Quantitative Blood Flow Measurement using C-Mode Doppler Ultrasound

by

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A thesis submitted in conformity with the requirements for the degree of Master of Science
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A new method of non-invasive blood flow measurement using Doppler ultrasound is presented and investigated. By applying pulsed Doppler ultrasound to make local measurements of blood velocity at constant depth in tissue, a velocity profile is estimated; spatial integration yields volume flow rate. This technique, known as C-mode velocity profiling, is plagued by flow estimation errors on the order of 20–60% due to partial volume effects. The hypothesis of this thesis is that application of attenuation compensation improves the accuracy and precision of C-mode velocity profiling by correcting for the partial volume effect. Systematic and random error for the new technique is investigated using a computational model and a steady state flow experiment. Both model and experiment confirmed the hypothesis, and determined that the remaining primary source of error is due to a correctable effect of signal processing. The mean error of the new flow measurement was –10 mL/min with a distribution that had a standard deviation of 18 mL/min. For physiologically relevant flow rates, this corresponds to estimation of blood flow to within 5%, with 95% confidence.
Acknowledgements

This work was supported in part by an Ontario Graduate Scholarship. That’s the easy bit.

Any piece of work of this magnitude is inevitably the result of the help and support of many. I can only hope to remember and recognize the people who have really helped to make the difference for me during my scientific trek here at Sunnybrook. These words below can only express the things that I value most from my mentors and my friends. It’s too difficult for me to form these feelings into sentences, so I’ll just express them in the way that they came to mind.

I’d like to recognize my thesis advisory committee, my mentors: Stuart Foster, who is always setting an example of optimism and inventiveness and balance. Graham Wright, who had the misfortune of having occasionally to wear awkwardly both hats of scientific advisor and personal friend; I learned scientific exactitude from him. And of course, my supervisor Peter Burns, who gave me a freedom that I did not even know to ask for. I learned, from his example, about speaking, about explaining, about idealism, and (I daresay) about doing things right.

At work and at play: Kasia Harasiewicz, who is perhaps the unseen glue of the ultrasound group; she is always saying the right things at the right time...not to mention helping me become a ski instructor. Don Knapik: late night idealism. Rudy Candela: enthusiasm. Jeff Stainsby: a compatriot in the outdoors. Geoff Lockwood, who inspired me to climb. Linda: genuinely one of the nicest people I’ve ever met; her kind words powered me through to the end.

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All my other friends for time well spent.

And my best friends, Katharine and Christopher, whose support I counted on, used, abused, and found solace in.
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Chapter 1

Blood Flow Measurement

1.1 Introduction

Quantitative measurement of blood flow has fundamental clinical and scientific significance in medical fields. Blood flow is defined in this thesis as the volumetric blood flow rate, that is, the volume of flow per unit time. Flow measurement has medical application in two broad areas: (1) for scientific understanding of physiology, and (2) for clinical assessment and patient management. This thesis is concerned with the quantitative measurement of blood flow in major vessels using ultrasound. The thesis describes the theory and experimental investigation of a new technique which is based on the combination of principles used in previous ultrasound methods. The strengths of this new technique include its non-invasive and non-destructive nature and the exclusion of dominant sources of error which plague existing ultrasound methods. Applications in both the areas of scientific exploration and clinical use are anticipated.

Flow measurement for scientific understanding of physiology has a long history. Several authors [46, 49, 68] have published brief summaries of this history of haemodynamics and blood flow measurement as introductions to their textbooks. William Harvey (1578–1657) is considered
the pioneer of modern cardiovascular physiology for his assertion that blood was forced from the left ventricle of the heart to be distributed in a uni-directional manner. Stephen Hales (1677-1761) first made measurements of blood pressure by arterial cannulation, and of ventricular volume in various species by using wax casts. Hales also introduced concepts of peripheral resistance, determined that the greatest resistance was due to arterioles and proposed a model which likened the dampening effect of the air-filled dome (the Windkessel) of contemporary fire engine pumps to the dampening effect of the arterial tree. All of this appeared in Hales' classic 1733 text Haemostatics [30]. Both Harvey and Hales are excellent examples of the parallel development of knowledge in physiology with experimental biophysical measurement.

Scientific studies of physiology today still use extensive animal experiments, with a focus on physiology in normal and disturbed conditions, as well as the evaluation of experimental surgical and medical treatment. As will be presented in Section 1.2.2, the traditionally accepted techniques of flow measurement are invasive. In light of the potential benefits of scientific inquiry, invasiveness is tolerated with some reservation. However, invasive procedures complicate the process of monitoring progressive changes in flow and currently require surgical implantation of probes. A second problem with invasive procedures is that flow is often disturbed by the measurement itself. A non-invasive and non-destructive method with similar accuracy would therefore be valuable. Development of such methods could lead to better understanding of physiology and of experimental medical and surgical procedures in humans.

Clinical blood flow measurement has been more limited, due to the demands of patient safety. Problems in the clinic range from diagnostic evaluation to assessment of a given treatment or procedure. Some of the methods used to investigate blood flow scientifically are not applicable in the clinic due to their invasive or destructive nature. Currently, the value of additional haemodynamic
information is set against the risk associated with flow measurement; using current techniques, this balance has been met in few clinical applications. Measurement of cardiac output for the evaluation of heart function is one of these, and it is described in greater detail in Section 1.2.3. The potential for clinical assessment in other areas such as the fetus, liver, and vessel grafts are also discussed briefly in Chapter 3.

This chapter surveys principles relevant to ultrasound blood flow measurement. The next section deals with motivation: the fundamental importance of blood flow, the current state of flow measurement, and the clinical problem of cardiac output measurement will be described. Next, some principles of flow physics will be introduced, including discussions on the flow profile and its meaning, the theory of laminar and turbulent flow in rigid vessels, and some physical parameters of the vascular system in vivo. Given this background, non-invasive transcutaneous ultrasound techniques of flow measurement will be discussed in greater detail. The chapter concludes with an outline of the work of this thesis.

1.2 Motivation

1.2.1 The Importance of Blood Flow

Blood flow has fundamental physiological relevance because it is an important parameter of circulatory transport, and it is an indicator of organ function. Blood transports oxygen, carbon dioxide, nutrients, waste, heat, hormones, and agents of the immune system. Under normal conditions, blood flow is regulated according to changing demand for the delivery or removal of these products. Under diseased and abnormal conditions, the circulation may become compromised. This results in the failure of tissues to receive sufficient quantities of vital substances, and/or toxic effects due to the build up of waste products. The basic relationships of blood flow, circulatory transport, and
flow regulation are discussed here to indicate the relevance of blood flow measurement.

Circulatory transport is vital to cell survival within the body. The maintenance of a consistent internal tissue environment (the concept of homeostasis) relies on the exchange of essential nutrients and waste between the cellular environment and the capillary blood supply. The activity of cells within a tissue bed determines the demand for substances and waste removal. Increased demand must be met by increased exchange of substances between the capillary blood supply and the tissue bed. This exchange can be limited either by the rate of transport across the capillary walls or by the quantity of a substance available in the capillary blood supply.

Blood flow is related to the availability of substances within the capillary supply. Figure 1.1 illustrates the macroscopic concept of circulatory transport. The parameters denoted in the figure are related according to an expression of the conservation of mass known as the Fick Principle:

\[
\dot{m} = \frac{dm}{dt} = Q(C_a - C_v)
\] (1.1)
where $\dot{m}$ is the mass of delivered substance per unit time, $Q$ is the blood flow, $C_a$ is the arterial concentration of the substance, and $C_v$ is the venous side concentration.

According to the Fick Principle, the exchange rate of a substance is equal to the product of the blood flow and the arteriovenous concentration difference. Knowledge of both the blood flow and arteriovenous concentration difference is thus important for physiological estimation of demand and use of oxygen and nutrients, as well as the elimination of waste.

Blood flow and arteriovenous concentration difference are determined by different aspects of circulatory physiology. Flow is determined by physical parameters including vascular resistance and blood pressures (this will be considered in greater detail in Section 1.3). Physiological alteration of vascular resistance and pressure difference is the primary means by which flow is controlled. Arteriovenous concentration differences reflect the efficiency of the transport process between capillary blood and tissue, and are the result of the Fick Principle mass balance. However, there are physiological limits to which the arteriovenous concentration difference can change.

The maximum degree to which arteriovenous concentration difference can change is reflected in a parameter known as the arteriovenous (AV) reserve, or buffer capacity. This reserve quantifies the maximum difference between venous concentration and normal arterial concentrations, as compared to the normal arteriovenous concentration difference:

$$AV\ Reserve = \frac{C_a(\text{normal}) - C_v(\text{minimum})}{C_a(\text{normal}) - C_v(\text{normal})}$$  \hspace{1cm} (1.2)

Table 1.1 summarizes reserve capacity for different substances in the systemic circulation. Some substances are extracted with great efficiency, and arterial concentrations are restored with each pass through the circulation (a process that normally takes a time on the order of 30 seconds to a minute). For example, oxygen and carbon dioxide levels are restored with each passage through the
pulmonary circulation. Other substances are restored on longer cycles. Exchange of these "longer cycle" substances results in a deficit or build-up in arterial concentration which is eventually restored to normal levels.

<table>
<thead>
<tr>
<th>Component</th>
<th>Arterio-Venous Reserve</th>
</tr>
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<tbody>
<tr>
<td>oxygen</td>
<td>3</td>
</tr>
<tr>
<td>glucose</td>
<td>30</td>
</tr>
<tr>
<td>fatty acids</td>
<td>28</td>
</tr>
<tr>
<td>amino acids</td>
<td>36</td>
</tr>
<tr>
<td>carbon dioxide</td>
<td>25</td>
</tr>
<tr>
<td>nitrogenous waste</td>
<td>480</td>
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Table 1.1: Systemic Arterio-Venous Reserve/Buffer Capacity (from Guyton [29])

Physiologically, both changes in flow and changes in arteriovenous concentration difference are important for increased delivery or extraction of substances. The Fick principle indicates that limitations in arteriovenous reserve reflect the relative importance of flow in the determination of availability of a given substance. Therefore, flow regulation is an important mechanism for maintaining sufficient oxygen levels, particularly in tissues where the concentration difference is near its maximum. Table 1.2 summarizes oxygen consumption and blood flow of different organs in the adult human (at rest). The table indicates, for example, that flow regulation is an important mechanism of maintaining oxygen availability in the heart muscle, even at rest. Under conditions of stress, such as in exercise, the demands for oxygen (and other nutrients) may rise dramatically, requiring both increased arteriovenous concentration difference and increased blood flow.

Blood flow is regulated locally according to the needs of each tissue bed. These needs may be different depending on function. Except in the kidneys and the skin, the most important factor in the regulation of flow in the systemic circulation appears to be the tissue need for oxygen [29]. Other factors affecting flow regulation include: pH, carbon dioxide levels (particularly in the skin and the brain), osmolality, and temperature [18,29]. The relationship of blood flow variation to
Table 1.2: Oxygen Consumption of Various Tissues in a 63kg adult human at rest [18].

<table>
<thead>
<tr>
<th>Organ</th>
<th>Arteriovenous Oxygen Difference (mL/L)</th>
<th>Arteriovenous Oxygen Consumption (mL/min)</th>
<th>Blood Flow (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>34</td>
<td>51</td>
<td>1500</td>
</tr>
<tr>
<td>Kidneys</td>
<td>14</td>
<td>18</td>
<td>1260</td>
</tr>
<tr>
<td>Brain</td>
<td>62</td>
<td>46</td>
<td>750</td>
</tr>
<tr>
<td>Skin</td>
<td>25</td>
<td>12</td>
<td>462</td>
</tr>
<tr>
<td>Skeletal Muscle</td>
<td>60</td>
<td>50</td>
<td>840</td>
</tr>
<tr>
<td>Heart Muscle</td>
<td>114</td>
<td>29</td>
<td>250</td>
</tr>
<tr>
<td>Rest of Body</td>
<td>129</td>
<td>44</td>
<td>336</td>
</tr>
<tr>
<td>Whole Body</td>
<td>46</td>
<td>250</td>
<td>5400</td>
</tr>
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function (due to its regulation) suggests that flow, in addition to being a fundamental circulatory transport parameter, is a physiological indicator.

Summary

In summary, measurement of blood flow has fundamental physiological relevance. Circulatory transport is intimately related to the blood volume flow rate ("blood flow"). Consequently, the function and viability of cells in tissues is related to the flow into capillaries which are fed upstream from major arteries. Furthermore, under normal conditions, blood flow is regulated according to the needs of each tissue bed. Blood flow through major vessels, and its variation, may therefore be a valuable indicator of organ function. Measurement is relevant in the basic study of human physiology, and may lead to new clinical insight into the pathophysiology of a wide spectrum of diseases. The use of blood flow measurement in the clinical evaluation of heart disease will be discussed as an example in Section 1.2.3, following a brief survey of flow measurement techniques.
1.2.2 Survey of Flow Measurement Techniques

The following section surveys existing techniques of blood flow measurement, and their fields of relevant application. Excellent descriptions of the theory, practice, and clinical application of blood flow measurement can be found in Mathie [43], Woodcock [68], and Nichols and O'Rourke [49].

**Timed Collection**

The gold standard technique of flow measurement precision for major vessels is timed collection. This involves cutting the vessel, and measuring its outflow as a function of time. Precision is improved by making measurements over longer periods of time. Timed collection determines a steady-state flow rate over many cardiac cycles; time variation in flow due to cardiac pulsation is not resolved. The technique is destructive, and the difficulty of ensuring physiologically similar outflow conditions make this method impractical for both the problems of physiological study and clinical assessment, as compared to other techniques. It is, however, an invaluable tool for evaluating the precision and accuracy of other flow measurement techniques.

**Indicator Techniques**

Flow measurement using indicator techniques is achieved by exploiting principles of mass transport. The techniques fall into categories of indicator dilution, indicator uptake, and indicator clearance. Indicator methods are considered good compromises between accuracy and invasiveness, and are the most widely used techniques for the clinical assessment of flow. Indicator methods are used, for example, in measuring liver flow using bromsulphalein (BSP) uptake, kidney flow using para-aminohippuric acid (PAH) uptake, and cardiac output using (i) pulmonary oxygen uptake (the Fick-Oxygen method), (ii) indicator dilution using cardiogreen, or (iii) thermal dilution. Like timed collection, indicator techniques depend on steady-state in the system, and measure an overall flow
rate that does not resolve variations due to cardiac pulsation. Indicator techniques also require intra-vascular catheterization, either for the introduction of indicator at a specific artery, and/or for the measurement of concentration at a particular site in the vasculature. This is a disadvantage both in its invasiveness and also in its disturbance of natural flow conditions.

**Perivascular Cuff Flowmeters**

Flow measurement devices have been developed which depend on surgical exposure of the vessel, in order to place a perivascular cuff. Currently two kinds of cuff flowmeters are used: electromagnetic (EM) flowmeters, and ultrasound transit time flowmeters. EM flowmeters measure induced transverse voltage as a result of blood flow through a magnetic field. Ultrasound transit-time meters measure the difference in pulse travel time between two opposing transducers due to fluid motion. Both EM and ultrasound transit time flowmeters are able to resolve cardiac pulsatility in blood flow. These devices are valuable in the physiological study of flow; implanted probes can also measure serial changes, and the perivascular nature of the probes allows them to make measurements without disturbing flow conditions. Perivascular cuff flowmeters are used for chronic implantation in animals and acute surgical monitoring in humans.

**Magnetic Resonance Techniques**

Magnetic resonance (MR) techniques of flow measurement have been pursued with great interest due to their non-invasive nature. Magnetic resonance techniques rely on the measurement of a precessing net magnetic moment induced in the test subject by a large static magnetic field and excitation using radiofrequency waves. The two broad MR techniques which are sensitive to flow are referred to as 2D time-of-flight (TOF) and phase contrast [40]. Time-of-flight techniques are based on the in-flow of fresh signals (due to blood flow) into a two dimensional plane where the signal from
stationary tissue has been suppressed. This technique is used in magnetic resonance angiography to map blood vessels based on flow. It is not suited, however, to quantitative flow measurement due to lack of quantitative sensitivity for physiological flow rates. Phase Contrast techniques make use of the accumulated phase of the precessing magnetic moment in the presence of a magnetic field gradient. When phase contrast techniques are applied, the signal from moving blood accumulates excess phase in linear proportion to its velocity (along the direction of the field gradient). Mean velocity measurements can be made, and multiplied with area measurements from MR imaging in order to calculate a flow rate. The current primary limitations of phase contrast techniques are its relatively long acquisition time (on the order of minutes), and spatial resolution. These techniques are currently quite experimental, and their ultimate utility is yet to be determined. MR techniques are a promising avenue of future research in flow measurement.

Non-invasive Ultrasound Techniques

Ultrasound offers another method for the non-invasive measurement of flow. Doppler ultrasound techniques for haemodynamic assessment are used extensively in clinical applications [60], however they are not currently used routinely for quantitative flow measurement. The various techniques of ultrasound flow measurement are described in detail in Section 1.4. In the context of this discussion, it is sufficient to mention that these techniques combine Doppler and imaging techniques to determine flow. Doppler ultrasound is used to determine a mean velocity. This mean velocity is subsequently multiplied by an area measurement, obtained either using ultrasound grey-scale imaging or from additional properties of the Doppler ultrasound signal, to calculate flow. The techniques are fast and are able to resolve changes in flow over the cardiac cycle. These advantages make ultrasound a very attractive approach for quantitative flow measurement. Although Doppler techniques have been applied in several clinical studies (summarized in Section 1.4), they are only
Summary

Currently accepted techniques of flow measurement, including timed collection, indicator methods, and perivascular flowmeters, are invasive. They are used in physiological studies, but their invasiveness limits clinical use. Non-invasive flow measurement has been pursued using ultrasound and magnetic resonance techniques. Although both of these are promising, ultrasound is more economical and has the advantages of speed and spatial resolution. It is anticipated that the development of a reasonably accurate and non-invasive ultrasound method will be tremendously valuable both for physiological study and for clinical assessment of blood flow.

1.2.3 Heart Disease and the Cardiac Output, an Example Application

Cardiovascular disease is the major cause of death, disability, and illness in Canada [31]. Thirty-nine percent of deaths in Canada in 1990 were due to cardiovascular disease. Ischaemic heart disease is a major subset of cardiovascular disease, accounting for twenty-three percent of all deaths (or fifty-eight percent of all deaths due to cardiovascular diseases). Ischaemic heart disease refers to impaired heart function due to reduced blood supply to the heart muscle.

Cardiac output is the volume of blood pumped by the heart per unit time. This blood flow is distributed through the branching vascular network into the various tissue beds of the body. The response of cardiac output to overall metabolic demand indicates function of the heart. This is an important method of evaluating both the severity of ischaemic heart disease, and the efficacy of heart disease treatment. In this section, the measurement of cardiac output is considered as an example application of clinical blood flow measurement.
In a healthy individual, the cardiac output and the arteriovenous oxygen difference increase together under increased metabolic demand. The maximum percentage by which cardiac output can increase above the resting value is known as the cardiac reserve. In the normal healthy individual, it is about 300–400 percent [28] (in athletes, it can be as high as 500–600 percent). Thus, the arteriovenous reserve and the cardiac reserve can combine to provide an eighteen-fold increase in oxygen delivery in trained athletes. But in heart disease the cardiac reserve is reduced, and in serious heart disease, there may be no cardiac reserve at all. Cardiac output is commonly normalised to body surface area; this value is known as the cardiac index. In a patient with progressively worsening heart disease, the cardiac index drops with increasing metabolic demand, while the arteriovenous oxygen difference increases to an even greater degree in order to accommodate the increased oxygen supply.
demand. This is because the heart becomes incapable of generating the increased pumping force that is required. Since the heart muscle itself requires oxygen for function, this can lead to a vicious cycle of increased oxygen demand, and insufficient supply which leads to death. Figure 1.2, modified from Grossman [27], illustrates this effect.

Cardiac reserve is reduced in ischaemic heart disease due to limitations in blood flow to the heart muscle. In severely diseased individuals, muscle fibres make maximal use of available oxygen when the body is at rest. When higher levels of cardiac output are required (due, for example, to physical exertion), the heart must work harder and requires more oxygen. In ischaemic heart disease, the coronary vessels are diseased and are unable to conduct more blood. This results in insufficient oxygen supply to the heart muscle and an inability to increase cardiac output.

Management and treatment of ischaemic heart disease is centred around restoring sufficient coronary blood supply. Medical treatment of disease may involve drugs which may use a variety of means to increase flow to the heart. Surgical intervention is necessary in more severe cases. In these situations, flow is restored to the heart either by grafting vessels into the coronary circulation (coronary bypass surgery), or by expanding the lumen of vessels using balloon-catheters (angioplasty) [3], which may also involve the permanent placement of an expanded wire mesh (stenting).

Role of Blood Flow (Cardiac Output) Measurement

The cardiac output is an indicator of the functional status of the heart. Of particular interest is the cardiac reserve, which requires measurement under conditions of various metabolic loads. This measurement is valuable because it would serve to indicate both the severity of disease, as well as the relative success of treatment. Thus, quantification of cardiac output is of direct relevance.

The two most common methods of assessing cardiac output are the Fick oxygen method, and thermal dilution. Other indicators are also used, such as indocyanine green. (Indicator dilution
methods were discussed in section 1.2.2). Measurement accuracies of approximately 5% have been reported using these techniques [29, 52]. These clinically accepted methods all require right heart catheterization. Consequently, these methods are not suitable for repeated application at intervals in the same patient [7], making it impractical for monitoring serial changes in cardiac function. Catheterization also comes with some discomfort and anxiety to the patient, and a slight risk [27, 53] (although the risk is much less than that for arterial catheters). On the other hand, catheterization facilitates additional measurements of pressure, and provide a means of injecting radio-opaque dyes for digital subtraction angiography, visualization of the right heart, and angiography of the pulmonary circulation.

A non-invasive and precise quantitative procedure for measuring cardiac output would be of immense value in evaluating heart function. It would open up the possibility of monitoring serial changes, and offer a haemodynamically relevant parameter by which to judge the effectiveness of disease treatment. The earliest work in Doppler ultrasound by Satornura was done with the goals of evaluating cardiac function [54]. Since then, a great number of investigators have attempted to measure cardiac output using ultrasound [8, 15, 33, 39, 41, 50]. None of the techniques have achieved widespread acceptance, but research continues in the development of these tools.

**Summary**

Cardiac reserve is a measure of the function of the heart which is important in characterising ischaemic heart disease and its treatment. The blood flow measurement of cardiac output is important for the determination of cardiac reserve. A non-invasive and precise tool would be useful for making this measurement, and would offer new potential since it could monitor progressive changes without added risk to delicate patients.
1.3 Relevant Principles from Flow Physics

Basic principles of flow physics are introduced here to facilitate a more precise and mathematical description of the blood flow measurement. Since this thesis is concerned with flow in major vessels, blood will be considered as a simple viscous and incompressible fluid. General principles will be introduced using a steady-state rigid-tube model. In particular, the following will be discussed:

- the concept of the velocity profile and its relationship to flow,
- the laminar flow model for incompressible viscous fluids in rigid tubes,
- turbulence, and
- the physical parameters of the vascular system in vivo.

1.3.1 Velocity Fields, the Velocity Profile, and Flow

The concepts of velocity field, velocity profile, and their relationship to volume flow are important for understanding ultrasound flow measurement techniques, since velocity measurements are the basis of these methods.

In the solution of fluid mechanics problems, the goal is to determine the properties of a fluid as continuous functions of space ($\vec{x}$) and time ($t$). The most important of these properties is the velocity field, $\vec{v}(\vec{x}, t)$. This vector field is the velocity vector of fluid at any given point in space and time; it generally has three scalar components (for directional mapping into three dimensions), all of which are functions of space and time. Most commonly, a rectangular orthogonal coordinate system is used, in which this field would be represented as follows:

$$\vec{v}(\vec{x}, t) = \vec{1}u(\vec{x}, t) + \vec{j}v(\vec{x}, t) + \vec{k}w(\vec{x}, t)$$  \hspace{1cm} (1.3)

where $\vec{v}$ is the velocity field as a function of space and time, and $\vec{1}, \vec{j}, \vec{k}$ are unit vectors in each of the orthogonal directions, $u, v, w$ are the scalar speeds in each of the directions.
Given a physical model, the velocity field can be used to determine other fields such as the pressure and/or temperature. Sometimes, other coordinate systems (such as polar or spherical) are used to exploit symmetry in the system, simplifying analysis.

Based purely on geometry, it is possible to calculate the volume flow of fluid, $Q$, through an arbitrary surface, $S$, given the velocity field. Mathematically, the volume flow is given by:

$$Q_S(t) = \int_S (\vec{v}(\vec{x}, t) \cdot \hat{n}) dA = \int_S V_n(\vec{x}, t) dA$$  \hspace{1cm} (1.4)

The flow $Q_S$ is calculated by integrating the dot product of the velocity field with the unit normal vector, $\hat{n}$, to an elemental surface area $dA$. This is the velocity $V_n$, normal to the surface of integration.

For the purpose of the physiological measurement of blood flow, the velocity field is constrained to be within closed blood vessels. Any arbitrary surface which completely transects the vessel can then be used to calculate volume blood flow rate. The problem is simplified somewhat by considering planar transectional surfaces, as shown in Figure 1.3.

