

CHAPTER 2

2 THEORY, METHODS, AND MODEL VALIDATION

2.1 Introduction

In this chapter, the equations governing Eulerian-Lagrangian particle hemodynamics analysis are presented. The computational methods used to solve these equations are discussed. Consistent with the objectives of this study, a computational point-force model for blood particle motion that is valid in both far- and near-wall regions is established. Lagrangian-style near-wall force terms, which are typically presented for simple two-dimensional shear flows, are extended to discretized three-dimensional complex flow domains. Operation of the Fortran 90 code for particle integration, originated by Buchanan (2000) is discussed in detail. Significant modifications to this code exclusive to this study are highlighted. Select validation case studies are then presented.

2.2 Governing Equations

2.2.1 Fluid Flow and Boundary Conditions

The flow field equations describing laminar incompressible hemodynamics are the conservation of mass

$$\nabla \cdot \vec{u} = 0 \quad (2.2.1)$$

and momentum

$$\frac{\partial \vec{u}}{\partial t} + (\vec{u} \cdot \nabla) \vec{u} = \frac{1}{\rho} \left(-\nabla p + \nabla \cdot \vec{\tau} \right) \quad (2.2.2a)$$

where \vec{u} is the velocity vector, p is the pressure, ρ is the fluid density, and the shear stress tensor is given by

$$\vec{\tau} = \eta(\dot{\gamma}) \left[\nabla \vec{u} + (\nabla \vec{u})^T \right] \quad (2.2.2b)$$

The shear rate ($\dot{\gamma}$) dependent absolute viscosity (η) is calculated by the transformed Quemada model (Buchanan and Kleinstreuer, 1998)

$$\eta(\dot{\gamma}) = \left(\sqrt{\eta_{\infty}} + \frac{\sqrt{\tau_0}}{\sqrt{\lambda} + \sqrt{\dot{\gamma}}} \right)^2 \quad (2.2.2c)$$

The advantage of the Quemada model over, for example, the popular Casson model is the additional shear-rate modifier, λ , that allows for a better blood data fit in low ranges of the shear rate (i.e., $\dot{\gamma} \sim 10^{-2} \text{ s}^{-1}$). Coefficients used in the original form of the Quemada model for a normal hematocrit (H) of 40% were taken from Cokelet (1987). The coefficients were transformed for Eq. (2.2.2c) using the methodology outlined in Buchanan (1996) resulting in empirical constants $\eta_{\infty} = 0.0309 \text{ dyn}\cdot\text{s}\cdot\text{cm}^{-2}$, $\tau_0 = 0.07687 \text{ dyn}\cdot\text{cm}^{-2}$, and $\lambda = 0.047723 \text{ s}^{-1}$. Using the above constants, the Quemada model predicts that absolute viscosity is within 5% of the Newtonian limit, i.e., $\eta_{\infty} = 0.0309 \text{ dyn}\cdot\text{s}\cdot\text{cm}^{-2}$, at a shear rate of $4,100 \text{ s}^{-1}$, cf. Fig. 2.2.1. Normal blood density has been assumed to be $\rho = 1.054 \text{ g/cm}^3$. The local shear rate, $\dot{\gamma}$, used in Eq. (2.2.2c) is computed from the second scalar invariant of the rate of deformation tensor, i.e.,

$$\dot{\gamma}^2 = \left| II_{2\bar{D}} \right| \quad (2.2.3)$$

where \bar{D} is the strain rate tensor such that

$$2\bar{D} = \nabla \bar{u} + (\nabla \bar{u})^T \quad (2.2.4)$$

The second scalar invariant can be expressed (Bird et al., 1967)

$$II_{2\bar{D}} = \frac{1}{2} \left[\left(I_{2\bar{D}} \right)^2 - \text{trace} \left(2\bar{D}^2 \right) \right] \quad (2.2.5a)$$

where the first scalar invariant is given by the trace of the rate of deformation tensor

$$I_{2\bar{D}} = \text{trace} \left(2\bar{D} \right) \quad (2.2.5b)$$

Expanding, the shear rate can be expressed as

$$\dot{\gamma}^2 = \left| 4D_{11}D_{22} + 4D_{11}D_{33} + 4D_{22}D_{33} + 4D_{12}D_{21} + 4D_{13}D_{31} + 4D_{23}D_{32} \right| \quad (2.2.6)$$

The femoral bypass configuration is the primary application of this research; however, a number of systems have been evaluated. General boundary conditions applied to all models will first be presented. The selection of an appropriate inlet waveform for the femoral bypass geometry will then be discussed.

Inlet and boundary conditions, in addition to the “no-slip” wall condition, were selected in a manner to: (a) match physiological conditions as closely as possible with the available data and (b) facilitate numerical computation. To generate the time varying inlet velocity profiles a transient Womersley (1955) solution was used. Flow rate information over variable time-steps was used to compute a complex Fourier series approximation of the pressure gradient pulse (Buchanan, 2000). The transient velocity profiles were then computed using the Womersley solution for Newtonian flow. An extended inlet of approximately three diameters was added to allow non-Newtonian aspects of the velocity profile to develop fully. Flow field outlets were extended far downstream such that the velocity was normal to the outlet plane, i.e., fully developed flow profiles with no significant radial velocity component. For single outlet conditions, a pressure boundary patch was typically used. For multiple outlets, constant mass flow rate boundaries and flow division ratios were specified, unless more detailed outlet flow rate waveforms were available, as with the carotid.

Flow rates through the femoral artery vary largely, depending on the quality of an individual's circulation system, location of the flow measurement, and conditions under which the measurements are made, e.g., resting or exercising. The various combinations of femoral diameter and flow rate can induce a wide range of Reynolds number waveforms. Lei (1995) and Kleinstreuer et al. (1996) employed a “resting pulse” derived from femoral flow velocity measurements made in a dog (cf. Nichols and O'Rourke, 1990) and assumed a second “exercise” pulse for patients under active conditions (provided by personal communication with JP Archie). These pulses are illustrated in Fig. 2.2.2 and are summarized in Table 2.1.

Table 2.1: Reynolds Number Waveforms for the Mid-Femoral Artery

	Re_{max}	Re_{min}	Re_{mean}	f (beats/min)
Resting Pulse (Lei, 1995)	600	-67.8	113.5	60
Exercise Pulse (Lei, 1995)	480	295	356.5	100
Standard Pulse (Steinman et al., 1993)	980	-375	125	60

Steinman et al. (1993) made Doppler ultrasonography measurements of a mid-femoral flow waveform, cf. Fig. 2.2.2. For consistency, this flow waveform has been used in a number of subsequent studies including Kunov et al. (1996), Ethier et al. (1998), and Moore et al. (1999).

The development of a significant stenosis is most likely accompanied by other changes throughout the circulatory system such as upstream occlusions and a general loss of wall compliance. The numeric study of Stroud (2000) took into account the presence of systemic plaque deposits and applied a pulse with damped local extreme during diastole, cf. Fig. 2.2.2. Furthermore, the inclusion of a bypass graft significantly alters waveform characteristics compared to measurements made in natural arteries.

A number of clinical studies have found significant correlations between post-operative femoropopliteal graft waveforms and long-term graft survival. In general, waveforms that vary significantly from the standard femoral pulse are typically associated with both early and late graft failure (Inokuchi et al., 1982; Okadome et al., 1986). Mid- or post-bypass graft waveforms are often characterized as Types 0-IV (cf. Fig. 2.2.3). Waveform Type 0 is characterized by a steep and smooth flow acceleration and a deceleration characterized by a deep negative deflection in diastole, followed by a small positive deflection. The Type I pattern resembles Type 0, except it lacks a portion of net retrograde flow. *Type I waveforms are widely observed in cases of mild atherosclerosis throughout the vasculature* (Okadome et al., 1991). Type II waveforms have a deceleration characterized by a gentle slope in the second half of diastole. With Type III patterns, the waveform decreases slowly though the diastolic period. Type IV classification is reserved

for waveforms that cannot be categorized as I through III (Okadome et al., 1990; Okadome et al., 1991).

Okadome et al. (1990) reviewed the outcome of 140 femoropopliteal grafts of which 75 were saphenous vein and 65 were PTFE. The distal grafting site was either the proximal (above-knee) or distal (below-knee) popliteal artery. The flow waveforms within the grafts were characterized immediately following surgery as Types 0-IV. Considering all grafts, those which displayed an initial Type 0 or Type I waveform had a significantly higher 4 year patency rate (56%) than grafts with Type II, III, or IV waveforms (35%). When only PTFE grafts were considered, Type 0 and I waveforms again showed a tendency toward increased patency; however, this result was not statistically significant. Okadome et al. (1991) indicated that flow rate waveforms Type III and IV are generally associated with surgical technical errors, such as thrombosis and stricture, or a significant degree of distal vascular occlusion. Grafts presenting such waveforms typically fail within 72 hours, i.e., early graft failure. Post-operative Type II waveforms are generally considered acceptable and not highly susceptible to early graft failure. However, Type II waveforms have been identified with an increased occlusion rate and reduced long-term patency (Okadome, 1990). Interestingly, Type II waveforms display less hemodynamic variability than observed with Type I configurations. *Hence, pulse severity alone does not necessarily indicate a predisposition for graft failure.* The frequency of waveform patterns measured by Okadome et al. (1991) at mid-graft level at the time of surgery is indicated in Table 2.2. Mean graft flow-rates characterized by waveform group are presented in Table 2.3 (Okadome et al., 1990).

Table 2.2: Frequency of Waveform Patterns at Time of Surgery (Okadome et al., 1991)

Waveform Type	Frequency	Percentage*
0	9	7.3 %
I	43	34.7 %
II	64	51.6 %
III or IV	8	6.5 %

* Based on 124 initial patients

Table 2.3: Mean Graft Flow Rates (Okadome et al., 1990)

Waveform Type	0 or I	II, III, or IV
Mean Flow Rate (ml/hr)	145.3 +/- 86.3	135.2 +/- 72.9

To formulate a representative baseline pulse for numeric investigation of the femoropopliteal bypass, a Type 0 or I waveform should be selected due to frequency of clinical occurrence and the absence of extraneous complications. The study of Okadome et al. (1991) indicates that of the 0/I category, Type I pulses are evident postoperatively in approximately 80% of grafts. Therefore, a Type I pulse has been selected as a representative basis for comparison and is illustrated in Fig. 2.2.4. This pulse is well within the range of mean flow-rates represented in Table 2.3 and falls within peak velocity and Reynolds numbers guidelines for non-stenosed grafts, cf. Table 2.4 (Nielsen et al., 1993; Papanicolaou et al., 1996). Consistent with Type I waveforms, only a small amount of net retrograde flow is observed in Table 2.4, which occurs around $t/T = 0$. The resulting velocity profiles display a significant amount of retrograde flow in the near-wall region throughout diastole.

Table 2.4: Characteristics of the Selected Type I Waveform

	Q_{mean}	Re_{mean}	Re_{max}	Re_{min}	V_{mean}	V_{max}	V_{min}
Arterial Conditions (Ø = 4 mm)	164.4 ml/hr	303.9	1054.	-5.9	21.8 cm/s	75.6 cm/s	-0.4 cm/s
Graft Conditions (Ø = 6 mm)	164.4 ml/hr	202.6	702.7	-3.9	9.7 cm/s	33.6 cm/s	-0.2 cm/s
Graft Conditions (Ø = 8 mm)	164.4 ml/hr	151.95	527.	-2.9	5.45 cm/s	18.9 cm/s	-0.1 cm/s

Note: All variables based on the Newtonian limiting viscosity of blood $\eta = 0.031 \text{ dyn*s/cm}^2$ and $\rho = 1.054 \text{ g/cm}^3$.

