One-dimensional Blood Flow Modelling with the Locally Conservative Galerkin (LCG) Method

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Abstract

One-dimensional blood flow modelling is becoming a useful tool for investigating normal arterial haemodynamics and the dynamics associated with cardiovascular diseases. While previous non-linear one-dimensional models have assessed pressure and flow throughout the systemic arterial tree, essential features of the real system have been excluded. Particularly, there is an important interaction between the left ventricle, systemic arterial and coronary arterial systems, however these have not yet been incorporated into a single model. The model presented in this study includes coronary and systemic arterial circulations, as well as ventricular pressure and an aortic valve that opens and closes ‘independently’ and based on local haemodynamics. The systemic circulation is modelled as a branching network of elastic tapering vessels. The terminal element applied at the extremities of the network is a single tapering vessel which is shown to adequately represent the input characteristics of the downstream vasculature. The coronary model consists of left and right coronary arteries which both branch into two ‘equivalent’ vessels that account for the lumped characteristics of subendocardial and subepicardial regional flows. Since contracting heart muscle causes significant compression of the subendocardial vessels, a time-varying external pressure proportional to ventricular pressure is applied to the distal part of the equivalent subendocardial vessel. The aortic valve consists of a variable reflection coefficient with respect to backward-running aortic waves, and a variable transmission coefficient with respect to forward-running ventricular waves. A realistic ventricular pressure is the input to the system, however an afterload-corrected ventricular pressure is calculated and results in pressure gradients between the ventricle and aorta that are similar to those observed in vivo. The one-dimensional equations of (viscous) fluid flow are solved using the Locally Conservative Galerkin (LCG) method, which provides explicit element-wise conservation, and can naturally incorporate vessel branching. Each component of the model is verified using a number of tests to ensure accuracy and reveal the underlying processes that give rise to complex pressure and flow waveforms. The complete model is then implemented, and simulations are performed with input parameters representing ‘at rest’ and exercise states for a normal adult. The resulting waveforms contain all of the important features seen in vivo, and standard measures of haemodynamic state are found to be normal. In addition, one or several characteristics of some common diseases are imposed on the model and are found to produce haemodynamic changes that agree with experimental observations in published literature.
Declarations

This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

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This thesis is the result of my own investigations, except where otherwise stated. Other sources are acknowledged in the appended bibliography.

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Symbols

\begin{itemize}
\item \(A\): Cross-sectional area \(\text{cm}^2\)
\item \(A_0\): Unstressed cross-sectional area \(\text{cm}^2\)
\item \(c\): Wave speed \(\text{cm/s}\)
\item \(c_0\): Intrinsic Wave speed (i.e. \(c\) when \(A = A_0\)) \(\text{cm/s}\)
\item \(E\): Young’s Modulus \(\text{dynes/cm}^2\)
\item \(h\): Vessel wall thickness \(\text{cm}\)
\item \(k_c\): Proportionality constant for applied coronary external pressure \((\text{dimensionless})\)
\item \(l_e\): Element length \(\text{cm}\)
\item \(L\): Vessel length \(\text{cm}\)
\item \(L_c\): Length of the ‘equivalent’ coronary vessel \(\text{cm}\)
\item \(n\): Current time step \((\text{integer value})\)
\item \(N_{\text{elem}}\): Number of elements
\item \(N_{\text{nodes}}\): Number of nodes
\item \(p\): Internal Pressure \(\text{dynes/cm}^2\) or \(\text{mmHg}\)
\item \(p_{\text{ext}}\): External pressure \(\text{dynes/cm}^2\) or \(\text{mmHg}\)
\item \(p_{LV}\): Afterload corrected ventricular pressure \(\text{mmHg}\)
\item \(p_{LVa}\): Prescribed component of \(p_{LV}\) \(\text{mmHg}\)
\item \(p_{LVa}\): Afterload component of \(p_{LV}\) \(\text{mmHg}\)
\item \(p_{AO}\): Aortic pressure \(\text{mmHg}\)
\item \(u\): Mean velocity over a cross-section \(\text{cm/s}\)
\item \(Q\): Volume Flow \(\text{L/min}\)
\item \(Q_{AO}\): Aortic Flow \(\text{L/min}\)
\item \(Q_{LCA}, Q_{RCA}\): Left & Right Coronary Flow \(\text{L/min}\)
\item \(Q_{Lepi}, Q_{Repi}\): Left & Right Subepicardial Coronary Flow \(\text{L/min}\)
\item \(Q_{Lendo}, Q_{Rendo}\): Left & Right Subendocardial Coronary Flow \(\text{L/min}\)
\item \(r\): Radial direction \(\text{cm}\)
\item \(t\): time \(\text{s}\)
\item \(\Delta t\): time step \(\text{s}\)
\item \(R\): Vessel radius \(\text{cm}\)
\item \(R_t\): Terminal reflection coefficient \((\text{dimensionless})\)
\item \(R_{Vr}\): Valve reflection coefficient \((\text{dimensionless})\)
\item \(RVCT\): Rapid Valve Closing Time \(\text{ms}\)
\end{itemize}
<table>
<thead>
<tr>
<th>Symbol</th>
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<tr>
<td>RVOT</td>
<td>Rapid Valve Opening Time</td>
</tr>
<tr>
<td>$T_{VP}$</td>
<td>Valve transmission coefficient</td>
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<tr>
<td>$x$</td>
<td>Axial direction</td>
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<tr>
<td>$w$</td>
<td>Characteristic variable</td>
</tr>
<tr>
<td>$w_{1in}$</td>
<td>Incoming characteristic at the inlet</td>
</tr>
<tr>
<td>$w_{1p}$</td>
<td>Component of $w_{1in}$ due to ventricular pump</td>
</tr>
<tr>
<td>$w_{1r}$</td>
<td>Component of $w_{1in}$ due to reflection of backward-running waves in the aorta</td>
</tr>
<tr>
<td>$Y = 1/Z$</td>
<td>Characteristic Admittance</td>
</tr>
<tr>
<td>$Z = \rho c / A$</td>
<td>Characteristic Impedance</td>
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<td>$C$</td>
<td>Vector of source terms for the characteristic system</td>
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<tr>
<td>$f_r$</td>
<td>Vector of boundary flux terms for $\Omega$</td>
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<td>$f_{re}$</td>
<td>Vector of boundary flux terms for $\Omega_e$</td>
</tr>
<tr>
<td>$F$</td>
<td>Vector of conservative variables</td>
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<tr>
<td>$F_U = \frac{\partial F}{\partial U} = H$</td>
<td>Jacobian matrix of the characteristic system</td>
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<td>$A$</td>
<td>Vector of eigenvalues</td>
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<tr>
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<td>Left Eigenvector</td>
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<td>$[K], [L]$</td>
<td>Coefficient Matrices for the Global Taylor-Galerkin Method</td>
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<td>$M$</td>
<td>Mass Matrix for the Global Taylor-Galerkin Method</td>
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<td>$N$</td>
<td>Finite element shape function</td>
</tr>
<tr>
<td>$S$</td>
<td>Vector of source terms for the non-linear system</td>
</tr>
<tr>
<td>$S_U = \frac{\partial S}{\partial U}$</td>
<td>Vector of primitive variables</td>
</tr>
<tr>
<td>$U = [A u]^T$</td>
<td>Vector of primitive variables</td>
</tr>
</tbody>
</table>

- $\alpha$: Womersley number (dimensionless)
- $\beta$: Parameter involving vessel material properties $(E, h & \sigma)$ and $A_0$ dynes/cm$^3$
- $\lambda_1, \lambda_2$: Eigenvalues of the characteristic system dynes/cm$^3$
- $\Gamma, \Gamma_e$: Boundary of $\Omega$ & $\Omega_e$ respectively
- $\mu = 0.035$: Blood viscosity poise
- $\nu = \frac{\mu}{\rho}$: Kinematic viscosity g/cm$^3$
- $\rho = 1.06$: Blood density g/cm$^3$
- $\sigma = 0.5$: Poisson ratio of vessel wall (dimensionless)
- $\omega$: Angular frequency rad/s
- $\Omega, \Omega_e$: Global Domain & Elemental Sub-domain
Chapter 1

Introduction

One-dimensional modelling is becoming a useful tool for gaining a better understanding of blood flow in the arterial circulation and how it is affected by various interventions or diseases [1, 2, 3, 4, 5, 6]. At present, 3D modelling of the entire arterial tree is not feasible. Apart from the unavailability of precise information regarding geometry and material properties, the computational time required to model such an extensive network of branching vessels, including the fluid-structure interaction between blood and vessel walls, is simply too great. However, it has long been recognized that since the wavelengths of the pressure-flow waves produced by the heart are much greater than the diameter of the vessels, it is valid to consider flow to be quasi one-dimensional [7, 8, 9, 10]. Chapter 2 presents the one-dimensional equations of flow expressed in terms of vessel cross-sectional area $A$, velocity $u$ and pressure $p$. Pressure is related to $A$ via the chosen non-linear elastic wall law (i.e. $p = p(A)$). There are indeed several to choose from (for example see [11]) which reflects the fact that the wall law is an empirical and/or mathematical simplification of the true mechanics of vessel walls, which are anisotropic and not perfectly cylindrical. It is also well-known [1, 12, 13] that the arterial wall is a visco-elastic material and thus pressure is determined not only by $A$ but its derivatives also, although these effects are generally considered small enough to be ignored [14]. Another consideration is the treatment of blood viscosity. While various approximations have been used [2, 9, 10], most authors [6, 14, 15, 16] calculate its effects in 1D by using an assumption of fully-developed steady flow with a parabolic velocity profile over a given cross-section (Poiseuille flow).

Given the equations governing flow in a single vessel, a branching network can be constructed by accounting for bifurcations and trifurcations. The geometry and material properties suitable for and used in past 1D models of the systemic arterial tree are almost exclusively sourced from work by Westerhof and Noordergraaf [8, 17], although these have been adjusted by Wang and Parker [18] and supplemented by Avolio [1]. Since the governing equations are hyperbolic and in physiological systems, flow is subsonic, boundary conditions are required at the inlet and at the terminals. Most previous models of the arterial tree [1, 2, 5, 6] have used the aorta as the input by prescribing a sine wave pressure [5] or an idealised or representative aortic flow [1, 2, 6, 19]. Both of these approaches avoid modelling the aortic valve. In a linear model, Westerhof et al [8]
Chapter 1. Introduction

used a waveform synthesizer to generate ventricular pressure or flow and an electrical network analog representing the aortic valve. The only non-linear model to incorporate an aortic valve is by Schaaf and Abbrecht [9] who prescribed aortic flow from a ventricular pressure gradient and an idealised (either open or closed) aortic valve. Neither of these models reflected the behaviour of the opening or closing valve which occurs over a finite time. In another linear model, Wang and Parker [18] modelled the closing aortic valve by specifying a linearly increasing aortic reflection coefficient (so that backward-running waves were variably reflected), but the timing of the closure was specified a priori. There was also no accounting for valve opening. In addition, none of these models demonstrated the effects of afterload on ventricular pressure. The afterload of the ventricular pump is the aortic pressure which the ventricle must overcome to achieve outflow. Afterload depends on ventricular performance which is the initial source of pressure and also on downstream haemodynamics such as reflected waves caused by bifurcations and vessel tapering. Conversely, the ventricle increases its force of contraction as a result of increased afterload. The haemodynamics of the ventricle and vasculature are thus highly coupled (the relationship is known as ventriculo-vascular coupling). Thus, in Chapter 3, in addition to providing a physical model of the arterial tree, a more realistic representation of ventricular pressure and the aortic valve is presented. This is done by first prescribing a physiologically realistic ventricular pump pressure. The valve, represented by a variable transmission coefficient from the perspective of the ventricle and a variable reflection coefficient from the perspective of the aorta, opens and closes ‘independently’. It opens when the pressure difference between ventricle and aorta rises above an opening pressure and it closes when aortic flow begins to fall below zero, both of which are physiological mechanisms. The valve also opens and closes over the finite times known clinically as Rapid Valve Opening Time (RVOT) and Rapid Valve Closing Time (RVCT) [20, 21]. Furthermore, the model includes an afterload-corrected ventricular pressure. This is calculated as the prescribed pressure plus an additional pressure due to the time-varying afterload.

Because of the extensive branching structure of the arterial tree and the fact that flow characteristics in very small vessels are quite different to those in large vessels, it is necessary to terminate the model at some point and represent all downstream parts of the tree in some ‘lumped’ way. There have been several approaches to this problem. The first is to represent the downstream network by a lumped resistance [1, 4, 5, 8, 9] and leads to the use of a reflection coefficient such that any forward-travelling change in pressure is reflected at the terminal by a given proportion. It has been recognized however [14] that the simple resistance terminal fails to account for vessel compliance which would result in a reflection coefficient that decreases as the frequency of a given harmonic of the pressure change increases, and would also introduce a frequency-dependant phase shift (that is, the reflection coefficient is complex and frequency-dependant). This has led to the use of the Windkessel element [2, 6, 14, 16], which consists of two resistors and a capacitor. This significantly improves the representation of downstream effects, however Olufsen [19] has pointed out that the Windkessel element still does not represent the effects of wave propagation which causes ripples in the input impedance spectrum (and thus the input reflection coefficient spectrum). Thus several authors have investigated directly applying the input impedance of linearised branching networks at the terminals [19, 22], however these are difficult to apply naturally to a non-linear model. Thus, also in Chapter 3, a new method is
investigated, where a single tapering vessel is used as the terminal element. This draws from several studies that have modelled the lumped behaviour of the entire arterial tree using one or two tapering vessels [23, 24, 25], although unlike these studies, linearity of pulse propagation is not assumed. The benefits of this method are that a tapering terminal vessel can naturally be incorporated into the non-linear model with no more coding than for the simple resistance terminal, and that the input characteristics can be manipulated by simply adjusting the vessel length and the taper gradient.

The performance of the heart and thus haemodynamics in general are highly dependant on coronary flow and vice versa. Compromise of coronary flow due to aortic valve stenosis or coronary arteriosclerosis can critically reduce the delivery of oxygen and other metabolic substrates to the myocardium and may lead to cell death and myocardial infarction. The coronary circulation provides blood flow to the heart muscle (myocardium) and begins in the aortic root behind the valve cusps via the left and right coronary arteries (LCA and RCA). These two main branches feed the left and right sides of the heart respectively. The coronary arterioles and capillaries throughout the heart wall are often functionally classified into subendocardial and subepicardial regions. This is because intramyocardial pressure (pressure inside the heart muscle) is greatest in regions close to the inner wall (endocardium) of the heart and least in regions close to the outer wall (epicardium). While the variation of intramyocardial pressure from endocardium to epicardium is smooth, the vasculature is often classified as being in a region of either high or low intramyocardial pressure. The high intramyocardial pressure developed during heart contraction causes significant compression of subendocardial vessels. However, this is not the case for subepicardial vessels where the intramyocardial pressure is low. Figure 1.1 shows an illustration of the idealised coronary flow dynamics during systole and diastole (see [26] for a similar illustration and more detailed explanation). In the subendocardial ‘layer’ of the left ventricle (LV) during systole (Figure 1.1a), the external pressure on coronary microvasculature is significant and has the effect of a) squeezing blood out of the subendocardial vessels and b) causing a reduction or even reversal in overall left coronary flow [26, 27]. The compression also occurs in the right ventricle (RV) but is less pronounced than in the LV which generates much greater pressures [28]. During diastole (Figure 1.1b), the heart muscle relaxes and thus removes the external pressure on the endocardial coronary vessels, thereby restoring endocardial flow in the LV. Both endocardial and epicardial flows then gradually decline during diastole as aortic pressure decreases.

Huo and Kassab [29] and Smith et al [30] have modelled blood flow in the coronary tree, however both of these studies did not take into account the external pressure applied by the contracting myocardium. Guiot et al [31] and Rammos et al [32] provided more complete models of coronary flow during the whole cardiac cycle by imposing a time-varying external pressure (equal to ventricular pressure) on subendocardial vessels. These models reproduced the physiological features of left coronary flow, but the effects of systemic arterial haemodynamics on coronary flow were not accounted for. In Chapter 3, in addition to the arterial model, a coronary model is incorporated. This consists of left and right coronary arteries which both bifurcate into two ‘equivalent’ vessels that represent the lumped characteristics of the subendocardial and subepicardial microvasculature on the left and right sides of the coronary tree. Drawing from studies that have
modelled the entire arterial tree with one or two tapering vessels [23, 24, 25], these equivalent vessels have a cross-sectional area with linear taper to account for reflections at branching sites and actual vessel taper. An external pressure directly proportional to ventricular pressure is then applied to the distal (i.e. further from the heart) part of the subendocardial vessels to account (in an approximate way) for the spatial and temporal variation in the intramyocardial pressure. It would be straightforward to include a more complete model of coronary geometry (as in [32] for example), however the simple model adequately reproduces the features seen in physiological waveforms [28, 31, 33, 34, 35], and is useful for investigating the effects of various disease states on coronary flow.

Various numerical and analytical methods have been used to solve the governing non-linear equations. The classic linear analytical solution known as Womersley flow [36] is a Fourier technique and enables calculation of axi-symmetric velocity profiles by treating each harmonic separately and adding the results together. This technique is commonly used [1, 22, 29] along with one-dimensional electrical analogs [8] but these do not account for non-linear effects, which are important particularly in the large arteries [5, 15, 37]. The non-linear equations have been discretised using the finite difference method [2, 14, 38], as well as various finite element methods such as the characteristic [9], Galerkin Least Squares [6] and Discontinuous Galerkin methods [3, 4, 5]. In Chapter 4, the recently developed Locally Conservative Galerkin (LCG) finite element method [39] is presented for use in solving the governing equations. The LCG method treats each element as an independent subdomain with weakly imposed Neumann boundary conditions. Information is transferred between subdomains via a post-processed boundary flux term. Previous work [39, 40, 41] has shown that in one-dimensional convection-diffusion problems, LCG produces identical results to Global Galerkin methods, but with the advantage that local conservation is explicitly enforced. The LCG method allows control over individual elements and thus eliminates the need for large matrix inversions, significantly reducing computation time and

Figure 1.1: Illustration of coronary flow dynamics during a) systole and b) diastole. Red and green boxes represent subendocardial and subepicardial vessels respectively. Red arrows indicate flow direction.

[Diagram of coronary flow dynamics during systole and diastole]
simplifying code. In addition, it is straightforward to include discontinuities and vessel branching points, where multiple nodes occupy the same spatial location.