A two-dimensional plot of $V_n(\vec{x}, t)$ as a function of position on a planar transectional surface provides a visual representation of the flow, known as a velocity profile. For the special case where the plane of transection is perpendicular to the vessel axis, this is commonly known as the "flow profile". The volume between the surface of the flow profile and the plane of transection represents the volume flow. This makes sense intuitively, by imagining that all fluid upstream of the transection plane is "marked" at one instance in time (Figure 1.3). After a given unit of time, some of the marked fluid will have passed through the transection plane. Given that unit of time, the velocity profile represents the leading surface of the moving fluid, thus the volume of fluid passing per unit time is the volume between the leading surface and the transection plane—a visual representation of volume flow, $Q$, and Equation 1.4.
Mathematical models of flow in haemodynamics range from simple steady-state (time independent) profiles to complex and dynamic profiles which include pulsatile components. The mathematics of these problems are greatly simplified by applying rules of symmetry. It is common to take a simplified approach where the velocities are considered to be mainly along the axis of the vessel, and neglecting any radial components. In the case of a cylindrically symmetric vessel, the flow profile is sometimes plotted along a single axis across a diameter of the vessel.

1.3.2 Laminar Flow in Rigid Tubes

Mathematical expressions for velocity profiles can be derived based on physical principles. Furthermore, these physical models can be used to relate velocity profiles with flow, pressure, and in more complicated cases, temperature. This section discusses a simple model of flow in rigid tubes known as the Poiseuille flow model. It is relevant to the work of this thesis, because experimental work
was done using a steady-flow experiment in a phantom which was negligibly distensible. The model is also important for qualitative understanding of important parameters in the vascular system in vivo.

Some of the most significant early work in cardiovascular physiology was done by the French physician J. L. M. Poiseuille (1799–1869). Poiseuille carefully and quantitatively determined the relationship between pressure and flow in rigid tubes in a steady flow experiment. This work was motivated by his earlier results from pressure measurement in arteries and veins using the mercury manometer—a technique that Poiseuille also pioneered. Unable to measure significant changes in pressure within the arterial system of vessels greater than 2 mm in diameter, and aware of the relatively low pressure in veins, Poiseuille focussed on the study of flow in small tubes. He found that:

$$Q = \frac{kD^4 \Delta P}{L}$$  \hspace{1cm} (1.5)

where $D$ and $L$ are the diameter and length of the tube, and $\Delta P$ is the pressure difference from the beginning to the end of the tube.

Poiseuille's empirical law was subsequently confirmed with an independent theoretical derivation for this geometry, relating the proportionality constant $k$ to the viscosity of the fluid:

$$Q = \frac{\pi R^4 \Delta P}{8\eta L}$$  \hspace{1cm} (1.6)

where $R$ is the radius of the tube, and $\eta$ is the viscosity of the fluid. The theoretical derivation gives rise to a characteristic parabolic flow profile. Beyond a minimum “entrance length” to the pipe, the velocity is a function of radius only, and is given by Equation 1.7:

$$\dot{v}(r) = \frac{\Delta P (R^2 - r^2)}{4L\eta}$$  \hspace{1cm} (1.7)
where $\vec{a}$ is the unit vector along the axis of the vessel. Flow as described by equations 1.6 and 1.7 is commonly called “Poiseuille Flow”.

In the region of entrance, the velocity profile is sometimes described using a family of curves given by:

$$v = v_m \left[ 1 - \left( \frac{r}{R} \right)^\alpha \right]$$

(1.8)

here $\alpha$ is a flow order parameter. Larger values of $\alpha$ correspond to profiles which appear more blunt.

Equations 1.7 and 1.8 can be used to describe laminar flow in straight-running rigid tubes.

**Concept of Vascular Resistance**

The linear relationship between flow and pressure difference in Poiseuille flow led to the development of the concept of “Vascular Resistance”. Vascular resistance, $R_V$, is simply the constant of proportionality between the pressure difference and the volume flow, as shown in Equation 1.9.

$$P_1 - P_2 = \Delta P = QR_V$$

(1.9)

where $Q$ is Flow,

$P_1$ and $P_2$ are the entrance and exit pressures, respectively, and

$R_V$ is the “Vascular Resistance”

In the case of Poiseuille flow, the vascular resistance can be related directly to the parameters of the tube through which a fluid is passing and the fluid’s viscosity. However, the value of the concept lies in its general application to vessels, regions of tissue, or even the entire systemic circulation for the purpose of qualitatively describing the demand for pressure in order to produce a given flow rate.

Equation 1.9 is similar to Ohm’s Law in electrical systems. This is a useful tool for understanding networks of vessels, and also for highlighting the importance of the flow measurement. The
implication is that measurement of flow is as fundamental as measurement of current in electronics!

1.3.3 Turbulence

In addition to the constraints of steady state and rigid wall conditions, Poiseuille’s law only applies for a limited range of flow rates. Beyond a certain flow rate (for a fixed geometry), velocities begin to fluctuate, both in direction and amplitude; this state is called “turbulence”. The well-behaved state is denoted “laminar flow”, since the fluid can be considered as layers which slide along each other with viscous friction. In the case of Poiseuille flow, the laminae are cylindrical in shape. In contrast, motion of fluid in turbulence is highly irregular. Recognition of the existence of this state is important, since the physical model, as well as the techniques which will be introduced in this thesis, generally depend on assumptions of laminar flow.

Turbulence is a consequence of the relative magnitude of inertial compared to viscous forces in fluid flow and is characterised by a dimensionless parameter called the Reynolds Number, $Re$. This parameter is named after Sir Osborne Reynolds who first investigated and precisely described the transition from laminar to turbulent flow.

$$Re = \frac{4\bar{v} \rho A}{\eta \text{Per}}.$$  

(1.10)

Equation 1.10 defines the Reynolds number for closed channels. $\bar{v}$ is the mean flow velocity; $\rho$ is the density of fluid; $\eta$ is the viscosity; “$A$” refers to the cross-sectional area of the channel; and, “Per” is its perimeter. Higher Reynolds numbers represent tendency towards turbulence. The normal transition from laminar to turbulent flow occurs in the range of Reynolds numbers of 2000 to 4000, though under special conditions, the transition may not occur until Reynolds numbers as high as 40,000 are reached [46].
1.3.4 Physical Parameters of the Vascular System \emph{in vivo}

A major difference between flows described thus far and physiological flow is pulsatility. Parameters vary \emph{in vivo} as a function of time.

Fortunately, the velocity field discussion and the relationship of velocity profiles to flow can be applied universally to physiological flow. Over the cardiac cycle, however, velocity profiles may take different shapes, and there may be both forward and reverse flow velocities through the plane of vessel transection. Volume flow is thus a function of time within blood vessels such as the arteries, where flow is significantly pulsatile. Problems with pulsatility can be partly overcome using systems that are capable of making measurements at rates that are fast compared to the physiological motions. Flow is then a function of time, and can be averaged over the cardiac cycle to produce a mean flow measurement:

\[
\bar{Q}_S = \frac{1}{T} \int_0^T \int_S (\vec{v}(\vec{x}, t) \cdot \vec{n}) \, dA \cdot dt
\]  

This expression assumes that the circulation can be considered to be in a general steady state over many cardiac cycles. In other words, it is assumed that the cardiac cycle does not change from pulse to pulse.

The Poiseuille flow model, however, applies quantitatively only under conditions of laminar and steady flow in rigid tubes. Although Poiseuille flow assumptions are not met in major arteries, the steady state rigid tube laminar flow model is useful conceptually for understanding the relative importance of changes in viscosity, vessel diameter, and length; changes in diameter have the most profound effect. Discrepancies from this model, especially in arteries, are due primarily to the compliance of vessels and the pulsatility of flow. In small vessels, non-Newtonian properties of blood also have significant effects. Physiological flow is almost universally laminar, although it is rarely “fully developed”, due to the effects of vessel branching, narrowing, and bending. Conditions of
Table 1.3: Physiological Flow Parameters for the Human Circulation [26]

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Diameter mm</th>
<th>Volume Flow mL/s</th>
<th>Mean Linear Velocity mm/s</th>
<th>Reynolds number mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending Aorta</td>
<td>23.0–43.5</td>
<td>---</td>
<td>364</td>
<td>3210–6075</td>
</tr>
<tr>
<td>Femoral Artery</td>
<td>5.0</td>
<td>-6.9 23.1 3.7</td>
<td>-350 1175 188</td>
<td>283</td>
</tr>
<tr>
<td>Common Carotid</td>
<td>5.9</td>
<td>2.7 10.6 5.1</td>
<td>99 388 187</td>
<td>332</td>
</tr>
<tr>
<td>Carotid Sinus</td>
<td>5.2</td>
<td>1.8 6.9 3.3</td>
<td>85 325 156</td>
<td>244</td>
</tr>
<tr>
<td>External Carotid</td>
<td>3.8</td>
<td>0.9 3.7 1.8</td>
<td>83 327 157</td>
<td>180</td>
</tr>
<tr>
<td>Thoracic inferior vena cava</td>
<td>20.0</td>
<td>--- 34–50</td>
<td>--- 107-160</td>
<td>323–482</td>
</tr>
</tbody>
</table>

Turbulence only occur for some cases in the ascending aorta, or in diseased narrowing of the lumen in some vessels. These complications are beyond the scope of this thesis; however, Milnor [46], Nichols and O'Rourke [49] can be consulted for a more complete treatment of this subject.

The vascular system can be considered qualitatively as follows. Major arteries serve as the low resistance conduits which deliver blood to local regions. For efficiency, the calibre is large, and blood velocities are high. Since arteries are subject to high pressures, arterial walls are correspondingly strong. Arterioles are the main resistance vessels in the circulatory system. They control flow to regional capillary beds by contracting to increase flow resistance, or by distending to decrease flow resistance. Muscular walls facilitate these large changes in lumen diameter. In the capillaries, nutrient, oxygen, and waste are exchanged between the blood and the interstitial fluid. Thus, walls of capillaries are thin and, to varying degrees, permeable. Venules collect blood from the capillaries, and grow together into progressively larger calibre veins. The major veins serve a dual purpose. First, the veins are conduits to return blood to the heart. Secondly, veins are also a reservoir for blood. Venous walls are thin, since the pressures are much lower than in the arterial side, but they are also muscular, which allows contraction and expansion to control the overall blood reservoir volume. Table 1.3 lists flow parameters for the vascular system in vivo.
1.3.5 Summary

In summary, physical models lead to understanding of both qualitative and quantitative aspects of blood flow in vivo. In particular, the relationship of velocity fields to volume flow has been introduced. Other concepts important to understanding of physiological flow such as vascular resistance, laminar flow, and turbulent flow have also been introduced. This knowledge serves as a foundation for understanding the flow measurement problem for major vessels.

1.4 Ultrasound Flow Measurement

This section discusses how ultrasound can be used to measure blood flow non-invasively and quantitatively using transcutaneous approaches. It begins with an introduction to relevant ultrasound fundamentals which leads into a discussion on the use of pulsed Doppler ultrasound to measure the distribution of velocities within a spatially localised sample volume. The various schemes that have been used to quantify flow using ultrasound are described and summarized, with emphasis on their accuracy and primary sources of error.

1.4.1 Background

The Ultrasound Beam

Ultrasound is generated and detected by piezoelectric transducers. Electrical and mechanical properties of the transducer determine the spatial and temporal characteristics of emitted ultrasound energy and, equivalently, its sensitivity to incident ultrasound signals. Piezoelectric transducers for ultrasound are usually shaped into thin discs, whose thickness determines the resonant vibrational frequency (for standard medical applications, generally 2–20 MHz). A matched backing is usually applied to the transducer to damp out oscillation such that a short pulse of ultrasound is produced.
when the transducer is excited with a high-amplitude voltage spike. The transducer material is also usually shaped to focus the ultrasound energy and sensitivity. The schematic representation of an ultrasound beam is shown in Figure 1.4 for the case of a single-element focussed circular ultrasound transducer. This beam represents the trajectory of an ultrasound pulse emitted from the transducer into an ideal uniform medium and also the spatial extent of the sensitivity to returning ultrasound.

![Ultrasound Beam Schematic](image)

**Figure 1.4: Ultrasound Beam: Spatial sensitivity of the ultrasound probe**

In medical imaging, transducers are generally built into handheld probes. These are used to direct the ultrasound energy into the body, when coupled through an acoustically matched medium, such as a water bath or ultrasound gel. Ultrasound pressure waves propagate through tissue and are scattered by variations in acoustic impedance, and absorbed. The scattered energy propagates back out of the tissue and is detected by the probe. Taken together, absorption and scattering result in gradual attenuation of the signal as it travels to deeper layers of tissue. The mechanisms of ultrasound propagation and scattering in tissue are complex. Absorption and scattering properties are dependent on ultrasound frequency and tissue type. Shung has compiled a text [56] discussing current understanding of ultrasonic scattering in tissue. Generally, scattering is considered to be a linear process; the scattered signal is usually thought of as a time delayed and scaled version of the incident ultrasound pulse. The strength of scattering is characterised by a parameter known
Ultrasound Imaging and Scan Modes

Figure 1.5: Ultrasound A-Mode Imaging. A signal with decreasing amplitude as a function of time (due to attenuation) is detected (a). Assuming a constant factor of attenuation, the received signal can be increasingly amplified as a function of time to eliminate approximately the depth dependence of the signal level (b). This process is called Time Gain Compensation (TGC). The final step is to detect the envelope of this signal, and display it (c).

A simple ultrasound imaging system is shown in Figure 1.5. A pulser transmits a signal to the probe transducer, causing it to emit an ultrasound pulse into the tissue. After the pulse is emitted, the probe transducer begins to receive the scattered signal (the "echo") from the tissue. By assuming a constant speed of sound, time is converted to depth within tissue. The envelope of the received signal is used as the image. Logarithmic compression is usually applied for display. This process is known as an A-mode scan ("amplitude"-mode), and the image is called an A-scan. The speed of the scan is limited by the depth of the scan—the system must wait until the echo from the deepest part of the scan has returned. This time is equivalent to twice the depth, divided
by the speed of sound. The speed of sound is approximately 1540 m/s in tissue, thus for a scan of 7.5 cm depth, approximately 100μs are required. This allows the line to be updated at a frequency of approximately 10 kHz.

It is possible to create a two dimensional image by moving the transducer in the lateral direction and combining the resulting series of A-scans. The same system is used, but now, position encoding must also be included. Signal level in each individual A-mode scan is shown as brightness, and the A-mode lines are displayed side by side. This process is called a B-mode scan ("brightness"-mode), and the image is often referred to as a B-scan. A simple B-scan system is shown in Figure 1.6.

![Ultrasound B-Mode Imaging](image)

**Figure 1.6: Ultrasound B-Mode Imaging.** A series of adjacent A-scans, encoded by brightness, is used to image a 2-dimensional plane.

The movement of the ultrasound beam can be achieved by mechanically translating the probe, but it is more convenient to use a probe which consists of an array of transducer elements; each element of the array can usually be controlled separately. By selectively activating array elements for both transmit and receive, the ultrasound beam can be scanned electronically. Assuming
that each successive line can be acquired instantly after the previous A-scan is made, and using 100 A-scans per image, this results in a scan rate (for the same parameters as used above: 7.5cm depth) of roughly 100 Hz. This is the "frame rate" for making B-scan images.

Figure 1.7: Ultrasound C-Mode Imaging. A series of A-scans in two orthogonal directions are used to insonate a 3 dimensional volume. By ranging and gating to detect signal from a depth range, the received signal from each A-mode scan is localised to a constant depth. The display of signal from a plane at constant depth is the C-scan.

A series of A-mode scans can be acquired by moving the transducer in orthogonal lateral directions to image a three dimensional volume. This also allows the construction of an image at constant depth away from the transducer. It can be achieved by setting a delay (ranging) for each A-mode scan, and taking data for a short window of time (gating). This is a C-mode scan (Figure 1.7). Until two dimensional arrays become widely available, C-mode scans must be performed either by mechanically scanning a single element transducer, or by using a linear array, and mechanically scanning it in the orthogonal direction. As with the calculation for B-scan frame rate the C-scan frame rate can be calculated by dividing the A-scan frame rate by the number of
A-scans used in the C-scan.

Due to the speed of imaging relative to motions within the body, each image is essentially a "snapshot". The tissue is roughly stationary with respect to each image acquisition, and due to the high frame rate, motion can be observed in real time.

Pulsed Doppler Ultrasound

Tissue motion can be analysed quantitatively using Doppler ultrasound techniques. These techniques can be broadly categorised into (1) continuous wave (CW) Doppler techniques which rely on the shift in ultrasound frequency of the scattered signal relative to a continuous emitted signal of one frequency, and (2) pulsed wave (PW, or pulsed) Doppler techniques which quantitatively detect the differences in received signals from a series of emitted pulses due to motion. Pulsed Doppler techniques are used in this thesis. A brief introduction to pulsed Doppler methods is provided in this section covering (i) concepts, (ii) instrumentation, and (iii) the Doppler spectrum. Several excellent texts have been written on the subject of Doppler ultrasound, including Jensen [35], Atkinson and Woodcock [1], and Taylor, Burns, and Wells [60]. These should be consulted for a more complete treatment of the subject. The following derivation will follow the argument presented by Jensen [35].

(i) Concepts

Figure 1.8 illustrates the interaction of an ultrasound pulse with a moving scatterer over three sequential pulses. Two effects due to motion are evident. First, the received echo of each pulse is temporally expanded or compressed due to relative motion between the source and receiver. Secondly, the time between the pulse and the echo is increased from pulse to pulse, due to changing distance between the transducer and the target object.
Two effects due to the motion of the scatterer are evident: (1) the received signal is expanded in the time domain, and (2) the received signal is delayed with each successive pulse by a time $\Delta t$, which is related to the pulse repetition time $T_R$, and the velocity of the scatterer in the direction of the axis of the ultrasound beam $v_a$. Pulsed Doppler systems detect the time shift $\Delta t$. 
These effects due to motion can be described mathematically. If scattering is assumed to be linear, the received signal can be considered as a transformation of the emitted signal. This is done by relating the time of reception $t_{r_i}$ for the scattered signal from a moving object to the emitted signal from time $t_{e_i}$, where $i$ denotes the pulse number. From the diagram,

$$t_{r_i} = \frac{2d_0}{c - v_a} + \frac{c + v_a}{c - v_a} t_{e_i}$$  \hspace{1cm} (1.12)

Emitted pulses are denoted $e_i(t)$, with the index $i$ representing pulse number. These pulses are emitted at a frequency of $f_R$, the pulse repetition frequency, and are spaced by time $T_R = 1/f_R$, the period of pulse repetition. Received signals are denoted $r_i$, with index $i$ denoting the response to the emitted pulse $e_i$. The received pulse $r_i(t)$ is a transformed copy of the emitted signal, according to the relationship between $t_{r_i}$ and $t_{e_i}$, thus,

$$r_i(t_{r_i}) = a_i e_i(t_{e_i})$$  \hspace{1cm} (1.13)

where $a_i$ is simply the scaling factor due to the strength of scattering, the attenuation due to ultrasound propagation, and also due to the sensitivity of the ultrasound transducer. Thus,

$$r_i(t) = a_i e_i \left( \frac{c - v_a}{c + v_a} t - \frac{2d_0}{c + v_a} \right)$$  \hspace{1cm} (1.14)

Pulsed "Doppler" systems use signal processing techniques to determine the blood flow velocities by quantifying the time shift $\Delta t$ of the received signal from pulse to pulse for a moving scatterer. This time shift is defined from the following equation:

$$r_{i+1}(t) = r_i(t - T_R - \Delta t)$$  \hspace{1cm} (1.15)

Assuming that the same emitted pulse is used, then

$$e_{i+1}(t) = e_i(t - T_R).$$  \hspace{1cm} (1.16)
Therefore,

\[ r_{i+1}(t) = a_{i+1} e_{i+1} \left( \frac{c-v_a t - \frac{2d_o}{c+v_a}}{c+v_a} \right) \]

\[ = a_{i+1} e_i \left( \frac{c-v_a t - \frac{2d_o}{c+v_a}}{c+v_a} - T_R \right) \]

\[ = a_{i+1} e_i \left( c-v_a \left( t - \frac{c+v_a T_R}{c-v_a} \right) - \frac{2d_o}{c+v_a} \right). \]

If it can be assumed that the scattered echo will have the same amplitude scaling \( (a_{i+1} = a_i) \), then,

\[ r_{i+1}(t) = r_i \left( t - \frac{1+v_a/c}{1-v_a/c} T_R \right). \]

Now applying the approximation \((1+x)^{-1} \approx 1 - x\) for \(x \ll 1\),

\[ \frac{1+v_a/c}{1-v_a/c} \approx \left( 1 + \frac{v_a}{c} \right)^2 \approx 1 + \frac{2v_a}{c} = \gamma. \]

Let this parameter, for simplicity, be denoted by \(\gamma\).

Physiologically, the highest velocities in the axial direction of the beam would be on the order of \(v_a \approx 1 \text{ m/s}\), and the speed of sound is roughly \(c \approx 1540 \text{ m/s}\). Therefore,

\[ r_{i+1}(t) = r_i(t - T_R - \frac{2v_a}{c} T_R). \]

Comparing with Equation 1.15,

\[ \Delta t = \frac{2v_a}{c} T_R. \]

(ii) Instrumentation

The purpose of pulsed Doppler instrumentation is to detect the time shift \(\Delta t\). Instrumentation for a traditional analogue pulsed Doppler system is shown in Figure 1.9.

At this point, it is convenient to shift to a time scale that is relative to time of emission. In other words, emitted pulses have characteristic:

\[ e_{i+1}(t) = e_i(t), \]
Figure 1.9: Conventional Analog Pulsed Doppler Ultrasound Instrumentation. For each pulse, the received signal is amplified, and divided into two channels (a). The first channel is multiplied by an in-phase signal from the master oscillator at the fundamental frequency of the insonating pulse. The second channel is multiplied by a quadrature-phase signal from the same master oscillator (b). Both channels are then low pass filtered to eliminate the summed frequency signal (of the oscillator versus the received signal); this leaves the difference frequency signal (c). This difference signal is a slowly varying sinusoid, as a function of velocity, depending on depth. To localise the signal along the axis of the ultrasound beam, this difference signal is ranged and gated (c), (a sample is taken over a range of time, which represents a range of depths). This is then integrated, and the resulting value is one sample of the “Doppler signal” (e). This value is held until the next sample (from the next pulse) is received.
without the extra time lag $T_R$. Likewise, Equation 1.20 becomes:

$$r_{i+1}(t) = r_i(t - \frac{2v_a}{c}T_R).$$  \hspace{1cm} (1.23)

A simple pulse that might be used by a Doppler system would be a rectangular gated sine wave. This can be expressed by:

$$e(t) = g(t)\sin(2\pi f_0 t)$$

$$g(t) = \begin{cases} 
1, & 0 < t < \frac{M}{f_o} \\
0, & \text{otherwise}
\end{cases} \hspace{1cm} (1.24)$$

where $M$ is an integral number of periods for the sinusoid. The Doppler instrumentation can be understood by examining its effect on each returning echo, from a succession of emitted pulses. For simplicity, we consider a single scatterer. (The analysis is applied to realistic situations by exploiting linear superposition.)

The response from the first emitted pulse, scattered from a single moving scatterer, according to Equation 1.14, and applying simplifications (Equation 1.19), will then be given by:

$$r_1(t) = ae(\gamma t - \phi_o)$$

$$= ag(\gamma t - \phi_o) \sin(2\pi f_0 (\gamma t - \phi_o))$$ \hspace{1cm} (1.25)

$$\phi_o = \frac{2\phi_o}{c + v_a}$$

Subsequent received pulses will be given by Equation 1.23. Therefore,

$$r_i(t) = r_1(t - \frac{2v_a}{c}(i - 1)T_R)$$ \hspace{1cm} (1.26)

Equations 1.25 and 1.26 describe the signals denoted (a) in Figure 1.9.

In the analysis of the Doppler system, we will consider the in-phase (I) component. The first stage in the Doppler instrumentation multiplies the received signal with a reference oscillation
Equation 1.27 describes the signal at (b) in Figure 1.9. The trigonometric identity

\[ \sin \psi \cos \phi = \frac{1}{2} (\sin(\psi + \phi) + \sin(\psi - \phi)) \]  

(1.28)

shows that there will be a summed frequency component and a difference frequency component. By applying a low pass filter, the summed frequency component is removed, leaving only the difference component,

\[
(Signal \ at \ Figure \ 1.9(c)) = \frac{a_i(t)}{2} \sin \left(2\pi f_o \left(\gamma(t - \frac{2v_a}{c} (i-1)T_R) - \phi_o - t\right)\right) \\
= \frac{a_i(t)}{2} \sin \left(2\pi f_o \left(\frac{2v_a}{c} t - \frac{2v_a}{c^2} + \frac{4v_a^2}{c^2} (i-1)T_R - \phi_o\right)\right) \\
\approx \frac{a_i(t)}{2} \sin \left(2\pi f_o \left(\frac{2v_a}{c} t - \frac{2v_a}{c} (i-1)T_R - \phi_o\right)\right). 
\]

\( t \) corresponds to depth within tissue. Consider a sample of the signal described by Equation 1.29.