2.2.2 Equations of Particle Motion and Near-Wall Forces

Basset-Boussinesq-Oseen Equation

Maxey and Riley (1983) have presented in detail the equation of motion for a small rigid sphere in a nonuniform flow with creeping relative motion, i.e., Stokes flow. Maxey and Riley (1983) begin with the equation of motion for a spherical particle as

$$m_p \frac{dv_i}{dt} = m_p g_i + \oint_S \sigma_{ij} n_j dS \quad (2.2.7)$$

where, v_i is a component of the particle velocity, the surface integral is over the sphere, n is the unit outward normal, and the fluid stress tensor is given by

$$\sigma_{ij} = -p \delta_{ij} + \mu \left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right) \quad (2.2.8)$$

This derivation makes clear the fact that contributions to the particle motion equation include forces from both (a) the undisturbed flow field (although it may be nonuniform); and (b) the local disturbance flow which is created by the presence of the sphere. These forces are applied to the centroid of a discrete particle, which is referred to as a point-force approximation. From Maxey (1987), the equation of motion for a small, rigid, spherical particle subjected to a nonuniform transient three-dimensional flow field of a Newtonian fluid is

$$\begin{aligned} m_p \frac{dv_i}{dt} = & \underbrace{m_f \frac{Du_i}{Dt}}_{\text{term 1}} - \underbrace{\frac{m_f}{2} \frac{d}{dt}(v_i - u_i)}_{\text{term 2}} - \underbrace{6\pi a_p \mu (v_i - u_i)}_{\text{term 3}} + \underbrace{(m_p - m_f)g}_{\text{term 4}} \\ & - \underbrace{\frac{6\pi a_p^2 \mu}{\sqrt{\pi v}} \left(\int_0^t \frac{d}{d\sigma} (v_i - u_i) \frac{d\sigma}{\sqrt{t - \sigma}} + \frac{v_i(0) - u_i(0)}{\sqrt{t}} \right)}_{\text{term 5}} \\ & + \underbrace{m_f \frac{d}{dt} \left(\frac{a^2 \nabla^2 u_i}{20} \right)}_{\text{term 6}} + \underbrace{\pi a_p^3 \mu \nabla^2 u_i}_{\text{term 7}} + \underbrace{a_p^4 \mu \sqrt{\frac{\pi}{v}} \left(\int_0^t \frac{d(\nabla^2 u_i)}{d\sigma} \frac{d\sigma}{\sqrt{t - \sigma}} + \frac{\nabla^2 u_i(0)}{\sqrt{t}} \right)}_{\text{term 8}} \end{aligned} \quad (2.2.9)$$

where v_i is the particle velocity, u_i is the fluid velocity, and a_p is the particle radius. This equation requires that the particle Reynolds number approaches zero

$$\text{Re}_p = \frac{2|u_i - v_i|a_p}{\nu} \ll 1 \quad (2.2.10a)$$

and, the particle radius is sufficiently small

$$\frac{a_p}{L} \ll 1 \quad (2.2.10b)$$

where L is a characteristic length of the flow field. Lift forces are assumed negligible due to the absence of particle rotation and the assumption of a small shear Reynolds number

$$\text{Re}_g = \frac{(2a_p)^2}{\nu_c} \frac{dU}{dy} \ll 1 \quad (2.2.10c)$$

The first term in Eq. (2.2.9) is the result of pressure gradients that exists in the undisturbed non-uniform flow. The second term is the added mass, which is a transient term resulting from the linear acceleration of the fluid surrounding a particle. A small particle Reynolds number allows for the application of Stokes drag, term 3, which accounts for both shear and pressure contributions in a uniform linear non-accelerating flow field, and implies a small difference between the particle and material derivatives d/dt and D/Dt . Auton et al. (1988) suggested that the added mass term be formulated as

$$\frac{m_f}{2} \frac{dv_i}{dt} - \frac{m_f}{2} \frac{Du_i}{dt} \quad (2.2.11)$$

however, the small Re_p assumption makes this difference negligible. The fifth term is the history integral, or Basset term, which is a transient consequence resulting from the delay in near-particle viscous effects as the relative velocity changes in a linear uniform flow field. The second term in the parentheses of the fifth component accounts for the effect of an initial relative velocity. Terms six through eight are the Faxen corrections to the added mass, the drag, and the history integral, respectively. These addenda account for the effects of nonuniform flow, such as swirl and curved particle paths, however, they do not account for or rely on particle rotation.

Relevant Forces in Blood Particle Free-Stream Flow

The dissertation of Buchanan (2000) includes an appendix that considers *analytic solutions* to a simplified version of Eq. (2.2.9) and carefully determines the forces that make a significant quantitative contribution to free-stream (i.e., no boundary effect) blood particle

motion. Analytic solutions to the equation of particle motion (including the history term) are available by several techniques. Michaelides and co-workers (1988, 1992, & 1996) have applied Laplace transforms to arrive at an analytic expression of particle motion that is explicit (cf. Michaelides, 1997). Assuming that the flow field could be represented using Fourier sums, Hjelmfelt and Mockros (1966) computed analytic solutions to the equation of particle motion as presented in Clift et al. (1978). Most recently, Buchanan (2000) followed the analysis of Coimbra and Rangel (1998) and used fractional-order derivative operators to evaluate the history term, neglecting the Faxen corrections.

The analytic analysis of Buchanan (2000) indicated that for a density ratio $\alpha = \rho_f/\rho_p < 8/5$, the history term is only important for values of $D \equiv T / \tau_p$ less than 100, where T is the pulse period and τ_p is the particle's relaxation time (or momentum response time)

$$\tau_p = \frac{2\rho_p a_p^2}{9\mu_c} \quad (2.2.12)$$

For blood flow in humans, the pulse period is relatively high at $T \approx 1$ s and density ratios are very near unity, i.e., in plasma $\alpha = 0.983$ for platelets and $\alpha = 0.964$ for monocytes. Blood particle relaxation times are on the order of $\tau_p = 10^{-6}$ s resulting in a very large value of D , i.e., $D \approx 10^5$ to 10^6 . Therefore, the history term may be neglected for the transport of platelets, monocytes, and red blood cells in plasma according to the findings of Buchanan (2000). Furthermore, Buchanan (2000) points out that the added mass term makes no significant contribution for liquid-solid multiphase flows or colloidal suspensions (such as blood) where the densities of the phases are very similar.

The resulting equation for blood particle motion, assuming only pressure and drag effects, is written

$$\frac{dv_i}{dt} = \alpha \frac{Du_i}{Dt} + \frac{1}{\tau_p} (u_i - v_i) \quad (2.2.13)$$

where, v_i and u_i are the components of the particle and local fluid element velocity, respectively. If virtual mass effects are to be included, the above equation can be written

$$\frac{dv_i}{dt} = \frac{3}{2} \beta \alpha \frac{Du_i}{Dt} + \frac{\beta}{\tau_p} (u_i - v_i) \quad (2.2.14a)$$

where

$$\beta = \frac{1}{1 + \alpha/2} := 0.693 \quad (2.2.14b)$$

It has been shown that the motion of a hardened red blood cell, as in the annular expansion of Karino and Goldsmith, can be modeled as a fluid element (cf. Appendix A.1). However, the analysis of Buchanan (2000) implies that both the drag and pressure terms make a significant contribution to the equation of particle motion. The question then arises if pressure and drag effects are insignificant in the Karino and Goldsmith (1977) annular expansion, or if these terms act in opposition to each other in a manner that results in a diminished net effect on the particle motion. This question has been investigated at length and is addressed in Appendix A.2. *The analysis in Appendix A.2 emphasizes the fundamental necessity of the pressure term to form an equation of particle motion that is physically relevant in an accelerating or decelerating flow field.*

As discussed in the literature review, the continued collisions and hydrodynamic interaction between, and deformations of, the red blood cells in flowing blood induces a form of mixing, similar on a macroscopic scale to the intermolecular collisions that result in Brownian motion. For platelets and white blood cells, the movement induced by this mixing results in a persistent dispersion, and is often modeled with effective diffusion coefficients which are two to three orders of magnitude greater than those due to Brownian motion. This motion becomes a major mechanism for permitting cells and possibly some of the larger proteins found in the blood to interact with the wall. To provide an accurate model for lateral motion, particle dispersion coefficients should be a function of the local velocity gradient, local red blood cell concentration, and cell deformation. Unfortunately, models for a realistic red blood cell concentration field are not present in the literature and models attempted in this study failed due to the highly deformable nature of the cells (cf. Appendix B.1). Therefore, local variations in hematocrit will be ignored in defining particle dispersion coefficients.

Assuming collision induced blood particle dispersion to be a Gaussian process, i.e., as would occur in a constant concentration shear field, the mean lateral displacement, Δr , is given by

$$\Delta r = \sqrt{2D_p \Delta t} \quad (2.2.15)$$

where Δt is a time-step much greater than τ_p . Interpreting the standard deviation of the Gaussian probability function to be Δr^2 , individual particle displacements are simulated using random walk theory, i.e., a Monte Carlo type approach (Balashazy, 1993). The above approximations do not consider red blood cell concentration gradients and, therefore, do not allow for the persistent motion that results in the appropriate concentration profiles over large distances (Phillips et al., 1991; Eckstein & Belgacem, 1991). Nevertheless, such approximations should be appropriate in the context of bifurcating blood vessel simulations, where distances of interest are relatively short. Appropriate values of the particle dispersion coefficients for both platelets and monocytes have been discussed in Section 1.7, and values selected are presented in Appendix B.2.

Near-Wall Forces

Assumptions required by the equation of particle motion, as presented above, include a relatively small shear Reynolds number and negligible particle rotation. These assumptions are most valid for fluid-particle flow in a boundless media. However, as a particle approaches a fluid boundary, at which a no-slip condition holds, the shear forces and the rotation rate of the particle increase. In the near-wall environment, the enhanced shear field and the particle rotation may influence the particle's trajectory by generating lift and modifying the drag term. The near-wall forces to be considered for bio-particle transport include near-wall drag modifications (i.e., the lubrication forces), as well as lift and biochemical interactions.

When a particle is close to a solid boundary, Eq. (2.2.13) should be modified to include the effects of the wall on the trajectory. Consider a particle moving near a wall with both a normal and tangential velocity component with respect to the boundary. The Stokes drag term in Eq. (2.2.13) cannot accurately predict the wall-normal motion. Specifically, the form drag component in the Stokes drag approximation assumes that there is not a boundary in the direction of particle motion acting to increase the pressure in front of the particle.

Hence, the Stokes drag approximation must be modified. Similarly, but to a lesser extent, the boundary influences the viscous drag on a particle moving tangential to a wall.

Cox and Brenner (1967) showed that for Stokes flow, the drag on a spherical particle of radius a_p moving normal to a wall is

$$F_n = -m_p \frac{1}{\tau_p} (v_n - u_n) - m_p \frac{1}{\tau_p} (v_n - u_n) \lambda_n \quad (2.2.16)$$

where n is the wall-normal direction and h_p is the distance between the center of the particle and the wall. In the above representation, the first term is the traditional Stokes drag while the second accounts for the drag modification due to the presence of the wall. It is this second term that is often referred to as the lubrication force and can be viewed as an interaction force as derived by Crowe et al. (1998) for the case of two approaching spheres. Dahneke (1974) suggested the following fit to the results of Cox and Brenner (1967) for the lubrication coefficient at all particle wall separations:

$$\lambda_n = \frac{a_p}{\delta} \quad (2.2.17a)$$

where δ is the distance between the particle surface and the wall, i.e.,

$$\delta = h_p - a_p \quad (2.2.17b)$$

For truly Stokesian flow, the lubrication coefficient may vary from zero to infinity in the limit, making it impossible for a particle to reach the wall in a finite amount of time. However, for particles moving through a gas, the continuum approximation breaks down when the gap between the surface of the particle and the wall becomes comparable with the molecular mean free path of the gas. Hence, the continuum model over predicts the magnitude of the stress on the particle surface in the gap. Hocking (1973), Goren (1973), and Dahneke (1974) suggested modifications of the lubrication coefficient to account for the effect of molecular slip in gas-particle flows.