In Chapter 5, various tests are performed to both verify the numerical scheme and to reveal the underlying processes at work in each component of the model. As well as comparisons with previously published data, these include demonstrations of wave reflection and transmission at branching points, an assessment of the suitability of tapering vessels as terminal elements and demonstrations of aortic valve function and the application of external pressure. Chapter 6 then provides tests of the full model which includes ventricular pressure, aortic valve and systemic and coronary arterial circulations. Waveforms for a normal human adult at rest and during exercise are obtained and found to contain all of the important features seen in real physiological waveforms measured \textit{in vivo}. Finally, one or several characteristics of various disease states are simulated and the changes observed are found to agree with published experimental work.

Chapter 7 provides some preliminary work on patient-specific three-dimensional modelling. Patient-specific modelling is a relatively new idea \cite{13, 42, 43} and involves using actual patient data (usually CT or MRI scans) to construct the geometry of a small arterial segment, such as the region surrounding a specific lesion or bifurcation. Although only a small anatomical region can be modelled in 3D, some investigators \cite{6, 13, 44} have suggested multi-dimensional models, where a small 3D segment is inserted into a more complete 1D network model. Similar to many others \cite{13, 42, 43, 45, 46, 47, 48}, this study focuses on the (normal) carotid bifurcation. A demonstration of the preprocessing stages required for patient-specific modelling is given. Then a comparison is made between the 3D results and the results of a 1D model representing the same bifurcation. While various assumptions are made, such as a rigid wall, the 3D and 1D results are shown to be very similar. This work may be extended in the future to allow patient-specific multi-dimensional modelling.
Chapter 2

One-Dimensional Equations for Blood Flow

2.1 Governing Equations for an Elastic Vessel

Given a cylindrical vessel with elastic walls, it can be shown [49] that in one dimension, continuity of mass and momentum leads to the following governing equations in terms of cross-sectional area ($A$), mean velocity over a cross-section ($u$) and internal pressure ($p$),

\[
\frac{\partial A}{\partial t} + \frac{\partial (Au)}{\partial x} = 0 \tag{2.1}
\]

\[
\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x} + \frac{1}{\rho} \frac{\partial p}{\partial x} - \frac{1}{\rho} \frac{\partial \tau}{\partial x} = 0 \tag{2.2}
\]

where $\rho \approx 1.06$ g/cm$^3$ is blood density [50], assumed constant for blood which is essentially incompressible, and $\tau = \mu \frac{\partial u}{\partial r}|_R$ is the shear stress, where $\mu$ is viscosity (approximately 0.035 poise for blood), $r$ is the radial direction in three-dimensional cylindrical coordinates, and $R$ is the vessel radius.

There are viscous and inertial components to the shear stress term [2, 9, 51], and these are proportional to $u$ and $du/dt$ respectively. However, it is common [3, 15, 38, 52] to ignore the inertial component which is relatively insignificant at low values of the Womersley parameter [36] $\alpha = R \sqrt{\omega \rho / \mu}$ where $\omega$ is the angular frequency of a given harmonic. For example, the inertial component would be most significant in a large artery (say $R = 3.5$cm) with a high frequency oscillation. Using a maximum expected frequency of 5 Hz, (since the significant frequency components of aortic blood pressure and flow are generally less than this), $\alpha = 3.3$. Referring to [9], pressure drops due to the inertial component only become significant at higher values of $\alpha$, thus neglecting this component is justified.

6
Chapter 2. One-Dimensional Equations for Blood Flow

Various formulations for the viscous resistance are possible and the field of blood rheology is a complex one [53]. However in the major arteries flow is often considered to be laminar and the expression for Poiseuille flow, which assumes fully developed ($\frac{\partial u}{\partial x} = 0$), steady ($\frac{\partial u}{\partial t} = 0$) flow, is used as follows:

$$\frac{dp}{dx} = \frac{d\tau}{dx} = \frac{8\mu Q}{\pi R^4} = \frac{8\pi \mu u}{A}$$

(2.3)

where $Q = Au$ is the volume flow. This expression will not be valid in arterioles or capillaries where flow is non-Newtonian (when the size of red blood cells becomes significant compared to vessel diameter) nor when flow is turbulent [10], which may occur in some disease states [54].

Incorporating Eq.(2.3) into Eq.(2.2), the coupled system of equations governing blood flow can be expressed in conservation form:

$$\frac{\partial U}{\partial t} + \frac{\partial F}{\partial x} = S$$

(2.4)

where $U = \begin{bmatrix} A \\ u \end{bmatrix}$, $F = \begin{bmatrix} uA \\ \frac{u^2}{2} + \frac{p}{\rho} \end{bmatrix}$ and $S = \begin{bmatrix} 0 \\ -8\pi \mu u/A \end{bmatrix}$

Since there are three variables, a third equation is required to close the system. This constitutive equation describes how vessel area varies with pressure and thus deals with the fluid-structure interaction of the problem. Table 2.1 shows various pressure-area relations that have been used in the past. These may be categorised as linear elastic models, where pressure is linearly related to area; non-linear elastic models, where this relation is non-linear; collapsible tube models, where special effort is made to accommodate tubes that can collapse as well as distend; and visco-elastic models, which account for the viscoelasticity of the vessel wall. While the visco-elastic models are the most complete, they are also the most complicated. Since the effects of wall viscosity are generally assumed to be small, a non-linear elastic relation is usually sufficient. The most common relation used in studies of this type is that used by Formaggia [55], Olufsen [56] and others (see Table 2.1) and is written here (following [5, 55]) as

$$p = p_{ext} + \beta \left( \sqrt{A} - \sqrt{A_0} \right)$$

(2.5)

where $p_{ext}$ is the external pressure from surrounding tissue, $A_0$ is the area when there is zero transmural pressure (i.e. $p = p_{ext}$) and $\beta$ accounts for the material properties of the elastic vessel (although it should be noted that $A_0$ also appears):

$$\beta = \frac{\sqrt{\pi h} E}{A_0(1 - \sigma)^2}$$

(2.6)

where $h$ is the vessel wall thickness, $E$ is Young’s Modulus and $\sigma$ is the Poisson ratio, assumed to be 0.5 (i.e. the vessel wall is incompressible). All of these values assumed to be independent of transmural pressure.
The intrinsic wave speed of a vessel is related to $\beta$ via

$$c_0 = \sqrt{\frac{\beta\sqrt{A_0}}{2\rho}} = \sqrt{\frac{hE}{2\rho R_0 (1-\sigma^2)}}$$

(2.7)

where the second expression is called the Moens-Korteweg equation (with $A_0 = \pi R_0^2$) and relates the material properties of the vessel to its intrinsic wave speed, that is, the speed at which an infinitesimally small pulse would propagate in an initially unstrained (i.e. $A(t=0) = A_0$ everywhere) vessel. Infinitesimally small pulses in initially stressed (i.e. $A(t=0) = A$ everywhere) vessels propagate at a slightly higher wave speed,

$$c = \sqrt{\frac{\beta\sqrt{A}}{2\rho}}$$

(2.8)

Note that finite amplitude pulses do not propagate at a speed $c$, but at $|u+c|$, as will be discussed in Section 2.2. As a consequence, the peak of a pressure wave propagates faster than its foot which would inevitably lead to shock formation (where the peak catches up with the foot) in a long enough tube. However, shocks generally do not form in the real arterial system since the

<table>
<thead>
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<th>Table 2.1: Various pressure-area relations used in the literature</th>
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<td><strong>Linear Elastic Models</strong></td>
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<tr>
<td>Raines et al [14]</td>
</tr>
<tr>
<td>$A = A_0 + a (p - p_{ext})$</td>
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<tr>
<td>Rammus et al [32]</td>
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<tr>
<td>$p = p_{ext} + \frac{Eh}{2R_0} \left( \frac{A}{A_0} \right) - 1$</td>
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<td><strong>Non-linear Elastic Models</strong></td>
</tr>
<tr>
<td>Formaggia et al [3, 44, 57]</td>
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<tr>
<td>$p = p_{ext} + \frac{\sqrt{\pi h_0 E}}{1-\sigma^2} \left( \sqrt{A} - \sqrt{A_0} \right)$</td>
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<tr>
<td>Urquiza et al [6]</td>
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<td>Canic and Kim [58]</td>
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<tr>
<td>$p = G_0 \left( \frac{A}{A_0} \right)^{\gamma/2} - 1$</td>
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<tr>
<td>Smith et al [30]</td>
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<td>Payne [59]</td>
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<tr>
<td>$p = p_{ext} \left( 1 + \frac{b}{a} \right) + \frac{h_0 E}{2R_0} \left( \frac{A}{A_0} \right)^{\gamma/2} - 1$</td>
</tr>
<tr>
<td>Porenta et al [16]</td>
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<tr>
<td>Stergiopulos et al [2]</td>
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<tr>
<td>$A = A_0 \left[ 1 + a (p - p_{ext}) + b (p - p_{ext})^2 \right]$</td>
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<tr>
<td>Kufahl and Clark [60]</td>
</tr>
<tr>
<td>$A = A_0 \left( 1 + \frac{2}{\sigma} \ln \left( \frac{\sigma}{\sigma_{ext}} \right) \right)$, $\frac{\partial A}{\partial p} = \frac{a}{p}$</td>
</tr>
<tr>
<td><strong>Collapsible Tube Models</strong></td>
</tr>
<tr>
<td>Shapiro [10]</td>
</tr>
</tbody>
</table>
| $P = \left\{ \begin{array}{ll} 
\rho \varepsilon^2 \left( \frac{A}{A_0} - 1 \right) 
\frac{\mu}{\pi} \left( 1 - \left( \frac{A}{A_0} \right)^{-1.5} \right) 
\frac{\partial A}{\partial p} \geq 1 
\frac{\mu}{\pi} \left( 1 - \left( \frac{A}{A_0} \right)^{-1.5} \right) 
\frac{\partial A}{\partial p} < 1 
\end{array} \right.$ |
| Brook et al [61]                                              |
| $p = p_{ext} + \frac{E}{12\sqrt{1-\varepsilon^2}} \left( \frac{\gamma}{\beta} \right)^3 \left( \frac{A}{A_0} \right)^{10} - \left( \frac{A}{A_0} \right)^{-1.5}$ |
| **Viscoelastic Models**                                       |
| Formaggia et al [57]                                          |
| $p = p_{ext} + \rho_c h \frac{\partial^2 u}{\partial t^2} - \frac{d^2 u}{dt^2} - a \frac{\partial^2 u}{\partial x^2} - c \frac{\partial^2 u}{\partial x^2} + b \eta$, $\eta = \frac{\sqrt{\Delta A}}{\sqrt{\sigma}}$ |
| Reuderink et al [15]                                          |
| $\frac{\partial A}{\partial p} = C_{v} \frac{\partial (\rho u^2 + p u^3)}{\partial \rho u}$ |
| Kitawaki and Shimizu [62]                                     |
| $\Delta p = \frac{1}{C_v} \left( \Delta A + \int_0^t \frac{dA(u)}{dt} du \right)$ |
| Kitawaki and Shimizu [62]                                     |
| $\Delta p = \frac{1}{C_v} \left( \Delta A + \int_0^t e^{-\beta(u-v)} \frac{dA(u)}{dt} du \right)$ |
frequency of the pulses and the length of the vessels are too low.

2.2 The Characteristic System

The system of equations Eq.(2.4) is non-linear and highly coupled, making direct analytical solutions impossible. Thus, a numerical solution is required. However when implementing the numerical solution, it is useful to have available a linearised de-coupled form of the equations which can be used when applying boundary conditions. Following the work of Formaggia et al and Sherwin et al [3, 5], the system is first written in quasi-linear form, which is then used to derive the characteristic system. By taking the spatial derivative of Eq.(2.5)

\[ \frac{\partial p}{\partial x} = \frac{\partial p_{ext}}{\partial x} + \frac{\beta}{2\sqrt{A}} \frac{\partial A}{\partial x} - \frac{\beta A_0}{2\sqrt{A_0}} \frac{\partial A_0}{\partial x} + \left( \sqrt{A} - \sqrt{A_0} \right) \frac{\partial \rho}{\partial x} \] (2.9)

the number of independent variables in the momentum equation can be reduced to two by replacing \( \frac{\partial p}{\partial x} \) with Eq.(2.9). Using Eq.(2.1), the quasi-linear form is

\[ \frac{\partial U}{\partial t} + H \frac{\partial U}{\partial x} = C \] (2.10)

where

\[ U = \begin{bmatrix} A \\ u \end{bmatrix}, H = \begin{bmatrix} u & A \\ \frac{\beta}{2\sqrt{A}} & u \end{bmatrix}, \]

\[ C = -\frac{1}{\rho} \begin{bmatrix} 8\pi \mu \frac{u}{A} + \frac{\partial p_{ext}}{\partial x} - \beta \frac{\partial A}{\partial x} + \left( \sqrt{A} - \sqrt{A_0} \right) \frac{\partial \rho}{\partial x} \\ 0 \end{bmatrix} \]

The eigenvalues (\( \Lambda \)) of Eq.(2.10) are given by \(|\Lambda I - H| = 0\) [63]. For physiological flows, \( u < c \), so there are two real eigenvalues and the system is hyperbolic [5, 50].

\[ \Lambda = \begin{bmatrix} \lambda_1 \\ \lambda_2 \end{bmatrix} = u \pm \sqrt{\frac{\beta \sqrt{A}}{2\rho}} = \begin{bmatrix} u + c \\ u - c \end{bmatrix} \] (2.11)

Next a set of characteristic variables [49, 64] is found. The set of left eigenvectors (\( l_i \)) are first found by solving the equation \( l_i H = \lambda_i l_i \), which leads to the left eigenmatrix

\[ L = \begin{bmatrix} l_1^T \\ l_2^T \end{bmatrix} = \begin{bmatrix} c/\rho & 1 \\ -c/\rho & 1 \end{bmatrix} \] (2.12)

Noting that \( LH^{-1} = \Lambda \), premultiplying Eq.(2.10) by \( L \) gives (in component form, \( i = 1, 2 \))

\[ l_i \frac{\partial U}{\partial t} + \lambda_i l_i \frac{\partial U}{\partial x} + l_i C = 0 \] (2.13)
Then the characteristic variables are defined by

\[ dw_i = \left( l_i \frac{dU}{dt} + l_i \mathbf{C} \right) dt \quad (2.14) \]

If this relation is integrable [64], the characteristic system can be expressed as

\[ \frac{\partial w_i}{\partial t} + \lambda_i \frac{\partial w_i}{\partial x} = 0 \quad (2.15) \]

If, in the region where the characteristic system must be valid (i.e. near the boundaries), a restriction is made that the spatial derivatives of \( \beta, A_0 \) and \( p_{ext} \) are zero, and if viscous resistance is small, then \( C \approx 0 \) and the following expression can be integrated:

\[ dw_{1,2} = du \pm \sqrt{\frac{\beta}{2\rho}} A^{-3/4} dA \quad (2.16) \]

where the expression for \( c \) has been substituted from Eq.(2.8). When \( C = 0 \) the characteristic variables are constant along the characteristic lines defined by \( \frac{dx}{dt} = \lambda \) and are called Riemann invariants which, upon integration, are

\[ \begin{bmatrix} w_1 \\ w_2 \end{bmatrix} = \begin{bmatrix} u + 4c \\ u - 4c \end{bmatrix} \quad (2.17) \]

Finally, the primitive variables can be calculated from the characteristic variables by adding or subtracting the two equations in Eq.(2.17), giving

\[ A = \frac{(w_1 - w_2)^4}{1024} \left( \frac{\rho}{\beta} \right)^2 \quad (2.18) \]

\[ u = \frac{1}{2} (w_1 + w_2) \quad (2.19) \]

The physical interpretation of the characteristic system is that pressure and velocity wavefronts propagate forwards (by convention, away from the heart) at a speed of \( u + c \) and backwards (towards the heart) at \( u - c \). A wavefront may be considered to be a particular point on a pulse [50] (for example, the peak or the foot) and will be discussed further in Section 2.4. Throughout this thesis, the terms ‘wave’ or ‘pulse’ refer to a finite amplitude, finite duration change in pressure and velocity, while a ‘wavefront’ strictly refers to an infinitesimal change in one of the characteristic variables, \( w_1 \) or \( w_2 \). Forward-running wavefronts are initially generated by the contraction of the heart which squeezes blood into the aorta. These wavefronts, which compose the forward-running pressure pulse, then propagate throughout the entire arterial tree. At branching points or whenever there is a change in vessel properties, the wavefronts are reflected and travel back towards the heart. These may re-reflect before reaching the heart, and thus the pressure and flow measured at any point in the arterial system may be explained as the combination of many forward and backward-running wavefronts.
Chapter 2. One-Dimensional Equations for Blood Flow

2.3 Boundary Conditions

The characteristic system is useful for calculating boundary conditions because the variables at any given point may be considered to arise from the combination of forward and backward-travelling wavefronts. Thus specifying boundary conditions becomes a matter of specifying the incoming wavefront (which can only arise from outside the computational domain) and predicting the effects of the outgoing wavefront on the boundary node (which cannot be affected by phenomena outside of the computational domain).

Since \( u < c, \lambda_1 > 0 \) and \( \lambda_2 < 0 \) (i.e. the system is subsonic), and so one boundary condition must be specified at both the inlet and outlet. In both cases, the outgoing characteristic may be calculated via linear extrapolation in the \( x-t \) plane, where for the next time step \( n+1 \),

\[
\left. w_2^{n+1} \right|_{x=x_0} = w_2^n |_{x=x_0 - \lambda_1^2 \Delta t} \tag{2.20}
\]

and

\[
\left. w_1^{n+1} \right|_{x=x_L} = w_1^n |_{x=x_L - \lambda_2^2 \Delta t} \tag{2.21}
\]

at the inlet and outlet respectively, where \( x_0 \) and \( x_L \) are the coordinates of the inlet and outlet. The incoming wave can be specified via a prescribed \( p, A \) or \( u \), and may be done in two ways. Traditionally, prescribing pressure at the inlet, for example, means forcing the pressure to be a certain value on the boundary node. This may seem obvious, but prescribing pressure in this way assumes \textit{a priori} knowledge regarding the timing and size of backward-running waves. It would be more intuitive to set a prescribed \textit{forward} pressure, that is, the forward component of the pressure, which will be equal to the actual pressure only if no backward-running waves arrive at the boundary. If backward-running waves do arrive at the boundary, the \textit{actual (or assigned) pressure at the boundary will not be equal to prescribed forward pressure}, but will consist of (prescribed) forward and (run-time calculated) backward components. Thus in what follows, \textit{prescribed pressure} in the traditional sense will be differentiated from \textit{prescribed forward pressure}. The same may be said for prescription of \( A \) or \( u \).