From pulse to pulse, if the sample is taken at constant depth (\( t = \) constant), only the second term in the equation changes since it is dependent on pulse number \( i \) (assuming that the velocity is constant). This sampled signal is the Doppler in-phase signal. In practice, ranging and gating are applied followed by integration over the gate length (Figure 1.9(c)–(e)). This can be considered as spatial integration, and the result is a superposition of signals described by Equation 1.29 from scatterers within the range gate. In this manner, the time shift \( \Delta t \) has been detected in the phase of the output in-phase “Doppler signal” \( I(i) \).

A similarly tedious derivation can be achieved by starting with a multiplication of the received signal \( r_i \) with a reference oscillation that is 90 degrees out of phase \( (\sin(2\pi f_o t)) \). It results in a quadrature Doppler signal \( Q(i) \), which is similarly 90 degrees out of phase. The combination of
in-phase and quadrature Doppler signals provides the necessary information to distinguish between forward and reverse flow.

The system produces one sample of the Doppler signal (including both in-phase and quadrature components) per pulse.

\[
I(i) = \cos \left( 2\pi \frac{2v_a}{c} f_o(i - 1)T_R + \phi \right)
\]
\[
Q(i) = \sin \left( 2\pi \frac{2v_a}{c} f_o(i - 1)T_R + \phi \right)
\]

To obtain a continuous audio-frequency signal, each sample of the Doppler signal is held until a new signal is received from the next pulse. This step-like function is low-pass filtered, resulting in the continuous signal, \( I(t) \) and \( Q(t) \).

The frequency of this signal is what is known as the “Doppler shift” frequency \( f_d \) for pulsed Doppler:

\[
f_d = \frac{2v_a}{c} f_o
\]

This equation corresponds with the expression for the frequency shift expected from continuous wave Doppler systems which exploit the classical Doppler effect. It is from this similarity that pulsed Doppler derives its name, despite the fact that the Doppler effect has little to do with the observed frequency shift in this case.

The derivation above makes several assumptions, the most important of which include (1) linearity of scattering, (2) the uniformity of scattering response of a changing target (due to mixing of blood), (3) uniformity of ultrasound beam sensitivity, (4) plane wave analysis. A complete description of these effects is beyond the scope of this introduction to pulsed Doppler systems; however, Evans [11] can be consulted for greater detail.
(iii) The Doppler Spectrum

So far, the system has been considered for the detection of velocity of individual scatterers. In reality, the scattered signal from blood is the linear superposition of many individual scattering events from structures within blood which may each be moving at different velocities. As a result of linearity, a flow velocity distribution within the sensitive volume results in a Doppler signal that is a superposition of the Doppler signals from each individual scatterer, with frequencies governed by Equation 1.31. Thus, instead of a single Doppler frequency $f_d$, the Doppler signal will have a spectrum of frequencies.

This spectrum of frequencies can be determined from the Doppler signal by applying the Fourier transform; the Doppler spectrum is the Fourier transform of the Doppler signal. This is the distribution of Doppler shift frequencies, and as a result of Equation 1.31, the distribution of flow velocities within the sample volume. The Doppler spectrum can thus be viewed as a histogram of velocities. The spectrum is represented by the power density function of Doppler shift frequency $P(f_d)$. An example of a Doppler signal and its associated Doppler spectrum is shown in Figure 1.10.
Useful quantitative parameters can be determined from the Doppler spectrum, including a mean frequency shift and total power.

Mean frequency shift is given by:

$$\bar{f} = \frac{\int_{-\infty}^{\infty} fP(f)df}{\int_{-\infty}^{\infty} P(f)df}$$  \hspace{1cm} (1.32)

This mean frequency shift can be used to estimate the mean velocity of scatterers (in the direction of the ultrasound beam) within the sample volume, simply by using Equation 1.31. Thus,

$$\bar{v}_a = \frac{c}{2f_0}\bar{f}.$$  \hspace{1cm} (1.33)

This mean velocity estimate requires some interpretation, because the ultrasound beam sensitivity is generally not spatially uniform. It is common for the velocities near the axis of the beam to be more heavily weighted due to higher sensitivity in that location.

Total power can also be calculated. Assuming linearity in the system, this quantity should be proportional to the overall scattered signal. Assuming that the scatterers have a uniform backscatter cross-section, that the beam is uniformly sensitive, and that attenuation is constant across the sensitive volume, this parameter is proportional to the number of scatterers within the sensitive volume. It is important to note that backscatter cross-section for blood has flow dependence; the assumption of its uniformity is violated in turbulence.

For pulsed Doppler systems, the spectrum is discrete, has frequency limits determined by the pulse repetition frequency ($1/T_R$), and has frequency resolution determined by the number of samples (and therefore pulses) used for measurement.
1.4.2 Principles of Ultrasound Flow Measurement

Non-invasive transcutaneous ultrasound flow measurement techniques are based on measurements of flow velocity using Doppler. Thus, the mathematical description of these techniques follows most naturally from the expression given in Equation 1.4 which relates flow to the velocity field:

\[ Q(t) = \int_S (\vec{v}(t) \cdot \vec{n}) dA \]

This equation can also be rewritten as follows:

\[ Q(t) = \int_S (\vec{v}(t) \cdot \vec{n}) dA = \left( \frac{\int_S (\vec{v}(t) \cdot \vec{n}) dA}{\int_S (\vec{n} \cdot \vec{n}) dA} \right) \int_S (\vec{n} \cdot \vec{n}) dA = \vec{v}_n(t) S \]

Here, \( \vec{v}_n(t) \) is the spatial mean of velocity perpendicular to the surface of transection across the entire surface of transection, and \( S \) is the area of the surface of transection. These are illustrated in Figure 1.11. In practice, if only one vessel crosses the surface of transection, and if there is no fluid motion outside of this vessel, then the equation can be rewritten:

\[ Q(t) = \vec{v}_n(t) A_{proj}(t), \quad (1.34) \]

where \( A_{proj}(t) \) is the area of the vessel lumen (which may change as a function of time) as projected onto the surface of transection. Note that Equation 1.34 is strictly valid only if (1) the area measured is perpendicular to the velocity, and (2) the area and the velocity are measured simultaneously.

These two expressions for flow (Equations 1.4 and 1.34) suggest two categories of flow measurement techniques: (1) measurement of a velocity profile which can be spatially integrated to yield flow, and (2) direct measurement of spatial mean velocity and vessel area which can be multiplied to give flow. Both of these approaches have been applied to the problem of ultrasound flow measurement.
Four transcutaneous ultrasound flow measurement techniques are discussed in this section, of which two are based on velocity profiling and two are based on mean velocity and area measurements. For each technique, the principle will be introduced, limitations and strengths will be discussed, and relevant studies will be summarized.

1.4.3 Velocity Profile Flowmeter

Principles

Figure 1.12 illustrates the velocity profile flowmeter. By scanning a small Doppler sample volume across a blood vessel, it is possible to estimate the velocity profile. Measured frequency shifts correspond to velocities in the direction of the beam, which can then be projected along the direction of the vessel. This projection requires the beam-vessel angle, which can be measured from a B-mode image. Assuming cylindrical symmetry, each velocity is applied to a semi-annular area, and integrated over the cross-section of the vessel.
Figure 1.12: **Velocity Profile Method.** A small sample volume is scanned along the ultrasound beam axis to sample the velocity profile. The velocities are projected to the direction along the vessel axis, using the Doppler beam vessel angle $\theta$. Each velocity is applied to a semi-annular area, and integrated over the transection plane. As shown, the transection plane in this case is perpendicular to the vessel axis.

\[
Q(t) = \sum_{r=-R}^{R} v_r(t) \pi r \Delta r = \pi \Delta r \sum_{r=-R}^{R} r \left( \frac{[f_d]_r c}{2 f_o \cos \theta} \right),
\]

where $R$ is the radius of the vessel, $\theta$ is the beam vessel angle, $v_r$ is the velocity of blood along the direction of the vessel axis, and $[f_d]_r$ is the mean Doppler shift frequency for a given location of the sample volume.

**Limitations and Strengths**

For single element Doppler transducer systems, a primary source of error for this method is the effect of the finite size of the sample volume [23]; the method requires a sample volume which is small relative to the size of the vessel. More recent implementations of the technique which use linear array transducers, however, appear to have sufficient spatial resolution for accurate flow measurement [51].
The uncertainty in the measurement of beam vessel angle is also a significant source of error. The $1/\cos \theta$ dependence of the velocity projection can result in significant flow measurement error if there is uncertainty in the determination of $\theta$. This is particularly true for large values of $\theta$, as shown in Figure 1.13. For example, for a 60 degree Doppler angle, an error in angle measurement of 5 degrees results in a flow measurement error of approximately 10 percent.

![Figure 1.13: Error due to Angle Uncertainty.](image)

**Figure 1.13: Error due to Angle Uncertainty.** For methods which have a $1/\cos \theta$ dependence due to projections (velocity profile and uniform insonation techniques), errors in flow measurement can be severe, especially for larger Doppler angles.

Velocities will not be registered properly to semi-annular areas if the vessel is not circular or if it does not have a cylindrically symmetric flow profile. The vessel axis must also lie within the same plane as the ultrasound beam axis. Although arteries generally have circular cross-sections, veins do not. Furthermore, the cross-sectional area may vary with time due to cardiac pulsations in arteries and due to respiration and blood pooling in veins.
The strength of the technique is that it provides additional information in the velocity profile. Spatial localisation also prevents interference of signal from adjacent vessels.

**Relevant Studies**

As one of the first techniques attempted with pulsed Doppler, the velocity profile method has been attempted in many *in vitro* as well as *in vivo* studies using single transducer systems. These are discussed by Gill [23], and summarized in Table 1.4. This technique had relatively disappointing results, primarily due to limitations in spatial resolution. Methods of deconvolution have been proposed to overcome this; however, Baker [4] suggested that the technique was best suited to large vessels (greater than 10mm in diameter). Nevertheless, these early *in vivo* results indicated reasonably good accuracy with errors of 15-20% using the method with duplex Doppler devices.

More recently, however, time domain correlation techniques of velocity estimation have been applied using array systems for velocity estimation across an entire scan plane [6]. These developments have led to a resurgence in interest in velocity profile techniques. Recently, Forsberg *et. al.* [17] have made *in vitro* and *in vivo* measurements of flow using this technique and compared the results with measurements using a perivascular ultrasound transit-time probe. Velocity profile flow measurement has also recently been attempted using standard Color Doppler [14]. These results are also included in the table. The *in vitro* results of Forsberg *et. al.* [17] in particular demonstrate excellent accuracy, with mean (absolute) errors of ±2%, and with a distribution of errors with 2 standard deviations less than ±10.5% with pulsatile flow. Clinical trials of velocity profiling *in vivo* using these array techniques are anticipated.
<table>
<thead>
<tr>
<th>Investigator</th>
<th>Subject</th>
<th>Vessels</th>
<th>Compared Against</th>
<th>Flow Rates</th>
<th>Error</th>
<th>Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keller et al. [37]</td>
<td>dog</td>
<td>-abdominal aorta</td>
<td>EM</td>
<td>within ±20%</td>
<td></td>
<td></td>
</tr>
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<td></td>
<td></td>
<td>-carotid arteries</td>
<td>flowmeter</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>-common iliac arteries</td>
<td></td>
<td></td>
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<tr>
<td>Marquis et al. [42]</td>
<td>dog</td>
<td>-femoral artery</td>
<td>timed blood</td>
<td>approx. 1.03</td>
<td>16 mL/min</td>
<td>0.99</td>
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<td></td>
<td></td>
<td>collection</td>
<td>collection</td>
<td>within ±15%</td>
<td></td>
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<td>Wood et al. [66]</td>
<td>dog</td>
<td>-carotid artery</td>
<td>timed collection</td>
<td></td>
<td></td>
<td>0.93</td>
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<td></td>
<td></td>
<td>-abdominal aorta</td>
<td>30-675 mL/min</td>
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<td></td>
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<tr>
<td>Stacey-Clear and Fish [58]</td>
<td>human</td>
<td>-femoral artery</td>
<td>repeatability</td>
<td>±12%</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td>standard deviation</td>
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<td>Fish [16]</td>
<td>in vitro</td>
<td>tubes</td>
<td></td>
<td></td>
<td></td>
<td>0.99, 0.95</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-4.9, -1 mL/min</td>
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<tr>
<td>Fillinger and Schwartz [14]</td>
<td>in situ</td>
<td>canine femoral, using pump</td>
<td>Timed Collection</td>
<td>±11%, 50% confidence = ±14 mL/min, 95% confidence = ±42 mL/min</td>
<td>1.02</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>0 to 300 mL/min</td>
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<td>-11.4 mL/min</td>
<td>r² = 0.928</td>
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<td>Forsberg et al. [17]</td>
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<td>latex tubes</td>
<td>accurate</td>
<td>±2% with 2 standard deviations less than ±10.5%</td>
<td>0.999</td>
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<td></td>
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<td>100–600 mL/min</td>
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<td>(carotid pulse)</td>
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<td></td>
<td></td>
<td>(pulsatile)</td>
<td></td>
<td>12.1 mL/min</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>0.91 (femoral pulse)</td>
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</table>

Table 1.4: Velocity Profile Technique: Results from Literature
1.4.4 Uniform Insonation Flowmeter

Principles

Figure 1.14: Uniform Insonation Volume Flowmeter. A spatial mean velocity is measured using a single large Doppler sample volume which encompasses the entire vessel. This is projected onto the direction of the vessel axis, and then multiplied by the cross-sectional area of the vessel which is measured independently.

The spatial mean velocity within a blood vessel can be measured directly by taking the mean Doppler shift frequency from a single large Doppler sample volume which encompasses the entire lumen of the vessel. Figure 1.14 illustrates this technique. The measured velocity is along the direction of the ultrasound beam. Area is measured using standard ultrasound grey-scale imaging. Most commonly, the lumen diameter, \( d \), is measured and circular symmetry is assumed. The Doppler beam vessel angle must also be measured in order to project either the velocity or the area such that the velocity measured is perpendicular to the area measured.

\[
Q = \left( \frac{\bar{f} \Delta c}{2f_o \cos \theta} \right) \left( \frac{\pi d^2}{4} \right). \tag{1.36}
\]
Limitations and Strengths

The use of pulsed Doppler ultrasound to determine spatial mean velocity along the vessel requires uniform sensitivity to velocities, uniform sensitivity to the entire vessel lumen, and a measurement of the angle between the ultrasound beam and the vessel. The dominant sources of error for the technique are: (1) non-uniform insonation, (2) beam vessel angle uncertainty, and (3) area measurement uncertainty.

Uniform sensitivity is the principal assumption of this technique, and violation of this results in significant errors [22]. Since conventional Doppler systems generally place spatial resolution at higher priority than uniform sensitivity, special instrumentation is usually required to implement this technique. Even specially designed ultrasound beams tend to overestimate flow since ultrasonic intensity is highest along the axis of the beam, and thus the higher velocities at the axis of the vessel are generally weighted too heavily. Gill [22] has demonstrated that for beamwidths (full width half maximum power of the ultrasound beam) 20% larger than the vessel diameter, error of flow measurement due to this effect is limited to a 5% overestimation. For a beam of half this width, the error can rise to 22%. Willink and Evans [65] have suggested correction methods to deal with this problem; however, these corrections make assumptions about the flow profile.

In practice, the use of a wide, uniformly sensitive beam has the advantage of relaxing the constraint on accurately locating the sample volume directly on the vessel. However, this also results in the disadvantage that flow in adjacent vessels may be measured as well. Directional sensitivity can be used to a limited degree to separate these signals since adjacent vessels tend to be arterial and venous pairs which run in opposite directions.

The method is also subject to the same $1/\cos\theta$ dependence and its associated errors, as described above for the velocity profile technique and illustrated in Figure 1.13.
Due to Diameter Measurement Error

Figure 1.15: **Error due to Area Measurement Uncertainty.** For methods which determine area from a diameter measurement, percentage error in flow is twice the percentage error in diameter.
The method is subject to errors due to uncertainty in the vessel area measurement. If diameter measurement is used, the percentage error in flow is twice the percentage error in diameter. Figure 1.15 illustrates this effect for physiological diameters. Errors in diameter measurement result from spatial resolution insufficient to locate vessel boundaries, off-vessel axis B-mode images, and the variation of vessel cross-sectional area with time due to pulsation. Unless separate transducers are used to measure area and Doppler signal, simultaneous measurement is not possible. Measurement over several cardiac cycles is common, with registration of vessel area and mean velocity assuming that beat-to-beat variation is negligible [10]. Alternatively, the cross-sectional area can be measured directly using a cross-sectional B-mode image of the vessel lumen. This depends on the lateral resolution of the ultrasound beam which tends to be poorer than the axial resolution of the beam normally used to calculate diameter.

Despite these sources of error, the uniform insonation technique is reasonably accurate, and has the strength of simplicity, with relaxed constraints on spatial resolution. In practice, relaxed constraints on spatial resolution result in better Doppler estimates, with greater signal relative to noise.

Relevant Studies

Gill [23] summarized results for the uniform insonation technique. These, and more recent studies, are collected in Table 1.5

For systems that were developed with appropriate ultrasound beam characteristics, accuracies were reasonably good, with errors of roughly 10–14% in vitro. Extensive in vivo trials of the system have not been published; however, several studies have implied reasonable accuracy. Gill [23] compared flow measurements in the portal vein and the sum of flows in downstream branches, which yielded results with rms differences of ±13%. He also measured flow in the splenic
<table>
<thead>
<tr>
<th>Investigator</th>
<th>Subject</th>
<th>Vessels</th>
<th>Compared Against</th>
<th>Flow Rates</th>
<th>Error</th>
<th>Slope</th>
<th>Offset</th>
<th>Regression R-value</th>
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<td>Gill [21]</td>
<td>in vitro</td>
<td>plastic tubes</td>
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<td>30–100 mL/min</td>
<td>±14%, ±32% maximum error</td>
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<td>excised human carotid artery</td>
<td>EM Flowmeter</td>
<td>0–700 mL/min (pulsatile)</td>
<td>±10% standard error</td>
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<td></td>
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<td>human main portal vein</td>
<td>vs. sum of branch flows</td>
<td></td>
<td>−Sum of branch flows exceeded portal flow by 3.5%, with rms difference value of ±13%</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>human splenic artery</td>
<td>vs. splenic vein</td>
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<td>−Venous flow exceeded arterial by 5.3%, with rms difference value of ±6.5%</td>
<td></td>
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<td>Eik-Nes et al. [10]</td>
<td>pig</td>
<td>abdominal aorta (surgically exposed)</td>
<td>EM Flowmeter</td>
<td>300–800 mL/min</td>
<td>0.96</td>
<td>8.9 mL/min</td>
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<td>in vitro</td>
<td>tubes</td>
<td>EM flowmeter</td>
<td></td>
<td>±34 mL/min</td>
<td>0.43</td>
<td>8 mL/min</td>
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<td>using standard</td>
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<td>human renal</td>
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<td>±21 mL/min</td>
<td>1.2</td>
<td>0.86</td>
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<td>Duplex scanner</td>
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<td>±53 mL/min</td>
<td>0.86</td>
<td>0.93</td>
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<tr>
<td>Uematsu [61]</td>
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<td>excised arteries</td>
<td>EM Flowmeter</td>
<td>630–815 mL/min (pulsatile)</td>
<td>±10% standard error</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uematsu [62]</td>
<td></td>
<td>human common carotid arteries</td>
<td>repeatability</td>
<td></td>
<td>intrasession variability: 2 standard deviations: ±6.7%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>using QFM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>week to week variability: 2 standard deviations: ±21.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hussain et al. [34]</td>
<td></td>
<td>human –common femoral artery</td>
<td>inter and intra</td>
<td></td>
<td>intraobserver variability: CFA 13%, SFA 15%, PFA 21%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>standard</td>
<td></td>
<td>–superficial femoral artery</td>
<td>operator</td>
<td></td>
<td>interobserver variability: CFA 16%, SFA 20%, PFA 40%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duplex scanner</td>
<td></td>
<td>–profunda femoris artery</td>
<td>variability</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Table 1.5: Uniform Insonation Technique: Results from Literature
artery versus in the vein in splenomegaly, yielding rms differences of ±6.5%. Uematsu [61] used a multi-transducer continuous wave Doppler system designed specifically for uniform insonation (the QFM—"quantitative flow meter" also known as VFM—"Volume Flow meter" system). Uematsu determined good in vitro accuracies using excised arteries, and went on to evaluate carotid flow in vivo [62] in a clinical study with over 650 subjects, including both healthy and neurologically diseased patients. Repeatability of measurement was excellent, with intrasession flow measurement variations of ±6.7% (2 standard deviations), and week-to-week variations of ±21.2% (also 2 standard deviations).

Evaluations of the technique have also been done on conventional duplex scanners. Hussain [34], considering error due to the instrumentation as systematic, evaluated inter- and intraobserver variability in flow measurement of the femoral artery using uniform insonation. He showed intraobserver variabilities of 13, 15, and 21% in the common femoral, superficial femoral, and profundum femoris arteries respectively. Interobserver variabilities were worse, at 16, 20, and 40%, respectively. Avasthi et. al. [2] also published somewhat disappointing results in vivo after an in vitro evaluation that had shown promising results. Gill has suggested that the relatively poor results using standard duplex Doppler instruments are a result of using an inappropriate ultrasound beam for the technique [23].

1.4.5 Attenuation Compensated Flowmeter

Principles

The attenuation compensated volume flowmeter is similar to the uniform insonation technique in the measurement of a mean flow velocity across the vessel lumen using a large sample volume; however, it makes use of the integrated power of the Doppler spectrum to determine the vessel area,
Figure 1.16: **Attenuation Compensated Volume Flowmeter.** Two beam geometries are required: (1) a wide beam which includes the entire projection of the vessel lumen (dotted ellipse), and (2) a narrow beam which is situated entirely inside the the vessel lumen (darkly shaded). Doppler frequency shifts received from the wide beam will correspond to velocities perpendicular to the projection of the lumen. Power in the Doppler spectrum from both geometries is used to estimate the area of the vessel as projected onto the surface of transection.

instead of relying on a grey-scale image. This measurement of area, however, requires a calibration, and compensation for attenuation, which is a function of depth. Compensation is achieved by using a smaller sample volume which is located entirely within the vessel. Figure 1.16 illustrates this technique.

The integrated power in the Doppler spectrum is proportional to the number of moving scatterers. If the density of scatterers within the sample volume is constant, then the power is a linear function of the proportion of the sample volume filled with moving scatterers. For a sample volume of uniform thickness, this proportion would correspond to a measurement of the proportion
of the transverse area filled with moving scatterers.

\[ P_{\text{total}} = k''(z)n_{\text{scatterers}} = k'(z)A_{\text{moving}}, \]  

(1.37)

where \( k''(z) \) and \( k'(z) \) are constants of proportionality, \( n_{\text{scatterers}} \) is the number of moving scatterers, and \( A_{\text{moving}} \) is the transverse area of the sample volume occupied by moving scatterers assuming a sample volume of constant thickness.

\[ k'(z) = T(z)\eta B(z), \]  

(1.38)

where \( T(z) \) is the attenuation, a function of depth; \( \eta \) is the back scattering cross section of blood; and, \( B(z) \) is the sensitivity of the ultrasound beam.

For the large sample volume, the power \([P_{\text{total}}]_1\) will be proportional to the projected area of the vessel \( A_{\text{proj}} \). For the small sample volume, the power \([P_{\text{total}}]_2\) will be proportional to the area of the sample volume itself \( A_2 \). Since the backscatter does not change, the use of the power from the small sample volume can be used to eliminate the dependence on attenuation.

Thus, the expression for flow using this method is:

\[ Q = \left( \frac{\bar{f}_d c}{2f_o \cos \theta} \right) \left( \frac{k(z)[P_{\text{total}}]_1}{[P_{\text{total}}]_2} \right), \]  

(1.39)

where \( \bar{f}_d \) is the mean Doppler shift frequency from the large sample volume, and \( k(z) \) is a calibration constant which is dependent on (1) the relative beam sensitivity for the small sample volume and large sample volume (a function of depth), and (2) the size of the small sample volume (also a function of depth).

**Limitations and Strengths**

Measurement of spatial mean velocity using a large sample volume results in similar limitations to those for the uniform insonation method. Thus, this technique still suffers primary sources of error
due to non-uniform insonation and interference with adjacent vessels. However, the ingenious use of Doppler power to estimate the vessel area projection eliminates sources of error due to dependence on separate angle and area measurements from imaging.

The technique does, however, have other sources of error and difficulties of implementation.

The area estimation based on Doppler power places additional importance on the uniformity of insonation in the large sample volume. In this technique, poor uniformity will cause both a poor mean velocity estimate and an inaccurate vessel area measurement.

The use of the small sample volume for calibration requires both similarity with the large sample volume and confirmation of position within the lumen of the vessel. The small beam is used to compensate for attenuation, which is dependent on the path of the beam through tissue and the ultrasound frequency. In practice, it is difficult to make a device which has, simultaneously, a large and uniform beam, and a small and focussed beam with sufficiently similar frequency and beam path. Although the technique eliminates the requirement of imaging for angle and area measurement, imaging may still be required to verify the location and relative size of the small sample volume with respect to the vessel. If the vessel to be examined is smaller than the small sample volume, then flow cannot be accurately calculated.