Similar to wall-normal motion, the drag coefficient in the tangential direction is also affected by the presence of the wall. Goldman et al. (1967a & b) showed that the drag force on a sphere near a wall in linear (uniform shear) flow is given by

$$F_t = -m_p \frac{1}{\tau_p} (v_t - u_t) - m_p \frac{1}{\tau_p} (v_t - u_t) \lambda_t \quad (2.2.18)$$

Goldman et al. (1967a & b) derived approximations for λ_r and illustrated that it was a function of shear rate, angular velocity, and the dimensionless ratio h_p/a_p . As the particle approaches a wall, λ_r diverges; however, unlike λ_n , it only diverges logarithmically.

The near-wall drag modifications given above, which were derived as asymptotic solutions in the limit of true Stokes flow, have proven to be reasonable estimates in comparison with experimental data (e.g., Young and Hanratty, 1991). Recently, Loth (2000) has reported near-wall drag modifications based on resolved-volume simulations of spherical particles for $Re_p \ll 1$. In the context of Eqs. 2.2.16 & 2.2.18, the approximations are expressed as

$$\lambda_n = \frac{1.1}{\left(\frac{h_p}{a_p} - 1\right)} \quad (2.2.19a)$$

and

$$\lambda_r = 0.7 \frac{a_p}{h_p} \quad (2.2.19b)$$

Loth (2000) reports that these approximations provide a solution that is within 2% of simulated results.

In a strongly sheared flow, inertial lift forces are likely to be important. These enter the BBO-equation at a higher order in the particle Reynolds number than the terms in Eq. (2.2.9). There is a lack of rigorous mathematical justification for using the available results for lift forces (McLaughlin, 1994). Furthermore, all the existing theories of lift forces at small but finite particle Reynolds numbers are derived for steady laminar flows.

There are two causes of a composite lateral lift force on a spherical particle. The first is known as the Magnus lift force and develops due to rotation of the particle. The lift is created by a pressure differential between opposite lateral sides of the particle resulting from a velocity differential due to rotation. The sphere may rotate because of collisions with the wall, inter-particle collisions, or due to the enhanced near-wall shear field. Calculation of the Magnus effect requires direct knowledge of the particle rotation rate, which must be different from the local fluid element rotation rate, otherwise no lift is produced (cf. Crowe et al., 1998). Calculation of the rotation rate requires solving the angular momentum equation.

Shear induced torque may be calculated directly if detailed knowledge of the particles influence on the flow field is known. Otherwise, a sum of terms must be used as with the BBO-Equation. Collisional induced torques further complicate the calculation. Due to the difficulties associated with the calculation of particle spin, particularly in the presence of a moderate number of collisions, the Magnus force is usually neglected (Michaelides, 1997).

The second source of lift is the shear field of the fluid, which may cause lateral lift on the sphere even in the absence of rotation. A velocity gradient may give rise to sufficiently high and low pressures on opposite sides of a particle, which induces the Saffman lateral lift force. The basic Saffman lift force is relatively easy to compute (Crowe et al., 1998), and has been corrected via an empirical correlation to allow for higher relative velocities (Mei, 1994). Non-empirical corrections, or analytic derivations, of the Saffman lateral lift component are based on perturbation methods. Briefly, a particle may attain some degree of translational inertia, relatively denoted by the particle Reynolds number Re_p , as well as rotational inertia, denoted by the shear Reynolds number Re_g . In the Stokes flow limit, both forms of particle inertia are absent and the solution does not allow for a lift force. Saffman (1965 & 1968) assumed that the shear Reynolds number was large compared to the slip velocity (or particle) Reynolds number, yet small compared to one, i.e., $Re_p \ll Re_g \ll 1$. This allowed for the use of a matched asymptotic expansion to obtain the expression for a lift force in an unbounded parallel linear shear flow. McLaughlin (1991) used a perturbation technique to generate results similar to Saffman's for unbounded shear flow with comparable, but small, shear and particle Reynolds numbers. Similarly, perturbation analyses have been used to study the effect of boundaries far from the particle with respect to the non-rotational lift force (Cox and Brenner, 1968; Ho and Leal, 1974; McLaughlin, 1993; Cherukat et al., 1994). Another line of research has analyzed lift forces on particles contacting a surface (Leighton and Acrivos, 1985; Krishnan and Leighton, 1995). Each of these perturbation analyses results in a complex integral equation that only applies for small particle and shear Reynolds numbers. Further limitations include laminar unidirectional flow, linear shear, a set distance from the wall, and only a few studies have considered the effect of particle rotation (e.g., Krishnan and Leighton, 1995). A number of studies regarding lift forces are listed in Table 2.5 (see end of chapter), along with their required limitations and conditions.

Cherukat and McLaughlin (1994) derived an expression for Saffman-style lift which is applicable when the distance between the particle and wall is on the order of the particle radius. Assuming that the wall lies within the inner region of the sphere's disturbance flow, the Cherukat and McLaughlin (1994) lift approximation can be written as

$$F_{lift} = \rho_f a_p^2 u_s^2 \cdot I \left(\frac{h_p}{a_p}, \frac{\dot{\gamma} a_p}{u_s} \right) \quad (2.2.20)$$

where u_s is taken to be the wall-tangent slip velocity

$$u_s = (v_t - u_t) \quad (2.2.21)$$

Assuming the particle to be a freely rotating sphere, Cherukat and McLaughlin (1994) numerically integrated their asymptotic result and found it could be approximated as

$$I = \left[1.7631 + 0.3561\kappa - 1.1837\kappa^2 + 0.845163\kappa^3 \right] - \left[\frac{3.24139}{\kappa} + 2.6760 - 0.8248\kappa - 0.4616\kappa^2 \right] \Lambda + \left[1.8081 + 0.8796\kappa - 1.9009\kappa^2 + 0.98149\kappa^3 \right] \Lambda^2 \quad (2.2.22)$$

where $\kappa = h_p / a_p$ and $\Lambda = \dot{\gamma} a_p / u_s$. For cases in which the slip velocity approaches zero, the velocity scale $\dot{\gamma} a_p$ should replace u_s in the above equations. Depending on the signs of $\dot{\gamma}$ and u_s , as well as the size of κ , the near-wall lift may be directed toward or away from the wall. However, as a particle approaches the wall in the limit, the lift force inevitably acts to separate the particle from the wall.

Application of the Cherukat & McLaughlin (1994) lift expression is based on the condition

$$a_p < h_p \ll \min\{L_S, L_G\} \quad (2.2.23a)$$

where the Stokes length scale is

$$L_S = \frac{\nu}{u_s} \quad (2.2.23b)$$

and the Saffman length scale is

$$L_G = \sqrt{\frac{\nu}{\dot{\gamma}}} \quad (2.2.23c)$$

For blood particle simulation, L_G is typically the limiting condition due to elevated shear fields and small particle response times. Assuming that Eq. (2.2.23a) implies that h_p should be one order of magnitude less than L_G , the near-wall lift expression is valid on the order of ten monocyte diameters.

For particle wall distances significantly greater than the particle radius, the near-wall lift expression of Cherukat and McLaughlin (1994) is no longer valid. To account for lift in wall bounded flow at all particle wall separations, Wang et al. (1997) suggested using a compilation of the available lift expressions, each valid in a band of wall separation distance. Lift expressions valid outside of the narrow near-wall region require significant axial lengths before a contribution to radial particle concentration is realized. In the context of bifurcating geometries, the region of interest is of insufficient length for significant radial motion away from the wall to occur as the result of lift. However, in the near-wall region, transverse motion on the order of a particle diameter becomes important with respect to particle deposition. Hence, for the case of blood particle deposition in bifurcating geometries, near-wall lift is the most critical. Beyond this region, insignificant particle lift will be assumed. Moreover, this is a necessary assumption owing to the fact that outside of the near-wall region collisional forces dominate lateral particle motion (cf. Section 1.7).

2.2.3 Hemodynamic Wall Parameters

As discussed in Chapter 1, endothelial cell injury or dysfunction and the interaction of critical blood particles with the vascular surface both play significant roles in the biophysical evolution of intimal thickening and thrombosis formation. Hemodynamic wall parameters are intended to identify sites where intimal thickening and thrombosis formation are likely, based on hemodynamic wall interactions. Traditionally, identifying sites of endothelial cell dysfunction has been a primary target of the wall shear stress (WSS) based hemodynamic parameters (Kleinstreuer et al., 2001). Sites of excessive particle-wall interaction have also been widely qualitatively considered. This work establishes a novel Lagrangian based

method to quantify particle-wall interactions. Hemodynamic wall parameters that are to be considered for the femoral bypass are reviewed below.

Wall Shear Stress

It is widely held that the arterial wall is capable of changing its diameter in response to changes in WSS. For example, Zarins et al. (1987) demonstrated *in vivo* that the arterial wall, when subjected to as much as a tenfold increase in blood flow, gradually increased in diameter until a mean WSS of 15 dyn/cm² was restored. Furthermore, the response of endothelial cells to the time-averaged direction and magnitude of WSS *in vitro* has been well documented (e.g., Helmlinger et al., 1991).

The shear stress is a tensor within the flow field and reduces to a vector on a surface

$$\bar{\tau}_w = \hat{n} \cdot \bar{\tau} \quad (2.2.24a)$$

where \hat{n} is the local surface normal vector. The magnitude of the time-averaged wall shear stress vector can be written as

$$WSS = |\overline{\bar{\tau}_w}| = \left| \frac{1}{T} \int_0^T \bar{\tau}_w dt \right| \quad (2.2.24b)$$

Alternatively, the time-average of the wall shear stress magnitude can be written

$$|\overline{\bar{\tau}_w}| = \frac{1}{T} \int_0^T |\bar{\tau}_w| dt \quad (2.2.24c)$$

The oscillatory shear index monitors differences in these two time-averaged values.

Oscillatory Shear Index

Cyclic departure of the wall shear stress vector from its predominant axial alignment indicates flow disruption over time and is known as the oscillatory shear index, or OSI (Ku et al., 1985). The OSI, therefore, quantifies disturbed flow interaction with the wall and is formulated as (He and Ku, 1996)

$$OSI = \frac{1}{2} \left(1 - \frac{\left| \int_0^T \bar{\tau}_w dt \right|}{\int_0^T |\bar{\tau}_w| dt} \right) \quad (2.2.25)$$

where $\vec{\tau}_w$ is the instantaneous wall shear stress vector. The numerator of the shear stress fraction represents the magnitude of the time-averaged WSS while the denominator represents the time-average of the WSS magnitude. The shear stress fraction can vary from 1 to 0 which indicates no cyclic variation to 180-degree cyclic variation of the wall shear stress direction with time, respectively. The OSI can vary from 0 to 1/2 indicating the least and most severe temporal shear rate conditions, respectively.