2.3.1 Prescribed Area, Pressure and Velocity

In general, prescribing area, pressure or velocity on a boundary node is achieved by simply setting the appropriate value on the boundary node after all other nodal values have been calculated. In this case, if area is being prescribed at the inlet, the velocity at the inlet would not be altered. This is valid for the Global Galerkin method, but for the LCG method, both primitive variables \((u \text{ and } A)\) on the boundary must be assigned, as there is no flux contribution from an adjacent element beyond the boundary (see Section 4). Thus at the inlet, the non-prescribed variable can be calculated from the outgoing characteristic via Eq.(2.20) and Eq.(2.11), while the prescribed value can be assigned directly.

To prescribe area at the inlet,

\[
A_{in}^{n+1} = A_{in}^{n+1} \tag{2.22}
\]

\[
u_{in}^{n+1} = w_2^{n+1} + 4A_{in}^{n+1} \sqrt{\frac{\beta}{2\rho}}
\]
where the over-bar represents a prescribed value, and the subscript \( \text{in} \) refers to the inlet node.

To prescribe pressure at the inlet,

\[
A_{\text{in}}^{n+1} = \left( \frac{p_{\text{in}}^{n+1} - p_{\text{ext}}}{\beta} + \sqrt{A_0} \right)^2
\]

\[
u_{\text{in}}^{n+1} = \frac{w_{2}^{n+1}}{2} + 4A_{\text{in}}^{n+1} \sqrt{\frac{T}{2\rho}}
\]  

(2.23)

To prescribe velocity at the inlet,

\[
A_{\text{in}}^{n+1} = \left( \frac{u_{\text{out}}^{n+1} - w_{2}^{n+1}}{64} \right)^4 \left( \frac{\beta}{\rho} \right)^2
\]

\[
u_{\text{in}}^{n+1} = \bar{u}^{n+1}
\]  

(2.24)

Similar expressions can readily be obtained for prescribing values at the outlet.

### 2.3.2 Prescribed Forward Area, Pressure and Velocity

Prescribing the forward component of a variable can be achieved by prescribing the incoming characteristic \((w_1)\) [3]. The actual values assigned to both \(A_{\text{in}}\) and \(u_{\text{in}}\) are determined at run time based on the prescribed incoming characteristic and the current value of the outgoing characteristic (from Eq. (2.20)) which is not known \textit{a priori}. Thus to prescribe forward area, rearrange (2.18) to give

\[
u_{1\text{in}}^{n+1} = w_{2}^{0} + 8 \left( A_{\text{in}}^{n+1} \right)^{1/4} \left( \frac{\beta}{2\rho} \right)
\]  

(2.25)

To prescribe forward pressure, substitute (2.5) into (2.25)

\[
u_{1\text{in}}^{n+1} = w_{2}^{0} + 4 \sqrt{\frac{T}{\rho}} \left( \frac{p_{\text{out}}^{n+1} - p_{\text{ext}}}{\rho} + \beta \sqrt{A_0} \right)
\]

(2.26)

Finally, forward velocity may be prescribed by rearranging (2.19)

\[
u_{1\text{in}}^{n+1} = 2\bar{u}^{n+1} - w_{2}^{0}
\]  

(2.27)

In these equations, \(w_{2}^{0}\) is the initial value of \(w_2\) and is also equal to the value of \(w_2\) at any time if no backward-running waves reach the inlet. The values assigned to \(A_{\text{in}}^{n+1}\) and \(u_{\text{in}}^{n+1}\) can then be calculated from one of Eq.(2.25), (2.26) or (2.27) and Eqs.(2.20), (2.18) and (2.19). Since prescribing the forward component of a variable is more physically intuitive, this approach will be adopted in the following sections unless otherwise stated. Prescribing backward components of the variables at the outlet could also be achieved in a similar manner. However, in keeping with the fact that the heart is the force generator and that the rest of the arterial system may be considered passive, the incoming characteristics at the terminal vessels are normally calculated using an approximation of the downstream circulation (see Section 3.4).
2.4 Lagrangian Solution for Uni-Directional Pulses in Uniform Vessels

In the foregoing sections, the concept of ‘wavefronts’ has been introduced. It is useful to consider a pressure-velocity pulse of finite size as being made up of an infinite number of these vanishingly small wavefronts. When viewed from a fixed spatial location, the arrival of a small wavefront is always associated with (and may be said to be the ‘cause’ of) a small change in pressure and velocity. Stated another way, a wavefront may be essentially equated with a small change in one of the characteristic variables. So if, at a location \( x \), \( w_1 \) changes by an amount \( \Delta w_1 \) over a small time \( dt \), this change will be associated with a corresponding change in pressure \( \Delta p \) and velocity \( \Delta u \) at \( x \) (considering Eqs. (2.18), (2.19) and (2.5)), and from Eq. (2.11) this change will propagate in the positive \( x \) direction at a speed of \( \lambda_1 = u + c \). A change in \( w_2 \) will also cause a corresponding change in pressure and velocity, but this wavefront will propagate in the negative \( x \) direction at a speed of \( \lambda_1 = u - c \). Thus a large pressure pulse can be viewed as being made up of many small wavefronts that each ‘ride’ on top of each other. A large change in amplitude occurring over a long time is the result of many small changes that occur over small times due to these wavefronts. The concept of wavefronts has been developed and applied in Wave Intensity Analysis [65], but is beyond the scope of the current work.

The concept of wavefronts can be used to develop a Lagrangian solution for uni-directional pulses in uniform vessels. The purpose of this is to enable verification of the Eulerian LCG method with a completely independent method. Since the following treatment is based on Eq. (2.15), the Lagrangian solution is valid only for inviscid flow in vessels with constant \( A_0 \) and \( \beta \). In the Lagrangian scheme each discrete node will move in space and will be associated with an individual wavefront. Therefore, a particular wavefront and its associated node will propagate at a speed \( u + c \), where from now on, only waves in the +\( x \) direction are considered. (The same treatment could be given for waves travelling in the −\( x \) direction, but there will be no way of treating two pulses that propagate in opposite directions and at some point superimpose, since there would then be two different types of wavefronts (\( \Delta w_1 \) and \( \Delta w_2 \) acting on the one node.) Each node has a constant pressure and velocity, since the characteristic paths are being followed. Thus the time step \( \Delta t \) is not restricted by a stability condition. From one time step \( t^n \) to the next \( t^{n+1} \), each node will shift by \( \Delta t(u + c) \) in the +\( x \) direction. That is,

\[
x^{n+1} = x^n + (u(x^n) + c(x^n))\Delta t
\]  

(2.28)

and

\[
p(x^{n+1}) = p(x^n)
\]  

(2.29)

\[
u(x^{n+1}) = u(x^n)
\]  

(2.30)

Assuming pressure is prescribed at the inlet, \( p \) is known at each Lagrangian node. To calculate velocity, linear transmission line theory can be used, which says [66] that pressure and flow are
linearly related via the vessel’s characteristic impedance \((Z_0)\), defined as

\[
Z_0 = \frac{\rho c_0}{A_0}
\]  

(2.31)

where \(c_0\) is given by Eq.(2.7). However, linearity (i.e. \(c \approx c_0\) and \(A \approx A_0\)) does not need to be assumed in this case since the actual wave speed \(c\) at each node is known from Eq.(2.8). Thus the pressure/flow ratio (or non-linear impedance) may be defined as

\[
Z(x) = \frac{\rho c(x)}{A(x)} = \frac{p(x)}{Q(x)}
\]  

(2.32)

But since \(Q = Au\), velocity can be found as

\[
u(x) = \frac{p(x)}{\rho c(x)}
\]  

(2.33)

which can be substituted into (2.28). The pressure at a fixed point in space can then be found via linear interpolation between the two closest nodes at each time step.
Chapter 3

A Model of Systemic and Coronary Arterial Flow

Most previous models [1, 2, 4, 5, 6, 13, 38, 49, 67] of arterial blood flow have not included the influence of the ventricle, aortic valve or coronary circulation. However, the function of the ventricle, the dynamics of the valve and the haemodynamics of the coronary and systemic arterial circulations are highly coupled and including each of these is important for achieving a physiologically relevant model. In this chapter, a model is presented which contains all of these components. The basic building blocks of the model are discontinuities and vessel branching. In addition, the treatment of inlet and terminal boundaries is addressed, along with additional features to account for the aortic valve and the unique coronary circulation.

3.1 Discontinuities

A discontinuity is a sudden jump in either material properties ($\beta$) or $A_0$. For example, a vascular stent (expandable mesh used to hold a stenosed vessel open) or a localised build-up of plaque may constitute a discontinuity. This may be realised as a jump from one discrete node to the next, although strictly speaking, this would not be a discontinuity since there is a finite distance over which the parameter is changing (i.e. the element length). A true discontinuity would occur over an infinitesimal distance. Since this type of discontinuity is a special case of vessel branching, it is treated in Section 3.2.

3.2 Vessel Branching

The arterial circulation has the structure of a tree, where blood from the LV is pumped into the aortic trunk, major branches direct blood to all parts of the body, feeding fractal-like asymmetric networks [22] of small arteries, arterioles and finally capillaries where oxygen and carbon dioxide transfer occurs. Deoxygenated blood then continues to the venous circulation, where
small venules connect to progressively larger veins and finally return blood to the right side of the heart. The pulmonary circulation may be treated as a separate circulation, fed from the RV, which provides blood flow to the lungs. This circulation has a fractal structure [68, 69] due to the rapid and almost immediate branching network that ends in the pulmonary capillaries. Here blood is reoxygenated and completes its journey back to the left heart via the pulmonary venous circulation.

Modelling part or all of the circulation therefore requires consideration of branching points such as bifurcations or trifurcations. In one dimension, branching points are a type of discontinuity in cross-sectional area and vessel material properties ($\beta$). Using the LCG method it is straightforward to implement such discontinuities since each element is treated as a separate domain, and thus two or more nodes are permitted to share exactly the same location. Figure 3.1 shows a variety of possible node connections. Connections of type A occur where one node belongs to two elements and this is the normal situation for interior nodes in a segment containing multiple elements. Type B has two nodes sharing the same location and the adjacent elements are therefore not connected in any intrinsic way. The benefit of such a connection is that unlike type A connections, true discontinuities can be realised, since for example, the co-located nodes can have different values of $A_0$ or $\beta$. In a similar way, bifurcations are formed by a connection of type C, with three co-located nodes belonging to the three weakly connected elements. A trifurcation would be of type D and indeed, any number of branches is possible. To transmit information between co-located nodes, the characteristics will again be used. (Note: the following treatment is a generalisation of that given in [5, 38]). Consider a parent vessel $p$ with $N$ daughter vessels. Each of the $N + 1$ co-located nodes are treated as boundaries and the boundary conditions (i.e. values of $A$ and $u$ for each node) will be set using upstream and downstream information. There are therefore $2(N + 1)$ unknowns and as many equations required to solve the system. Half of these equations can be determined from the outgoing characteristics as discussed in Section 2.3. The known value of the characteristic can then be related to the primitive variables for the nodes as follows:

$$w_{1p} = u_p + 4A_p^{1/4} \sqrt{\frac{\beta_p}{2\rho}}$$  \hspace{1cm} (3.1)

for the parent vessel and

$$w_{2i} = u_i - 4A_i^{1/4} \sqrt{\frac{\rho}{2\beta}}$$  \hspace{1cm} (3.2)
Chapter 3. A Model of Systemic and Coronary Arterial Flow

for the $i$-th daughter vessel. Note that it is possible to have multiple ‘parent’ vessels, but for this example only a single parent vessel branching to multiple daughter vessels is considered. Next, equations are found that ensure continuity of mass flow and total pressure. These provide the necessary information that is external to a given branch (and so in this case the incoming characteristics are not needed). Conservation of mass provides one equation and requires that

$$Q = A_p u_p = \sum_{i=1}^{N} A_i u_i$$  \hfill (3.3)

Continuity of total pressure (i.e. dynamic pressure ($\rho u^2/2$) + static pressure Eq.(2.5)) provides the remaining $N$ equations, where for the $i$-th daughter vessel,

$$\frac{\rho u^2}{2} + p_{ext(p)} + \beta \left( \sqrt{A_p} - \sqrt{A_{i0}} \right) = \frac{\rho u^2}{2} + p_{ext(i)} + \beta \left( \sqrt{A_i} - \sqrt{A_{i0}} \right)$$  \hfill (3.4)

This set of non-linear equations is solved using the Newton-Raphson method [70]. The $N+1$ equations are first written in the following form:

\begin{align*}
    f_1 &= u_p + 4A_p^{1/4} \sqrt{\frac{\beta_p}{2\rho}} - w_{1p} = 0 \\
    f_{1+i} &= u_i - 4A_i^{1/4} \sqrt{\frac{\beta_i}{2\rho}} - w_{2i} = 0 \quad i = 1, N \\
    f_{2+N} &= \sum_{j=1}^{N} u_j A_j - u_p A_p = 0 \\
    f_{2+N+i} &= \frac{\rho}{2} u_p^2 + \beta_p \left( \sqrt{A_p} - \sqrt{A_{i0}} \right) - \frac{\rho}{2} u_i^2 - \beta_i \left( \sqrt{A_i} - \sqrt{A_{i0}} \right) = 0 \quad i = 1, N
\end{align*}  \hfill (3.5)

defining the vector of equations $\mathbf{f} = \left[ f_1 \; \cdots \; f_{2(N+1)} \right]^T$. The Jacobian matrix ($\mathbf{J}$) of $\mathbf{f}$ is defined as

$$\mathbf{J} = \begin{bmatrix}
\frac{\partial f_1}{\partial u_p} & \frac{\partial f_1}{\partial u_{i=1}} & \cdots & \frac{\partial f_1}{\partial u_{i=N}} & \frac{\partial f_1}{\partial A_p} & \frac{\partial f_1}{\partial A_{i=1}} & \cdots & \frac{\partial f_1}{\partial A_{i=N}} \\
\vdots & \vdots & \cdots & \vdots & \vdots & \vdots & \cdots & \vdots \\
\frac{\partial f_{2(N+1)}}{\partial u_p} & \frac{\partial f_{2(N+1)}}{\partial u_{i=1}} & \cdots & \frac{\partial f_{2(N+1)}}{\partial u_{i=N}} & \frac{\partial f_{2(N+1)}}{\partial A_p} & \frac{\partial f_{2(N+1)}}{\partial A_{i=1}} & \cdots & \frac{\partial f_{2(N+1)}}{\partial A_{i=N}}
\end{bmatrix}$$  \hfill (3.6)

The set of equations can then be solved by applying the following iterative procedure

$$\mathbf{x}^{k+1} = \mathbf{x}^k - [\mathbf{J}^k]^{-1} \mathbf{f}^k$$  \hfill (3.7)

where $\mathbf{x} = [u_p, u_{i=1,N}, A_p, A_{i=1,N}]^T$ is the vector of variables and $k$ is the iteration number. The iteration may be stopped when the norm of $\mathbf{f}$ is below a predetermined threshold $\theta$, that is, when $\mathbf{f}^T \mathbf{f} < \theta$.

### 3.3 Reflections

It is well-known from linear transmission line theory that whenever there is a change in characteristic impedance due to changes in vessel properties or branching, wave reflections occur. The characteristic impedance of a vessel relates the velocity of a wave with the pressure applied (and
is therefore analogous to Ohm’s Law, i.e. \( Z_0 = \frac{4}{Q} \) and may be expressed as

\[
Z_0 = \frac{1}{Y_0} = \frac{\rho c_0}{A_0} \quad (3.8)
\]

Considering Eq. (2.7), it can be seen that \( Z_0 \) depends only on vessel geometric and material properties. \( Y_0 \) is called the characteristic admittance. The reflection coefficient \( (R) \) is commonly used to express the ratio of the amplitudes of incoming and reflected waves and is given by (using the same subscripts as in Section 3.2)

\[
R = \frac{Y_{op} - \sum_{i=1}^{n} Y_{0i}}{Y_{op} + \sum_{i=1}^{n} Y_{0i}} \quad (3.9)
\]

For a dead end terminal (i.e. \( \sum Y_{0i} = 0 \)), there is a total positive reflection \( (R = 1) \) and for an opening with no downstream resistance \( (\sum Y_{0i} \rightarrow \infty) \), there is a total negative reflection \( (R \rightarrow -1) \), while for a well-matched branching no reflection occurs \( (R = 0) \). While Eq. (3.9) is strictly valid only in a linear model, it is useful for verifying the results of the non-linear model and to make general predictions about reflections at discontinuities or vessel branching points. A reflection coefficient can also be used to set boundary conditions of simple resistance terminal vessels (see following section).

3.4 Terminal Vessels

The number of branches in the arterial tree increases dramatically towards the periphery, with approximately \( 2.7 \times 10^9 \) capillaries [28]. While the vast number of small vessels and capillaries cannot be modelled individually, their combined effect may be approximated and imposed at the terminal boundaries of a model of larger arteries. Many investigators \([1, 4, 5, 8, 9]\) have treated the downstream effects on flow as being purely resistive, that is, there is no phase difference between reflected pressure and flow, and the reflection coefficient is the same for all frequency harmonics. In this case, the change in the incoming characteristic could be determined from the change in the outgoing characteristic. For a wavefront travelling in the +x direction the terminal reflection coefficient is

\[
R_t = -\frac{\Delta w_2}{\Delta w_1} = -\frac{w_2^{n+1} - w_2^0}{w_1^{n+1} - w_1^0} \quad (3.10)
\]

The value of \( w_1 \) for the next time step \( (t = n + 1) \) can be determined via extrapolation (see section 2.3), while \( w_1^0 \) and \( w_2^0 \) are the initial values of the characteristic variables. The unknown \( (w_2^{n+1}) \) can then be determined by simply rearranging Eq. (3.10),

\[
w_2^{n+1} = w_2^0 - R_t (w_1^{n+1} - w_1^0) \quad (3.11)
\]

The drawback of the simple resistance terminal is that the arterial bed is known to have capacitive as well as resistive properties. This leads to a phase lag between reflected pressure and velocity and means that higher frequency harmonics undergo smaller reflections. Thus the reflection coefficient is frequency dependant and complex \( (R = R(j\omega)) \). This has led others
to use the Windkessel element (which consists of two resistors and a capacitor) as vessel terminals. Here the input impedance and reflection coefficient spectra have peaks at zero frequency, fall rapidly over the first several harmonics and remain small and relatively constant at high frequencies [19]. While this model is a vast improvement, Olufsen [19] points out that the Windkessel element does not take into account the effects of wave propagation in a branching network. The short-coming is that in real branching networks there are ripples in the input impedance spectrum (and thus reflection coefficient) after the low frequency peak [8, 22]. An alternative is to use a generalised branching network model at the terminal [19, 22]. While these models do produce ripples in the input impedance and reflection coefficient spectra, they rely on the assumption of linearity and can only be applied to sinusoidal harmonics.