Furthermore, the angle independence of the technique is also limited, since large beam-vessel angles result in wide luminal projections. Thus large beam-vessel angles require larger and wider beams of uniform insonation.

These considerations taken together, the method has limited practical application. It appears to be suited to larger vessels (for ease of locating the small sample volume) and to situations where the beam-vessel angle is not excessively large.
Relevant Studies

In vitro trials of the attenuation compensated technique were described in the original paper which introduced the method [32]. Flow measurements were made in 12 mm and 16 mm diameter plastic tubing for a range of beam-vessel angles between 43 and 57 degrees. Angle independence is shown in principle, and measurements in the flow range of 15–40 mL/s were shown to deviate within ±6% from a regression fit.

More recently, Evans et al. have developed an attenuation compensated flowmeter instrument [13] for cardiac output measurement which uses an annular array. In vitro evaluation of this instrument [12] has demonstrated that it is independent of vessel angle to within 4% (within a limited range of angles), independent of vessel diameter to within ±5% (within a limited range of diameters), and that linearity is better than ±3%. Comparison with indicator dilution techniques in vivo had a correlation coefficient of $r = 0.96$.

1.4.6 C-Mode Velocity Profile Flowmeter

Principles

The C-mode velocity profile technique consists of measuring the mean velocity within each pixel of a C-mode scan using pulsed Doppler ultrasound. In this way, the entire two dimensional flow profile can be measured. Since the beam is always perpendicular to the scan plane (in the case of C-mode), projection of velocities is not required. Integrating over the entire scan plane yields flow, and is therefore independent of Doppler beam-vessel angle:

$$Q(t) = \int_{\delta(t)} \bar{v}(t) \cdot \vec{n} dA = \sum_{x,y} \bar{v}(x,y) \delta x \delta y = \sum_{x,y} \frac{c[f_d](x,y)}{2f_0} \delta x \delta y. \quad (1.40)$$
Figure 1.17: C-Mode Velocity Profile Method. A small sample volume is scanned in two lateral directions; mean velocity measurements are made at each pixel location to determine a velocity profile. This profile of velocities is naturally perpendicular to the scan plane; no projection is required. Integration of mean velocity over the entire plane yields flow.

Limitations and Strengths

The sources of error for this technique are not well understood, although clearly the vessel lumen projection must be entirely located within the C-mode scan plane. The technique requires high spatial resolution relative to the vessel size; however, the relative importance of this effect in the C-mode geometry has not yet been explored. Moser [47] cites partial volume effects at the vessel boundary as a source of overestimation error for the technique.

The technique is significantly limited by the requirement of scanning the beam in two dimensions. This can be impractically slow if mechanical beam translation is used. For this reason, the method is more suited to array implementations.

Theoretically, the inherent strengths of the method are that it does not require the mea-
measurement of the beam vessel angle, nor does it require the direct independent measurement of the vessel luminal area.

**Relevant Studies**

Research on this relatively new technique has been limited; however, significant preliminary work on the method has been done at the Institute of Biomedical Engineering, at the University of Zürich. This group has developed a real-time two-dimensional transducer array system for C-Mode Flow Measurement. Schumacher [55] describes an *in vitro* validation of the system using a 63 element (7 by 9) array, using a 10mm diameter flow phantom vessel. Angle independence was studied by making measurements of the same flow, but with Doppler angles varying between 30 and 70 degrees. Standard deviation of this measurement was used by the authors to characterise the angle independence. The variation depended on distance between the transducer and measurement plane. This standard deviation was found to be 3 percent of the flow for a 40mm distance, and 2 percent for 50mm distance. Linearity was evaluated by measuring flows of 0 to 42 mL/s. The authors found that the correlation coefficient of the linear least squares fit to the measurement data was 0.9986 for flows of 2 to 38mL/s, and that the slope of the line comparing measured to actual flow was 1.06. Finally, the authors studied symmetric and asymmetric stenoses and slowly oscillating flow profiles in the phantom using their system. They noted good agreement in the stenotic cases with known flows, and less than 4 percent standard deviation of measurements of 25mL/s flow in the slowly oscillating case.

1.4.7 **Summary Discussion of Ultrasound Techniques**

The various ultrasound techniques for measuring flow are summarized in Table 1.6. The parallel development of velocity profile and uniform insonation techniques has led to transcutaneous non-
<table>
<thead>
<tr>
<th>Method</th>
<th>Instrumentation Requirements</th>
<th>Assumptions</th>
<th>Primary Error Sources</th>
<th>Demonstrated Accuracy</th>
<th>Applications</th>
</tr>
</thead>
</table>
| Velocity Profile             | - Multi-gate (or scanned single gate) pulsed Doppler  
- High spatial resolution  
- Imaging for beam-vessel angle and sample volume registration | - Vessel axis in line with scan plane  
- Circular vessel  
- Cylindrically symmetric profile | - Insufficient spatial resolution  
- Angle estimation  
- Non-circular vessel  
- Asymmetric profile  
- Variation in vessel cross-section with time | in vivo: ±15-20%  
 in vitro: ±10%  
 (Table 1.4) | - Large Vessels |
| Uniform Insonation           | - Single gate pulsed Doppler, or continuous wave Doppler  
- Appropriate beam width to cover vessel lumen  
- Imaging for beam-vessel angle and area measurement | - Uniformly sensitive sample volume  
- Entire vessel lumen insonated | - Non-uniform insonation  
- Area estimation  
- Angle estimation  
- Interference from adjacent vessels  
- Variation in vessel cross-section with time | in vivo: ±10-14%  
 in vitro: ±10%  
 (Table 1.5) | - General |
| Attenuation Compensated Uniform Insonation | - pulsed Doppler in narrow and wide sample volume geometries  
- appropriate beam width in both geometries | - Uniformly sensitive large sample volume  
- large sample volume insonates entire vessel lumen  
- small sample volume entirely within vessel lumen | - Non-uniform insonation  
- Small sample volume not completely within vessel lumen  
- Interference from adjacent vessels  
- others? | in vitro: ±5-10%  
 [32] | - Large vessels  
- Small vessels ?? |
| C-mode Velocity Profile      | - Two-dimensional Doppler array, or scanned sample volume, to sample C-mode plane  
- High spatial resolution (appropriate beam width) | - Vessel lumen completely included in C-mode scan plane | - partial volume effect  
- others?  
 (Table 1.6) | in vitro: ±2-4%  
 [55] | - Large vessels  
- Small Vessels?? |

Table 1.6: Summary of Ultrasound Flow Measurement Techniques.
invasive flow measurement techniques with reasonably good demonstrated accuracy. Despite this, none of the techniques has received widespread clinical acceptance.

This may be due to several factors. First, accurate flow measurement requires a high degree of technical knowledge in order to limit the effect of many error sources. Many of the quoted accuracies were achieved under idealised conditions. Second, some techniques require special instrumentation that is not widely available. Third, the use of ultrasound for quantitative flow measurement is still a relatively new idea.

The relatively recent advent of linear transducer arrays and the demand for high quality images has resulted in clinical ultrasound scanners that are optimized to provide spatial resolution. For this reason, modern scanners are better suited to techniques based in principle on velocity profiling; consequently, the use of uniform insonation techniques has become more rare. With modern systems, the problem of angle measurement is most severe. Spatial localisation of the sample volume is simplified due to the use of color Doppler schemes and time domain correlation techniques which map flow velocity across a two dimensional section of the imaging plane. Accuracy of flow velocity determination for these techniques is an important new source of error. The use of modern linear array systems greatly simplifies clinical use of the velocity profile technique.

The new C-mode velocity profiling technique poses a solution to the problem of uncertainty due to angle estimation, and mapping velocities to semi-annular areas. Upcoming two-dimensional array technologies and early results from the literature indicate that this technique deserves further research, particularly with regard to determining the primary sources of error and accuracy.
1.5 Summary and Thesis Outline

This thesis began as an attempt to characterise the C-Mode Velocity Profile technique, and to establish the method’s place in Table 1.6. Over time, the work evolved into a novel technique which combines Attenuation Compensation and C-Mode Velocity Profiling in order to improve accuracy and precision of flow measurement by elimination of partial volume effects. Understanding of this new technique matured through a process of experimentation and computational modelling. The body of work presented in this thesis is the theory, computational modelling, and experimental validation of attenuation compensated C-mode Doppler. Results indicate that this method has excellent potential for blood flow measurement in major vessels.

**Chapter one** has been an introduction to the problem of quantitative blood flow measurement. In this chapter, I have attempted to make a case for the importance of non-invasive and quantitative blood flow measurement, and to set the context of the ultrasound blood flow measurement problem. Standard techniques of flow measurement are invasive, ranging from relatively low-risk catheter insertion to surgical exposure of the vessel to be interrogated. Ultrasound techniques are plagued by sources of error, among the most important of which are uncertainty in beam-vessel angle measurement and area estimation.

**Chapter two** describes a new ultrasound flow measurement technique, that is independent of beam-vessel angle measurement and explicit area measurement. Theory of the new technique is discussed, starting with the origin of the Doppler spectrum, and leading to the formulation of the C-mode velocity profiling technique. This formulation is shown to suffer from serious partial volume effects, and a new correction based on attenuation compensation is proposed. The hypothesis of this thesis is that the precision and accuracy of C-mode velocity profiling is improved by applying attenuation compensation to correct for the error due to partial volume effects. A
computational model is described next. This model was used to determine the systematic error as a result of relevant geometric and signal processing parameters. Results of the model confirm improvement using attenuation compensated C-mode and predict important relationships of error with signal processing parameters. It is also significant that the model predicts a decreasing error with increasing flow, suggesting that errors predicted using slow flow experiments can be used as upper limits of error for in vivo application. Following this theoretical treatment of the problem, experimental validation using a steady state flow model is described. Measurements of flow were compared against timed collection. The experiment verifies improved flow measurement accuracy and the efficacy of a correction for the dominant source of error. Ultimately, the accuracy of the technique is determined to be at least as good as those of existing techniques presented in Chapter 1.

Chapter three discusses future work and potential of this method. Design considerations for implementing this technique for cardiac output measurement are determined. Concepts of transducer arrays are introduced and described in the context of use for flow measurement with the new technique. Suggestions for refinement of the computational model are described briefly, for the purpose of answering new questions concerning array implementation. Finally, speculation is made on potential areas of future application.
Chapter 2

Attenuation Compensated C-Mode Doppler

2.1 Introduction

A new technique for quantitative blood flow measurement is presented in this chapter. It is based on the application of attenuation compensation to correct for partial volume errors in the C-mode velocity profiling technique. Accuracy and sources of error are investigated using a computational model and an experiment. The objective was to quantify both overall accuracy and improvement over the standard C-mode technique.

The new method is investigated for a C-mode scan plane that is insonated at each pixel using an identical sample volume. The model and the experiment deal with flow in steady-state in vitro models, and thus effects such as in vivo pulsatility, and refraction are not investigated. Relevance of these effects are addressed briefly in the summary.
2.2 Theory

2.2.1 Velocity Estimation using the Doppler Spectrum

The techniques of this chapter rely on the estimation of blood velocities from Doppler spectra obtained from a sample volume set at constant depth, but at different lateral positions. These spectra are either computed using models, or measured in experiments. As shown in Figure 2.1, a Doppler spectrum is obtained for a given geometry of ultrasound beam relative to vessel.

![Diagram of Doppler Spectrum](image)

**Figure 2.1: Origin of Doppler Spectrum.** A spectrum is acquired for a given geometry of ultrasound beam and blood vessel. The Doppler beam-vessel angle $\theta$ is illustrated, and the pixel within the C-mode scan is denoted by $(\delta x_i, \delta y_j)$.

The Doppler spectrum is a power density function of Doppler shift frequency. This function is denoted $P'(f)$. It is calculated as the magnitude of the complex Fourier transform of the in-phase (real) and quadrature (imaginary) components of the audio frequency Doppler signal as described in Section 1.4.1. The frequencies of the Doppler spectrum correspond to velocities according to the
Doppler equation

\[ f = \frac{2vn}{c} f_o. \]  

Thus, as discussed in Chapter 1, the Doppler spectrum can be viewed as a histogram of velocities within the “sample volume”, spatially weighted by the sensitivity of the ultrasound beam.

Pulsed Doppler systems generate Doppler spectra that are discretely sampled functions. The discrete representation is limited in extent, between maximal frequencies determined by the frequency of sampling \((f_R)\) in the time domain. Thus, the spectrum is defined between maximal frequencies \(-f_R\) and \(f_R\). In the discrete case, the power density function is represented by \(P'_f\), and \(f\) represents a frequency among the discrete range frequencies over which the spectrum is computed. These spectra are also functions of pixel number \((\delta x_i, \delta y_j)\), and each pixel corresponds to a physical position \((x, y)\). Doppler spectra are a function of pixel number, and are therefore denoted \(P'_f(\delta x_i, \delta y_j)\).

**Components of the Doppler Spectrum**

The Doppler spectrum is the superposition of the spectra that would be arise from motion due to the individual scatterers within the sample volume. The detected signal may be due to the motion of the blood vessel wall, due to the movement of blood, or may simply be random noise in the system. Figure 2.2(a) illustrates the contribution of these three effects. Expressed as this superposition, the Doppler spectrum function is

\[ P'_f = P_{Nf} + P_{Wf} + P_{Qf}, \]  

where \(P_{Nf}\) is the power spectrum due to noise, \(P_{Wf}\) is the power spectrum due to vessel wall motion, and \(P_{Qf}\) is the power spectrum due to blood flow. Normally the signal \(P_{Qf}\) is of interest. This signal can be extracted from the Doppler spectrum \(P'_f\) using foreknowledge of characteristics
Figure 2.2: **Doppler Spectrum Components and Processing.** (a) **Spectrum Components.** Three components that contribute to the Doppler spectrum $P'_f$ are shown. The separate components are highlighted for clarity. (i) The signal due to flowing blood is highlighted in black. (ii) The signal due to motion of the vessel wall is shown in dark grey, and results in low Doppler shift frequencies. The flow signal and the "clutter" signal due to vessel wall motion have Doppler frequency shifts corresponding to the velocity of motion in the axial direction of the ultrasound beam. These signals are superimposed over (iii) baseline noise (light grey). The noise signal is relatively uniform across the whole spectrum. (b) **Spectrum Processing.** The flow signal is extracted using two techniques of processing. (i) Thresholding can be used to reduce the effect of noise. All signals below a power density threshold are ignored (set to zero). (ii) "Wall" filtering can be used to remove the component due to vessel wall motion. All signals below a cut-off Doppler frequency ($f_c$) are scaled down (or set to zero).
Power Thresholding to reduce Noise Signal

A signal exists due to thermal noise in the transducer and electronics of the Doppler system. This noise is relatively uniform in amplitude across the Doppler spectrum with some random fluctuation. The level of this baseline noise establishes a limit on the sensitivity of the system for the detection of flow. In practice, the power density from flow is typically up to 30–40dB above baseline noise. When the power density contribution of the flow signal falls to the level of baseline noise, it becomes masked by the random variation in the noise signal. By applying a threshold of inclusion on the basis of power density, the effect of signal due to noise can be reduced, as shown in Figure 2.2(b); however, this also eliminates any signal due to flow that is below the threshold level.

Wall Filtering to reduce Vessel Wall Motion Signal

The signal due to motion of the vessel wall is high in amplitude, but low in Doppler shift frequency. Signals from the vessel wall can be 20-30dB higher than that from blood due to the higher scattering efficiency of tissue structures. It is critical to remove such signals before processing the Doppler spectrum for flow information. Milnor [46] summarizes work on pulsation of arteries, showing that changes in radius are on the order of 5–10%. Assuming that the arterial wall motion is mainly in the radial direction of the vessel, its velocity in the direction of the ultrasound beam has a sinusoidal relationship with beam vessel angle, and is on the order of 0–5cm/s. Blood in major vessels has velocity on the order of 100cm/s (see Table 1.3). Therefore, Doppler shift frequencies associated with wall motion are low compared to those of blood in major vessels (except for blood close to the vessel wall) and can be removed by applying a high pass filter to the Doppler spectrum. Figure 2.2(b) illustrates digital wall filtering by applying a cutoff frequency $f_c$. All signals with
absolute frequency above this cut-off are included (\(|f| > f_c\)), and all frequencies below (\(|f| < f_c\)) are excluded.

Formulation of Spectrum Parameters

Several parameters can be calculated from processed Doppler spectra to characterise detected flow. Throughout this thesis, these parameters are always calculated for spectra after a wall filter has been applied, but different degrees of power thresholding will be discussed. Wall filter processed Doppler spectra are denoted \(P_f\) (without the prime). Among the most important parameters of the Doppler spectrum are the integrated Doppler spectrum power (or "Doppler power"), and the mean frequency.

(i) Doppler Power

The integrated power (Doppler power) \(P_{total}\), is calculated as the sum of the discrete spectrum:

\[
P_{total}(\delta x_i, \delta y_j) = \sum_{f=-f_R}^{f_R} P_f(\delta x_i, \delta y_j)
\]

In other words, Doppler power is the area under the curve representing the spectrum. Note that the Doppler power parameter has arbitrary units.

If the spectrum can be considered as the weighted histogram of velocities, then the sum over the entire spectrum should be related to the number of moving scatterers. Assuming that the weighting is roughly uniform over the entire sample volume, then

\[
P_{total} \propto \eta T(z) B(z) n_{moving}.
\]

The integrated power in the Doppler spectrum is proportional to the backscatter cross-section \(\eta\), a scaling factor due to attenuation \(T\), the sensitivity of the transducer to the backscattered signal \(B\), and the number of moving scatterers within the sample volume \(n_{moving}\). The backscatter
The cross-section is essentially constant; however, the attenuation and sensitivity of the transducer are functions of depth. If the Doppler spectrum has been processed to eliminate signals from the vessel wall and noise, then the Doppler power can be considered as a measure of the volume of moving blood within the sample volume.

(ii) Mean Frequency

The mean frequency of a Doppler spectrum is determined by

\[
\bar{f}(\delta x_i, \delta y_j) = \frac{\sum_{f=-f_R}^{f_R} P_f(\delta x_i, \delta y_j) \cdot f}{\sum_{f=-f_R}^{f_R} P_f(\delta x_i, \delta y_j)}. \tag{2.5}
\]

The mean frequency is the first moment of the Doppler spectrum normalised by the zeroth moment. Assuming a uniform spatial weighting (uniform ultrasound beam sensitivity), then this mean frequency corresponds to a mean velocity, using the Doppler equation:

\[
\bar{v}_n = \frac{c\bar{f}}{2f_o}. \tag{2.6}
\]

The mean frequency is the centroid of the Doppler spectrum curve. When the noise in the Doppler spectrum is significant, it can bias the centroid significantly. This has been described in detail by Gerzberg and Meindl [19] and Gill [20]. Due to linearity, this effect can be expressed as follows:

\[
\bar{f} = \frac{\bar{f}_N \sum_f P_{Nf} + \bar{f}_Q \sum_f P_{Qf}}{\sum_f P_{Nf} + \sum_f P_{Qf}}, \tag{2.7}
\]

where \( \bar{f} \) is the overall spectrum mean frequency, \( \bar{f}_N \) is the mean frequency of the spectrum due to noise, and \( \bar{f}_Q \) is the mean frequency of the spectrum due to flow.
Doppler spectra $P_f(\delta x_i, \delta y_j)$ are obtained for sample volume positions in the C-mode scan plane. The signal from blood flow is extracted by applying wall filters to eliminate large amplitude signals due to vessel wall motion, and sometimes by applying power thresholds to reduce noise effects. Processed spectra $P_f(\delta x_i, \delta y_j)$ can be characterised using parameters of (i) Doppler power (Equation 2.3), and (ii) mean frequency (Equation 2.5). Doppler power is related to the number of moving scatterers, and mean frequency is related to their mean velocity within the sample volume.

### 2.2.2 C-Mode Doppler Velocity Profiling

The C-Mode velocity profiling technique of blood flow measurement was introduced in Section 1.4.6. It is reformulated here in greater detail, with a discussion of its most serious defect, the partial volume problem.

Applying the expression for flow using the C-mode velocity profiling technique,

$$Q_{C-Mode} = \sum_{\delta x_i, \delta y_j} \bar{v}_n(\delta x_i, \delta y_j) \Delta x \Delta y,$$

where $\Delta x$ and $\Delta y$ are the pixel dimensions in the C-mode scan plane. Combining with the Doppler equation (Equation 2.1), the overall flow measured using the conventional C-mode velocity profile technique is

$$Q_{C-Mode} = \sum_{\delta x_i, \delta y_j} \frac{c \Delta x \Delta y}{2f_o} \left( \sum_{f=\pm f_R} \frac{f}{P_f(\delta x_i, \delta y_j) \cdot f} \right).$$

### The Partial Volume Problem

The C-mode velocity profiling technique suffers from a systematic partial volume error. The partial volume problem is illustrated in Figure 2.3. Realistic ultrasound beams have lateral sensitivity that
Figure 2.3: The Partial Volume Problem for C-Mode Velocity Profiling. Realistic lateral sensitivity of the ultrasound beam falls off gradually. As the sample volume passes through the vessel wall and out of the vessel, Doppler spectra change as shown on the right. Doppler power (the area under the curve) decreases, as less and less moving blood is detected in the sample volume. The mean detected velocity corresponds to the centroid of the curve, which also decreases. The partial volume problem is a result of applying the mean frequency to the entire volume of the pixel, regardless of the proportion of blood within it.

falls off gradually. The mean Doppler frequency estimates mean velocity of moving scatterers within the lateral sensitive range of the ultrasound beam, but this mean velocity is applied to the entire scan pixel, regardless of the proportion of moving scatterers within the pixel. This means that the use of mean frequency of the Doppler spectrum to estimate mean velocity in a C-mode scan pixel is prone to severe error under conditions of a sample volume only partially filled with blood (the component of moving scatterers). As the proportion of moving scatterers within the sample volume decreases, the error increases in severity.

Ultimately, this partial volume error results in a distorted velocity profile, from which the volume flow is calculated. The edges of the vessel will appear to be ill defined, with velocities detected in pixels outside of the vessel boundary. Clearly the severity of this problem will be a function of the extent of the sample volume, both laterally and axially. Severity will also be affected
by techniques of processing that are applied to the Doppler spectrum.

2.2.3 A New Proposal: Attenuation Compensated C-Mode

The hypothesis of this thesis is that the precision and accuracy of C-mode velocity profiling is improved by applying attenuation compensation to correct for error due to the partial volume effect. Correction of the partial volume error can be achieved by determining the proportion of the sample volume that contains moving scatterers. It is possible to make use of the Doppler power (the integrated power of the Doppler spectrum, Equation 2.3) for this purpose. Attenuation compensation as it is used in this thesis refers to the use of the Doppler power from a reference measurement in order to calibrate other power measurements. Calibrated Doppler power is proportional to the number of moving scatterers and, therefore, volume of blood within the Doppler sample volume.

Attenuation compensation is illustrated conceptually in Figure 2.4. Mathematically, this concept is expressed as follows. Equation 2.4 defined the major dependencies of Doppler power. Using the same ultrasound beam to scan each pixel of the C-mode plane, and assuming that attenuation is a function of depth only, the relative proportion of moving scatterers within the sample volume can be determined by comparing the Doppler Power in any given pixel to the Doppler Power in a reference pixel \((P_{\text{total}}(\text{ref}))\) that is known to be completely within the vessel (at the depth of the C-mode scan plane). The true mean Doppler frequency shift for the pixel is therefore

\[
 \bar{f}_{A.C.}(\delta x_i, \delta y_j) = \bar{f}(\delta x_i, \delta y_j) \left( \frac{P_{\text{total}}(\delta x_i, \delta y_j)}{P_{\text{total}}(\text{ref})} \right)
\]

\[
= \left( \frac{\sum_f P_f(\delta x_i, \delta y_j)}{\sum_f P_f(\delta x_i, \delta y_j)} \right) \left( \frac{\sum_f P_f(\delta x_i, \delta y_j)}{P_{\text{total}}(\text{ref})} \right).
\]
Figure 2.4: **Attenuation Compensation.** The spectrum from a reference pixel known to be within the vessel is used to calibrate measurements from other pixels. The area under the spectrum for the reference pixel is its Doppler power. Doppler power is a function of depth due to beam sensitivity and attenuation, but for sample volumes at the same depth, and using the same ultrasound beam, power indicates the number of moving scatterers within the sample volume. Therefore, the ratio of Doppler power between a measurement pixel and the reference pixel (shaded areas) indicates the proportion of the sample volume that is filled with blood.
Throughout these formulations, the subscript "A.C." refers to the attenuation compensated result.

\[
\bar{f}_{A.C.}(\delta x_i, \delta y_j) = \frac{\sum f \mathcal{P}_f(\delta x_i, \delta y_j)}{\mathcal{P}_{\text{total}}(\text{ref})} \tag{2.9}
\]

Using Equation 2.9 instead of 2.5 for the velocity estimation, flow is calculated using 2.10:

\[
Q_{A.C.} = \sum_{\delta x_i, \delta y_j} \frac{c \Delta x \Delta y}{2 f_o} \left( \frac{\sum_{f=-f_R}^{f_R} \mathcal{P}_f(\delta x_i, \delta y_j) \cdot f}{\sum_{f=-f_R}^{f_R} \mathcal{P}_f(\text{ref})} \right) \tag{2.10}
\]

Thus, the flow within each pixel is proportional to the integrated first moment of the Doppler spectrum, and attenuation compensated (normalised) according to the integrated Doppler power for a reference pixel (\(\mathcal{P}_{\text{total}}(\text{ref})\)) where the sample volume is found to be entirely within the vessel.