Wall Shear Stress Gradient

From a biological standpoint, endothelial cells have been shown to align themselves with the mean flow direction which corresponds to the local direction of the time-averaged wall shear stress. Surface coordinates that elucidate the interaction of instantaneous wall shear stress vectors and endothelial cells are defined as

- m - temporal mean wall shear stress direction
- n - tangential to the surface and normal to m
- l - surface normal direction

The wall shear stress gradient can be obtained by calculating spatial derivatives of the wall shear stress vector ($\tau_{w,i}$), which results in a nine component tensor

$$\nabla \vec{\tau}_w = \left(\frac{\partial}{\partial x} \hat{i} + \frac{\partial}{\partial y} \hat{j} + \frac{\partial}{\partial z} \hat{k} \right) (\tau_{w,x} \hat{i} + \tau_{w,y} \hat{j} + \tau_{w,z} \hat{k}) = \begin{bmatrix} \frac{\partial \tau_{w,x}}{\partial x} & \frac{\partial \tau_{w,x}}{\partial y} & \frac{\partial \tau_{w,x}}{\partial z} \\ \frac{\partial \tau_{w,y}}{\partial x} & \frac{\partial \tau_{w,y}}{\partial y} & \frac{\partial \tau_{w,y}}{\partial z} \\ \frac{\partial \tau_{w,z}}{\partial x} & \frac{\partial \tau_{w,z}}{\partial y} & \frac{\partial \tau_{w,z}}{\partial z} \end{bmatrix} \quad (2.2.26)$$

The $\nabla \vec{\tau}_w$ tensor with respect to the xyz -coordinates (x_1, x_2, x_3) can be transformed to the mnl -coordinate system (s_1, s_2, s_3) by a standard component-wise tensor transformation

$$\frac{\partial \tau'_{w,i}}{\partial s_j} = a_{ik} a_{jl} \frac{\partial \tau_{w,k}}{\partial x_l} \quad (2.2.27a)$$

where the primes denotes the mnl -coordinate system. The terms a_{ik} and a_{jl} represent the directional cosines of the xyz -coordinates rotated to the mnl -coordinates. The resultant tensor is

$$\nabla \bar{\tau}_w = \begin{bmatrix} \frac{\partial \tau_{w,m}}{\partial m} & \frac{\partial \tau_{w,m}}{\partial n} & \frac{\partial \tau_{w,m}}{\partial \ell} \\ \frac{\partial \tau_{w,n}}{\partial m} & \frac{\partial \tau_{w,n}}{\partial n} & \frac{\partial \tau_{w,n}}{\partial \ell} \\ \frac{\partial \tau_{w,\ell}}{\partial m} & \frac{\partial \tau_{w,\ell}}{\partial n} & \frac{\partial \tau_{w,\ell}}{\partial \ell} \end{bmatrix} \quad (2.2.27b)$$

Due to the coordinate system chosen, i.e., mnl , the components of the $\nabla \bar{\tau}_w$ tensor affect the endothelial cell in normal and tangential directions. However, the components related to the l -directional wall shear stress and l -coordinate, i.e., all normal components and variations, are of no interest because the aggravating effects on the endothelium are caused by changes in surface, i.e., tangential, forces. Specifically,

$$\nabla \bar{\tau}_w := \begin{bmatrix} \frac{\partial \tau_{w,m}}{\partial m} & \frac{\partial \tau_{w,m}}{\partial n} \\ \frac{\partial \tau_{w,n}}{\partial m} & \frac{\partial \tau_{w,n}}{\partial n} \end{bmatrix} \quad (2.2.27c)$$

The diagonal components $\partial \tau_{w,m} / \partial m$ and $\partial \tau_{w,n} / \partial n$ generate intracellular tension which causes widening and shrinking of cellular gaps. The off-diagonal components $\partial \tau_{w,m} / \partial n$ and $\partial \tau_{w,n} / \partial m$ cause relative movement of adjacent cells. Lei (1995) suggested that the normal components of the $\nabla \bar{\tau}_w$ tensor, i.e., those creating tension, are the most important ones with respect to intimal thickening due to atherosclerosis or hyperplasia. A scalar combination of the normal components can be written as

$$WSSG(t) = \left[\left(\frac{\partial \tau_m}{\partial m} \right)^2 + \left(\frac{\partial \tau_n}{\partial n} \right)^2 \right]^{1/2} \quad (2.2.28)$$

In order to employ the WSSG-concept to assess the impact of non-uniform hemodynamics, the absolute value of the local instantaneous wall shear stress gradient is either used directly or in its time-averaged dimensionless form. Specifically,

$$WSSG_{nd} = \frac{1}{T} \frac{d_o}{\tau_o} \int_0^T WSSG(t) dt \quad (2.2.29)$$

in which d_o is a reference diameter and $\tau_o = 8\eta u_{mean}/d_o$ is the reference Poiseuille-type wall shear stress corresponding to the mean flow rate.

Wall Shear Stress Angle Gradient

Hyun et al. (2000) proposed that a measure of the angle between adjacent wall shear stress vectors would indicate regions of dysfunctional endothelial cells, and, hence, sites of intimal thickening. The wall shear stress angle deviation (WSSAD) for a control volume of area dA_i is formulated

$$WSSAD = \frac{1}{T} \int_0^T \left(\frac{1}{A_S} \int \arccos \left(\frac{\bar{\tau}_o \cdot \bar{\tau}_n}{|\bar{\tau}_o| \cdot |\bar{\tau}_n|} \right) dA_i \right) dt \quad (2.2.30)$$

where the surface stress vector at the location of interest is represented by $\bar{\tau}_o$, and $\bar{\tau}_n$ represents the four surrounding surface stress vectors. A similar, mesh independent parameter, the wall shear stress angle gradient, was devised for the publication of Longest and Kleinstreuer (2000). The rationale for this parameter, which has not appeared elsewhere, is provided in the following discussion.

Considering Eq. (2.2.30), the WSSAD can be used to evaluate single geometries and make comparisons among designs if and only if the inter-nodal distances between adjacent surface nodes are approximately equal. Grids should therefore be constructed to ensure that, in the region of interest, the inter-nodal distances at the wall are nearly equivalent. It is usually difficult to meet this requirement with the use of structured meshes for complex geometries.

A mesh independent wall shear stress directional parameter may be formulated using a gradient operation. For example, the WSSG scalar reports how much $\tau_{w,m}$ and $\tau_{w,n}$ vary in the m and n directions, respectively. Similarly, the WSSAD reports spatial variation of the

mean shear stress direction, i.e., variation of the m and n directions. If the WSSG components $\partial\tau_{w,m}/\partial m$ and $\partial\tau_{w,n}/\partial n$ were calculated as the WSSAD is, they would simply be the differences in $\tau_{w,m}$ and $\tau_{w,n}$ values across one control volume in the m and n directions, respectively. In this formulation, the distance between the locations at which $\tau_{w,m}$ and $\tau_{w,n}$ values are sampled would be ignored resulting in a mesh dependent formulation. A mesh independent measure of change in $\tau_{w,m}$ and $\tau_{w,n}$ in the m and n directions is formed using the gradient operation (or directional derivatives). Similarly, to formulate a mesh independent measure of spatial variation in the WSS direction, the gradient operation can be used. The region of interest is a surface area segment defined by a central control-volume face and its four surrounding nodes. Using the central mean WSS vector as a reference, a scalar field of angular differences can be computed as with the WSSAD. In this formulation

$$\phi = \arccos\left(\frac{\bar{\tau}_o \cdot \bar{\tau}_n}{|\bar{\tau}_o| |\bar{\tau}_n|}\right) \quad (2.2.31a)$$

where again, the stress vector at the location of interest is represented by $\bar{\tau}_o$, and $\bar{\tau}_n$ represents the surrounding stress vectors, i.e., vectors over each surface control-volume edge. The gradient of the scalar field of angular variations is then taken on an area-average basis assuming that each angular difference is constant for its respective control volume edge. The resulting wall shear stress angular gradient (WSSAG) is composed of three components

$$\overrightarrow{WSSAG} = \frac{1}{A_i} \int_S \frac{\partial\phi}{\partial x} dA_i \hat{i} + \frac{1}{A_i} \int_S \frac{\partial\phi}{\partial y} dA_i \hat{j} + \frac{1}{A_i} \int_S \frac{\partial\phi}{\partial z} dA_i \hat{k} \quad (2.2.31b)$$

or

$$\overrightarrow{WSSAG} = \Phi_x \hat{i} + \Phi_y \hat{j} + \Phi_z \hat{k} \quad (2.2.31c)$$

The gradient vector can then be transformed to the m and n coordinate system (such that the normal component l vanishes) to quantify specific directional changes in the surface coordinates. Alternately, the magnitude of the WSSAG vector is a coordinate independent scalar that can be computed on a time-average basis

$$WSSAG = \frac{1}{T} \int_0^T \left(\Phi_x^2 + \Phi_y^2 + \Phi_z^2 \right)^{1/2} dt \quad (2.2.31d)$$

or, more succinctly,

$$WSSAG = \frac{1}{T} \int_0^T \left| \frac{1}{A_i} \int_S \nabla \phi \, dA_i \right| dt \quad (2.2.32)$$

which represents the magnitude of the shear stress angle deviation over a distance. Due to the use of the gradient operation this parameter is mesh independent even though the central vector was used to compute the scalar field of angles. This is because the mean shear stress vector is simply a reference, i.e., any other surface vector could be used for this purpose.

Lagrangian Based Wall Parameters

As discussed, blood particle depositions and stasis have been widely implicated with intimal thickening and thrombosis formation. In the absence of near-wall forces, it is often assumed that the initial point of particle wall contact represents a critical location of interest (cf. Hyun, 1998; Buchanan, 2000). However, the inclusion of near-wall forces coupled with the assumption of spherical particles and Stokes flow prevents particle wall contact. Blood particle stasis may then serve as a qualitative hemodynamic wall parameter. Ehrlich and Friedman (1977) examined the distribution of blood particle stasis in a Y-branch two-dimensional (2-D) model by tracking Lagrangian fluid elements assumed to be blood particles. For pulsatile axisymmetric stenotic flow, Kunov et al. (1996) tracked Lagrangian fluid elements which were assumed to be groups of activated platelets in a symmetric (2-D) stenosis and applied the quantitative concept of a local volumetric residence time which takes into account where particles accumulate and how long they remain there. For a similar stenotic configuration, Buchanan et al. (2000) generated maps of localized fluid element residence time for various input pulse frequencies.

This research hypothesizes that blood particle deposition is most likely in regions of near-wall particle stasis and/or elevated concentrations, coincident with regions of dysfunctional endothelial cells. Regions of enhanced particle-wall interaction may be quantified by the proposed non-dimensional near-wall residence time (NWRT) parameter. To derive a general model for the near-wall residence time (NWRT) and hence for the probability of blood particle deposition, the following factors have been considered:

1. Time that a particle spends in close proximity to an attached site
2. Availability of particles

3. Distance between the particle and the vascular surface
4. Bio-particle activation and surface reactivity (which may be proportional to flow induced surface dysfunction)
5. Independence of mesh size and particle loading

In conjunction with the correct particle dynamics equations (cf. Eqs. 2.2.13-2.2.22), a non-dimensional near-wall residence time parameter, NWRT, is proposed, which indicates the probability of particle deposition. Specifically,

$$NWRT = \frac{Q_{av}}{n_o V_{NW}} \sum_{p=1}^n \int_{path,p} \left(\frac{a_p}{h_p} \right)^s \frac{\vec{v}}{\|\vec{v}\|^2} \cdot d\hat{r} \quad (2.2.33)$$

For a local near-wall region of volume V_{NW} , $\|\vec{v}\|$ is the magnitude of the particle velocity, n is the number of activated blood particles that pass through the local volume, and $d\hat{r}$ is the local directional unit vector for integration along each trajectory. A near-wall layer of biophysical interaction is defined by $h = 50 \mu\text{m}$. The near-wall volume, $V_{NW} = A_{surf} \times h$, accounts for variations in near-wall control-volume size, such that the solution is practically mesh independent for a limiting value of local surface area, A_{surf} . Inclusion of the total number of particles, n_o , results in convergent profiles once a sufficient quantity of particles has been simulated. The average flow rate term Q_{av} , is a physically relevant constant, which is included to form a dimensionless parameter. The distance between a particle center and the wall, h_p , is a key scaling (or probability) factor in the term $(a_p/h_p)^s$, where a_p is the particle radius and, to match experimental results, s is set to unity for monocytes and a factor of 2 for platelets (cf. Sect. 3.2).

The NWRT concept is an approximate method which is particularly useful and necessary given that biophysical factors such as vessel surface roughness, actual blood particle shape, and nano-scale bond formations responsible for possible blood cell attachment, rolling, or re-suspension, cannot feasibly be included in simulations involving relatively large-scale 3-D geometries. For the calculation of NWRT, at least 50,000 blood particles have been released *randomly* in both space and time over one pulse period at an upstream

slice prior to the junction area. Simulations are continued until all particles exit the flow field.

The development and testing of the NWRT, as well as a composite model for blood particle deposition that takes into account endothelial cell reactivity, is presented in Chapter 3. The NWRT parameter will then be applied to identify and mitigate regions susceptible to intimal thickening and thrombosis formation in the distal femoral bypass geometry in Chapters 5 and 6.