### 3.4.1 Tapering Vessels as Terminal Elements

Another possible approach is to use a tapering vessel as the terminal element. Consider a vessel with multiple step decreases in \( A_0 \) or step increases in \( \beta \). Each step corresponds to a local increase in characteristic impedance \( Z_0 \) and thus reflections will occur at each stepping point. Since these reflections occur at different distances along the vessel, backward running waves will reach the start of the vessel at different times. Note however that waves travelling back towards the inlet will also experience partial and negative re-reflections, since in this direction there are step decreases in characteristic impedance. Thus, from the perspective of the inlet, reflections that occur at more distant reflection sites have a smaller effect. This is similar to what occurs in the arterial system. Forward-travelling waves undergo relatively small reflections at branching points, but backward-travelling waves undergo relatively large negative re-reflections. In the limit where there is an infinite number of very small steps, there will an infinite number of small reflections and re-reflections at every point along the vessel. It is thus possible to approximate the behaviour of a branching network at its input with a single tapering vessel. In fact, several investigators [23, 24, 25, 50] have modelled the input characteristics of the entire arterial tree with some success using only one or two tapering vessels. These models predict an input impedance spectrum with ripples which is similar to the input characteristics of branching networks. An exact solution to the Riccati equation which governs the input impedance of a tapering vessel has only recently been formulated [71]. This and other approximate solutions [23, 24, 25] assume linearity and ignore viscous effects, which become important in small vessels. No known analytical solution exists for the input impedance of a tapering vessel for non-linear viscous flow. An empirical approach has thus been taken in this study and the relationship between input reflection coefficient and vessel length and taper gradient (a linear taper is assumed throughout) has been investigated.

A boundary condition still needs to be specified at the end of the tapering vessel. This boundary condition can be set by using a pure resistance or a Windkessel impedance (as discussed above). For simplicity, the terminal (or load) impedance of each tapering vessel has been chosen to provide good matching. To achieve this, a reflection coefficient of zero is applied according to Eq.(3.10). While using a Windkessel load impedance at the output would result in more degrees of freedom for adjusting the input characteristics of the tapering vessel, setting a zero
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reflection coefficient at the output means that the input characteristics of the tapering vessel will be determined entirely by the length of the vessel and the gradient (or severity) of the taper.

3.5 Aortic Valve and Ventricular Pressure

There have been various approaches to modelling the aortic valve. For example, Wippermann [72] modelled the valve in 1D, but this was not coupled to an arterial tree model. Regarding arterial tree models, the effects of the valve have been included implicitly by prescribing experimental aortic root pressures at the inlet [1, 2, 38, 50]. While some [3, 5] have ignored it’s effects completely by treating the heart as a perfect absorber during the whole cardiac cycle, others have idealised the valve so that during systole the heart is a complete absorber of backward waves while during diastole it is a complete reflector [8, 9, 67]. This idealisation was relaxed by Wang and Parker [18] in a linear model of the circulation, where the heart reflection coefficient changed linearly from 0 to 1 over 10ms. However, the timing of valve opening and closing was fixed a priori. In the current study, this idea is extended further so that the valve opens and closes ‘independently’ and based on local haemodynamics as is the case physiologically. The input to the model is a ventricular (forward) pressure which drives aortic flow during systole. During diastole, when the valve is closed, the aortic pressure becomes independent of this ventricular pressure, simulating the effective isolation of the aorta and ventricle during this time.

In the ventricle, a normal heart cycle consists of four phases. 1) In the isovolumic contraction phase, the ventricle begins to contract but the valve is closed. During this time there is a rapid increase in ventricular pressure since the ventricle is a closed cavity. 2) The ejection phase begins when ventricular pressure rises above aortic pressure, causing the valve to open. Further contraction causes ventricular pressure to rise above aortic pressure resulting in flow output, but this pressure difference is relatively small since (under normal conditions) there is little resistance to flow. 3) In the isovolumic relaxation phase, the heart muscle relaxes causing a drop in pressure and flow in both the ventricle and aorta. When aortic flow reaches zero, the valve closes, but there is often a small amount of reverse aortic flow before the valve is fully closed. After the valve closes, ventricular pressure continues to fall rapidly to near zero pressure. 4) The final phase is diastolic filling, where the heart muscle is relaxed and, similar to a compliant balloon, increases in volume but with little increase in pressure.

The inlet of this model is a point in the ventricle just before the valve. A realistic pressure waveform is generated using two sigmoid functions fused at mid-ejection (see Figure 3.2). Each sigmoid has the form

\[ p_{sig}(t) = a_1 + \frac{(a_2 - a_1)}{1 + e^{(a_3 - t)/a_4}} \]  

(3.12)

where

\[ a_1 = p_{ed} - 9.11 \times 10^{-4} p_{peak} \]
\[ a_2 = p_{peak} \]
\[ a_3 = 7 t_c \]
\[ a_4 = t_c \]

Here, \( p_{ed} \) is end-diastolic pressure, \( p_{peak} \) is peak pressure, and \( t_c \) is a time constant that determines the slope of the isovolumic upstroke or downstroke. From end-diastole to peak pressure
Figure 3.2: An example of a realistic ventricular pressure constructed using two sigmoid functions and used (in combination with a valve model) as the input to the arterial model. Important physiological features are labelled (i.e. the first sigmoid) Eq. (3.12) is used as is, but from peak pressure onwards (the second sigmoid) the relation is calculated backwards in time and applied forwards in time. Where the two sigmoids join (peak pressure), an iterative technique is used to ensure the pressures of the adjacent points are similar to within a threshold. This avoids a jump in pressure that would occur when fusing two sigmoids that have different shapes (for example, when using a different value of $t_c$ for isovolumic contraction and relaxation). The benefit of this input is that important features of real ventricular pressures can be emulated and manipulated independently. These features are end-diastolic pressure, peak pressure, ejection time, contraction rate, relaxation rate and diastolic filling time as shown in Figure 3.2, as well as heart rate which results from a combination of the other parameters. Prescription of ventricular forward pressure at the input is achieved via the incoming characteristic ($w_{1in}$) using Eq. (2.26). To include the effects of the valve, $w_{1in}$ is split into components such that

$$w_{1in} = \Delta w_{1p} + \Delta w_{1r} + w_1^0$$

(3.13)

where $w_1^0$ is the initial value (corresponding to the no-pulse situation), $\Delta w_{1p}$ is the change in the incoming characteristic associated with the ventricular pump and $\Delta w_{1r}$ is the change associated with backward-travelling waves that are partially or completely reflected from the valve. Making use of Eq. (3.10)

$$\Delta w_{1r} = R_{Vr}(t)\Delta w_2$$

(3.14)

where $R_{Vr}(t)$ is a time-varying valve reflection coefficient for backward-travelling waves. It is then assumed that $R_{Vr} = 0$ when the valve is open, $R_{Vr} = 1$ when it is closed, and that this value varies exponentially when the valve is opening or closing. An exponential variation was chosen based on axial displacement waveforms of leaflet tips in normal aortic valves given in [73]. The valve function $V(t)$ used was as follows:

$$V(t) = B\left(e^{-kt} - 1\right)$$

(3.15)

where $0 < t < 1$, while the constants are $B = 1/(e^{-k} - 1)$ and $k = 3$. This expression results in variation between 0 and 1 over 1 second. A scaled (in time or amplitude) and/or reversed
version of this expression is then applied to the opening or closing valve as necessary. The ventricular pump contribution to $\Delta w_{1n}$ may be expressed as

$$\Delta w_{1p} = T_{VP}(t)\Delta w_1$$  \hfill (3.16)

where $T_{VP}$ is a transmission coefficient and in what follows $T_{VP} = 1 - R_{VR}(t)$. The valve begins to open when the ventricular-aortic pressure difference rises above a set threshold. The valve begins to close when aortic velocity falls below a threshold. These thresholds have been set to 0 dynes/cm$^2$ and -0.01 cm/s respectively. Normal values of ‘Rapid Valve Opening Time’ (RVOT) and ‘Rapid Valve Closing Time’ (RVCT) are relatively similar and approximately 57 ms \footnote{20} for heart rates of 70 beats/min, and the reasonable assumption is made here that RVCT and RVOT are inversely related to heart rate \footnote{21}.

### 3.5.1 Afterload Adjusted Ventricular Pressure

The force and duration of heart contraction is determined by a host of interacting factors such as humoral control, neural control, preload and afterload. Afterload is the pressure in the aorta which the heart must overcome to achieve flow. Thus if arterial pressure increases, the ventricle maintains output by increasing pressure accordingly. In this model ventricular forward pressure is prescribed. However, an afterload corrected ventricular pressure can be derived from the prescribed forward pressure ($\bar{p}_{LV}(t)$) and a contribution due to the instantaneous afterload ($p_{LVa}(t)$). The afterload corrected ventricular pressure is then simply

$$p_{LV}(t) = \bar{p}_{LV}(t) + p_{LVa}(t)$$ \hfill (3.17)

Consider the case where no reflections from the arterial tree reach the ventricle, then ventricular pressure should equal prescribed pressure. The extra pressure is thus caused by backward-running wavefronts, that is, changes in $w_2$. Using Eq.(2.18) and Eq.(2.5), an expression relating a change in $w_2$ to a corresponding change in pressure can be derived. This is then weighted with the valve reflection coefficient $R_{VR}$ to yield

$$p_{LVa}(t) = (1 - R_{VR})\frac{\rho}{32} \left[ w_2(t)^2 - (w_0^2)^2 + 2w_1(t)(w_0^2 - w_2(t)) \right]$$ \hfill (3.18)

### 3.6 Coronary Flow

Coronary arteries supply blood to the heart muscle. There are two inlets to the coronary circulation (the left and right coronary arteries, LCA and RCA respectively) and these are located behind two of the three cusps of the aortic valve. It is well-known \footnote{28} that the majority of coronary flow to the LV occurs during diastole when the valve is closed. This is because during systole, the contracting muscle compresses the subendocardial coronary arterioles and capillaries, which reduces or even reverses total left coronary flow. However, during diastole the heart muscle is relaxed and there is no restriction to flow.

The situation is somewhat different in the right coronary artery which feeds the RV. Since the
pressure generated by the RV is lower than the LV, there is less compression of the subendocardial coronary vessels and thus greater systolic flow. Similar to Wang and Parker [18], the effect of coronary flow on arterial flow could be approximated by assuming there is no coronary flow during systole, and by making $R_{V,r} < 1$ when the valve is fully closed (see Section 3.5). However, in this study, regional coronary flow is modelled explicitly, with LCA and RCA both branching into two ‘equivalent’ vessels that represent the lumped behaviour of the left and right coronary arterial circulations respectively. Each of these equivalent vessels have a linear taper in $A_0$. This is a similar approach to that taken by Rumberger [74], who used an equivalent vessel with an elastic taper (i.e. taper of $\beta$ rather than $A_0$) to represent the coronary circulation. As mentioned in Section 3.4.1, tapering vessels have also previously been used to model the entire systemic arterial circulation [24, 25]. Thus in the current model, blood flows from the ventricle (input) into the aortic root, where a trifurcation is formed from the two coronary equivalent vessels and ascending aorta (see Figure 3.3b). Furthermore, and similar to Guiot et al [31], the effect of the surrounding heart muscle on the subendocardial vessels is simulated by applying a time-varying external pressure $p_{ext}(t)$ to the distal part (Figure 3.3c). More precisely,

$$p_{ext}(x, t) = \begin{cases} 
0 & x < \frac{L_c}{3} \\
\frac{k_c p_{LV}(t)}{k_c p_{LV}(t)} & \frac{L_c}{3} \leq x \leq \frac{2L_c}{3} \\
\frac{k_c p_{LV}(t)}{k_c p_{LV}(t)} & x > \frac{2L_c}{3}
\end{cases} \quad (3.19)$$

where $p_{LV}(t)$ is the time-varying LV pressure (see Section 3.5), $L_c = 7$ is the length of the equivalent coronary vessel, $x$ is assumed to be zero at the inlet and $k_c$ is a constant that determines the proportion of ventricular pressure to be applied as external pressure. For the left subendocardial equivalent vessel, $k_c = 1$, while $k_c = 0.2$ for the right subendocardial vessel, thus reflecting the fact that the right coronary arteries undergo less compression than the left. The cross-sectional area of the LCA and RCA at the inlet were taken as 0.21 and 0.18 cm$^2$ respectively, which is slightly larger than measurements performed in vivo at more distal sites, where the cross-sectional area would be somewhat smaller than at the coronary inlet [75, 76]. The value of $\beta$ for LCA and RCA were found by using the Young’s Modulus of the femoral artery [75] and a wall thickness of 0.08cm.

### 3.7 Arterial Tree

There is very little data available regarding geometry and material properties of the systemic arterial tree. The data used in essentially all 1D models comes originally from Noordergraaf et al [17] and Westerhof et al [8]. However Avolio [1] added more segments and changed the segment connectivity, while Stergiopulos et al [2] made adjustments to include linear vessel taper. Wang and Parker [18] did not include vessel taper but made additional adjustments to enforce good matching at branch points in the forward direction, since it is generally accepted that reflection coefficients are relatively small in this direction (but not in the backward direction). The result was that essentially all reflections occurred at the (pure resistance) terminals. However, this required significant increases (by up to 53%) in most of the vessel radii. In this work, a slightly different approach has been taken. Beginning with the data (i.e. connectivity, geometry and
Chapter 3. A Model of Systemic and Coronary Arterial Flow

Figure 3.3: a) The arterial tree model which consists of 61 major arteries including left and right coronary circulation. Tapering vessels are used at the model terminals (see Section 3.4.1). b) Detailed view of the coronary circulation model. Left and right coronary arteries branch into two equivalent vessels each, representing subepicardial and subendocardial microvasculatures, which taper in $A_0$ by a factor $k$ (see c)). c) An external pressure equal to the ventricular pressure weighted by $k_c$ is applied to the subendocardial equivalent vessels (segments 3 and 6) with zero external pressure at the proximal end and a linear increase towards the distal end as shown.

Material properties) of Stergiopulos et al [2] it was found that including vessel taper reduced the amount of adjustment required to achieve good matching at branch points in the forward direction. Note that taper causes distributed reflections and this is a potentially significant physiological phenomenon [16]. Since the Young’s moduli of the vessel walls are quite approximate in the original data (either 0.4, 0.8 or 1.6 MPa), changes were primarily made to $\beta$ rather than $A_0$ to achieve good matching in the forward direction. In several cases, to avoid large reductions in $\beta$, the radii of Wang and Parker [18] were adopted. In addition, the arrangement used by Wang and Parker [18] and Stergiopulos et al [2] for the Coeliac, Hepatic, Splenic and Gastric arteries involving two bifurcations resulted in a very large negative reflection coefficient, which is not likely to be physiological. However the arrangement of Avolio [1] of a single trifurcation resulted in a very low reflection coefficient in the forward direction and was thus employed in this study. For full details, see Figure 3.3a and Table 3.1.
Table 3.1: Geometry and material properties of the arterial tree model. Data adapted from [1, 2, 8, 18]