**Spectrum Summation Formulation**

It is possible to rearrange the sums in Equation 2.10 as follows:

\[
Q_{A.C.} = \sum_{\delta x_i, \delta y_j} \frac{c \Delta x \Delta y}{2 f_o} \left( \frac{\sum_{f=-f_{\text{max}}}^{f_{\text{max}}} \mathcal{P}_f(\delta x_i, \delta y_j) \cdot f}{\mathcal{P}_{\text{total}}(\text{ref})} \right) = \frac{c \Delta x \Delta y}{2 f_o \mathcal{P}_{\text{total}}(\text{ref})} \sum_{f=-f_{\text{max}}}^{f_{\text{max}}} f \sum_{\delta x_i, \delta y_j} \mathcal{P}_f(\delta x_i, \delta y_j) \tag{2.11}
\]

In other words, all spectra can be summed spatially to determine the "total" Doppler spectrum for the entire C-mode scan plane. This total spectrum is \(\mathcal{P}_f(\text{Cplane})\):

\[
\mathcal{P}_f(\text{Cplane}) = \sum_{\delta x_i, \delta y_j} \mathcal{P}_f(\delta x_i, \delta y_j) \tag{2.12}
\]

which gives an alternate formulation of the method:

\[
Q_{A.C.} = \frac{c \Delta x \Delta y}{2 f_o \mathcal{P}_{\text{total}}(\text{ref})} \sum_{f=-f_{\text{max}}}^{f_{\text{max}}} f \mathcal{P}_f(\text{Cplane}) \tag{2.13}
\]
This can be related readily to formulations of other methods in terms of a mean velocity multiplied by an effective area, as follows. Since

$$
\sum_{f=-f_{max}}^{f_{max}} fP(f)\mathcal{P}(Cplane) = \mathcal{F}(Cplane)\mathbf{P}_{total}(Cplane),
$$

therefore,

$$
Q_{A,C.} = \left( \frac{c\mathcal{F}(Cplane)}{2f_o} \right) \left( \frac{\mathbf{P}_{total}(Cplane)\Delta x\Delta y}{\mathbf{P}_{total}(ref)} \right)_{A_{proj}}^{v_n}
$$

(2.14)

2.2.4 Comparison with Existing Techniques

The principles of this new technique are founded upon the concepts of the uniform insonation method [21], the attenuation compensated method [32], and the conventional C-mode method [63]. However, it is an improvement on each of these previous techniques. Theoretical improvement over conventional C-mode has already been discussed above.

Like uniform insonation, a mean velocity is calculated from a spectrum for the whole vessel lumen. Unlike uniform insonation, however, the area used comes from a comparison of the Doppler power from the spectra over the whole plane and the Doppler power from a single sample volume location. This determines the area of the vessel lumen as a function of pixel size, $\Delta x\Delta y$. The advantage of angle independence and not requiring an additional measurement of luminal area was already discussed in Chapter 1. After these errors, Gill [22] cited non-uniform insonation and interference with other vessels as the main sources of error. In effect, attenuation compensated C-mode simulates a wide uniform beam by sampling points in the C-mode scan.

Comparison of Equations 2.14 and 1.39 demonstrates similarity with the conventional attenuation compensated method. The difference with the new technique is that the same beam is used to generate both narrow and wide geometries. This has two advantages. First, the wide geometry is not as severely limited by transducer design parameters, since it is simulated by sampling a C-mode
scan plane. Second, the relative characteristics of the narrow and wide insonating geometries do not require calibration as a function of depth (since the same beam is used for both geometries).

In addition to these geometrical advantages, attenuation compensated C-mode also generates a representation of the velocity profile, which could be of additional value.

The remaining sections of this chapter deal with characterisation of the newly proposed attenuation compensated C-mode technique, and comparison of its accuracy with that of the conventional C-mode technique. The theoretical derivation given above has not considered problems due to lack of uniformity in the ultrasound beam, nor has it considered effects of spectrum processing such as baseline thresholding and wall filtering. A computational model which includes these parameters is used to evaluate the accuracy of the technique and to determine the most important sources of systematic error. Results from the computational model are then validated in a comparison with results from an experimental flow measurement. The experiment provides a means of assessing the effects of random error.

2.3 Computational Modelling

2.3.1 Objective

A computational model was developed for the purpose of investigating the accuracy of flow measurement using C-mode velocity profiling techniques. The goals were (1) to compare the conventional C-mode technique with the proposed attenuation compensated C-mode technique, and (2) to determine the relative severity of error due to modelled system parameters; this would lead to the identification of primary sources of error. The following system parameters were incorporated into the model: velocity profile, beam-vessel angle, relative beam-vessel size, C-mode sampling resolution, wall filtering, and baseline thresholding. Inclusion of these parameters permitted the
investigation of the effects of beam non-uniformity and spatial sensitivity, as well as the effect of spectrum processing. The model was computed for an ideal steady-state system where flow is fully developed and laminar. The model also provides a means for testing out new methods based on C-mode Doppler scanning schemes.

2.3.2 Methods

Basis of Model

The model is based on the computation of a theoretical Doppler spectrum for each pixel location in the C-mode scan. This spectrum is calculated as the histogram of velocities within a theoretical sample volume, weighted by the sensitivity of the ultrasound beam. The computational model was implemented in three dimensions; however, it is convenient to reduce the problem to one dimension for purposes of explanation. An overview of the model in the ideal case is presented in figure 2.5, and is described below.

The velocity profile is given by \( V(x) \), as shown in Figure 2.5a. In the one dimensional case, the true volume flow would be equivalent to the area under this curve,

\[
Q = \int V(x) \, dx.
\]

This velocity profile is sampled by an ultrasound beam, which has a sensitivity that is a spatial function, \( B(x) \) (Figure 2.5b). In the ideal case, as shown in the figure, a rectangular beam is used; it is uniformly sensitive to scatterers over a limited spatial region, and completely insensitive to scatterers outside of the spatial region.

A weighted histogram is computed for each pixel by combining these functions (positions are denoted by a number, \( n \)). The pixel positions taken together are represented by a sampling function \( S(x) \) (Figure 2.5c), whereas each individual pixel position is given by a single delta function, denoted
For one pixel location, at n=2...

Figure 2.5: Model of C-Mode Doppler. (a) \( V(x) \) is the velocity profile and (b) \( B(x) \) is the ultrasound beam sensitivity. (c) This beam is moved across the x-axis in pixel widths of \( \Delta x \) to sample the velocity profile. (d) The sensitivity of the beam to velocities is given by \( M(v) \). (e) For a single pixel measurement, the beam is convolved with the appropriate sampling location \( S_n(x) \). The histogram computation of \( V(x) \), scaled spatially by the beam sensitivity from \( B(x) * S_n(x) \) gives (f), the spectrum power density function \( P'_v(\delta x_2) \). This is scaled by the sampled sensitivity to velocities \( M_v \) to get (g), the final modelled spectrum \( P_v(\delta x_2) \).
For each pixel, the velocity profile and the beam sensitivity are spatially sampled at fixed resolution. The histogram is computed by integrating through space. The velocity \( V(x) \) determines the bin number for the histogram \( P'(\delta x_n) \) and the value placed in the bin is the sensitivity of the beam for that location, given by \( B(x) * S_n(x) \). Once all of the points along the x-axis have been added, then a spectrum \( P'(\delta x_n) \) is obtained. Since \( P'(\delta x_n) \) is a histogram, the spectrum resolution is defined by the number of bins used for \( v \).

The function \( M(v) \) (Figure 2.5d) is required in order to account for velocity dependent sensitivity. In the ideal case, \( M(v) \) is uniform for all velocities except for \( v = 0 \) where it is zero (Doppler is not sensitive to stationary scatterers). The spectrum is multiplied by a version of velocity sensitivity \( M_v \) (sampled to correspond with the bin sizes in the spectrum) to generate the theoretical processed spectrum \( P_v \).

Finally, this theoretical spectrum must be converted to a frequency spectrum \( P_f \) by scaling velocities to frequencies using the Doppler Equation 1.31. Once this theoretical spectrum \( P_f \) has been obtained for each pixel location \( (\delta x_n) \), the process of analysis is identical to that of using real Doppler spectra obtained by experiment.

3-Dimensional Implementation

The computational model was implemented in Matlab (Mathworks, Cambridge), a matrix-oriented data analysis language, and C (the programming language), on a Sun Workstation.

Geometry for the implementation of the model is shown in Figure 2.6. A rectangular coordinate system is used, with the origin along the axis of the ultrasound beam, at its focal length. Analytical expressions for the beam sensitivity and the flow profile were both calculated in this coordinate system. Thus, the different beam and vessel geometries were achieved by simple coordinate transformations. The \( x-y \) plane was considered to be the C-mode scan plane, and the
Figure 2.6: Model Geometry and Parameters. A rectangular coordinate system is used, with the origin centred on the sample volume (shaded cylinder), such that the $x$-$y$ plane is the C-mode scan plane, and such that the vessel lies in the $x$-$z$ plane. (Directions shown have been displaced from the origin for clarity) The beam-vessel angle is $\theta$. 

Geometric Parameters of Computational Model

- Parabolic velocity profile
- Gaussian lateral sensitivity of sample volume (cylindrically symmetric)
- Rectangular axial sensitivity of sample volume
- Scan plane
- $\Delta x$, $\Delta y$
- Beam-vessel angle $\theta$
- $P = 42 \Omega$
The $x$-$z$ plane was used as the bisecting plane along the length of the vessel. In the three dimensional implementation, the vessel was moved relative to the coordinate system of the sample volume.

Each beam-vessel geometry yielded a single simulated Doppler spectrum. Spectra are determined for a simulated C-mode scan plane. From this series of spectra, flow is calculated using the equations formulated above in the theory section (Section 2.2). For the conventional C-mode technique, mean frequency is calculated using Equation 2.5, volume flow is calculated using Equation 2.8, and, if desired, total Doppler power can be calculated using Equation 2.3. For the attenuation compensated C-mode technique, mean frequency is calculated using Equation 2.9 and volume flow is calculated using Equation 2.10.

Model Parameters

The parameters of the model are described below. (i) Parameters that are related to the geometry of scanning are introduced; (ii) Parameters related to the processing of the Doppler spectrum are described in general; and, (iii) fixed parameters used for calculation are summarized.

(i) Geometric Parameters

Figure 2.6 illustrates the geometric parameters of the model, which make it possible to include the effects of (1) Velocity profile and beam-vessel angle, (2) C-mode sampling strategy, and (3) Relative size of ultrasound beam and blood vessel.

In the model, a parabolic flow profile is used, as would be expected for steady flow in rigid tubes under conditions of fully developed laminar flow. The expression for this velocity profile in the coordinate system is:

$$v_n(x, y, z) = V_{max} \cos \theta \left( 1 - \frac{(x - n\Delta x) \cos \theta - z \sin \theta)^2 + (y - m\Delta y)^2}{R^2} \right),$$

(2.15)
where \( v_n \) is the velocity in the direction of the axis of the ultrasound beam, \( V_{\text{max}} \) is the maximum flow velocity in the vessel, \( \theta \) is the beam-vessel angle, and \( R \) is the radius of the vessel. \( n \) and \( m \) are integer values which represent the various positions in a C-mode scan of constant pixel size. Note, as the beam-vessel angle increases, more pixels are required to keep the vessel lumen projection contained within the scan plane.

The ultrasound beam sensitivity \( B(x, y, z) \) is modelled as a cylindrically symmetric function. It is gaussian in its lateral extent, and is rectangular in the axial extent. This is expressed analytically by:

\[
B(x, y, z) = \begin{cases} 
  e^{-\frac{x^2+y^2}{\beta^2}} & \frac{W}{2} > z > -\frac{W}{2} \\
  0 & \text{otherwise}
\end{cases}
\]

where \( W \) is the axial length of the sample volume and \( \beta \) is a parameter which characterises the width of the beam (\( \beta = \sqrt{2}\sigma \), where \( \sigma \) is the standard deviation of the gaussian). The relative size of the beam and the vessel is adjusted by changing \( R \) and/or by changing \( \beta \).

(ii) Spectrum Analysis Parameters

Modelled spectra were processed using standard techniques to determine mean velocity and Doppler power. Spectrum analysis parameters are illustrated in Figure 2.7.

Both baseline thresholding and wall filtering are applied in the computational model. This processing is applied individually to each spectrum (a pixel-by-pixel basis). Baseline thresholding is applied by zeroing all signals that do not have power density above the threshold level. The baseline threshold level is defined as a fractional level below the maximum power density \( \max(P_m) \) of the spectrum across the entire scan plane, in units of decibels (dB). Hence,

\[
\text{Baseline Threshold (dB)} = 10 \log \left( \frac{P_t}{\max(P_m)} \right).
\]
Figure 2.7: Spectrum Analysis Parameters for Model. The curve represents the flow spectrum calculated. Signal below an absolute frequency cutoff $f_c$ is removed to simulate wall filtering. Various levels of baseline thresholding can be applied by zeroing signal in bins with power density below the selected threshold $P_t$. The maximum power density for a spectrum is $P_m$.

A simple digital wall filter is used; a cutoff frequency $f_c$ is selected, and all signals in bins with absolute frequency below the frequency cutoff are ignored.

(iii) Fixed Parameters Used in all Calculations

For this thesis, a fixed relative size of beam to vessel radius of $R/\beta = 5$ was used in the model. Scan pixel sizes were also fixed, at $\Delta x = \Delta y = \beta$. The spatial sampling resolution was 20 divisions per $\beta$. In the lateral extent, the sampling of the functions went out to limits of $-3\beta$ and $3\beta$ from the centre of the sample volume. Modelled spectra were calculated using histograms with 2000 bins.

Effects Studied Using the Model

The model was used to study several effects by variation of four parameters; these were: axial sample volume size ($W$), baseline threshold level ($P_t$), wall filter cutoff ($f_c$), and Doppler beam-vessel angle ($\theta$).

Use of the model to determine relative error severity is summarized as follows.
Table 2.1: Summarized Computational Model Variables and Results

(a) The effects of axial sample volume size and Doppler beam-vessel angle were studied by varying $W$ and $\theta$, and fixing $P_t$ and $f_c$.

(b) The effects of baseline thresholding and wall filtering were studied by varying $P_t$ and $f_c$, and fixing $\theta$ and $W$.

(c) The effect of wall filtering and Doppler beam-vessel angle were studied by varying $f_c$ and $\theta$, and fixing $P_t$ and $W$.

Given the results from (a)–(c), the overall accuracy and linearity of the new technique could be computed as functions of the most severe sources of error. Variation of $f_c$ in flow measurements while keeping $V_{\text{max}}$ constant simulates flow variation in a steady-state system. The effects of wall filter and beam-vessel angle on overall accuracy were predicted using this technique.

2.3.3 Model Results

Table 2.1 summarizes the variable model parameters and results from the computational model.
Figure 2.8 illustrates the modelled effect of changing the axial sample volume size, and how this effect varies as a function of the beam-vessel angle. Flows using four different sample volume sizes were calculated: \( W = \frac{\theta}{2}, \beta, \frac{3\theta}{2}, 2\beta \). For each of these cases, measurements were simulated for beam-vessel angles \( (\theta) \) between 40 and 70 degrees, in 5 degree increments. For these results, the lowest possible value of wall filter was used \( (f_c = V_{\text{max}}/1000) \). The lowest baseline threshold was used, which corresponded to \( (P_t \approx -90\text{dB}) \). With the standard C-mode technique, errors range from 20–40% for the range of axial sample volume sizes used; this error also had an angle dependence. For C-mode, the range in error was \( \Delta 9\% \) for beam-vessel angles of 40–70 degrees for axially thin sample volumes, and this range decreased to approximately \( \Delta 1\% \) as axial sample volume size increased by a factor of 4. For the attenuation compensated C-mode techniques, error was negligible \( (-0.002-0.0001\%) \) over the range of axial sample volume sizes used.

**Figure 2.8: Modelled Effect of Axial Sample Volume Size and Angle**
(b) Effect of Baseline Thresholding and Wall Filter

Figure 2.9 illustrates the effect of varying the baseline threshold in spectrum processing for the two
techniques. $P_t$ was varied in 5 dB increments from $-10$ dB to $-90$ dB. Wall filter cutoffs were
incremented in steps of 25 units ($V_{\text{max}} = 1000$ units), from 0 to 900 units. The axial sample volume
size was set at $W = \beta$ and the beam vessel angle was set at $\theta = 60$ degrees. Figure 2.9a illustrates
that for C-mode, errors ranged from $-100$--$120\%$, depending on both baseline threshold and wall
filter. Variations in baseline threshold result in large ranges of error. Figure 2.9b illustrates results
for the same parameters using attenuation compensated C-mode. Errors ranged from 0 to $-100\%$. 
Variations in baseline threshold existed, but were small (with $\approx2\%$) for thresholds from $-20$ dB--
$-90$ dB. The $-100\%$ error line can be considered as a baseline 0 dB threshold (all signal removed).
This gives an indication in the maximum spread of error. The wall filter setting at 50% (500 units)
is equivalent to the projection of the maximum velocity in the direction of the ultrasound beam
(proportional to $\cos \theta$) for $\theta = 60$ degrees.

(c) Effect of wall filter and beam-vessel angle

Figure 2.10 shows the modelled error in flow measurements as functions of wall-filter setting and
beam-vessel angle. Wall filter cutoffs were incremented in steps of 25 units ($V_{\text{max}} = 1000$ units),
from 0 to 900 units. The axial sample volume size was set at $W = \beta$, and the baseline threshold
was set at a constant level of $-30$ dB. Calculations of flow were made for beam vessel angles of
$\theta = 40, 50, 60$, and 70 degrees. Errors for standard C-mode were in the range of $-100$--$20\%$, and
had dependence on both wall filter and angle. For attenuation compensated C-mode, errors ranged
from $-100\%$ to nearly 0%, and had angle dependence. For both techniques, the maximum spread
in error was at a wall filter cutoff corresponding to the maximum velocity for a 70 degree angle, and
Figure 2.9: Modelled Effect of Baseline Thresholding and Wall Filter (a) for standard C-mode, and (b) for Attenuation Compensated (A.C.) C-mode.
Figure 2.10: Modelled effect of wall filter and beam-vessel angle. The four lower curves are for the attenuation compensated C-mode technique, whereas the four upper curves are for the conventional C-mode technique.
for standard C-mode, this was \( \Delta 160\% \); for attenuation compensated C-mode, maximum spread in error was \( \Delta 80\% \).

Modelled Flow Dependence of Error

The flow dependence of error was simulated in the computational model by varying the wall filter cut-off level. In real systems, the wall filter setting is constant and the flow velocities change with increasing flow. Flow is proportional in this model to the maximum velocity; therefore, flow variations could be simulated by applying changing ratios of \( f_c/V_{\max} \). This was done for various angles \( \theta \), and for various baseline thresholds \( P_t \).

Figure 2.11: Effect of Flow on Error: Angle effects.

Figure 2.11 shows the effect of beam-vessel angle on the flow dependence of error. Calcula-
tions of flow were made for beam vessel angles of $\theta = 40, 50, 60,$ and $70$ degrees. The axial sample volume size was set at $W = \beta$, and the baseline threshold was set at a constant level of $-30$ dB. This simulation represents the effect of a constant wall filter which corresponds to a cutoff at 10% of the frequency shift corresponding to maximum blood velocity, if it were in line with an ultrasound beam. This condition was chosen because it corresponds to conditions of the flow experiment (Section 2.4). Errors for C-mode ranged from $-100$--55%, corresponding to an error range of $-0.2$ to 0.48 arbitrary flow units (maximum flow was 1). For attenuation compensated C-mode errors ranged from $-100$--2%, corresponding to an error range of $-0.26$ to $-0.03$ arbitrary flow units. The error in flow units can be used to infer the linearity characteristics of the measurement. If the actual flow is given by $x$, and its error in the same units $\varepsilon$, then the measured flow is $x + \varepsilon$.

Figure 2.12: Effect of Flow on Error: Baseline Threshold effects.
Figure 2.12 shows the effect of baseline threshold on the flow dependence of error. Calculations of flow were made for thresholds of $-20 \text{ dB}$, $-30 \text{ dB}$, and $-40 \text{ dB}$. The beam vessel angle was fixed in this case at 60 degrees. Axial sample volume size was set at $W = \beta$. For C-mode, the variation in error for this range increased significantly after error went from underestimation to overestimation, resulting in an error range of $\Delta 50\%$ to a range of $\Delta 30\%$. These corresponded to changing errors in flow that were as much as 0.3 flow units. For attenuation compensated C-mode, this variation was smaller, with a maximum spread of $\approx \Delta 2\%$.

### 2.3.4 Discussion

The results of the computational model determine systematic error in flow measurement as a function of various parameters; given a priori knowledge of all parameters, these results could be used to make corrections. The variability of flow error as a result of unknown variation in measurement parameters determines contribution to actual errors in experimental conditions. Superimposed upon this variability is random error which has not yet been considered. Although the variables correspond to parameters which are set by the user (and therefore known precisely), the effects are dependent on inherent assumptions such as the characteristic of the flow profile (in this case parabolic) and the shape of the ultrasound beam, which vary depending on tissue characteristics.

Recalling the objective of the model, the results of Figures 2.8–2.12 can be used to quantify systematic improvement in flow measurement for the attenuation compensated C-mode technique, in comparison to its predecessor, the C-mode technique. The range of measurement parameters chosen in this thesis correspond to relevant ranges for biophysical measurement. Furthermore, critical parameters can be determined.

In the discussion below, C-mode and attenuation compensated C-mode will be compared. This will be followed by notes which will help to interpret the various graphs of the model results,
in order to understand the technique. Finally, the various assumptions and compromises used in
the computational model will be discussed.

Comparison of C-Mode versus Attenuation Compensated C-Mode

Comparison indicates striking improvement with the application of the attenuation compensa-
tion correction to C-mode velocity profiling. In the cases computed, accuracy of the attenuation
compensated C-mode technique was better than its conventional C-mode counterpart (with the
exception of a narrow range of high wall filter cutoff settings for which C-mode flow error happens
to cross through a point of zero error). Since the attenuation compensation correction is primarily
concerned with the elimination of partial volume effects, this suggests that partial volume effects
dominate error in the conventional C-mode technique. Error appears to be relatively well-behaved
for attenuation compensated C-mode in comparison to the conventional technique. All results of the
attenuation compensated C-mode technique indicate systematic underestimation of flow, whereas
the regular C-mode technique swings through both overestimation and underestimation. The effect
of baseline thresholds in the range of -20dB and lower (more negative), in particular, causes large
variability in flow measurement error for C-mode, but not for attenuation compensated C-mode.

Interpretation: (a) Axial Sample Volume Size and Angle

Figure 2.8 can be interpreted as a pure treatment of the partial volume effect. By examining
Figure 2.4, it is clear that a longer axial sample volume (a taller cylinder) results in a larger
region of partial volume; the sample volume can be moved further laterally, while still picking up
signal from the vessel. This effect is exacerbated by increasing the beam-vessel angle. The use of
attenuation compensation to correct for this error is clearly apparent in the reduction of error, both
in terms of its magnitude, and spread due to angle.
Interpretation: (b) Spectrum Processing: Baseline Threshold and Wall Filter

Figure 2.9 is interpreted as the gradual elimination of the flow signal due to processing of the Doppler spectrum; this is made more clear by analysing Figure 2.7. The shaded region of Figure 2.7 represents the flow signal that is included in the measurement. As the wall filter cutoff frequency $f_c$ increases, more and more of the signal is lost. When the cutoff frequency reaches the maximum Doppler shift frequency, no flow is detected, resulting in a final error of -100% for both techniques.

The baseline threshold also reduces signal. As the threshold height increases, the shaded area becomes narrower, until the threshold is so high that the flow signal is completely lost.

The C-mode technique uses the centroid of this curve to estimate mean velocity of the pixel; it is clear that the centroid increases as low frequency shift components are removed from the spectrum. This is a critical problem with C-mode. As wall filter increases, the mean velocity of each pixel will approach an estimation of maximum velocity. A pixel will not register zero flow until its highest spectrum frequency is exceeded by the wall filter cutoff. Eventually, the filter setting is high enough to eliminate flow from all pixels. This accounts for the shape dependency on wall filter for the curves of C-mode measurement in Figure 2.9. It also provides a clue for interpreting the effect of baseline threshold. As the threshold gets lower (more negative $P_t$), the system is more sensitive to flow. This results in the increasing likelihood of detecting higher frequency components, since it increases the effective lateral sensitivity of the ultrasound beam.