2.3 Methods

2.3.1 Computational Fluid Dynamics Solution

The solution of the time varying velocity field has been carried out with a validated finite-volume based algorithm (CFX 4.4, AEA Technology) with user-Fortran programs added to account for the blood rheology, the input pulse, and the hemodynamic parameters. A structured, multiblock, body-fitted coordinate discretization scheme was employed. Parameters necessary for both temporal and mesh convergence were evaluated for a sample femoral-bypass configuration. These conditions will provide a starting point for convergence validation in all subsequent configurations studied.

Solution of Governing Equations

The finite-volume solution relies on a modified form of the governing equations, i.e.,

$$\frac{\partial \rho \vec{u}}{\partial t} + \nabla \cdot (\rho \vec{u} \vec{u} - \eta \nabla \vec{u}) = -\nabla p + \nabla \cdot (\eta (\nabla \vec{u})^T) \quad (2.3.1)$$

Integration of this equation for individual control-volumes results in

$$\int \frac{\partial \rho \vec{u}}{\partial t} dV + \int \rho \vec{u} \vec{u} \cdot \vec{n} dA - \int \eta \nabla \vec{u} \cdot \vec{n} dA = \int S dA \quad (2.3.2)$$

where the pressure gradient and stress divergence have been included in the source term, S . With the exception of advection, all terms in Eq. (2.3.2) are discretized in space using second-order central differences. The advection terms are discretized using the higher-order upwind (huw) differencing scheme of Thompson and Wilkes (1982). This upwind scheme

was derived by integrating fluxes over the control-volume and is completely conservative and consistent with the control-volume formulation (Shyy et al., 1992). The coefficients of the convective terms are obtained using the Rhie-Chow (Rhie & Chow, 1983) interpolation formula which has been extended to include non-uniform grid corrections. Continuity is enforced by solving a pressure-correction equation to update the pressure and velocity fields. Specifically, the SIMPLEC algorithm of Van Doormal and Raithby (1984) is used.

A fully implicit backward Euler scheme was used for temporal discretization. Higher-order schemes, which allow for larger time-steps, such as the Crank-Nicholson method are available. However, time-step size and not method order determine the accuracy of the solution. That is, the first-order scheme selected with sufficiently small time-steps is capable of the accuracy achieved by higher order schemes with larger time-steps. The fully implicit backward Euler scheme was chosen to rapidly generate a sufficiently large number of temporal velocity field solutions such that linear interpolation in time could be used for the integration of particle trajectories. The computational cost incurred by implementing this first-order method was reduced by a variable time-step routine for the solution of the velocity field.

The discretized transport equations are solved iteratively. There are two levels of iteration: (1) a linear inner iteration which solves for spatial coupling for a particular variable, and (2) a non-linear outer iteration which solves for the coupling among variables. The outer iteration is a Picard scheme used to update the non-linearities of the problem. Each variable is taken in sequence, regarding all other variables as fixed. The coefficients of the discretized equations are always reformed, using the most recently calculated values of the variables, before each inner iteration. For each outer iteration, the set of linearized difference equations is passed to a simultaneous linear equation solver which uses an iterative solution method. An exact solution is not required because this is just one step in the non-linear outer iteration. With the exception of the pressure correction equation, all variables were solved for using an algebraic multigrid method. This method solves the discretized equations on a series of coarsening meshes (cf. Lonsdale, 1993) chosen algebraically. The AMG method takes advantage of the properties of multigrid schemes which can converge in an ideal number of iterations for certain problems (Ferziger and Peric, 1999). However, rather than

using nested grids which vary by a factor of two in mesh size to obtain approximate solutions on finer grids, the AMG method performs restriction and prolongation operations on the linearized matrix itself using non-square matrices to reduce the problem size and then performs smoothing operations. This “algebraic” method of prolongation and restriction is what gives the algorithm its name as well as its performance boost. The advantage of the AMG scheme is that it reaches a convergent solution monotonically and in fewer total (outer) iterations than the other schemes. The cost is that each iteration is more expensive in both CPU time and memory required, but the overall computational time is reduced. In general, for the transient three-dimensional problems solved, the AMG method has been used.

The typical convergence criterion for hemodynamic simulations is to halt the outer iteration procedure and advance the time-step when the global mass residual has been reduced from its original value by three orders of magnitude, in cgs units. However, Longest (1999) demonstrated that this criterion is often insufficient for variable viscosity conditions. Furthermore, the above convergence criterion often halts a solution process that is significantly reducing the mass residual. Therefore, monitoring the rate of both momentum and mass residual reduction, in addition to mass residual size is recommended. To monitor convergence rate, a residual reduction factor (rrf) can be defined as

$$rrf = \frac{\text{avg. residual reduction over the last 5 outer iterations}}{\text{current residual magnitude}} \quad (2.3.3)$$

The inverse of the rrf indicates the number of outer iterations that would be required to drive the residual to zero, at the current rate of reduction. Appropriate values that resulted in a sufficiently convergent solution without excessive outer iterations were found to be $rrf_{mass} = 0.01$ and $rrf_{mom.} = 0.06$. The composite convergence criterion is then:

- i. mass residual \leq mass flow rate $\times 10^{-3}$
- ii. $rrf_{mass} \leq 0.01$
- iii. $rrf_{mom.} \leq 0.06$

The mean mass flow rate divided by a factor of two was used in condition i when the time varying mass flow rate dropped below this value. To ensure that a converged solution had been reached, the above factors were reduced by an order of magnitude and results were compared. The stricter convergence criteria produced a negligible effect on both velocity and wall shear stress fields.

An adaptive time-stepping routine was implemented to maintain a highly efficient routine throughout the widely varying input pulse. Time-step size selection was based on the convergence rate of the previous time-step. Time-step size was either increased or decreased to maintain the total number of outer iterations around 75. This is a reasonable number of iterations considering typically under-relaxation factors for the AMG solver were 0.6 for momentum and 0.25 for viscosity. The resulting time-step size varied from 0.001 to 0.01 s and was found to sufficiently resolve Lagrangian particle tracks.

Mesh Construction and Grid Convergence

Realistic femoropopliteal distal anastomotic models with the common graft-to-artery diameter ratios of 2:1 and 1.5:1 have been considered. Synthetic PTFE grafts of 8 and 6 mm were cut at 45-degree angles as well as beveled curves and sutured in end-to-side fashion to 4 mm grafts by Dr. J. P. Archie, Jr. The grafts were then filled with RTV polyurethane rubber (Poly 74-30TM, Polytek, Inc.) to a static pressure of 100 mmHg and cured. Internal cast of the grafts were excised and digitized via three-dimensional laser scanning (First Article Corp., New Hope, MN). Surface models were constructed to maintain key geometric features, such as graft and artery cross-sectional variations due to the construction of the anastomosis (Fig. 2.3.1). The opening of the artery in the region of the anastomosis induces an elliptical arterial cross-section and results in a raised vessel floor. This feature is more evident with the larger diameter ratio. The natural artery configuration, which is due to the pressurized anastomosis, has also been faithfully reproduced. A gently curving graft was assumed and consistently reproduced for all models. The vessel walls were assumed to be rigid and symmetric about a centerline-plane, i.e., in-plane.

Construction of a valid multiblock computational mesh requires consideration of three primary facets. First and most obvious, the computational domain boundaries, or surfaces, must model as accurately as possible the physical domain. Matching a series of blocks to the curved surfaces of the anastomoses requires distorting some of the control volumes which compose the block structure. The blocks should be arranged in a manner that minimizes control volume distortions. The reduction of mesh skewness by proper block formation and connection is the second aspect that must be considered in mesh construction. The degree of

control volume distortion is directly related to the numerical truncation error inherent in solving discretized equations for a given computational domain. Truncation error also relates to control volume size, which is the third aspect of mesh construction to be addressed. Mesh cell size must be small enough such that the assumptions made when generating the discretized equations, e.g. conversion of a derivative to a difference, are valid. The lower limit on mesh cell size is dictated by the round-off error of the machine and computational resources.

The computational fluid dynamics package CFX 4.4 (AEA Technology) is a control volume based solver which allows for the use of multiblock meshes. Multiblock structure is characterized by topologically rectangular blocks composed of irregular hexahedrons or control volumes. CFX 4.4 incorporates the surface modeler and mesh generator BUILD which enables the generation of complex curved surfaces and junction boundaries. The multiblock mesh construction for all graft geometries studied was done in accordance with a validated blocking structure (Longest, 1999) with the goal of minimizing control volume distortions. Local refinements were made to reduce control-volume distortions which are inherent to the heel area. Specifically, a new “scalloped” blocking structure applied in the artery near the heel dramatically reduced the severity of mesh skewness in this region at the expense of moderate curvatures away from the wall (Fig. 2.3.1). This technique allowed for refined near-wall mesh spacing without the threat of collapsing near-wall control volumes. Furthermore, this scalloped blocking structure was a necessary requirement when the butterfly cross-sectional design was applied to lower-angle grafts. All control-volumes in the completed meshes were within acceptable orthogonality parameters thereby minimizing one aspect of truncation error. As discussed, control-volume sizes that are too large result in significant truncation errors, and, hence unrealistic, grid-dependent solutions. To ensure grid convergence, the computational domain size and configuration was adjusted until an acceptable level of grid-independence was achieved. Assuming planar symmetry, end-to-side anastomosis-style grids consisting of 90,000 and 210,000 control-volumes were tested under steady-state mean flow conditions. The finer mesh was constructed to provide 1.5 times the resolution of the coarser mesh in the region of the anastomosis, particularly with regard to cross-sectional subdivisions. The maximum relative error, ϵ , of the velocity and

shear stress magnitude was $\epsilon = 0.9\%$ and $\epsilon = 3.88\%$, respectively. Relative errors were also calculated for the WSSG over one pulse and found to be, at maximum, $\epsilon = 8.6\%$. Refining the grid by a factor of 1.5 had a negligible effect on both the velocity and wall shear stress fields; therefore, all solutions have been based on meshes with approximately 90,000 control-volumes.

2.3.2 Particle Trajectory Solution

Blood Particle Properties and Simulation

Human blood is a concentrated suspension of various types and shapes of deformable interacting cells in a complex aqueous solution. The platelets are very small oblate spheroids, or discoids, (White, 1994) and constitute less than $1/800^{\text{th}}$ of the cellular volume. Monocytes are a subclass of leukocytes, or white blood cells, that are also a dilute cellular constituent and are generally spherical in shape. More important to blood rheology are red cells which occupy about 45% of the blood volume and are capable of deforming their shape, in 0.006 seconds, under the influence of shear. The cellular contents of blood (including red cells, white cells, and platelets) are immersed in plasma, which displays Newtonian characteristics. Specific details of blood components are given in Table 2.6 (Caro et al., 1978; Cokelet, 1987; Goldsmith, 1999). It is the red cells which, at the macroscopic level, determine the flow properties of blood, and which, at the microscopic level, determine the motions of the platelets and white cells.

Based on a dimensional analysis of blood particles, it has been shown that the inter-particle hydrodynamic effects are significant and the effect of the red blood cells on the flow field cannot be ignored. However, due to a low Stokes number, the two-phase flow can be considered a multi-component mixture (homogeneous flow) with modified properties. Specifically, blood in sufficiently large vessels (i.e., the vessel diameter being much greater than d_p) is typically modeled as a multi-component flow with a constant density influenced by components of the mixture and a variable viscosity dependent on shear rate and the mean hematocrit. The mixture density of whole blood is simply the sum of the bulk densities of the constituents. The viscosity of blood will be modeled with the semi-empirical Quemada

formulation (Cokelet, 1987) which captures the red blood cell based shear thinning nature (cf. Eq. (2.2.2c)).