<table>
<thead>
<tr>
<th>Vessel</th>
<th>ID</th>
<th>L (cm)</th>
<th>(A_0) (cm²)</th>
<th>(\beta) (10⁶ dyne/cm³)</th>
<th>Vessel</th>
<th>ID</th>
<th>L (cm)</th>
<th>(A_0) (cm²)</th>
<th>(\beta) (10⁶ dyne/cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic Root</td>
<td>1</td>
<td>1</td>
<td>7.010</td>
<td>0.227</td>
<td>L Ulnar B</td>
<td>32</td>
<td>47.8</td>
<td>0.113 → 0.105</td>
<td>5.751 → 6.200</td>
</tr>
<tr>
<td>L Coronary</td>
<td>2</td>
<td>3</td>
<td>0.210</td>
<td>7.121</td>
<td>Intercostals</td>
<td>33</td>
<td>8</td>
<td>1.208 → 0.679</td>
<td>0.288 → 0.511</td>
</tr>
<tr>
<td>L Subendocardial</td>
<td>3</td>
<td>7</td>
<td>0.120 → 0.060</td>
<td>12.462 → 24.924</td>
<td>Thoracic Aorta B</td>
<td>34</td>
<td>10.4</td>
<td>1.431 → 1.307</td>
<td>0.660 → 0.723</td>
</tr>
<tr>
<td>L Subepicardial</td>
<td>4</td>
<td>7</td>
<td>0.120 → 0.060</td>
<td>12.462 → 24.924</td>
<td>Abdom. Aorta A</td>
<td>35</td>
<td>5.3</td>
<td>1.169</td>
<td>0.728</td>
</tr>
<tr>
<td>R Coronary</td>
<td>5</td>
<td>3</td>
<td>0.180</td>
<td>7.604</td>
<td>Coeliac</td>
<td>36</td>
<td>2</td>
<td>0.126</td>
<td>4.814</td>
</tr>
<tr>
<td>R Subendocardial</td>
<td>6</td>
<td>7</td>
<td>0.103 → 0.052</td>
<td>13.289 → 26.577</td>
<td>Hepatic</td>
<td>37</td>
<td>12.5</td>
<td>0.152</td>
<td>3.046</td>
</tr>
<tr>
<td>R Subepicardial</td>
<td>7</td>
<td>7</td>
<td>0.103 → 0.052</td>
<td>13.289 → 26.577</td>
<td>Splenic</td>
<td>38</td>
<td>6.3</td>
<td>0.102</td>
<td>4.179</td>
</tr>
<tr>
<td>Asc. Aorta</td>
<td>8</td>
<td>4</td>
<td>6.780 → 6.514</td>
<td>0.227 → 0.266</td>
<td>Gastric</td>
<td>39</td>
<td>7.1</td>
<td>0.238</td>
<td>2.149</td>
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<tr>
<td>Aortic Arch A</td>
<td>9</td>
<td>2</td>
<td>3.941</td>
<td>0.302</td>
<td>Sup. Mesenteric</td>
<td>40</td>
<td>17.2</td>
<td>0.283</td>
<td>2.307</td>
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<tr>
<td>Brachioceph.</td>
<td>10</td>
<td>3.4</td>
<td>1.535 → 1.208</td>
<td>0.277 → 0.528</td>
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<td>41</td>
<td>1</td>
<td>1.094</td>
<td>0.692</td>
</tr>
<tr>
<td>R Subclavian A</td>
<td>11</td>
<td>3.4</td>
<td>0.919 → 0.562</td>
<td>0.689 → 1.127</td>
<td>L Renal</td>
<td>42</td>
<td>3.2</td>
<td>0.212</td>
<td>2.359</td>
</tr>
<tr>
<td>R Carotid</td>
<td>12</td>
<td>17.7</td>
<td>0.430</td>
<td>1.385</td>
<td>Abdom. Aorta C</td>
<td>43</td>
<td>1</td>
<td>1.094</td>
<td>0.692</td>
</tr>
<tr>
<td>R Vertebral</td>
<td>13</td>
<td>14.8</td>
<td>0.111 → 0.105</td>
<td>7.662 → 8.087</td>
<td>R Renal</td>
<td>44</td>
<td>3.2</td>
<td>0.212</td>
<td>2.359</td>
</tr>
<tr>
<td>R Subclavian B</td>
<td>14</td>
<td>42.2</td>
<td>0.510 → 0.175</td>
<td>1.862 → 7.239</td>
<td>Abdom. Aorta D</td>
<td>45</td>
<td>10.6</td>
<td>1.057 → 0.943</td>
<td>0.671 → 0.751</td>
</tr>
<tr>
<td>R Radius</td>
<td>15</td>
<td>29</td>
<td>0.053 → 0.036</td>
<td>22.968 → 33.698</td>
<td>Inf. Mesenteric</td>
<td>46</td>
<td>5</td>
<td>0.080</td>
<td>5.054</td>
</tr>
<tr>
<td>R Ulnar A</td>
<td>16</td>
<td>6.7</td>
<td>0.145</td>
<td>8.983</td>
<td>Abdom. Aorta E</td>
<td>47</td>
<td>1</td>
<td>0.849</td>
<td>0.723</td>
</tr>
<tr>
<td>R Interosseous</td>
<td>17</td>
<td>7.9</td>
<td>0.026</td>
<td>40.697</td>
<td>L Common Iliac</td>
<td>48</td>
<td>5.9</td>
<td>0.425 → 0.385</td>
<td>1.333 → 1.474</td>
</tr>
<tr>
<td>R Ulnar B</td>
<td>18</td>
<td>30.3</td>
<td>0.120 → 0.105</td>
<td>6.718 → 8.266</td>
<td>R Common Iliac</td>
<td>49</td>
<td>5.8</td>
<td>0.425 → 0.385</td>
<td>1.333 → 1.474</td>
</tr>
<tr>
<td>R Int. Carotid</td>
<td>19</td>
<td>17.6</td>
<td>0.283 → 0.062</td>
<td>3.009 → 13.817</td>
<td>L Ext. Iliac</td>
<td>50</td>
<td>14.4</td>
<td>0.322 → 0.229</td>
<td>3.115 → 4.375</td>
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<tr>
<td>R Ext. Carotid</td>
<td>20</td>
<td>17.7</td>
<td>0.283 → 0.062</td>
<td>2.808 → 12.896</td>
<td>L Int. Iliac</td>
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<td>5</td>
<td>0.285</td>
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<tr>
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<td>3.597</td>
<td>0.302</td>
<td>L Femoral</td>
<td>52</td>
<td>44.3</td>
<td>0.211 → 0.113</td>
<td>4.486 → 8.335</td>
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<tr>
<td>L Carotid</td>
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<td>20.8</td>
<td>0.430</td>
<td>1.385</td>
<td>L Deep Femoral</td>
<td>53</td>
<td>7.3</td>
<td>0.091 → 0.049</td>
<td>19.574 → 36.373</td>
</tr>
<tr>
<td>L Int. Carotid</td>
<td>23</td>
<td>17.6</td>
<td>0.283 → 0.062</td>
<td>3.009 → 13.817</td>
<td>L Post. Tibial</td>
<td>54</td>
<td>21</td>
<td>0.126 → 0.062</td>
<td>13.541 → 27.243</td>
</tr>
<tr>
<td>L Ext. Carotid</td>
<td>24</td>
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<td>0.283 → 0.062</td>
<td>2.808 → 12.896</td>
<td>L Ant. Tibial</td>
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<td>1.110</td>
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<td>7.662 → 8.087</td>
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<td>58</td>
<td>44.4</td>
<td>0.211 → 0.113</td>
<td>4.486 → 8.335</td>
</tr>
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<td>1.862 → 7.239</td>
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<td>59</td>
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<td>0.091 → 0.049</td>
<td>19.574 → 36.373</td>
</tr>
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<td>22.968 → 33.698</td>
<td>R Post. Tibial</td>
<td>60</td>
<td>32.2</td>
<td>0.126 → 0.062</td>
<td>13.541 → 27.243</td>
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Chapter 4

The Locally Conservative Galerkin Method

Standard Galerkin discretisation of Eq.(2.4) leads to spatial instability due to the presence of the convective term. One possible way of achieving better spatial stability is by including the Taylor-Galerkin stabilisation, which is the finite element equivalent of Lax-Wendroff stabilisation for the finite difference method, and also gives a second order time accuracy. Derivation of the Taylor-Galerkin discretisation for the $A, Q$ system has been performed by Formaggia and Sherwin [3, 5] and is the same for the $A, u$ system. For completeness it is included here. Eq.(2.4) can be rearranged to give

$$\frac{\partial U}{\partial t} = S - \frac{\partial F}{\partial x}$$  (4.1)

where $U$, $F$ and $S$ are the vectors of primitive variables, conservative variables and source term respectively. Differentiating with respect to time and applying the chain rule,

$$\frac{\partial^2 U}{\partial t^2} = S_U \frac{\partial U}{\partial t} - \frac{\partial}{\partial x} \left( F_U \frac{\partial U}{\partial t} \right)$$  (4.2)

where $F_U = \frac{\partial F}{\partial U}$ (= $H$ in Eq.(2.10)) and $S_U = \frac{\partial S}{\partial U}$. Substituting Eq.(4.2) into Eq.(4.1) removes the time derivatives from the right-hand side.

$$\frac{\partial^2 U}{\partial t^2} = S_U \left( S - \frac{\partial F}{\partial x} \right) - \frac{\partial}{\partial x} \left( F_U \frac{\partial U}{\partial t} \right) + \frac{\partial}{\partial x} \left( F_U \frac{\partial F}{\partial x} \right)$$  (4.3)

The Taylor series expansion in time is

$$U^{n+1} = U^n + \Delta t \frac{\partial U^n}{\partial t} + \frac{\Delta t^2}{2} \frac{\partial^2 U^n}{\partial t^2} + O (\Delta t^3)$$  (4.4)

where $\Delta t$ is the time step and $n$ refers to the current time step. Ignoring 3rd and higher order terms, and substituting Eq.(4.1) and Eq.(4.3) yields the final explicit semi-discrete form:

$$\frac{U^{n+1} - U^n}{\Delta t} = S^n - \frac{\partial F^n}{\partial x} - \frac{\Delta t}{2} \left[ \frac{\partial}{\partial x} \left( F^n_U S^n - F^n_U \frac{\partial F^n}{\partial x} \right) - S^n_U \frac{\partial F^n}{\partial x} - S^n_U S^n \right]$$  (4.5)
Note that the second bracketed term is the Taylor-Galerkin stabilisation term.

### 4.1 Global Taylor-Galerkin Method

The standard spatial discretisation for the finite element method is performed over the global domain $\Omega$ which has boundaries denoted by $\Gamma$. Galerkin weighting $N^T$ along with a linear spatial discretisation provides a residual equation which converges to the exact solution when the element size approaches zero, that is,

$$\int_{\Omega} \left( N^T \frac{\Delta \hat{U}}{\Delta t} - N^T \hat{R} \right) d\Omega = 0 \quad (4.6)$$

where $\hat{R}$ is the right-hand side of Eq.(4.5). The hat signifies that these variables are approximated by the finite element method, where for any variable $\Phi$, for example, $\hat{\Phi} = N_i \tilde{\Phi}_i + N_j \tilde{\Phi}_j = N\tilde{\Phi}$ means that the value of $\hat{\Phi}$ anywhere in a given one-dimensional element is interpolated between two discrete nodes $(i, j)$ with nodal values $\tilde{\Phi}_{i,j}$ via the linear interpolation functions $N_i = (x_j - x)/{(x_j - x_i)}$ and $N_j = (x - x_i)/{(x_j - x_i)}$. Evaluation of Eq.(4.6) results in the following equation in compact matrix form:

$$[M] \{ \Delta U \} = \Delta t ([K] \{ F \}^n + [L] \{ S \}^n + \{ f \}^n) \quad (4.7)$$

where $[M]$ is called the mass matrix and $[K]$ and $[L]$ are coefficient matrices for convection, Taylor-Galerkin and source terms; each of these are $N_{\text{nodes}} \times N_{\text{nodes}}$ matrices, where $N_{\text{nodes}}$ is the number of nodes in $\Omega$. $U$, $F$ and $S$ are the vectors of primitive variables ($\Delta U = U^{n+1} - U^n$), conservative variables and source terms respectively, while $f$ contains boundary fluxes. On internal nodes these fluxes are usually ignored for the Global Galerkin method (thus $f = f_{\Gamma}$), since the flux contributions from the two adjoining elements exactly cancel. While this not so on boundaries, this term is still not used since Dirichlet boundary conditions are set explicitly (see section 2.3).

### 4.2 Locally Conservative Taylor-Galerkin Method

The Locally Conservative Galerkin (LCG) method is a technique introduced by Thomas and Nithiarasu [39, 40, 41] which treats each element as a sub-domain with its own boundaries. In this case Eq.(4.7) is written over an elemental sub-domain ($\Omega_e$):

$$[M_e] \{ \Delta U \} = \Delta t ([K_e] \{ F \}^n + [L_e] \{ S \}^n + \{ f_{\Gamma} \}^n) \quad (4.8)$$

Now $[M_e]$, $[K_e]$ and $[L_e]$ are 2x2 matrices, and this system of equations is solved on individual elements, independent of surrounding elements. Information is transmitted between elements via the flux term which is imposed as a Neumann boundary condition. It can be shown that the LCG method is equivalent to the Global Galerkin method for convection-diffusion type problems except on global boundaries [39]. One advantage of LCG method is that only small equations
need to be solved; for one-dimensional problems, the 2x2 matrices can be evaluated directly before coding, which removes the need for any matrix inversions. For brevity, only the derivation for the inviscid case will be considered, which is achieved by removing all terms involving \( S \) and \( S_U \). This reduced form is as follows:

\[
\int_{\Omega_e} N^T \frac{\Delta \hat{U}^n}{\Delta t} = - \int_{\Omega_e} N^T \frac{\partial \hat{F}^n}{\partial x} + \frac{\Delta t}{2} \int_{\Omega_e} N^T \frac{\partial}{\partial x} \left( \hat{F}^n_U \frac{\partial \hat{F}^n}{\partial x} \right) d\Omega_e = 0 \tag{4.9}
\]

The time integral is treated in the usual way resulting in the element mass matrix

\[
[M_e] = \frac{l_e}{6} \begin{bmatrix} 2 & 1 \\ 1 & 2 \end{bmatrix} \tag{4.10}
\]

where \( l_e \) is the element length. The lumped mass matrix may also be used,

\[
[M_e] = \frac{l_e}{2} \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix} \tag{4.11}
\]

While the lumped mass matrix is sometimes considered undesirable for transient problems, Section 5.1 demonstrates that there is negligible difference when comparing consistent and lumped mass matrices. Thus, in what follows, the lumped mass matrix has been used since it is somewhat more efficient. The convection term is integrated by parts,

\[
- \int_{\Omega_e} N^T \frac{\partial \hat{F}^n}{\partial x} d\Omega_e = \int_{\Omega_e} \frac{\partial N^T}{\partial x} \hat{F}^n d\Omega_e - \int_{\Gamma_e} N^T \hat{F}^n U \frac{\partial \hat{F}^n}{\partial x} d\Gamma_e \tag{4.12}
\]

where \( \hat{F} \) is computed in a small post-processing step as the average value of \( F \) from adjacent elements. Similarly the Taylor-Galerkin term is integrated by parts,

\[
\int_{\Omega_e} N^T \frac{\partial}{\partial x} \left( F^n_U \frac{\partial \hat{F}^n}{\partial x} \right) d\Omega_e = - \int_{\Omega_e} \frac{\partial N^T}{\partial x} F^n_U \frac{\partial \hat{F}^n}{\partial x} d\Omega_e + \int_{\Gamma_e} N^T \bar{F}^n_U \frac{\partial \hat{F}^n}{\partial x} d\Gamma_e \tag{4.13}
\]

Evaluation of Eq.(4.12) and Eq.(4.13) provides the coefficient matrix \([K_e]\) for the inviscid case. If source terms are also included, the full matrix is found to be

\[
[K_e] = \left( \frac{1}{2} + \frac{\Delta t}{4} S_U \right) \begin{bmatrix} -1 & -1 \\ 1 & 1 \end{bmatrix} - \frac{\Delta t}{2l_e} F_U \begin{bmatrix} 1 & -1 \\ -1 & 1 \end{bmatrix} \tag{4.14}
\]

where \( \bar{F}_U \) and \( \bar{S}_U \) are the average values over the elemental sub-domain (not to be confused with the post-processed flux value which is the average of adjacent elements). This is an alternative to numerical integration, which is equivalent when using linear shape functions. Similarly the coefficient matrix \([L_e]\) is found to be

\[
[L_e] = \left( \frac{l_e}{6} + \frac{\Delta t l_e}{12} S_U \right) \begin{bmatrix} 2 & 1 \\ 1 & 2 \end{bmatrix} + \frac{\Delta t}{4} F_U \begin{bmatrix} -1 & -1 \\ 1 & 1 \end{bmatrix} \tag{4.15}
\]
For the flux term, the contributions from the Taylor-Galerkin terms are not included since these arise from the numerical technique and will be zero on the boundaries. Thus,

$$\{f_e\} = \begin{cases} \tilde{F}^n_i \\ -\tilde{F}^n_j \end{cases}$$ \hfill (4.16)

The system can then be implemented in computer code by substituting Eqs. (4.10), (4.14), (4.15) and (4.16) into Eq. (4.8) and implementing the boundary conditions (see section 2.3). It can be shown that the stability condition for the characteristic system Eq. (2.15) is

$$\Delta t_{max} = \frac{\Delta x_{min}}{c_{max}}$$ \hfill (4.17)

although for a non-zero source term (C) this will be slightly lower. Experience has shown that Eq. (4.17) with a small safety factor (i.e. using a $\Delta t$ slightly small than $\Delta t_{max}$) works well for the coupled system (Eq. (2.4)).
Chapter 5

Model Verification

5.1 Numerical Scheme Verification

Results obtained using a lumped or consistent mass matrix are compared in Figure 5.1. Pressure waveforms in the Ascending Aorta and two of the most distal locations in the arterial tree (Right Anterior Tibial and Left Ulnar B) reveal that there is no perceptible difference. The lumped mass matrix is slightly more computationally efficient and has thus been used in all subsequent calculations.

Figure 5.2 shows the convergence of the numerical scheme as element length (Figure 5.2a) and time step (Figure 5.2b) are decreased. Results are shown for three input pressure pulses, all with an amplitude of 2000 dynes/cm$^2$, but with pulse widths of 0.005, 0.01 and 0.05s. All results in Figure 5.2a were obtained with a time step of 5μs, while the results in Figure 5.2b were obtained with an element length of 0.1cm. Note that as element length or time step is decreased, the solution converges to an asymptotic value. Moreover, longer pulses tend to converge to this asymptote at larger element lengths and time steps. In other words, time step and mesh density become less limiting for long pulses. Thus for physiological pulses (which generally contain only

![Figure 5.1: Comparison of the results obtained when using a lumped or consistent mass matrix. Pressure obtained in the aorta and two of the most distal sites in the arterial tree.](image-url)
Figure 5.2: a) Spatial and b) temporal convergence of the LCG and Global Galerkin (GG) methods in a single uniform vessel. Results are shown for three different input pressure pulses of amplitude 2000 dynes/cm$^2$ and pulse widths (Pwidth) given in the legend, with values obtained at $x = 15$. In b), error is calculated as the amplitude of the pressure peak minus the value for the smallest time step ($1\mu$s).

low frequency harmonics), very small time steps and element lengths are not required. Figure 5.2 also compares the LCG and Global Galerkin methods, which are identical.

5.2 Pulse Propagation in a Single Uniform Vessel

In order to compare the numerical model with results found in published literature, a test case is taken from Formaggia et al and Sherwin et al [3, 5]. Consider a single vessel of length $L = 15$ which has a uniform $A_0$ and $\beta = \beta_0$. A half-sinusoidal pressure of amplitude 20000 dynes/cm$^2$ and width 0.165s is applied at the inlet ($x = 0$) and the pressure is monitored at three points ($x = 0, 0.25L, 0.5L, 0.75L$) along the vessel. The value of $\beta_0$ taken from [3, 5] is 451352 dynes/cm$^3$.

Regarding the value of $A_0$, these references claim that a radius of 0.5cm ($A_0 = 0.78cm^2$) was used, however it is most likely that this is an error and that in fact the cross-sectional area had this value (i.e. $A_0 = 0.5$). This conclusion was based on the fact that using $A_0 = 0.78cm^2$ with the LCG method gave significantly different results (the waves propagated too fast), while using $A_0 = 0.5$ produced very close results to those published. This was confirmed by the Lagrangian solution (see Section 2.4) which gave very similar results. These two solutions, as well as the data given in [3, 5] are plotted in Figure 5.3. Here it can be seen that the pulse propagates from inlet to outlet with essentially no distortion.