For the attenuation compensated C-mode technique, the error due to these effects is well behaved. The removal of signal components due to both the wall filter and the baseline threshold result simply in a loss of flow signal. The effect of baseline threshold is only significant for values of $P_t > -20dB$, corresponding to thresholds a factor of 100 below the peak amplitude. Wall filter has the expected effect of gradually removing the detected signal from slow moving blood, until
the cutoff is so high as to remove the entire signal.

**Interpretation: (c) Spectrum Processing: Wall Filter and Beam-Vessel Angle**

Figure 2.10 can be interpreted as the wall filter effect that was described above, but with increasing severity due to the cosine dependence of frequency shift. In fact, the curves will map closely onto each other by linear stretching in the horizontal direction.

In practice, the lowest possible wall filter settings should always be used. This is defined by the maximum velocities of interfering tissue motion. Physiologically, these wall filters usually correspond to what was calculated as filters of 5-10%\(V_{\text{max}}\) in the model. Beam vessel angles of \(\theta < 60^\circ\) are used in practice. Therefore, modelled systematic errors for conventional C-mode are 30–40%. For attenuation compensated C-mode, modelled severity of this error is limited to systematic underestimations only up to 5% (Figure 2.10). These results also demonstrate the degree of angle dependence. For wall filters between 0–10%, the C-mode has variations in error of approximately 20–40%, and for attenuation compensated C-mode, this results in a variation in error of only 0–(-10)%.

**Interpretation: Effects of Flow on Error**

Figures 2.11 and 2.12 represent an alternative method of analysing the results presented in Figures 2.9 and 2.10. As the flow increases, the relative proportion of blood moving at low velocity decreases, therefore the wall filter has less of an effect. For C-mode, the effect is not easily interpreted due to the competing effects of overestimation due to partial volume effects, and underestimation due to the wall filter. The modelled result for C-mode is one of underestimations at low flow (corresponding to relatively high wall filter), a crossover as partial volume effects begin to dominate, followed by systematic overestimation. Beam vessel angle also has an effect (Figure 2.11),
complicated by large variations due to the level of baseline threshold (Figure 2.12). Effects for attenuation compensated C-mode are more straightforward. All flows are underestimated; however, as the relative proportion of signal removed by the wall filter decreases, accuracy improves. As will be discussed in the experiment, physiological flows correspond more or less to the right hand side of these graphs. In this region, errors are stabilized at approximately 50% overestimation for C-mode; errors decrease from 5% for attenuation compensated C-mode.

**Significance of Effects**

The partial volume effect is a debilitating source of error for the conventional C-mode technique. The attenuation compensation correction of this thesis results in significant improvements to both the overall accuracy and the predictability of error.

The predictable nature of error for the attenuation compensated technique depends on the relative level of noise compared to flow signal. In the model, it is assumed that thresholding is used to eliminate the noise signal from the spectrum (Figure 2.2). In other words, the model results only apply for a maximum power density of noise in the Doppler spectrum that is below the level of the threshold. Therefore, the baseline threshold establishes a minimum ratio of signal power density as compared to noise power density. In the model results, baseline threshold effects were < 2% for a threshold below -20dB. This level of signal is observed in real biophysical flow measurement in major vessels.

Given the well behaved nature of the errors for attenuation compensated C-mode, it would be possible to reverse these results from the computational model to correct for error given knowledge of the various system parameters. Of course this has limited application, since it depends on the validity of the assumptions and matching the model geometry with experimental conditions.
Validity of Major Assumptions

Several important assumptions were made in the formulation of the model. These included:

1. a one-to-one relationship between velocity and frequency shift,
2. a parabolic flow profile,
3. sufficiency of integration range for the sample volume, and
4. no baseline noise bias.

(1) One to one mapping: velocity→frequency

A one-to-one relationship between velocity and frequency shift is assumed in the model so that the histogram of velocities can be considered equivalent to the Doppler spectrum measured within the sample volume. In reality, this is not the case. Spatial localisation makes Doppler estimation prone to spectral broadening, an effect where a scatterer moving at a single velocity generates a spectrum of frequencies centred about the Doppler shift frequency for this velocity. The degree of spread is directly related to the degree of focussing. However, since the C-mode methods are based on estimates of mean velocity, the frequency spreading effect is not expected to have a primary effect on the accuracy of the technique. Incorporation of these effects into the model is discussed in Chapter 3.

(2) Non-parabolic Flow Profiles

Results of were computed using only parabolic flow profiles. Other profiles were not considered, although these could be readily implemented in future. Investigations of the effects of non-parabolic flow on error will be particularly important for predicting error in vivo.
A simple analysis using non-parabolic flow profiles will be used here to demonstrate the first order wall filter effects on flow measurement linearity. This discussion uses a much simpler system than the computational model that has been described thus far. A simple velocity profile expression for axially symmetric laminar flow in rigid tubes is used to further characterise the underestimation due to wall filter, for the attenuation compensated C-mode technique.

As described in the first chapter, flow profiles are expected to take the theoretical form:

\[
v = v_m \left[ 1 - \left( \frac{r}{R} \right)^\alpha \right]
\]

The analytical expression for the overall Doppler spectrum (equivalent to calculating \( P_f(C_{\text{plane}}) \)) resulting from this flow profile is:

\[
P(f) = \frac{2}{\alpha f_{\text{max}}} \left( 1 - \frac{f}{f_{\text{max}}} \right)^{\frac{2-\alpha}{\alpha}}
\]

(2.18)

The spectra calculated from this equation for \( \alpha = 2 \rightarrow 6 \) are shown in Figure 2.13.

Wall filters can be applied to these theoretical spectra, to predict effect on flow. Since the experiment will characterise accuracy as a function of flow rate, the error due to wall filter was also
calculated as a function of flow rate. Flow measured (proportional to first moment of spectrum) is plotted as a function of a theoretical flow rate in Figure 2.14.

This figure shows that the expected effect of the wall filter on accuracy is to offset the measured flows from the identity. In other words, the precision of the experiment should not be greatly affected, but flows will tend to be underestimated. The constancy of the offset begins to break down for flows of higher order ($\alpha$) and at lower flow rates.

The conclusion of this short analysis is that the errors predicted for non-parabolic profiles that can be described by Equation 1.8 result in improved accuracy. Overall, it is reasonable to suggest that profiles which have a greater proportion of blood moving at higher velocity will result in more accurate flow measurements, since the wall filter (the dominant source of error) will have less influence in these cases.

(3) Range of Integration for Sample Volume

A range of integration of the velocity profile and beam was used for the calculation of the computational model. The relative amount of lost signal power in the excluded region can be calculated as follows:

$$\frac{\int_0^{2\pi} \int_{3\beta}^\infty e^{-\frac{r^2}{\beta^2}} r dr d\theta}{\int_0^{2\pi} \int_0^{\infty} e^{-\frac{r^2}{\beta^2}} r dr d\theta} = \frac{1}{e^{\beta}}$$

(2.19)

Although the detection of velocities at very low power is important in terms of the partial volume effect, once the correction has been made, it is safe to assume that this level of lost signal power is insignificant. The limitation of this range of integration is observed in the choppy variation apparent in some of the results for conventional C-mode measurement. This is due to the fact that mean velocity estimates are made with very low power results, and that low power results come from the edges of the sample volume.
Figure 2.14: Theory of Wall Filter effect on Flow Measurement. For parabolic flow ($\alpha = 2$), the wall filter causes the measured flows to be offset from the identity line. The effect for higher order flow ($\alpha = 6$) is also an offset, but has a more pronounced curvature at lower flow rates. Wall filters are indexed as a percentage of the maximum flow velocity for the maximum flow rate. (In parabolic flow, maximum flow velocity is proportional to flow).
Finally, the model does not consider noise above the baseline threshold. It is always assumed in the model that the spectra used will be pre-processed using baseline thresholding and wall filtering. If no baseline threshold is applied, then the spectrum will contain some component of random variation that would influence both the mean frequency estimation and the Doppler power. Noise in the reference power estimate could have a large effect on the estimated flow, however averaging techniques can be applied.

2.3.5 Conclusions from Computational Model

A computational model has been used to investigate the efficacy of the C-mode velocity profiling method and a new technique that I have termed attenuation compensated C-mode. Results from this model have been used to compare the techniques, and to indicate the primary sources of systematic error. Results were calculated for a system with geometric parameters in the range of those used in the clinical measurement of major blood vessels. The conclusions from the computational model are as follows:

Conventional C-mode. The conventional C-mode technique is prone to large errors of flow estimation ranging from negative flow errors at low flow rates to overestimations which approach a constant 50% overestimation under physiologically relevant conditions. The primary source of error for this technique is the partial volume effect (which results in flow overestimation), which is dealt with using attenuation compensation.

Attenuation Compensated C-mode. The attenuation compensated C-mode technique reduces the effect of partial volume. Application of this correction in the model demonstrated improved accuracy and well behaved error in comparison to conventional C-mode. The largest
errors are at low flow rates, but in the range of wall filters that are below 10% of maximum
flow velocity, error continues to decrease from a maximum of 5%, given a beam vessel angle
less than 60 degrees. The primary source of systematic error for the technique is the wall
filter, which has decreasing effect with larger relative flow rates. Furthermore, errors are well
behaved, suggesting that correction is possible.

2.4 Experimental Validation

2.4.1 Objectives

A flow experiment was used for the purposes of (1) validating improvement of attenuation compensated C-mode over the conventional C-mode technique, and (2) investigating the random error for the new attenuation compensated C-mode velocity profiling technique in a more realistic physical system.

The specific goal was to compare the accuracy of conventional C-mode velocity profiling against the accuracy of the new technique of attenuation compensated C-mode velocity profiling. Measurements of flow were made using the two techniques, and were compared against the standard of timed collection. Measurement accuracy was investigated as functions of flow rate, Doppler beam-vessel angle, and vessel size.

2.4.2 Methods

In the flow experiments, C-mode Doppler techniques were investigated using a mechanically scanned single-element transducer to probe steady-state flow in an in vitro vessel model. Figure 2.15 is a schematic overview of the experimental apparatus used. The experimental methods are described in the following order:
(a) flow model,  
(b) C-mode Doppler scan implementation,  
(c) C-mode velocity profile analysis methods,  
(d) attenuation compensated C-mode velocity profile analysis methods, and  
(e) correction methods to account for wall filter and noise.

(a) Flow Model  

The flow model consisted of (i) an in vitro vessel phantom, (ii) a blood mimicking fluid, and (iii) a flow system for driving the fluid through the vessel phantom. The goal was to produce repeatable
steady-state fully developed laminar flow within a cylindrical vessel phantom.

(i) Vessel Phantoms

The requirements for a vessel phantom for these experiments are simply that attenuation is approximately homogeneous (and has a value that is reasonably close to that for human tissues) and that the phantom can withstand the intraluminal pressures generated by the flow system. A constant coefficient of attenuation would ensure that the attenuation was mainly a function of depth, making the attenuation relatively constant across the C-mode scan plane. Since the flow was generated with a pressure head, intraluminal pressures required to generate the high velocities reached approximately 75 mmHg, or roughly 10 kPa. The required strength of material is also a function of the circumference of the vessel cross-section; larger diameter vessels experience greater wall stresses.

A cross-linked gelatin-graphite vessel phantom was designed and constructed for the flow experiment. This material was chosen for its similarity to living tissue in terms of backscatter images (see Figure 2.17) and speed of sound (~1540m/s). This material consisted of small graphite particles, used as scatterers, suspended in a gelatin matrix which was cross-linked to increase the strength.

The phantom material was cast into a special mould which could be mounted at arbitrary angles between approximately 50 and 90 degrees from the vertical. The material was moulded around a metal rod which was later removed, leaving a cylindrical channel (the phantom vessel) through the material. The phantom is shown in Figure 2.16. Two diameters of phantom vessel were used: 6.4mm and 9.4mm. Figure 2.17(b) shows an ultrasound image of the 6.4mm diameter phantom.
Figure 2.16: Gelatin-Graphite Phantom

Figure 2.17: Ultrasound Grey-Scale Images: (a) Clinical Carotid Bifurcation (CCA = Common Carotid Artery, ICA = Internal Carotid Artery, and ECA = External Carotid Artery), (b) Phantom. Images were obtained using an ATL HDI-3000 Ultrasound Scanner with a linear array transducer. The hash marks in the scale on the right represent divisions of 1 cm (with dots indicating 5 mm). Arrows indicate the transmit focal zones for the ultrasound beam.
(ii) **Blood Mimicking Fluid**

For the experiment, the blood mimicking fluid need only have scattering properties reasonably similar to that of blood, and be uniformly distributed within the vessel lumen. A simple mixture of water and Sigmacell Type 20 Microcrystalline Cellulose particles (Sigma Chemical Co., St. Louis, MO) was used. The low viscosity of water reduced the required pressure head to generate higher velocity flows, eliminating the need for a pump. It also made the use of a gelatin based phantom practical. The documentation for the cellulose particles cited diameters smaller than 20 µm, well within the range of Rayleigh scattering for diagnostic ultrasound frequencies of 5-10MHz. The negative aspect of the low viscosity was that maximum flow velocities were reduced (to ensure laminar flow).

(iii) **Flow System**

The flow system was designed to produce a steady flow rate of blood mimicking fluid through the phantom vessel. The system consisted of high and low reservoirs, a flow control valve, a pump, and a magnetic stirrer.

A fixed pressure head between high and low reservoirs was used as the driving force for fluid motion. Using a pressure head instead of a pump reduced extraneous vibrations and pulsations. Flow in this case is described by the Bernouilli equation, with an extra term which represents frictional losses in the system. The valve also provides flow control. The pump returns fluid from the low reservoir to the high one, and the stirrer is used to maintain a uniform distribution of scatterers within the fluid medium.

In order to maintain conditions of laminar flow, conditions were kept such that the Reynolds number was below 2000. For fully developed flow, a tube entrance length $L_e$ of straight running
and uniform diameter tubing is required. \( L_e \) is given by:

\[
\frac{L_e}{D} \approx 0.06 R e D
\]  

(2.20)

where \( D \) is the diameter of the tubing. This entrance length was required both before and after the site of measurement within the vessel phantom.

(iv) **Timed Collection**

For all flow experiments, measurements were compared to timed collection. Timed collection was simply achieved by swapping out the low reservoir for a graduated cylinder. Volumes of 100–200\text{mL} of fluid were collected. The filling time was measured using a stopwatch. The precision of this measurement was approximately 1–2\% (based on a test of repeated measurement of flow in the experiment).

(b) **C-Mode Doppler Scan Implementation**

The C-mode scan was implemented using a clinical single-element transducer mounted on a computer-controlled positioning stage. Custom software allowed the user to control scan dimensions, step sizes, and time taken at each data point.

An Interspec XL Doppler ultrasound system (ATL Technologies, Seattle, WA) was used to acquire the Doppler data. The Interspec XL system uses standard analog Doppler processing, as described in the introductory chapter. A modification to the system allows the In-phase (I) and Quadrature (Q) Doppler signals to be extracted, and output onto the right and left analog recording channels of a Panasonic SV-3700 DAT recorder. These signals were then re-digitized for analysis on a Sun Workstation.

Data was acquired using the Interspec XL 5.0 MHz imaging and Doppler probe. The factory
specifications for this probe indicate that it is focussed at 5.5 cm depth, and that its aperture has a diameter of 13 mm. The shortest possible axial sample volume length for the probe is 1.0 mm, which was used for all experiments.

Data acquisition was performed by positioning the Doppler sample volume in the middle of the vessel, at the focal distance of 5.5 cm. The central position was verified both in the imaging mode, and by maximizing the intensity and frequency shifts of the Doppler spectrogram in the Doppler mode. From this position, the C-mode scan and DAT tape recording were started. Acquired data took the form of a long stream of digitised Doppler I and Q data, which was later synchronized with data from the positioning system in the analysis.

(c) C-Mode Velocity Profile Analysis Methods

The analysis of data for a given measurement involves the calculation of Doppler spectra for each C-mode scan location, from the digitised Doppler I and Q data. In this section, the analysis method
is followed through for a single example flow measurement.

The stream of Doppler data is broken into segments which are registered to pixel locations. A window of data is used for calculations at each pixel; a user-defined region at the beginning and end of each segment is discarded, to eliminate the signals which were acquired as the transducer was moving from one pixel to the next.

A discrete Fourier transform (Matlab's Fast Fourier Transform) was applied to the Doppler data for each position, generating a series of spatially localized Doppler spectra. Due to the long length of the time window (generally 1.5–2.5 seconds), a simple rectangular window was used in the time domain. (At a sampling frequency of 4kHz, this corresponds to 6,000–10,000 points.) An example Doppler spectrum for a single spatial location is shown in Figure 2.19.

Now, all of the C-mode velocity profiling parameters from Section 2.2 can be calculated, and the mean frequency can be plotted as a function of pixel position (this is a scaled version of the measured velocity profile). Figure 2.20 shows a typical plot of mean frequency as a function of position in an experiment, for a vessel diameter of 6.35 mm, at a beam-vessel angle of 70 degrees.

Flow for the C-mode technique is calculated according to Equation 2.8. Finally, Figure 2.21 shows a typical map of Doppler power as a function of position, for the same dataset as seen above.

(d) Attenuation Compensation Analysis Methods

Theory and computational modelling suggested a simple attenuation correction where the Doppler power in a single reference pixel that was known to be within the vessel could be used to properly calibrate flow measurement for the entire C-mode scan plane (Equation 2.11).

Several schemes could be used to automatically determine which pixel should be used as a reference. For example, the pixel with the maximum Doppler power could be used, if it were known that at least one pixel should be completely enclosed within the vessel. Some sort of power-
Figure 2.19: Analysis Example: Doppler spectrum from experiment, for a single transducer location. A flow signal, observed between frequency shifts of approximately zero to 500 Hz is evident above baseline noise, which is at a level of approximately a factor of 1000 below the signal peak power. The notch in the middle of the spectrum corresponds to the analogue wall filter of the Doppler system, which in this case is set at a level of 184 Hz.

thresholded average could also be used to determine a valid pixel. Early attempts to perform attenuation compensation with single pixel values resulted in a failure to show consistent improvements in accuracy due to fluctuations in the power, as is evident in Figure 2.21. These variations resulted in flow measurements in error by as much as a factor of 2.

In a vessel that has a large lumen projection compared to the sample volume size, there should be many pixels in which the sample volume falls completely within the vessel. Spatial averaging of the Doppler power within these pixels could be used to improve the accuracy of the normalisation factor $P_{\text{total}}(\text{ref})$. 
Figure 2.20: Analysis Example: Map of mean frequency from experiment (2 dimensional velocity profile). Axis one corresponds to the y-direction, and axis two corresponds to the x-direction.

The approach taken in this thesis is to fit a flat surface to the highest Doppler power pixels in a logarithmically compressed spatial map of Doppler power (in effect, a mono-exponential fit). The surface is also constrained to tilt only in the z-x plane where the vessel is diving. This makes some allowance for attenuation compensation which includes effects of variations in attenuation along the diving direction of the vessel. Thus, instead of using a single valued normalisation power, the attenuation compensation factor is a function of the long axis direction, and is given by $P_{total}(x)$, which is determined by the fitting routine described next.

An automated algorithm selects the highest power amplitude lines of the Doppler power spatial map (Figure 2.21), along the diving direction (in the example case, Axis 2). The criteria for the automatic selection of these lines is simply that more than 25 percent of the points on the
Figure 2.21: Analysis Example: Map of Doppler power

Line are the maxima in the orthogonal direction. These are plotted for the example data set in Figure 2.22. User intervention is then required to determine the range over which the fit should be made. In the case of the example, the fit is made over the region of 5 mm to 17 mm. Fits are made for each of the lines individually (dotted lines), and then for the points in the region, taken together (solid line). The fits are made in a least squares sense. The solid line is the function $P'_{\text{total}}(\delta x_i)$.

Therefore, the attenuation compensated mean frequencies are given by a modification to Equation 2.9:

$$
\bar{f}(\delta x_i, \delta y_j) = \frac{\sum_{f=-f_{\text{max}}}^{f_{\text{max}}} P_f(\delta x_i, \delta y_j) \cdot f}{P'_{\text{total}}(\delta x_i)},
$$

(2.21)

and the Volume flow, after attenuation compensation, is given by Equation 2.22:
Figure 2.22: Analysis Example: Mono-Exponential Fit of Total Power for Attenuation Compensation. The user has selected the region of 5mm to 17mm to apply the fitting procedure. Dotted lines show the fit for each of the two data lines, and the solid line shows the fit for all of the points in the region selected.

\[
Q_{A.C.} \approx \sum_{\delta x_i, \delta y_j} \frac{c\Delta x \Delta y}{2f_o} \left( \frac{\sum_{f=-f_{max}}^{f_{max}} P_f(\delta x_i, \delta y_j) \cdot f}{P'_{total}(\delta x_i)} \right).
\]  (2.22)

(e) Wall Filter Correction and Baseline Thresholding

Angle independent corrections were used to reduce the errors due to wall filtering. A simple method of baseline thresholding was also applied. These corrections were based on manipulating the summed overall spectrum, denoted in the theory section (2.2). Due to the modified application of attenuation compensation, the summed spectrum can no longer be expressed by Equation 2.12, since the attenuation correction term \( P'_{total}(x) \) is now a function of position.
The spectrum cannot be correctly calculated without applying the attenuation compensation first. Thus, the following expression will be referred to as the summed spectrum:

\[
\hat{P}_f(C\text{plane}) = \sum_{\delta x_i, \delta y_j} \frac{P_f(\delta x_i, \delta y_j)}{P'_{\text{total}}(\delta x_i)}
\]  

(2.23)

This also changes the formulation of flow to:

\[
Q_{A.C.} = \frac{c\Delta x \Delta y}{2f_o} \sum_{f=-f_{\text{max}}}^{f_{\text{max}}} f \hat{P}_f(C\text{plane})
\]

(2.24)

(i) Wall-Filter Correction by Extrapolation

In principle, it is possible to make an angle independent correction for wall filter by making use of the summed spectrum \(\hat{P}_f(C\text{plane})\), and by making some assumptions about the velocity profile. A simple example of this type of correction is used in this experiment, as a proof of concept.

An example of a summed spectrum from an experiment is shown in Figure 2.23a. The plot is of \(\hat{P}_f(C\text{plane})\). The effect of the wall filter is clearly seen, with slow flow cut out from frequency shifts of 0 to approximately 200 Hz. For this data set, the wall filter setting was 184Hz (the lowest possible for the Interspec XL system). Figure 2.23b shows the theoretical spectra (same as Figure 2.13 from the discussion of the computational model), which correspond to flow profiles for axially symmetric laminar flow. For this family of theoretical curves, the power density function at low velocity parts of the spectrum is relatively constant. In this thesis, the “missing” flow from the wall filter is restored using a simple extrapolation of data.

The extrapolation used in the experimental analysis required some user intervention. A region over which to average and a region over which to use that average to extrapolate data were chosen. This is illustrated in Figure 2.24. In this case, the user has chosen to average over the range of 250 to 300Hz, and extrapolate this data to the region of 0 to 250 Hz.
Theoretical Doppler Spectra for alpha = 2—6

Power Density (arbitrary units)

Frequency Shift (percentage of maximum)

Figure 2.23: Analysis Example: Total Spectrum
Figure 2.24: Analysis Example: Extrapolation and Windowing. For wall filter correction, the user has selected to average over the range of 250 to 300 Hz, and extrapolate this data from 0 to 250 Hz, as shown by the straight line. In order to minimize bias due to noise, the user also chooses to perform the calculation using data from the range of frequency shifts of 0 to 900 Hz.
Thus, in this case, the low frequency portion of $\hat{P}_f(C\text{plane})$ is replaced by the averaged value, generating $\hat{P}'_f(C\text{plane})$.

$$\hat{P}'_f(C\text{plane}) = \begin{cases} \bar{P}_{f \in \text{(averaging range)}}(C\text{plane}) & \forall f \in \text{(extrapolation range)} \\ \mathcal{P}_f(C\text{plane}) & \text{otherwise} \end{cases}$$  \hspace{1cm} (2.25)

The corrected flow measurement is given by:

$$Q \approx \frac{c\Delta x \Delta y}{2f_o} \sum_{f=-f_{\text{max}}}^{f_{\text{max}}} f \hat{P}'_f(C\text{plane})$$  \hspace{1cm} (2.26)

(ii) Baseline Thresholding

In this experiment, baseline thresholding was not applied on a pixel by pixel basis. Without baseline correction, the mean frequency estimation will be biased based on Equation 2.7. Therefore, an overall baseline is applied on the summed spectrum. This is achieved by applying a user-defined window of frequencies to be used for calculation. The size and location of the window was determined by visual inspection of the spectrum. (This process corresponds to an approximate baseline threshold of $-25--30 \text{ dB}$). Plots similar to Figure 2.23a were generated. The user was able to zoom in and select a region of the spectrum to use for the flow calculation. In the case shown, the user chose to calculate the flow only using frequency shifts from 0 to 900Hz. If we denote these limits by $f_{\text{low}}$ and $f_{\text{high}}$, the flow equation can be modified to give:

$$Q \approx \frac{c\Delta x \Delta y}{2f_o} \sum_{f=f_{\text{low}}}^{f_{\text{high}}} f \hat{P}'_f(C\text{plane}).$$  \hspace{1cm} (2.27)
Summary of Analysis Methods

Equations 2.23, 2.25 and 2.27, summarize all of the corrections that are used to-date, to improve the C-mode velocity profiling in the experiment. \( \hat{P}_{total}(x) \) is used to make the partial volume correction using attenuation compensation, \( \hat{P}_{s}(C_{plane}) \) is used to make the wall filter correction, and the restricted limits of summation correspond to baseline thresholding.