Table 2.6: Properties of Blood Constituents

Material	Density (g/cm ³)	Viscosity (dyn•s/cm ²)	Blood cell count (#/cm ³)	Volume (μm ³)	Size (μm)	Volume fraction	τ _p (s)	α = ρ _f /ρ _p
Red Blood Cell	1.09	--	5 × 10 ⁹	88	7.7 × 2.8	0.42 – 0.46	1.45 × 10 ⁻⁶	.967
Platelet	1.069 [†]	--	3 × 10 ⁸	5.17 ^{†,††}	3.0 ^{††}	1.9 × 10 ⁻³	1.12 × 10 ⁻⁶	0.983
Leukocytes (all)	1.07-1.09	--	7.0 × 10 ⁶ (total)	460	9.5	1.2 × 10 ⁻³ (total)	3.35 × 10 ^{-6♦}	0.964♦
Plasma	1.03	0.014 [*]	--	--	--	--	--	--
Whole Blood	1.054	0.0309 ^{**}	--	--	--	--	--	--

† representative mean value for unactivated platelet (Corash et al., 1977)

†† platelet dimensions vary considerably

* at 37°C (may vary from 0.012 to 0.018)

** Newtonian limit at H = 40%

♦ value for monocytes

The low concentration and low Stokes number of monocytes and platelets allows for the motion of these cells to be computed in a one-way coupled manner, i.e., these particles do not affect flow field momentum. However, the continued collisions and hydrodynamic interactions with red blood cells results in a persistent lateral motion of platelets and monocytes, as discussed in Sections 1.7 & 2.2.2.

Hyun (1998) devised a one-way coupled blood particle tracking scheme which implements 4th-order Runge-Kutta integration and a fixed time-step. This method computed trajectories as the flow field solution advanced, and produced qualitatively accurate results for the motion of a hardened red blood cell in the sudden annular expansion geometry of Karino and Goldsmith (1977). Buchanan (2000) introduced a variable time-step code which computed particle trajectories as a post-processing step. The inclusion of a variable time-step allowed for a dramatic increase in computational efficiency; however, storing a three-dimensional transient velocity field is extremely memory intensive (e.g., 4096 MB) requiring access to supercomputer style machines. The Fortran 90 (f90) code of Buchanan (2000) was parallelized using OpenMP and SGI-directives for the SGI Origin 2400 machine (NCSC, RTP, NC) allowing for efficient multiprocessor application. These codes were intended

primarily for pathline integration; however, a luminal particle trajectory routine and mechanisms for particle dispersion were also included.

The basic methodology and code construct implemented by Buchanan (2000) have been applied to this study. Indeed, the overall science of particle-hemodynamics in branching blood vessels is best served by researchers collaborating and building upon others contributions. For this study, the particle tracking code originated by Buchanan (2000) has been extended to better simulate particle trajectories, particularly in the near-wall region. Details of the current solution procedure are presented below, followed by performance characteristics.

Particle Tracking Algorithm

The f90 particle-tracking algorithm calculates trajectories as a post-processing step using an adaptive step-size control integration scheme based on the second-order improved Euler predictor corrector method. Geometry data and velocity at all control-volume vertices are extracted from the CFD solution and written to arrays for one complete transient pulse cycle. Each computational time-step results in one velocity array of approximately 15 MB for a geometry of approximately 90,000 control-volumes. Boundary flags and surrounding-cell-pointers are also extracted from the flow field solution and stored in array format. Once all geometry and flow field solution data has been determined, it is loaded into the f90 particle trajectory code as a separate step, i.e., ‘off-line’ code operation valid for the one-way coupled solution approach. The large volume of geometric and velocity solution data to be held in main memory (e.g., 4096 MB) typically requires a super-computer style machine, e.g., the SGI Origin 2400.

As indicated by Eq. (2.2.13), computation of the particle trajectories requires knowledge of the flow field solution at the location of the particle within a specific control-volume. Linear interpolation in time has been applied between arrays to determine the appropriate vertex velocity values. The application of linear interpolation was the primary motivation behind selecting the fully implicit backward Euler routine for the flow field solution. Shape-function interpolation, as implemented in finite-element applications (Pepper and Heinrich, 1992), was then used to determine particle velocity at a location within

a specific control-volume. The implementation of common shape functions usually requires knowledge of the particle position in local computational space, i.e., $-1 \leq \xi \leq 1$, $-1 \leq \eta \leq 1$, $-1 \leq \zeta \leq 1$, cf. Fig. 2.3.2. In this study, the Jacobian matrix, which is the link between physical and computational coordinates, has been defined consistent with typically CFD applications, i.e.,

$$J1 = \begin{bmatrix} \frac{\partial x}{\partial \xi} & \frac{\partial x}{\partial \eta} & \frac{\partial x}{\partial \zeta} \\ \frac{\partial y}{\partial \xi} & \frac{\partial y}{\partial \eta} & \frac{\partial y}{\partial \zeta} \\ \frac{\partial z}{\partial \xi} & \frac{\partial z}{\partial \eta} & \frac{\partial z}{\partial \zeta} \end{bmatrix} \quad (2.3.4)$$

Computational particle positions within a control-volume of interest can then be evaluated as

$$\begin{bmatrix} \xi \\ \eta \\ \zeta \end{bmatrix} = J1^{-1} \begin{bmatrix} \bar{x} \\ \bar{y} \\ \bar{z} \end{bmatrix} \quad (2.3.5)$$

where $\bar{x}, \bar{y}, \bar{z}$ are with respect to the control-volume center. A field variable, ϕ , such as fluid velocity, u_i , can then be interpolated for a point within the control-volume, based on computational coordinates, as

$$\phi(\xi, \eta, \zeta) = \sum_{i=1}^8 N_i \phi_i \quad (2.3.6)$$

where i represents the eight vertices defined in Figure 2.3.2. The shape functions, N_i , consistent with this notation are (Pepper and Heinrich, 1992)

$$\begin{bmatrix} N_1 \\ N_2 \\ N_3 \\ N_4 \\ N_5 \\ N_6 \\ N_7 \\ N_8 \end{bmatrix} = \frac{1}{8} \begin{bmatrix} (1-\xi)(1-\eta)(1-\zeta) \\ (1+\xi)(1-\eta)(1-\zeta) \\ (1-\xi)(1+\eta)(1-\zeta) \\ (1+\xi)(1+\eta)(1-\zeta) \\ (1-\xi)(1-\eta)(1+\zeta) \\ (1+\xi)(1-\eta)(1+\zeta) \\ (1-\xi)(1+\eta)(1+\zeta) \\ (1+\xi)(1+\eta)(1+\zeta) \end{bmatrix} \quad (2.3.7)$$

The evaluation of particle-surface contact also relies on particle computational space representation. Specifically, the particle radius normal to the wall can be represented in terms of computational coordinates as

$$\begin{bmatrix} \xi_{rad} \\ \eta_{rad} \\ \zeta_{rad} \end{bmatrix} = J1^{-1} \begin{bmatrix} a_p n_1 \\ a_p n_2 \\ a_p n_3 \end{bmatrix} \quad (2.3.8a)$$

where the outward surface normal vector is $\hat{n} = n_1 \hat{i} + n_2 \hat{j} + n_3 \hat{k}$. Either ξ_{rad} , η_{rad} , or ζ_{rad} is of interest, depending on the computational space orientation of the wall. Particle-to-surface contact can then be evaluated depending on the computational space location of the particle. For example, with a high- ζ wall, surface contact occurs when

$$\zeta + \zeta_{rad} \geq 1 \quad (2.3.8b)$$

Particles that cross control-volume boundaries are identified as having a computational space coordinate outside of the range $-1 \leq \xi \leq 1$, $-1 \leq \eta \leq 1$, or $-1 \leq \zeta \leq 1$. The new local control-volume is specified by determining which computational space coordinate range is exceeded, and then referencing a pointer array. For cases when a particle crosses through a control-volume corner, a full domain search is employed to determine the new control-volume location.

A problem with the earlier version of the f90 code and with the code of Hyun (1998) was that particles were often lost and appeared to ‘float-out’ of the domain. It was identified that CFX4 was inappropriately reporting the surrounding cell-pointer array near block boundaries in some cases. Specifically, when a control-volume identification call was made across a block-boundary and then to a third control-volume, an errant identification was reported. Identifying and correcting these instances in the f90 code practically eliminated the occurrence of lost particles.

The variable time-step scheme used for trajectory integration was based on a method given in detail by Press et al. (1992) where:

1. An initial time-step, Δt , is used to generate a solution, x_i (a new position in a particular coordinate direction, where $i = 1, 2$, or 3), at $t + \Delta t$ using the second-order Euler method.

2. The initial time-step is cut in half and applied twice to generate a second solution, x_i' , at $t+\Delta t$.
3. The difference in the solutions at $t+\Delta t$ is evaluated, and x_i' is accepted if it is of sufficient accuracy (the time-step size is increased for the next step).
4. Otherwise, the solution is rejected, the time-step is decreased, and the process restarts.

For each trajectory, the error that is monitored at a given step is

$$\Delta_i = \max |x_i - x_i'| \quad (2.3.9a)$$

The solution for an individual trajectory is accepted if all errors, Δ_i , remain within the bounds of a fractional error reference scale $\Delta_{o,i}$, i.e.,

$$\Delta_i \leq \Delta_{o,i} \quad (2.3.9b)$$

where

$$\Delta_{o,i} = \varepsilon \cdot \{ |x_i| + |\Delta t \cdot dx_i / dt| \} \quad (2.3.9c)$$

In the above equation, ε is the accuracy tolerance level and the remaining term is a scale factor commonly used to obtain constant fractional errors. The appropriate accuracy tolerance for most applications is $10^{-6} \leq \varepsilon \leq 10^{-3}$. However, it was found that the use of the above expression results in serious inconsistencies regarding trajectory accuracy, particularly in the near-wall region or as any coordinate location nears zero. An alternative is to select a constant value for the reference scale as follows

$$\Delta_{o,i} = \varepsilon \cdot const. \quad (2.3.9d)$$

The problem with this scheme is that the condition for acceptable accuracy may always be artificially satisfied if a small enough time-step is selected. However, if the resulting time-step isn't appropriate for the surrounding flow conditions, an arbitrary solution results. A more dynamic condition can be realized by setting the reference scale relative to the local step size, as follows

$$\Delta_{o,i} = \varepsilon \cdot dx_i \quad (2.3.9e)$$

This approach avoids the particle location dependent artifact introduced with Eq. (2.3.9c), yet allows for a dynamic adaptation of step-size when extremely small time-steps are required, as

in the near-wall region. For particle hemodynamic simulations of monocytes and platelets, appropriate values for the accuracy tolerance were found to range $10^{-3} \leq \epsilon \leq 10^{-2}$.

The adaptive time-step integration, as described, allowed for trajectory time-step size to be controlled on an individual particle basis and maintained a specified accuracy even in the near-wall control volumes. Comparing the second-order method, with a sufficiently small time-step, to a fourth-order Runge-Kutta method, the results were nearly identical from a practical point of view. This observation is explained by the fact that order is only the rate at which the error goes to zero as the step-size is decreased, and it is the step-size that controls accuracy.

The f90 adaptive time-step integration scheme was parallelized for the SGI Origin 2400 using both SGI and OpenMP directives. The Origin 2400 machine has a ccNUMA (cache coherent Non-Uniform Memory Access) architecture that allows CPUs to easily address non-local or shared memory. Therefore, the Origin 2400 was an excellent candidate considering the massive geometry and velocity arrays to be stored. OpenMP was selected so that a fork-join model could be created to parallelize the computationally intensive portions of the code. The main components of the code are initialization, solution by integration, and the output phase, as illustrated in Fig. 2.3.3. In the initialization phase, the *section* directive is used to read in files (primarily the velocity arrays) over different processors. The majority of parallelism is achieved in the solution portion by solving groups of trajectories over multiple processors. The SGI *distribute* directive is used to split the arrays allowing for simultaneous trajectory integrations. To optimize data access from the cache lines, multidimensional arrays were stored with their dominant dimension second, i.e., defining the number of array columns.