A second example taken from references [3, 5] considers a similar vessel but with an increased value of $\beta = k\beta_0$ in the central third of its length, with a smooth transition between the two values with a half-width of 0.05cm, as shown in Figure 5.4a. This simulates placement of a stent, which is an expandable metal mesh which is surgically implanted into a vessel. This is a common treatment of stenosis, a localised narrowing of the vessel lumen due to the build-up of plaques on the wall. Taking $k = 100$ from [3, 5], and again using $A_0 = 0.5$ and the same half-sinusoidal input as for Figure 5.3, the calculated waveforms show good agreement with the published data. These results are plotted in Figure 5.4b. In this case, the Lagrangian solution cannot be used
due to the presence of reflections (i.e. pulse(s) are not uni-directional). The nature of these reflections are best seen by using a very short pulse, so that forward and backward-running pulses do not overlap (Figure 5.4c). This short half-sinusoidal pulse has a width of 0.0025s. Positive reflections occur whenever there is an increase in $\beta$ and negative reflections where $\beta$ decreases. For the system given in Figure 5.4c, the individual reflections of the pulse can be explained as follows:

1. The incoming pulse (marked a) passes the first monitoring point ($x = 0.25L$) at around $t=0.01s$, and at some time later reaches the sudden increase in $\beta$ around $x = 5$, thereby undergoing a partial positive reflection (b) and a partial transmission (c).
2. The reflected pulse (b) propagates back toward the inlet and passes $x = 0.25L$ at around $t=0.015s$.
3. The transmitted pulse (c) continues propagating in the $+x$ direction, however it reaches $x = 0.5L$ faster than (b) reaches $x = 0.25L$ since the wave speed inside the stent is much higher. Also, the amplitude of (c) is high because the wall stiffness is high.
4. Pulse (c) continues toward the sudden drop in $\beta$ at $x = 10$ where it undergoes a partial negative reflection. This negative pulse (d) propagates back to the $x = 0.5L$ point, while the small transmitted pulse (e) continues in the $+x$ direction towards the $x = 0.75L$ point.
5. The backward-running pulse (d) encounters a drop in $\beta$ at $x = 5$, and again reflects to produce pulses (f) and (g). This process continues such that the pulse in the stent propagates back and forth, and each time it encounters the step in $\beta$, a partial reflection and partial transmission occurs. The result is that energy is trapped in the stent and gradually escapes via transmitted waves, leading to the steady decline in amplitude of these pulses as time progresses. Turning now to the long pulse in Figure 5.4b, it can be seen that the peak pressure at $x = 0.25L$ is somewhat increased compared with the uniform vessel (Figure 5.3). The increase is relatively small due to the pressure increasing effect of the positive reflection at the start of the stent and the fact that...
Figure 5.4: a) A stent in the middle third of the vessel’s length is represented by an increased value of $\beta$. b) Pressure obtained at three locations for a long and c) short pressure pulse (see text for explanation of wave labels). Waveforms from [3, 5] are shown in b) for comparison.

this only slightly outweighs the pressure decreasing effect of the negative reflection(s) that occur at the end of the stent and are transmitted back to $x = 0.25L$. Thus for the large pulse, the positive and negative effects of the large reflections partially cancel, leaving a relatively moderate overall effect. At the end of the pulse, the pressure drops below zero for a short time, which shows that the positive reflection has finished passing $x = 0.25L$ but the negative reflections have not.

The same short pulse example is provided in the uniform and stented vessels by Formaggia et al [3], but with a reported amplitude of 20000 dynes/cm$^2$. Their figure showing this pulse propagating with little distortion in the uniform vessel cannot be valid however. A simple calculation will show that within a 15cm length, such a pulse will form a shock. The propagation speed of the pulse’s foot is equal to $u_0 + c_0$ which is simply $c_0$ given by Eq.(2.7) since $u_0 = 0$, which is approximately 399.5 cm/s. The propagation speed of the peak, $u + c$ (from Eqs.(2.5),(2.8),(2.33)), is 460.4 cm/s. The width of the pulse in space is equal to the distance the leading foot propagates over 0.0025s (the pulse width in time), i.e. 0.0025s × 399.5 cm/s ≈ 1 cm. Since the peak is propagating 60.9 cm/s faster than the foot, a shock is expected to form at approximately $t = 0.0082s$ or $x = 3.27cm$. (Note: The shock will actually occur slightly earlier because of the convex shape of the pulse with respect to the $x$-axis, so that some point on the upstroke of the pulse will catch up with the foot before the peak does). Figure 5.5a confirms these calculations. Both the LCG
method and the Lagrangian method reveal that for an input amplitude of 20000 dynes/cm$^2$, a shock forms at approximately $t = 0.0082 s$. However, Figure 5.5b shows the results for a small pulse (amplitude 1 dynes/cm$^2$) which propagates with little distortion over the 15cm tubing (note: for comparison with Figure 5.5a, Figure 5.5b only shows propagation up to a length of approximately 5cm). Using the same calculations as above for the small amplitude pulse, a shock would be expected to form at a distance of 637 m! Figure 5.6 shows a log-log plot of calculated distance to shock formation vs. input amplitude for two values of $A_0$ and the two pulse widths presented above (0.0025s and 0.33s). It can be seen that shock formation occurs sooner with larger amplitude pulses, with short duration (high frequency) pulses, and in larger vessels where the wave speed is low. The filled red circle and blue triangle in Figure 5.6 correspond to approximate upper limits of the amplitude and propagation distance for harmonics in physiological signals that correspond to the two pulse widths, while the arrows indicate that given amplitudes and distances below these upper limits, shock formation is even less likely. The conclusion that can be drawn (see also [12]) is that physiological pulses are unlikely to undergo shock formation since a) high frequency harmonics are very small in amplitude and b) wave speed increases at greater distances from the heart (since vessel diameter decreases and wall stiffness increases).

### 5.3 Viscous Effects

Figure 5.7 shows the propagation of a Gaussian pressure pulse and compares inviscid and viscous flow. In this case, the vessel has a uniform $A_0 = 1.0$cm and $\beta = 229674$ dynes/cm$^3$. The width of this pulse (0.03s) is very short compared to a normal heart beat ($\approx$1 s). In Figure 5.7a it can be seen that for inviscid flow, the pulse propagates with little distortion. However viscous flow is associated with a gradual decay in the amplitude of the peak. This is also seen in a large amplitude ($10^4$ dynes/cm$^2$) pressure pulse (Figure 5.7b), which displays significant distortion due to both viscous effects and the non-linear effects discussed in the previous section. Figure 5.7c shows that the attenuation of the pressure pulse due to viscosity is dependant on
vessel cross-sectional area. As predicted from Eq. (2.3), the decay of the pressure peak \( \Delta p_{\text{peak}} \) is greater for small vessels and for large amplitude pulses.

### 5.4 Discontinuities

Figure 5.8a shows the effect of a sudden decrease in \( A_0 \). Since this corresponds to an increase in characteristic impedance, there is a partial positive reflection. The calculated linear reflection coefficient Eq. (3.9) is \( R = 0.25 \) while the transmission coefficient (from transmission line theory, \( T = 1 + R \)) is \( T = 1.25 \). The amplitudes of the reflected and transmitted waves are close to these values, and while it is important to stress that the linear reflection coefficient is not strictly valid for the non-linear system, small pulses do approach the linear behaviour. Conversely, Figure 5.8b demonstrates that there is a partial negative reflection when \( A_0 \) is increased (with \( R = -0.25 \) and \( T = 0.75 \)).

Another possible type of discontinuity is in \( \beta \). Assuming \( A_0 \) is constant, this reflects a sudden change in material properties (Young’s modulus or wall thickness) of the vessel (see Eq. (2.6)). This situation is encountered clinically when arterial stents are used to hold a stenosed vessel open. Since the stents are stiffer than the vessel there is a sudden increase in characteristic impedance followed by a decrease at the other end. Figure 5.9 shows reflected and transmitted waves for a single reflection site where \( \beta \) doubles or halves. Note that wave speed increases or decreases along with \( \beta \) (Eq. (2.8)) as shown by changes in the width of the pulse.

### 5.5 Vessel Branching

The branching nature of the arterial tree and the fact that parent and daughter branches are not perfectly matched Eq. (3.9) gives rise to a great number of reflections, re-reflections and so on.
Figure 5.7: Propagation of a short a) low and b) high pressure pulse in a single vessel for inviscid (black) and viscous flow (red), with snapshots taken at $t=0.03s$ (solid lines), $0.045s$ (dashed lines) and $0.06s$ (dotted lines). For low pressures, propagation is approximately linear and the pulse does not distort. At high pressures, non-linear effects distort the pulse and lead to shock formation. c) Log-log plot of pressure peak decay $\Delta p_{peak}$ over 20cm due to viscosity with different vessel cross-sectional areas ($A_0$) and for initial pulse amplitudes of 100, 1000 and 2000 dynes/cm$^2$.

Figure 5.8: Reflected and transmitted waves in a single vessel due to a) a step decrease and b) a step increase in $A_0$. 
Figure 5.9: Reflected and transmitted waves in a single vessel due to a) a step increase and b) a step decrease in $\beta$ with constant $A_0$.

throughout the system. To illustrate this, Figure 5.10 shows the propagation of a short pressure pulse in a single bifurcation. The parent vessel (A) (with $A_0 = 4$, $\beta_A = 113487$ and $L = 10$) branches into a narrow open-ended branch (B) ($A_0 = 0.5$, $\beta_B = 4\beta_A$, $L = 5$) and a larger close-ended branch (C) ($A_0 = 0.35$, $\beta_B = 2\beta_A$, $L = 10$). When pressure is monitored mid-way along each branch, it can be seen that a single input pulse (a) gives rise to several reflected waves in each segment in addition to the primary wave. The first reflection occurs when the wave reaches the bifurcation, partly reflecting back along A (wave b) and partly transmitting to both daughter branches (e and h). In branch B, wave e arrives at the monitoring point before wave h in branch C, due to the shorter distance and greater wave speed in B. Since B is well-matched to any downstream vessels (that is, the terminal reflection coefficient is zero), there are no further reflections of wave e. Conversely, wave h in C reflects completely at the closed end producing i which has the same magnitude. This backward-running wave then propagates toward the bifurcation, reflecting once again to produce the forward-running wave j in C, the backward-running wave c in A and the forward-running wave f in B. Note that the effective reflection coefficient of the bifurcation from the perspective of C is negative (since the combined characteristic impedance of A and C is less than that of B), causing wave j to be negative. This re-reflected wave is reflected again at the terminal of C producing k, which is then partially reflected once again as l and transmitted as waves g and d.

Several points should be noted. First, the input pulse is very short to enable clear view of backward and forward-running waves without overlap. The heart pulse however is much longer making individual waves more difficult to distinguish. It is then important to note that the principle of superposition, where the overlapping waves can simply be considered as the sum of individual waves, is only valid in a linear model. In non-linear models, this is not the case and will only hold approximately. This is because linear models assume a constant wave speed whereas non-linear models do not. Thus a wave travelling by itself will propagate at a different speed to the same wave when it encounters other waves [78]. Therefore, forward-running waves do in fact influence backward-running waves, although this effect is small. Secondly, the results in Figure 5.10 are for inviscid flow. For viscous flow there would be some attenuation of the waves (Figure 5.7) which in turn, would lead to a slightly lower peak wave speed. However since the signals in Figure 5.10 are small, these effects are negligible.
The input characteristics of the chosen terminal elements should represent, as closely as possible, the downstream branching network of small arteries and capillaries. Previous research [22] has shown that the effective reflection coefficient at the input of a branching network is complex and frequency dependent ($R_{in} = R_{in}(j\omega)$, where $\omega$ is the angular frequency). Other studies [23, 24, 25] have shown that the input characteristics of tapering vessels are similar to those of branching networks. To investigate the use of tapering vessels as terminal elements, the input characteristics of both a branching network and various tapering vessels were determined. Using an empirical approach, the assumptions required for analytical methods can be avoided and the response of the full non-linear system determined. The frequency-dependent input reflection coefficient, $R_{in}(j\omega)$, was determined by prescribing sinusoidal forward pressures of various frequencies at the inlet (1-10 Hz in steps of 1 Hz and 12,15,20,25 Hz). Since this input was a time-varying forward pressure, the time-varying backward pressure (which arises from reflections in the tapering vessel) was determined by subtracting the actual (or assigned) value of pressure (see Section 2.3.2) at the inlet from the forward pressure. Thus for each sinusoidal inlet forward pressure, the inlet backward pressure was calculated, which, after an initial stabilisation period, was also sinusoidal with the same frequency as the forward pressure. The magnitude of the effective input reflection coefficient could then be calculated for each frequency as the ratio of the amplitudes of the forward and backward sine waves. The phase could also be determined via the time delay between the occurrence of peaks in the forward and backward sine waves. It should be stressed that while the concept of a spectrum requires linearity, determining the spectrum of non-linear systems (such as measurement of the input impedance spectrum arteries in vivo) is common practice.
Figure 5.11a shows the frequency-dependent magnitude and phase of a 4 generation branching network and various tapering vessels, while Figure 5.11b shows an example of the calculated pressure and velocity at the input of the different terminal elements given a signal with amplitude and frequency characteristics that are similar to physiological signals. Note that from here on the pressure units of mmHg are used (where 1 mmHg = 1333 dynes/cm²), which is standard for physiological signals. As predicted by theory, the simple resistance network reflects all frequencies by the same amount and the phase is constant. However for the branching network and tapering vessels, there is an initial peak in magnitude at low frequencies followed by a decline with gentle ripples as frequency increases. Also, the phase in both branching networks and tapering vessels displays similar oscillations. These results accord with work by Brown [22] who showed the input reflection coefficient spectrum for a branching network with more generations, with the first minimum in magnitude occurring between 2 and 7 Hz. It is also worth noting several observations regarding tapering vessels. The first magnitude minimum occurs at higher frequencies in shorter tapering vessels (approximately 15 Hz for L=10 compared with 5-6 Hz for L=30). Also, the difference in response between viscous and inviscid conditions is small. Finally, the magnitude of the reflection coefficient at very small or zero frequencies increases with greater taper severity (0.53 when \( A_0(L) = 0.2 A_0(0) \) compared with 0.67 when \( A_0(L) = 0.2 A_0(0) \)), which is to be expected since in the limit where \( A_0(L) = 0 \), complete reflection must occur. In the time domain (Figure 5.11b), the tapering vessel is seen to match the behaviour of the branching network closely, while the simple resistance terminal does not. Particularly, due to the distributed delay in arrival of backward-travelling waves, the increase in pressure and decrease in velocity associated with these waves is also delayed and gradual, but this is not the case for the simple resistance terminals. For all of these reasons, it is concluded that tapering vessels are an adequate representation of branching networks and thus for use as terminal elements.

5.7 Aortic Valve and Ventricular Pressure

The unique feature of the aortic valve presented in this study is that forward-running ventricular waves are partially or fully transmitted to the aorta according to the valve transmission coefficient, \( T_{Vp} \), while backward-running waves in the aorta are partially or fully reflected according to the valve reflection coefficient, \( R_{Vr} \). To demonstrate these principles, two examples are presented here which involve a series of short Gaussian pressure pulses (width 0.04 s) as the input to a single aortic segment with a valve at the proximal end. In Figure 5.12, forward pressure is prescribed at the inlet (i.e. at the valve) according to Eq.(3.13). Since no reflections occur there are no backward-running waves and afterload-corrected left-ventricular pressure (\( p_{LV} \)) is equal to the prescribed forward pressure. Pressure values obtained at two points in the vessel (\( p_1 \) at \( x = 0 \) and \( p_2 \) at \( x = 10 \)) show that progressively smaller fractions of the input pulses are transmitted through the valve as \( T_{Vp} \) decreases, and greater fractions as \( T_{Vp} \) increases. In other words, Figure 5.12 shows the valve closing in a linear fashion over the first 0.2 s and opening again over the subsequent 0.2 s. This example thus demonstrates how the valve variably transmits forward-running ventricular waves.

In the second example (Figure 5.13), the same vessel is used but now the input pulses are prescribed as a *backward pressure* at the outlet, while prescribed forward pressure at the inlet is
Figure 5.11: a) Input reflection coefficient spectrum (magnitude and phase) of a branching network (blue), a simple resistance terminal (green), and various tapering vessels: (red) $L = 30, A_0(L) = 0.2A_0(0)$, (black dashed) $L = 10, A_0(L) = 0.3A_0(0)$, (black solid) $L = 30, A_0(L) = 0.1A_0(0)$, all for viscous flow. ($\times$) is the same as (black solid) but with inviscid flow. b) An example of the pressure and velocity calculated at the input of different types of terminals (colours as in a)) for a non-sinusoidal pulse. Dotted black line represents the case where the terminal is perfectly matched (and thus measured pressure = prescribed pressure).

zero. This enables demonstration of the valve response to backward-running waves without interference from forward-running waves. Note that the frequency of the input pressure pulses is also halved. It can be seen in Figure 5.13 that each backward-running pulse gives rise to a $p_{LV}$ (which in this case consists of only an afterload contribution) equal to zero when the valve is fully closed and non-zero contributions when $R_{Vr} < 1$. It is important to point out that the valve behaviour is not the same as for a partial reflection and transmission at a discontinuity, as in Section 5.4. For a discontinuity, a total positive reflection (corresponding to a closed valve) would cause a transmitted wave double the size of the reflected wave (since $T = R + 1$, and if $R = 1$, then $T = 2$). However this is clearly not realistic for a valve, where a total reflection should correspond to zero transmission and vice versa. Turning now to the reflection characteristics of the valve, $p_1$ and $p_2$ both demonstrate that a proportion (equal to $R_{Vr}$) of each backward-running wave is reflected. This is not so obvious in $p_1$ since backward-running and forward-running (reflected) waves are superimposed; note the wave at 0.2s which is double the amplitude of the input pulse. However, the reflected waves are clearly seen in $p_2$, where every second wave is a partial reflection of the previous backward-running wave. In summary, these examples have demonstrated that forward-running waves from the ventricle are partially transmitted by the valve according to the value of $T_{Vp}$, while backward-running waves from the aorta are partially reflected according to $R_{Vr}$. These backward-running waves also determine the afterload contribution of $p_{LV}$. 
Figure 5.12: Demonstration of the transmission characteristics of the aortic valve. The input is a prescribed forward pressure at the inlet.

