, but the trend of increasing elastic modulus during a simulation leading to solution divergence is present. The Weissenberg number is not computed and so it cannot be said for certain what influence the High Weissenberg Number Problem has on simulation results. Based on the inverse relationship between the elastic modulus and Weissenberg number seen in Chapter 4, the HWNP is not suspected to play a role. It should be noted that the platelet aggregation model, due to its variable viscosity and relaxation time, is different from the model of an Oldroyd-B fluid and therefore conclusions drawn in Chapter 4 may not always pertain to
results in Chapter 5. Placing an upper limit on the elastic modulus in the platelet aggregation
model dramatically improves stability and allows simulations to converge out to much later times.
Simulations with a limited elastic modulus develop a platelet stress field that is well controlled.
This behavior is responsible for the marked improvement in stability. There may be a more
representative parameter of stability that could be used in a similar manner instead of the elastic
modulus, and locating it might be a subject for future work. Another possible subject for future
work might be the investigation of the solution of the platelet aggregation model using the form
for the stress transport equation often seen in the viscoelastic literature. This form is solved for
the Oldroyd-B fluid in Chapter 4 and shown to yield the same results as the form presented in
Fogelson’s literature, which is used exclusively in Chapter 5. The idea of using $\tau$, rather than $\sigma$
to couple the momentum equation with Fogelson’s model is discussed in [18] where it is explained
that only the pressure field will change as a result. This approach, too, might be investigated in
future work.

6.2 General Model Considerations

As shown in Chapter 5, numerical solution of the platelet aggregation model using OpenFOAM
and the computational methodology described in Chapter 3 yields results with clots that grow
with time starting at the initial injury zone. The fluid velocity within the clot is reduced,
representing a solid body within the flow field. This general behavior is required, however, other
fields within the model may not have such physically relevant values. Activated platelets within
the clot, for example, do not rise above the initial dormant platelet concentration of blood.
As discussed in [18] actual platelet aggregates should have a higher concentration of activated
platelets and therefore an inconsistency exists between the model results and reality. The physical
relevance of other predicted thrombosis related fields in the model has not yet been investigated.
Physically relevant predictions for the thrombosis portion of the model are not a requirement for
developing a clot that grows and couples to the flow field as results in Chapter 5 make evident.
The method of clot initiation used in this thesis is simple and may lack physical relevance. Results
presented in this thesis use arbitrary chemical concentrations in the injury zone that are selected
based on qualitative clot growth behavior. The physical relevance of the values used for $C_o$ is
presently unclear. Furthermore, the initiation of clot growth could be performed in a manner that
captures more of the physics of platelet-wall adhesion. Essentially, the method in this thesis is
used in order to generate results for the purpose of evaluating of the remainder of the model. One
particularly important limitation of the model itself is the fact that no mechanism for predicting
where a clot might start to grow is included. In the model’s current form, simulations require
the specification of an injury zone independent of the method used to initiate clot growth. For
the design of artificial blood contacting devices, it would be useful to have a model capable of
predicting where within a given geometry a clot might begin to form. The model in its current
form can only predict the clot growth behavior given a specified starting location. The model
does not specify the actual physical boundary of the clot. Results do show that many of the field variable solutions clearly indicate the general shape and size of the clot, but a definitive clot boundary would be a useful addition. With a known boundary, the pressure and velocity fields could be solved for by using a standard Navier-Stokes solver in the presence of a no-slip wall and compared to the pressure and velocity fields predicted by the model equations. Such a validation will eventually be necessary and should be considered in future work.

The effects of various model parameters on the behavior of results are presented in Chapter 5. One major limitation of the model is that clots tend to grow downstream in a seemingly unphysical manner. Results indicate, however, that the breaking rate shows potential for limiting this downstream growth. Simulations indicate that breaking rates which increase more sharply with the energy per link, present with decreased downstream growth. Although, results still show a thin patch of clot that forms along the wall reaching downstream. The link breaking rate shows promise for limiting clot growth, though other functional forms might be a subject for future work. For example, a breaking rate that becomes infinite as the energy per link approaches some maximum value might more accurately represent the physics of link breaking. Degradation of chemical activator is also observed to limit clot growth. In this instance as the chemical concentration falls below the threshold value for platelet activation, clots are observed to stop growing altogether in the presence of a variable breaking rate. Importantly, both of these clot growth inhibition mechanisms represent processes that are physically relevant to platelet aggregation.