2.4.3 Parameters and Results of Experiment

Parameters of Experiment

Experiments were performed at beam-vessel angles of 50, 60, 65, and 70 degrees. Flow rates ranged between approximately 60 mL/min, and 345 mL/min. All of the above were measured on a 6.35 mm diameter vessel phantom. One dataset was taken for a phantom with a 9.42 mm diameter. Data were analysed blindly; that is, no foreknowledge of system parameters were used to aid in flow calculation. The parameters of the experiment are summarized in Table 2.2.

<table>
<thead>
<tr>
<th>Set Name</th>
<th>Angle (degrees)</th>
<th>Diameter (mm)</th>
<th>Flow Rates (mL/min)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>960503</td>
<td>65</td>
<td>6.35</td>
<td>60-280</td>
<td>10</td>
</tr>
<tr>
<td>960726</td>
<td>60</td>
<td>6.35</td>
<td>75-340</td>
<td>7</td>
</tr>
<tr>
<td>960727</td>
<td>50</td>
<td>6.35</td>
<td>60-315</td>
<td>6</td>
</tr>
<tr>
<td>960909-2</td>
<td>70</td>
<td>6.35</td>
<td>85-330</td>
<td>6</td>
</tr>
<tr>
<td>960916</td>
<td>60</td>
<td>9.42</td>
<td>120-345</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>50-70</td>
<td>60-345</td>
<td>36</td>
<td></td>
</tr>
</tbody>
</table>

Table 2.2: Parameters of Experiment

Table 2.3 summarizes results from the experiment. Flow calculations were performed using the conventional C-mode technique, the attenuation compensated C-mode technique without baseline thresholding, and finally, for the attenuation compensated C-mode technique with all corrections. For each of these, plots of linearity and error are presented below. Linearity is char-
characterised by the correlation coefficient, \( r \). Distributions of error for the attenuation compensated C-mode technique with and without corrections are also plotted. These error distributions were characterised by mean error and standard deviation, \( \sigma \). Assuming that the measurement process can be considered to have Gaussian distributed error, then the 95% confidence interval for error will be given by \( \pm 2\sigma \).

<table>
<thead>
<tr>
<th>Method</th>
<th>Least Squares Fit</th>
<th>Error Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>slope (mL/min)</td>
<td>offset (mL/min)</td>
</tr>
<tr>
<td>Conventional C-Mode</td>
<td>1.60 ± 0.11</td>
<td>-112 ± 25</td>
</tr>
<tr>
<td>Atten. Comp. C-Mode</td>
<td>1.05 ± 0.04</td>
<td>-63 ± 9</td>
</tr>
<tr>
<td>Corrected A.C. C-Mode</td>
<td>0.92 ± 0.03</td>
<td>7.8 ± 7.5</td>
</tr>
</tbody>
</table>

Table 2.3: Results of Experiment. Results of linearity and accuracy are listed. Slope (and its standard error) and offset (and standard error) for linear least squares fitting are shown. Linearity is quantified by the linear correlation coefficient, \( r \). The distribution in measurement error is also characterised in terms of its mean and its standard deviation. Assuming a Gaussian distribution, the 95% confidence interval is given by \( \pm 2\sigma \). (This is not done for the conventional C-mode technique because there is a strong dependence on error with flowrate).

Performance of C-Mode Velocity Profiling

Figure 2.25 compares the C-mode velocity profile technique to timed collection. Flows on this graph were calculated using Equation 2.8. Measurements are scattered, with both underestimations and overestimations. Overestimations tend to occur at the higher flowrates, and underestimations at the lower flowrates. This is reflected in the slope and error of the least squares fit of the data (a slope of 1.60 ± 0.1); for this fit, \( r = 0.93 \). In the lower half of Figure 2.25 the absolute error and percentage error are plotted. These plots accentuate the systematic dependence of error on flow rate (because of this systematic dependence, error distributions were not plotted for this technique).
Figure 2.25: Experimental Results for C-Mode Flowmeter.
Figure 2.26: Experimental Results for Attenuation Compensated C-Mode Flowmeter (without corrections).
Figure 2.27: Attenuation Compensated C-mode Error Distribution (without corrections). The solid line represents the Gaussian distribution with equivalent standard deviation.

Performance of AC C-Mode velocity profiling

Figure 2.26 compares the attenuation compensated C-mode technique to timed collection. This graph plots the same data taken for Figure 2.25, but uses Equation 2.22 to calculate flow. With one exception, all measurements are underestimated. The slope of the least squares fit is $1.05 \pm 0.04$, and the correlation coefficient was 0.98. In the lower half of Figure 2.26 absolute error and percentage error are plotted. Figure 2.27 plots the error distribution. Overall mean error for attenuation compensated C-mode was $-51.7$ mL/min, and the distribution has a standard deviation of 19.3 mL/min. Therefore, this method had a 95% confidence interval of measurement that was approximately equal to $\pm 40$ mL/min about the mean error.
Performance of All Corrections Taken Together

Figure 2.28 illustrates the linearity of flow measurement following application of all corrections to the data. This included attenuation compensation, wall filter correction by spectrum extrapolation, and noise thresholding by spectrum windowing. The slope of the least squares fit is $0.92 \pm 0.03$. The correlation coefficient of this fit was 0.98. The lower half of the figure shows absolute error and percentage error. Figure 2.29 is a plot of the error distribution. Overall mean error for the corrected attenuation compensated C-mode method was $-10.5$ mL/min, and the distribution had standard deviation of $17.4$ mL/min. Therefore, this method had a 95% confidence interval of measurement that was approximately equal to $\pm 35$ mL/min about the mean error.

2.4.4 Discussion

The experimental results confirm improvement in flow measurement accuracy and precision with the application of attenuation compensation to the C-mode velocity profiling technique. Improved accuracy is reflected in the slope and the correlation coefficient of linear least squares fitting versus timed collection, which was considered in this experiment to be truth. Results clearly indicate progressive improvement from the use of C-mode velocity profiling to attenuation compensated C-mode to corrected attenuation compensated C-mode. In this discussion, the results will be interpreted according to the understanding of C-mode Doppler that has been developed from theory and the computational model. This is followed by notes on the limitations of in vivo relevance and then a comparison against other experimental methods of dealing with partial volume.
Figure 2.28: Experimental Results for Attenuation Compensated C-Mode Flowmeter (including all corrections).
Interpretation of Results

The general characteristics of the error for C-mode measurement are commensurate with understanding of the technique from the computational model. This can be observed by direct comparison of Figures 2.25, 2.11, and 2.12. Figures 2.11 and 2.12 were calculated for parameters that correspond to the flow experiment, with flow unit of 1 corresponding to approximately 350–400 mL/min. Systematic underestimation and overestimation are observed in the experiment as predicted by the model, and have a cross-over that is roughly in the same range of flows as predicted. Random error, however, appears to prevent precise prediction, and therefore, inability to make corrections based on the model.

For the uncorrected attenuation compensated measurement, model results help to explain the observed offset as an effect of wall filter. This is somewhat complicated by the lack of baseline thresholding for these results; however, errors in the experiment follow roughly on track with those
in the model. Matched results with the model indicate that these errors are systematic and subject to correction. This is confirmed with the degree of error variation, which is significantly lower than the error offset. Furthermore, the distribution of errors appears to be independent of flow rate in the range of flows used.

Finally, the application of a proof-of-concept angle independent correction of wall filter illustrates good agreement between the measured results with actual flow as determined by timed collection. The predicted flow appears to be increasingly underestimated with higher flows, as indicated by the slope of the regression fit which is slightly less than one. However, this effect may be due more to problematic application of the correction at low flow rates. The correction has greater error at low flow rates since flow velocities are closer to the wall filter, leaving less data from which to extrapolate a curve to zero velocity. As with the uncorrected attenuation compensated results, the variation in error does not appear to depend significantly on flow rate. The efficacy of more complicated corrections such as linear squares fitting of theoretical spectrum curves to the experimental data have yet to be investigated for this technique. For the purposes of illustrating a systematic correction, the extrapolation used in this experiment is sufficient.

The model also predicts variations as a function of angle. While there are some trends in the data with angle, more data points would be required in order to achieve the statistical significance required to test these against the computational model results.

**Limitations on In Vivo Relevance**

The following considerations limit the relevance of the flow experiment in application to *in vivo* flow measurement:

(a) Validity of wall filter correction

(b) Uniformity of Attenuation in C-Mode
(a) Validity of Wall Filter Correction

The wall filter correction that was applied in the experiment made assumptions about the flow profile. The validity of these assumptions was tested qualitatively for the dataset at 70 degree angle, and 6.35 mm diameter (the most severe case in terms of angle, according to the computational model). It was not possible to set the wall filter below the minimum 184Hz setting; however, it was possible to effectively increase the wall filter by performing a spectrum truncation. In this way, the effect for increasing wall filters was examined.

The results appear in Figure 2.30. Increasing wall filter resulted in increasing offset from the identity line.

The effect on accuracy of the wall filter behaved as predicted in the simple theoretical treatment of Section 2.3.4. Figure 2.24 shows the spectrum of the highest flow data point in the dataset illustrated in Figure 2.30. According to the spectrum, the flow order appears to be within the order $2 < \alpha < 6$. Thus, the wall filter behaviour is expected to be similar to that depicted earlier in Figure 2.14.

The experimental data appear to have a slightly larger offset from the identity line than in the theory. This is consistent with the effect of noise, which also causes the flow to be underestimated.

*In vivo* application of this correction would likely result in a more erroneous estimate. This is due to the fact that the family of curves used to interpret the spectrum were valid for flow in rigid tubes. *In vivo* correction would require the use of a more complicated model of flow such as the Womersely model which is based on the steady-state decomposition of pulsatile flow (described
Figure 2.30: Experimental Results: Wall Filter Effects for 70 degree beam-vessel angle and 6.35 mm diameter vessel phantom. The effect of increasing wall filter is examined by truncating the Doppler spectrum (the opposite to the correction method, which was extrapolation of the spectrum).
(b) Uniformity of Attenuation

In theory, the vessel model was cast in such a way that the attenuation was uniform across the C-mode scan. In both model and experiment, the attenuation of the signal is assumed to be a function of depth only. As a result, the model does not include any component of attenuation variation, and the experiment does not have a significantly varying attenuation at the C-mode scan plane. In reality, variations in attenuation in the tissue above the C-mode plane may cause variations in the power of the ultrasound signal. This is an important effect particularly for the attenuation compensated C-mode technique. If the tissue above a blood vessel is stratified into uniform layers, and the attenuation is relatively uniform within each layer, then the variations in attenuation should not be particularly significant. If, however, there are large variations over the lumen, large errors could result. For example, in the case of a calcified plaque which partially occludes the vessel, significant variations in attenuation might be expected. Clearly the assumption of attenuation as a function of depth only must be re-visited with more extensive modelling and experimentation to determine the potential effects on accuracy for the new technique.

(c) Steady flow versus Pulsatile Flow

On the timescale of the Doppler system, the measurement of velocities in a steady state system is not very different from that of the pulsatile case, since pulsatility is on the order of Hz, whereas pulsed Doppler sampling rates are on the order of 10 kHz. Pulsatility also introduces the possible requirement of cardiac gating in slow scanning systems. Pulsatile flow also requires averaging over several cardiac cycles in order to get a mean flow.

However, the distribution of the velocities for the same quantitative flow rate to be detected
will be very different. In this context, the steady state flow model actually represents a “worst case” scenario. This is due to the fact that a large proportion of volume flow is delivered during systole, where flow rates and velocities are high. In addition, flow profiles tend to be more blunted, resulting in fewer velocities that will be influenced by the wall filter. And yet, partial volumes are likely to have higher flow velocities, which accentuates the difficulties of the conventional C-mode result. As a result, physiological pulsatility results in less severe errors due to wall filter and partial volume effects for attenuation compensated C-mode.

(d) Refraction effects

Refraction effects have not been considered in this thesis. These effects are the result of variation in the speed of sound between intervening tissue layers, and the boundary between blood vessel and moving blood. The effect of refraction will be to alter the accuracy of the velocity estimation of the vessel, and also to cause the vessel lumen to be enlarged or reduced in the C-mode scan projection. Further study is required to determine the quantitative effects of refraction on accuracy of the technique.

Alternative Means of Addressing the Partial Volume Effect

Other ways of addressing the partial volume effect include: (1) the use of imaging information to segment the vessel within the scan plane, and (2) thresholding on the basis of Doppler power. These are considered here briefly, for comparison with attenuation compensated C-mode.

Using images, or *a priori* knowledge of the vessel boundary is a way of reducing the partial volume effect. By simply excluding pixels external to the vessel, the partial volume effect will be reduced. A method similar to this may have been used by Schumacher, *et al.* [55] for their 2D array C-mode measurements to achieve a 2–4% accuracy of *in vitro* flow measurement. Since it is
possible to make the measurement without additional information with attenuation compensated C-mode, the method presented in this thesis is preferred (unless it can be demonstrated that these other techniques will consistently be more accurate, particularly *in vivo*).

Segmentation can also be achieved using Doppler power maps. The edge of the vessel is depicted more clearly in the spatial map of Doppler power (Example Figure 2.21). Since the Doppler power is proportional to the number of moving scatterers, this quantity serves as a better delineator (than mean frequency) of the vessel boundaries, as can be seen by comparing Figures 2.21 and 2.20. However, power thresholding is less attractive than attenuation compensation. Although the power threshold technique could solve the partial volume problem empirically, attenuation compensation has physical relevance. Secondly, power thresholding preferentially eliminates low power signals, reducing the sensitivity of the system. This corresponds to the use of a high level of baseline threshold, which was shown in the computational model to be a significant source of systematic error for both attenuation compensated C-mode, and C-mode. Power thresholding can be understood as a choice of baseline threshold in Figure 2.9(a) that results in small error. Variation in the effect of threshold for this purpose indicates that this method is sensitive to changes in relative signal power.

Given the alternatives described above, it appears that attenuation compensated C-mode is currently the most appropriate way to deal with the partial volume effect which plagues C-mode velocity profiling.

### 2.4.5 Conclusions from Experiment

The measurement of flow in a steady-state experiment using C-mode velocity profiling techniques has illustrated the efficacy of the attenuation compensated C-mode method of measuring blood flow. Clear improvement was observed over conventional C-mode techniques. This was quantified
in terms of slope of linear fit and correlation coefficient of linear fit. For the attenuation compensated technique, error was quantitatively characterised by mean error, and standard deviation. Experimental results corresponded qualitatively with the computational model. Random errors in the new technique were small enough such that corrections to the dominant effects of wall filter were applicable. Taken together, these results indicate that the attenuation compensated C-mode method is well understood according to principles presented in this chapter. The experiment has demonstrated accuracy of the technique, with a 95% confidence level of $\pm 35$ mL/min about a mean of $-10.5$ mL/min.

### 2.5 Summary Conclusions

Using a C-mode velocity profiling technique to quantitatively measure volume flow overcomes problems with error due to uncertainties in the Doppler angle and vessel area measurements which have plagued existing techniques. However, this method is crippled by a systematic error due to partial volume effects. This error can be overcome by applying attenuation compensation. In essence, this involves using the integrated first moment of the Doppler spectrum to estimate flow in the pixel, and normalising by the integrated Doppler power in pixels where the sample volume is entirely within the vessel.

The hypothesis of this thesis is that the accuracy and precision of the C-mode velocity profile technique is significantly improved by using attenuation compensation to correct for partial volume effects. This hypothesis is verified both by the computational model and by a steady-state experiment using a gelatin-graphite flow phantom.

This thesis contributes to the field of ultrasound blood flow measurement in two ways. First, it has proposed a novel technique of flow measurement which is a hybrid of the previous techniques
of C-mode velocity profiling and attenuation compensation. Secondly, systematic and random errors have been analysed using a computational model and a steady state flow experiment. This analysis has determined primary sources of error and has predicted effects on accuracy. The result is a more comprehensive understanding of both C-mode and attenuation compensated C-mode flow measurement methods.

Taken together, the results of this thesis have established the required information to add the new technique to Table 1.6, and to update the information on C-mode as shown in Table 2.4.
<table>
<thead>
<tr>
<th>Method</th>
<th>Instrumentation Requirements</th>
<th>Assumptions</th>
<th>Primary Error Sources</th>
<th>Accuracy</th>
<th>Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-mode Velocity Profile</td>
<td></td>
<td></td>
<td>(quantified) partial volume effects</td>
<td>in vitro: ±30-40% (without a priori knowledge)</td>
<td>Large vessels</td>
</tr>
<tr>
<td>Attenuation Compensated C-Mode</td>
<td>-Two-dimensional Doppler array, or scanned sample volume to sample C-mode plane</td>
<td>- Vessel lumen completely included in C-mode scan plane</td>
<td>Wall Filter</td>
<td>in vitro: ±10%</td>
<td>large vessels small vessels?</td>
</tr>
<tr>
<td></td>
<td>-Sufficient spatial location to locate reference pixel inside vessel</td>
<td>- small sample volume entirely within vessel lumen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- uniformity of attenuation in C-mode plane</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2.4: Ultrasound Flow Measurement Techniques: New Information from Thesis
Chapter 3

Future Work

3.1 Summary and Outline of Future Work

Chapter 1 covered background concepts important to understanding the context and concept of non-invasive blood flow measurement using ultrasound. Clinically accepted techniques have the disadvantage of being invasive and current ultrasound techniques are plagued with sources of error.

Chapter 2 introduced a new technique of measuring blood flow using pulsed Doppler ultrasound. This technique is based on a correction to the C-mode velocity profiling technique using attenuation compensation. The new technique is independent of Doppler angle measurement, and does not require the explicit measurement of vessel cross-sectional area. The technique has the additional benefit of separating the effect of partial volume error (which causes overestimation in flow), from other error sources (which cause underestimation in flow). Results from both theoretical modelling and experimental measurement in a steady flow phantom showed that the new “attenuation compensated C-mode” method has improved accuracy over the existing C-mode technique. The accuracy of the new technique in the steady state flow experiment appeared to be at least as good as that of existing ultrasound methods (Tables 1.4 and 1.5). Error for the new technique
was determined to be due primarily to effects of the wall filter and noise. Preliminary methods of dealing with these errors were used in the analysis of data from the experiment. The work presented in Chapter 2 indicates that the Attenuation Compensated C-Mode Velocity Profile technique for measuring volume blood flow has good potential for investigation of blood flow physiology and for clinical measurement.

This chapter establishes practical and concrete directions for taking the work of this thesis forward. The ultimate goal is to develop a practical instrument capable of non-invasively measuring flow in vivo. Figure 3.1 is a flow chart of future work, outlining directions that will be discussed in this chapter. Implementation of the attenuation compensated C-mode volume flow technique is proposed for cardiac output measurement. Section 3.2 establishes ultrasound design specifications. Section 3.3 discusses the use of arrays to deal with the speed constraint using both existing and future transducer array technology. Design considerations of clinical implementation lead to new questions about the effects of error. Section 3.4 considers future directions for continuing and developing a more realistic computational model for analysis of the new technique. Finally, in Section 3.5, speculation is made on the long term future of attenuation compensated C-mode Doppler. Other clinical problems are suggested for study, and the application of the method for regional flow mapping and bulk flow measurement is proposed.
Figure 3.1: Flowchart Summary of Future Work
3.2 Cardiac Output Measurement

In the discussion below, design specifications, including both geometric and haemodynamic clinical parameters, will be used to determine ultrasound parameters for a proposed device to measure cardiac output using the attenuation compensated C-mode method. (The clinical significance of measuring cardiac output was discussed in Section 1.2.3.) The factors of ultrasound frequency, pulse repetition frequency, speed, and accuracy are considered.

3.2.1 Design Specifications for Cardiac Output Measurement

Cardiac output can be measured in the ascending aorta, the outlet vessel of the left ventricle of the heart. The network of great vessels in the proximity of the ascending aorta make interfering flow an important source of error for current measurement techniques such as uniform insonation (Section 1.4.4) and the traditional attenuation compensated method (Section 1.4.5) where a wide uniform scan plane is required. A spatially resolved flow profile, as generated with the new attenuation compensated C-mode method, will help to alleviate this problem.

Figure 3.2 illustrates the concept of an attenuation compensated C-mode flow meter for measuring cardiac output. In the figure, various geometric design specifications are established. Table 3.1 summarizes the relevant clinical parameters for cardiac output. These parameters determine the design specifications for the ultrasound system.

3.2.2 Ultrasound Parameters

Ultrasound Frequency and Pulse Repetition Frequency

A fundamental trade-off exists between insonation depth and maximum velocity for pulsed Doppler systems. This is due to the relationship between maximum range depth, pulse repetition frequency,
Figure 3.2: Concept of Attenuation Compensated C-Mode Device for Cardiac Output Measurement. The cardiac output can be measured in the ascending aorta using a probe placed at the suprasternal notch, as shown on the right. This establishes geometric design specifications. A C-mode scan plane at a depth of approximately 6 cm is required. The beam vessel angle is small and is expected to be within $\theta < 20^\circ$. The projected lumen diameter will be 2–4 cm (with flow pulsatility) and it must be contained within the scan plane. Interference with surrounding vessels, as shown on the left, will complicate the problem. Flow profile mapping with increased spatial resolution will help to alleviate interference.

<table>
<thead>
<tr>
<th>Specification</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter (Ascending Aorta)</td>
<td>$\approx 25$ mm</td>
</tr>
<tr>
<td>Vessel Depth</td>
<td>$\approx 6$ cm</td>
</tr>
<tr>
<td>&quot;Footprint&quot; (size of suprasternal notch)</td>
<td>$\approx 1$–$2$ cm</td>
</tr>
<tr>
<td>Angle of Insonation</td>
<td>$\approx -20$–$20$ degrees</td>
</tr>
<tr>
<td>Cardiac Output Range</td>
<td>2–30 L/min</td>
</tr>
<tr>
<td>Maximum Velocity (at rest)</td>
<td>120 cm/s</td>
</tr>
<tr>
<td>Maximum Velocity (maximum exertion)</td>
<td>$\sim 250$ cm/s</td>
</tr>
<tr>
<td>Real Time Frame Rate</td>
<td>1/20 s</td>
</tr>
<tr>
<td>Accuracy (to match other techniques)</td>
<td>5%</td>
</tr>
</tbody>
</table>

Table 3.1: Clinical Specifications for Cardiac Output Measurement
The finite wave propagation velocity of ultrasound in tissue establishes a minimum limit on time between successive pulse emissions $T_R$. Time is required for the ultrasound pulse to travel to a certain depth and return. The pulse repetition frequency is $f_R = 1/T_R$. Therefore range depth limitation establishes a maximum pulse repetition frequency $f_R$, given by:

$$f_R < \frac{c}{2d},$$  \hspace{1cm} (3.1)

where $d$ is the insonation depth.

The Nyquist theorem determines a minimum limit on the pulse repetition frequency required in pulsed Doppler systems. It states that the maximum frequency that can be unambiguously determined using a sampled system is equal to $1/2$ of the sampling frequency (in this case, $f_R$). Applying the Doppler equation, this establishes the maximum velocity $\vec{v}$ that can be unambiguously detected, as a function of the following fundamental parameters: ultrasound frequency $f_o$, pulse repetition frequency $f_R$, Doppler angle $\theta$, and speed of sound $c$.

$$\frac{f_R}{2} > \frac{2|\vec{v}_{max}| \cos \theta}{c} f_o.$$  \hspace{1cm} (3.2)

Taken together, the range depth limitation and the Nyquist limitation give

$$\frac{c}{2d} > f_R > \frac{4|\vec{v}_{max}| \cos \theta}{c} f_o,$$  \hspace{1cm} (3.3)

which establishes the fundamental tradeoff between depth, maximum velocity, and fundamental ultrasound frequency for a given speed of sound and angle.

Figure 3.3 illustrates this tradeoff in the range of depths and velocities that are relevant in the cardiac output measurement problem. The scan plane is at a depth of 6cm, although there should be some allowance for variation from patient to patient. The resulting maximum pulse repetition frequencies are in the range of 10–15kHz. Fixing the ultrasound frequency determines a
Figure 3.3: Tradeoff of Depth with Maximum Velocity. For cardiac output measurements, a depth of 6 cm is used. This corresponds (at the top of the graph) to a maximum pulse repetition frequency of 12.8 kHz. For a 2.0 MHz system, the maximum unambiguously detectable velocity is slightly less than 250 cm/s.
maximum detectable velocity due to the Nyquist limit. To detect the range of velocities from rest through to maximum exertion, it is necessary to be able to detect velocities up to 250 cm/s. This establishes an ultrasound frequency in the range of 1.5–2.0 MHz.