Figure 5.13: Demonstration of the reflection characteristics of the aortic valve and how backward-running waves contribute to afterload-corrected left-ventricular pressure ($p_{LV}$). The input is a prescribed backward pressure at the outlet.
5.8 External Pressure and Subendocardial Coronary Vessels

In this section, the effects of applied external pressure on a subendocardial coronary vessel are investigated in the context of a realistic ventricular pressure and an opening and closing aortic valve. To this aim, a simplified model has been constructed as follows (see Figure 5.14h): The ventricular pressure and aortic valve (at \(x = 0\)) are as specified in Section 3.5. The aortic root has \(A_0 = 7.01\text{cm}^2\) and \(\beta = 10^6\text{dynes/cm}^3\) and at \(x = 1\) branches into a single straight (subendocardial) coronary vessel of length 7cm, \(A_0 = 0.12\text{cm}^2\) and \(\beta = 12.462 \times 10^6\text{ dynes/cm}^3\) and an aortic trunk, which has the same value of \(\beta\) as the root. The trunk is 10cm long with \(A_0 = 6.9\text{cm}^2\) and terminates in a single tapering vessel (\(A_0\) tapers by 90%) with a length of 30cm. This terminal vessel represents, in a very rough way, the rest of the systemic circulation and has the sole purpose of producing reflected waves that arrive back at the aortic root during diastole. A ventricular forward pressure is then prescribed as specified in Section 3.5. The external pressure is applied to the coronary vessel as in Figure 3.3, with \(k_c = 1\). Note that this simple model does not include a representation of subepicardial coronary flow where there is no applied external pressure.

Figure 5.14 shows a 3D representation of the 1D coronary vessel at different times during the cardiac cycle, where changes in cross-sectional area are exaggerated by a factor of 20.
5.14g gives the timing of each snapshot along with afterload-corrected ventricular pressure $p_{LV}$, aortic pressure $p_{AO}$, valve reflection coefficient $R_{Vr}$ and velocity obtained mid-way along the coronary vessel $u_{coro}$. In early systole, at a time just before the valve has opened (Figure 5.14a), ventricular pressure and thus external coronary pressure has increased. This leads to compression of the distal portion of the coronary vessel. At a slightly later time (Figure 5.14b), when the valve is opening, the external pressure is even more pronounced. This results in blood being squeezed out of the distal part of the vessel, with the proximal part expanding to accommodate the resulting backflow. During ejection (Figure 5.14c), the coronary compression is relatively constant, but the increased aortic pressure gives rise to a forward component to flow in the coronary vessel. This forward component of total flow reduces the large negative flow but does not overcome it. This is seen as an expansion of the whole coronary vessel in Figure 5.14c compared with Figure 5.14b. Around the time of valve closure (Figure 5.14d), both the ventricular and aortic pressure fall, which leads to some relaxation of the coronary vessel. As ventricular pressure continues to fall after valve closure (Figure 5.14e), the compression of distal part of the coronary vessel is removed, and thus the backflow is also removed. At the same time, reflected waves from the systemic circulation arriving at the aorta cause a forward flow in the coronary vessel which expands accordingly. Later in diastole, as aortic pressure gradually declines (Figure 5.14f), the forward coronary flow also declines, leading to complete relaxation of the coronary vessel until the start of the next cardiac cycle.
Chapter 6

Investigation of Various Normal and Disease States

6.1 Integration of Model Components

In chapter 5, each component of the model was verified. The full model incorporates all of these components, including systemic and coronary arterial circulations, ventricular pressure and aortic valve. Before showing results obtained from the full model, an overview of the implementation will be provided. This consists of three stages: pre-processing, the main processing unit and post-processing. All of these stages were programmed in Matlab using custom-written m-files (i.e. matlab scripts).

Pre-processing
The two key inputs to the model are the mesh and the ventricular input waveform.
1. The 1D mesh contains the geometry and material properties of each segment of the arterial tree, as well as information regarding how segments are connected. The characteristics of each terminal element (i.e. length and taper gradient) are also set in the mesh.
2. The ventricular input waveform is generated using user-defined input parameters such as end-diastolic pressure, peak pressure, isovolumic contraction/relaxation rates and systolic/diastolic time intervals.

The 1D mesh and ventricular input waveforms are both written to files for use in the main program. The preprocessing stages in the main program are as follows:
3. Read in the 1D mesh and calculate the inverse mass matrices for each elemental sub-domain (Eq.(4.11)).
4. Read in the ventricular input waveform and calculate the incoming characteristic at the inlet for each time step (Eq.(2.26)).
5. Calculate the valve opening and closing function (Eq.(3.15)).
6. Calculate an external pressure weighting factor for each node in the subendocardial coronary ‘equivalent’ vessels (Eq.(3.19)).
Main Processing Unit

The main processing unit consists of the following stages for every time step.

7. Using the value of afterload-corrected ventricular pressure ($p_{LV}$) from the previous time step (or initial value for the first iteration), calculate the external pressure for each node of the subendocardial coronary vessels (Eq. (3.19)).

8. Solve the governing equations using the LCG method.

9. Calculate the outgoing characteristic at the inlet (Eq. (2.20)).

10. Based on the values of pressure and flow in the previous time step, calculate the valve reflection and transmission coefficients ($R_{Vr}$ and $T_{Vp}$) (see Section 3.5).

11. Using the prescribed incoming (ventricular) characteristic (step 4) and the valve coefficients (step 10), calculate the incoming (aortic) characteristic (Eq. (3.13)).

12. Based on the incoming and outgoing characteristics, calculate and assign the boundary conditions at the inlet (see Section 2.3.2).

13. Calculate the afterload-corrected ventricular pressure (Eq. (3.18)).

14. For each discontinuity or branching point (i.e. bifurcation, trifurcation etc), calculate the boundary conditions for all co-located nodes (see Section 3.2).

15. For all tapering terminal vessels, calculate the outgoing characteristic (Eq. (2.21)). Using a reflection coefficient of zero, calculate the incoming characteristic and the boundary conditions for each outlet.

Post-processing

In post-processing, the results are stored, visualised and analysed.

16. The pressure, velocity and flow at pre-specified ‘monitoring points’ throughout the arterial tree are written to a text file for storage.

17. Particular waveforms of interest are graphed and viewed.

18. Analysis of waveforms is performed as necessary.

6.2 Waveforms in the Arterial Tree

Having implemented the full model of the arterial tree, ventricular pressure, aortic valve and coronary circulation, various tests of the validity and potential applicability of the model are considered below. These includes simulation of ‘normal’ states and disease states. The waveforms produced by the model display considerable concordance with haemodynamics measured in vivo. For each disease state, one or several changes to the input parameters have been made in order to draw comparisons with the normal state. However, it should be stressed that while these changes are based on known phenomena associated with each disease found in the literature, they do not take into account all of the complex physiological interactions that are present in reality. Therefore, the results may not represent the disease precisely.
For all simulations, unless otherwise stated, the initial pressure in all arterial segments was 50 mmHg, which corresponds to the non-zero asymptote seen in vivo during asystole [79], prescribed LV pressure $p_{LV} = 85/5$ (max/min), RVOT = RVCT = 57ms and heart rate (HR) = 73 bpm. Tapering vessel terminals tapered to an $A_0$ of 0.03cm$^2$ or 0.9$A_0(0)$, whichever was smaller. The maximum element length was 1.5cm and $\Delta t = 25\mu s$ (slightly lower than the value calculated from the Eq.(4.17)). Variables were monitored at the mid-point of each arterial segment.

6.3 Normal ‘At Rest’ State

Figure 6.1 shows various waveforms for a normal adult at rest. The model produces waveforms that contain all the well-known features that are obtained from in vivo measurements, with regularity arising after the first beat. The plot of aortic valve reflection coefficient ($R_{Vr}$) shows that the valve opens and closes at the appropriate times based on local haemodynamics as discussed in Section 3.5. Prescribed ($\bar{p}_{LV}$) and afterload corrected ($p_{LV}$) LV pressure are shown along with ascending aortic pressure ($p_{AO}$) and aortic flow ($Q_{AO}$), all which display normal morphologies [80, 81]. It can be seen that during systole, afterload has the effect of increasing ventricular pressure. Also during systole, $p_{AO}$ is almost equal to $p_{LV}$, with a small positive pressure difference ($p_{LV} - p_{AO}$) in early systole (marked feature b) which drives forward flow, and a small negative pressure difference in mid-to-late systole caused by backward-running waves and the relaxing ventricle which cause reductions in aortic flow and lead to valve closure. Relatively early in systole, there is a pressure-increasing and flow-decreasing hump in $p_{AO}$ and $Q_{AO}$ (feature c). This is the well-known pressure augmentation [82] that is due to reflected waves arriving at the aorta and causes the shape of $p_{LV}$ and $p_{AO}$ waveforms to depart from that of $\bar{p}_{LV}$. Valve closure is associated with the dicrotic notch in $p_{AO}$ (feature a). This jump in pressure can be explained by noting that the valve reflection coefficient is rapidly increasing during this time and thus backward-running waves begin to reflect from the valve. At this time there is also a small amount of reverse flow across the valve. During diastole, $Q_{AO}$ is effectively zero while $p_{AO}$ gradually declines. This decline is governed by reflected waves and for the case of asystole, when the heart stops beating for an extended period, it can be seen in Figure 6.2 that the pressure falls in a roughly exponential fashion (a non-linear least squares fit to a mono-exponential function yields $R^2=0.96$) to a non-zero plateau, as is observed in vivo [79, 83]. Using the data shown in Figure 6.1, the common haemodynamic measures of systolic/diastolic(mean) aortic pressures of 110/73(94), cardiac output (CO = mean $Q_{AO_{mean}}$) of 4.5 L/min, contractility index (maximum $dp_{LV}/dt$) of 1179 mmHg/s, and systemic vascular resistance (SVR = mean $p_{AO}$ / CO with central venous pressure taken to be zero) of 1671 dynes/s/cm$^5$ would all be considered normal for an adult human at rest.

The morphology of coronary flow also accords with in vivo data. Mean flow in the LCA and RCA was 0.127 and 0.181 L/min respectively, with total coronary flow accounting for 6.8% of cardiac output, which again is in the range of normal values. In the LCA, the majority of flow ($Q_{LCA}$) occurs during diastole [26, 27, 28] and there are two well-defined local minima [28, 31]. To explain these features, it is helpful to observe that $Q_{LCA}$ is equal to the sum of subepicardial and
subendocardial flows ($Q_{\text{Lepi}}$ and $Q_{\text{Lendo}}$). $Q_{\text{Lepi}}$ has a similar morphology to aortic pressure which shows that forward-running waves are predominant throughout the cardiac cycle. In contrast, $Q_{\text{Lendo}}$ reveals a large amount of backflow during systole when the heart squeezes blood out of the subendocardial equivalent vessel, while during diastole when there is almost no external pressure applied, $Q_{\text{Lendo}}$ follows $Q_{\text{Lepi}}$. Such large systolic subendocardial backflows have been observed in [84]. The first minimum (feature e) in $Q_{\text{LCA}}$ occurs in early systole and is caused by the fall in $Q_{\text{Lendo}}$. The presence of reverse flow in $Q_{\text{LCA}}$ thus depends on whether the negative $Q_{\text{Lendo}}$ outweighs the positive end-diastolic $Q_{\text{Lepi}}$. The $Q_{\text{LCA}}$ second minimum occurs at the time of valve closure and is accompanied by decreases in both $Q_{\text{Lepi}}$ and $Q_{\text{Lendo}}$. This is most likely associated with the fact that $Q_{\text{AO}}$ falls rapidly just before the external pressure is removed and $Q_{\text{Lendo}}$ begins to rise. In the right coronary circulation, $Q_{\text{RCA}}$, $Q_{\text{Repi}}$ and $Q_{\text{Rendo}}$ always remain positive [33], since the external pressure exerted on subendocardial vessels is less pronounced. The effect of external pressure is seen, however, by the reduced flow in $Q_{\text{Rendo}}$ compared with $Q_{\text{Repi}}$ during systole.
Chapter 6. Investigation of Various Normal and Disease States

Figure 6.2: Simulation of asystole, where the heart stops beating for an extended time. Aortic pressure decreases in an approximately exponential fashion to a non-zero plateau.

Figure 6.3: a) Pressure, b) flow and c) velocity profiles obtained in locations progressing from the aorta to the leg.

Figure 6.3 shows pressure, flow and velocity in arteries progressing from the aorta to the leg. There are several notable features of such a progression which are supported by previous findings [1, 2, 8, 50]. First, the peak pressure increases with distance from the heart due to the progressive decrease in vessel cross-sectional area. Second, the slope of the initial pressure rise is steeper at more distal sites due to the non-linearity of the system, such that if the arterial system were longer, shocks would eventually form. Third, flow rate decreases at more distal sites since flow is being distributed between many branches of the arterial tree. Finally, peak velocity increases initially due to the decreasing cross-sectional area, however the reduction in flow rate due to branching eventually causes velocity to decrease also.

6.3.1 Exercise

Exercise is characterised by an increase in heart rate (HR), force of ventricular contraction and peak pressure. Systemic vascular resistance also drops because more small blood vessels are recruited for oxygen transfer [85]. To simulate moderate exercise, the model parameters
were adjusted as follows: HR = 115 bpm, $\bar{p}_{LV} = 115/5$ mmHg and RVOT = RVCT = 35 ms. Vascular resistance was reduced by decreasing the taper severity of terminal elements so that $A_0(L) = 0.1 \text{cm}^2$ or $0.9A_0(0)$, whichever was smaller. Figure 6.4b shows a regular beat under these conditions and may be compared to the ‘at rest’ case in Figure 6.4a. Of particular note is a 3.3 fold increase in cardiac output and an associated increase in coronary flow. There is also an increase in peak $p_{AO} - p_{LV}$ to 17.8 mmHg (compared with 6.7 mmHg at rest). Contractility also increased by 133%. These results accord well with in vivo measurements [85].

6.3.2 Cardiomyopathy

Cardiomyopathy may take several forms but is generally characterised by a reduction in the capacity of the heart to generate force. Accordingly, peak $\bar{p}_{LV}$ was reduced to 60 mmHg, while the isovolumic contraction and relaxation times were increased by 30% compared with the normal ‘at rest’ case. Figure 6.4c shows that cardiomyopathy has the opposite effect to exercise in a normal heart, with cardiac output dropping to 1.79 L/min, contractility by 47% and $p_{AO} - p_{LV}$ by 43%. Similar trends have been observed in [86]. While [86] showed only small reductions in left coronary flow, the model predicted a 64% decrease. This may reflect that the amount of external pressure applied by the failing heart is actually less than applied in the model.
6.3.3 Aortic Valve Regurgitation (or Aortic Insufficiency)

Compromise of the structural integrity of the aortic valve can lead to leakage of blood from aorta to ventricle during diastole. To model mild valve regurgitation, the maximum valve reflection coefficient was set to $R_{Vr}(\text{max}) = 0.9$. This led (Figure 6.4d) to sustained $Q_{AO}$ backflow during the whole period of diastole, and although peak $Q_{AO}$ was higher, cardiac output fell by 37%. Valve leakage also led to a small amount of negative flow in $Q_{Lepi}$ as well as both right coronary flows. End-diastolic and mean $p_{AO}$ fell while peak $p_{AO}$ was preserved (40/114(76)) and peak $p_{AO} - p_{LV}$ increased by 64%. These findings are in good agreement with [87].

6.3.4 Aortic Valve Stenosis

Aortic valve stenosis (or just ‘Aortic Stenosis’) is a narrowing of the aortic valve which impedes systolic flow. This leads to a significant pressure gradient between the LV and the aorta, and to compensate, the LV must generate much greater pressures to maintain adequate arterial pressures and flows. This may be modelled with a reduced maximum valve transmission coefficient or non-zero reflection coefficient during systole as well as an increased $\bar{p}_{LV}$. Using $R_{Vr}(\text{min}) = 0.8$ and $\bar{p}_{LV} = 100/5$, Figure 6.4e reveals a large ventricular-aortic pressure gradient (peak $p_{AO} - p_{LV}$ of 26 mmHg compared with 6.7 mmHg in the normal state) which lasts for all of systole. Despite the increased ventricular pressure, aortic pressure is lower (64/89(77)), and this leads to compromised coronary flow. Due to increased external pressure during systole, there is a greater negative $Q_{Lendo}$ which overcomes $Q_{Lepi}$ and is revealed in $Q_{LCA}$ as a sustained systolic backflow. These trends have been observed in [88, 89].

6.3.5 Coronary Arteriosclerosis

Coronary arteriosclerosis is a stiffening of the coronary vessel walls due to the deposition of lipids, lipid by-products and calcium. To provide a basic model of arteriosclerosis, Young’s modulus of the coronary vessels was increased by a factor of 4. Since this is equivalent to a reduction in characteristic admittance (see Section 3.3), mean $Q_{LCA}$ and $Q_{RCA}$ fell by 52% and 46% respectively (Figure 6.4f) [28], although there was little change to the morphology of coronary flow. Systemic haemodynamics did not change significantly, although in reality, the reduced coronary flow would lead to compromised ventricular function and thus haemodynamics in general. To model this interaction, cardiac metabolism and gas transport between myocardium and coronary capillaries would need to be accounted for.

In summary, various normal and disease states have been simulated. While the model does not account for all physiological interactions or physical characteristics of the diseases, the waveforms obtained from the model are consistent with in vivo measurements and suggest that the model is physiologically relevant.
Chapter 7

Preliminary Comparison of 1D and 3D Modelling

The one-dimensional (1D) modelling presented in this work is an approximation of the true three-dimensional (3D) flow in real vessels. A major assumption of 1D models is that vessels have a circular cross-section and a flat or parabolic velocity profile. However, true vessels, while roughly axi-symmetric, have complex geometries and flow dynamics. This is especially true at vessel branching points such as bifurcations. One bifurcation that has commonly been studied in 3D is the carotid bifurcation [13, 42, 43, 45, 46, 47], where the common carotid branches into the internal and external carotids. Research on this particular bifurcation has been so extensive because carotid artery disease (stenosis of the carotid) is a high prevalence and serious disease. While earlier studies used idealised geometries of the bifurcation [45, 46, 48], there has been a more recent emphasis on using patient-specific geometries [13, 42, 43]. Using multiple 2D image slices from CT, MRI or ultrasound scans, the 3D geometry of a patient’s carotid bifurcation can be obtained. Although there are challenges to this process, such as limited resolution, the resulting geometry is more authentic than any idealised version. In addition, there is potential for patient-specific modelling to aid medical decision-making, since flow characteristics of each specific stenosis geometry can be assessed.