The second-order improved Euler predictor-corrector method has been used for the integration of particle motion equations including near-wall effects, cf. Eqs. (2.2.13 & 2.2.16-2.2.23). Using superscripts n and $n+1$ to denote times t and $t+dt$, discretized equations for the predictor or trail step of the routine are

$$v_i^{*n+1} = v_i^n + \frac{dt}{\tau_p} (u_i^n - v_i^n) + \alpha dt \left. \frac{Du_i}{Dt} \right|^{n+1} + dt f_{i,lubrication}^n + dt f_{i,lift}^n \quad (2.3.10a)$$

and

$$x_i^{*n+1} = x_i^n + dt v_i^{*n+1} \xrightarrow{\text{interpolate}} u_i^{*n+1} \quad (2.3.10b)$$

where $f_{i,lubrication}$ and $f_{i,lift}$ represent the near-wall lubrication and lift forces described in Eqs. (2.2.16-2.2.23) divided by particle mass, m_p . Once a trial particle position, x_i^{*n+1} , has been determined, the local fluid velocity may be evaluated at that location using shape function interpolation, as described above. The use of the trial velocity, v_i^{*n+1} , in Eq. (2.3.10b) was found to improve solution stability, compared to the use of v_i^n . The second step of the integration routine provides the particle velocity and position at time $t+dt$,

$$v_i^{n+1} = v_i^n + \frac{dt}{2\tau_p} (u_i^n - v_i^n + u_i^{*n+1} - v_i^{*n+1}) + \alpha dt \left. \frac{Du_i}{Dt} \right|^{n+1} + dt f_{i,lubrication}^n + dt f_{i,lift}^n \quad (2.3.11a)$$

and

$$x_i^{n+1} = x_i^n + \frac{dt}{2} (v_i^n + v_i^{n+1}) \xrightarrow{\text{interpolate}} u_i^{n+1} \quad (2.3.11b)$$

Again, shape-function interpolation is used to evaluate fluid velocity, u_i^{n+1} , at the new particle location.

In the near-wall region, pressure gradients in front of a particle generally have a more dramatic impact than conditions behind the particle. Therefore, the pressure gradient term, represented by the material derivative in the above equations, should be based on conditions at n and $n+1$, as opposed to $n-1$ and n . The explicit nature of the solution routine can be maintained by taking advantage of the fact that the material derivative is equivalent to the acceleration of a fluid element. The pressure gradient term is then evaluated by a call to a second improved Euler routine that integrates a fluid element over a time, dt , and evaluates the new velocity, $u_i'^{n+1}$. The pressure gradient term may then be expressed as

$$\left. \frac{Du_i}{Dt} \right|^{n+1} = \frac{u_i'^{n+1} - u_i^n}{dt} \quad (2.3.12)$$

While this operation is expensive, it eliminates the need to store old velocity values and time-steps. Furthermore, only one evaluation of the pressure gradient term is required per time-step, cf. Eqs. (2.3.10 & 2.3.11).

The near-wall drag modifications, or lubrication forces presented in Eqs. (2.2.16 & 2.2.18) including the approximations of Loth (2000) (cf. Eqs. (2.2.19a & b)), have been discretized for an arbitrary three-dimensional surface as

$$f_{i,lubrication}^n = \frac{1}{\tau_p} \left[\text{sgn}_{n,i} |u_{n,i} - v_{n,i}| \left(\frac{1.1}{\frac{h_p}{a_p} - 1} \right) + \text{sgn}_{t,i} |u_{t,i} - v_{t,i}| \left(\frac{0.7a_p}{h_p} \right) \right]^n \quad (2.3.13)$$

Consistent with the previous notation, superscripts refer to the time level of interest and velocity subscripts n and t represent the wall-normal and wall-tangential directions, respectively. The surface-normal unit vector pointing out of the geometry is defined as

$$\hat{n} = n_1 \hat{i} + n_2 \hat{j} + n_3 \hat{k} \quad (2.3.14a)$$

and, the surface tangent unit vector on an individual particle basis in the direction of particle motion is defined as

$$\hat{t} = t_1 \hat{i} + t_2 \hat{j} + t_3 \hat{k} \quad (2.3.14b)$$

Wall-normal fluid and particle velocity components can be expressed as

$$u_{n,i} = (\vec{u} \cdot \hat{n}) n_i \quad (2.3.15a)$$

and

$$v_{n,i} = (\vec{v} \cdot \hat{n}) n_i \quad (2.3.15b)$$

Similarly, wall-tangent fluid and particle velocity components can be expressed as

$$u_{t,i} = (\vec{u} \cdot \hat{t}) t_i \quad (2.3.15c)$$

and

$$v_{t,i} = (\vec{v} \cdot \hat{t}) t_i \quad (2.3.15d)$$

To generate an expression that resists particle motion both toward and away from the wall in a three-dimensional geometry for a non-quiescent fluid, the appropriate sign on the first component of expression (2.3.13) is

$$\text{sgn}_{n,i} = \begin{cases} +1 & \text{for } v_{n,i} < 0 \\ -1 & \text{for } v_{n,i} > 0 \end{cases} \quad (2.3.16a)$$

As indicated, the wall normal drag modification is valid for Stokes flow. For cases in which the particle Reynolds number violates the required condition, $Re_p \ll 1$, particle motion toward the wall is resisted more stringently than particle motion away from the wall (Brenner, 1961). Such a condition can be approximated by only including the drag modification for particle motion toward the wall, i.e.,

$$\text{sgn}_{n,i} = \begin{cases} 0 & \text{for } \vec{v} \cdot \hat{n} < 0 \\ +1 & \text{for } v_{n,i} < 0 \text{ and } \vec{v} \cdot \hat{n} > 0 \\ -1 & \text{for } v_{n,i} > 0 \text{ and } \vec{v} \cdot \hat{n} > 0 \end{cases} \quad (2.3.16b)$$

Appropriate evaluation of viscous shear on the particle resulting from the presence of the wall, which resists particle motion, requires that the tangential drag modification assume the sign of

$$\text{sgn}_{t,i} = \begin{cases} +1 & \text{for } v_{t,i} < 0 \\ -1 & \text{for } v_{t,i} > 0 \end{cases} \quad (2.3.17)$$

As indicated by the n -superscript in Eq. (2.3.13), the near-wall forces are evaluated once for the current time level. Multiple evaluations of the near-wall forces per time-step, e.g., computing $f_{i,lubrication}^{*n+1}$ using velocities at the trail $n+1$ time-level, were found to result in serious instabilities in some instances.

The near-wall lift expression of Cherukat and McLaughlin (1994) (cf. Eqs. 2.2.20-2.2.22) has been discretized on a component basis as

$$f_{i,lift}^n = \frac{-\rho_f a_p^2 n_i}{m_p} \left[u_s^2 \cdot I \left(\frac{h_p}{a_p}, \frac{\dot{\gamma} a_p}{u_s} \right) \right]^n \quad (2.3.18a)$$

where the wall-tangent slip velocity is represented as

$$u_s = \vec{v} \cdot \hat{t} - \vec{u} \cdot \hat{t} \quad (2.3.18b)$$

To preserve the sign of $\Lambda = \dot{\gamma} a_p / u_s$ used to evaluate the integral, I , the shear rate has been approximated at the particle location as

$$\dot{\gamma} \approx \frac{\vec{u} \cdot \hat{t}}{h_p} \quad (2.3.18c)$$

which is reasonable near the wall. Particle lift is only applied within the near-wall region for which conditions (2.2.23) are satisfied.

Evaluation of the near-wall expressions requires knowledge of the distance between the particle center and the wall, h_p . This distance can be evaluated using computational space particle coordinates (ξ, η, ζ) and the Jacobian matrix. Specifically, the wall-normal vector describing the physical distance between the particle center and the wall, \vec{r}_n , for particles within a control-volume with a high-oriented wall, can be evaluated as

$$\begin{bmatrix} r_{n,1} \\ r_{n,2} \\ r_{n,3} \end{bmatrix} = J1 \begin{bmatrix} \text{for high-}\xi \text{ wall : } (1-\xi) \\ \text{otherwise : } 0 \\ \text{for high-}\eta \text{ wall : } (1-\eta) \\ \text{otherwise : } 0 \\ \text{for high-}\zeta \text{ wall : } (1-\zeta) \\ \text{otherwise : } 0 \end{bmatrix} \quad (2.3.19a)$$

The distance between the particle and wall is then computed as

$$h_p = |\vec{r}_n| \quad (2.3.19b)$$

The f90 code contains modifications to the above expression that account for particles in control-volumes removed from the wall, as well as low-oriented walls.

Knowledge of the instantaneous velocity gradient during particle integration is necessary for several applications, e.g., computation of fluid viscosity and particle shear history used to establish activation. For an individual control-volume, the velocity gradient will be assumed constant, i.e.,

$$\nabla \vec{u} \approx \frac{1}{V} \int_{CV} \nabla \vec{u} dV \quad (2.3.20a)$$

In addition to interpolation and integration, the shape functions for hexahedral control-volumes may also be used to evaluate individual terms of the gradient operation, as follows,

$$\frac{\partial \phi}{\partial x_j} = \sum_{i=1}^8 \frac{\partial N_i}{\partial x_j} \phi_i \quad (2.3.20b)$$

where i represents the eight control-volume vertices. Derivatives of the shape functions with respect to physical space can be calculated as

$$\begin{bmatrix} \frac{\partial N_1}{\partial x} & \frac{\partial N_2}{\partial x} & \dots & \frac{\partial N_8}{\partial x} \\ \frac{\partial N_1}{\partial y} & \frac{\partial N_2}{\partial y} & \dots & \frac{\partial N_8}{\partial y} \\ \frac{\partial N_1}{\partial z} & \frac{\partial N_2}{\partial z} & \dots & \frac{\partial N_8}{\partial z} \end{bmatrix} = [J_1^{-1}]^T \begin{bmatrix} \frac{\partial N_1}{\partial \xi} & \frac{\partial N_2}{\partial \xi} & \dots & \frac{\partial N_8}{\partial \xi} \\ \frac{\partial N_1}{\partial \eta} & \frac{\partial N_2}{\partial \eta} & \dots & \frac{\partial N_8}{\partial \eta} \\ \frac{\partial N_1}{\partial \zeta} & \frac{\partial N_2}{\partial \zeta} & \dots & \frac{\partial N_8}{\partial \zeta} \end{bmatrix} \quad (2.3.20c)$$

Assuming a constant gradient for a control-volume centered at $\xi=0, \eta=0, \zeta=0$, the shape function computational space derivatives are given by

$$\begin{bmatrix} \frac{\partial N_1}{\partial \xi} & \frac{\partial N_2}{\partial \xi} & \dots & \frac{\partial N_8}{\partial \xi} \\ \frac{\partial N_1}{\partial \eta} & \frac{\partial N_2}{\partial \eta} & \dots & \frac{\partial N_8}{\partial \eta} \\ \frac{\partial N_1}{\partial \zeta} & \frac{\partial N_2}{\partial \zeta} & \dots & \frac{\partial N_8}{\partial \zeta} \end{bmatrix} = \begin{bmatrix} -\frac{1}{8} & \frac{1}{8} & -\frac{1}{8} & \frac{1}{8} & -\frac{1}{8} & \frac{1}{8} & -\frac{1}{8} & \frac{1}{8} \\ -\frac{1}{8} & -\frac{1}{8} & \frac{1}{8} & \frac{1}{8} & -\frac{1}{8} & -\frac{1}{8} & \frac{1}{8} & \frac{1}{8} \\ -\frac{1}{8} & \frac{1}{8} & -\frac{1}{8} & -\frac{1}{8} & \frac{1}{8} & \frac{1}{8} & -\frac{1}{8} & -\frac{1}{8} \end{bmatrix} \quad (2.3.20d)$$

Due to the extremely small momentum response times of platelets and monocytes (cf. Table 2.6) the velocity difference between the particle and the surrounding fluid is very small, and often beyond the range of single-precision calculations. Hence, instabilities may arise during particle integration, especially in the near-wall region. Furthermore, the rapid response of particles to the flow field often requires an extremely small time integration step. The variable time-step routine then compares corresponding solutions to evaluate accuracy and time-step acceptability. Differences between corresponding solutions can often drop below single-precision resolution, resulting in the next time-step being set too large for the given system characteristics. Significant particle stalls often result. *To avoid these round-off errors, Lagrangian-style hemodynamic particle tracking should only be conducted in double-precision.* While double-precision calculations are generally more expensive, the resolution of stability issues was found to significantly reduce the total number of calculations required resulting in a moderate decrease in run time.