**Lateral Resolution**

The ultrasound frequency determines, in part, the resolution of the ultrasound beam. The lateral resolution for a focussed circular ultrasound transducer is proportional to the wavelength, $\lambda$, and the “f-number”, which characterises the degree of focusing. The f-number is the focal length $l_f$ divided by the aperture diameter $d_a$. Lateral resolution can be defined as the full off-axis width of the ultrasound beam at which the pressure falls to half its maximum value. In this case, lateral resolution, $\Delta b$, is given by:

$$\Delta b \approx \frac{l_f}{d_a} = \frac{c}{f_o d_a}.$$  

(3.4)

For cardiac output measurement, the maximum aperture diameter will be fixed by the size of the suprasternal notch, at 1–2cm. Using 1cm, and a focal length of 6cm, this gives an f-number of 6. For a 2 MHz ultrasound transducer, $\lambda = 0.77\text{mm}$ in tissue, therefore the lateral resolution is approximately 5mm.

**Speed (Scan Rate)**

Long scan times (relative to other ultrasound methods) are a fundamental limitation of C-mode techniques. This is because each pixel in the scan plane corresponds to a different transducer position. In contrast, a single transducer position corresponds to an entire A-mode scan, and a line of data in a B-mode scan.

Figure 3.4 shows the frequency components of aortic flow from which the required speed of measurement can be inferred. Sampling of flow at $1/20 \text{s}$ corresponds to a bandwidth of 20Hz,
which is sufficiently large to include all of the components shown in Figure 3.4. Milnor [46] has suggested that pulsatile flow is closely approximated by using as few as the first 10 harmonics of the fundamental cardiac frequency (the heart rate) of approximately 1–1.25 Hz. This corresponds to a bandwidth as low as 10–12.5 Hz. The scan time is the inverse of this bandwidth, and corresponds, therefore to scan times on the order of 50-100ms.

![Frequency components of flow pulsatility](image)

Figure 3.4: **Frequency Components of Typical Aortic Flow Pulsatility.** Data from Milnor [46] is plotted to illustrate the pulsatility of flow. A Fourier transform has been applied to measurements of flow as a function of time in order to characterise pulsatility. The level of the signal as a function of frequency provides a means for estimating the required speed of a system to capture fully the pulsatile qualities.

The time required to make a measurement using the attenuation compensated C-mode method, $T_{A.C.}$, is given by

$$T_{A.C.} = N_{\text{pix}} \left( T_{\text{move}} + \frac{N_R}{f_R} \right). \quad (3.5)$$

where $N_{\text{pix}}$ is the number of C-mode scan pixels used, $T_{\text{move}}$ is the amount of time required to position the ultrasound beam, $N_R$ is the number of pulses used for each pixel measurement, and $f_R$ is the pulse repetition frequency.

In practical terms, $f_R$ has already been fixed, above, at 10-15kHz. The time required to
position the ultrasound beam $T_{\text{move}}$ is determined by the implementation; the use of arrays to effectively eliminate this time is described in Section 3.3. The remaining variables are $N_{\text{pix}}$ and $N_R$. In other words, there is a trade-off in terms of speed between using more pixels in the C-mode scan and using more pulses at each pixel to get better estimates of mean velocity and power. This trade-off merits further study.

Several strategies have been proposed to characterise mean flow velocities using a small number of pulses (minimization of $N_R$). These are the strategies that are used currently in the colour Doppler mode of modern ultrasound scanners which are capable of making mean velocity measurements with only 3–10 pulses. Kasai and Namekawa [36] proposed a scheme which makes use of the Wiener-Khinchin theorem which relates the autocorrelation function to the Doppler power density function $P(f)$. They derived expressions for mean frequency and its variance as a function of the autocorrelation of the Doppler signal. Another method of using a small number of pulses to measure velocity is to apply cross-correlation techniques to the time domain ultrasound signal directly in order to estimate velocity as suggested by Bonnefous and Pesqué [6]. This has additional advantages of eliminating problems to do with aliasing. Both of these techniques require very reproducible ultrasound pulses emitted into tissue, and repeatable scattering response from the target. A full description of these techniques is beyond the scope of this thesis; however, Jensen [35] and Evans [11] provide detailed explanations. In the context of this discussion, the important point is that modern colour Doppler flow mapping instruments have demonstrated an order of magnitude reduction (over traditional Doppler instruments) in the number of pulses required to estimate a mean velocity.

The use of 10 pulses at 10kHz for mean velocity estimation would result in an allotted time of 1ms for each C-mode scan pixel. If the goal is to achieve a scan in 1/20s, this allows for 50–100
pixels to be scanned sequentially, not counting the time required to move the ultrasound beam between each pixel.

Cardiac gating is an alternative means of dealing with this problem, however it greatly extends the examination time. Gated measurements are also subject to problems with spatial mis-registration (due to gross movement of surrounding tissue structures). Gated measurements also become inaccurate with variations from heartbeat to heartbeat. Given the alternative choices for this technique cardiac gating should be considered only as a last resort.

3.2.3 Predicted Accuracy

Accuracy is anticipated to be sufficient for this method, based on the results of Chapter 2. An accuracy of approximately 5% for the cardiac output corresponds to an absolute accuracy of about 250 mL/min (for a resting cardiac output of 5 L/min). The steady-state experiment had a mean error of $-10$ mL/min, more than an order of magnitude better than what is required. Variations in error of less than $\pm 35$ mL/min were also predicted with 95% confidence. These results cannot be applied directly to the cardiac output problem, but there are reasonable similarities between the problems. The transducer used in the experiment had an $f$-number of 4.23, and a wavelength (1540 m/s $\pm$ 5 MHz) of 0.3 mm, thus lateral resolution was approximately 1.3 mm. This is compared to the vessel size in the experiment, which was 6.35 mm in diameter. For the transducer characteristics described above, a 5 mm lateral resolution was predicted, for measurement in a vessel of 25 mm diameter. Thus the experiment and the proposed application have similar beam-vessel lateral size ratios. In the experiment, high beam-vessel angles were used whereas clinical cardiac output measurements will be made with beam-vessel angle near zero degrees. Results from the computational model (Figure 2.11) suggest that errors decrease with smaller beam vessel angles. The most obvious difference between the experiment and the measurement of cardiac output would
be in the effect of gross motion of the vessel, and Doppler clutter noise from the vessel walls which are significant in vivo, but were not present in the steady flow experiment. As discussed in the theory of Chapter 2, tissue motion signal is eliminated using a wall filter. Although the wall filter was a dominant source of error, the wall filter levels (5% of maximum velocity) required for this application would result in predicted errors from the computational model of less than 2% for beam vessel angles less than 40 degrees. Furthermore, the effect of the wall filter is less for aortic flow, since it has a plug-like velocity profile (and therefore less blood moving at slow velocities that might be eliminated by the wall filter). These considerations taken together, accuracy should be on the order of those determined for the steady state experiment of Chapter 2, if not better. For a 40 mL/min error, this corresponds to an accuracy better than ±1%. This is better than what is required and leaves a large margin for unexpected errors.

3.2.4 Summary

Preliminary considerations have been made for the clinical implementation of the attenuation compensated C-mode technique for measuring cardiac output. An ultrasound device used for this measurement should have fundamental frequency of 1.5–2 MHz, and pulse repetition frequency of 10–15 kHz. 2 MHz gives a lateral resolution of approximately 5 mm. The most serious constraint on the system is the scan rate. To capture the pulsatility of flow, it is desired to have a system capable of producing velocity profiles within 50 ms. Predicted accuracy (on the order of 1%) is good enough to exceed that of existing techniques, with a wide margin for increased error due to effects that have not yet been considered. The discussion above has also raised additional issues which merit study for this technique. In particular, the following should be studied in order to optimize device design and to improve fundamental understanding: (1) the trade-off between number of pixels and number of pulses used to estimate mean velocity and power, (2) the relationship between the pixel
geometry and the lateral resolution, and (3) the explicit effect of pulsatility on flow measurement accuracy.

3.3 Array Implementation

The use of transducer arrays has revolutionized ultrasound medical imaging techniques. Arrays facilitate fast high-resolution images by effectively eliminating transducer motion that was previously required to scan the ultrasound beam. Furthermore, arrays offer flexibility and control of ultrasound beam shape and direction. The advantage of arrays is particularly relevant to the implementation of the flow measurement technique described in this thesis, since it provides a means for reducing the scan time, currently a limiting factor. In this section, transducer array concepts will be briefly introduced, followed by suggestions for array implementation of C-mode Doppler.

3.3.1 Transducer Array Concepts

Figure 3.5 illustrates the basic concepts of one dimensional transducer arrays for ultrasound B-mode scanning. Two approaches are described. Both of these techniques are used clinically. Linear arrays have the constraint that transducers must be spaced apart by a maximum distance of $\lambda$. Phased arrays have a more stringent constraint: maximum separation of phased array transducers is $\lambda/2$. These array concepts can also be applied in the elevation direction. Electronic scanning of a beam in the orthogonal direction requires a two dimensional array of transducers. Arrays are described in greater detail in the texts that have been referenced throughout this thesis [11,35,60].

Figure 3.6 illustrates various methods of acquiring a C-mode scan using arrays; the next sections deal with these techniques. The use of arrays for C-mode scanning effectively eliminates the term $T_{move}$ from Equation 3.5 (except in mechanical linear scanning which still requires $T_{move}$.
Figure 3.5: **One Dimensional Transducer Array Concepts.** Many individual transducers are lined up in one dimension. All transducers are focussed physically in the elevation direction. The ultrasound beam can be scanned in two ways. **Linear transducer arrays** (top) use the selective activation of a subset of transducer elements to create a localised beam. The beam is moved laterally by activating different subsets of transducers. Furthermore, by appropriately timing the activation of transducers, the beam can be electronically focussed in the lateral direction. **Phased transducer arrays** (bottom) apply timing for all transducers both to focus in the lateral direction and to sweep the beam through a wedge-shaped scan plane.
3.3.2 Existing Technology: Linear Array Implementation

The attenuation compensated C-Mode velocity profile flow measurement can be implemented on existing clinical scanners with minimal modification by mechanically scanning a standard linear or phased transducer array in the direction orthogonal to the array. A constant depth line from a B-mode image scanned in the orthogonal direction is equivalent to a C-mode scan. It is unlikely that such an implementation could perform a scan within the 50-100ms time frame. Therefore, each line would have to be measured over the entire cardiac cycle, and the lateral mechanical scan would have to be cardiac gated.

A major advantage of using this technique is that fast acquisition of mean velocity and Doppler power measurement have already been implemented in state of the art scanners such as the HDI-3000 (ATL, Seattle, Wash.). In Colour and Power modes, maps of mean velocity and power can be determined at real-time frame rates. This facilitates immediate implementation of the technique.

A current technique known as colour power angiography (CPA) successfully uses unregistered orthogonal scanning of a linear transducer array to map vessels using the Doppler Power imaging mode. This technique simply relies on the steadiness of the hand of the sonographer; the user smoothly tilts the linear array such that the scan plane sweeps through the volume of interest. Reconstruction simply assumes a constant angular velocity. This technique works surprisingly well. Figure 3.7 shows two CPA images of the author’s splenic vasculature.
Figure 3.6: **Array Implementations of C-mode Doppler.** Using existing one dimensional array technology (top left), a C-mode scan can be achieved by mechanically translating or tilting the scan plane in the orthogonal direction to sweep out a three dimensional volume. In future, use of two dimensional arrays will allow electronic scanning in the two lateral directions (top right). Two dimensional arrays may also be employed using the “Explososcan” technique [64]. The C-mode plane is insonated in unison, and electronic focussing is used to separate the pixels as the signal is received in parallel.
Figure 3.7: Ultrasound colour power angiography images of the author’s spleen. These images are three dimensional reconstructions of splenic vasculature based on manual handheld scanning of a linear transducer array with a modern ultrasound scanner.

3.3.3 Future Technology: Two Dimensional Array Implementations

Sequential Scanning

Ultimately the attenuation compensated C-Mode scan should be implemented using a two-dimensional array, obviating the need for mechanical scanning completely. The C-mode scan plane could be insonated sequentially. Two dimensional array implementations would offer great flexibility in both the pixel scanning sequence, and also in the lateral resolution of the beam. It would be possible to do a low resolution scan, followed by a higher resolution scan to fill in detail. Furthermore, since focal length is not determined by transducer shaping in two dimensional arrays, implementation may also turn out to be more generally applicable.
Smith and von Ramm [57, 64] have suggested an interesting implementation of volume imaging using two dimensional arrays. This is exactly the geometry required for C-mode Doppler. The technique trades off some degree of spatial isolation with the ability to scan a large volume quickly. As shown already in Figure 3.6, a wide transmit beam is used, and the signals from different areas are received in parallel by appropriately time delaying and summing signals from individual array elements. Effectively, this reduces $N_{pix}$ to 1 for Equation 3.5, a significant savings in time. Doppler measurements using this scanning sequence would suffer no loss in time resolution over the traditional spectral Doppler techniques.

The first implementation of C-mode velocity profiling described in Chapter 1 used a specially designed two dimensional array for implementation [47] by applying precisely this strategy. The scan requirements for attenuation compensated C-mode are identical.

The effect of reducing the spatial isolation between pixels versus the increase in Doppler data is unclear. Further evaluation will be required to characterise this trade off.

### 3.4 Computational Model Improvements

Design considerations and the discussion on transducer array implementations of attenuation compensated C-mode Doppler have raised new questions for the technique. These can be addressed in part by improving the existing model and subsequent investigation through simulation. In this section, improvements to the model will be suggested, including the addition of noise, spectral broadening, pulsatility, and pulsing strategy.

The next improvement in the computational model should be the addition realistic noise. To this point, the model has only been used to investigate systematic errors as a result of different
parameters. A prediction of the resulting random error in flow measurement based on noise in the system would be valuable in helping to investigate correction methods. The addition of noise is relatively straightforward. Noise due to signal from vessel wall and gross tissue motion could be added as high amplitude random variation at low frequency in the spectrum. This could be useful for evaluating conditions of low wall filter settings where flow measurement has, to this point, been most accurate. Thermal noise in the transducer and electronics can be added by applying random variation to the function $M(v)$ in the model, which represents a weighting of the Doppler spectrum.

Spectral broadening is another effect that may be worth modelling, particularly for the evaluation of arrays which have a large aperture and high degree of focussing. Spectral broadening (as was mentioned briefly in the discussion of the model) is simply the effect where a scatterer moving at a single frequency gives rise to a spectrum of frequency shifts centred about the Doppler shift frequency for this velocity. Spectral broadening is explained according to two arguments: one is geometric, and the other relates to movement through a non-uniform ultrasound beam. Newhouse [48] has demonstrated that these are the same effect. The geometric argument is that the Doppler beam-vessel angle is a function of position on the transducer surface for any given position in space. This results in a variation in frequency shift across the transducer surface, which is summed together to determine the response for the entire transducer. This concept can be readily used to adapt the model for inclusion of spectral broadening effects. Referring back to Figure 2.5, the calculation between of the weighted histogram going from (e) to (f) can be modified to include spectral broadening. The weighting of the histogram can be determined using an integration across the surface of the transducer; weighting would therefore apply to both the bin in the histogram, as well as the value placed within that bin.

Since the technique is constrained by limitations in speed, it may be valuable to examine
the effect of pulsatility. This can be simulated simply by calculation of more realistic profiles based, for example, on Womersley’s model of pulsatile flow. These time varying profiles can be applied in the calculation in a step-wise fashion, from pixel measurement to pixel measurement. By changing the time steps between pixel and flow profile, it will be possible to estimate systematic error due to changing flow during the acquisition of the velocity profile.

Finally, the relative penalty in accuracy of flow measurement for using a small number of pulses to make estimates of mean velocity and Doppler power within a pixel element can be studied by applying a more complex model such as the one suggested by Kerr [38]. Kerr’s model considers the scattering nature of blood and the acoustic impulse response of the transducer to simulate the entire ultrasound signal received for each pulse. With this simulated data, the various strategies of velocity estimation can be applied directly and compared. A clear and quantitative understanding of the advantages and disadvantages of these various techniques would provide information for making an informed choice about the optimal strategy for assessing mean velocity and Doppler power at each pixel.

The improvements described above will help to provide a more realistic model for the determination of errors and optimal parameters. Simulation will help to address the questions brought forth in the discussion on a cardiac output measurement device and in the discussion of array usage.

3.5 Potential Applications

The rest of this chapter briefly discusses potential applications of attenuation compensated C-mode Doppler which are more speculative in nature. Some additional areas of clinical interest are suggested, followed by a proposal for using the technique to map flow regionally within an arbitrary C-mode plane and to measure bulk flow across it.
3.5.1 Other Areas of Clinical Interest

The proposal of using volume flow measurement in the evaluation of cardiac function is only one of many possible areas of clinical interest. It was chosen since it is an area of widespread clinical evaluation of blood flow using current techniques which are relatively invasive. Due to the grave consequences of heart disease, and the current use of catheters for other procedures of heart function evaluation such as angiography, relatively invasive procedures of measurement can be used without much additional risk.

One of the areas where ultrasound flow measurement has been proposed is in the evaluation of umbilical vein flow. Ultrasound imaging is ubiquitous in obstetrics. Due to its non-invasiveness, ultrasound is a natural choice for evaluating fetal well-being. There is clinical potential for the use of Doppler ultrasound in measuring blood flow rate through the umbilical vein for the purpose of diagnosing Intrauterine Growth Retardation (IUGR), a condition in which the growth of the fetus is retarded due to insufficient oxygen and nutrient supply [44]. Since the fetus receives all of its nutrients and oxygen through the umbilical vein, flow through this vessel is an indicator of fetal well-being. IUGR affects 3–7% of all pregnancies, and is responsible for significant fetal mortality and morbidity. Currently, the diagnosis of this condition comes from estimations of fetal size and weight from ultrasound imaging. However, there are other conditions which may cause variations in size of the fetus, including normal variations, and growth failure from congenital anomaly. Blood flow measurement may therefore be a valuable adjunct to imaging for the diagnosis of this problem. Currently, the clinically accepted use of Doppler in this problem is limited to the measurement of various indices of pulsatility which are used indirectly to infer information about the flow. Gill has demonstrated non-invasive ultrasound measurement of fetal umbilical flow using uniform insonation [25] as early as in 1981. In a study comparing umbilical flow in normal and complicated
pregnancies, Gill et al. [24] also demonstrated that ultrasound flow measurement could be used to separate fetuses into low and high risk categories with better sensitivity and accuracy than existing methods. Use of flow has not progressed very far since then, although there have been several attempts, because of inaccuracy [44] and lack of availability of the appropriate instrumentation for uniform insonation measurement. Perhaps an instrument less prone to clinical error such as the one proposed in this thesis might achieve better success.

Another area of potential clinical interest in flow measurement is flow in the liver. The liver is a special area of circulation in the body, in that one of its inlet vessels, the portal vein, comes from the downstream end of a capillary bed—that of the gut. This facilitates the liver’s function as a filter for blood which is rich in nutrients from the process of digestion. In this haemodynamic situation, the pressure in the portal vein is very low (approximately 9 mmHg for normal patients) in comparison to other inlet vessels (arterial pressures are normally in the range of 80–120 mmHg). It is the very low vascular resistance of the liver which allows significant blood flow (\( \sim 1500 \text{ mL/min} \)) through this vessel with such a small pressure difference. Liver diseases such as cirrhosis can result in an increase in resistance, which results in portal hypertension (an increase in portal venous pressure). Portal hypertension can result in conditions such as varices and spleen engorgement [59], with associated risk of hemorrhage. Knowledge of the blood flow could be useful both for physiological understanding of the problem, as well as the clinical evaluation of portal hypertension and its treatment [5].

Flow measurement is also relevant in the problem of evaluating the patency of vessel grafts. There are many clinical situations in which the evaluation of vessel graft patency is important. For example, vessels are grafted in transplants, and in bypass surgery both for the coronary and peripheral vascular disease. Vessel grafts are performed for the purpose of providing sufficient
blood flow for the survival of downstream tissues; thus, blood flow is the relevant parameter for determining the function and efficacy of these grafts. A common complication of vessel graft procedures is gradual stenosis and occlusion. The quantitative measurement of flow could be of diagnostic value to complement other ultrasound methods which are currently used to evaluate vessel graft patency, which include Doppler assessments to detect turbulent flow, high-velocity jets, and tissue noise, as well as the use of pulsatility and resistive indices [45].

The applications that have been mentioned in this thesis only serve as examples to help indicate the universal physiological importance of flow. For further information, the reader is directed to references such as Taylor, Burns, and Wells [60], Woodcock [67], Evans [11], and Atkinson and Woodcock [1].

3.5.2 Bulk Flow Measurement

Throughout this thesis, the use of ultrasound for the measurement of flow in major vessels has been considered. According to the theoretical derivation, however, there is no reason to constrain flow measurement to that of a single vessel through the scan plane. The passage of multiple vessels through the scan plane would simply result in a bulk flow measurement. The only requirement for applying the new flow measurement technique is that a pixel is required where the sample volume is located entirely within the vessel, in order to provide a calibration for quantitative flow measurement.

Practically, the use of this bulk flow measurement is somewhat limited in that arteries are generally situated in close proximity to veins which have flow running in the opposite direction. In steady state, flow in artery-vein pairs for a given organ should cancel out. Doppler frequency shifts can be used, however, to separate directionally the flows such that forward and reverse bulk flow measurements through the plane can be made.
The application of this bulk flow measurement is not yet clear; however, it is a haemodynamic parameter that is related to the supply of oxygen and nutrients to a region downstream or upstream of the scan plane. An interesting consideration is that this can be used to quantify flows within vessels that are smaller than the pixel size. Doppler ultrasound using conventional frequencies is capable of measuring flow in vessels smaller than 100 μm in diameter [60]. The detection of flow in small vessels is limited by the velocity, which must be significantly different in terms of Doppler frequency shift from that of the bulk motion of the surrounding tissue, and it must have sufficient signal in comparison to noise in the system for detection. Thus a bulk flow measurement across a C-mode scan plane would result in the integrated forward and reverse flows of all detectable vessels, including some smaller than 100 μm. The interpretation of this number is complicated by the fact that smaller vessels may weave through the plane, resulting in multiple forward and reverse signals. More detailed frequency analysis of these signals might also yield information of additional value. Bulk flow measurement is something of a curiosity, and the value of its determination remains to be seen.

3.5.3 Regional Flow Mapping

The process of bulk flow measurement across a C-mode scan plane can be carried one step further to the regional mapping of flow. Flow measurement of the sort described in the previous section can be made for each scan pixel. Without separating flows into forward and reverse components, the bulk flow in each pixel can be mapped spatially across the C-mode scan. This is simply an application of the theoretical derivation given in Section 2.2, which demonstrated that flow was proportional to the first moment of the Doppler spectrum for that pixel:

\[ \Delta Q(\delta x_i, \delta y_j) \propto \sum fP_f(\delta x_i, \delta y_j). \]  \hspace{1cm} (3.6)
A map of the first moment as a function of position would represent relative flow across the entire C-mode scan plane. This can be realised either by calculation from the Doppler spectrum directly, or by applying alternative techniques to measuring mean velocity and Doppler power, and multiplying the two.

The use of this first moment parameter has been suggested by others such as Dymling [9] as a means of characterising blood perfusion, or, in other words, a way of more directly quantifying flow into the capillary bed. The first moment is proportional to the flow, however the theory of the attenuation compensated technique indicates that it is now possible to make a calibrated flow measurement directly. If it is possible to locate pixels completely within blood vessels somewhere in the plane, then these could be used to calibrate the relative flow map to provide an absolute flow measurement across the plane.

Currently, maps of mean velocity as a function of position (Color Doppler mode) and Doppler power as a function of position (Power Doppler mode) are implemented on most state of the art ultrasound scanners. The parameter of flow is more relevant physiologically, and a map of first moment at constant depth would correspond to a map of relative flow. This can easily be calculated by multiplying mean velocity by the Doppler power. Regions of interest could be selected by the user, and flow in multiple vessels could be measured.

3.6 Summary of Future Work

The future of the attenuation compensated C-mode velocity profiling technique looks bright. There are many potential areas for future work. In this chapter, several specific suggestions for future work have been made. The next stage is to extend the model, and to attempt an implementation of the system using a more practical one dimensional array system that is mechanically scanned.
Finally, a comprehensive model can be used which would include effects of blood scattering and full effects of transducer geometry. Implementation should be attempted on a two dimensional array system.

3.7 Final Remarks

Blood flow is a fundamental parameter both of physiology and of flow physics, yet its quantitative measurement in vivo has been difficult. Recent technological advances in ultrasound have recently made feasible the direct non-invasive measurement of a two dimensional flow profile from which blood flow can be quantitatively determined. This thesis has investigated this technique in some detail. The early investigators of medical ultrasound did not have the luxury of high quality fast electronics, massive computational power, and materials science expertise that are all required for the modern ultrasound scanner and its arsenal of array transducers. It is somewhat ironic that with all this power, we propose finally to set aside such esthetic and elegant indirect methods of flow measurement as the Fick oxygen method. Still, the benefits of using the new technique for flow measurement proposed in this thesis are tantalising. With an accurate non-invasive tool for measuring blood flow, we can expect better understanding of fundamental physiological phenomenon, and we can hope that additional haemodynamic information will aid in patient management. The simple idea of adding attenuation compensation to the C-mode technique has also resulted in a more unified understanding for the author (and, in hope, for the reader) of the ultrasound flow measurement problem.
References