6.3 Model Application to Flow Over a Backward Facing Step

One particular application of thrombosis modeling and the model employed in this thesis is the backward facing step. As previously discussed, this geometry promotes thrombus formation on the downstream side of the step due to the increased residence time experienced by platelets and other constituents. Numerical results for clot growth over this flow field are presented in Chapter 5. The model shows promise, predicting clot growth that fills in the region on the downstream side of the step. One limitation is that the model appears to be sensitive to the location of the specified injury zone. For example, prescribing an injury zone in grid cells located near the corner at the base of the step yields unphysical results as previously discussed. It is found that the most physical results are generated in the presence of an injury zone defined along the wall spanning the entire recirculation zone. In this instance, the clot fills the entire recirculation zone and continues to grow downstream. Due to this initial condition, a thin clot forms immediately along the wall within the recirculation zone, which may not be physical. Though general experimental observations are reproduced with the model, physical relevance of the thrombosis related portion of the model is lacking as described in the section on general model applicability. Still, the model could potentially be used to predict experimental results for clot growth within the flow field.
around a backward facing step geometry. With the general experimental observations predicted by the model the next likely course of action is to match the time scales observed in experimental results. Multiple parameters within the platelet aggregation model can change the time over which clots are predicted to grow. The stress formation rate constant, $\alpha_2$, and the link breaking rate, $\beta$, have both been shown to alter the time scale of predicted clot growth. In addition, variation of the platelet activation time, $t_{act}$, which is not investigated in the work performed in this thesis, would likely alter the time over which clots develop. Investigation of model clot growth time scales is a subject for future work and will be necessary for obtaining numerical results that coincide with experiments. As previously discussed, the activated platelet concentrations within the clot are not physically representative of real blood clots. Fitting the current form of the model to experimental measurements of the thrombosis related fields, therefore seems an unlikely route for future research. Experimentally determined clot geometry, however, has been shown to correspond to the numerical results for the flow over a backward facing step as discussed. With appropriate matching of the time scales numerically predicted clot shapes and sizes could potentially be fitted to experimental results. Furthermore, the general shape of the clot is important for determining the surrounding flow field which in turn determines the shear and pressure forces on the clot. These forces become useful when determining the potential for embolization, a clinically significant event. In future work, experimental clots might be defined in terms of geometric parameters, for example maximum dimension in the cross flow and streamwise directions for the case of the backward facing step flow. These metrics could then be used to determine model parameters that yield results close to those from the experiments. The backward facing step is an important case to be investigated in future research due its clinical importance and the model’s apparent ability to capture experimentally observed clot growth behavior.
Appendix A

Model Dimensions

All variables and constants within an OpenFOAM solver must have their dimensions specified. In this manner, OpenFOAM is able to check for dimensional consistency upon execution of a solver and does not run unless this condition is met. Dimension specification is performed at run time and each of the seven primary dimensions is specified. Model variable and parameter dimensions used in this thesis are listed in tables A.1 and A.2 respectively.

Table A.1. Dimensional units used within OpenFOAM for model field variables. 1 kgmol = 1000 mol.

<table>
<thead>
<tr>
<th>Field Variable</th>
<th>Dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>velocity</td>
<td>m</td>
</tr>
<tr>
<td>pressure</td>
<td>m$^2$</td>
</tr>
<tr>
<td>cohesive stress</td>
<td>m$^2$</td>
</tr>
<tr>
<td>activated platelet concentration</td>
<td>platelets</td>
</tr>
<tr>
<td>non-activated platelet concentration</td>
<td>platelets</td>
</tr>
<tr>
<td>chemical activator concentration</td>
<td>kgmol</td>
</tr>
<tr>
<td>inter-platelet link concentration</td>
<td>links</td>
</tr>
</tbody>
</table>

Table A.2. Dimensional units used within OpenFOAM for model parameters. 1 kgmol = 1000 mol.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>$D_n$</td>
<td>m$^2$</td>
</tr>
<tr>
<td>$D_c$</td>
<td>m$^2$</td>
</tr>
<tr>
<td>$A$</td>
<td>kgmol platelet</td>
</tr>
<tr>
<td>$K, R, \beta$</td>
<td>m$^2$</td>
</tr>
<tr>
<td>$\mu$</td>
<td>kg m$^{-2}$</td>
</tr>
<tr>
<td>$\rho$</td>
<td>kg m$^{-3}$</td>
</tr>
<tr>
<td>$\alpha_2$</td>
<td>kg m$^{-1}$ links</td>
</tr>
<tr>
<td>$\alpha_0$</td>
<td>m$^2$ links</td>
</tr>
</tbody>
</table>
Bibliography