Most of the systems considered in this study are in-plane, such that particles often encounter a symmetry-plane boundary condition. In regions of significant secondary flow, particle momentum may result in minor symmetry plane encroachments. Such instances were dramatically reduced with the double-precision version of the code. However, a full

domain search is required when any particle crosses the symmetry plane for every additional particle integration step. Considering that 10^6 integration steps may be required for a single particle, it becomes apparent that any symmetry plane encroachment becomes extremely computationally expensive. The current version of the f90 code contains a symmetry-plane particle correction where particles that cross the plane of symmetry, due to momentum driven impaction or collisional diffusion, are artificially restored to the flow field such that full geometry searches are not required. While this condition is only applied to a very small number of particles, the total computational time is generally reduced by an order of magnitude.

Code Performance

Multiprocessor computational speedup and efficiency for the initial and computational portions of the code are given in Figs. 2.3.4a & b. For the initial phase of the code, speedups and efficiencies were relatively low, particularly past four processors. In the computational phase of the code (which accounts for 95+% of the total time), speedups were excellent with efficiencies above 90% through six processors. The overall performance of the code is illustrated in Figure 2.3.4c for 50,000 particles. Despite the relatively low performance of the initialization phase, the overall efficiency is above 80% with the use of four threads. Hence, a four thread allocation seems an appropriate use of computational resources and will be applied in subsequent trials. Typical run times for 50,000 particles over four threads are on the order of two hours. The memory requirement for a geometry with 90,000 cells and 300 transient velocity field time-step arrays is on the order of 4096 MB.

A comparison of run-times using the f90 particle-tracking algorithm versus the commercial software package CFX4.4 is provided in Table 2.7 for several systems of interest. Procedure times reported include generation of the flow field solution. For a single recirculating particle in the asymmetric expansion geometry of Karino and Goldsmith (1977), the f90 algorithm provided a substantial reduction in run-time due to the fact that only one cycle of the flow field solution needed to be computed and stored. Considering 50,000 particles in a realistic femoral geometry (cf. Chapter 4) for approximately ten pulse cycles, an order of magnitude reduction in run time was observed with the f90 algorithm, largely due to

the ‘off-line’ construct and parallel implementation. Finally, for 500,000 particles computed in successive 50,000 particle groups, as required to establish NWRT convergence for a standard femoral anastomosis, the necessity of the implemented f90 algorithm is realized.

Summary

Blood particle transport is characterized by highly pulsatile flow and large discrepancies in luminal and near-wall time scales. Hence, it was found necessary to adopt a highly flexible step-size adaptive integration routine. Particle tracking algorithms that are coupled to commercial flow field solvers often limit user access to step-size control parameters, if active step-size control is even implemented. Furthermore, commercial routines solve for the transient flow field as the particle trajectory is progressed; i.e., transient flow field solutions are usually not stored. Particles that remain in the flow domain for multiple pulse cycles and/or successive simulations within a single domain result in hundreds or even thousands of unnecessary flow field solution steps. To overcome the limitations of available commercial software, blood particle simulations have been computed in an effective ‘off-line’ manner using a separate Fortran 90 (f90) routine. As described, this routine stores all velocity and geometry data in array format for all time-steps of one complete pulse cycle. The f90 routine then repeatedly accesses and interpolates velocity field data for the calculation of particle trajectories over multiple pulses, in this one-way coupled formulation. Furthermore, the off-line f90 code provides full access to all adaptive step-size control parameters, allows for the specification of near-wall approximations, and has been effectively parallelized. The resulting algorithm is capable of computing 50,000 particles within a geometry of 90,000 control-volumes for approximately 10 pulse cycles within 22.5 hours, compared to approximately 200 hours required by a typical commercial CFD package (Table 2.7). Furthermore, once the flow field solution has been generated and stored in array format, each additional group of 50,000 particles may be computed in 2.5 hours. The drawback of the f90 algorithm is the massive amount of storage required to accommodate the transient flow field solution. Nevertheless, the SGI Origin 2400 (NCSC, RTP, NC) was found to be highly capable of maintaining and rapidly accessing the required data in shared memory for the realistic femoral geometry.

Table 2.7: Run times for the f90 and CFX4.4 particle tracking algorithms including flow field solutions

System	Off-line f90 Algorithm	CFX4.4 particle tracking algorithm
Single particle in the axisymmetric expansion	1.5	2.5
50,000 particles in the realistic femoral anastomosis	22.5*	200
500,000 particles computed in groups of 50,000 in the femoral anastomosis	45.0*	2000

* Implementing parallel processing over four threads for the particle solution only.

2.4 Model Validation

2.4.1 Flow Field

The CFD approach described in Section 2.3.1 has been extensively validated in Longest (1999). Briefly, selected case studies for CFD method validation were the two-dimensional pulsatile T-junction experiment of Khodadadi et al. (1988), a three-dimensional end-to-side anastomosis model by Ojha (1993), and an analytic solution for fully developed non-Newtonian pipe flow implementing the Quemada viscosity model. Second-order grid independent temporally resolved solutions generated using CFX4 and supplemented with user-Fortran routines were found to be in good agreement with the experimental and analytic case studies selected (Longest, 1999).

2.4.2 Luminal Trajectories

Validation of the particle tracking algorithm applied in the vessel lumen away from wall boundaries has been established by comparison to the annular expansion results of Karino and Goldsmith (1977). The motion of an elliptical hardened red blood cell in an annular expansion under sinusoidal flow for a specific initialization position was reported as illustrated in the upper panels of Fig. 2.4.1. The lower panels of this figure illustrate the comparable numeric result, including drag and pressure gradient effects in the equation for particle motion. Indeed, the agreement is qualitatively very good. Further details of this

study along with a parametric sensitivity analysis of the effect of various terms in the equation for particle motion are included in Appendix A.1.

As another comparison, numeric pathlines which pass through a certain slice of finite thickness over a time interval can be displayed for comparison to snapshots from planar laser illumination experiments. For the end-to-side geometry with a sinusoidal input waveform, Fig. 2.4.2 illustrates the results of an experiment conducted by Hughes and How (1996) compared to a snapshot of numeric blood element pathlines near peak flow and prior to zero flow in the region of the midplane. Some discrepancy may be attributed to elasticity in the experimental model and differences in the heel geometry, however, agreement is observed to be acceptable.

The near-wall terms in the equation of particle motion are grounded in analytic derivations. Hence, their inclusion is fundamentally valid. As described in Section 1.5, the interaction of blood particles with a responsive vascular surface is dependent on a variety of complex physico-biological mechanisms including particle pseudo-pod extension, receptor-ligand molecular binding, and active surface response. Hence, experimental studies reporting near-wall particle interaction and particle deposition cannot be used to evaluate the validity of the near-wall forces without the inclusion of a particle-wall deposition or wall-interaction model. In this study, the NWRT model for particle deposition has been proposed. Validation of this model, which is inseparably coupled to the validity of the appropriate near-wall expression, is the subject of Chapter 3.

2.4.3 Convergence of the NWRT Parameter

The NWRT model quantifies Lagrangian-based particle wall interactions as a continuous Eulerian parameter. As indicated in Eq. (2.2.33), the NWRT is divided by the total number of particles, resulting in convergent profiles once a sufficient number of particles have been simulated. To establish convergence, groups of 50,000 particles have been initialized randomly at an upstream slice over one pulse period within a model end-to-side femoral anastomosis. Particles are distributed radially consistent with the instantaneous local mass flux and temporally corresponding to the mean flow rate waveform. The simulation is continued until all particles have exited the flow field. Due to the Lagrangian

nature of the particles and the potential for random dispersion, a mean relative error of the NWRT was tested for successive groups of 50,000 particles, defined as

$$\varepsilon_{mean} = \frac{1}{m} \sum_{CV=1}^m \frac{NWRT_{50k \cdot n} - NWRT_{50k \cdot (1+n)}}{NWRT_{50k \cdot (1+n)}} \cdot 100 \quad (2.4.1)$$

where m is the number of control-volume locations with a non-zero NWRT-value and n is an integer. Considering a mean relative error of 10% to represent a sufficiently converged solution, approximately 400,000 monocyte trajectories without dispersion were required for the calculation of the NWRT field (Fig. 2.4.3). Including the random effects of red blood cells required 500,000 monocyte trajectories to satisfy the convergence criterion (Fig. 2.4.3). Results are similar for activated platelets.

Table 2.5: Selected Studies that Model Lift Forces

Researcher	Flow Description		Particle Location w.r.t. a Boundary	Particle Re_p and Re_g Restrictions	Rotational Effects	
	Flow Condition	Type				Re_d
Saffman (1965 and 1968)		unbounded linear shear flow*	laminar flow**	NA	$Re_p \ll Re_g^{1/2}$ Re_p and $Re_g \ll 1$	Y
Cox and Brenner (1968)		bounded parabolic velocity	$\ll 1$	far from wall $a_p \ll h_p$ and $Re_h \ll 1$	$Re_p \ll Re_g^{1/2}$ Re_p and $Re_g \ll 1$	N
Cox and Hsu (1977)		bounded parabolic velocity	$= 0$ and $\ll 1$	near wall $a_p \ll h_p \ll \min(L_G, L_S)$	$Re_p \ll Re_g^{1/2}$ Re_p and $Re_g \ll 1$	N
Vasseur and Cox (1977)		bounded stagnant fluid	$= 0$	near wall	$Re_p \ll 1$	N
Drew (1978)		generalized unbounded 2-D shear flow*	$\ll 1$	NA	$Re_p \ll Re_g^{1/2}$ Re_p and $Re_g \ll 1$	N
Leighton and Acrivos (1985)		linear shear flow* over a flat surface	NDR	contacting wall stationary sphere	$Re_g \ll 1$	N
Drew (1988)		linear shear flow* over a flat surface		distant wall $h_p \gg a_p$	$Re_p \ll Re_g^{1/2}$ Re_p and $Re_g \ll 1$	N
Schonberg and Hinch (1989)		bounded parabolic velocity	$O(1)$ (< 150)	NR	$Re_g \ll 1$	N

Table 2.5 (cont.): Selected Studies that Model Lift Forces

Researcher	Flow Description		Particle Location w.r.t. a Boundary	Particle Re_p and Re_g Restrictions	Rotational Effects	
	Flow Condition	Type				Re_d
Drew et al. (1991)		bounded parabolic velocity	$(a_p/h_p)^2$ * $Re_d \ll 1$	NR	$Re_g \ll 1$	N
McLaughlin (1991)		unbounded linear* shear flow	NDR	NA	Re_p and $Re_g \ll 1$	N
McLaughlin (1993)		linear shear flow* over a flat surface		distant wall $h_p \gg a_p$		N
Cherukat and McLaughlin (1994)		linear shear flow* over a flat surface	NDR	very near wall $h_p \ll \min(L_G, L_S)$ and $h_p/a_p > 0.1$	$Re_p \ll 1$ $Re_p \ll a_p/h_p$ $Re_g \ll (a_p/h_p)^2$	Y
Krishnan and Leighton (1995)		linear shear flow* over a flat surface	NDR	contacting wall rolling sphere	$Re_g \ll 1$	Y

Note: All approximations are for steady flow only

* Implies an unchanging linear velocity profile

** Applies to all models

NA – not applicable

NR – no restriction

NDR – no direct restriction

a_p – particle radius

$d_p = 2a_p$

D – characteristic length scale of channel or boundary

h_p – distance between particle center and a boundary

$$Re_p = \frac{\rho|u - v|d_p}{\mu}$$

$$L_g = \left(\frac{\mu}{\rho\dot{\gamma}}\right)^{1/2}$$

$$Re_D = \frac{\rho UD}{\mu}$$

$$L_s = \frac{\mu}{\rho|u - v|}$$

$$Re_g = \frac{\rho d_p^2 \dot{\gamma}}{\mu}$$