Another emerging technique that has been approached by several investigators [6, 13, 44] is coupled 1D/3D models, or multi-dimensional modelling. For example a 3D model of a localised anatomical segment (such as the carotid bifurcation) is coupled to a 1D model of the whole arterial network. In this way, the detailed fluid dynamics of the region of interest may be investigated, while the boundary conditions to the 3D model can be set in a more realistic way via the 1D network. In addition, the global haemodynamic effects of specific 3D geometry may be assessed. At present it is not feasible to create patient-specific 3D or even 1D models of the entire arterial network, but it is possible to use patient-specific data for a localised 3D model, of a lesion such as stenosis or aneurysm for example, and couple this to a generic 1D arterial network model. While multi-dimensional modelling is beyond the scope of this work, development of these techniques may provide important information for clinical decision-making that would not otherwise be available.
Chapter 7. Preliminary Comparison of 1D and 3D Modelling

This chapter presents a preliminary comparison between 1D and 3D patient-specific modelling of the carotid bifurcation. Few comparisons of this type exist in the literature, although some non-patient-specific examples are found in [4, 6]. Since the main scope of this work is 1D modelling, the 3D modelling is only preliminary in the following ways. First, fluid-structure interaction between blood flow and vessels walls (which is a rather complex undertaking) will not be treated. Thus the vessel walls will be assumed to be rigid. Second, only laminar flow will be considered and therefore a higher value of blood viscosity will be used to avoid high Reynold’s numbers. Lastly, simulation of carotid artery disease will not be considered. While it may be argued that these simplifications make the 3D model irrelevant, the primary purpose of this chapter is to provide a comparison between 1D and 3D models, as well as provide some preliminary experience in patient-specific modelling. The construction of the 3D model consists of the following steps: 1) Data Preparation, 2) Segmentation, 3) Surface Generation, 4) Mesh Generation, 5) Boundary Conditions and 6) Simulation. Following a description of each of these stages, a comparison with the 1D model will be made.

7.1 The 3D Model

A set of anonymous computed tomography (CT) images was obtained from Singleton Hospital, Swansea, and consisted of 390 axial slices, from the thorax to the nasal passage. Data preparation, segmentation, surface and mesh generation was performed with the data visualisation software AMIRA (Mercury Computer Systems, Chelmsford, MA, USA). Generation of boundary conditions and all post-processing was performed in Matlab. The simulations were performed using an in-house computational fluid dynamics solver [90].

7.1.1 Data Preparation

One slice of the raw image set is shown in Figure 7.1. In the context of this image, the carotid artery is a relatively small artery, with a cross-sectional area of approximately 0.4cm$^2$ in the common carotid and less for its branches. Cross-sections of the left internal and external carotid arteries just above the bifurcation are indicated in Figure 7.1 with the red and blue arrows respectively (note that all images shown are mirror images). Since the anatomical region covered by the images is much greater than desired, the first step is to crop them down to a more suitable region of interest. Figure 7.2a shows the cropped image. It can be seen that the resolution is quite low resulting in severe pixelation of the carotid arteries. This is a common problem encountered in biomedical imaging where resolution is often limited. The resolution can be improved however by resampling the image, for example with a Lanzcos filter (see AMIRA documentation for details). Figure 7.2b shows an example where the pixel size has been decreased from $0.088 \times 0.088 \times 0.1$cm to $0.02 \times 0.02 \times 0.02$cm. It can be seen that this removes the large pixelations and vastly improves the shape and clarity of the lumen boundaries.
Chapter 7. Preliminary Comparison of 1D and 3D Modelling

Figure 7.1: One of 390 axial slices from a CT scan between thorax and nasal passage. The red and blue arrows point to the left internal and external carotid arteries respectively. The red dotted box corresponds to the cropped region displayed in Figure 7.2

Figure 7.2: a) A cropped version of Figure 7.1 showing a small region surrounding the carotid arteries before resampling. b) The same region after resampling using a Lanzcos filter. The red and blue arrows point to the internal and external carotid arteries respectively.
7.1.2 Segmentation

For each 2D slice, the region corresponding to the internal lumen of each artery is then identified and marked. This process, called segmentation, is done on a per-pixel basis and can thus be rather time consuming. However, several software tools make segmentation less laborious. For example, with a magic wand tool, clicking on a single pixel causes selection of all surrounding pixels that are within a user-defined contrast limit (with the aid of an image histogram). There are also other standard image editing tools that may be used. Figure 7.3 shows an example of segmentation for the internal carotid artery. Once the lumen area is selected, the appropriate pixels are labelled in readiness for surface generation.

7.1.3 Surface Generation

The next step is generation of a 3D surface represented by a triangular mesh, where the regions marked on each 2D slice are connected. The surface is smoothed to remove any unwanted corners or points that arise from the segmentation. Figure 7.4 shows three surface meshes with different triangle densities. The regions on the surface that correspond to the inlet and outlets are manually marked and given specific boundary IDs (Figure 7.5). Boundary conditions can then be generated in the preprocessing stage and assigned in the main processing unit to the appropriate nodes based on these surface element IDs.
Figure 7.4: Three surface meshes with different triangle density.

Figure 7.5: Assignment of boundary IDs to the inlet (left) and outlets (right).
7.1.4 Volume Mesh Generation

The final stage in preparing the geometry of the problem is volume mesh generation. This is generated from the surface mesh using standard tools. Various operations and tests can then be performed to optimise the quality (e.g. aspect ratio) of the tetrahedral elements. An example volume mesh is shown in Figure 7.6, with a group of elements hidden so that some inside elements become visible. In order to investigate mesh convergence, a number of meshes were generated, each with a different density ranging from 16,079 elements to approximately 1.2 million elements.

7.1.5 Boundary Conditions

In 1D, the mean pressure, velocity or cross-sectional area at the inlet can be prescribed in a straightforward manner via the entering characteristic (Section 2.3). In the 3D, however, the no-slip condition \( (u|_R = 0) \) must be satisfied. A velocity profile for the inlet boundary condition may be obtained from Hagen-Poiseuille flow, but this is only appropriate for fully-developed steady flows. A better alternative is a fully-developed unsteady solution known as Womersley flow \([36, 91, 92]\). This is a 2D linear viscous solution of the Navier-Stokes equations in cylindrical tubes, and has been used in previous 3D modelling studies (for example, in \([48, 53]\)). Consider a sinusoidal mean pressure gradient at a given cross-section given by

\[
\frac{\partial p}{\partial x} = B \cos(\omega t + \phi) \tag{7.1}
\]

where \( B \) is the amplitude, \( \omega = 2\pi f \) is the angular frequency (radians/s) and \( \phi \) is the phase angle (radians). \( x \) refers to the axial direction and in cylindrical coordinates, \( \frac{\partial p}{\partial r} = \frac{\partial p}{\partial \theta} = 0 \), where \( r \) is the radial component and \( \theta \) is the tangential component. The velocity profile in that
Table 7.1: Harmonics used to construct the inlet velocity profile

<table>
<thead>
<tr>
<th>Harmonic</th>
<th>Frequency (Hz)</th>
<th>Amplitude (dynes cm(^{-2}) s(^{-1}))</th>
<th>Phase (rad)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>126.88125</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1.63548</td>
<td>219.048</td>
<td>-1.59841</td>
</tr>
<tr>
<td>2</td>
<td>3.27097</td>
<td>156.0645</td>
<td>3.04933</td>
</tr>
<tr>
<td>3</td>
<td>4.90645</td>
<td>80.2545</td>
<td>1.81371</td>
</tr>
<tr>
<td>4</td>
<td>6.54193</td>
<td>57.64425</td>
<td>1.22483</td>
</tr>
<tr>
<td>5</td>
<td>8.17742</td>
<td>56.193375</td>
<td>-0.107859</td>
</tr>
<tr>
<td>6</td>
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<td>25.0012125</td>
<td>-1.55024</td>
</tr>
<tr>
<td>7</td>
<td>11.4484</td>
<td>17.1054</td>
<td>-1.40587</td>
</tr>
<tr>
<td>8</td>
<td>13.0839</td>
<td>24.2474625</td>
<td>-2.93862</td>
</tr>
<tr>
<td>9</td>
<td>14.7194</td>
<td>8.1630375</td>
<td>1.45781</td>
</tr>
<tr>
<td>10</td>
<td>16.3548</td>
<td>10.90725</td>
<td>2.74547</td>
</tr>
<tr>
<td>11</td>
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<td>12.6963375</td>
<td>0.490823</td>
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<tr>
<td>12</td>
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<td>5.02695</td>
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</tr>
<tr>
<td>15</td>
<td>24.5323</td>
<td>2.558115</td>
<td>0.376408</td>
</tr>
</tbody>
</table>

Eq. (7.2) can only be applied to signals of the type in Eq. (7.1). However using the assumption of linearity, the velocity profile for an arbitrary pressure gradient may be obtained by adding the profiles of a number of sinusoidal harmonics. While in theory, exact representation of an arbitrary signal may require an infinite number of harmonics, physiological signals can be represented with sufficient accuracy using only a few harmonics. Table 7.1 provides the 15 harmonics used in this model which were obtained by performing a Fourier Series analysis on a measured aortic velocity waveform (see Acknowledgements). For each of these harmonics, the radial velocity profile was calculated from Eq. (7.2). (Note: For the ‘zero’ frequency component, a very small frequency (\(\omega = 10^{-5}\)) was used to avoid division by zero). All velocity profiles were then added together to yield the resultant velocity profile. The final result was also scaled to provide the desired peak velocity. Figure 7.7a,b shows the velocity profile at various times during the initial upstroke and around the time of flow reversal, while Figure 7.7c shows the mean velocity for the whole cardiac cycle. For large mean velocities, the velocity profiles are essentially parabolic. However more complex profiles are seen at near-zero velocities, where it is possible to have positive velocities near the centre of the vessel but negative velocities near the walls [53].

The velocity profile must then be mapped to the 2D inlet surface. If the inlet were perfectly circular, each node could be assigned a velocity for each time step based on its normalised radius. However, the input surface is generally not circular and so prescribing nodal velocities is
somewhat more complex. The mapping, illustrated in Figure 7.8, may thus be performed as follows.

1. Identify the inlet edge nodes based on the surface IDs of the surrounding elements.
2. Determine the centroid of the inlet, calculated as the average of \( x \) and \( y \) values, and perform a mapping on all nodes so that the centroid is at \((0,0)\).
3. Express the positions of all inlet surface nodes in 2D polar coordinates \((r, \theta)\), with the third co-ordinate assumed constant over the whole inlet surface.
4. Calculate a normalised radius for each inside node. This is found by first identifying the two edges nodes with the closest value of \( \theta \). From the absolute radii of these two edge nodes \((R_i \text{ and } R_j)\), a linearly interpolated radius \((R_{int})\) of an imaginary edge node is found. This imaginary edge node is on the same line that connects the inside node with the centroid.
5. Based on the radius of the imaginary edge node, the normalised radius \((r_n)\) of the inside node can be calculated as \(r_n = \frac{r}{R_{int}}\), and the appropriate velocity prescribed. This mapping results in a smooth 3D inlet velocity profile, as shown in Figure 7.9 at four different times during the cardiac cycle.

7.1.6 Simulation

Simulation was performed using an in-house computational fluid dynamics solver, which uses the Characteristic Base Split (CBS) method to solve the transient incompressible Navier-Stokes...
equations in 3D. A full description of the CBS method is beyond the scope of this work and is described elsewhere (for example, in [41, 77, 93, 94]). Briefly, the method solves the Navier-Stokes equations in three steps. In the first step, the pressure term is dropped and an intermediate velocity field is calculated. This intermediate equation is then readily solvable using the Characteristic Galerkin (CG) method. In the second step the pressure is calculated via an artificial compressibility method, which requires dual time stepping. In dual time stepping, each real time step is broken into a number of instantaneous steady-state time steps. Finally, using the equations from the first two steps, the corrected velocity field is calculated. The velocity profile (Figure 7.7) was discretised into 50 (real) time steps. The peak velocity was set to 66 cm/s, while the peak mean velocity was 45 cm/s. The blood viscosity was assumed to be 3.5 poise due to difficulty in attaining convergence with a lower value. This was possibly due to the fact that turbulence modelling was not included and the peak Reynold’s number (using a blood viscosity of 0.035 poise) was approaching the range for turbulent flow. Increasing the viscosity thus ensured laminar flow by reducing the Reynold’s number and resulted in acceptable convergence to instantaneous steady states.

To investigate mesh convergence, several meshes were generated, where the number of elements
(N\textsubscript{elem}) approximately doubled each time and it was found that little change occurred above \(N\textsubscript{elem} = 35,863\).

### 7.2 Comparison of 1D and 3D Models

The primary limitation of the 3D model is that the fluid-structure interaction between blood and vessel walls has been neglected, and thus the vessels walls are rigid. This makes direct comparison with the 1D model difficult, since the 1D equations Eq.(2.4) implicitly include this interaction. A rigid wall in 1D corresponds to an infinite value of \(\beta\) and thus wave speed (Eq.2.8), and consequently, unconditional instability (Eq.(4.17)). The best that can be done is to make the wall stiffness very large by including a large \(\beta\) value (i.e. large Young’s Modulus). Implicit in any 1D model is a rather simplified geometry. In the current model, the cross-sections of both the common carotid artery and its branches were not circular, but an average radius at the inlet and outlets was obtained. The resulting cross-sectional areas used in the 1D model were 0.309, 0.035 and 0.153 cm\(^2\) for the common, external and internal carotid arteries respectively. A small amount of linear taper in \(A_0\) was also used for the two branches \((A_{0\text{ext}}(L) = 1.2A_{0\text{ext}}(0)\) and \(A_{0\text{int}}(L) = 1.1A_{0\text{int}}(0)\)), since in the 3D geometry (Figure 7.4) it is clear that the cross-sectional area in both at the bifurcation is slightly lower at the outlets. The value of \(\beta\) for the inlet was chosen rather arbitrarily to be \(5 \times 10^6\) dynes/cm\(^3\). Since, in the 3D model, the mean velocities in parent and daughter branches had very similar shapes, it was assumed that the bifurcation was relatively well matched in the forward direction. Since \(A_0\) was known in both branches, the value of \(\beta\) (assumed the same for both branches) calculated to obtain good matching was \(3.1 \times 10^6\) dynes/cm\(^3\). The boundary conditions were set in a similar way to the 3D model. More precisely, and in contrast to the 1D results presented in previous sections, actual velocity was prescribed at the inlet via Eq.(2.24) (previous sections have used forward pressure), while actual pressure \((p = 0)\) was prescribed at both outlets. Figure 7.10 shows a comparison between the 1D and 3D models using the (mean) velocity waveforms obtained at the two outlets. Given the assumptions introduced to the 1D model, the agreement between the two models is striking.
While slightly different results may be obtained with different input parameters used in the 1D model, such as the ratio of $\beta$ between the two branches, this shows that 1D modelling is indeed generally adequate for representing flow in branching vessels.
Chapter 8

Conclusions, Limitations and Future Work

8.1 Conclusions

A one-dimensional model of the major arteries in the systemic arterial tree using the Locally Conservative Galerkin (LCG) method has been presented. This model includes a realistic ventricular pressure as the input, as well as an aortic valve that opens and closes independently and based on local haemodynamics. In addition, left and right coronary circulations were modelled with inclusion of regional (subendocardial and subepicardial) flow. An external pressure related to ventricular pressure was imposed on the distal portion of the subendocardial equivalent vessel to simulate the compressive force applied by the contracting myocardium. Tapering vessels were introduced for use as the model terminals, and it was shown that these adequately represent the input characteristics of the downstream vasculature, while being easy to incorporate into the model. Combining arterial and coronary circulations, as well as the aortic valve and ventricular pressure, and terminal elements with realistic input characteristics, makes this the most complete one-dimensional circulation model to date. Waveforms produced by the model contain all the important features observed in \textit{in vivo} measurements. In addition to the ‘at rest’ and exercise states, several disease states (Cardiomyopathy, Aortic Valve Regurgitation, Aortic Stenosis and Coronary Arteriosclerosis) were modelled and the resulting changes in haemodynamics agreed well with published literature. It should be noted however that it was not the aim of this study to provide comprehensive models of the various disease states, although it has been found that including one or several of the most important features of each disease does produce the expected changes in ventricular, arterial and coronary haemodynamics. Finally, a comparison was made between 1D and 3D representations of a patient-specific carotid bifurcation, and good agreement was observed. The design of a more complete 1D network model presented in this work as well as the development of 3D patient-specific modelling has great potential for future use in cardiovascular research and in aiding clinical decision-making.


8.2 Limitations and Future Work

The model does not account for the viscoelasticity of vessel walls and the viscosity model used assumed fully-developed steady flow (Poiseuille flow). While the inaccuracies introduced by such simplifications are expected to be small, such effects could readily be included in future studies. In modelling the arterial tree, it is difficult to obtain accurate data regarding geometry and material properties of all the major arteries. Similar to others [1, 2, 18], it was necessary to make some adjustments to the original data [8, 17] to obtain good matching of bifurcations in the forward direction. Overall, however, fewer adjustments were made to vessel radii than in [18] by including vessel taper, which is an important feature of real vessels. The geometry of the coronary circulation was also simplified. While this allowed idealised delineation of subendocardial and subepicardial flow, the equivalent vessels used may not precisely represent the actual coronary tree. It was also assumed that external pressure on left subendocardial vessels is equal to LV pressure, with a smaller proportion for right endocardial vessels. While others have used such an approach [31], this is only an approximation. Thus, future studies could incorporate a more extensive geometric model as well as a more accurate representation of intramyocardial pressure distribution.

There are many complex feedback systems and coupled processes that were not accounted for. For example, the effects of preload, humoral and neural control were not accounted for. Also, the model did not account for the dependency of heart performance on coronary perfusion. Future models could incorporate the metabolism of the myocardium as well as oxygen and carbon dioxide transfer to and from coronary blood. The calculation of an afterload corrected ventricular pressure has produced realistic ventricular pressures as well as ventricle-aorta pressure differences. While this works under most circumstances, the true ventricular pressure and pressure gradients would require a more complete model of the ventricle and aortic valve. For example, if systemic vascular resistance were high enough, it would be possible to achieve a situation where the valve does not open at all. While physically realistic, this simply shows that the true behaviour of the ventricle, which responds to arterial and coronary haemodynamics on an intra- and inter-beat basis, has been simplified.
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